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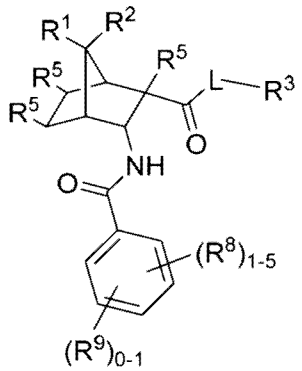
申請實體審查：無 申請專利範圍項數：22 項 圖式數：0 共 1036 頁

(54)名稱

RXFP1 促效劑

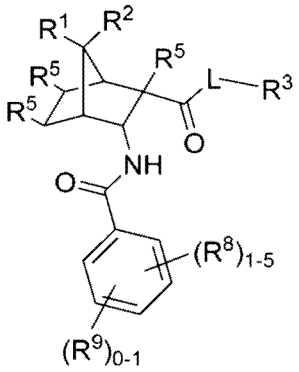
(57)摘要

本發明係關於 RXFP1 受體促效劑之式(I)化合物；含有該等化合物之組合物；及使用該等化合物之方法，例如用於治療心臟衰竭、纖維變性疾病及相關疾病，諸如肺病(例如特發性肺纖維化)、腎病(例如慢性腎病)或肝病(例如非酒精性脂肪變性肝炎及門靜脈高血壓)之方法。



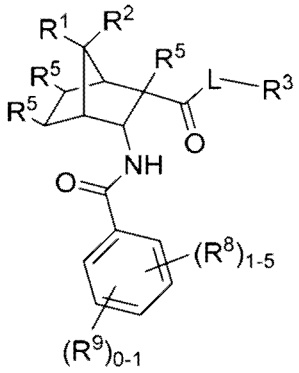
(I)

The disclosure relates to compounds of Formula (I), which are RXFP1 receptor agonists, compositions containing them, and methods of using them, for example, in the treatment of heart failure, fibrotic diseases, and related diseases such as lung disease (e.g., idiopathic pulmonary fibrosis), kidney disease (e.g., chronic kidney disease), or hepatic disease (e.g., non-alcoholic steatohepatitis and portal hypertension).



(I)

特徵化學式：



(I)

202333003 專利案號：111141101
202333003

[(發明摘要)]

[(中文發明名稱)]

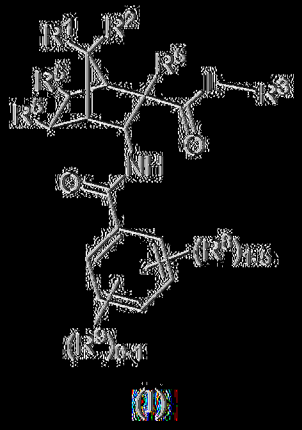
RXFP1促效劑

[(英文發明名稱)]

RXFP1 AGONISTS

[(中文)]

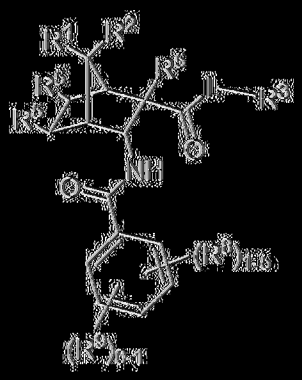
本發明係關於RXFP1受體促效劑之式(I)化合物；含有該等化合物之組合物；及使用該等化合物之方法，例如用於治療心臟衰竭、纖維變性疾病及相關疾病，諸如肺病(例如特發性肺纖維化)、腎病(例如慢性腎病)或肝病(例如非酒精性脂肪變性肝炎及門靜脈高血壓)之方法。



(I)

[(英文)]

The disclosure relates to compounds of Formula (I), which are RXFP1 receptor agonists, compositions containing them, and methods of using them, for example, in the treatment of heart failure, fibrotic diseases, and related diseases such as lung disease (e.g., idiopathic pulmonary fibrosis), kidney disease (e.g., chronic kidney disease), or hepatic disease (e.g., non-alcoholic steatohepatitis and portal hypertension).



(I)

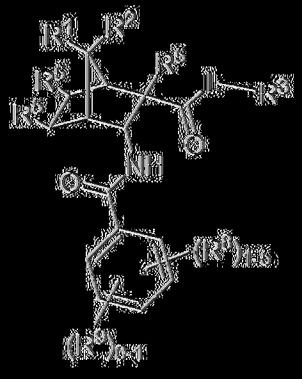
[指定代表圖]

無

[代表圖之符號簡單說明]

無

[特徵化學式]



(I)

【發明說明書】

【中文發明名稱】

RXFP1促效劑

【英文發明名稱】

RXFP1 AGONISTS

【技術領域】

【先前技術】

【0001】 本發明係關於作為鬆弛素家族肽受體1 (RXFP1)促效劑之新穎化合物、含有其之組合物，及其使用方法，例如用於治療心臟衰竭、纖維變性疾病及相關疾病，諸如肺病(例如特發性肺纖維化)、腎病(例如慢性腎病)或肝病(例如非酒精性脂肪變性肝炎及門靜脈高血壓)之方法。

【0002】 人類鬆弛素激素(亦稱為鬆弛素或H2鬆弛素)係由53個胺基酸構成之6-kDa肽，其活性最初係在當Frederick Hisaw在1926年將來自豬黃體之粗提取物注射至原生天竺鼠中且觀測到纖維軟骨恥骨聯合關節鬆弛時發現(Hisaw FL., *Proc. Soc. Exp. Biol. Med., 1926, 23, 661-663*)。鬆弛素受體先前稱為Lgr7，但現時常稱為鬆弛素家族肽受體1 (RXFP1)，且在2002年使其脫孤成為鬆弛素受體(Hsu SY.,等人，*Science, 2002, 295*, 671-674)。RXFP1在具有85%胺基酸一致性之小鼠與人類之間具有相當良好的保守性且基本上廣泛地表現於人類及其他物種中*(Halls ML.*等人，*Br. J. Pharmacol., 2007, 150*, 677-691)。鬆弛素及RXFP1之細胞信號傳導路徑具有細胞類型依賴性且相當複雜(Halls ML.等人，*Br. J. Pharmacol., 2007, 150*, 677-691；Halls ML.等人，*Ann. N Y Acad. Sci., 2009, 1160*, 108-111；Halls ML., *Ann N Y Acad. Sci., 2007, 1160*, 117-120)。最佳研

究之路徑為cAMP之細胞水平之鬆弛素依賴性增加，其中鬆弛素充當RXFP1促效劑以促進腺苷酸環化酶之GαS偶合及活化(Halls ML等人，*Mol. Pharmacol., 2006, 70*, 214-226)。

【0003】 自鬆弛素之初始發現以來，許多實驗工作著重於描繪鬆弛素已在女性生殖生物學中發揮的作用及在哺乳動物妊娠期間出現之生理變化(Sherwood OD., *Endocr. Rev., 2004, 25*, 205-234)。在人妊娠期間，為了滿足胎兒強制性營養需求，女性身體會經歷全身血管阻力(SVR)顯著降低約30%且伴隨心輸出量增加約50% (Jeyabalan AC., K.P., *Renal and Electolyte Disorders. 2010*, 462-518)、(Clapp JF. & Capeless E., *Am. J. Cardio., 1997, 80*, 1469-1473)。其他血管適應性包括：全局動脈順應性之約30%增加，其對於維持高效心室-動脈耦合很重要，以及腎血流量(RBF)及腎絲球過濾率(GFR)兩者之約50%增加，其對於代謝廢料消除很重要(Jeyabalan AC., K.P., *Renal and Electolyte Disorders. 2010*, 462-518), (Poppas A.等人，*Circ., 1997, 95*, 2407-2415)。在嚙齒動物之臨床前研究以及在多種患者環境中進行之臨床研究提供證據表明，至少在某種程度上涉及鬆弛素會介導此等適應性生理變化(Conrad KP., *Regul. Integr. Comp. Physiol., 2011, 301*, R267-275), (Teichman SL.等人，*Heart Fail. Rev., 2009, 14*, 321-329)。重要的是，許多此等適應性反應可能有益於HF患者，係因為過度纖維化、不良動脈順應性及不良腎功能為心臟衰竭患者共有的全部特徵(Mohammed SF.等人，*Circ., 2015, 131*, 550-559)、(Wohlfahrt P.等人，*Eur. J. Heart Fail., 2015, 17*, 27-34)、(Damman K.等人，*Prog. Cardiovasc. Dis., 2011, 54*, 144-153)。

【0004】 心臟衰竭(HF)，在血液動力學上定義為「全身灌流由於心

泵功能減弱而不足以滿足身體代謝需求」，表示對當今保健系統造成巨大負擔，其中估計在美國的流行率為580萬且在全球超過2300萬(Roger VL.等人，*Circ. Res., 2013, 113*, 646-659)。據估計，到2030年，美國將再有300萬人患有HF，自2010以來增加25%。2010年與HF相關之估計直接成本(2008年，以美元為單位)為250億美元，預計到2030年會增長至780億美元(Heidenreich PA.等人，*Circ., 2011, 123*, 933-944)。令人驚奇的是，在美國，9例死亡中有1例的死亡證明上提及了HF (Roger VL.等人，Circ., 2012, 125, e2-220)，且在HF診斷之後的存活期隨時間推移而提高(Matsushita K.等人，*Diabetes, 2010, 59*, 2020-2026)、(Roger VL.等人，*JAMA, 2004, 292*, 344-350)，約50%具有HF之人的死亡率仍然較高，會在確診後5年內死亡(Roger VL.等人，*Circ., 2012, 125*, e2-220)、(Roger VL.等人，*JAMA*, *2004, 292*, 344-350)。

【0005】 HF之症狀由心輸出量不足引起，且該等症狀視晚期疾病而定可使人相當衰弱。HF之主要症狀及病徵包括：1)由肺水腫引起之呼吸困難(dyspnea) (難以呼吸)，肺水腫由自左心室之低效正向流動及肺毛細管床中之壓力增加引起；2)當右心室不能適應全身性靜脈回流時，出現下肢水腫；及3)由於心臟衰竭而無法承受足夠的心輸出量(CO)以滿足身體代謝需求造成的疲勞(Kemp CD., & Conte JV., *Cardiovasc. Pathol., 2011, 21*, 365-371)。此外，與症狀嚴重程度相關，HF患者通常被描述為「代償」或「代償不全」在代償心臟衰竭中，症狀為穩定的，且不存在水腫(fluid retention)及肺水腫之許多明顯特徵。代償不全之心臟衰竭係指惡化(其可以肺水腫急性發作形式存在)、運動耐量降低且在運動時呼吸急促增加(Millane T.等人，*BMJ, 2000, 320*, 559-562)。

【0006】 相比於不能滿足代謝需求的不良心臟功效之簡單定義，大量連帶性疾病、多種風險因素及最終導致心臟衰竭之許多病理變化使得此疾病極其複雜(Jessup M. & Brozena S., *N. Engl. J. Med., 2003, 348*, 3007-2018)。認為與HF之病理生理學有關的嚴重事件的範圍為非常急性(諸如心肌梗塞)至更慢性損害(諸如終生高血壓)。歷史上，HF主要描述為「收縮性HF」，其中左心室(LV)收縮功能減少限制血液排出且因此導致射出分率降低(EF為心搏出量/舒張末期容積)，或描述為「舒張性HF」，其中主動鬆弛降低且被動變剛度增加，從而在心臟舒張期間限制LV填充，但會維持總體EF (Borlaug BA. & Paulus WJ., *Eur Heart J., 2011, 32*, 670-679)。近年來，應理解，由於舒張及收縮LV功能不全並非此等兩個群組所特有的，所以採用以下新術語：「射出分率降低型心臟衰竭」(HFrEF)及「射出分率正常型心臟衰竭」(HFpEF) (Borlaug BA. & Paulus WJ., *Eur Heart J., 2011, 32*, 670-679)。儘管此兩個患者群體具有極類似的病徵及症狀，但HFrEF及HFpEF是否表示兩種不同形式之HF或共用常見發病機制之單一光譜的兩個極值目前仍處於心血管界爭論之中(Borlaug BA. & Redfield MM., *Circ., 2011, 123*, 2006-2013)、 (De Keulenaer GW., & Brutsaert DL., *Circ., 2011, 123*, 1996-2004)。

【0007】 目前正在研發具有0.09小時的相對短的第一階段藥物動力學半衰期之重組人類鬆弛素肽之靜脈內(IV)調配物用於治療HF (Novartis，2014)。塞雷拉辛(serelaxin)已給予正常健康志願者(NHV)且證實會增加RBF(Smith MC.等人，*J. Am. Soc. Nephrol. 2006, 17*, 3192-3197)及經估計GFR (Dahlke M.等人，*J. Clin. Pharmacol., 2015, 55*, 415-422)。亦在代償穩定之HF患者中觀測到RBF增加(Voors AA.等人，*Cir.*

Heart Fail., 2014, 7, 994-1002)。在大型臨床研究中，在急性代償不全之HF (ADHF)患者中回應於住院48小時IV輸注塞雷拉辛觀測到腎功能惡化、HF惡化以及死亡較少之有利變化(Teerlink JR.等人，*Lancet, 2013, 381*, 29-39)，(Ponikowski P.等人，*Eur. Heart, 2014, 35*, 431-441)。表明了長期給藥塞雷拉辛可向HF患者提供持續益處，即在使用皮下泵向持續給予塞雷拉辛6個月的硬皮病患者中觀測到基於血清肌酐含量之腎功能改善(Teichman SL.等人，*Heart Fail. Rev., 2009, 14*, 321-329)。除了有可能作為治療劑來治療HF以外，亦已證明連續皮下投與釋放素對肺(Unemori EN.等人，*J. Clin. Invet., 1996, 98*, 2739-2745)、腎(Garber SL.等人，*Kidney Int., 2001, 59*, 876-882)及肝損傷(Bennett RG., *Liver Int., 2014, 34*, 416-426)之各種動物模型有效。

【0008】 概言之，有大量證據支援RXFP1介導在哺乳動物妊娠期間出現之適應性變化的鬆弛素依賴性促效作用，且此等變化在向HF患者給予鬆弛素時轉變成有利的生理作用及結果。在肺、腎臟及肝臟損傷之各種疾病模型中之其他臨床前動物研究提供證據表明，當長期投與時，鬆弛素可能對除HF以外之多種適應症提供治療益處。更特定言之，長期投與鬆弛素可有益於罹患肺病(例如特發性肺纖維化)、腎病(例如慢性腎病)或肝病(例如非酒精性脂肪變性肝炎及門靜脈高血壓)之患者。

【發明內容】

【0009】 本發明提供新穎的經取代之降冰片烷基化合物、其類似物，包括其立體異構物、互變異構物、醫藥學上可接受之鹽或溶劑合物，其適用作RXFP1受體促效劑。

【0010】 本發明亦提供製造本發明化合物之方法及中間物。

[0011] 本發明亦提供醫藥組合物，其包含醫藥學上可接受之載劑及本發明化合物或其立體異構物、互變異構物、醫藥學上可接受之鹽或溶劑合物中之至少一者。

[0012] 本發明化合物可用於例如治療及/或預防心臟衰竭、纖維變性疾病及相關疾病，諸如肺病(例如特發性肺纖維化)、腎病(例如慢性腎病)或肝病(例如非酒精性脂肪變性肝炎及門靜脈高血壓)。

[0013] 本發明化合物可以用於療法中。

[0014] 本發明化合物可用於製造用於治療及/或預防心臟衰竭之藥劑。

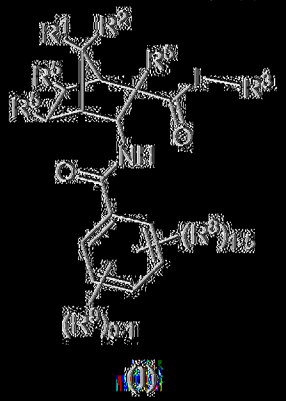
[0015] 本發明化合物可單獨使用、與其他本發明化合物組合或與一或多種、較佳一至兩種其他藥劑組合使用。

[0016] 本發明之此等及其他特徵將隨繼續揭示而以擴展形式闡述。

[實施方式]

[0017] 本發明涵蓋式(I)化合物，其為RXFP1受體促效劑；含有其之組合物；及其使用方法。

[0018] 在第一態樣中，本發明尤其提供式(I)化合物：



(I)

或其醫藥學上可接受之鹽，其中：

L為-O-或-NH-；

R^1為經0至1個芳基或C_{3-6}環烷基取代基取代之C_{1-3}烷基；

R^2為H；其限制條件為，當R^1為經0個芳基或C_{3-6}環烷基取代基取代之C_{1-3}烷基時，R^9為不存在；

或R^1及R^2組合為$=CR^6R^7$或$=NOC_{1-4}$烷基，其中「=」為雙鍵；或R^1及R^2與該兩者所連接之碳原子一起形成經0至1個芳基取代基取代之二氧戊環基；

R^3為經0至5個鹵基、CN、-OH或$-OC_{1-3}$烷基取代基取代之C_{1-8}烷基、經0至5個R^4取代之$-(CR^dR^d)_n-C_{3-10}$碳環基或包含1至4個選自O、$S(=O)_p$、N及NR^{4c}之雜原子且經0至5個R^4取代之$-(CR^dR^d)_n$-3員至12員雜環基；

R^4為鹵基、CN、-OH、$-SF_5$、$-S(=O)_pR^c$、經0至5個鹵基、-OH或$-OC_{1-4}$烷基取代基取代之C_{1-4}烷基、經0至5個鹵基取代基取代之OC_{1-4}烷基、經0至5個R^e取代之$-(CR^dR^d)_n-C_{3-10}$碳環基、或包含1至4個選自O、$S(=O)_p$、N及NR^{4c}之雜原子且經0至5個R^e取代之$-(CR^dR^d)_n$-4員至6員雜環基；

R^{4c}為H、C_{1-4}烷基或$-S(=O)_2CF_3$；

各R^5為H、鹵基、-OH、經0至5個鹵基取代基取代之C_{1-4}烷基、或經0至5個鹵基取代基取代之$-OC_{1-4}$烷基；

R^6為H、鹵基、CN、經0至3個R^{6a}取代之C_{1-7}烷基、經0至3個R^{6a}取代之C_{2-7}烯基、經0至3個R^{6a}取代之C_{2-7}炔基、$-C(=O)OR^{6b}$、$-CONR^{6b}R^{6b}$、經0至5個R^{14}取代之$-(CH_2)_n-C_{3-10}$碳環基、或包含1至4個選自O、$S(=O)_p$、N或NR^{14a}之雜原子且經0至5個R^{14}取代之3員至12員雜環基；

R^{6a}為鹵基、-OH、-OC_{1-4}烷基、C_{1-4}烷基、芳基、或經0至4個鹵基取代基取代之C_{3-6}環烷基；

R^{6b}為H、經0至1個芳基取代基取代之C_{1-4}烷基、或經0至4個鹵基取代基取代之C_{3-6}環烷基；

R^{7}為H或C_{1-4}烷基；

或R^{6}及R^{7}與該兩者所連接之碳原子一起形成環戊二烯基、二氫茚基或茚基；

R^{8}為H、鹵基、CN、-$NR^{7}R^{7}$、經0至5個鹵基或-OH取代基取代之C_{1-4}烷基、或經0至5個鹵基取代之-OC_{1-4}烷基、-OH、C_{3-6}環烷基、芳基、包含1至4個選自O、$S(=O)_p$及N之雜原子的4員至9員雜環基或經0至1個-OC_{1-3}烷基取代基取代之-OC_{1-3}烷基；

R^{9}為經0至3個R^{10}及0至2個R^{11}取代之芳基、或包含1至5個選自O、$S(=O)_p$、N及NR^{11a}之雜原子且經0至3個R^{10}及0至2個R^{11}取代之3員至12員雜環基；

R^{10}為鹵基、CN、C_{1-4}烷基、=O、-OH或-OC_{1-4}烷基；

R^{11}為經0至4個R^{12}及0至2個R^{13}取代之C_{1-5}烷基、-OR^{b}、-$NR^{a}R^{a}$、-$NR^{a}C(=O)R^{b}$、-$NR^{a}C(=O)OR^{b}$、-$NR^{a}C(=O)NR^{a}R^{a}$、-$NR^{a}S(=O)_pR^{c}$、-$C(=O)R^{b}$、-$C(=O)OR^{b}$、-$C(=O)NR^{a}R^{a}$、-$C(=O)NR^{a}S(=O)_pR^{c}$、-$OC(=O)R^{b}$、-$S(=O)_pR^{c}$、-$S(=O)_pNR^{a}R^{a}$、經0至5個R^{e}取代之C_{3-9}碳環基、或包含1至4個選自O、$S(=O)_p$、N及NR^{15}之雜原子且經0至5個R^{e}取代之3員至12員雜環基；

R^{11a}為H、經0至4個R^{11b}取代之C_{1-5}烷基、-$C(=O)R^{b}$、-$C(=O)OR^{b}$、-$C(=O)NR^{a}R^{a}$、經0至5個R^{e}取代之C_{3-6}環烷基、經0至5個R^{e}取代之芳基、

包含1至4個選自O、$S(=O)_p$、N及NR^{15}之雜原子且經0至5個R^e取代之4員至6員雜環基；

R^{11b}為鹵基、-OH、$-C(=O)OH$、$-C(=O)OC_{1-4}$烷基或芳基；

R^{12}為鹵基、$-C(=O)OR^b$、$-C(=O)NR^aR^a$、$-C(=O)NR^aOR^b$、經0至3個鹵基或-OH取代基取代之C_{1-4}烷基、或C_{3-6}環烷基；

R^{13}為$-OR^b$、$-NR^aR^a$、$-NR^aC(=O)R^b$、$-NR^aC(=O)OR^b$、$-NR^aC(=O)NR^aR^a$、$-NR^aS(=O)_pR^c$、$-NR^aS(=O)_pNR^aR^a$、$-OC(=O)NR^aR^a$、$-OC(=O)NR^aOR^b$、$-S(=O)_pNR^aR^a$、$-S(=O)_pR^c$、經0至3個R^e取代之$-(CH_2)_n-C_{3-10}$碳環基、或包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至3個R^e取代之$(CH_2)_n$-3員至12員雜環基；

R^{14}為鹵基、CN、經0至3個鹵基取代基取代之C_{1-4}烷基、經0至3個鹵基取代基取代之$-OC_{1-4}$烷基、$-(CH_2)_n-NR^aR^a$、經0至3個R^e取代之$-(CH_2)_n$-芳基、經0至3個R^e取代之-O-芳基、或包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至3個R^e取代之$-(CH_2)_n$-3員至12員雜環基；

R^{14a}為H、$C(=O)C_{1-4}$烷基或經以下取代之C_{1-3}烷基：0至3個$Si(C_{1-3}$烷基$)_3$或經0至2個鹵基取代基取代之芳基；

R^{15}為H、C_{1-4}烷基或芳基；

R^a為H、$-OC_{1-6}$烷基、經0至5個R^e取代之C_{1-6}烷基、經0至5個R^e取代之C_{2-6}烯基、經0至5個R^e取代之C_{2-6}炔基、經0至5個R^e取代之$(CH_2)_nC_{3-10}$碳環基、或包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至5個R^e取代之$(CH_2)_n$-3員至12員雜環基；或R^a及R^a與該兩者所連接之氮原子一起形成包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至5個R^e取代之3員至12員雜環基；

R^b為H、經0至5個R^e取代之C_{1-6}烷基、經0至5個R^e取代之C_{2-6}烯基、經0至5個R^e取代之C_{2-6}炔基、經0至5個R^e取代之-$(CH_2)_n$-C_{3-10}碳環基、或包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至5個R^e取代之$(CH_2)_n$-3員至12員雜環基；

R^c為經0至5個R^e取代之C_{1-6}烷基、經0至5個R^e取代之C_{2-6}烯基、經0至5個R^e取代之C_{2-6}炔基、經0至5個R^e取代之C_{3-6}碳環基、或包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至5個R^e取代之3員至12員雜環基；

R^d為H、C_{1-4}烷基或C_{3-6}環烷基；

R^e為鹵基、CN、NO_2、=O、經0至5個R^g取代之C_{1-6}烷基、經0至5個-R^g取代之C_{2-6}烯基、經0至5個-R^g取代之C_{2-6}炔基、經0至5個R^g取代之-$(CH_2)_n$-C_{3-10}碳環基、包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至5個R^g取代之-$(CH_2)_n$-3員至12員雜環基、-$(CH_2)_nOR^f$、-$C(=O)OR^f$、-$C(=O)NR^fR^f$、-$NR^fC(=O)R^f$、-$S(=O)_pR^f$、-$S(=O)_pNR^fR^f$、-$NR^fS(=O)_pR^f$、-$NR^fC(=O)OR^f$、-$OC(=O)NR^fR^f$或-$(CH_2)_nNR^fR^f$；

R^f為H、經0至2個-OH或-OC_{1-4}烷基取代基取代之C_{1-6}烷基、C_{3-6}環烷基、芳基、或包含1至4個選自O、$S(=O)_p$及N之雜原子的3員至12員雜環基，及；或R^f及R^f與該兩者所連接之氮原子一起形成包含1至4個選自O、$S(=O)_p$及N之雜原子的3員至12員雜環基；

R^g為鹵基、CN、-OH、C_{1-6}烷基、C_{3-6}環烷基或芳基；

n為0、1、2或3；及

p為0、1或2。

【0019】 在第一態樣之範疇內的第二態樣中，本發明提供式(I)化合物或其醫藥學上可接受之鹽，其中：

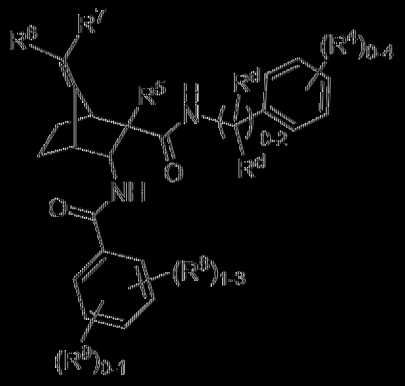
R^3為經0至4個鹵基或-OH取代基取代之C_{1-6}烷基、經0至4個R^4取代之-$(CHR^d)_{0-1}$-C_{3-6}環烷基、經0至4個R^4取代之C_{6-9}螺環烷基、經0至4個R^4取代之C_{6-10}雙環碳環基、或包含1至2個選自O、S(=O)$_p$、N及NR^{4c}之雜原子且經0至4個R^4取代之3員至6員雜環基；

R^4為鹵基或經0至4個鹵基取代基取代之C_{1-3}烷基；

R^{4c}為H或C_{1-4}烷基；

R^d為C_{1-3}烷基。

[0020] 在第一態樣之範疇內的第二態樣中，本發明提供式(II)化合物



(II)

或其醫藥學上可接受之鹽，其中：

R^4為鹵基、經0至4個鹵基取代基取代之-S(=O)$_p$$C_{1-4}$烷基、經0至4個鹵基取代基取代之$C_{1-4}$烷基、經0至4個鹵基取代基取代之-O$C_{1-4}$烷基；

R^5為H或鹵基；

R^6為鹵基、CN、經0至3個R^{6a}取代之C_{1-7}烷基、經0至3個R^{6a}取代之C_{2-7}烯基、經0至3個R^{6a}取代之C_{2-7}炔基、-C(=O)OR^{6b}、CO$NR^{6b}R^{6b}$、經0至3個R^{14}取代之C_{3-6}環烷基、經0至3個R^{14}取代之C_{3-6}環烯基、經0至3個R^{14}取代之芳基、或包含1至3個選自O、S(=O)$_p$、N及NR^{14a}之雜原子且經0至3個R^{14}取代之4員至6員雜環基；

R^{6a}為鹵基、-OH、C_{3-6}環烷基或芳基；

R^{6b}為H、經0至1個芳基取代基取代之C_{1-4}烷基、或經0至4個鹵基取代基取代之C_{3-6}環烷基；

R^{7}為H或C_{1-3}烷基；

R^{8}為鹵基、CN、-N(C_{1-2}烷基)$_2$、經0至5個鹵基或-OH取代基取代之C_{1-4}烷基、或經0至4個鹵基、-OH、芳基或-OC_{1-4}烷基取代基取代之-OC_{1-4}烷基；

R^{9}為經0至3個R^{10}及0至2個R^{11}取代之C_6芳基、或包含1至4個選自O、S(=O)$_p$、N及NR^{11a}之雜原子且經0至3個R^{10}及0至1個R^{11}取代之3員至12員雜環基；

R^{10}為鹵基、CN、C_{1-4}烷基、=O、-OH或-OC_{1-4}烷基；

R^{11}為經0至1個R^{12}及0至1個R^{13}取代之C_{1-4}烷基、-OR^b、-NR^aR^a、-$NR^aC(=O)R^b$、-$NR^aC(=O)OR^b$、-$NR^aC(=O)NR^aR^a$、-$NR^aS(=O)_pR^c$、-$C(=O)R^b$、-$C(=O)OR^b$、-$C(=O)NR^aR^a$、-$C(=O)NR^aS(=O)_pR^c$、-$OC(=O)R^b$、-$S(=O)_pR^c$、-$S(=O)_pNR^aR^a$、經0至5個R^e取代之C_{3-6}環烷基、包含1至4個選自O、S(=O)$_p$、N及NR^{15}之雜原子且經0至5個R^e取代之4員至12員雜環基；

R^{11a}為H、經0至2個R^{11b}取代之C_{1-4}烷基、-$C(=O)R^b$、-$C(=O)OR^b$、-$C(=O)NR^aR^a$、經0至5個R^e取代之C_{3-6}環烷基、包含1至4個選自O、S(=O)$_p$、N及NR^{15}之雜原子且經0至5個R^e取代之4員至6員雜環基；

R^{11b}為-OH、-C(=O)OH或芳基；

R^{12}為鹵基、-$C(=O)OR^b$、-$C(=O)NHR^a$、-$C(=O)NHOR^b$、或經0至3個鹵基或-OH取代基取代之C_{1-4}烷基；

R^{13} 為 $-OR^b$ 、 $-NR^aR^a$ 、 $-NR^aC(=O)R^b$ 、 $-NR^aC(=O)OR^b$ 、 $-NR^aS(=O)_pR^c$ 、 $-NR^aS(=O)_pNR^aR^a$ 、 $-OC(=O)NR^aR^a$ 、 $-OC(=O)NR^aOR^b$ 、 $-S(=O)_pNR^aR^a$ 或 $-S(=O)_pR^c$ ；

R^{14} 為鹵基、CN、經0至3個鹵基取代基取代之 C_{1-4} 烷基、經0至3個鹵基取代基取代之 $-OC_{1-4}$ 烷基、$-(CH_2)_{0-2}-NR^aR^a$ 、經0至3個 R^e 取代之 $-(CH_2)_{0-3}-$ 芳基、經0至3個 R^e 取代之 $-O-$ 芳基、或包含1至4個選自O、$S(=O)_p$ 及N之雜原子且經0至3個 R^e 取代之 $-(CH_2)_{0-3}-$ 3員至12員雜環基；

R^{14a} 為H、$C(=O)C_{1-4}$ 烷基或經以下取代之 C_{1-3} 烷基：0至3個經0至2個鹵基取代基取代之芳基、；

R^{15} 為H、C_{1-3} 烷基或芳基；

R^a 為H、經0至5個 R^e 取代之 C_{1-5} 烷基、經0至5個 R^e 取代之 C_{2-5} 烯基、經0至5個 R^e 取代之 C_{2-5} 炔基、經0至5個 R^e 取代之 $-(CH_2)_n-C_{3-10}$ 碳環基、或包含1至4個選自O、$S(=O)_p$ 及N之雜原子且經0至5個 R^e 取代之 $-(CH_2)_n-$ 3員至12員雜環基；或 R^a 及 R^a 與該兩者所連接之氮原子一起形成包含1至4個選自O、$S(=O)_p$ 及N之雜原子且經0至5個 R^e 取代之3員至12員雜環基；

R^b 為H、經0至5個 R^e 取代之 C_{1-5} 烷基、經0至5個 R^e 取代之 C_{2-5} 烯基、經0至5個 R^e 取代之 C_{2-5} 炔基、經0至5個 R^e 取代之 $-(CH_2)_n-C_{3-10}$ 碳環基、或包含1至4個選自O、$S(=O)_p$ 及N之雜原子且經0至5個 R^e 取代之 $-(CH_2)_n-$ 3員至12員雜環基；

R^c 為經0至5個 R^e 取代之 C_{1-5} 烷基、經0至5個 R^e 取代之 C_{2-5} 烯基、經0至5個 R^e 取代之 C_{2-5} 炔基、經0至5個 R^e 取代之 C_{3-6} 碳環基、或包含1至4個選自O、$S(=O)_p$ 及N之雜原子且經0至5個 R^e 取代之3員至12員雜環基；

R^d 為H或 C_{1-4} 烷基；

R^c為鹵基、CN、=O、經0至5個R^g取代之C_{1-6}烷基、經0至5個R^g取代之C_{2-6}烯基、經0至5個R^g取代之C_{2-6}炔基、經0至5個R^g取代之$-(CH_2)_n-C_{3-6}$環烷基、經0至5個R^g取代之$-(CH_2)_n-$芳基、包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至5個R^g取代之$-(CH_2)_n-3$員至12員雜環基、$-(CH_2)_nOR^f$、$-C(=O)OR^f$、$-C(=O)NR^fR^f$、$-NR^fC(=O)R^f$、$-S(=O)_pR^f$、$-NR^fC(=O)OR^f$、$-OC(=O)NR^fR^f$或$-(CH_2)_nNR^fR^f$；

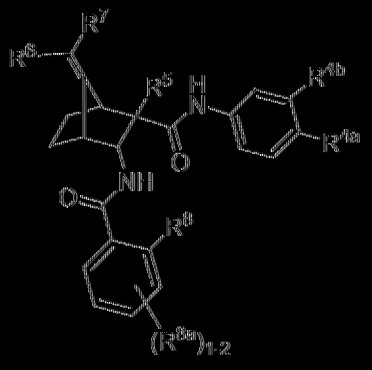
R^f為H、C_{1-5}烷基、C_{3-6}環烷基或芳基；或R^f及R^f與該兩者所連接之氮原子一起形成雜環基；

R^g為鹵基、CN、-OH、C_{1-5}烷基、C_{3-6}環烷基或芳基；

n為0、1、2或3；及

p為0、1或2。

[0021] 在第一態樣之範疇內之第四態樣中，本發明提供式(III)化合物：



(III)

或其醫藥學上可接受之鹽，其中：

R^{4a}為鹵基；

R^{4b}為經0至4個鹵基取代基取代之C_{1-4}烷基；

R^5為H或F；

R^6為鹵基、經0至3個R^{6a}取代之C_{1-4}烷基、經0至1個苯基或-OH取代

基取代之C_{2-4}烯基、-C(=O)OR^{6b}、C(=O)NHR^{6b}、經0至3個R^{14}取代之C_{3-6}環烷基、經0至3個R^{14}取代之C_{3-6}環烯基、經0至3個R^{14}取代之苯基、經0至3個R^{14}取代之萘基、或包含1至3個選自O、S、N及NR^{14a}之雜原子且經0至3個R^{14}取代之5員至6員雜環基；

R^{6a}為鹵基、-OH、C_{3-6}環烷基或苯基；

R^{6b}為H或C_{1-4}烷基；

R^{7}為H或C_{1-3}烷基；

或R^{6}及R^{7}與該兩者所連接之碳原子一起形成環戊二烯基、二氫茚基或茚基；

R^{8}為-N(C_{1-4}烷基)$_2$或經0至1個-OC_{1-4}烷基取代基取代之-OC_{1-4}烷基；

R^{8a}為鹵基；

R^{14}為鹵基、CN、經0至3個鹵基取代基取代之C_{1-4}烷基、經0至3個鹵基取代基取代之-OC_{1-4}烷基、-$(CH_2)_{0-2}$-NR^aR^a、經0至3個R^e取代之-$(CH_2)_{0-2}$-芳基、經0至3個R^e取代之-O-芳基、或包含1至4個選自O、S(=O)$_p$及N之雜原子且經0至3個R^e取代之-$(CH_2)_{0-2}$-3員至12員雜環基；

R^{14a}為H、C(=O)C_{1-3}烷基或經以下取代之C_{1-3}烷基：0至3個經0至2個鹵基取代基取代之芳基；

R^a為H、經0至5個R^e取代之C_{1-6}烷基、經0至5個R^e取代之-$(CH_2)_n$-苯基、或包含1至4個選自O、S(=O)$_p$及N之雜原子且經0至5個R^e取代之-$(CH_2)_n$-3員至12員雜環基；或R^a及R^a與該兩者所連接之氮原子一起形成包含1至4個選自O、S(=O)$_p$及N之雜原子且經0至5個R^e取代之3員至12員雜環基；

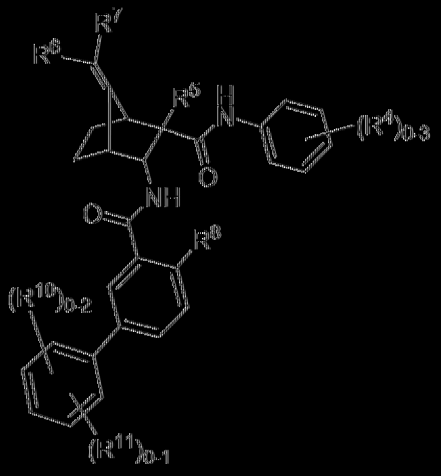
R^b為H、經0至5個R^e取代之C_{1-6}烷基、經0至5個R^e取代之-$(CH_2)_{0-1}$-

苯基、或包含1至4個選自O、S(=O)$_p$及N之雜原子且經0至5個R^c取代之-(CH$_2$)$_n$-3員至12員雜環基；

R^c為鹵基、CN、=O、C$_{1-6}$烷基或C(=O)OH；及

n為0、1、2或3。

[0022] 在第一至第二態樣之範疇內的第三態樣中，本發明提供式(IV)化合物：



(IV)

或其醫藥學上可接受之鹽，其中：

R^4為鹵基、經0至3個鹵基取代基取代之C$_{1-4}$烷基或經0至3個鹵基取代基取代之-OC$_{1-4}$烷基；

R^5為H或F；

R^6為鹵基、CN、經0至3個R^{6a}取代之C$_{1-6}$烷基、經0至3個R^{6a}取代之C$_{2-6}$烯基、經0至3個R^{6a}取代之C$_{2-6}$炔基、-C(=O)OR^{6b}、C(=O)N$R^{6b}R^{6b}$、經0至3個R^{14}取代之C$_{3-6}$環烷基、經0至3個R^{14}取代之C$_{3-6}$環烯基、經0至3個R^{14}取代之苯基、或包含1至3個選自O、S(=O)$_p$、N及NR^{14a}之雜原子且經0至3個R^{14}取代之5員至6員雜芳基；

R^{6a}為鹵基、C$_{3-6}$環烷基或苯基；

R^{6b}為H、經0至1個芳基取代基取代之C$_{1-3}$烷基、或經0至4個鹵基取

代基取代之C_{3-6}環烷基；

R^7為H或C_{1-2}烷基；

R^8為經0至4個鹵基、-OH、芳基或-OC_{1-4}烷基取代基取代之-OC_{1-4}烷基；

R^{10}為鹵基、CN、C_{1-3}烷基、-OH或-OC_{1-4}烷基；

R^{11}為經0至2個R^{12}及0至1個R^{13}取代之C_{1-4}烷基、-OR^b、-NR^aR^a、-$NR^aC(=O)R^b$、-$NR^aC(=O)NR^aR^a$、-$NR^aS(=O)_pR^c$、-$C(=O)R^b$、-$C(=O)OR^b$、-$C(=O)NR^aR^a$、-$C(=O)NR^aS(=O)_pR^c$、-$OC(=O)R^b$、-$S(=O)_pR^c$、-$S(=O)_pNR^aR^a$、C_{3-6}環烷基、包含1至4個選自O、$S(=O)_p$、N及NR^{15}之雜原子且經0至4個R^e取代之4員至9員雜環基；

R^{12}為鹵基、-$C(=O)OR^b$、-$C(=O)NHR^a$、-$C(=O)NHOR^b$、或經0至3個鹵基或-OH取代基取代之C_{1-4}烷基；

R^{13}為-OR^b、-NR^aR^a、-$NR^aC(=O)R^b$、-$NR^aC(=O)OR^b$、-$NR^aS(=O)_pR^c$、-$NR^aS(=O)_pNR^aR^a$、-$OC(=O)NR^aR^a$、-$OC(=O)NR^aOR^b$、-$S(=O)_pNR^aR^a$或-$S(=O)_pR^c$；

R^{14}為鹵基、CN、經0至3個鹵基取代基取代之C_{1-4}烷基、經0至3個鹵基取代基取代之-OC_{1-4}烷基、-$(CH_2)_{0-2}$-NR^aR^a、經0至3個R^e取代之-$(CH_2)_{0-2}$-芳基、經0至3個R^e取代之-O-芳基、或包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至3個R^e取代之-$(CH_2)_{0-2}$-3員至12員雜環基；

R^{14a}為H、$C(=O)C_{1-3}$烷基、經以下取代之C_{1-3}烷基：0至2個經0至2個鹵基取代基取代之芳基；

R^{15}為H、C_{1-2}烷基或苯基；

R^a為H、經0至4取代之C_{1-5}烷基、經0至4個R^e取代之C_{2-5}烯基、經0至

4個R^e取代之C_{2-5}炔基、經0至4個R^e取代之-$(CH_2)_n$-C_{3-10}碳環基、或包含1至4個選自O、S(=O)$_p$及N之雜原子且經0至4個R^e取代之-$(CH_2)_n$-3員至12員雜環基；或R^a及R^a與該兩者所連接之氮原子一起形成包含1至4個選自O、S(=O)$_p$及N之雜原子且經0至4個R^e取代之3員至12員雜環基；

R^b為H、經0至4個R^e取代之C_{1-5}烷基、經0至4個R^e取代之C_{2-5}烯基、經0至4個R^e取代之C_{2-5}炔基、經0至4個R^e取代之-$(CH_2)_n$-C_{3-10}碳環基、或包含1至4個選自O、S(=O)$_p$及N之雜原子且經0至4個R^e取代之-$(CH_2)_n$-3員至12員雜環基；

R^c為經0至4個R^e取代之C_{1-5}烷基、經0至4個R^e取代之C_{2-5}烯基、經0至4個R^e取代之C_{2-5}炔基、C_{3-6}碳環基、或包含1至4個選自O、S(=O)$_p$及N之雜原子之3員至12員雜環基；

R^e為鹵基、CN、NO_2、=O、經0至5個R^g取代之C_{1-6}烷基、經0至5個R^g取代之C_{2-6}烯基、經0至5個R^g取代之C_{2-6}炔基、-$(CH_2)_n$-C_{3-6}環烷基、-$(CH_2)_n$-芳基、包含1至4個選自O、S(=O)$_p$及N之雜原子之-$(CH_2)_n$-3員至12員雜環基、-$(CH_2)_n$$OR^f$、S(=O)$_p$$R^f$、C(=O)$NR^fR^f$、C(=O)$OR^f$、$NR^f$C(=O)$R^f$、S(=O)$_p$$NR^fR^f$、$NR^f$S(=O)$_p$$R^f$、$NR^f$C(=O)$OR^f$、OC(=O)$NR^fR^f$或-$(CH_2)_n$$NR^fR^f$；

R^f為H、C_{1-6}烷基、C_{3-6}環烷基或芳基；或R^f及R^f與該兩者所連接之氮原子一起形成雜環基；

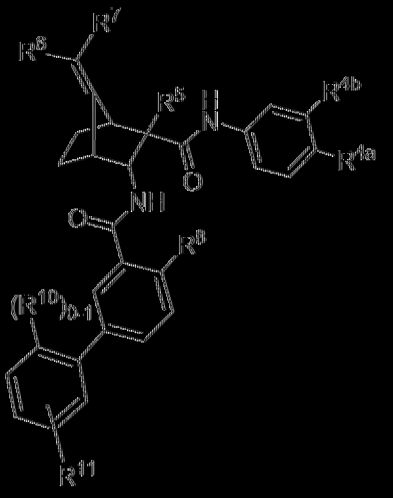
R^g為鹵基、CN、-OH、C_{1-5}烷基、C_{3-6}環烷基或芳基；

n為0、1、2或3；及

p為0、1或2。

【0023】在第五態樣之範疇內的第六態樣中，本發明提供式(V)化

合物：



(V)

或其醫藥學上可接受之鹽，其中：

R^{4a}為鹵基或C_{1-2}烷基；

R^{4b}為經0至4個鹵基取代基取代之C_{1-4}烷基；

R^5為H或F；

R^6為鹵基、CN、經0至3個R^{6a}取代之C_{1-4}烷基、經0至3個R^{6a}取代之C_{2-4}烯基、-C(=O)OR^{6b}、C(=O)$ONR^{6b}R^{6b}$、經0至3個R^{14}取代之C_{3-6}環烷基、經0至3個R^{14}取代之苯基、或包含1至3個選自O、S(=O)$_p$、N及NR^{14a}之雜原子且經0至3個R^{14}取代之5員至6員雜芳基；

R^{6a}為鹵基、-OH、C_{3-6}環烷基或苯基；

R^{6b}為H、經0至1個芳基取代基取代之C_{1-3}烷基或C_{3-6}環烷基；

R^7為H或C_{1-2}烷基；

R^8為經0至4個鹵基、-OH、-OC_{1-4}烷基或芳基取代基取代之-OC_{1-4}烷基；

R^{10}為鹵基或C_{1-3}烷基；

R^{11}為經0至2個R^{12}及0至1個R^{13}取代之C_{1-4}烷基、-OH、-OC_{1-4}烷基、$NR^aC(=O)R^b$、$NR^aC(=O)NR^aR^a$、$NR^aS(=O)_pR^c$、$C(=O)R^b$、

$-C(=O)OR^b$ 、 $-C(=O)NR^aR^a$ 、 $-C(=O)NR^aS(=O)_pR^c$ 、 $-OC(=O)R^b$ 、 $-S(=O)_pR^c$、$-S(=O)_pNR^aR^a$、C_{3-6}環烷基、包含1至4個選自O、$S(=O)_p$、N及NR^{15}之雜原子且經0至3個R^e取代之4員至9員雜環基；

R^{12}為鹵基、$-C(=O)OR^b$、$-C(=O)NHR^a$、$-C(=O)NHOR^b$、或經0至3個鹵基或-OH取代基取代之C_{1-4}烷基；

R^{13} 為 $-OR^b$ 、 $-NR^aR^a$ 、 $-NR^aC(=O)R^b$ 、 $-NR^aC(=O)OR^b$ 、 $-NR^aS(=O)_pR^c$、$-NR^aS(=O)_pNR^aR^a$、$-OC(=O)NR^aR^a$或$-OC(=O)NR^aOR^b$；

R^{14}為鹵基、CN、經0至3個鹵基取代基取代之C_{1-4}烷基、經0至3個鹵基取代基取代之$-OC_{1-4}$烷基、$-(CH_2)_{0-2}-NR^aR^a$、經0至3個R^e取代之$-(CH_2)_{0-1}-$芳基、經0至3個R^e取代之-O-芳基、或包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至3個R^e取代之$-(CH_2)_{0-1}-$3員至9員雜環基；

R^{14a}為H、$C(=O)C_{1-3}$烷基、經以下取代之C_{1-3}烷基：0至1個經0至2個鹵基取代基取代之芳基；

R^{15}為H、C_{1-2}烷基或苯基；

R^a為H、經0至5個R^e取代之C_{1-4}烷基、經0至5個R^e取代之C_{2-4}烯基、經0至5個R^e取代之C_{2-4}炔基、經0至5個R^e取代之$-(CH_2)_n-C_{3-10}$碳環基、或包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至5個R^e取代之$-(CH_2)_n-$3員至12員雜環基；或R^a及R^a與該兩者所連接之氮原子一起形成包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至5個R^e取代之3員至9員雜環基；

R^b為H、經0至5個R^e取代之C_{1-4}烷基、經0至5個R^e取代之C_{2-4}烯基、經0至5個R^e取代之C_{2-4}炔基、經0至5個R^e取代之$-(CH_2)_n-C_{3-10}$碳環基、或包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至5個R^e取代之$-(CH_2)_n-$3員至9員雜環基；

R^c為經0至5個R^e取代之C_{1-4}烷基、經0至5個R^e取代之C_{2-4}烯基、經0至5個R^e取代之C_{2-4}炔基、C_{3-6}碳環基、或包含1至4個選自O、$S(=O)_p$及N之雜原子之3員至9員雜環基；

R^e為鹵基、CN、=O、經0至5個R^g取代之C_{1-6}烷基、經0至5個R^g取代之C_{2-6}烯基、經0至5個R^g取代之C_{2-6}炔基、$-(CH_2)_n-C_{3-6}$環烷基、$-(CH_2)_n-$芳基、包含1至4個選自O、$S(=O)_p$及N之雜原子之$-(CH_2)_n-$4員至6員雜環基、$-(CH_2)_nOR^f$、$S(=O)_pR^f$、$C(=O)NR^fR^f$、$C(=O)OR^f$、$NR^fC(=O)R^f$、$S(=O)_pNR^fR^f$、$NR^fS(=O)_pR^f$、$NR^fC(=O)OR^f$、$OC(=O)NR^fR^f$或$-(CH_2)_nNR^fR^f$；

R^f為H、C_{1-6}烷基、C_{3-6}環烷基或芳基；或R^f及R^f與該兩者所連接之氮原子一起形成雜環基；

R^g為鹵基、CN、-OH、C_{1-6}烷基、C_{3-6}環烷基或芳基；

n為0、1、2或3；及

p為0、1或2。

【0024】 在式(V)之一個實施例中，R^{4a}為F或CH_3；R^{4b}為CF_3；R^6為苯基或包含1至2個選自O及N之雜原子之5員雜芳基；R^7為H；R^8為$-OC_{1-2}$烷基；R^{10}為鹵基；R^{11}為$-CH_3$、$-CH_2CH_3$、$-CF_3$ $-OCF_3$、$-NHS(=O)_2C_{1-2}$烷基、-C(=O)OH、$-C(=O)OC_{1-4}$烷基、經0至1個R^e取代之$-C(=O)NHC_{1-4}$烷基、或包含1至4個選自O、N及NR^{15}之雜原子且經0至3個R^e取代之5員雜環基；R^{15}為H、C_{1-2}烷基或苯基；且R^e為=O或C(=O)OH。

【0025】 在第六態樣之範疇內的第七態樣中，本發明提供式(V)化合物或其醫藥學上可接受之鹽，其中：

R^{4a}為鹵基；

R^{4b}為CF_3；

R^6為經0至3個鹵基取代基取代之C_{1-4}烷基或經0至3個鹵基取代基取代之C_{3-6}環烷基；

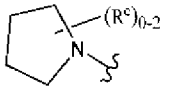
R^8為-OC_{1-4}烷基；

R^{10}為F；

R^{11}為-OH、-OC_{1-4}烷基、-$NR^aC(=O)R^b$、-$NR^aS(=O)_pR^c$、-$C(=O)OR^b$、-$C(=O)NR^aR^a$、-$C(=O)NR^aS(=O)_pR^c$、包含1至4個選自O、$S(=O)_p$、N及NR^{15}之雜原子且經0至5個R^e取代之4員至9員雜環基；

R^{15}為H或C_{1-2}烷基；

R^a為H或經0至5個R^e取代之C_{1-4}烷基；

或R^a及R^a一起為  ；

R^b為H或經0至5個R^e取代之C_{1-4}烷基；

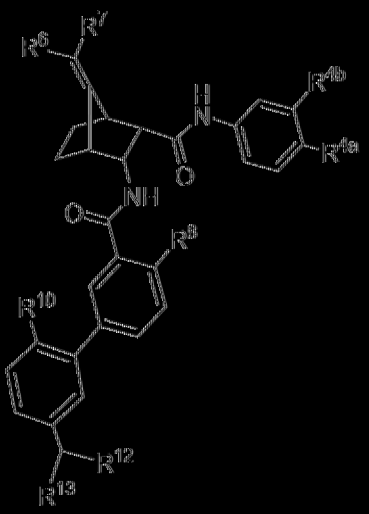
R^c為經0至5個R^e取代之C_{1-3}烷基或C_{3-6}碳環基；

R^e為鹵基、=O、經0至5個R^g取代之C_{1-4}烷基、C(=O)OH、-OR^f或-NR^fR^f；及

R^f為H及C_{1-6}烷基；或R^f及R^f與該兩者所連接之氮原子一起形成雜環基；及

R^g為鹵基。

【0026】在第六態樣之範疇內之第八態樣中，本發明提供式(VI)化合物：



(VI)

或其醫藥學上可接受之鹽，其中：

R^{4a}為鹵基；

R^{4b}為CF_3；

R^6為經0至3個鹵基取代基取代之C_{1-4}烷基或經0至3個鹵基取代基取代之C_{3-6}環烷基；

R^7為H；

R^8為經0至1個芳基取代基取代之-OC_{1-4}烷基；

R^{10}為鹵基；

R^{12}為-C(=O)OH、-C(=O)OC_{1-4}烷基、-C(=O)NHC_{1-4}烷基、-C(=O)$NHOC_{1-3}$烷基、或經0至3個鹵基取代基取代之C_{1-3}烷基；

R^{13}為-OR^b、-NR^aR^a、-$NR^aC(=O)R^b$、-$NR^aC(=O)OR^b$、-$NR^aS(=O)_pR^c$、-$NR^aS(=O)_pNR^aR^a$、-$OC(=O)NR^aR^a$或-$OC(=O)NR^aOR^b$；

R^a為H、經0至5個鹵基取代基取代之C_{1-4}烷基、經0至4個R^c取代之苯基、經0至4個R^c取代之C_{3-10}環烷基、經0至4個R^c取代之螺環烷基、或包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至4個R^c取代之3員至9員雜環基；或R^a及R^a與該兩者所連接之氮原子一起形成包含1至4個選自O、

$S(=O)_p$及N之雜原子且經0至4個R^e取代之3員至12員雜環基；

R^b為H、經0至5個R^e取代之C_{1-4}烷基、經0至4個R^e取代之-$(CH_2)_n$-苯基、經0至4個鹵基取代基取代之C_{3-6}環烷基、或包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至4個R^e取代之3員至12員雜環基；

R^c為經0至4個R^e取代之C_{1-4}烷基，

R^e為鹵基、CN、=O、經0至5個R^g取代之C_{1-5}烷基、C_{3-6}環烷基、芳基、包含1至4個選自O、$S(=O)_p$及N之雜原子之4員至6員雜環基、或-OR^f；

R^f為H、C_{1-4}烷基、C_{3-6}環烷基或芳基；

R^g為鹵基；

n為0或1；及

p為0、1或2。

【0027】 在第八態樣之範疇內之第九態樣中，本發明提供式(VI)化合物或其醫藥學上可接受之鹽，其中：

R^{4a}為F

R^{4b}為CF_3；

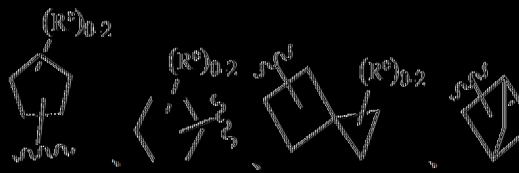
R^6為CF_3或C_{3-6}環烷基；

R^8為-OCH_3或-OCH_2-苯基；

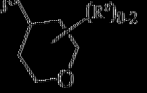
R^{10}為F；

R^{12}為-C(=O)OH、-C(=O)OC_{1-4}烷基、-C(=O)NHC_{1-4}烷基、-C(=O)$NHOC_{1-4}$烷基、CH_3、CHF_2或CF_3；

R^{13}為-OH、-NR^aR^a、-NHC(=O)R^b、-$NHS(=O)_pC_{1-4}$烷基、-$OC(=O)NR^aR^a$或-$OC(=O)NHOC_{1-4}$烷基；

R^a為H、經0至4個F取代其取代之C_{1-4}烷其、  、  ；

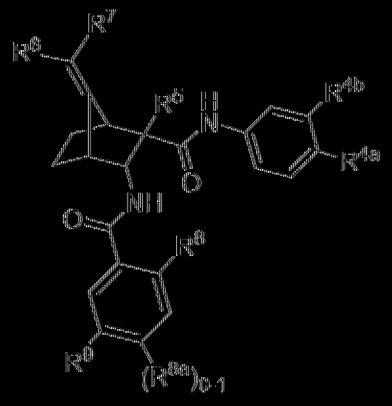
或R^a及$R^{a'}$一起為  ，

R^b為H、經0至5個R^c取代之C_{1-4}烷其、苯其，或  ；及

R^c為鹵其、=O、芳其、包含1至4個選自O、$S(=O)_p$及N之雜原子的4員至6員雜環其或$-OR^f$；及

R^f為H、C_{1-3}烷其、C_{3-6}環烷其或苯其。

〔0028〕在第二態樣之範疇內的第十態樣中，本發明提供式(VII)化合物：



(VII)

或其醫藥學上可接受之鹽，其中：

R^{4a}為鹵其；

R^{4b}為經0至3個鹵其取代其取代之C_{1-4}烷其或經0至3個鹵其取代其取代之$-OC_{1-4}$烷其；

R^5為H或F；

R^6為鹵基、CN、經0至3個R^{6a}取代之C_{1-6}烷基、經0至3個R^{6a}取代之C_{2-6}烯基、經0至3個R^{6a}取代之C_{2-6}炔基、經0至3個R^{14}取代之C_{3-6}環烷基、0至3個R^{14}經取代之C_{3-6}環烯基、經0至3個R^{14}取代之苯基、或包含1至3個選自O、$S(=O)_p$、N及NR^{14a}之雜原子且經0至3個R^{14}取代之5員至6員雜芳基；

R^{6a}為鹵基、C_{3-6}環烷基或苯基；

R^7為H或C_{1-2}烷基；

R^8為鹵基、CN或經0至4個鹵基、-OH或-OC_{1-4}烷基取代基取代之-OC_{1-4}烷基；

R^{8a}為鹵基或CN；

R^9為包含1至4個選自O、$S(=O)_p$、N及NR^{11a}之雜原子且經0至3個R^{10}及0至1個R^{11}取代之3員至12員雜環基；

R^{10}為鹵基、CN、C_{1-3}烷基、=O、-OH或-OC_{1-3}烷基；

R^{11}為經0至1個R^{12}及0至1個R^{13}取代之C_{1-3}烷基、$-OR^b$、$-NR^aR^a$、$-NR^aC(=O)R^b$、$-NR^aC(=O)OR^b$、$-NR^aC(=O)NR^aR^a$、$-NR^aS(=O)_pR^c$、$-C(=O)R^b$、$-C(=O)OR^b$、$-C(=O)NR^aR^a$、$-C(=O)NR^aS(=O)_pR^c$、$-OC(=O)R^b$、$-S(=O)_pR^c$、$-S(=O)_pNR^aR^a$、經0至5個R^e取代之C_{3-6}環烷基、包含1至4個選自O、$S(=O)_p$、N及NR^{15}之雜原子且經0至4個R^e取代之4員至6員雜環基；

R^{11a}為H、經0至2個R^{11b}取代之C_{1-4}烷基、$-C(=O)R^b$、$-C(=O)OR^b$、$-C(=O)NR^aR^a$、C_{3-6}環烷基、包含1至4個選自O、$S(=O)_p$、N及NR^{15}之雜原子且經0至4個R^e取代之4員至6員雜環基；

R^{11b}為-OH、-C(=O)OH或芳基；

R^{12}為-C(=O)OR^b、-C(=O)NHR^a、-C(=O)$NHOR^b$或經0至3個鹵基或-OH取代基取代之C_{1-4}烷基；

R^{13}為-OR^b、-NR^aR^a、-$NR^aC(=O)R^b$、-$NR^aC(=O)OR^b$、-$NR^aS(=O)_pR^c$、-$NR^aS(=O)_pNR^aR^a$、-$OC(=O)NR^aR^a$、-$S(=O)_pNR^aR^a$或-$S(=O)_pR^c$；

R^{14}為鹵基、CN、經0至3個鹵基取代之C_{1-4}烷基、經0至3個鹵基取代之-OC_{1-4}烷基、-$(CH_2)_{0-2}$-NR^aR^a、經0至3個R^e取代之-$(CH_2)_{0-2}$-芳基、經0至3個R^e取代之-O-芳基、或包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至3個R^e取代之-$(CH_2)_{0-2}$-3員至12員雜環基；

R^{14a}為H、C(=O)C_{1-3}烷基或經以下取代之C_{1-3}烷基：0至2個經0至2個鹵基取代基取代之芳基；

R^{15}為H、C_{1-2}烷基或苯基；

R^a為H、經0至4取代之C_{1-5}烷基、經0至4個R^e取代之C_{2-5}烯基、經0至4個R^e取代之C_{2-5}炔基、經0至4個R^e取代之-$(CH_2)_n$-C_{3-10}碳環基、或包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至4個R^e取代之-$(CH_2)_n$-3員至12員雜環基；或R^a及R^a與該兩者所連接之氮原子一起形成包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至4個R^e取代之3員至12員雜環基；

R^b為H、經0至4個R^e取代之C_{1-5}烷基、經0至4個R^e取代之C_{2-5}烯基、經0至4個R^e取代之C_{2-5}炔基、經0至4個R^e取代之-$(CH_2)_n$-C_{3-10}碳環基、或包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至4個R^e取代之-$(CH_2)_n$-3員至12員雜環基；

R^c為經0至4個R^e取代之C_{1-5}烷基、經0至4個R^e取代之C_{2-5}烯基、經0至4個R^e取代之C_{2-5}炔基、C_{3-6}碳環基、或包含1至4個選自O、$S(=O)_p$及N

之雜原子之3員至12員雜環基；

R^e為鹵基、CN、=O、經0至4個R^g取代之C_{1-6}烷基、經0至5個R^g取代之C_{2-6}烯基、經0至5個R^g取代之C_{2-6}炔基、經0至4個R^g取代之-$(CH_2)_n$-C_{3-6}環烷基、經0至4個R^g取代之-$(CH_2)_n$-芳基、包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至4個R^g取代之-$(CH_2)_n$-4員至6員雜環基、-$(CH_2)_nOR^f$、$C(=O)OR^f$、$C(=O)NR^fR^f$、$NR^fC(=O)R^f$、$S(=O)_pR^f$、$NR^fS(=O)_pR^f$、$NR^fC(=O)OR^f$、$OC(=O)NR^fR^f$或-$(CH_2)_nNR^fR^f$；

R^f為H、C_{1-6}烷基、C_{3-6}環烷基或芳基；

R^g為鹵基、CN、-OH、C_{1-4}烷基、C_{3-6}環烷基或芳基；

n為0、1、2或3；及

p為0、1或2。

【0029】 在第十態樣之範疇內之第十一態樣中，本發明提供式(VII)化合物或其醫藥學上可接受之鹽，其中：

R^{4a}為鹵基；

R^{4b}為經0至3個鹵基取代基取代之C_{1-4}烷基；

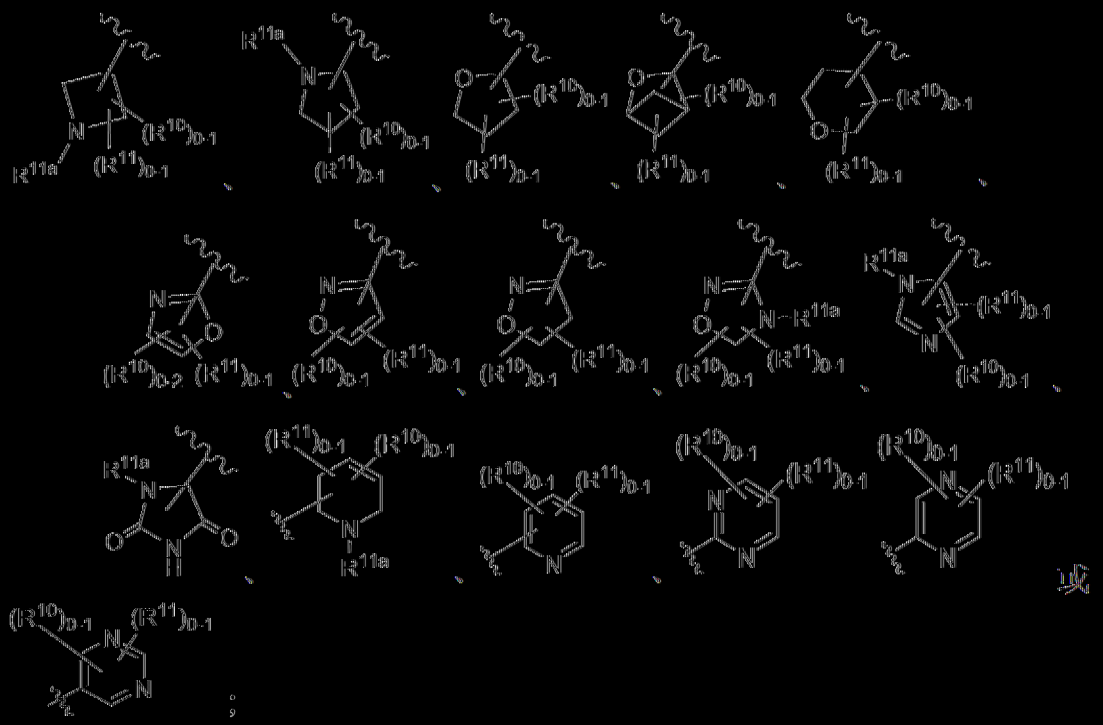
R^5為H；

R^6為經0至2個F取代基取代之C_{1-2}烷基或C_{3-6}環烷基；

R^8為-OC_{1-3}烷基；

R^{8a}為F或CN；

R^9為



R^{10}為鹵基、CN、C_{1-2}烷基、=O、-OH或-OC_{1-2}烷基；

R^{11}為經0至1個R^{12}及0至1個R^{13}取代之C_{1-3}烷基、-OR^b、-NR^aR^a、-$NR^aC(=O)R^b$、-$C(=O)R^b$、-$C(=O)OR^b$、-$C(=O)NR^aR^a$或經0至5個R^c取代之C_{3-6}環烷基；

R^{11a}為H、-$C(=O)R^b$、-$C(=O)NR^aR^a$或經0至1個R^{11b}取代之C_{1-4}烷基；

R^{11b}為-OH或芳基；

R^{12}為-$C(=O)OR^b$、-$C(=O)NHR^a$、-$C(=O)NHOR^b$或經0至2個鹵基或-OH取代基取代之C_{1-4}烷基；

R^{13}為-OH、經0至2個-OH取代基取代之-OC_{1-4}烷基、或-$S(=O)_2C_{1-4}$烷基；

R^a為H或C_{1-6}烷基，或R^a及R^a與該兩者所連接之氮原子一起形成經0至4個R^c取代之3員至9員雜環基；

R^b為H、經0至1個R^c取代之C_{1-4}烷基或經0至1個R^c取代之C_{3-6}環烷基；

R^e為-OR^f；及

R^f為H或C_{1-4}烷基。

【0030】在第十一態樣之範疇內之第十二態樣中，本發明提供式(VII)化合物或其醫藥學上可接受之鹽，其中：

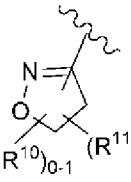
R^{4a}為鹵基；

R^{4b}為CF_3；

R^5為H；

R^6為CF_3或C_{3-6}環丙基；

R^8為-OC_{1-3}烷基；

R^9為  ；

R^{10}為C_{1-2}烷基、-OH或-OC_{1-4}烷基；

R^{11}為經0至1個R^{12}及0至1個R^{13}取代之C_{1-2}烷基、-C(=O)OR^b或-C(=O)NR^aR^a；

R^{12}為-C(=O)OR^b；

R^{13}為-OH；

R^a為H或C_{1-4}烷基；及

R^b為H或C_{1-4}烷基。

【0031】在第十態樣之範疇內之第十三態樣中，本發明提供式(VI)化合物或其醫藥學上可接受之鹽，其中：

R^{4a}為鹵基；

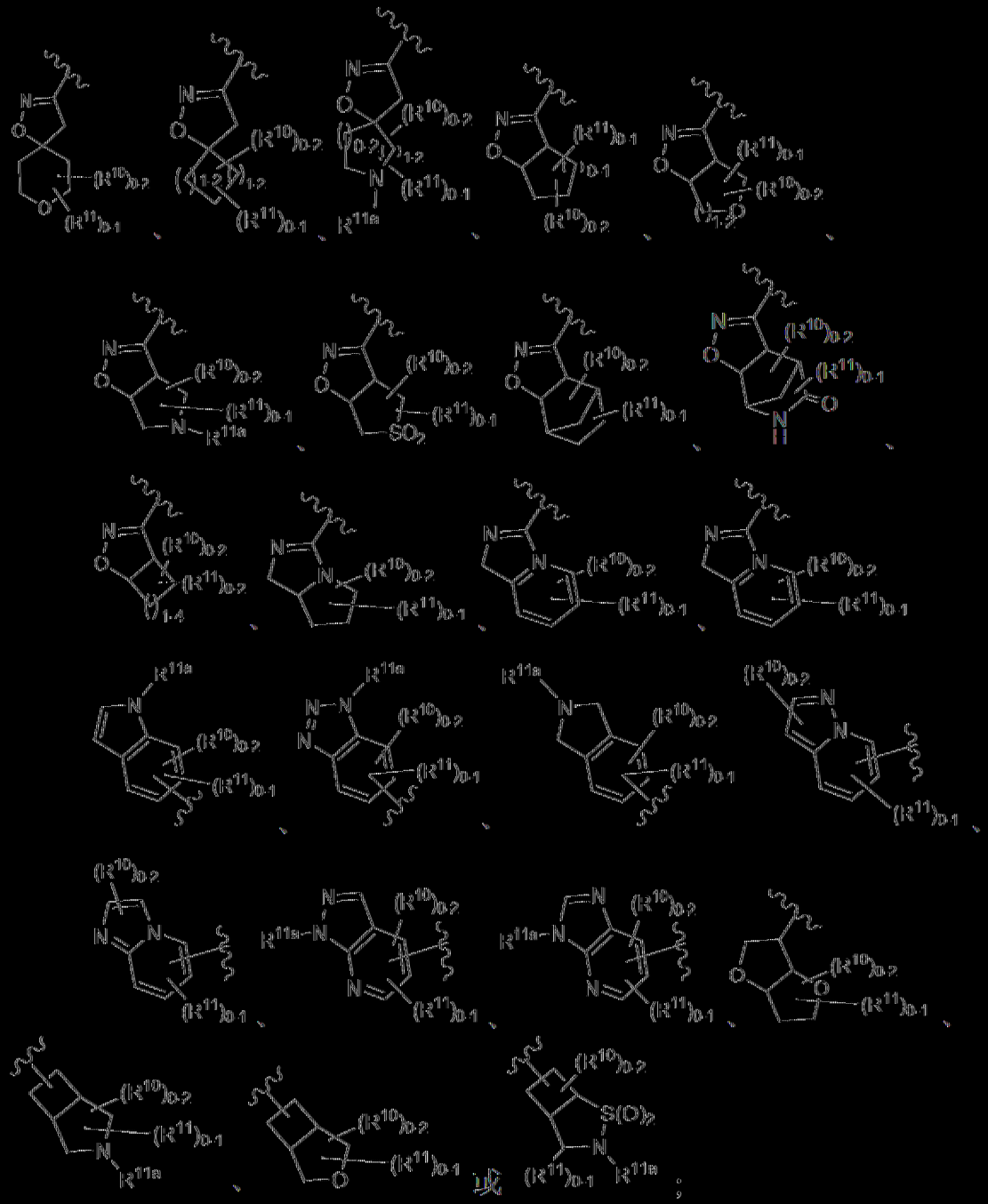
R^{4b}為經0至3個鹵基取代基取代之C_{1-4}烷基；

R^5為H；

R^6為經0至3個F取代其取代之C_{1-3}烷基或C_{3-6}環烷基；

R^8為-OC_{1-3}烷基；

R^9為



R^{10}為鹵基、C_{1-3}烷基、-OH或-OC_{1-3}烷基；

R^{11}為經0至1個R^{12}及0至1個R^{13}取代之C_{1-3}烷基或-C(=O)NH_2；

R^{11a}為H、經0至2個R^{11b}取代之C_{1-4}烷基或-C(=O)OC_{1-4}烷基；

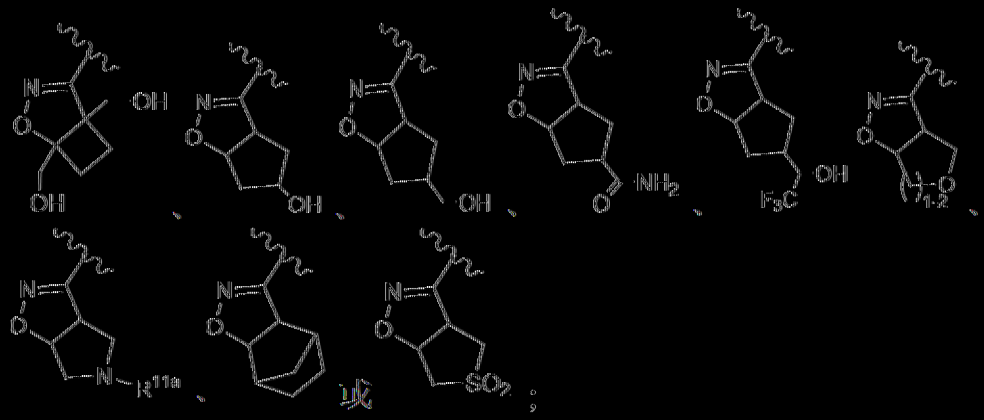
R^{11b}為-OH、-C(=O)OH或芳基；

R^{12}為C(=O)OR^b或經0至3個鹵基取代基取代之C_{1-3}烷基；

R^{13}為-OH；及

R^b為H或C_{1-4}烷基。

[0032] 在式(VII)之一個實施例中，R^{4a}為F；R^{4b}為CF_3；R^5為H；R^6為經0至3個F取代基取代之C_{1-4}烷基或C_{3-6}環烷基；R^8為-OCH_3或-$OCH_3(CH_2)_2OCH_3$；R^9為



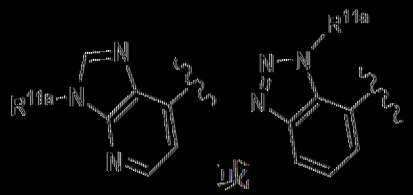
；

R^{11}為經0至1個R^{13}取代之C_{1-2}烷基；

R^{11a}為H、經0至2個R^{11b}取代之C_{1-3}烷基、經0至1個R^{11b}取代之-C(=O)C_{1-4}烷基、或-C(=O)OC_{1-4}烷基；且R^{11b}為-OH、-C(=O)OH或芳基；及

R^{13}為-OH。

[0033] 在式(VII)之一個實施例中，R^{4a}為F；R^{4b}為CF_3；R^5為H；R^6為經0至3個F取代基取代之C_{1-3}烷基或C_{3-6}環烷基；R^8為-OCH_3；R^9為

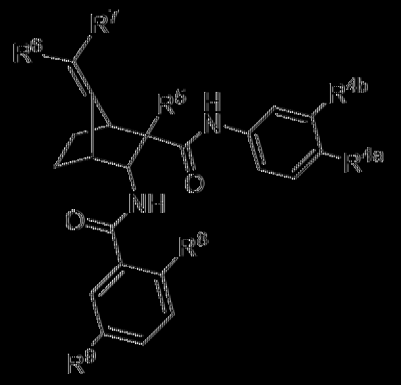


；

R^{11a}為H或經0至1個R^{11b}取代之C_{1-2}烷基；且R^{11b}為-C(=O)OH。

[0034] 在第三態樣之範疇內之第十四態樣中，本發明提供式

(VIII)化合物：



(VIII)

或其醫藥學上可接受之鹽，其中：

R^{4a}為鹵基；

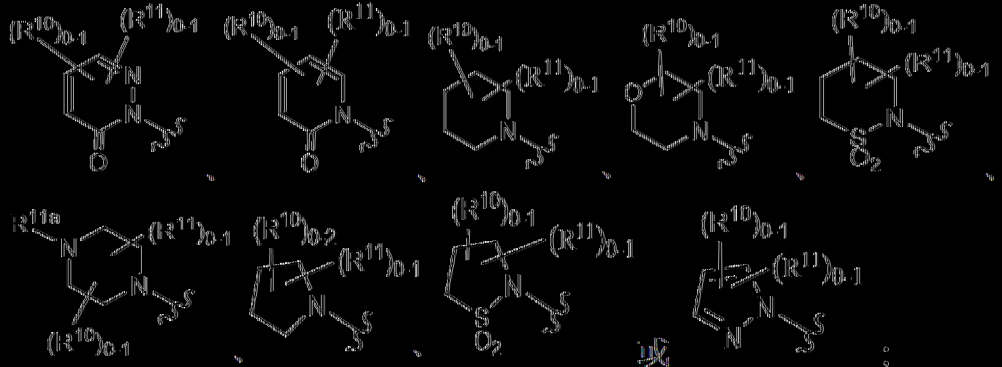
R^{4b}為經0至4個鹵基取代基取代之C_{1-4}烷基；

R^{6}為經0至2個F取代基取代之C_{1-2}烷基、C_{3-6}環烷基或芳基；

R^{7}為H；

R^{8}為-OC_{1-3}烷基；

R^{9}為



；

R^{10}為鹵基、CN、C_{1-4}烷基、=O、-OH或-OC_{1-4}烷基；

R^{11}為經0至1個R^{12}及0至1個R^{13}取代之C_{1-2}烷基、-NR^aR^a、-$NR^aC(=O)R^b$、-$NR^aC(=O)OR^b$或-$C(=O)OR^b$；

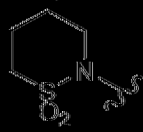
R^{12}為-$C(=O)OR^b$、-$C(=O)NHR^a$、-$C(=O)NHOR^b$或經0至3個鹵基或-OH取代基取代之C_{1-4}烷基；

R^{13}為-OH或-$NR^aC(=O)R^b$；

R^a為H或C_{1-4}烷基；及

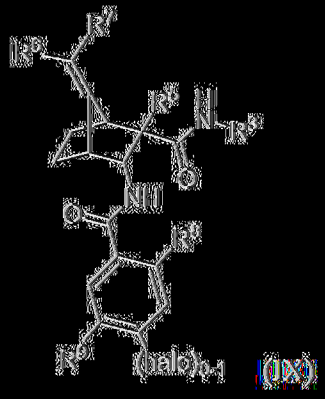
R^b為H、C_{1-4}烷基、或包含1至4個選自O、$S(=O)_p$及N之雜原子的3員至9員雜環基。

[0035] 在式(VIII)之一個實施例中，R^{4a}為F；R^{4b}為CF_3；R^5為H；R^6為CF_3或環內基；R^8為-OCH_3；R^9為



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[0036] 在第一態樣之範疇內的第十五態樣中，本發明提供式(IX)化合物：



或其醫藥學上可接受之鹽，其中：

R^3為C_{1-6}烷基、CF_3、經0至4個R^4取代之-$(CR_dR_d)_{0-1}$-C_{3-6}環烷基或經0至4個R^4取代之苯基；

R^4為鹵基、CN、CH_3或CF_3；

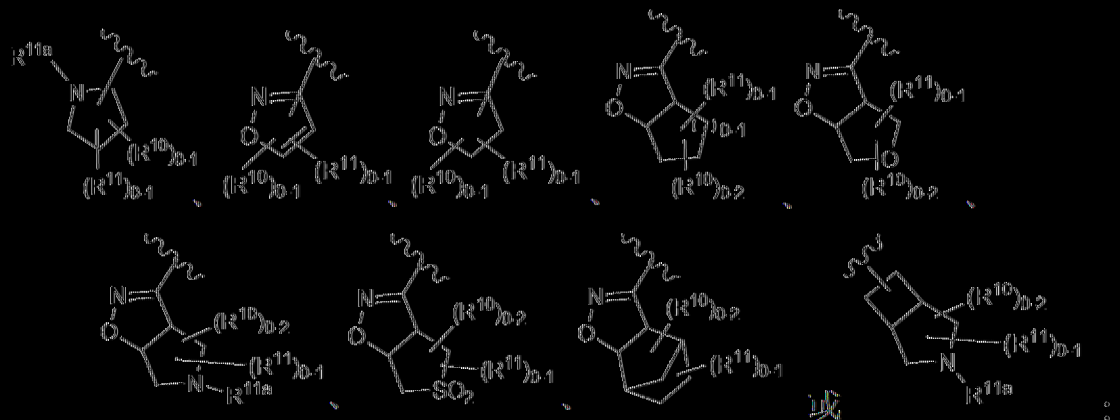
R^5為H；

R^6為C_{1-5}烷基、CF_3或經0至2個F取代基取代之C_{3-6}環烷基；

R^7為H；

R^8為鹵基、-$N(C_{1-3}$烷基$)_2$、經0至1個-OC_{1-4}烷基取代基取代之-OC_{1-3}烷基；

R^9為



；

R^{10}為鹵基、C_{1-4}烷基、-OH或-OC_{1-4}烷基；

R^{11}為經0至2個R^{12}及0至2個R^{13}取代之C_{1-4}烷基、-C(=O)OR^b、-C(=O)NR^aR^a或經0至2個R^c取代之C_{3-6}環烷基；

R^{11a}為H、經0至2個R^{11b}取代之C_{1-4}烷基、-C(=O)R^b或-C(=O)OC_{1-4}烷基；

R^{11b}為-OH；

R^{12}為經0至3個鹵基取代基取代之C_{1-3}烷基或-C(=O)OR^b；

R^{13}為-OH；

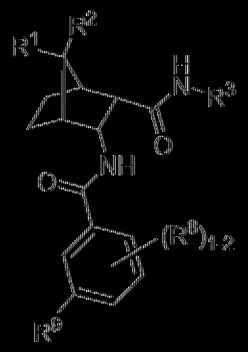
R^a為H或C_{1-3}烷基；

R^b為H或經0至1個R^c取代之C_{1-4}烷基；

R^c為-OR^f；及

R^f為H或C_{1-6}烷基。

[0037] 在第一態樣之範疇內之第十六態樣中，本發明提供式(X)化合物：



(X)

或其醫藥學上可接受之鹽，其中：

R^1為經C_{3-6}環烷基取代之C_{1-2}烷基；

R^2為H；

或R^1及R^2組合為-CR^6R^7；

R^3為經0至5個鹵基、CN或-OC_{1-3}烷基取代基取代之C_{1-6}烷基、經0至5個R^4取代之-$(CHR^d)_n$-C_{3-10}碳環基、或包含1至3個選自O、S(=O)$_p$、N之雜原子且經0至3個R^4取代之5員至6員雜芳基；

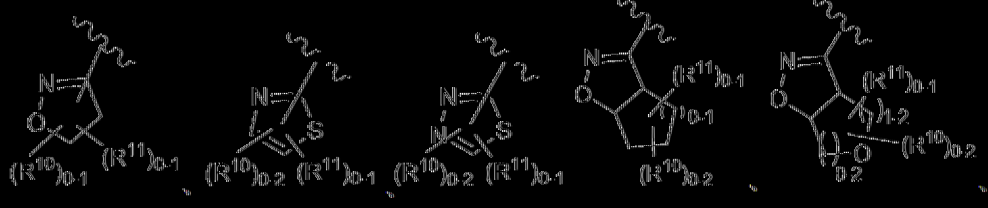
R^4為鹵基、CN、S(=O)$_2CF_3$或經0至5個鹵基取代基取代之C_{1-4}烷基；

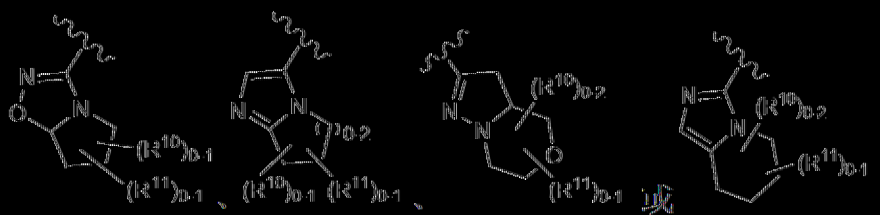
R^6為鹵基、經0至3個R^{6a}取代之C_{1-5}烷基、經0至3個R^{14}取代之C_{3-6}環烷基、或包含1至3個選自O、S及N之雜原子且經0至3個R^{14}取代之5員至6員雜環基；

R^{6a}為鹵基、-OH或C_{3-6}環烷基；

R^7為H；

R^8為H、鹵基、CN、C_{1-4}烷基或經0至5個鹵基、-OH、C_{3-6}環烷基或-OC_{1-4}烷基取代基取代之-OC_{1-4}烷基；

R^9為 



；

R^{10}為鹵基、CN、C_{1-4}烷基或-OH；

R^{11}為經0至3個R^{12}及0至1個R^{13}取代之C_{1-3}烷基、-OR^b、-$NHC(=O)R^b$或$C(=O)OR^b$；

R^{12}為鹵基；

R^{13}為-OR^b或C_{3-6}碳環基；

R^{14}為鹵基、CN或經0至3個鹵基取代基取代之C_{1-4}烷基；

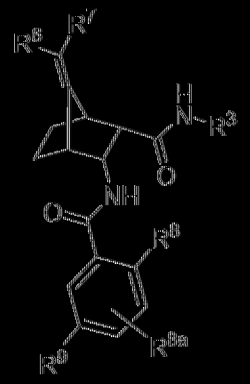
R^b為H或經0至5個R^a取代之C_{1-3}烷基；

R^d為H或C_{1-4}烷基；

R^a為-OH；及

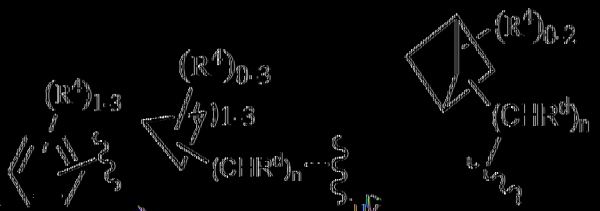
n為0或1。

〔0038〕在第一態樣之範疇內之第十七態樣中，本發明提供式(XI)化合物：



(XI)

或其醫藥學上可接受之鹽，其中：

R^3為C_{1-5}烷基或  ；

R^4為鹵基、CN、-S(=O)$_2$$CF_3$或經0至5個鹵基取代基取代之$C_{1-4}$烷基；

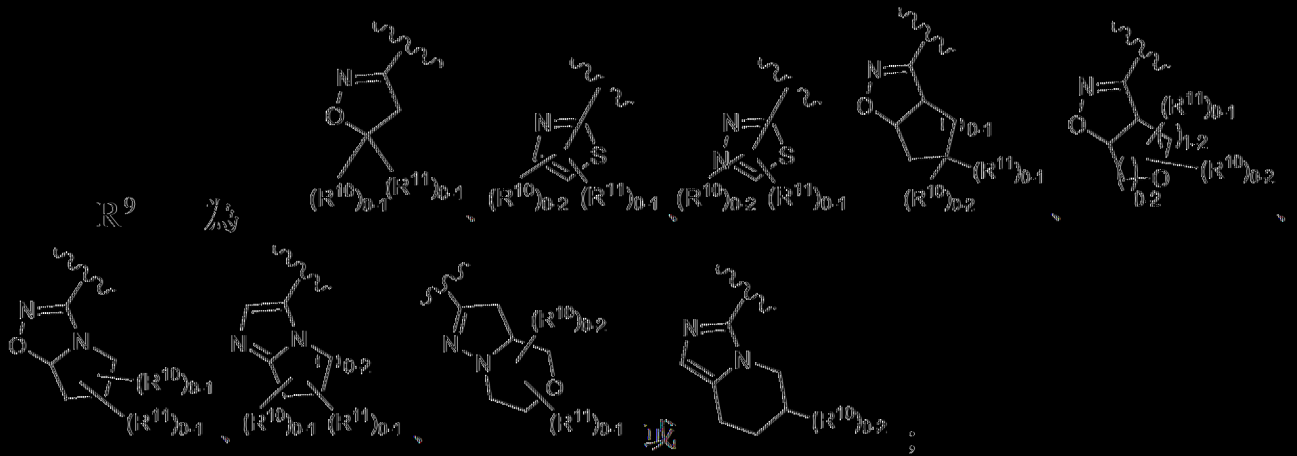
R^6為經0至4個R^{6a}取代之C_{1-5}烷基、經0至2個R^{14}取代之C_{3-6}環烷基、或包含1至3個選自O、S及N之雜原子且經0至2個R^{14}取代之5員至6員雜環基；

R^{6a}為鹵基、-OH或C_{3-6}環烷基；

R^7為H；

R^8為經0至5個鹵基、-OH、C_{3-6}環烷基或-OC_{1-3}烷基取代基取代之-OC_{1-3}烷基；

R^{8a}為H、鹵基、CN或C_{1-3}烷基；

R^9為  ；

R^{10}為鹵基、CN、C_{1-4}烷基或-OH；

R^{11}為經0至3個R^{12}及0至1個R^{13}取代之C_{1-3}烷基、-OR^b、-$NHC(=O)R^b$或-$C(=O)OR^b$；

R^{12}為鹵基；

R^{13}為-OR^b或C_{3-6}碳環基；

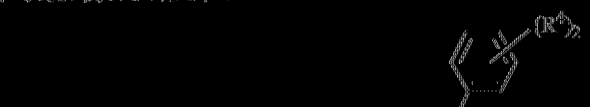
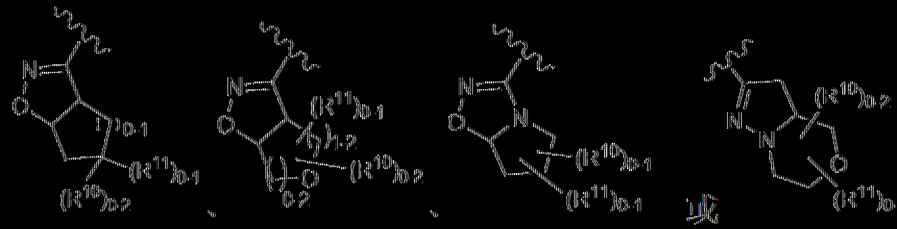
R^{14}為鹵基或經0至3個鹵基取代基取代之C_{1-4}烷基；

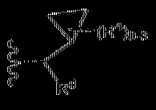
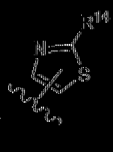
R^b為H或經0至5個R^c取代之C_{1-3}烷基；

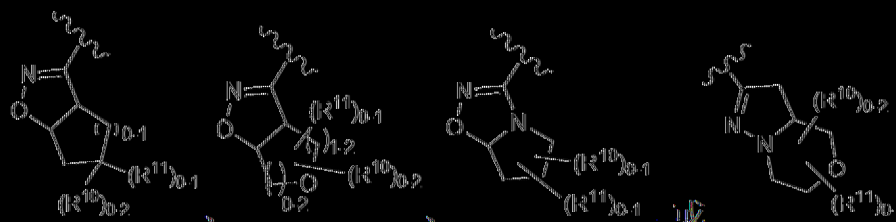
R^d為H或C_{1-2}烷基；及

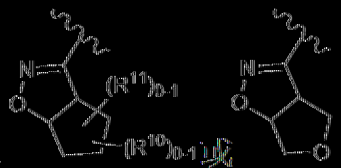
n為0或1。

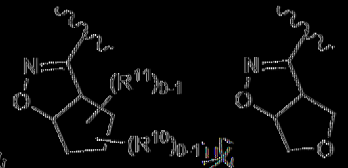
[0039] 對於式(I)化合物，可變取代基(包括R^1、R^2、R^3、R^4(R^{4a}、R^{4b}、R^{4c})、R^5、R^6、R^7、R^8(R^{8a})、R^9、R^{10}、R^{11}、R^{12}、R^{13}、R^{14}及R^{15})之任何例項之範疇可與可變取代基之任何其他例項之範疇獨立地使用。因而，本發明包括不同態樣之組合。

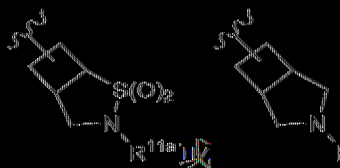
[0040] 在式(XI)之一個實施例中，R^3為  ；R^4為鹵基、CF_3或OCF_3；R^6為C_{3-6}環烷基或經0至3個R^{6a}取代之C_{1-3}烷基；R^{6a}為鹵基；R^7為H；R^8為經0至1個CF_3或OCH_3取代基取代之OC_{1-3}烷基；R^9為  ；R^{10}為C_{1-4}烷基或OH；R^{11}為經0至3個R^{12}及0至1個R^{13}取代之C_{1-3}烷基；R^{12}為鹵基；且R^{13}為OH。

[0041] 在式(XI)之另一個實施例中，R^3為  ；R^4為鹵基或經0至3個鹵基取代基取代之C_{1-2}烷基；R^d為C_{1-2}烷基；R^6為  、經0至3個R^{6a}取代之C_{3-6}環烷基或經0至3個R^{6a}取代之C_{1-3}烷基；R^{6a}為鹵基或OH；R^{14}為經0至3個鹵基取代基取代之C_{1-2}烷基；R^7為H；R^8為經0至1個C_{3-6}環烷基取代基取代之OC_{1-2}烷基；R^{8a}為H或鹵基；R^9為

 、、或；R^{10}為C_{1-4}烷基或-OH；R^{11}為經0至3個R^{12}及0至1個R^{13}取代之C_{1-3}烷基；R^{12}為鹵基；且R^{13}為-OH。

[0042] 在式(IX)之一個實施例中，R^3為C_{1-4}烷基；R^6為CF_3或環內基；R^7為H；R^8為-OC_{1-2}烷基；R^9為  ；R^{10}為-OH或-OC_{1-4}烷基；R^{11}為經0至2個R^{12}及0至2個R^{13}取代之C_{1-2}烷基；R^{12}為經0至3個鹵基取代之C_{1-3}烷基或-C(=O)OR^b；且R^{13}為-OH。

[0043] 在式(IX)之另一個實施例中，R^3為經0至1個R^4取代之環戊基、R^4為CN或C_{1-2}烷基；R^6為CF_3或環內基；R^7為H；R^8為-OC_{1-2}烷基；R^9為  ；R^{10}為-OH或-OC_{1-4}烷基；R^{11}為經0至2個R^{12}及0至2個R^{13}取代之C_{1-2}烷基；R^{12}為經0至3個鹵基取代基取代之C_{1-3}烷基或-C(=O)OR^b；且R^{13}為-OH。

[0044] 在式(IX)之另一個實施例中，R^3為經0至2個R^4取代之苯基、R^4為鹵基或CF_3；R^6為CF_3或環內基；R^7為H；R^8為-OC_{1-2}烷基；R^9為  ；R^{11a}為H、經0至2個R^{11b}取代之C_{1-2}烷基；R^{11b}為-OH。

[0045] 在式(I)之另一個實施例中，R^1及R^2與該兩者所連接之碳原子形成二氧戊環基。

【0046】 在式(I)之另一個實施例中，R^1及R^2組合為=NOC_{1-4}烷基，其中「=」為雙鍵。

【0047】 在式(I)之另一個實施例中，R^1及R^2組合為=CR^6R^7，其中「=」為雙鍵。

【0048】 在式(I)之另一個實施例中，R^1及R^2組合為=CR^6R^7；R^6及R^7皆為甲基。

【0049】 在式(I)之另一個實施例中，R^1及R^2組合為=CR^6R^7；R^6為甲基、乙基、丙基或丁基，其各自視情況經-OH或鹵基取代；R^7為H。

【0050】 在式(I)之另一個實施例中，R^1及R^2組合為=CR^6R^7；R^6為CF_3；R^7為H。

【0051】 在式(I)之另一個實施例中，R^1及R^2組合為=CR^6R^7；R^6為鹵基；R^7為H。

【0052】 在式(I)之另一個實施例中，R^1及R^2組合為=CR^6R^7；R^6為經0至1個R^{14}取代之苯基；R^7為H；R^{14}為鹵基、-OC_{1-4}烷基或苯基。

【0053】 在式(I)之另一個實施例中，R^1及R^2組合為=CR^6R^7；R^6為包含1至3個選自O及N之雜原子的5員雜環基；R^7為H。

【0054】 在式(I)之另一個實施例中，R^1及R^2組合為=CR^6R^7；R^6為C(=O)NH-苯基；R^7為H。

【0055】 在式(I)之另一個實施例中，R^1及R^2組合為=CR^6R^7；R^6為C(=O)OC_{1-4}烷基；R^7為H。

【0056】 在式(I)之另一個實施例中，R^1及R^2組合為=CR^6R^7；R^6為C(=O)$N(Me)_2$；R^7為H。

【0057】 在式(I)之另一個實施例中，R^1及R^2組合為=CR^6R^7；R^6為

C_{3-6}環烷基；R^7為H。

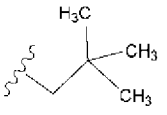
【0058】 在式(I)之另一個實施例中，R^1及R^2組合為=CR^6R^7；R^6為經鹵基取代之-CH_2-C_{3-6}環烷基；R^7為H。

【0059】 在式(I)之另一個實施例中，R^1及R^2組合為=CR^6R^7；R^6為環丙基；R^7為H。

【0060】 在式(I)之另一個實施例中，R^1及R^2組合為=CR^6R^7；R^6及R^7與該兩者所連接之碳原子形成環戊二烯基、二氫茚基或茚基。

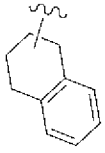
【0061】 在式(I)之一個實施例中，R^3為經0至2個R^4取代之C_{1-6}烷基。

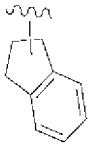
【0062】 在式(I)之另一個實施例中，R^3為甲基、乙基、丙基或丁基或戊基。

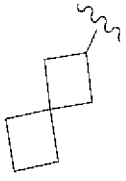
【0063】 在式(I)之另一個實施例中，R^3為 

。

【0064】 在式(I)之另一個實施例中，R^3為經0至2個R^4取代之C_{3-6}環烷基。

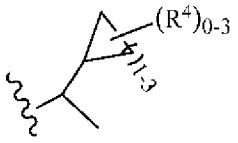
【0065】 在式(I)之另一個實施例中，R^3為經0至2個R^4取代之C_{3-6}環烯基。在式(I)之另一個實施例中，R^3為 
。

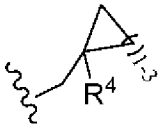
【0066】 在式(I)之另一個實施例中，R^3為 
。

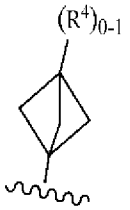
【0067】 在式(I)之另一個實施例中，R^3為 
。

【0068】 在式(I)之另一個實施例中，R^3為經0至2個R^4取代之-(CR^dR^d)$_{1-2}$-苯基；R^4為鹵基、CF_3或OCF_3；R^d為H或甲基。

【0069】 在式(I)之另一個實施例中，R^3為經0至2個R^4取代之-(CHR^d)-C_{3-6}環烷基；R^4為鹵基或C_{1-2}烷基；R_d為H或C_{1-2}烷基。

【0070】 在式(I)之另一個實施例中，R^3為  ；R^4為鹵基或C_{1-3}烷基。

【0071】 在式(I)之另一個實施例中，R^3為  ；R^4為C_{1-2}烷基。

【0072】 在式(I)之另一個實施例中，R^3為  ；R^4為鹵基或CN。

【0073】 在式(I)之另一個實施例中，R^3為包含1至2個選自O及N之雜原子之-$(CR^dR^d)_{1-2}$-5員雜環基；R^d為H或甲基。

【0074】 在式(I)之另一個實施例中，R^4為鹵基、CN、經0至3鹵基取代之C_{1-2}烷基。

【0075】 在式(I)之另一實施例中，R^3為環丙基、環丁基、經0至1個R^4取代之環戊基、或環己基；R^4為CN或C_{1-2}烷基。

【0076】 在式(I)之一個實施例中，R^5為H、鹵基或-OH。

【0077】 在式(I)之另一個實施例中，R^5為H或-OH。

【0078】 在式(I)之一個實施例中，R^6為經0至3個R^{6a}取代之C_{1-4}烷基或經0至3個R^{14}取代之C_{3-6}環烷基、或包含1至3個選自O、S、N及NR^{14a}之雜原子且經0至3個R^{14}取代之5員至6員雜環基；R^{6a}為鹵基、-OH或經0至3個鹵基取代基取代之C_{3-6}環烷基；R^{14}為鹵基或經0至3個鹵基取代基取代

之C_{1-3}烷基。

【0079】 在式(I)之另一個實施例中，R^6為經0至3個R^{14}取代之C_{3-6}環烷基；R^{14}為鹵基取代基。

【0080】 在式(I)之另一個實施例中，R^6為異丙基。

【0081】 在式(I)之一個實施例中，R^7為H或C_{1-2}烷基。

【0082】 在式(I)之一個實施例中，存在兩個R^8變數。一個R^8為-OC_{1-3}烷基。有時稱為R^{8a}之另一R^8為鹵基或CN。

【0083】 在式(I)之一個實施例中，R^9為經0至3個R^{10}及0至2個R^{11}取代之苯基。

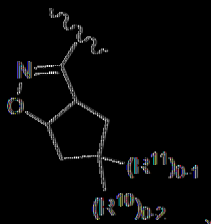
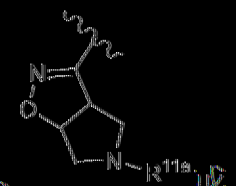
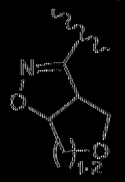
【0084】 在式(I)之另一實施例中，R^9為經0至3個R^{10}及0至2個R^{11}取代之苯基；R^{10}為鹵基；R^{11}為經0至4個R^{12}及0至2個R^{13}取代之C_{1-5}烷基；R^{12}為鹵基或C(=O)OH；R^{13}為-$OC(=O)NHR^a$；R^a為C_{1-4}烷基、C_{3-6}烷基或苯基。

【0085】 在式(I)之另一實施例中，R^9為經0至3個R^{10}及0至2個R^{11}取代之苯基；R^{10}為鹵基；R^{11}為經0至4個R^{12}及0至2個R^{13}取代之C_{1-5}烷基；R^{12}為鹵基或C(=O)OH；R^{13}為-$NHC(=O)R^b$；R^b為包含1至3個選自O、S及N之雜原子的3員至6員雜環基。

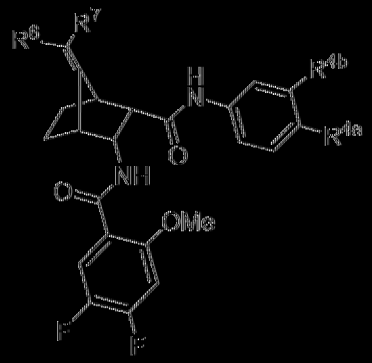
【0086】 在式(I)之另一個實施例中，R^9為經0至1個R^{10}及0至1個R^{11}取代之苯基；R^{10}為鹵基；R^{11}為包含1至4個選自O、$S(=O)_p$、N及NR^{15}之雜原子且經0至3個R^e取代之4員至9員雜環基；R^e為-COOH或經0至5個R^g取代之C_{1-3}烷基；R^g為-OH。

【0087】 在式(I)之一個實施例中，R^9為包含1至5個選自O、$S(=O)_p$、N及NR^{11a}之雜原子且經0至3個R^{10}及0至2個R^{11}取代之3員至12員

雜環基。

[0088] 在式(I)之另一個實施例中，R^9為  、  或  ；R^{10}為C_{1-2}烷基；R^{11}為經-OH取代基取代之C_{1-3}烷基，R^{11a}為經0至1個R^{11b}取代之-C(=O)C_{1-4}烷基；R^{11b}為-OH。

[0089] 在另一態樣中，本發明提供式(IIIa)化合物：



(IIIa)

或其醫藥學上可接受之鹽，其中：

R^{4a}為鹵基；

R^{4b}為經0至4個鹵基取代基取代之C_{1-4}烷基；

R^6為鹵基、經0至3個R^{6a}取代之C_{1-4}烷基、經0至1個苯基或-OH取代之C_{2-4}烯基、-C(=O)OR^b、C(=O)NR^aR^a、C_{3-6}環烷基、經0至3個R^{14}取代之C_{3-6}環烯基、經0至3個R^{14}取代之苯基、萘基、或包含1至3個選自O、S、N及NR^{14a}之雜原子且經0至3個R^{14}取代之5員至6員雜環基；

R^{6a}為鹵基、-OH、C_{3-6}環烷基或苯基；

R^7為H；

或R^6及R^7與該兩者所連接之碳原子一起形成環戊烯基、二氫茚基

或前述；

R^{14}為鹵基、CN、經0至3個鹵基取代基取代之C_{1-4}烷基、經0至3個鹵基取代基取代之$-OC_{1-4}$烷基、$-(CH_2)_{0-2}NR^aR^a$、經0至3個R^c取代之$-(CH_2)_{0-2}$芳基、經0至3個R^c取代之-O-芳基、或包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至3個R^c取代之$-(CH_2)_{0-2}$-3員至12員雜環基；

R^{14a}為H或C_{1-3}烷基；

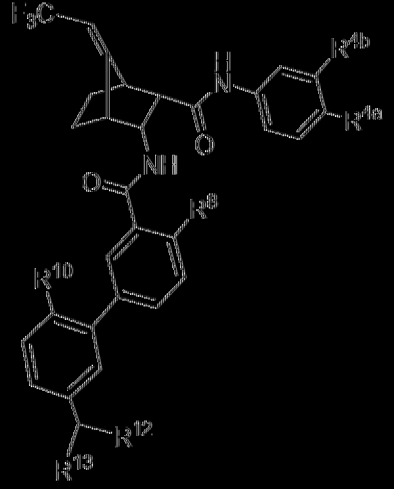
R^a為H或C_{1-3}烷基；

R^b為H或C_{1-3}烷基；及

p為0或2。

[0090] 在式(V)之一個實施例中，R^{4a}為F或CH_3；R^{4b}為CF_3；R^6為苯基或包含1至2個選自O及N之雜原子之5員雜芳基；R^7為H；R^8為$-OC_{1-2}$烷基；R^{10}為鹵基；R^{11}為$-NHS(=O)_2C_{1-2}$烷基、$-C(=O)OH$、$-C(=O)OC_{1-4}$烷基、經0至1個R^c取代之$-C(=O)NHC_{1-4}$烷基、或包含1至4個選自O、N及NR^{15}之雜原子且經0至3個R^c取代之5員雜環基；R^{15}為H、C_{1-2}烷基或苯基；且R^c為=O或$C(=O)OH$。

[0091] 在另一態樣中，本發明提供式(VIb)化合物：



(VIb)

或其醫藥學上可接受之鹽，其中：

R^{4a}為鹵基；

R^{4b}為CF_3；

R^8為-OC_{1-4}烷基；

R^{10}為鹵基；

R^{12}為-C(=O)OH、-C(=O)OC_{1-4}烷基、-C(=O)NHC_{1-4}烷基、-C(=O)$NHOC_{1-3}$烷基、或經0至3個鹵基取代之C_{1-3}烷基；

R^{13}為$-OR^b$、$-NR^aR^a$、$-NR^aC(=O)R^b$、$-NR^aC(=O)OR^b$、$-NR^aS(=O)_pR^c$、$-NR^aS(=O)_pNR^aR^a$、$-OC(=O)NR^aR^a$、$-OC(=O)NR^aOR^b$、$-S(=O)_pNR^aR^a$或$-S(=O)_pR^c$；

R^a為H、經0至5個鹵基取代基取代之C_{1-6}烷基、苯基、經0至4個R^e取代之C_{3-6}環烷基、螺環烷基、或經0至4個R^e取代之雜環基；或R^a及R^a與該兩者所連接之氮原子一起形成經0至4個R^e取代之雜環基；

R^b為H、經0至5個R^e取代之C_{1-6}烷基、$-(CH_2)_n$-苯基、經0至4個鹵基取代基取代之C_{3-6}環烷基、或包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至4個R^e取代之3員至9員雜環基；

R^c為經0至4個R^e取代之C_{1-6}烷基，

R^e為鹵基、CN、=O、經0至5個R^g取代之C_{1-5}烷基、C_{3-6}環烷基、芳基、4員至6員雜環基或$-OR^f$；

R^f為H、C_{1-6}烷基、C_{3-6}環烷基或芳基；

R^g為鹵基；

n為0或1；及

p為0、1或2。

【0092】在另一態樣中，本發明提供式(VII)化合物或其醫藥學上可

接受之鹽，其中：

R^{4a}為F；

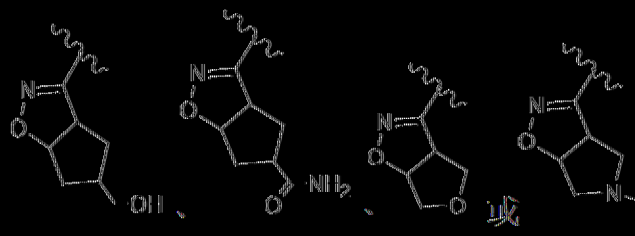
R^{4b}為CF_3；

R^5為H；

R^6為經0至3個F取代基取代之C_{1-3}烷基或C_{3-6}環烷基；

R^8為$-OCH_3$；

R^9為



；

R^{11a}為H、經0至2個R^{11b}取代之C_{1-3}烷基、經0至1個R^{11b}取代之$C(=O)C_{1-4}$烷基、或$C(=O)OC_{1-4}$烷基；及

R^{11b}為-OH、$-C(=O)OH$或芳基。

[0093] 除非另有指定，否則此等術語具有以下含義。

[0094] 「鹵基」包括氟、氯、溴及碘。

[0095] 「烷基」或「伸烷基」意欲包括具有指定數目個碳原子之分支鏈與直鏈飽和脂族烴基。舉例而言，「C_1至C_{10}烷基」或「C_{1-10}烷基」(或伸烷基)意欲包括C_1、C_2、C_3、C_4、C_5、C_6、C_7、C_8、C_9及C_{10}烷基。此外，例如「C_1至C_6烷基」或「C_1-C_6烷基」表示具有1至6個碳原子之烷基。烷基可未經取代或經取代，其中至少一個氫經另一化學基團置換。實例甲基包括(但不限於)甲基(Me)、乙基(Et)、丙基(例如正丙基及異丙基)、丁基(例如正丁基、異丁基、二級丁基)及戊基(例如正戊基、異戊基、新戊基)。當使用「C_0烷基」或「C_0伸烷基」時，其意欲表示直接

鍵。「烷基」亦包括氘代烷基，諸如CD_3。

【0096】「烯基」或「伸烯基」意欲包括具有一或多個、較佳一個至三個碳-碳雙鍵的直鏈或分支鏈組態的烴鏈，碳-碳雙鍵可存在於沿該鏈的任何穩定點處。舉例而言，「C_2至C_6烯基」或「C_{2-6}烯基」(或伸烯基)意欲包括C_2、C_3、C_4、C_5及C_6烯基；諸如乙烯基、丙烯基、丁烯基、戊烯基及己烯基。

【0097】「炔基」或「伸炔基」意欲包括具有一或多個、較佳一至三個碳-碳參鍵的直鏈或分支鏈組態的烴鏈，碳-碳參鍵可存在於沿該鏈的任何穩定點處。舉例而言，「C_2 至C_6炔基」或「C_{2-6}炔基」(或伸炔基)意欲包括C_2、C_3、C_4、C_5及C_6炔基；諸如乙炔基、丙炔基、丁炔基、戊炔基及己炔基。

【0098】「碳環」、「碳環基」或「碳環殘基」欲意謂任何穩定3員、4員、5員、6員、7員或8員單環或雙環，或7員、8員、9員、10員、11員、12員或13員雙環或三環烴環，其中任一者可為飽和、部分不飽和、不飽和或芳族的。此類碳環基之實例包括(但不限於)環丙基、環丁基、環丁烯基、環戊基、環戊烯基、環己基、環庚烯基、環庚基、金剛烷基、環辛基、環辛烯基、環辛二烯基、[3.3.0]二環辛烷、[4.3.0]二環壬烷、[4.4.0]二環癸烷(十氫萘)、[2.2.2]二環辛烷、茚基、苯基、萘基、二氫茚基、金剛烷基、蒽基及四氫萘基(四氫萘)。如上文所示，碳環基定義亦包括橋接環(例如[2.2.2]二環辛烷)。當一或多個碳原子連接兩個非相鄰碳原子時，產生橋接環。較佳橋為一或兩個碳原子。應注意，橋鍵始終將單環轉化成三環。當環橋接時，關於環敍述之取代基亦可存在於橋上。當使用術語「碳環基」時，其意欲包括「芳基」、「環烷基」、「螺環烷

基」、「環烯基」。除非另外指定，否則較佳碳環基為環丙基、環丁基、環戊基、環己基、苯基及二氫茚基。

【0099】「環烷基」意欲指環化烷基，包括單環、雙環或多環環系統。「C_3至C_7環烷基」或「C_{3-7}環烷基」意欲包括C_3、C_4、C_5、C_6及C_7環烷基。單環環烷基之非限制性實例包括環丙基、環丁基、環戊基、環己基、環庚基及環辛基。多環環烷基之非限制性實例包括1-十氫萘基、降冰片烷基及金剛烷基。

【0100】「環烯基」欲意謂環化烯基，包括在至少一個環中含有一或多個雙鍵之單環或多環環系統；但是若存在一個以上雙鍵，則雙鍵不能在所有環中形成完全非定域π電子系統(否則該基團將為如本文所定義之「芳基」)。「C_3至C_7環烯基」或「C_{3-7}環烯基」意欲包括C_3、C_4、C_5、C_6及C_7環烯基。

【0101】「螺環烷基」欲意謂兩個環經由單一原子連接之烴雙環系統。環在大小及性質方面可不同，或在大小及性質方面相同。實例包括螺戊烷、螺己烷、螺庚烷、螺辛烷、螺壬烷或螺癸烷。

【0102】「雙環碳環基(bicyclic carbocyclyl)」或「雙環碳環基(bicyclic carbocyclic group)」欲意謂含有兩個稠合環且由碳原子組成的穩定9員或10員碳環環系統。在兩個稠合環中，一個環為與第二環稠合之苯并環；且第二個環為5員或6員飽和、部分不飽和或不飽和碳環。雙環碳環基可在任何可產生穩定結構之碳原子處連接至其側基。若所得化合物穩定，則本文中所描述之雙環碳環基可在任何碳上經取代。雙環碳環基之實例係(但不限於)萘基、1,2-二氫萘基、1,2,3,4-四氫萘基及二氫茚基。

【0103】「芳基」係指單環或多環芳族烴，其包括例如苯基、萘基

及菲基。芳基部分為吾人所熟知且描述於例如Lewis, R.J.編, *Hawley's Condensed Chemical Dictionary*, 第13版，John Wiley & Sons, Inc., New York (1997)中。

【0104】「苯甲基」欲意謂其中一個氫原子經苯基置換的甲基，其中該苯基可視情況經1至5個基團，較佳1至3個基團取代。

【0105】「雜環(heterocycle)」、「雜環基(heterocyclyl)」或「雜環(heterocyclic ring)」欲意謂穩定3員、4員、5員、6員或7員單環或雙環、或7員、8員、9員、10員、11員、12員、13員或14員多環雜環，其為飽和、部分不飽和或完全不飽和的且含有碳原子及1個、2個、3個或4個獨立地選自由N、O及S組成之群的雜原子；且包括其中任一上文所定義之雜環與苯環稠合的任何多環基團。氮及硫雜原子可視情況經氧化(亦即，N→O及$S(O)_p$，其中p為0、1或2)。氮原子可經取代或未經取代(亦即N或NR，其中R為H或另一取代基(若定義))。雜環可在產生穩定結構之任何雜原子或碳原子處連接至其側基。若所得化合物穩定，則本文所描述之雜環可在碳原子或氮原子上經取代。雜環基中之氮可視情況經四級銨化。較佳的係，當雜環基中之S及O原子之總數超過1時，此等雜原子則彼此不相鄰。較佳的係，雜環基中之S及O原子之總數不超過1。雜環基之定義亦包括橋接環。當使用術語「雜環基」時，意欲包括「雜芳基」。

【0106】雜環基之實例包括(但不限於)吖啶基、氮雜環丁烷基、吖辛因基、苯并咪唑基、苯并呋喃基、苯并硫代呋喃基、苯并噻吩基、苯并噁唑基、苯并噁唑啉基、苯并噻唑基、苯并三唑基、苯并四唑基、苯并異噁唑基、苯并異噻唑基、苯并咪唑啉基、咔唑基、4a*H*-咔唑基、咔啉基、咭烷基、咭烯基、咝啉基、十氫喹啉基、2*H*,6*H*-1,5,2-二噻吩基、二

氫呋喃并[2,3-*b*]四氫呋喃、呋喃基、呋呫基、咪唑啶基、咪唑啉基、咪唑基、1*H*-吲唑基、咪唑并吡啶基、吲哚烯基、吲哚啉基、吲哚吩基、吲哚基、3*H*-吲哚基、靛紅醯基、異苯并呋喃基、異唍烷基、異吲唑基、異吲哚啉基、異吲哚基、異喹啉基、異噻唑基、異噻唑并吡啶基、異噁唑基、異噁唑并吡啶基、亞甲基二氧基苯基、味啉基、嗪啶基、八氫異喹啉基、噁二唑基、1,2,3-噁二唑基、1,2,4-噁二唑基、1,2,5-噁二唑基、1,3,4-噁二唑基、噁唑啶基、噁唑基、噁唑并吡啶基、噁唑啶基呸啶基、羥吲哚基、嘧啶基、啡啶基、啡啉基、啡吩基、啡噻唑基、啡噁吩基、呔吩基、哌吩基、哌啶基、哌啶酮基、4-哌啶酮基、向日葵基(piperonyl)、喋啶基、嘌呤基、哌喃基、吡吩基、吡唑啶基、吡唑啉基、吡唑并吡啶基、吡唑基、嗒吩基、吡啶并噁唑基、吡啶并咪唑基、吡啶并噻唑基、吡啶基、嘧啶基、吡咯啶基、吡咯啉基、2-吡咯啶酮基、2H-吡咯基、吡咯基、喹唑啉基、喹啉基、4H-喹吩基、喹喏啉基、喔啶基、四唑基、四氫呋喃基、四氫異喹啉基、四氫喹啉基、6*H*-1,2,5-噻二吩基、1,2,3-噻二唑基、1,2,4-噻二唑基、1,2,5-噻二唑基、1,3,4-噻二唑基、噻嗯基、噻唑基、噻吩基、噻唑并吡啶基、噻吩并噻唑基、噻吩并噁唑基、噻吩并咪唑基、噻吩基、三吩基、1,2,3-三唑基、1,2,4-三唑基、1,2,5-三唑基、1,3,4-三唑基及呫基。亦包括含有例如上述雜環基的稠環及螺合化合物。

【0107】「雙環雜環基(Bicyclic heterocyclyl)」、「雙環雜環基(bicyclic heterocyclyl)」或「雙環雜環基(bicyclic heterocyclic group)」欲意謂穩定的9員或10員雜環系統，其含有兩個稠環且由碳原子及1、2、3或4個獨立地選自由N、O及S組成之群的雜原子組成。在兩個稠合環

中，一個環為5員或6員單環芳環，其包含5員雜芳基環、6員雜芳基環或苯并環，各稠合至第二環。第二環為5員或6員單環，其為飽和、部分不飽和或不飽和的且包含5員雜環基、6員雜環基或碳環基(限制條件為若第二環為碳環基，則第一環不為苯并環)。

【0108】 雙環雜環基可在產生穩定結構之任何雜原子或碳原子處連接至其側基。若所得化合物穩定，則本文中所描述之雙環雜環基可在碳原子或氮原子上經取代。較佳的係，當雜環基中之S及O原子之總數超過1時，此等雜原子則彼此不相鄰。較佳的係，雜環基中之S及O原子之總數不超過1。

【0109】 雙環雜環基之實例係(但不限於)喹啉基、異喹啉基、呔啡基、喹唑啉基、吲哚基、異吲哚基、吲哚啉基、1H-吲唑基、苯并咪唑基、1,2,3,4-四氫喹啉基、1,2,3,4-四氫異喹啉基、5,6,7,8-四氫喹啉基、2,3-二氫苯并呋喃基、唍烷基、1,2,3,4-四氫喹喏啉基及1,2,3,4-四氫喹唑啉基。

【0110】 「雜芳基」欲意謂穩定的單環及多環芳族烴，其包括至少一個雜原子環成員，諸如硫、氧或氮。雜芳基包括(但不限於)吡啶基、嘧啶基、吡啡基、嗒啡基、三啡基、呋喃基、喹啉基、異喹啉基、噻吩基、咪唑基、噻唑基、吲哚基、吡咯基、噁唑基、苯并呋喃基、苯并噻吩基、苯并噻唑基、異噁唑基、吡唑基、三唑基、四唑基、吲唑基、1,2,4-噻二唑基、異噻唑基、嘌呤基、咔唑基、苯并咪唑基、吲哚啉基、苯并二氧戊環基及苯并二噁烷。雜芳基經取代或未經取代。氮原子經取代或未經取代(亦即N或NR，其中R為H或另一取代基(若定義))。氮及硫雜原子可視情況經氧化(亦即，N→O及$S(O)_p$，其中p為0、1或2)。

【0111】 如本文中所提及，術語「經取代」意謂至少一個氫原子置換為非氫基團，其限制條件為維持正常價數且取代產生穩定化合物。當取代基為酮基(亦即=O)時，則原子上之2個氫經置換。酮基取代基不存在於芳族部分上。當環系統(例如碳環或雜環)據稱經羰基或雙鍵取代時，該羰基或雙鍵意欲為該環之一部分(亦即在該環內)。如本文所用之環雙鍵為在兩個相鄰環原子之間所形成的雙鍵(例如，C=C、C=N或N=N)。

【0112】 在本發明化合物上存在氮原子(例如胺)的情況下，此等氮原子可藉由用氧化劑(例如mCPBA及/或過氧化氫)處理而轉化成N-氧化物，得到其他本發明化合物。因此，所展示及所主張之氮原子視為涵蓋所展示之氮及其N-氧化物(N→O)衍生物。

【0113】 當任何變數在化合物之任何組分或式中出現一次以上時，其在每次出現時的定義獨立於其在其他每次出現時的定義。因此，例如，若基團經展示經0至3個R基團取代，則該基團可視情況經至多3個R基團取代，且R在每次出現時獨立地選自R之定義。此外，取代基及/或變數之組合僅當此等組合產生穩定化合物時為容許的。

【0114】 若連至取代基之一鍵顯示與連接環中之兩個原子的一鍵交叉，則此類取代基可鍵結至該環上的任何原子。若所列取代基未指示此取代基鍵結至指定式之化合物的其餘部分的原子，則此取代基可經此取代基中的任何原子鍵結。取代基及/或變數之組合僅在此類組合產生穩定化合物時為容許的。

【0115】 本發明包括化合物之所有醫藥學上可接受之鹽形式。醫藥學上可接受之鹽為相對離子不顯著促成化合物之生理學活性或毒性且本身用作藥理學等效物的鹽。此等鹽可根據常見有機技術、採用市售試劑製

得。一些陰離子鹽形式包括乙酸鹽、醋硬脂酸鹽、苯磺酸鹽、溴化物、氯化物、檸檬酸鹽、反丁烯二酸鹽、葡萄糖醛酸鹽、氫溴酸鹽、鹽酸鹽、氫碘酸鹽、碘化物、乳酸鹽、順丁烯二酸鹽、甲磺酸鹽、硝酸鹽、雙羥萘酸鹽、磷酸鹽、丁二酸鹽、硫酸鹽、酒石酸鹽、甲苯磺酸鹽及羥萘甲酸鹽。一些陽離子鹽形式包括銨、鋁、苄星青黴素(benzathine)、鉍、鈣、膽鹼、二乙胺、二乙醇胺、鋰、鎂、葡甲胺、4-苯基環已胺、哌啡、鉀、鈉、緩血酸胺及鋅。

【0116】 在整個說明書及隨附申請專利範圍中，既定化學式或名稱應涵蓋其所有立體異構物及光學異構物及外消旋物(若此等異構物存在)。除非另外指明，否則所有對掌性(鏡像異構物及非鏡像異構物)及外消旋形式屬於本發明之範疇內。鏡像異構物及非鏡像異構物為立體異構物之實例。術語「鏡像異構物」係指彼此互為鏡像且不可重疊之分子物種對之一。術語「非鏡像異構物」係指不為鏡像之立體異構物。術語「外消旋物」或「外消旋混合物」係指由等莫耳量之兩種鏡像異構物物質構成的組合物，其中該組合物缺乏光學活性。

【0117】 本發明包括化合物、滯轉異構物及旋轉異構物之所有互變異構形式。

【0118】 術語「相對離子」用於表示帶負電之物質，諸如氯離子、溴離子、氫氧根、乙酸根及硫酸根。

【0119】 用於製備本發明化合物之所有方法及其中製備的中間物視為本發明之一部分。

【0120】 符號「R」及「S」代表對掌性碳原子周圍之取代基的組態。異構物描述詞「R」及「S」如本文所述用於表明相對於核心分子之

原子組態且意欲如文獻(IUPAC Recommendations 1996, *Pure and Applied Chemistry*, 68:2193-2222 (1996))中所定義般使用。

【0121】 術語「對掌性」係指分子之使其不可能疊印於其鏡像上的結構特徵。術語「同對掌性」係指鏡像異構純度之狀態。術語「光學活性」係指同對掌性分子或對掌性分子之非外消旋混合物使偏振光平面旋轉的程度。

【0122】 本發明意欲包括存在於化合物中之原子的所有同位素。同位素包括具有相同原子數但質量數不同之彼等原子。作為一般實例且非限制性地，氫之同位素包括氘及氚。碳之同位素包括^{13}C及^{14}C。本發明之同位素標記化合物一般可藉由熟習此項技術者已知之習知技術或藉由類似於本文所述之方法，使用經適當同位素標記之試劑代替原來使用之未經標記之試劑來製備。此類化合物可具有多種潛在用途，例如在測定生物活性時用作標準物及試劑。在穩定同位素之情況下，此類化合物可具有有利地調節生物學、藥理學或藥物動力學特性之潛能。

生物方法

【0123】 RXFP1環單磷酸腺苷(cAMP)分析。將人類胚胎腎細胞293(HEK293)細胞及穩定表現人類RXFP1之HEK293細胞在補充有10%合格FBS及300 μg/ml潮黴素(Life Technologies)之MEM培養基中培養。將細胞解離且懸浮於分析緩衝液中。分析緩衝液為含有20 mM HEPES、0.05% BSA及0.5 mM IBMX之HBSS緩衝液(具有鈣及鎂)。將細胞(每孔3000個細胞，除穩定表現人類RXFP1之HEK293細胞的每孔1500個細胞外)添加至384孔Proxiplates (Perkin-Elmer)中。將細胞立即用DMSO (最終2%)中之測試化合物以0.010 nM至50 μ M範圍內之最終濃度處理。將細

胞在室溫下培育30 min。根據製造商說明書使用HTRF HiRange cAMP分析試劑套組(Cisbio)測定細胞內cAMP之含量。分別在所供應裂解緩衝液中製備穴狀化合物結合之抗cAMP及d2螢光團標記之cAMP之溶液。反應完成後，用等體積的d2-cAMP溶液及抗cAMP溶液裂解細胞。在1 h室溫培育後，使用Envision (Perkin-Elmer)在400 nm激發及590 nm及665 nm之雙重發射下來量測時差式螢光強度。藉由繪製665 nm發射之螢光強度與590 nm發射之強度對照cAMP濃度之比率，以2.7 μM至0.1 pM之濃度範圍下之外部cAMP標準建構校準曲線。隨後藉由根據cAMP含量對化合物濃度之繪圖擬合4參數邏輯方程式來測定化合物抑制cAMP產生之效力及活性。

【0124】 在上文所描述之人類RXFP1 (hRXFP1) HEK293 cAMP分析中測試下文所揭示之實例，且發現其具有促效活性。表1列出針對實例量測之hRXFP1 HEK293 cAMP分析中之EC_{50}值。

表1

實例	cAMP hRXFP1 HEK293 分析 EC_{50} (nM)
5	2,200
6	140
7	270
8	110
9	310
10	1,100
11	230
12	410
13	1,100
14	220
15	110
16	770
17	120
18	630
19	720
20	940
21	55
22	700

實例	cAMP hRXFP1 HEK293 分析 EC_{50} (nM)
23	1,400
24	94
25	200
26	77
27	380
28	400
29	110
30	55
33	310
34	4,600
35	30
36	19
37	15
38	360
39	88
40	20
41	27
42	130
43	70
44	26
45	59
46	120
47	47
48	220
49	200
50	150
51	790
52	3,000
53	240
54	160
55	230
56	270
57	550
58	1,100
59	890
60	920
61	570
62	710
63	510
64	520
65	2,000
66	1,700
67	1,700
68	3,200
69	3,700
70	2,900
71	350

實例	cAMP hRXFP1 HEK293 分析 EC_{50} (nM)
72	250
73	2,400
74	3,800
75	2,600
76	400
77	330
78	1,900
79	11
80	11
81	39
82	41
83	66
84	110
85	130
86	150
87	160
88	190
89	330
90	330
91	360
92	380
93	390
94	400
95	420
96	460
97	490
98	510
99	540
100	560
101	580
102	590
103	910
104	1,600
105	1,200
106	2,700
107	180
108	330
109	390
110	800
111	860
113	1,800
114	1,100
115	1,100
119	3,900
120	7
121	16
122	13

實例	cAMP hRXFP1 HEK293 分析 EC_{50} (nM)
123	210
124	210
125	240
126	23
127	49
128	55
129	60
130	440
131	130
132	220
133	1,700
134	1,400
135	370
136	270
137	480
138	370
139	550
140	700
141	720
142	2,900
143	2,800
144	2,100
145	1,300
146	2,200
147	1,800
148	910
149	4,500
150	190
151	240
152	8
153	140
154	33
155	87
156	11
157	610
158	100
159	21
160	26
161	110
162	40
163	13
164	14
165	40
166	11
167	16
168	11
169	44

實例	cAMP hRXFP1 HEK293 分析 EC_{50} (nM)
170	59
171	5
172	5
173	7
174	8
175	17
176	57
177	5
178	11
179	5
180	5
181	6
182	5
183	5
184	11
185	15
186	25
187	19
188	20
189	10
190	74
191	42
192	135
193	300
194	5
195	29
196	45
197	51
198	76
199	128
200	37
201	76
202	180
203	322
204	3,200
205	1
206	1
207	1
208	1
209	1
210	1
211	1
212	1
213	2
214	2
215	2
216	2

實例	cAMP hRXFP1 HEK293 分析 EC_{50} (nM)
217	2
218	2
219	3
220	8
221	26
222	1
223	2
224	2
225	3
226	3
227	3
228	3
229	7
230	1
231	1
232	1
233	2
234	1
235	1
236	3
237	2
238	1
239	1
240	1
241	3
242	3
243	4
244	7
245	3
246	9
247	73
248	4
249	5
250	12
251	36
252	11
253	17
254	71
255	3
256	14
257	16
258	283
259	815
260	2,972
261	1,883
262	139
263	294

實例	cAMP hRXFP1 HEK293 分析 EC_{50} (nM)
264	3,183
265	5
266	3,947
267	505
268	15
269	370
270	25
271	664
272	3,826
274	16
275	25
276	72
277	12
278	32
279	15
280	12
281	15
282	25
283	69
284	109
285	7
286	5
287	7
288	127
289	548
290	20
291	506
292	1,858
293	32
294	47
295	53
296	205
297	73
298	70
299	227
300	575
301	850
302	889
303	1,697
304	1,713
305	1,384
306	540
307	958
308	2,391
309	4,380
310	162
311	38

實例	cAMP hRXFP1 HEK293 分析 EC_{50} (nM)
312	9
313	90
314	5
315	60
316	81
317	31
318	11
319	13
320	1,949
321	91
322	1,088
323	854
324	2,244
325	4,835
326	2,270
327	2,039
328	673
329	4,810
330	369
331	601
331	534
333	1,362
334	1,371
335	3,561
336	1,933
337	2,075
338	750
339	67
340	62
341	1,175
342	390
343	707
344	757
345	1,405
346	169
347	62
348	1,307
349	2,792
350	2,521
351	2,871
352	64
353	11
354	11
355	3
356	5
357	211
358	18

實例	cAMP hRXFP1 HEK293 分析 EC_{50} (nM)
359	2
360	1,944
361	747
362	807
363	254
364	2,231
365	234
366	1,663
367	267
368	639
369	65
370	788
371	338
372	12
373	9
374	59
375	213
376	662
377	1,042
378	16
379	26
380	23
381	20
382	118
383	127
384	123
385	8
386	71
387	11
388	152
389	54
390	37
391	49
392	50
393	73
394	49
395	104
396	320
397	912
398	37
399	42
400	31
401	786
402	70
403	1,394
404	45
406	48

實例	cAMP hRXFP1 HEK293 分析 EC_{50} (nM)
407	21
408	3
409	9
410	168
411	435
412	85
413	39
414	364
415	1,200
416	1
417	172
418	170
419	17
420	1
421	831
422	55
423	28
424	11
425	19
426	45
427	54
428	6
429	2
430	194
431	250
432	2
433	2
434	24
435	49
436	4
437	31
438	24
439	30
440	25
441	360
442	25
443	5
444	410
445	0.5
446	0.6
447	0.8
448	1.2
449	1.6
450	1.6
452	1.8
453	1.9
454	1.9

實例	cAMP hRXFP1 HEK293 分析 EC_{50} (nM)
455	2.0
457	2.1
458	2.2
459	2.5
460	2.5
461	2.6
462	3.0
463	3.1
464	3.2
465	3.5
466	3.9
467	4.0
469	4.3
471	4.5
472	4.7
473	4.9
474	5.0
475	5.6
476	6.1
477	6.4
478	6.5
480	6.7
481	6.7
482	6.8
483	7.3
484	7.4
485	7.8
486	7.8
488	8.2
489	8.5
491	8.7
493	9.5
494	10.4
495	10.5
496	10.5
497	10.6
499	11.0
500	11.0
501	11.6
502	11.9
504	12.1
505	12.1
506	12.7
507	12.9
508	13.0
509	15.2
510	15.2

實例	cAMP hRXFP1 HEK293 分析 EC_{50} (nM)
511	15.3
512	15.7
513	16.5
514	17.2
515	17.2
516	17.6
517	18.0
518	18.4
520	19.3
521	19.5
522	21.1
523	21.3
524	21.9
526	22.4
527	22.4
528	22.4
530	22.7
531	22.7
532	22.9
533	23.4
534	23.9
535	24.0
536	24.7
537	26.0
538	26.3
539	29.3
540	29.4
541	30.0
543	30.5
545	31.5
546	32.1
548	32.6
549	33.0
550	34.9
551	36.6
552	36.7
553	37.4
554	37.6
555	41.4
556	41.7
558	44.3
559	44.9
560	45.3
564	47.3
565	50.7
566	56.3
567	58.1

實例	cAMP hRXFP1 HEK293 分析 EC_{50} (nM)
568	59.4
570	62.7
571	65.3
572	66.4
573	67.4
574	67.8
575	68.8
576	69.2
577	70.7
578	70.8
579	71.6
580	72.8
582	74.9
583	74.9
584	77.3
585	78.3
586	79.1
587	80.8
588	82.0
589	83.5
590	86.1
591	86.6
592	87.1
593	89.8
594	91.4
595	92.7
596	101.9
597	101.9
598	102.0
599	104.2
600	106.3
601	108.0
602	110.0
603	111.7
605	118.3
606	120.7
607	128.4
609	130.4
610	132.2
611	132.7
612	133.7
613	137.1
614	138.3
615	139.2
616	141.4
617	153.0
618	154.7

實例	cAMP hRXFP1 HEK293 分析 EC_{50} (nM)
619	156.4
620	163.0
621	163.9
622	167.7
623	168.7
624	168.7
626	171.3
627	175.6
628	177.0
629	179.5
630	185.1
631	185.3
632	190.1
633	190.4
634	190.7
635	191.0
636	195.8
637	206.1
638	207.2
639	212.2
640	213.7
641	216.6
642	219.0
644	238.4
645	239.1
646	240.4
647	241.4
648	241.9
649	250.4
650	261.6
651	269.4
652	277.9
653	285.3
654	299.5
655	303.2
656	311.4
657	312.0
658	314.1
659	347.3
660	349.9
661	359.1
662	359.9
664	367.2
665	372.6
666	373.2
667	384.1
669	416.4

實例	cAMP hRXFP1 HEK293 分析 EC_{50} (nM)
670	447.6
671	450.8
672	454.9
673	476.6
674	481.0
675	485.2
676	485.8
677	500.5
678	507.4
679	562.7
680	581.6
681	605.7
682	612.2
683	626.1
684	642.1
685	644.8
686	653.2
687	658.0
688	675.0
689	683.6
690	711.6
691	734.7
692	789.0
693	791.4
694	796.3
695	836.1
696	965.8
697	972.0
698	1,007
699	1,026
700	1,046
701	1,086
702	1,150
703	1,194
704	1,298
705	1,302
706	1,305
707	1,333
708	1,357
710	1,470
711	1,561
712	1,599
713	1,673
714	1,745
715	1,960
716	1,982
717	2,319

實例	cAMP hRXFP1 HEK293 分析 EC_{50} (nM)
718	2,347
719	2,491
720	3,139
721	3,907
722	4,181
723	4,984
724	4,995
725	360
726	417
727	381
728	41
729	82
730	263
731	10
732	99
733	6.3
734	23
735	1.3
736	2.4
737	3.2
738	3.3
739	3.4
740	3.4
741	1.7
742	4.7
743	5.0
744	2.5
745	1.2
748	3.3
749	3.3
750	3.5
751	2.2
752	2.5
753	3.3
754	3.6
755	5.0
756	0.4
757	0.9
758	0.9
759	1.0
760	1.2
761	1.9
762	2.0
763	2.1
764	2.3
765	2.5
766	2.7

實例	cAMP hRXFP1 HEK293 分析 EC_{50} (nM)
767	3.0
768	3.0
769	3.3
770	3.6
771	3.8
772	3.8
773	3.9
774	4.1
775	4.4
776	5.0
777	13.9
778	1.1
779	1.6
780	1.8
781	2.7
782	3.2
783	3.4
784	3.4
785	4.0
786	4.0
787	4.2
788	4.3
789	4.4
790	4.9
791	0.8
792	1.4
793	2.2
794	3.2
795	3.5
796	3.7
797	4.1
798	4.7
799	4.7
800	1.0
801	2.0
802	3.0
803	3.5
804	4.0
805	4.1
806	4.9
807	2.1
808	4.2
809	4.6
810	4.7
811	0.6
812	0.8
813	1.0

實例	cAMP hRXFP1 HEK293 分析 EC_{50} (nM)
814	1.2
815	1.5
816	1.6
817	1.9
818	2.2
819	2.3
820	2.4
821	2.5
822	2.5
823	2.6
824	2.9
825	2.9
826	3.0
827	3.1
828	3.3
829	3.4
830	3.4
831	3.5
832	3.6
833	3.7
834	3.8
835	3.9
836	4.1
837	4.3
838	4.4
839	4.4
840	4.5
841	4.7
842	4.9
843	0.9
844	1.2
845	1.3
846	1.8
847	2.5
848	2.5
849	2.7
850	2.7
851	2.8
852	3.1
853	3.6
854	3.9
855	4.5
856	4.7
857	5.0
858	1.3
859	1.8
862	3.4

實例	cAMP hRXFP1 HEK293 分析 EC_{50} (nM)
864	3.8
866	4.8
867	3.7
868	3.8
869	1.4
870	2.2
871	4.8
872	8.0
873	3.3
875	1.8
876	0.9
878	5.1
879	0.9
880	1.6
881	3.1
883	2.5
884	1.0
886	2.7
887	5.5
888	2.7
889	8.5
890	2.4
891	3.7
892	9.9
893	2.2
894	1.3
895	0.2
896	8.2
897	1.0
898	3.9
899	3.0
901	4.5
902	8.7
905	7.0
906	6.8
907	0.1
908	3.5
909	4.0
910	3.4
911	7.6
913	9.0
914	7.8
915	4.0
916	3.6
917	1.3
918	5.5
919	3.6

實例	cAMP hRXFP1 HEK293 分析 EC_{50} (nM)
920	2.4
921	8.2
922	2.2
923	4.7
924	5.7
925	5.2
926	2.8
927	0.4
928	1.4
929	1.6
930	1.1
931	2.5
932	3.9
933	0.9
934	1.4
935	2.5
936	1.4
937	5.8
938	1.7
939	0.6
940	4.1
941	1.2
942	1.3
943	1.7
944	1.9
945	5.4
946	0.9
947	8.6
948	8.6
949	3.6
950	4.9
951	1.0
952	1.5
953	7.0
954	5.3
955	0.1
956	6.1
957	5.3
958	0.9
959	6.1
960	0.4
961	1.0
962	3.1
963	2.9
964	6.2
965	4.8
966	6.9

實例	cAMP hRXFP1 HEK293 分析 EC_{50} (nM)
967	2.1
969	3.6
970	2.0
971	2.8
972	1.9
973	5.8
974	4.5
975	1,000
976	710

醫藥組合物及使用方法

【0125】 式(I)化合物為RXFP1受體促效劑，且可用於治療醫學適應症，諸如心臟衰竭、纖維變性疾病及相關疾病，諸如肺病(例如特發性肺纖維化)、腎病(例如慢性腎病)或肝病(例如非酒精性脂肪變性肝炎及門靜脈高血壓)。

【0126】 本發明之另一態樣為一種醫藥組合物，其包含式(I)化合物及醫藥學上可接受之載劑。

【0127】 本發明之另一態樣為一種醫藥組合物，其包含用於治療鬆弛素相關病症之式(I)化合物及醫藥學上可接受之載劑。

【0128】 本發明之另一態樣係一種治療與鬆弛素相關之疾病的方法，其包含投與有效量之式(I)化合物。

【0129】 本發明之另一態樣為一種治療心血管疾病之方法，其包含向有需要之患者投與有效量之式(I)化合物。

【0130】 本發明之另一態樣為一種治療心臟衰竭之方法，其包含向有需要之患者投與有效量之式(I)化合物。

【0131】 本發明之另一態樣為一種治療纖維化之方法，其包含向有需要之患者投與治療有效量之式(I)化合物。

【0132】 本發明之另一態樣為一種治療與纖維化相關之疾病的方

法，其包含向有需要之患者投與治療有效量之式(I)化合物。

【0133】 本發明之另一態樣為一種治療特發性肺纖維化的方法，其包含向有需要之患者投與治療有效量之式(I)化合物。

【0134】 本發明之另一態樣為一種治療腎病(例如慢性腎病)之方法，其包含向有需要之患者投與治療有效量之式(I)化合物。

【0135】 本發明之另一態樣為一種治療或預防腎衰竭之方法，其包含向有需要之患者投與治療有效量之式(I)化合物。

【0136】 本發明之另一態樣為一種改善、穩定或恢復有需要之患者之腎功能的方法，其包含向該患者投與治療有效量之式(I)化合物。

【0137】 本發明之另一態樣為一種治療特發性肺纖維化的方法，其包含向有需要之患者投與治療有效量之式(I)化合物。

【0138】 本發明之另一態樣為一種治療腎病(例如慢性腎病)之方法，其包含向有需要之患者投與治療有效量之式(I)化合物。

【0139】 除非另有指定，否則以下術語具有所陳述之含義。

【0140】 如本領域中之從業者所理解，術語「患者」或「個體」係指可能受益於使用RXFP1促效劑之治療的任何人類或非人類有機體。例示性個體包括任何年齡的具有心血管疾病風險因素的人類。常見風險因素包括(但不限於)年齡、性別、體重、家族病史、睡眠呼吸暫停、酒精或煙草使用、缺乏運動性心律不整或胰島素抗性之徵象，諸如黑棘皮病(acanthosis nigricans)、高血壓、血脂異常或多囊性卵巢症候群(PCOS)。

【0141】 「治療(treating)」或「治療(treatment)」涵蓋治療如此領域之從業者所瞭解之疾病病況，且包括以下：(a)抑制疾病病況，亦即遏制其發展；(b)緩解疾病病況，亦即使得疾病病況消退；及/或(c)預防在哺

乳動物中出現疾病病況，尤其在此類哺乳動物易感染疾病病況但尚未診斷為患有該疾病病況時如此。

【0142】如本領域中之從業者所瞭解，「預防(preventing/prevention)」涵蓋預防性治療(亦即防治及/或風險降低)亞臨床疾病病況，旨在降低出現臨床疾病病況之機率。基於已知相較於一般群體增加罹患臨床疾病病況之風險的因素而選擇用於預防性療法之患者。「防治」療法可分成(a)初級預防及(b)次級預防。初級預防定義為在尚未呈現臨床疾病病況之個體中治療，而次級預防定義為預防第二次出現相同或類似臨床疾病病況。「風險降低(risk reduction)」或「降低風險(reducing risk)」涵蓋降低臨床疾病病況發展之發生率的療法。因而，初級及次級預防療法為風險降低之實例。

【0143】如本領域中之從業者所瞭解，「治療有效量」意欲包括當單獨或與其他藥劑組合投與時有效治療病症的本發明化合物之量。在應用於組合時，該術語係指無論組合、依序或是同時投與，均產生預防或治療效果的活性成分之組合量。

【0144】「心血管系統病症」或「心血管病症」包括例如以下病症：高血壓(hypertension) (高血壓(high blood pressure))、周邊及心血管病症、冠心病、穩定型及不穩定型心絞痛、心臟病發作、心肌功能不全、異常心律(或心律不整)、持續缺血性功能障礙(「冬眠心肌(hibernating myocardium)」)、暫時缺血後功能障礙(「頓抑心肌(stunned myocardium)」)、心臟衰竭、末梢血流紊亂、急性冠狀動脈症候群、心臟衰竭、心肌疾病(心肌病(cardiomyopathy))、心肌梗塞及血管疾病(vascular disease) (血管疾病(blood vessel disease))。

【0145】「心臟衰竭」包括心臟衰竭之急性及慢性表現，以及更具體或相關類型之疾病，諸如晚期心臟衰竭、急性期後心臟衰竭、心腎症候群、心臟衰竭伴腎功能受損、慢性心臟衰竭、射出分率中程型慢性心臟衰竭(HFmEF)、代償型心臟衰竭、代償不全型心臟衰竭、右心衰竭、左心衰竭、全身衰竭、缺血性心肌症、擴張型心肌症、與先天性心臟缺損相關之心臟衰竭、心臟瓣膜缺損、與心臟瓣膜缺損相關之心臟衰竭、二尖瓣狹窄、二尖瓣閉鎖不全、主動脈瓣狹窄、主動脈瓣閉鎖不全、三尖瓣狹窄、三尖瓣閉鎖不全、肺狹窄、肺瓣膜閉鎖不全、與合併心臟瓣膜缺損相關之心臟衰竭、心肌發炎(心肌炎)、慢性心肌炎、急性心肌炎、病毒性心肌炎、糖尿病性心臟衰竭、酒精性心肌病、與心臟儲積病症相關之心臟衰竭、舒張性心臟衰竭、收縮性心臟衰竭、急性心臟衰竭惡化期、射出分率正常型心臟衰竭(HFpEF)、射出分率降低型心臟衰竭(HFrEF)、慢性射出分率降低型心臟衰竭(HFrEF)、長期射出分率正常型心臟衰竭(HFpEF)、心肌梗死後重塑(post myocardial remodeling)、心絞痛、高血壓、肺高血壓及肺動脈高血壓。

【0146】「纖維變性病症」涵蓋特徵為纖維化之疾病及病症，尤其包括以下疾病及病症：肝纖維化、肝硬化、NASH、肺纖維化(pulmonary fibrosis)或肺部纖維化(lung fibrosis)、心臟纖維化、心內膜心肌纖維化、腎病、絲球體腎炎、間質性腎纖維化、由糖尿病引起之纖維變性損傷、骨髓纖維化及類似纖維變性病症、硬皮病、硬斑病、瘢痕瘤、肥大性瘢痕形成(亦在手術操作後)、痣、糖尿病性視網膜病變、增生性玻璃體視網膜病變及結締組織病症(例如類肉瘤病)。

【0147】鬆弛素相關病症包括(但不限於)心血管系統病症及纖維變

性病症。

【0148】 本發明化合物可藉由任何適合之手段投與，例如經口，諸如錠劑、膠囊(其各自包括持續釋放或定時釋放調配物)、丸劑、散劑、顆粒劑、酏劑、酊劑、懸浮液(包括奈米懸浮液、微懸浮液、噴霧乾燥分散液)、糖漿及乳液；舌下；經頰；非經腸，諸如藉由皮下、靜脈內、肌肉內或胸骨內注射，或輸注技術(例如作為無菌可注射水溶液或非水溶液或懸浮液)；經鼻，包括向鼻膜投與，諸如藉由吸入噴霧投與；表面，諸如以乳霜或軟膏形式；或經直腸，諸如以栓劑形式投與。其可單獨投與，但一般將與基於所選投與途徑及標準醫藥實踐而選擇之醫藥載劑一起投與。

【0149】 「醫藥組合物」意謂包含本發明化合物與至少一種其他醫藥學上可接受之載劑之組合的組合物。「醫藥學上可接受之載劑」係指此項技術中一般接受用於向動物(尤其哺乳動物)遞送生物活性劑之介質，視投與模式之性質及劑型而定，包括(亦即)佐劑、賦形劑或媒劑，諸如稀釋劑、防腐劑、填充劑、流動調節劑、崩解劑、濕潤劑、乳化劑、懸浮劑、甜味劑、調味劑、芳香劑、抗細菌劑、抗真菌劑、潤滑劑及分散劑。

【0150】 醫藥學上可接受之載劑根據一般熟習此項技術者見識內的許多因素來調配。此等因素包括但不限於：所調配之活性劑的類型及性質；要投與含該藥劑之組合物的個體；組合物之預期投與途徑；以及所靶向之治療適應症。醫藥學上可接受之載劑包括水性及非水性液體介質，以及各種固體及半固體劑型。此類載劑可包括除活性劑之外的許多不同成分及添加劑，此類其他成分出於一般熟習此項技術者熟知的多種原因包括於調配物中，例如穩定活性劑、黏合劑等。對於適合的醫藥學上可接受之載劑及其選擇所設計之因素之描述見於多種容易獲得之來源，諸如Allen,

L.V., Jr.等人, *Remington: The Science and Practice of Pharmacy* (2卷), 第22版, Pharmaceutical Press (2012)。

【0151】 本發明化合物之給藥方案當然將視已知因素而變化，諸如特定藥劑之藥效學特徵及其投與模式及途徑；接受者之物種、年齡、性別、健康狀況、醫學條件及體重；症狀之性質及程度；同時發生之治療的種類；治療頻率；投與途徑；患者之腎功能及肝功能；以及所需作用。

【0152】 藉助於一般導引，各活性成分在用於指定作用時的每日口服劑量將在每天約0.01至約5000 mg之間，較佳每天約0.1至約1000 mg之間，且最佳每天約0.1至約250 mg之間的範圍內。靜脈內投與時，在恆定速率輸注期間最佳劑量將在每分鐘約0.01至約10 mg/kg之範圍內。本發明化合物可以單次日劑量形式投與，或每日總劑量可分成每日兩次、三次或四次分次劑量投與。

【0153】 化合物通常以與針對預期投與形式(例如口服錠劑、膠囊、酏劑及糖漿)適當選擇且與習知醫藥實踐相符的適合醫藥稀釋劑、賦形劑或載劑(在本文中統稱為醫藥載劑)之混雜物形式投與。

【0154】 適合於投與之劑型(醫藥組合物)可含有每劑量單位約1毫克至約2000毫克之活性成分。在此等醫藥組合物中，活性成分通常將以按該組合物之總重量計約0.1-95重量%之量存在。用於經口投與之典型膠囊含有本發明化合物中之至少一者(250 mg)、乳糖(75 mg)及硬脂酸鎂(15 mg)。混合物通過60目篩且裝入1號明膠膠囊中。藉由將本發明化合物中之至少一者(250 mg)以無菌方式放入小瓶中、以無菌方式冷凍乾燥及密封來製造典型可注射製劑。對於使用，將小瓶之內含物與2 mL生理食鹽水混合產生可注射製劑。

【0155】 化合物可與適用於治療疾病或病症之其他適合治療劑組合使用，該等治療劑包括：抗動脈粥樣硬化劑、抗脂質異常劑、抗糖尿病劑、抗高血糖劑、抗高胰島素劑、抗血栓劑、抗視網膜病變劑、抗神經病劑、抗腎病劑、抗缺血劑、抗高血壓劑、抗肥胖劑、抗高血脂劑、抗高三酸甘油酯劑、抗高膽固醇劑、抗再狹窄藥劑、抗胰臟病劑、降脂劑、厭食劑、記憶增強劑、抗癡呆劑、認知促進劑、食慾抑制劑、治療心臟衰竭之藥劑、治療周邊動脈疾病之藥劑、治療惡性腫瘤之藥劑及消炎劑。

【0156】 其他治療劑可包括ACE抑制劑、β-阻斷劑、利尿劑、鹽皮質激素受體拮抗劑、利阿諾定(ryanodine)受體調節劑、SERCA2a活化劑、腎素抑制劑、鈣離子通道阻斷劑、腺苷A1受體促效劑、部分腺苷A1受體、多巴胺β-羥化酶抑制劑、血管收縮素II受體拮抗劑、具有用於選擇細胞信號傳導路徑之偏壓促效作用的血管收縮素II受體拮抗劑、血管收縮素II受體拮抗劑與腦啡肽酶酶抑制劑之組合、腦啡肽酶酶抑制劑、可溶性鳥苷酸環化酶活化劑、肌凝蛋白ATP酶活化劑、rho-激酶1抑制劑、rho-激酶2抑制劑、愛帕琳肽(apelin)受體促效劑、硝醯基供體化合物、鈣依賴性激酶II抑制劑、抗纖維化劑、半乳糖凝集素-3抑制劑、血管加壓素受體拮抗劑、RXFP1受體調節劑、利尿鈉肽受體促效劑、瞬時受體電位辣椒素-4通道阻斷劑、抗心律不整劑、I_f「起搏電流」通道阻斷劑、硝酸鹽、毛地黃(digitalis)化合物、強心劑(inotropic agent)及β-受體促效劑、細胞膜再密封劑(例如泊洛沙姆(Poloxamer) 188) 抗高血脂劑、血漿HDL增強劑、抗高膽固醇血症劑、膽固醇生物合成抑制劑(諸如HMG CoA還原酶抑制劑)、LXR促效劑、FXR促效劑、普羅布考(probucol)、雷諾昔芬(raloxifene)、菸鹼酸、菸鹼醯胺、膽固醇吸收抑制劑、膽酸螯合劑、陰

離子交換樹脂、四級胺、消膽胺(cholestyramine)、考來替泊(colestipol)、低密度脂蛋白受體誘導劑、氯貝特(clofibrate)、非諾貝特(fenofibrate)、苯紮貝特(bezafibrate)、環丙貝特(ciprofibrate)、吉非貝齊(gemfibrizol)、維生素B6、維生素B12、抗氧化劑維生素、抗糖尿病劑、血小板凝集抑制劑、血纖維蛋白原受體拮抗劑、阿司匹林(aspirin)及纖維酸衍生物、PCSK9抑制劑、阿司匹林及P2Y12抑制劑，諸如氯吡格雷(Clopidogrel)。

【0157】其他治療劑亦可包括尼達尼布(nintedanib)、吡非尼酮(Pirfenidone)、LPA1拮抗劑、LPA1受體拮抗劑、GLP1類似物、曲羅蘆單抗(tralokinumab)(IL-13，AstraZeneca)、維莫德吉(vismodegib)(刺蝟拮抗劑，Roche)、PRM-151 (正五聚素蛋白-2，TGFβ-1，Promedior)、SAR-156597 (雙特異性Mab IL-4&IL-13，Sanofi)、辛妥珠單抗(simtuzumab)((抗離胺醯氧化酶樣2 (抗LOXL2)抗體，Gilead)、CKD-942、PTL-202 (PDE抑制劑/己酮可可鹼(pentoxifylline)/NAC經口控制釋放，Pacific Ther.)、奧米昔布(omipalisib) (經口PI3K/mTOR抑制劑，GSK)、IW-001 (適度經口V型牛膠原蛋白溶液，ImmuneWorks)、STX-100 (整合素αV/β-6 ant，Stromedix/Biogen)、阿克姆(Actimmune)(IFNγ)、PC-SOD (中度歧化酶(midismase)；吸入型，LTT Bio-Pharma/CKD Pharm)、來瑞組單抗(lebrikizumab)(抗IL-13 SC人源化mAb，Roche)、AQX-1125 (SHIP1活化劑，Aquinox)、CC-539 (JNK抑制劑，Celgene)、FG-3019 (FibroGen)、SAR-100842 (Sanofi)及奧貝膽酸(OCA或INT-747，Intercept)。

【0158】以上其他治療劑與本發明化合物組合使用時可以例如

Physicians' Desk Reference (如以上所陳述的專利中)中所指示的量或另外由此項技術中之從業者確定的量使用。

【0159】 尤其當以單個劑量單元形式提供時，組合之活性成分之間可能存在化學相互作用。因此，當本發明化合物及第二治療劑在單個劑量單元中組合時，其經調配使得儘管活性成分在單個劑量單元中組合，但活性成分之間的物理接觸降至最低(亦即降低)。舉例而言，一種活性成分可包覆腸溶包衣。藉由對活性成分中的一種包覆腸溶包衣，不僅可使組合之活性成分之間的接觸降至最低，而且可控制此等組分中之一者在胃腸道中的釋放，使得此等組分中之一者不在胃中釋放，而是在腸中釋放。活性成分中之一者亦可包覆有影響在整個胃腸道中持續釋放的物質，且亦用以使組合之活性成分之間的物理接觸降至最低。此外，持久釋放之組分可另外包覆腸溶包衣，使得此組分之釋放僅在腸道中發生。另一方法將涉及組合產物之調配，其中一種組分包覆有持續及/或腸釋放聚合物，且另一組分亦包覆有諸如低黏度級別之羥丙基甲基纖維素(HPMC)的聚合物或此項技術中已知的其他適當物質，以進一步分離活性組分。聚合物包衣用以形成與另一組分之相互作用的其他障壁。

【0160】 本發明化合物亦適用作涉及RXFP1之測試或分析中的標準或參考化合物，例如作為品質標準或對照。此類化合物可提供於例如用於涉及RXFP1活性之醫藥研究的市售套組中。舉例而言，本發明化合物可在分析中用作參考物以使其已知活性與具有未知活性的化合物相比較。此將確保實驗者正確進行分析法且提供比較基礎，尤其當測試化合物為參考化合物之衍生物時。當研發新的分析或方案時，根據本發明之化合物可用以測試其有效性。本發明化合物亦可用於涉及RXFP1之診斷分析中。

【0161】 本發明亦涵蓋一種製品。如本文中所使用，製品意欲包括但不限於套組及套裝。本發明製品包含：(a)第一容器；(b)位於該第一容器內之醫藥組合物，其中該組合物包含第一治療劑，該第一治療劑包含本發明化合物或其醫藥學上可接受之鹽形式；以及(c)藥品說明書，其陳述該醫藥組合物可用於治療血脂異常及其後遺症。在另一實施例中，藥品說明書陳述該醫藥組合物可與第二治療劑組合(如上文所定義)用於治療血脂異常及其後遺症。製品可進一步包含：(d)第二容器，其中組分(a)及(b)位於第二容器中，且組分(c)位於第二容器內或外。位於第一及第二容器內意謂各別容器將物品固持於其邊界內。

【0162】 第一容器為用以容納醫藥組合物之盛器。此容器可用於製造、儲存、運送及/或個別/整體出售。第一容器意欲涵蓋瓶、罐、小瓶、燒瓶、注射器、管(例如用於乳膏製劑)或任何其他用於製造、容納、儲存或分配醫藥產品之容器。

【0163】 第二容器為用以容納第一容器及視情況選用之藥品說明書的容器。第二容器之實例包括(但不限於)盒(例如卡紙板或塑膠)、板條箱、紙盒、袋(例如紙或塑膠袋)、小袋及大袋。藥品說明書可經由膠帶、膠、卡釘(staple)或另一附著方法物理附著於第一容器之外部，或其可留在第二容器內部而不藉助於任何物理方式附著於第一容器。或者，藥品說明書位於第二容器之外部。當位於第二容器之外部時，藥品說明書較佳經膠帶、膠、卡釘或另一附著方法物理附著。或者，其可與第二容器外部相鄰或接觸但不以物理方式附著。

【0164】 藥品說明書為敍述與位於第一容器內之醫藥組合物有關之資訊的標記、標籤、標記物等。所敍述資訊通常將由控管出售製品之地區

的監管機構(例如美國食品與藥物管理局(United States Food and Drug Administration))決定。較佳地，藥品說明書具體敍述醫藥組合物已審批通過之適應症。藥品說明書可由個人可讀取其中或其上所含之資訊之任何材料製成。較佳地，藥品說明書為上面已形成所需資訊(例如印刷或塗覆)之可印刷材料(例如紙、塑膠、卡紙板、箔、膠黏紙或塑膠等)。

化學方法

【0165】 本發明化合物可藉由此項技術中已知之多種方法製備，包括以下流程及特定實施例部分中之方法。合成流程中所示的結構編號及變數編號與申請專利範圍或說明書其餘部分之結構或變數編號不同，且不應混淆。流程中之變數僅欲說明如何製備一些本發明化合物。

【0166】 本發明不限於前述說明性實例，且該等實例應在所有方面被視為說明性的而非限定性的，且因此意欲涵蓋申請專利範圍之等效意義及範圍內出現的所有變化。

【0167】 亦將認識到，在本領域中，任何合成途徑之規劃中的另一主要考慮因素為審慎選擇用於保護本發明中所描述之化合物中存在之反應性官能基的保護基。向經培訓之從業者描述多種替代方式的權威性說明為Greene, T.W.等人, *Protecting Groups in Organic Synthesis*,第4版，Wiley (2007))。

【0168】 縮寫定義如下：「1×」：一次；「2×」：兩次；「3×」：三次；「℃」：攝氏度；「aq」：水溶液；「eq」或「equiv.」：當量；「g」：公克；「mg」：毫克；「L」：公升；「mL」：毫升；「μL」：微升；「N」：正常；「M」：莫耳；「nM」：奈莫耳；「pM」：皮莫耳；「mol」：莫耳；「mmol」：毫莫耳；「min」：分

鐘；「h」：小時；「rt」：室溫；「RT」：滯留時間；「atm」：大氣壓；「psi」：磅/平方吋；「conc.」：濃縮物；「aq」：「水溶液」；「sat.」：飽和；「MW」：分子量；「MS」或「Mass Spec」：質譜；「ESI」：電噴霧電離質譜；「LC-MS」：液相層析質譜；「HPLC」：高壓液相層析；「RP HPLC」：逆相HPLC；「NMR」：核磁共振光譜；「SFC」：超臨界流體層析；「^{1}H」：質子；「δ」：德耳塔(δ)；「s」：單重峰；「d」：雙重峰；「t」：三重峰；「q」：四重峰；「m」：多重峰；「br」：寬峰；「Hz」：赫茲；「MHz」：百萬赫；且「α」、「β」、「R」、「S」、「E」及「Z」為熟習此項技術者熟悉之立體化學標示。

AcCl	乙醯氯
AcOH	乙酸
AIBN	偶氮二異丁腈
BHFFT	雙(四亞甲基)氟甲脒鎓六氟磷酸鹽
Boc	三級丁氧羰基
BuLi	丁基鋰
DAST	二乙基胺基硫三氟化物
DCE	二氯乙烷
DCM	二氯甲烷
DIEA	二乙丙基乙胺
DMAP	4-二甲胺基吡啶
DMF	二甲基甲醯胺
DPPA	二苯基磷醯基疊氮化物
Et_2O	二乙醚
EtOAc	乙酸乙酯
EtOH	乙醇
HATU	(1-[雙(二甲胺基)亞甲基]-1H-1,2,3-三唑并[4,5-b]吡啶鎓3-氧化物六氟磷酸鹽)
HMPA	六甲基磷醯胺
IPA	異丙醇
i-Pr	異丙基
KHMDS	雙(三甲基矽基)胺基鉀\
LDA	二異丙胺基鋰
MeCN	乙腈
MeOH	甲醇
Me	甲基

NBS	N-溴代丁二醯亞胺
Pd/C	鈀/碳
pTsOH	對甲苯磺酸
PyBroP	溴三吡咯啶鏻六氟磷酸鹽
T3P	2,4,6-三丙基-1,3,5,2,4,6-三氧雜三磷雜環已烷-2,4,6-三氧化物
TBAF	四正丁基氟化銨
t-Bu	三級丁基
Teoc	甲酸2-(三甲基矽基)乙酯
TFA	三氟乙酸
TFAA	三氟乙酸酐
THF	四氫呋喃
TsOH	甲苯磺酸
XPhos-Pd-G2	第2代XPhos預催化劑CAS編號1310584-14-5

【0169】 除了另外標記之處以外，在例示性實例中使用以下方法。經由正相或逆相層析進行中間物及最終產物之純化。除非另有指示，否則使用預填充之SiO_2濾筒，用己烷及乙酸乙酯或DCM及MeOH之梯度溶離來進行正相層析。使用C18管柱，藉由UV 220 nm或製備型LCMS偵測，用以下梯度溶離來進行逆相製備型HPLC：溶劑A (90%水、10%甲醇、0.1% TFA)及溶劑B (10%水、90%甲醇、0.1% TFA)之梯度；或溶劑A (95%水、5% ACN、0.1% TFA)及溶劑B (5%水、95% ACN、0.1% TFA)之梯度；或溶劑A (95%水、2% ACN、0.1% HCOOH)及溶劑B (98% ACN、2%水、0.1% HCOOH)之梯度；或溶劑A (95%水、5% ACN、10 mM NH_4OAc)及溶劑B (98% ACN、2%水、10 mM NH_4OAc)之梯度；或溶劑A (98%水、2% ACN、0.1% NH_4OH)及溶劑B (98% ACN、2%水、0.1% NH_4OH)之梯度。

【0170】 用於實例之表徵中之LC/MS方法列於下文。

【0171】

方法A:

儀器：Waters Acquity聯合Waters MICROMASS® ZQ質譜儀

線性梯度：2至98% B，經1 min，其中在98% B下的保持時間為0.5

min

UV觀測：220 nm

管柱：Waters BEH C18，2.1 × 50 mm

流動速率：0.8 mL/min (方法A)

移動相A：0.05% TFA，100%水

移動相B：0.05% TFA，100%乙腈

【0172】

方法B：

儀器：Shimadzu Prominence HPLC聯合Shimadzu LCMS-2020質譜儀

線性梯度：0至100% B，經3 min，其中在100% B下的保持時間為0.75 min

UV觀測：220 nm

管柱：Waters Xbridge C18，2.1 × 50 mm，1.7 μm粒子

流動速率：1 mL/min

移動相A：10 mM乙酸銨，95:5水：乙腈

移動相B：10 mM乙酸銨，5:95水：乙腈

【0173】

方法C：

儀器：Shimadzu Prominence HPLC聯合Shimadzu LCMS-2020質譜儀

線性梯度：0至100% B，經3 min，其中在100% B下的保持時間為0.75 min

UV觀測：220 nm

管柱：Waters Xbridge C18，2.1 × 50 mm，1.7 μm粒子

流動速率：1 mL/min

移動相A：0.1% TFA，95:5水：乙腈

移動相B：0.1% TFA，5:95水：乙腈

【0174】

方法D：

儀器：Waters Acquity聯合Waters MICROMASS® ZQ質譜儀

線性梯度：10% B至98% B，經1 min，其中在98% B下的保持時間為0.5 min

UV觀測：220 nm

管柱：Waters Acquity GEN C18，2.1 × 50 mm，1.7 μm粒子

流動速率：1 mL/min

移動相A：0.05% TFA，100%水

移動相B：0.05% TFA，100%乙腈

【0175】

方法E：

儀器：Shimadzu Prominence HPLC聯合Shimadzu LCMS-2020質譜儀

線性梯度：0至100% B，經1 min，其中在100% B下的保持時間為0.5 min

UV觀測：220 nm

管柱：Waters Acquity BEH C18，2.1 × 50 mm，1.7 μm粒子

流動速率：1 mL/min

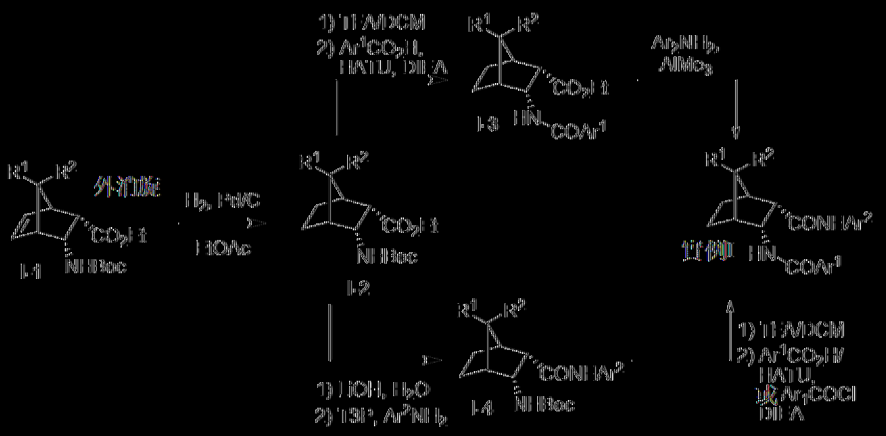
移動相A：10 mM乙酸銨，95:5水：乙腈

移動相B：10 mM乙酸銨，5:95水：乙腈

【0176】實例之表徵中採用之NMR。使用在如下頻率下操作之Bruker或JEOL®傅立葉變換光譜儀獲得^{1}H NMR光譜：^{1}H NMR：400 MHz (Bruker或JEOL®)或500 MHz (Bruker或JEOL®)。光譜資料以如下格式報導：化學位移(多重性、偶合常數及氫之數目)。以四甲基矽烷內標(δ單元，四甲基矽烷=0 ppm)之ppm下場及/或參考溶劑峰指定化學位移，其在^{1}H NMR光譜中呈現為2.51 ppm (對於DMSO-d_6)、3.30 ppm(對於CD_3OD)、1.94 ppm (對於CD_3CN)及7.24 ppm (對於$CDCl_3$)。

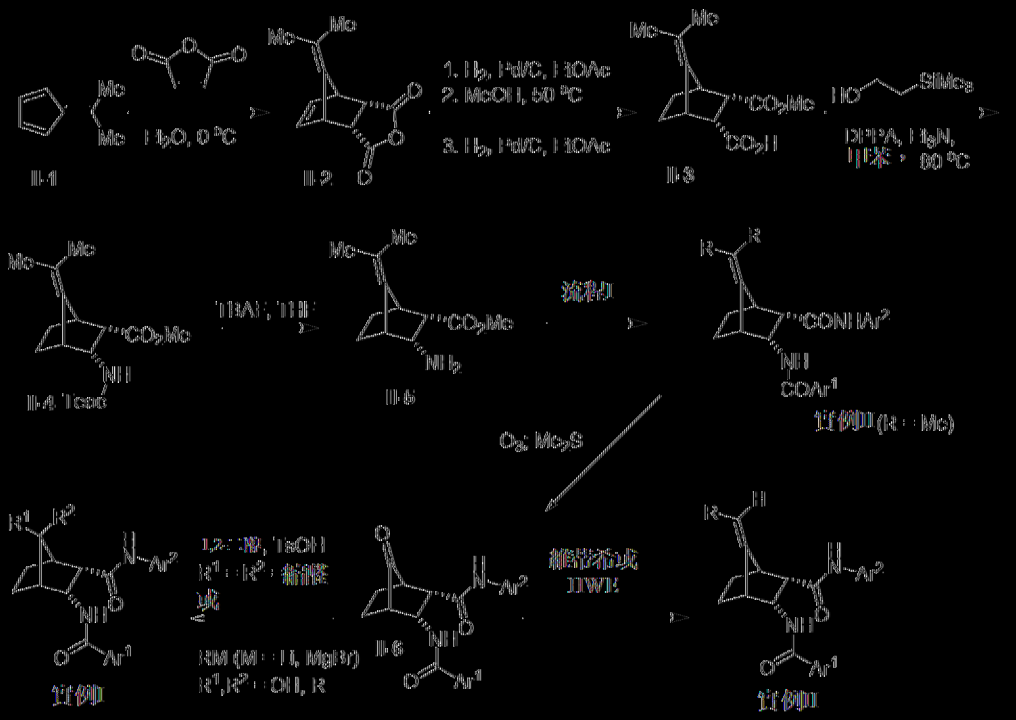
【0177】流程I描述降冰片烷基實例可如何以降冰片烷基中間物**I-1**為起始物質來製備或如何如後續流程中所描述來製備，該等降冰片烷基中間物為市售的($R^1 = R^2 = H$)。以經保護之胺基酯(諸如**I-1**)為起始物質，可在氫化條件(例如Pd/C、H_2)下還原烯烴。所得受Boc保護之胺**I-2**接著可使用TFA脫除保護基，隨後採用各種醯胺鍵形成條件(例如HATU或BOP-Cl，DIEA)用苯甲酸進行後續醯化，得到**I-3**。酯**I-3**可隨後藉由用適合的胺及$AlMe_3$處理而直接轉化為通式結構**I**之實例。或者，醯胺鍵形成反應之順序可顛倒，以**I-2**之皂化開始，隨後用T3P®及適當胺處理，得到**I-4**。根據先前所描述之條件的脫除保護基及醯化接著亦得到通式結構**I**之實例。另外，初始氫化步驟可延遲至該順序中之任何點，而不改變流程1中所描述之步驟之結果。

流程I



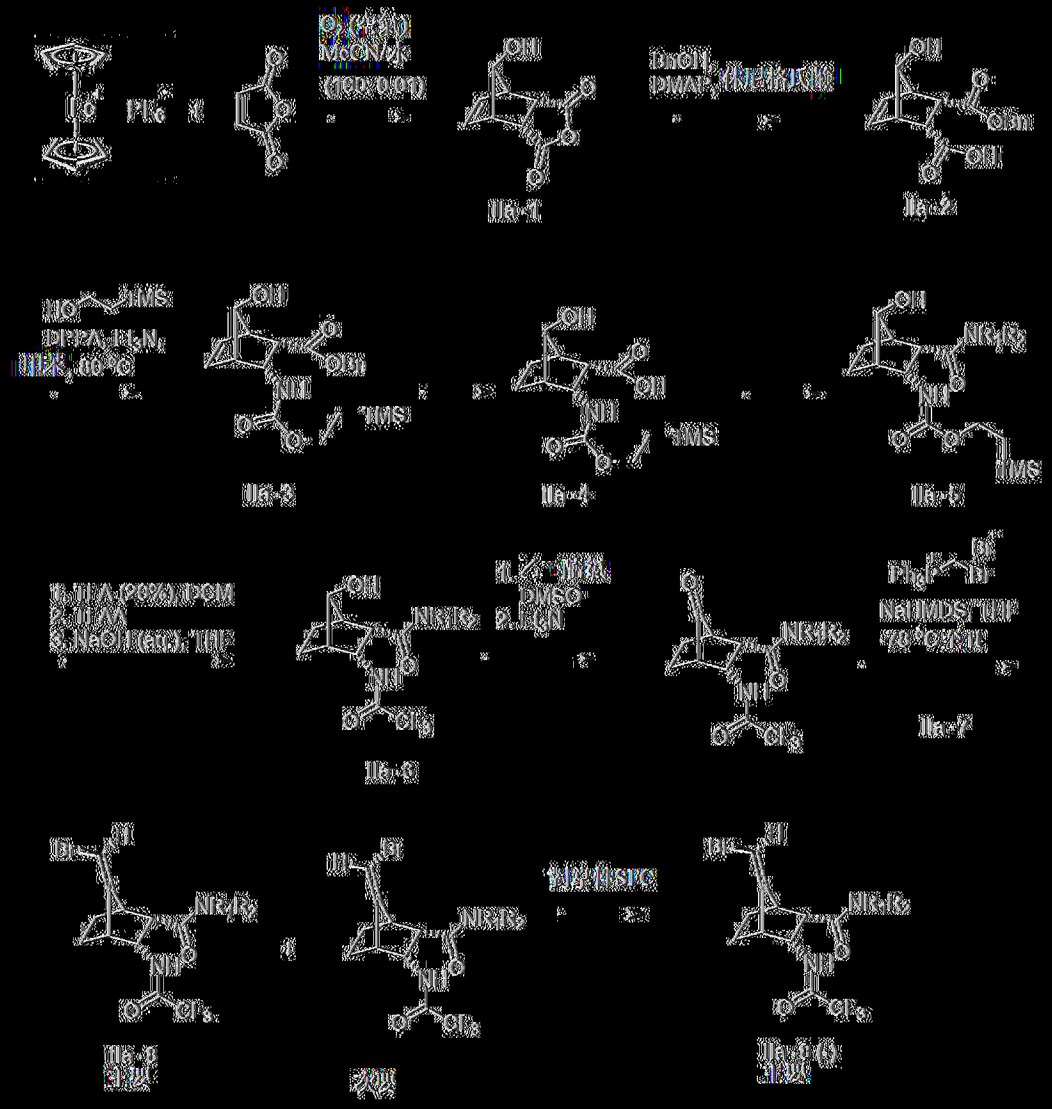
[0178] 流程II展示一種用於以II-1為起始物質產生在C7位置具有取代之降冰片烷基類似物的方法。用鄰果酸酐處理II-1得到II-2，其選擇性地經氫化且溶劑化以產生II-3。II-3與DPPA在三甲基矽烷醇存在下發生柯提斯反應(Curtius reaction)，以便形成II-4。在標準條件下使Troc基團脫除保護基使胺II-5形成，胺II-5可經直接加工為通式結構II之實例。或者，可用臭氧處理結構II，得到酮II-6，酮II-6又可經由多種標準變換而官能化，包括(但不限於)有機金屬添加(例如，R-Li、R-MgBr)、維蒂希(Wittig)或霍納-沃茲沃思-埃蒙斯(Horner-Wadsworth-Emmons；HWE)烯化或縮醛形成。此等產物可充當通式結構I或II本身之實例，或可替代地可充當中間物以用於進一步加工。另外，臭氧化反應步驟可出於策略原因而在合成順序中較早進行，而不改變流程II中概述之合成步驟的結果。

流程II



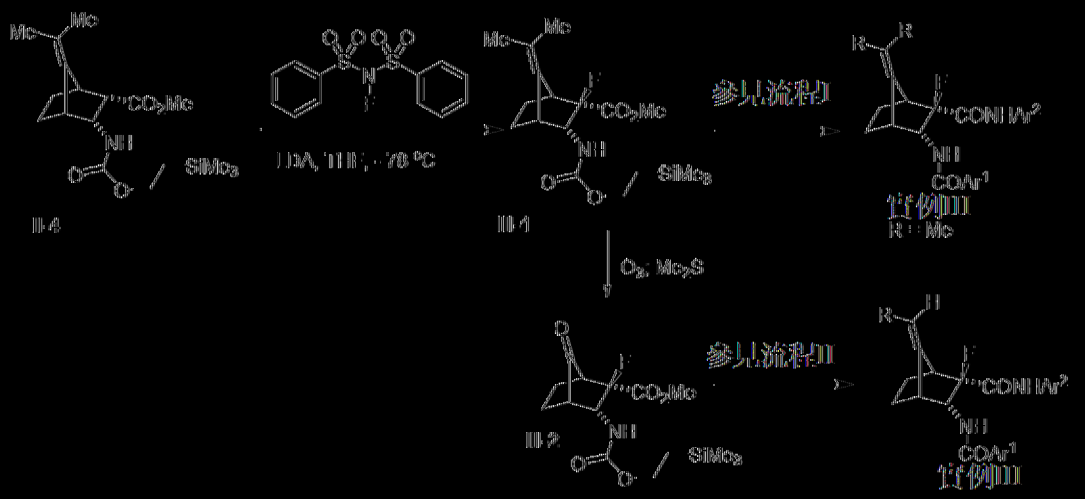
流程IIa

〔0179〕降冰片烷基中間物IIa-8亦可藉由流程IIa中所示之通用途徑由呋喃-2,5-二酮及六氟磷酸三苯鋶製備。進行狄耳士-阿爾德縮合(Diels Alder condensation)，隨後水解得到IIa-2，經柯提斯重排反應得到中間物胺，其在氧化條件還原且隨後受保護，得到中間物IIa-3使苯甲基酯裂解且與NHR_1R_2發生交叉偶合，產生具有通式結構IIa-5之中間物。C7經基轉化成酮，隨後進行維蒂希烯化，產生主要異構物中間物IIa-8。藉由拆析將主要異構物與次要異構物分離且外消旋物經分離成鏡像純IIa-8(-)。



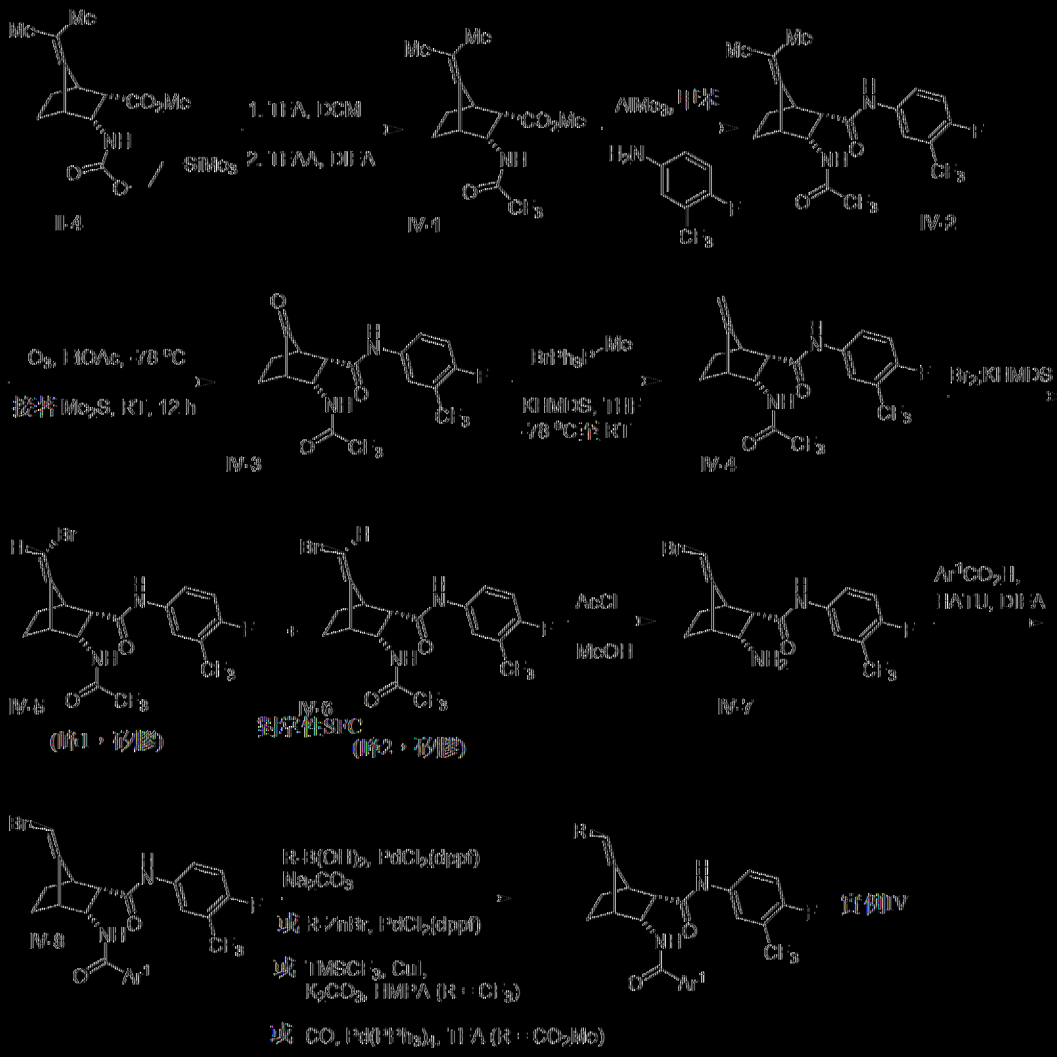
〔0180〕流程III展示降冰片烷基核心可如何氟化。以III-4為起始物質，將該物質用LDA去質子化且用N-氟-二苯基磺醯胺氟化，隨後根據流程II中所概述之路徑加工為通式結構III之實例。或者，III-1可與流程II中類似用臭氧處理，得到III-2。中間物III-2可隨後用維蒂希或HWE條件處理且如流程II中加工，得到通式結構(III)之實例。

流程III



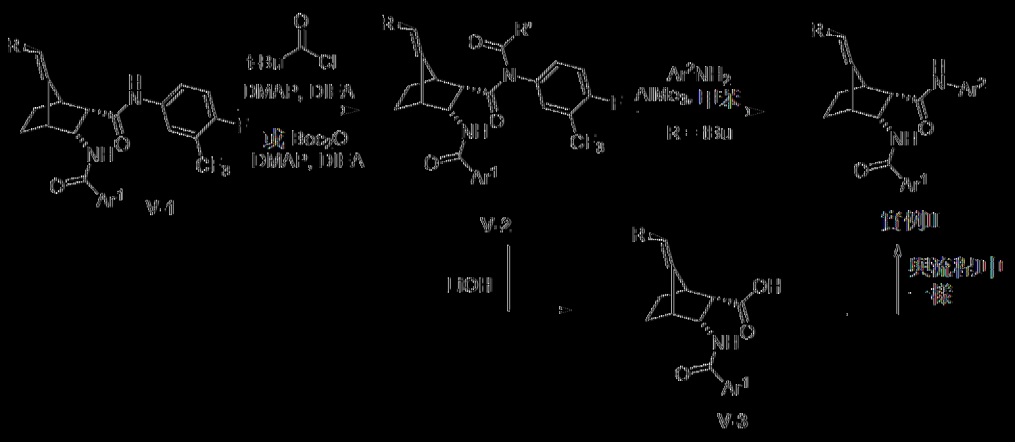
[0181] 流程IV展示由常見中間物溴化物製備多種不同的經C-7甲基取代之降冰片烷基核心。經由標準Teoc脫除保護基、TFA醯化程序將II-4轉化成IV-1。根據流程II中所概述之AlMe3程序將酯IV-1轉化成醯胺IV-2，且與流程II中一樣使IV-2發生臭氧化反應，得到酮IV-3。維蒂希甲基化得到烯烴IV-4，其經溴及KHMDS處理，得到呈藉由矽膠層析分離之異構物混合物形式之IV-5及IV-6。隨後對異構物IV-6進行對掌性SFC純化，產生IV之單一鏡像異構物，接著使其脫除保護基，得到IV-7。胺IV-7可隨後根據流程1中所概述之方法醯化，得到IV-8。溴乙烯亦可進一步官能化(例如鈴木、根岸及Sonnelhack反應條件及其他)，其產生通式結構IV之不同實例或可隨後進一步加工之對應中間物。或者，可對IV-6進行溴乙烯官能化步驟，且以通式結構IV之實例類似之方式處理所得物質。

流程IV



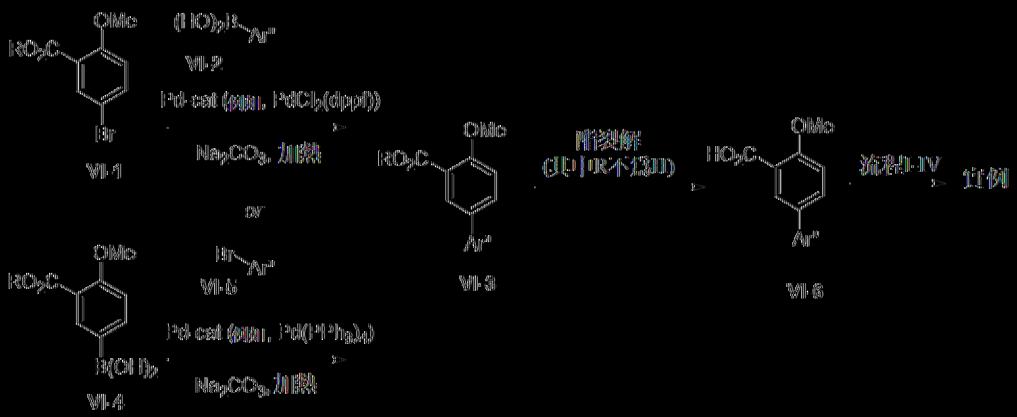
[0182] 流程V展現在高度加工之甲酸降冰片烷基酯上引入不同醯胺之方法。根據流程I-IV中所描述之方法製備之中間物V-1可用特戊醯氯、DMAP及DIEA處理，得到V-2。所得醯亞胺可在AlMe3存在下用胺直接置換，得到通式結構II之實例。或者，可經由使用氫氧化物(例如LiOH、NaOH等)水解V-2，得到V-3，其可根據流程I中所概述之方法進一步官能化，得到通式結構II之實例。

流程V



[0183] 流程VI描述用於流程I-IV中之雙環苯甲酸酯(Ar1 - -Ar'-Ar"，其中"Ar"-經取代之苯基、雜芳基或雜環烯烴)之合成。在鈴木反應條件下用芳基、雜芳基及雜環乙烯基硼酸(或酯) VI-2、鈀催化劑(例如$Pd(PPh_3)_4$、$PdCl_2(dppf)$等)、適當的鹼(例如，Na_2CO_3、K_3PO_4等)處理芳基溴化物VI-1 (其中R可為H、Me、Bn、tBu及其他)，得到雙環VI-3。或者，可在類似條件下使用芳基硼酸VI-4及鹵化物VI-5來頭倒偶合搭配物，以同樣產生VI-3。在VI-3，R/H的情況下，可採用鹼化條件(例如LiOH，針對R=Me之水)、酸性條件(例如，針對R=tBu之TFA/DCM)或氫解條件(例如Pd/C，針對R=Bn之H_2)裂解苯甲酸酯，得到VI-6。接著可如流程I-IV中所概述使苯甲酸VI-6與降冰片烷基核心偶合，得到通式結構I或II之實例或可進一步加工為實例之中間物。

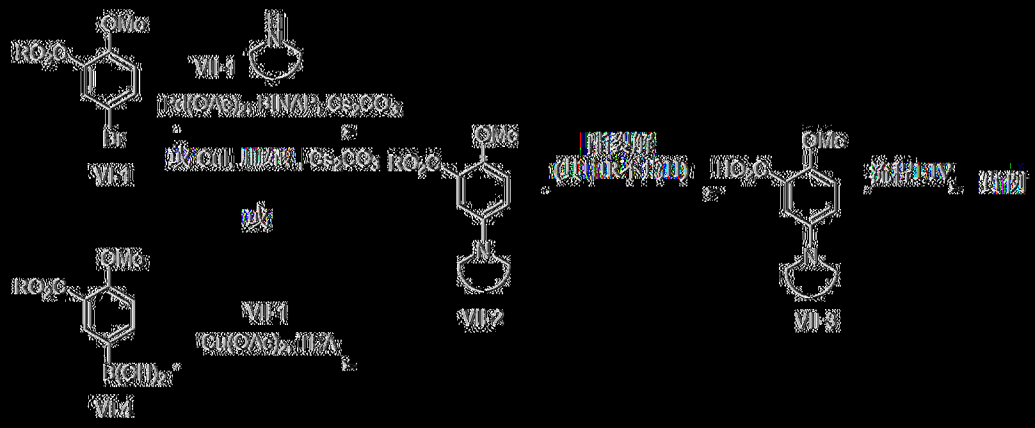
流程VI



[0184] 流程VII概述由苯甲酸酯中間物VI-1或VI-4合成N-鍵聯之

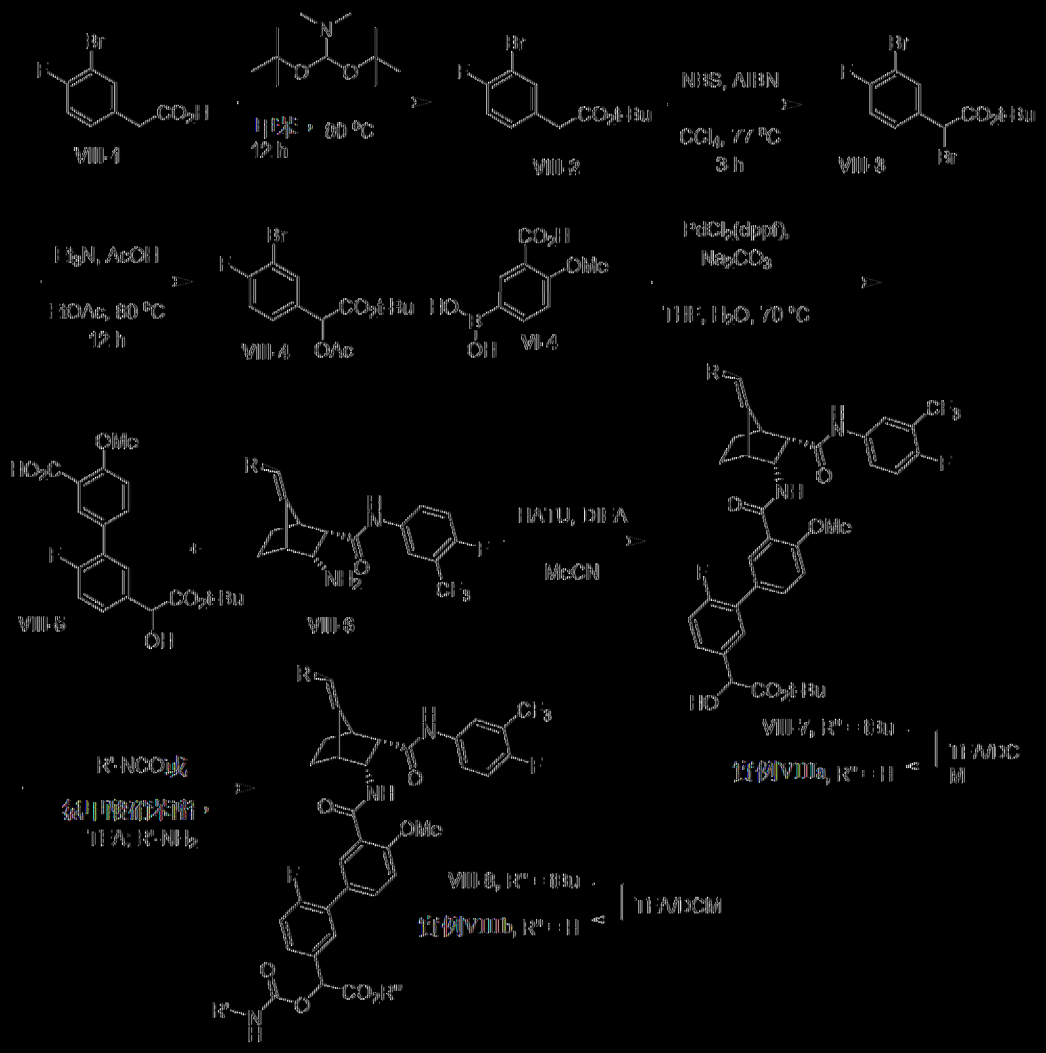
氫雜環雙環苯甲酸酯。在布赫瓦爾德-哈特維希(Hartwig-Buchwald)反應條件(例如$Pd(OAc)_2$、BINAP、Cs_2CO_3及其他)或烏爾曼(Ullman)反應條件(例如CuI、脯胺酸、Cs_2CO_3及其他)下用胺VIII-1處理VII-1，得到雙環VIII-2。或者，可根據Chan-Evans-Lam條件(例如$Cu(OAc)_2$、TEA、O_2及其他)由VII-4製備VIII-2。中間物VIII-2可隨後在需要時經由酯裂解以與流程VI中之VI-3類似之方式進一步官能化，且根據流程I-IV進一步操作，直接得到通式結構I或II之實例或可進一步加工成實例之中間物。

流程VII



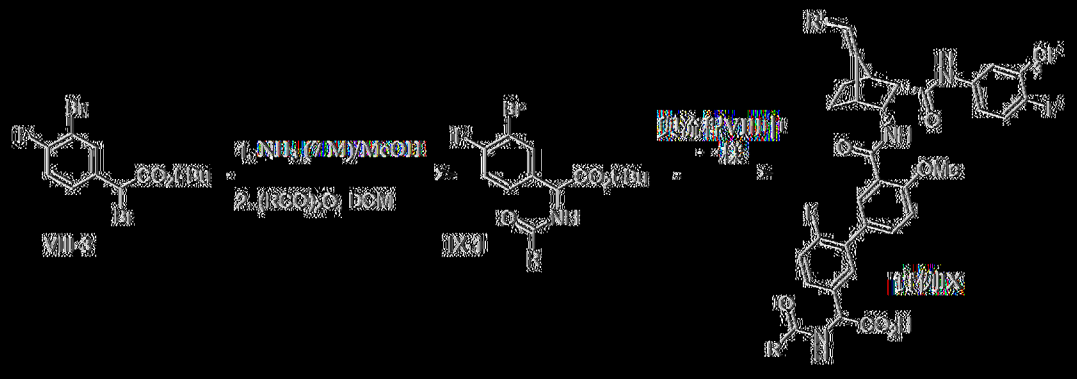
[0185] 流程VIII說明得到其於杏仁酸之聯芳基類似物的通用途徑。將市售VIII-1轉化為三級丁酯VIII-2，接著溴化，得到VIII-3。溴化物經乙酸置換得到中間物VIII-4，接著如流程VI中所描述進行鈴木反應，得到VIII-5(乙酸酯裂解伴隨聯芳基形成)。如流程II中所描述將所得酸直接與降冰片烷基中間物VIII-6偶合，得到VIII-7。接著可裂解(TFA/DCM)三級丁酯VIII-7，得到通式結構VIIIa之實例。或者，VIII-7中之溴基可用適當異氰酸根或兩步胺基甲酸酯形成方案(例如氯甲酸硝苯酯、TEA，接著胺)加工，得到VIII-8，其接著可經裂解(TFA/DCM)，得到通式結構VIIIb之實例。

流程VIII



[0186] 流程IX展示對流程VIII中允許製備其於苯基甘胺酸之聯芳基類似物的步驟之修改。用氨處理中間物VIII-3，接著進行醯化，得到中間物IX-1，其根據流程VIII中所概述之方法加工，得到通式結構IX之實例。

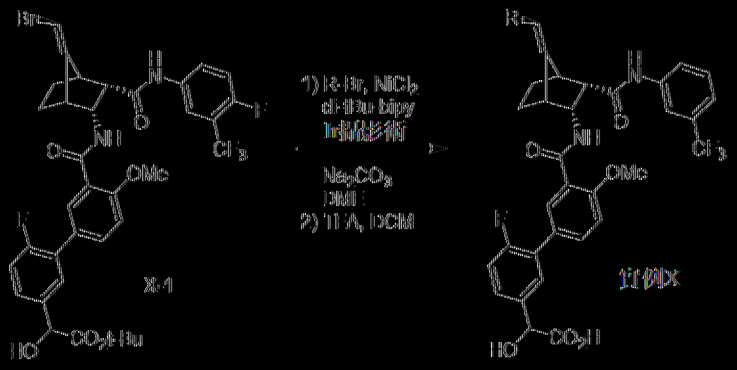
流程IX



[0187] 流程X描述一種可由中間物X-1製備具有不同脂族C-7取代

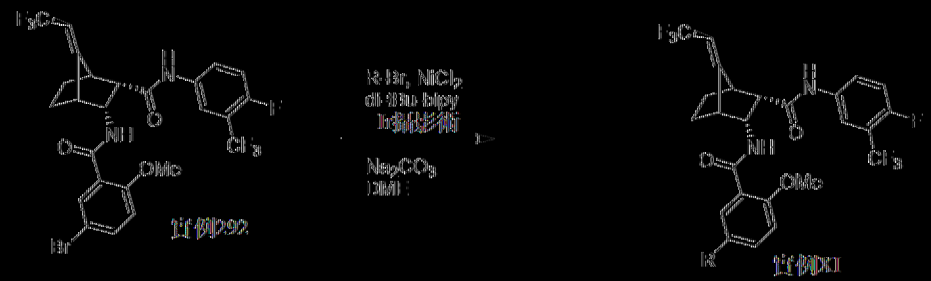
其之類似物之方法，該中間物X-1本身根據流程VIII中概述之途徑製備。在MacMillan等人(*J. Am. Chem. Soc.* 2016, *138*, 8084−8087)中概述之條件下用烷基溴化物處理中間物X-1，隨後對tBu酯進行後續脫除保護基，產生通式結構X之實例。

流程X



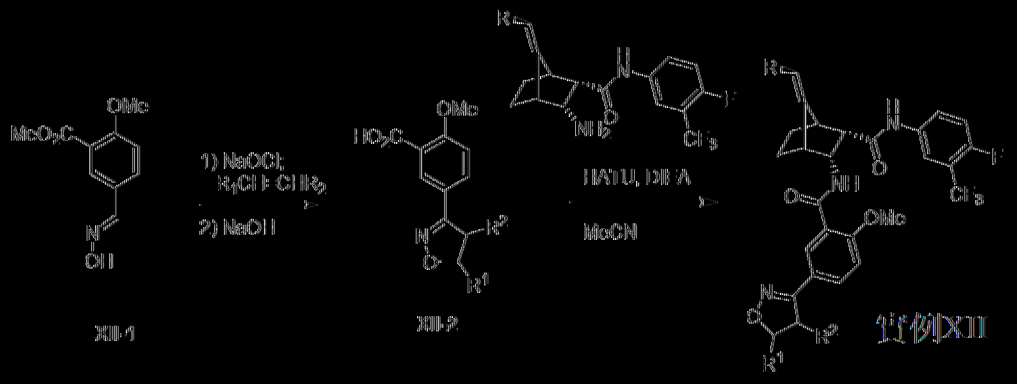
[0188] 流程XI表明製備可由實例292製備之具有不同脂族芳基取代基(R)之類似物的途徑。在MacMillan等人(*J. Am. Chem. Soc.* 2016, *138*, 8084−8087)中概述之條件下用烷基溴化物處理實例292，得到通式結構XI之類似物。

流程XI



[0189] 流程XII描述一種產生經取代之異吲哚啉類似物之途徑。用NaOCl處理XII-1，隨後藉由後續酯還原用經取代之烯烴處理，得到中間物XII-2。此等中間物係根據流程1中所概述之方法與降冰片烷基胺偶合，得到通式結構XII之實例。

流程XII



[0190] 流程XIII描述用於產生具有不同芳基取代基(Ar)之類似物的途徑。用四甲基乙二醇處理硼酸VI-4，隨後與降冰片烷基醯胺(根據以上流程製備)進行醯胺偶合，得到XIII-1。在標準無水鈴木條件下用芳基鹵化物處理XIII-1，以便形成類似物XIII。

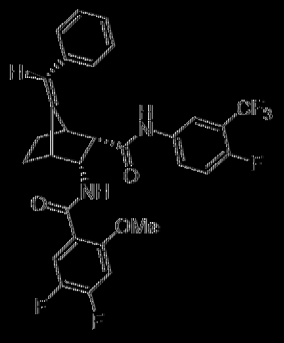
流程XIII

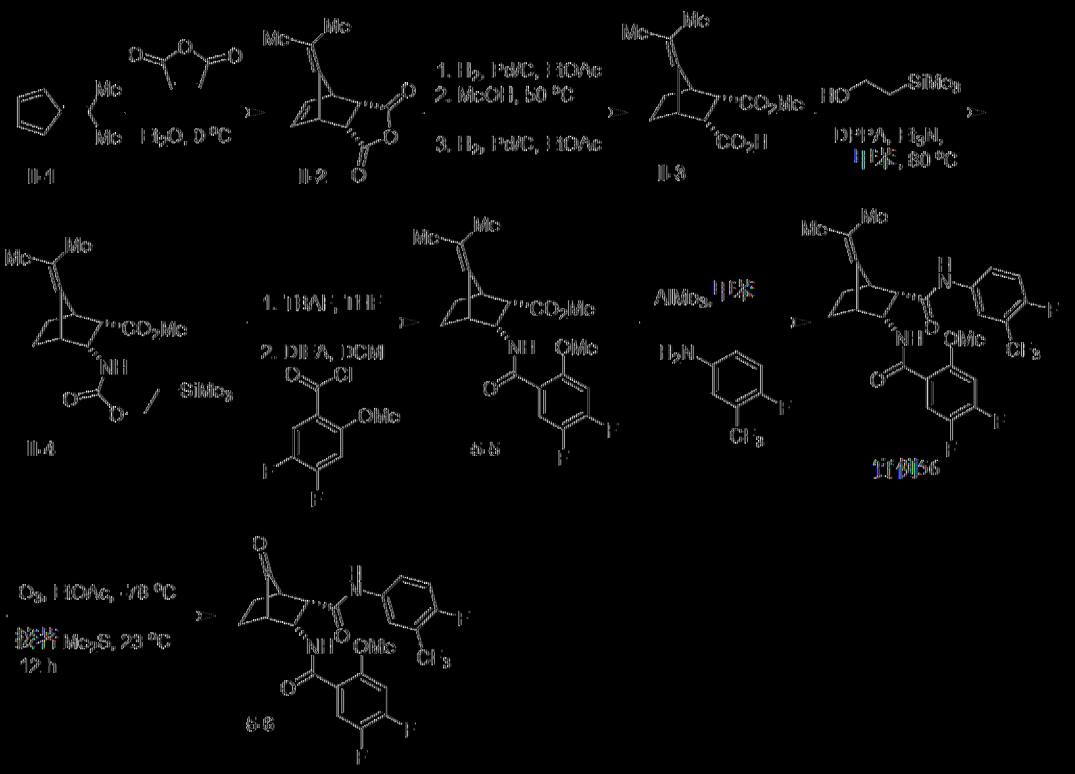


實例

[0191]

實例5





中間物10-2：在0℃向反應容器中添加Et_2O (100 mL)、5-內烷-2-基(其)環戊-1,3-二烯(10-1，10 g，94 mmol)及呋喃-2,5-二酮(10 g，102 mmol)。將反應混合物在0℃攪拌18 h，在減壓下濃縮且經由矽膠層析純化，得到10-2 (3.74 g，18.3 mmol，19.0%產率)。中間物10-2為已知化合物；請參見：2011年12月29日的PCT國際申請案2011163502。

[0192] 中間物10-3：向反應容器中添加10-2 (2.74 g，13.4 mmol)、EtOAc (100 mL)、吡啶(0.540 mL，6.71 mmol)及Pd/C (70 mg，0.070 mmol)。將反應混合物在23℃在1 atm H_2 (H_2氣球)下攪拌60 min，經矽藻土過濾，且在減壓下濃縮。將所得中間物溶解於甲醇(50 mL)中且在50℃加熱12 h。在減壓下濃縮反應混合物(與甲苯3×15 mL共沸)，產生10-3 (3.21 g，13.5 mmol，100%產率)，其不經進一步純化即使用。

[0193] 中間物10-4：向反應容器中添加10-3 (3.2 g，13 mmol)、Et_3N (3.38 mL，24.3 mmol)、甲苯(75 mL)及二苯基磷醯基疊氮化物(4.35 mL，20.2 mmol)。在23℃攪拌反應混合物1 h。隨後在85℃加熱反應混合

物30 min且添加2-(三甲基矽基)乙醇(4.83 mL，33.7 mmol)。在85℃攪拌66 h之後，使反應混合物冷卻至23℃且經由矽膠層析純化，得到外消旋**II-4** (3.71 g，10.5 mmol，78.0%產率) LC-MS RT = 1.25 min；(M+H) = 354.1。方法A。使用對掌性SFC將外消旋**II-4**分離成個別鏡像異構物。製備型層析條件：儀器：Thar 350 SFC；管柱：Whelko-RR，5×50 cm，10微米；移動相：13% IPA/87% CO_2；流動條件：300 mL/min，100巴，35℃；偵測器波長：220 nm；注射詳情：注射4次3.5 mL 59 g / 490 mL MeOH:DCM (4:1) 120 mg/mL於IPA中。分析型層析條件：儀器：Thar分析型SFC；管柱：Whelko-RR (0.46×25 cm，5微米；移動相：5% IPA/95% CO_2；流動條件：3 mL/min，140巴，40℃；偵測器波長：200-400 nm UV。峰1，RT = 3.496 min，>99% ee；峰2，RT = 4.417 min，>99% ee。收集中間物**II-4**產物峰#1且繼續使用以產生對掌性**5-5**。

【0194】 中間物**5-5**：向反應容器中添加對掌性**II-4** (3.71 g，10.5 mmol)、THF (80 mL)及TBAF (31.5 mL，31.5 mmol)。將反應混合物在23℃攪拌12 h，用EtOAc (15 mL)稀釋，且用飽和$NaHCO_3$ (15 mL)洗滌有機部分。收集有機相，經Na_2SO_4乾燥，在減壓下濃縮且溶解於DCM (50 mL)中。冷卻至0℃之後，添加DIEA (5.50 mL，31.5 mmol)及4,5-二氟-2-甲氧基苯甲醯氯(2.4 g，12 mmol)。將反應混合物在0℃攪拌1 h，隨後升溫至23℃，在減壓下濃縮，且經由矽膠層析純化殘餘物，得到**5-5** (2.9 g，7.7 mmol，產率74%)。LC-MS RT = 1.13 min；(M+H) = 380.1。方法A。

【0195】 **實例56**：向反應容器中添加4-氟-3-(三氟甲基)苯胺(4.87 g，27.2 mmol)、甲苯(40 mL)及三甲基鋁(13.59 mL，27.20 mmol)。在

23℃攪拌30 min之後，添加含**5-6** (2.95 g，7.76 mmol)之甲苯(80 mL)。在65℃攪拌反應混合物30 min。在冷卻至23℃之後，將反應混合物用EtOAc (50 mL)稀釋且用羅謝爾鹽飽和水溶液洗滌。將有機層經Na_2SO_4乾燥，過濾，在減壓下濃縮且經由矽膠層析純化，得到實例**56** (3.23 g，6.14 mmol，79.0%產率)。LCMS RT = 1.23 min；(M+H) = 527.1；方法A。

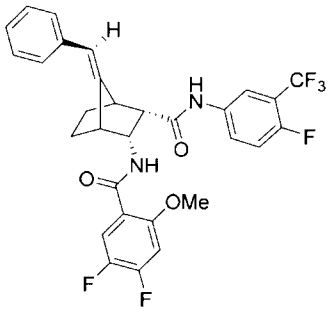
【0196】 中間物**5-6**：向反應容器中添加**實例56** (110 mg，0.210 mmol)及EtOAc (5 mL)。使反應混合物冷卻至-78℃，且使O_3鼓泡通過溶液10 min (直至出現藍色)。在使N_2鼓泡以移除過量O_3之後，隨後添加二硫二甲烷(0.370 mL，4.18 mmol)且使反應混合物升溫至23℃且攪拌12 h。在減壓下濃縮反應混合物，得到殘餘物**5-6** (100 mg，0.20 mmol，96%產率)，其不經進一步純化即使用。LC-MS RT = 1.08 min；(M+H) = 501.1；方法A。

【0197】 針對**實例5**之程序：向反應容器中添加苯甲基膦酸二乙酯(0.290 mL，1.40 mmol)、THF (10 mL)。使混合物冷卻至-78℃且添加KHMDS (1.4 mL，1.4 mmol)。在-78℃攪拌此混合物15 min且在-78℃添加**5-6**。在-78℃攪拌10 min之後，使混合物升溫至23℃，在23℃攪拌1 h，用飽和$NaHCO_3$淬滅且用EtOAc萃取。收集有機相，經Na_2SO_4乾燥，過濾，濃縮，且經由矽膠層析純化，得到*E*-異構物**實例5** (59 mg，0.10 mmol，51%產率)及Z-異構物**實例6** (34 mg，0.060 mmol，29%產率)。^{1}H NMR (400MHz, $CDCl_3$) δ 9.53 (d, J=7.7 Hz, 1H), 8.03 (dd, J=11.2, 9.5 Hz, 1H), 7.93 (dd, J=6.1, 2.5 Hz, 1H), 7.83 (s, 1H), 7.55 - 7.47 (m, 1H), 7.37 - 7.21 (m, 5H), 7.10 (t, J=9.4 Hz, 1H), 6.78 (dd, J=11.6, 6.1 Hz,

1H), 6.31 (s, 1H), 4.83 - 4.72 (m, 1H), 4.00 (s, 3H), 3.46 - 3.39 (m, 1H), 3.12 (dd, J=10.7, 4.1 Hz, 1H), 2.89 (t, J=4.0 Hz, 1H), 2.31 - 2.20 (m, 1H), 1.94 - 1.84 (m, 1H), 1.79 - 1.65 (m, 2H)。LC-MS RT: 1.25 min；MS (ESI) m/z = 575.2 (M+H)+；方法A。

【0198】

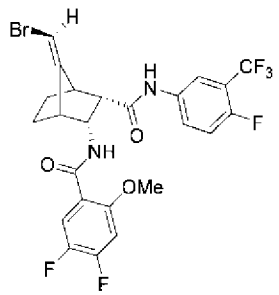
實例6



針對**實例6**之程序：**實例6**經製備作為**實例5**之副產物。^{1}H NMR (400MHz, $CDCl_3$) δ 9.51 (d, J=7.7 Hz, 1H), 8.03 (dd, J=11.4, 9.5 Hz, 1H), 7.94 (dd, J=6.2, 2.6 Hz, 1H), 7.72 (s, 1H), 7.53 (dt, J=8.5, 3.7 Hz, 1H), 7.37 - 7.30 (m, 4H), 7.25 - 7.19 (m, 1H), 7.12 (t, J=9.4 Hz, 1H), 6.78 (dd, J=11.7, 6.2 Hz, 1H), 6.33 (s, 1H), 4.83 (ddd, J=10.9, 7.6, 3.9 Hz, 1H), 3.99 (s, 3H), 3.49 (br. s., 1H), 3.16 (dd, J=10.8, 3.7 Hz, 1H), 2.87 (br. s., 1H), 2.22 (t, J=8.8 Hz, 1H), 1.91 (t, J=8.7 Hz, 1H), 1.69 (d, J=6.4 Hz, 2H)。LC-MS RT: 1.25 min；MS (ESI) m/z = 575.2 (M+H)+；方法A。

【0199】

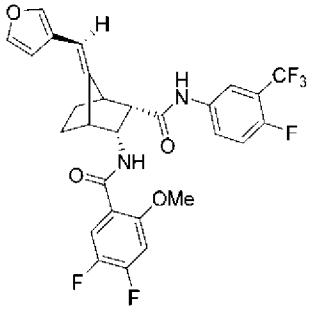
實例11



針對**實例11**之程序：**實例11**係根據針對**實例5**所描述之方法，採用溴(溴甲基)三苯基磷烷，由**5-6**製備。^{1}H NMR (500MHz, $CDCl_3$) δ 9.31 (d, J=8.0 Hz, 1H), 8.01 (dd, J=11.3, 9.4 Hz, 1H), 7.94 - 7.86 (m, 2H), 7.51 (dt, J=8.7, 3.6 Hz, 1H), 7.10 (t, J=9.4 Hz, 1H), 6.78 (dd, J=11.6, 6.1 Hz, 1H), 5.98 (s, 1H), 4.87 - 4.76 (m, 1H), 3.97 (s, 3H), 3.28 (t, J=3.7 Hz, 1H), 3.16 - 3.09 (m, 1H), 2.93 (t, J=3.7 Hz, 1H), 2.35 - 2.25 (m, 1H), 1.91 - 1.82 (m, 1H), 1.75 - 1.63 (m, 2H)。LC-MS RT: 1.22 min；MS (ESI) m/z = 578.9 (M+H)+；方法A。

【0200】

實例12

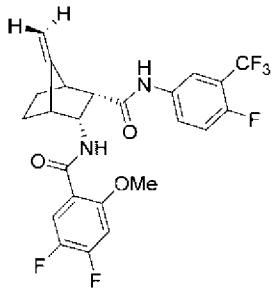


針對**實例12**之程序：向反應容器添加**實例11** (10 mg，0.020 mmol)，隨後添加呋喃-3-基硼酸(9.7 mg，0.090 mmol)、$PdCl_2$(dppf)-CH_2Cl_2加合物(4.2 mg，5.2 μmol)、THF (2 mL)及Na_2CO_3 (0.5 mL，1.00 mmol)。藉由使N_2鼓泡使反應混合物脫氣10 min，密封，且在60℃攪拌2 h。在使反應混合物冷卻至23℃之後，濃縮反應混合物且經由製備型RP-HPLC純化殘餘物，得到**實例12** (7.7 mg，0.010 mmol，77%產率)。^{1}H NMR (500MHz, $CDCl_3$) δ 9.54 (d, J=7.4 Hz, 1H), 8.03 (dd, J=11.3, 9.4 Hz, 1H), 7.94 (dd, J=6.3, 2.8 Hz, 1H), 7.69 (s, 1H), 7.53 (dt, J=8.9, 3.4 Hz, 1H), 7.44 (d, J=0.8 Hz, 1H), 7.39 (t, J=1.7 Hz, 1H), 7.12 (t, J=9.4 Hz, 1H), 6.79 (dd, J=11.6, 6.3 Hz, 1H), 6.54 (d, J=1.1 Hz, 1H), 6.08 (s, 1H), 4.82

- 4.73 (m, 1H), 4.00 (s, 3H), 3.37 (t, J=3.6 Hz, 1H), 3.12 (dd, J=10.7, 3.9 Hz, 1H), 2.84 (t, J=3.3 Hz, 1H), 2.20 - 2.14 (m, 1H), 1.90 (t, J=8.5 Hz, 1H), 1.69-1.65 (m, 2H)。LC-MS RT: 1.22 min；MS (ESI) m/z = 565.0 (M+H)+；方法C。

【0201】

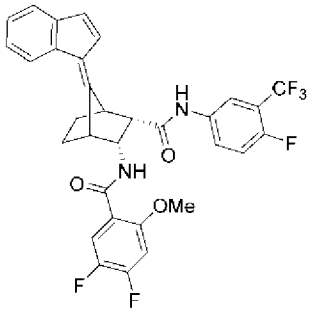
實例13



針對**實例13**之程序：**實例13**係根據針對**實例12**所描述之方法，採用[1,1'-聯苯]-4-基硼酸，由**5-6** (5.0 mg，8.7 μmol)製備。在形成**實例13**之情況下，未獲得交叉偶合產物，但觀測到去鹵化副產物且將其分離(2.3 mg，4.6 μmol，53%)。^{1}H NMR (500MHz, $CDCl_3$) δ 9.44 (d, J=6.6 Hz, 1H), 8.05 (dd, J=11.3, 9.5 Hz, 1H), 7.99 - 7.93 (m, 1H), 7.76 (bs, 1H), 7.58 - 7.50 (m, 1H), 7.13 (t, J=9.3 Hz, 1H), 6.80 (dd, J=11.6, 6.1 Hz, 1H), 4.86 (s, 1H), 4.85 (s, 1H), 4.79 - 4.73 (m, 1H), 3.11 (dd, J=10.8, 4.0 Hz, 1H), 2.83 (br. s., 1H), 2.79 (br. s., 1H), 2.24 - 2.15 (m, 1H), 1.88 - 1.80 (m, 1H), 1.69 - 1.63 (m, 2H)。LC-MS RT: 1.17 min；MS (ESI) m/z = 499.1 (M+H)+；方法C。

【0202】

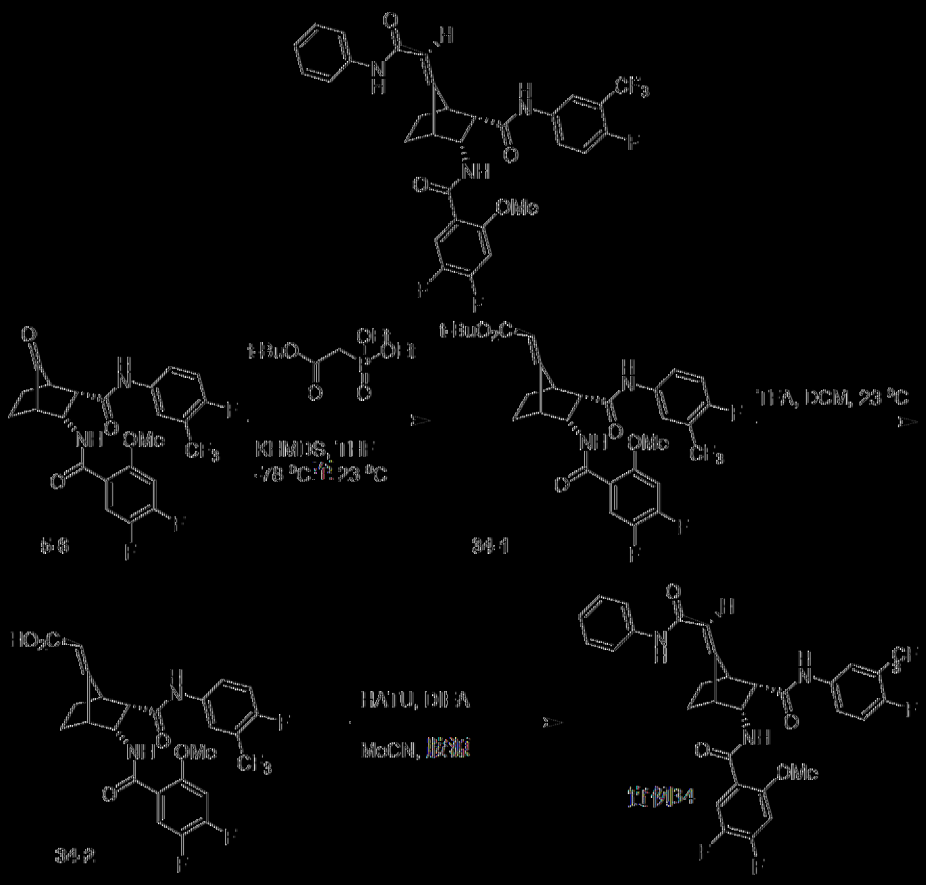
實例33



針對**實例33**之程序：向反應容器中添加1H-茚(34.8 mg，0.300 mmol)及THF (2 mL)。使反應混合物冷卻至-78℃且添加nBuLi (0.19 mL，0.30 mmol)。在-78℃攪拌10 min且在23℃攪拌10 min之後，將反應混合物再次冷卻至-78℃且添加**5-6** (15 mg，0.030 mmol)。使反應混合物升溫至23℃，攪拌15 min，且藉由添加飽和$NaHCO_3$淬滅且用EtOAc萃取。將有機相經Na_2SO_4乾燥，過濾，濃縮且溶解於Et_2O (2 mL)中。在添加柏傑士試劑(Burgess reagent) (14.3 mg，0.0600 mmol) (添加1 equiv.且接著在3 h之後再添加1 equiv.)之後，在45℃攪拌反應混合物12 h。濃縮所得溶液且經由矽膠層析純化，得到E-異構產物(3.4 mg，5.6 μmol，19%產率)及Z-異構物**實例33** (4.6 mg，7.5 μmol，25%產率)。^{1}H NMR (500MHz, $CDCl_3$) δ 9.63 (d, J=7.7 Hz, 1H), 8.07 (dd, J=11.3, 9.4 Hz, 1H), 8.00 (dd, J=6.2, 2.6 Hz, 1H), 7.87 (d, J=7.4 Hz, 1H), 7.80 (s, 1H), 7.57 (dt, J=8.7, 3.5 Hz, 1H), 7.37 (d, J=7.4 Hz, 1H), 7.32 - 7.26 (m, 1H), 7.25 - 7.21 (m, 1H), 7.17 (t, J=9.4 Hz, 1H), 6.90 (d, J=5.5 Hz, 1H), 6.83 (dd, J=11.6, 6.1 Hz, 1H), 6.67 (d, J=5.5 Hz, 1H), 4.94 - 4.86 (m, 1H), 4.04 (s, 3H), 3.98 (t, J=4.0 Hz, 1H), 3.43 (t, J=3.9 Hz, 1H), 3.19 (dd, J=10.9, 4.0 Hz, 1H), 2.40 - 2.33 (m, 1H), 2.14 - 2.07 (m, 1H), 1.84 - 1.70 (m, 2H)。LC-MS RT: 1.27 min；MS (ESI) m/z = 599.1 (M+H)+；方法A。

【0203】

實例34



中間物34-1：中間物34-1係以與實例5中之一般維蒂希反應相同之方式由5-6及2-(二乙氧基磷醯基)乙酸三級丁酯製備。LC-MS RT = 1.25 min；(M+H)+ = 599.1；方法A。

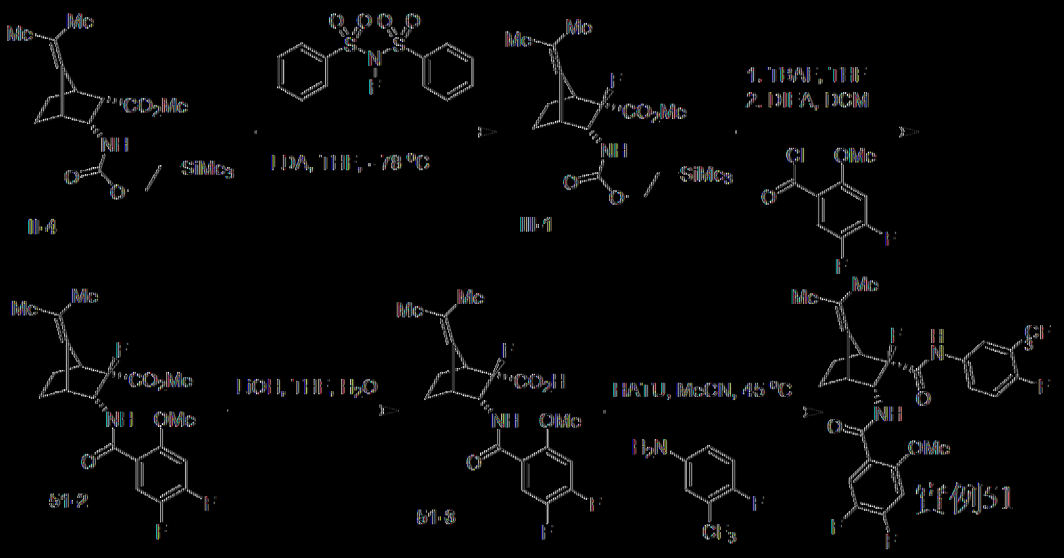
[0204] 中間物34-2：向反應容器中添加34-1 (50 mg，0.080 mmol)、DCM (2 mL)及TFA (0.200 mL，2.59 mmol)。在23℃攪拌12 h之後，在減壓下濃縮反應內容物，得到34-2 (46 mg，0.080 mmol，98%產率)，其不經進一步純化即使用。LC-MS RT = 1.08 min，(M+H)+ = 543.1；方法A。

[0205] 針對實例34之程序：向反應容器中添加34-2 (5 mg，9 μmol)、MeCN (1 mL)、DIEA (5 μl、0.03 mmol)及HATU (7 mg，0.02 mmol)。在23℃攪拌反應混合物3 h，在減壓下濃縮溶液，且經由製備型

HPLC純化殘餘物，得到實例34 (3.8 mg，6.8 mmol，74%產率)。LC-MS RT: 1.18 min；MS (ESI) m/z：618.1 (M+H)+；方法B。

[0206]

實例51



中間物III-1：向反應容器中添加III-4 (100 mg，0.28 mmol)及THF (5 mL)。在冷卻至-78℃之後，添加LDA (在0℃由BuLi (0.53 mL，0.85 mmol)及二異丙胺(0.12 mL，0.85 mmol)製備)且在-78℃攪拌反應混合物15 min。隨後，在-78℃添加N-氟-N-(苯基磺醯基)苯磺醯胺(223 mg，0.710 mmol)。在-78℃攪拌1 h之後，藉由添加飽和$NaHCO_3$淬滅反應混合物且用EtOAc萃取水性部分。將合併之有機部分經Na_2SO_4乾燥，在減壓下濃縮，且經由矽膠層析純化，得到III-1 (59.5 mg，0.160 mmol，57.0%產率) (第1峰)以及反式異構物(17.5 mg，0.0500 mmol，17.0%產率) (第2峰)。LC-MS RT：1.21 min，(M+H)：372.1；方法A。

[0207] 中間物51-2：向反應容器中添加III-1 (20 mg，0.050 mmol)、THF (1 mL)及TBAF (0.270 mL，0.270 mmol)。將反應混合物在23℃攪拌3 h，用EtOAc稀釋，且用飽和$NaHCO_3$洗滌有機部分。收集有機相，經Na_2SO_4乾燥，在減壓下濃縮且再溶解於DCM (1 mL)中。隨後添加

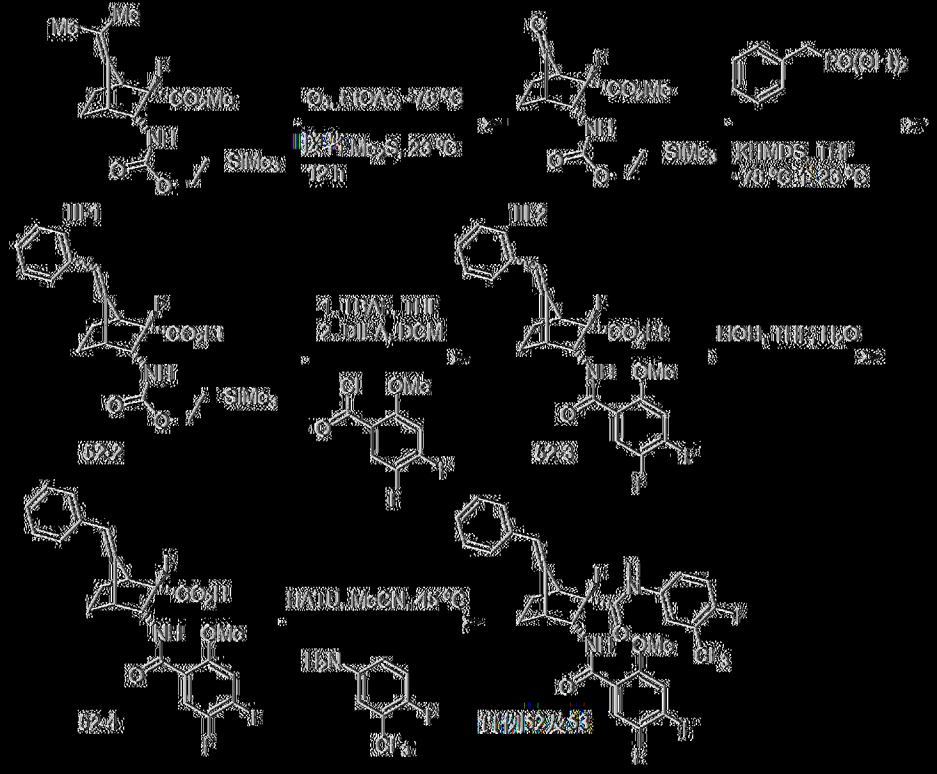
DIEA (0.02 mL，0.11 mmol)及4,5-二氟-2-甲氧苯甲醯氯(16.7 mg，0.0800 mmol)。在23℃攪拌1 h之後，在減壓下濃縮反應混合物且經由矽膠層析純化，得到**51-2** (7.2 mg，0.020 mmol，34%產率)。LC-MS RT = 1.11 min，(M+H) = 398.1；方法A。

【0208】 中間物**51-3**：向反應容器中添加**51-2** (7.5 mg，0.020 mmol)、THF (1 mL)、水(0.5 mL)及單水合氫氧化鋰(4.0 mg，0.090 mmol)。在23℃攪拌反應混合物1 h，用EtOAc (10 mL)稀釋，且用10 mL含有0.1 mmol HCl之飽和NH_4Cl洗滌有機部分。將有機相經Na_2SO_4乾燥，過濾且在減壓下濃縮，得到**51-3** (7.5 mg，0.020 mmol，100%產率)，其不經進一步純化即使用。LC-MS RT = 0.98 min，(M+H) = 384.1；方法A。

【0209】 針對**實例51**之程序：向反應容器中添加**51-3** (7.0 mg，0.020 mmol)、4-氟-3-(三氟甲基)苯胺(6.5 mg，0.040 mmol)、MeCN (1 mL)、DIEA (6 µl，0.04 mmol)及HATU (14 mg，0.040 mmol)。在50℃攪拌反應混合物1 h，使其冷卻至23℃，在減壓下濃縮，且經由矽膠層析純化，得到**實例51** (4.7 mg，8.3 mmol，45%產率)。^{1}H NMR (500MHz, $CDCl_3$) δ 9.21 (d, J=8.3 Hz, 1H), 8.33 (d, J=8.8 Hz, 1H), 8.09 (dd, J=6.2, 2.6 Hz, 1H), 8.02 (dd, J=11.3, 9.4 Hz, 1H), 7.54 (dt, J=8.8, 3.4 Hz, 1H), 7.18 (t, J=9.2 Hz, 1H), 6.78 (dd, J=11.7, 6.2 Hz, 1H), 4.70 - 4.54 (m, 1H), 3.13 (t, J=3.9 Hz, 1H), 2.98 (dd, J=9.4, 3.9 Hz, 1H), 2.07 - 2.00 (m, 1H), 1.79 (s, 3H), 1.74 (s, 3H), 1.57 - 1.43 (m, 3H)。LC-MS RT: 1.23 min；MS (ESI) m/z = 545.1 (M+H)+；方法A。

【0210】

實例52



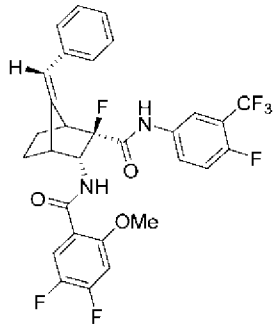
中間物I00-2：向反應容器中添加I00-1 (50 mg，0.14 mmol)及EtOAc (3 mL)。使反應混合物冷卻至-78℃，且使O_3鼓泡通過溶液10 min。隨後添加二硫二甲烷(0.24 mL，2.7 mmol)且使反應混合物升溫至23℃且攪拌12 h。在減壓下濃縮之後，將殘餘物溶解於EtOAc中且經由矽膠過濾。在減壓下濃縮濾液，得到I00-2 (50.5 mg，0.15 mmol，100%產率)，其不經進一步純化即使用。LCMS RT = 1.24 min，(M+H)+ = 346.0；方法A。

[0211] 中間物52-2：向反應容器中添加苯甲基膦酸二乙酯(0.14 mL，0.65 mmol)、THF (5 mL)。使反應混合物冷卻至-78℃且添加KHMDS (0.65 mL，0.65 mmol)。在-78℃攪拌此混合物20 min且在-78℃添加I00-2 (45 mg，0.13 mmol)。在-78℃攪拌5 min且在23℃攪拌1 h之後，藉由添加飽和$NaHCO_3$淬滅反應混合物且用EtOAc萃取水性部分。合併有機部分，經Na_2SO_4乾燥，在減壓下濃縮，且經由矽膠層析純化，得到52-2 (17.4 mg，0.0400 mmol，31.0%產率，烯烴異構物之1.45:1混合

物)。LC-MS RT = 1.27 min，(M+H-Et) = 406.0；方法A。

【0212】 中間物**52-3**：中間物**52-3**係利用針對中間物**51-2**之合成所描述的程序來製備。

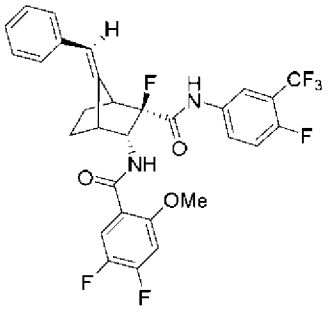
【0213】 中間物**52-4**：中間物**52-4**係利用針對中間物**51-3**之合成所描述的程序來製備。



【0214】 針對**實例52**之程序：**實例52**係根據**實例51**所描述之方法由**52-4**製備。^{1}H NMR (500MHz, $CDCl_3$) δ 9.25 (d, J=8.0 Hz, 1H), 8.33 (d, J=8.5 Hz, 1H), 8.10 (dd, J=6.2, 2.6 Hz, 1H), 8.04 (dd, J=11.1, 9.5 Hz, 1H), 7.58 - 7.50 (m, 1H), 7.39 - 7.31 (m, 4H), 7.18 (t, J=9.4 Hz, 1H), 6.79 (dd, J=11.6, 6.1 Hz, 1H), 6.56 (s, 1H), 4.92 - 4.73 (m, 1H), 4.00 (s, 3H), 3.41 (dd, J=8.7, 3.4 Hz, 1H), 3.06 (t, J=3.9 Hz, 1H), 2.24 - 2.13 (m, 1H), 1.79 - 1.72 (m, 1H), 1.71 - 1.57 (m, 3H)。LC-MS RT: 1.27 min；MS (ESI) m/z = 593.0 (M+H)+；方法A。

【0215】

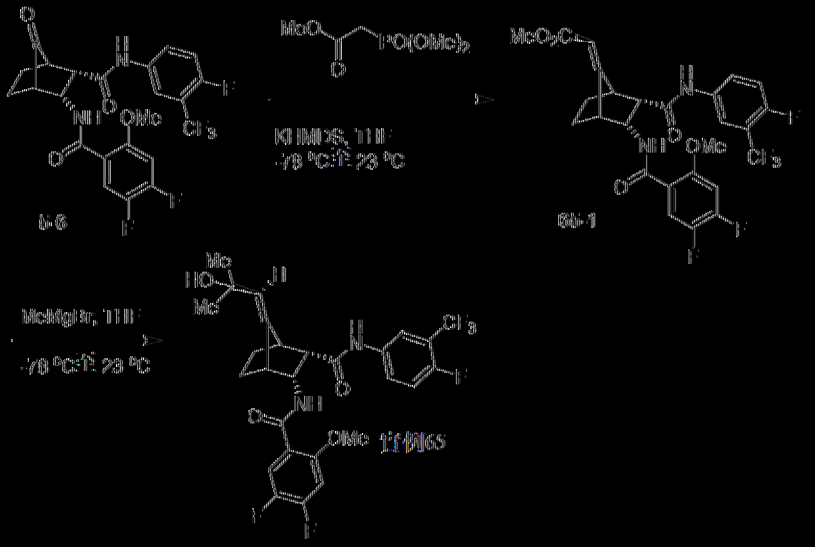
實例53



針對實例53之程序：實例53係根據實例51所描述之方法由52-4製備。^{1}H NMR (500MHz, $CDCl_3$) δ 9.28 (d, J = 7.4 Hz, 1H), 8.33 (d, J = 8.3 Hz, 1H), 8.11 (d, J = 4.1 Hz, 1H), 8.02 (t, J = 10.3 Hz, 1H), 7.55 (d, J = 7.7 Hz, 1H), 7.40 – 7.31 (m, 4H), 7.19 (t, J = 9.2 Hz, 1H), 6.79 (dd, J = 11.6, 6.1 Hz, 1H), 6.45 (s, 1H), 4.89 – 4.72 (m, 1H), 4.01 (s, 3H), 3.61 (br. s., 1H), 2.85 (d, J = 6.1 Hz, 1H), 2.25 – 2.13 (m, 1H), 1.85 – 1.76 (m, 1H), 1.75 – 1.58 (m, 3H)。LC-MS RT: 1.27 min；MS (ESI) m/z = 593.0 (M+H)+；方法A。

[0216]

實例65



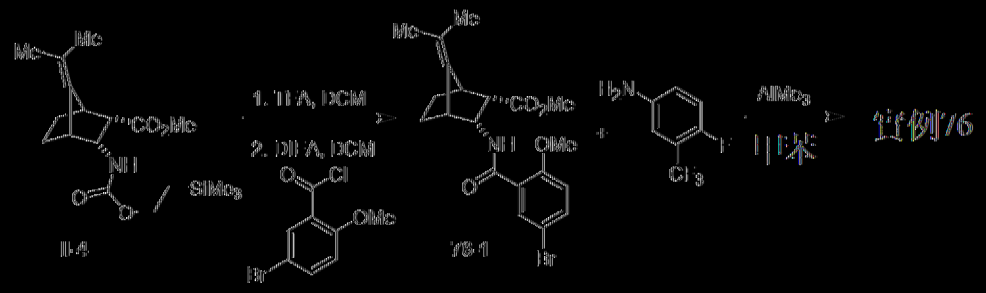
中間物65-1：中間物65-1係以與實例5中所描述之維蒂希反應類似之方式由5-6及2-(二甲氧基磷醯基)乙酸甲酯製備。

[0217] 針對實例65之程序：向反應容器中添加65-1 (5.0 mg，9.0 mmol)及THF (1 mL)。在冷卻反應混合物至-78℃之後，添加氯化甲基鎂(0.06 mL，0.2 mmol)。使反應混合物升溫至23℃，在23℃攪拌2 h。藉由添加飽和$NaHCO_3$淬滅反應物且用EtOAc萃取溶液。將有機層經Na_2SO_4乾燥，過濾，在減壓下濃縮，且經由製備型RP-HPLC純化來純化，得到實

例65 (3.2 mg，5.3 μmol，59%產率)。^{1}H NMR (500MHz, $CDCl_3$) δ 9.46 (d, J = 7.7 Hz, 1H), 8.03 – 7.91 (m, 3H), 7.53 (dt, J = 8.6, 3.5 Hz, 1H), 7.10 (t, J = 9.4 Hz, 1H), 6.78 (dd, J = 11.6, 6.3 Hz, 1H), 5.49 (s, 1H), 4.77 – 4.67 (m, 1H), 3.98 (s, 3H), 3.49 (t, J = 4.0 Hz, 1H), 3.07 (dd, J = 11.0, 4.1 Hz, 1H), 2.69 (t, J = 3.9 Hz, 1H), 2.17 – 2.09 (m, 1H), 1.89 – 1.81 (m, 1H), 1.68 – 1.55 (m, 2H), 1.42 (s, 6H)。LC-MS RT: 1.14 min；MS (ESI) m/z = 557.0 (M+H)+；方法C。

[0218]

實例76



中間物76-1：向含有II-4 (1.77 g，5.00 mmol)之20 mL小瓶中添加DCM (20 mL)。隨後添加TFA (2.02 mL，26.3 mmol)且在23℃攪拌反應混合物48 h。在減壓下濃縮所得溶液且在高真空下乾燥5小時。殘餘物不經進一步純化即繼續用於醯化步驟。以下列方式製備5-溴-2-甲氧苯甲醯氯：向裝有5-溴-2-甲氧基苯甲酸(1.39 g，6.00 mmol)之100 mL燒瓶中添加DCM (30 mL)，隨後添加乙二醯氯(0.6 mL，7 mmol)及DMF (0.05 mL，0.6 mmol)。在23℃攪拌溶液18 h且以與針對中間物5-5所描述相同之方式轉化成醯胺，得到76-1 (878 mg，2.10 mmol，56.0%產率)。^{1}H NMR (500MHz, DMSO-d_6) δ 9.49 (d, J = 7.0 Hz, 1H), 8.04 – 7.87 (m, 1H), 7.74 – 7.59 (m, 1H), 7.17 (d, J = 8.8 Hz, 1H), 4.26 (br. s., 1H), 3.98 (s, 3H), 3.63 (s, 1H), 3.51 (br. s., 1H), 3.42 (d, J = 18.1 Hz, 3H), 3.13 – 3.01 (m,

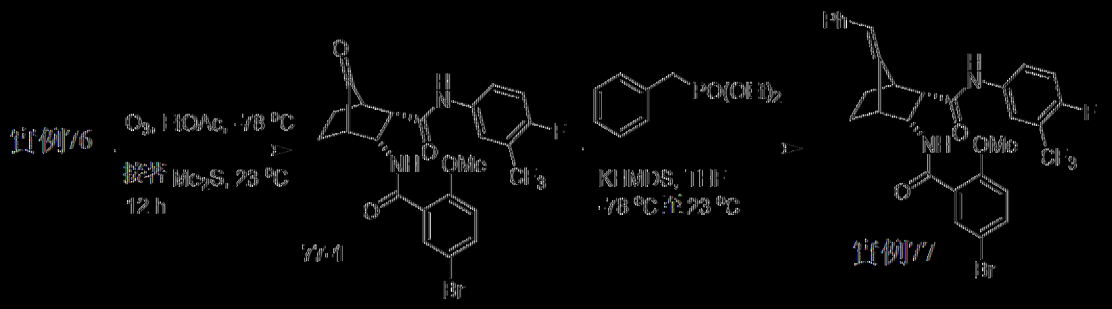
1H), 2.92 (d, J = 13.5 Hz, 2H), 1.67 (s, 5H), 1.64 – 1.47 (m, 3H), 1.36 (br. s., 2H)。

[0219] 針對實例76之程序：實例76係根據針對實例56所描述之方法，採用4-氟-3-(三氟甲基)苯胺，由76-1製備。^{1}H NMR (500MHz, DMSO-d6) δ 10.52 (s, 1H), 9.88 (d, J = 7.0 Hz, 1H), 8.19 (d, J = 4.3 Hz, 1H), 7.97 (d, J = 2.7 Hz, 1H), 7.78 (d, J = 8.5 Hz, 1H), 7.65 (dd, J = 8.7, 2.6 Hz, 1H), 7.47 (t, J = 9.8 Hz, 1H), 7.16 (d, J = 8.9 Hz, 1H), 4.31 (br. s., 1H), 3.98 (s, 3H), 3.55 – 3.40 (m, 3H), 3.09 (dd, J = 10.7, 4.0 Hz, 1H), 3.02 (br. s., 1H), 2.91 (br. s., 1H), 1.80 (t, J = 8.9 Hz, 1H), 1.75 – 1.62 (m, 7H), 1.33 (d, J = 6.1 Hz, 2H)。

LC-MS RT: 2.69 min；MS (ESI) m/z = 569.1 (M+H)+；方法B。

[0220]

實例77



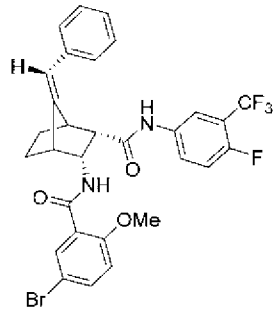
中間物77-1：中間物77-1係以與針對中間物56所描述之相同通用方式，由實例76製備。LC-MS RT = 1.0 min；(M+H)+ = 544.0；方法A。

[0221] 針對實例77之程序：實例77係根據針對實例5所描述之通用方法，使用苯甲基膦酸二乙酯，由77-1製備。^{1}H NMR (500 MHz, DMSO-d6) δ 10.66 – 10.50 (m, 1H), 10.06 – 9.88 (m, 1H), 8.27 – 8.13 (m, 1H), 8.06 – 7.94 (m, 1H), 7.86 – 7.73 (m, 1H), 7.71 – 7.59 (m, 1H), 7.53 – 7.43 (m, 1H), 7.43 – 7.31 (m, 4H), 7.31 – 7.21 (m, 1H), 7.21 – 7.09 (m,

1H), 6.47 - 6.22 (m, 1H), 4.55 - 4.37 (m, 1H), 4.09 - 3.95 (m, 3H), 3.33 - 3.19 (m, 1H), 2.90 - 2.76 (m, 1H), 2.02 - 1.88 (m, 1H), 1.87 - 1.71 (m, 1H), 1.64 - 1.42 (m, 2H), 1.06 - 0.91 (m, 1H)。LC-MS RT: 2.83 min；MS (ESI) m/z = 617.20 (M-H)+；方法B。

【0222】

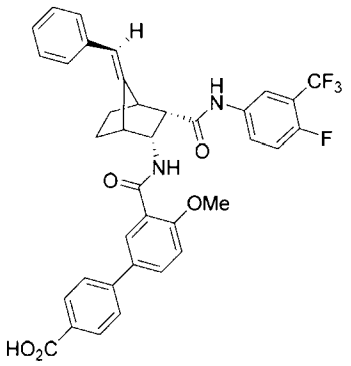
實例78



針對**實例78**之程序：在實例77之生產中製備呈副產物形式之**實例78**。^{1}H NMR (500 MHz, DMSO-d6) δ 10.66 - 10.50 (m, 1H), 10.06 - 9.88 (m, 1H), 8.27 - 8.13 (m, 1H), 8.06 - 7.94 (m, 1H), 7.86 - 7.73 (m, 1H), 7.71 - 7.59 (m, 1H), 7.53 - 7.43 (m, 1H), 7.43 - 7.31 (m, 4H), 7.31 - 7.21 (m, 1H), 7.21 - 7.09 (m, 1H), 6.47 - 6.22 (m, 1H), 4.55 - 4.37 (m, 1H), 4.09 - 3.95 (m, 3H), 3.33 - 3.19 (m, 1H), 2.90 - 2.76 (m, 1H), 2.02 - 1.88 (m, 1H), 1.87 - 1.71 (m, 1H), 1.64 - 1.42 (m, 2H), 1.06 - 0.91 (m, 1H)。LC-MS RT: 2.82 min；MS (ESI) m/z = 617.35 (M-H)+；方法B。

【0223】

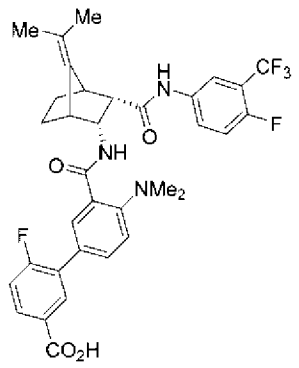
實例79

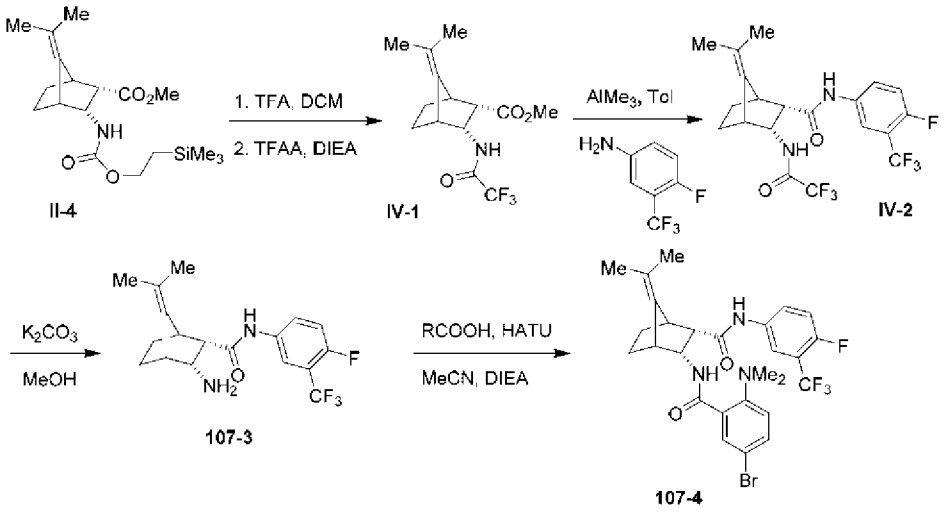


針對**實例79**之程序：向裝有**實例77** (15 mg，0.024 mmol)之0.5至2.0 mL微波反應小瓶中添加4-溴苯甲酸(6 mg，0.04 mmol)，隨後添加THF (490 µl)及K_3PO_4 (97 µl，0.049 mmol)於水中之溶液。最後，添加XPhos-Pd-G2 (CAS 1310584-14-5) (2 mg，0.002 mmol，小刮勺尖端)。將小瓶加蓋且在微波中加熱至100℃持續30 min。將反應物用DMF稀釋至2 mL總體積，過濾，且藉由製備型RP-HPLC純化，得到**實例79** (5.2 mg，0.01 mmol，33%產率)。^{1}H NMR (500MHz, DMSO-d6) δ 9.95 (d, J=7.0 Hz, 1H), 8.26 (d, J=4.3 Hz, 1H), 7.94 (d, J=6.7 Hz, 1H), 7.81 (br. s., 1H), 7.50 (t, J=8.2 Hz, 3H), 7.44 - 7.32 (m, 6H), 7.25 (br. s., 2H), 7.18 (d, J=8.2 Hz, 1H), 7.04 (t, J=7.5 Hz, 1H), 6.39 (s, 1H), 4.52 (br. s., 1H), 3.28 (br. s., 1H), 2.93 (br. s., 1H), 2.02 - 1.79 (m, 3H), 1.53 (br. s., 3H)。LC-MS RT: 2.2 min；MS (ESI) m/z = 659.4 (M-H)+；方法B。

【0224】

實例107





中間物**IV-1**：將**II-4**脫除保護基得到中間物**IV-1**係利用與**76-1**中所描述之相同條件。如下進行三氟乙醯基保護基之安裝：將**II-4**脫除保護基得到對應的胺中間物且添加胺(1.7 g，8.1 mmol)，添加DCM (41 mL)且經由冰浴使燒瓶冷卻至0℃。添加TFAA (1.26 mL，8.90 mmol)及DIEA (5.7 mL，33 mmol)。5 min之後，自冰浴中移出反應燒瓶，且在23℃攪拌30 min。將反應混合物用飽和$NaHCO_3$ (50 mL)淬滅且用EtOAc (3×50 mL)萃取。將合併之有機部分經Na_2SO_4乾燥，過濾且在減壓下濃縮，得到**IV-1** (2.48 g，8.12 mmol，100%產率)，其不經進一步純化即使用。LC-MS RT = 1.11 min；MS (ESI) m/z = 306.1 $(M+H)^+$；方法A。

【0225】 中間物**IV-2**：中間物**IV-2**係以如針對**5-6**所描述之相同方式由**IV-1**製備。(2.5 g，5.5 mmol，63%產率)；LC-MS RT = 1.20 min；MS (ESI) m/z = 453.0 $(M+H)^+$；方法A。

【0226】 中間物**107-3**：將中間物**IV-2** (133 mg，0.290 mmol)溶解於水(2.9 mL)及MeOH (2.9 mL)中。添加K_2CO_3 (2.03 g，1.47 mmol)且在40℃攪拌反應混合物4 h。使反應混合物冷卻至室溫，隨後添加水(5 mL)。用EtOAc (3×10 mL)萃取所得混合物。將合併之有機萃取物經Na_2SO_4乾燥，過濾且在減壓下濃縮，得到**107-3** (105 mg，0.290 mmol，

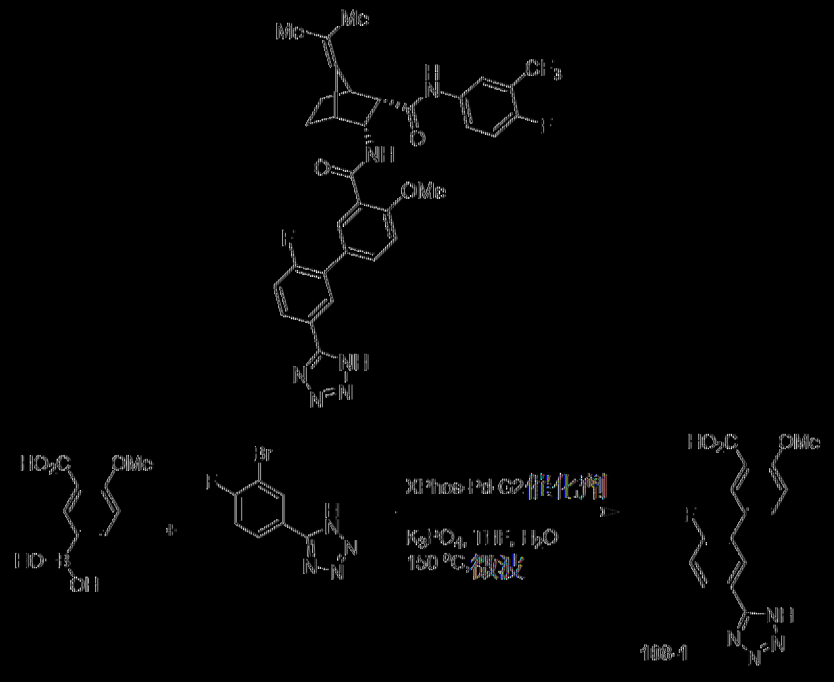
100%產率)，其不經進一步純化即使用。LC-MS RT = 0.82 min；MS (ESI) m/z = 357.1 $(M+H)^+$；方法A。

[0227] 中間物107-4係使用針對76-1使用之樣本程序由107-3製備。

[0228] 針對實例107之程序：實例107係根據針對實例79所描述之方法，採用3-溴-4-氟苯甲酸，由107-4製備。^{1}H NMR (500 MHz, DMSO-d6) δ 10.64 (s, 1H), 10.34 (br d, J = 7.3 Hz, 1H), 8.23 (dd, J = 6.1, 1.8 Hz, 1H), 7.99 (br d, J = 7.6 Hz, 1H), 7.93 (s, 1H), 7.91 – 7.86 (m, 1H), 7.80 (br d, J = 8.2 Hz, 1H), 7.61 (br d, J = 8.2 Hz, 1H), 7.44 (br t, J = 9.8 Hz, 1H), 7.33 (d, J = 8.5 Hz, 1H), 7.24 (br t, J = 9.6 Hz, 1H), 4.46 – 4.38 (m, 1H), 3.13 (br dd, J = 10.4, 4.0 Hz, 1H), 3.03 (br s, 1H), 2.93 (br s, 1H), 2.71 (s, 6H), 1.94 – 1.87 (m, 2H), 1.84 – 1.75 (m, 1H), 1.71 (s, 6H), 1.45 – 1.30 (m, 2H)。LC-MS RT: 2.2 min；MS (ESI) m/z = 642.2 $(M+H)^+$；方法B。

[0229]

實例108

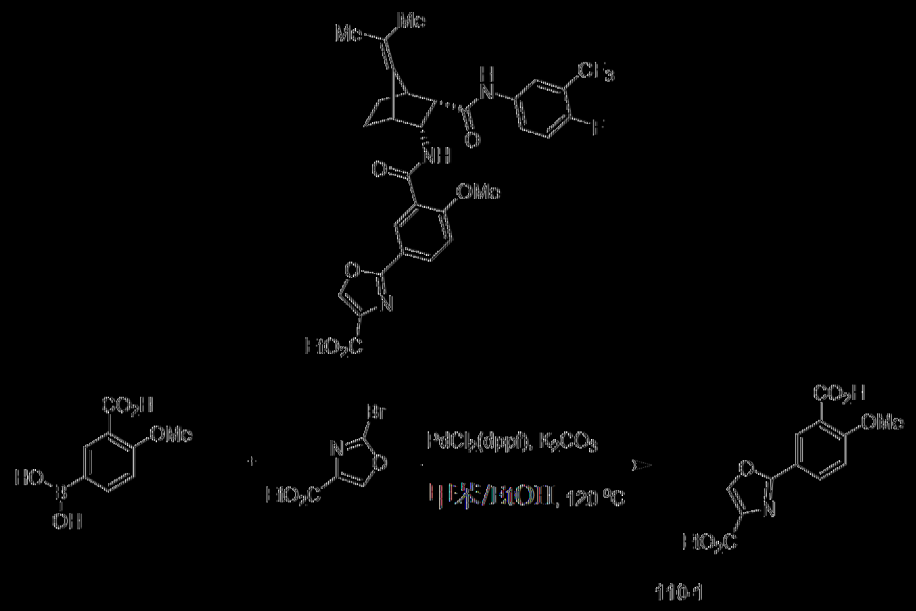


中間物**108-1**：向小瓶中添加5-(3-溴-4-氟苯基)-1H-四唑(50 mg，0.21 mmol)、5-溴-2-甲氧基苯甲酸(60.5 mg，0.309 mmol)、XPhos-Pd-G2催化劑(32 mg，0.042 mmol)及K_3PO_4 (131 mg，0.617 mmol) ，隨後添加THF (1.8 mL)及水(257 µl)。將反應混合物用氮氣脫氣2 min，接著密封且在微波照射下在150℃加熱2.5 h。使反應混合物分配於1 N HCl (5 mL)之間且用EtOAc (3×5 mL)萃取。將合併之有機部分經Na_2SO_4乾燥，過濾且在減壓下濃縮。藉由製備型RP-HPLC純化所得殘餘物，得到**108-1** (13 mg，0.041 mmol，20%產率)。LC-MS RT = 0.77 min；MS (ESI) m/z = 315.1 $(M+H)^+$；方法A。

【0230】針對**實例108**之程序：向反應容器中添加**107-3** (10 mg，0.03 mmol)、**108-1** (13.2 mg，0.0400 mmol)、MeCN (1 mL)、DIEA (0.02 mL，0.1 mmol)及HATU (16 mg，0.040 mmol)。將反應混合物在23℃攪拌3 h，在減壓下濃縮，且進行製備型RP-HPLC純化，得到**實例108** (12.3 mg，0.0200 mmol，65.0%產率)。^{1}H NMR (500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.93 (d, J=7.0 Hz, 1H), 8.26 - 8.19 (m, 2H), 8.17 (br d, J=6.4 Hz, 1H), 8.09 - 8.02 (m, 1H), 7.83 - 7.75 (m, 2H), 7.54 (dd, J=10.2, 9.0 Hz, 1H), 7.47 (t, J=9.8 Hz, 1H), 7.34 (d, J=8.5 Hz, 1H), 4.41 - 4.34 (m, 1H), 4.05 (s, 3H), 3.11 (dd, J=10.8, 4.1 Hz, 1H), 3.05 - 3.02 (m, 1H), 2.99 - 2.92 (m, 1H), 1.86 - 1.80 (m, 1H), 1.77 - 1.69 (m, 7H), 1.41 - 1.31 (m, 2H)。LC-MS RT: 2.17 min；MS (ESI) m/z = 653.6 (M+H)+；方法B。

【0231】

實例110



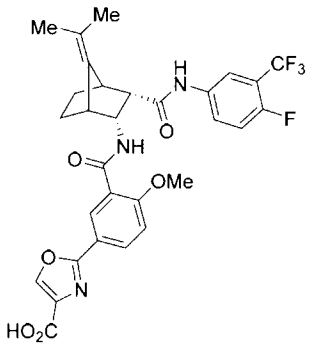
110-1

中間物110-1：向小瓶中添加5-溴-2-甲氧基苯甲酸(100 mg，0.51 mmol)、2-溴噁唑-4-甲酸乙酯(75 mg，0.34 mmol)、$PdCl_2(dppf)\cdot CH_2Cl_2$加合物(28 mg，0.030 mmol)、$K_2CO_3$ (470 mg，3.40 mmol)、甲苯(1.7 mL)及乙醇(1.7 mL)。在120℃加熱反應混合物3 h，其後其變成凝膠。將反應混合物用DMF稀釋，過濾且藉由製備型RP-HPLC純化，得到110-1 (24 mg，0.080 mmol，24%產率)。RT：0.73 min；MS (ESI) m/z：292.1 $(M+H)^+$；方法A。

[0232] 針對實例110之程序：實例110係根據針對實例108所描述之方法，採用110-1，由107-3製備。^1H NMR (500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.93 (d, J=7.0 Hz, 1H), 8.88 (s, 1H), 8.58 (d, J=2.4 Hz, 1H), 8.20 (dd, J=6.4, 2.1 Hz, 1H), 8.12 (dd, J=8.7, 2.3 Hz, 1H), 7.81 (br dd, J=8.4, 4.1 Hz, 1H), 7.48 (t, J=9.8 Hz, 1H), 7.37 (d, J=8.9 Hz, 1H), 4.41 - 4.35 (m, 1H), 4.31 (q, J=7.0 Hz, 2H), 4.08 (s, 3H), 3.12 (br dd, J=10.7, 4.0 Hz, 1H), 3.07 - 3.02 (m, 1H), 2.98 - 2.93 (m, 1H), 1.86 - 1.79 (m, 1H), 1.78 - 1.69 (m, 7H), 1.38 - 1.33 (m, 2H), 1.31 (t, J=7.0 Hz, 3H)。LC-MS RT: 2.61 min；MS (ESI) m/z：630.5 $(M+H)^+$；方法B。

【0233】

實例113

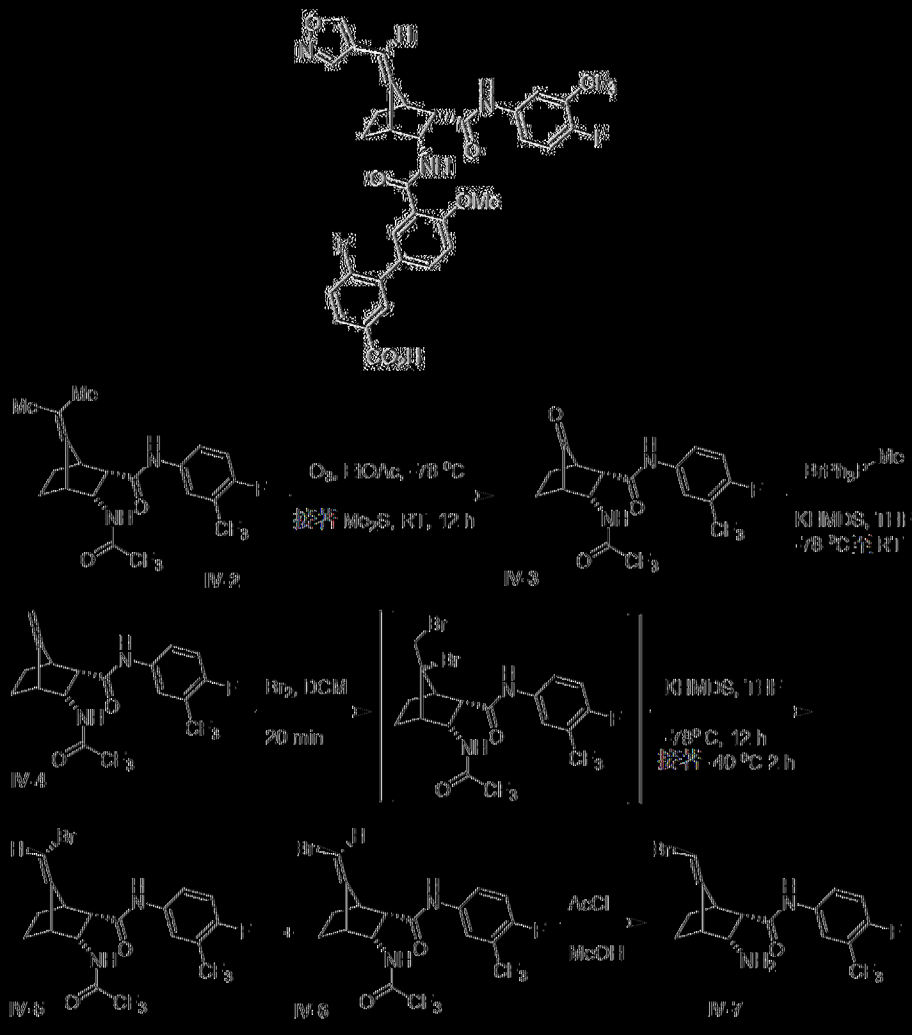


針對**實例113**之程序：向含有**實例110** (11.5 mg，0.02 mmol)於THF (180 µl)/水(90 µl)/MeOH (90 µl)中之小瓶中添加1.5 M氫氧化鋰溶液(61 µl，0.09 mmol)，且在23℃攪拌反應物5 min。藉由添加1N HCl (1 mL)淬滅反應混合物且用EtOAc (3×5 mL)萃取。將合併之有機物經Na_2SO_4乾燥且在減壓下濃縮。經由製備型RP-HPLC純化所得粗產物，得到**實例113** (6.3 mg，0.01 mmol，56%產率)。^{1}H NMR (500 MHz, DMSO-d6) δ 10.57 (s, 1H), 9.93 (d, J=7.3 Hz, 1H), 8.57 (s, 1H), 8.54 (d, J=2.1 Hz, 1H), 8.18 (dd, J=6.1, 2.1 Hz, 1H), 8.10 (dd, J=8.7, 2.3 Hz, 1H), 7.79 (dd, J=8.1, 3.8 Hz, 1H), 7.46 (t, J=9.8 Hz, 1H), 7.35 (d, J=8.9 Hz, 1H), 4.41 - 4.30 (m, 1H), 4.06 (s, 3H), 3.10 (dd, J=10.7, 4.0 Hz, 1H), 3.05 - 2.99 (m, 1H), 2.98 - 2.91 (m, 1H), 1.81 (t, J=8.7 Hz, 1H), 1.76 - 1.65 (m, 7H), 1.41 - 1.28 (m, 2H)。LC-MS RT: 1.92 min；MS (ESI) m/z = 601.9 (M+H)+；方法B。

【0234】 針對**實例114**之程序：**實例114**係根據針對**實例108**所描述之方法，採用5-氰基-2-氟苯甲酸，由**14-3**製備。^{1}H NMR. LC-MS RT: 2.53 min；MS (ESI) m/z = 504.1 (M+H)+；方法C。

【0235】

實例120



中間物IV-3：中間物IV-3係以如針對5-6所描述之相同方式由IV-2製備。(101 g，0.240 mmol，97.0%產率)。^{1}H NMR (500 MHz, $CDCl_3$) δ 9.61 (br d, J = 6.3 Hz, 1H), 7.76 (dd, J = 5.9, 2.6 Hz, 1H), 7.71 (d1, J = 8.9, 3.4 Hz, 1H), 7.66 (s, 1H), 7.23 (t, J = 9.4 Hz, 1H), 4.70 (d1, J = 10.3, 5.3 Hz, 1H), 3.33 (dd, J = 10.5, 4.4 Hz, 1H), 2.54 (t, J = 4.3 Hz, 1H), 2.42 (t, J = 4.1 Hz, 1H), 2.20 – 2.10 (m, 1H), 2.06 – 1.99 (m, 1H), 1.96 – 1.81 (m, 2H)。

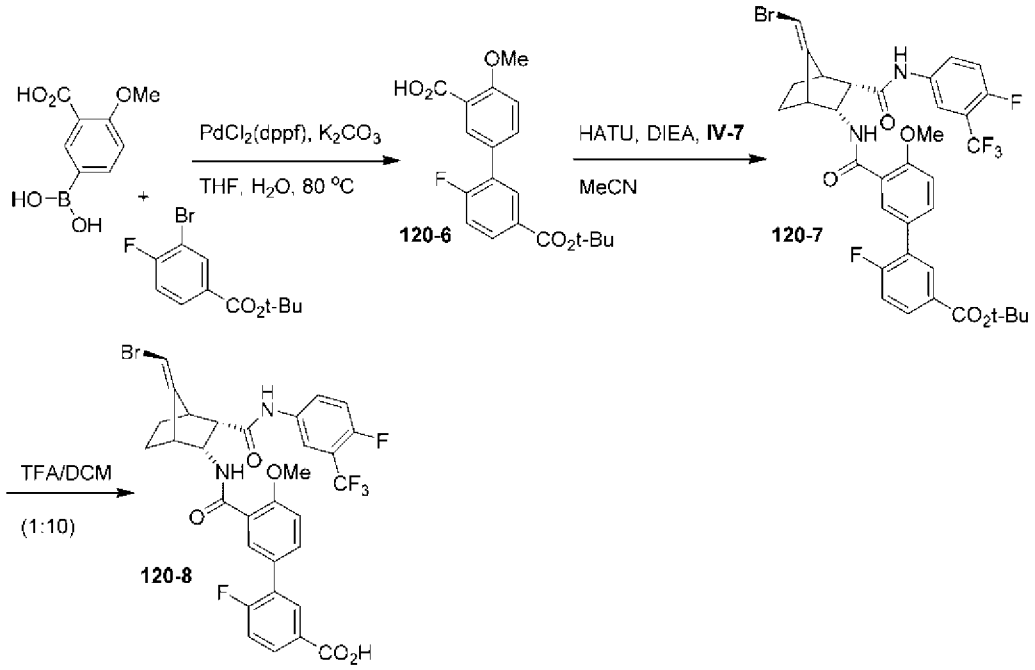
[0236] 中間物IV-4：向反應容器中添加溴(甲基)三苯基磷烷(419 mg，1.17 mmol)(藉由研磨市售材料之精細粉末)及THF (7 mL)。使反應混合物冷卻至-78℃且添加KHMDS (1.2 mL，1.17 mmol)。在-78℃劇烈

攪拌此反應混合物30 min且在-78℃添加**IV-3** (100 mg，0.240 mmol)。在-78℃再攪拌10 min之後，使反應混合物升溫至23℃且攪拌1.5 h。使反應混合物冷卻至-40℃且藉由添加飽和$NaHCO_3$淬滅。用EtOAc萃取溶液。將有機相經Na_2SO_4乾燥，過濾，在減壓下濃縮，且經由矽膠層析純化，得到**IV-4** (71 mg，0.17 mmol，71%產率)。LCMS RT = 1.16 min；(M+H) = 425.0；方法A。

【0237】 中間物**IV-5**及**IV-6**：向反應容器中添加**IV-4** (71 mg，0.17 mmol)、DCM (3 mL)及Br_2 (0.03 mL，0.6 mmol)。在23℃攪拌反應混合物20 min且在減壓下用飽和$Na_2S_2O_3$捕獲劑濃縮以淬滅過量Br_2。將所得二溴化物溶解於THF (3 mL)中。在將燒瓶冷卻至-78℃之後，添加KHMDS (1.0 mL，1.0 mmol)。使反應混合物在-78℃保持12 h且在-40℃保持2 h，隨後藉由在-40℃添加飽和$NaHCO_3$淬滅。用EtOAc萃取所得溶液。收集有機相，經Na_2SO_4乾燥，過濾，在減壓下濃縮，且經由矽膠層析純化，得到**IV-6** (27 mg，0.050 mmol，32%產率) (Z-異構物，峰2。LCMS RT = 1.19 min；(M+H) = 504.9；方法A，及相對應的*E*-異構物**IV-5** (28 mg，0.060 mmol，33%產率) (峰1)。**IV-6**係如上文所概述以外消旋物形式產生且使用對掌性SFC分離成個別鏡像異構物。製備型層析條件：儀器：Thar 350 SFC；管柱：Chiralcel OD-H，5×50 cm，5微米；移動相：20% MeOH/80% CO_2；流動條件：340 mL/min，100巴，35℃；偵測器波長：220 nm；注射詳情：3.75 mL 30 mg/mL於MeOH中。峰1，RT = 7.81 min，>99% ee；峰2，RT = 10.97 min，>99% ee。收集中間物**IV-6**產物峰#1 (1.9公克)且繼續使用以產生對掌性**IV-7**。

【0238】 中間物**IV-7**：向反應物中添加MeOH (3 mL)及AcCl (0.3

mL，4.2 mmol)。在攪拌5 min之後，添加對掌性**IV-6** (來自對掌性SFC之第1溶離峰，75 mg，0.15 mmol)且在40℃攪拌反應混合物48 h。在減壓下濃縮所得溶液，得到**IV-7** (67 mg，0.16 mmol，100%)，其不經進一步純化即使用。LC-MS RT = 0.78 min；(M+H) = 408.9；方法A。



【0239】 中間物**120-6**：向小瓶中添加5-溴-2-甲氧基苯甲酸(500 mg，2.55 mmol)、3-溴-4-氟苯甲酸三級丁酯(842 mg，3.06 mmol)、3-溴-4-氟苯甲酸三級丁酯(842 mg，3.06 mmol)、K_2CO_3 (1.76 g，12.8 mmol)、$PdCl_2$(dppf)-CH_2Cl_2加合物(313 mg，0.380 mmol)及THF (22.3 mL)。將反應混合物用氮氣脫氣2 min，接著在80℃加熱18 h。冷卻至室溫之後，用1N HCl (25 mL)稀釋反應混合物且用EtOAc (3×25 mL)萃取溶液。將合併之有機部分經Na_2SO_4乾燥，過濾，在減壓下濃縮，且將所得殘餘物溶解於DMF中且藉由製備型RP-HPLC純化，得到**120-6** (586 mg，1.69 mmol，66.0%產率)。LC-MS RT = 1.02 min；(M+H) = 347.1；方法A。

【0240】 可用替代性芳基鹵化物進行鈴木反應，且以與聯芳基類似

物產生類似之方式進行其餘步驟。

【0241】 中間物**120-7**：在反應容器中添加**IV-7** (7 mg，0.02 mmol)及**120-6** (6.6 mg，0.020 mmol)、MeCN (1 mL)、DIEA (9.64 uL、0.0600 mmol)及HATU (12.0 mg，0.0300 mmol)。將反應混合物在23℃攪拌3 h，在減壓下濃縮且經由矽膠層析純化，得到**120-7** (10 mg，0.014 mmol，86%產率)。LC-MS RT = 1.33 min；(M+H) = 735.2；方法A。

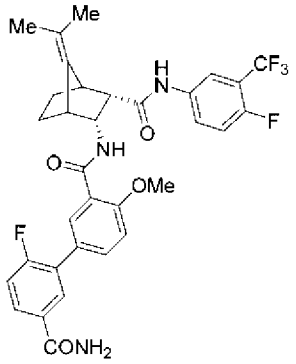
【0242】 中間物**120-8**：中間物**120-8**係以與中間物**34-2**相同之方式由**120-7**製備(5 mg，0.07 mmol，100%產率)。LC-MS RT = 1.15 min；(M+H) = 679.08；方法A。

【0243】 針對**實例120**之程序：向含有**120-8** (10 mg，0.01 mmol)之反應容器中添加4-(4,4,5,5-四甲基-1,3,2-二氧雜硼雜環戊-2-基)異喔唑(13.3 mg，0.07 mmol)、$PdCl_2$(dppf)-CH_2Cl_2加合物(3 mg，0.004 mmol，小刮勺尖端)及Na_2CO_3 (0.5 mL，1.0 mmol)。藉由使N_2鼓泡使反應混合物脫氣10 min，密封，且在60℃攪拌2 h。在冷卻至23℃之後，在減壓下濃縮反應混合物且經由製備型RP-HPLC純化，得到中間物三級丁酯。用10:1 DCM/TFA處理酯，隨後藉由逆相HPLC純化，得到**實例120** (7.0 mg，0.01 mmol，72%產率)。^{1}H NMR (500 MHz, $CDCl_3$) δ 10.03 (br d, J=6.3 Hz, 1H), 8.50 (br s, 1H), 8.43 (br s, 1H), 8.31 (br s, 1H), 8.21 (br d, J=5.2 Hz, 1H), 8.10 - 7.91 (m, 3H), 7.73 (br d, J=8.3 Hz, 1H), 7.53 (br d, J=3.9 Hz, 1H), 7.27 - 7.19 (m, 1H), 7.19 - 7.08 (m, 2H), 6.06 (s, 1H), 4.86 (br s, 1H), 4.11 (br s, 3H), 3.31 (br s, 1H), 3.22 (br d, J=7.2 Hz, 1H), 2.93 (br s, 1H), 2.37 - 2.25 (m, 1H), 2.03 (br d, J=11.8 Hz, 1H), 1.75 - 1.65 (m, 2H)。LC-MS RT: 1.14 min；MS (ESI) m/z = 668.3 (M+H)+；

方法A。

【0244】

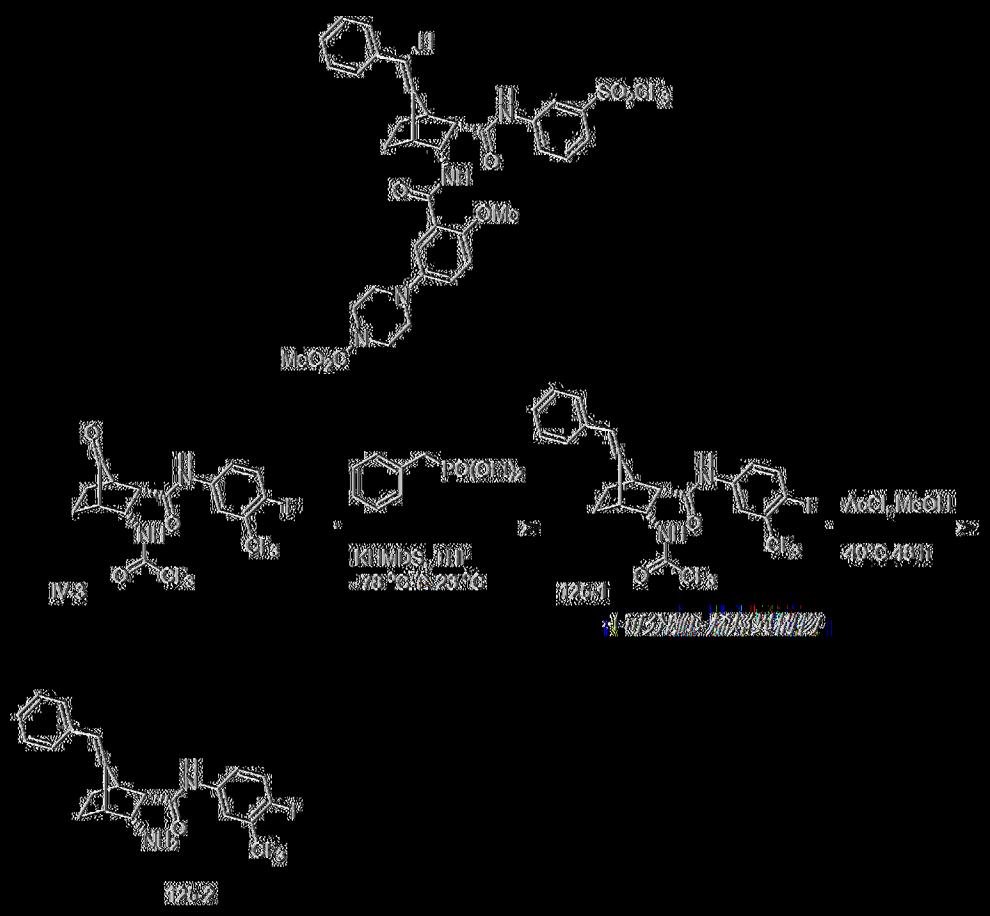
實例121



針對**實例121**之程序：向反應容器中添加**實例87** (3 mg，4.77 μmol)、乙磺醯胺(1.6 mg，0.01 mmol)、MeCN (1 mL)、DIEA (3 μl，0.017 mmol)及BOP-Cl (4 mg，0.01 mmol)。將反應物在40℃攪拌12 h，在減壓下濃縮且經由製備型RP-HPLC純化，以僅產生初級醯胺副**產物121** (3.0 mg，0.0040 mmol，93%產率)。^{1}H NMR (500 MHz, $CDCl_3$) δ 9.65 (br d, J=8.0 Hz, 1H), 8.41 (d, J=2.2 Hz, 1H), 7.96 (dd, J=7.2, 2.2 Hz, 2H), 7.90 - 7.83 (m, 2H), 7.73 (dt, J=8.5, 2.2 Hz, 1H), 7.56 (dt, J=8.7, 3.5 Hz, 1H), 7.25 (dd, J=9.9, 8.8 Hz, 1H), 7.16 - 7.06 (m, 2H), 6.69 - 6.68 (m, 1H), 4.72 (br t, J=11.0 Hz, 1H), 4.08 (s, 3H), 3.06 (br d, J=8.8 Hz, 3H), 2.21 - 2.14 (m, 1H), 1.84 (br t, J=8.7 Hz, 1H), 1.76 (s, 3H), 1.75 (s, 3H), 1.64 - 1.54 (m, 2H)。LC-MS RT: 1.26 min；MS (ESI) m/z = 628.3 (M+H)+；方法A。

【0245】

實例125



中間物125-1：中間物125-1係以與實例5相同之方式由IV-3製備且經由矽膠層析純化(49 mg，0.10 mmol，30%產率)。RT：1.23 min；MS (ESI) m/z：501.1 (M+H)+；方法A。

[0246] 中間物125-2：中間物125-2係以與中間物IV-7相同之方式由125-1製備(73 mg，0.18 mmol，96%產率)。RT：0.87 min；MS (ESI) m/z：405.1 (M+H)+；方法A。



[0247] 中間物125-3：向反應容器中添加哌啶-1-甲酸甲酯(103

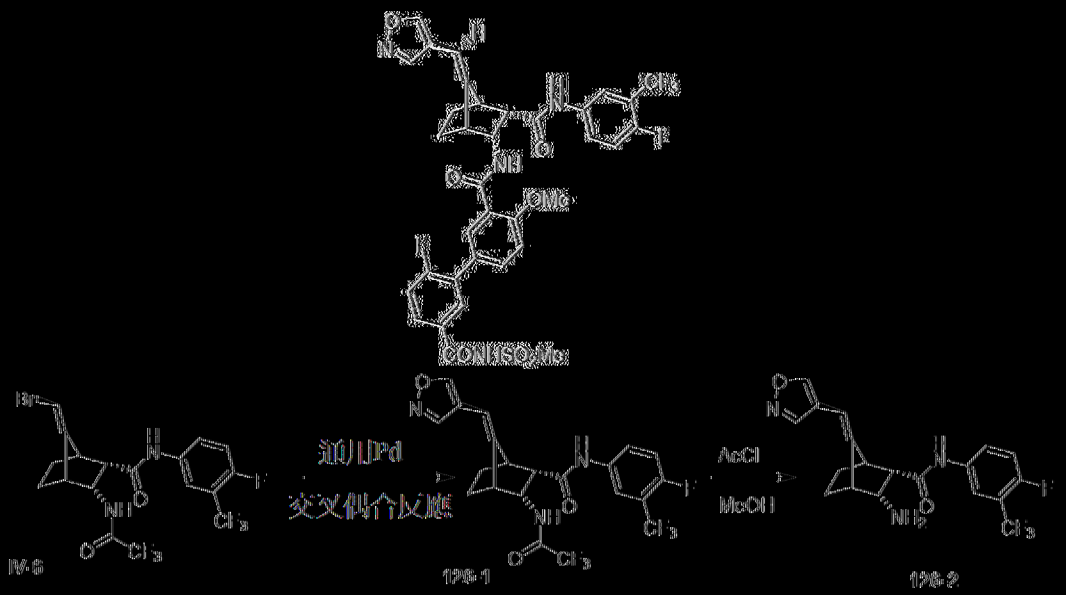
mg，0.710 mmol)、DCE (1 mL)、MeCN (1 mL)、乙酸銅(II) (130 mg，0.71 mmol)、(4-甲氧基-3-(甲氧基羰基)苯基)酮酸(50 mg，0.24 mmol)及4Å分子篩(300 mg)。將反應混合物在23℃攪拌12 h (露天)，過濾，在減壓下濃縮且經由製備型RP-HPLC純化，得到125-3 (37 mg，0.12 mmol，50%產率)。LC-MS RT = 0.72 min；MS (ESI) m/z = 309.1 $(M+H)^+$；方法A。

【0248】 中間物**125-4**：向反應容器中添加**125-3** (37 mg, 0.12 mmol)、THF (1 mL)、水(0.5 mL)及單水合氫氧化鋰(34.4 mg, 0.820 mmol)。將反應混合物在23℃攪拌2.5 h，用EtOAc (10 mL)稀釋且用10 mL含有0.82 mmol HCl之飽和NH_4Cl洗滌。將有機相經Na_2SO_4乾燥且在減壓下濃縮，得到**125-4** (35.3 mg，0.120 mmol，100%產率)，其不經進一步純化即使用。LC-MS RT = 0.62 min；MS (ESI) m/z = 295.0 $(M+H)^+$；方法A。

【0249】 針對**實例125**之程序：**實例125**係根據針對**實例108**所描述之方法，採用**125-4**，由**125-2**製備。^1H NMR (500 MHz, $CDCl_3$) δ 9.63 (br d, J=7.7 Hz, 1H), 7.96 - 7.84 (m, 3H), 7.59 (dt, J=8.8, 3.4 Hz, 1H), 7.33 (d, J=4.1 Hz, 4H), 7.29 (dd, J=8.9, 3.2 Hz, 1H), 7.25 - 7.20 (m, 1H), 7.10 (t, J=9.4 Hz, 1H), 6.95 (d, J=9.1 Hz, 1H), 6.33 (s, 1H), 4.89 - 4.80 (m, 1H), 3.99 (s, 3H), 3.75 (s, 3H), 3.74 - 3.69 (m, 4H), 3.49 (t, J=3.3 Hz, 1H), 3.23 - 3.14 (m, 5H), 2.89 (m, 1H), 2.27 - 2.19 (m, 1H), 1.97 - 1.87 (m, 1H), 1.75 - 1.66 (m, 2H)。LC-MS RT: 1.16 min；MS (ESI) m/z = 681.3 (M+H)+；方法A。

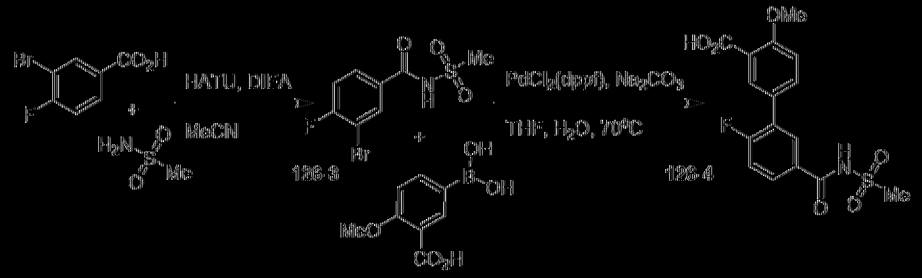
【0250】

實例126



中間物126-1：向含有IV-6 (125 mg，0.25 mmol)之反應容器中添加4-(4,4,5,5-四甲基-1,3,2-二氧雜硼雜環戊-2-基)異噁唑(125 mg，0.610 mmol)、$PdCl_2(dppf)\cdot CH_2Cl_2$加合物(50.7 mg，0.0620 mmol)及Na_2CO_3 (1.5 mL，3.0 mmol)。藉由使氮氣鼓泡使反應混合物脫氣3 min，密封，且在60℃攪拌2 h。在冷卻至23℃之後，用EtOAc萃取反應混合物，將合併之有機部分經Na_2SO_4乾燥，過濾，在減壓下濃縮，且經由矽膠層析純化，得到126-1 (101 mg，0.210 mmol，83.0%產率)。LC-MS RT = 1.07 min；MS (ESI) m/z = 492.1 $(M+H)^+$；方法A。

[0251] 中間物126-2：中間物126-2係以與中間物IV-7相同之方式由126-1製備(67 mg，0.16 mmol，100%產率)。RT = 0.76 min；MS (ESI) m/z = 396.0 $(M+H)^+$；方法A。



[0252] 中間物126-3：向反應容器中添加甲磺醯胺(521 mg，5.48

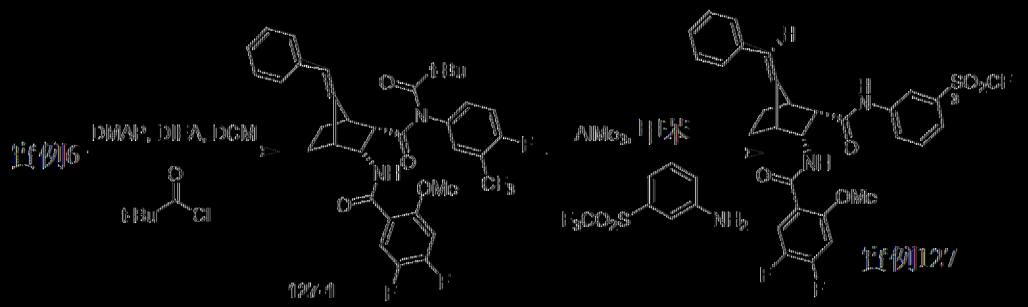
mmol)、3-溴-4-氟苯甲酸(400 mg，1.83 mmol)、MeCN (3.7 mL)、DIEA (1.1 mL，6.40 mmol)及HATU (833 mg，2.19 mmol)。將反應混合物在40℃攪拌12 h，使其冷卻，在減壓下濃縮，且進行製備型RP-HPLC純化，得到**126-3** (450 mg，1.52 mmol，83%產率)。LC-MS RT = 0.76 min；(M+H) = 297.7；方法A

【0253】 中間物**126-4**：向含有**126-3** (200 mg，0.68 mmol)之反應容器中添加5-溴-2-甲氧基苯甲酸(199 mg，1.01 mmol)、$PdCl_2$(dppf)-CH_2Cl_2加合物(83 mg，0.10 mmol)、THF (6.7 mL)及1 M Na_2CO_3 (4.0 mL，4.1 mmol)。藉由使氮氣鼓泡使反應混合物脫氣10 min，密封，且在70℃攪拌2 h。在冷卻至23℃之後，在減壓下濃縮反應混合物且經由製備型RP-HPLC純化，得到**126-4** (158 mg，0.430 mmol，64.0%產率)。LC-MS RT = 0.70 min；MS (ESI) m/z = 368.1 (M+H)+；方法A。

【0254】 針對**實例126**之程序：**實例126**係根據針對**實例108**所描述之方法，採用**126-4**，由**126-2**製備。^{1}H NMR (500 MHz, $CDCl_3$) δ 10.32 (br s, 1H), 9.86 (br d, J=7.7 Hz, 1H), 8.41 (s, 1H), 8.34 (s, 1H), 8.25 (d, J=1.7 Hz, 1H), 8.10 (br s, 1H), 8.04 (dd, J=6.1, 2.5 Hz, 1H), 7.98 (dd, J=7.3, 2.1 Hz, 1H), 7.89 (ddd, J=8.5, 4.5, 2.2 Hz, 1H), 7.68 (br d, J=8.8 Hz, 1H), 7.58 (dt, J=8.6, 3.5 Hz, 1H), 7.19 - 7.06 (m, 3H), 5.95 (s, 1H), 4.72 - 4.63 (m, 1H), 4.08 (s, 3H), 3.45 (s, 3H), 3.25 - 3.20 (m, 1H), 3.15 (dd, J=10.7, 4.1 Hz, 1H), 2.89 - 2.84 (m, 1H), 2.28 - 2.23 (m, 1H), 2.01 - 1.96 (m, 1H), 1.71 - 1.62 (m, 2H)。LC-MS RT: 1.09 min；MS (ESI) m/z = 745.2 (M+H)+；方法A。

【0255】

實例127

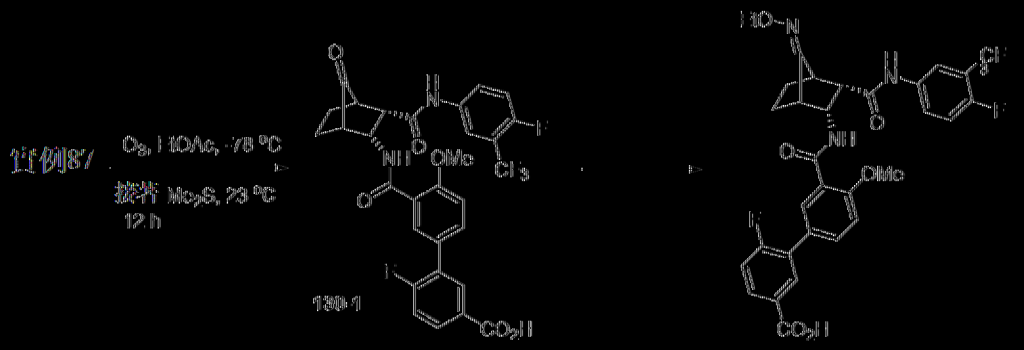


中間物127-1：向反應容器中添加實例6 (10 mg，0.017 mmol)、DCM (1 mL)、DIEA (0.015 mL，0.087 mmol)及DMAP (1.06 mg，8.70 μmol)。在23℃攪拌12 h之後，經由矽膠層析純化殘餘物，得到127-1 (10.5 mg，0.0160 mmol，92.0%產率)。LC-MS RT：1.31 min；MS (ESI) m/z：659.3 (M+H)+；方法A。

[0256] 針對實例127之程序：向反應容器中添加3-((二氟甲基)磺醯基)苯胺(24 mg，0.11 mmol)、甲苯(0.5 mL)及三甲基鋁(0.05 mL，0.11 mmol)。在23℃攪拌15 min之後，添加含中間物127-1 (5 mg，7.6 μmol)之甲苯(0.5 mL)。將反應物在23℃攪拌1 h，用飽和羅謝鹽淬滅且用EtOAc萃取。將有機相經Na_2SO_4乾燥，濃縮且經由製備型RP-HPLC純化，得到實例127 (3.6 mg，5.80 μmol，76%產率)。^{1}H NMR (500 MHz, $CDCl_3$) δ 9.56 (br d, J=7.7 Hz, 1H), 8.56 - 8.47 (m, 1H), 8.06 - 7.98 (m, 2H), 7.78 - 7.71 (m, 2H), 7.58 (t, J=8.0 Hz, 1H), 7.37 - 7.30 (m, 4H), 7.25 - 7.21 (m, 1H), 6.79 (dd, J=11.7, 6.2 Hz, 1H), 6.33 (s, 1H), 4.88 - 4.81 (m, 1H), 4.03 (s, 3H), 3.52 - 3.47 (m, 1H), 3.20 (dd, J=10.7, 3.9 Hz, 1H), 2.91 - 2.87 (m, 1H), 2.26 - 2.18 (m, 1H), 1.95 - 1.88 (m, 1H), 1.74 - 1.70 (m, 2H)。LC-MS RT: 1.25 min；MS (ESI) m/z：621.2 (M+H)+；方法A。

[0257]

實例130

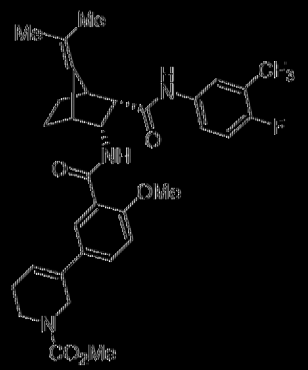


中間物130-1：中間物130-1係以與如針對77-1所描述之相同方式由實例87製備(19 mg，0.030 mmol，100%產率)。LC-MS RT：1.06 min；MS (ESI) m/z：603.1 $(M+H)^+$；方法A。

[0258] 針對實例130之程序：向含有130-1 (17 mg，0.03 mmol)之反應容器中添加DCE (1.5 mL)、DIEA (0.09 mL，0.51 mmol)及O-乙基羥胺HCl (41.3 mg，0.42 mmol)。將混合物在23℃攪拌24 h，在減壓下濃縮，且進行製備型RP-HPLC純化，得到呈Z/E異構物之混合物形式之實例130 (15 mg，0.023 mmol，82%產率)。LC-MS RT: 1.13 min；MS (ESI) m/z：464.2 $(M+H)^+$；方法A。

[0259]

實例134

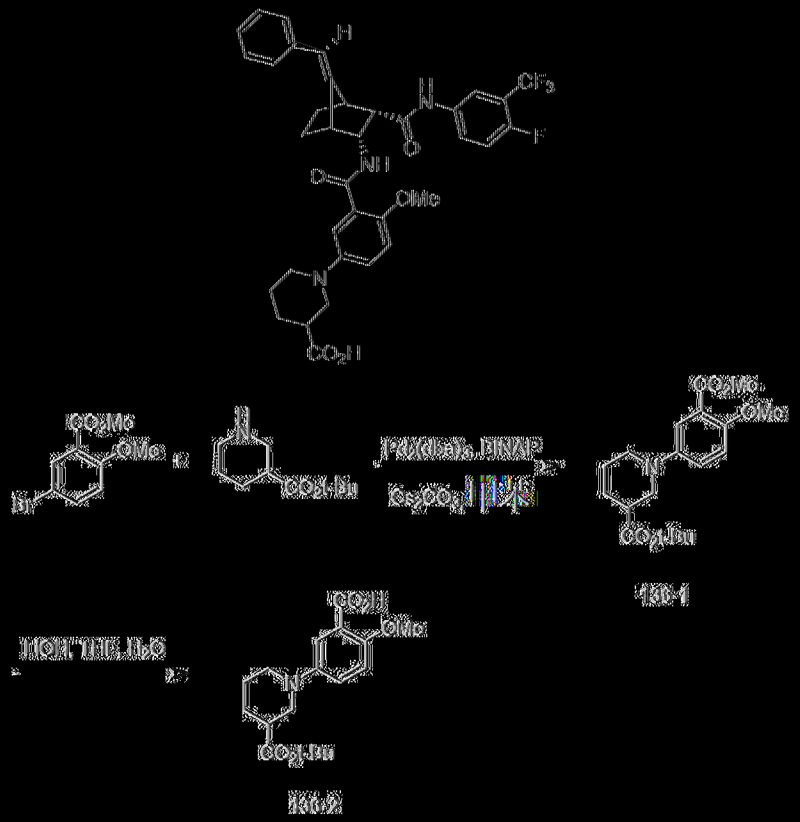


針對實例134之程序：向反應容器中添加實例140 (6 mg，10 μmol)、DCM (1 mL)、DIEA (6 μl，0.03 mmol)及氫甲酸甲酯(2 μl，0.02

mmol)。在23℃攪拌30 min之後，在減壓下濃縮反應混合物且經由製備型RP-HPLC純化，得到實例134 (3.5 mg，5.4 μmol，51%產率)。^{1}H NMR (500 MHz, $CDCl_3$) δ 9.42 - 9.17 (m, 1H), 8.25 - 8.02 (m, 2H), 7.87 (dd, J = 6.1, 2.4 Hz, 1H), 7.62 - 7.53 (m, 1H), 7.43 (br s, 1H), 7.07 (t, J = 9.5 Hz, 1H), 6.92 (br d, J = 8.6 Hz, 1H), 6.17 (br s, 1H), 4.78 - 4.66 (m, 1H), 4.38 - 4.23 (m, 2H), 3.98 (s, 3H), 3.75 (s, 3H), 3.66 - 3.52 (m, 2H), 3.08 - 2.97 (m, 3H), 2.37 - 2.26 (m, 2H), 2.23 - 2.11 (m, 1H), 1.83 - 1.75 (m, 1H), 1.74 - 1.72 (m, 3H), 1.72 (s, 3H), 1.62 - 1.53 (m, 2H)。LC-MS RT: 1.25 min；MS (ESI) m/z = 630.3 (M+H)+；方法B。

|(0260)|

實例136



中間物136-1：向反應容器中添加5-溴-2-甲氧基苯甲酸甲酯(33.1 mg，0.135 mmol)、哌啶-3-甲酸三級丁酯(25 mg，0.14 mmol)、甲苯(1

mL)、哌啶-3-甲酸三級丁酯(25 mg，0.14 mmol)、BINAP (10.5 mg，0.0200 mmol)及$Pd_2(dba)_3$ (6 mg，0.01 mmol)。將反應混合物用氮氣脫氣3 min且在100℃攪拌12 h，使其冷卻至23℃，用EtOAc稀釋，且用飽和$NaHCO_3$ (2×10 mL)洗滌溶液。將有機層經Na_2SO_4乾燥，過濾，在減壓下濃縮，且經由製備型RP-HPLC純化，得到**136-1** (39 mg，0.084 mmol，62%產率)。LC-MS RT = 0.82 min；MS (ESI) m/z = 350.1 $(M+H)^+$；方法A。

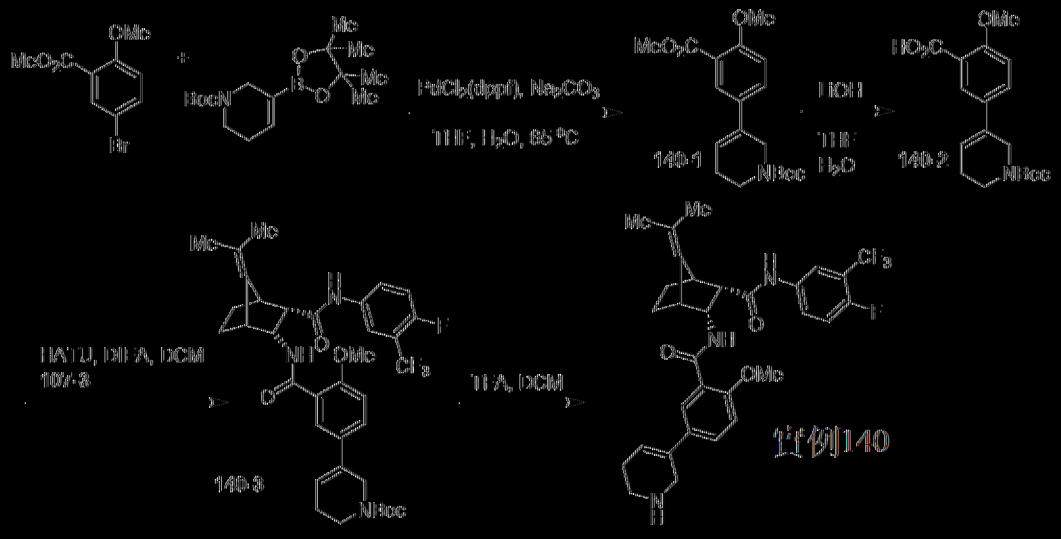
【0261】 中間物**136-2**：向反應容器中添加**136-1** (26 mg，0.060 mmol)、THF (1 mL)、水(0.5 mL)及單水合氫氧化鋰(19.1 mg，0.460 mmol)。將反應混合物在23℃攪拌3 h，用EtOAc (10 mL)稀釋且用10 mL含有0.5 mmol HCl之飽和NH_4Cl洗滌。將有機相經Na_2SO_4乾燥且在減壓下濃縮，得到**136-2** (19 mg，0.060 mmol，100%產率)，其不經進一步純化即使用。LC-MS RT = 0.74 min；MS (ESI) m/z = 336.1 $(M+H)^+$；方法A。

【0262】 針對**實例136**之程序：**實例136**係根據針對**實例108**所描述之方法，採用外消旋**136-2**，由**125-2**製備。與製備**實例120**之程序中一樣實現三級丁酯之後續移除。經由SFC層析將**實例136** (峰1)與其非鏡像異構物(峰2)**實例138**分離。峰1，RT = 8.80 min，>99.5% ee；峰2，RT = 9.97 min，> 99.5% ee。製備型層析條件：儀器：Berger MG II；管柱：Chiralpak IA，30×250 mm，5微米；移動相：25% EtOH / 75% CO_2；流動條件：70 mL/min，150巴，40℃；偵測器波長：220 nm；注射詳情：0.5 mL ~3 mg/mL於CAN中。分析型層析條件：儀器：Berger Analytical SFC；管柱：Chiralpak IA，4.6×250 mm，5微米；移動相：25% EtOH /

75% CO_2；流動條件：2.0 mL/min，150巴，40℃；偵測器波長：220 nm；注射詳情：10 μL濃縮樣本於EtOH中。LC-MS RT: 1.07 min；MS (ESI) m/z：666.3 $(M+H)^+$；方法A。

[0263]

實例140



中間物140-1：向含有5-溴-2-甲氧基苯甲酸甲酯(47.6 mg，0.190 mmol)之反應容器中添加3-(4,4,5,5-四甲基-1,3,2-二氧雜硼雜環戊-2-基)-5,6-二氫吡啶-1(2H)-甲酸三級丁酯(50 mg，0.16 mmol)、$PdCl_2(dppf)$-CH_2Cl_2加合物(19.8 mg，0.0240 mmol)及Na_2CO_3 (1 mL，2 mmol)。藉由使氮氣鼓泡使反應混合物脫氣3 min，密封，且在65℃攪拌2 h。在冷卻至23℃之後，用EtOAc萃取反應混合物。將有機相經Na_2SO_4乾燥，過濾，在減壓下濃縮，且經由矽膠層析純化，得到140-1 (57.4 mg，0.17 mmol，100%產率)。LC-MS RT：1.04 min；MS (ESI) m/z：348.0 $(M+H)^+$；方法A。

[0264] 中間物140-2：向反應容器中添加140-1 (28 mg，0.081 mmol)、THF (1 mL)、水(0.5 mL)及單水合氫氧化鋰(16.9 mg，0.400 mmol)。將反應混合物在23℃攪拌1 h，用EtOAc (10 mL)稀釋且用10 mL

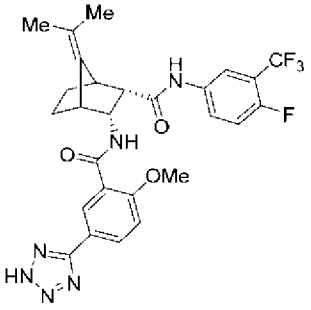
含有0.5 mmol HCl之飽和NH_4Cl洗滌所得溶液。將有機相經Na_2SO_4乾燥且在減壓下濃縮，得到**140-2** (25 mg，0.080 mmol，93%產率)，其不經進一步純化即使用。

【0265】 中間物**140-3**：中間物**140-3**係使用實例**108**中所採用之通用醯胺偶合程序，由**140-2**及**107-3**製備(67 mg，0.16 mmol，100%產率)。RT = 1.32 min；MS (ESI) m/z = 672.3 $(M+H)^+$；方法A。

【0266】 針對**實例140**之程序：向反應容器中添加**140-3** (11.4 mg，0.02 mmol)、DCM (1 mL)及TFA (0.1 mL，1.30 mmol)。在23℃攪拌3 h之後，在減壓下濃縮反應內容物，得到**實例140** (3.7 mg，5.13 μmol，30%產率)。^1H NMR (500 MHz, $CDCl_3$) δ 9.29 (br d, J=7.9 Hz, 1H), 8.59 (br s, 1H), 8.08 (d, J=2.3 Hz, 1H), 7.94 (br d, J=4.5 Hz, 1H), 7.67 - 7.57 (m, 1H), 7.18 (br d, J=8.3 Hz, 1H), 7.06 (t, J=9.4 Hz, 1H), 6.82 (d, J=8.6 Hz, 1H), 6.16 (br s, 1H), 4.75 - 4.60 (m, 1H), 3.97 (s, 3H), 3.79 - 3.59 (m, 2H), 3.20 - 3.12 (m, 1H), 3.11 - 3.05 (m, 2H), 3.04 - 3.00 (m, 1H), 2.98 - 2.95 (m, 1H), 2.46 - 2.34 (m, 2H), 2.22 (br t, J=8.7 Hz, 1H), 1.77 (br t, J=8.7 Hz, 1H), 1.72 (s, 3H), 1.71 (s, 3H), 1.60 - 1.53 (m, 2H)。LC-MS RT: 0.98 min；MS (ESI) m/z = 572.4 (M+H)+；方法B。

【0267】

實例144

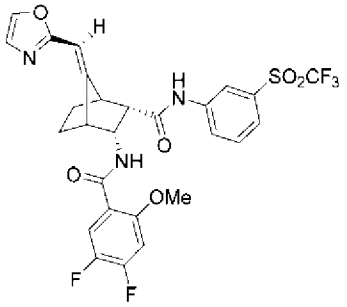


針對**實例144**之程序：向反應容器中添加**實例114** (3.4 mg，6.6

μmol)、疊氮化鈉(12.9 mg，0.198 mmol)、氯化銨(10.6 mg，0.198 mmol)及DMF。在105℃攪拌反應混合物4 h，使其冷卻至23℃，用MeOH稀釋，過濾，且經由製備型RP-HPLC純化，得到**實例144** (2.3 mg，4.0 μmol，60%產率)。^{1}H NMR (500 MHz, $CDCl_3$) δ 10.01 (d, J=9.4 Hz, 1H), 9.30 (d, J=2.5 Hz, 1H), 8.51 (dd, J=8.8, 2.5 Hz, 1H), 8.44 (s, 1H), 8.11 (dd, J=6.3, 2.8 Hz, 1H), 7.41 (dt, J=8.7, 3.3 Hz, 1H), 7.25 - 7.22 (m, 1H), 7.08 - 6.99 (m, 1H), 4.96 (td, J=9.8, 4.3 Hz, 1H), 4.21 (s, 3H), 3.31 (dd, J=10.7, 3.9 Hz, 1H), 3.04 (t, J=3.7 Hz, 1H), 2.88 (t, J=4.0 Hz, 1H), 2.51 - 2.44 (m, 1H), 1.87 - 1.80 (m, 2H), 1.67 (s, 3H), 1.60 - 1.50 (m, 2H), 1.48 (s, 3H)。LC-MS RT: 1.11 min；MS (ESI) m/z = 559.1 (M+H)+；方法A。

【0268】

實例145

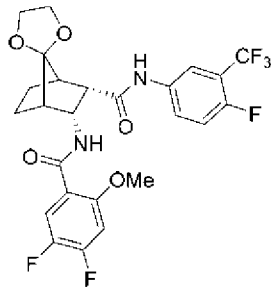


針對**實例145**之程序：**實例145**係採用2-甲基噁唑，由**5-6**製備。向反應容器中添加2-甲基噁唑(24.9 mg，0.300 mmol)及THF (1 mL)。在使反應混合物冷卻至-78℃之後，添加KHMDS (0.30 mL，0.30 mmol)。在-78℃攪拌混合物10 min且再添加2-甲基噁唑(24.9 mg，0.300 mmol)。使混合物升溫至23℃，在23℃攪拌3 h，且藉由添加飽和Na_2CO_3淬滅。將有機相經Na_2SO_4乾燥，過濾，濃縮，且經由矽膠層析純化，得到中間物醇(17 mg，0.029 mmol，97%產率)。根據**實例33**中所描述之方法使中間物醇脫水。^{1}H NMR (500 MHz, $CDCl_3$) δ 9.53 (br d, J=7.4 Hz, 1H), 8.06 -

7.99 (m, 2H), 7.97 (dd, J=6.2, 2.6 Hz, 1H), 7.63 (s, 1H), 7.53 (dt, J=8.9, 3.4 Hz, 1H), 7.18 - 7.09 (m, 2H), 6.80 (dd, J=11.6, 6.1 Hz, 1H), 6.28 (s, 1H), 4.88 - 4.80 (m, 1H), 4.00 (s, 3H), 3.93 (t, J=4.0 Hz, 1H), 3.19 (dd, J=10.9, 3.7 Hz, 1H), 2.99 - 2.92 (m, 1H), 2.35 - 2.27 (m, 1H), 2.02 - 1.94 (m, 1H), 1.78 - 1.71 (m, 2H)。LC-MS RT: 1.17 min；MS (ESI) m/z = 566.0 (M+H)+；方法A。

【0269】

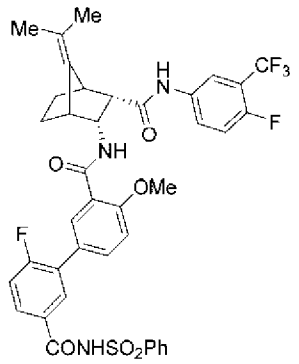
實例147



針對**實例147**之程序：向反應容器中添加**5-6** (10 mg，0.020 mmol)、苯(1 mL)、乙烷-1,2-二醇(24.81 mg，0.4000 mmol)、$MgSO_4$ (200 mg，1.66 mmol)及pTsOH單水合物(3.8 mg，0.020 mmol)。在50℃攪拌12 h之後，過濾反應混合物，在減壓下濃縮且經由製備型RP-HPLC純化，得到**實例147** (2.1 mg，3.8 μmol，19%產率)。^{1}H NMR (500 MHz, $CDCl_3$) δ 9.35 (br d, J=7.8 Hz, 1H), 8.04 (dd, J=11.4, 9.4 Hz, 1H), 7.93 (dd, J=6.3, 2.6 Hz, 1H), 7.77 (s, 1H), 7.52 (dt, J=8.7, 3.6 Hz, 1H), 7.12 (t, J=9.4 Hz, 1H), 6.79 (dd, J=11.6, 6.1 Hz, 1H), 5.05 - 4.97 (m, 1H), 4.08 - 4.01 (m, 4H), 3.99 (s, 3H), 3.49 - 3.41 (m, 1H), 2.23 (t, J=4.0 Hz, 1H), 2.20 - 2.11 (m, 2H), 1.93 - 1.81 (m, 2H), 1.75 - 1.67 (m, 1H)。LC-MS RT: 1.14 min；MS (ESI) m/z = 545.1 (M+H)+；方法C。

【0270】

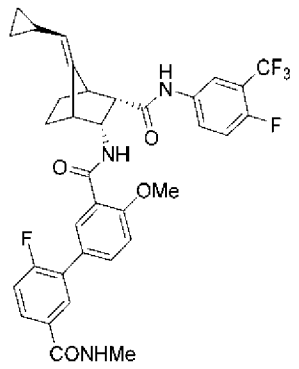
實例150



針對**實例150**之程序：向反應容器中添加**實例87** (5 mg，8 μmol)、苯磺醯胺(3.8 mg，0.020 mmol)、MeCN (1 mL)、DIEA (5 μl，0.03 mmol)及BOP-Cl (6.0 mg，0.024 mmol)。將反應混合物在40℃攪拌12 h，在減壓下濃縮且經由製備型RP-HPLC純化，得到**實例150** (2.2 mg，2.7 μmol，34%產率)。^{1}H NMR (500 MHz, $CDCl_3$) δ 9.65 (br d, J=8.0 Hz, 1H), 8.41 (d, J=2.2 Hz, 1H), 7.96 (dd, J=7.2, 2.2 Hz, 2H), 7.90 - 7.84 (m, 2H), 7.73 (dt, J=8.5, 2.2 Hz, 1H), 7.56 (dt, J=8.7, 3.5 Hz, 1H), 7.25 (dd, J=9.9, 8.8 Hz, 1H), 7.16 - 7.03 (m, 2H), 4.75 - 4.68 (m, 1H), 4.08 (s, 3H), 3.06 (br d, J=8.8 Hz, 3H), 2.21 - 2.14 (m, 1H), 1.87 - 1.81 (m, 1H), 1.76 (s, 3H), 1.75 (s, 3H), 1.63 - 1.56 (m, 2H)。LC-MS RT: 1.4 min；MS (ESI) m/z = 768.2 (M+H)+；方法C。

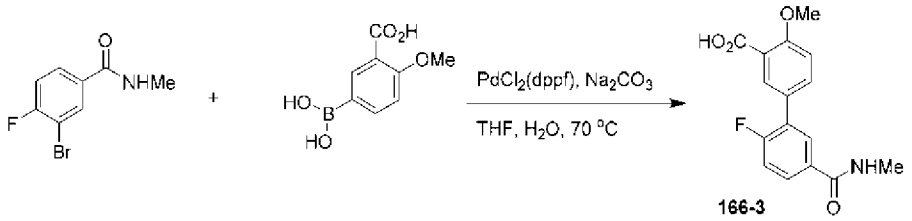
【0271】

實例166



中間物**166-1**：中間物**166-1**係以與中間物**126-1**相同之方式由**IV-6**製備(5.1 mg，0.010 mmol，23%產率)。RT = 1.21 min；MS (ESI) m/z = 465.1 $(M+H)^+$；方法A。

【0272】 中間物**166-2**：中間物**166-2**係以與中間物**IV-7**相同之方式由**166-1**製備(4.0 mg，0.010 mmol，100%產率)。RT = 0.84 min；MS (ESI) m/z = 369.1 $(M+H)^+$；方法A。



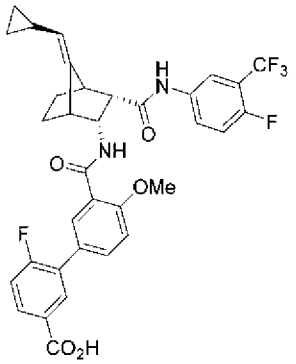
【0273】 中間物**166-3**：中間物**166-3**係以與中間物**140-1**相同之方式，由3-溴-4-氟-N-甲基苯甲醯胺及5-溴-2-甲氧基苯甲酸製備(28 mg，0.080 mmol，41%產率)。LC-MS RT = 0.99 min；MS (ESI) m/z = 304.9 $(M+H)^+$；方法A。

【0274】 針對**實例166**之程序：**實例166**係根據針對**實例108**所描述之方法，採用**166-3**，由**166-2**製備。^{1}H NMR (500 MHz, $CDCl_3$) δ 9.73 (br d, J=7.7 Hz, 1H), 8.39 (d, J=1.9 Hz, 1H), 7.97 (dd, J=6.2, 2.3 Hz, 1H), 7.90 (s, 1H), 7.85 (dd, J=7.4, 2.2 Hz, 1H), 7.81 (ddd, J=8.5, 4.7, 2.2 Hz, 1H), 7.72 (dt, J=8.8, 2.2 Hz, 1H), 7.56 (dt, J=8.7, 3.4 Hz, 1H), 7.24 - 7.19 (m, 1H), 7.15 - 7.10 (m, 1H), 7.08 (d, J=8.8 Hz, 1H), 6.47 (br s, 1H), 4.85 - 4.76 (m, 1H), 4.66 (d, J=9.6 Hz, 1H), 4.09 (s, 3H), 3.22 (t, J=3.7 Hz, 1H), 3.10 (dd, J=10.7, 3.3 Hz, 1H), 3.05 (d, J=4.7 Hz, 3H), 2.77 - 2.67 (m, 1H), 2.19 - 2.12 (m, 1H), 1.94 - 1.86 (m, 1H), 1.71 - 1.61 (m, 2H),

1.53 - 1.46 (m, 1H), 0.81 - 0.71 (m, 2H), 0.41 - 0.30 (m, 2H)。LC-MS RT: 1.18 min；MS (ESI) m/z = 654.2 (M+H)+；方法A。

【0275】

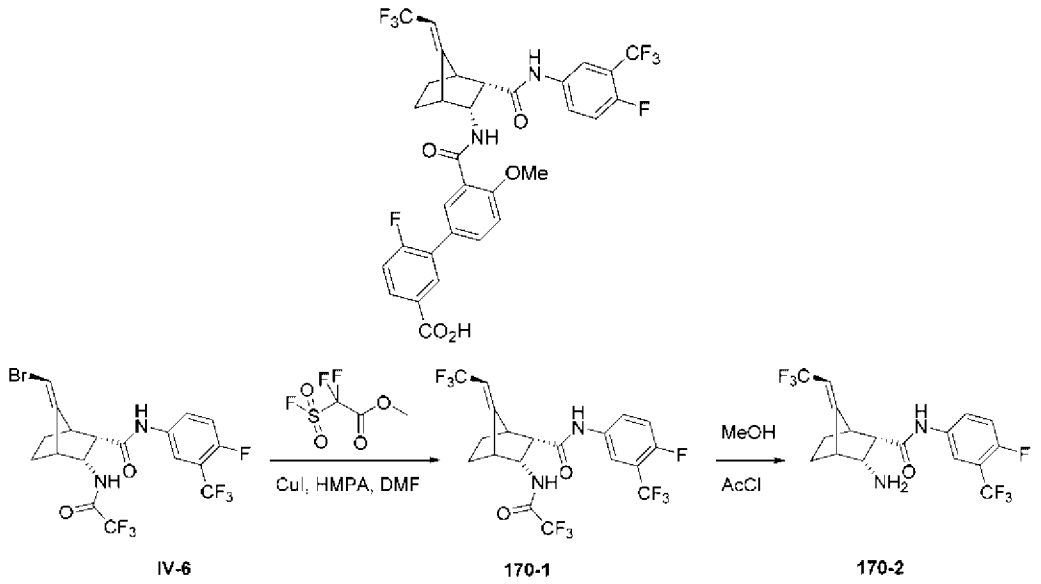
實例168



針對**實例168**之程序：**實例168**係根據針對**實例108**所描述之方法，採用**120-6**，由**166-2**製備。在DCM (1 mL)中實現三級丁酯之裂解且在23℃與$ZnBr_2$ (20 equiv.)一起攪拌12 h。在藉由添加HCl (1.0 M)淬滅反應物且用乙酸乙酯萃取所得溶液之後，將有機相經Na_2SO_4乾燥，過濾，在減壓下濃縮，且經由製備型RP-HPLC純化殘餘物，得到**實例168**。**實例168**之分析資料：^{1}H NMR (500 MHz, $CDCl_3$) δ 9.42 (br d, J=7.7 Hz, 1H), 8.43 (br s, 1H), 8.30 - 8.21 (m, 1H), 8.12 - 8.02 (m, 1H), 7.96 (br s, 2H), 7.71 (dt, J=8.7, 2.0 Hz, 1H), 7.54 - 7.47 (m, 1H), 7.26 - 7.21 (m, 1H), 7.13 - 7.06 (m, 2H), 4.95 - 4.85 (m, 1H), 4.66 (d, J=9.6 Hz, 1H), 4.07 (s, 3H), 3.27 - 3.19 (m, 1H), 3.14 (br dd, J=10.9, 3.2 Hz, 1H), 2.75 (t, J=3.9 Hz, 1H), 2.32 - 2.23 (m, 1H), 1.94 - 1.87 (m, 1H), 1.74 - 1.63 (m, 2H), 1.54 - 1.48 (m, 1H), 0.76 (m, 2H), 0.36 (m, 2H)。LC-MS RT: 1.19 min；MS (ESI) m/z = 641.1 (M+H)+；方法A。

【0276】

實例170



中間物**170-1**：在氮氣氛圍下，在75℃經由注射器向裝有含2,2-二氟-2-(氟磺醯基)乙酸甲酯(體積?，0.15 mmol)之無水DMF (0.5 mL)的20 mL小瓶中逐滴添加**IV-6**及CuI (質量?，0.07 mmol)於無水DMF (1 mL)及HMPA (0.5 mL)中之懸浮液持續30 min。在相同溫度下攪拌所得混合物12 h。使反應混合物冷卻且經由HPLC過濾器過濾且藉由RP-HPLC純化，得到**170-1** (24 mg，81%產率)。^{1}H NMR (500 MHz, $CDCl_3$) δ 9.38 (br d, J=6.1 Hz, 1H), 7.77 - 7.69 (m, 2H), 7.46 (s, 1H), 7.24 (t, J=9.1 Hz, 1H), 5.62 (q, J=7.2 Hz, 1H), 4.50 (dt, J=10.5, 5.3 Hz, 1H), 3.50 - 3.42 (m, 1H), 3.13 - 3.04 (m, 1H), 2.89 (t, J=4.0 Hz, 1H), 2.02 - 1.90 (m, 2H), 1.76 - 1.60 (m, 2H)。

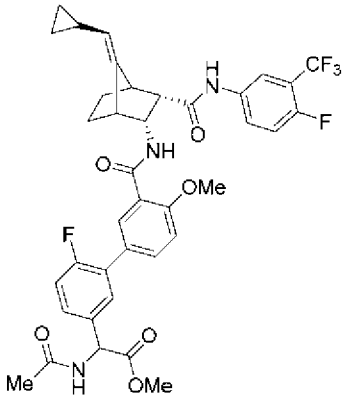
【0277】 中間物**170-2**：中間物**170-2**係由**170-1**製備。將MeOH (1.5 mL)及乙醯氯(2.1 mmol)裝入2打蘭小瓶中且在23℃攪拌5 min。向反應小瓶中添加**170-1**且將內容物加熱至40℃持續24 h。用氮氣流濃縮反應混合物，得到呈HCl鹽形式之**170-2**，其不經進一步純化即使用。LC-MS RT = 0.75 min；MS (ESI) m/z = 397.1 $(M+H)^+$；方法A。

【0278】 針對**實例170**之程序：**實例170**係根據針對**實例120**所描述

之方法，採用**120-6**，由**170-2**製備。**實例170**之分析資料：^{1}H NMR (500 MHz, $CDCl_3$) δ 9.28 (br d, J=6.6 Hz, 1H), 8.41 (br s, 1H), 8.37 (br s, 1H), 8.27 (br d, J=6.1 Hz, 1H), 8.08 (br s, 1H), 7.92 (br s, 1H), 7.80 - 7.70 (m, 1H), 7.47 (dt, J=8.6, 3.7 Hz, 1H), 7.27 - 7.20 (m, 1H), 7.13 - 7.02 (m, 2H), 5.60 (q, J=7.3 Hz, 1H), 5.05 - 4.92 (m, 1H), 4.06 (s, 3H), 3.42 (br s, 1H), 3.25 (br dd, J=10.6, 3.4 Hz, 1H), 2.95 (t, J=4.0 Hz, 1H), 2.61 - 2.50 (m, 1H), 2.05 - 1.97 (m, 1H), 1.82 - 1.72 (m, 2H)。LC-MS RT: 1.15 min；MS (ESI) m/z = 669.2 (M+H)+；方法A。

【0279】

實例171

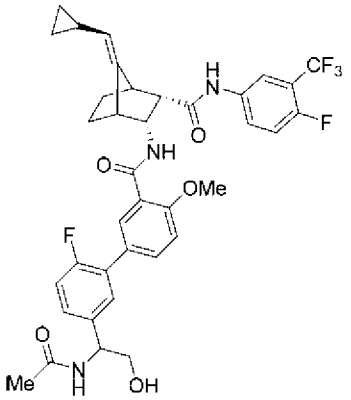


針對**實例171**之程序：**實例171**係由**實例186**製備。向裝有**實例186** (0.008 mmol)、DCM (0.3 mL)及MeOH (0.1 mL)之1打蘭小瓶中添加TMS-重氮甲烷(0.5 M於DCM中，0.34 mL，0.17 mmol，20 equiv.)，且在23℃攪拌反應混合物1 h。在減壓下濃縮反應混合物且經由矽膠正相層析純化，得到6.1 mg實例**171**。**實例171**之分析資料：^{1}H NMR (500 MHz, $CDCl_3$) δ 9.45 (br d, J=8.0 Hz, 1H), 8.38 - 8.35 (m, 1H), 8.00 - 7.92 (m, 2H), 7.64 (dt, J=8.7, 2.0 Hz, 1H), 7.54 (dt, J=8.7, 3.5 Hz, 1H), 7.43 (dd, J=7.3, 2.3 Hz, 1H), 7.32 (ddd, J=8.4, 4.5, 2.5 Hz, 1H), 7.17 - 7.03 (m,

3H), 6.59 (br d, J=6.9 Hz, 1H), 5.61 (d, J=6.9 Hz, 1H), 4.89 - 4.81 (m, 1H), 4.65 (d, J=9.6 Hz, 1H), 4.06 (s, 3H), 3.77 (s, 3H), 3.21 (t, J=4.1 Hz, 1H), 3.15 - 3.08 (m, 1H), 2.73 (t, J=4.0 Hz, 1H), 2.24 - 2.16 (m, 1H), 2.08 (s, 3H), 1.95 - 1.86 (m, 1H), 1.72 - 1.63 (m, 2H), 1.54 - 1.45 (m, 1H), 0.79 - 0.72 (m, 2H), 0.39 - 0.32 (m, 2H)。LC-MS RT: 1.15 min；MS (ESI) m/z = 726.3 (M+H)+；方法A。

【0280】

實例172

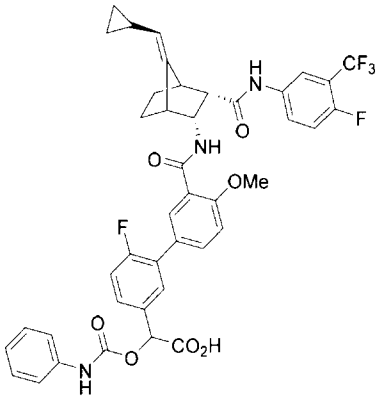


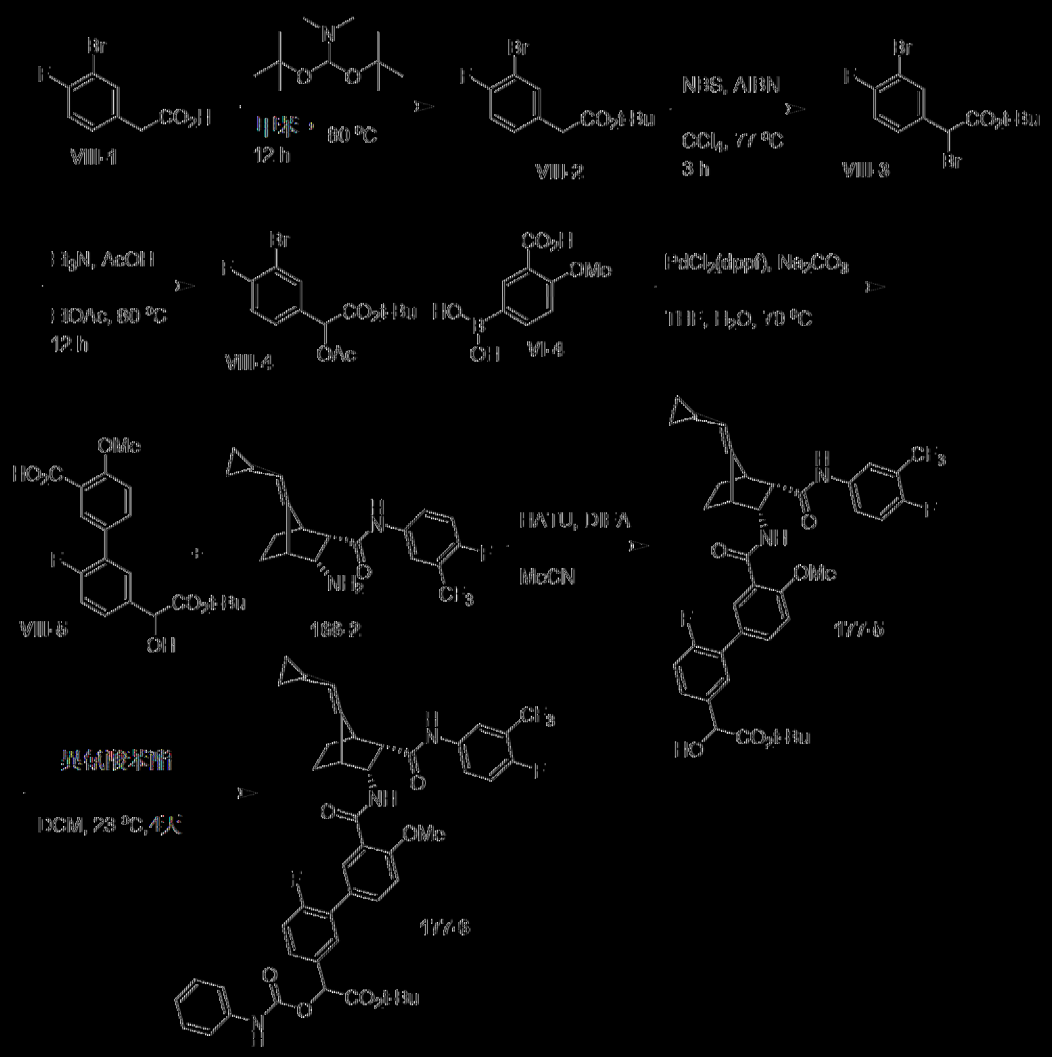
針對**實例172**之程序：**實例172**係由**實例171**製備。向裝有**實例171** (0.009 mmol)及THF (0.5 mL)之經冰浴冷卻之1打蘭小瓶中添加$LiBH_4$ (0.027 mmol，3.0 quiv.)。在0℃攪拌反應混合物5 min，且隨後升溫至23℃且再攪拌30 min 用乙酸乙酯(10 mL)稀釋反應混合物。用飽和氯化銨水溶液(20 mL)洗滌溶液。用EtOAc萃取水相，將合併之有機部分經Na_2SO_4乾燥，過濾且在減壓下濃縮，且經由製備型RP-HPLC純化殘餘物，得到**實例172**。**實例172**之分析資料：^{1}H NMR (500 MHz, $CDCl_3$) δ 9.54 (d, J=8.0 Hz, 1H), 8.29 (d, J=1.7 Hz, 1H), 8.21 (s, 1H), 7.96 (dd, J=6.1, 2.5 Hz, 1H), 7.57 - 7.47 (m, 2H), 7.32 - 7.29 (m, 1H), 7.23 (ddd, J=8.3, 4.6, 2.5 Hz, 1H), 7.12 - 7.00 (m, 3H), 6.45 (br d, J=6.9 Hz, 1H),

5.10 - 5.03 (m, 1H), 4.85 - 4.76 (m, 1H), 4.62 (d, J=9.4 Hz, 1H), 4.08 (s, 3H), 3.93 - 3.86 (m, 2H), 3.18 (t, J=4.1 Hz, 1H), 3.13 - 3.06 (m, 1H), 2.71 (t, J=4.0 Hz, 1H), 2.26 - 2.18 (m, 1H), 2.08 (s, 3H), 1.95 - 1.87 (m, 1H), 1.70 - 1.62 (m, 2H), 1.51 - 1.43 (m, 1H), 0.77 - 0.72 (m, 2H), 0.37 - 0.30 (m, 2H)。LC-MS RT: 1.08 min；MS (ESI) m/z = 698.4 (M+H)+；方法A。

【0281】

實例177





中間物VIII-2：除了將反應溫度維持在80℃持續12 h之外，間物VIII-2係採用關於類似受質之已知條件(Ludwig, J.；Lehr, M. Syn. Comm. 2004, 34, 3691–3695)製備。^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (dd, J = 6.6, 2.2 Hz, 1H), 7.20 (ddd, J = 8.3, 4.6, 2.2 Hz, 1H), 7.13 – 7.03 (m, 1H), 3.49 (s, 2H), 1.46 (s, 9H)。

[0282] 中間物VIII-3：向裝有中間物VIII-2 (266 mg，0.920 mmol)之20 mL反應小瓶中添加NBS (196 mg，1.10 mmol)、四氯化碳(10 mL)及AIBN (15 mg，0.090 mmol)。在77℃攪拌溶液3 h 在減壓下濃縮溶液且藉由正相矽膠層析純化，得到中間物VIII-3 (308 mg，0.840 mmol，91.0%產率)。

【0283】 中間物**VIII-4**：向裝有中間物**VIII-3**之2打蘭小瓶中添加乙酸乙酯(2 mL)、三乙胺(0.27 mL，2.0 mmol)及乙酸(0.1 mL，2 mmol)。在80℃攪拌反應混合物12 h。在減壓下濃縮反應混合物且藉由正相矽膠層析純化，得到中間物**VIII-4**。^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (dd, J=6.6, 2.2 Hz, 1H), 7.41 (ddd, J=8.4, 4.7, 2.1 Hz, 1H), 7.15 (t, J=8.4 Hz, 1H), 5.77 (s, 1H), 2.22 (s, 3H), 1.43 (s, 9H)。

【0284】 中間物**VIII-5**：中間物**VIII-5**係以用於中間物**140-1**之相同條件，採用5-溴-2-甲氧基苯甲酸，由中間物**VIII-4**製備。分離出呈O-乙酸酯形式之一半物質(85 mg，0.60 mmol，34%)；^{1}H NMR (500 MHz, $CDCl_3$) δ 8.43 - 8.36 (m, 1H), 7.81 (dt, J=8.7, 2.0 Hz, 1H), 7.56 (dd, J=7.3, 2.3 Hz, 1H), 7.45 (ddd, J=8.5, 4.6, 2.3 Hz, 1H), 7.23 - 7.16 (m, 2H), 5.84 (s, 1H), 4.17 (s, 3H), 2.23 (s, 3H), 1.45 (s, 9H) 同時分離出呈游離醇形式之另一半(70 mg，0.19 mmol，31%)；^{1}H NMR (500 MHz, $CDCl_3$) δ 8.40 (d, *J*=2.2 Hz, 1H), 7.82 (dt, *J*=8.6, 2.2 Hz, 1H), 7.54 (dd, *J*=7.4, 2.5 Hz, 1H), 7.41 (ddd, *J*=8.4, 4.8, 2.2 Hz, 1H), 7.19 - 7.14 (m, 2H), 5.09 (s, 1H), 4.16 (s, 3H), 1.47 (s, 9H)。使用對掌性SFC將外消旋**VIII-5**分離成個別鏡像異構物。製備型層析條件：儀器：Berger MG II；管柱：Chiralpak ID，21×250 mm，5微米；移動相：25% IPA / 75% CO_2；流動條件：45 mL/min，120巴， 40℃；偵測器波長：220 nm；注射詳情：注射8次0.36 mL ~20 mg/mL於IPA中。分析型層析條件：儀器：Waters UPC2分析型SFC；管柱：Chiralpak ID 4.6×100 mm，3微米；移動相：25% IPA / 75% CO_2；流動條件：2 mL/min，150巴， 40℃；偵測器波長：220 nm。峰1，RT = 3.89 min，>99.5% ee；峰2，RT = 5.44 min，>99.5%

ee。收集中間物**VIII-5**產物峰#2且繼續使用以產生對掌性中間物**177-5**。

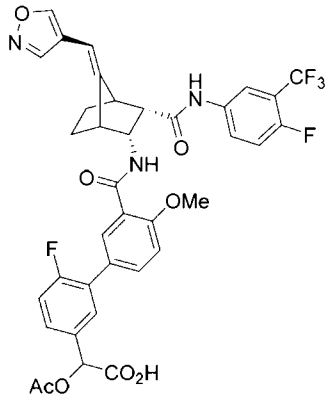
【0285】 中間物**177-5**：中間物**177-5**係根據針對**實例108**所描述之方法，由**VIII-5**峰2製備。中間物**177-5** (14.2 mg，0.0200 mmol，79.0%產率)。LC-MS RT = 1.22 min；MS (ESI) m/z = 727.1 $(M+H)^+$；方法A。

【0286】 中間物**177-6**：向裝有**177-5**之1打蘭小瓶中添加DCM (1 mL)及異氰酸苯酯(82 mg，0.69 mmol)。將溶液在23℃攪拌4天，在減壓下濃縮且藉由RP-HPLC純化，得到中間物**177-6** (6.2 mg，0.0070 mmol，53%產率)。

【0287】 針對**實例177**之程序：**實例177**係藉由採用針對**實例168**所描述之三級丁酯裂解方法，由**177-6**製備。**實例177**之分析資料：^{1}H NMR (500 MHz, $CDCl_3$) δ 9.74 (br d, J=8.0 Hz, 1H), 8.22 (d, J=2.2 Hz, 1H), 8.06 - 7.97 (m, 2H), 7.73 (br s, 1H), 7.65 (td, J=8.7, 2.1 Hz, 2H), 7.46 (dt, J=8.8, 3.4 Hz, 1H), 7.41 - 7.33 (m, 3H), 7.24 (t, J=7.8 Hz, 2H), 7.09 - 6.98 (m, 4H), 6.15 (s, 1H), 4.84 - 4.74 (m, 1H), 4.59 (d, J=9.6 Hz, 1H), 4.04 (s, 3H), 3.16 (t, J=4.0 Hz, 1H), 3.09 (br dd, J=10.6, 3.7 Hz, 1H), 2.67 (br t, J=3.7 Hz, 1H), 2.21 - 2.14 (m, 1H), 1.91 - 1.82 (m, 1H), 1.68 - 1.52 (m, 2H), 1.51 - 1.41 (m, 1H), 0.79 - 0.69 (m, 2H), 0.36 - 0.29 (m, 2H)。LC-MS RT: 1.26 min；MS (ESI) m/z = 790.4 (M+H)+；方法A。

【0288】

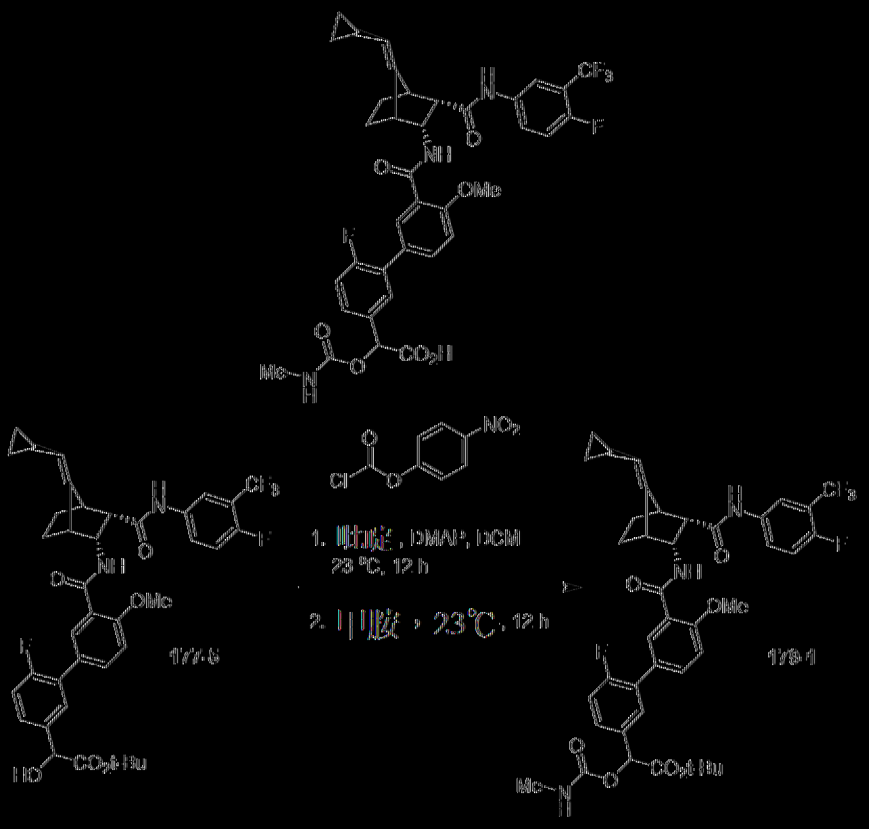
實例178



針對**實例178**之程序：**實例178**係由**34-1**製備。向裝有**34-1**、DCM (1.5 mL)及DIEA (0.12 mL，0.70 mmol，30 equiv.)之2打蘭小瓶中添加乙醯氯(0.03，0.5 mmol，20 equiv.)且在23℃攪拌1 h。藉由添加MeOH (1 mL)淬滅反應物且根據針對**實例168**所描述之方法移除三級丁酯。**實例178**之分析資料：^{1}H NMR (500 MHz, $CDCl_3$) δ 9.82 (d, J=8.3 Hz, 1H), 8.45 (s, 1H), 8.36 (s, 1H), 8.29 (s, 1H), 8.26 (d, J=2.5 Hz, 1H), 8.00 (dd, J=6.3, 2.5 Hz, 1H), 7.70 (dt, J=8.5, 2.2 Hz, 1H), 7.62 (dd, J=7.4, 2.2 Hz, 1H), 7.46 (ddd, J=8.5, 4.3, 2.6 Hz, 2H), 7.14 (dd, J=10.0, 8.7 Hz, 1H), 7.08 - 7.00 (m, 2H), 5.98 (s, 1H), 5.98 (s, 1H), 4.88 - 4.79 (m, 1H), 4.06 (s, 3H), 3.25 - 3.19 (m, 2H), 2.91 - 2.86 (m, 1H), 2.40 - 2.33 (m, 1H), 2.19 (s, 3H), 2.00 - 1.93 (m, 1H), 1.72 - 1.60 (m, 2H)。LC-MS RT: 1.11 min；MS (ESI) m/z = 740.1 (M+H)+；方法A。

【0289】

實例179



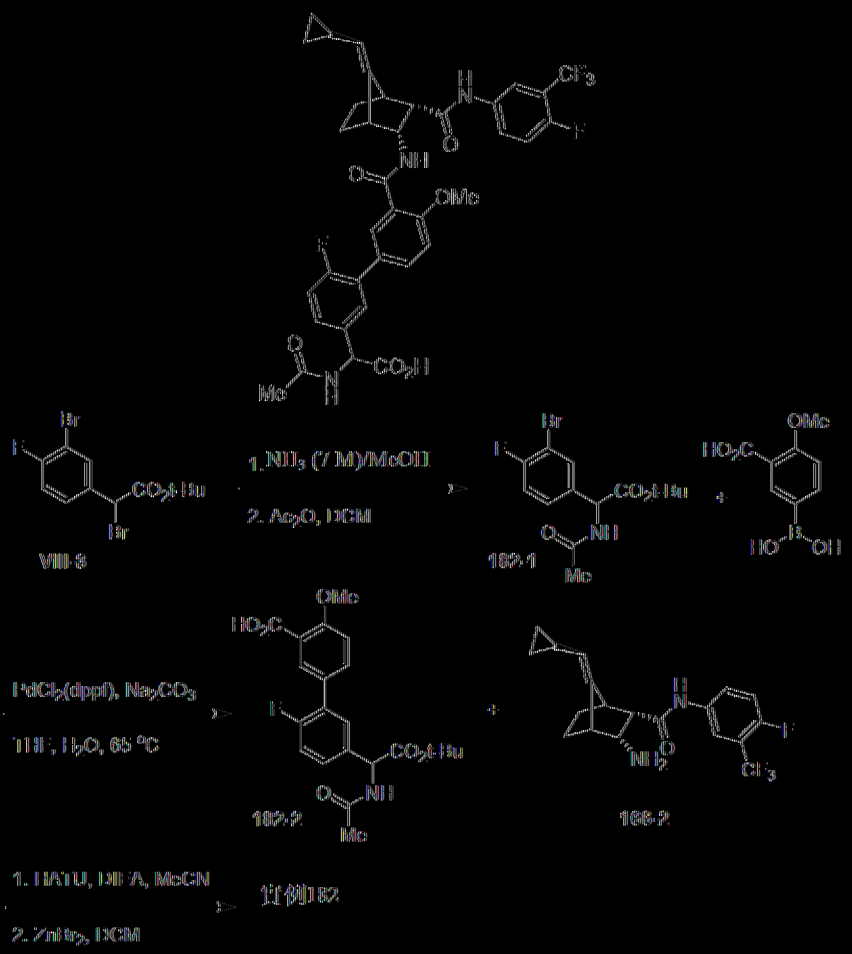
中間物179-1：向裝有177-5之20 mL小瓶中添加DCM (4 mL)、氯甲酸4-硝基苯酯(體積或質量，0.43 mmol)及DMAP (質量，0.04 mmol)。在23℃攪拌反應溶液12 h。添加甲胺(0.85 mmol)且再攪拌反應溶液1 h。在減壓下濃縮反應溶液且藉由RP-HPLC純化，得到中間物179-1 (65 mg，0.083 mmol，97%)。LC-MS RT = 1.24 min；MS (ESI) m/z = 784.4 (M+H)+；方法A。

[0290] 針對實例179之程序：實例179係根據如實例168中針對三級丁酯裂解所描述之方法由179-1製備。實例179之分析資料：^{1}H NMR (500 MHz, $CDCl_3$) δ 9.70 (br d, J = 8.0 Hz, 1H), 8.28 (d, J = 1.9 Hz, 1H), 8.19 (s, 1H), 8.01 (dd, J = 6.2, 2.6 Hz, 1H), 7.68 (dt, J = 8.6, 2.2 Hz, 1H), 7.60 (br d, J = 5.5 Hz, 1H), 7.52 – 7.45 (m, 1H), 7.45 – 7.37 (m, 1H), 7.15 – 7.00 (m, 3H), 6.05 (s, 1H), 5.38 – 5.28 (m, 1H), 4.82 – 4.75 (m, 1H), 4.60 (d, J = 9.4 Hz, 1H), 4.07 (s, 3H), 3.16 (t, J = 4.1 Hz, 1H), 3.10 (dd, J = 10.5,

3.3 Hz, 1H), 2.85 (br d, J = 3.3 Hz, 3H), 2.71 – 2.67 (m, 1H), 2.25 – 2.20 (m, 1H), 1.92 – 1.86 (m, 1H), 1.68 – 1.53 (m, 2H), 1.49 – 1.42 (m, 1H), 0.78 – 0.69 (m, 2H), 0.36 – 0.30 (m, 2H)。LC-MS RT: 1.13 min；MS (ESI) m/z = 728.3 (M+H)+；方法A。

[0291]

實例182



中間物182-1：向裝有中間物VIII-3之1打蘭小瓶中添加氨(0.5 mL，4 mmol，7 M於MeOH中)。在23℃攪拌溶液12 h。在減壓下濃縮溶液，用含乙酸酐(7.2 μL，0.076 mmol)之DCM (1 mL)處理殘餘物，在23℃攪拌1 h。藉由正相矽膠層析純化所得殘餘物，得到中間物182-1 (26 mg，0.074 mmol，97%產率)。LC-MS RT = 0.92 min；MS (ESI) m/z = 346.1 (M+H)+；方法A。

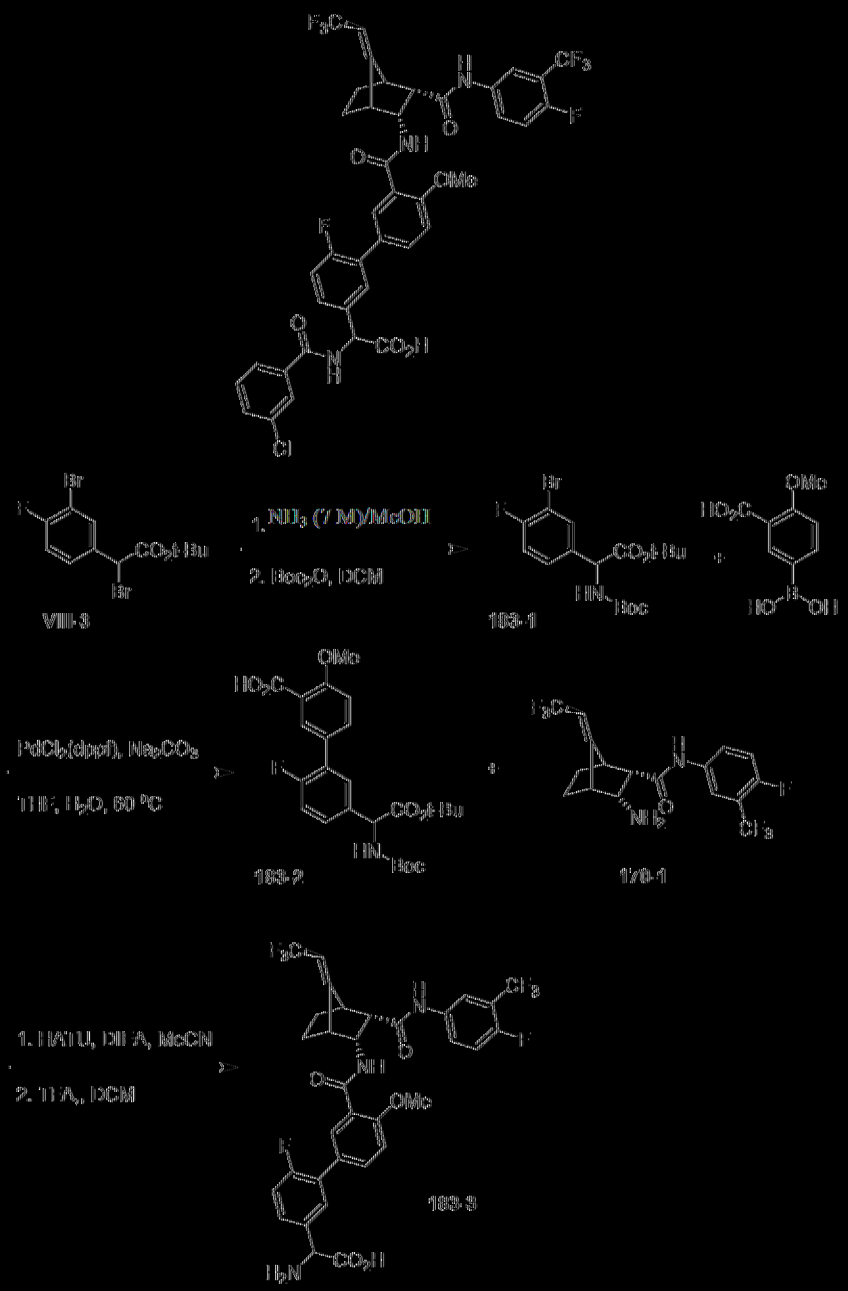
【0292】 中間物**182-2**：除了在65℃之溫度下持續18 h以外，中間物**182-2**係採用針對中間物**140-1**所描述之類似條件來製備。^{1}H NMR (500 MHz, CDCl3) δ 8.37 (d, J=1.9 Hz, 1H), 7.81 (dt, J=8.5, 2.1 Hz, 1H), 7.45 (dd, J=7.3, 2.3 Hz, 1H), 7.35 (ddd, J=8.5, 4.6, 2.3 Hz, 1H), 7.21 - 7.13 (m, 2H), 6.74 (br d, J=6.9 Hz, 1H), 5.51 (d, J=6.9 Hz, 1H), 4.17 (s, 3H), 2.12 (s, 3H), 1.45 (s, 9H)。外消旋**182-2**係使用對掌性SFC分離成其鏡像異構物。製備型層析條件：儀器：Berger MG II；管柱：Chiralpak ID，21×250 mm，5微米；移動相：20% IPA / 80% CO_2；流動條件：45 mL/min，120巴， 40℃；偵測器波長：215 nm；注射詳情：注射3次15 mg/mL於MeOH中。分析型層析條件：儀器：Aurora Infinity分析型SFC；管柱：Chiralpak AD-H，4.6×100 mm，3微米；移動相：20% IPA / 80% CO_2；流動條件：2 mL/min，150巴，40℃；偵測器波長：220 nm。峰1, RT = 3.49 min，>99.5% ee；峰2, RT = 4.43 min，>99.5% ee。收集中間物**182-2**產物峰#2且繼續使用以產生**實例182**。

【0293】 針對**實例182**之程序：**實例182**係根據針對**實例108**所描述之方法，採用**182-2** (峰2，異構物2)，由**166-2**製備。與製備**實例168**之程序中一樣實現三級丁酯之後續移除。**實例182** (異構物1)之分析資料：^{1}H NMR (500 MHz, $CDCl_3$) δ 10.14 (d, J=7.7 Hz, 1H), 8.72 (br d, J=9.1 Hz, 1H), 8.46 (d, J=2.5 Hz, 1H), 8.00 (dd, J=6.1, 2.8 Hz, 1H), 7.80 - 7.70 (m, 2H), 7.61 (s, 1H), 7.46 - 7.38 (m, 2H), 7.11 - 7.01 (m, 2H), 6.98 (d, J=8.8 Hz, 1H), 5.96 (d, J=9.1 Hz, 1H), 4.73 - 4.65 (m, 2H), 4.04 (s, 3H), 3.18 (br t, J=3.7 Hz, 1H), 3.03 (dd, J=10.6, 4.0 Hz, 1H), 2.69 (br t, J=3.7 Hz, 1H), 2.13 (s, 3H), 2.06 - 1.98 (m, 1H), 1.88 - 1.80 (m, 1H), 1.64 - 1.49

(m, 3H), 0.89 – 0.76 (m, 2H), 0.44 – 0.34 (m, 2H)。LC-MS RT: 1.11 min；MS (ESI) m/z = 712.2 (M+H)+；方法A。

[0294]

實例183



中間物183-1：中間物183-1係根據針對中間物182-1所描述之方法，用Boc_2O置換Ac_2O，由VIII-3來製備。LC-MS RT = 1.14 min；MS (ESI) m/z = 406.0 $(M+H)^+$；方法A。

【0295】 中間物**183-2**：除了在60℃之溫度下持續18 h以外，中間物**183-2**係採用用於中間物**140-1**之相同條件來製備。^{1}H NMR (500 MHz, $CDCl_3$) δ 8.38 (d, *J*=1.9 Hz, 1H), 7.80 (dt, *J*=8.7, 2.0 Hz, 1H), 7.46 (dd, *J*=7.4, 2.5 Hz, 1H), 7.36 (dddd, *J*=8.8, 4.4, 2.2, 1.1 Hz, 1H), 7.19 - 7.13 (m, 2H), 5.67 (br d, *J*=5.2 Hz, 1H), 5.25 (br d, *J*=6.3 Hz, 1H), 4.16 (s, 3H), 1.46 (br s, 9H), 1.44 (s, 9H)。使用對掌性SFC將外消旋**183-2**分離成個別鏡像異構物。製備型層析條件：儀器：Berger MG II；管柱：Chiralpak ID，21×250 mm，5微米；移動相：20% MeOH / 80% CO_2；流動條件：45 mL/min，120巴， 40℃；偵測器波長：209 nm；注射詳情：注射49次於MeOH中。分析型層析條件：儀器：Waters UPC2分析型SFC；管柱：Chiralpak IC，4.6×100 mm，3微米；移動相：25% MeOH / 75% CO_2；流動條件：2 mL/min，150巴， 40℃；偵測器波長：220 nm。峰1，RT = 4.22 min，95.7% ee；峰2，RT = 5.11 min，>99% ee。收集中間物**183-2**產物峰#2且繼續使用以產生中間物**183-3**。

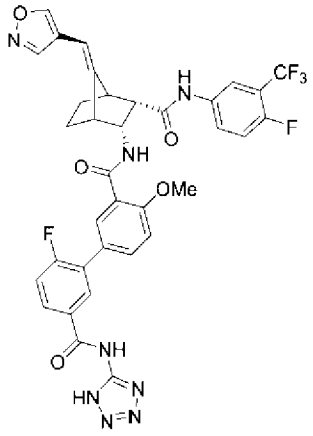
【0296】 中間物**183-3**：中間物**183-3**係根據針對**實例108**所描述之方法，由**183-2**製備。與製備**實例120**之程序中一樣實現三級丁酯之後續移除。LC-MS RT = 0.99 min；MS (ESI) m/z = 698.3 $(M+H)^+$；方法A。

【0297】 針對**實例183**之程序：**實例183**係由**183-3**製備。向2打蘭小瓶中裝入**183-3**、DIEA (0.06 mmol，5 equiv.)及4-氯苯甲醯氯(0.035 mmol，3.0 equiv.)。將溶液在23℃攪拌30 min且隨後用MeOH淬滅。在減壓下濃縮反應內容物得到粗產物，該粗產物經由製備型RP-HPLC純化，得到**實例183**。**實例183**之分析資料：^{1}H NMR (500 MHz, $CDCl_3$) δ 9.98 (br d, J=8.0 Hz, 1H), 8.77 - 8.68 (m, 1H), 8.49 (d, J=2.5 Hz, 1H), 7.96

(dd, J=6.3, 2.5 Hz, 1H), 7.91 - 7.84 (m, 2H), 7.77 - 7.71 (m, 1H), 7.69 (t, J=1.7 Hz, 1H), 7.60 (d, J=8.0 Hz, 1H), 7.55 (ddd, J=8.3, 4.3, 2.2 Hz, 1H), 7.43 - 7.39 (m, 1H), 7.37 - 7.31 (m, 1H), 7.27 - 7.24 (m, 1H), 7.08 (dd, J=10.6, 8.7 Hz, 1H), 7.01 - 6.95 (m, 2H), 6.21 (d, J=8.5 Hz, 1H), 5.61 (q, J=7.4 Hz, 1H), 4.83 - 4.74 (m, 1H), 4.04 (s, 3H), 3.41 (br s, 1H), 3.14 (dd, J=10.5, 4.1 Hz, 1H), 2.88 (t, J=3.9 Hz, 1H), 2.30 - 2.22 (m, 1H), 2.01 - 1.95 (m, 1H), 1.73 - 1.62 (m, 2H)。LC-MS RT: 1.21 min；MS (ESI) m/z = 836.3 (M+H)+；方法A。

【0298】

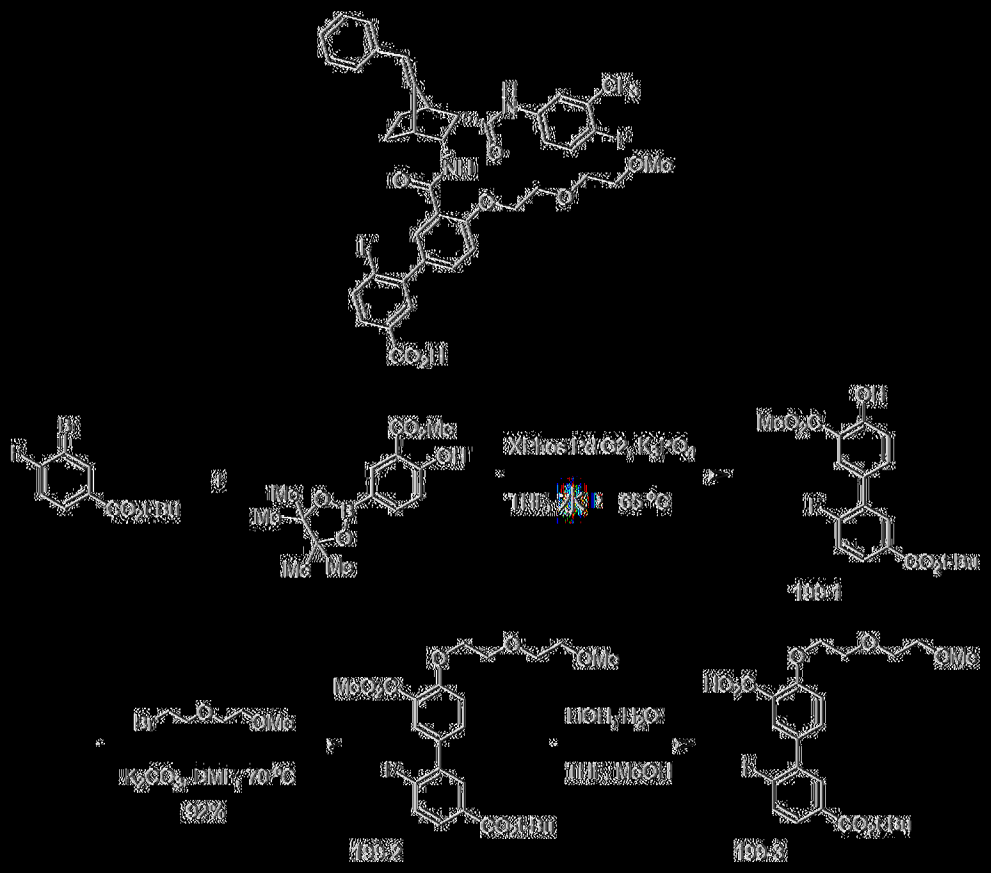
實例192



針對**實例192**之程序：**實例192**係採用BHFFT作為偶合劑，由**實例120**製備。向裝有**實例120** (0.043 mmol，1.3 equiv.)之2打蘭額定壓力小瓶中添加BHFFT (0.049 mmol，2.0 equiv.)，隨後添加DCM (1 mL)及DIEA (0.15 mmol，4.5 equiv.)。將反應混合物在23℃攪拌30 min，隨後加熱至80℃持續18 h。使反應混合物冷卻至23℃，將小瓶內容物溶解於DMF (1.5 mL)中，且藉由RP-HPLC純化殘餘物。**實例192**之分析資料：LC-MS RT: 2.41 min；MS (ESI) m/z = 735.1 (M+H)+；方法C。

【0299】

實例199



中間物199-1：除了在65℃之溫度下持續18 h以外，中間物199-1係採用用於中間物140-1之相同條件來製備。^{1}H NMR (500 MHz, $CDCl_3$) δ 10.87 (s, 1H), 8.11 – 8.04 (m, 2H), 7.95 (ddd, J = 8.5, 4.8, 2.3 Hz, 1H), 7.68 (d, J = 8.5, 1.9 Hz, 1H), 7.18 (dd, J = 10.0, 8.7 Hz, 1H), 7.09 (d, J = 8.5 Hz, 1H), 3.99 (s, 3H), 1.66 – 1.59 (m, 9H)。LC-MS RT = 1.20 min；MS (ESI) m/z = 347.1 $(M+H)^+$

[0300] 中間物199-2：向裝有中間物199-1之1打蘭小瓶中添加碳酸鉀(53.5 mg，0.39 mmol)、DMF (0.4 mL)及1-溴-2-(2-甲氧基乙氧基)乙烷(70.8 mg，0.39 mmol)。將反應混合物在23℃攪拌18 h，隨後加熱至40℃再持續18 h。用氮氣流濃縮反應混合物，用乙酸乙酯及水稀釋殘餘物且用乙酸乙酯(3×10 mL)萃取所得溶液。將合併之有機部分經硫酸鈉乾燥，過濾，且在減壓下濃縮，得到199-2 (80 mg，0.18 mmol，92%產

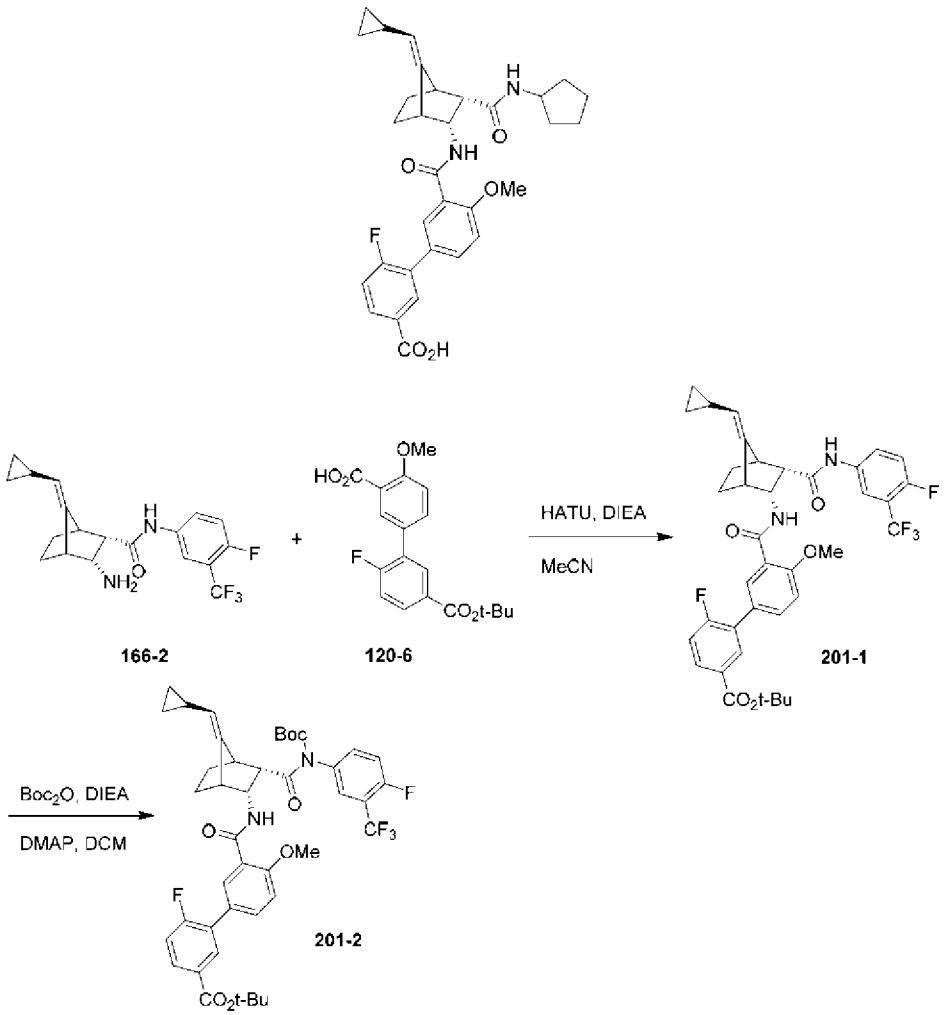
率)。^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (dd, J=7.7, 2.2 Hz, 1H), 8.00 (dd, J=2.2, 1.1 Hz, 1H), 7.94 (ddd, J=8.5, 4.8, 2.3 Hz, 1H), 7.66 (dt, J=8.7, 2.0 Hz, 1H), 7.17 (dd, J=10.0, 8.7 Hz, 1H), 7.09 (d, J=8.8 Hz, 1H), 4.28 (t, J=5.1 Hz, 2H), 3.97 - 3.93 (m, 2H), 3.91 (s, 3H), 3.81 - 3.77 (m, 2H), 3.61 - 3.57 (m, 2H), 3.44 - 3.39 (m, 3H), 1.61 (s, 9H)。LC-MS RT = 1.11 min；MS (ESI) m/z = 449.1 $(M+H)^+$；方法A。

【0301】 中間物**199-3**：中間物**199-3**係以與中間物**3-3**類似之方式，藉由中間物**199-2**之氫氧化鋰水解來製備。LC-MS RT = 1.02 min；MS (ESI) m/z = 348.1 $(M+H)^+$；方法A。

【0302】 針對**實例199**之程序：**實例199**係根據針對**實例108**所描述之方法，採用**199-3**，由**125-2**製備。與製備**實例120**之程序中一樣實現三級丁酯之後續移除。**實例199**之分析資料：LC-MS RT: 1.15 min；MS (ESI) m/z = 765.2 (M+H)+；方法A。

【0303】

實例201



中間物**201-1**：**中間物201-1**係根據針對**實例108**所描述之方法，採用**120-6**，由**166-2**製備。^{1}H NMR (500 MHz, $CDCl_3$) δ 9.40 (br d, J=8.0 Hz, 1H), 8.40 (d, J=1.1 Hz, 1H), 8.08 (dd, J=7.7, 2.2 Hz, 1H), 8.02 - 7.93 (m, 3H), 7.64 (dt, J=8.6, 1.9 Hz, 1H), 7.49 (dt, J=8.6, 3.5 Hz, 1H), 7.18 (dd, J=10.0, 8.7 Hz, 1H), 7.12 - 7.03 (m, 2H), 4.89 - 4.81 (m, 1H), 4.63 (d, J=9.4 Hz, 1H), 4.05 (s, 3H), 3.20 (t, J=3.9 Hz, 1H), 3.10 (dd, J=10.6, 3.2 Hz, 1H), 2.72 (t, J=3.9 Hz, 1H), 2.24 - 2.16 (m, 1H), 1.93 - 1.85 (m, 1H), 1.71 - 1.63 (m, 2H), 1.61 (s, 9H), 1.53 - 1.41 (m, 1H), 0.74 (dt, J=7.8, 3.7 Hz, 2H), 0.41 - 0.30 (m, 2H)。LC-MS RT = 1.30 min；MS (ESI) m/z = 697.3 $(M+H)^+$；方法A。

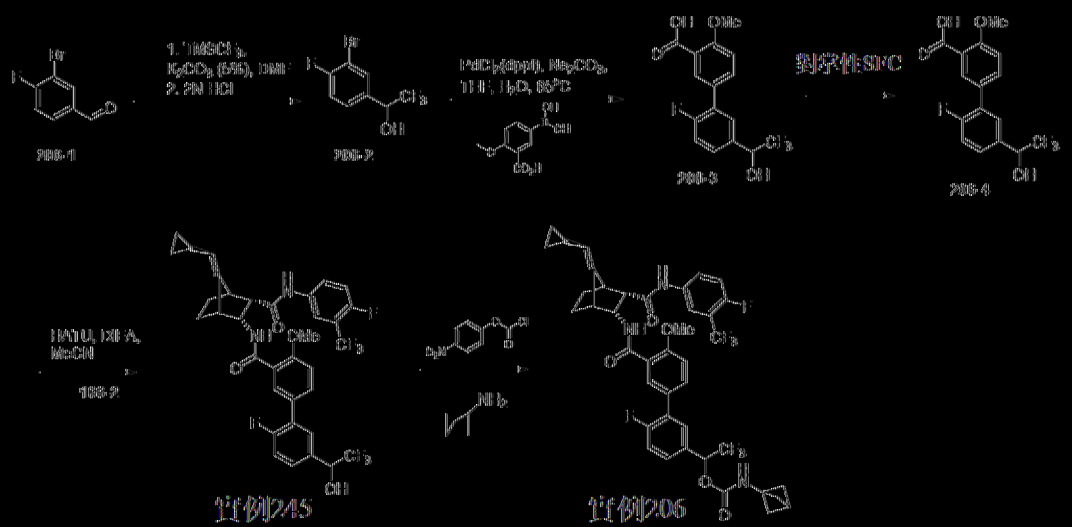
【0304】 中間物**201-2**：向裝有中間物**201-1** (88 mg，0.126 mmol)

之2打蘭小瓶中添加DCM (1.25 mL)，隨後添加Boc_2O (0.51 mmol)、DMAP (0.06 mmol)及DIEA (0.51 mmol)。將溶液在23℃攪拌18 h，且隨後在減壓下濃縮。藉由正相矽膠層析純化所得粗物質，得到中間物**201-2** (94 mg，0.12 mmol，93%產率)。LC-MS RT = 1.34 min；MS (ESI) m/z = 797.5 $(M+H)^+$；方法A。

【0305】 針對**實例201**之程序：**實例201**係由**201-2**製備。向裝有**201-2** (0.013 mmol)之1打蘭小瓶中添加DCM (0.3 mL)及環戊基胺(0.125 mmol，10 equiv.)。將溶液在23℃攪拌18 h且在減壓下濃縮，得到粗中間物。與製備**實例120**之程序中一樣實現三級丁酯之後續移除。**實例201**之分析資料：^1H NMR (500 MHz, DMSO-d6) δ 9.78 (br d, J=7.0 Hz, 1H), 7.85 - 7.75 (m, 3H), 7.74 - 7.67 (m, 1H), 7.48 (br d, J=8.5 Hz, 1H), 7.16 (br t, J=9.5 Hz, 1H), 7.05 (d, J=8.9 Hz, 1H), 4.36 (d, J=9.5 Hz, 1H), 4.04 (dt, J=10.0, 5.2 Hz, 1H), 3.81 - 3.73 (m, 4H), 2.83 - 2.76 (m, 1H), 2.66 - 2.60 (m, 1H), 1.69 - 1.45 (m, 4H), 1.40 - 1.29 (m, 2H), 1.28 - 1.16 (m, 3H), 1.15 - 1.01 (m, 4H), 0.53 - 0.39 (m, 2H), 0.06 (br d, J=3.1 Hz, 2H)。LC-MS RT: 2.33 min；MS (ESI) m/z = 547.4 (M+H)+；方法C。

【0306】

實例206



中間物206-2：向反應容器中添加3-溴-4-氟苯甲醛(206-1，235 mg，1.15 mmol)、DMF (3.5 mL)、(三氟甲基)三甲基矽烷(0.34 mL，2.3 mmol)及K_2CO_3 (8.0 mg，0.058 mmol)。在室溫下攪拌反應混合物60 min且添加2N HCl (3 mL)。在室溫下再攪拌1 h之後，用EtOAc (15 mL)稀釋反應混合物，且用飽和NH_4Cl洗滌溶液。藉由添加EtOAc (10 mL×2)萃取水相。將合併之有機部分經Na_2SO_4乾燥，過濾，濃縮，且藉由矽膠層析純化，得到206-2 (205 mg，0.751 mmol，64.9%產率)。^{1}H NMR (500 MHz, $CDCl_3$) d 7.74 (dd, *J* = 6.5, 2.1 Hz, 1H), 7.43 (ddd, *J* = 8.4, 4.8, 2.2 Hz, 1H), 7.19 (t, *J* = 8.4 Hz, 1H), 5.11 – 4.98 (m, 1H), 2.69 (d, *J* = 4.4 Hz, 1H)。

[0307] 中間物206-3：向含有206-2 (100 mg, 0.366 mmol)之反應容器中添加5-溴-2-甲氧基苯甲酸(93 mg，0.48 mmol)、$PdCl_2$(dppf)-CH_2Cl_2加合物(45 mg，0.055 mmol)、Na_2CO_3 (155 mg，1.46 mmol)及H_2O (1 mL)。藉由使N_2鼓泡使反應混合物脫氣10 min，密封，且在65℃攪拌3h。在冷卻至室溫之後，藉由添加1N HCl淬滅反應混合物，將溶液用EtOAc萃取，經Na_2SO_4乾燥，過濾，濃縮且藉由HPLC純化，得到206-3 (50.5 mg，0.147 mmol，40.1%產率)。^{1}H NMR (500 MHz, $CDCl_3$) δ

8.39 (d, *J*=1.9 Hz, 1H), 7.83 (dt, *J*=8.7, 2.1 Hz, 1H), 7.59 (dd, *J*=7.3, 2.1 Hz, 1H), 7.53 - 7.45 (m, 1H), 7.23 (dd, *J*=10.2, 8.8 Hz, 1H), 7.18 (d, *J*=8.5 Hz, 1H), 5.11 (q, *J*=6.6 Hz, 1H), 4.17 (s, 3H)。

【0308】 中間物**206-4**：使用對掌性SFC將外消旋**206-3**分離成個別鏡像異構物。製備型層析條件：儀器：Berger MG II；管柱：Kromasil 5-CelluCoat，21×250 mm，5微米；移動相：15% IPA-ACN (0.1% DEA) / 85% CO_2；流動條件：45 mL/min，120巴， 40℃；偵測器波長：220 nm；注射詳情：0.4 mL ~15 mg/mL於ACN-IPA (1:1)中。收集峰#2，得到中間物**206-4**。分析型層析條件：儀器：Aurora Infinity Analytical SFC；管柱：Kromasil 5-CelluCoat，4.6×250 mm，5微米；移動相：20% IPA-ACN (0.1% DEA) / 80% CO_2；流動條件：2 mL/min，150巴，40℃；偵測器波長：220 nm。峰1，RT = 9.12 min，99% ee；峰2，RT = 10.19 min，98% ee。

【0309】 實例**245**：向反應容器中添加中間物**166-2** (7.0 mg，0.017 mmol)、中間物**206-4** (6.2 mg，0.018 mmol)、MeCN (1 mL)、DIEA (9.1 µl，0.052 mmol)及HATU (7.2 mg，0.019 mmol)。將反應混合物在室溫下攪拌12 h，在減壓下濃縮，且進行製備型HPLC純化，得到實例**245** (9.5 mg，0.014 mmol，78%產率)。^{1}H NMR (500 MHz, $CDCl_3$) δ 9.57 (d, *J*=7.7 Hz, 1H), 8.33 (dd, *J*=2.2, 0.8 Hz, 1H), 8.05 (s, 1H), 7.99 (dd, *J*=6.3, 2.5 Hz, 1H), 7.66 (dt, *J*=8.7, 2.0 Hz, 1H), 7.57 (dd, *J*=7.3, 2.1 Hz, 1H), 7.56 - 7.52 (m, 1H), 7.45 - 7.40 (m, 1H), 7.17 (dd, *J*=10.2, 8.5 Hz, 1H), 7.11 - 7.04 (m, 2H), 5.11 - 5.04 (m, 1H), 4.77 - 4.70 (m, 1H), 4.57 (d, *J*=9.4 Hz, 1H), 4.06 (s, 3H), 3.42 (br s, 1H), 3.19 (t, *J*=4.1 Hz, 1H), 3.08

(ddd, *J*=10.7, 4.1, 1.2 Hz, 1H), 2.67 (t, *J*=4.0 Hz, 1H), 2.18 - 2.07 (m, 1H), 1.92 - 1.82 (m, 1H), 1.67 - 1.58 (m, 2H), 1.53 - 1.45 (m, 1H), 0.79 - 0.68 (m, 2H), 0.38 - 0.27 (m, 2H)。LC-MS RT: 1.38 min；MS (ESI) *m/z* 695.3 $(M+H)^+$；方法A。

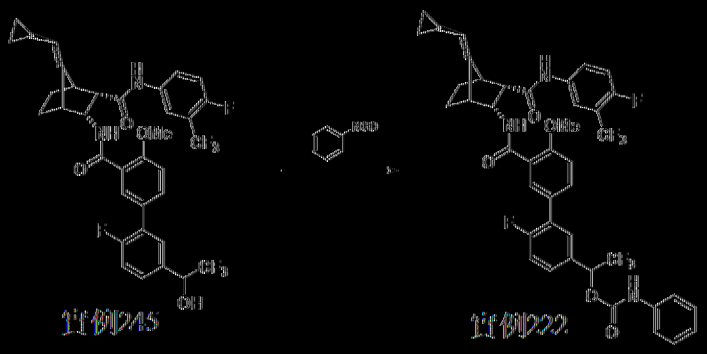
【0310】實例**246**：遵循合成實例**246**之程序，由中間物**166-2**及**206-4**之鏡像異構物(來自對掌性SFC純化之峰1)製備。^{1}H NMR (500 MHz, $CDCl_3$) δ 9.53 (d, *J*=7.7 Hz, 1H), 8.34 (dd, *J*=2.5, 0.8 Hz, 1H), 8.01 (s, 1H), 7.97 (dd, *J*=6.2, 2.6 Hz, 1H), 7.66 (dt, *J*=8.7, 2.0 Hz, 1H), 7.57 - 7.50 (m, 2H), 7.48 - 7.40 (m, 1H), 7.18 (dd, *J*=10.2, 8.5 Hz, 1H), 7.12 - 7.02 (m, 2H), 5.13 - 5.03 (m, 1H), 4.81 - 4.71 (m, 1H), 4.60 (d, *J*=9.6 Hz, 1H), 4.06 (s, 3H), 3.19 (t, *J*=3.7 Hz, 2H), 3.09 (ddd, *J*=10.8, 4.1, 1.1 Hz, 1H), 2.70 (t, *J*=4.0 Hz, 1H), 2.19 - 2.11 (m, 1H), 1.92 - 1.84 (m, 1H), 1.70 - 1.60 (m, 2H), 1.51 - 1.42 (m, 1H), 0.77 - 0.70 (m, 2H), 0.36 - 0.30 (m, 2H)。LC-MS RT: 1.38 min；MS (ESI) *m/z* 695.3 $(M+H)^+$；方法A。

【0311】實例**206**：向反應容器中添加實例**245** (6.0 mg，8.6 μmol)、DCM (1 mL)、吡啶(7.0 μl，0.086 mmol)、氯甲酸4-硝基苯酯(8.7 mg，0.043 mmol)及DMAP (1.0 mg，8.6 μmol)。在室溫下攪拌2 h之後，添加雙環[1.1.1]戊-1-胺(7.2 mg，0.086 mmol)。將反應混合物在室溫下攪拌1h，在減壓下濃縮且進行製備型HPLC純化，得到雙環[1.1.1]戊烷-1-基胺基甲酸1-(3'-(((1R,2R,3S,4R,Z)-7-(環丙基亞甲基)-3-((4-氟-3-(三氟甲基)苯基)胺甲醯基)雙環[2.2.1]庚烷-2-基)胺甲醯基)-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2,2,2-三氟乙酯(實例**206**，3.8 mg，4.7 μmol，54%產率)。^{1}H NMR (500 MHz, DMSO-d6) *δ* 10.54 (s, 1H), 9.95 (br d, *J*=6.3

Hz, 1H), 8.55 (br s, 1H), 8.24 (br d, *J* = 4.2 Hz, 1H), 8.13 (br s, 1H), 7.86 – 7.75 (m, 1H), 7.69 (br t, *J* = 9.4 Hz, 2H), 7.58 – 7.38 (m, 3H), 7.33 (d, *J* = 8.8 Hz, 1H), 6.43 – 6.30 (m, 1H), 4.69 (d, *J* = 9.6 Hz, 1H), 4.51 – 4.41 (m, 1H), 4.06 (s, 3H), 3.16 (br dd, *J* = 10.1, 3.8 Hz, 1H), 3.11 (br s, 1H), 2.72 (br s, 1H), 2.39 – 2.34 (m, 1H), 2.02 – 1.89 (m, 6H), 1.88 – 1.77 (m, 2H), 1.54 – 1.47 (m, 1H), 1.45 – 1.36 (m, 2H), 0.79 – 0.69 (m, 2H), 0.35 (br s, 2H)。LC-MS RT: 1.27 min；MS (ESI) *m/z* 804.5 $(M+H)^+$；方法A。

[0312]

實例222



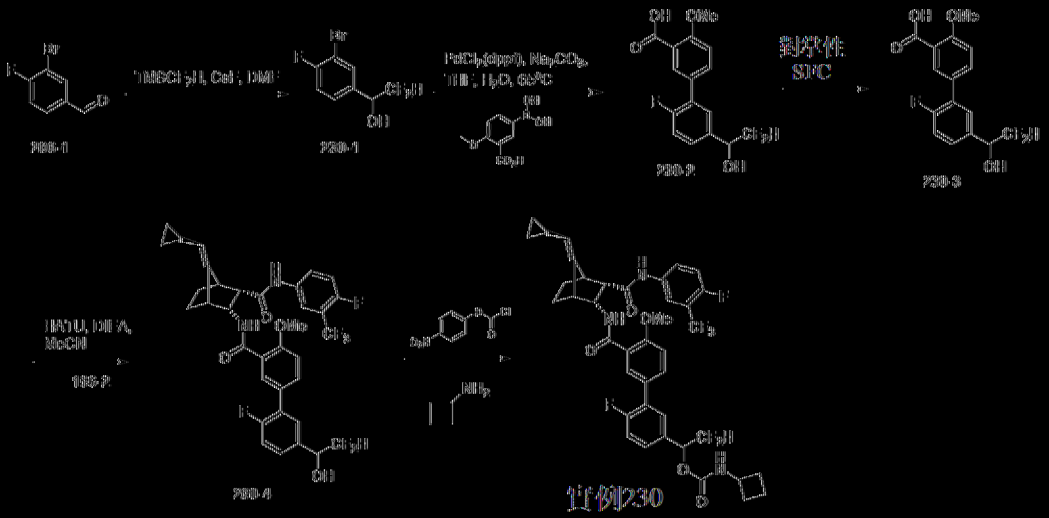
實例245　　實例222

實例222：向反應容器中添加實例246 (11 mg，0.017 mmol)、DCM (1 mL)、吡啶(8.0 µl，0.099 mmol)及異氰酸苯酯(9.9 mg，0.083 mmol)。在室溫下攪拌12h之後，將反應混合物濃縮且進行製備型HPLC純化，得到苯胺基甲酸1-(3'-(((1R,2R,3S,4R,7*Z*)-7-(環內基亞甲基)-3-((4-氟-3-(三氟甲基)苯基)胺甲醯基)雙環[2.2.1]庚烷-2-基)胺甲醯基)-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)乙酯(實例222，11.8 mg，0.0160 mmol，94.0%產率)。^{1}H NMR (500 MHz, DMSO-d6) δ 10.52 (s, 1H), 9.92 (br d, *J* = 7.3 Hz, 1H), 9.72 (br s, 1H), 8.22 (br d, *J* = 4.9 Hz, 1H), 8.14 (s, 1H), 7.81 – 7.75 (m, 1H), 7.70 (br d, *J* = 8.2 Hz, 1H), 7.54 (br d, *J* = 6.7 Hz, 1H), 7.50 – 7.38 (m, 4H), 7.35 – 7.27 (m, 2H), 7.25 (br t, *J* = 7.8 Hz, 2H), 6.96 (t, *J* = 7.5

Hz, 1H), 5.89 – 5.80 (m, 1H), 4.69 (d, *J* = 9.5 Hz, 1H), 4.49 – 4.41 (m, 1H), 4.05 (s, 3H), 3.16 (br dd, *J* = 10.8, 3.5 Hz, 1H), 3.11 (br s, 1H), 2.72 (br s, 1H), 1.92 – 1.74 (m, 2H), 1.56 (br d, *J* = 6.1 Hz, 3H), 1.53 – 1.47 (m, 1H), 1.45 – 1.35 (m, 2H), 0.82 – 0.66 (m, 2H), 0.39 – 0.29 (m, 2H)。LC-MS RT: 1.26 min；MS (ESI) *m/z* 760.5 $(M+H)^+$；方法A。

[0313]

實例230



中間物230-1：向反應容器中添加206-1 (577 mg，2.84 mmol)、DMF (15 mL)、(二氟甲基)三甲基矽烷(530 mg，4.26 mmol)及CsF (216 mg，1.42 mmol)。在50℃攪拌12h之後，用EtOAc (15 mL)稀釋反應混合物，且用飽和NH_4Cl洗滌溶液。再用EtOAc (10 mL×2)萃取水相。將合併之有機部分經Na_2SO_4乾燥，過濾，濃縮，且藉由矽膠層析純化，得到1-(3-溴-4-氟苯基)-2,2-二氟乙-1-醇(230-1，98 mg，0.38 mmol，13%產率)。^1H NMR (500 MHz, $CDCl_3$) δ 7.67 (dd, *J* = 6.6, 2.1 Hz, 1H), 7.36 (ddd, *J* = 8.4, 4.6, 2.1 Hz, 1H), 7.16 (t, *J* = 8.4 Hz, 1H), 5.87 – 5.57 (m, 1H), 4.86 – 4.78 (m, 1H), 2.50 (br s, 1H)。

[0314] 中間物230-2：向含有230-1 (220 mg，0.863 mmol)之反應

容器中添加5-溴-2-甲氧基苯甲酸(220 mg，1.12 mmol)、$PdCl_2$(dppf)-CH_2Cl_2加合物(106 mg，0.129 mmol、Na_2CO_3 (366 mg，3.45 mmol)及H_2O (3.5 mL)。藉由使N_2鼓泡使反應混合物脫氣10 min，密封，且在65℃攪拌3h。在冷卻至室溫之後，藉由添加1N HCl淬滅反應混合物，將所得溶液用EtOAc萃取，經Na_2SO_4乾燥，過濾，濃縮且進行製備型HPLC純化，得到5'-(2,2-二氟-1-羥基乙基)-2'-氟-4-甲氧基-[1,1'-聯苯]-3-甲酸(**230-2**，186 mg，0.570 mmol，66.1%產率)。^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, *J*=1.8 Hz, 1H), 7.82 (dt, *J*=8.7, 2.0 Hz, 1H), 7.53 (dd, *J*=7.4, 2.1 Hz, 1H), 7.45 - 7.39 (m, 1H), 7.24 - 7.14 (m, 2H), 6.01 - 5.59 (m, 1H), 4.89 (td, *J*=10.1, 4.7 Hz, 1H), 4.15 (s, 3H)。

【0315】 中間物**230-3**：使用對掌性SFC將外消旋**230-2**分離成個別鏡像異構物。製備型層析條件：儀器：PIC Solution SFC Prep-200；管柱：Chiralpak IC，30×250 mm，5微米；移動相：10% MeOH / 90% CO_2；流動條件：85 mL/min，150巴，40℃；偵測器波長：220 nm；注射詳情：10μL ~1mg/mL於MeOH中。收集峰#2，得到中間物**230-3**。分析型層析條件：儀器：Aurora Infinity分析型SFC；管柱：Chiralpak ID，4.6×250 mm，5微米；移動相：10%MeOH / 90% CO_2；流動條件：2 mL/min，150巴，40℃；偵測器波長：220 nm。峰1，RT = 11.85 min，96% ee；峰2，RT = 13.65 min，>99.5% ee。

【0316】 中間物**230-4**：向反應容器中添加中間物**166-2** (20 mg，0.054 mmol)、中間物**230-3** (18 mg，0.057 mmol)、MeCN (1 mL)、DIEA (0.028 mL，0.16 mmol)及HATU (23 mg，0.060 mmol)。將反應混合物在室溫下攪拌12h，在減壓下濃縮且進行矽膠層析純化，得到

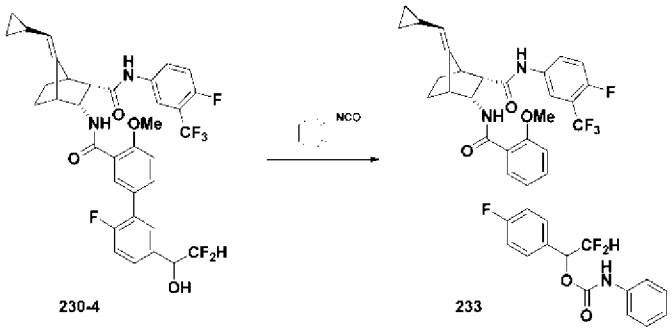
(1R,2S,3R,4R,Z)-7-(環丙基亞甲基)-3-(5'-(2,2-二氟-1-羥基乙基)-2'-氟-4-甲氧基-[1,1'-聯苯]-3-甲醯胺基)-N-(4-氟-3-(三氟甲基)苯基)雙環[2.2.1]庚烷-2-甲醯胺(**230-4**，25 mg，0.037 mmol，68%產率)。^{1}H NMR (400 MHz, $CDCl_3$) δ 9.49 (br d, *J*=7.7 Hz, 1H), 8.40 - 8.33 (m, 1H), 8.01 (s, 1H), 7.98 - 7.91 (m, 1H), 7.66 (dt, *J*=8.7, 2.0 Hz, 1H), 7.57 - 7.48 (m, 2H), 7.38 (dq, *J*=6.4, 4.2 Hz, 1H), 7.18 (ddd, *J*=10.2, 8.6, 1.2 Hz, 1H), 7.11 - 7.01 (m, 2H), 6.03 - 5.59 (m, 1H), 4.91 - 4.83 (m, 1H), 4.81 - 4.73 (m, 1H), 4.61 (d, *J*=9.5 Hz, 1H), 4.06 (s, 3H), 3.19 (t, *J*=3.7 Hz, 1H), 3.09 (dd, *J*=10.8, 3.3 Hz, 1H), 2.82 (br d, *J*=12.5 Hz, 1H), 2.70 (t, *J*=3.9 Hz, 1H), 2.22 - 2.12 (m, 1H), 1.95 - 1.85 (m, 1H), 1.72 - 1.61 (m, 2H), 1.50 - 1.41 (m, 1H), 0.79 - 0.69 (m, 2H), 0.39 - 0.28 (m, 2H)。

【0317】實例**230**：向反應容器中添加中間物**230-4** (6.0 mg，8.9 μmol)、DCM (1 mL)、吡啶(7.2 μl，0.089 mmol)、氯甲酸4-硝基苯酯(8.9 mg，0.044 mmol)及DMAP (1.1 mg，8.9 μmol)。在室溫下攪拌2h之後，添加環丁胺(6.3 mg，0.089 mmol)。將反應混合物在室溫下攪拌1h，在減壓下濃縮且進行製備型HPLC純化，得到環丁基胺基甲酸1-(3'-(((1R,2R,3S,4R,Z)-7-(環丙基亞甲基)-3-((4-氟-3-(三氟甲基)苯基)胺甲醯基)雙環[2.2.1]庚烷-2-基)胺甲醯基)-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2,2-二氟乙酯(實例**230**，4.5 mg，5.8 μmol，66%產率)。^{1}H NMR (500 MHz, DMSO-d6) *δ* 10.55 (s, 1H), 9.94 (br d, *J*=7.2 Hz, 1H), 8.19 (br d, *J*=5.1 Hz, 1H), 8.09 (s, 1H), 7.94 (br d, *J*=7.8 Hz, 1H), 7.80 - 7.71 (m, 1H), 7.68 (br d, *J*=8.8 Hz, 1H), 7.53 (br d, *J*=6.7 Hz, 1H), 7.48 - 7.39 (m, 2H), 7.38 - 7.27 (m, 2H), 6.49 - 6.13 (m, 1H), 5.93 - 5.81 (m, 1H), 4.67 (d, *J*=9.6

Hz, 1H), 4.48 - 4.38 (m, 1H), 4.03 (s, 3H), 3.94 - 3.85 (m, 1H), 3.19 - 3.11 (m, 1H), 3.08 (br s, 1H), 2.70 (br s, 1H), 2.15 - 2.01 (m, 2H), 1.92 - 1.73 (m, 4H), 1.58 - 1.45 (m, 3H), 1.43 - 1.35 (m, 2H), 0.77 - 0.66 (m, 2H), 0.37 - 0.28 (m, 2H)。LC-MS RT: 1.22 min；MS (ESI) *m/z* 774.3 $(M+H)^+$；方法A。

【0318】

實例233

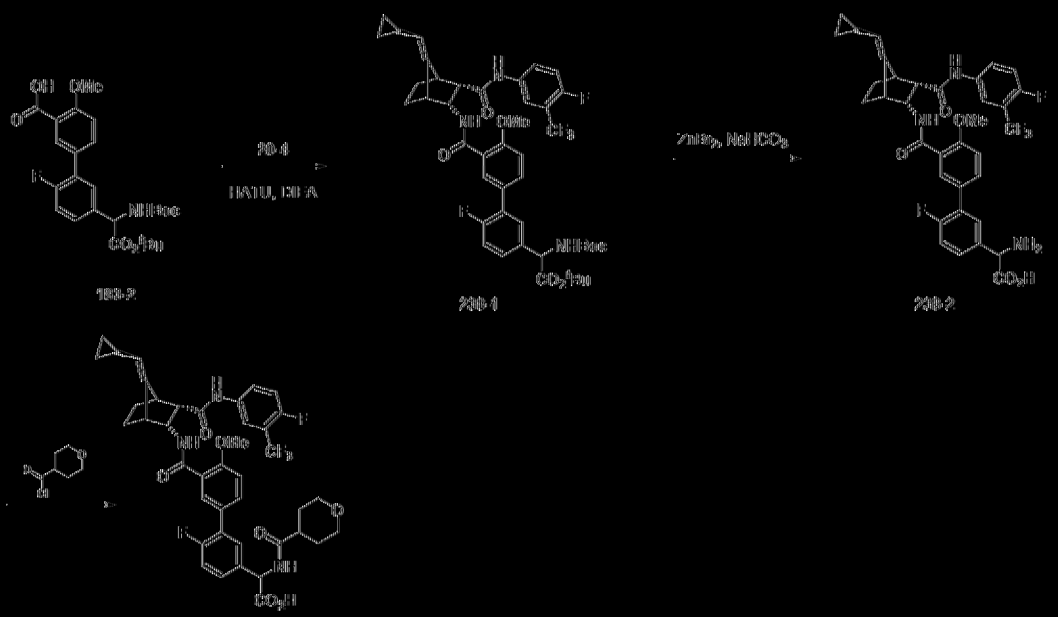


實例**233**：向反應容器中添加**230-4** (6.0 mg，8.9 μmol)、DCM (1 mL)、吡啶(0.014 mL，0.17 mmol)及異氰酸基苯(5.3 mg，0.044 mmol)。在室溫下攪拌12h之後，在減壓下濃縮混合物且進行製備型HPLC純化，得到苯基胺基甲酸1-(3'-(((1R,2R,3S,4R,Z)-7-(環丙基亞甲基)-3-((4-氟-3-(三氟甲基)苯基)胺甲醯基)雙環[2.2.1]庚烷-2-基)胺甲醯基)-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2,2-二氟乙酯(實例**233**，4.9 mg，5.9 μmol，67%產率)。^{1}H NMR (500 MHz, DMSO-d6) δ 10.54 (s, 1H), 10.07 (br s, 1H), 9.93 (br d, *J*=7.0 Hz, 1H), 8.17 (br d, *J*=4.6 Hz, 1H), 8.10 (s, 1H), 7.79 - 7.59 (m, 3H), 7.50 (br s, 1H), 7.47 - 7.34 (m, 4H), 7.34 - 7.24 (m, 3H), 7.01 (br t, *J*=7.2 Hz, 1H), 6.55 - 6.25 (m, 1H), 6.08 - 5.98 (m, 1H), 4.68 (d, *J*=9.5 Hz, 1H), 4.48 - 4.39 (m, 1H), 4.02 (s, 3H), 3.19 - 3.10 (m, 1H), 3.08 (br s, 1H), 2.72 - 2.67 (m, 1H), 1.87 - 1.72 (m, 2H), 1.53 - 1.45 (m,

1H), 1.44 – 1.34 (m, 2H), 0.77 – 0.65 (m, 2H), 0.37 – 0.26 (m, 2H)。LC-MS RT: 1.23 min；MS (ESI) *m/z* 796.2 $(M+H)^+$；方法A。

|(0319)|

實例238：



實例238

中間物238-1：向反應容器中添加166-2 (75 mg，0.19 mmol)、183-2 (92 mg，0.20 mmol)、MeCN (5 mL)、DIEA (0.097 mL，0.56 mmol)及HATU (77 mg，0.200 mmol)。將反應混合物在室溫下攪拌12h，在減壓下濃縮且對殘餘物進行矽膠層析純化，得到2-((三級丁氧基羰基)胺基)-2-(3'-(((1R,2R,3S,4R,Z)-7-(環內基亞甲基)-3-((4-氟-3-(三氟甲基)苯基)胺甲醯基)雙環[2.2.1]庚烷-2-基)胺甲醯基)-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)乙酸三級丁酯(238-1，147 mg，0.178 mmol，96.0%產率)。^{1}H NMR (400 MHz, $CDCl_3$) δ 9.42 (br d, *J* = 7.9 Hz, 1H), 8.41 (dd, *J* = 2.2, 1.3 Hz, 1H), 8.09 – 8.04 (m, 1H), 8.06 (s, 1H), 8.00 (dd, *J* = 6.3, 2.5 Hz, 1H), 7.67 – 7.61 (m, 1H), 7.55 – 7.48 (m, 1H), 7.44 (dd, *J* = 7.3, 2.4 Hz, 1H), 7.36 – 7.31 (m, 1H), 7.20 – 7.04 (m, 3H), 5.66 (br d, *J* = 6.6 Hz, 1H), 5.24 (br d, *J* = 7.0 Hz,

1H), 4.92 - 4.82 (m, 1H), 4.65 (d, *J*=9.5 Hz, 1H), 4.07 (s, 3H), 3.22 (t, *J*=3.9 Hz, 1H), 3.13 (dd, *J*=10.5, 3.6 Hz, 1H), 2.74 (t, *J*=3.7 Hz, 1H), 2.27 - 2.16 (m, 1H), 1.95 - 1.86 (m, 1H), 1.74 - 1.66 (m, 2H), 1.46 (br s, 9H), 1.43 (s, 9H), 1.39 - 1.34 (m, 1H), 0.81 - 0.72 (m, 2H), 0.43 - 0.33 (m, 2H)。

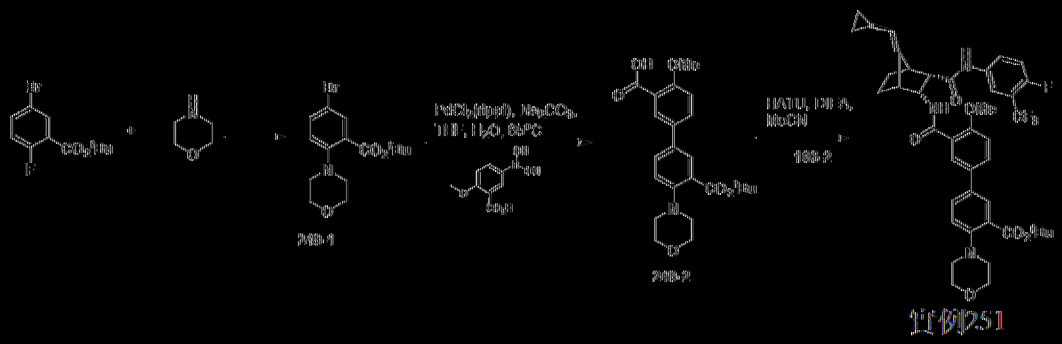
【0320】 中間物**238-2**：向反應容器中添加**238-1** (147 mg，0.178 mmol)、DCM (10 mL)、碳酸氫鈉(112 mg，1.33 mmol)及溴化鋅(1200 mg，5.34 mmol)。在攪拌24h之後，藉由添加1N HCl淬滅反應混合物且用EtOAc萃取溶液。將合併之有機部分經Na_2SO_4乾燥，過濾，濃縮，且進行製備型HPLC純化，得到2-胺基-2-(3'-(((1R,2R,3S,4R,Z)-7-(環丙基亞甲基)-3-((4-氟-3-(三氟甲基)苯基)胺甲醯基)雙環[2.2.1]庚烷-2-基)胺甲醯基)-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)乙酸TFA (**238-2**，62 mg，0.079 mmol，44%產率)。MS (ESI) *m/z* 670.4 (M+H)。

【0321】 實例**238**：向反應容器中添加**238-2** (9 mg，0.01 mmol)、MeCN (1 mL)、吡啶(2.8 µl，0.034 mmol)及四氫-2*H*-哌喃-4-碳醯氯(1.7 mg，0.012 mmol)。在室溫下攪拌30 min之後，藉由添加MeOH來淬滅反應混合物，在減壓下濃縮，且對殘餘物進行製備型HPLC純化，得到2-(3'-(((1R,2R,3S,4R,Z)-7-(環丙基亞甲基)-3-((4-氟-3-(三氟甲基)苯基)胺甲醯基)雙環[2.2.1]庚烷-2-基)胺甲醯基)-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2-(四氫-2H-哌喃-4-甲醯胺基)乙酸(實例**238**，8.9 mg，0.011 mmol，99%產率)。^{1}H NMR (500 MHz, $CDCl_3$) δ 9.89 (br d, *J*=7.7 Hz, 1H), 8.26 (d, *J*=2.2 Hz, 1H), 7.99 (dd, *J*=6.2, 2.3 Hz, 1H), 7.84 (s, 1H), 7.74 - 7.62 (m, 2H), 7.54 (dd, *J*=7.3, 2.3 Hz, 1H), 7.49 - 7.42 (m, 1H), 7.37 - 7.31 (m,

1H), 7.12 – 7.05 (m, 1H), 7.02 – 6.94 (m, 2H), 5.80 (d, *J* = 8.0 Hz, 1H), 4.77 – 4.69 (m, 1H), 4.64 (d, *J* = 9.4 Hz, 1H), 4.06 (s, 3H), 4.03 – 3.90 (m, 2H), 3.49 – 3.36 (m, 2H), 3.14 – 3.09 (m, 1H), 3.06 (dd, *J* = 10.6, 4.0 Hz, 1H), 2.73 – 2.66 (m, 1H), 2.57 – 2.48 (m, 1H), 2.16 – 2.10 (m, 1H), 1.92 – 1.84 (m, 2H), 1.82 – 1.74 (m, 4H), 1.67 – 1.54 (m, 2H), 1.54 – 1.46 (m, 1H), 0.86 – 0.74 (m, 2H), 0.41 – 0.32 (m, 2H)。LC-MS RT: 1.26 min；MS (ESI) *m/z* 782.5 $(M+H)^+$；方法A。

[0322]

實例249：



中間物249-1：向反應容器中添加5-溴-2-氟苯甲酸三級丁酯(120 mg，0.436 mmol)、味啉(0.19 mL，2.2 mmol)及甲苯(2 mL)。在90℃攪拌12h之後，在減壓下濃縮反應混合物且對殘餘物進行矽膠層析純化，得到5-溴-2-N-味啉基苯甲酸三級丁酯(249-1，117 mg，0.342 mmol，78.0%產率)。^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 2.4 Hz, 1H), 7.49 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.91 (d, *J* = 8.8 Hz, 1H), 3.89 – 3.85 (m, 4H), 3.07 – 3.03 (m, 4H), 1.62 (s, 9H)。

[0323] 中間物249-2：向含有249-1 (30 mg，0.088 mmol)之反應容器中添加5-溴-2-甲氧基苯甲酸(25.8 mg，0.131 mmol)、$PdCl_2$(dppf)-CH_2Cl_2加合物(14 mg，0.018 mmol)及Na_2CO_3 (46 mg，0.44 mmol)。藉

由使N_2鼓泡使反應混合物脫氣10 min，密封，且在65℃攪拌2h。在冷卻至室溫之後，在減壓下濃縮反應混合物，且對殘餘物進行製備型HPLC純化，得到3'-(三級丁氧基羰基)-4-甲氧基-4'-N-味啉基-[1,1'-聯苯]-3-甲酸(**249-2**，40 mg，0.097 mmol，110%產率)。MS (ESI) *m/z* 414.0 (M+H)。

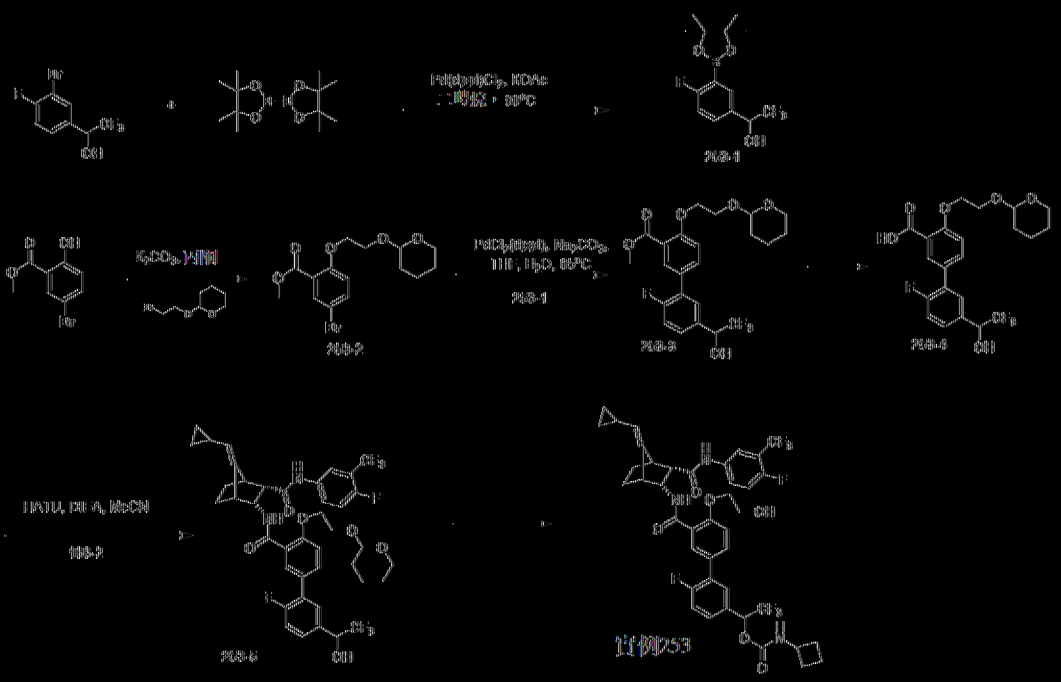
【0324】實例**251**：向反應容器中添加中間物**166-2** (15 mg，0.037 mmol)、**249-2** (20 mg，0.048 mmol)、MeCN (1 mL)、DIEA (0.02 mL，0.1 mmol)及HATU (18 mg，0.048 mmol)。將反應混合物在室溫下攪拌12h，在減壓下濃縮，且對殘餘物進行矽膠層析純化，得到3'-(((1R,2R,3S,4R,Z)-7-(環丙基亞甲基)-3-((4-氟-3-(三氟甲基)苯基)胺甲醯基)雙環[2.2.1]庚烷-2-基)胺甲醯基)-4'-甲氧基-4-N-味啉基-[1,1'-聯苯]-3-甲酸三級丁酯(實例**251**,12 mg，0.016 mmol，42%產率)。^{1}H NMR (500 MHz, $CDCl_3$) δ 9.87 (br d, *J*=7.7 Hz, 1H), 8.31 (d, *J*=2.2 Hz, 1H), 8.22 (s, 1H), 8.04 (dd, *J*=6.3, 2.5 Hz, 1H), 7.94 (d, *J*=2.2 Hz, 1H), 7.76 (br dd, *J*=8.3, 1.9 Hz, 1H), 7.60 (dd, *J*=8.7, 2.3 Hz, 1H), 7.56 (dt, *J*=8.7, 3.4 Hz, 1H), 7.47 (br d, *J*=8.0 Hz, 1H), 7.11 (t, *J*=9.4 Hz, 1H), 7.03 (d, *J*=8.8 Hz, 1H), 4.62 (d, *J*=9.6 Hz, 2H), 4.07 (s, 3H), 4.07 - 4.04 (m, 4H), 3.50 - 3.38 (m, 4H), 3.17 (t, *J*=3.9 Hz, 1H), 2.97 (dd, *J*=10.7, 3.9 Hz, 1H), 2.69 (t, *J*=3.9 Hz, 1H), 2.12 - 2.05 (m, 1H), 1.90 - 1.81 (m, 1H), 1.62 (s, 9H), 1.61 - 1.54 (m, 2H), 1.50 - 1.43 (m, 1H), 0.78 - 0.69 (m, 2H), 0.37 - 0.28 (m, 2H)。LC-MS RT: 1.23 min；MS (ESI) *m/z* 764.3 $(M+H)^+$；方法A。

【0325】實例**249**：向反應容器中添加實例**251** (12 mg，0.016 mmol)、CH_2Cl_2 (2 mL)、碳酸氫鈉(13.2 mg，0.157 mmol)及溴化鋅(142 mg，0.628 mmol)。在35℃攪拌3h之後，藉由添加1N HCl淬滅反應混合

物且用EtOAc萃取溶液。將合併之有機部分經Na_2SO_4乾燥，過濾，濃縮，且進行製備型HPLC純化，得到3'-(((1R,2R,3S,4R,Z)-7-(環丙基亞甲基)-3-((4-氟-3-(三氟甲基)苯基)胺甲醯基)雙環[2.2.1]庚烷-2-基)胺甲醯基)-4'-甲氧基-4-N-味啉基-[1,1'-聯苯]-3-甲酸TFA (實例**249**，5.2 mg，6.2 μmol，40%產率)。^{1}H NMR (500 MHz, $CDCl_3$) δ 9.71 (br d, *J*=7.7 Hz, 1H), 8.53 (d, *J*=2.2 Hz, 1H), 8.41 (d, *J*=2.5 Hz, 1H), 7.96 (dd, *J*=6.1, 2.5 Hz, 1H), 7.91 - 7.84 (m, 2H), 7.76 (dd, *J*=8.7, 2.6 Hz, 1H), 7.59 (dt, *J*=8.7, 3.5 Hz, 1H), 7.54 (d, *J*=8.3 Hz, 1H), 7.13 (t, *J*=9.4 Hz, 1H), 7.09 (d, *J*=8.8 Hz, 1H), 4.83 - 4.74 (m, 1H), 4.67 (d, *J*=9.6 Hz, 1H), 4.09 (s, 3H), 4.02 (br s, 4H), 3.23 (br t, *J*=4.0 Hz, 1H), 3.17 (br s, 4H), 3.10 (br dd, *J*=10.9, 3.4 Hz, 1H), 2.74 (t, *J*=3.9 Hz, 1H), 2.22 - 2.15 (m, 1H), 1.93 - 1.86 (m, 1H), 1.73 - 1.59 (m, 2H), 1.55 - 1.47 (m, 1H), 0.80 - 0.73 (m, 2H), 0.39 - 0.34 (m, 2H)。LC-MS RT: 1.15 min；MS (ESI) *m/z* 708.4 $(M+H)^+$；方法A。

【0326】

實例253：



中間物253-1：向反應容器中添加1-(3-溴-4-氟苯基)-2,2,2-三氟乙-1-醇(100 mg，0.366 mmol)、4,4,4',4',5,5,5',5'-八甲基-2,2'-雙(1,3,2-二氧雜硼雜環戊烷) (126 mg，0.494 mmol)及1,4-二噁烷(3 mL)。隨後添加$PdCl_2(dppf)\cdot CH_2Cl_2$加合物(29.9 mg，0.037 mmol)及乙酸鉀(90 mg，0.91 mmol)，且藉由使N_2鼓泡使反應混合物脫氣10 min。在65℃攪拌反應混合物5h，使其冷卻至室溫且用EtOAc萃取溶液。將合併之有機部分經Na_2SO_4乾燥，過濾且濃縮。所得物質(253-1)不經進一步純化即用於下一步驟。

[0327] 中間物253-2：向反應容器中添加5-溴-2-羥基苯甲酸甲酯(200 mg，0.866 mmol)、2-(2-溴乙氧基)四氫-2H-哌喃(217 mg，1.039 mmol)、丙酮(3 mL)及K_2CO_3 (239 mg，1.73 mmol)。在50℃攪拌12h之後，在減壓下濃縮反應混合物且對殘餘物進行矽膠層析純化，得到5-溴-2-(2-((四氫-2H-哌喃-2-基)氧基)乙氧基)苯甲酸甲酯(253-2，112 mg，0.312 mmol，36.0%產率)。^1H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, *J* = 2.6 Hz, 1H), 7.55 (dd, *J* = 8.9, 2.6 Hz, 1H), 6.94 (d, *J* = 8.9 Hz, 1H), 4.76 (t,

J=3.5 Hz, 1H), 4.30 - 4.16 (m, 2H), 4.08 (dt, *J*=11.5, 4.6 Hz, 1H), 3.94 - 3.84 (m, 5H), 3.59 - 3.52 (m, 1H), 1.88 - 1.79 (m, 1H), 1.79 - 1.71 (m, 1H), 1.67 - 1.60 (m, 2H), 1.58 - 1.50 (m, 2H)。

【0328】 中間物**253-3**：向含有**253-2** (80 mg，0.22 mmol)之反應容器中添加**253-1** (93 mg，0.29 mmol)、$PdCl_2$(dppf)-CH_2Cl_2加合物(27 mg，0.033 mmol)、Na_2CO_3 (94 mg，0.89 mmol)及H_2O (0.5 mL)。藉由使N_2鼓泡使反應混合物脫氣10 min，密封，且在65℃攪拌3h。在冷卻至室溫之後，藉由添加水來淬滅反應混合物，且用EtOAc萃取溶液。將合併之EtOAc部分經Na_2SO_4乾燥，過濾，濃縮且進行矽膠層析純化，得到2'-氟-4-(2-((四氫-2H-哌喃-2-基)氧基)乙氧基)-5'-(2,2,2-三氟-1-羥基乙基)-[1,1'-聯苯]-3-甲酸甲酯(**253-3**，66 mg，0.14 mmol，62%產率)。^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (dd, *J*=2.4, 1.0 Hz, 1H), 7.64 (dt, *J*=8.7, 1.8 Hz, 1H), 7.52 (dd, *J*=7.3, 2.1 Hz, 1H), 7.47 - 7.40 (m, 1H), 7.19 (dd, *J*=10.2, 8.5 Hz, 1H), 7.09 (d, *J*=8.7 Hz, 1H), 5.10 - 5.03 (m, 1H), 4.77 (t, *J*=3.5 Hz, 1H), 4.31 - 4.25 (m, 2H), 4.15 - 4.08 (m, 1H), 3.95 - 3.87 (m, 5H), 3.60 - 3.52 (m, 1H), 2.98 (br d, *J*=3.5 Hz, 1H), 1.89 - 1.81 (m, 1H), 1.79 - 1.71 (m, 1H), 1.67 - 1.61 (m, 2H), 1.59 - 1.51 (m, 2H)。

【0329】 中間物**253-4**：將**253-3** (66 mg，0.14 mmol)溶解於THF (4 mL)中且添加單水合氫氧化鋰(31.7 mg，0.754 mmol)於水(2 mL)中之溶液。在室溫下攪拌反應混合物12 h，用EtOAc (10 mL)稀釋，且藉由添加1.0 eq的1N HCl淬滅。將有機相經Na_2SO_4乾燥，過濾且在減壓下濃縮，得到2'-氟-4-(2-((四氫-2H-哌喃-2-基)氧基)乙氧基)-5'-(2,2,2-三氟-1-羥基乙基)-[1,1'-聯苯]-3-甲酸(**253-4**，64 mg，0.14 mmol，100%產率)，其不

經進一步純化即用於下一步驟。

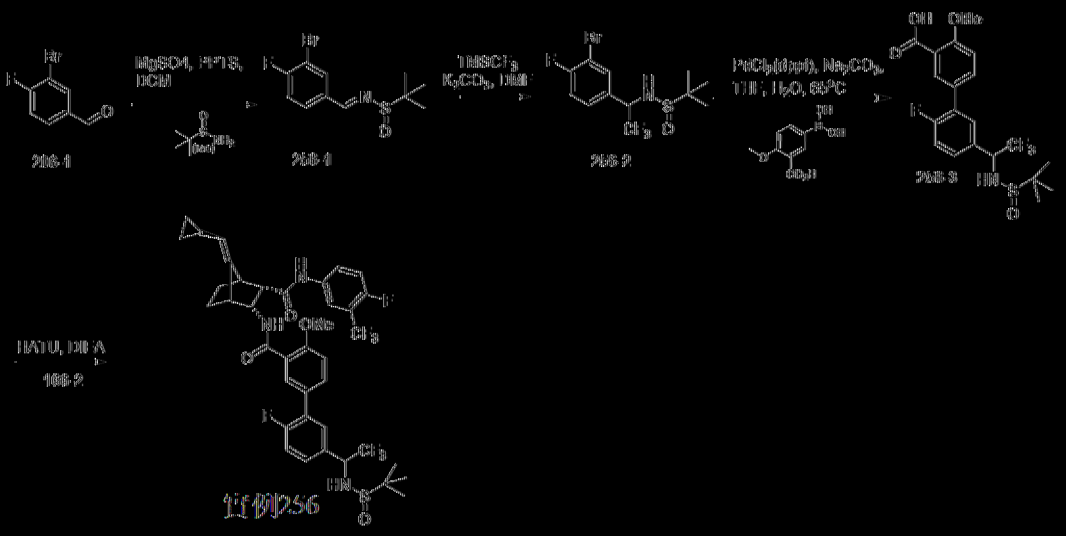
【0330】 中間物**253-5**：向反應容器中添加中間物**166-2** (25 mg，0.068 mmol)、**253-4** (31 mg，0.068 mmol)、MeCN (1 mL)、DIEA (0.036 mL，0.20 mmol)及HATU (28.4 mg，0.0750 mmol)。在室溫下攪拌反應混合物12h，在減壓下濃縮且對殘餘物進行製備型HPLC純化，得到(1R,2S,3R,4R,Z)-7-(環丙基亞甲基)-N-(4-氟-3-(三氟甲基)苯基)-3-(2'-氟-4-(2-((四氫-2H-哌喃-2-基)氧基)乙氧基)-5'-(2,2,2-三氟-1-羥基乙基)-[1,1'-聯苯]-3-甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺(**253-5**，39 mg，0.049 mmol，72%產率)。MS (ESI) *m/z* 809.2 (M+H)。

【0331】 實例**253**：向反應容器中添加**253-5** (15 mg，0.019 mmol)、DCM (1 mL)、吡啶(0.015 mL，0.19 mmol)、氯甲酸4-硝基苯酯(19 mg，0.093 mmol)及DMAP (2.3 mg，0.019 mmol)。在室溫下攪拌2h之後，添加環丁胺(13.2 mg，0.185 mmol)。在室溫下攪拌反應混合物1h且在減壓下濃縮。對殘餘物進行製備型HPLC純化，產生相應胺基甲酸酯。此產物由於存在TFA而不穩定。在室溫下靜置12h，隨後濃縮且進行製備型HPLC純化，得到環丁基胺基甲酸1-(3'-(((1R,2R,3S,4R,Z)-7-(環丙基亞甲基)-3-((4-氟-3-(三氟甲基)苯基)胺甲醯基)雙環[2.2.1]庚烷-2-基)胺甲醯基)-6-氟-4'-(2-羥基乙氧基)-[1,1'-聯苯]-3-基)-2,2,2-三氟乙酯(實例**253**，11.0 mg，0.0130 mmol，70.0%產率)。^{1}H NMR (500 MHz, $CDCl_3$) δ 9.54 (br d, *J*=8.5 Hz, 1H), 8.29 (d, *J*=2.0 Hz, 1H), 7.76 - 7.67 (m, 2H), 7.57 - 7.47 (m, 3H), 7.43 - 7.36 (m, 1H), 7.21 - 7.14 (m, 2H), 7.10 (br d, *J*=8.9 Hz, 1H), 6.11 - 6.05 (m, 1H), 5.32 (br d, *J*=8.2 Hz, 1H), 4.93 - 4.85 (m, 1H), 4.69 (d, *J*=9.6 Hz, 1H), 4.49 - 4.43 (m, 1H), 4.32 - 4.24 (m, 2H),

4.17 – 4.09 (m, 2H), 3.17 (t, *J* = 4.1 Hz, 1H), 3.13 (dd, *J* = 10.5, 3.8 Hz, 1H), 2.75 (t, *J* = 4.0 Hz, 1H), 2.42 – 2.24 (m, 2H), 2.20 – 2.14 (m, 1H), 1.98 – 1.85 (m, 3H), 1.80 – 1.61 (m, 4H), 1.53 – 1.46 (m, 1H), 0.82 – 0.73 (m, 2H), 0.40 – 0.33 (m, 2H)。LC-MS RT: 1.33 min；MS (ESI) *m/z* 822.1 $(M+H)^+$；方法A。

|0332|

實例256：



中間物256-1：向反應容器中添加3-溴-4-氟苯甲醛(1670 mg，8.25 mmol)、2-甲基丙烷-2-亞磺醯胺(500 mg，4.13 mmol)、DCM (2 mL)、$MgSO_4$ (2483 mg，20.63 mmol)及PPTS (52 mg，0.21 mmol)。在室溫下攪拌反應混合物24h，裝載至二氧化矽濾筒，且對其進行矽膠層析純化，得到(*E*)-*N*-(3-溴-4-氟苯甲亞基)-2-甲基丙烷-2-亞磺醯胺(256-1，1220 mg，3.98 mmol，97%產率)。^{1}H NMR (500 MHz, $CDCl_3$) δ 8.51 (s, 1H), 8.11 (dd, *J* = 6.6, 2.2 Hz, 1H), 7.77 (ddd, *J* = 8.5, 4.7, 1.9 Hz, 1H), 7.24 (t, *J* = 8.4 Hz, 1H), 1.28 (s, 9H)。

|0333| 中間物256-2：向反應容器中添加256-1 (200 mg，0.653 mmol)、DMF (3 mL)、(三氟甲基)三甲基矽烷(0.19 mL，1.3 mmol)及

K_2CO_3 (45 mg，0.33 mmol)。在室溫下攪拌反應混合物60 min且添加2N HCl (15 mL)。在室溫下攪拌1h之後，用EtOAc (30 mL)稀釋反應混合物，且用飽和NH_4Cl洗滌有機部分。藉由添加EtOAc (10 mL×2)萃取水相。將合併之有機部分經Na_2SO_4乾燥，濃縮，過濾且藉由矽膠層析純化，得到N-(1-(3-溴-4-氟苯基)-2,2,2-三氟乙基)-2-甲基丙烷-2-亞磺醯胺(**256-2**，163 mg，0.433 mmol，66%產率)。^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (dd, *J*=6.3, 2.1 Hz, 1H), 7.42 - 7.37 (m, 1H), 7.18 (t, *J*=8.4 Hz, 1H), 4.81 (quin, *J*=7.1 Hz, 1H), 3.58 (br d, *J*=6.6 Hz, 1H), 1.27 (s, 9H)。

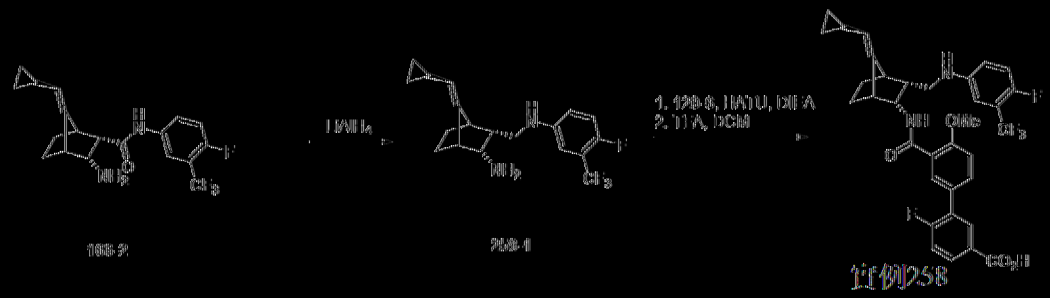
【0334】 中間物**256-3**：向含有**256-2** (50. mg，0.13 mmol)之反應容器中添加5-溴-2-甲氧基苯甲酸(31 mg，0.16 mmol)、$PdCl_2$(dppf)-CH_2Cl_2加合物(16 mg，0.020 mmol)、Na_2CO_3 (56 mg，0.53 mmol)及H_2O (0.5 mL)。藉由使N_2鼓泡使反應混合物脫氣10 min，密封，且在65℃攪拌3h。在冷卻至室溫之後，藉由添加1N HCl淬滅反應混合物，用EtOAc萃取溶液，將合併之有機部分經Na_2SO_4乾燥，過濾，濃縮且進行製備型HPLC純化，得到5'-(1-((三級丁基亞磺醯基)胺基)-2,2,2-三氟乙基)-2'-氟-4-甲氧基-[1,1'-聯苯]-3-甲酸(**256-3**，47 mg，0.10 mmol，79%產率)。MS (ESI) *m/z* 448.1 (M+H)。

【0335】 實例**256**：向反應容器中添加**166-2** (10 mg，0.027 mmol)、**256-3** (12 mg，0.027 mmol)、MeCN (1 mL)、DIEA (0.014 mL，0.081 mmol)及HATU (11 mg，0.030 mmol)。在室溫下攪拌反應混合物12h，在減壓下濃縮且對殘餘物進行製備型HPLC純化，得到(1R,2S,3R,4R,Z)-3-(5'-(1-((三級丁基亞磺醯基)胺基)-2,2,2-三氟乙基)-2'-氟-4-甲氧基-[1,1'-聯苯]-3-甲醯胺基)-7-(環丙基亞甲基)-N-(4-氟-3-(三氟

甲基)苯基)雙環[2.2.1]庚烷-2-甲醯胺(實例256，7.5 mg，9.3 μmol，34%產率)。^{1}H NMR (500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.95 (br t, *J* = 6.4 Hz, 1H), 8.27 – 8.19 (m, 1H), 8.16 (s, 1H), 7.87 – 7.74 (m, 2H), 7.70 (br d, *J* = 8.8 Hz, 1H), 7.66 – 7.58 (m, 1H), 7.48 (br t, *J* = 9.7 Hz, 1H), 7.40 – 7.29 (m, 2H), 6.51 (d, *J* = 9.6 Hz, 1H), 5.39 – 5.27 (m, 1H), 4.68 (d, *J* = 9.7 Hz, 1H), 4.51 – 4.41 (m, 1H), 4.05 (s, 3H), 3.19 – 3.14 (m, 1H), 3.11 (br s, 1H), 1.88 – 1.75 (m, 2H), 1.56 – 1.46 (m, 1H), 1.44 – 1.35 (m, 2H), 1.14 (s, 9H), 0.79 – 0.68 (m, 2H), 0.39 – 0.30 (m, 2H)。LC-MS RT: 1.25 min；MS (ESI) *m/z* 798.1 (M+H)$^+$；方法A。

[0336]

實例258：



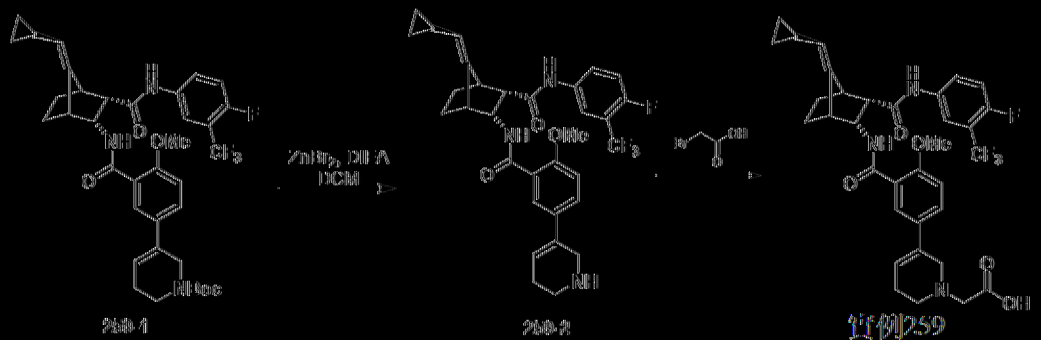
中間物258-1：向反應容器中添加中間物166-2 (15 mg，0.041 mmol)及THF (1 mL)。在冷卻至0℃之後，添加$LiAlH_4$ (0.5 mL，0.500 mmol)。在0℃攪拌5 min之後，使反應混合物升溫至室溫且在室溫下攪拌20 min。用EtOAc稀釋反應混合物。在用飽和$NaHCO_3$洗滌有機溶液之後，經Na_2SO_4乾燥有機相且在減壓下濃縮，得到(1R,2R,3R,4R,7*S*)-7-(環丙基甲基)-3-(((4-氟-3-(三氟甲基)苯基)胺基)甲基)雙環[2.2.1]庚烷-2-胺(258-1，7.0 mg，0.020 mmol，49%產率)。此物質不經進一步純化即用於下一步驟。MS (ESI) *m/z* 355.3 (M+H)。

[0337] 實例258：向反應容器中添加258-1 (7.0 mg，0.020

mmol)、120-6 (6.5 mg，0.019 mmol)、MeCN (1 mL)、DIEA (9.4 µl，0.054 mmol)及HATU (7.5 mg，0.020 mmol)。在室溫下攪拌反應混合物12h，在減壓下濃縮且對殘餘物進行矽膠層析純化，得到殘餘物，將其在室溫下用2:1 DCM/TFA處理30 min。濃縮所得溶液且藉由HPLC純化殘餘物，得到3'-(((1R,2R,3R,4R,7S)-7-(環丙基甲基)-3-(((4-氟-3-(三氟甲基)苯基)胺基)甲基)雙環[2.2.1]庚烷-2-基)胺甲醯基)-6-氟-4'-甲氧基-[1,1'-聯苯]-3-甲酸(實例258，6.5 mg，8.4 µmol，47%產率)。^{1}H NMR (500 MHz, $CDCl_3$) δ 8.59 (br d, *J* = 7.4 Hz, 1H), 8.41 (d, *J* = 1.4 Hz, 1H), 8.23 (dd, *J* = 7.6, 2.1 Hz, 1H), 8.09 (ddd, *J* = 8.5, 4.6, 2.1 Hz, 1H), 7.71 (br d, *J* = 8.8 Hz, 1H), 7.26 - 7.22 (m, 1H), 7.08 - 7.02 (m, 2H), 6.99 - 6.94 (m, 2H), 4.65 (d, *J* = 9.6 Hz, 1H), 4.63 - 4.57 (m, 1H), 4.03 (s, 3H), 3.32 (dd, *J* = 11.4, 2.9 Hz, 1H), 3.09 (t, *J* = 4.1 Hz, 1H), 3.04 - 2.97 (m, 1H), 2.59 - 2.52 (m, 2H), 1.83 - 1.74 (m, 1H), 1.73 - 1.67 (m, 1H), 1.64 - 1.55 (m, 2H), 1.47 - 1.39 (m, 1H), 0.76 - 0.69 (m, 2H), 0.41 - 0.31 (m, 2H)。LC-MS RT: 1.31 min；MS (ESI) *m/z* 683.5 $(M+H)^+$；方法A。

|0338|

實例259



中間物259-1：259-1係遵循針對實例168所描述之程序由中間物166-2及140-2製備。^{1}H NMR (500 MHz, $CDCl_3$) δ 9.58 - 9.15 (br. s, 1H), 8.20

(d, *J*=2.2 Hz, 1H), 8.17 - 7.93 (m, 1H), 7.90 (dd, *J*=6.1, 2.5 Hz, 1H), 7.56 (dt, *J*=8.9, 3.4 Hz, 1H), 7.41 (dd, *J*=8.5, 2.5 Hz, 1H), 7.08 (t, *J*=9.4 Hz, 1H), 6.92 (br d, *J*=7.7 Hz, 1H), 6.16 (dt, *J*=4.0, 2.1 Hz, 1H), 4.87 - 4.79 (m, 1H), 4.63 (d, *J*=9.6 Hz, 1H), 4.32 - 4.18 (m, 2H), 3.99 (s, 3H), 3.55 (br s, 2H), 3.18 (t, *J*=3.7 Hz, 1H), 3.11 - 3.06 (m, 1H), 2.71 (t, *J*=3.7 Hz, 1H), 2.31 (br d, *J*=2.8 Hz, 2H), 2.23 - 2.12 (m, 1H), 1.91 - 1.80 (m, 1H), 1.71 - 1.61 (m, 2H), 1.50 (s, 9H), 1.49 - 1.42 (m, 1H), 0.77 - 0.70 (m, 2H), 0.40 - 0.30 (m, 2H)。

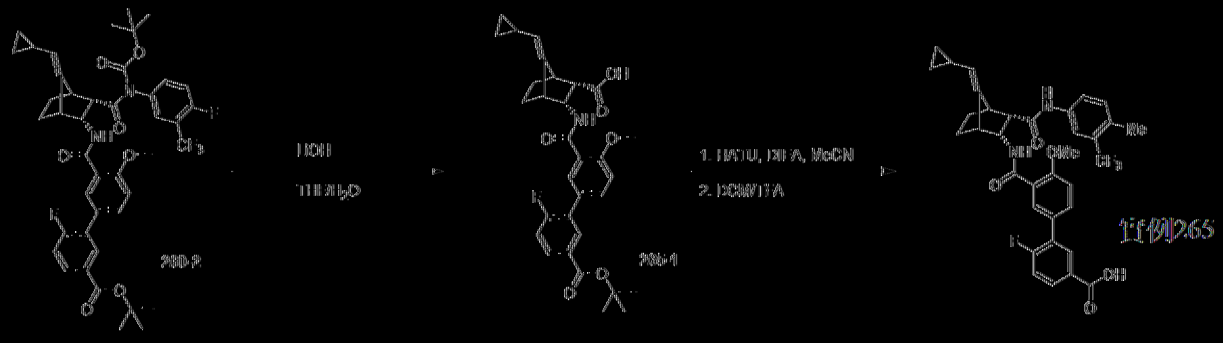
【0339】 中間物**259-2**：向反應容器中添加**259-1** (13 mg，0.019 mmol)、DCM (1.5 mL)、DIEA (0.012 mL，0.067 mmol)及溴化鋅(150 mg，0.665 mmol)。在攪拌12h之後，藉由添加飽和$NaHCO_3$淬滅反應混合物且用EtOAc萃取溶液。將合併之有機部分經Na_2SO_4乾燥，過濾且濃縮，得到(1R,2S,3R,4R,Z)-7-(環丙基亞甲基)-N-(4-氟-3-(三氟甲基)苯基)-3-(2-甲氧基-5-(1,2,5,6-四氫吡啶-3-基)苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺(**259-2**，12 mg，0.021 mmol，110%產率)。此中間物不經進一步純化即用於下一步驟中。MS (ESI) *m/z* 584.4 (M+H)。

【0340】 實例**259**：向反應容器中添加**259-2** (11 mg，0.019 mmol)、MeCN (1 mL)、2-溴乙酸(1.5 mg，0.011 mmol)及DIEA (9.9 µl、0.057 mmol)。在室溫下攪拌反應混合物1h且在減壓下濃縮。對所得殘餘物進行製備型HPLC，隨後進行SFC純化，得到2-(5-(3-(((1R,2R,3S,4R,Z)-7-(環丙基亞甲基)-3-((4-氟-3-(三氟甲基)苯基)胺甲醯基)雙環[2.2.1]庚烷-2-基)胺甲醯基)-4-甲氧基苯基)-3,6-二氫吡啶-1(2H)-基)乙酸(實例**259**，4.1 mg，5.4 µmol，28%產率)。^{1}H NMR (500 MHz,

CD_3OD) δ 10.31 (br d, *J*= 7.2 Hz, 1H), 10.12 (s, 1H), 8.15 (dd, *J*= 6.2, 2.6 Hz, 1H), 8.05 (d, *J*= 2.5 Hz, 1H), 7.78 – 7.68 (m, 1H), 7.59 (dd, *J*= 8.8, 2.5 Hz, 1H), 7.28 (t, *J*= 9.6 Hz, 1H), 7.23 – 7.17 (m, 1H), 6.38 – 6.32 (m, 1H), 4.74 (d, *J*= 9.4 Hz, 1H), 4.60 – 4.52 (m, 1H), 4.25 (br s, 4H), 4.09 (s, 3H), 3.25 – 3.19 (m, 1H), 3.17 – 3.11 (m, 1H), 2.77 – 2.68 (m, 3H), 2.01 – 1.89 (m, 2H), 1.59 – 1.47 (m, 3H), 0.80 – 0.71 (m, 2H), 0.41 – 0.29 (m, 2H)。LC-MS RT: 0.94 min；MS (ESI) *m/z* 642.3 $(M+H)^+$；方法A。

|0341|

實例265



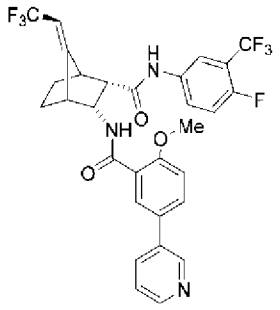
中間物265-1：向含有含260-2 (10 mg，0.013 mmol)之THF (1.3 mL)的小瓶中添加呈1M水溶液形式之LiOH (63 μl，0.063 mmol)。在室溫下攪拌反應混合物18 h，接著用1N HCl稀釋。用EtOAc (3x5 mL)萃取所得混合物。將合併之有機物經Na_2SO_4乾燥，過濾且濃縮，得到(1R,2S,3R,4R,Z)-3-(5'-(三級丁氧基羰基)-2'-氟-4-甲氧基-[1,1'-聯苯]-3-甲醯胺基)-7-(環內基亞甲基)雙環[2.2.1]庚烷-2-甲酸(7.0 mg，0.013 mmol，100%產率)，其不經進一步純化即使用。^{1}H-NMR (500 MHz, DMSO-d6) δ 10.05 (br s, 1H), 8.12 (s, 1H), 8.01 – 7.97 (m, 1H), 7.96 – 7.92 (m, 1H), 7.74 (d, J= 8.9 Hz, 1H), 7.45 (t, J= 9.5 Hz, 1H), 7.33 (d, J= 8.9 Hz, 1H), 4.66 (d, J= 9.5 Hz, 1H), 4.34 – 4.25 (m, 1H), 4.04 (s, 3H), 3.15 –

3.09 (m, 1H), 2.99 (dd, J=10.8, 3.8 Hz, 1H), 2.68 - 2.61 (m, 1H), 1.76 - 1.63 (m, 2H), 1.56 (s, 9H), 1.47 (dt, J=8.7, 4.2 Hz, 1H), 1.42 (s, 2H), 0.84 - 0.60 (m, 2H), 0.44 - 0.23 (m, 2H)。LC-MS RT: 1.17 min；MS (ESI) *m/z* 536 $(M+H)^+$；方法D。

【0342】**實例265**：向反應容器中添加**265-1** (4.0 mg，0.022 mmol)、MeCN (1 mL)、DIEA (10 µl，0.060 mmol)及HATU (6.8 mg，0.018 mmol)。在室溫下攪拌反應混合物12h，隨後在減壓下濃縮且將殘餘物溶解於1:2 TFA/DCM中且攪拌30 min。將反應混合物在減壓下濃縮，溶解於DMSO中，且藉由HPLC純化，得到3'-(((1R,2R,3S,4R,Z)-7-(環丙基亞甲基)-3-((4-甲基-3-(三氟甲基)苯基)胺甲醯基)雙環[2.2.1]庚烷-2-基)胺甲醯基)-6-氟-4'-甲氧基-[1,1'-聯苯]-3-甲酸(3.4 mg，5.3 µmol，35%產率)。^{1}H-NMR (500 MHz, DMSO-d6) δ 10.41 (s, 1H), 9.98 (d, J=6.7 Hz, 1H), 8.21 - 8.09 (m, 2H), 8.05 - 7.99 (m, 1H), 7.99 - 7.90 (m, 1H), 7.77 - 7.70 (m, 1H), 7.64 (dd, J=7.8, 1.1 Hz, 1H), 7.45 - 7.36 (m, 2H), 7.33 (d, J=8.5 Hz, 1H), 4.69 (d, J=9.5 Hz, 1H), 4.55 - 4.36 (m, 1H), 4.06 (s, 3H), 3.19 - 3.13 (m, 1H), 3.13 - 3.08 (m, 1H), 2.78 - 2.66 (m, 1H), 2.37 (s, 3H), 1.90 - 1.84 (m, 1H), 1.83 - 1.76 (m, 1H), 1.55 - 1.47 (m, 1H), 1.47 - 1.37 (m, 2H), 0.84 - 0.60 (m, 2H), 0.42 - 0.23 (m, 2H)。LC-MS RT: 2.21 min；MS (ESI) *m/z* 653 $(M+H)^+$；方法A。

【0343】

實例310



中間物310-1

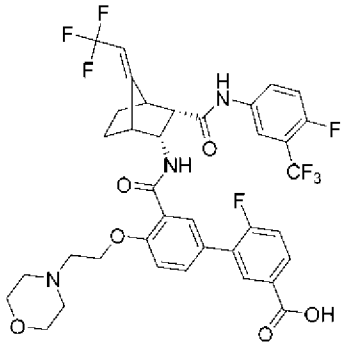
用四甲基乙二醇(0.121 g，1.02 mmol)處理5-溴-2-甲氧基苯甲酸(0.200 g，1.02 mmol)於EtOAc (10ml)中之溶液且在室溫下攪拌所得溶液過夜。接著濃縮反應混合物且呈2-甲氧基-5-(4,4,5,5-四甲基-1,3,2-二氧硼雜環己烷-2-基)苯甲酸(0.284 g，1.02 mmol，100%產率)形式之所得固體不經進一步操作即使用。此固體係根據與實例**108**相同之程序與中間物**170-2**偶合，得到中間物**310-1**。

【0344】 將**310-1** (50 mg，0.076 mmol)、$PdCl_2$(dppf) (5.6 mg，7.6 μmol)、3-溴吡啶(0.1 mL)及K_3PO_4 (48.5 mg，0.229 mmol)之反應混合物加熱至80℃。使反應混合物冷卻至室溫且分配於水與EtOAc之間。濃縮有機層且藉由逆相HPLC純化殘餘物，得到(1R,2S,3R,4R,Z)-N-(4-氟-3-(三氟甲基)苯基)-3-(2-甲氧基-5-(吡啶-3-基)苯甲醯胺基)-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-甲醯胺(11.4 mg，0.019 mmol，24%產率)。^{1}H NMR (500 MHz, DMSO-d6) δ 10.68 (s, 1H), 9.99 (br d, J=6.8 Hz, 1H), 8.85 (s, 1H), 8.55 (br d, J=3.4 Hz, 1H), 8.24 (br d, J=2.3 Hz, 2H), 8.07 - 8.00 (m, 1H), 7.90 (dd, J=8.6, 2.4 Hz, 1H), 7.83 - 7.73 (m, 1H), 7.56 - 7.45 (m, 2H), 7.34 (d, J=8.8 Hz, 1H), 6.05 - 5.92 (m, 1H), 4.60 - 4.51 (m, 1H), 4.06 (s, 3H), 3.47 (s, 1H), 3.00 (br s, 1H), 2.74 (s, 1H), 2.02 - 1.95 (m, 1H), 1.94 - 1.87 (m, 1H), 1.51 (br d, J=6.6 Hz, 2H)。LC-MS RT 2.47 min；MS (ESI) m/z = 608.3 (M+H)+；方法C。

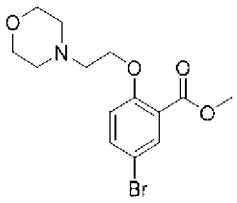
【0345】 **實例320**係經由以下中間物，以類似於**實例253**之方式製備。

【0346】

實例320



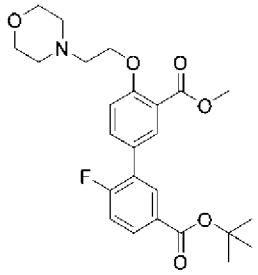
中間物320-1



向5-溴-2-羥基苯甲酸甲酯(750 mg，3.25 mmol)及4-(2-溴乙基)味啉(756 mg，3.90 mmol)於DMF (12 mL)中之溶液中添加K_2CO_3 (1346 mg，9.74 mmol)，在70℃加熱4 h。用EtOAc稀釋反應混合物，且用水及鹽水溶液洗滌溶液。使所分離之有機層經Na_2SO_4乾燥，過濾且在減壓下濃縮。藉由二氧化矽管柱純化殘餘物，得到5-溴-2-(2-N-味啉基乙氧基)苯甲酸甲酯(**320-1**，0.800 g，2.32 mmol，71.6%產率)。MS, *m/z*: 343.9 (M+2H)。

【0347】

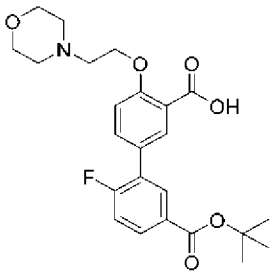
中間物320-2



向**320-1** (300 mg，0.872 mmol)及4-氟-3-(4,4,5,5-四甲基-1,3,2-二氧雜硼雜環戊-2-基)苯甲酸三級丁酯(309 mg，0.959 mmol)於1,4-二噁烷(10 mL)及水(1 mL)中之溶液中添加磷酸三鉀(555 mg，2.61 mmol)，且用氮氣吹掃所得混合物5 min。添加$PdCl_2$(dppf)-CH_2Cl_2加合物(71 mg，0.087 mmol)且用氮氣吹掃反應混合物2 min，隨後在密封管中在85℃加熱16 h。經由矽藻土過濾反應混合物。用EtOAc稀釋濾液且用水及鹽水溶液洗滌有機相。使有機層經Na_2SO_4乾燥，過濾且在減壓下濃縮。藉由二氧化矽管柱層析純化殘餘物，得到6'-氟-4-(2-N-味啉基乙氧基)-[1,1'-聯苯]-3,3'-二甲酸3'-(三級丁酯)3-甲酯(**320-2**，0.310 g，0.675 mmol，77%產率)。MS, *m/z*: 460.2 (M+H)。

【0348】

中間物320-3

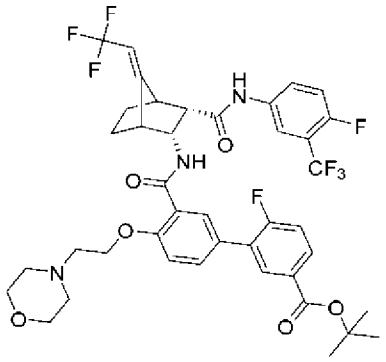


向**320-2** (100 mg，0.218 mmol)於THF (2 mL)中之溶液中添加NaOH (0.87 mL，2.2 mmol)溶液且在50℃攪拌30 min。在真空下移除THF，添加1 ml水且用1.5N HCl酸化至pH 4。用EtOAc (2×20 ml)萃取水層。將合併之有機層用水及鹽水溶液洗滌，經Na_2SO_4乾燥，過濾且在減壓下濃

縮，得到5'-(三級丁氧基羰基)-2'-氟-4-(2-N-味啉基乙氧基)-[1,1'-聯苯]-3-甲酸(40 mg，0.090 mmol，41%產率)。MS, *m/z*: 446.2 (M+H)。

【0349】

中間物320-4



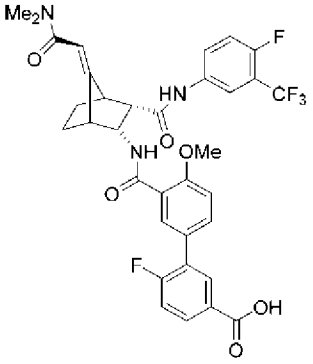
向**320-3** (30 mg，0.076 mmol)及**170-2** (334 mg，0.0760 mmol)於DMF (2 mL)中之溶液中添加DIPEA (0.07 mL，0.4 mmol)及HATU (57.6 mg，0.151 mmol)，且在室溫下攪拌12h。將反應混合物用EtOAc稀釋，用水及鹽水溶液洗滌。使經分離之有機層經Na_2SO_4乾燥，過濾且濃縮。藉由矽膠層析純化殘餘物產物，得到6-氟-3'-(((1R,2R,3S,4R,Z)-3-((4-氟-3-(三氟甲基)苯基)胺甲醯基)-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基)胺甲醯基)-4'-(2-N-味啉基乙氧基)-[1,1'-聯苯]-3-甲酸三級丁酯(**320-4**，50 mg，0.061 mmol，80%產率)。MS, *m/z*: 824.3 (M+H)。

【0350】 在0℃向**320-4** (50 mg，0.061 mmol)於DCM (2 mL)中之溶液中添加TFA (0.094 mL，1.2 mmol)，在室溫下攪拌4 h。在減壓下濃縮反應混合物且藉由逆相HPLC純化殘餘物，得到呈白色固體之6-氟-3'-(((1R,2R,3S,4R,Z)-3-((4-氟-3-(三氟甲基)苯基)胺甲醯基)-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基)胺甲醯基)-4'-(2-N-味啉基乙氧基)-[1,1'-聯苯]-3-甲酸(20 mg，0.025 mmol，42%產率)。^{1}H NMR (400MHz, DMSO-d6) δ ppm 13.27 - 13.08 (m, 1H), 10.47 - 10.37 (m, 1H), 10.02 - 9.81 (m,

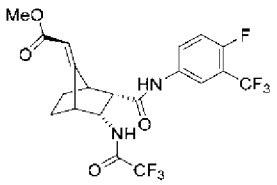
1H), 8.91 - 8.75 (m, 1H), 8.16 - 7.94 (m, 3H), 7.89 - 7.79 (m, 1H), 7.76 - 7.60 (m, 2H), 5.82 - 5.67 (m, 1H), 4.68 - 4.61 (m, 1H), 4.61 - 4.43 (m, 1H), 4.01 - 3.83 (m, 2H), 3.75 - 3.61 (m, 2H), 3.58 - 3.48 (m, 3H), 2.84 - 2.78 (m, 2H), 2.70 - 2.63 (m, 5H), 2.02 - 1.85 (m, 2H), 1.81 - 1.65 (m, 2H), 1.62 - 1.45 (m, 2H)。MS, *m/z*: 768.2 (M+H)。

【0351】

實例323



中間物323-1

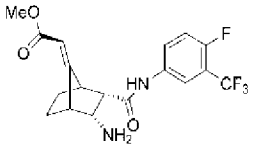


將溶解於MeOH (0.5 mL)及THF (0.5 mL)中之**120-4** (0.05 g，0.1 mmol)中添加休尼格氏鹼(0.021 mL，0.12 mmol)、三苯基膦(0.8 mg，3 μmol)及雙(三苯基膦)氯化鈀(II) (2 mg，3 μmol)。在60 psi下用一氧化碳加壓容器且在70℃加熱36 h。將反應溶液在真空下濃縮且經由急驟層析純化，得到(Z)-2-((1R,2S,3R,4R)-2-((4-氟-3-(三氟甲基)苯基)胺甲醯基)-3-(2,2,2-三氟乙醯胺基)雙環[2.2.1]庚烷-7-亞基)乙酸甲酯**323-1**。^{1}H NMR (500 MHz, $CDCl_3$) δ 9.49 (br d, *J*=6.9 Hz, 1H), 7.96 (s, 1H), 7.86 - 7.72 (m, 2H), 7.23 (t, *J*=9.4 Hz, 1H), 5.76 (s, 1H), 4.51 (dt, *J*=10.5, 5.3 Hz,

1H), 3.93 (t, *J*=4.1 Hz, 1H), 3.86 - 3.75 (m, 3H), 3.18 - 3.05 (m, 1H), 2.89 (t, *J*=4.0 Hz, 1H), 2.06 - 1.87 (m, 2H), 1.78 - 1.64 (m, 2H)。

【0352】

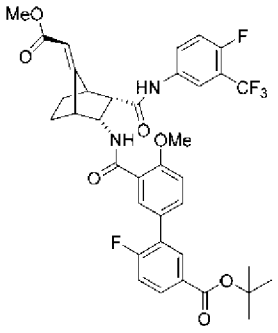
中間物323-2



向MeOH (0.8 mL)中添加AcCl (0.080 mL，1.1 mmol)且攪拌5分鐘，並添加**323-1** (0.029 g，0.060 mmol)，且攪拌反應混合物32 h。在真空下濃縮反應混合物，得到(Z)-2-((1R,2R,3S,4R)-2-胺基-3-((4-氟-3-(三氟甲基)苯基)胺甲醯基)雙環[2.2.1]庚烷-7-亞基)乙酸甲酯氯化氫鹽(**323-2**，0.025 g，0.060 mmol，100%產率)，其不經進一步純化即使用。MS (ESI) *m/z* 387.0 (M+H)。

【0353】

中間物323-3

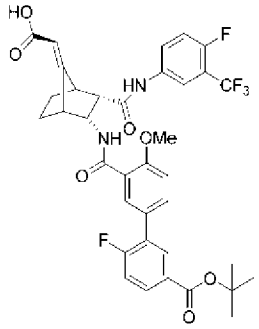


向溶解於MeCN (0.6 mL)中之**323-2**及**120-6** (0.025 g，0.072 mmol)中添加DIEA (0.03 mL，0.2 mmol)，隨後添加HATU (0.034 g，0.090 mmol)。將反應混合物攪拌16 h，在真空下濃縮且經由急驟層析純化，得到6-氟-3'-(((1R,2R,3S,4R,Z)-3-((4-氟-3-(三氟甲基)苯基)胺甲醯基)-7-(2-甲氧基-2-側氧基亞乙基)雙環[2.2.1]庚烷-2-基)胺甲醯基)-4'-甲氧基-[1,1'-

聯苯]-3-甲酸三級丁酯(**323-3**，0.028 g，0.039 mmol，65%產率)。MS (ESI) *m/z* 715.3 (M+H)。

【0354】

中間物323-4



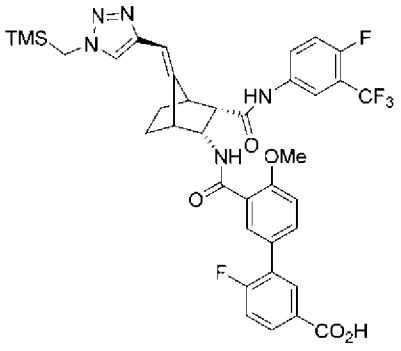
向溶解於THF (1 mL)中之**323-3** (0.028 g，0.040 mmol)中添加水(0.5 mL)及單水合氫氧化鋰(2 mg，0.05 mmol)且攪拌16 h。將反應混合物用水稀釋，用1M HCl中和且萃取至EtOAc中。分離有機層且經Na_2SO_4乾燥且在減壓下濃縮，得到(Z)-2-((1R,2R,3S,4R)-2-(5'-(三級丁氧基羰基)-2'-氟-4-甲氧基-[1,1'-聯苯]-3-甲醯胺基)-3-((4-氟-3-(三氟甲基)苯基)胺甲醯基)雙環[2.2.1]庚烷-7-亞基)乙酸(**323-4**，0.025 g，0.036 mmol，90%產率)。^{1}H NMR (500 MHz, $CDCl_3$) δ 8.43 (s, 1H), 8.30 - 8.18 (m, 1H), 8.16 - 8.06 (m, 1H), 8.02 - 7.94 (m, 1H), 7.71 (br d, *J*=8.5 Hz, 1H), 7.25 - 7.13 (m, 2H), 7.00 (br d, *J*=8.8 Hz, 1H), 5.82 (s, 1H), 4.85 - 4.65 (m, 1H), 4.29 (br s, 1H), 3.97 (s, 3H), 3.16 - 2.96 (m, 2H), 2.22 - 2.09 (m, 1H), 2.04 - 1.86 (m, 2H), 1.75 - 1.58 (m, 9H) MS (ESI) *m/z* 701.3 (M+H)。

【0355】 **實例323**係藉由首先根據**實例34**之程序製造醯胺，隨後根據**實例120**之程序移除三級丁基，由**中間物323-4**來製備。^{1}H NMR (500 MHz, DMSO-d6) δ 10.67 (s, 1H), 9.85 (br d, J=7.0 Hz, 1H), 8.24 (br d, J=4.3 Hz, 1H), 8.11 (br s, 1H), 8.01 (br d, J=7.0 Hz, 1H), 7.93 (br s, 1H),

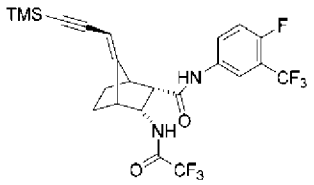
7.80 (br d, J=8.2 Hz, 1H), 7.72 (br d, J=8.2 Hz, 1H), 7.48 (br t, J=9.5 Hz, 1H), 7.37 (br t, J=9.5 Hz, 1H), 7.31 (br d, J=8.9 Hz, 1H), 6.14 (s, 1H), 4.58 - 4.44 (m, 1H), 4.06 (s, 3H), 3.54 (br s, 1H), 3.05 (s, 3H), 2.99 (s, 1H), 2.88 (s, 4H), 2.03 - 1.95 (m, 1H), 1.90 - 1.73 (m, 1H), 1.45 (br s, 2H)。LC-MS RT: 2.19 min；MS (ESI) m/z = 627.14 (M-H)+；方法C。

【0356】

實例325



中間物325-1

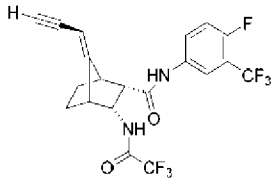


向在三乙胺(0.2 mL)中製成漿液之**120-4** (0.05 g，0.1 mmol)中添加乙炔基三甲基矽烷(0.02 mL，0.1 mmol)、雙(三苯基膦)氯化鈀(II) (3 mg，5 μmol)及碘化銅(I) (2 mg，10 μmol)。在90℃加熱反應混合物16 h。使反應混合物分配於EtOAc與pH 7.4緩衝液之間且萃取至EtOAc中。分離有機層且經Na_2SO_4乾燥，傾析且在真空下濃縮，且經由急驟層析純化殘餘物，得到(1R,2S,3R,4R,Z)-N-(4-氟-3-(三氟甲基)苯基)-3-(2,2,2-三氟乙醯胺基)-7-(3-(三甲基矽基)丙-2-炔-1-亞基)雙環[2.2.1]庚烷-2-甲醯胺(**325-1**，40 mg，0.077 mmol，77%產率)。^{1}H NMR (500 MHz, $CDCl_3$) δ 9.39 (br d, *J*=6.9 Hz, 1H), 7.78 - 7.67 (m, 2H), 7.33 (s, 1H), 7.26 - 7.18

(m, 1H), 5.45 (s, 1H), 4.60 - 4.41 (m, 1H), 3.32 (t, *J*=4.1 Hz, 1H), 3.05 (ddd, *J*=10.5, 4.4, 1.4 Hz, 1H), 2.81 (t, *J*=4.1 Hz, 1H), 1.98 - 1.90 (m, 1H), 1.90 - 1.81 (m, 1H), 1.76 - 1.59 (m, 2H), 0.31 - 0.17 (m, 9H)。MS (ESI) *m/z* 521.0 (M+H)。

【0357】

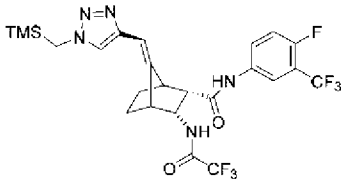
中間物325-2



向溶解於THF (0.8 mL)中之**325-1** (40 mg，0.077 mmol)中添加1 M TBAF/THF (0.2 mL，0.2 mmol)且攪拌反應物16 h。在減壓下濃縮反應混合物且經由急驟層析純化，得到(1R,2S,3R,4R,Z)-N-(4-氟-3-(三氟甲基)苯基)-7-(丙-2-炔-1-亞基)-3-(2,2,2-三氟乙醯胺基)雙環[2.2.1]庚烷-2-甲醯胺(**325-2**，38 mg，0.084 mmol，定量產率)。MS (ESI) *m/z* 499.0 (M+H)。

【0358】

中間物325-3

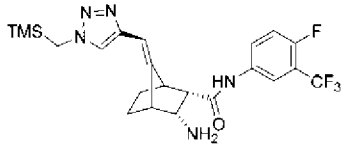


向**325-2** (0.017 g，0.038 mmol)、(疊氮基甲基)三甲基矽烷(0.011 mL，0.076 mmol)溶解於DMF (0.3 mL)及水(0.1 mL)中之溶液中添加五水合硫酸銅(II) (7 mg，0.03 mmol)及抗壞血酸鈉(8 mg，0.04 mmol)且攪拌3h。使反應混合物分配於EtOAc與水之間，且將有機層用EtOAc洗滌2次，經$MgSO_4$乾燥，過濾且真空濃縮，得到(1R,2S,3R,4R,Z)-N-(4-氟-3-

(三氟甲基)苯基)-3-(2,2,2-三氟乙醯胺基)-7-((1-((三甲基矽基)甲基)-1H-1,2,3-三唑-4-基)亞甲基)雙環[2.2.1]庚烷-2-甲醯胺**325-3**，其不經進一步純化即使用。MS (ESI) *m/z* 578.1 (M+H)。

【0359】

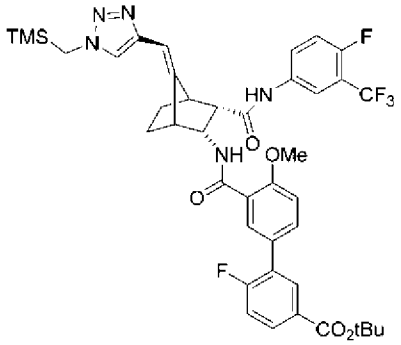
中間物325-4



向MeOH (0.5 ml)中添加AcCl (0.050 ml，0.70 mmol)且攪拌反應混合物5 min。添加**325-3** (0.022 g，0.038 mmol)且在40℃攪拌反應混合物48 h。在減壓下濃縮反應混合物且在高真空下移除殘餘溶劑，以產生(1R,2S,3R,4R,Z)-3-胺基-N-(4-氟-3-(三氟甲基)苯基)-7-((1-((三甲基矽基)甲基)-1H-1,2,3-三唑-4-基)亞甲基)雙環[2.2.1]庚烷-2-甲醯胺(**325-4**，0.018 g，0.038 mmol，100%產率)，其不經進一步純化即使用。MS (ESI) *m/z* 482.2 (M+H)。

【0360】

中間物325-5



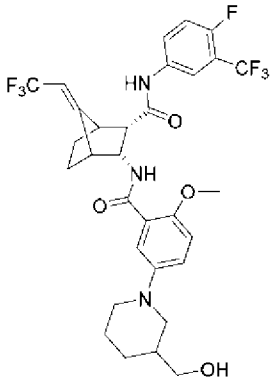
中間物325-5係根據**實例108**之程序由**325-4**及**120-6**製備。

【0361】 **實例325**係根據**實例120**之程序由**325-5**製備。^{1}H NMR (500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.85 (br d, J=7.0 Hz, 1H), 8.15 (br

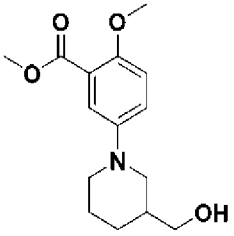
d, J=4.6 Hz, 1H), 8.05 (br s, 1H), 7.99 - 7.81 (m, 3H), 7.71 (br s, 1H), 7.65 (br d, J=8.2 Hz, 1H), 7.40 (br t, J=9.6 Hz, 1H), 7.33 (br t, J=9.6 Hz, 1H), 7.24 (br d, J=8.5 Hz, 1H), 6.18 (s, 1H), 4.44 (br s, 1H), 3.98 (s, 3H), 3.90 (s, 2H), 3.48 (br s, 1H), 3.27 - 3.09 (m, 1H), 2.83 (br s, 1H), 1.96 - 1.72 (m, 2H), 1.41 (br d, J=5.8 Hz, 2H), 0.00 (s, 9H)。LC-MS RT: 2.54 min；MS (ESI) m/z = 754.36 (M-H)+；方法C。

【0362】

實例329



中間物329-1

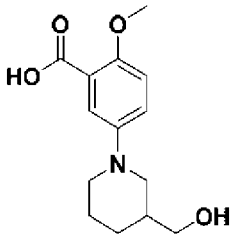


向5-碘-2-甲氧基苯甲酸甲酯(500 mg，1.71 mmol)及哌啶-3-基甲醇(394 mg，3.42 mmol)於DMSO (10 mL)中之溶液中添加K_2CO_3 (710 mg，5.14 mmol)、CuI (98 mg，0.51 mmol)及L-脯胺酸(59 mg，0.51 mmol)。將所得溶液用N_2脫氣10 min，隨後在90℃加熱12 h。將反應混合物用乙酸乙酯稀釋，用水、鹽水洗滌，經Na_2SO_4乾燥且在減壓下濃縮。藉由矽膠層析純化殘餘物，得到5-(3-(羥基甲基)哌啶-1-基)-2-甲氧基苯甲酸甲酯(**329-1**，350 mg，1.25 mmol，73.2%產率)。MS (ESI) *m/z* 280.2

(M+H)。

【0363】

中間物329-2

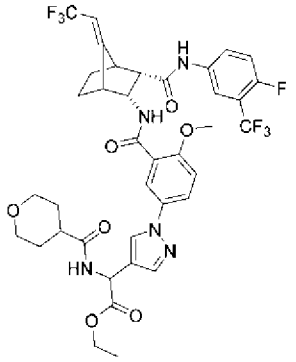


向**329-1** (350 mg，1.253 mmol)於MeOH (5 mL)、THF (5 mL)及水(3 mL)中之溶液中添加LiOH (150 mg，6.26 mmol)且在室溫下攪拌3h。在減壓下濃縮反應物質，用HCl將水層酸化至pH約4-5，且過濾所得沈澱物且乾燥，得到呈白色固體之5-(3-(羥基甲基)哌啶-1-基)-2-甲氧基苯甲酸(300 mg，1.13 mmol，90%產率)。MS (ESI) *m/z* 266.2 (M+H)。

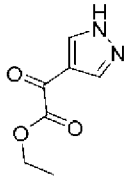
【0364】 **實例329**係根據**實例108**之程序，由**中間物166-2**及**329-2**製備。藉由製備型HPLC管柱Chiralcel OD-H (250 × 4.6)mm,5u分離立體異構物，得到(1R,2R,3R,4R,Z)-N-(4-氟-3-(三氟甲基)苯基)-3-(5-(3-(羥基甲基)哌啶-1-基)-2-甲氧基苯甲醯胺基)-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-甲醯胺(2.1 mg，3.231 μmol，3.51%產率)。MS (ESI) *m/z* 644.2 (M+H)。^{1}H NMR (400 MHz, DMSO-d6) δ ppm 10.43 (s, 1H), 8.41 (d, *J* = 6.5 Hz, 1H), 8.12 (dd, *J* = 2.5, 6.5 Hz, 1H), 7.88 - 7.75 (m, 1H), 7.48 (t, *J* = 9.8 Hz, 1H), 7.20 (d, *J* = 2.5 Hz, 1H), 7.11 - 6.95 (m, 2H), 5.82 - 5.64 (m, 1H), 4.65 - 4.56 (m, 1H), 4.52 (t, *J* = 5.3 Hz, 1H), 3.83 (s, 3H), 3.51 (br s, 1H), 3.44 - 3.41 (m, 1H), 3.25 - 3.20 (m, 2H), 2.78 (d, *J* = 4.0 Hz, 1H), 2.58 - 2.55 (m, 3H), 2.32 - 2.27 (m, 1H), 1.92 (td, *J* = 4.7, 12.2 Hz, 1H), 1.80 - 1.65 (m, 6H), 1.56 (br s, 2H), 1.09 - 0.94 (m, 1H)。

【0365】

實例346



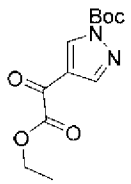
中間物346-1



在-78℃向4-溴-1H-吡唑(2.00 g，13.6 mmol)於THF (100 mL)中之溶液中逐滴添加正丁基鋰(25.5 mL，40.8 mmol)。添加完成後，使反應混合物升高至室溫且在室溫下攪拌1.5小時。隨後將混合物冷卻回至-78℃且添加草酸二乙酯(2.8 mL，20 mmol)於THF (2.5 mL)中之溶液且攪拌20分鐘。藉由添加飽和氯化銨淬滅反應混合物且用乙酸乙酯萃取溶液。合併有機層，在減壓下濃縮且使用矽膠層析純化，得到**346-1** (496 mg，20.6%)。MS (ESI) *m/z*: 168.9 (M+H)。

【0366】

中間物346-2

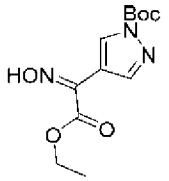


向**346-1** (150 mg，0.892 mmol)於乙腈(5 mL)中之溶液中添加DMAP (10.90 mg，0.089 mmol)、二碳酸二-三級丁酯(0.249 mL，1.07 mmol)，

隨後添加TEA (0.149 mL，1.07 mmol)。隨後在室溫下攪拌反應混合物18h。隨後在減壓下濃縮反應混合物且使用矽膠層析純化，得到**346-2** (185 mg，73.4%)。MS (ESI) *m/z*: 269.1 (M+H)。

【0367】

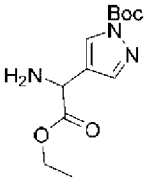
中間物346-3



在回流下加熱**346-2** (185 mg，0.690 mmol)、乙酸鈉(62.2 mg，0.759 mmol)及羥胺鹽酸鹽(86 mg，1.241 mmol)於乙醇(3 mL)中之溶液1小時。隨後在真空下濃縮反應混合物且用乙酸乙酯稀釋。將有機層用5% HCl溶液洗滌，得到**346-3** (190 mg，88%)，其不經進一步純化即使用。MS (ESI) *m/z*: 183.9 (M+H-Boc)。

【0368】

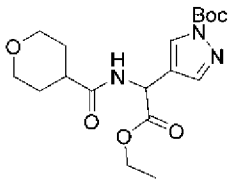
中間物346-3



向**346-3** (190 mg，0.671 mmol)於乙醇(5 mL)中之經脫氣溶液中添加鈀/碳(143 mg，0.134 mmol)且用氮氣脫氣。在氫氣球下攪拌反應混合物1.5小時。經矽藻土墊過濾反應混合物，得到**346-4** (181 mg，100%)。MS (ESI) *m/z*: 270.1 (M+H)。

【0369】

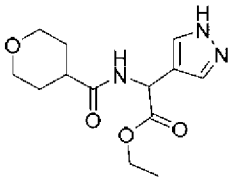
中間物346-5



向**346-4** (181 mg，0.672 mmol)及四氫-2H-哌喃-4-甲酸(87 mg，0.672 mmol)於無水DMF (2 mL)中之溶液中添加DIEA (0.587 mL，3.36 mmol)，隨後添加BOP (327 mg，0.739 mmol)。在室溫下攪拌反應混合物1小時且過濾。在減壓下濃縮殘餘物且使用矽膠層析純化，得到**346-5** (120 mg，44.5%)。MS (ESI) *m/z*: 382.3 (M+H)。

【0370】

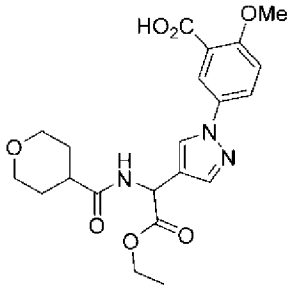
中間物346-6



向**346-5** (120 mg，0.315 mmol)於DCM (4 mL)中之溶液中添加TFA (1.5 mL，19.47 mmol)，且在室溫下攪拌反應混合物1小時。在減壓下濃縮反應混合物，得到**346-6** (125 mg，90%)。MS (ESI) *m/z*: 282.2 (M+H)。

【0371】

中間物346-7



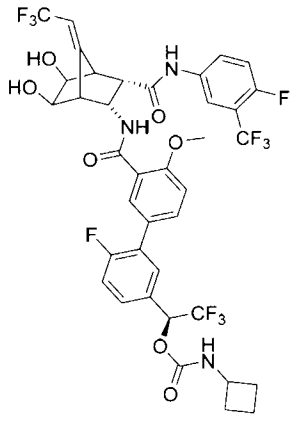
向5-溴-2-甲氧基苯甲酸(87 mg，0.444 mmol)、**346-6** (125 mg，0.444 mmol)及硼酸(boric acid) (82 mg，1.3 mmol)之經N_2脫氣溶液中添

加乙酸銅(II) (81 mg，0.44 mmol)，且在室溫下攪拌反應混合物18h。在減壓下濃縮反應混合物且使用矽膠層析純化。MS (ESI) *m/z*: 432.3 (M+H)。

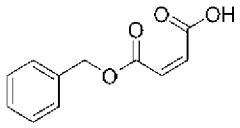
【0372】 **實例346**係以與**實例108**類似之方式由**170-2**及**346-7**製備。^{1}H NMR (500MHz, DMSO-d_6) δ 10.66 (s, 1H), 10.03 (d, *J*=6.7 Hz, 1H), 8.59 - 8.51 (m, 1H), 8.46 (br. s., 1H), 8.32 (br. s., 1H), 8.24 (d, *J*=4.6 Hz, 1H), 7.98 - 7.88 (m, 1H), 7.79 (br. s., 1H), 7.72 (s, 1H), 7.50 (t, *J*=9.8 Hz, 1H), 7.33 (d, *J*=8.8 Hz, 1H), 6.00 - 5.88 (m, 1H), 5.38 (d, *J*=6.4 Hz, 1H), 4.54 (br. s., 1H), 4.17 - 4.09 (m, 2H), 4.05 (s, 3H), 3.36 - 3.20 (m, 2H), 3.00 (br. s., 1H), 2.01 - 1.82 (m, 2H), 1.69 - 1.55 (m, 5H), 1.50 (d, *J*=6.1 Hz, 2H), 1.17 (t, *J*=7.0 Hz, 3H)；LC-MS (M+H) = 810.1；HPLC RT = 2.44 min；方法B。

【0373】

實例348



中間物348-1：

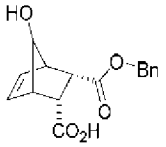


將呋喃-2,5-二酮(10 g，102 mmol)及苯甲醇(31.7 mL，306 mmol)於甲苯(50 mL)中之混合物加熱至80℃持續24小時。隨後在減壓下濃縮反應

混合物且使用矽膠層析純化，得到**348-1** (15.5 g，73%)。MS (ESI) *m/z*: 206.9 (M+H)。

【0374】

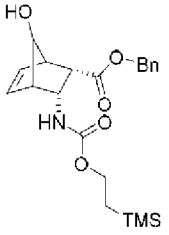
中間物348-2



向**348-1** (3.6 g，17 mmol)於MeCN (40 mL)及水(0.400 mL)中之溶液中添加六氟磷酸二茂鐵(11.6 g，34.9 mmol)且在開放氛圍中攪拌18小時。在減壓下濃縮反應混合物且用DCM稀釋。用1N HCl (40 mL)處理反應混合物30分鐘。接著分離有機層且用DCM洗滌水層且分離。合併有機層且用鹽水洗滌。在減壓下濃縮有機層且使用矽膠層析純化，得到**348-2** (1.8 g，35%)。MS (ESI) *m/z*: 289.1 (M+H)。

【0375】

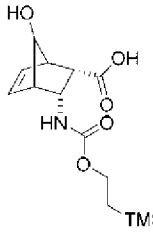
中間物348-3



向3頸圓底燒瓶中添加**348-2** (1.99 g，6.90 mmol)及甲苯(45 mL)，隨後添加TEA (2.1 mL，15 mmol)及二苯基磷醯基疊氮化物(1.26 mL，5.87 mmol)。在室溫下攪拌反應混合物2.5小時。向此反應混合物中添加2-(三甲基矽基)乙-1-醇(3.94 mL，28.3 mmol)且在80℃加熱所得反應混合物28小時。使反應混合物冷卻至室溫，在減壓下濃縮且使用矽膠層析純化，得到**348-3** (1.52 g，51.8%)。MS (ESI) *m/z*: 403.9 (M+H)。

【0376】

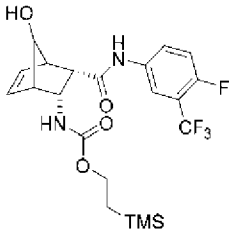
中間物348-4



向**348-3** (1.52 g，3.77 mmol)於THF (24 mL)及水(8.0 mL)中之溶液中添加LiOH (5.65 mL，11.3 mmol)且在室溫下攪拌溶液1小時。將反應混合物酸化且用乙酸乙酯萃取。合併有機層且在減壓下濃縮，得到**348-4** (1.1 g，92%)。MS (ESI) *m/z*: 313.9 (M+H)。

【0377】

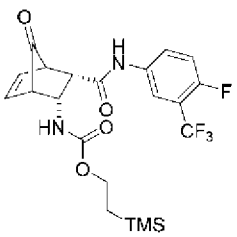
中間物348-5



向**348-4** (680 mg，2.17 mmol)於無水DMF (12 mL)中之溶液中添加4-氟-3-(三氟甲基)苯胺(0.28 mL，2.2 mmol)、1-羥基苯并三唑水合物(515 mg，3.36 mmol)及1-(3-二甲基胺基丙基)-3-乙基碳化二亞胺鹽酸鹽(624 mg，3.25 mmol)。在室溫下攪拌反應混合物18 h且在減壓下濃縮。使用矽膠層析純化殘餘物，得到**348-5** (260 mg，25%)。MS (ESI) *m/z*: 474.9 (M+H)。

【0378】

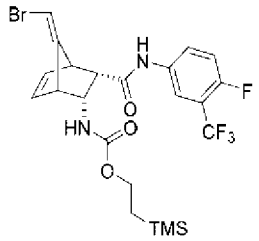
中間物348-6



在0℃在N_2下向燒瓶中添加DMSO (4 mL)及吡啶三氧化硫(279 mg，1.75 mmol)、至**348-5** (260 mg，0.548 mmol)及TEA (0.61 mL，4.4 mmol)於DMSO (4 mL)中之溶液。攪拌反應混合物1小時且用EtOAc稀釋且用鹽水洗滌有機相。在減壓下濃縮有機層且使用矽膠層析純化殘餘物，得到**348-6** (280 mg，100%)。MS (ESI) *m/z*: 473.0 (M+H)。

【0379】

中間物348-7

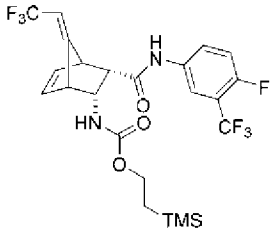


向圓底燒瓶中添加溴化(溴甲基)三苯基鏻(388 mg，0.889 mmol)及THF (5.0 mL)。使反應混合物冷卻至-78℃，且接著經2分鐘逐滴添加1M NaHMDS (0.89 mL，0.89 mmol)於THF中之溶液，同時保持內部溫度低於-70℃。在-78℃攪拌所得亮黃色懸浮液1小時。向此反應混合物中添加**348-6** (280 mg，0.593 mmol)於無水THF (1.0 mL)中之溶液，先前經2分鐘用NaHMDS (1.12 mL，1.12 mmol)處理該溶液，同時保持內部溫度低於-70℃。在-78℃攪拌所得反應混合物3小時。隨後藉由緩慢添加水(6 mL)，接著添加乙酸乙酯(6 mL)來淬滅反應混合物。將所得反應混合物攪拌5分鐘且接著用EtOAc稀釋。用鹽水洗滌合併之有機部分且使用矽膠層析純化。使用以下對殘餘物進行對掌性分離：Chiralcel OD-H，21 × 250 mm，5微米管柱，移動相5% MeOH/CAN/95% CO_2，流動速率45 mL/min及150巴。在40℃進行分離且在240 nm之波長下量測。對掌性分離產生四個峰，滯留時間為9.29 min (>99.9% ee)，11.16 min (>99.9% ee)，13.98

min (>99.9% ee)及15.30 min (>81.0% ee)。在11.16 min發現所需產物且其ee>99.9% (來自對掌性SFC之峰2)，其藉由2D NMR分析確認，得到**348-7** (82 mg，25.16%)。MS (ESI) *m/z*: 473.1 (M+H)。

【0380】

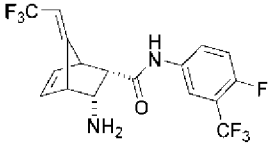
中間物348-8



在75℃在N_2下，經10 min之時段向**348-7** (83 mg，0.15 mmol)及CuI (43.2 mg，0.227 mmol)於無水DMF (1 mL)及HMPA (1.2 mL，7.0 mmol)中之懸浮液中逐滴添加含2,2-二氟-2-(氟磺醯基)乙酸甲酯(0.048 mL，0.38 mmol)之無水DMF (0.5 mL)。在75℃在氮氣下攪拌所得懸浮液12小時。使反應混合物冷卻至室溫，藉由添加$NaHCO_3$ (20 mL)及溶液淬滅，用EtOAc萃取。將有機層濃縮且進行矽膠層析，得到**348-8** (52 mg，61%)。MS (ESI) *m/z*: 539.1 (M+H)。

【0381】

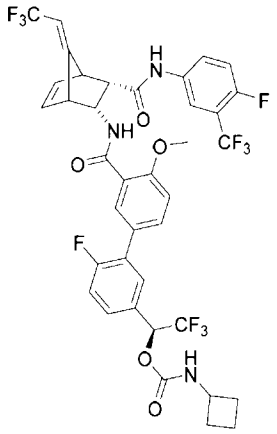
中間物348-9



向**348-8** (52 mg，0.097 mmol)於1,4-二噁烷(1.5 mL)中之溶液中添加DCM (1.6 mL)及TFA (0.4 mL)。在室溫下攪拌反應混合物30分鐘且在減壓下濃縮，得到**348-9**，其不經進一步純化即使用(49 mg，95%)。MS (ESI) *m/z*: 394.9 (M+H)。

【0382】

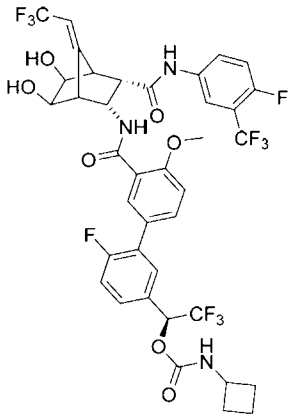
中間物348-10



348-10係根據**實例230**之程序製備。MS (ESI) *m/z*: 818.2 (M+H)。

【0383】

實例348



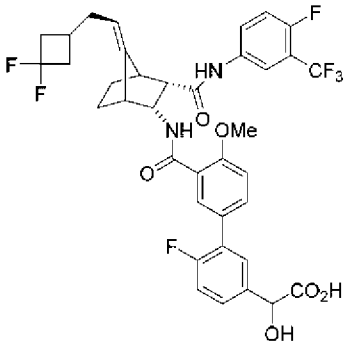
向**348-10** (35 mg，0.043 mmol)於丙酮(1 mL)中之溶液中添加*N*-甲基味啉*N*-氧化物(10 mg，0.086 mmol)，隨後添加含OsO_4之三級丁醇(0.054 mL，4.2 μmol)。在室溫下攪拌反應混合物18h。用EtOAc稀釋反應混合物且用硫代硫酸鈉洗滌溶液。分離有機層且在減壓下濃縮，且使用製備型逆相HPLC純化殘餘物，得到**實例348** (14.6 mg，38.0%)。^{1}H NMR (400MHz, CD_3OD) δ 10.41 (s, 1H), 10.15 (d, *J*=7.3 Hz, 1H), 8.27 (d, *J*=1.3 Hz, 1H), 8.19 (dd, *J*=6.3, 2.5 Hz, 1H), 7.84 - 7.72 (m, 2H), 7.69 - 7.61 (m, 1H), 7.56 - 7.48 (m, 1H), 7.38 - 7.24 (m, 3H), 6.18 (q, *J*=7.0 Hz, 1H), 5.94 (q, *J*=7.5 Hz, 1H), 4.70 (ddd, *J*=10.9, 7.1, 4.2 Hz, 1H), 4.55 (d,

J=6.4 Hz, 1H), 4.45 (d, *J*=6.4 Hz, 1H), 4.13 (s, 3H), 4.12 - 3.99 (m, 1H), 3.42 (d, *J*=1.5 Hz, 1H), 3.38 (s, 1H), 2.90 (d, *J*=4.0 Hz, 1H), 2.39 - 2.19 (m, 2H), 2.09 - 1.90 (m, 2H), 1.78 - 1.63 (m, 2H)；LC-MS (M+H) = 852.1；HPLC RT = 11.48 min；方法C.

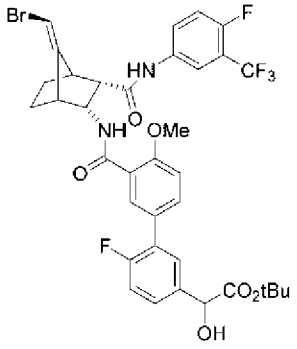
【0384】在環境溫度下攪拌**351-5** (120 mg，0.176 mmol)及LiOH (21.05 mg，0.879 mmol)於MeOH (2 mL)、THF (2 mL)及水(1 mL)中之溶液12 h。濃縮反應物質且用1.5N HCl酸化。用DCM萃取反應物且濃縮有機層。藉由製備型逆相HPLC純化殘餘物，得到4-氟-3'-(1R,2R,3R,4R,Z)-3-((4-氟-3-(三氟甲基)苯基)胺甲醯基)-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基)胺甲醯基)-4'-甲氧基-[1,1'-聯苯]-3-甲酸(11.5 mg，0.016 mmol，9%產率)。^{1}H NMR. MS (E^-) *m/z*: 669.2 (M+H)。

【0385】

實例352



中間物352-1



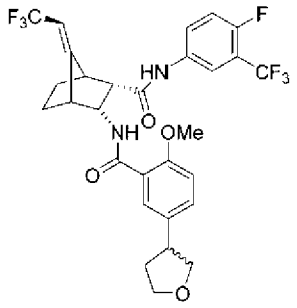
中間物352-1係根據針對**實例108**所描述之方法由**120-5**及**177-4**製

備。LC-MS (M+H) = 767.1；HPLC RT = 1.25 min；方法A。

【0386】將**352-1** (0.038 g，0.050 mmol)、Na_2CO_3 (5.30 mg，0.0500 mmol)、(4,4'-二-三級丁基-2,2'-聯吡啶)雙[3,5-二氟-2-[5-三氟甲基-2-吡啶基-κ_N)苯基-κ_C]銥(III) PF_6 (0.515 mg，0.500 μmol)、$NiCl_2$-乙二醇二甲醚複合物(0.549 mg，2.50 μmol)、4,4'-二-三級丁基-2,2'-聯吡啶(0.551 mg，2.50 μmol)、$(TMS)_3SiH$ (0.03 mL)及3-(溴甲基)-1,1-二氟環丁烷(0.019 g，0.10 mmol)於DME中之漿液用N_2脫氣，且用藍色LED照射96小時。將反應混合物用EtOAc稀釋，經由矽膠過濾且在減壓下濃縮。將殘餘物溶解於DCM (0.4 mL)中，用TFA (0.08 mL)處理。15 min之後，用甲苯稀釋溶液且在減壓下濃縮。藉由製備型逆相HPLC純化殘餘物，得到2-(3'-(((1R,2R,3S,4R,Z)-7-(2-(3,3-二氟環丁基)亞乙基)-3-((4-氟-3-(三氟甲基)苯基)胺甲醯基)雙環[2.2.1]庚烷-2-基)胺甲醯基)-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2-羥基乙酸(2.6 mg，3.2 μmol，6.5%產率)。^1H NMR (500 MHz, DMSO-d6) δ 10.56 (br s, 1H), 9.92 (br dd, J=15.4, 7.2 Hz, 1H), 8.18 (br t, J=4.9 Hz, 1H), 8.08 (br d, J=11.0 Hz, 1H), 7.81 - 7.61 (m, 2H), 7.52 - 7.35 (m, 3H), 7.32 - 7.13 (m, 2H), 5.26 - 5.13 (m, 1H), 4.92 (br d, J=1.8 Hz, 1H), 4.38 (br d, J=4.3 Hz, 1H), 4.02 (s, 1H), 3.89 - 3.71 (m, 3H), 3.19 - 3.09 (m, 1H), 2.88 (s, 1H), 2.72 (s, 2H), 2.64 (br s, 2H), 2.32 - 2.06 (m, 5H), 1.89 - 1.66 (m, 2H), 1.38 (br s, 2H)。LC-MS (M+H) = 734.24；HPLC RT = 2.48 min；方法C。

【0387】

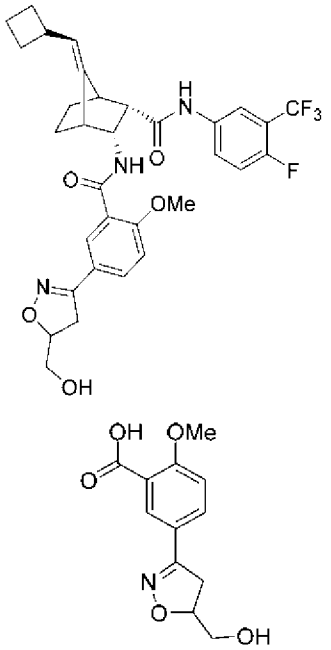
實例360



使**實例292** (0.025 g，0.041 mmol)、Na_2CO_3 (4.35 mg，0.0410 mmol)、(4,4'-二-三級丁基-2,2'-聯吡啶)雙[3,5-二氟-2-[5-三氟甲基-2-吡啶基-k_N)苯基-k_C]Ir(III) PF_6 (0.423 mg，0.410 μmol)、$NiCl_2$乙二醇二甲醚複合物(0.451 mg，2.05 μmol)、4,4'-二-三級丁基-2,2'-聯吡啶(0.551 mg，2.50 μmol)、$(TMS)_3SiH$ (0.03 mL)及3-溴四氫呋喃(0.012 g，0.082 mmol)於DME (1.641 ml)中之漿液脫氣，掩蓋於N_2下且用藍色LED照射。96 h之後，將反應混合物用EtOAc稀釋，經由矽膠過濾且在減壓下濃縮。藉由製備型逆相HPLC純化殘餘物，得到呈非鏡像異構物混合物形式之(1R,2S,3R,4R,Z)-N-(4-氟-3-(三氟甲基)苯基)-3-(2-甲氧基-5-(四氫呋喃-3-基)苯甲醯胺基)-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-甲醯胺(3.5 mg，5.5 μmol，13%產率)。^{1}H NMR (500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.78 (br d, J=5.8 Hz, 1H), 8.14 (br d, J=4.6 Hz, 1H), 7.81 - 7.65 (m, 2H), 7.49 - 7.28 (m, 2H), 7.04 (br d, J=8.5 Hz, 1H), 5.84 (q, J=7.9 Hz, 1H), 4.43 (br s, 1H), 3.95 - 3.78 (m, 5H), 3.74 - 3.64 (m, 1H), 3.37 - 3.07 (m, 2H), 2.89 (br s, 1H), 2.81 (s, 1H), 2.71 - 2.62 (m, 1H), 2.24 - 2.11 (m, 1H), 1.99 - 1.87 (m, 1H), 1.83 - 1.71 (m, 2H), 1.50 - 1.26 (m, 2H)。LC-MS (M+H) = 601.16；HPLC RT = 2.58 min；方法C。

【0388】

實例378



中間物**378-1**：製備(E)-5-((羥基亞胺基)甲基)-2-甲氧基苯甲酸甲酯。將市售5-甲醯基-2-甲氧基苯甲酸酯(1.16 g，5.97 mmol)溶解於DCM (5 mL)中，且向此溶液中添加羥胺.HCl (415 mg，5.97 mmol)，隨後添加TEA (1 mL)，且在室溫下攪拌反應混合物18h。添加水(100 mL)且用EtOAc (2×25 mL)萃取溶液，將合併之有機部分乾燥($MgSO_4$)，過濾且在減壓下蒸發，產生**378-1**，1.19 g，95%產率。^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (s, 1H), 8.03 (d, *J*=2.4 Hz, 1H), 7.78 - 7.67 (m, 1H), 7.03 (d, *J*=8.8 Hz, 1H), 3.97 (s, 3H), 3.93(s, 3H)。MS (ESI) *m/z* = 210.1 (M+H)。

【0389】 中間物**378-2**：製備5-(5-(羥基甲基)-4,5-二氫異噁唑-3-基)-2-甲氧基苯甲酸甲酯。將中間物**378-1** (55 mg，0.26 mmol)溶解於DMF (2 mL)中，且向此溶液中添加NCS (35 mg，0.26 mmol)，且在室溫下攪拌反應混合物4h。添加水且用EtOAc (2×25 mL)萃取溶液，將合併之有機部分乾燥($MgSO_4$)，過濾，在減壓下濃縮且使殘餘物立即再溶解於DCM (5 mL)中。向溶液中添加烯丙醇(61 mg，1.05 mmol)，隨後添加TEA (0.5 mL)，且在室溫下攪拌所得反應混合物18 h。添加水(20 mL)且

用EtOAc (2×20 mL)萃取溶液，將合併之有機部分乾燥($MgSO_4$)，過濾且藉由正相層析，用己烷/EtOAc溶離來純化，得到**378-2**，58 mg，85%產率。^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (d, *J*=2.4 Hz, 1H), 7.89 (dd, *J*=8.8, 2.4 Hz, 1H), 7.05 (d, *J*=8.9 Hz, 1H), 4.90 (dddd, *J*=10.8, 7.7, 4.6, 3.2 Hz, 1H), 4.08 - 3.85 (ss, 6H), 3.81 - 3.68 (m, 1H), 3.46 - 3.36 (m, 1H), 1.89 (br t, *J*=6.2 Hz, 1H), 1.57 (s, 2H)。MS (ESI) *m/z* = 266.1 (M+H)。

【0390】 中間物**378-3**：將**378-2** (58 mg，0.22 mmol)溶解於THF (2 mL)中且向其中添加LiOH (6.3 g，0.26 mmol)，隨後添加水(2 mL)及甲醇(1 mL)且在室溫下攪拌4h。用稀釋HCl (1N)淬滅至pH 7且用EtOAc (2×25 mL)萃取溶液，將合併之有機部分乾燥($MgSO_4$)，過濾且蒸發成**378-3**。^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (d, *J*=2.3 Hz, 1H), 8.14 (dd, *J*=8.8, 2.4 Hz, 1H), 7.28 - 7.14 (m, 1H), 4.92 (dddd, *J*=10.8, 7.7, 4.6, 3.1 Hz, 1H), 4.16 (s, 3H), 4.09 - 3.89 (m, 1H), 3.72 (dd, *J*=12.4, 4.6 Hz, 1H), 3.48 - 3.39 (m, 1H), 3.38 - 3.29 (m, 1H), 1.94 - 1.72 (m, 1H), 1.60 (br s, 1H)。MS (ESI) *m/z* = 252.3 (M+H)。

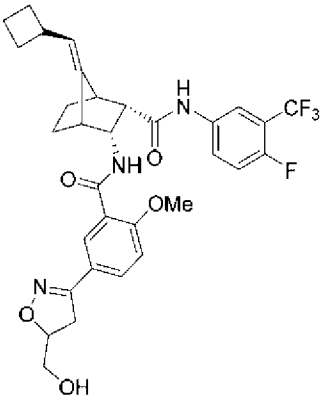
【0391】 中間物**378-4**及**378-5**. 根據以下製備型方法對**378-3**進行對掌性SFC分離：儀器：Berger MG II，管柱：Chiralpak IC，21×250 mm，5微米，移動相：20%甲醇/ 80% CO_2，流動條件：2 mL/min，150巴， 40℃ 偵測器波長：220 nm，注射詳情：0.7 mL ~35mg/mL於MeOH中，得到**378-4** (峰1，> 99% de，分析型RT = 5.6 min) and **378-5** (峰2，99% de，分析型RT = 6.6 min)，分析型層析條件：儀器：Shimadzu Nexera SFC (CTR-L410-SFC3)，管柱：Chiralpak IC，4.6×100 mm，3微米，移動相：20% 甲醇/ 80% CO_2，流動條件：2.0 mL/min，150巴，

40℃，偵測器波長：220 nm，注射詳情：5 μL ~1 mg/mL於MeOH中

【0392】 藉由使中間物**378-3** (4.6 mg，0.018 mmol)與環丁基降冰片烷基中間物**369-1** (7 mg，0.02 mmol)、BOP試劑(8.1 mg，0.018 mmol)及休尼格氏鹼(0.05 ml)在DMF中偶合來製備(1R,2S,3R,4R,Z)-7-(環丁基亞甲基)-N-(4-氟-3-(三氟甲基)苯基)-3-(5-(5-(羥基甲基)-4,5-二氫異噁唑-3-基)-2-甲氧基苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺**378** (非鏡像異構混合物)。經由逆相HPLC純化得到呈固體之**378** (5 mg，44%產率)。^{1}H NMR (500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.89 (dd, J=7.1, 2.8 Hz, 1H), 8.26 - 8.17 (m, 2H), 7.84 - 7.73 (m, 2H), 7.48 (br t, J=9.7 Hz, 1H), 7.26 (d, J=8.8 Hz, 1H), 5.37 (d, J=8.4 Hz, 1H), 4.78 - 4.65 (m, 1H), 4.35 (br s, 1H), 4.03 (s, 3H), 3.63 (br s, 1H), 3.22 - 3.05 (m, 3H), 2.96 (br s, 1H), 2.70 (br s, 1H), 2.23 - 2.06 (m, 3H), 1.91 - 1.70 (m, 7H), 1.43 - 1.22 (m, 2H)。MS (ESI) m/z =616.1 (M+H)。HPLC純度：100%；滯留時間：2.54 min；方法C。

【0393】

實例379

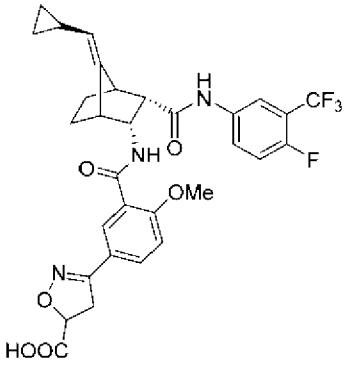


實例379. 藉由針對實例**378**所描述之偶合方法，使用環丁基降冰片烷基中間物**369-1**及中間物**378-5**來製備(1R,2S,3R,4R,Z)-7-(環丁基亞甲基)-

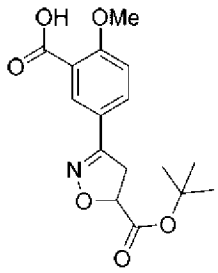
N-(4-氟-3-(三氟甲基)苯基)-3-(5-(5-(羥基甲基)-4,5-二氫異噁唑-3-基)-2-甲氧基苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺(同對掌性異構物-2) (49%產率)。^{1}H NMR (500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.88 (br d, *J*=7.0 Hz, 1H), 8.22 (s, 1H), 8.23 (d, *J*=7.0 Hz, 1H), 7.79 (br d, *J*=8.2 Hz, 2H), 7.49 (br t, *J*=9.6 Hz, 1H), 7.27 (d, *J*=8.5 Hz, 1H), 5.38 (br d, *J*=8.5 Hz, 1H), 4.70 (br d, *J*=3.1 Hz, 2H), 4.36 (br s, 1H), 4.04 (s, 3H), 3.51 (br s, 1H), 3.37 (br s, 2H), 3.22 - 3.04 (m, 2H), 2.97 (br s, 1H), 2.71 (br s, 1H), 2.19 (br d, *J*=5.8 Hz, 1H), 2.14 (br s, 1H), 1.92 - 1.71 (m, 6H), 1.37 (br s, 2H)。MS (ESI) *m/z* = 616.1 (M+H)。HPLC純度：100%；滯留時間：2.54 min；方法C。

【0394】

實例384



中間物384-1 (外消旋物)及384-2 (同對掌性峰-1)及384-3 (同對掌性峰-2)



中間物**384-1**：中間物5-(5-(三級丁氧基羰基)-4,5-二氫異噁唑-3-基)-2-甲氧基苯甲酸係如針對**378-2**所描述經由水解酯且用NCS/DMF處理由來

自**378-1**之產物製備，得到5-(氯(羥基亞胺基)甲基)-2-甲氧基苯甲酸，在用過量丙烯酸三級丁酯處理後得到所需中間物5-(5-(三級丁氧基羰基)-4,5-二氫異噁唑-3-基)-2-甲氧基苯甲酸(**384-1**)，產率為76%。^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (d, *J*=2.3 Hz, 1H), 8.19 (dd, *J*=8.8, 2.4 Hz, 1H), 7.16 (d, *J*=8.9 Hz, 1H), 5.10 (dd, *J*=9.9, 8.7 Hz, 1H), 4.16 (s, 3H), 3.67 - 3.60 (m, 2H), 1.74 - 1.51 (m, 9H)。MS (ESI) *m/z* = 322.1 (M+H)。

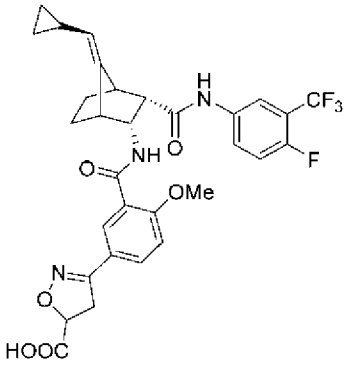
【0395】 中間物**384-2**及**384-3**：藉由對掌性SFC，藉由以下製備型層析方法分離**384-1**對掌性中間物：儀器：Berger MG II，管柱：Chiralpak IC，21×250 mm，5微米，移動相：20%甲醇/80% CO_2，流動條件：2 mL/min，150巴，40℃，偵測器波長：220 nm，注射詳情：0.7 mL ~35mg/mL於MeOH中，得到**384-2** (峰1，> 99% de，分析型RT = 7.93 min)及**384-3** (峰2，> 99% de，分析型RT = 9.65 min)。分析型層析條件：儀器：Shimadzu Nexera SFC (CTR-L410-SFC3)，管柱：Chiralpak IC，4.6×100 mm，3微米，移動相：20%甲醇/80% CO_2，流動條件：2.0 mL/min，150巴，40℃，偵測器波長：220 nm，注射詳情：5 μL ~1 mg/mL於甲醇中。

【0396】 藉由針對實例**378**所描述之偶合方法，使用降冰片烷基中間物**166-2**及中間物**384-1**來製備3-(3-(((1R,2R,3S,4R,Z)-7-(環丙基亞甲基)-3-((4-氟-3-(三氟甲基)苯基)胺甲醯基)雙環[2.2.1]庚烷-2-基)胺甲醯基)-4-甲氧基苯基)-4,5-二氫異噁唑-5-甲酸(非鏡像異構混合物) (7%產率)。^{1}H NMR (500 MHz, DMSO-d6) δ 10.56 (s, 1H), 9.92 (d, *J*=7.0 Hz, 1H), 8.32 - 8.20 (m, 2H), 7.87 - 7.75 (m, 2H), 7.49 (t, *J*=9.8 Hz, 1H), 7.34 - 7.22 (m, 1H), 5.15 (dd, *J*=11.6, 6.7 Hz, 1H), 4.70 (d, *J*=9.5 Hz, 1H), 4.45

(br s, 1H), 4.05 (s, 3H), 3.74 (dd, *J*=17.1, 11.6 Hz, 1H), 3.23 - 3.13 (m, 2H), 3.11 (br s, 2H), 2.86 - 2.64 (m, 1H), 1.88 - 1.68 (m, 2H), 1.62 - 1.46 (m, 1H), 1.42 (br s, 2H), 0.88 - 0.68 (m, 2H), 0.36 (br s, 2H)。MS (ESI) *m/z* = 616.3 (M+H)。HPLC純度：100%；滯留時間：2.38 min。方法C。

【0397】

實例385

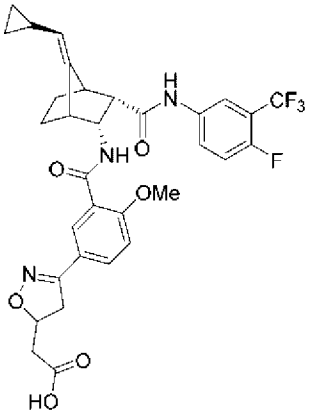


藉由使中間物**384-2** (13.9 mg，0.04 mmol)與中間物**166-2** (16 mg，0.04 mmol)在DMF中在BOP試劑(19 mg，0.04 mmol)及休尼格氏鹼(0.05 mL)存在下偶合來製備3-(3-(((1R,2R,3S,4R,Z)-7-(環丙基亞甲基)-3-((4-氟-3-(三氟甲基)苯基)胺甲醯基)雙環[2.2.1]庚烷-2-基)胺甲醯基)-4-甲氧基苯基)-4,5-二氫異噁唑-5-甲酸同對掌性異構物-1。在減壓下濃縮反應混合物且添加水(25 mL)，且用EtOAc (2×25 mL)萃取溶液，將合併之有機部分乾燥($MgSO_4$)，過濾且在減壓下濃縮。將殘餘物溶解於DCM (1 ml)中且向其中添加TFA (0.2 mL)且在室溫下攪拌15 min。將溶液在減壓下濃縮且用DMF (1 mL)使其再溶解且經由逆相HPLC純化，得到**385**，即呈固體之3-(3-(((1R,2R,3S,4R,Z)-7-(環丙基亞甲基)-3-((4-氟-3-(三氟甲基)苯基)胺甲醯基)雙環[2.2.1]庚烷-2-基)胺甲醯基)-4-甲氧基苯基)-4,5-二氫異噁唑-5-甲酸(同對掌性) (12 mg，99%產率)。^{1}H NMR (500 MHz, DMSO-d_6) δ 10.62 (s, 1H), 9.92 (br d, *J*=7.0 Hz, 1H), 8.24 (br s, 2H), 7.88 - 7.76 (m,

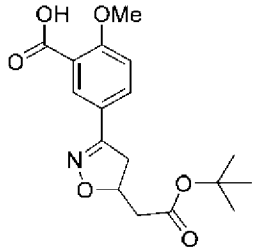
2H), 7.49 (br t, *J*=9.5 Hz, 1H), 7.27 (d, *J*=8.9 Hz, 1H), 5.01 - 4.84 (m, 1H), 4.69 (d, *J*=9.5 Hz, 1H), 4.45 (br s, 1H), 4.05 (s, 3H), 3.67 - 3.43 (m, 1H), 3.18 (br d, *J*=7.3 Hz, 1H), 3.12 (br s, 1H), 2.73 (br s, 1H), 1.92 (s, 1H), 1.88 - 1.66 (m, 2H), 1.51 (br d, *J*=4.3 Hz, 1H), 1.42 (br s, 2H), 0.89 - 0.68 (m, 2H), 0.35 (br s, 2H)。HPLC純度100%。分析型LC-MS: 2.33 min；(ESI) *m/z* = 616.28 (M+H)+, 方法C。

【0398】

實例390



中間物**390-1**



中間物**390-1**係以針對中間物378-3所描述之相同方式製備(71%產率)，在此情況下係藉由用丁-3-炔酸三級丁酯取代烯丙醇來製備。^{1}H NMR (400 MHz, $CDCl_3$) δ 10.40 (br s, 1H), 8.29 - 8.25 (m, 1H), 8.18 (dd, *J*=8.8, 2.4 Hz, 1H), 7.16 (d, *J*=8.8 Hz, 1H), 5.21 - 5.09 (m, 1H), 4.23 - 4.12 (m, 3H), 3.58 (dd, *J*=16.8, 10.5 Hz, 1H), 3.17 (dd, *J*=16.7, 7.5 Hz, 1H), 2.82 (dd, *J*=15.8, 5.9 Hz, 1H), 2.61 (dd, *J*=15.8, 7.5 Hz, 1H), 1.52 -

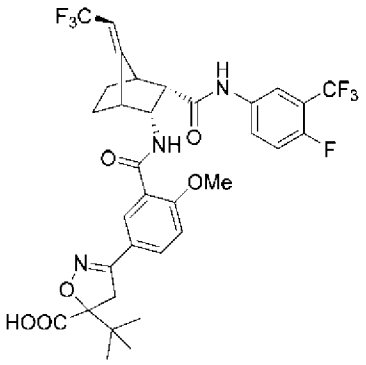
1.43 (m, 9H)。MS (ESI) *m/z* = 336.1 (M+H)。

【0399】 中間物**390-2**及**390-3**：藉由對掌性SFC，藉由以下製備型層析方法分離**390-1**之對掌性中間物：儀器：PIC Solution SFC Prep-200，管柱：Chiralpak IC，30×250 mm，5微米，移動相：15% MeOH / 85% CO_2，流動條件：85 mL/min，150巴， 40℃，偵測器波長：227 nm，注射詳情：0.5 mL ~53mg/mL於MeOH中， 得到**390-2** (峰1，100% de，分析型RT = 11.3 min)及**390-3** (峰2，93.8% de，分析型RT = 12.6 min)。分析型層析條件：儀器：Aurora Infinity SFC。管柱：Chiralpak IC，4.6×250 mm，3微米，移動相：20% MeOH / 80% CO_2，流動條件：2.0 mL/min，150巴， 40℃，偵測器波長：220 nm，注射詳情：5 μL ~1 mg/mL於MeOH中。

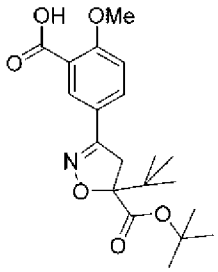
【0400】 藉由針對實例**378**所描述之偶合方法，使用環丙基降冰片烷基中間物**166-2**及中間物**390-3**，隨後用TFA脫除保護基來製備2-(3-(3-(((1R,2R,3S,4R,Z)-7-(環丙基亞甲基)-3-((4-氟-3-(三氟甲基)苯基)胺甲醯基)雙環[2.2.1]庚烷-2-基)胺甲醯基)-4-甲氧基苯基)-4,5-二氫異噁唑-5-基)乙酸同對掌性異構物-2 **390** (47%產率)。^{1}H NMR (500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.92 (br d, *J*=7.2 Hz, 1H), 8.26 - 8.19 (m, 2H), 7.84 - 7.77 (m, 2H), 7.49 (t, *J*=9.6 Hz, 1H), 7.28 (d, *J*=8.9 Hz, 1H), 5.04 - 4.90 (m, 1H), 4.70 (d, *J*=9.5 Hz, 1H), 4.46 (br s, 1H), 4.05 (s, 3H), 3.22 - 3.09 (m, 2H), 2.73 (br s, 1H), 2.70 - 2.59 (m, 2H), 2.55 (s, 2H), 1.89 - 1.71 (m, 2H), 1.51 (br d, *J*=4.9 Hz, 1H), 1.42 (br s, 2H), 0.87 - 0.69 (m, 2H), 0.36 (br s, 2H)。MS (ESI) *m/z* = 630.3 (M+H)。HPLC純度：100%；滯留時間：2 min。方法B。

【0401】

實例397



中間物397-1



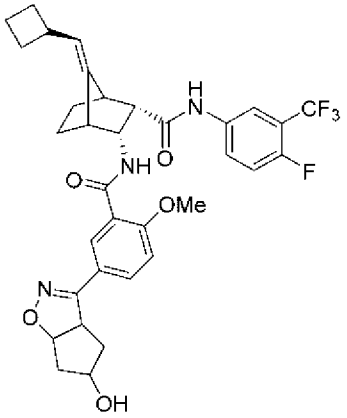
中間物**397-1**係以針對中間物**378-3**所描述之相同方式製備(81%產率)，在此情況下係藉由用3,3-二甲基-2-亞甲基丁酸三級丁酯取代烯丙醇來製備。^{1}H NMR (500 MHz, CD_3OD) δ 8.12 (d, *J*=2.3 Hz, 1H), 7.88 (d, *J*=8.5 Hz, 1H), 7.22 (d, *J*=8.9 Hz, 1H), 4.06 - 3.88 (s, 3H), 3.62 (q, *J*=18.0 Hz, 2H), 1.61 - 1.39 (m, 9H)。MS (ESI) m/z = 378.3 (M+H)。

【0402】 藉由針對實例**378**所描述之偶合方法，使用三氟甲基降冰片烷基中間物**170-2**及中間物**397-1**，隨後用TFA處理來製備5-(三級丁基)-3-(3-(((1R,2R,3S,4R,Z)-3-((4-氟-3-(三氟甲基)苯基)胺甲醯基)-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基)胺甲醯基)-4-甲氧基苯基)-4,5-二氫異噁唑-5-甲酸非鏡像異構混合物**397** (54%產率)。^{1}H NMR (500 MHz, DMSO-d6) δ 10.74 - 10.63 (m, 1H), 9.98 - 9.88 (m, 1H), 8.21 (br d, *J*=5.2 Hz, 1H), 7.79 (br s, 1H), 7.50 (br t, *J*=9.2 Hz, 1H), 7.26 (br s, 1H), 7.08 (br s, 1H), 5.99 - 5.86 (m, 1H), 4.50 (br s, 1H), 4.03 (s, 3H), 3.51 (br s,

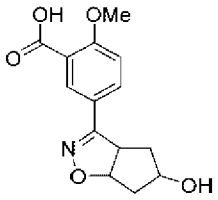
3H), 3.24 (br s, 1H), 2.99 (s, 1H), 2.11 - 1.90 (m, 1H), 1.86 (br s, 1H), 1.49 (br s, 1H), 0.99 (br s, 9H)。MS (ESI) *m/z* = 700.3 (M+H)。HPLC純度：98.8%；滯留時間：2.07 min。方法B。

【0403】

實例406



中間物**406-1**



中間物**406-1**係以針對中間物**378-3**所描述之相同方式製備(31%產率)，在此情況下係以非鏡像異構物之混合物形式，藉由用環戊-3-烯-1-基醇取代烯丙醇來製備。^{1}H NMR (600 MHz, $CDCl_3$) δ 8.04 (d, *J*=2.3 Hz, 1H), 7.85 (dd, *J*=8.8, 2.3 Hz, 1H), 7.03 (d, *J*=8.8 Hz, 1H), 5.30 (ddd, *J*=9.4, 6.2, 2.9 Hz, 1H), 4.50 (quin, *J*=5.9 Hz, 1H), 4.19 (td, *J*=9.3, 4.7 Hz, 1H), 3.92 (s, 3H), 2.33 - 2.27 (m, 1H), 2.18 - 2.06 (m, 3H)。MS (ESI) *m/z* = 292.0 (M+H)。

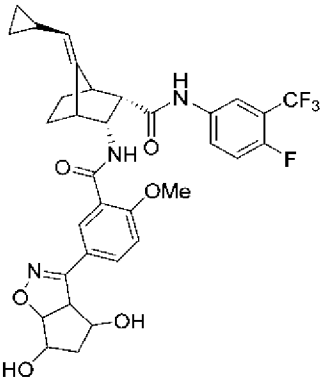
【0404】 中間物**406-2至406-5 (對掌性).** 藉由對掌性SFC，藉由以下製備型層析方法分離**406-1**之對掌性中間物：儀器：Berger SFC (LVL-L4021 Lab)管柱：IC 25×3 cm ID，5μm，溫度：40℃，流動速率：85

mL/min，移動相：梯度75/25 CO_2/MeOH，持續12 min，接著達到45% MeOH，偵測器波長：235 nm，注射量：1000 μL，得到對掌性**406-2** 峰-1，> 99% de，分析型RT = 8.80 min)、對掌性**406-3** (峰-2，>95% de，分析型RT = 9.86 min)、對掌性**406-4** (峰-3，> 99% de，分析型RT = 13.53 min)、對掌性**406-5** (峰-4，> 99% de，分析型RT = 16.67 min)。分析型層析條件：儀器：Agilent SFC (LVL-L4021 Lab)，管柱：IC 250×4.6 mm ID，5 μm，溫度：環境溫度，流動速率：2.0 mL/min，移動相：梯度75/25 CO_2/MeOH 12 min，接著達到45% MeOH。

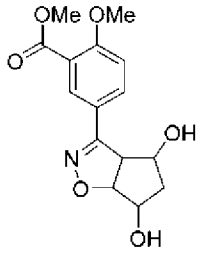
【0405】 藉由針對實例**378**所描述之偶合方法，使用環丁基降冰片烷基中間物**369-1**及中間物**406-1**來製備(1R,2S,3R,4R,Z)-7-(環丁基亞甲基)-N-(4-氟-3-(三氟甲基)苯基)-3-(5-(5-羥基-3a,5,6,6a-四氫-4H-環戊并[d]異噁唑-3-基)-2-甲氧基苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺非鏡像異構混合物**406** (74%產率)。^{1}H NMR (500 MHz, DMSO-d6) δ 10.56 (s, 1H), 9.89 (d, *J*=7.3 Hz, 1H), 8.21 (br s, 2H), 7.78 (br d, *J*=8.7 Hz, 2H), 7.48 (br t, *J*=9.6 Hz, 1H), 7.26 (br d, *J*=8.8 Hz, 1H), 5.37 (d, *J*=8.3 Hz, 1H), 5.10 (br t, *J*=7.2 Hz, 1H), 4.34 (br s, 1H), 4.15 (br s, 1H), 4.12 - 4.05 (m, 1H), 4.03 (s, 3H), 3.72 - 3.56 (m, 3H), 3.20 - 3.02 (m, 2H), 2.95 (br s, 1H), 2.70 (br s, 1H), 2.16 (br s, 1H), 2.13 - 2.01 (m, 2H), 1.92 - 1.70 (m, 6H), 1.36 (br s, 2H)。MS (ESI) *m/z* = 642.1 (M+H)。HPLC純度：100%；滯留時間：2.49 min。方法C。

【0406】

實例413



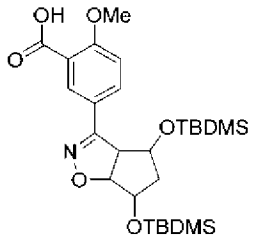
中間物413-1 (非鏡像異構混合物)



中間**413-1**係以與針對中間物**378-3**所描述相同之方式製備(10%產率)，在此情況下係呈非鏡像異構物之混合物形式，藉由用(1R,3S)-環戊-4-烯-1,3-二醇取代烯丙醇來製備。^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 - 7.91 (m, 1H), 7.30 (s, 1H), 7.11 - 7.01 (m, 1H), 5.46 - 5.21 (m, 1H), 4.45 - 4.23 (m, 1H), 4.04 - 3.88 (ss, 6H), 3.02 - 2.98 (m, 1H), 2.92 (d, *J*=0.7 Hz, 1H), 2.45 - 2.35 (m, 1H), 2.02 (s, 2H)。MS (ESI) *m/z* = 294.1 (M+H)。

【0407】

中間物413-2 (非鏡像異構混合物)



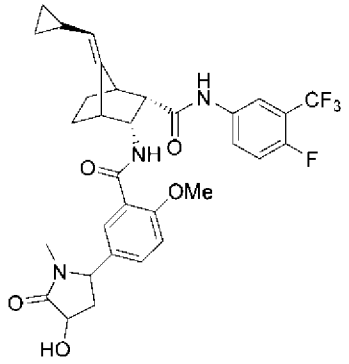
經由兩步順序，藉由用過量TBDMS三氟甲磺酸鹽(2.64 g，9.99 mmol)及含2,6-二甲基吡啶(1.61 g，14.9 mmol)之DCM (5 mL)進行保護，隨後在THF/MeOH/水(1:1:1，5 mL)中用LiOH水解酯以自中間物**413-1**獲

得**413-2**。^{1}H NMR (500 MHz, $CDCl_3$) δ 8.48 - 8.46 (m, 1H), 8.04 - 8.00 (m, 1H), 7.10 - 7.05 (m, 1H), 5.06 - 5.02 (m, 1H), 4.33 - 4.29 (m, 1H), 4.23 - 4.18 (s, 3H), 4.15 - 4.13 (m, 1H), 4.12 - 4.10 (m, 1H), 4.00 - 3.94 (m, 1H), 1.29 - 1.24 (m, 1H), 0.93 (ss, 18H), 0.12 (s, 3H), 0.12 - 0.03 (m, 3H), 0.03 (s, 1H), 0.02 (s, 3H), -0.05 - 0.06 (m, 3H)。MS (ESI) m/z 522.5 (M+H)。

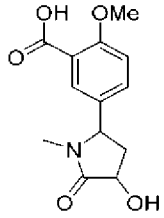
【0408】 藉由針對實例**378**所描述之偶合方法，使用環丙基降冰片烷基中間物**166-2**及中間物**413-2**，隨後用氟化四丁銨(1M於THF中，1 mL)脫除保護基來製備(1R,2S,3R,4R,Z)-7-(環丙基亞甲基)-3-(5-(4,6-二羥基-3a,5,6,6a-四氫-4H-環戊并[d]異噁唑-3-基)-2-甲氧基苯甲醯胺基)-N-(4-氟-3-(三氟甲基)苯基)雙環[2.2.1]庚烷-2-甲醯胺非鏡像異構混合物**413** (36%產率)。^{1}H NMR (500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.90 (br d, *J*=7.3 Hz, 1H), 8.43 - 8.37 (m, 1H), 8.21 (br d, *J*=6.1 Hz, 1H), 7.89 (dd, *J*=8.7, 2.3 Hz, 1H), 7.83 - 7.66 (m, 1H), 7.48 (t, *J*=9.6 Hz, 1H), 7.29 (d, *J*=8.9 Hz, 1H), 4.96 (dd, *J*=10.2, 2.0 Hz, 1H), 4.70 (d, *J*=9.5 Hz, 1H), 4.45 (br s, 1H), 4.05 (s, 3H), 3.54 (br s, 1H), 3.21 - 3.07 (m, 2H), 3.00 (s, 1H), 2.54 (s, 1H), 2.85 - 2.64 (m, 1H), 1.92 - 1.76 (m, 3H), 1.76 - 1.62 (m, 1H), 1.52 (br s, 1H), 1.42 (br s, 2H), 0.85 - 0.68 (m, 2H), 0.36 (br s, 2H)。MS (ESI) *m/z* = 644.4 (M+H)。HPLC純度：100%；滯留時間：2.36 min。方法C。

【0409】

實例414



中間物414-3 (外消旋物)及對掌性414-4 (對掌性峰-1)、對掌性414-5 (對掌性峰-2)、對掌性414-6 (對掌性峰-3)、對掌性414-7 (對掌性峰-4)。



中間物**414-1**：將市售5-甲醯基-2-甲氧基苯甲酸甲酯(948 mg，4.88 mmol)溶解於EtOH (10 mL)中且向此溶液中添加NMeNHOH.HCl (408 mg，4.88 mmol)，隨後添加K_2CO_3 (675 mg，4.88 mmol)且在室溫下攪拌反應混合物1h。添加水(100 mL)且用EtOAc (2×25 mL)萃取溶液，將合併之有機部分乾燥($MgSO_4$)且在減壓下蒸發成固體。將固體轉移至小瓶中且添加甲苯(7 mL)，隨後添加丙烯酸甲酯(3 mL)且密封小瓶。在95℃加熱反應混合物18h。在減壓下濃縮經冷卻之反應混合物且藉由矽膠層析純化殘餘物。單離呈油狀物之**414-3** (200 mg，13%)。^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (m, 1H), 7.88 (m, 1), 7.02 (d, *J*=8.8 Hz, 1H), 4.01 - 3.84 (mss, 8H), 3.79 - 3.71 (m, 3H), 3.17 - 3.01 (m, 3H), 2.92 - 2.67 (m, 1H), 2.07 - 1.81 (m, 2H)。MS (ESI) *m/z* = 310.0 (M+H)。

【0410】 中間物**414-2**：在Parr燒瓶中將產物**414-1** (49 mg，0.158 mmol)溶解於甲醇(5 mL)中，且向其中添加10% Pd/C (20 mg)且在60 psi下氫化5 h。經矽藻土墊過濾反應混合物且在減壓下蒸發，得到呈油狀物

之5-(4-羥基-1-甲基-5-側氧基吡咯啶-2-基)-2-甲氧基苯甲酸甲酯(35 mg，79%)。^{1}H NMR (500 MHz, CD_3OD) δ 7.71 (d, *J*=2.4 Hz, 1H), 7.50 (dd, *J*=8.7, 2.4 Hz, 1H), 7.18 (d, *J*=8.7 Hz, 1H), 4.51 - 4.42 (m, 1H), 4.38 (t, *J*=8.5 Hz, 1H), 3.90 (s, 3H), 3.86 (s, 3H), 2.84 (ddd, *J*=13.1, 8.4, 6.9 Hz, 1H), 2.58 (s, 3H), 1.74 (dt, *J*=13.0, 8.5 Hz, 1H)。MS (ESI) *m/z* = 280.2 (M+H)。

【0411】 中間物**414-3**：將產物**414-2** (30 mg)溶解於MeOH (1 mL)中，且向此溶液中添加LiOH，隨後添加水(1 mL)，且在室溫下攪拌5 h。添加稀釋HCl，且將所得溶液在減壓下濃縮為膠狀固體。添加甲醇且過濾反應混合物且在減壓下濃縮以產生**414-3** (20 mg，71%產率)。MS m/z = 266.08 (M+H)。

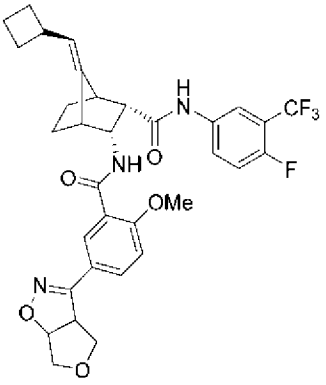
【0412】 對掌性中間物**414-(4-7)**：在以下製備型條件下藉由SFC分離**414-3**：儀器：Berger SFC (LVL-L4021 Lab)，管柱：IG 25×3 cm ID，5μm，溫度：40℃，流動速率：85 mL/min，移動相：82/18 CO_2/MeOH-0.1% DEA，偵測器波長：220 nm，注射量：1200 μL，得到對掌性**414-4** (峰-1，> 99% de，分析型RT = 15.56 min)、對掌性**414-5** (峰-2 > 95% de，分析型RT = 18.09 min)、對掌性**414-6** (峰-3，>99% de，分析型RT = 26.38 min)及對掌性**414-7** (峰-4，> 95% de，分析型RT = 29.29 min)。分析型層析條件：儀器：Agilent SFC (LVL-L4021 Lab)，管柱：IG 250×4.6 mm ID，5 μm，溫度：環境溫度，流動速率：2.0 mL/min，移動相：80/20 CO_2/MeOH-0.1%DEA

【0413】 藉由針對實例**378**所描述之偶合方法，使用環丙基降冰片烷基中間物**166-2**及中間物**414-4**來製備(1R,2S,3R,4R,Z)-7-(環丙基亞甲

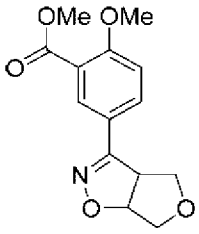
基)-N-(4-氟-3-(三氟甲基)苯基)-3-(5-(4-羥基-1-甲基-5-側氧基吡咯啶-2-基)-2-甲氧基苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺同對掌性異構物-1 **414** (48%產率)。^{1}H NMR (500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.89 (d, *J*=7.3 Hz, 1H), 8.23 (dd, *J*=6.6, 2.3 Hz, 1H), 7.89 (d, *J*=2.1 Hz, 1H), 7.84 - 7.67 (m, 1H), 7.49 (t, *J*=9.2 Hz, 1H), 7.44 (d, *J*=8.3 Hz, 1H), 7.24 (d, *J*=8.5 Hz, 1H), 4.70 (d, *J*=9.8 Hz, 1H), 4.34 (m, 1H), 4.20 (br s, 1H), 4.02 (s, 3H), 3.16 (br dd, *J*=10.7, 4.0 Hz, 1H), 3.09 (br s, 1H), 2.80 - 2.63 (m, 2H), 2.50 - 2.39 (m, 2H), 1.94 - 1.74 (m, 2H), 1.65 - 1.45 (m, 1H), 1.45 - 1.24 (m, 2H), 0.88 - 0.67 (m, 2H), 0.36 (br s, 2H)。MS (ESI) *m/z* = 616.2 (M+H)。HPLC純度：100%；滯留時間：2.12 min。方法C。

【0414】

實例416



中間物**416-1**：(外消旋物)及對掌性**416-2** (對掌性峰-1)、**416-3** (對掌性峰-2)。



中間物**416-1**係以與針對中間物**378-1**所描述相同之方式製備(50%產率)。^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, J=2.3 Hz, 1H), 7.86 (dd,

J=8.8, 2.4 Hz, 1H), 7.04 (d, J=8.7 Hz, 1H), 5.38 (dd, J=9.2, 3.9 Hz, 1H), 4.34 - 4.26 (m, 2H), 4.20 - 4.09 (m, 1H), 3.96 (s, 3H), 3.91 (s, 3H), 3.83 - 3.76 (m, 1H), 2.92 - 2.70 (m, 1H)。MS (ESI) *m/z* = 278.3 (M+H)。

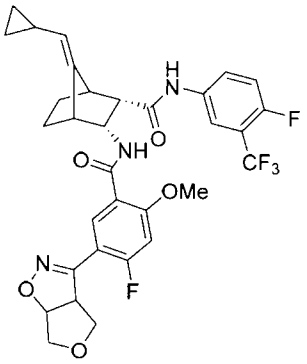
【0415】 **416-2及416-3**：藉由對掌性SFC，藉由以下製備型層析方法將以下對掌性中間物與外消旋物DP39-1分離：儀器：Berger MG II管柱：Chiralpak IA，21×250 mm，5微米，移動相：20% MeOH / 80% CO_2，流動條件：45 mL/min，150巴， 40℃，偵測器波長：220 nm，得到對掌性**416-2** (峰-1，> 99% de，分析型RT = 3.80 min)及對掌性**416-3** (峰-2，> 98% de，分析型RT = 7.43 min)。分析型層析條件：儀器：Shimadzu Nexera SFC，管柱：Chiralpak IA，4.6×100 mm，3微米，移動相：20% MeOH / 80% CO_2，流動條件：2.0 mL/min，150巴， 40℃，偵測器波長：220 nm，注射詳情：5 μL ~1mg/mL於MeOH中。

【0416】 藉由針對實例**378**所描述之方法，使用環丁基降冰片烷基中間物**369-1**及中間物**416-2**來製備(1R,2S,3R,4R,Z)-7-(環丁基亞甲基)-N-(4-氟-3-(三氟甲基)苯基)-3-(2-甲氧基-5-(3a,4,6,6a-四氫呋喃并[3,4-d]異噁唑-3-基)苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺同對掌性異構物-2 **416** (62%產率)。^{1}H NMR (500 MHz, DMSO-d6) δ 10.56 (s, 1H), 9.93 (dd, *J*=10.8, 7.2 Hz, 1H), 8.25 - 8.20 (m, 2H), 7.84 - 7.76 (m, 2H), 7.48 (t, *J*=9.8 Hz, 1H), 7.28 (d, *J*=8.9 Hz, 1H), 5.35 (dd, *J*=9.0, 3.2 Hz, 1H), 4.70 (d, *J*=9.5 Hz, 1H), 4.54 - 4.41 (m, 2H), 4.12 - 4.02 (m, 3H), 3.90 (br d, *J*=9.5 Hz, 1H), 3.84 - 3.73 (m, 1H), 3.50 (br s, 1H), 3.16 (br dd, *J*=10.8, 4.4 Hz, 1H), 3.11 (br s, 1H), 2.73 (br s, 1H), 2.56 (s, 4H), 1.91 - 1.71 (m, 2H), 1.50 (br s, 1H), 1.42 (br s, 2H), 0.87 - 0.68 (m, 2H), 0.35 (br s, 2H)。

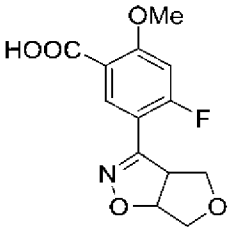
MS (ESI) *m/z* = 614.2 (M+H)。HPLC純度：100%；滯留時間：2.42 min。方法C。

【0417】

實例419



中間物419-5 (對掌性峰-1)及419-6 (對掌性峰-2)



中間物**419-1**：向含4-氟-5-甲醯基-2-甲氧基苯甲酸甲酯(0.15 g，0.68 mmol) (如Chen, Xiao-Yang, Sorensen, Eric, J. *JACS*, **2018**, 140, 2789-2792中所描述來製備)及NH_2OH HCl (48 mg，0.68 mmol)之DCM (10 mL)中添加DIEA (0.12 mL, 0.68 mmol)。24h之後，用水稀釋反應混合物且藉由過濾收集(*E*)-4-氟-5-((羥基亞胺基)甲基)-2-甲氧基苯甲酸甲酯白色固體(0.15 g，96%)，乾燥且按原樣使用。^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 - 8.37 (m, 1H), 8.33 - 8.22 (m, 2H), 6.79 - 6.61 (m, 1H), 3.94 (s, 3H), 3.91 (s, 3H)。MS (ESI) *m/z* 228.2 $(M+H)^+$。

【0418】 中間物**419-2**：向中間物**419-1** (0.15 g，0.66 mmol)及DMF (1 mL)中添加NCS (88 mg，0.66 mmol)。24h之後，用水(20 mL)及乙酸乙酯(50 mL)分配反應混合物。用乙酸乙酯(2×20 mL)萃取水層。將合

併之有機層用鹽水(15 mL)洗滌且乾燥(Na_2SO_4)，得到固體。向含固體之DCM (3 mL)中添加2,5-二氫呋喃(0.46 g，6.6 mmol)及TEA (0.1 mL，0.66 mmol)。24h之後，將反應混合物用水(20 mL)淬滅且用DCM (3×30 mL)萃取。將合併之有機層用鹽水(15 mL)洗滌且乾燥($MgSO_4$)。經由矽膠層析，使用己烷/EtOAc作為溶離劑純化殘餘物，得到呈茶色固體之4-氟-2-甲氧基-5-(3a,4,6,6a-四氫呋喃并[3,4-d]異噁唑-3-基)苯甲酸甲酯(0.13 g，66%)。MS (ESI) *m/z* = 296.2 $(M+H)^+$。

【0419】對掌性中間物**419-3及419-4**：中間物**419-2**係在具有Chiralpak IA，21×250 mm管柱之Jasco SFC Prep上，用20% MeOH/80% CO_2溶離(45 mL/min，150巴， 40℃，偵測器波長267 nm)分離，得到**419-3** (33 mg，0.11 mmol，17%產率) (峰-1，99% ee，分析型RT = 1.693 min.)；^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (d, *J*=8.8 Hz, 1H), 6.75 (d, *J*=13.2 Hz, 1H), 5.39 (dd, *J*=9.1, 3.9 Hz, 1H), 4.40 (dt, *J*=4.6, 2.3 Hz, 1H), 4.34 (d, *J*=10.8 Hz, 1H), 4.11 (br d, *J*=9.7 Hz, 1H), 3.97 (s, 3H), 3.91 (s, 3H), 3.86 (dd, *J*=9.7, 6.8 Hz, 1H), 3.79 (dd, *J*=10.8, 4.0 Hz, 1H)；**419-4** (32 mg，0.11 mmol，6%產率) (峰-2，99% ee，分析型RT = 5.463 min.)；^{1}H NMR (400 MHz,$CDCl_3$) δ 8.45 (d, *J*=8.6 Hz, 1H), 6.75 (d, *J*=13.4 Hz, 1H), 5.39 (dd, *J*=9.5, 4.0 Hz, 1H), 4.46 - 4.38 (m, 1H), 4.34 (d, *J*=11.0 Hz, 1H), 4.16 - 4.09 (m, 1H), 3.97 (s, 3H), 3.91 (s, 3H), 3.86 (dd, *J*=9.7, 6.8 Hz, 1H), 3.79 (dd, *J*=10.8, 4.0 Hz, 1H)。分析型層析條件：儀器：Shimadzu Nexera SFC，管柱：Chiralpak IC，4.6×100 mm，3微米，移動相：20%甲醇/ 80% CO_2，流動條件：2.0 mL/min，150巴，40℃，偵測器波長：220 nm

【0420】 中間物**419-5**：向冷卻至0℃的含**419-3** (33 mg，0.11 mmol)之THF (2 mL)/MeOH(0.1 mL)中添加2 M LiOH水溶液(0.17 ml，0.34 mmol)。攪拌18h之後，將反應物用稀釋HCl (10 mL)淬滅且用EtOAc (3×30 mL)萃取。將合併之有機層用鹽水(15 mL)洗滌，乾燥($MgSO_4$)，過濾且濃縮，得到呈白色固體之**419-5** (31 mg，0.11 mmol，99%產率)。^{1}H NMR (600 MHz, DMSO-d6) δ 12.90 (br s, 1H), 8.07 (d, *J*=8.7 Hz, 1H), 7.17 (d, *J*=13.8 Hz, 1H), 5.34 (dd, *J*=9.2, 3.7 Hz, 1H), 4.49 - 4.42 (m, 1H), 4.09 (d, *J*=10.7 Hz, 1H), 3.90 (br d, *J*=9.7 Hz, 1H), 3.88 (s, 3H), 3.73 (dd, *J*=9.5, 6.9 Hz, 1H), 3.64 (dd, *J*=10.8, 3.7 Hz, 1H)。LCMS(ESI) *m/z* = 282.2 $(M+H)^+$。

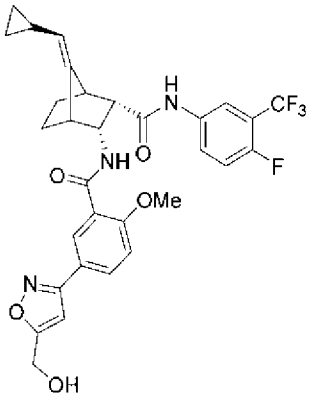
【0421】 中間物**419-6**：**419-6** (30 mg，0.11 mmol，96%產率)係以與**419-5**類似之方式，以**419-3**取代**419-4**來製備。^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (d, *J*=8.6 Hz, 1H), 6.86 (d, *J*=12.5 Hz, 1H), 5.40 (dd, *J*=9.2, 4.0 Hz, 1H), 4.55 - 4.28 (m, 2H), 4.11 (s, 3H), 4.08 (s, 1H), 3.87 (dd, *J*=9.7, 6.8 Hz, 1H), 3.79 (dd, *J*=10.8, 4.0 Hz, 1H)。LCMS(ESI) *m/z* = 282.2 $(M+H)^+$。

【0422】 **實例419.** 以與實例**378**類似之方式，藉由使用環丙基降冰片烷基中間物**20-4**及中間物**419-5**來製備(1R,2S,3R,4R,Z)-7-(環丙基亞甲基)-3-(4-氟-2-甲氧基-5-(3a,4,6,6a-四氫呋喃并[3,4-d]異噁唑-3-基)苯甲醯胺基)-*N*-(4-氟-3-(三氟甲基)苯基)雙環[2.2.1]庚烷-2-甲醯胺**419** (5.9 mg，67%产率)。^{1}H NMR (500 MHz, DMSO-d_6) δ 10.67 - 10.38 (m, 1H), 9.89 (br d, *J*=7.0 Hz, 1H), 8.33 (br d, *J*=8.9 Hz, 1H), 8.20 (br d, *J*=4.0 Hz, 1H), 7.85 - 7.71 (m, 1H), 7.48 (br t, *J*=9.8 Hz, 1H), 7.22 (br d, *J*=13.1 Hz, 1H),

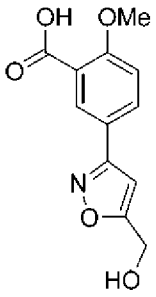
5.35 (br dd, *J*=9.5, 3.4 Hz, 1H), 4.69 (br d, *J*=9.5 Hz, 1H), 4.52 - 4.36 (m, 2H), 4.10 (br d, *J*=10.7 Hz, 1H), 4.05 (s, 3H), 3.77 - 3.66 (m, 1H), 3.66 - 3.54 (m, 2H), 3.22 - 3.12 (m, 1H), 3.09 (br s, 1H), 2.72 (br s, 1H), 1.90 - 1.79 (m, 1H), 1.79 - 1.66 (m, 1H), 1.50 (br dd, *J*=8.5, 4.3 Hz, 1H), 1.45 - 1.32 (m, 2H), 0.87 - 0.61 (m, 2H), 0.35 (br d, *J*=2.7 Hz, 2H)。HPLC純度98%。分析型LC-MS: 2.48 min；MS (ESI) *m/z* = 631.9 $(M+H)^+$。方法B。

【0423】

實例423



中間物423-1



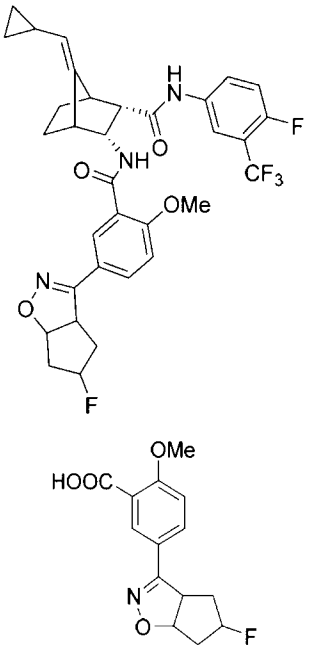
中間物**423-1**係以針對中間物**378-3**所描述之相同方式製備，在此情況下係藉由用炔丙醇取代烯丙醇來製備。^{1}H NMR (500 MHz, CD_3OD) δ 8.28 (d, J=2.3 Hz, 1H), 8.01 (dd, J=8.7, 2.3 Hz, 1H), 7.27 (d, J=8.7 Hz, 1H), 6.75 (s, 1H), 4.91 - 4.82 (m, 5H), 4.73 (s, 2H), 4.00 - 3.96 (m, 3H)。MS (ESI) *m/z* = 250.3 (M+H)。

【0424】 藉由針對實例**378**所描述之偶合方法，使用降冰片烷基中

間物**20-4**及中間物**423-1**來製備(1R,2S,3R,4R,Z)-7-(環丙基亞甲基)-N-(4-氟-3-(三氟甲基)苯基)-3-(5-(5-(羥基甲基)異噁唑-3-基)-2-甲氧基苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺**423** (77%產率)。^{1}H NMR (500 MHz, DMSO-d6) δ 10.56 (s, 1H), 9.95 (br d, *J*=7.0 Hz, 1H), 8.40 (d, *J*=1.8 Hz, 1H), 8.19 (br d, *J*=4.3 Hz, 1H), 7.97 (dd, *J*=8.5, 2.1 Hz, 1H), 7.77 (br d, *J*=8.9 Hz, 1H), 7.46 (br t, *J*=9.8 Hz, 1H), 7.32 (d, *J*=8.5 Hz, 1H), 6.84 (s, 1H), 4.69 (d, *J*=9.8 Hz, 1H), 4.61 (d, *J*=5.8 Hz, 2H), 4.45 (br s, 1H), 4.05 (s, 3H), 3.21 - 3.06 (m, 2H), 2.72 (br s, 1H), 1.92 - 1.73 (m, 2H), 1.62 - 1.45 (m, 1H), 1.41 (br s, 2H), 0.84 - 0.67 (m, 2H), 0.35 (br d, *J*=4.3 Hz, 2H)。MS (ESI) *m/z* = 600.1 (M+H)。HPLC純度：100%；滯留時間：2.39 min；方法B。

【0425】

實例427



製備5-(5-氟-3a,5,6,6a-四氫-4*H*-環戊并[*d*]異噁唑-3-基)-2-甲氧基苯甲酸甲酯(非鏡像異構物混合物)。向含**406-1**酯(0.1 g，0.3 mmol)之DCM

(2 mL)中添加DAST (0.05 mL，0.412 mmol)。24 h之後，在減壓下濃縮反應混合物且藉由矽膠層析純化，得到呈透明膜形式之相應氟化物(66 mg，0.23 mmol，66%產率)。^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J*=2.4 Hz, 1H), 7.88 (dd, *J*=8.7, 2.3 Hz, 1H), 7.06 (d, *J*=8.8 Hz, 1H), 5.53 - 5.38 (m, 1H), 4.25 (dd, *J*=9.5, 2.0 Hz, 1H), 4.01 - 3.97 (m, 4H), 3.94 - 3.92 (m, 3H), 2.76 - 2.47 (m, 2H), 2.33 - 2.12 (m, 1H), 2.10 - 1.90 (m, 1H)。LCMS(ESI) *m/z* = 294.2 $(M+H)^+$。

【0426】 中間物**427-2**：製備5-(5-氟-3a,5,6,6a-四氫-4H-環戊并[d]異噁唑-3-基)-2-甲氧基苯甲酸。向含中間物**427-1** (14 mg，0.048 mmol)之THF (1 mL)中添加2M LiOH水溶液(72 µl，0.14 mmol)。24 h之後，添加稀釋HCl (10 mL)且用EtOAc (3×30 mL)萃取溶液。將合併之有機層用鹽水(15 mL)洗滌，乾燥($MgSO_4$)，過濾，且在減壓下濃縮，得到**427-2** (13 mg，0.047 mmol，98%產率)。^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, *J*=2.2 Hz, 1H), 8.13 (dd, *J*=8.8, 2.4 Hz, 1H), 7.20 - 7.12 (m, 1H), 5.95 - 5.83 (m, 1H), 5.45 (ddd, *J*=10.0, 6.8, 4.7 Hz, 1H), 5.38 - 5.18 (m, 1H), 4.28 (td, *J*=9.4, 7.5 Hz, 1H), 4.16 (s, 3H), 2.75 - 2.55 (m, 2H), 2.32 - 2.17 (m, 1H), 2.06 - 1.92 (m, 1H)。LCMS(ESI) *m/z* = 280.2 $(M+H)^+$。

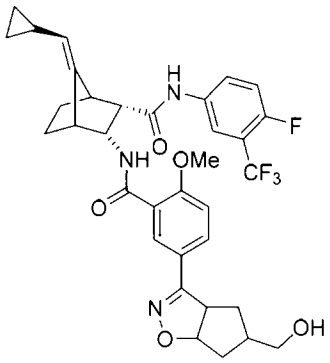
【0427】 藉由使用環丙基降冰片烷基中間物**20-4**及中間物**427-2**，以與實例**378**類似之方式，使用環丙基降冰片烷基中間物**20-4**來製備(1R,2S,3R,4R,Z)-7-(環丙基亞甲基)-N-(4-氟-3-(三氟甲基)苯基)-3-(5-(5-氟-3a,5,6,6a-四氫-4H-環戊并[d]異噁唑-3-基)-2-甲氧基苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺非鏡像異構混合物**427** (5.7 mg，9.1 µmol，67%產率)。^{1}H NMR (500 MHz, DMSO-d_6) δ 10.69 - 10.39 (m, 1H), 9.92 (br t,

J=7.0 Hz, 1H), 8.49 - 8.08 (m, 2H), 7.91 - 7.71 (m, 2H), 7.50 (br t, *J*=9.6 Hz, 1H), 7.29 (d, *J*=8.9 Hz, 1H), 5.45 - 5.26 (m, 1H), 4.71 (br d, *J*=9.2 Hz, 1H), 4.46 (br s, 1H), 4.39 - 4.30 (m, 1H), 4.06 (d, *J*=2.4 Hz, 3H), 3.41 (br s, 1H), 3.18 (br dd, *J*=10.8, 3.5 Hz, 1H), 3.12 (br s, 1H), 2.74 (br s, 1H), 2.51 - 2.35 (m, 2H), 2.17 - 2.06 (m, 1H), 2.06 - 2.00 (m, 1H), 1.92 - 1.84 (m, 1H), 1.80 (br d, *J*=11.3 Hz, 1H), 1.61 - 1.50 (m, 1H), 1.49 - 1.36 (m, 2H), 0.86 - 0.68 (m, 2H), 0.37 (br s, 2H)。HPLC純度100%。分析型LC-MS: 2.65 min；MS (ESI) *m/z* = 630.3 $(M+H)^+$。方法B。

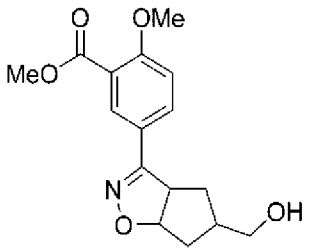
【0428】 **428**係以與實例**379**類似之方式，藉由使用環丙基降冰片烷基中間物**20-4**及中間物**428-1**來製備(6.1 mg，69%產率)。^{1}H NMR。HPLC純度100%。分析型LC-MS: 2.84 min；MS (ESI) *m/z* = 638.2 $(M+H)^+$。方法B。

【0429】

實例429



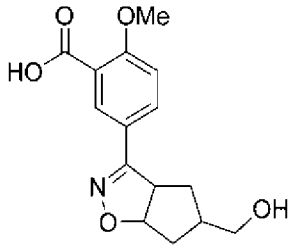
中間物429-1：製備5-(5-(羥基甲基)-3a,5,6,6a-四氫-4H-環戊并[d]異噁唑-3-基)-2-甲氧基苯甲酸甲酯。



中間物**429-1**係以針對中間物**378-3**所描述之相同方式製備(75%產率)，在此情況下係藉由用環戊-3-烯-1-基甲醇取代烯丙醇來製備。

【0430】

中間物429-2：製備5-(5-(羥基甲基)-3a,5,6,6a-四氫-4H-環戊并[d]異噁唑-3-基)-2-甲氧基苯甲酸。



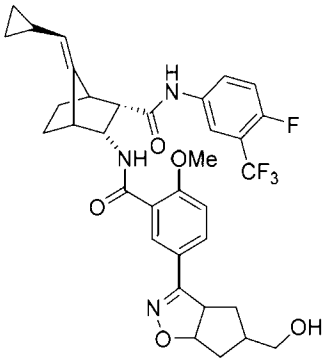
將5-(5-(羥基甲基)-3a,5,6,6a-四氫-4H-環戊并[d]異噁唑-3-基)-2-甲氧基苯甲酸甲酯(58 mg，0.22 mmol)溶解於THF (1 mL)/MeOH (1 mL)中，在室溫下用含LiOH單水合物(36 mg，0.86 mmol)之H_2O (1 mL)處理。3 h之後，用H_2O (5 mL)稀釋反應混合物且釋放有機物。用1M HCl溶液將剩餘水層之pH調節至pH 7，用EtOAc (2×25 mL)萃取，用鹽水洗滌，乾燥(Na_2SO_4)，過濾且蒸發，得到中間物**429-2** (62 mg，74.2%)。甲酸不經進一步純化即繼續用於下一反應。MS (ESI) *m/z* = 292.3 (M+H)。

【0431】 **實例429**係藉由使中間物**429-2** (3.95 mg，0.014 mmol)與溶解於無水THF (2 mL)中之中間物**166-2** (5 mg，0.014 mmol)在DIEA (0.012 mL，0.068 mmol)及BOP (6.60 mg，0.015 mmol)存在下偶合來製備。3 h之後，過濾反應混合物且藉由逆相製備型HPLC純化，得到所需產物(1R,2S,3R,4R,Z)-7-(環丙基亞甲基)-N-(4-氟-3-(三氟甲基)苯基)-3-(5-(5-(羥基甲基)-3a,5,6,6a-四氫-4H-環戊并[d]異噁唑-3-基)-2-甲氧基苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺非鏡像異構混合物**429** (5.1 mg，0.0079 mmol，58%產率)。^{1}H NMR (500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.90

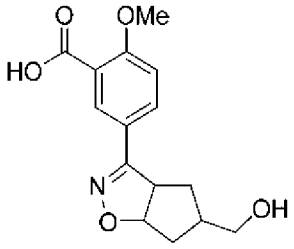
(br d, *J*=6.4 Hz, 1H), 8.23 - 8.17 (m, 2H), 7.81 - 7.74 (m, 2H), 7.46 (br t, *J*=9.8 Hz, 1H), 7.26 (d, *J*=8.9 Hz, 1H), 5.15 - 5.07 (m, 1H), 4.68 (br d, *J*=9.5 Hz, 1H), 4.42 (br s, 1H), 4.20 - 4.14 (m, 1H), 4.02 (s, 3H), 3.58 - 3.47 (m, 2H), 3.39 - 3.18 (m, 2H), 3.17 - 3.06 (m, 2H), 2.73 - 2.68 (m, 1H), 1.99 - 1.73 (m, 5H), 1.66 - 1.59 (m, 1H), 1.56 - 1.37 (m, 4H), 0.78 - 0.68 (m, 2H), 0.38 - 0.29 (m, 2H)。HPLC純度：99.2%。分析型LC-MS: 2.53 min；MS (ESI) *m/z* = 642.2 (M+H)；方法B。

【0432】

實例430



中間物429-4 (對掌性峰-1)、429-6 (對掌性峰-2)、429-8 (對掌性峰-3)及429-10 (對掌性峰-4)



藉由非鏡像異構混合物中間物**429** (524.9 mg，1.72 mmol)之對掌性SFC獲得個別對掌性非鏡像異構物酯中間物**429-4A**、**429-6A**、**429-8A**及**429-10A**。對掌性SFC製備型層析條件：儀器：Berger MG II (SFC)；管柱：Chiralpak AD-H，21×250 mm，5微米；移動相：15% MeOH / 85% CO_2；流動條件：45 mL/min，150巴， 40℃；偵測器波長：210 nm；注

射詳情：0.5 mL ~35mg/mL於MeOH中。分析型層析條件：儀器：Shimadzu Nexera SFC；管柱：Chiralpak AD-H，4.6×100 mm，3微米；移動相：15% MeOH / 85% CO_2；流動條件：2.0 mL/min，150巴，40℃；偵測器波長：220 nm；注射詳情：5 μL ~1mg/mL於MeOH中。

【0433】 獲得呈膜形式之中間物**429-4A** (峰-1，>99% de，分析型RT = 4.02 min) (152.8 mg, 29.1%)。^{1}H NMR (600 MHz, $CDCl_3$) δ 8.04 (d, *J*=2.3 Hz, 1H), 7.87 (dd, *J*=8.7, 2.3 Hz, 1H), 7.01 (d, *J*=8.8 Hz, 1H), 5.23 (dd, *J*=8.8, 5.1 Hz, 1H), 4.10 (t, *J*=8.7 Hz, 1H), 3.94 (s, 3H), 3.90 (s, 3H), 3.72 - 3.66 (m, 1H), 3.61 (dt, *J*=10.5, 5.2 Hz, 1H), 2.30 - 2.16 (m, 2H), 2.05 (dd, *J*=13.0, 6.1 Hz, 1H), 1.76 (ddd, *J*=12.9, 11.5, 9.4 Hz, 1H), 1.68 - 1.62 (m, 1H), 1.39 (br t, *J*=4.8 Hz, 1H)。

【0434】 中間物**429-4** (104.4 mg，78%)係以與中間物**429-2**類似之方式，藉由水解中間物**429-4A**來製備。MS (ESI) *m/z* = 292.3 (M+H)。

【0435】 獲得呈膜形式之中間物**429-6A** (峰-2，>99% de，分析型RT = 4.56 min) (33.2 mg，6.3%)。^{1}H NMR (600 MHz, $CDCl_3$) δ 8.05 (d, *J*=2.3 Hz, 1H), 7.87 (dd, *J*=8.8, 2.3 Hz, 1H), 7.02 (d, *J*=8.8 Hz, 1H), 5.25 (ddd, *J*=10.1, 6.2, 4.2 Hz, 1H), 4.04 - 3.98 (m, 1H), 3.94 (s, 3H), 3.90 (s, 3H), 3.63 - 3.57 (m, 1H), 3.56 - 3.50 (m, 1H), 2.38 - 2.26 (m, 3H), 1.92 - 1.85 (m, 1H), 1.73 - 1.66 (m, 1H), 1.51 (t, *J*=5.3 Hz, 1H)。

【0436】 中間物**429-6** (20.2 mg，92%)係以與中間物**429-2**類似之方式，藉由水解中間物**429-6**來製備。MS (ESI) *m/z* = 292.3 (M+H)。

【0437】 獲得呈膜形式之中間物**429-8A** (峰-3，>99% de，分析型RT = 5.67 min) (160.8 mg，30.6%)。^{1}H NMR: (600 MHz, $CDCl_3$) δ 8.05

- 8.03 (m, 1H), 7.86 (dd, *J*=8.7, 2.3 Hz, 1H), 7.01 (d, *J*=8.8 Hz, 1H), 5.23 (dd, *J*=8.7, 5.2 Hz, 1H), 4.10 (t, *J*=8.7 Hz, 1H), 3.94 (s, 3H), 3.90 (s, 3H), 3.69 (br dd, *J*=10.6, 5.2 Hz, 1H), 3.63 - 3.58 (m, 1H), 2.28 - 2.17 (m, 2H), 2.05 (br dd, *J*=12.9, 6.2 Hz, 1H), 1.76 (ddd, *J*=13.0, 11.5, 9.4 Hz, 1H), 1.64 - 1.60 (m, 1H), 1.49 (br s, 1H)。

【0438】 中間物**429-8** (121 mg，85%)係以與中間物**429-2**類似之方式，藉由水解中間物**429-8a**來製備。MS (ESI) *m/z* = 292.3 (M+H)。

【0439】 獲得呈膜形式之中間物**429-10A** (峰-4，>99%de，分析型RT=9.78 min) (47.1 mg，9.0%)。^{1}H NMR: (600 MHz, $CDCl_3$) δ 8.04 (d, J=2.3 Hz, 1H), 7.87 (dd, J=8.7, 2.3 Hz, 1H), 7.02 (d, J=8.8 Hz, 1H), 5.24 (ddd, J=10.1, 6.2, 4.2 Hz, 1H), 4.03 - 3.98 (m, 1H), 3.94 (s, 3H), 3.90 (s, 3H), 3.63 - 3.57 (m, 1H), 3.56 - 3.49 (m, 1H), 2.38 - 2.25 (m, 3H), 1.91 - 1.85 (m, 1H), 1.72 - 1.66 (m, 1H), 1.55 (br s, 1H)。

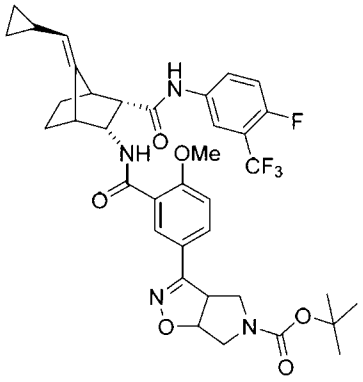
【0440】 中間物**429-10** (18.2 mg，51.6%)係以與中間物**429-2**類似之方式，藉由水解中間物**429-10A**來製備。MS (ESI) *m/z* = 292.3 (M+H)。

【0441】 實例**430**係以與實例**429**類似之方式，用中間物**429-4** (來自SFC之峰-1)來製備。(1R,2S,3R,4R,Z)-7-(環丙基亞甲基)-N-(4-氟-3-(三氟甲基)苯基)-3-(5-(5-(羥基甲基)-3a,5,6,6a-四氫-4H-環戊并[d] 異噁唑-3-基)-2-甲氧基苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺同對掌性異構物-1 (10.5 mg，0.016 mmol，60.3%產率)。^{1}H NMR (500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.90 (br d, *J*=7.0 Hz, 1H), 8.23 - 8.18 (m, 2H), 7.81 - 7.75 (m, 2H), 7.47 (br t, *J*=9.5 Hz, 1H), 7.26 (d, *J*=8.5 Hz, 1H), 5.11 (br dd,

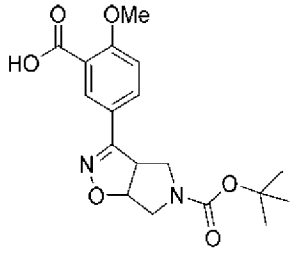
J=8.2, 5.5 Hz, 1H), 4.68 (d, *J*=9.8 Hz, 1H), 4.46 - 4.39 (m, 1H), 4.22 - 4.13 (m, 1H), 4.03 (s, 3H), 3.49 - 3.28 (m, 1H), 3.19 - 3.05 (m, 2H), 2.73 - 2.68 (m, 1H), 1.98 (br dd, *J*=13.6, 5.0 Hz, 1H), 1.93 - 1.74 (m, 4H), 1.69 - 1.60 (m, 1H), 1.58 - 1.36 (m, 4H), 0.77 - 0.68 (m, 2H), 0.37 - 0.30 (m, 2H)。HPLC純度：100%。分析型LC-MS: 2.3 min；MS (ESI) *m/z* = 642.3 (M+H)；方法B。

【0442】

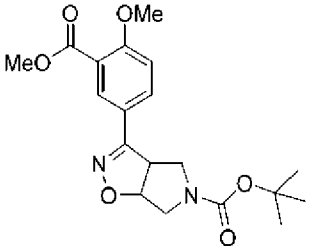
實例434



中間物434-2 (非鏡像異構混合物)



中間物**434-1**：製備3-(4-甲氧基-3-(甲氧基羰基)苯基)-3a,4,6,6a-四氫-5H-吡咯并[3,4-d]異噁唑-5-甲酸三級丁酯。



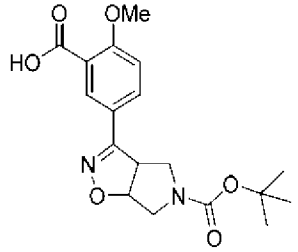
【0443】 中間物**434-1** (499.5 mg，46%)係藉由針對中間物**429-1**所

描述之方法製備，在此情況下係藉由用2,5-二氫-1H-吡咯-1-甲酸三級丁酯取代環戊-3-烯-1-基甲醇來製備。^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.99 (d, *J*=2.4 Hz, 1H), 7.84 (dd, *J*=8.7, 2.3 Hz, 1H), 7.04 (d, *J*=8.8 Hz, 1H), 5.31 (ddd, *J*=9.2, 5.4, 1.2 Hz, 1H), 4.21 (br dd, *J*=12.4, 9.1 Hz, 1H), 3.96 (s, 3H), 3.91 (s, 3H), 3.72 - 3.61 (m, 2H), 1.43 (s, 9H)。MS (ESI) *m/z* = 377.4 (M+H)。

【0444】 中間物**434-2**：製備5-(5-(三級丁氧基羰基)-3a,5,6,6a-四氫-4H-吡咯并[3,4-d]異噁唑-3-基)-2-甲氧基苯甲酸。**434-2** (151.4 mg，43.7%，經三個步驟)係藉由針對中間物**429-2**所描述之方法，用中間物**434-1**置換中間物**429-1**來製備。MS (ESI) *m/z* = 363.4 (M+H)。

【0445】

中間物**434-4及434-6** (同對掌性)



中間物**434-3**及**434-4**係藉由非鏡像異構混合物中間物**434-2** (499 mg，1.33 mmol)之對掌性SFC獲得。對掌性SFC製備型層析條件：儀器：Berger MG II (SFC)；管柱：Regis Whelk-01，21×250 mm，5微米；移動相：15% MeOH / 85% CO_2；流動條件：45 mL/min，150巴， 40℃；偵測器波長：220 nm；注射詳情：1.0 mL ~31mg/mL於MeOH-ACN中。分析型層析條件：儀器：Shimadzu Nexera SFC；管柱：Regis Whelk-01，4.6×100 mm，3微米；移動相：15% MeOH / 85% CO_2；流動條件：2.0 mL/min，150巴， 40℃；偵測器波長：220 nm；注射詳情：5 μL

~1mg/mL於乙腈。

【0446】 獲得呈白色固體之中間物**434-3** (峰-1，>99% de，分析型RT = 4.02 min) (95.9 mg，19.2%產率)。^{1}H NMR: (600 MHz, $CDCl_3$) δ 7.99 (d, *J*=2.3 Hz, 1H), 7.86 - 7.82 (m, 1H), 7.04 (br d, *J*=8.7 Hz, 1H), 5.31 (ddd, *J*=9.2, 5.4, 1.3 Hz, 1H), 4.24 - 4.18 (m, 1H), 4.01 - 3.93 (m, 4H), 3.91 (s, 3H), 3.83 - 3.76 (m, 1H), 3.71 - 3.67 (m, 1H), 3.63 (br s, 1H), 1.43 (br s, 9H)。

【0447】 中間物**434-4**. 製備5-(5-(三級丁氧基羰基)-3a,5,6,6a-四氫-4H-吡咯并[3,4-d]異噁唑-3-基)-2-甲氧基苯甲酸。中間物**434-4** (52 mg，67.5%產率)係以與中間物**434-2**類似之方式，藉由水解中間物**434-3**來製備。MS (ESI) *m/z* = 363.1 (M+H)。

【0448】 獲得呈白色固體之中間物**434-5** (峰-2，99.6% de，分析型RT = 4.56 min) (96.7 mg，19.4%產率)。1H NMR (600 MHz, $CDCl_3$) δ 7.98 (d, *J*=2.3 Hz, 1H), 7.83 (dd, *J*=8.8, 2.2 Hz, 1H), 7.03 (d, *J*=8.7 Hz, 1H), 5.32 - 5.28(m, 1H), 4.21 (td, *J*=8.8, 4.0 Hz, 1H), 4.01 - 3.94 (m, 1H), 3.95 (s, 3H), 3.90 (s, 3H), 3.83 - 3.73 (m, 1H), 3.68 (dd, *J*=11.4, 8.9 Hz, 1H), 3.65 - 3.58 (m, 1H), 1.43 (s, 9H)。

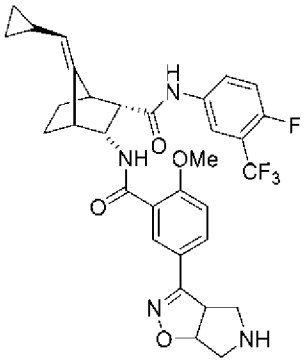
【0449】 中間物**434-6**. 製備5-(5-(三級丁氧基羰基)-3a,5,6,6a-四氫-4H-吡咯并[3,4-d]異噁唑-3-基)-2-甲氧基苯甲酸。中間物**434-6** (48 mg，62.3%產率)係以與中間物**434-2**類似之方式，藉由水解中間物**434-5**來製備。MS (ESI) *m/z* = 363.1 (M+H)。

【0450】 實例**434**係以與實例**429**類似之方式，用中間物**434-2**置換中間物**429-2**來製備。3-(3-(((1R,2R,3S,4R,Z)-7-(環丙基亞甲基)-3-((4-氟

-3-(三氟甲基)苯基) 胺甲醯基) 雙環[2.2.1]庚烷-2-基)胺甲醯基)-4-甲氧基苯基)-3a,4,6,6a-四氫-5H-吡咯并[3,4-d]異噁唑-5-甲酸三級丁酯非鏡像異構混合物**434** (7.1 mg，0.0098 mmol，72.3%產率，非鏡像異構混合物)。^{1}H NMR (500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.91 (br d, *J*=6.7 Hz, 1H), 8.21 (br s, 2H), 7.78 (br d, *J*=7.0 Hz, 2H), 7.47 (br t, *J*=9.5 Hz, 1H), 7.28 (d, J=8.5 Hz, 1H), 5.25 (br dd, J=8.9, 4.9 Hz, 1H), 4.68 (br d, J=9.5 Hz, 1H), 4.46 - 4.39 (m, 2H), 4.04 (d, J=3.1 Hz, 3H), 3.80 - 3.69 (m, 1H), 3.15 (br dd, J=11.0, 3.7 Hz, 1H), 3.10 (br d, J=3.4 Hz, 1H), 2.73 - 2.68 (m, 1H), 1.90 (s, 1H), 1.85 - 1.74 (m, 2H), 1.55 - 1.15 (m, 14H), 0.79 - 0.67 (m, 2H), 0.40 - 0.24 (m, 2H)。HPLC純度：98.5%。分析型LC-MS: 2.81 min；MS (ESI) *m/z* = 713.2 (M+H)；方法B。

【0451】

實例437

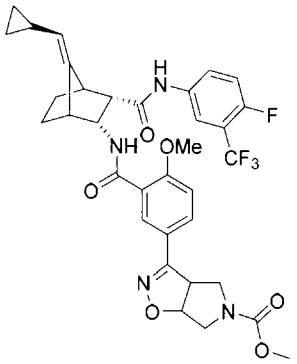


藉由使中間物**434-2** (9.84 mg，0.027 mmol)與溶解於無水THF (2 mL)中之中間物**166-2** (10 mg，0.027 mmol)在DIEA (0.024 mL，0.136 mmol)及BOP (13.21 mg，0.030 mmol)存在下偶合來製備。1 h之後，濃縮反應混合物，溶解於DCM (1 mL)中，且用50% TFA/DCM (1 mL)處理。1 h之後，在減壓下濃縮反應混合物且藉由逆相製備型HPLC純化，得到**437** (1R,2S,3R,4R,Z)-7-(環丙基亞甲基)-N-(4-氟-3-(三氟甲基)苯基)-3-

(2-甲氧基-5-(3a,5,6,6a-四氫-4H-吡咯并[3,4-d]異噁唑-3-基)苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺非鏡像異構混合物(10.3 mg，0.0140 mmol，51.5%產率)。^{1}H NMR (500 MHz, DMSO-d6) δ 10.58 - 10.55 (m, 1H), 9.94 (dd, *J*=18.8, 7.1 Hz, 1H), 8.25 (dd, *J*=10.2, 2.0 Hz, 1H), 8.22 - 8.17 (m, 1H), 7.83 - 7.78 (m, 1H), 7.78 - 7.74 (m, 1H), 7.46 (br t, *J*=9.5 Hz, 1H), 7.29 (d, *J*=8.7 Hz, 1H), 5.43 (dd, *J*=9.3, 4.6 Hz, 1H), 4.69 - 4.64 (m, 2H), 4.44 - 4.37 (m, 1H), 4.04 (d, *J*=1.7 Hz, 3H), 3.72 - 3.65 (m, 2H), 3.46 - 3.38 (m, 1H), 3.16 - 3.11 (m, 1H), 3.09 - 3.05 (m, 1H), 2.73 - 2.68 (m, 1H), 1.83 - 1.70 (m, 2H), 1.51 - 1.34 (m, 4H), 0.76 - 0.66 (m, 2H), 0.33 (br d, J=3.2 Hz, 2H)。HPLC純度：98.6%。分析型LC-MS: 2.32 min；MS (ESI) *m/z* = 613.2 (M+H)；方法C。

【0452】

實例438

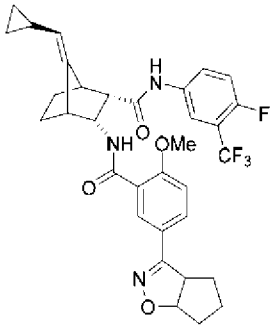


將中間物**434-2** (9.84 mg，0.027 mmol)及環丙基降冰片烷基中間物**166-2** (10 mg，0.027 mmol)溶解於無水THF (2.0 mL)中，接著添加DIEA (0.024 mL，0.136 mmol)及BOP (13.21 mg，0.030 mmol)。2 h之後，濃縮反應混合物，將所得殘餘物再溶解於DCM (0.25 mL)中，且用50% TFA/DCM (0.25 mL)處理。1h之後，將反應混合物濃縮至乾燥。將胺溶解於THF (2.0 mL)中且在0℃用TEA (0.019 mL，0.13 mmol)處理，隨後

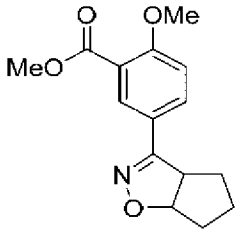
用氯甲酸甲酯(2.6 mg，0.027 mmol)處理。在室溫下攪拌2h之後，在減壓下濃縮反應混合物且藉由製備型RP-HPLC純化，得到3-(3-(((1R,2R,3S,4R,Z)-7-(環丙基亞甲基)-3-((4-氟-3-(三氟甲基)苯基) 胺甲醯基)雙環[2.2.1]庚烷-2-基)胺甲醯基)-4-甲氧基苯基)-3a,4,6,6a-四氫-5H-吡咯并[3,4-d]異噁唑-5-甲酸甲酯(非鏡像異構混合物)**438** (2.6 mg，0.0036 mmol，14.2%產率)。^{1}H NMR (500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.92 (br t, *J*=6.1 Hz, 1H), 8.18 (br s, 2H), 7.81 - 7.74 (m, 2H), 7.45 (br t, *J*=9.8 Hz, 1H), 7.29 - 7.26 (m, 1H), 5.28 (br dd, *J*=8.5, 4.9 Hz, 1H), 4.68 (br d, *J*=9.5 Hz, 1H), 4.48 - 4.38 (m, 2H), 4.03 (d, *J*=3.1 Hz, 2H), 3.81 - 3.74 (m, 1H), 3.64 - 3.48 (m, 4H), 3.17 - 3.06 (m, 2H), 2.73 - 2.66 (m, 1H), 1.84 - 1.72 (m, 2H), 1.52 - 1.33 (m, 4H), 0.77 - 0.67 (m, 2H), 0.33 (br d, J=3.4 Hz, 2H)。HPLC純度：99.1%。分析型LC-MS: 2.48 min；MS (ESI) *m/z* = 671.1 (M+H)；方法B。

【0453】

實例439



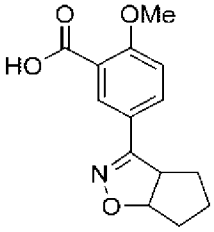
中間物439-1：製備2-甲氧基-5-(3a,5,6,6a-四氫-4H-環戊并[d]異噁唑-3-基)苯甲酸甲酯。



中間物**439-1**係以針對中間物**378-3**所描述之相同方式製備(128 mg，23%產率)，在此情況下係藉由用環戊烯取代烯丙醇來製備。

【0454】

中間物439-2：製備2-甲氧基-5-(3a,5,6,6a-四氫-4H-環戊并[d]異噁唑-3-基)苯甲酸。



中間物**439-2** (45.2 mg，60.3%)係以與中間物**429-2**類似之方式，藉由水解中間物**439-1**來製備。MS (ESI) *m/z* = 262.2 (M+H)。

【0455】藉由非鏡像異構混合物中間物**439-1** (128 mg，0.465 mmol)之對掌性SFC獲得個別對掌性非鏡像異構物酯中間物**439-4A (對掌性峰-1)**及**439-6A (對掌性峰-2)**。對掌性SFC製備型層析條件：儀器：Jasco SFC Prep；管柱：Chiralpak OJ-H，21×250 mm，5微米；移動相：5% IPA / 95% CO_2；流動條件：45 mL/min，150巴， 40℃；偵測器波長：220 nm；注射詳情：0.5 mL ~35mg/mL於IPA-ACN中。分析型層析條件：儀器：Shimadzu Nexera SFC；管柱：Chiralpak OJ-H，4.6×100 mm，3微米；移動相：10% IPA / 90% CO_2；流動條件：2.0 mL/min，150巴， 40℃；偵測器波長：220 nm；注射詳情：5 μL ~1mg/mL於MeOH中。

【0456】獲得呈膜形式之中間物**439-4A** (峰-1，>99% de，分析型

RT=2.84 min) (48.8 mg，38.1%)。^{1}H NMR: (400 MHz, 氯仿-d) δ 8.06 (d, *J*=2.4 Hz, 1H), 7.86 (dd, *J*=8.8, 2.2 Hz, 1H), 7.01 (d, *J*=8.8 Hz, 1H), 5.21 (dd, *J*=8.8, 4.6 Hz, 1H), 4.03 (td, *J*=8.4, 3.0 Hz, 1H), 3.94 (s, 3H), 3.90 (s, 3H), 2.21 - 2.14 (m, 1H), 1.94 - 1.85 (m, 2H), 1.83 - 1.72 (m, 2H), 1.60 - 1.47 (m, 1H)。

【0457】 中間物**439-4** (41.9 mg，90%)係以與中間物**429-2**類似之方式，藉由水解中間物**439-4A**來製備。MS (ESI) *m/z* = 262.3 (M+H)。

【0458】 獲得呈膜形式之中間物**439-6A** (峰-2，>95%de，分析型RT=3.60 min) (51.5 mg，40.2%)。^{1}H NMR: (400 MHz, $CDCl_3$) δ 8.06 (d, J=2.4 Hz, 1H), 7.86 (dd, J=8.8, 2.4 Hz, 1H), 7.01 (d, J=8.8 Hz, 1H), 5.21 (dd, J=8.8, 4.6 Hz, 1H), 4.07 - 4.00 (m, 1H), 3.94 (s, 3H), 3.90 (s, 3H), 2.21 - 2.15 (m, 1H), 1.94 - 1.87 (m, 2H), 1.83 - 1.71 (m, 2H), 1.60 - 1.49 (m, 1H)。

【0459】 中間物**439-6** (45.3 mg，93%)係以與中間物**429-2**類似之方式，藉由水解中間物**439-6A**來製備。MS (ESI) *m/z* = 262.3 (M+H)。

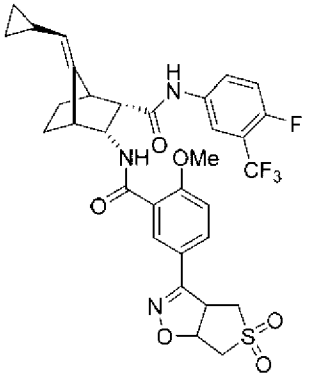
【0460】 實例**439**係以與實例**429**類似之方式，用中間物**439-2**置換中間物**429-2**來製備。(1R,2S,3R,4R,Z)-7-(環丙基亞甲基)-N-(4-氟-3-(三氟甲基)苯基)-3-(2-甲氧基-5-(3a,5,6,6a-四氫-4H-環戊并[d]異噁唑-3-基)苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺非鏡像異構混合物**439** (6.2 mg，0.010 mmol，74.2%產率)。^{1}H NMR (500 MHz, DMSO-d6) δ 10.57 - 10.50 (m, 1H), 9.93 - 9.85 (m, 1H), 8.23 - 8.17 (m, 2H), 7.80 - 7.73 (m, 2H), 7.49 - 7.44 (m, 1H), 7.28 - 7.24 (m, 1H), 5.16 - 5.09 (m, 1H), 4.71 - 4.66 (m, 1H), 4.46 - 4.37 (m, 1H), 4.18 - 4.12 (m, 1H), 4.05 - 3.99 (m,

3H), 3.17 - 3.06 (m, 2H), 2.73 - 2.67 (m, 1H), 1.99 - 1.90 (m, 1H), 1.86 - 1.63 (m, 6H), 1.52 - 1.26 (m, 4H), 0.78 - 0.68 (m, 2H), 0.39 - 0.29 (m, 2H)。HPLC純度：99.4%。分析型LC-MS: 2.82 min；MS (ESI) *m/z* 612.2 (M+H)；方法B。

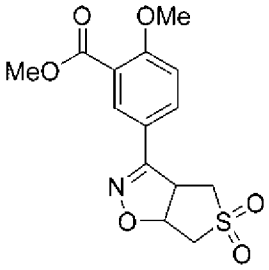
【0461】 以與實例**429**類似之方式，用中間物**439-6** (來自SFC之峰-2)置換中間物**429-2**來製備。(1R,2S,3R,4R,Z)-7-(環丙基亞甲基)-N-(4-氟-3-(三氟甲基)苯基)-3-(2-甲氧基-5-(3a,5,6,6a-四氫-4H-環戊并[d]異噁唑-3-基)苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺同對掌性異構物-2，**441** (10.9 mg，0.017 mmol，63.1%產率)。^{1}H NMR。HPLC純度：100%。分析型LC-MS: 2.71 min；MS (ESI) *m/z* = 612.3 (M+H)；方法B。

【0462】

實例442



中間物442-1：製備5-(5,5-二氧離子基-3a,4,6,6a-四氫噻吩并[3,4-d]異噁唑-3-基)-2-甲氧基苯甲酸甲酯。

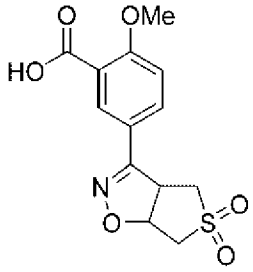


中間物**442-1**係以針對中間物**378-3**所描述之相同方式製備(128 mg，23%產率)，在此情況下係藉由用2,5-二氫噻吩1,1-二氧化物取代烯丙醇來

製備。

【0463】

中間物442-2：製備5-(5,5-二氧離子基-3a,4,6,6a-四氫噻吩并[3,4-d]異噁唑-3-基)-2-甲氧基苯甲酸。



中間物**442-2** (59.0 mg，39.6%)係以與中間物**429-2**類似之方式，藉由水解中間物**442-1**來製備。MS (ESI) *m/z* = 312.2 (M+H)。

【0464】 藉由非鏡像異構混合物中間物**441-1**之對掌性SFC獲得個別對掌性非鏡像異構物酯中間物**442-4A**及**442-6A** (600 mg，1.84 mmol)。對掌性SFC製備型層析條件：儀器：PIC Solution SFC Prep-200；管柱：Chiralcel OD-H，21×250 mm，5微米；移動相：25% MeOH / 75% CO_2；流動條件：45 mL/min，150巴， 40℃；偵測器波長：271 nm；注射詳情：1.0 mL ~50mg/mL於MeOH:ACN中。分析型層析條件：儀器：Shimadzu Nexera SFC；管柱：Chiralcel OD-H，4.6×100 mm，3微米；移動相：15% MeOH / 85% CO_2；流動條件：2.0 mL/min，150巴，40℃；偵測器波長：220 nm；注射詳情：5 µL ~1mg/mL於MeOH中。

【0465】 獲得呈白色固體之中間物**442-4A** (峰-1，>99% de，分析型RT=3.74 min) (108.1 mg，18%)。^{1}H NMR: (400 MHz, 氯仿-d) δ 7.96 (d, J=2.4 Hz, 1H), 7.85 (dd, J=8.8, 2.2 Hz, 1H), 7.07 (d, J=9.0 Hz, 1H), 5.43 (ddd, J=10.1, 7.2, 4.1 Hz, 1H), 4.52 - 4.44 (m, 1H), 3.97 (s, 3H), 3.92 (s, 3H), 3.66 - 3.47 (m, 3H), 3.14 (dd, J=13.6, 8.1 Hz, 1H)。

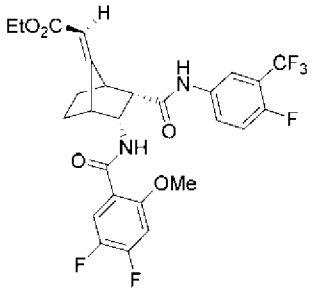
【0466】 中間物**442-4** (82 mg，79%)係以與中間物**429-2**類似之方

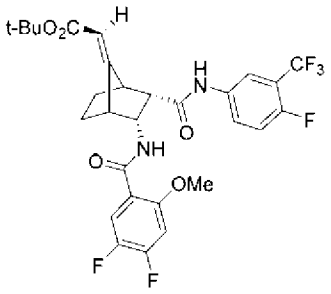
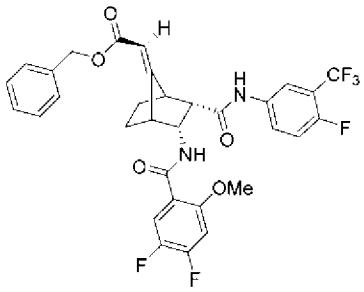
式，藉由水解中間物**442-4A**來製備。MS (ESI) *m/z* = 312.3 (M+H)。

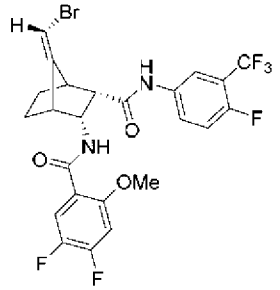
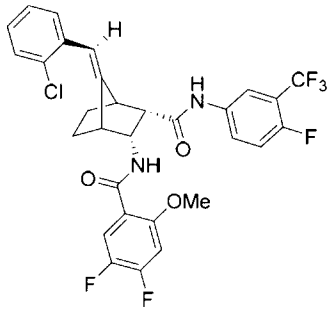
【0467】 獲得呈白色固體之中間物**442-6A** (峰-2，>99% de，分析型RT=5.44 min) (108.8 mg，18%)。^{1}H NMR: (400 MHz, 氯仿-d) δ 7.96 (d, J=2.4 Hz, 1H), 7.85 (dd, J=8.8, 2.2 Hz, 1H), 7.06 (d, J=8.8 Hz, 1H), 5.42 (ddd, J=10.1, 7.2, 4.1 Hz, 1H), 4.52 - 4.44 (m, 1H), 3.97 (s, 3H), 3.91 (s, 3H), 3.66 - 3.46 (m, 3H), 3.14 (dd, J=13.6, 8.4 Hz, 1H)。

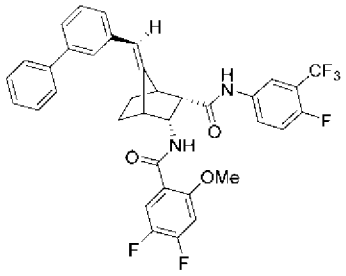
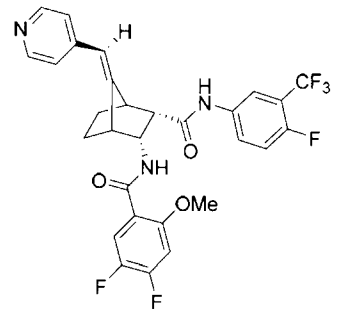
【0468】 中間物**442-6** (89.6 mg，87%)係以與中間物**429-2**類似之方式，藉由水解中間物**442-6A**來製備。MS (ESI) *m/z* = 312.3 (M+H)。

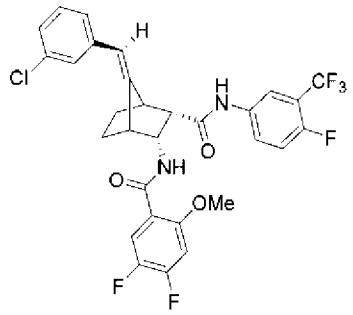
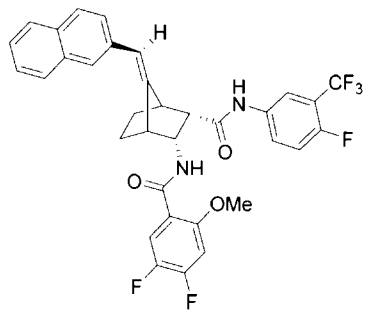
【0469】 實例**442**係以與實例**429**類似之方式，用中間物**442-2**置換中間物**429-2**來製備。(1R,2S,3R,4R,Z)-7-(環丙基亞甲基)-3-(5-(5,5-二氧離子基-3a,4,6,6a-四氫噻吩并[3,4-d]異噁唑-3-基)-2-甲氧基苯甲醯胺基)-N-(4-氟-3-(三氟甲基)苯基)雙環[2.2.1]庚烷-2-甲醯胺非鏡像異構混合物**442** (4.8 mg，0.0072 mmol，53.0%產率)。^{1}H NMR (500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.91 (br t, *J*=8.4 Hz, 1H), 8.26 - 8.20 (m, 2H), 7.81 - 7.74 (m, 2H), 7.48 (br t, *J*=9.9 Hz, 1H), 7.28 (d, *J*=8.9 Hz, 1H), 5.43 - 5.38 (m, 1H), 4.78 - 4.72 (m, 1H), 4.69 (br d, *J*=9.8 Hz, 1H), 4.43 (br s, 1H), 4.05 (s, 3H), 3.65 (br dd, *J*=14.3, 6.7 Hz, 1H), 3.44 - 3.33 (m, 1H), 3.18 - 3.08 (m, 3H), 2.72 (br s, 1H), 1.85 - 1.74 (m, 2H), 1.52 - 1.46 (m, 1H), 1.45 - 1.34 (m, 2H), 0.79 - 0.68 (m, 2H), 0.34 (br s, 2H)。HPLC純度：99.2%。分析型LC-MS：2.33 min；MS (ESI) *m/z* 662.2 (M+H)；方法B。

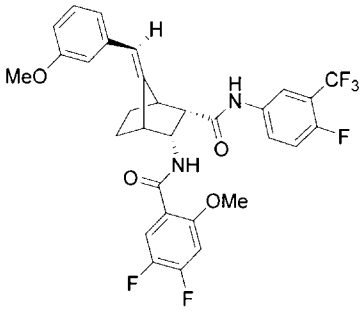
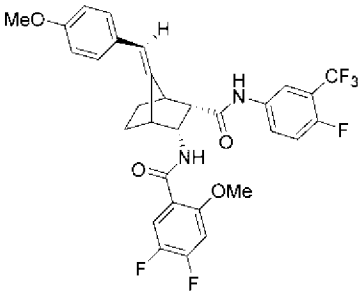
表2					
實例編號	**結構**	**名稱**	**MS (ESI) (M+H)**	**^{1}H NMR**	**LC RT Meth. (min)**
7		2-[(2R,3S,7Z)-2-(4,5-二氟-2-甲氧基苯甲醯胺基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-7-亞基]乙酸乙酯	571.1	(400MHz, $CDCl_3$) δ 9.30 (d, J=7.9 Hz, 1H), 8.26 (s, 1H), 7.99 (dd, J=11.2, 9.2 Hz, 1H), 7.92 (dd, J=6.3, 2.5 Hz, 1H), 7.56 (dt, J=8.7, 3.5 Hz, 1H), 7.10 (t, J=9.4 Hz, 1H), 6.78 (dd, J=11.4, 6.2 Hz, 1H), 5.72 (s, 1H), 4.85 - 4.76 (m, 1H), 4.21 (qd, J=7.2, 1.0 Hz, 2H), 3.98 (s, 3H), 3.91 (t, J=4.1 Hz, 1H), 3.14 (dd, J=10.7, 3.0 Hz, 1H), 2.86 (t, J=4.0 Hz, 1H), 2.39 - 2.30 (m, 1H), 1.97 - 1.87 (m, 1H), 1.78 - 1.65 (m, 2H), 1.32 (t, J=7.2 Hz, 3H)	1.20, A

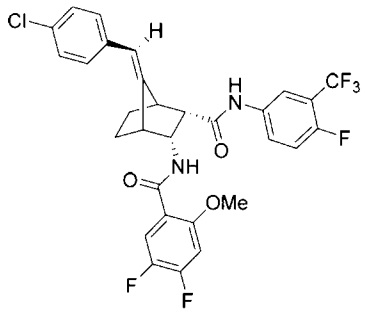
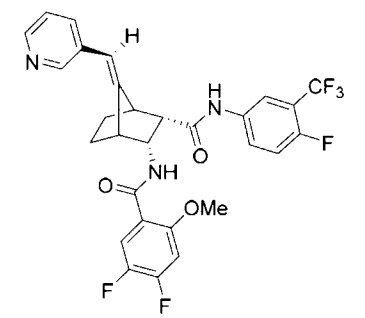
8		2-[(2R,3S,7Z)-2-(4,5-二氟-2-甲氧基苯甲醯胺基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-7-亞基]乙酸三級丁酯	599.1	(500MHz, $CDCl_3$) δ 9.50 (d, J=7.7 Hz, 1H), 8.74 (s, 1H), 8.00 (dd, J=6.3, 2.5 Hz, 1H), 7.97 - 7.92 (m, 1H), 7.66 (dt, J=8.6, 3.5 Hz, 1H), 7.11 (t, J=9.4 Hz, 1H), 6.78 (dd, J=11.6, 6.1 Hz, 1H), 5.64 (s, 1H), 4.78 - 4.68 (m, 1H), 4.00 (s, 3H), 3.86 (t, J=4.1 Hz, 1H), 3.16 (dd, J=10.7, 3.3 Hz, 1H), 2.83 (t, J=4.0 Hz, 1H), 2.33 - 2.25 (m, 1H), 1.98 - 1.92 (m, 1H), 1.74 - 1.59 (m, 3H), 1.50 (s, 9H)	1.25, C
9		2-[(2R,3S,7Z)-2-(4,5-二氟-2-甲氧基苯甲醯胺基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-7-亞基]乙酸苯甲酯	633.2	(500MHz, $CDCl_3$) δ 9.29 (d, J=7.9 Hz, 1H), 8.21 (s, 1H), 8.02 (dd, J=11.3, 9.3 Hz, 1H), 7.93 (dd, J=6.3, 2.6 Hz, 1H), 7.56 (dt, J=8.7, 3.5 Hz, 1H), 7.45 - 7.33 (m, 5H), 7.12 (t, J=9.3 Hz, 1H), 6.80 (dd, J=11.4, 6.1 Hz, 1H), 5.78 (s, 1H), 5.27 - 5.18 (m, 2H), 4.90 - 4.79 (m, 1H), 3.99 (s, 3H), 3.99 - 3.96 (m, 1H), 3.19 - 3.11 (m, 1H), 2.87 (t, J=4.0 Hz, 1H), 2.41 - 2.32 (m, 1H), 1.98 - 1.89 (m, 1H), 1.79 - 1.66 (m, 2H)	1.25, B

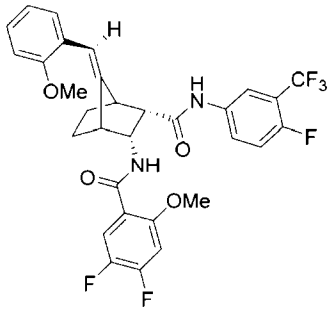
10		(2S,3R,7E)-7-(溴亞甲基)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	578.9	(500MHz, $CDCl_3$) δ 9.65 (d, J=7.4 Hz, 1H), 8.03 - 7.96 (m, 2H), 7.84 (s, 1H), 7.53 (dt, J=8.7, 3.5 Hz, 1H), 7.14 (t, J=9.4 Hz, 1H), 6.79 (dd, J=11.6, 6.1 Hz, 1H), 5.95 (s, 1H), 4.75 - 4.67 (m, 1H), 4.00 (s, 3H), 3.24 (t, J=3.9 Hz, 1H), 3.12 (dd, J=10.7, 4.1 Hz, 1H), 2.98 (t, J=4.0 Hz, 1H), 2.22 - 2.13 (m, 1H), 1.96 - 1.88 (m, 1H), 1.70 - 1.61 (m, 1H)	2.60, B
14		(2S,3R,7Z)-7-[(2-氯苯基)亞甲基]-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4- 氟 -3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	609.1	-	1.28, B

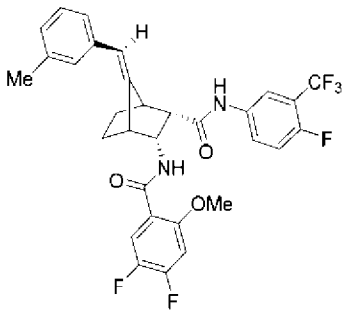
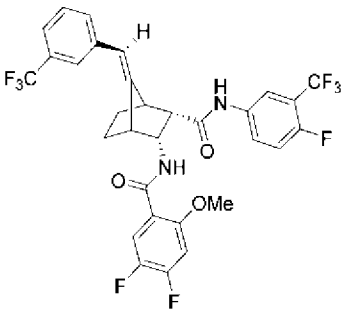
15		(2S,3R,7Z)-7-({[1,1'-聯苯]-3-基}亞甲基)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	651.2	(500MHz, $CDCl_3$) δ 9.51 (d, J=7.6 Hz, 1H), 8.04 (dd, J=11.2, 9.4 Hz, 1H), 7.97 (dd, J=6.1, 2.4 Hz, 1H), 7.84 (s, 1H), 7.66 - 7.62 (m, 2H), 7.58 - 7.52 (m, 2H), 7.51 - 7.42 (m, 4H), 7.40 - 7.35 (m, 2H), 7.14 (t, J=9.3 Hz, 1H), 6.80 (dd, J=11.6, 6.1 Hz, 1H), 6.41 (s, 1H), 4.92 - 4.84 (m, 1H), 4.01 (s, 3H), 3.56 - 3.51 (m, 1H), 3.21 (dd, J=10.7, 4.0 Hz, 1H), 2.92 (br. s., 1H), 2.30 - 2.23 (m, 1H), 1.98 - 1.92 (m, 1H), 1.79 - 1.69 (m, 2H)	1.35, B
16		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-[(吡啶-4-基)亞甲基]雙環[2.2.1]庚烷-2-甲醯胺	576.1	(500MHz, $CDCl_3$) δ 9.65 (d, J=7.3 Hz, 1H), 8.58 (br. s., 2H), 8.10 - 7.98 (m, 2H), 7.61 - 7.54 (m, 1H), 7.27 (br. s., 1H) 7.15 (t, J=9.3 Hz, 1H), 6.82 (dd, J=11.6, 6.1 Hz, 1H), 6.27 (s, 1H), 4.83 (t, J=10.8 Hz, 1H), 4.03 (s, 3H), 3.51 (d, J=2.6 Hz, 1H), 3.22 (dd, J=11.0, 4.0 Hz, 1H), 2.94 (br. s., 1H), 2.26 (t, J=9.2 Hz, 1H), 2.00 (t, J=8.7 Hz, 1H), 1.73 (m, 2H)	0.96, C

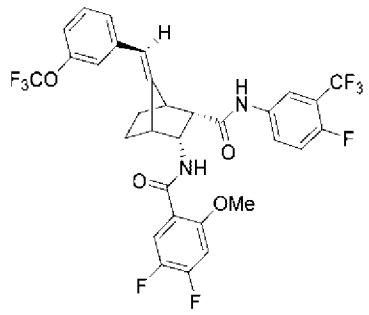
17		(2S,3R,7Z)-7-[(3-氯苯基)亞甲基]-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	609.0	(500MHz, $CDCl_3$) δ 9.49 (d, J=7.9 Hz, 1H), 8.05 (dd, J=11.3, 9.3 Hz, 1H), 7.96 (dd, J=6.1, 2.6 Hz, 1H), 7.77 (s, 1H), 7.59 - 7.52 (m, 1H), 7.33 - 7.27 (m, 2H), 7.26 - 7.22 (m, 2H), 7.15 (t, J=9.4 Hz, 1H), 6.81 (dd, J=11.4, 6.1 Hz, 1H), 6.29 (s, 1H), 4.89 - 4.81 (m, 1H), 4.02 (s, 3H), 3.49 - 3.41 (m, 1H), 3.19 (dd, J=10.8, 3.8 Hz, 1H), 2.91 (br. s., 1H), 2.28 (t, J=8.9 Hz, 1H), 1.96 (t, J=8.7 Hz, 1H), 1.78 - 1.67 (m, 2H)	1.29, B
18		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-[(萘-2-基)亞甲基]雙環[2.2.1]庚烷-2-甲醯胺	625.1	(500MHz, $CDCl_3$) δ 9.51 (d, J=7.6 Hz, 1H), 8.06 (dd, J=11.3, 9.3 Hz, 1H), 7.97 (dd, J=6.2, 2.7 Hz, 1H), 7.87 - 7.81 (m, 3H), 7.78 (d, J=13.9 Hz, 2H), 7.59 - 7.52 (m, 2H), 7.51 - 7.43 (m, 2H), 7.15 (t, J=9.3 Hz, 1H), 6.81 (dd, J=11.6, 6.1 Hz, 1H), 6.52 (s, 1H), 4.97 - 4.88 (m, 1H), 4.02 (s, 3H), 3.61 (t, J=3.4 Hz, 1H), 3.24 (dd, J=10.8, 3.8 Hz, 1H), 2.96 (br. s., 1H), 2.29 (t, J=8.6 Hz, 1H), 1.97 (t, J=8.6 Hz, 1H), 1.82 - 1.69 (m, 2H)	1.31, B

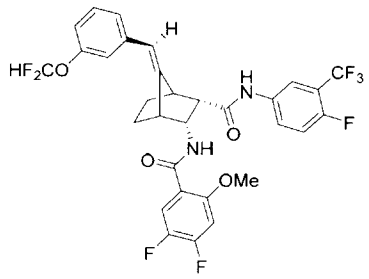
19		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-[(3-甲氧基苯基)亞甲基]雙環[2.2.1]庚烷-2-甲醯胺	605.2	-	1.25, B
20		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-[(4-甲氧基苯基)亞甲基]雙環[2.2.1]庚烷-2-甲醯胺	605.1	(500MHz, $CDCl_3$) δ 9.57 (d, J=7.6 Hz, 1H), 8.04 (dd, J=11.4, 9.4 Hz, 1H), 7.98 (dd, J=6.1, 2.6 Hz, 1H), 7.80 (s, 1H), 7.55 (dt, J=8.7, 3.5 Hz, 1H), 7.31 - 7.29 (m, 1H), 7.14 (t, J=9.3 Hz, 1H), 6.92 - 6.87 (m, 2H), 6.80 (dd, J=11.5, 6.2 Hz, 1H), 6.27 (s, 1H), 4.87 - 4.77 (m, 1H), 4.02 (s, 3H), 3.83 (s, 3H), 3.49 (t, J=3.4 Hz, 1H), 3.16 (dd, J=10.8, 3.8 Hz, 1H), 2.88 - 2.84 (m, 1H), 2.21 (t, J=8.9 Hz, 1H), 1.93 (t, J=8.6 Hz, 1H), 1.73 - 1.64 (m, 2H)	1.26, C

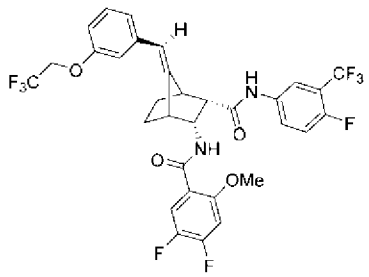
21		(2S,3R,7Z)-7-[(4-氯苯基)亞甲基]-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	609.1	(500MHz, $CDCl_3$) δ 9.56 (d, J=7.6 Hz, 1H), 8.05 (dd, J=11.4, 9.4 Hz, 1H), 7.97 (dd, J=6.1, 2.6 Hz, 1H), 7.75 (s, 1H), 7.55 (dt, J=8.7, 3.5 Hz, 1H), 7.34 - 7.30 (m, 2H), 7.28 - 7.26 (m, 2H), 7.15 (t, J=9.3 Hz, 1H), 6.81 (dd, J=11.4, 6.1 Hz, 1H), 6.29 (s, 1H), 4.90 - 4.78 (m, 1H), 4.02 (s, 3H), 3.51 - 3.42 (m, 1H), 3.18 (dd, J=10.8, 4.0 Hz, 1H), 2.90 (br. s., 1H), 2.30 - 2.19 (m, 1H), 1.99 - 1.90 (m, 1H), 1.76 - 1.65 (m, 2H)	1.29, C
22		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-[(吡啶-3-基)亞甲基]雙環[2.2.1]庚烷-2-甲醯胺	576.0	(500MHz, $CDCl_3$) δ 9.62 (d, J=7.5 Hz, 1H), 8.57 (d, J=2.0 Hz, 1H), 8.49 (dd, J=4.7, 1.5 Hz, 1H), 8.16 (br. s., 1H), 8.06 - 7.99 (m, 2H), 7.74 (dt, J=8.0, 1.8 Hz, 1H), 7.59 (dt, J=8.6, 3.5 Hz, 1H), 7.31 (dd, J=7.8, 4.9 Hz, 1H), 7.16 (t, J=9.3 Hz, 1H), 6.81 (dd, J=11.4, 6.1 Hz, 1H), 6.33 (s, 1H), 4.88 - 4.76 (m, 1H), 4.03 (s, 3H), 3.46 (t, J=3.6 Hz, 1H), 3.21 (dd, J=10.8, 3.9 Hz, 1H), 2.96 (t, J=3.4 Hz, 1H), 2.28 (t, J=9.0 Hz, 1H), 2.03 - 1.97 (m, 1H), 1.79 - 1.69 (m, 2H)	0.95, B

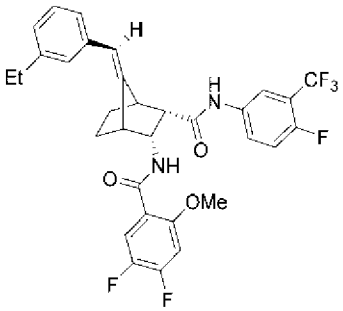
23		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-[(2-甲氧基苯基)亞甲基]雙環[2.2.1]庚烷-2-甲醯胺	605.1	(500MHz, $CDCl_3$) δ 9.49 (d, J=7.8 Hz, 1H), 8.04 (dd, J=11.4, 9.4 Hz, 1H), 7.97 (dd, J=6.1, 2.6 Hz, 1H), 7.75 (s, 1H), 7.55 (dt, J=8.8, 3.5 Hz, 1H), 7.33 (dd, J=7.5, 1.5 Hz, 1H), 7.27 - 7.22 (m, 1H), 7.14 (t, J=9.4 Hz, 1H), 7.01 - 6.94 (m, 1H), 6.91 (d, J=8.4 Hz, 1H), 6.80 (dd, J=11.6, 6.1 Hz, 1H), 6.49 (s, 1H), 4.90 - 4.81 (m, 1H), 4.01 (s, 3H), 3.89 (s, 3H), 3.36 (t, J=3.9 Hz, 1H), 3.22 (dd, J=10.8, 4.0 Hz, 1H), 2.93 (t, J=3.7 Hz, 1H), 2.29 - 2.20 (m, 1H), 1.95 - 1.88 (m, 1H), 1.80 - 1.67 (m, 2H)	1.26, C

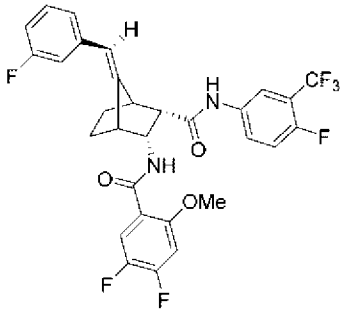
24		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-[(3-甲基苯基)亞甲基]雙環[2.2.1]庚烷-2-甲醯胺	589.2	(500MHz, $CDCl_3$) δ 9.53 (d, J=7.9 Hz, 1H), 8.03 (dd, J=11.3, 9.3 Hz, 1H), 7.97 (dd, J=6.3, 2.6 Hz, 1H), 7.91 (s, 1H), 7.56 (dt, J=8.6, 3.6 Hz, 1H), 7.27 - 7.23 (m, 1H), 7.20 - 7.11 (m, 3H), 7.07 (d, J=7.5 Hz, 1H), 6.80 (dd, J=11.5, 6.2 Hz, 1H), 6.31 (s, 1H), 4.87 - 4.80 (m, 1H), 4.01 (s, 3H), 3.50 (t, J=3.7 Hz, 1H), 3.18 (dd, J=10.5, 3.7 Hz, 1H), 2.87 (t, J=3.7 Hz, 1H), 2.38 (s, 3H), 2.24 (t, J=8.9 Hz, 1H), 1.98 - 1.91 (m, 1H), 1.74 - 1.67 (m, 2H)	1.30, C
25		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-{[3-(三氟甲基)苯基]亞甲基}雙環[2.2.1]庚烷-2-甲醯胺	643.0	(500MHz, CDCl3) δ 9.53 (d, J=7.8 Hz, 1H), 8.04 (dd, J=11.4, 9.4 Hz, 1H), 7.97 (dd, J=6.2, 2.7 Hz, 1H), 7.83 (s, 1H), 7.59 - 7.46 (m, 5H), 7.15 (t, J=9.3 Hz, 1H), 6.81 (dd, J=11.4, 6.1 Hz, 1H), 6.37 (s, 1H), 4.89 - 4.81 (m, 1H), 4.02 (s, 3H), 3.43 (t, J=3.4 Hz, 1H), 3.20 (dd, J=10.8, 3.8 Hz, 1H), 2.93 (br. s., 1H), 2.29 (t, J=8.9 Hz, 1H), 1.97 (t, J=8.6 Hz, 1H), 1.80 - 1.65 (m, 2H)	1.29, C

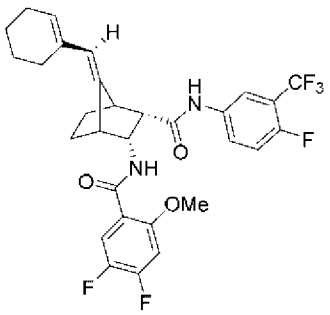
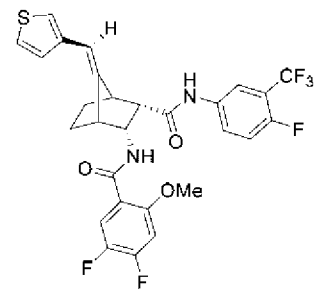
26		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-{[3-(三氟甲氧基)苯基]亞甲基}雙環[2.2.1]庚烷-2-甲醯胺	659.1	(500MHz, $CDCl_3$) δ 9.51 (d, J=7.6 Hz, 1H), 8.04 (dd, J=11.2, 9.4 Hz, 1H), 7.96 (dd, J=6.2, 2.5 Hz, 1H), 7.85 (s, 1H), 7.55 (dt, J=8.7, 3.5 Hz, 1H), 7.41 - 7.36 (m, 1H), 7.31 (d, J=7.8 Hz, 1H), 7.14 (q, J=9.5 Hz, 3H), 6.81 (dd, J=11.6, 6.1 Hz, 1H), 6.32 (s, 1H), 4.90 - 4.80 (m, 1H), 4.02 (s, 3H), 3.44 (br. s., 1H), 3.19 (dd, J=10.8, 4.0 Hz, 1H), 2.91 (br. s., 1H), 2.28 (t, J=9.0 Hz, 1H), 2.01 - 1.91 (m, 1H), 1.79 - 1.68 (m, 2H)	1.31, C

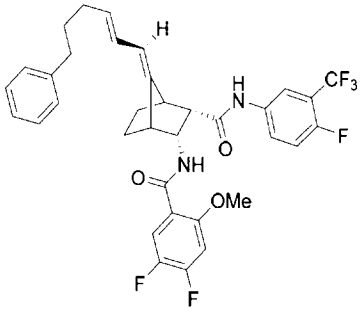
27		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-7-{[3-(二氟甲氧基)苯基]亞甲基}-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	641.0	(500MHz, $CDCl_3$) δ 9.55 (d, J=7.8 Hz, 1H), 8.03 (dd, J=11.3, 9.3 Hz, 1H), 7.97 (dd, J=6.1, 2.6 Hz, 1H), 7.87 (s, 1H), 7.56 (dt, J=8.8, 3.4 Hz, 1H), 7.39 - 7.32 (m, 1H), 7.22 (d, J=7.8 Hz, 1H), 7.14 (t, J=9.3 Hz, 1H), 7.06 (s, 1H), 7.01 (dd, J=8.0, 1.9 Hz, 1H), 6.81 (dd, J=11.6, 6.1 Hz, 1H), 6.74 - 6.41 (m, 1H), 6.31 (s, 1H), 4.89 - 4.76 (m, 1H), 4.02 (s, 3H), 3.45 (br. s., 1H), 3.19 (dd, J=10.8, 4.0 Hz, 1H), 2.90 (br. s., 1H), 2.26 (t, J=8.9 Hz, 1H), 2.01 - 1.90 (m, 1H), 1.77 - 1.67 (m, 2H)	1.27, C

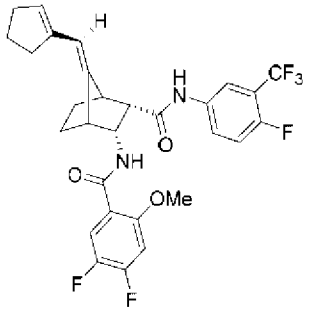
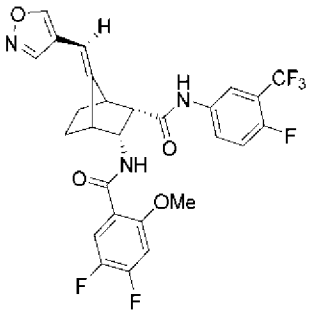
28		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-{[3-(2,2,2-三氟乙氧基)苯基]亞甲基}雙環[2.2.1]庚烷-2-甲醯胺	673.1	(500MHz, $CDCl_3$) δ 9.56 (d, J=7.8 Hz, 1H), 8.04 (dd, J=11.3, 9.5 Hz, 1H), 7.98 (dd, J=6.1, 2.4 Hz, 1H), 7.79 (s, 1H), 7.60 - 7.53 (m, 1H), 7.34 - 7.29 (m, 1H), 7.15 (t, J=9.3 Hz, 1H), 7.05 (d, J=7.8 Hz, 1H), 6.94 (s, 1H), 6.88 - 6.78 (m, 2H), 6.32 (s, 1H), 4.90 - 4.79 (m, 1H), 4.44 (q, J=8.2 Hz, 2H), 4.02 (s, 3H), 3.48 (br. s., 1H), 3.20 (dd, J=10.7, 4.1 Hz, 1H), 2.91 (br. s., 1H), 2.23 (t, J=9.0 Hz, 1H), 1.95 (t, J=8.8 Hz, 1H), 1.76 - 1.66 (m, 2H)	1.29, B

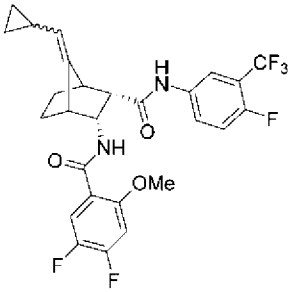
29		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-7-[(3-乙基苯基)亞甲基]-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	603.2	(500MHz, $CDCl_3$) δ 9.50 (d, J=7.8 Hz, 1H), 8.04 (dd, J=11.3, 9.5 Hz, 1H), 7.97 (dd, J=6.2, 2.4 Hz, 1H), 7.88 (s, 1H), 7.56 (dt, J=8.7, 3.3 Hz, 1H), 7.31 - 7.26 (m, 1H), 7.21 (d, J=7.6 Hz, 1H), 7.17 - 7.08 (m, 3H), 6.80 (dd, J=11.4, 6.1 Hz, 1H), 6.33 (s, 1H), 4.91 - 4.82 (m, 1H), 4.01 (s, 3H), 3.53 - 3.46 (m, 1H), 3.19 (dd, J=10.7, 3.8 Hz, 1H), 2.90 - 2.86 (m, 1H), 2.68 (q, J=7.5 Hz, 2H), 2.30 - 2.19 (m, 1H), 1.97 - 1.87 (m, 1H), 1.77 - 1.66 (m, 2H), 1.28 (t, J=7.6 Hz, 3H)	1.34, C

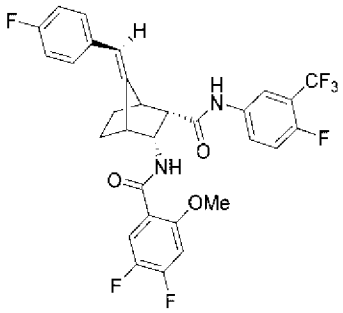
30		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-[(3-氟苯基)亞甲基]雙環[2.2.1]庚烷-2-甲醯胺	593.0	(500MHz, $CDCl_3$) δ 9.52 (d, J=7.6 Hz, 1H), 8.04 (dd, J=11.3, 9.3 Hz, 1H), 7.97 (dd, J=6.3, 2.6 Hz, 1H), 7.84 (s, 1H), 7.55 (dt, J=8.7, 3.4 Hz, 1H), 7.32 (td, J=7.9, 6.1 Hz, 1H), 7.19 - 7.12 (m, 2H), 7.01 (dt, J=10.1, 1.9 Hz, 1H), 6.95 (td, J=8.2, 2.3 Hz, 1H), 6.81 (dd, J=11.5, 6.2 Hz, 1H), 6.30 (s, 1H), 4.89 - 4.78 (m, 1H), 4.02 (s, 3H), 3.47 (t, J=3.6 Hz, 1H), 3.19 (dd, J=10.8, 3.9 Hz, 1H), 2.90 (t, J=3.5 Hz, 1H), 2.27 (t, J=8.9 Hz, 1H), 2.00 - 1.92 (m, 1H), 1.76 - 1.67 (m, 2H)	1.28, C

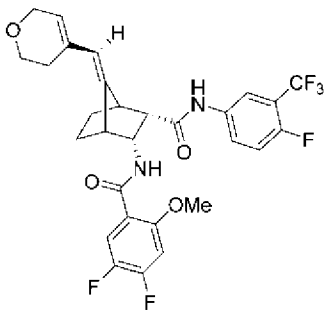
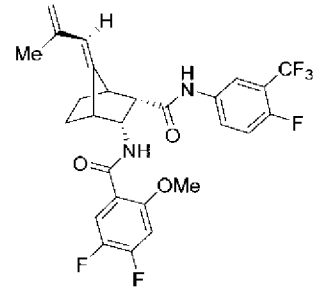
35		(2S,3R,7Z)-7-[(環己-1-烯-1-基)亞甲基]-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	579.1	(500MHz, $CDCl_3$) δ 9.55 (d, J=7.6 Hz, 1H), 8.06 (dd, J=11.4, 9.4 Hz, 1H), 7.97 (dd, J=6.2, 2.5 Hz, 1H), 7.69 (s, 1H), 7.61 - 7.50 (m, 1H), 7.14 (t, J=9.3 Hz, 1H), 6.80 (dd, J=11.5, 6.2 Hz, 1H), 5.84 (s, 1H), 5.74 (br. s., 1H), 4.80 - 4.69 (m, 1H), 4.01 (s, 3H), 3.41 (t, J=3.9 Hz, 1H), 3.06 (dd, J=10.7, 3.5 Hz, 1H), 2.74 (t, J=3.9 Hz, 1H), 2.42 - 2.33 (m, 1H), 2.29 - 2.20 (m, 1H), 2.18 - 2.06 (m, 3H), 1.92 - 1.85 (m, 1H), 1.73 - 1.66 (m, 2H), 1.65 - 1.53 (m, 4H)	1.35, B
36		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-[(噻吩-3-基)亞甲基]雙環[2.2.1]庚烷-2-甲醯胺	581.0	(500MHz, $CDCl_3$) δ 9.59 (d, J=7.6 Hz, 1H), 8.05 (dd, J=11.4, 9.4 Hz, 1H), 7.98 (dd, J=6.1, 2.6 Hz, 1H), 7.74 (s, 1H), 7.56 (dt, J=8.6, 3.5 Hz, 1H), 7.31 (dd, J=4.5, 3.4 Hz, 1H), 7.22 - 7.19 (m, 2H), 7.15 (t, J=9.2 Hz, 1H), 6.81 (dd, J=11.5, 6.2 Hz, 1H), 6.30 (s, 1H), 4.87 - 4.78 (m, 1H), 3.54 - 3.45 (m, 1H), 3.17 (dd, J=10.7, 4.0 Hz, 1H), 2.86 (br. s., 1H), 2.24 - 2.16 (m, 1H), 1.99 - 1.89 (m, 1H), 1.74 - 1.65 (m, 2H)	1.26, B

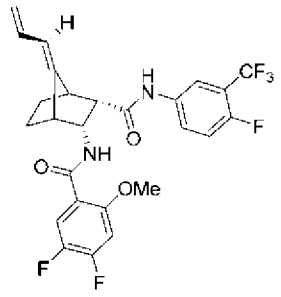
37		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-[(2E)-6-苯基己-2-烯-1-亞基]雙環[2.2.1]庚烷-2-甲醯胺	643.3	(500MHz, $CDCl_3$) δ 9.53 (d, J=7.8 Hz, 1H), 8.05 (dd, J=11.4, 9.4 Hz, 1H), 7.96 (dd, J=6.2, 2.5 Hz, 1H), 7.69 (s, 1H), 7.58 - 7.50 (m, 1H), 7.34 - 7.29 (m, 2H), 7.24 - 7.19 (m, 3H), 7.14 (t, J=9.2 Hz, 1H), 6.80 (dd, J=11.6, 6.1 Hz, 1H), 6.20 (dd, J=15.2, 10.8 Hz, 1H), 5.88 (d, J=10.7 Hz, 1H), 5.76 - 5.67 (m, 1H), 4.76 - 4.68 (m, 1H), 4.01 (s, 3H), 3.23 (br. s., 1H), 3.07 (dd, J=10.7, 4.0 Hz, 1H), 2.77 (br. s., 1H), 2.69 - 2.64 (m, 2H), 2.22 - 2.13 (m, 3H), 1.87 (t, J=8.6 Hz, 1H), 1.77 (quin, J=7.6 Hz, 2H), 1.60 (d, J=8.5 Hz, 4H)	1.33, B

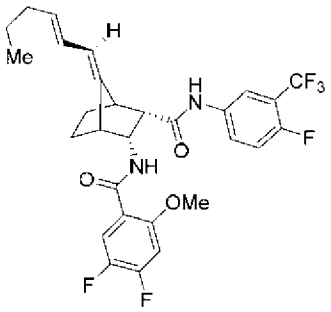
38		(2S,3R,7Z)-7-[(環戊-1-烯-1-基)亞甲基]-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	565.0	(500MHz, $CDCl_3$) δ 9.53 (d, J=7.6 Hz, 1H), 8.06 (dd, J=11.4, 9.3 Hz, 1H), 7.96 (dd, J=6.2, 2.5 Hz, 1H), 7.68 (s, 1H), 7.58 - 7.52 (m, 1H), 7.14 (t, J=9.3 Hz, 1H), 6.80 (dd, J=11.6, 6.1 Hz, 1H), 6.11 (s, 1H), 5.74 (s, 1H), 4.79 - 4.70 (m, 1H), 4.01 (s, 3H), 3.38 (t, J=3.9 Hz, 1H), 3.08 (dd, J=10.8, 4.0 Hz, 1H), 2.78 (t, J=3.7 Hz, 1H), 2.73 - 2.66 (m, 1H), 2.60 - 2.53 (m, 1H), 2.44 - 2.38 (m, 2H), 2.16 - 2.10 (m, 1H), 1.98 (quin, J=7.2 Hz, 2H), 1.92 - 1.86 (m, 1H), 1.67 - 1.61 (m, 2H)	1.28, B
39		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-[(1,2-噁唑-4-基)亞甲基]雙環[2.2.1]庚烷-2-甲醯胺	566.2	(500MHz, $CDCl_3$) δ 9.54 (d, J=7.4 Hz, 1H), 8.44 (s, 1H), 8.35 (s, 1H), 8.03 (dd, J=11.3, 9.4 Hz, 1H), 7.94 (dd, J=6.1, 2.5 Hz, 1H), 7.65 (s, 1H), 7.56 - 7.49 (m, 1H), 7.13 (t, J=9.4 Hz, 1H), 6.79 (dd, J=11.6, 6.1 Hz, 1H), 6.02 (s, 1H), 4.83 - 4.74 (m, 1H), 4.03 - 3.97 (m, 3H), 3.26 (br. s., 1H), 3.14 (dd, J=10.7, 4.1 Hz, 1H), 2.88 (br. s., 1H), 2.23 (t, J=8.9 Hz, 1H), 1.95 (t, J=8.7 Hz, 1H), 1.72 - 1.63 (m, 2H)	1.03, A

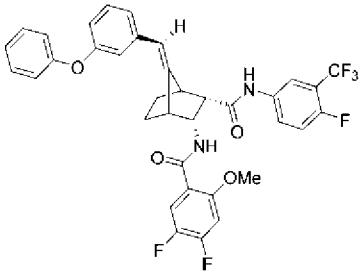
40		(2S,3R)-7-(環丙基亞甲基)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	539.1	(500MHz, $CDCl_3$) δ 9.48 (d, J=7.7 Hz, 1H), 9.38 (d, J=7.7 Hz, 1H), 8.03 (ddd, J=11.4, 9.4, 4.8 Hz, 2H), 7.92 (dt, J=6.1, 2.9 Hz, 2H), 7.78 (s, 1H), 7.70 (s, 1H), 7.58 - 7.47 (m, 2H), 7.11 (t, J=9.4 Hz, 2H), 6.78 (ddd, J=11.6, 6.2, 4.3 Hz, 2H), 4.78 - 4.71 (m, 1H), 4.71 - 4.65 (m, 1H), 4.63 (d, J=3.3 Hz, 1H), 4.61 (d, J=3.3 Hz, 1H), 3.99 (s, 3H), 3.98 (s, 3H), 3.20 - 3.13 (m, 2H), 3.13 - 3.07 (m, 1H), 3.04 (ddd, J=10.7, 4.1, 1.1 Hz, 1H), 2.72 (t, J=4.3 Hz, 1H), 2.68 (t, J=3.9 Hz, 1H), 2.17 (ddd, J=12.1, 8.8, 3.6 Hz, 1H), 2.13 - 2.06 (m, 1H), 1.87 - 1.81 (m, 1H), 1.80 - 1.74 (m, 1H), 1.68 - 1.53 (m, 2H), 1.51 - 1.40 (m, 2H), 0.76 - 0.66 (m, 4H), 0.40 - 0.29 (m, 4H)	1.23, A

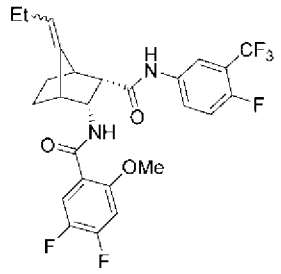
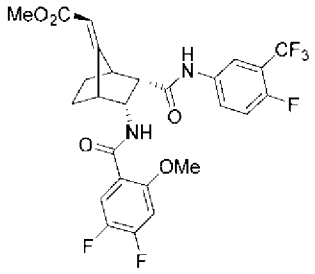
41		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-[(4-氟苯基)亞甲基]雙環[2.2.1]庚烷-2-甲醯胺	593.0	(500MHz, $CDCl_3$) δ 9.56 (d, J=7.6 Hz, 1H), 8.05 (dd, J=11.4, 9.4 Hz, 1H), 7.97 (dd, J=6.1, 2.6 Hz, 1H), 7.72 (s, 1H), 7.55 (dt, J=8.7, 3.5 Hz, 1H), 7.33 - 7.29 (m, 2H), 7.15 (t, J=9.3 Hz, 1H), 7.07 - 7.02 (m, 2H), 6.81 (dd, J=11.6, 6.1 Hz, 1H), 6.30 (s, 1H), 4.88 - 4.79 (m, 1H), 4.02 (s, 3H), 3.45 (t, J=3.4 Hz, 1H), 3.18 (dd, J=10.8, 3.7 Hz, 1H), 2.89 (t, J=3.3 Hz, 1H), 2.23 (t, J=8.9 Hz, 1H), 1.98 - 1.90 (m, 1H), 1.76 - 1.65 (m, 2H)	1.29, C

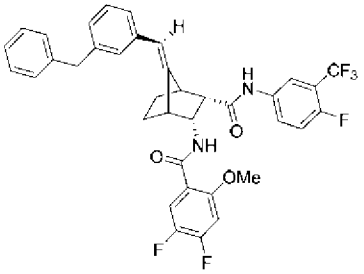
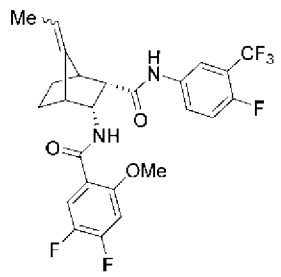
42		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-7-[(3,6-二氫-2H-哌喃-4-基)亞甲基]-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	581.2	(500MHz, $CDCl_3$) δ 9.60 (d, J=7.5 Hz, 1H), 8.07 - 7.96 (m, 2H), 7.80 (s, 1H), 7.56 (dt, J=8.7, 3.5 Hz, 1H), 7.15 (t, J=9.4 Hz, 1H), 6.80 (dd, J=11.6, 6.1 Hz, 1H), 5.85 (s, 1H), 5.72 (d, J=0.8 Hz, 1H), 4.77 - 4.69 (m, 1H), 4.27 (d, J=2.6 Hz, 2H), 4.01 (s, 3H), 3.91 - 3.80 (m, 2H), 3.39 (t, J=3.9 Hz, 1H), 3.08 (dd, J=10.7, 4.3 Hz, 1H), 2.76 (t, J=3.8 Hz, 1H), 2.52 - 2.44 (m, 1H), 2.43 - 2.35 (m, 1H), 2.16 - 2.09 (m, 1H), 1.95 - 1.87 (m, 1H), 1.67 - 1.58 (m, 2H)	1.19, C
43		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-(2-甲基丙-2-烯-1-亞基)雙環[2.2.1]庚烷-2-甲醯胺	539.1	(500MHz, $CDCl_3$) δ 9.53 (d, J=7.5 Hz, 1H), 8.05 (dd, J=11.4, 9.3 Hz, 1H), 7.96 (dd, J=6.3, 2.6 Hz, 1H), 7.72 (s, 1H), 7.54 (dt, J=8.8, 3.5 Hz, 1H), 7.14 (t, J=9.3 Hz, 1H), 6.81 (dd, J=11.6, 6.1 Hz, 1H), 5.95 (s, 1H), 4.97 (s, 2H), 4.82 - 4.71 (m, 1H), 4.01 (s, 3H), 3.45 (t, J=4.0 Hz, 1H), 3.12 - 3.06 (m, 1H), 2.77 (t, J=3.9 Hz, 1H), 2.18 - 2.11 (m, 1H), 2.01 (s, 3H), 1.94 - 1.87 (m, 1H), 1.70 - 1.61 (m, 2H)	1.25, B

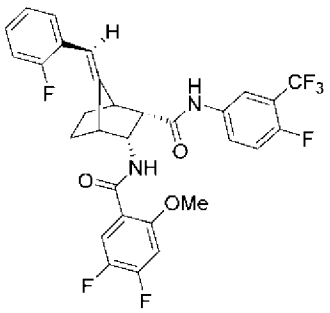
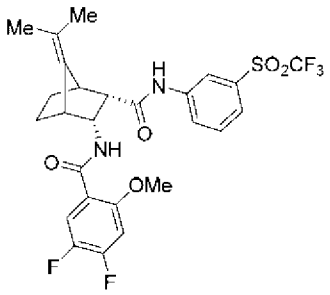
44		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-(丙-2-烯-1-亞基)雙環[2.2.1]庚烷-2-甲醯胺	525.0	(500MHz, $CDCl_3$) δ 9.51 (d, J=7.6 Hz, 1H), 8.05 (dd, J=11.4, 9.4 Hz, 1H), 7.96 (dd, J=6.3, 2.6 Hz, 1H), 7.73 (s, 1H), 7.54 (dt, J=8.8, 3.5 Hz, 1H), 7.14 (t, J=9.3 Hz, 1H), 6.81 (dd, J=11.6, 6.1 Hz, 1H), 6.51 (dt, J=16.9, 10.5 Hz, 1H), 5.93 (d, J=10.8 Hz, 1H), 5.22 (dd, J=16.9, 1.4 Hz, 1H), 5.12 (dd, J=10.1, 1.5 Hz, 1H), 4.78 - 4.68 (m, 1H), 4.01 (s, 3H), 3.24 (t, J=3.6 Hz, 1H), 3.08 (dd, J=10.8, 3.9 Hz, 1H), 2.79 (t, J=3.4 Hz, 1H), 2.19 (t, J=8.9 Hz, 1H), 1.95 - 1.85 (m, 1H), 1.68 - 1.60 (m, 2H)	1.21, B

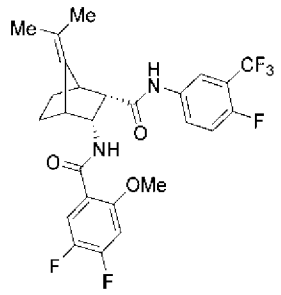
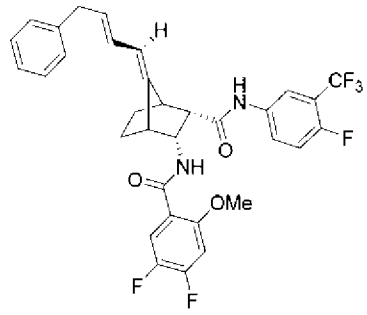
45		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-[(2E)-己-2-烯-1-亞基]雙環[2.2.1]庚烷-2-甲醯胺	567.1	(500MHz, $CDCl_3$) δ 9.57 (d, J=7.8 Hz, 1H), 8.06 (dd, J=11.4, 9.4 Hz, 1H), 7.98 (dd, J=6.2, 2.7 Hz, 1H), 7.73 (s, 1H), 7.58 - 7.50 (m, 1H), 7.15 (t, J=9.3 Hz, 1H), 6.81 (dd, J=11.6, 6.1 Hz, 1H), 6.19 (dd, J=15.1, 10.8 Hz, 1H), 5.87 (d, J=10.7 Hz, 1H), 5.75 - 5.64 (m, 1H), 4.77 - 4.66 (m, 1H), 4.06 - 3.97 (m, 3H), 3.23 (br. s., 1H), 3.07 (dd, J=10.8, 3.9 Hz, 1H), 2.76 (br. s., 1H), 2.17 - 2.06 (m, 3H), 1.86 (t, J=8.6 Hz, 1H), 1.70 - 1.55 (m, 2H), 1.45 (sxt, J=7.4 Hz, 2H), 0.98 - 0.91 (m, 3H)	1.33, C

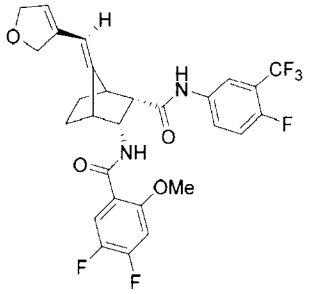
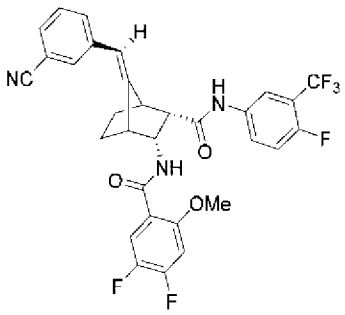
46		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-[(3-苯氧基苯基)亞甲基]雙環[2.2.1]庚烷-2-甲醯胺	667.3	(500MHz, $CDCl_3$) δ 9.43 (d, J=7.6 Hz, 1H), 8.05 (dd, J=11.3, 9.3 Hz, 1H), 7.95 (dd, J=6.3, 2.6 Hz, 1H), 7.76 (s, 1H), 7.59 - 7.51 (m, 1H), 7.40 - 7.35 (m, 2H), 7.33 - 7.29 (m, 1H), 7.17 - 7.11 (m, 3H), 7.08 - 7.04 (m, 2H), 6.96 (t, J=1.9 Hz, 1H), 6.89 (dd, J=8.2, 1.7 Hz, 1H), 6.81 (dd, J=11.6, 6.1 Hz, 1H), 6.30 (s, 1H), 4.88 - 4.80 (m, 1H), 4.01 (s, 3H), 3.47 (br. s., 1H), 3.18 (dd, J=10.8, 3.7 Hz, 1H), 2.91 - 2.87 (m, 1H), 2.27 (t, J=8.7 Hz, 1H), 1.96 - 1.90 (m, 1H), 1.76 - 1.68 (m, 2H)	1.31, B

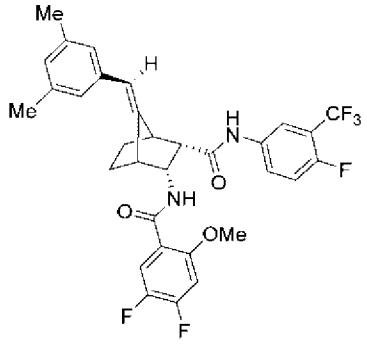
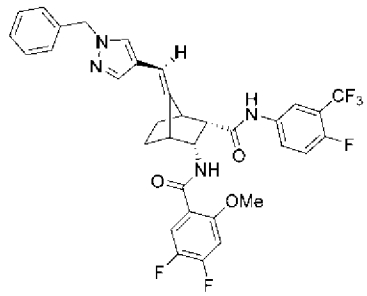
47		(2S,3R)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-亞丙基雙環[2.2.1]庚烷-2-甲醯胺	527.2	(500MHz, $CDCl_3$) δ 9.45 (d, J=7.7 Hz, 1H), 9.34 (d, J=8.0 Hz, 1H), 8.02 (dd, J=11.3, 9.4 Hz, 2H), 7.96 - 7.88 (m, 2H), 7.77 (s, 1H), 7.68 (s, 1H), 7.52 (tt, J=9.2, 3.6 Hz, 2H), 7.10 (t, J=9.4 Hz, 2H), 6.77 (ddd, J=11.6, 6.3, 3.0 Hz, 2H), 5.23 (t, J=7.3 Hz, 2H), 4.74 - 4.63 (m, 2H), 3.98 (s, 3H), 3.97 (s, 3H), 3.09 - 2.98 (m, 4H), 2.70 (dt, J=13.1, 3.9 Hz, 2H), 2.21 - 2.03 (m, 6H), 1.84 - 1.74 (m, 2H), 1.63 - 1.53 (m, 4H), 1.00 (m, 6H)	1.24, A
48		2-[(2R,3S,7Z)-2-(4,5-二氟-2-甲氧基苯甲醯胺基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-7-亞基]乙酸甲酯	599.1	(500MHz, $CDCl_3$) δ 9.33 (d, J=7.8 Hz, 1H), 8.21 (s, 1H), 8.02 (dd, J=11.3, 9.3 Hz, 1H), 7.94 (dd, J=6.2, 2.7 Hz, 1H), 7.58 (dt, J=8.5, 3.6 Hz, 1H), 7.12 (t, J=9.4 Hz, 1H), 6.81 (dd, J=11.4, 6.1 Hz, 1H), 5.75 (s, 1H), 4.89 - 4.77 (m, 1H), 4.01 (s, 3H), 3.93 (t, J=4.2 Hz, 1H), 3.78 (s, 3H), 3.16 (ddd, J=10.8, 4.1, 1.2 Hz, 1H), 2.89 (t, J=4.0 Hz, 1H), 2.42 - 2.32 (m, 1H), 1.99 - 1.90 (m, 1H), 1.81 - 1.65 (m, 2H)	1.25, B

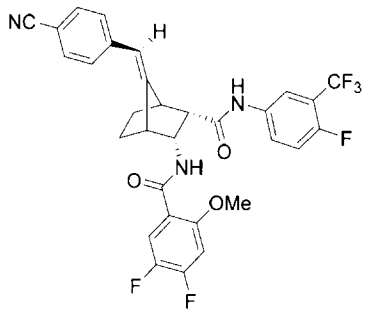
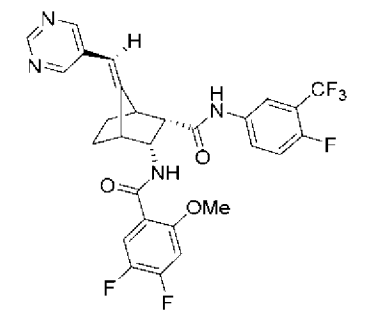
49		(2S,3R,7Z)-7-[(3-苯甲基苯基)亞甲基]-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	665.1	(500MHz, $CDCl_3$) δ 9.44 (d, J=7.8 Hz, 1H), 8.06 (dd, J=11.4, 9.4 Hz, 1H), 7.95 (dd, J=6.3, 2.7 Hz, 1H), 7.77 (s, 1H), 7.55 (dt, J=8.7, 3.5 Hz, 1H), 7.34 - 7.29 (m, 3H), 7.26 - 7.19 (m, 4H), 7.16 - 7.07 (m, 3H), 6.81 (dd, J=11.5, 6.2 Hz, 1H), 6.30 (s, 1H), 4.89 - 4.80 (m, 1H), 4.01 (s, 5H), 3.43 (t, J=3.4 Hz, 1H), 3.17 (dd, J=10.9, 3.9 Hz, 1H), 2.87 (br. s., 1H), 2.24 (t, J=8.9 Hz, 1H), 1.95 - 1.86 (m, 1H), 1.75 - 1.64 (m, 2H)	1.33, B
50		(2S,3R)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-7-亞乙基-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	513.1	(500MHz, $CDCl_3$) δ 9.49 (d, J=7.7 Hz, 1H), 9.38 (d, J=8.0 Hz, 1H), 8.02 (ddd, J=11.6, 9.4, 3.0 Hz, 2H), 7.92 (td, J=5.6, 2.8 Hz, 2H), 7.83 (s, 1H), 7.76 (s, 1H), 7.57 - 7.48 (m, 2H), 7.10 (t, J=9.4 Hz, 2H), 6.78 (ddd, J=11.6, 6.1, 3.0 Hz, 2H), 5.25 (q, J=6.8 Hz, 2H), 4.71 - 4.62 (m, 2H), 3.98 (s, 3H), 3.97 (s, 3H), 3.11 - 3.00 (m, 4H), 2.71 (dt, J=14.9, 3.7 Hz, 2H), 2.20 - 2.07 (m, 2H), 1.84 - 1.73 (m, 2H), 1.69 (d, J=3.0 Hz, 3H), 1.68 (d, J=3.0 Hz, 3H), 1.62 - 1.51 (m, 4H)	1.20, A

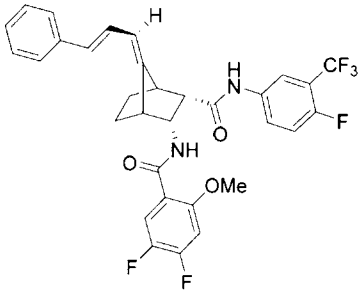
54		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-[(2-氟苯基)亞甲基]雙環[2.2.1]庚烷-2-甲醯胺	593.0	(500MHz, $CDCl_3$) δ 9.57 (d, J=7.6 Hz, 1H), 8.04 (dd, J=11.4, 9.4 Hz, 1H), 7.99 (dd, J=6.2, 2.5 Hz, 1H), 7.80 (s, 1H), 7.55 (dt, J=8.7, 3.5 Hz, 1H), 7.38 (td, J=7.6, 1.5 Hz, 1H), 7.27 - 7.21 (m, 1H), 7.18 - 7.11 (m, 2H), 7.10 - 7.04 (m, 1H), 6.81 (dd, J=11.6, 6.1 Hz, 1H), 6.39 (s, 1H), 4.88 - 4.79 (m, 1H), 4.02 (s, 3H), 3.35 (t, J=3.6 Hz, 1H), 3.21 (dd, J=10.5, 3.8 Hz, 1H), 2.93 (t, J=3.7 Hz, 1H), 2.31 - 2.20 (m, 1H), 2.00 - 1.91 (m, 1H), 1.79 - 1.68 (m, 2H)	1.30, B
55		(2S,3R)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-7-丙烷-2-亞基)-N-(3-三氟甲磺醯基苯基)雙環[2.2.1]庚烷-2-甲醯胺	573.3	(500MHz, $CDCl_3$) δ 9.45 (d, J=7.6 Hz, 1H), 8.48 (s, 1H), 8.13 (br. s., 1H), 8.07 (dd, J=11.4, 9.4 Hz, 1H), 7.80 (dt, J=8.2, 1.0 Hz, 1H), 7.74 (d, J=7.6 Hz, 1H), 7.59 (t, J=8.0 Hz, 1H), 6.81 (dd, J=11.4, 6.1 Hz, 1H), 4.74 - 4.63 (m, 1H), 4.04 (s, 3H), 3.11 - 2.99 (m, 3H), 2.18 - 2.07 (m, 1H), 1.84 - 1.77 (m, 1H), 1.75 (s, 3H), 1.75 (s, 3H), 1.66 - 1.52 (m, 2H)	1.21, B

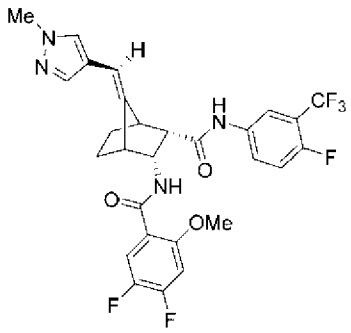
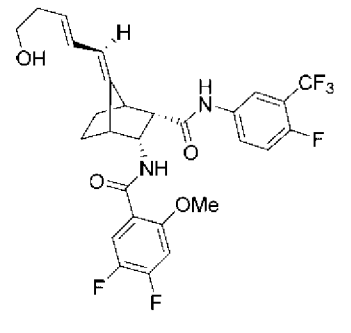
56		(2S,3R)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-丙烷-2-亞基)雙環[2.2.1]庚烷-2-甲醯胺	527.2	(500MHz, $CDCl_3$) δ 9.35 (d, J=7.4 Hz, 1H), 8.03 (dd, J=11.6, 9.4 Hz, 1H), 7.91 (dd, J=6.2, 2.6 Hz, 1H), 7.75 (s, 1H), 7.57 - 7.50 (m, 1H), 7.10 (t, J=9.4 Hz, 1H), 6.77 (dd, J=11.6, 6.1 Hz, 1H), 4.65 (d, J=4.4 Hz, 1H), 3.97 (s, 3H), 3.03 - 2.95 (m, 3H), 2.14 - 2.08 (m, 1H), 1.79 - 1.73 (m, 1H), 1.72 (s, 3H), 1.71 (s, 3H), 1.57 - 1.53 (m, 2H)	1.24, A
57		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-(2-苯基亞乙基)雙環[2.2.1]庚烷-2-甲醯胺	589.0	(500MHz, $CDCl_3$) δ 9.52 (d, J=7.5 Hz, 1H), 8.10 - 8.02 (m, 1H), 7.98 - 7.93 (m, 1H), 7.69 (br. s., 1H), 7.57 - 7.50 (m, 1H), 7.37 - 7.30 (m, 2H), 7.25 - 7.18 (m, 3H), 7.13 (t, J=9.2 Hz, 1H), 6.81 (dd, J=11.5, 6.2 Hz, 1H), 5.43 (t, J=7.5 Hz, 1H), 4.77 (t, J=10.9 Hz, 1H), 4.01 (s, 3H), 3.45 (m, 2H), 3.22 (br. s., 1H), 3.10 (dd, J=10.6, 3.7 Hz, 1H), 2.76 (br. s., 1H), 2.21 - 2.13 (m, 1H), 1.94 - 1.87 (m, 1H), 1.64 (d, J=8.5 Hz, 2H)	1.26, A

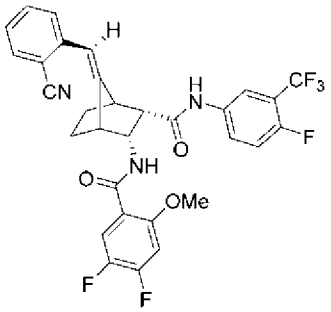
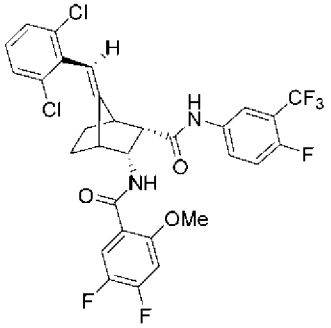
58		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-7-[(2,5-二氫呋喃-3-基)亞甲基]-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	567.0	(500MHz, $CDCl_3$) δ 9.48 (d, J=7.7 Hz, 1H), 8.00 (dd, J=11.3, 9.4 Hz, 1H), 7.93 (dd, J=6.2, 2.6 Hz, 1H), 7.85 (s, 1H), 7.52 (dt, J=8.9, 3.4 Hz, 1H), 7.11 (t, J=9.2 Hz, 1H), 6.78 (dd, J=11.6, 6.3 Hz, 1H), 6.05 (s, 1H), 5.83 (t, J=1.8 Hz, 1H), 4.92 - 4.85 (m, 1H), 4.81 - 4.74 (m, 1H), 4.73 - 4.66 (m, 3H), 3.98 (s, 3H), 3.08 (dd, J=10.7, 3.9 Hz, 1H), 2.97 (t, J=3.4 Hz, 1H), 2.79 (t, J=3.3 Hz, 1H), 2.19 - 2.14 (m, 1H), 1.89 (t, J=8.7 Hz, 1H), 1.65 - 1.59 (m, 2H)	1.18, B
59		(2S,3R,7Z)-7-[(3-氰基苯基)亞甲基]-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	600.1	(500MHz, $CDCl_3$) δ 9.59 (d, J=7.6 Hz, 1H), 8.05 - 7.96 (m, 2H), 7.86 (s, 1H), 7.60 - 7.52 (m, 4H), 7.51 - 7.44 (m, 1H), 7.16 (t, J=9.3 Hz, 1H), 6.80 (dd, J=11.6, 6.1 Hz, 1H), 6.29 (s, 1H), 4.86 - 4.77 (m, 1H), 4.01 (s, 3H), 3.42 (br. s., 1H), 3.23 (dd, J=10.8, 4.1 Hz, 1H), 2.95 (br. s., 1H), 2.31 - 2.22 (m, 1H), 1.99 (t, J=8.7 Hz, 1H), 1.77 - 1.67 (m, 2H)	1.29, B

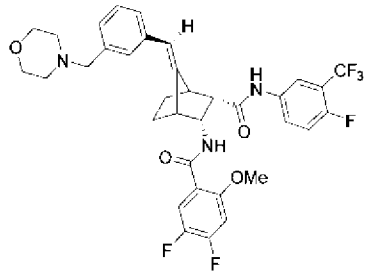
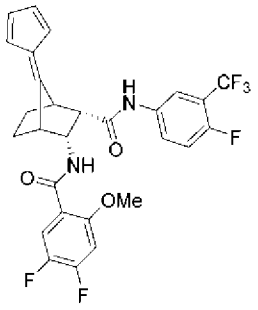
60		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-7-[(3,5-二甲基苯基)亞甲基]-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	603.1	(500MHz, $CDCl_3$) δ 9.42 (d, J=7.8 Hz, 1H), 8.05 (dd, J=11.3, 9.3 Hz, 1H), 7.94 (dd, J=6.2, 2.5 Hz, 1H), 7.80 (s, 1H), 7.60 - 7.52 (m, 1H), 7.13 (t, J=9.4 Hz, 1H), 6.97 (s, 2H), 6.91 (s, 1H), 6.84 - 6.76 (m, 1H), 6.29 (s, 1H), 4.90 - 4.83 (m, 1H), 4.03 - 3.99 (m, 3H), 3.51 - 3.47 (m, 1H), 3.18 (dd, J=10.9, 3.9 Hz, 1H), 2.88 (t, J=3.6 Hz, 1H), 2.34 (s, 6H), 2.29 - 2.23 (m, 1H), 1.96 - 1.89 (m, 1H), 1.77 - 1.68 (m, 2H)	1.35, B
61		(2S,3R,7Z)-7-[(1-苯甲基-1H-吡唑-4-基)亞甲基]-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	655.1	(500MHz, $CDCl_3$) δ 9.60 (d, J=7.6 Hz, 1H), 8.05 (dd, J=11.3, 9.5 Hz, 1H), 7.98 (dd, J=6.1, 2.4 Hz, 1H), 7.87 (s, 1H), 7.60 (s, 1H), 7.57 - 7.52 (m, 1H), 7.49 (s, 1H), 7.40 - 7.31 (m, 4H), 7.27 - 7.23 (m, 2H), 7.14 (t, J=9.3 Hz, 1H), 6.81 (dd, J=11.4, 6.1 Hz, 1H), 6.07 (s, 1H), 5.38 - 5.28 (m, 2H), 4.82 - 4.74 (m, 1H), 4.06 - 3.98 (m, 3H), 3.33 (br. s., 1H), 3.12 (dd, J=10.8, 3.9 Hz, 1H), 2.83 (br. s., 1H), 2.18 (t, J=8.9 Hz, 1H), 1.96 - 1.88 (m, 1H), 1.71 - 1.62 (m, 2H)	1.23, C

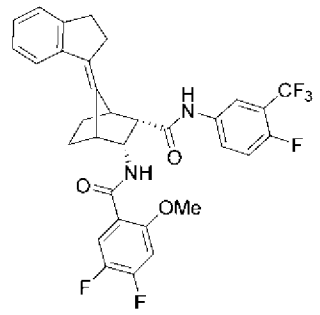
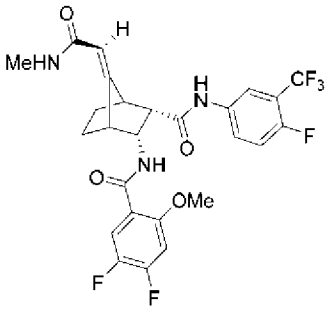
62		(2S,3R,7Z)-7-[(4-氰基苯基)亞甲基]-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	600.0	(500MHz, $CDCl_3$) δ 9.61 (d, J=7.6 Hz, 1H), 8.05 (dd, J=11.3, 9.3 Hz, 1H), 7.98 (dd, J=6.3, 2.6 Hz, 1H), 7.71 (s, 1H), 7.66 - 7.66 (m, 1H), 7.67 - 7.61 (m, 2H), 7.55 (dt, J=8.8, 3.5 Hz, 1H), 7.44 (d, J=8.1 Hz, 2H), 7.16 (t, J=9.3 Hz, 1H), 6.82 (dd, J=11.4, 6.1 Hz, 1H), 6.36 (s, 1H), 4.89 - 4.78 (m, 1H), 4.03 (s, 3H), 3.46 (t, J=3.4 Hz, 1H), 3.19 (dd, J=10.7, 4.0 Hz, 1H), 2.97 - 2.89 (m, 1H), 2.31 - 2.20 (m, 1H), 2.06 - 1.94 (m, 1H), 1.78 - 1.67 (m, 2H)	1.29, B
63		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-[(嘧啶-5-基)亞甲基]雙環[2.2.1]庚烷-2-甲醯胺	577.1	(500MHz, $CDCl_3$) δ 9.52 (d, J=7.5 Hz, 1H), 9.11 (br. s., 1H), 8.72 (br. s., 2H), 8.02 (dd, J=11.2, 9.4 Hz, 1H), 7.97 (dd, J=6.1, 2.4 Hz, 1H), 7.86 (s, 1H), 7.56 (dt, J=8.7, 3.4 Hz, 1H), 7.16 (t, J=9.3 Hz, 1H), 6.81 (dd, J=11.6, 6.1 Hz, 1H), 6.25 (s, 1H), 4.89 - 4.79 (m, 1H), 4.02 (s, 3H), 3.38 (br. s., 1H), 3.21 (dd, J=10.8, 4.0 Hz, 1H), 2.98 (br. s., 1H), 2.33 (t, J=9.1 Hz, 1H), 2.02 (t, J=8.7 Hz, 1H), 1.79 - 1.71 (m, 2H)	1.14, B

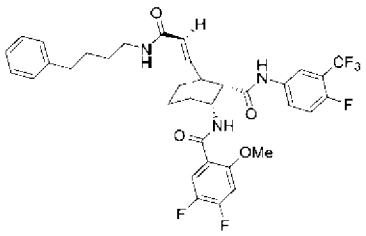
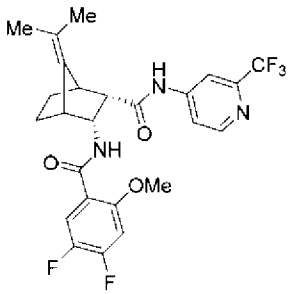
64		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-[(2E)-3-苯基丙-2-烯-1-亞基]雙環[2.2.1]庚烷-2-甲醯胺	601.1	(500MHz, $CDCl_3$) δ 9.59 (d, J=7.6 Hz, 1H), 8.07 (dd, J=11.4, 9.4 Hz, 1H), 7.98 (dd, J=6.2, 2.5 Hz, 1H), 7.69 (s, 1H), 7.58 - 7.52 (m, 1H), 7.44 (d, J=7.5 Hz, 2H), 7.38 - 7.31 (m, 3H), 7.27 - 7.22 (m, 1H), 7.15 (t, J=9.4 Hz, 1H), 6.93 (dd, J=15.6, 10.8 Hz, 1H), 6.82 (dd, J=11.5, 6.0 Hz, 1H), 6.56 (d, J=15.6 Hz, 1H), 6.10 (d, J=10.8 Hz, 1H), 4.81 - 4.74 (m, 1H), 4.02 (s, 3H), 3.38 (br. s., 1H), 3.12 (dd, J=10.8, 4.0 Hz, 1H), 2.85 (br. s., 1H), 2.21 (t, J=8.6 Hz, 1H), 1.96 - 1.90 (m, 1H), 1.65 (d, J=6.6 Hz, 2H)	1.35, C

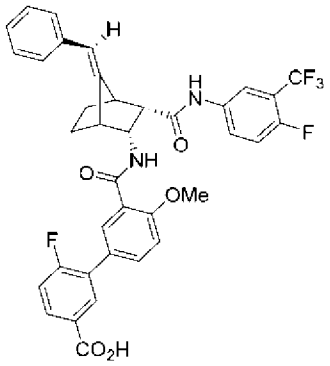
66		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-[(1-甲基-1H-吡唑-4-基)亞甲基]雙環[2.2.1]庚烷-2-甲醯胺	579.1	(500MHz, $CDCl_3$) δ 9.66 (d, J=7.6 Hz, 1H), 8.05 (dd, J=11.3, 9.3 Hz, 1H), 8.02 - 7.98 (m, 1H), 7.86 (s, 1H), 7.56 (dt, J=8.7, 3.5 Hz, 1H), 7.50 (s, 1H), 7.46 (s, 1H), 7.16 (t, J=9.2 Hz, 1H), 6.82 (dd, J=11.6, 6.1 Hz, 1H), 6.08 (s, 1H), 4.80 - 4.71 (m, 1H), 4.03 (s, 3H), 3.91 (s, 3H), 3.37 - 3.33 (m, 1H), 3.17 - 3.08 (m, 1H), 2.84 (br. s., 1H), 2.17 (t, J=8.9 Hz, 1H), 1.97 - 1.87 (m, 1H), 1.71 - 1.65 (m, 2H)	1.14, C
67		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-[(2E)-5-羥基戊-2-烯-1-亞基]雙環[2.2.1]庚烷-2-甲醯胺	569.2	(500MHz, $CDCl_3$) δ 9.66 (d, J=7.6 Hz, 1H), 8.05 (dd, J=11.3, 9.3 Hz, 1H), 8.02 - 7.98 (m, 1H), 7.86 (s, 1H), 7.56 (dt, J=8.7, 3.5 Hz, 1H), 7.50 (s, 1H), 7.46 (s, 1H), 7.16 (t, J=9.2 Hz, 1H), 6.82 (dd, J=11.6, 6.1 Hz, 1H), 6.08 (s, 1H), 4.80 - 4.71 (m, 1H), 4.03 (s, 3H), 3.91 (s, 3H), 3.37 - 3.33 (m, 1H), 3.17 - 3.08 (m, 1H), 2.84 (br. s., 1H), 2.17 (t, J=8.9 Hz, 1H), 1.97 - 1.87 (m, 1H), 1.71 - 1.65 (m, 2H)	1.13, C

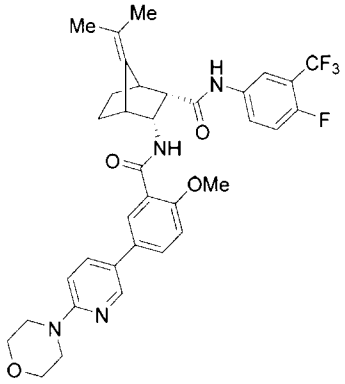
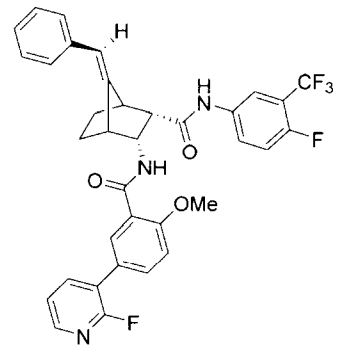
68		(2S,3R,7Z)-7-[(2-氰基苯基)亞甲基]-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	600.0	(500MHz, $CDCl_3$) δ 9.81 (d, J=7.5 Hz, 1H), 8.13 - 8.05 (m, 2H), 8.01 (dd, J=11.4, 9.4 Hz, 1H), 7.67 (d, J=7.6 Hz, 1H), 7.60 - 7.52 (m, 3H), 7.38 - 7.31 (m, 1H), 7.18 (t, J=9.3 Hz, 1H), 6.82 (dd, J=11.6, 6.1 Hz, 1H), 6.62 (s, 1H), 4.84 - 4.75 (m, 1H), 4.04 (s, 3H), 3.40 (t, J=3.7 Hz, 1H), 3.26 (dd, J=10.7, 3.8 Hz, 1H), 2.96 (t, J=3.7 Hz, 1H), 2.25 - 2.17 (m, 1H), 2.07 - 1.98 (m, 1H), 1.78 - 1.67 (m, 2H)	1.29, B
69		(2S,3R,7Z)-7-[(2,6-二氯苯基)亞甲基]-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	643.0	(500MHz, $CDCl_3$) δ 9.81 (d, J=7.5 Hz, 1H), 8.13 - 8.05 (m, 2H), 8.01 (dd, J=11.4, 9.4 Hz, 1H), 7.67 (d, J=7.6 Hz, 1H), 7.60 - 7.52 (m, 3H), 7.38 - 7.31 (m, 1H), 7.18 (t, J=9.3 Hz, 1H), 6.82 (dd, J=11.6, 6.1 Hz, 1H), 6.62 (s, 1H), 4.84 - 4.75 (m, 1H), 4.04 (s, 3H), 3.40 (t, J=3.7 Hz, 1H), 3.26 (dd, J=10.7, 3.8 Hz, 1H), 2.96 (t, J=3.7 Hz, 1H), 2.25 - 2.17 (m, 1H), 2.07 - 1.98 (m, 1H), 1.78 - 1.67 (m, 2H)	1.29, B

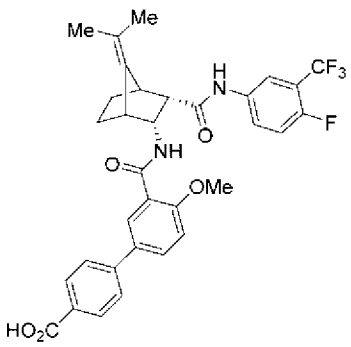
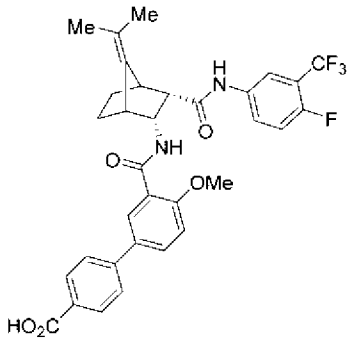
70		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-({3-[(味啉-4-基)甲基]苯基}亞甲基)雙環[2.2.1]庚烷-2-甲醯胺	674.2	(500MHz, DMSO-d_6) δ 1H NMR (500MHz, CDCl3) d 9.65 (br. s., 1H), 8.02 (t, J=10.2 Hz, 2H), 7.63 - 7.54 (m, 1H), 7.31 (br. s., 3H), 7.21 (br. s., 1H), 7.15 (t, J=9.3 Hz, 1H), 6.80 (dd, J=11.5, 6.2 Hz, 1H), 6.33 (s, 1H), 4.80 (br. s., 1H), 4.02 (s, 3H), 3.80 (br. s., 4H), 3.65 (br. s., 2H), 3.47 (br. s., 1H), 3.21 (dd, J=10.7, 4.0 Hz, 1H), 2.89 (br. s., 1H), 2.64 (br. s., 2H), 2.26 - 2.15 (m, 1H), 2.00 - 1.91 (m, 1H), 1.69 (br. s., 3H)	1.02, B
71		(2S,3R)-7-(環戊-2,4-二烯-1-亞基)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	567.0	(500MHz, $CDCl_3$) δ 9.39 (d, J=7.7 Hz, 1H), 7.85 (dd, J=11.3, 9.4 Hz, 1H), 7.79 (dd, J=6.2, 2.6 Hz, 1H), 7.61 (s, 1H), 7.37 (dt, J=8.7, 3.5 Hz, 1H), 6.97 (t, J=9.4 Hz, 1H), 6.62 (dd, J=11.6, 6.3 Hz, 1H), 6.44 - 6.39 (m, 2H), 6.30 - 6.26 (m, 1H), 6.21 (dt, J=4.3, 2.1 Hz, 1H), 4.70 - 4.60 (m, 1H), 3.83 (s, 3H), 3.20 (t, J=3.9 Hz, 1H), 3.14 (t, J=3.7 Hz, 1H), 2.99 (dd, J=10.9, 4.0 Hz, 1H), 2.23 - 2.15 (m, 1H), 1.86 - 1.79 (m, 1H), 1.60 - 1.51 (m, 2H)	1.19, A

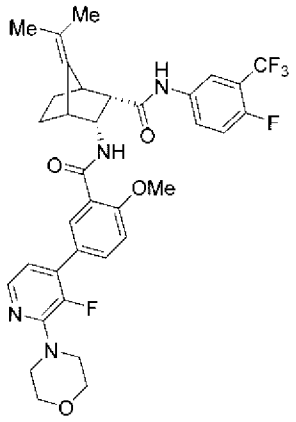
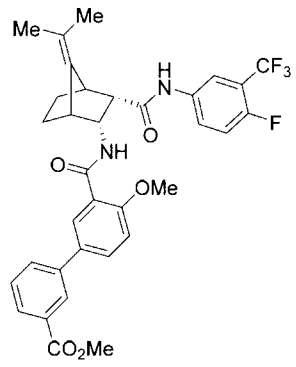
72		(2S,3R)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-7-[(1Z)-2,3-二氫-1H-茚-1-亞基]-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	601.1	(400MHz, $CDCl_3$) δ 9.48 (d, J=7.5 Hz, 1H), 8.06 (dd, J=11.4, 9.2 Hz, 1H), 7.94 (dd, J=6.2, 2.6 Hz, 1H), 7.80 (s, 1H), 7.71 - 7.63 (m, 1H), 7.59 - 7.51 (m, 1H), 7.31 - 7.24 (m, 2H), 7.22 - 7.17 (m, 2H), 7.12 (t, J=9.5 Hz, 1H), 6.79 (dd, J=11.7, 6.2 Hz, 1H), 4.86 - 4.77 (m, 1H), 4.00 (s, 3H), 3.71 (t, J=4.2 Hz, 1H), 3.12 (dd, J=10.1, 3.5 Hz, 1H), 3.06 (t, J=3.9 Hz, 1H), 3.03 - 2.96 (m, 2H), 2.84 - 2.75 (m, 2H), 2.26 - 2.16 (m, 1H), 1.97 - 1.89 (m, 1H), 1.75 - 1.66 (m, 2H)	1.34, A
73		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-[(甲基胺甲醯基)亞甲基]雙環[2.2.1]庚烷-2-甲醯胺	556.1	(500MHz, $CDCl_3$) δ 10.00 (br. s., 1H), 9.75 (br. s., 1H), 8.16 (dd, J=6.2, 2.4 Hz, 1H), 7.92 (t, J=10.2 Hz, 1H), 7.73 - 7.61 (m, 1H), 7.14 - 7.05 (m, 1H), 6.79 (dd, J=11.4, 6.1 Hz, 1H), 6.38 (br. s., 1H), 5.73 (s, 1H), 4.62 (br. s., 1H), 4.03 (s, 3H), 3.81 (br. s., 1H), 3.26 (dd, J=10.8, 3.7 Hz, 1H), 2.86 (br. s., 3H), 2.22 - 2.09 (m, 1H), 2.03 - 1.94 (m, 1H), 1.70 - 1.51 (m, 2H)	1.04, C

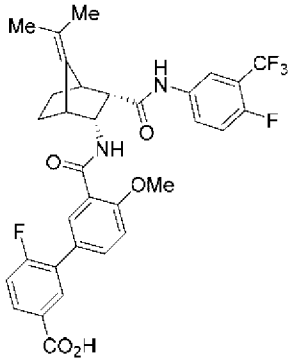
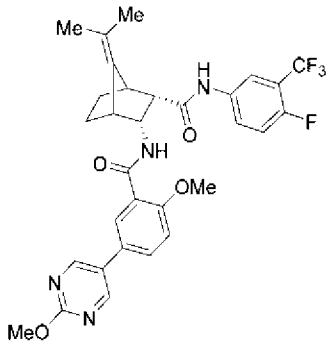
74		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-{[(4-苯基丁基)胺甲醯基]亞甲基}雙環[2.2.1]庚烷-2-甲醯胺	674.1	(500MHz, $CDCl_3$) δ 9.75 (br. s., 1H), 9.44 (br. s., 1H), 8.11 (d, J=4.0 Hz, 1H), 7.93 (t, J=10.2 Hz, 1H), 7.73 - 7.60 (m, 1H), 7.26 (d, J=7.6 Hz, 2H), 7.21 - 7.16 (m, 1H), 7.15 - 7.06 (m, 3H), 6.76 (dd, J=11.5, 6.0 Hz, 1H), 5.97 (br. s., 1H), 5.68 (s, 1H), 4.67 (br. s., 1H), 3.99 (s, 3H), 3.85 (br. s., 1H), 3.30 (br. s., 2H), 3.24 (dd, J=10.7, 3.8 Hz, 1H), 2.83 (br. s., 1H), 2.61 - 2.54 (m, 2H), 2.22 (t, J=9.4 Hz, 1H), 1.99 - 1.90 (m, 1H), 1.85 (m, 2H), 1.59 (d, J=16.6 Hz, 4H)	1.20, B
75		(2S,3R)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-7-丙烷-2-亞基)-N-[2-(三氟甲基)吡啶-4-基]雙環[2.2.1]庚烷-2-甲醯胺	510.3	(500MHz, $CDCl_3$) δ 9.20 (d, J=7.9 Hz, 1H), 8.55 (d, J=5.5 Hz, 1H), 8.47 (s, 1H), 8.05 (dd, J=11.2, 9.4 Hz, 1H), 8.00 (d, J=1.8 Hz, 1H), 7.54 (dd, J=5.5, 2.0 Hz, 1H), 6.80 (dd, J=11.4, 6.1 Hz, 1H), 4.74 - 4.68 (m, 1H), 4.01 (s, 3H), 3.14 - 3.00 (m, 3H), 2.17 - 2.07 (m, 1H), 1.80 - 1.71 (m, 7H), 1.68 - 1.56 (m, 2H)	1.18, B

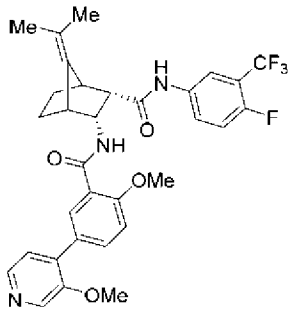
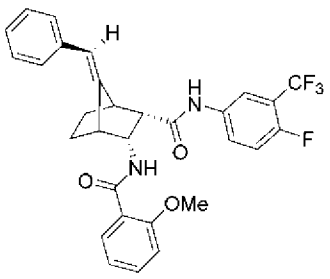
80		6-氟-3'-{[(1R,2R,3S,4R,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(苯基亞甲基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-3-甲酸	677.4	(500MHz, DMSO-d6) δ 10.65 (s, 1H), 10.04 (d, J=6.7 Hz, 1H), 8.25 (d, J=4.3 Hz, 1H), 8.14 (s, 1H), 8.02 (d, J=7.6 Hz, 1H), 7.94 (br. s., 1H), 7.81 (br. s., 1H), 7.74 (d, J=8.2 Hz, 1H), 7.49 (t, J=9.6 Hz, 1H), 7.43 - 7.35 (m, 5H), 7.33 (d, J=8.5 Hz, 1H), 7.29 - 7.20 (m, 1H), 6.38 (s, 1H), 4.53 (br. s., 1H), 4.07 (s, 3H), 3.45 (br. s., 1H), 3.36 - 3.24 (m, 1H), 2.97 - 2.88 (m, 1H), 1.91 (dd, J=20.0, 10.8 Hz, 2H), 1.53 (br. s., 2H)	2.18, B

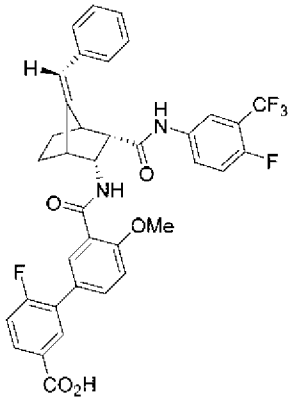
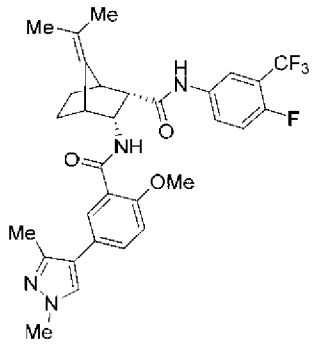
81		(1R,2S,3R,4R)-N-[4-氟-3-(三氟甲基)苯基]-3-{2-甲氧基-5-[6-(味啉-4-基)吡啶-3-基]苯甲醯胺基}-7-丙烷-2-亞基)雙環[2.2.1]庚烷-2-甲醯胺	652.9	(500MHz, DMSO-d6) δ 10.52 (s, 1H), 9.87 (d, J=7.0 Hz, 1H), 8.38 (s, 1H), 8.20 (d, J=4.3 Hz, 1H), 8.13 - 8.07 (m, 1H), 7.84 - 7.76 (m, 2H), 7.76 - 7.69 (m, 1H), 7.52 - 7.41 (m, 1H), 7.23 (d, J=8.5 Hz, 1H), 6.90 (d, J=8.9 Hz, 1H), 4.36 (br. s., 1H), 4.00 (s, 3H), 3.75 - 3.64 (m, 4H), 3.51 (d, J=7.0 Hz, 1H), 3.49 - 3.41 (m, 2H), 3.16 (d, J=4.6 Hz, 1H), 3.10 (dd, J=10.7, 4.0 Hz, 1H), 3.02 (br. s., 1H), 2.93 (br. s., 1H), 1.83 (s, 1H), 1.72 (d, J=9.5 Hz, 7H), 1.34 (d, J=5.8 Hz, 2H)	2.19, C
82		(1R,2S,3R,4R,7Z)-N-[4-氟-3-(三氟甲基)苯基]-3-[5-(2-氟吡啶-3-基)-2-甲氧基苯甲醯胺基]-7-(苯基亞甲基)雙環[2.2.1]庚烷-2-甲醯胺	634.2	(500MHz, DMSO-d6) δ 10.70 - 10.59 (m, 1H), 10.05 (d, J=6.3 Hz, 1H), 8.26 (br. s., 1H), 8.18 (s, 1H), 8.22 (s, 1H), 8.11 (t, J=8.2 Hz, 1H), 7.88 - 7.72 (m, 2H), 7.55 - 7.43 (m, 2H), 7.43 - 7.30 (m, 5H), 7.26 (d, J=4.5 Hz, 1H), 6.43 - 6.34 (m, 1H), 4.53 (br. s., 1H), 4.07 (s, 3H), 3.29 (br. s., 1H), 2.94 (br. s., 1H), 1.99 - 1.82 (m, 2H), 1.53 (br. s., 2H)。	2.72, B

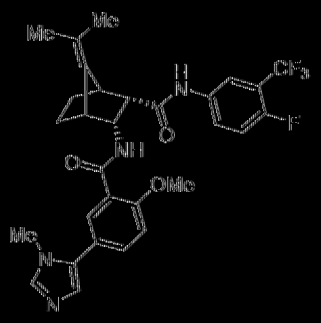
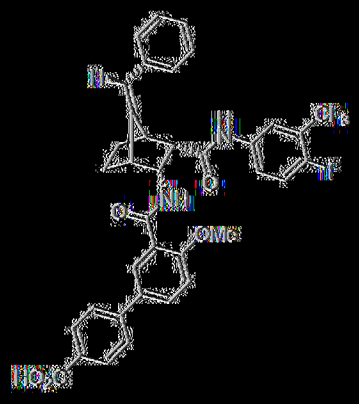
83		3'-{[(1R,2R,3S,4R)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-丙烷-2-亞基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-4-甲酸	611.3	(500MHz, DMSO-d6) δ 10.53 (s, 1H), 9.89 (d, J=7.0 Hz, 1H), 8.26 (s, 1H), 8.21 (d, J=4.9 Hz, 1H), 8.00 (d, J=7.9 Hz, 2H), 7.88 (d, J=8.5 Hz, 1H), 7.84 - 7.68 (m, 3H), 7.47 (t, J=9.6 Hz, 1H), 7.30 (d, J=8.5 Hz, 1H), 4.38 (br. s., 1H), 4.04 (s, 3H), 3.11 (d, J=10.7 Hz, 1H), 3.03 (br. s., 1H), 2.98 (s, 1H), 2.95 (br. s., 1H), 1.88 - 1.79 (m, 1H), 1.72 (d, J=9.2 Hz, 7H), 1.35 (d, J=5.5 Hz, 2H)	2.54, C
84		2-氟-3'-{[(1R,2R,3S,4R)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-丙烷-2-亞基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-4-甲酸	629.5	(500 MHz, DMSO-d6) δ 10.66 - 10.45 (m, 1H), 10.00 - 9.83 (m, 1H), 8.25 - 8.18 (m, 1H), 8.18 - 8.12 (m, 1H), 7.88 - 7.67 (m, 4H), 7.68 - 7.59 (m, 1H), 7.54 - 7.42 (m, 1H), 7.34 - 7.25 (m, 1H), 4.45 - 4.28 (m, 1H), 4.11 - 3.92 (m, 3H), 3.14 - 3.06 (m, 1H), 3.06 - 2.98 (m, 1H), 2.97 - 2.85 (m, 1H), 1.90 - 1.75 (m, 2H), 1.80 - 1.58 (m, 7H), 1.41 - 1.25 (m, 2H)	2.07, B

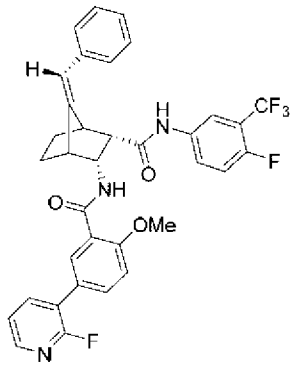
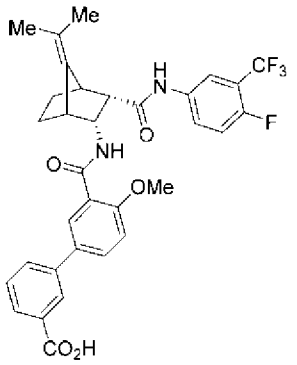
85		(1R,2S,3R,4R)-3-{5-[3-氟-2-(味啉-4-基)吡啶-4-基]-2-甲氧基苯甲醯胺基}-N-[4-氟-3-(三氟甲基)苯基]-7-丙烷-2-亞基)雙環[2.2.1]庚烷-2-甲醯胺	671.4	(500MHz, DMSO-d6) δ 10.54 (s, 1H), 9.90 (d, J=7.0 Hz, 1H), 8.19 (d, J=4.3 Hz, 1H), 8.15 (s, 1H), 8.03 (d, J=5.2 Hz, 1H), 7.83 - 7.68 (m, 2H), 7.46 (t, J=9.8 Hz, 1H), 7.30 (d, J=8.9 Hz, 1H), 6.99 (t, J=5.0 Hz, 1H), 4.34 (br. s., 1H), 4.03 (s, 3H), 3.76 - 3.67 (m, 3H), 3.60 - 3.51 (m, 5H), 3.10 (dd, J=10.5, 3.8 Hz, 1H), 3.02 (br. s., 1H), 2.93 (br. s., 1H), 1.85 - 1.77 (m, 1H), 1.70 (s, 4H), 1.72 (s, 3H), 1.34 (d, J=5.5 Hz, 2H)	2.78, C
86		3'-{[(1R,2R,3S,4R)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-丙烷-2-亞基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-3-甲酸甲酯	625.4	(500MHz, DMSO-d6) δ 10.53 (s, 1H), 9.92 (d, J=7.3 Hz, 1H), 8.26 - 8.16 (m, 2H), 8.13 (s, 1H), 7.91 (t, J=7.0 Hz, 2H), 7.85 (dd, J=8.5, 2.1 Hz, 1H), 7.79 (d, J=8.2 Hz, 1H), 7.61 (t, J=7.8 Hz, 1H), 7.46 (t, J=9.8 Hz, 1H), 7.30 (d, J=8.5 Hz, 1H), 4.37 (br. s., 1H), 4.03 (s, 3H), 3.88 (s, 3H), 3.14 - 3.07 (m, 1H), 3.03 (br. s., 1H), 2.95 (br. s., 1H), 1.88 - 1.78 (m, 1H), 1.72 (d, J=8.9 Hz, 7H), 1.35 (d, J=6.1 Hz, 2H)	2.84, B

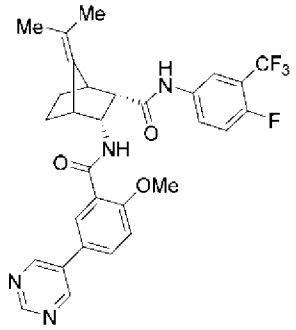
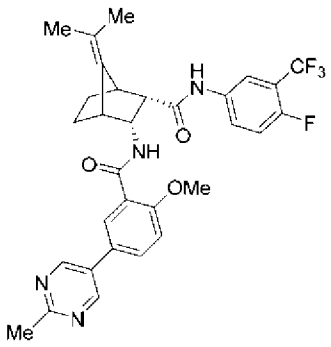
87		6-氟-3'-{[(1R,2R,3S,4R)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-丙烷-2-亞基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-3-甲酸	629.4	(500MHz, DMSO-d6) δ 10.53 (br. s., 1H), 9.92 (br. s., 1H), 8.22 (br. s., 1H), 8.13 (br. s., 1H), 8.02 (d, J=5.8 Hz, 1H), 7.96 (br. s., 1H), 7.80 (br. s., 1H), 7.73 (d, J=7.9 Hz, 1H), 7.52 - 7.38 (m, 2H), 7.31 (d, J=8.2 Hz, 1H), 4.37 (br. s., 1H), 4.05 (br. s., 3H), 3.11 (d, J=10.4 Hz, 1H), 3.04 (br. s., 1H), 2.95 (br. s., 1H), 1.84 (br. s., 1H), 1.71 (s, 3H), 1.73 (s, 4H), 1.35 (br. s., 2H)	2.09, B
88		(1R,2S,3R,4R)-N-[4-氟-3-(三氟甲基)苯基]-3-[2-甲氧基-5-(2-甲氧基嘧啶-5-基)苯甲醯胺基]-7-丙烷-2-亞基)雙環[2.2.1]庚烷-2-甲醯胺	599.1	(500MHz, DMSO-d6) δ 10.54 (s, 1H), 9.88 (d, J=7.0 Hz, 1H), 8.86 (s, 2H), 8.22 (d, J=4.3 Hz, 1H), 8.19 - 8.13 (m, 1H), 7.80 (d, J=7.9 Hz, 1H), 7.84 (d, J=8.5 Hz, 1H), 7.48 (t, J=9.8 Hz, 1H), 7.30 (d, J=8.9 Hz, 1H), 4.37 (br. s., 1H), 4.03 (s, 3H), 3.95 (s, 3H), 3.15 - 3.07 (m, 1H), 3.04 (br. s., 1H), 2.94 (br. s., 1H), 1.89 - 1.78 (m, 1H), 1.72 (s, 4H), 1.74 (s, 3H), 1.35 (d, J=6.1 Hz, 2H)	2.59, B

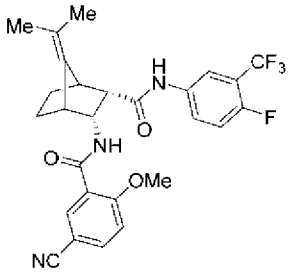
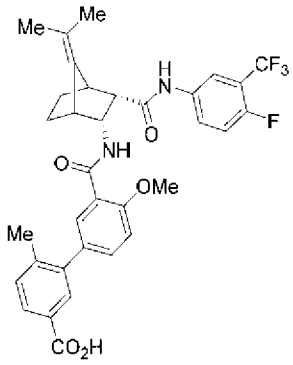
89		(1R,2S,3R,4R)-N-[4-氟-3-(三氟甲基)苯基]-3-[2-甲氧基-5-(3-甲氧基吡啶-4-基)苯甲醯胺基]-7-丙烷-2-亞基)雙環[2.2.1]庚烷-2-甲醯胺	598.2	(500MHz, DMSO-d6) δ 10.55 (s, 1H), 9.89 (d, J=7.3 Hz, 1H), 8.41 (br. s., 1H), 8.23 (br. s., 1H), 8.19 (d, J=4.3 Hz, 1H), 8.14 (d, J=2.1 Hz, 1H), 7.78 (d, J=8.5 Hz, 1H), 7.72 (dd, J=8.5, 2.1 Hz, 1H), 7.45 (t, J=9.8 Hz, 1H), 7.32 (d, J=4.6 Hz, 1H), 7.26 (d, J=8.5 Hz, 1H), 4.34 (br. s., 1H), 4.02 (s, 3H), 3.86 (s, 3H), 3.16 (s, 1H), 3.09 (dd, J=10.7, 4.0 Hz, 1H), 3.02 (br. s., 1H), 2.92 (br. s., 1H), 1.87 - 1.78 (m, 1H), 1.70 (s, 4H), 1.72 (s, 4H), 1.34 (d, J=5.8 Hz, 2H)	2.53, B
90		(1R,2S,3R,4R,7Z)-N-[4-氟-3-(三氟甲基)苯基]-3-(2-甲氧基苯甲醯胺基)-7-(苯基亞甲基)雙環[2.2.1]庚烷-2-甲醯胺	539.4	(500MHz, DMSO-d6) δ 9.95 (d, J=7.0 Hz, 1H), 8.26 (d, J=4.3 Hz, 1H), 7.94 (d, J=6.7 Hz, 1H), 7.81 (br. s., 1H), 7.50 (t, J=8.2 Hz, 3H), 7.44 - 7.32 (m, 6H), 7.25 (br. s., 2H), 7.18 (d, J=8.2 Hz, 1H), 7.04 (t, J=7.5 Hz, 1H), 6.39 (s, 1H), 4.52 (br. s., 1H), 3.28 (br. s., 1H), 2.93 (br. s., 1H), 2.02 - 1.79 (m, 3H), 1.53 (br. s., 3H)	2.64, C

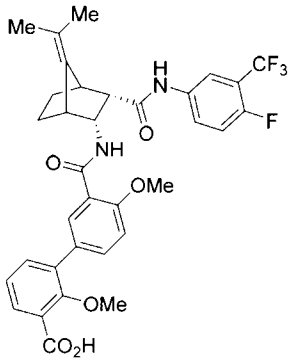
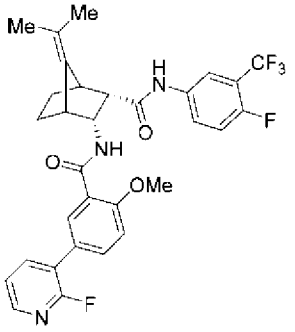
91		6-氟-3'-{[(1R,2R,3S,4R,7E)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(苯基亞甲基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-3-甲酸	677.5	(500MHz, DMSO-d6) δ 10.62 (s, 1H), 10.00 (d, J=7.0 Hz, 1H), 8.21 (d, J=4.3 Hz, 1H), 8.14 (s, 1H), 8.02 (d, J=7.6 Hz, 1H), 7.95 (br. s., 1H), 7.80 (br. s., 1H), 7.73 (d, J=8.5 Hz, 1H), 7.48 (t, J=9.8 Hz, 1H), 7.44 - 7.28 (m, 6H), 7.25 (t, J=7.0 Hz, 1H), 6.36 (s, 1H), 4.52 (br. s., 1H), 4.07 (s, 3H), 3.45 (d, J=15.3 Hz, 1H), 3.35 - 3.22 (m, 1H), 2.85 (br. s., 1H), 2.02 - 1.94 (m, 1H), 1.89 - 1.79 (m, 1H), 1.54 (t, J=14.2 Hz, 2H)	2.21, B
92		(1R,2S,3R,4R)-3-[5-(1,3-二甲基-1H-吡唑-4-基)-2-甲氧基苯甲醯胺基]-N-[4-氟-3-(三氟甲基)苯基]-7-丙烷-2-亞基)雙環[2.2.1]庚烷-2-甲醯胺	585.2	(500MHz, DMSO-d6) δ 10.51 (s, 1H), 9.85 (d, J=7.3 Hz, 1H), 8.21 (d, J=4.3 Hz, 1H), 7.97 (d, J=2.1 Hz, 1H), 7.85 - 7.74 (m, 2H), 7.55 - 7.41 (m, 2H), 7.18 (d, J=8.5 Hz, 1H), 4.36 (br. s., 1H), 3.99 (s, 3H), 3.76 (s, 3H), 3.47 - 3.35 (m, 2H), 3.10 (dd, J=10.5, 3.8 Hz, 1H), 3.03 (br. s., 1H), 2.93 (br. s., 1H), 2.24 (s, 3H), 1.89 - 1.79 (m, 1H), 1.71 (s, 3H), 1.73 (s, 4H), 1.35 (d, J=6.1 Hz, 2H)	2.51, B

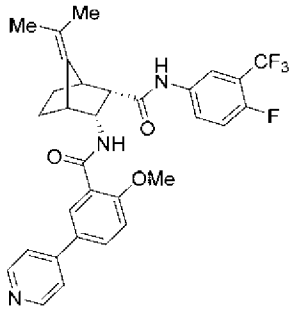
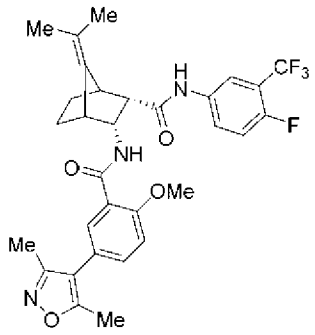
93		(1R,2S,3R,4R)-N-[4-氟-3-(三氟甲基)苯基]-3-[2-甲氧基-5-(1-甲基-1H-咪唑-5-基)苯甲醯胺基]-7-丙烷-2-亞基雙環[2.2.1]庚烷-2-甲醯胺	571.2	(500MHz, DMSO-d6) δ 10.58 (s, 1H), 9.93 (d, J=7.0 Hz, 1H), 8.78 (br. s., 1H), 8.21 (d, J=4.3 Hz, 1H), 8.05 (s, 1H), 7.79 (d, J=8.5 Hz, 1H), 7.70 (d, J=8.5 Hz, 1H), 7.63 (br. s., 1H), 7.48 (t, J=9.8 Hz, 1H), 7.34 (d, J=8.9 Hz, 1H), 4.34 (br. s., 1H), 4.05 (s, 3H), 3.74 (s, 3H), 3.52 (br. s., 1H), 3.11 (dd, J=10.7, 4.0 Hz, 1H), 3.04 (br. s., 1H), 2.93 (br. s., 1H), 1.81 (t, J=8.7 Hz, 1H), 1.70 (s, 4H), 1.73 (s, 3H), 1.35 (d, J=6.4 Hz, 2H)	2.37, B
94		3'-{[(1R,2R,3S,4R,7E)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(苯基亞甲基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-4-甲酸	659.2	(500MHz, DMSO-d6) δ 10.62 (s, 1H), 9.98 (d, J=7.0 Hz, 1H), 8.27 (s, 1H), 8.22 (d, J=4.6 Hz, 1H), 8.03 - 7.97 (m, J=8.2 Hz, 2H), 7.88 (d, J=8.5 Hz, 1H), 7.80 (br. s., 1H), 7.78 - 7.68 (m, J=8.2 Hz, 2H), 7.48 (t, J=9.8 Hz, 1H), 7.44 - 7.35 (m, 4H), 7.32 (d, J=8.5 Hz, 1H), 7.29 - 7.20 (m, 1H), 6.37 (s, 1H), 4.54 (br. s., 1H), 4.06 (s, 3H), 3.29 (d, J=7.3 Hz, 1H), 2.86 (br. s., 1H), 2.03 - 1.94 (m, 1H), 1.84 (br. s., 1H), 1.55 (t, J=13.7 Hz, 2H)	2.69, C

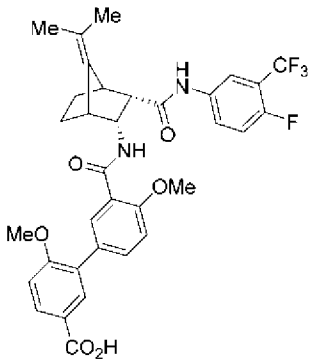
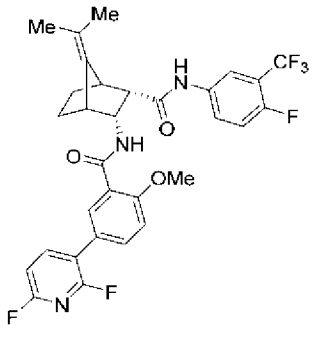
95		(1R,2S,3R,4R,7E)-N-[4-氟-3-(三氟甲基)苯基]-3-[5-(2-氟吡啶-3-基)-2-甲氧基苯甲醯胺基]-7-(苯基亞甲基)雙環[2.2.1]庚烷-2-甲醯胺	634.5	(500MHz, DMSO-d6) δ 10.61 (s, 1H), 9.99 (d, J=7.0 Hz, 1H), 8.21 (d, J=4.6 Hz, 2H), 8.18 (s, 1H), 8.10 (t, J=8.2 Hz, 1H), 7.85 - 7.72 (m, 2H), 7.51 - 7.43 (m, 2H), 7.43 - 7.30 (m, 5H), 7.25 (t, J=7.2 Hz, 1H), 6.37 (s, 1H), 4.52 (br. s., 1H), 4.07 (s, 3H), 3.46 - 3.36 (m, 2H), 3.32 - 3.24 (m, 1H), 2.85 (br. s., 1H), 1.97 (d, J=9.2 Hz, 1H), 1.89 - 1.78 (m, 1H), 1.65 - 1.46 (m, 2H)	2.69, B
96		3'-{[(1R,2R,3S,4R)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-丙烷-2-亞基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-3-甲酸	611.3	(500MHz, DMSO-d6) δ 10.63 (s, 1H), 9.91 (d, J=7.3 Hz, 1H), 8.23 (br. s., 2H), 8.13 (br. s., 1H), 7.90 - 7.75 (m, 3H), 7.69 (d, J=7.6 Hz, 1H), 7.53 - 7.40 (m, 2H), 7.28 (d, J=8.9 Hz, 1H), 4.39 (br. s., 1H), 4.04 (s, 3H), 3.17 - 3.11 (m, 1H), 3.04 (br. s., 1H), 2.99 (s, 1H), 2.96 (br. s., 1H), 1.72 (d, J=6.1 Hz, 6H), 1.35 (d, J=5.8 Hz, 2H), 1.22 (s, 3H), 1.15 (d, J=7.0 Hz, 1H), 0.92 - 0.79 (m, 1H)	2.61, C

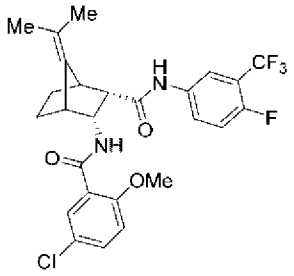
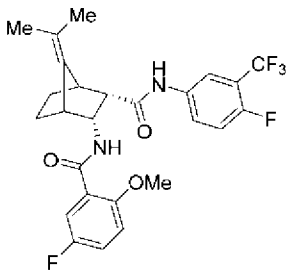
97		(1R,2S,3R,4R)-N-[4-氟-3-(三氟甲基)苯基]-3-[2-甲氧基-5-(嘧啶-5-基)苯甲醯胺基]-7-丙烷-2-亞基)雙環[2.2.1]庚烷-2-甲醯胺	569.3	(500MHz, DMSO-d6) δ 10.54 (s, 1H), 9.90 (d, J=7.0 Hz, 1H), 9.13 (s, 1H), 9.06 (s, 2H), 8.24 (d, J=1.8 Hz, 1H), 8.19 (d, J=4.3 Hz, 1H), 7.97 - 7.89 (m, 1H), 7.78 (br. s., 1H), 7.46 (t, J=9.8 Hz, 1H), 7.34 (d, J=8.9 Hz, 1H), 4.36 (br. s., 1H), 4.03 (s, 3H), 3.10 (dd, J=10.7, 4.0 Hz, 1H), 3.03 (br. s., 1H), 2.94 (br. s., 1H), 1.88 - 1.76 (m, 1H), 1.71 (d, J=9.8 Hz, 7H), 1.35 (d, J=6.1 Hz, 2H)	2.42, B
98		(1R,2S,3R,4R)-N-[4-氟-3-(三氟甲基)苯基]-3-[2-甲氧基-5-(2-甲基嘧啶-5-基)苯甲醯胺基]-7-丙烷-2-亞基)雙環[2.2.1]庚烷-2-甲醯胺	583.2	(500MHz, DMSO-d6) δ 10.53 (s, 1H), 9.91 (d, J=7.0 Hz, 1H), 8.90 (s, 2H), 8.22 - 8.11 (m, 2H), 7.87 (d, J=8.5 Hz, 1H), 7.74 (br. s., 1H), 7.43 (t, J=9.6 Hz, 1H), 7.30 (d, J=8.5 Hz, 1H), 4.33 (br. s., 1H), 4.00 (s, 2H), 3.08 (d, J=10.7 Hz, 1H), 3.00 (br. s., 1H), 2.92 (br. s., 1H), 2.62 (s, 3H), 1.69 (d, J=8.5 Hz, 7H), 1.33 (d, J=6.1 Hz, 2H), 1.17 (br. s., 1H)	2.50, B

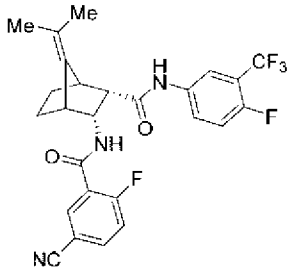
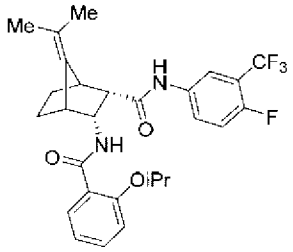
99		(1R,2S,3R,4R)-3-(5-氰基-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-丙烷-2-亞基)雙環[2.2.1]庚烷-2-甲醯胺	516.2	(500MHz, DMSO-d6) δ 10.56 (s, 1H), 9.91 (d, J=7.0 Hz, 1H), 8.25 - 8.13 (m, 2H), 7.97 (d, J=8.5 Hz, 1H), 7.79 (d, J=8.9 Hz, 1H), 7.47 (t, J=9.8 Hz, 1H), 7.37 (d, J=8.9 Hz, 1H), 4.32 (br. s., 1H), 4.07 (s, 3H), 3.49 - 3.38 (m, 1H), 3.10 (dd, J=10.7, 4.0 Hz, 1H), 3.03 (br. s., 1H), 2.93 (br. s., 1H), 1.79 (d, J=9.5 Hz, 1H), 1.78 - 1.65 (m, 8H), 1.34 (d, J=5.5 Hz, 2H)	2.59, B
100		3'-{[(1R,2R,3S,4R)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-丙烷-2-亞基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-6-甲基-[1,1'-聯苯]-3-甲酸	625.5	(500 MHz, DMSO-d6) δ 10.63 - 10.51 (m, 1H), 9.98 - 9.86 (m, 1H), 8.30 - 8.17 (m, 1H), 7.95 - 7.86 (m, 1H), 7.86 - 7.77 (m, 2H), 7.77 - 7.64 (m, 1H), 7.56 - 7.44 (m, 2H), 7.44 - 7.34 (m, 1H), 7.33 - 7.17 (m, 1H), 4.44 - 4.29 (m, 1H), 4.10 - 3.98 (m, 3H), 3.15 - 3.08 (m, 1H), 3.08 - 2.99 (m, 1H), 2.97 - 2.83 (m, 2H), 2.32 - 2.21 (m, 2H), 1.95 - 1.81 (m, 2H), 1.80 - 1.61 (m, 7H), 1.41 - 1.29 (m, 2H), 1.21 - 1.10 (m, 1H)	2.19, B

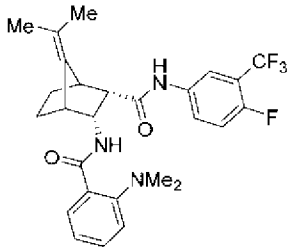
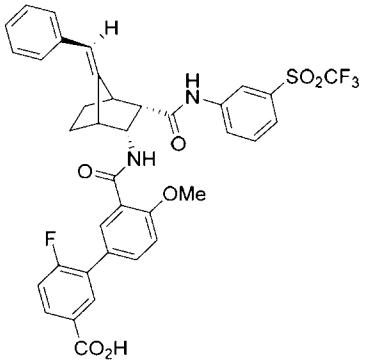
101		3'-{[(1R,2R,3S,4R)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-丙烷-2-亞基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-2,4'-二甲氧基-[1,1'-聯苯]-3-甲酸	641.2	(500MHz, DMSO-d6) δ 10.54 (s, 1H), 9.89 (d, J=7.0 Hz, 1H), 8.19 (d, J=4.6 Hz, 1H), 8.07 (s, 1H), 7.92 (s, 1H), 7.77 (br. s., 1H), 7.64 (d, J=8.8 Hz, 1H), 7.53 (br. s., 1H), 7.45 (t, J=9.8 Hz, 1H), 7.39 (d, J=7.0 Hz, 1H), 7.29 - 7.15 (m, 2H), 4.35 (br. s., 1H), 4.02 (s, 3H), 3.39 (s, 3H), 3.09 (d, J=10.4 Hz, 1H), 3.01 (br. s., 1H), 2.92 (br. s., 1H), 1.88 - 1.79 (m, 1H), 1.70 (d, J=9.5 Hz, 7H), 1.39 - 1.29 (m, 2H)	2.04, B
102		(1R,2S,3R,4R)-N-[4-氟-3-(三氟甲基)苯基]-3-[5-(2-氟吡啶-3-基)-2-甲氧基苯甲醯胺基]-7-丙烷-2-亞基)雙環[2.2.1]庚烷-2-甲醯胺	586.3	(500MHz, DMSO-d6) δ 10.52 (s, 1H), 9.91 (d, J=7.3 Hz, 1H), 8.20 - 8.13 (m, 2H), 8.11 (br. s., 1H), 8.04 (t, J=8.7 Hz, 1H), 7.79 - 7.69 (m, 2H), 7.47 - 7.38 (m, 2H), 7.30 (d, J=8.9 Hz, 1H), 4.33 (br. s., 1H), 4.01 (s, 3H), 3.12 - 3.04 (m, 1H), 3.00 (br. s., 1H), 2.92 (br. s., 1H), 1.80 (t, J=8.7 Hz, 1H), 1.69 (d, J=8.9 Hz, 6H), 1.33 (d, J=6.4 Hz, 2H), 1.17 (br. s., 1H)	2.71, B

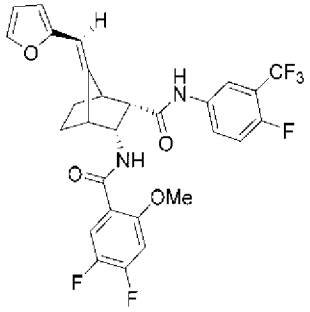
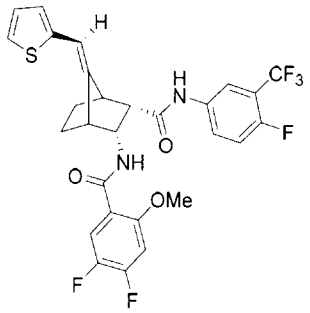
103		(1R,2S,3R,4R)-N-[4-氟-3-(三氟甲基)苯基]-3-[2-甲氧基-5-(吡啶-4-基)苯甲醯胺基]-7-丙烷-2-亞基)雙環[2.2.1]庚烷-2-甲醯胺	568.2	(500MHz, DMSO-d6) δ 10.59 (s, 1H), 9.93 (d, J=6.7 Hz, 1H), 8.80 (br. s., 2H), 8.45 (s, 1H), 8.22 (d, J=4.6 Hz, 1H), 8.12 (d, J=6.1 Hz, 3H), 7.80 (br. s., 1H), 7.48 (t, J=9.8 Hz, 1H), 7.40 (d, J=8.9 Hz, 1H), 4.37 (br. s., 1H), 4.08 (s, 3H), 3.51 (br. s., 1H), 3.16 (s, 1H), 3.12 (dd, J=10.4, 4.0 Hz, 1H), 3.05 (br. s., 1H), 2.95 (br. s., 1H), 1.87 - 1.77 (m, 1H), 1.72 (d, J=9.8 Hz, 7H), 1.36 (d, J=5.8 Hz, 2H)	2.12, C
104		(1R,2S,3R,4R)-3-[5-(3,5-二甲基-1,2-噁唑-4-基)-2-甲氧基苯甲醯胺基]-N-[4-氟-3-(三氟甲基)苯基]-7-丙烷-2-亞基)雙環[2.2.1]庚烷-2-甲醯胺	586.3	(500MHz, DMSO-d6) δ 10.57 (br. s., 1H), 9.90 (d, J=6.3 Hz, 1H), 8.23 (d, J=5.0 Hz, 1H), 7.86 (d, J=2.0 Hz, 1H), 7.79 (d, J=8.8 Hz, 1H), 7.55 - 7.44 (m, 2H), 7.27 (d, J=8.6 Hz, 1H), 4.35 (br. s., 1H), 4.03 (s, 3H), 3.46 (br. s., 5H), 3.10 (dd, J=10.6, 4.0 Hz, 1H), 3.03 (br. s., 1H), 2.93 (br. s., 1H), 2.35 (s, 3H), 2.17 (s, 3H), 1.83 (t, J=9.0 Hz, 1H), 1.70 (s, 3H), 1.73 (s, 4H), 1.35 (d, J=6.0 Hz, 2H)	2.69, B

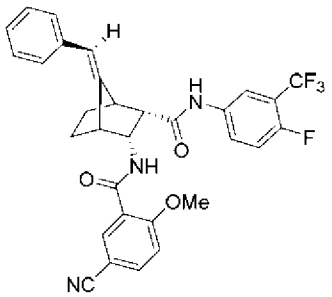
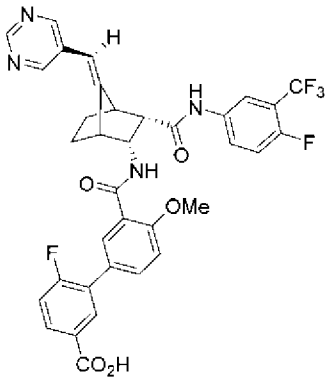
105		3'-{[(1R,2R,3S,4R)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-丙烷-2-亞基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4',6-二甲氧基-[1,1'-聯苯]-3-甲酸	641.2	(500 MHz, DMSO-d6) δ 10.63 - 10.50 (m, 1H), 9.98 - 9.85 (m, 1H), 8.26 - 8.16 (m, 1H), 8.09 - 8.00 (m, 1H), 8.00 - 7.86 (m, 1H), 7.86 - 7.71 (m, 2H), 7.71 - 7.59 (m, 1H), 7.51 - 7.40 (m, 1H), 7.27 - 7.10 (m, 2H), 4.41 - 4.28 (m, 1H), 4.10 - 3.97 (m, 3H), 3.88 - 3.73 (m, 2H), 3.72 - 3.61 (m, 1H), 3.19 - 3.14 (m, 1H), 3.13 - 3.05 (m, 1H), 3.05 - 2.98 (m, 1H), 2.98 - 2.85 (m, 1H), 1.87 - 1.79 (m, 1H), 1.79 - 1.64 (m, 7H), 1.44 - 1.27 (m, 2H)	2.24, B
106		(1R,2S,3R,4R)-3-[5-(2,6-二氟吡啶-3-基)-2-甲氧基苯甲醯胺基]-N-[4-氟-3-(三氟甲基)苯基]-7-丙烷-2-亞基)雙環[2.2.1]庚烷-2-甲醯胺	604.3	(500MHz, DMSO-d6) δ 10.53 (s, 1H), 9.90 (d, J=7.3 Hz, 1H), 8.31 - 8.22 (m, 1H), 8.19 (d, J=4.6 Hz, 1H), 8.11 (s, 1H), 7.77 (br. s., 1H), 7.72 (d, J=8.8 Hz, 1H), 7.46 (t, J=9.6 Hz, 1H), 7.31 (d, J=8.5 Hz, 1H), 7.24 (d, J=6.7 Hz, 1H), 4.35 (br. s., 1H), 4.03 (s, 3H), 3.10 (dd, J=10.8, 3.8 Hz, 1H), 3.02 (br. s., 1H), 2.93 (br. s., 1H), 1.87 - 1.77 (m, 1H), 1.70 (s, 4H), 1.72 (s, 3H), 1.34 (d, J=6.4 Hz, 2H)	2.77, B

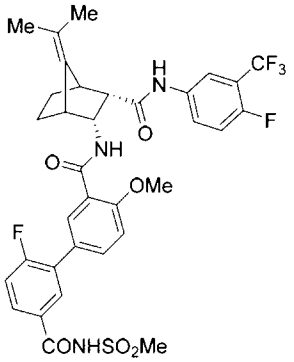
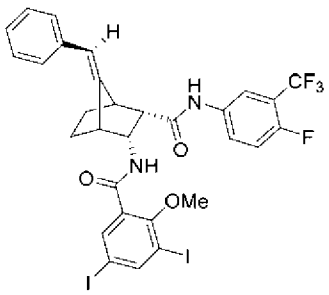
109		(2S,3R)-3-(5- 氯 -2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-丙烷-2-亞基)雙環[2.2.1]庚烷-2-甲醯胺	525.2	(500 MHz, DMSO-d6) δ 10.52 (s, 1H), 9.90 (br d, J=7.0 Hz, 1H), 8.17 (br d, J=4.0 Hz, 1H), 7.83 (d, J=2.4 Hz, 1H), 7.80 - 7.71 (m, 1H), 7.52 (dd, J=8.9, 2.4 Hz, 1H), 7.45 (br t, J=9.6 Hz, 1H), 7.20 (d, J=8.9 Hz, 1H), 4.35 - 4.25 (m, 1H), 3.97 (s, 3H), 3.08 (br dd, J=10.7, 4.0 Hz, 1H), 3.03 - 2.98 (m, 1H), 2.93 - 2.88 (m, 1H), 1.82 - 1.75 (m, 1H), 1.73 - 1.65 (m, 7H), 1.40 - 1.25 (m, 2H)	2.60, B
111		(2S,3R)-3-(5- 氟 -2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-丙烷-2-亞基)雙環[2.2.1]庚烷-2-甲醯胺	509.0	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.94 (d, J=7.0 Hz, 1H), 8.19 (d, J=4.3 Hz, 1H), 7.84 - 7.72 (m, 1H), 7.63 (dd, J=9.5, 3.1 Hz, 1H), 7.47 (t, J=9.8 Hz, 1H), 7.38 - 7.29 (m, 1H), 7.20 (dd, J=9.2, 4.3 Hz, 1H), 4.42 - 4.24 (m, 1H), 3.97 (s, 3H), 3.09 (dd, J=10.7, 4.0 Hz, 1H), 3.05 - 2.99 (m, 1H), 2.95 - 2.88 (m, 1H), 1.81 (t, J=8.7 Hz, 1H), 1.75 - 1.63 (m, 7H), 1.40 - 1.26 (m, 2H)	2.64, B

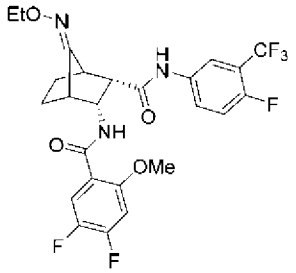
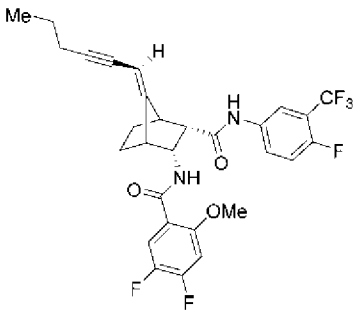
114		(2S,3R)-3-(5-氰基-2-氟苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-丙烷-2-亞基)雙環[2.2.1]庚烷-2-甲醯胺	504.1	(500 MHz, DMSO-d6) δ 10.51 (s, 1H), 9.34 (br t, J=6.0 Hz, 1H), 8.14 - 8.10 (m, 1H), 8.07 - 8.02 (m, 1H), 8.02 - 7.99 (m, 1H), 7.83 - 7.76 (m, 1H), 7.56 (t, J=9.6 Hz, 1H), 7.46 (t, J=9.8 Hz, 1H), 4.36 - 4.27 (m, 1H), 3.09 (dd, J=10.4, 4.0 Hz, 1H), 3.06 - 3.01 (m, 1H), 2.95 - 2.90 (m, 1H), 1.80 - 1.74 (m, 2H), 1.72 (s, 3H), 1.70 (s, 3H), 1.41 - 1.32 (m, 2H)	2.53, C
115		(2S,3R)-N-[4-氟-3-(三氟甲基)苯基]-7-丙烷-2-亞基)-3-[2-丙烷-2-基氧基)苯甲醯胺基]雙環[2.2.1]庚烷-2-甲醯胺	519.4	(500 MHz, DMSO-d6) δ 10.46 (s, 1H), 9.54 (d, J=7.9 Hz, 1H), 8.26 (d, J=4.3 Hz, 1H), 7.85 (d, J=7.6 Hz, 1H), 7.66 - 7.57 (m, 1H), 7.47 - 7.37 (m, 2H), 7.15 (d, J=8.2 Hz, 1H), 6.96 (t, J=7.5 Hz, 1H), 4.87 (dt, J=11.9, 6.0 Hz, 1H), 4.48 - 4.38 (m, 1H), 3.05 (dd, J=10.7, 3.7 Hz, 1H), 3.02 - 2.98 (m, 1H), 2.89 - 2.84 (m, 1H), 1.86 (dd, J=15.6, 9.2 Hz, 2H), 1.71 (s, 3H), 1.69 (s, 3H), 1.46 (d, J=5.8 Hz, 3H), 1.41 (d, J=6.1 Hz, 3H), 1.39 - 1.34 (m, 2H)	2.75, C

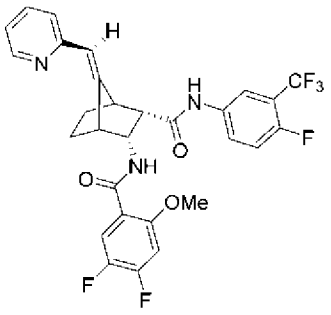
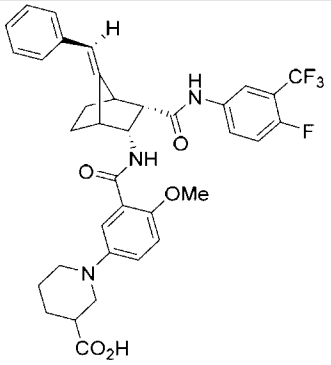
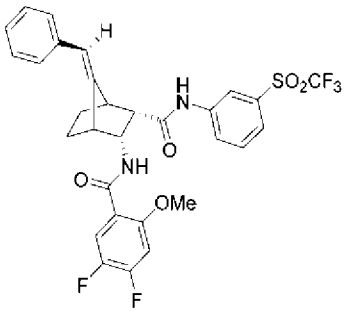
119		(2S,3R)-3-[2-(二甲基胺基)苯甲醯胺基]-N-[4-氟-3-(三氟甲基)苯基]-7-丙烷-2-亞基)雙環[2.2.1]庚烷-2-甲醯胺	504.3	(500 MHz, DMSO-d6) δ 10.52 (br d, J=7.4 Hz, 1H), 10.47 (br s, 1H), 8.21 (d, J=5.1 Hz, 1H), 7.77 (d, J=7.7 Hz, 1H), 7.76 - 7.70 (m, 1H), 7.50 - 7.36 (m, 2H), 7.26 (d, J=8.0 Hz, 1H), 7.09 (t, J=7.4 Hz, 1H), 4.48 - 4.32 (m, 1H), 3.08 (dd, J=10.8, 4.0 Hz, 1H), 3.03 - 2.97 (m, 1H), 2.93 - 2.87 (m, 1H), 2.63 (s, 6H), 1.90 (t, J=9.2 Hz, 1H), 1.80 - 1.65 (m, 7H), 1.45 - 1.26 (m, 2H)	2.71, B
122		6-氟-4'-甲氧基-3'-{[(2R,3S,7Z)-7-(苯基亞甲基)-3-[(3-三氟甲磺醯基苯基)胺甲醯基]雙環[2.2.1]庚烷-2-基]胺甲醯基}-[1,1'-聯苯]-3-甲酸	723.2	(500 MHz, $CDCl_3$) δ 9.94 - 9.64 (m, 1H), 8.61 (br d, J=7.7 Hz, 1H), 8.45 - 7.97 (m, 3H), 7.80 - 7.65 (m, 3H), 7.63 - 7.56 (m, 1H), 7.42 - 7.30 (m, 3H), 7.25 - 7.15 (m, 2H), 7.10 (br d, J=8.3 Hz, 1H), 6.35 (br s, 1H), 4.97 (br s, 1H), 4.15 (br s, 3H), 3.52 (br s, 1H), 3.37 - 3.23 (m, 1H), 2.94 (br s, 1H), 2.40 - 2.33 (m, 1H), 2.02 - 1.96 (m, 1H), 1.80 - 1.68 (m, 2H)	1.21, A

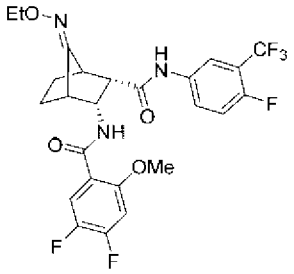
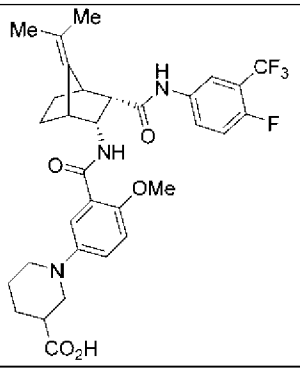
123		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-[(呋喃-2-基)亞甲基]雙環[2.2.1]庚烷-2-甲醯胺	565.0	(500 MHz, $CDCl_3$) δ 9.43 (br d, J=7.4 Hz, 1H), 8.04 (br t, J=10.3 Hz, 1H), 7.93 (br d, J=4.0 Hz, 1H), 7.88 (br s, 1H), 7.60 - 7.49 (m, 1H), 7.36 (s, 1H), 7.11 (br t, J=9.3 Hz, 1H), 6.79 (br dd, J=11.4, 6.1 Hz, 1H), 6.38 (br s, 1H), 6.25 (d, J=2.9 Hz, 1H), 6.08 (s, 1H), 4.82 (br t, J=11.0 Hz, 1H), 3.74 (br s, 1H), 3.14 (br dd, J=10.6, 3.2 Hz, 1H), 2.85 (br s, 1H), 2.31 - 2.17 (m, 1H), 1.98 - 1.85 (m, 1H), 1.76 - 1.63 (m, 2H)	1.23, C
124		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-[(噻吩-2-基)亞甲基]雙環[2.2.1]庚烷-2-甲醯胺	581.0	(500 MHz, $CDCl_3$) δ 9.49 (br d, J=7.4 Hz, 1H), 8.05 (br t, J=10.3 Hz, 1H), 7.94 (br d, J=5.7 Hz, 1H), 7.84 (br s, 1H), 7.59 - 7.48 (m, 1H), 7.20 (br d, J=4.6 Hz, 1H), 7.12 (br t, J=9.3 Hz, 1H), 7.01 - 6.94 (m, 2H), 6.79 (dd, J=11.4, 6.1 Hz, 1H), 6.43 (s, 1H), 4.84 - 4.77 (m, 1H), 3.66 - 3.60 (m, 1H), 3.19 - 3.12 (m, 1H), 2.89 - 2.83 (m, 1H), 2.26 - 2.18 (m, 1H), 1.96 - 1.87 (m, 1H), 1.75 - 1.63 (m, 2H)	1.25, C

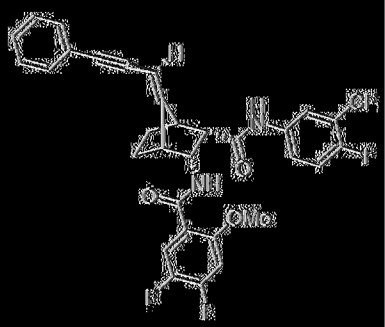
128		(2S,3R,7Z)-3-(5-氰基-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-(苯基亞甲基)雙環[2.2.1]庚烷-2-甲醯胺	564.1	(500 MHz, $CDCl_3$) δ 9.67 (br d, J=7.7 Hz, 1H), 8.49 (d, J=2.2 Hz, 1H), 8.01 (dd, J=6.2, 2.6 Hz, 1H), 7.72 (dd, J=8.5, 2.2 Hz, 1H), 7.63 (s, 1H), 7.50 (dt, J=8.5, 3.6 Hz, 1H), 7.34 (d, J=4.4 Hz, 4H), 7.25 - 7.21 (m, 1H), 7.15 (t, J=9.2 Hz, 1H), 7.05 (d, J=8.5 Hz, 1H), 6.33 (s, 1H), 4.85 - 4.79 (m, 1H), 4.10 (s, 3H), 3.55 - 3.50 (m, 1H), 3.16 (dd, J=10.7, 3.9 Hz, 1H), 2.90 - 2.85 (m, 1H), 2.20 - 2.14 (m, 1H), 1.96 - 1.90 (m, 1H), 1.67 - 1.64 (m, 2H)	1.22, A
129		6-氟-3'-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-[(嘧啶-5-基)亞甲基]雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-3-甲酸	679.3	-	1.08, A

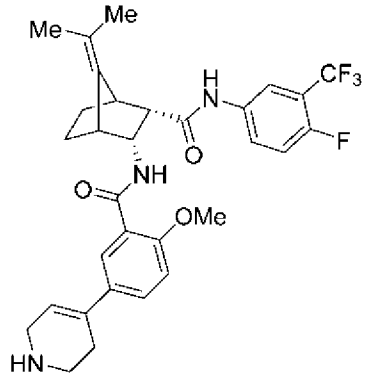
131		6'- 氟 -N3-[(2R,3S)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-丙烷-2-亞基)雙環[2.2.1]庚烷-2-基]-N3'-甲磺醯基-4-甲氧基-[1,1'-聯苯]-3,3'-二甲醯胺	706.3	(500 MHz, $CDCl_3$) δ 10.44 (br s, 1H), 9.77 (d, J=7.7 Hz, 1H), 8.30 (d, J=1.9 Hz, 1H), 8.12 (s, 1H), 8.07 - 7.99 (m, 2H), 7.92 (ddd, J=8.6, 4.5, 2.3 Hz, 1H), 7.72 - 7.66 (m, 1H), 7.61 (dt, J=8.8, 3.4 Hz, 1H), 7.20 (dd, J=9.9, 8.5 Hz, 1H), 7.13 (t, J=9.4 Hz, 1H), 7.07 (d, J=8.8 Hz, 1H), 4.45 - 4.37 (m, 1H), 4.06 (s, 3H), 3.46 (s, 3H), 2.99 - 2.91 (m, 3H), 2.11 - 2.04 (m, 1H), 1.83 - 1.77 (m, 1H), 1.66 (s, 3H), 1.62 (s, 3H), 1.55 - 1.46 (m, 2H)	1.23, A
132		(2S,3R,7Z)-3-(3,5-二碘-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-(苯基亞甲基)雙環[2.2.1]庚烷-2-甲醯胺	791.0	(500 MHz, $CDCl_3$) δ 9.10 (br d, J=8.0 Hz, 1H), 8.25 (d, J=2.2 Hz, 1H), 8.19 (d, J=2.2 Hz, 1H), 7.83 - 7.72 (m, 2H), 7.66 (dt, J=8.5, 3.6 Hz, 1H), 7.38 - 7.30 (m, 4H), 7.26 - 7.22 (m, 1H), 7.13 (t, J=9.4 Hz, 1H), 6.34 (s, 1H), 4.89 - 4.81 (m, 1H), 3.78 (s, 3H), 3.47 - 3.41 (m, 1H), 3.24 - 3.17 (m, 1H), 2.93 - 2.88 (m, 1H), 2.31 - 2.24 (m, 1H), 1.97 - 1.88 (m, 1H), 1.79 - 1.68 (m, 2H)	1.35, A

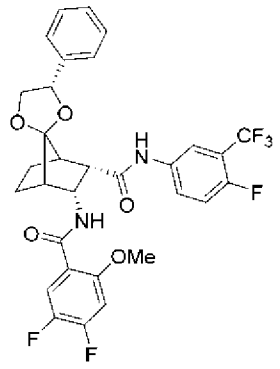
133		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-7-(乙氧基亞胺基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	544.1	(500 MHz, $CDCl_3$) δ 9.49 (br d, J=7.3 Hz, 1H), 8.05 - 7.93 (m, 3H), 7.51 (dt, J=8.8, 3.5 Hz, 1H), 7.13 (t, J=9.3 Hz, 1H), 6.79 (dd, J=11.5, 6.1 Hz, 1H), 4.90 - 4.81 (m, 1H), 4.09 (q, J=7.0 Hz, 2H), 3.99 (s, 3H), 3.50 (t, J=3.9 Hz, 1H), 3.22 (dd, J=10.8, 4.0 Hz, 1H), 2.86 (t, J=3.8 Hz, 1H), 2.38 - 2.26 (m, 1H), 1.98 - 1.87 (m, 1H), 1.81 - 1.70 (m, 2H), 1.27 (t, J=7.1 Hz, 3H)	1.18, B
135		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-(己-2-炔-1-亞基)雙環[2.2.1]庚烷-2-甲醯胺	565.1	(500 MHz, $CDCl_3$) δ 9.32 (br d, J=7.6 Hz, 1H), 8.06 (dd, J=11.3, 9.3 Hz, 1H), 7.91 (dd, J=6.3, 2.6 Hz, 1H), 7.84 (s, 1H), 7.53 (dt, J=8.7, 3.5 Hz, 1H), 7.17 - 7.05 (m, 1H), 6.80 (dd, J=11.6, 6.1 Hz, 1H), 5.37 (t, J=2.0 Hz, 1H), 4.87 - 4.77 (m, 1H), 4.00 (s, 3H), 3.25 (t, J=4.0 Hz, 1H), 3.11 (dd, J=11.3, 3.5 Hz, 1H), 2.82 (t, J=3.8 Hz, 1H), 2.35 - 2.23 (m, 3H), 1.94 - 1.82 (m, 1H), 1.74 - 1.66 (m, 2H), 1.63 - 1.57 (m, 2H), 1.03 (t, J=7.3 Hz, 3H)	1.28, B

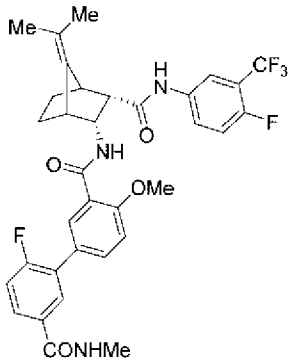
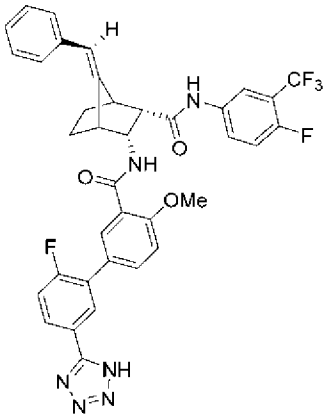
137		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-[(吡啶-2-基)亞甲基]雙環[2.2.1]庚烷-2-甲醯胺	576.0	-	0.96, C
138		1-(3-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(苯基亞甲基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)哌啶-3-甲酸	666.3	-	1.07, A
139		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-(3-甲磺醯基苯基)-7-(苯基亞甲基)雙環[2.2.1]庚烷-2-甲醯胺	567.1	(500 MHz, $CDCl_3$) δ 9.58 (br d, J=7.7 Hz, 1H), 8.34 (t, J=1.8 Hz, 1H), 8.03 (dd, J=11.6, 9.4 Hz, 1H), 7.91 (s, 1H), 7.68 - 7.61 (m, 2H), 7.53 - 7.44 (m, 1H), 7.34 (d, J=4.4 Hz, 4H), 7.25 - 7.20 (m, 1H), 6.79 (dd, J=11.6, 6.3 Hz, 1H), 6.33 (s, 1H), 4.87 - 4.80 (m, 1H), 4.04 (s, 3H), 3.51 - 3.47 (m, 1H), 3.21 - 3.16 (m, 1H), 3.04 (s, 3H), 2.91 - 2.86 (m, 1H), 2.24 - 2.19 (m, 1H), 1.96 - 1.88 (m, 1H), 1.73 - 1.67 (m, 2H)	1.11, A

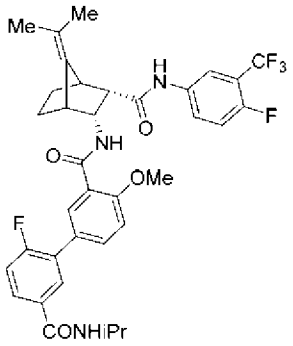
141		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-7-(乙氧基亞胺基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	544.1	(500 MHz, $CDCl_3$) δ 9.52 (br d, J=7.6 Hz, 1H), 8.01 (dd, J=11.2, 9.4 Hz, 1H), 7.96 (dd, J=6.2, 2.4 Hz, 1H), 7.83 (br s, 1H), 7.50 (dt, J=8.8, 3.4 Hz, 1H), 7.13 (t, J=9.3 Hz, 1H), 6.78 (dd, J=11.5, 6.1 Hz, 1H), 4.91 - 4.82 (m, 1H), 4.11 (q, J=7.0 Hz, 2H), 4.00 (s, 3H), 3.50 - 3.45 (m, 1H), 3.18 (dd, J=10.6, 4.0 Hz, 1H), 2.92 - 2.87 (m, 1H), 2.33 - 2.23 (m, 1H), 1.98 - 1.86 (m, 1H), 1.81 - 1.70 (m, 2H), 1.28 (t, J=7.1 Hz, 3H)	1.18, B
142		1-(3-{[(2R,3S)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-丙烷-2-亞基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)哌啶-3-甲酸	618.3	-	0.98, A

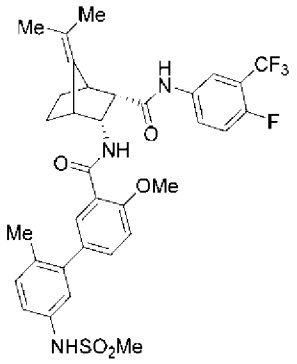
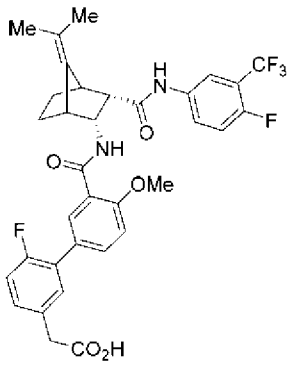
143		4-(3-{[(2R,3S)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-丙烷-2-基-雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-1,2,3,6-四氫吡啶-1-甲酸甲酯	630.4	(500 MHz, $CDCl_3$) δ 9.27 (br d, J = 8.2 Hz, 1H), 8.20 (br s, 1H), 8.08 (br s, 1H), 7.83 (dd, J = 6.1, 2.5 Hz, 1H), 7.64 – 7.56 (m, 1H), 7.44 (dd, J = 8.5, 2.1 Hz, 1H), 7.05 (t, J = 9.3 Hz, 1H), 6.92 (d, J = 8.7 Hz, 1H), 6.06 – 5.94 (m, 1H), 4.78 – 4.67 (m, 1H), 4.11 (br s, 2H), 3.98 (s, 3H), 3.75 (s, 3H), 3.68 (br s, 2H), 3.09 – 2.99 (m, 3H), 2.51 (br s, 2H), 2.20 – 2.13 (m, 1H), 1.82 – 1.76 (m, 1H), 1.73 (s, 3H), 1.72 (s, 3H), 1.64 – 1.58 (m, 2H)	1.25, C
146		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-(3-苯基丙-2-炔-1-亞基)雙環[2.2.1]庚烷-2-甲醯胺	598.6	(500 MHz, $CDCl_3$) δ 9.34 (br d, J = 8.1 Hz, 1H), 8.06 (dd, J = 11.4, 9.4 Hz, 1H), 7.92 (dd, J = 6.2, 2.7 Hz, 1H), 7.81 (s, 1H), 7.54 (dt, J = 9.0, 3.4 Hz, 1H), 7.50 – 7.43 (m, 2H), 7.36 – 7.31 (m, 3H), 7.13 (t, J = 9.3 Hz, 1H), 6.81 (dd, J = 11.4, 6.1 Hz, 1H), 5.62 (s, 1H), 4.94 – 4.84 (m, 1H), 4.01 (s, 3H), 3.36 (t, J = 4.0 Hz, 1H), 3.21 – 3.13 (m, 1H), 2.91 (t, J = 3.8 Hz, 1H), 2.38 – 2.30 (m, 1H), 1.96 – 1.88 (m, 1H), 1.80 – 1.66 (m, 2H)	2.84, C

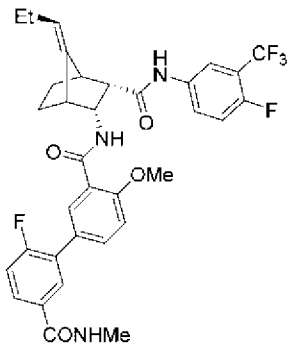
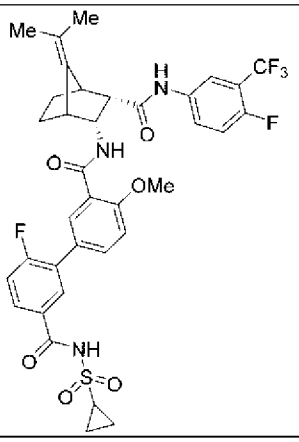
148		(2S,3R)-N-[4-氟-3-(三氟甲基)苯基]-3-[2-甲氧基-5-(1,2,3,6-四氫吡啶-4-基)苯甲醯胺基]-7-丙烷-2-亞基)雙環[2.2.1]庚烷-2-甲醯胺	572.4	(500 MHz, $CDCl_3$) δ 9.36 (br d, J=7.7 Hz, 1H), 8.41 (br s, 1H), 8.15 (d, J=2.4 Hz, 1H), 7.91 (dd, J=5.9, 1.9 Hz, 1H), 7.66 - 7.58 (m, 1H), 7.44 (dd, J=8.7, 2.4 Hz, 1H), 7.06 (t, J=9.3 Hz, 1H), 6.93 (d, J=8.7 Hz, 1H), 6.03 (br s, 1H), 4.70 - 4.62 (m, 1H), 3.99 (s, 3H), 3.62 (br d, J=2.4 Hz, 2H), 3.22 (t, J=5.8 Hz, 2H), 3.06 (dd, J=10.8, 3.9 Hz, 1H), 3.01 - 2.95 (m, 2H), 2.57 (br d, J=2.7 Hz, 2H), 2.19 - 2.14 (m, 1H), 1.81 - 1.75 (m, 1H), 1.71 (s, 3H), 1.69 (s, 3H), 1.59 - 1.52 (m, 2H)	0.98, B

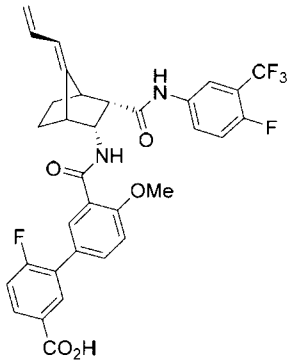
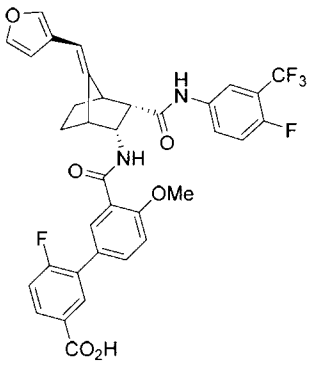
149		6'-氟-N3-((1R,2R,3S,4R)-3-((4-氟-3-(三氟甲基)苯基)胺甲醯基)-7-丙烷-2-亞基)雙環[2.2.1]庚烷-2-基)-4-甲氧基-N3'-甲基-[1,1'-聯苯]-3,3'-二甲醯胺	621.2	(400 MHz, $CDCl_3$) δ 9.32 (br d, J=8.1 Hz, 1H), 8.02 (dd, J=11.4, 9.5 Hz, 1H), 7.91 (dd, J=6.3, 2.5 Hz, 1H), 7.81 (s, 1H), 7.54 - 7.47 (m, 1H), 7.42 - 7.34 (m, 5H), 7.09 (t, J=9.2 Hz, 1H), 6.78 (dd, J=11.6, 6.1 Hz, 1H), 5.16 (t, J=6.8 Hz, 1H), 5.09 - 4.98 (m, 1H), 4.34 (dd, J=8.1, 6.4 Hz, 1H), 3.98 (s, 3H), 3.83 (t, J=7.8 Hz, 1H), 3.55 (dd, J=10.6, 3.7 Hz, 1H), 2.36 - 2.31 (m, 1H), 2.31 - 2.26 (m, 1H), 2.23 - 2.17 (m, 1H), 1.96 - 1.83 (m, 2H), 1.78 - 1.68 (m, 1H)	1.24, A

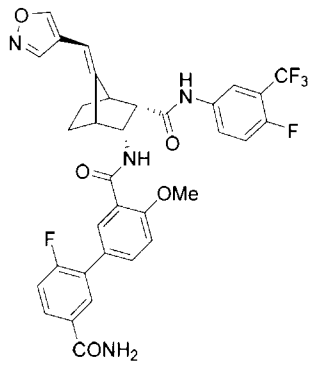
151		6'-氟-N3-((1R,2R,3S,4R)-3-((4-氟-3-(三氟甲基)苯基)胺甲醯基)-7-丙烷-2-亞基)雙環[2.2.1]庚烷-2-基)-4-甲氧基-N3'-甲基-[1,1'-聯苯]-3,3'-二甲醯胺	642.2	(500 MHz, $CDCl_3$) δ 9.41 (d, J=7.9 Hz, 1H), 8.36 (d, J=1.8 Hz, 1H), 8.14 (s, 1H), 7.94 (dd, J=6.2, 2.5 Hz, 1H), 7.81 (dd, J=7.3, 2.2 Hz, 1H), 7.76 (ddd, J=8.4, 4.6, 2.3 Hz, 1H), 7.66 (dt, J=8.6, 1.9 Hz, 1H), 7.56 (dt, J=8.7, 3.4 Hz, 1H), 7.19 (dd, J=10.0, 8.7 Hz, 1H), 7.08 (t, J=9.3 Hz, 1H), 7.04 (d, J=8.6 Hz, 1H), 6.29 (br d, J=4.3 Hz, 1H), 4.74 - 4.64 (m, 1H), 4.04 (s, 3H), 3.07 - 3.00 (m, 6H), 2.18 - 2.11 (m, 1H), 1.84 - 1.78 (m, 1H), 1.72 (s, 3H), 1.71 (s, 3H), 1.60 - 1.53 (m, 2H)	1.18, B
152		2'-氟-N-[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(苯基亞甲基)雙環[2.2.1]庚烷-2-基]-4-甲氧基-5'-(1H-1,2,3,4-四唑-5-基)-[1,1'-聯苯]-3-甲醯胺	701.2	(500 MHz, DMSO-d6) δ 10.64 (s, 1H), 10.07 (br d, J=7.0 Hz, 1H), 8.27 (d, J=4.3 Hz, 1H), 8.23 (br s, 1H), 8.20 - 8.15 (m, 1H), 8.10 - 8.00 (m, 1H), 7.87 - 7.76 (m, 2H), 7.58 - 7.46 (m, 2H), 7.42 - 7.34 (m, 5H), 7.29 - 7.23 (m, 1H), 6.39 (s, 1H), 4.64 - 4.47 (m, 1H), 4.08 (s, 3H), 3.31 (br dd, J=10.1, 4.0 Hz, 1H), 3.16 (s, 1H), 2.97 - 2.91 (m, 1H), 1.91 (dd, J=17.5, 8.7 Hz, 2H), 1.64 - 1.44 (m, 2H)	2.26, B

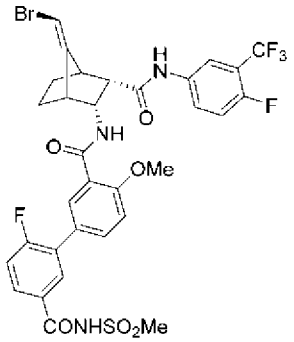
153		6'-氟-N3-[(2R,3S)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-丙烷-2-亞基)雙環[2.2.1]庚烷-2-基]-4-甲氧基-N3'-丙烷-2-基)-[1,1'-聯苯]-3,3'-二甲醯胺	670.2	(500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.92 (br d, J=7.3 Hz, 1H), 8.34 (d, J=7.6 Hz, 1H), 8.22 (d, J=4.0 Hz, 1H), 8.15 (s, 1H), 8.01 - 7.94 (m, 1H), 7.90 - 7.84 (m, 1H), 7.83 - 7.78 (m, 1H), 7.74 (d, J=8.5 Hz, 1H), 7.48 (t, J=9.8 Hz, 1H), 7.37 (t, J=9.5 Hz, 1H), 7.32 (d, J=8.9 Hz, 1H), 4.41 - 4.33 (m, 1H), 4.14 - 4.07 (m, 1H), 4.05 (s, 3H), 3.11 (dd, J=10.5, 3.8 Hz, 1H), 3.06 - 3.01 (m, 1H), 2.98 - 2.92 (m, 1H), 1.88 - 1.80 (m, 1H), 1.78 - 1.67 (m, 7H), 1.41 - 1.31 (m, 2H), 1.17 (s, 3H), 1.16 (s, 3H)	2.69, C

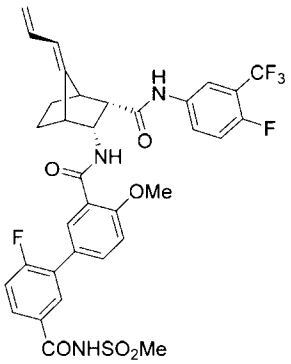
154		N-[(2R,3S)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-丙烷-2-亞基)雙環[2.2.1]庚烷-2-基]-5'-甲磺醯胺基-4-甲氧基-2'-甲基-[1,1'-聯苯]-3-甲醯胺	674.4	(500 MHz, DMSO-d6) δ 10.52 (s, 1H), 9.91 (br d, J=7.0 Hz, 1H), 8.22 (d, J=4.0 Hz, 1H), 7.86 (d, J=2.1 Hz, 1H), 7.83 - 7.75 (m, 1H), 7.54 - 7.43 (m, 2H), 7.25 (dd, J=8.5, 1.5 Hz, 2H), 7.12 (dd, J=8.2, 2.1 Hz, 1H), 7.02 (d, J=1.8 Hz, 1H), 4.44 - 4.30 (m, 1H), 4.03 (s, 3H), 3.10 (dd, J=10.7, 4.0 Hz, 1H), 3.05 - 3.00 (m, 1H), 2.99 - 2.90 (m, 4H), 2.14 (s, 3H), 1.90 - 1.81 (m, 1H), 1.79 - 1.65 (m, 7H), 1.43 - 1.28 (m, 2H)	2.66, C
155		2-(6-氟-3'-{[(2R,3S)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-丙烷-2-亞基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-3-基)乙酸	643.1	(500 MHz, $CDCl_3$) δ 10.01 (br d, J=8.0 Hz, 1H), 8.53 (br s, 1H), 8.24 (d, J=2.2 Hz, 1H), 7.92 (dd, J=6.3, 2.5 Hz, 1H), 7.84 (s, 1H), 7.71 (dt, J=8.7, 2.0 Hz, 1H), 7.49 (dt, J=8.6, 3.5 Hz, 1H), 7.36 (dd, J=7.4, 2.2 Hz, 1H), 7.27 - 7.21 (m, 1H), 7.15 - 7.05 (m, 3H), 4.72 - 4.64 (m, 1H), 4.08 (s, 3H), 3.73 (s, 2H), 3.11 - 2.98 (m, 3H), 2.20 - 2.13 (m, 1H), 1.87 - 1.80 (m, 1H), 1.76 (s, 3H), 1.75 (s, 3H), 1.59 - 1.54 (m, 2H)	1.19, A

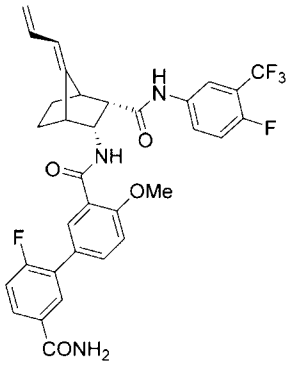
156		6'- 氟 -N3-[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-亞丙基雙環[2.2.1]庚烷-2-基]-4- 甲 氧 基 -N3'-甲基-[1,1'-聯苯]-3,3'- 二 甲 醯 胺	642.2	(500 MHz, $CDCl_3$) δ 10.02 (br d, J=7.4 Hz, 1H), 8.40 (d, J=2.2 Hz, 1H), 8.00 (dd, J=6.2, 2.6 Hz, 1H), 7.89 - 7.83 (m, 2H), 7.80 - 7.75 (m, 2H), 7.55 (dt, J=8.7, 3.5 Hz, 1H), 7.22 (dd, J=10.3, 8.4 Hz, 1H), 7.14 (t, J=9.4 Hz, 1H), 7.09 (d, J=8.8 Hz, 1H), 6.82 (br d, J=3.3 Hz, 1H), 5.27 (t, J=7.3 Hz, 1H), 4.72 - 4.63 (m, 1H), 4.11 (s, 3H), 3.13 - 3.07 (m, 2H), 3.06 (d, J=5.0 Hz, 3H), 2.73 (t, J=3.7 Hz, 1H), 2.16 - 2.08 (m, 3H), 1.91 - 1.84 (m, 1H), 1.68 - 1.53 (m, 2H), 1.04 (t, J=7.6 Hz, 3H)	1.20, A
157		N3'-(環丙烷磺醯基)-6'- 氟 -N3-[(2R,3S)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-丙烷-2-亞基)雙環[2.2.1]庚烷-2-基]-4- 甲 氧 基 -[1,1'- 聯 苯]-3,3'-二甲醯胺	732.2	-	1.18, B

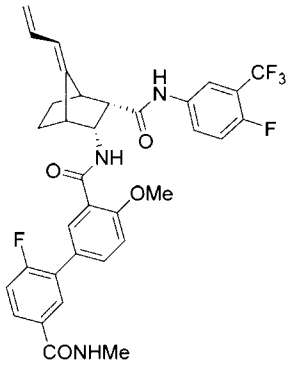
158		6-氟-3'-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(丙-2-烯-1-亞基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-3-甲酸	627.2	(500 MHz, $CDCl_3$) δ 9.43 (br d, J=8.3 Hz, 1H), 8.43 (br s, 1H), 8.25 (br d, J=6.6 Hz, 1H), 8.11 - 7.94 (m, 3H), 7.72 (br d, J=8.8 Hz, 1H), 7.51 (br d, J=8.3 Hz, 1H), 7.26 - 7.21 (m, 1H), 7.10 - 7.03 (m, 2H), 6.59 - 6.45 (m, 1H), 5.95 (br d, J=10.7 Hz, 1H), 5.23 (br d, J=16.5 Hz, 1H), 5.12 (br d, J=9.1 Hz, 1H), 4.92 - 4.83 (m, 1H), 4.07 (s, 3H), 3.31 - 3.23 (m, 1H), 3.19 - 3.13 (m, 1H), 2.87 - 2.80 (m, 1H), 2.40 - 2.33 (m, 1H), 1.96 - 1.90 (m, 1H), 1.71 - 1.64 (m, 2H)	1.15, A
159		6-氟-3'-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-[(呋喃-3-基)亞甲基]雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-3-甲酸	667.2	-	1.17, A

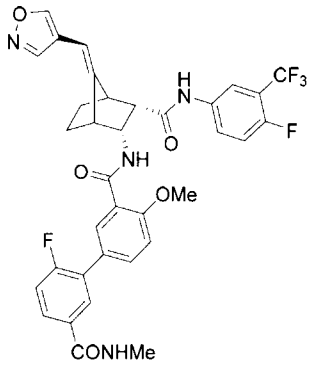
160		6'- 氟 -N3-[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-[(1,2-噁唑-4-基)亞甲基]雙環[2.2.1]庚烷-2-基]-4- 甲氧基-[1,1'- 聯苯]-3,3'-二甲醯胺	667.2	(500 MHz, $CDCl_3$) δ 9.68 (br d, J=7.4 Hz, 1H), 8.47 (s, 1H), 8.42 - 8.33 (m, 2H), 8.00 (br d, J=3.6 Hz, 1H), 7.94 (br dd, J=7.3, 2.1 Hz, 2H), 7.87 - 7.78 (m, 1H), 7.71 (br d, J=8.5 Hz, 1H), 7.60 - 7.52 (m, 1H), 7.27 - 7.20 (m, 1H), 7.14 (t, J=9.2 Hz, 1H), 7.09 (d, J=8.8 Hz, 1H), 6.04 (s, 1H), 4.90 - 4.80 (m, 1H), 4.10 (s, 3H), 3.33 - 3.27 (m, 1H), 3.20 (dd, J=10.7, 3.9 Hz, 1H), 2.96 - 2.89 (m, 1H), 2.33 - 2.24 (m, 1H), 2.05 - 1.95 (m, 1H), 1.76 - 1.66 (m, 2H)	1.08, A

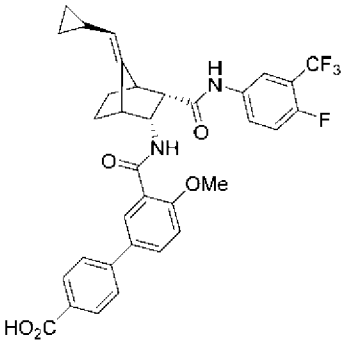
161		N3-[(2R,3S,7Z)-7-(溴亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]-6'-氟-N3'-甲磺醯基-4-甲氧基-[1,1'-聯苯]-3,3'-二甲醯胺	756.1	(400 MHz, $CDCl_3$) δ 10.85 - 10.61 (m, 1H), 9.93 (d, J=7.7 Hz, 1H), 8.43 (s, 1H), 8.34 (d, J=1.3 Hz, 1H), 8.15 (dd, J=6.2, 2.4 Hz, 1H), 8.09 (dd, J=7.3, 2.2 Hz, 1H), 7.91 (ddd, J=8.5, 4.5, 2.2 Hz, 1H), 7.76 (br d, J=8.8 Hz, 1H), 7.61 (dt, J=8.6, 3.5 Hz, 1H), 7.25 - 7.15 (m, 2H), 7.11 (d, J=8.8 Hz, 1H), 5.74 (s, 1H), 4.47 - 4.33 (m, 1H), 4.10 (s, 3H), 3.49 (s, 3H), 3.18 (br s, 1H), 3.09 (dd, J=10.8, 4.0 Hz, 1H), 2.83 (br s, 1H), 2.15 - 2.10 (m, 1H), 1.95 - 1.83 (m, 1H), 1.68 - 1.55 (m, 2H)	1.14, A

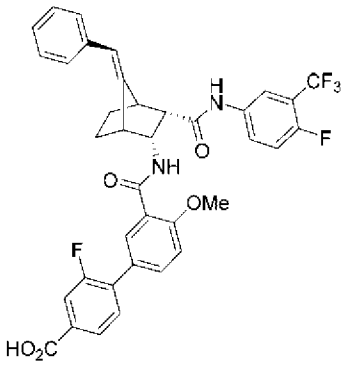
162		6'-氟-N3-[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(丙-2-烯-1-亞基)雙環[2.2.1]庚烷-2-基]-N3'-甲磺醯基-4-甲氧基-[1,1'-聯苯]-3,3'-二甲醯胺	704.3	(400 MHz, $CDCl_3$) δ 10.41 (br s, 1H), 10.00 (br d, J=7.7 Hz, 1H), 8.36 (d, J=1.5 Hz, 1H), 8.16 (s, 1H), 8.11 (dd, J=6.1, 2.1 Hz, 1H), 8.05 (dd, J=7.2, 1.9 Hz, 1H), 7.92 (ddd, J=6.3, 4.3, 2.1 Hz, 1H), 7.75 (br d, J=8.6 Hz, 1H), 7.63 - 7.58 (m, 1H), 7.27 - 7.13 (m, 2H), 7.11 (d, J=8.8 Hz, 1H), 6.42 (dt, J=16.9, 10.5 Hz, 1H), 5.77 (d, J=10.8 Hz, 1H), 5.24 - 5.11 (m, 2H), 4.48 - 4.38 (m, 1H), 4.11 (s, 3H), 3.48 (s, 3H), 3.20 - 3.12 (m, 1H), 3.06 (br dd, J=10.5, 4.1 Hz, 1H), 2.74 - 2.70 (m, 1H), 2.15 - 2.10 (m, 1H), 1.94 - 1.86 (m, 1H), 1.64 - 1.51 (m, 2H)	1.16, A

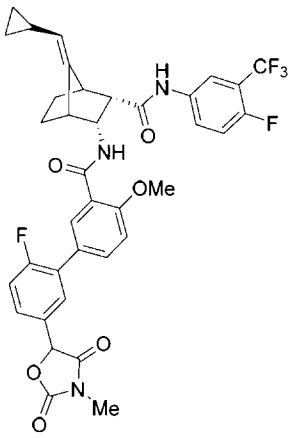
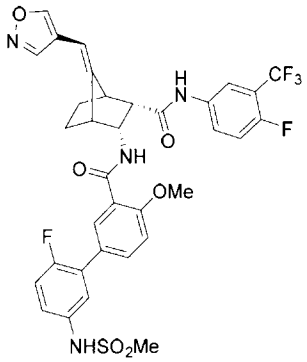
163		6'-氟-N3-[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(丙-2-烯-1-亞基)雙環[2.2.1]庚烷-2-基]-4-甲氧基-[1,1'-聯苯]-3,3'-二甲醯胺	626.3	(400 MHz, $CDCl_3$) δ 9.61 (br d, J=7.7 Hz, 1H), 8.41 (d, J=1.8 Hz, 1H), 8.02 - 7.90 (m, 3H), 7.86 (ddd, J=8.4, 4.7, 2.3 Hz, 1H), 7.73 (dt, J=8.5, 2.1 Hz, 1H), 7.56 (dt, J=8.3, 3.6 Hz, 1H), 7.26 (dd, J=10.0, 8.5 Hz, 1H), 7.17 - 7.07 (m, 2H), 6.53 (dt, J=16.9, 10.6 Hz, 1H), 5.95 (d, J=10.8 Hz, 1H), 5.24 (dd, J=16.8, 1.2 Hz, 1H), 5.17 - 5.11 (m, 1H), 4.85 - 4.73 (m, 1H), 4.10 (s, 3H), 3.31 - 3.23 (m, 1H), 3.13 (dd, J=10.8, 3.7 Hz, 1H), 2.85 - 2.80 (m, 1H), 2.31 - 2.21 (m, 1H), 1.99 - 1.93 (m, 1H), 1.72 - 1.63 (m, 2H)	1.15, A

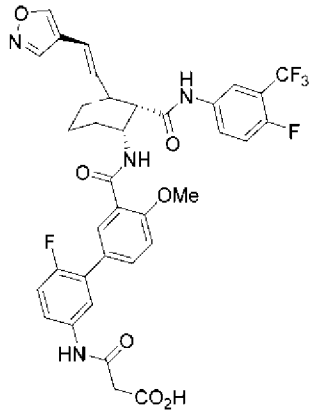
164		6'-氟-N3-[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(丙-2-烯-1-亞基)雙環[2.2.1]庚烷-2-基]-4-甲氧基-N3'-甲基-[1,1'-聯苯]-3,3'-二甲醯胺	640.2	(400 MHz, $CDCl_3$) δ 9.84 (br d, J=7.7 Hz, 1H), 8.40 (d, J=2.2 Hz, 1H), 8.00 (dd, J=6.2, 2.4 Hz, 1H), 7.91 - 7.81 (m, 3H), 7.75 (dt, J=8.6, 2.2 Hz, 1H), 7.57 (dt, J=8.6, 3.2 Hz, 1H), 7.23 (dd, J=10.2, 8.5 Hz, 1H), 7.15 (t, J=9.4 Hz, 1H), 7.10 (d, J=8.6 Hz, 1H), 6.65 - 6.47 (m, 2H), 5.95 (d, J=10.8 Hz, 1H), 5.25 (dd, J=16.8, 1.2 Hz, 1H), 5.18 - 5.11 (m, 1H), 4.81 - 4.70 (m, 1H), 4.11 (s, 3H), 3.31 - 3.25 (m, 1H), 3.16 - 3.09 (m, 1H), 3.06 (d, J=4.8 Hz, 3H), 2.85 - 2.81 (m, 1H), 2.21 - 2.16 (m, 1H), 1.98 - 1.91 (m, 1H), 1.72 - 1.61 (m, 2H)	1.17, A

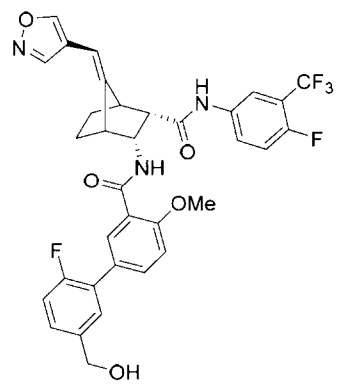
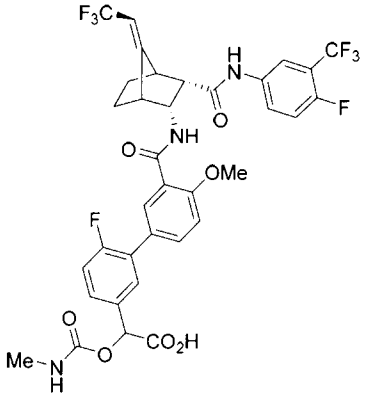
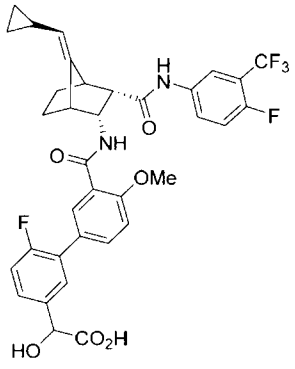
165		6'-氟-N3-[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-[(1,2-噁唑-4-基)亞甲基]雙環[2.2.1]庚烷-2-基]-4-甲氧基-N3'-甲基-[1,1'-聯苯]-3,3'-二甲醯胺	681.2	(500 MHz, $CDCl_3$) δ 9.93 (br d, J=7.2 Hz, 1H), 8.46 (s, 1H), 8.38 (br s, 2H), 8.15 - 7.98 (m, 2H), 7.86 (dd, J=7.3, 2.3 Hz, 1H), 7.80 (ddd, J=8.5, 4.6, 2.3 Hz, 1H), 7.72 (br d, J=8.3 Hz, 1H), 7.63 - 7.56 (m, 1H), 7.23 - 7.11 (m, 2H), 7.08 (br d, J=9.1 Hz, 1H), 6.59 (br s, 1H), 6.02 (s, 1H), 4.86 - 4.69 (m, 1H), 4.46 - 4.46 (m, 1H), 4.10 (s, 3H), 3.33 - 3.27 (m, 1H), 3.19 (dd, J=10.7, 4.1 Hz, 1H), 3.04 (br d, J=4.1 Hz, 3H), 2.91 (br s, 1H), 2.23 (br t, J=8.4 Hz, 1H), 2.01 (br t, J=8.8 Hz, 1H), 1.73 - 1.64 (m, 2H)	1.12, A

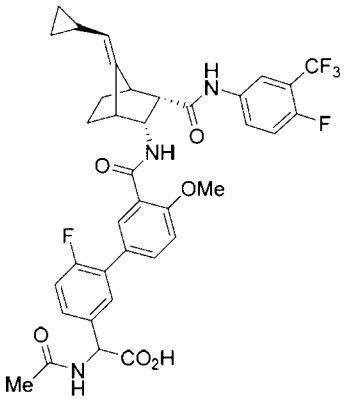
167		3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-4-甲酸	623.2	(500 MHz, $CDCl_3$) δ 9.51 (d, J=8.3 Hz, 1H), 8.52 (d, J=2.5 Hz, 1H), 8.17 (d, J=8.5 Hz, 2H), 7.94 (dd, J=6.2, 2.6 Hz, 1H), 7.84 (s, 1H), 7.75 (dd, J=8.5, 2.5 Hz, 1H), 7.71 (d, J=8.3 Hz, 2H), 7.56 (dt, J=8.7, 3.3 Hz, 1H), 7.10 (d, J=8.8 Hz, 2H), 4.92 - 4.83 (m, 1H), 4.67 (d, J=9.6 Hz, 1H), 4.08 (s, 3H), 3.24 (t, J=4.0 Hz, 1H), 3.12 (dd, J=10.7, 3.0 Hz, 1H), 2.74 (t, J=3.9 Hz, 1H), 2.25 - 2.18 (m, 1H), 1.94 - 1.87 (m, 1H), 1.74 - 1.60 (m, 2H), 1.56 - 1.47 (m, 1H), 0.81 - 0.71 (m, 2H), 0.37 (dt, J=2.9, 1.6 Hz, 2H)	1.17, A

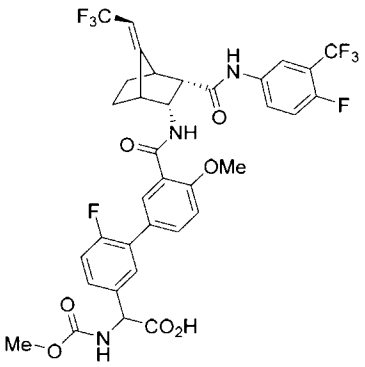
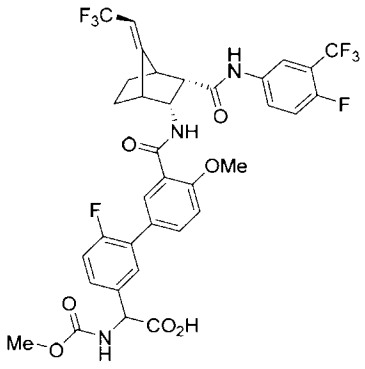
169		2-氟-3'-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(苯基亞甲基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-4-甲酸	677.1	(500 MHz, DMSO-d6) δ 10.69 (s, 1H), 10.06 (br d, J=6.7 Hz, 1H), 8.28 (br d, J=4.6 Hz, 1H), 8.20 (s, 1H), 7.85 (br d, J=7.6 Hz, 2H), 7.82 - 7.72 (m, 2H), 7.63 (br t, J=7.9 Hz, 1H), 7.52 (br t, J=9.8 Hz, 1H), 7.44 - 7.34 (m, 5H), 7.29 (br d, J=4.3 Hz, 1H), 6.41 (s, 1H), 4.56 (br s, 1H), 4.09 (s, 3H), 3.57 (br s, 1H), 3.42 (br s, 1H), 3.38 - 3.27 (m, 1H), 3.20 (s, 1H), 2.96 (br s, 1H), 2.59 - 2.56 (m, 6H), 2.02 - 1.84 (m, 2H), 1.56 (br s, 2H), 1.24 (s, 1H)	2.59, C

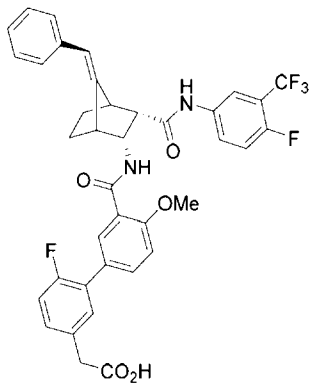
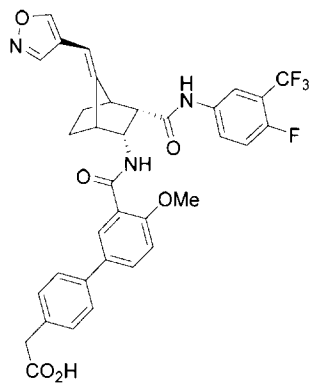
173		N-[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]-2'-氟-4-甲氧基-5'-(3-甲基-2,4-二側氧基-1,3-噁唑啶-5-基)-[1,1'-聯苯]-3-甲醯胺	710.4	(500 MHz, $CDCl_3$) δ 9.45 (br d, J=8.0 Hz, 1H), 8.38 (d, J=1.4 Hz, 1H), 7.97 (dd, J=6.2, 2.6 Hz, 1H), 7.86 (s, 1H), 7.66 (dt, J=8.5, 2.1 Hz, 1H), 7.53 (dd, J=6.9, 2.5 Hz, 2H), 7.40 (ddd, J=8.4, 4.3, 2.2 Hz, 1H), 7.25 (dd, J=9.9, 8.8 Hz, 1H), 7.14 - 7.05 (m, 2H), 5.79 (s, 1H), 4.91 - 4.81 (m, 1H), 4.66 (d, J=9.4 Hz, 1H), 4.07 (s, 3H), 3.22 (t, J=4.1 Hz, 1H), 3.18 (s, 3H), 3.11 (dd, J=10.5, 3.3 Hz, 1H), 2.74 (t, J=3.9 Hz, 1H), 2.25 - 2.18 (m, 1H), 1.94 - 1.86 (m, 1H), 1.55 - 1.49 (m, 1H)	1.20, A
174		2'-氟-N-[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-[(1,2-噁唑-4-基)亞甲基]雙環[2.2.1]庚烷-2-基]-5'-甲磺醯胺基-4-甲氧基-[1,1'-聯苯]-3-甲醯胺	717.1	(500 MHz, DMSO-d6) δ 10.47 (s, 1H), 9.89 (br d, J=7.2 Hz, 1H), 8.96 (s, 1H), 8.69 (s, 1H), 8.21 - 8.14 (m, 1H), 8.11 (s, 1H), 7.86 - 7.75 (m, 1H), 7.67 (br dd, J=9.4, 1.1 Hz, 1H), 7.45 (t, J=9.8 Hz, 1H), 7.34 - 7.20 (m, 4H), 6.13 (s, 1H), 4.58 - 4.42 (m, 1H), 4.05 (s, 3H), 3.87 (s, 1H), 3.18 (d, J=5.2 Hz, 1H), 2.98 (s, 3H), 2.93 (br s, 1H), 2.02 - 1.84 (m, 2H), 1.64 - 1.45 (m, 2H)	2.40, C

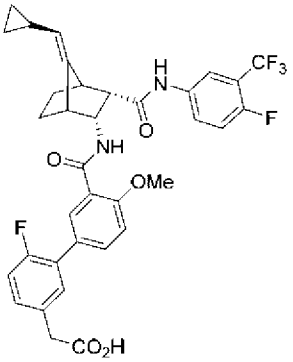
175		2-[(6-氟-3'-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-[(1,2-噁唑-4-基)亞甲基]雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-3-基)胺甲醯基]乙酸	725.3	(500 MHz, DMSO-d6) δ 10.50 (s, 1H), 9.90 (d, J=7.2 Hz, 1H), 8.98 (s, 1H), 8.71 (s, 1H), 8.20 (br d, J=5.0 Hz, 1H), 8.14 (s, 1H), 7.83 (br s, 1H), 7.75 (br d, J=5.0 Hz, 1H), 7.68 (br d, J=8.6 Hz, 1H), 7.54 (br d, J=8.5 Hz, 1H), 7.47 (t, J=9.8 Hz, 1H), 7.32 (d, J=8.7 Hz, 1H), 7.23 (t, J=9.7 Hz, 1H), 6.14 (s, 1H), 4.55 (br s, 1H), 4.07 (s, 3H), 3.34 - 3.23 (m, 1H), 3.19 (s, 2H), 2.94 (br s, 1H), 2.57 - 2.53 (m, 10H), 2.00 (br t, J=10.2 Hz, 1H), 1.92 (s, 2H), 1.63 - 1.47 (m, 2H), 1.18 (s, 1H)	2.29, C

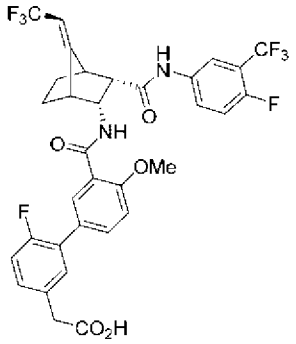
176		2'-氟-N-[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-[(1,2-噁唑-4-基)亞甲基]雙環[2.2.1]庚烷-2-基]-5'-(羥基甲基)-4-甲氧基-[1,1'-聯苯]-3-甲醯胺	654.3	(500 MHz, DMSO-d6) δ 10.47 (s, 1H), 9.90 (br d, J=7.2 Hz, 1H), 8.97 (s, 1H), 8.70 (s, 1H), 8.23 - 8.13 (m, 2H), 8.00 - 7.79 (m, 1H), 7.70 (br d, J=8.7 Hz, 1H), 7.53 - 7.38 (m, 2H), 7.35 - 7.28 (m, 2H), 7.23 (dd, J=10.8, 8.5 Hz, 1H), 6.15 (s, 1H), 4.54 (br d, J=4.0 Hz, 3H), 4.07 (s, 3H), 3.19 (br s, 2H), 2.94 (br s, 1H), 2.58 - 2.53 (m, 8H), 2.07 - 1.96 (m, 1H), 1.96 - 1.86 (m, 2H), 1.55 (br t, J=13.9 Hz, 2H)	2.41, C
180		2-(6-氟-3'-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-3-基)-2-[(甲基胺甲醯基)氧基]乙酸	756.3	-	1.11, A
181		2-(3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2-羥基乙酸	671.2	-	1.14, A

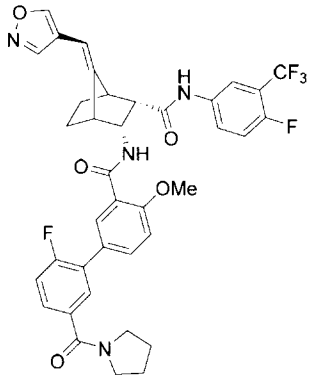
184		2-(3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2-乙醯胺基乙酸	712.2	(500 MHz, $CDCl_3$) δ 10.11 (d, J=7.4 Hz, 1H), 8.66 (br d, J=8.8 Hz, 1H), 8.48 (d, J=2.2 Hz, 1H), 7.99 (dd, J=6.1, 2.5 Hz, 1H), 7.82 (dt, J=8.5, 2.5 Hz, 1H), 7.74 (dd, J=7.4, 2.2 Hz, 1H), 7.65 (s, 1H), 7.53 (dt, J=8.8, 3.4 Hz, 1H), 7.42 (ddd, J=8.3, 4.4, 2.2 Hz, 1H), 7.13 (t, J=9.4 Hz, 1H), 7.08 (dd, J=10.7, 8.3 Hz, 1H), 7.02 (d, J=8.8 Hz, 1H), 5.97 (d, J=9.4 Hz, 1H), 4.70 - 4.62 (m, 2H), 4.08 (s, 3H), 3.14 - 3.10 (m, 1H), 3.04 (dd, J=10.7, 4.1 Hz, 1H), 2.69 (br s, 1H), 2.09 (s, 3H), 2.05 - 2.00 (m, 1H), 1.85 - 1.79 (m, 1H), 1.61 - 1.47 (m, 3H), 0.90 - 0.78 (m, 2H), 0.43 - 0.35 (m, 2H)	1.10, A

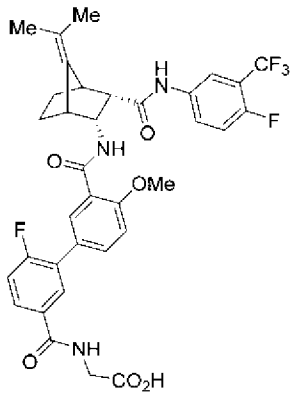
185		2-(6-氟-3'-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-3-基)-2-[(甲氧基羰基)胺基]乙酸	756.3	(500 MHz, $CDCl_3$) δ 9.75 (br d, J=8.0 Hz, 1H), 8.40 (br s, 1H), 8.08 (br s, 1H), 7.98 (dd, J=6.1, 2.2 Hz, 1H), 7.76 (br d, J=8.5 Hz, 1H), 7.67 (br d, J=5.8 Hz, 1H), 7.50 - 7.42 (m, 2H), 7.15 - 7.05 (m, 2H), 7.05 - 6.94 (m, 2H), 5.63 - 5.53 (m, 2H), 4.86 - 4.76 (m, 1H), 4.06 (s, 3H), 3.67 (s, 3H), 3.34 (br s, 1H), 3.15 (dd, J=10.7, 4.1 Hz, 1H), 2.89 (br s, 1H), 2.36 (br d, J=11.3 Hz, 1H), 2.00 - 1.89 (m, 1H), 1.70 - 1.60 (m, 2H)	1.10, A
186		2-(6-氟-3'-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-3-基)-2-[(甲氧基羰基)胺基]乙酸	756.3	-	1.11, A

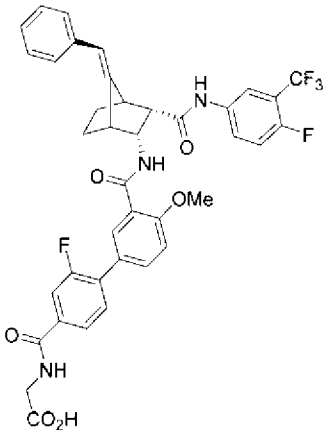
187		2-(6-氟-3'-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(苯基亞甲基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-3-基)乙酸	691.3	(500 MHz, DMSO-d6) δ 10.50 (s, 1H), 9.93 (d, J=7.1 Hz, 1H), 8.22 (dd, J=6.3, 2.2 Hz, 1H), 8.14 (s, 1H), 7.89 - 7.80 (m, 1H), 7.69 (br d, J=8.5 Hz, 1H), 7.48 (t, J=9.8 Hz, 1H), 7.43 - 7.36 (m, 5H), 7.34 - 7.19 (m, 4H), 6.40 (s, 1H), 4.62 - 4.52 (m, 1H), 4.07 (s, 3H), 3.62 - 3.56 (m, 1H), 3.46 - 3.38 (m, 1H), 2.98 - 2.92 (m, 1H), 2.07 - 1.87 (m, 2H), 1.63 - 1.49 (m, 2H)	2.64, C
188		2-(3'-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-[(1,2-噁唑-4-基)亞甲基]雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-4-基)乙酸	664.2	(500 MHz, DMSO-d6) δ 10.46 (br s, 1H), 9.87 (br d, J=6.7 Hz, 1H), 8.98 (s, 1H), 8.71 (s, 1H), 8.27 - 8.18 (m, 2H), 7.88 - 7.77 (m, 2H), 7.57 (br d, J=7.5 Hz, 2H), 7.47 (br t, J=9.6 Hz, 1H), 7.35 (br d, J=7.5 Hz, 2H), 7.29 (br d, J=8.5 Hz, 1H), 6.15 (s, 1H), 4.56 (br s, 1H), 4.06 (s, 3H), 3.60 (s, 2H), 3.29 (br s, 1H), 2.95 (br s, 1H), 2.06 - 1.97 (m, 1H), 1.97 - 1.87 (m, 1H), 1.65 - 1.47 (m, 2H)	1.09, A

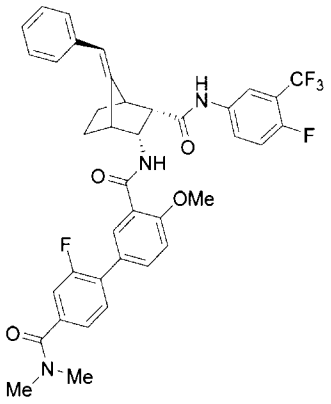
189		2-(3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)乙酸	655.2	(500 MHz, $CDCl_3$) δ 9.55 (d, J=8.0 Hz, 1H), 8.33 (d, J=1.9 Hz, 1H), 8.03 (s, 1H), 7.97 (dd, J=6.2, 2.6 Hz, 1H), 7.68 (dt, J=8.7, 2.0 Hz, 1H), 7.55 - 7.47 (m, 1H), 7.38 (dd, J=7.3, 2.3 Hz, 1H), 7.24 (ddd, J=8.2, 4.6, 2.3 Hz, 1H), 7.15 - 7.03 (m, 3H), 4.86 - 4.79 (m, 1H), 4.64 (d, J=9.4 Hz, 1H), 4.06 (s, 3H), 3.70 (s, 2H), 3.22 - 3.18 (m, 1H), 3.13 - 3.07 (m, 1H), 2.74 - 2.71 (m, 1H), 2.26 - 2.19 (m, 1H), 1.93 - 1.86 (m, 1H), 1.73 - 1.58 (m, 2H), 1.53 - 1.44 (m, 1H), 0.79 - 0.71 (m, 2H), 0.39 - 0.32 (m, 2H)	1.17

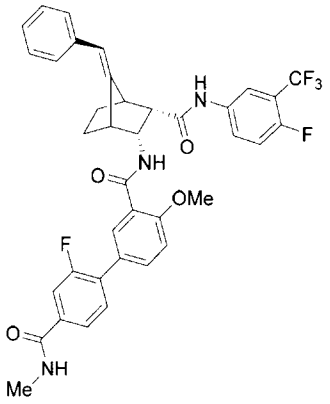
190		2-(6-氟-3'-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-3-基)乙酸	655.2	(500 MHz, $CDCl_3$) δ 9.41 (br d, J=8.3 Hz, 1H), 8.37 (s, 1H), 8.30 (d, J=1.9 Hz, 1H), 7.95 (dd, J=6.2, 2.6 Hz, 1H), 7.67 (dt, J=8.5, 2.1 Hz, 1H), 7.45 (dt, J=8.7, 3.3 Hz, 1H), 7.34 (dd, J=7.4, 2.2 Hz, 1H), 7.26 - 7.21 (m, 1H), 7.10 (dd, J=10.3, 8.4 Hz, 1H), 7.06 - 6.99 (m, 2H), 5.57 (q, J=7.4 Hz, 1H), 4.94 - 4.85 (m, 1H), 4.05 (s, 3H), 3.69 (s, 2H), 3.39 (br s, 1H), 3.18 (dd, J=10.6, 3.4 Hz, 1H), 2.91 (br t, J=3.9 Hz, 1H), 2.49 - 2.42 (m, 1H), 2.02 - 1.95 (m, 1H), 1.79 - 1.67 (m, 2H)	1.17, A

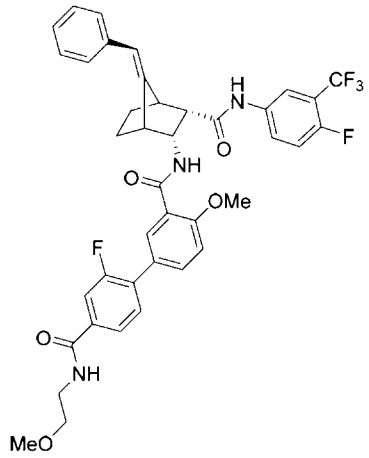
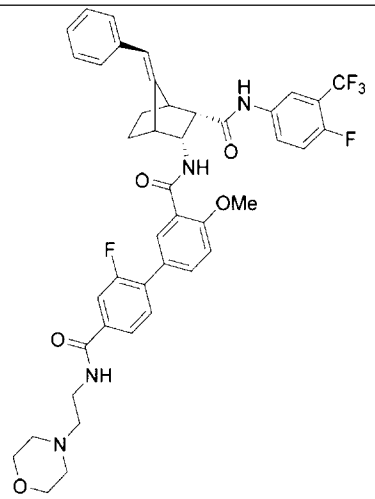
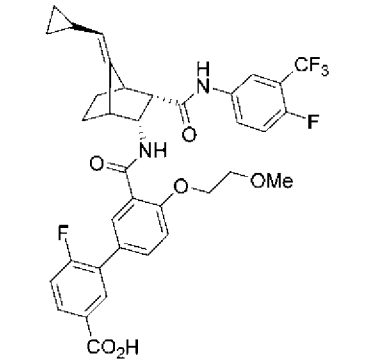
191		2'-氟-N-[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-[(1,2-噁唑-4-基)亞甲基]雙環[2.2.1]庚烷-2-基]-4-甲氧基-5'-(吡咯啶-1-羰基)-[1,1'-聯苯]-3-甲醯胺	721.1	(500 MHz, DMSO-d6) δ 10.48 (s, 1H), 9.89 (br d, J=7.2 Hz, 1H), 8.97 (s, 1H), 8.70 (s, 1H), 8.20 (d, J=6.7 Hz, 1H), 8.16 (s, 1H), 7.83 (br d, J=8.5 Hz, 1H), 7.73 (br d, J=8.5 Hz, 1H), 7.62 (br d, J=7.7 Hz, 1H), 7.55 (t, J=6.8 Hz, 1H), 7.47 (t, J=9.8 Hz, 1H), 7.40 - 7.27 (m, 2H), 6.14 (s, 1H), 4.54 (br s, 1H), 4.07 (s, 3H), 3.48 (br s, 3H), 3.19 (s, 1H), 2.94 (br s, 1H), 2.58 - 2.53 (m, 5H), 2.07 - 1.96 (m, 1H), 1.95 - 1.89 (m, 2H), 1.86 (br s, 4H), 1.55 (br t, J=14.2 Hz, 2H)	2.38

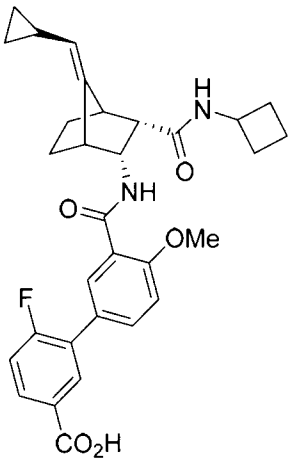
193		2-[(6-氟-3'-{[(2R,3S)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-丙烷-2-亞基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-3-基)甲醯胺基]乙酸	686.1	(500 MHz, DMSO-d6) δ 10.56 (s, 1H), 9.94 (br d, J=7.0 Hz, 1H), 8.97 (br s, 1H), 8.31 - 8.14 (m, 2H), 8.05 (br d, J=7.0 Hz, 1H), 7.91 (br s, 1H), 7.83 (br d, J=7.9 Hz, 1H), 7.77 (br d, J=8.5 Hz, 1H), 7.50 (t, J=9.0 Hz, 1H), 7.44 (t, J=9.0 Hz, 1H), 7.34 (d, J=8.5 Hz, 1H), 4.40 (br s, 1H), 4.07 (s, 3H), 3.99 - 3.88 (m, 2H), 3.19 - 3.10 (m, 1H), 3.06 (br s, 1H), 2.97 (br s, 1H), 2.57 - 2.54 (m, 6H), 1.86 (br t, J=9.2 Hz, 1H), 1.75 (br d, J=11.3 Hz, 6H), 1.38 (br d, J=5.8 Hz, 2H)	2.37, C

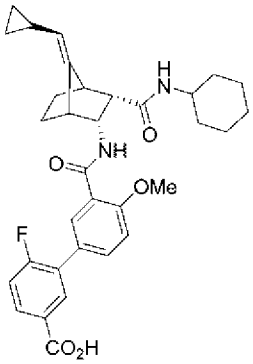
194		2-[(2-氟-3'-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(苯基亞甲基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-4-基)甲醯胺基]乙酸	734.1	(500 MHz, DMSO-d6) δ 10.57 (s, 1H), 9.94 (br d, J=7.1 Hz, 1H), 8.28 (br s, 1H), 8.26 - 8.05 (m, 2H), 7.85 (br s, 2H), 7.80 - 7.70 (m, 3H), 7.62 (br t, J=8.1 Hz, 1H), 7.48 (br t, J=9.6 Hz, 1H), 7.39 (d, J=4.1 Hz, 3H), 7.33 (d, J=8.7 Hz, 1H), 7.30 - 7.18 (m, 1H), 6.40 (s, 1H), 4.58 (br s, 1H), 4.08 (s, 3H), 3.90 (s, 1H), 3.72 (br s, 2H), 3.43 (br s, 1H), 2.96 (br s, 1H), 2.70 - 2.54 (m, 1H), 2.00 (br d, J=10.0 Hz, 1H), 1.97 - 1.76 (m, 2H), 1.56 (br s, 2H), 1.25 (br s, 2H), 0.87 (br s, 1H)	2.53, C

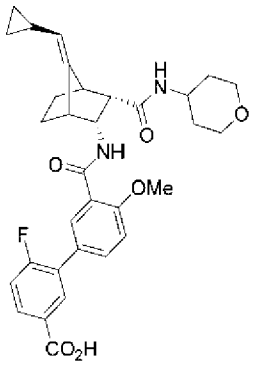
195		2'-氟-N3-[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(苯基亞甲基)雙環[2.2.1]庚烷-2-基]-4-甲氧基-N4',N4'-二甲基-[1,1'-聯苯]-3,4'-二甲醯胺	704.1	(500 MHz, DMSO-d6) δ 10.49 (s, 1H), 9.90 (br d, J=7.1 Hz, 1H), 8.21 - 8.10 (m, 2H), 7.79 (br s, 1H), 7.72 (br d, J=8.7 Hz, 1H), 7.55 (t, J=7.9 Hz, 1H), 7.49 - 7.40 (m, 1H), 7.37 (d, J=4.2 Hz, 4H), 7.34 - 7.23 (m, 4H), 6.38 (s, 1H), 4.55 (br s, 1H), 4.05 (s, 3H), 3.86 (s, 1H), 3.62 - 3.49 (m, 12H), 3.38 (br s, 1H), 3.29 (br dd, J=10.6, 3.9 Hz, 1H), 2.97 (br s, 5H), 2.93 (br s, 1H), 2.56 - 2.54 (m, 1H), 1.98 (br d, J=10.0 Hz, 1H), 1.90 (br d, J=10.1 Hz, 1H), 1.54 (br s, 2H), 1.22 (s, 1H)	2.58, C

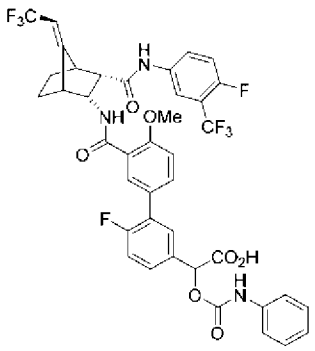
196		2'-氟-N3-[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(苯基亞甲基)雙環[2.2.1]庚烷-2-基]-4-甲氧基-N4'-甲基-[1,1'-聯苯]-3,4'-二甲醯胺	690.1	(500 MHz, DMSO-d6) δ 9.95 (br d, J=6.9 Hz, 1H), 8.48 (br d, J=4.4 Hz, 1H), 8.24 (br d, J=4.5 Hz, 1H), 8.19 (s, 1H), 7.97 - 7.82 (m, 1H), 7.80 - 7.71 (m, 3H), 7.62 (t, J=8.0 Hz, 1H), 7.50 - 7.37 (m, 5H), 7.33 (d, J=8.4 Hz, 1H), 7.27 (d, J=7.4 Hz, 1H), 6.40 (s, 1H), 4.57 (br s, 1H), 4.08 (s, 3H), 3.42 (br s, 1H), 3.35 (br dd, J=10.7, 4.3 Hz, 1H), 2.96 (br s, 1H), 2.83 (d, J=4.5 Hz, 3H), 2.65 - 2.54 (m, 1H), 2.00 (br d, J=9.9 Hz, 1H), 1.93 (br d, J=10.4 Hz, 1H), 1.72 (br s, 2H), 1.56 (br s, 2H), 1.25 (br s, 1H)	2.76, C

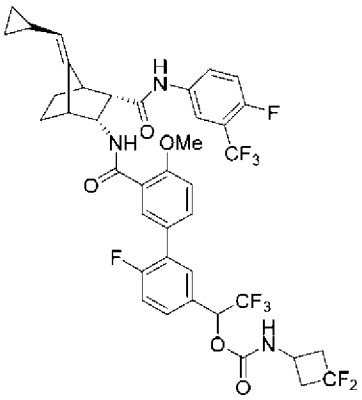
197		2'-氟-N3-[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(苯基亞甲基)雙環[2.2.1]庚烷-2-基]-4-甲氧基-N4'-(2-甲氧基乙基)-[1,1'-聯苯]-3,4'-二甲醯胺	734.1	(500 MHz, DMSO-d6) δ 9.94 (br d, J=7.0 Hz, 1H), 8.59 - 8.48 (m, 1H), 8.23 (d, J=6.9 Hz, 1H), 8.19 (s, 1H), 7.85 (br d, J=8.6 Hz, 1H), 7.81 - 7.73 (m, 3H), 7.62 (t, J=8.0 Hz, 1H), 7.48 (br t, J=9.8 Hz, 1H), 7.39 (d, J=4.2 Hz, 4H), 7.33 (d, J=8.7 Hz, 1H), 7.30 - 7.23 (m, 1H), 6.40 (s, 1H), 4.57 (br s, 1H), 4.08 (s, 3H), 3.55 - 3.39 (m, 4H), 3.38 - 3.25 (m, 1H), 2.96 (br s, 1H), 2.00 (br d, J=9.9 Hz, 1H), 1.97 - 1.88 (m, 1H), 1.56 (br s, 2H)	2.55, C
198		2'-氟-N3-[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(苯基亞甲基)雙環[2.2.1]庚烷-2-基]-4-甲氧基-N4'-[2-(味啉-4-基)乙基]-[1,1'-聯苯]-3,4'-二甲醯胺	789.1	-	2.90, C
200		3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-(2-甲氧基乙氧基)-[1,1'-聯苯]-3-甲酸	685.1	-	1.14, A

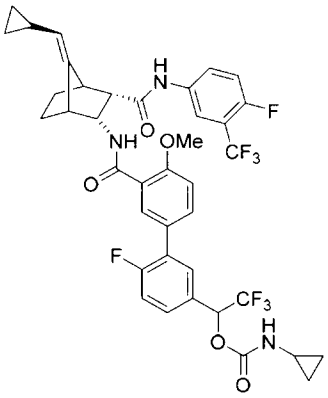
202		3'-{[(2R,3S,7Z)-3-(環丁基胺甲醯基)-7-(環丙基亞甲基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-甲酸	533.1	(500 MHz, DMSO-d6) δ 9.74 (br d, J=7.0 Hz, 1H), 8.10 (br d, J=7.6 Hz, 1H), 7.81 (s, 1H), 7.76 (br d, J=7.3 Hz, 1H), 7.69 (br d, J=18.3 Hz, 1H), 7.47 (br d, J=8.5 Hz, 1H), 7.16 (br t, J=9.5 Hz, 1H), 7.04 (d, J=8.9 Hz, 1H), 4.36 (d, J=9.8 Hz, 1H), 4.03 (br s, 1H), 3.98 - 3.92 (m, 1H), 3.76 (s, 2H), 2.79 (br s, 1H), 2.64 - 2.59 (m, 1H), 2.48 (s, 1H), 2.28 (br d, J=18.9 Hz, 9H), 1.90 (br s, 2H), 1.66 - 1.53 (m, 3H), 1.51 - 1.45 (m, 1H), 1.39 - 1.32 (m, 2H), 1.23 - 1.17 (m, 1H), 1.08 (br t, J=12.5 Hz, 2H), 0.45 (br t, J=8.1 Hz, 2H), 0.08 - 0.02 (m, 2H)	2.29, C

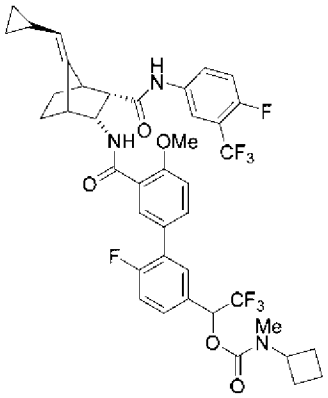
203		3'-{[(2R,3S,7Z)-3-(環己基胺甲醯基)-7-(環丙基亞甲基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-甲酸	561.2	(500 MHz, DMSO-d6) δ 10.00 (br d, J=6.7 Hz, 1H), 8.09 (s, 1H), 8.06 - 8.02 (m, 1H), 8.00 - 7.92 (m, 2H), 7.74 (br d, J=8.9 Hz, 1H), 7.44 (t, J=9.5 Hz, 1H), 7.30 (d, J=8.9 Hz, 1H), 4.61 (d, J=9.5 Hz, 1H), 4.35 - 4.26 (m, 1H), 4.03 (s, 3H), 3.65 - 3.53 (m, 1H), 3.05 (br s, 1H), 2.89 (br dd, J=10.8, 3.8 Hz, 1H), 1.89 (br t, J=9.8 Hz, 1H), 1.81 - 1.59 (m, 5H), 1.57 - 1.43 (m, 2H), 1.41 - 1.18 (m, 4H), 1.12 (br d, J=8.9 Hz, 3H), 0.71 (quin, J=9.5 Hz, 2H), 0.32 (br d, J=2.1 Hz, 2H)	2.38, C

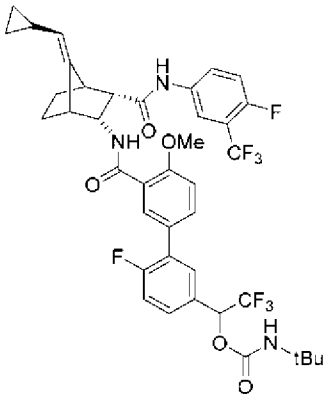
204		3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-[(噁烷-4-基)胺甲醯基]雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-甲酸	563.4	(500 MHz, DMSO-d6) δ 9.99 (br d, J=7.0 Hz, 1H), 8.12 - 8.06 (m, 2H), 8.06 - 8.01 (m, 1H), 8.00 - 7.94 (m, 1H), 7.74 (br d, J=8.5 Hz, 1H), 7.44 (t, J=9.6 Hz, 1H), 7.30 (d, J=8.5 Hz, 1H), 4.62 (d, J=9.8 Hz, 1H), 4.32 (br s, 1H), 4.03 (s, 3H), 3.79 (br t, J=10.2 Hz, 3H), 3.40 - 3.27 (m, 2H), 3.05 (br s, 1H), 2.90 (br dd, J=10.8, 3.8 Hz, 1H), 1.90 - 1.82 (m, 1H), 1.81 - 1.73 (m, 1H), 1.73 - 1.62 (m, 2H), 1.52 - 1.43 (m, 1H), 1.42 - 1.28 (m, 4H), 0.71 (quin, J=9.3 Hz, 2H), 0.32 (br d, J=2.4 Hz, 2H)	2.02, C

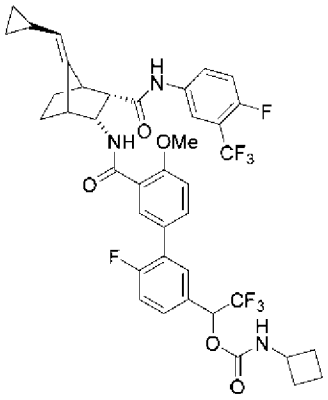
205		2-(6-氟-3'-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-3-基)-2-[(苯基胺甲醯基)氧基]乙酸	818.6	(500 MHz, $CDCl_3$) δ 9.58 (br d, *J*=8.5 Hz, 1H), 8.37 (br s, 1H), 8.26 (br s, 1H), 7.98 (dd, *J*=5.9, 2.3 Hz, 1H), 7.68 (br d, *J*=8.5 Hz, 1H), 7.62 (br d, *J*=5.5 Hz, 1H), 7.48 - 7.36 (m, 5H), 7.31 - 7.26 (m, 2H), 7.12 - 7.01 (m, 4H), 6.10 (s, 1H), 5.43 (q, *J*=7.3 Hz, 1H), 4.92 - 4.83 (m, 1H), 4.05 (s, 3H), 3.33 (br s, 1H), 3.15 (br dd, *J*=10.6, 3.4 Hz, 1H), 2.81 (br s, 1H), 2.50 - 2.43 (m, 1H), 2.01 - 1.95 (m, 2H), 1.73 - 1.62 (m, 2H)	1.13, A

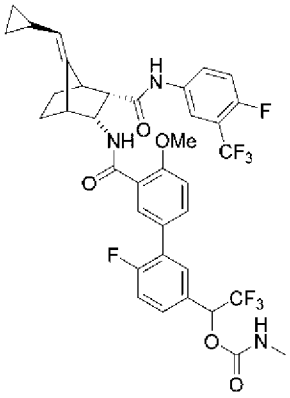
207		N-(3,3-二氟環丁基)胺基甲酸1-(3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2,2,2-三氟乙酯	828.5	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.94 (br d, J=7.4 Hz, 1H), 8.40 (br d, J=6.7 Hz, 1H), 8.21 (br d, J=3.2 Hz, 1H), 8.10 (br s, 1H), 7.77 (br dd, J=4.5, 2.9 Hz, 1H), 7.68 (br t, J=10.3 Hz, 2H), 7.53 (br d, J=4.4 Hz, 1H), 7.49 - 7.36 (m, 2H), 7.32 (d, J=8.8 Hz, 1H), 6.47 - 6.29 (m, 1H), 4.68 (d, J=9.7 Hz, 1H), 4.43 (br d, J=5.6 Hz, 1H), 4.04 (s, 3H), 3.91 - 3.81 (m, 1H), 3.19 - 3.12 (m, 1H), 3.09 (br s, 1H), 2.94 - 2.78 (m, 2H), 2.71 (br s, 1H), 2.63 - 2.54 (m, 2H), 1.89 - 1.72 (m, 2H), 1.55 - 1.32 (m, 3H), 0.79 - 0.65 (m, 2H), 0.40 - 0.27 (m, 2H)	1.24, A

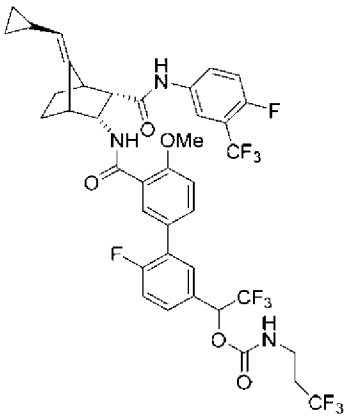
208		N-環丙基胺基甲酸 1-(3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2,2,2-三氟乙酯	778.4	(400 MHz, CDCl3) δ 9.66 (br d, J=7.7 Hz, 1H), 8.38 (d, J=1.5 Hz, 1H), 7.97 (dd, J=6.2, 2.6 Hz, 1H), 7.81 (s, 1H), 7.70 (br d, J=8.6 Hz, 1H), 7.61 - 7.50 (m, 2H), 7.46 - 7.37 (m, 1H), 7.21 (br t, J=9.6 Hz, 1H), 7.15 - 7.06 (m, 2H), 6.18 - 6.08 (m, 1H), 5.30 (br s, 1H), 4.88 - 4.80 (m, 1H), 4.68 (d, J=9.5 Hz, 1H), 4.09 (s, 3H), 3.27 - 3.21 (m, 1H), 3.11 (dd, J=10.7, 3.9 Hz, 1H), 2.78 - 2.71 (m, 1H), 2.65 (br d, J=1.8 Hz, 1H), 1.97 - 1.86 (m, 1H), 1.75 - 1.60 (m, 2H), 1.56 - 1.46 (m, 1H), 0.82 - 0.72 (m, 4H), 0.67 - 0.55 (m, 2H), 0.41 - 0.32 (m, 2H)	1.23, A

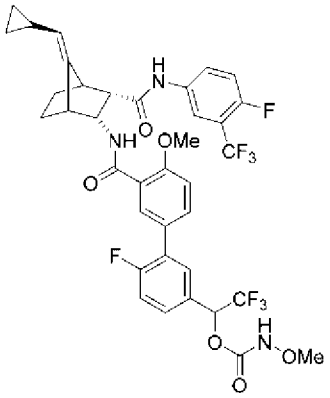
209		N-環丁基-N-甲基胺基甲酸1-(3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2,2,2-三氟乙酯	806.3	(500 MHz, DMSO-d6) δ 10.52 (s, 1H), 9.91 (d, J=7.0 Hz, 1H), 8.22 (dd, J=6.4, 2.7 Hz, 1H), 8.12 (s, 1H), 7.82 - 7.75 (m, 1H), 7.69 (br d, J=7.9 Hz, 2H), 7.55 (br s, 1H), 7.50 - 7.36 (m, 2H), 7.32 (d, J=8.9 Hz, 1H), 6.47 - 6.35 (m, 1H), 4.69 (d, J=9.5 Hz, 1H), 4.50 - 4.34 (m, 2H), 4.05 (s, 3H), 3.16 (br dd, J=10.2, 3.8 Hz, 1H), 3.10 (br s, 1H), 2.97 - 2.76 (m, 3H), 2.72 (br s, 1H), 2.21 - 2.01 (m, 4H), 1.89 - 1.75 (m, 2H), 1.67 - 1.54 (m, 2H), 1.53 - 1.45 (m, 1H), 1.44 - 1.35 (m, 2H), 0.77 - 0.66 (m, 2H), 0.38 - 0.30 (m, 2H)	1.31, A

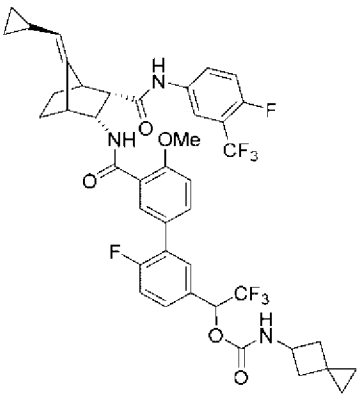
210		N-三級丁基胺基甲酸 1-(3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2,2,2-三氟乙酯	794.3	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.93 (br d, J=7.0 Hz, 1H), 8.22 (dd, J=6.4, 2.4 Hz, 1H), 8.12 (s, 1H), 7.81 - 7.75 (m, 1H), 7.72 - 7.66 (m, 2H), 7.59 (br s, 1H), 7.57 - 7.53 (m, 1H), 7.50 - 7.44 (m, 1H), 7.41 (br t, J=9.6 Hz, 1H), 7.33 (d, J=8.5 Hz, 1H), 6.37 - 6.27 (m, 1H), 4.69 (d, J=9.5 Hz, 1H), 4.49 - 4.41 (m, 1H), 4.05 (s, 3H), 3.16 (br dd, J=11.0, 4.3 Hz, 1H), 3.10 (br s, 1H), 2.72 (br s, 1H), 1.89 - 1.75 (m, 2H), 1.54 - 1.46 (m, 1H), 1.45 - 1.35 (m, 2H), 1.20 (s, 9H), 0.78 - 0.67 (m, 2H), 0.38 - 0.30 (m, 2H)	1.28, A

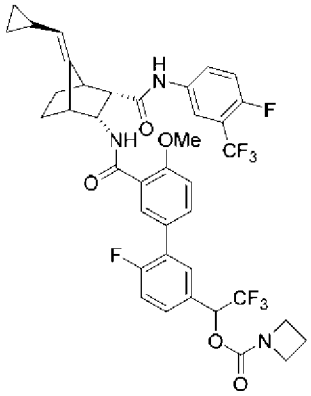
211		N-環丁基胺基甲酸 1-(3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2,2,2-三氟乙酯	792.5	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.93 (br d, J=6.7 Hz, 1H), 8.24 - 8.17 (m, 1H), 8.14 - 8.07 (m, 2H), 7.81 - 7.74 (m, 1H), 7.70 - 7.62 (m, 2H), 7.52 (br s, 1H), 7.48 - 7.37 (m, 2H), 7.32 (d, J=8.5 Hz, 1H), 6.35 - 6.28 (m, 1H), 4.68 (d, J=9.5 Hz, 1H), 4.48 - 4.40 (m, 1H), 4.04 (s, 3H), 3.95 - 3.86 (m, 1H), 3.19 - 3.12 (m, 1H), 3.09 (br s, 1H), 2.71 (br s, 1H), 2.17 - 2.04 (m, 2H), 1.96 - 1.74 (m, 4H), 1.62 - 1.52 (m, 2H), 1.52 - 1.46 (m, 1H), 1.44 - 1.34 (m, 2H), 0.78 - 0.65 (m, 2H), 0.39 - 0.27 (m, 2H)	1.25, A

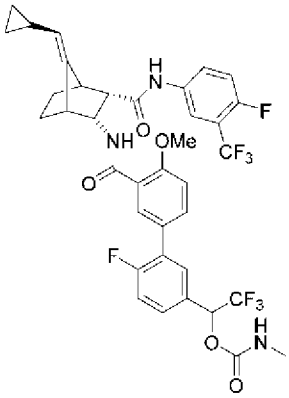
212		N-甲基胺基甲酸1-(3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2,2,2-三氟乙酯	752.4	(500 MHz, CDCl3) δ 9.92 (br d, J=8.0 Hz, 1H), 8.33 (d, J=1.9 Hz, 1H), 7.97 (dd, J=6.1, 2.5 Hz, 1H), 7.76 - 7.71 (m, 1H), 7.69 (s, 1H), 7.62 - 7.57 (m, 1H), 7.54 - 7.49 (m, 1H), 7.43 - 7.38 (m, 1H), 7.19 (dd, J=10.2, 8.5 Hz, 1H), 7.15 - 7.08 (m, 2H), 6.13 (q, J=6.8 Hz, 1H), 5.19 - 5.13 (m, 1H), 4.84 - 4.77 (m, 1H), 4.68 (d, J=9.6 Hz, 1H), 4.10 (s, 3H), 3.24 (t, J=4.0 Hz, 1H), 3.13 - 3.07 (m, 1H), 2.86 (d, J=4.7 Hz, 3H), 2.74 (t, J=4.1 Hz, 1H), 2.20 - 2.14 (m, 1H), 1.95 - 1.87 (m, 1H), 1.72 - 1.58 (m, 2H), 1.56 - 1.49 (m, 1H), 0.83 - 0.73 (m, 2H), 0.40 - 0.33 (m, 2H)	1.23, A

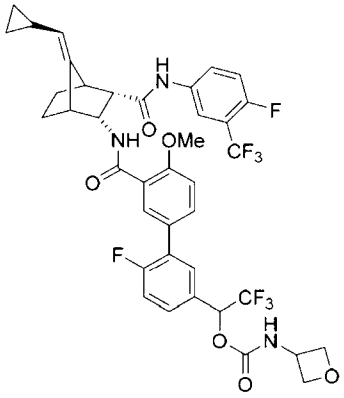
213		N-(3,3,3-三氟丙基)胺基甲酸1-(3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2,2,2-三氟乙酯	834.5	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.94 (br d, J=7.2 Hz, 1H), 8.27 - 8.17 (m, 1H), 8.10 (s, 1H), 8.06 (br t, J=5.6 Hz, 1H), 7.80 - 7.74 (m, 1H), 7.67 (br dd, J=13.8, 7.8 Hz, 2H), 7.54 (br d, J=4.5 Hz, 1H), 7.49 - 7.36 (m, 2H), 7.32 (d, J=8.6 Hz, 1H), 6.42 - 6.31 (m, 1H), 4.68 (d, J=9.7 Hz, 1H), 4.49 - 4.37 (m, 1H), 4.04 (s, 3H), 3.34 - 3.19 (m, 2H), 3.18 - 3.12 (m, 1H), 3.09 (br s, 1H), 2.71 (br s, 1H), 2.46 - 2.33 (m, 2H), 1.89 - 1.74 (m, 2H), 1.53 - 1.45 (m, 1H), 1.40 (br t, J=9.2 Hz, 2H), 0.78 - 0.66 (m, 2H), 0.40 - 0.26 (m, 2H)	1.24, A

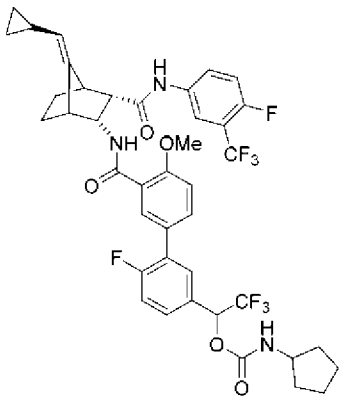
214		N-甲氧基胺基甲酸 1-(3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2,2,2-三氟乙酯	768.3	(500 MHz, $CDCl_3$) δ 9.63 - 9.55 (m, 1H), 8.37 (dd, J=5.1, 1.8 Hz, 1H), 7.97 (ddd, J=9.5, 6.5, 2.8 Hz, 1H), 7.90 - 7.76 (m, 2H), 7.72 - 7.66 (m, 1H), 7.61 - 7.55 (m, 1H), 7.53 (dt, J=4.7, 2.1 Hz, 1H), 7.46 - 7.38 (m, 1H), 7.25 - 7.18 (m, 1H), 7.14 - 7.06 (m, 2H), 6.15 (qd, J=6.6, 3.0 Hz, 1H), 4.89 - 4.80 (m, 1H), 4.66 (d, J=9.6 Hz, 1H), 4.08 (d, J=2.2 Hz, 3H), 3.80 (s, 3H), 3.23 (t, J=4.0 Hz, 1H), 3.11 (dd, J=10.6, 3.2 Hz, 1H), 2.74 (t, J=3.9 Hz, 1H), 2.23 - 2.16 (m, 1H), 1.95 - 1.87 (m, 1H), 1.73 - 1.59 (m, 2H), 1.56 - 1.46 (m, 1H), 0.80 - 0.73 (m, 2H), 0.39 - 0.33 (m, 2H)	1.27, A

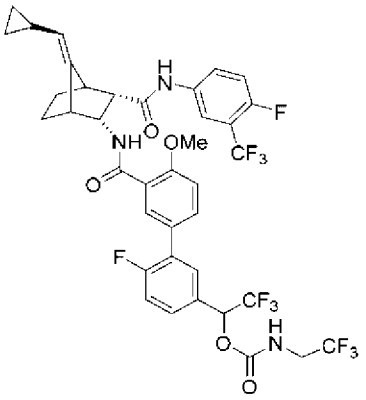
215		N-{螺[2.3]己烷-5-基}胺基甲酸1-(3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2,2,2-三氟乙酯	818.5	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.95 (br d, J=7.1 Hz, 1H), 8.28 - 8.17 (m, 2H), 8.10 (br s, 1H), 7.82 - 7.74 (m, 1H), 7.70 - 7.63 (m, 2H), 7.53 (br d, J=4.1 Hz, 1H), 7.49 - 7.36 (m, 2H), 7.32 (br d, J=8.7 Hz, 1H), 6.47 - 6.24 (m, 1H), 4.68 (br d, J=9.7 Hz, 1H), 4.49 - 4.36 (m, 1H), 4.17 - 4.07 (m, 1H), 4.04 (s, 3H), 3.19 - 3.12 (m, 1H), 3.09 (br s, 1H), 2.71 (br s, 1H), 2.27 - 2.03 (m, 4H), 1.88 - 1.74 (m, 2H), 1.54 - 1.45 (m, 1H), 1.44 - 1.32 (m, 2H), 0.78 - 0.67 (m, 2H), 0.45 - 0.37 (m, 2H), 0.34 (br s, 4H)	1.27, A

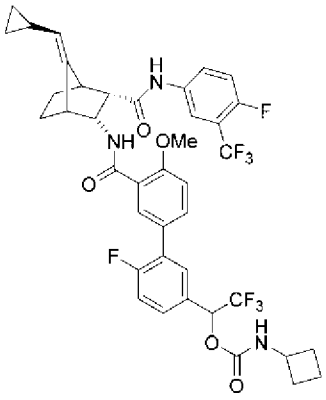
216		氮雜環丁烷-1-甲酸 1-(3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2,2,2-三氟乙酯	778.3	(500 MHz, DMSO-d6) δ 10.52 (s, 1H), 9.92 (d, J=7.3 Hz, 1H), 8.23 (dd, J=6.4, 2.4 Hz, 1H), 8.13 (d, J=1.2 Hz, 1H), 7.79 (br dd, J=8.5, 4.0 Hz, 1H), 7.73 - 7.63 (m, 2H), 7.61 - 7.52 (m, 1H), 7.50 - 7.36 (m, 2H), 7.33 (d, J=8.5 Hz, 1H), 6.41 - 6.33 (m, 1H), 4.69 (d, J=9.5 Hz, 1H), 4.54 - 4.41 (m, 1H), 4.17 - 4.08 (m, 2H), 4.06 (s, 3H), 3.97 - 3.86 (m, 2H), 3.21 - 3.14 (m, 1H), 3.11 (br s, 1H), 2.72 (br d, J=2.7 Hz, 1H), 2.22 (br dd, J=7.5, 5.6 Hz, 2H), 1.89 - 1.75 (m, 2H), 1.55 - 1.47 (m, 1H), 1.47 - 1.34 (m, 2H), 0.79 - 0.67 (m, 2H), 0.40 - 0.29 (m, 2H)	1.26, A

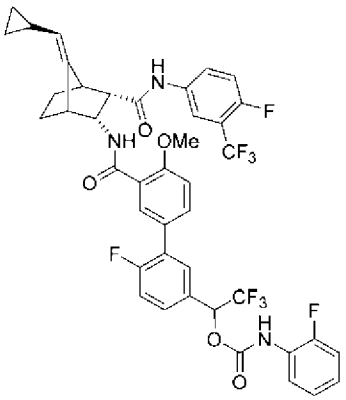
217		N-甲基胺基甲酸1-(3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2,2,2-三氟乙酯	752.3	(500 MHz, $CDCl_3$) δ 9.92 (br d, J=7.4 Hz, 1H), 8.33 (t, J=2.5 Hz, 1H), 8.02 - 7.94 (m, 1H), 7.73 (br d, J=8.8 Hz, 2H), 7.59 (br d, J=7.2 Hz, 1H), 7.54 - 7.48 (m, 1H), 7.44 - 7.37 (m, 1H), 7.19 (t, J=8.9 Hz, 1H), 7.15 - 7.07 (m, 2H), 6.13 (q, J=6.8 Hz, 1H), 5.22 - 5.14 (m, 1H), 4.83 - 4.75 (m, 1H), 4.68 (d, J=9.6 Hz, 1H), 4.10 (d, J=3.3 Hz, 3H), 3.24 (br d, J=3.0 Hz, 1H), 3.10 (dd, J=10.7, 3.3 Hz, 1H), 2.86 (d, J=4.7 Hz, 3H), 2.73 (t, J=3.9 Hz, 1H), 2.20 - 2.14 (m, 1H), 1.95 - 1.84 (m, 1H), 1.75 - 1.58 (m, 2H), 1.55 - 1.47 (m, 1H), 0.82 - 0.74 (m, 2H), 0.44 - 0.32 (m, 2H)	1.27, A

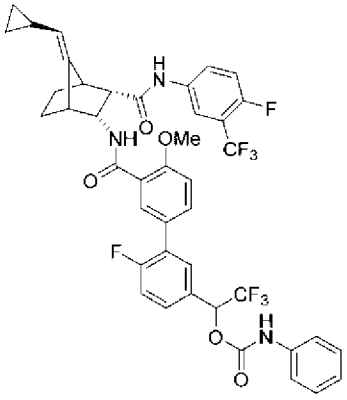
218		N-(氧雜環丁烷-3-基)胺基甲酸1-(3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2,2,2-三氟乙酯	794.5	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.95 (br d, J=7.2 Hz, 1H), 8.69 (br d, J=6.5 Hz, 1H), 8.26 - 8.18 (m, 1H), 8.11 (br s, 1H), 7.81 - 7.74 (m, 1H), 7.72 - 7.65 (m, 2H), 7.58 - 7.52 (m, 1H), 7.50 - 7.38 (m, 2H), 7.33 (d, J=8.8 Hz, 1H), 6.43 - 6.32 (m, 1H), 4.71 - 4.65 (m, 2H), 4.65 - 4.58 (m, 2H), 4.49 - 4.37 (m, 3H), 4.05 (s, 3H), 3.15 (br dd, J=8.8, 4.5 Hz, 1H), 3.10 (br s, 1H), 2.75 - 2.67 (m, 1H), 1.87 - 1.74 (m, 2H), 1.53 - 1.47 (m, 1H), 1.45 - 1.36 (m, 2H), 0.78 - 0.66 (m, 2H), 0.39 - 0.26 (m, 2H)	1.19, A

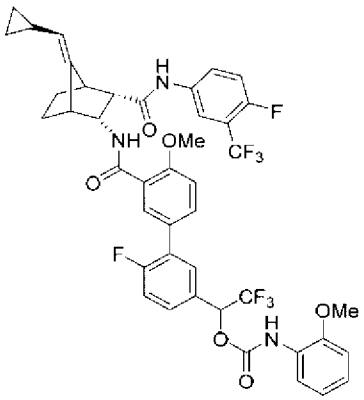
219		N-環戊基胺基甲酸 1-(3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2,2,2-三氟乙酯	806.5	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.92 (br d, J=7.0 Hz, 1H), 8.19 (br d, J=6.1 Hz, 1H), 8.09 (s, 1H), 7.82 (br d, J=7.0 Hz, 1H), 7.78 - 7.73 (m, 1H), 7.67 (br dd, J=14.2, 8.1 Hz, 2H), 7.53 (br d, J=1.8 Hz, 1H), 7.49 - 7.35 (m, 2H), 7.31 (d, J=8.9 Hz, 1H), 6.37 - 6.24 (m, 1H), 4.68 (d, J=9.8 Hz, 1H), 4.48 - 4.39 (m, 1H), 4.03 (s, 3H), 3.81 - 3.67 (m, 1H), 3.14 (br dd, J=11.0, 4.0 Hz, 1H), 3.09 (br s, 1H), 2.70 (br s, 1H), 1.87 - 1.67 (m, 4H), 1.65 - 1.52 (m, 2H), 1.52 - 1.28 (m, 7H), 0.76 - 0.66 (m, 2H), 0.38 - 0.26 (m, 2H)	1.27, A

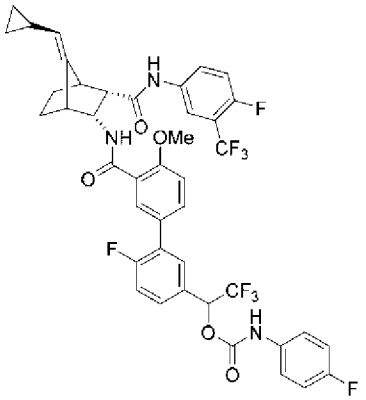
220		N-(2,2,2-三氟乙基)胺基甲酸1-(3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2,2,2-三氟乙酯	820.3	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.92 (br d, J=6.7 Hz, 1H), 8.65 (br t, J=6.4 Hz, 1H), 8.19 (br d, J=5.8 Hz, 1H), 8.10 (s, 1H), 7.80 - 7.72 (m, 1H), 7.68 (br d, J=7.9 Hz, 2H), 7.55 (br d, J=4.6 Hz, 1H), 7.43 (dt, J=19.1, 9.5 Hz, 2H), 7.32 (d, J=8.9 Hz, 1H), 6.51 - 6.35 (m, 1H), 4.68 (d, J=9.5 Hz, 1H), 4.43 (br s, 1H), 4.03 (s, 3H), 3.90 - 3.68 (m, 2H), 3.18 - 3.12 (m, 1H), 3.09 (br s, 1H), 2.70 (br s, 1H), 1.89 - 1.74 (m, 2H), 1.53 - 1.45 (m, 1H), 1.43 - 1.34 (m, 2H), 0.79 - 0.65 (m, 2H), 0.38 - 0.28 (m, 2H)	1.23, A

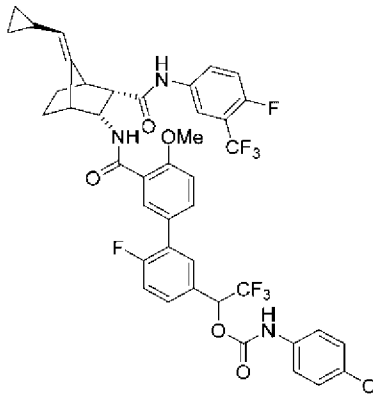
221		N-環丁基胺基甲酸 1-(3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2,2,2-三氟乙酯	792.4	(500 MHz, DMSO-d6) δ 10.56 (s, 1H), 9.94 (br d, J=7.2 Hz, 1H), 8.20 (dd, J=5.9, 2.0 Hz, 1H), 8.14 (br d, J=7.9 Hz, 1H), 8.09 (s, 1H), 7.81 - 7.74 (m, 1H), 7.66 (br dd, J=19.9, 8.2 Hz, 2H), 7.52 (br d, J=1.7 Hz, 1H), 7.48 - 7.36 (m, 2H), 7.32 (d, J=8.8 Hz, 1H), 6.37 - 6.25 (m, 1H), 4.67 (d, J=9.5 Hz, 1H), 4.48 - 4.41 (m, 1H), 4.04 (s, 2H), 3.94 - 3.86 (m, 1H), 3.14 (br dd, J=10.2, 4.0 Hz, 1H), 3.08 (br s, 1H), 2.71 (br s, 1H), 2.18 - 2.04 (m, 2H), 1.95 - 1.75 (m, 4H), 1.59 - 1.43 (m, 3H), 1.43 - 1.32 (m, 2H), 0.76 - 0.64 (m, 2H), 0.41 - 0.27 (m, 2H)	1.26, A

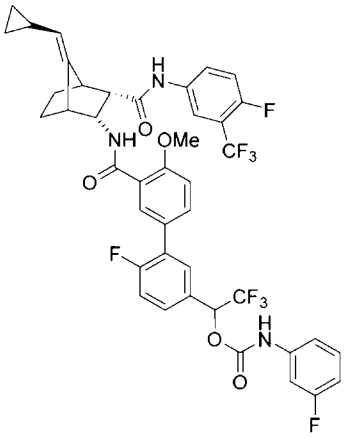
223		N-(2-氟苯基)胺基甲酸1-(3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2,2,2-三氟乙酯	832.3	(500 MHz, DMSO-d6) δ 10.54 (s, 1H), 10.14 - 9.99 (m, 1H), 9.95 (br d, J=7.2 Hz, 1H), 8.22 (br d, J=4.4 Hz, 1H), 8.14 (br s, 1H), 7.82 - 7.74 (m, 2H), 7.70 (br d, J=7.7 Hz, 1H), 7.65 - 7.52 (m, 2H), 7.51 - 7.40 (m, 2H), 7.33 (d, J=8.8 Hz, 1H), 7.27 - 7.11 (m, 3H), 6.54 (br d, J=6.1 Hz, 1H), 4.68 (d, J=9.6 Hz, 1H), 4.45 (br t, J=10.6 Hz, 1H), 4.05 (s, 3H), 3.15 (br dd, J=7.9, 4.6 Hz, 1H), 3.10 (br s, 1H), 2.71 (br s, 1H), 1.91 - 1.74 (m, 2H), 1.54 - 1.47 (m, 1H), 1.45 - 1.34 (m, 2H), 0.78 - 0.66 (m, 2H), 0.40 - 0.28 (m, 2H)	1.27, A

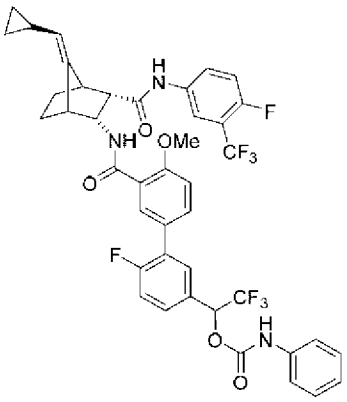
224	 異構物1	N-苯基胺基甲酸1-(3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2,2,2-三氟乙酯	814.5	(500 MHz, $CDCl_3$) δ 9.62 (br d, J=7.7 Hz, 1H), 8.39 (d, J=1.9 Hz, 1H), 7.97 (dd, J=6.2, 2.6 Hz, 1H), 7.79 (s, 1H), 7.74 - 7.67 (m, 1H), 7.63 (br d, J=5.8 Hz, 1H), 7.53 (dt, J=8.6, 3.5 Hz, 1H), 7.49 - 7.44 (m, 1H), 7.42 (br d, J=8.0 Hz, 2H), 7.37 - 7.32 (m, 2H), 7.22 (dd, J=10.2, 8.5 Hz, 1H), 7.16 - 7.05 (m, 3H), 7.02 (br s, 1H), 6.20 (q, J=6.8 Hz, 1H), 4.88 - 4.81 (m, 1H), 4.67 (d, J=9.6 Hz, 1H), 4.08 (s, 3H), 3.23 (t, J=4.0 Hz, 1H), 3.15 - 3.07 (m, 1H), 2.74 (t, J=3.9 Hz, 1H), 2.23 - 2.14 (m, 1H), 1.95 - 1.85 (m, 1H), 1.72 - 1.59 (m, 2H), 1.55 - 1.47 (m, 1H), 0.82 - 0.72 (m, 2H), 0.40 - 0.33 (m, 2H)	1.28, A

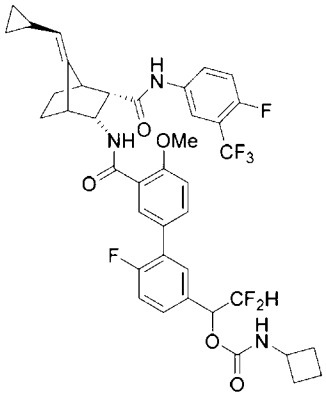
225		N-(2-甲氧基苯基)胺基甲酸1-(3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2,2,2-三氟乙酯	844.2	(500 MHz, $CDCl_3$) δ 9.88 (br d, J=7.9 Hz, 1H), 8.32 (d, J=1.7 Hz, 1H), 8.03 (br d, J=6.7 Hz, 1H), 7.96 (dd, J=6.3, 2.6 Hz, 1H), 7.74 (s, 1H), 7.72 - 7.68 (m, 1H), 7.64 - 7.60 (m, 1H), 7.56 (br s, 1H), 7.52 - 7.47 (m, 2H), 7.22 (dd, J=10.1, 8.5 Hz, 1H), 7.14 - 7.08 (m, 2H), 7.07 - 7.02 (m, 1H), 6.96 (td, J=7.8, 1.1 Hz, 1H), 6.89 (dd, J=8.2, 1.1 Hz, 1H), 6.21 (q, J=6.8 Hz, 1H), 4.86 - 4.77 (m, 1H), 4.67 (d, J=9.6 Hz, 1H), 4.09 (s, 3H), 3.91 (s, 3H), 3.24 (t, J=4.1 Hz, 1H), 3.14 - 3.05 (m, 1H), 2.73 (t, J=4.0 Hz, 1H), 2.23 - 2.15 (m, 1H), 1.93 - 1.86 (m, 1H), 1.74 - 1.57 (m, 2H), 1.55 - 1.48 (m, 1H), 0.83 - 0.73 (m, 2H), 0.41 - 0.32 (m, 2H)	1.36, A

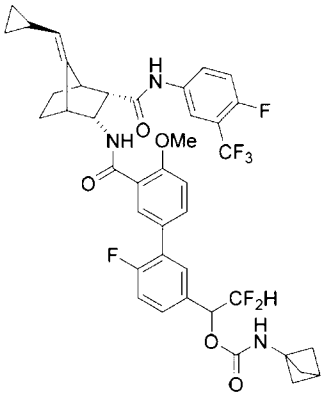
226		N-(4-氟苯基)胺基甲酸 1-(3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)乙酯	778.2	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.92 (br d, J=6.7 Hz, 1H), 9.76 (br s, 1H), 8.21 (br d, J=4.9 Hz, 1H), 8.12 (s, 1H), 7.81 - 7.74 (m, 1H), 7.69 (br d, J=8.9 Hz, 1H), 7.53 (br s, 1H), 7.49 - 7.36 (m, 4H), 7.34 - 7.27 (m, 2H), 7.08 (br t, J=8.7 Hz, 2H), 5.87 - 5.81 (m, 1H), 4.68 (d, J=9.8 Hz, 1H), 4.44 (br d, J=7.0 Hz, 1H), 4.04 (s, 3H), 3.15 (br dd, J=10.5, 3.2 Hz, 1H), 3.10 (br s, 1H), 2.71 (br s, 1H), 1.89 - 1.74 (m, 2H), 1.55 (br d, J=6.7 Hz, 3H), 1.50 - 1.43 (m, 1H), 1.43 - 1.34 (m, 2H), 0.78 - 0.67 (m, 2H), 0.40 - 0.29 (m, 2H)	1.30, A

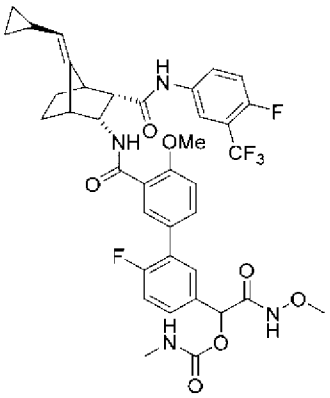
227		N-(4-氯苯基)胺基甲酸1-(3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2,2,2-三氟乙酯	848.5	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 10.44 (br s, 1H), 9.94 (br d, J=7.3 Hz, 1H), 8.22 (br d, J=4.6 Hz, 1H), 8.13 (s, 1H), 7.83 - 7.75 (m, 2H), 7.71 (br d, J=7.6 Hz, 1H), 7.66 - 7.58 (m, 1H), 7.52 - 7.39 (m, 4H), 7.36 - 7.29 (m, 3H), 6.62 - 6.50 (m, 1H), 4.69 (br d, J=9.5 Hz, 1H), 4.51 - 4.42 (m, 1H), 4.05 (s, 3H), 3.18 - 3.14 (m, 1H), 3.10 (br d, J=1.2 Hz, 1H), 2.72 (br d, J=2.4 Hz, 1H), 1.90 - 1.78 (m, 2H), 1.55 - 1.49 (m, 1H), 1.45 - 1.36 (m, 2H), 0.79 - 0.68 (m, 2H), 0.35 (br s, 2H)	1.30, A

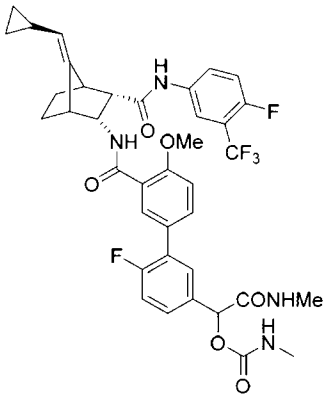
228		N-(3-氟苯基)胺基甲酸1-(3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2,2,2-三氟乙酯	832.4	(500 MHz, DMSO-d6) δ 10.53 (br s, 2H), 9.94 (br d, J=7.0 Hz, 1H), 8.21 (br d, J=4.9 Hz, 1H), 8.13 (s, 1H), 7.82 - 7.73 (m, 2H), 7.70 (br d, J=8.2 Hz, 1H), 7.61 (br d, J=4.3 Hz, 1H), 7.50 - 7.40 (m, 2H), 7.33 (br d, J=8.9 Hz, 3H), 7.23 (br d, J=8.2 Hz, 1H), 6.86 (br t, J=8.1 Hz, 1H), 6.63 - 6.50 (m, 1H), 4.68 (d, J=9.5 Hz, 1H), 4.45 (br t, J=10.2 Hz, 1H), 4.05 (s, 3H), 3.16 (br dd, J=10.5, 4.1 Hz, 1H), 3.10 (br s, 1H), 2.71 (br s, 1H), 1.90 - 1.73 (m, 2H), 1.56 - 1.44 (m, 1H), 1.44 - 1.34 (m, 2H), 0.80 - 0.66 (m, 2H), 0.34 (br d, J=1.2 Hz, 2H)	1.28, A

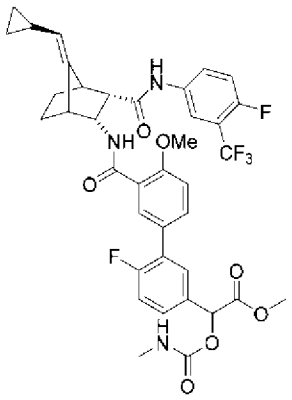
229	 異構物2	N-苯基胺基甲酸1-(3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2,2,2-三氟乙酯	814.5	1H NMR (500 MHz, 氯仿-d) Shift 9.60 (br d, J=8.0 Hz, 1H), 8.36 (d, J=2.2 Hz, 1H), 7.98 (dd, J=6.2, 2.6 Hz, 1H), 7.83 (s, 1H), 7.74 - 7.66 (m, 1H), 7.64 - 7.58 (m, 1H), 7.51 (dt, J=8.7, 3.5 Hz, 1H), 7.46 - 7.38 (m, 3H), 7.32 (t, J=8.0 Hz, 2H), 7.20 (dd, J=10.2, 8.5 Hz, 1H), 7.14 - 7.04 (m, 4H), 6.18 (q, J=6.9 Hz, 1H), 4.86 - 4.78 (m, 1H), 4.64 (d, J=9.4 Hz, 1H), 4.07 (s, 3H), 3.22 (t, J=4.0 Hz, 1H), 3.09 (ddd, J=10.8, 4.1, 1.1 Hz, 1H), 2.72 (t, J=3.9 Hz, 1H), 2.20 - 2.13 (m, 1H), 1.94 - 1.84 (m, 1H), 1.71 - 1.58 (m, 2H), 1.54 - 1.45 (m, 1H), 0.79 - 0.69 (m, 2H), 0.37 - 0.31 (m, 2H)	1.28, A

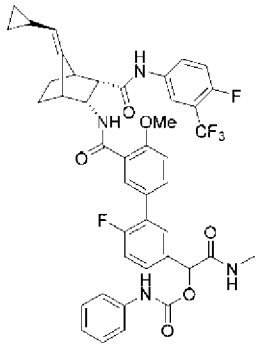
231		N-環丁基胺基甲酸 1-(3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2,2-二氟乙酯	774.4	1H NMR (500 MHz, DMSO-d6) Shift 10.52 (s, 1H), 9.98 - 9.87 (m, 1H), 8.23 (br d, J=4.6 Hz, 1H), 8.12 (br s, 1H), 7.95 (br d, J=7.6 Hz, 1H), 7.82 - 7.74 (m, 1H), 7.69 (br d, J=8.2 Hz, 1H), 7.56 (br d, J=7.3 Hz, 1H), 7.50 - 7.41 (m, 2H), 7.40 - 7.26 (m, 2H), 6.49 - 6.19 (m, 1H), 5.91 (br t, J=12.5 Hz, 1H), 4.69 (d, J=9.8 Hz, 1H), 4.49 - 4.41 (m, 1H), 4.05 (s, 3H), 3.97 - 3.86 (m, 1H), 3.20 - 3.13 (m, 1H), 3.10 (br s, 1H), 2.72 (br s, 1H), 2.17 - 2.03 (m, 2H), 1.95 - 1.77 (m, 4H), 1.62 - 1.46 (m, 3H), 1.46 - 1.34 (m, 2H), 0.78 - 0.67 (m, 2H), 0.38 - 0.30 (m, 2H)	1.22, A

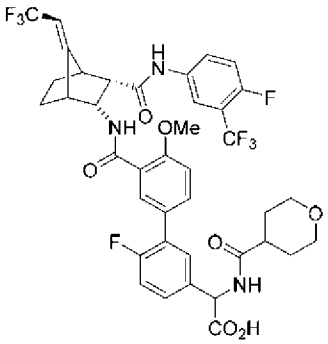
232		N-{雙環[1.1.1]戊烷-1-基}胺基甲酸 1-(3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2,2-二氟乙酯	786.3	1H NMR (500 MHz, DMSO-d6) Shift 10.55 (s, 1H), 9.95 (br d, J=6.3 Hz, 1H), 8.37 (br s, 1H), 8.24 (br d, J=4.2 Hz, 1H), 8.13 (br s, 1H), 7.85 - 7.76 (m, 1H), 7.70 (br d, J=8.5 Hz, 1H), 7.57 (br d, J=5.7 Hz, 1H), 7.52 - 7.30 (m, 4H), 6.56 - 6.17 (m, 1H), 6.02 - 5.84 (m, 1H), 4.69 (d, J=9.5 Hz, 1H), 4.51 - 4.39 (m, 1H), 4.05 (s, 3H), 3.16 (br dd, J=10.1, 4.3 Hz, 1H), 3.11 (br s, 1H), 2.72 (br s, 1H), 2.36 (s, 1H), 1.90 (br s, 6H), 1.88 - 1.76 (m, 2H), 1.56 - 1.47 (m, 1H), 1.46 - 1.35 (m, 2H), 0.79 - 0.68 (m, 2H), 0.40 - 0.30 (m, 2H)	1.23, A

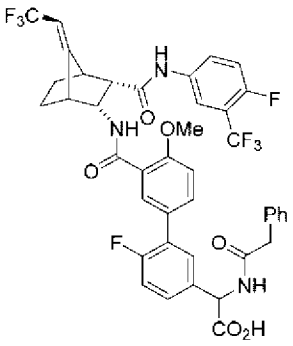
234		N-甲基胺基甲酸(3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)(甲氧基胺甲醯基)甲酯	757.3	(500 MHz, $CDCl_3$) δ 9.84 - 9.58 (m, 2H), 8.30 (br s, 1H), 8.11 (br s, 1H), 8.01 (br d, *J*=3.9 Hz, 1H), 7.63 (br d, *J*=8.8 Hz, 1H), 7.55 - 7.48 (m, 2H), 7.47 - 7.39 (m, 1H), 7.17 - 7.07 (m, 2H), 7.04 (d, *J*=8.5 Hz, 1H), 6.06 (br s, 1H), 5.25 (br s, 1H), 4.78 (br s, 1H), 4.62 (d, *J*=9.6 Hz, 1H), 4.09 (s, 3H), 3.77 (s, 3H), 3.20 (t, *J*=4.0 Hz, 1H), 3.10 (dd, *J*=10.5, 3.6 Hz, 1H), 2.81 (br d, *J*=2.8 Hz, 3H), 2.71 (br s, 1H), 2.20 - 2.13 (m, 1H), 1.94 - 1.86 (m, 1H), 1.71 - 1.55 (m, 2H), 1.52 - 1.42 (m, 1H), 0.74 (dd, *J*=8.0, 1.7 Hz, 2H), 0.39 - 0.27 (m, 2H)	1.17, A

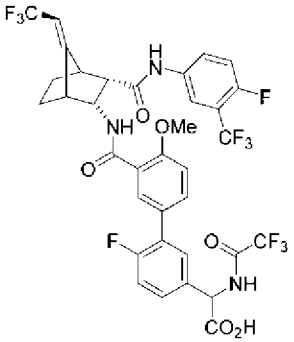
235		N-甲基胺基甲酸(3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)(甲基胺甲醯基)甲酯	741.5	(500 MHz, CDCl3) δ 9.53 (br d, J=7.3 Hz, 1H), 8.36 - 8.31 (m, 1H), 8.09 (br s, 1H), 7.99 (dd, J=6.0, 2.5 Hz, 1H), 7.64 (dt, J=8.5, 2.0 Hz, 1H), 7.53 (dt, J=8.4, 3.4 Hz, 1H), 7.50 - 7.45 (m, 1H), 7.44 - 7.37 (m, 1H), 7.17 - 7.02 (m, 3H), 6.51 - 6.43 (m, 1H), 6.08 (s, 1H), 5.13 - 5.05 (m, 1H), 4.87 - 4.77 (m, 1H), 4.63 (d, J=9.5 Hz, 1H), 4.07 (s, 3H), 3.19 (t, J=3.8 Hz, 1H), 3.10 (dd, J=10.2, 3.5 Hz, 1H), 2.87 (d, J=4.9 Hz, 3H), 2.82 (d, J=4.9 Hz, 3H), 2.72 (t, J=3.7 Hz, 1H), 2.22 - 2.14 (m, 1H), 1.94 - 1.86 (m, 1H), 1.71 - 1.62 (m, 2H), 1.51 - 1.47 (m, 1H), 0.78 - 0.71 (m, 2H), 0.38 - 0.30 (m, 2H)	1.11, A

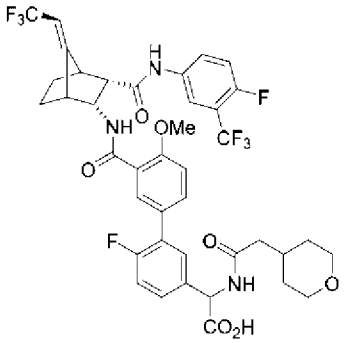
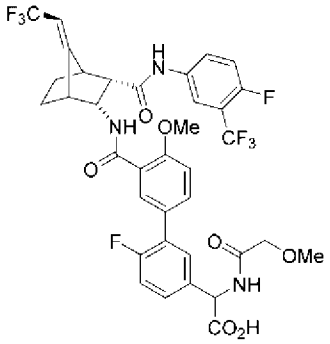
236		2-(3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2-[(甲基胺甲醯基)氧基]乙酸甲酯	741.5	(500 MHz, $CDCl_3$) δ 9.41 (br d, *J*=7.7 Hz, 1H), 8.40 (d, *J*=1.7 Hz, 1H), 7.97 (dd, *J*=6.1, 2.5 Hz, 1H), 7.90 (s, 1H), 7.66 (dt, *J*=8.5, 2.1 Hz, 1H), 7.58 - 7.50 (m, 2H), 7.45 - 7.37 (m, 1H), 7.18 (dd, *J*=10.0, 8.7 Hz, 1H), 7.13 - 7.03 (m, 2H), 5.98 (s, 1H), 4.97 (br d, *J*=4.1 Hz, 1H), 4.90 - 4.82 (m, 1H), 4.66 (d, *J*=9.4 Hz, 1H), 4.07 (s, 3H), 3.77 (s, 3H), 3.22 (t, *J*=4.0 Hz, 1H), 3.14 - 3.07 (m, 1H), 2.87 (d, *J*=5.0 Hz, 3H), 2.74 (t, *J*=3.9 Hz, 1H), 2.25 - 2.17 (m, 1H), 1.93 - 1.85 (m, 1H), 1.73 - 1.62 (m, 2H), 1.55 - 1.47 (m, 1H), 0.80 - 0.73 (m, 2H), 0.40 - 0.33 (m, 2H)	1.23, A

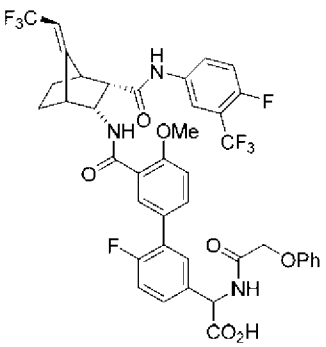
237		N-苯基胺基甲酸(3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)(甲基胺甲醯基)甲酯	803.3	(500 MHz, $CDCl_3$) δ 9.64 (br d, J=7.9 Hz, 1H), 8.37 (d, J=2.3 Hz, 1H), 7.99 (dd, J=6.0, 2.2 Hz, 1H), 7.96 - 7.90 (m, 1H), 7.74 - 7.66 (m, 1H), 7.59 - 7.52 (m, 3H), 7.50 - 7.46 (m, 1H), 7.43 - 7.43 (m, 1H), 7.43 - 7.39 (m, 1H), 7.35 - 7.29 (m, 3H), 7.20 - 7.04 (m, 5H), 6.45 - 6.37 (m, 1H), 6.15 (s, 1H), 4.86 - 4.77 (m, 1H), 4.63 (d, J=9.6 Hz, 1H), 4.08 (s, 3H), 3.21 (t, J=3.9 Hz, 1H), 3.09 (br dd, J=10.5, 3.1 Hz, 1H), 2.88 (d, J=4.7 Hz, 3H), 2.77 - 2.70 (m, 1H), 2.22 - 2.13 (m, 1H), 1.97 - 1.87 (m, 1H), 1.65 - 1.59 (m, 2H), 1.50 - 1.45 (m, 1H), 1.54 - 1.43 (m, 2H), 0.78 - 0.71 (m, 2H), 0.79 - 0.69 (m, 3H), 0.38 - 0.29 (m, 2H)	1.17, A

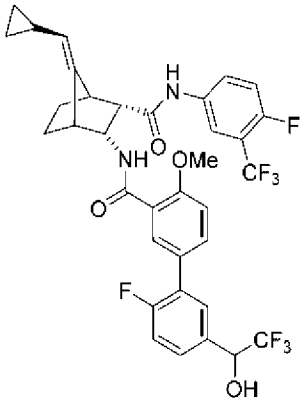
239		2-(6-氟-3'-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-3-基)-2-[(噁烷-4-基)甲醯胺基]乙酸	810.4	(500 MHz, $CDCl_3$) δ 10.00 (br d, *J*=7.7 Hz, 1H), 8.24 (br s, 1H), 8.14 (s, 1H), 7.98 (dd, *J*=6.1, 2.5 Hz, 1H), 7.67 (br d, *J*=8.3 Hz, 1H), 7.52 - 7.39 (m, 3H), 7.09 (br t, *J*=9.4 Hz, 1H), 7.05 - 6.96 (m, 2H), 5.63 (br d, *J*=7.2 Hz, 1H), 5.57 (q, *J*=7.3 Hz, 1H), 4.81 - 4.72 (m, 1H), 4.08 (s, 3H), 4.07 - 4.00 (m, 2H), 3.50 - 3.42 (m, 2H), 3.32 (br s, 1H), 3.16 (dd, *J*=10.6, 4.0 Hz, 1H), 2.88 (br s, 1H), 2.62 - 2.54 (m, 1H), 2.35 - 2.28 (m, 1H), 2.02 - 1.96 (m, 1H), 1.88 - 1.74 (m, 4H), 1.73 - 1.60 (m, 2H)	1.07, A

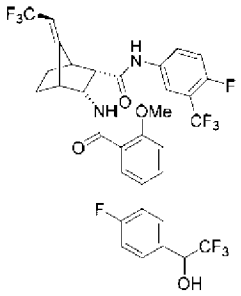
240		2-(6-氟-3'-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-3-基)-2-(2-苯基乙醯胺基)乙酸	816.5	(500 MHz, $CDCl_3$) δ fin9.71 (br d, J=8.5 Hz, 1H), 8.24 (d, J=2.5 Hz, 1H), 8.11 (br s, 1H), 8.02 - 7.93 (m, 1H), 7.67 - 7.59 (m, 1H), 7.48 - 7.42 (m, 2H), 7.32 (s, 1H), 7.26 - 7.18 (m, 5H), 7.05 - 6.94 (m, 4H), 5.73 (d, J=7.4 Hz, 1H), 5.61 - 5.54 (m, 1H), 4.87 - 4.75 (m, 1H), 4.05 (s, 3H), 3.64 (s, 2H), 3.40 (br s, 1H), 3.19 - 3.11 (m, 1H), 2.90 - 2.84 (m, 1H), 2.43 - 2.32 (m, 1H), 2.03 - 1.97 (m, 1H), 1.73 - 1.57 (m, 2H)	1.11, A

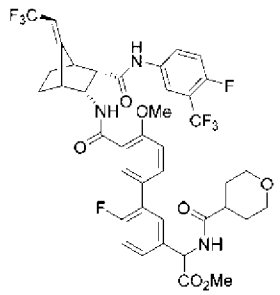
241		2-(6-氟-3'-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-3-基)-2-(2,2,2-三氟乙醯胺基)乙酸	794.3	(500 MHz, $CDCl_3$) δ 10.02 (br d, J=7.7 Hz, 1H), 9.14 (br d, J=8.0 Hz, 1H), 8.42 (d, J=2.5 Hz, 1H), 7.98 (dd, J=6.2, 2.6 Hz, 1H), 7.82 - 7.73 (m, 2H), 7.61 (s, 1H), 7.54 - 7.47 (m, 1H), 7.45 - 7.37 (m, 1H), 7.12 (dd, J=10.6, 8.4 Hz, 1H), 7.08 - 7.03 (m, 1H), 7.01 (d, J=8.8 Hz, 1H), 5.92 (d, J=8.5 Hz, 1H), 5.60 (q, J=7.3 Hz, 1H), 4.79 - 4.71 (m, 1H), 4.05 (s, 3H), 3.40 (br s, 1H), 3.09 (dd, J=10.7, 4.1 Hz, 1H), 2.90 - 2.84 (m, 1H), 2.28 - 2.22 (m, 1H), 2.03 - 1.92 (m, 1H), 1.73 - 1.62 (m, 2H)	1.12, A

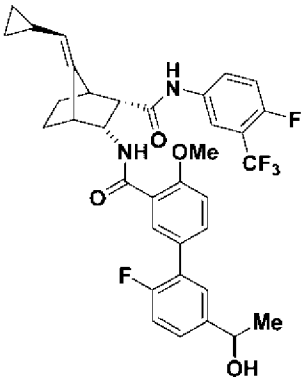
242		2-(6-氟-3'-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-3-基)-2-[2-(噁烷-4-基)乙醯胺基]乙酸	824.3	(500 MHz, $CDCl_3$) δ 9.78 - 9.41 (m, 1H), 8.22 - 8.04 (m, 1H), 7.91 (br d, J=5.3 Hz, 1H), 7.63 - 7.31 (m, 4H), 7.23 - 7.17 (m, 1H), 7.04 - 6.80 (m, 3H), 5.65 - 5.45 (m, 2H), 4.80 - 4.68 (m, 1H), 4.01 (s, 3H), 3.88 - 3.72 (m, 2H), 3.33 - 3.19 (m, 3H), 3.18 - 3.10 (m, 1H), 2.82 (br s, 1H), 2.44 - 2.32 (m, 1H), 2.21 - 2.09 (m, 2H), 2.03 - 1.91 (m, 2H), 1.70 - 1.58 (m, 2H), 1.57 - 1.45 (m, 2H), 1.32 - 1.18 (m, 2H)	1.07, A
243		2-(6-氟-3'-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-3-基)-2-(2-甲氧基乙醯胺基)乙酸	770.4	(500 MHz, $CDCl_3$) δ 9.51 - 9.36 (m, 1H), 8.59 - 8.30 (m, 1H), 8.21 (br s, 1H), 8.00 - 7.90 (m, 1H), 7.67 - 7.53 (m, 2H), 7.51 - 7.36 (m, 2H), 7.37 - 7.30 (m, 1H), 7.11 - 6.92 (m, 3H), 5.73 - 5.61 (m, 1H), 5.53 (q, J=7.4 Hz, 1H), 4.84 (br s, 1H), 4.04 (s, 3H), 3.93 (br s, 2H), 3.41 (br s, 3H), 3.34 (br s, 1H), 3.21 - 3.13 (m, 1H), 2.87 (br s, 1H), 2.52 - 2.42 (m, 1H), 2.05 - 1.94 (m, 1H), 1.77 - 1.59 (m, 2H)	1.09, A

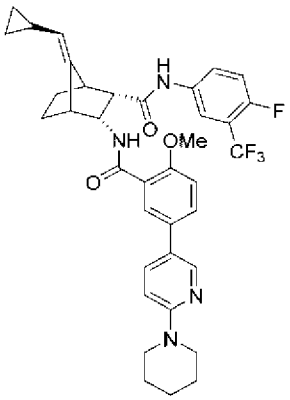
244		2-(6-氟-3'-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-3-基)-2-(2-苯氧基乙醯胺基)乙酸	832.2	(500 MHz, $CDCl_3$) δ 9.57 (br d, J=7.8 Hz, 1H), 8.26 (br s, 1H), 8.21 (br s, 1H), 8.02 - 7.91 (m, 2H), 7.60 (br d, J=8.3 Hz, 1H), 7.50 (br d, J=5.9 Hz, 1H), 7.42 - 7.35 (m, 1H), 7.32 (br d, J=0.9 Hz, 1H), 7.21 (br t, J=7.8 Hz, 2H), 7.05 - 6.92 (m, 4H), 6.89 (br d, J=8.0 Hz, 2H), 5.74 (br d, J=6.7 Hz, 1H), 5.53 (q, J=7.1 Hz, 1H), 4.86 - 4.76 (m, 1H), 4.51 (q, J=15.0 Hz, 2H), 4.03 (s, 3H), 3.36 (br s, 1H), 3.14 (br dd, J=10.5, 3.9 Hz, 1H), 2.84 (br s, 1H), 2.44 - 2.36 (m, 1H), 2.06 - 1.97 (m, 1H), 1.78 - 1.60 (m, 2H)	1.22, A

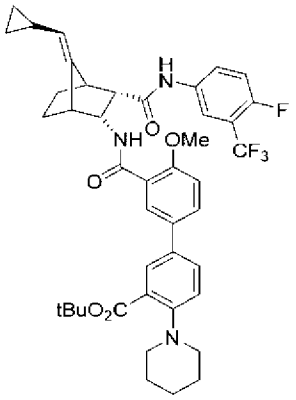
245		N-[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]-2'-氟-4-甲氧基-5'-(2,2,2-三氟-1-羥基乙基)-[1,1'-聯苯]-3-甲醯胺	695.3	(500 MHz, $CDCl_3$) δ 9.57 (d, J=7.7 Hz, 1H), 8.33 (dd, J=2.2, 0.8 Hz, 1H), 8.05 (s, 1H), 7.99 (dd, J=6.3, 2.5 Hz, 1H), 7.66 (dt, J=8.7, 2.0 Hz, 1H), 7.57 (dd, J=7.3, 2.1 Hz, 1H), 7.56 - 7.52 (m, 1H), 7.45 - 7.40 (m, 1H), 7.17 (dd, J=10.2, 8.5 Hz, 1H), 7.11 - 7.04 (m, 2H), 5.11 - 5.04 (m, 1H), 4.77 - 4.70 (m, 1H), 4.57 (d, J=9.4 Hz, 1H), 4.06 (s, 3H), 3.42 (br s, 1H), 3.19 (t, J=4.1 Hz, 1H), 3.08 (ddd, J=10.7, 4.1, 1.2 Hz, 1H), 2.67 (t, J=4.0 Hz, 1H), 2.18 - 2.07 (m, 1H), 1.92 - 1.82 (m, 1H), 1.67 - 1.58 (m, 2H), 1.53 - 1.45 (m, 1H), 0.79 - 0.68 (m, 2H), 0.38 - 0.27 (m, 2H)	1.38, A

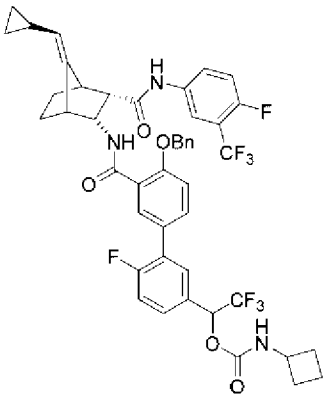
246		N-[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]-2'-氟-4-甲氧基-5'-(2,2,2-三氟-1-羥基乙基)-[1,1'-聯苯]-3-甲醯胺	695.3	(500 MHz, $CDCl_3$) δ 9.53 (d, J=7.7 Hz, 1H), 8.34 (dd, J=2.5, 0.8 Hz, 1H), 8.01 (s, 1H), 7.97 (dd, J=6.2, 2.6 Hz, 1H), 7.66 (dt, J=8.7, 2.0 Hz, 1H), 7.57 - 7.50 (m, 2H), 7.48 - 7.40 (m, 1H), 7.18 (dd, J=10.2, 8.5 Hz, 1H), 7.12 - 7.02 (m, 2H), 5.13 - 5.03 (m, 1H), 4.81 - 4.71 (m, 1H), 4.60 (d, J=9.6 Hz, 1H), 4.06 (s, 3H), 3.19 (t, J=3.7 Hz, 2H), 3.09 (ddd, J=10.8, 4.1, 1.1 Hz, 1H), 2.70 (t, J=4.0 Hz, 1H), 2.19 - 2.11 (m, 1H), 1.92 - 1.84 (m, 1H), 1.70 - 1.60 (m, 2H), 1.51 - 1.42 (m, 1H), 0.77 - 0.70 (m, 2H), 0.36 - 0.30 (m, 2H)	1.38, A

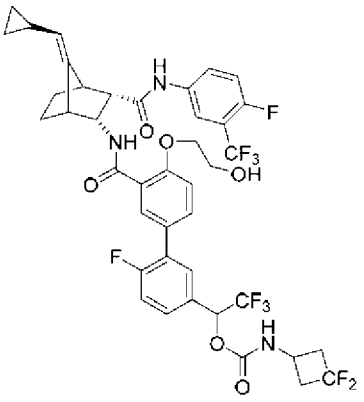
247		2-(6-氟-3'-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-3-基)-2-[(噁烷-4-基)甲醯胺基]乙酸甲酯	824.4	(500 MHz, $CDCl_3$) δ 9.25 (br d, *J*=8.0 Hz, 1H), 8.40 - 8.33 (m, 1H), 8.11 (s, 1H), 7.89 (dd, *J*=6.3, 2.5 Hz, 1H), 7.67 - 7.62 (m, 1H), 7.51 (dt, *J*=8.5, 3.6 Hz, 1H), 7.40 (dd, *J*=7.2, 2.2 Hz, 1H), 7.31 (ddd, *J*=8.4, 4.4, 2.3 Hz, 1H), 7.15 (dd, *J*=10.2, 8.5 Hz, 1H), 7.09 - 7.01 (m, 2H), 6.56 (br d, *J*=6.6 Hz, 1H), 5.62 - 5.53 (m, 2H), 4.96 - 4.88 (m, 1H), 4.04 (s, 3H), 4.03 - 3.99 (m, 2H), 3.76 (s, 3H), 3.47 - 3.39 (m, 3H), 3.17 (dd, *J*=10.9, 2.9 Hz, 1H), 2.93 (t, *J*=3.7 Hz, 1H), 2.49 - 2.39 (m, 2H), 2.01 - 1.94 (m, 1H), 1.87 - 1.80 (m, 3H), 1.79 - 1.72 (m, 3H)。	1.17, A

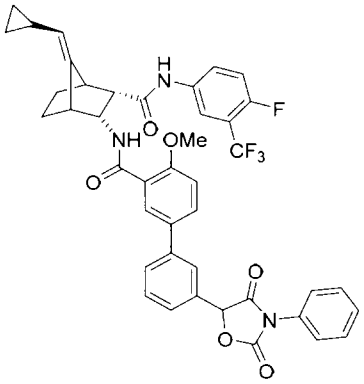
248		N-[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]-2'-氟-5'-(1-羥基乙基)-4-甲氧基-[1,1'-聯苯]-3-甲醯胺	641.4	(500 MHz, $CDCl_3$) δ 9.43 (br d, *J*=7.7 Hz, 1H), 8.38 (dd, *J*=2.5, 0.8 Hz, 1H), 8.02 (s, 1H), 7.96 (dt, *J*=6.1, 3.0 Hz, 1H), 7.67 (dt, *J*=8.7, 2.0 Hz, 1H), 7.56 - 7.50 (m, 1H), 7.44 (dt, *J*=7.4, 1.9 Hz, 1H), 7.38 - 7.29 (m, 1H), 7.16 - 7.02 (m, 3H), 4.94 (q, *J*=6.3 Hz, 1H), 4.85 - 4.76 (m, 1H), 4.62 (d, *J*=9.4 Hz, 1H), 4.05 (s, 3H), 3.20 (t, *J*=4.0 Hz, 1H), 3.10 (ddd, *J*=10.8, 4.1, 1.1 Hz, 1H), 2.71 (t, *J*=4.0 Hz, 1H), 2.22 - 2.14 (m, 1H), 1.92 - 1.86 (m, 1H), 1.70 - 1.56 (m, 2H), 1.53 (d, *J*=6.3 Hz, 3H), 1.51 - 1.44 (m, 1H), 0.76 - 0.69 (m, 2H), 0.37 - 0.30 (m, 2H)	1.18, A

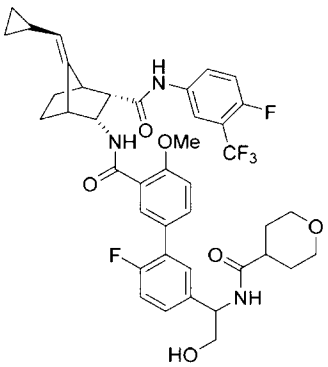
250		(2S,3R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{2-甲氧基-5-[6-(味啉-4-基)吡啶-3-基]苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	665.3	(500 MHz, $CDCl_3$) δ 9.73 (d, J=7.4 Hz, 1H), 8.55 - 8.46 (m, 2H), 8.24 (d, J=2.5 Hz, 1H), 8.15 (dd, J=9.4, 2.2 Hz, 1H), 8.10 (dd, J=6.3, 2.5 Hz, 1H), 7.64 (dt, J=8.7, 3.5 Hz, 1H), 7.54 (dd, J=8.5, 2.5 Hz, 1H), 7.13 (t, J=9.4 Hz, 1H), 7.06 (d, J=9.6 Hz, 1H), 6.93 (d, J=8.8 Hz, 1H), 4.65 (d, J=9.4 Hz, 1H), 4.58 - 4.49 (m, 1H), 4.04 (s, 3H), 3.95 - 3.90 (m, 4H), 3.79 - 3.73 (m, 4H), 3.14 (t, J=3.7 Hz, 1H), 3.06 (dd, J=10.7, 4.1 Hz, 1H), 2.74 - 2.68 (m, 1H), 2.11 - 2.04 (m, 1H), 1.88 - 1.81 (m, 1H), 1.63 - 1.52 (m, 2H), 1.51 - 1.42 (m, 1H), 0.77 - 0.70 (m, 2H), 0.38 - 0.32 (m, 2H)	1.00, A

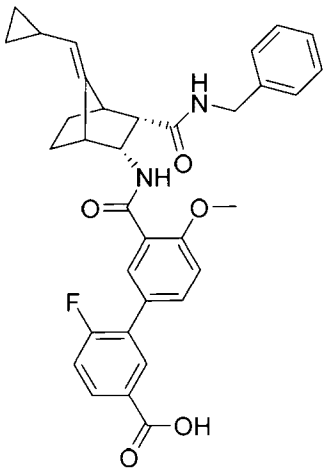
251		3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-4-(味啉-4-基)-[1,1'-聯苯]-3-甲酸三級丁酯	764.3	(500 MHz, $CDCl_3$) δ 9.87 (br d, J=7.7 Hz, 1H), 8.31 (d, J=2.2 Hz, 1H), 8.22 (s, 1H), 8.04 (dd, J=6.3, 2.5 Hz, 1H), 7.94 (d, J=2.2 Hz, 1H), 7.76 (br dd, J=8.3, 1.9 Hz, 1H), 7.60 (dd, J=8.7, 2.3 Hz, 1H), 7.56 (dt, J=8.7, 3.4 Hz, 1H), 7.47 (br d, J=8.0 Hz, 1H), 7.11 (t, J=9.4 Hz, 1H), 7.03 (d, J=8.8 Hz, 1H), 4.62 (d, J=9.6 Hz, 2H), 4.07 (s, 3H), 4.07 - 4.04 (m, 4H), 3.50 - 3.38 (m, 4H), 3.17 (t, J=3.9 Hz, 1H), 2.97 (dd, J=10.7, 3.9 Hz, 1H), 2.69 (t, J=3.9 Hz, 1H), 2.12 - 2.05 (m, 1H), 1.90 - 1.81 (m, 1H), 1.62 (s, 9H), 1.61 - 1.54 (m, 2H), 1.50 - 1.43 (m, 1H), 0.78 - 0.69 (m, 2H), 0.37 - 0.28 (m, 2H)	1.23, A

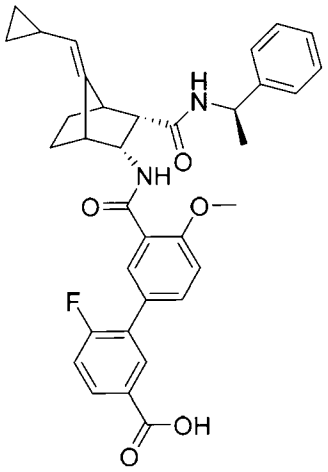
252		N-環丁基胺基甲酸 1-[4'-(苯甲基氧基)-3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-[1,1'-聯苯]-3-基]-2,2,2-三氟乙酯	868.2	(500 MHz, DMSO-d6) δ 10.46 (s, 1H), 9.88 - 9.81 (m, 1H), 8.14 - 8.08 (m, 2H), 8.06 (s, 1H), 7.75 - 7.69 (m, 1H), 7.64 (br d, J=7.0 Hz, 1H), 7.59 (br d, J=8.5 Hz, 1H), 7.54 (br d, J=7.3 Hz, 3H), 7.43 - 7.36 (m, 2H), 7.30 (td, J=13.5, 7.8 Hz, 4H), 6.38 - 6.30 (m, 1H), 5.50 (s, 2H), 4.67 (d, J=9.8 Hz, 1H), 4.54 - 4.42 (m, 1H), 3.98 - 3.86 (m, 1H), 3.15 (br dd, J=10.8, 3.8 Hz, 1H), 3.05 (br s, 1H), 2.69 (br s, 1H), 2.17 - 2.03 (m, 2H), 1.95 - 1.81 (m, 2H), 1.76 - 1.65 (m, 2H), 1.60 - 1.52 (m, 2H), 1.51 - 1.44 (m, 1H), 1.36 - 1.28 (m, 2H), 0.79 - 0.67 (m, 2H), 0.39 - 0.28 (m, 2H)	1.34, A

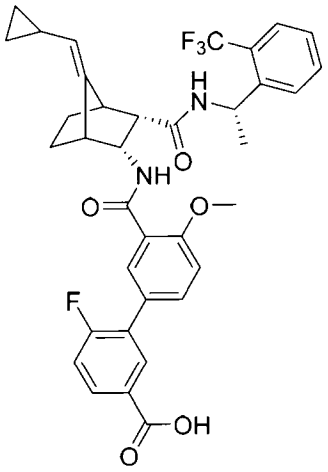
254		N-(3,3-二氟環丁基)胺基甲酸1-(3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-(2-羥基乙氧基)-[1,1'-聯苯]-3-基)-2,2,2-三氟乙酯	858.0	(500 MHz, $CDCl_3$) δ 9.55 (br d, J=8.4 Hz, 1H), 8.30 (d, J=2.3 Hz, 1H), 7.73 (br d, J=8.7 Hz, 1H), 7.65 (s, 1H), 7.59 - 7.51 (m, 3H), 7.42 - 7.35 (m, 1H), 7.21 - 7.14 (m, 2H), 7.11 (d, J=8.7 Hz, 1H), 6.08 (q, J=6.7 Hz, 1H), 5.51 (br d, J=7.0 Hz, 1H), 4.92 - 4.83 (m, 1H), 4.69 (d, J=9.6 Hz, 1H), 4.51 - 4.42 (m, 1H), 4.29 - 4.21 (m, 2H), 4.13 - 4.03 (m, 2H), 3.18 (t, J=4.0 Hz, 1H), 3.12 (dd, J=10.9, 3.9 Hz, 1H), 3.07 - 2.89 (m, 2H), 2.75 (t, J=4.0 Hz, 1H), 2.63 - 2.48 (m, 2H), 2.20 - 2.13 (m, 1H), 1.95 - 1.87 (m, 1H), 1.79 - 1.70 (m, 1H), 1.68 - 1.58 (m, 1H), 1.54 - 1.45 (m, 1H), 0.84 - 0.74 (m, 2H), 0.41 - 0.32 (m, 2H)	1.31, A

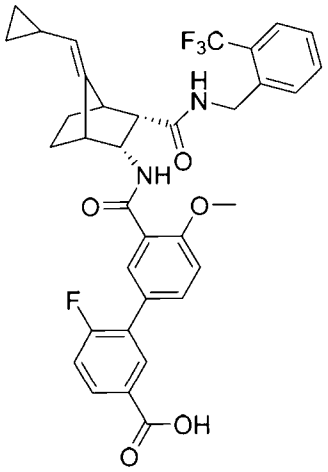
255		N-[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]-5'-(2,4-二側氧基-3-苯基-1,3-噁唑啶-5-基)-2'-氟-4-甲氧基-[1,1'-聯苯]-3-甲醯胺	772.3	(500 MHz, $CDCl_3$) δ 9.48 (dd, *J*=7.9, 2.4 Hz, 1H), 8.44 - 8.37 (m, 1H), 8.03 - 7.94 (m, 1H), 7.86 (s, 1H), 7.68 (dt, *J*=8.6, 1.8 Hz, 1H), 7.64 - 7.59 (m, 1H), 7.56 - 7.43 (m, 7H), 7.15 - 7.07 (m, 2H), 5.96 (s, 1H), 4.89 - 4.81 (m, 1H), 4.66 (d, *J*=9.5 Hz, 1H), 4.08 (s, 3H), 3.22 (t, *J*=4.2 Hz, 1H), 3.14 - 3.06 (m, 1H), 2.74 (t, *J*=4.0 Hz, 1H), 2.25 - 2.16 (m, 1H), 1.94 - 1.87 (m, 1H), 1.71 - 1.61 (m, 2H), 1.55 - 1.48 (m, 1H), 0.80 - 0.72 (m, 2H), 0.36 (td, *J*=4.0, 2.4 Hz, 2H)	1.20, A

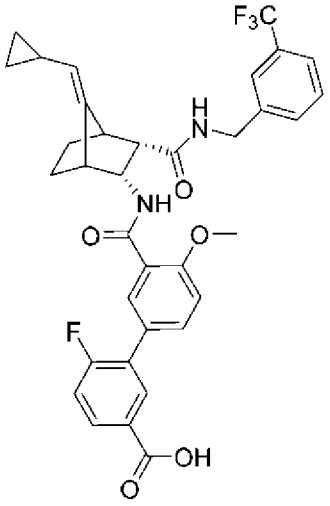
257		N-[1-(3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2-羥基乙基]喔烷-4-甲醯胺	768.6	(500 MHz, $CDCl_3$) δ 9.55 (br d, *J*=7.7 Hz, 1H), 8.32 (s, 1H), 8.01 - 7.89 (m, 2H), 7.59 (br d, *J*=8.5 Hz, 1H), 7.55 - 7.48 (m, 1H), 7.35 - 7.30 (m, 1H), 7.24 - 7.19 (m, 1H), 7.15 - 7.02 (m, 2H), 6.40 - 6.24 (m, 1H), 5.12 - 5.04 (m, 1H), 4.84 - 4.75 (m, 1H), 4.63 (d, *J*=9.6 Hz, 1H), 4.06 (s, 3H), 4.04 - 3.97 (m, 2H), 3.91 (br d, *J*=4.4 Hz, 2H), 3.42 (tt, *J*=11.5, 3.2 Hz, 2H), 3.19 (br t, *J*=3.9 Hz, 1H), 3.08 (br dd, *J*=10.5, 3.0 Hz, 1H), 2.71 (t, *J*=3.9 Hz, 1H), 2.48 - 2.41 (m, 1H), 2.21 - 2.17 (m, 1H), 1.92 - 1.76 (m, 4H), 1.70 - 1.59 (m, 2H), 1.51 - 1.44 (m, 1H), 0.78 - 0.71 (m, 2H), 0.37 - 0.30 (m, 2H)	1.10, A

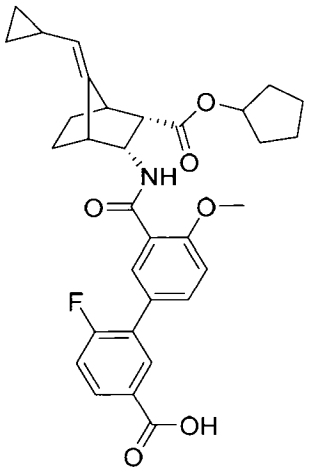
260		3'-{[(2R,3S,7Z)-3-(苯甲基胺甲醯基)-7-(環丙基亞甲基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-甲酸	569.0	(500 MHz, $CDCl_3$) 9.71 (d, J=6.9 Hz, 1H), 8.37 (s, 1H), 8.22 (dd, J=5.1, 1.9 Hz, 1H), 8.02 - 7.89 (m, 1H), 7.66 - 7.56 (m, 1H), 7.23 - 7.15 (m, 5H), 7.14 - 7.06 (m, 1H), 6.99 (d, J=7.5 Hz, 1H), 6.12 - 5.79 (m, 1H), 4.75 - 4.64 (m, 1H), 4.57 (d, J=9.0 Hz, 1H), 4.39 (d, J=5.6 Hz, 2H), 4.00 (s, 3H), 3.27 - 3.14 (m, 1H), 2.87 (br dd, J=10.6, 3.0 Hz, 1H), 2.57 - 2.49 (m, 1H), 2.20 - 2.08 (m, 1H), 1.99 - 1.85 (m, 1H), 1.61 - 1.39 (m, 3H), 0.75 - 0.60 (m, 2H), 0.35 - 0.18 (m, 2H)	1.91, A

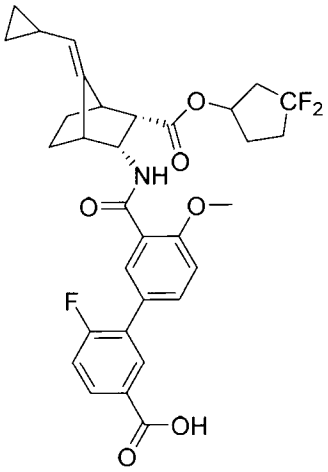
261		3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[(1R)-1-苯基乙基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-甲酸	582.9	(500 MHz, $CDCl_3$) δ 9.72 (br d, J=7.5 Hz, 1H), 8.42 (d, J=1.8 Hz, 1H), 8.26 (dd, J=7.5, 1.7 Hz, 1H), 8.05 - 7.97 (m, 1H), 7.69 - 7.64 (m, 1H), 7.34 - 7.21 (m, 6H), 7.18 (t, J=9.3 Hz, 1H), 7.07 (d, J=8.6 Hz, 1H), 5.82 (br d, J=7.6 Hz, 1H), 5.07 (quin, J=7.1 Hz, 1H), 4.74 - 4.67 (m, 1H), 4.58 (d, J=9.2 Hz, 1H), 4.09 (s, 2H), 3.71 (s, 1H), 3.21 (t, J=4.1 Hz, 1H), 2.92 - 2.80 (m, 1H), 2.60 (s, 1H), 2.51 (t, J=4.1 Hz, 1H), 2.08 - 1.99 (m, 1H), 1.92 - 1.84 (m, 1H), 1.57 - 1.42 (m, 3H), 1.39 (d, J=6.9 Hz, 3H), 0.75 - 0.64 (m, 2H), 0.28 (dd, J=4.5, 2.0 Hz, 2H)	1.94, A

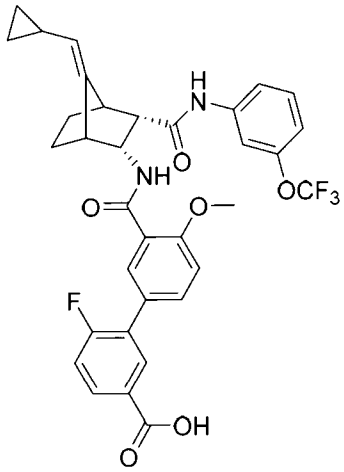
262		3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[(1S)-1-[2-(三氟甲基)苯基]乙基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-甲酸	651.48	(500 MHz, DMSO-d6) δ 9.82 (br d, J=6.8 Hz, 1H), 8.39 (br d, J=6.6 Hz, 1H), 7.89 (s, 1H), 7.83 - 7.76 (m, 1H), 7.71 (ddd, J=8.3, 4.9, 2.1 Hz, 1H), 7.47 (br d, J=8.4 Hz, 1H), 7.44 - 7.38 (m, 3H), 7.20 (br dt, J=8.0, 4.2 Hz, 1H), 7.14 (br dd, J=10.4, 8.7 Hz, 1H), 7.05 (d, J=8.7 Hz, 1H), 5.08 - 4.91 (m, 1H), 4.42 (d, J=9.2 Hz, 1H), 4.09 (dt, J=9.9, 4.8 Hz, 1H), 3.76 (s, 3H), 2.82 (br t, J=3.7 Hz, 1H), 2.80 - 2.77 (m, 1H), 2.37 (br t, J=4.0 Hz, 1H), 1.45 - 1.32 (m, 1H), 1.22 (td, J=8.7, 4.0 Hz, 1H), 1.19 - 1.14 (m, 1H), 1.09 (br d, J=6.8 Hz, 3H), 1.06 - 0.99 (m, 1H), 0.97 - 0.87 (m, 1H), 0.55 - 0.39 (m, 2H), 0.08 (br d, J=4.5 Hz, 2H)	2.05, B

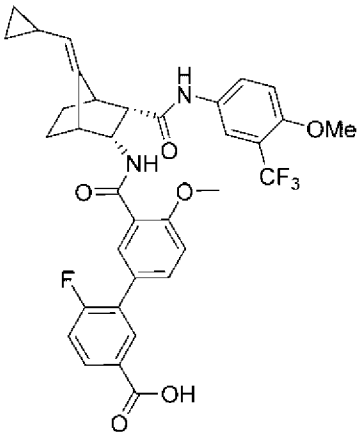
263		3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-({[2-(三氟甲基)苯基]甲基}胺甲醯基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-甲酸	637.15	(500 MHz, CDCl3) δ 9.69 (br d, J=6.9 Hz, 1H), 8.36 (br s, 1H), 8.22 (br d, J=6.0 Hz, 1H), 8.03 - 7.90 (m, 1H), 7.63 (br d, J=7.2 Hz, 1H), 7.57 (br d, J=7.7 Hz, 1H), 7.42 (br d, J=7.7 Hz, 1H), 7.33 - 7.28 (m, 1H), 7.27 (br d, J=7.9 Hz, 1H), 7.19 - 7.08 (m, 1H), 7.01 (br d, J=8.3 Hz, 1H), 6.07 - 5.95 (m, 1H), 4.75 - 4.66 (m, 1H), 4.66 - 4.53 (m, 3H), 4.01 (s, 3H), 3.20 (br s, 1H), 2.90 (br dd, J=10.6, 3.5 Hz, 1H), 2.54 (br t, J=3.7 Hz, 1H), 2.09 (br t, J=9.8 Hz, 1H), 1.97 - 1.84 (m, 1H), 1.60 - 1.41 (m, 3H), 0.75 - 0.58 (m, 2H), 0.36 - 0.19 (m, 2H)	2.09, A

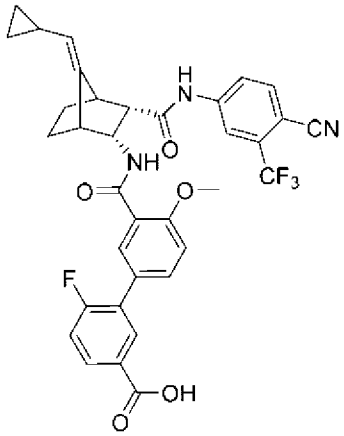
264		3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-({[3-(三氟甲基)苯基]甲基}胺甲醯基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-甲酸	637.27	(400 MHz, CDCl3) δ 9.76 (br d, J=7.4 Hz, 1H), 8.42 (s, 1H), 8.36 - 8.24 (m, 1H), 8.09 - 7.94 (m, 1H), 7.77 - 7.67 (m, 1H), 7.53 - 7.48 (m, 1H), 7.47 - 7.36 (m, 2H), 7.34 - 7.28 (m, 1H), 7.21 (t, J=9.5 Hz, 1H), 7.06 (d, J=8.8 Hz, 1H), 6.45 - 6.14 (m, 1H), 4.86 - 4.69 (m, 1H), 4.60 (d, J=9.6 Hz, 1H), 4.54 - 4.38 (m, 2H), 4.11 - 3.92 (m, 3H), 3.23 (d, J=3.7 Hz, 1H), 2.99 (dd, J=10.3, 4.2 Hz, 1H), 2.70 - 2.51 (m, 1H), 2.16 (t, J=8.4 Hz, 1H), 2.02 - 1.80 (m, 1H), 1.73 - 1.41 (m, 3H), 0.81 - 0.62 (m, 2H), 0.42 - 0.19 (m, 2H)	1.88, A

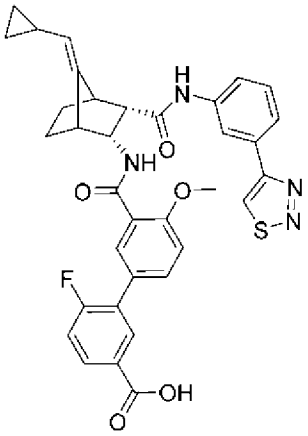
266		3'-{[(2R,3S,7Z)-3-[(環戊基氧基)羰基]-7-(環丙基亞甲基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-甲酸	582.9	(500 MHz, $CDCl_3$) δ 9.72 (br d, J=7.5 Hz, 1H), 8.42 (d, J=1.8 Hz, 1H), 8.26 (dd, J=7.5, 1.7 Hz, 1H), 8.05 - 7.97 (m, 1H), 7.69 - 7.64 (m, 1H), 7.34 - 7.21 (m, 6H), 7.18 (t, J=9.3 Hz, 1H), 7.07 (d, J=8.6 Hz, 1H), 5.82 (br d, J=7.6 Hz, 1H), 5.07 (quin, J=7.1 Hz, 1H), 4.74 - 4.67 (m, 1H), 4.58 (d, J=9.2 Hz, 1H), 4.09 (s, 2H), 3.71 (s, 1H), 3.21 (t, J=4.1 Hz, 1H), 2.92 - 2.80 (m, 1H), 2.60 (s, 1H), 2.51 (t, J=4.1 Hz, 1H), 2.08 - 1.99 (m, 1H), 1.92 - 1.84 (m, 1H), 1.57 - 1.42 (m, 3H), 1.39 (d, J=6.9 Hz, 3H), 0.75 - 0.64 (m, 2H), 0.28 (dd, J=4.5, 2.0 Hz, 2H)	2.19, B

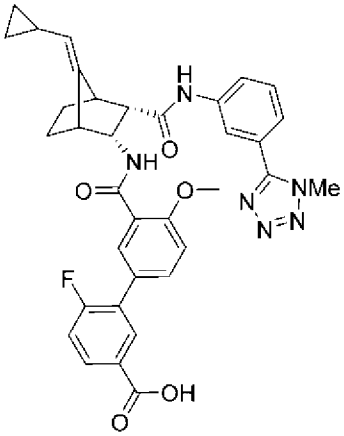
267		3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-[(3,3-二氟環戊基)胺甲醯基]雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-甲酸	651.48	(500 MHz, DMSO-d6) δ 9.82 (br d, J=6.8 Hz, 1H), 8.39 (br d, J=6.6 Hz, 1H), 7.89 (s, 1H), 7.83 - 7.76 (m, 1H), 7.71 (ddd, J=8.3, 4.9, 2.1 Hz, 1H), 7.47 (br d, J=8.4 Hz, 1H), 7.44 - 7.38 (m, 3H), 7.20 (br dt, J=8.0, 4.2 Hz, 1H), 7.14 (br dd, J=10.4, 8.7 Hz, 1H), 7.05 (d, J=8.7 Hz, 1H), 5.08 - 4.91 (m, 1H), 4.42 (d, J=9.2 Hz, 1H), 4.09 (dt, J=9.9, 4.8 Hz, 1H), 3.76 (s, 3H), 2.82 (br t, J=3.7 Hz, 1H), 2.80 - 2.77 (m, 1H), 2.37 (br t, J=4.0 Hz, 1H), 1.45 - 1.32 (m, 1H), 1.22 (td, J=8.7, 4.0 Hz, 1H), 1.19 - 1.14 (m, 1H), 1.09 (br d, J=6.8 Hz, 3H), 1.06 - 0.99 (m, 1H), 0.97 - 0.87 (m, 1H), 0.55 - 0.39 (m, 2H), 0.08 (br d, J=4.5 Hz, 2H)	2.2, A

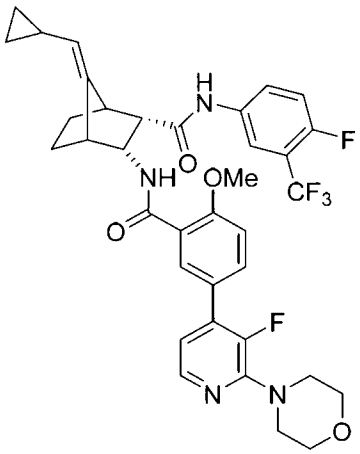
268		3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[3-(三氟甲氧基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-甲酸	637.15	(500 MHz, $CDCl_3$) δ 9.69 (br d, J=6.9 Hz, 1H), 8.36 (br s, 1H), 8.22 (br d, J=6.0 Hz, 1H), 8.03 - 7.90 (m, 1H), 7.63 (br d, J=7.2 Hz, 1H), 7.57 (br d, J=7.7 Hz, 1H), 7.42 (br d, J=7.7 Hz, 1H), 7.33 - 7.28 (m, 1H), 7.27 (br d, J=7.9 Hz, 1H), 7.19 - 7.08 (m, 1H), 7.01 (br d, J=8.3 Hz, 1H), 6.07 - 5.95 (m, 1H), 4.75 - 4.66 (m, 1H), 4.66 - 4.53 (m, 3H), 4.01 (s, 3H), 3.20 (br s, 1H), 2.90 (br dd, J=10.6, 3.5 Hz, 1H), 2.54 (br t, J=3.7 Hz, 1H), 2.09 (br t, J=9.8 Hz, 1H), 1.97 - 1.84 (m, 1H), 1.60 - 1.41 (m, 3H), 0.75 - 0.58 (m, 2H), 0.36 - 0.19 (m, 2H)	2.61, A

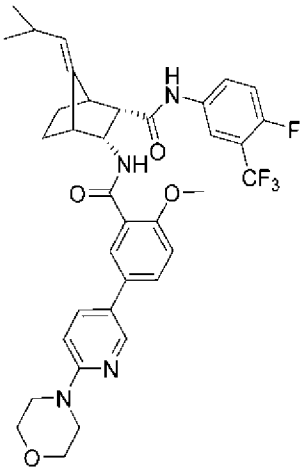
269		3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-甲氧基-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-甲酸	637.27	(400 MHz, $CDCl_3$) δ 9.76 (br d, J=7.4 Hz, 1H), 8.42 (s, 1H), 8.36 - 8.24 (m, 1H), 8.09 - 7.94 (m, 1H), 7.77 - 7.67 (m, 1H), 7.53 - 7.48 (m, 1H), 7.47 - 7.36 (m, 2H), 7.34 - 7.28 (m, 1H), 7.21 (t, J=9.5 Hz, 1H), 7.06 (d, J=8.8 Hz, 1H), 6.45 - 6.14 (m, 1H), 4.86 - 4.69 (m, 1H), 4.60 (d, J=9.6 Hz, 1H), 4.54 - 4.38 (m, 2H), 4.11 - 3.92 (m, 3H), 3.23 (d, J=3.7 Hz, 1H), 2.99 (dd, J=10.3, 4.2 Hz, 1H), 2.70 - 2.51 (m, 1H), 2.16 (t, J=8.4 Hz, 1H), 2.02 - 1.80 (m, 1H), 1.73 - 1.41 (m, 3H), 0.81 - 0.62 (m, 2H), 0.42 - 0.19 (m, 2H)	2.48, B

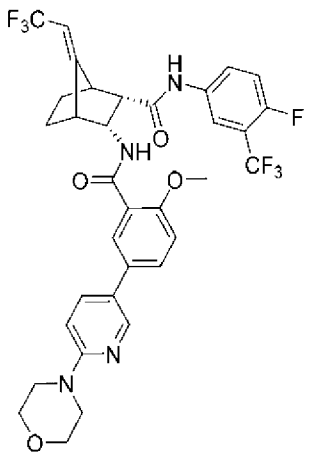
270		3'-{[(2R,3S,7Z)-3-{[4-氰基-3-(三氟甲基)苯基]胺甲醯基}-7-(環丙基亞甲基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-甲酸	648.18	(500 MHz, DMSO-d6) δ 10.99 (s, 1H), 9.84 (br d, J=7.0 Hz, 1H), 8.38 (s, 1H), 8.12 (s, 1H), 8.08 (d, J=8.5 Hz, 1H), 8.03 - 7.97 (m, 1H), 7.97 - 7.93 (m, 1H), 7.93 - 7.88 (m, 1H), 7.78 - 7.64 (m, 1H), 7.41 - 7.22 (m, 2H), 4.69 (d, J=9.5 Hz, 1H), 4.55 - 4.38 (m, 1H), 4.07 (s, 3H), 3.22 (dd, J=10.8, 3.8 Hz, 1H), 3.13 - 3.08 (m, 1H), 2.80 - 2.67 (m, 1H), 1.90 (s, 1H), 1.86 - 1.73 (m, 2H), 1.62 - 1.46 (m, 1H), 1.46 - 1.33 (m, 2H), 0.86 - 0.60 (m, 2H), 0.42 - 0.23 (m, 2H)	1.95, A

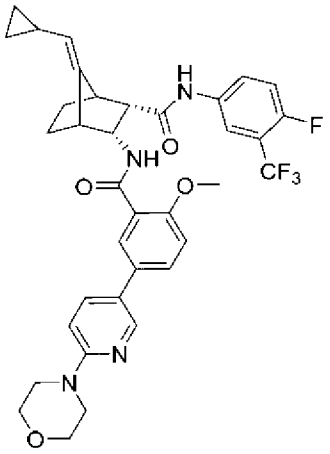
271		3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[3-(1,2,3-噻二唑-4-基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-甲酸	639.3	(500 MHz, DMSO-d6) δ 10.37 (s, 1H), 10.02 (br d, J=7.0 Hz, 1H), 9.50 (s, 1H), 8.57 (s, 1H), 8.13 (s, 1H), 8.01 (d, J=7.0 Hz, 1H), 7.98 - 7.91 (m, 1H), 7.74 (dd, J=18.6, 7.9 Hz, 2H), 7.66 (d, J=7.9 Hz, 1H), 7.53 - 7.47 (m, 1H), 7.40 (t, J=9.5 Hz, 1H), 7.30 (d, J=8.5 Hz, 1H), 4.69 (d, J=9.8 Hz, 1H), 4.52 - 4.40 (m, 1H), 4.08 (s, 3H), 3.24 - 3.18 (m, 1H), 3.15 - 3.09 (m, 1H), 2.77 - 2.70 (m, 1H), 1.96 - 1.88 (m, 1H), 1.86 - 1.78 (m, 1H), 1.55 - 1.47 (m, 1H), 1.47 - 1.34 (m, 2H), 0.80 - 0.66 (m, 2H), 0.41 - 0.28 (m, 2H)	2.35, B

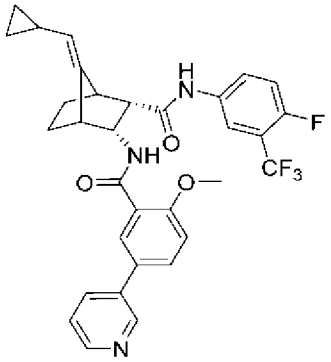
272		3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[3-(1-甲基-1H-1,2,3,4-四唑-5-基)苯氧基]羰基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-甲酸	638.16	(500 MHz, DMSO-d6) δ 10.46 (s, 1H), 9.97 (br d, J=7.0 Hz, 1H), 8.21 (s, 1H), 8.14 (s, 1H), 8.05 - 7.98 (m, 1H), 7.98 - 7.92 (m, 1H), 7.82 (d, J=7.6 Hz, 1H), 7.74 (d, J=8.2 Hz, 1H), 7.61 - 7.53 (m, 2H), 7.42 (t, J=9.3 Hz, 1H), 7.32 (d, J=8.5 Hz, 1H), 4.70 (d, J=9.5 Hz, 1H), 4.54 - 4.40 (m, 1H), 4.17 (s, 3H), 4.07 (s, 3H), 3.20 (dd, J=10.4, 3.4 Hz, 1H), 3.15 - 3.07 (m, 1H), 2.73 (br d, J=3.1 Hz, 1H), 1.96 - 1.87 (m, 1H), 1.86 - 1.79 (m, 1H), 1.57 - 1.48 (m, 1H), 1.47 - 1.35 (m, 2H), 0.79 - 0.66 (m, 2H), 0.45 - 0.25 (m, 2H)	1.57, A

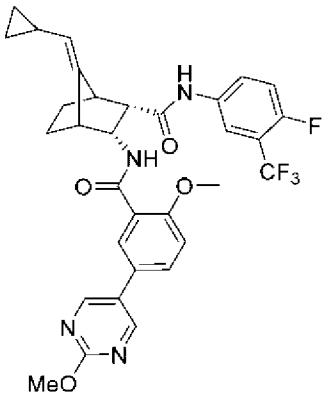
274		(2S,3R,7Z)-7-(環丙基亞甲基)-3-{5-[3-氟-2-(味啉-4-基)吡啶-4-基]-2-甲氧基苯甲醯胺基}-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	683.0	(500 MHz, $CDCl_3$) δ 9.47 (br d, J=7.5 Hz, 1H), 8.42 (s, 1H), 8.04 (d, J=4.9 Hz, 1H), 7.98 - 7.91 (m, 1H), 7.86 (s, 1H), 7.73 - 7.64 (m, 1H), 7.59 - 7.46 (m, 1H), 7.13 - 7.02 (m, 2H), 6.88 (t, J=4.8 Hz, 1H), 4.90 - 4.76 (m, 1H), 4.64 (d, J=9.5 Hz, 1H), 4.07 (s, 3H), 3.95 - 3.82 (m, 4H), 3.58 - 3.44 (m, J=4.1 Hz, 4H), 3.24 - 3.16 (m, 1H), 3.09 (dd, J=10.7, 3.1 Hz, 1H), 2.78 - 2.65 (m, 1H), 2.25 - 2.09 (m, 1H), 1.97 - 1.81 (m, 1H), 1.74 - 1.61 (m, 2H), 1.54 - 1.41 (m, 1H), 0.82 - 0.65 (m, 2H), 0.45 - 0.26 (m, 2H)	2.52, A

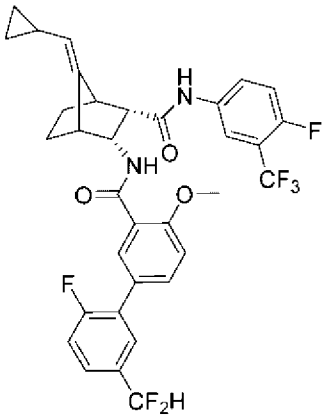
275		(2S,3R,7Z)-N-[4-氟-3-(三氟甲基)苯基]-3-{2-甲氧基-5-[6-(味啉-4-基)吡啶-3-基]苯甲醯胺基}-7-(2-甲基亞丙基)雙環[2.2.1]庚烷-2-甲醯胺	667.1	(500 MHz, $CDCl_3$) δ 9.40 (br d, J=7.7 Hz, 1H), 8.43 (d, J=2.1 Hz, 1H), 8.36 (d, J=2.3 Hz, 1H), 7.97 - 7.89 (m, 2H), 7.73 (dd, J=8.7, 2.4 Hz, 1H), 7.60 (dd, J=8.5, 2.4 Hz, 1H), 7.56 - 7.50 (m, 1H), 7.12 - 6.97 (m, 2H), 6.71 (d, J=8.7 Hz, 1H), 5.07 (d, J=9.1 Hz, 1H), 4.80 - 4.70 (m, 1H), 4.03 (s, 3H), 3.90 - 3.83 (m, 4H), 3.64 - 3.50 (m, 4H), 3.13 - 3.03 (m, 2H), 2.73 - 2.66 (m, 1H), 2.59 - 2.43 (m, 1H), 2.25 - 2.10 (m, 1H), 1.92 - 1.78 (m, 1H), 1.01 (dd, J=15.1, 6.6 Hz, 6H)	2.21, C

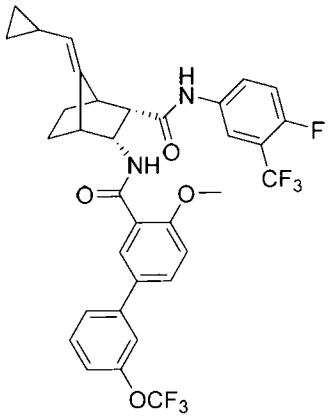
276		(2S,3R,7Z)-N-[4-氟-3-(三氟甲基)苯基]-3-{2-甲氧基-5-[6-(味啉-4-基)吡啶-3-基]苯甲醯胺基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-甲醯胺	693.3	(500 MHz, $CDCl_3$) δ 9.29 (d, J=8.0 Hz, 1H), 8.42 (d, J=2.3 Hz, 1H), 8.33 (d, J=2.5 Hz, 1H), 8.21 (s, 1H), 7.89 (dd, J=6.2, 2.6 Hz, 1H), 7.70 (dd, J=8.8, 2.6 Hz, 1H), 7.61 (dd, J=8.5, 2.6 Hz, 1H), 7.53 (dt, J=8.8, 3.5 Hz, 1H), 7.08 - 6.98 (m, 2H), 6.71 (d, J=8.8 Hz, 1H), 5.58 (q, J=7.4 Hz, 1H), 4.96 - 4.84 (m, 1H), 3.89 - 3.82 (m, 3H), 3.60 - 3.52 (m, 4H), 3.44 - 3.37 (m, 1H), 3.18 (dd, J=10.9, 3.9 Hz, 1H), 2.92 (t, J=3.9 Hz, 1H), 2.63 (s, 1H), 2.46 - 2.36 (m, 1H), 2.02 - 1.94 (m, 1H), 1.81 - 1.66 (m, 2H), 1.59 (s, 3H)	2.08, C

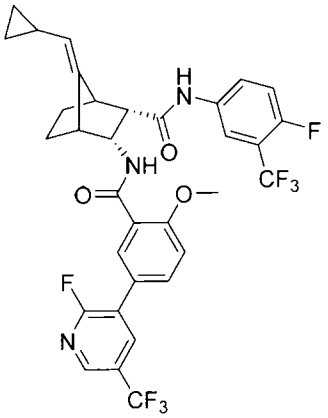
277		(2S,3R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{2-甲氧基-5-[6-(味啉-4-基)吡啶-3-基]苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	366.1	(500 MHz, $CDCl_3$) δ 9.57 (br d, J=7.7 Hz, 1H), 8.52 (d, J=1.9 Hz, 1H), 8.30 (d, J=2.5 Hz, 1H), 8.26 (br s, 1H), 8.09 (dd, J=9.1, 2.2 Hz, 1H), 8.04 (dd, J=5.9, 2.3 Hz, 1H), 7.70 - 7.61 (m, 1H), 7.57 (dd, J=8.8, 2.5 Hz, 1H), 7.13 (t, J=9.4 Hz, 1H), 7.03 - 6.96 (m, 2H), 4.67 (d, J=9.4 Hz, 2H), 4.06 (s, 3H), 3.98 - 3.88 (m, 4H), 3.83 - 3.70 (m, 4H), 3.18 (t, J=4.0 Hz, 1H), 3.11 (dd, J=10.9, 4.0 Hz, 1H), 2.73 (t, J=3.6 Hz, 1H), 1.91 - 1.84 (m, 2H), 1.69 - 1.57 (m, 2H), 1.50 (tt, J=12.9, 4.7 Hz, 1H), 0.82 - 0.71 (m, 2H), 0.43 - 0.29 (m, 2H)	0.70, A

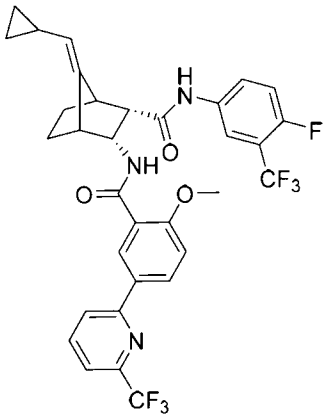
278		(2S,3R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-[2-甲氧基-5-(吡啶-3-基)苯甲醯胺基]雙環[2.2.1]庚烷-2-甲醯胺	580.3	(500 MHz, DMSO-d6) δ 10.50 (s, 1H), 9.87 (br d, J=7.0 Hz, 1H), 8.78 (s, 1H), 8.49 (d, J=3.7 Hz, 1H), 8.21 - 8.09 (m, 2H), 7.98 (d, J=7.3 Hz, 1H), 7.83 (dd, J=8.9, 1.5 Hz, 1H), 7.78 - 7.65 (m, 1H), 7.50 - 7.37 (m, 2H), 7.28 (d, J=8.5 Hz, 1H), 4.64 (d, J=9.8 Hz, 1H), 4.48 - 4.36 (m, 1H), 4.00 (s, 2H), 3.60 - 3.46 (m, 1H), 3.11 (dd, J=10.5, 4.1 Hz, 1H), 3.08 - 3.03 (m, 1H), 2.71 - 2.63 (m, 1H), 1.89 - 1.66 (m, 2H), 1.55 - 1.27 (m, 3H), 0.69 (br dd, J=11.4, 9.0 Hz, 2H), 0.37 - 0.21 (m, 2H)	2.05, C

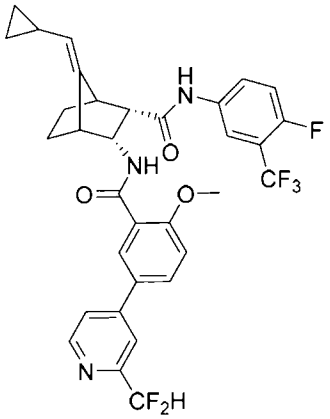
279		(2S,3R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-[2-甲氧基-5-(2-甲氧基嘧啶-5-基)苯甲醯胺基]雙環[2.2.1]庚烷-2-甲醯胺	611.3	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.89 (br d, J=7.3 Hz, 1H), 8.84 (s, 2H), 8.19 (dd, J=6.6, 2.0 Hz, 1H), 8.16 (d, J=2.1 Hz, 1H), 7.83 (dd, J=8.2, 2.4 Hz, 1H), 7.80 - 7.72 (m, 1H), 7.46 (t, J=9.6 Hz, 1H), 7.30 (d, J=8.5 Hz, 1H), 4.68 (d, J=9.5 Hz, 1H), 4.50 - 4.39 (m, 1H), 4.02 (s, 3H), 3.94 (s, 3H), 3.14 (dd, J=10.8, 3.2 Hz, 1H), 3.11 - 3.07 (m, 1H), 2.76 - 2.65 (m, 1H), 1.90 - 1.72 (m, 2H), 1.56 - 1.33 (m, 4H), 0.82 - 0.61 (m, 3H), 0.42 - 0.24 (m, 2H)	2.54, C

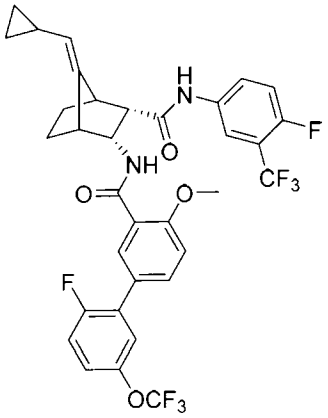
280		N-[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]-5'-(二氟甲基)-2'-氟-4-甲氧基-[1,1'-聯苯]-3-甲醯胺	647.1	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.91 (d, J=7.3 Hz, 1H), 8.19 (dd, J=6.3, 2.3 Hz, 1H), 8.12 (s, 1H), 7.82 - 7.67 (m, 3H), 7.61 (br d, J=8.9 Hz, 1H), 7.45 (t, J=9.6 Hz, 2H), 7.31 (d, J=8.9 Hz, 1H), 7.21 - 6.90 (m, 1H), 4.67 (d, J=9.8 Hz, 1H), 4.49 - 4.39 (m, 1H), 4.04 (s, 3H), 3.20 - 3.11 (m, 1H), 3.11 - 3.05 (m, 1H), 2.74 - 2.66 (m, 1H), 1.90 - 1.81 (m, 1H), 1.81 - 1.72 (m, 1H), 1.55 - 1.45 (m, 1H), 1.44 - 1.34 (m, 2H), 0.72 (quin, J=9.5 Hz, 2H), 0.39 - 0.27 (m, 2H)	2.78, C

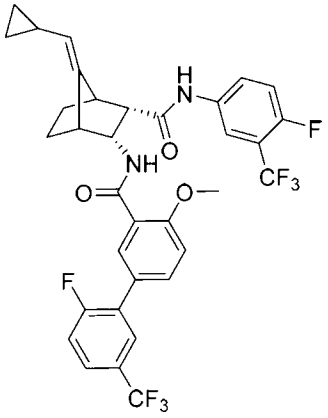
281		N-[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]-4-甲氧基-3'-(三氟甲氧基)-[1,1'-聯苯]-3-甲醯胺	663.2	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.93 (d, J=7.2 Hz, 1H), 8.28 - 8.17 (m, 2H), 7.88 (dd, J=8.6, 2.4 Hz, 1H), 7.82 - 7.76 (m, 1H), 7.68 (d, J=8.1 Hz, 1H), 7.63 - 7.55 (m, 2H), 7.49 (t, J=9.8 Hz, 1H), 7.34 (d, J=8.4 Hz, 1H), 7.31 (d, J=8.8 Hz, 1H), 4.70 (d, J=9.6 Hz, 1H), 4.55 - 4.41 (m, 1H), 4.05 (s, 3H), 3.24 - 3.14 (m, 1H), 3.14 - 3.05 (m, 1H), 2.78 - 2.68 (m, 1H), 1.96 - 1.71 (m, 2H), 1.58 - 1.46 (m, 1H), 1.46 - 1.31 (m, 2H), 0.87 - 0.62 (m, 2H), 0.44 - 0.29 (m, 2H)	2.92, C

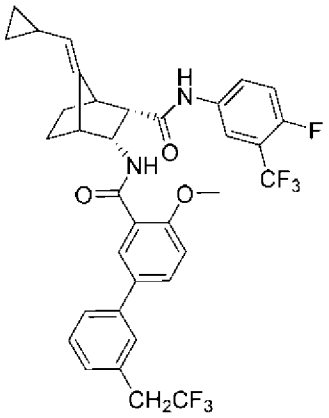
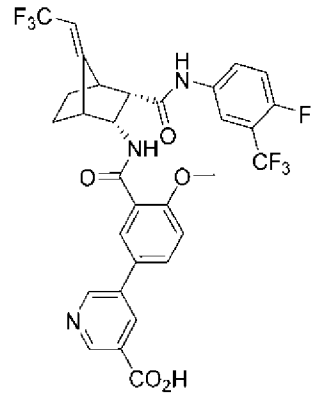
282		(2S,3R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[2-氟-5-(三氟甲基)吡啶-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	666.3	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.90 (d, J=7.3 Hz, 1H), 8.66 (s, 1H), 8.53 - 8.44 (m, 1H), 8.24 - 8.19 (m, 2H), 7.85 (d, J=9.2 Hz, 1H), 7.81 - 7.72 (m, 1H), 7.47 (t, J=9.6 Hz, 1H), 7.35 (d, J=8.9 Hz, 1H), 4.69 (d, J=9.5 Hz, 1H), 4.50 - 4.40 (m, 1H), 4.06 (s, 3H), 3.16 (dd, J=10.7, 3.7 Hz, 1H), 3.13 - 3.07 (m, 1H), 2.75 - 2.68 (m, 1H), 1.90 - 1.75 (m, 2H), 1.57 - 1.45 (m, 1H), 1.45 - 1.34 (m, 2H), 0.73 (quin, J=9.6 Hz, 2H), 0.41 - 0.28 (m, 2H)	2.83, C

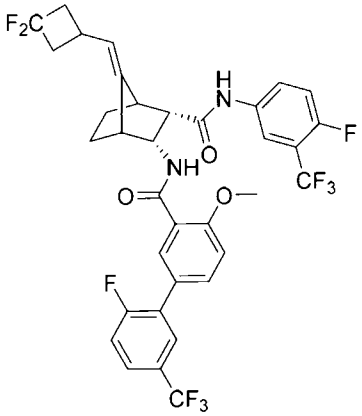
283		(2S,3R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{2-甲氧基-5-[6-(三氟甲基)吡啶-2-基]苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	647.9	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.93 (br d, J=6.8 Hz, 1H), 8.73 (d, J=2.1 Hz, 1H), 8.31 - 8.19 (m, 3H), 8.14 (t, J=7.8 Hz, 1H), 7.81 (d, J=7.9 Hz, 1H), 7.79 - 7.74 (m, 1H), 7.48 (t, J=9.8 Hz, 1H), 7.35 (d, J=8.8 Hz, 1H), 4.69 (d, J=9.4 Hz, 1H), 4.53 - 4.41 (m, 1H), 4.07 (s, 3H), 3.23 - 3.14 (m, 1H), 3.14 - 3.10 (m, 1H), 2.75 - 2.70 (m, 1H), 1.88 - 1.71 (m, 2H), 1.59 - 1.47 (m, 1H), 1.47 - 1.34 (m, 2H), 0.82 - 0.64 (m, 2H), 0.43 - 0.28 (m, 2H)	2.85, C

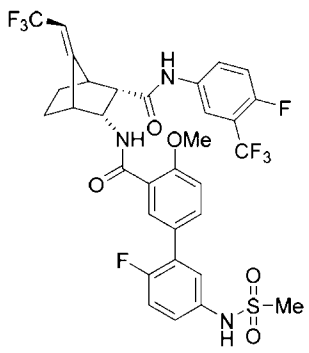
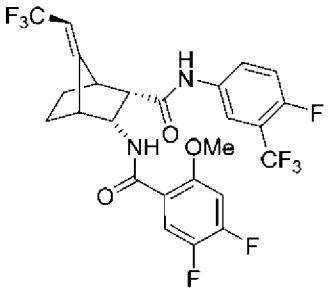
284		(2S,3R,7Z)-7-(環丙基亞甲基)-3-{5-[2-(二氟甲基)吡啶-4-基]-2-甲氧基苯甲醯胺基 }-N-[4- 氟 -3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	630.3	(500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.92 (d, J=7.0 Hz, 1H), 8.72 (d, J=2.4 Hz, 1H), 8.28 - 8.17 (m, 2H), 8.16 - 8.00 (m, 2H), 7.82 - 7.76 (m, 1H), 7.62 (d, J=7.3 Hz, 1H), 7.48 (t, J=9.8 Hz, 1H), 7.34 (d, J=8.9 Hz, 1H), 7.18 - 6.83 (m, 1H), 4.70 (d, J=9.8 Hz, 1H), 4.55 - 4.39 (m, 1H), 4.07 (s, 3H), 3.17 (br dd, J=10.7, 4.0 Hz, 1H), 3.15 - 3.11 (m, 1H), 2.76 - 2.70 (m, 1H), 1.95 - 1.72 (m, 2H), 1.61 - 1.47 (m, 1H), 1.47 - 1.32 (m, 2H), 0.85 - 0.64 (m, 2H), 0.47 - 0.25 (m, 2H)	2.77, C

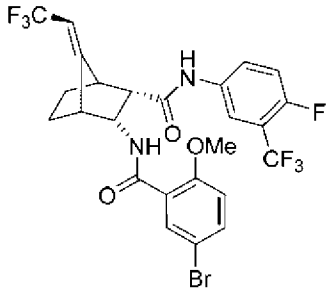
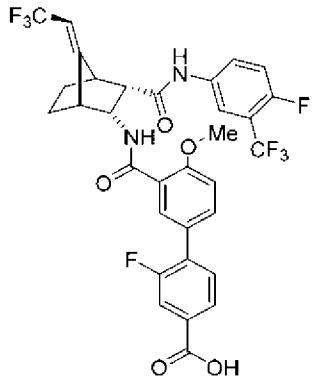
285		N-[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]-2'-氟-4-甲氧基-5'-(三氟甲氧基)-[1,1'-聯苯]-3-甲醯胺	681.3	(500 MHz, DMSO-d6) δ 10.51 (s, 1H), 9.87 (d, J=7.1 Hz, 1H), 8.20 - 8.11 (m, 1H), 8.11 - 8.01 (m, 1H), 7.78 - 7.64 (m, 2H), 7.50 - 7.33 (m, 4H), 7.27 (d, J=8.8 Hz, 1H), 4.63 (d, J=9.6 Hz, 1H), 4.47 - 4.31 (m, 1H), 3.99 (s, 3H), 3.14 - 3.07 (m, 1H), 3.04 (br s, 1H), 2.66 (br d, J=19.2 Hz, 1H), 1.87 - 1.76 (m, 1H), 1.76 - 1.67 (m, 1H), 1.50 - 1.41 (m, 1H), 1.40 - 1.29 (m, 2H), 0.76 - 0.58 (m, 2H), 0.36 - 0.24 (m, 2H)	2.99, C

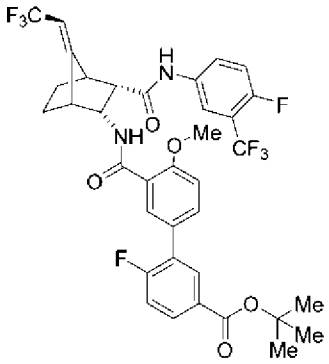
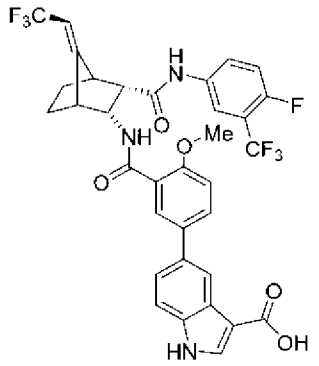
286		N-[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]-2'-氟-4-甲氧基-5'-(三氟甲基)-[1,1'-聯苯]-3-甲醯胺	665.1	(500 MHz, DMSO-d6) δ 10.52 (s, 1H), 9.90 (br d, J=7.0 Hz, 1H), 8.22 - 8.16 (m, 1H), 8.12 (s, 1H), 7.82 (d, J=7.0 Hz, 1H), 7.80 - 7.72 (m, 3H), 7.54 (t, J=9.3 Hz, 1H), 7.45 (t, J=9.8 Hz, 1H), 7.32 (d, J=8.5 Hz, 1H), 4.68 (d, J=9.8 Hz, 1H), 4.49 - 4.39 (m, 1H), 4.04 (s, 3H), 3.14 (dd, J=10.8, 4.4 Hz, 1H), 3.11 - 3.05 (m, 1H), 2.77 - 2.65 (m, 1H), 1.88 - 1.82 (m, 1H), 1.81 - 1.72 (m, 1H), 1.54 - 1.45 (m, 1H), 1.44 - 1.35 (m, 2H), 0.83 - 0.63 (m, 2H), 0.40 - 0.25 (m, 2H)	2.88, C

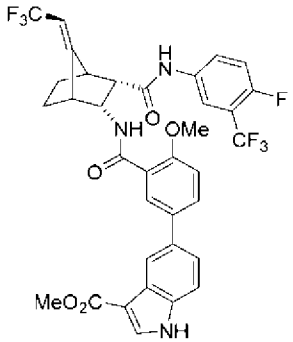
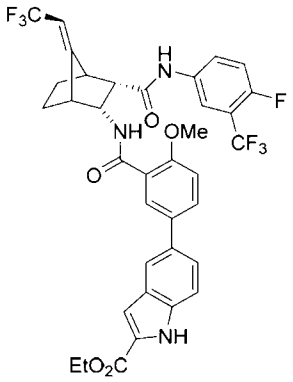
287		N-[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]-4-甲氧基-3'-(2,2,2-三氟乙基)-[1,1'-聯苯]-3-甲醯胺	661.3	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.94 (d, J=7.1 Hz, 1H), 8.28 - 8.20 (m, 2H), 7.85 - 7.74 (m, 2H), 7.67 - 7.57 (m, 2H), 7.53 - 7.43 (m, 2H), 7.32 (dd, J=16.3, 8.0 Hz, 2H), 4.70 (d, J=9.6 Hz, 1H), 4.56 - 4.39 (m, 1H), 4.05 (s, 3H), 3.80 - 3.65 (m, 2H), 3.17 (dd, J=10.4, 4.1 Hz, 1H), 3.14 - 3.08 (m, 1H), 2.78 - 2.68 (m, 1H), 1.92 - 1.73 (m, 2H), 1.55 - 1.48 (m, 1H), 1.47 - 1.35 (m, 2H), 0.81 - 0.66 (m, 2H), 0.42 - 0.30 (m, 2H)	2.86, C
288		5-(3-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)吡啶-3-甲酸	652.0	(500 MHz, $CDCl_3$) δ 10.32 - 9.84 (m, 2H), 9.73 (br s, 1H), 9.27 (br s, 1H), 9.14 (s, 1H), 8.72 (br d, J=2.1 Hz, 2H), 7.81 - 7.68 (m, 1H), 7.54 - 7.41 (m, 1H), 7.28 - 7.23 (m, 1H), 6.71 - 6.51 (m, 1H), 5.63 (q, J=7.4 Hz, 1H), 4.44 - 4.25 (m, 1H), 4.06 (s, 3H), 3.39 (br dd, J=10.6, 4.0 Hz, 1H), 3.19 (br s, 1H), 2.93 (br s, 1H), 2.40 - 2.28 (m, 1H), 1.92 - 1.80 (m, 1H), 1.70 - 1.53 (m, 2H)	1.19, D

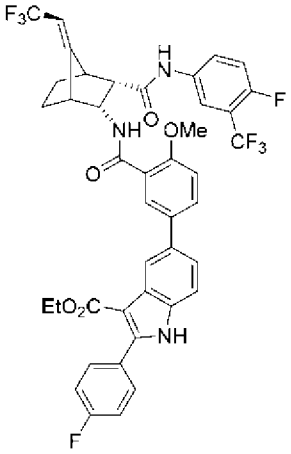
289		N-[(2R,3S,7Z)-7-[(3,3-二氟環丁基)亞甲基]-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]-2'-氟-4-甲氧基-5'-(三氟甲基)-[1,1'-聯苯]-3-甲醯胺	715.0	(500 MHz, $CDCl_3$) δ 11.63 (s, 1H), 8.87 (br d, J=6.3 Hz, 1H), 8.50 (dd, J=2.4, 1.0 Hz, 1H), 8.13 (dd, J=6.3, 2.7 Hz, 1H), 7.87 (dt, J=8.5, 3.8 Hz, 1H), 7.80 - 7.74 (m, 2H), 7.68 - 7.62 (m, 1H), 7.35 - 7.30 (m, 1H), 7.19 (d, J=8.7 Hz, 1H), 7.16 (t, J=9.5 Hz, 1H), 5.41 (d, J=8.7 Hz, 1H), 4.41 - 4.31 (m, 1H), 4.15 (s, 3H), 3.26 (d, J=4.9 Hz, 1H), 2.99 (t, J=3.8 Hz, 1H), 2.92 - 2.82 (m, 1H), 2.81 - 2.68 (m, 2H), 1.98 - 1.89 (m, 1H), 1.86 - 1.72 (m, 2H), 1.53 (ddd, J=12.3, 8.9, 5.6 Hz, 1H), 1.29 - 1.27 (m, 2H), 0.97 - 0.77 (m, 2H)	1.21, D

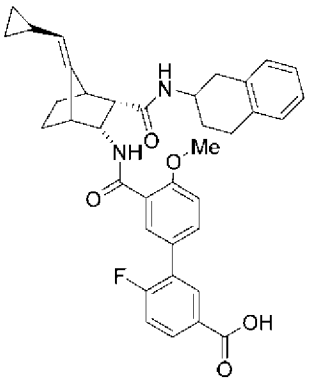
290		2'-氟-N-[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]-5'-甲磺醯胺基-4-甲氧基-[1,1'-聯苯]-3-甲醯胺	718.0	(500 MHz, DMSO-d_6) δ 10.65 (s, 1H), 9.97 (br d, *J*=6.7 Hz, 1H), 8.23 (br d, *J*=4.6 Hz, 1H), 8.11 (br s, 1H), 7.80 (br s, 1H), 7.67 (br d, *J*=8.2 Hz, 1H), 7.50 (br t, *J*=9.5 Hz, 1H), 7.34 - 7.26 (m, 2H), 7.23 (br s, 1H), 5.93 (br d, *J*=7.9 Hz, 1H), 4.53 (br s, 1H), 4.05 (s, 2H), 3.30 (br s, 2H), 2.99 (s, 3H), 2.55 - 2.51 (m, 10H), 1.97 (br d, *J*=8.9 Hz, 1H), 1.90 (br s, 1H), 1.49 (br d, *J*=6.1 Hz, 2H)	2.56, C
291		(2S,3R,7Z)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-甲醯胺	567.0	(500 MHz, DMSO-d6) δ 10.65 (s, 1H), 9.97 (br d, J=6.4 Hz, 1H), 8.23 (br d, J=4.6 Hz, 1H), 7.86 (br t, J=10.4 Hz, 1H), 7.77 (br s, 1H), 7.50 (br t, J=9.8 Hz, 1H), 7.39 (br dd, J=12.5, 6.4 Hz, 1H), 5.94 (q, J=7.9 Hz, 1H), 4.49 (br s, 1H), 4.01 (s, 3H), 3.29 - 3.21 (m, 1H), 2.99 (br s, 1H), 2.55 - 2.53 (m, 1H), 1.96 - 1.91 (m, 1H), 1.87 - 1.82 (m, 1H), 1.49 (br d, J=6.4 Hz, 2H)	2.60, C

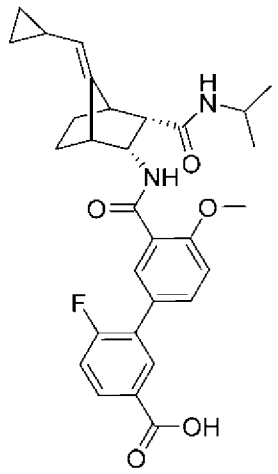
292		(2S,3R,7Z)-3-(5-溴-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-甲醯胺	609.0	(500 MHz, DMSO-d6) δ 10.51 (s, 1H), 9.82 (br d, J=6.9 Hz, 1H), 8.16 (br d, J=5.7 Hz, 1H), 7.98 (d, J=1.9 Hz, 1H), 7.85 - 7.72 (m, 1H), 7.65 (dd, J=8.8, 2.4 Hz, 1H), 7.46 (t, J=9.7 Hz, 1H), 7.17 (d, J=8.8 Hz, 1H), 5.89 (q, J=7.8 Hz, 1H), 4.58 - 4.45 (m, 1H), 3.99 (s, 3H), 3.49 - 3.34 (m, 3H), 3.28 - 3.18 (m, 1H), 2.99 (br s, 1H), 2.57 - 2.54 (m, 4H), 2.08 - 1.95 (m, 1H), 1.95 - 1.83 (m, 1H), 1.50 (br d, J=6.6 Hz, 2H)	2.78, C
293		2-氟-3'-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-4-甲酸	669.0	(500 MHz, DMSO-d_6) δ 10.57 (s, 1H), 9.85 (br d, *J*=7.1 Hz, 1H), 8.22 - 8.13 (m, 2H), 7.87 - 7.78 (m, 2H), 7.78 - 7.70 (m, 2H), 7.60 (t, *J*=8.0 Hz, 1H), 7.46 (t, *J*=9.7 Hz, 1H), 7.33 (d, *J*=8.7 Hz, 1H), 5.90 (q, *J*=7.7 Hz, 1H), 4.56 (br t, *J*=10.7 Hz, 1H), 4.06 (s, 3H), 3.32 - 3.25 (m, 1H), 3.00 (br d, *J*=6.9 Hz, 1H), 2.58 - 2.53 (m, 6H), 2.05 (br t, *J*=9.2 Hz, 1H), 1.94 (br t, *J*=8.7 Hz, 1H), 1.52 (br d, *J*=6.3 Hz, 2H)	2.55, C

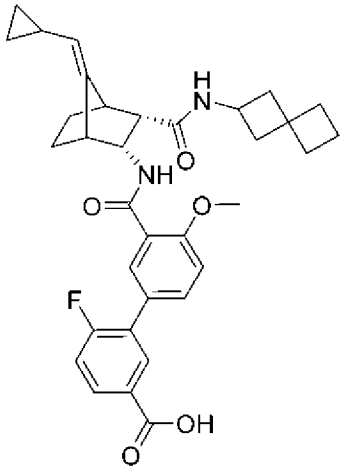
294		6-氟-3'-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-3-甲酸三級丁酯	725.0	(500 MHz, DMSO-d_6) δ 10.65 (s, 1H), 9.94 (br d, *J*=7.0 Hz, 1H), 8.22 (br d, *J*=4.3 Hz, 1H), 8.16 (s, 1H), 7.81 - 7.69 (m, 4H), 7.64 (br t, *J*=7.9 Hz, 1H), 7.49 (br t, *J*=9.6 Hz, 1H), 7.33 (d, *J*=8.9 Hz, 1H), 5.93 (q, *J*=7.9 Hz, 1H), 4.53 (br s, 1H), 4.05 (s, 3H), 3.48 - 3.41 (m, 1H), 3.29 - 3.23 (m, 1H), 2.99 (br s, 1H), 1.99 (br t, *J*=9.3 Hz, 1H), 1.90 (br t, *J*=8.7 Hz, 1H), 1.56 (s, 9H), 1.50 (br d, *J*=6.4 Hz, 2H)	3.00, C
295		5-(3-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-1H-吲哚-3-甲酸	690.0	(500 MHz, DMSO-d_6) δ 10.52 (s, 1H), 9.87 (br d, *J*=7.0 Hz, 1H), 8.30 - 8.18 (m, 3H), 8.01 (d, *J*=2.2 Hz, 1H), 7.89 - 7.74 (m, 2H), 7.55 (d, *J*=8.5 Hz, 1H), 7.52 - 7.42 (m, 2H), 7.29 (d, *J*=8.7 Hz, 1H), 5.92 (q, *J*=7.9 Hz, 1H), 4.71 - 4.53 (m, 1H), 4.06 (s, 3H), 3.31 (br s, 1H), 3.01 (br s, 1H), 2.91 (s, 1H), 2.75 (s, 1H), 2.57 - 2.53 (m, 4H), 2.08 (br t, *J*=9.3 Hz, 1H), 2.02 - 1.91 (m, 1H), 1.53 (br d, *J*=6.5 Hz, 2H)	2.33, C

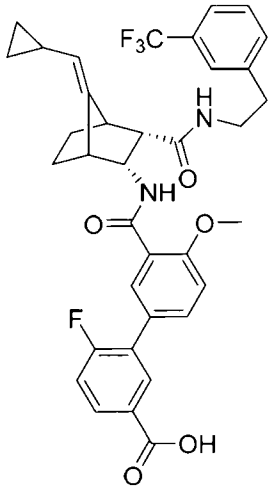
296		6-(3-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-1H-吲哚-3-甲酸甲酯	704	(500 MHz, DMSO-d6) δ 10.67 (s, 1H), 9.97 (br d, J=7.0 Hz, 1H), 8.27 - 8.22 (m, 2H), 8.11 (s, 1H), 8.04 (d, J=8.5 Hz, 1H), 7.95 (s, 1H), 7.87 - 7.77 (m, 2H), 7.68 (s, 1H), 7.52 - 7.44 (m, 2H), 7.29 (d, J=8.5 Hz, 1H), 5.94 (q, J=7.4 Hz, 1H), 4.55 (br s, 1H), 4.05 (s, 3H), 3.36 (br s, 2H), 3.33 - 3.23 (m, 1H), 3.00 (br s, 1H), 2.89 (s, 2H), 2.73 (s, 2H), 2.56 - 2.53 (m, 1H), 1.99 (br d, J=9.8 Hz, 1H), 1.95 - 1.86 (m, 1H), 1.50 (br d, J=6.1 Hz, 2H), 1.22 (br d, J=7.6 Hz, 3H)	2.63, C
297		5-(3-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-1H-吲哚-2-甲酸乙酯	718	(500 MHz, DMSO-d6) δ 9.96 (br d, J=6.7 Hz, 1H), 8.24 (br s, 2H), 7.89 (s, 1H), 7.84 - 7.78 (m, 2H), 7.56 - 7.48 (m, 3H), 7.28 (d, J=8.5 Hz, 1H), 7.20 (s, 1H), 5.94 (q, J=7.8 Hz, 1H), 4.56 (br s, 1H), 4.35 (q, J=7.0 Hz, 2H), 4.04 (s, 3H), 3.31 - 3.25 (m, 1H), 3.00 (br s, 1H), 2.56 - 2.53 (m, 6H), 2.02 - 1.96 (m, 1H), 1.96 - 1.88 (m, 1H), 1.50 (br d, J=6.1 Hz, 2H), 1.35 (t, J=7.2 Hz, 3H)	2.78, C

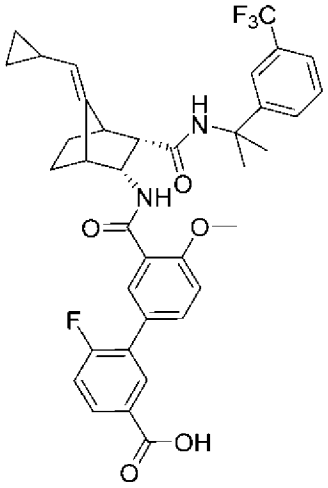
298		5-(3-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-2-(4-氟苯基)-1H-吲哚-3-甲酸乙酯	812	(500 MHz, DMSO-d6) δ 9.97 (br d, J=6.7 Hz, 1H), 8.29 - 8.23 (m, 3H), 7.83 - 7.73 (m, 4H), 7.54 - 7.46 (m, 3H), 7.36 - 7.29 (m, 3H), 5.93 (q, J=7.7 Hz, 1H), 4.56 (br s, 1H), 4.20 (q, J=7.0 Hz, 2H), 4.05 (s, 3H), 3.33 - 3.25 (m, 1H), 3.00 (br s, 1H), 2.88 (s, 1H), 2.72 (s, 1H), 2.55 - 2.52 (m, 1H), 2.00 (br d, J=9.2 Hz, 1H), 1.95 - 1.89 (m, 1H), 1.66 (br s, 1H), 1.54 - 1.46 (m, 2H), 1.22 (br t, J=7.0 Hz, 3H)	2.87, C

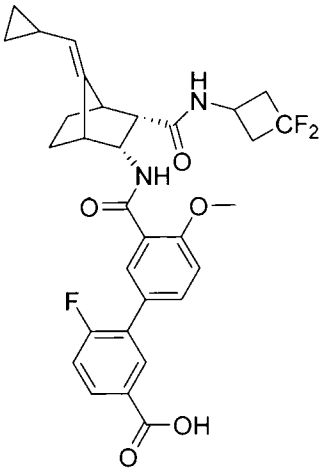
299		3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-[(1,2,3,4-四氫萘-2-基)胺甲醯基]雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-甲酸	609.0	(500 MHz, DMSO-d_6) δ 10.01 (br d, *J*=6.7 Hz, 1H), 8.17 (br d, *J*=7.3 Hz, 1H), 8.11 (br s, 1H), 8.03 (br d, *J*=7.0 Hz, 1H), 7.94 (br d, *J*=5.8 Hz, 1H), 7.72 (br s, 1H), 7.36 (br t, *J*=9.5 Hz, 1H), 7.29 (d, *J*=8.2 Hz, 1H), 7.06 (br s, 4H), 4.61 (br d, *J*=9.2 Hz, 1H), 4.33 (br s, 1H), 4.06 - 3.98 (m, 4H), 3.06 (br s, 1H), 2.95 (br d, *J*=6.4 Hz, 2H), 2.89 (s, 1H), 2.79 (br s, 2H), 2.73 (s, 1H), 2.61 - 2.57 (m, 1H), 2.56 - 2.52 (m, 8H), 1.90 (s, 9H), 1.79 (br s, 1H), 1.63 (br s, 1H), 1.47 (br s, 1H), 1.36 (br s, 2H), 0.71 (br t, *J*=9.2 Hz, 2H), 0.31 (br s, 2H)	2.52, C

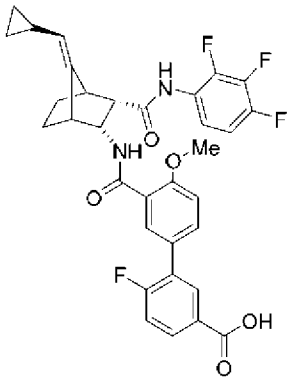
300		3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-[丙烷-2-基)胺甲醯基]雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-甲酸	521	(500 MHz, DMSO-d6) δ 10.03 (br d, J=7.0 Hz, 1H), 8.09 (s, 1H), 7.97 (br dd, J=15.9, 7.6 Hz, 1H), 7.85 (br t, J=6.9 Hz, 1H), 7.69 (br d, J=8.5 Hz, 1H), 7.28 (d, J=8.9 Hz, 1H), 7.17 (t, J=8.9 Hz, 1H), 4.61 (d, J=9.5 Hz, 1H), 4.30 (br s, 1H), 4.03 (s, 2H), 3.92 - 3.86 (m, 1H), 3.57 - 3.48 (m, 2H), 3.06 (br s, 1H), 2.86 (br dd, J=10.7, 4.0 Hz, 1H), 2.55 (s, 6H), 1.90 (br t, J=9.6 Hz, 1H), 1.78 (s, 2H), 1.48 (br d, J=8.9 Hz, 1H), 1.34 (br t, J=13.4 Hz, 1H), 1.04 (t, J=7.0 Hz, 4H), 0.75 - 0.67 (m, 1H), 0.31 (br s, 1H)	2.28, C

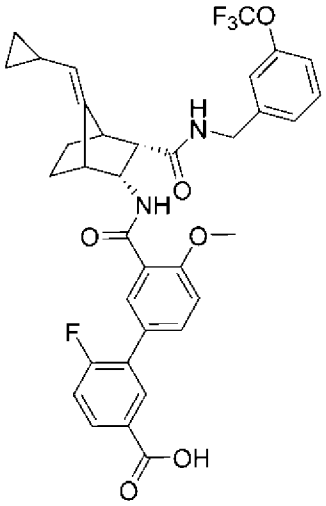
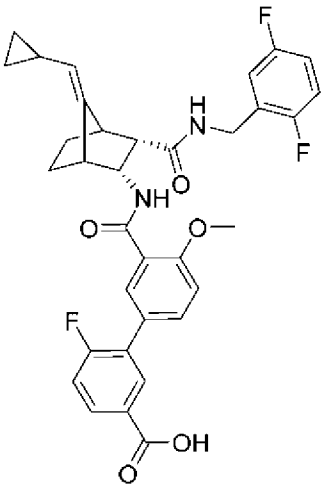
301		3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-({螺[3.3]庚烷-2-基}胺甲醯基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-甲酸	573	(500 MHz, DMSO-d6) d 9.98 (br d, J=6.4 Hz, 1H), 8.24 (br d, J=7.0 Hz, 1H), 8.14 - 7.98 (m, 2H), 7.90 (br s, 1H), 7.70 (br d, J=8.5 Hz, 1H), 7.35 - 7.20 (m, 2H), 4.62 (br d, J=9.5 Hz, 1H), 4.30 (br s, 1H), 4.08 - 3.98 (m, 4H), 3.33 (br s, 1H), 3.05 (br s, 1H), 2.85 (br d, J=6.7 Hz, 1H), 2.65 (br s, 1H), 2.56 - 2.54 (m, 5H), 2.27 (br d, J=7.9 Hz, 2H), 1.98 (br d, J=6.4 Hz, 2H), 1.90 - 1.72 (m, 8H), 1.46 (br s, 1H), 1.34 (br s, 2H), 0.80 - 0.59 (m, 2H), 0.32 (br s, 2H)	2.55, C

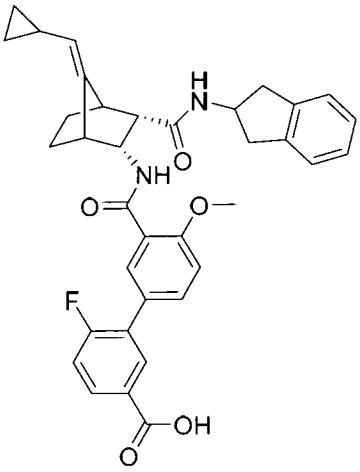
302		3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-({2-[3-(三氟甲基)苯基]乙基}胺甲醯基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-甲酸	651	(500 MHz, DMSO-d6) δ 9.64 (br d, J=6.9 Hz, 1H), 7.86 (s, 1H), 7.80 (br d, J=5.7 Hz, 2H), 7.76 - 7.68 (m, 1H), 7.47 (br d, J=8.5 Hz, 1H), 7.32 - 7.14 (m, 5H), 7.04 (d, J=8.7 Hz, 1H), 4.38 (d, J=9.3 Hz, 1H), 4.06 (br s, 1H), 3.24 (dq, J=13.3, 6.7 Hz, 1H), 2.81 (br s, 1H), 2.68 - 2.56 (m, 3H), 2.53 - 2.43 (m, 1H), 2.33 - 2.22 (m, 9H), 2.18 (br t, J=3.9 Hz, 1H), 1.50 (br t, J=6.2 Hz, 2H), 1.22 (br dd, J=8.6, 4.1 Hz, 1H), 1.10 (br s, 1H), 1.01 (br s, 1H), 0.54 - 0.39 (m, 2H), 0.08 (br d, J=2.7 Hz, 2H)	2.64, C

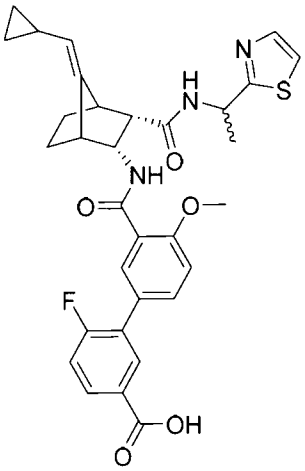
303		3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-({2-[3-(三氟甲基)苯基]丙烷-2-基}胺甲醯基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-甲酸	664	(500 MHz, DMSO-d6) δ 9.81 (br d, J=6.9 Hz, 1H), 8.35 (s, 1H), 8.12 (s, 1H), 7.99 (br d, J=6.6 Hz, 1H), 7.92 - 7.75 (m, 1H), 7.74 - 7.55 (m, 3H), 7.54 - 7.31 (m, 2H), 7.29 - 7.13 (m, 2H), 4.69 (d, J=9.3 Hz, 1H), 4.35 (br s, 1H), 3.90 (s, 1H), 3.65 (s, 2H), 3.12 - 2.94 (m, 1H), 2.77 - 2.60 (m, 1H), 2.59 - 2.54 (m, 1H), 2.48 - 2.24 (m, 1H), 2.07 (s, 1H), 1.90 (s, 2H), 1.75 - 1.54 (m, 7H), 1.54 - 1.40 (m, 1H), 1.38 - 1.18 (m, 2H), 1.17 - 0.96 (m, 2H), 0.89 - 0.69 (m, 2H), 0.34 (br s, 2H)	2.22, C

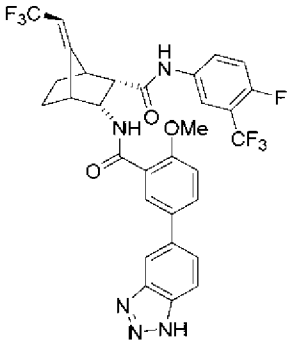
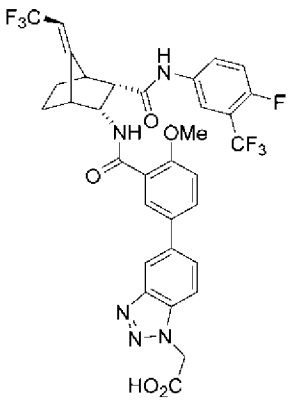
304		3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-[(3,3-二氟環丁基)胺甲醯基]雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-甲酸	569	(500 MHz, DMSO-d6) δ 9.87 (br d, J=7.0 Hz, 1H), 8.47 (br d, J=6.5 Hz, 1H), 8.12 (s, 1H), 8.03 (br d, J=8.8 Hz, 1H), 7.89 (br s, 1H), 7.69 (br d, J=8.8 Hz, 1H), 7.28 (br d, J=8.7 Hz, 1H), 7.22 (br d, J=9.7 Hz, 1H), 4.67 (d, J=9.4 Hz, 1H), 4.37 (br s, 1H), 4.15 - 3.99 (m, 3H), 3.09 (br s, 1H), 3.00 - 2.78 (m, 2H), 2.65 (br s, 1H), 2.59 - 2.54 (m, 3H), 1.87 (br d, J=8.8 Hz, 1H), 1.79 (br s, 1H), 1.50 (br s, 1H), 1.38 (br s, 1H), 1.26 (s, 1H), 0.80 - 0.67 (m, 1H), 0.33 (br s, 2H)	1.84, C

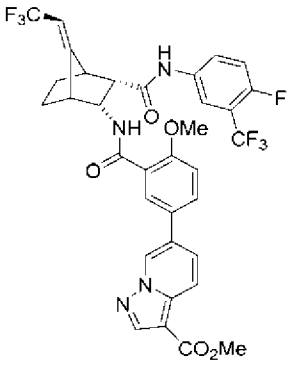
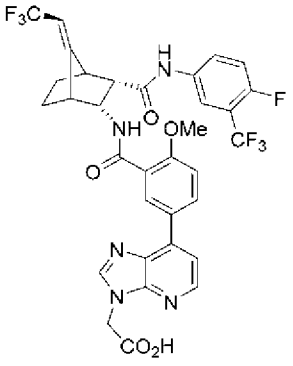
305		3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-[(2,3,4-三氟苯基)胺甲醯基]雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-甲酸	609.0	(500 MHz, DMSO-d_6) δ 9.82 (br d, *J*=7.0 Hz, 1H), 8.13 (s, 1H), 8.02 (br d, *J*=7.3 Hz, 1H), 7.88 (br s, 1H), 7.69 (br d, *J*=8.2 Hz, 1H), 7.53 (br s, 1H), 7.34 - 7.18 (m, 3H), 4.69 (br d, *J*=9.5 Hz, 1H), 4.46 (br s, 1H), 3.96 (s, 3H), 3.35 (br s, 1H), 3.10 (br s, 1H), 2.73 (br s, 1H), 2.56 - 2.53 (m, 8H), 1.88 (br d, *J*=10.1 Hz, 1H), 1.83 - 1.76 (m, 1H), 1.72 (br s, 1H), 1.50 (br s, 1H), 1.42 (br s, 2H), 0.74 (br dd, *J*=13.1, 8.9 Hz, 2H), 0.35 (br s, 2H)	2.49, C

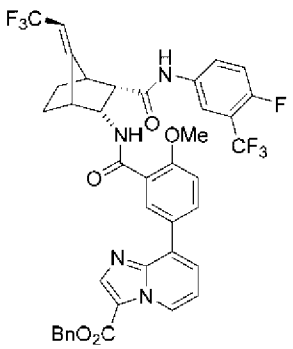
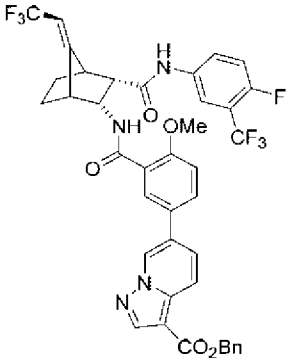
306		3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-({[2-(三氟甲氧基)苯基]甲基}胺甲醯基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-甲酸	653	(500 MHz, DMSO-d6) δ 9.95 (br d, J=6.7 Hz, 1H), 8.66 (br s, 1H), 8.12 (br s, 1H), 8.04 (br d, J=7.3 Hz, 1H), 7.97 (br s, 1H), 7.73 (br d, J=8.5 Hz, 1H), 7.45 (br t, J=9.5 Hz, 1H), 7.39 - 7.30 (m, 2H), 7.30 - 7.22 (m, 2H), 4.64 (br d, J=9.5 Hz, 1H), 4.37 (br s, 2H), 3.91 (s, 2H), 3.09 - 3.01 (m, 1H), 2.60 (br s, 1H), 2.56 - 2.52 (m, 6H), 1.89 - 1.82 (m, 1H), 1.80 - 1.70 (m, 1H), 1.47 (br s, 1H), 1.35 (br t, J=12.4 Hz, 2H), 0.76 - 0.67 (m, 1H), 0.33 (br s, 1H)	2.5, C
307		3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[1-(2,5-二氟苯基)乙基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-甲酸	619	(500 MHz, DMSO-d6) δ 8.63 (br dd, J=16.6, 7.5 Hz, 1H), 8.12 - 8.00 (m, 1H), 7.95 (br s, 1H), 7.75 - 7.66 (m, 1H), 7.42 (br t, J=8.1 Hz, 1H), 7.18 - 7.05 (m, 2H), 5.17 - 5.10 (m, 1H), 4.66 - 4.62 (m, 1H), 4.34 (br s, 1H), 4.01 (s, 1H), 3.67 (s, 1H), 3.06 - 2.98 (m, 1H), 2.61 (br s, 1H), 2.55 - 2.52 (m, 5H), 1.70 (br s, 1H), 1.47 (br s, 1H), 1.32 (br d, J=6.7 Hz, 4H), 0.76 - 0.67 (m, 1H), 0.32 (br s, 1H)	2.41, C

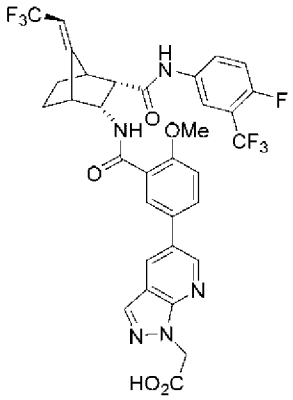
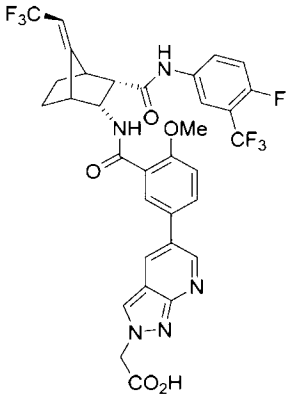
308		3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-[(2,3-二氫-1H-茚-2-基)胺甲醯基]雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-甲酸	595	(500 MHz, DMSO-d6) δ 10.04 (br d, J=7.0 Hz, 1H), 8.41 (br d, J=6.7 Hz, 1H), 8.12 (br s, 1H), 8.05 (br d, J=7.6 Hz, 1H), 7.97 (br s, 1H), 7.75 (br d, J=7.6 Hz, 1H), 7.44 (br t, J=9.5 Hz, 1H), 7.32 (br d, J=8.5 Hz, 1H), 7.21 (br d, J=6.4 Hz, 1H), 7.13 (br d, J=7.0 Hz, 3H), 4.60 (br d, J=9.5 Hz, 1H), 4.54 - 4.45 (m, 1H), 4.32 (br s, 1H), 4.07 (s, 3H), 3.24 - 3.10 (m, 1H), 3.06 (br s, 1H), 2.96 - 2.83 (m, 1H), 2.78 - 2.64 (m, 2H), 2.55 - 2.53 (m, 3H), 2.08 - 1.86 (m, 1H), 1.79 (br s, 1H), 1.46 (br s, 1H), 1.36 (br s, 2H), 1.27 - 1.11 (m, 1H), 1.04 (d, J=6.1 Hz, 3H), 0.71 (br t, J=9.2 Hz, 2H), 0.31 (br s, 2H)	2.47, C

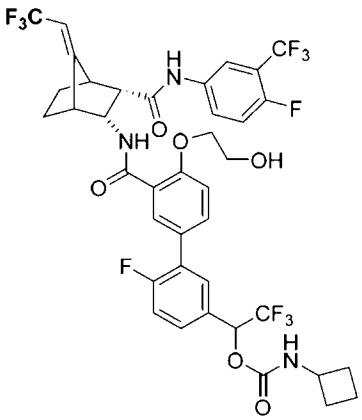
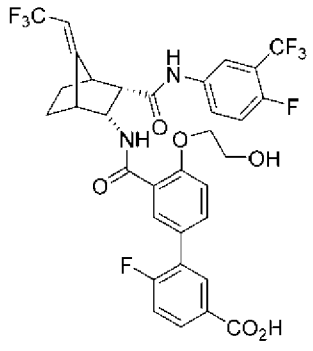
309		3'-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[1-(1,3-噻唑-2-基)乙基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-甲酸	590	(500 MHz, DMSO-d6) δ 10.00 (br d, J=7.0 Hz, 1H), 8.90 (t, J=8.4 Hz, 1H), 8.11 (br s, 1H), 8.03 (br d, J=7.0 Hz, 1H), 7.95 (br s, 1H), 7.77 - 7.68 (m, 2H), 7.62 (dd, J=17.7, 3.1 Hz, 1H), 7.46 - 7.38 (m, 1H), 7.30 (br d, J=8.9 Hz, 1H), 5.31 - 5.19 (m, 1H), 4.65 (br t, J=9.2 Hz, 1H), 4.37 (br s, 1H), 4.02 (s, 2H), 3.90 (s, 1H), 3.80 (s, 1H), 3.17 (s, 1H), 3.07 (br s, 1H), 3.05 - 2.97 (m, 1H), 2.89 (s, 1H), 2.73 (s, 1H), 2.63 (br d, J=15.3 Hz, 1H), 2.55 - 2.52 (m, 8H), 1.97 - 1.86 (m, 1H), 1.86 - 1.70 (m, 2H), 1.48 (br d, J=6.4 Hz, 4H), 1.36 (br s, 2H), 0.85 - 0.66 (m, 2H), 0.33 (br s, 2H)	2.04, C

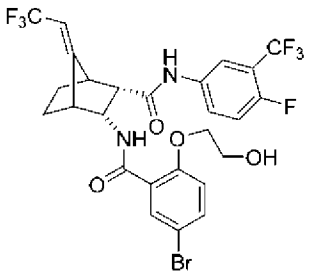
311		(2S,3R,7Z)-3-[5-(1H-1,2,3-苯并三唑-5-基)-2-甲氧基苯甲醯胺基]-N-[4-氟-3-(三氟甲基)苯基]-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-甲醯胺	684.3	(500 MHz, DMSO-d6) δ 10.69 (br s, 1H), 9.97 (br d, J=7.0 Hz, 1H), 8.33 - 8.22 (m, 2H), 8.01 (s, 1H), 7.94 - 7.86 (m, 2H), 7.83 - 7.76 (m, 1H), 7.59 (br d, J=8.5 Hz, 1H), 7.52 - 7.44 (m, 1H), 7.31 (d, J=8.5 Hz, 1H), 5.94 (q, J=7.7 Hz, 1H), 4.56 (br s, 1H), 4.06 (s, 3H), 3.36 - 3.24 (m, 2H), 2.99 (s, 2H), 2.10 - 1.90 (m, 2H), 1.50 (br d, J=6.4 Hz, 2H)	2.48, C
312		2-[5-(3-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-1H-1,2,3-苯并三唑-1-基]乙酸	706.18	(500 MHz, DMSO-d6) δ 10.68 (br d, J=4.3 Hz, 1H), 9.98 (br s, 1H), 8.39 - 8.18 (m, 2H), 8.08 (br d, J=7.9 Hz, 1H), 7.98 - 7.76 (m, 3H), 7.68 (br d, J=8.9 Hz, 1H), 7.49 (br t, J=9.6 Hz, 1H), 7.32 (br dd, J=8.4, 4.7 Hz, 1H), 5.93 (br d, J=7.9 Hz, 1H), 5.59 - 5.46 (m, 2H), 4.61 - 4.44 (m, 1H), 4.05 (s, 3H), 3.47 - 3.38 (m, 1H), 3.27 (br s, 1H), 2.99 (br s, 1H), 2.06 - 1.85 (m, 2H), 1.55 - 1.45 (m, 2H), 1.22 (s, 1H)	2.35, C

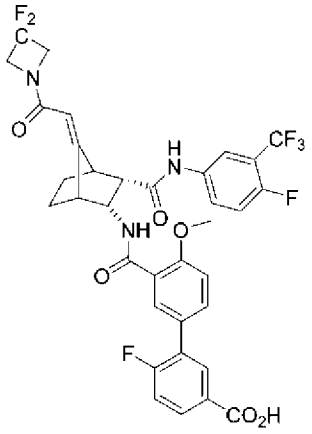
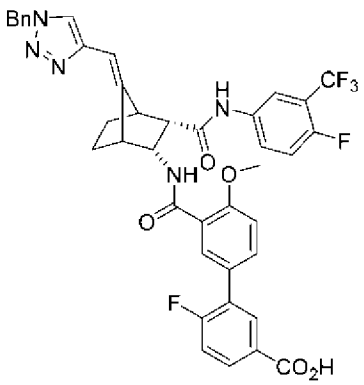
313		6-(3-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)吡唑并[1,5-a]吡啶-3-甲酸甲酯	705.2	(500 MHz, DMSO-d6) δ 10.66 (s, 1H), 9.94 (br d, J=7.0 Hz, 1H), 9.06 (s, 1H), 8.44 (s, 1H), 8.24 (s, 1H), 8.18 (br d, J=5.5 Hz, 1H), 8.11 (br d, J=9.2 Hz, 1H), 7.96 - 7.83 (m, 2H), 7.75 (br s, 1H), 7.45 (br t, J=9.6 Hz, 1H), 7.30 (br d, J=8.5 Hz, 1H), 5.89 (q, J=7.7 Hz, 1H), 4.51 (br s, 1H), 4.02 (s, 3H), 3.82 (s, 1H), 3.65 - 3.59 (m, 3H), 3.24 (br s, 1H), 2.97 (br s, 1H), 2.00 - 1.82 (m, 2H), 1.56 - 1.40 (m, 2H)	2.70, C
314		2-[7-(3-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-3H-咪唑并[4,5-b]吡啶-3-基]乙酸	705.9	(500 MHz, DMSO-d6) δ 10.66 (br d, J=4.9 Hz, 1H), 9.97 (br t, J=5.8 Hz, 1H), 8.58 (br d, J=4.6 Hz, 1H), 8.46 (br d, J=4.9 Hz, 1H), 8.30 - 8.19 (m, 3H), 7.90 (br s, 1H), 7.80 (br s, 1H), 7.50 (br d, J=5.8 Hz, 1H), 7.35 - 7.27 (m, 1H), 6.00 - 5.90 (m, 1H), 5.03 (br s, 2H), 4.55 (br s, 1H), 4.05 (br d, J=5.8 Hz, 3H), 3.26 (br s, 1H), 2.99 (br s, 1H), 2.04 - 1.87 (m, 2H), 1.50 (br s, 2H), 1.23 (br d, J=4.6 Hz, 2H)	1.92, C

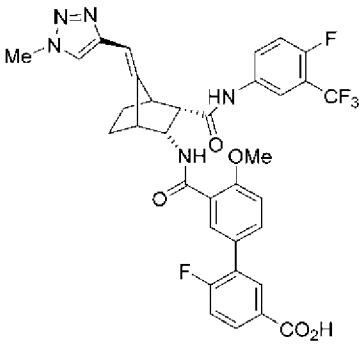
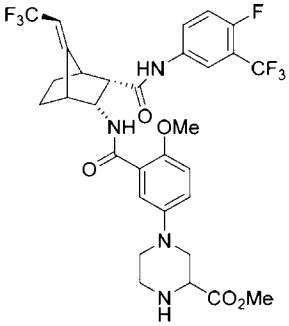
315		8-(3-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)咪唑并[1,2-a]吡啶-3-甲酸苯甲酯	781.1	(500 MHz, DMSO-d6) δ 9.97 (br d, J=6.7 Hz, 1H), 9.23 (br d, J=7.3 Hz, 1H), 8.41 - 8.34 (m, 2H), 8.26 - 8.18 (m, 1H), 8.11 - 8.00 (m, 2H), 7.87 - 7.78 (m, 1H), 7.60 (s, 1H), 7.53 - 7.43 (m, 3H), 7.42 - 7.37 (m, 1H), 7.35 (br t, J=9.0 Hz, 2H), 5.97 - 5.89 (m, 1H), 5.41 (s, 2H), 4.54 (br dd, J=9.9, 4.1 Hz, 1H), 4.06 (s, 3H), 3.43 (br d, J=1.5 Hz, 1H), 3.31 - 3.24 (m, 1H), 3.00 (br s, 1H), 2.53 - 2.51 (m, 1H), 2.00 - 1.87 (m, 2H), 1.80 (br s, 1H), 1.56 - 1.42 (m, 2H)	2.76, C
316		6-(3-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)吡唑并[1,5-a]吡啶-3-甲酸苯甲酯	781.36	(500 MHz, DMSO-d6) δ 10.70 (s, 1H), 9.98 (br d, J=6.8 Hz, 1H), 9.17 (s, 1H), 8.53 (s, 1H), 8.29 (br d, J=2.4 Hz, 2H), 8.12 (d, J=9.3 Hz, 1H), 8.02 - 7.90 (m, 2H), 7.86 - 7.77 (m, 1H), 7.53 - 7.47 (m, 3H), 7.46 - 7.29 (m, 4H), 5.94 (br d, J=7.6 Hz, 1H), 5.37 (s, 2H), 4.60 - 4.49 (m, 1H), 4.06 (s, 3H), 3.33 - 3.23 (m, 1H), 2.94 - 2.89 (m, 2H), 2.01 - 1.85 (m, 2H), 1.50 (br d, J=5.6 Hz, 2H)	2.89, C

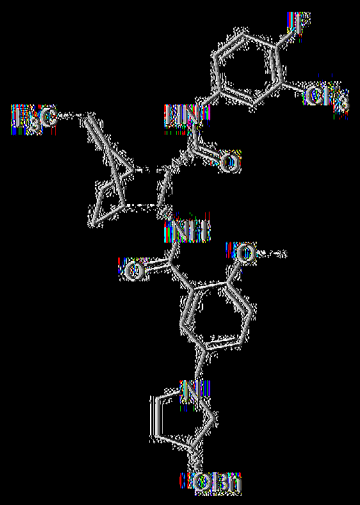
317		2-[5-(3-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-1H-吡唑并[3,4-b]吡啶-1-基]乙酸	706.29	(500 MHz, DMSO-d6) δ 10.75 - 10.68 (m, 1H), 9.99 (d, J=6.7 Hz, 1H), 8.79 (d, J=1.9 Hz, 1H), 8.45 (d, J=1.9 Hz, 1H), 8.30 - 8.20 (m, 3H), 7.96 - 7.87 (m, 2H), 7.84 - 7.74 (m, 1H), 7.50 (t, J=9.8 Hz, 1H), 7.34 (d, J=8.8 Hz, 1H), 5.94 (d, J=7.7 Hz, 1H), 5.22 (s, 2H), 4.61 - 4.51 (m, 1H), 4.05 (s, 3H), 3.36 - 3.20 (m, 1H), 2.89 (s, 1H), 2.73 (s, 1H), 2.03 - 1.83 (m, 2H), 1.50 (br d, J=6.7 Hz, 2H)	1.97, C
318		2-[5-(3-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-2H-吡唑并[3,4-b]吡啶-2-基]乙酸	706.18	(500 MHz, DMSO-d6) δ 10.82 - 10.71 (m, 1H), 9.99 (br d, J=6.7 Hz, 1H), 8.82 (s, 1H), 8.36 (d, J=10.4 Hz, 2H), 8.29 - 8.21 (m, 2H), 7.90 (br d, J=10.1 Hz, 1H), 7.84 - 7.76 (m, 1H), 7.50 (t, J=9.6 Hz, 1H), 7.33 (d, J=8.9 Hz, 1H), 6.00 - 5.91 (m, 1H), 4.85 (s, 2H), 4.63 - 4.50 (m, 1H), 4.06 (s, 3H), 3.36 - 3.23 (m, 1H), 3.01 (br s, 1H), 2.07 - 1.86 (m, 3H), 1.51 (br d, J=5.5 Hz, 3H)	1.92, C

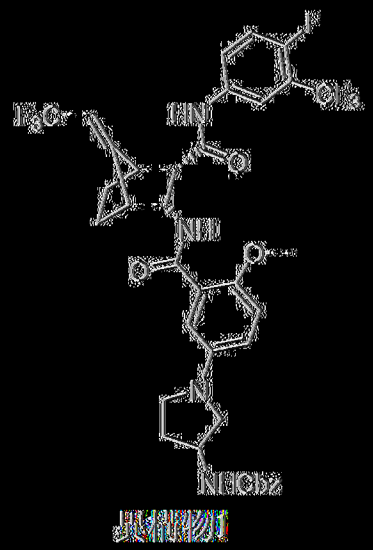
319		N-環丁基胺基甲酸 (1S)-2,2,2- 三氟 -1-(6- 氟 -3'-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-(2-羥基乙氧基)-[1,1'-聯苯]-3-基)乙酯	850.19	(500 MHz, DMSO-d6) δ 10.61 (s, 1H), 9.67 (br d, J=7.3 Hz, 1H), 8.23 - 8.04 (m, 3H), 7.81 - 7.73 (m, 1H), 7.69 (br d, J=7.6 Hz, 2H), 7.56 (br d, J=2.1 Hz, 1H), 7.51 - 7.34 (m, 3H), 6.47 - 6.27 (m, 1H), 5.96 (q, J=8.0 Hz, 1H), 4.90 (t, J=5.5 Hz, 1H), 4.69 - 4.56 (m, 1H), 4.45 - 4.30 (m, 2H), 4.06 - 3.83 (m, 3H), 3.29 (br dd, J=10.8, 4.1 Hz, 1H), 3.23 (br s, 1H), 3.01 (s, 1H), 2.28 - 2.00 (m, 4H), 2.00 - 1.82 (m, 2H), 1.70 - 1.48 (m, 4H)	2.62, C
321		6- 氟 -3'-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-(2-羥基乙氧基)-[1,1'-聯苯]-3-甲酸	699.33	(500 MHz, DMSO-d6) δ 10.61 (s, 1H), 9.63 (br d, J=7.6 Hz, 1H), 8.07 (br s, 2H), 8.04 - 7.91 (m, 2H), 7.78 - 7.68 (m, 2H), 7.52 - 7.32 (m, 3H), 5.93 (q, J=7.7 Hz, 1H), 4.70 - 4.54 (m, 1H), 4.43 - 4.18 (m, 2H), 4.07 - 3.84 (m, 2H), 3.27 (br dd, J=11.0, 4.3 Hz, 1H), 3.23 - 3.15 (m, 1H), 2.99 (br s, 1H), 2.07 (br d, J=7.9 Hz, 2H), 1.53 (br d, J=7.0 Hz, 2H)	2.19, C

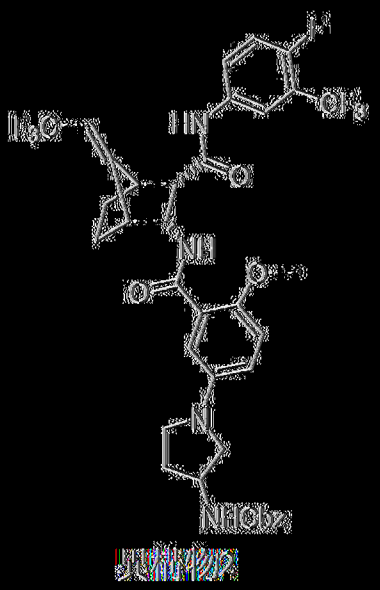
322		(2S,3R,7Z)-3-[5-溴-2-(2-羥基乙氧基)苯甲醯胺基]-N-[4-氟-3-(三氟甲基)苯基]-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-甲醯胺	639.22	(500 MHz, DMSO-d6) δ 10.59 (s, 1H), 9.60 (br d, J=7.3 Hz, 1H), 8.12 - 8.02 (m, 1H), 7.92 (d, J=2.4 Hz, 1H), 7.74 (br dd, J=8.2, 3.1 Hz, 1H), 7.64 (dd, J=8.9, 2.7 Hz, 1H), 7.47 (t, J=9.8 Hz, 1H), 7.22 (d, J=8.9 Hz, 1H), 5.93 (q, J=7.8 Hz, 1H), 4.91 (t, J=5.5 Hz, 1H), 4.64 - 4.49 (m, 1H), 4.35 - 4.20 (m, 2H), 3.98 - 3.80 (m, 2H), 3.25 (br dd, J=10.5, 4.4 Hz, 1H), 3.19 (br s, 1H), 2.98 (br s, 1H), 2.02 (br d, J=7.9 Hz, 2H), 1.51 (br d, J=8.5 Hz, 2H)	2.38, C

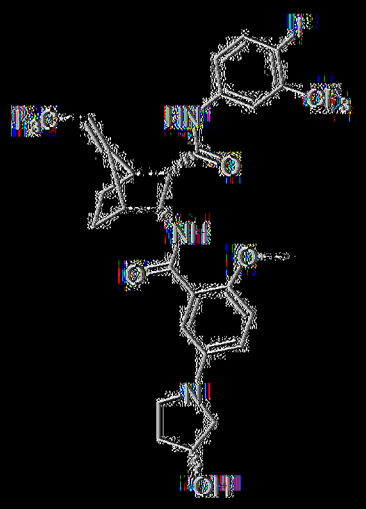
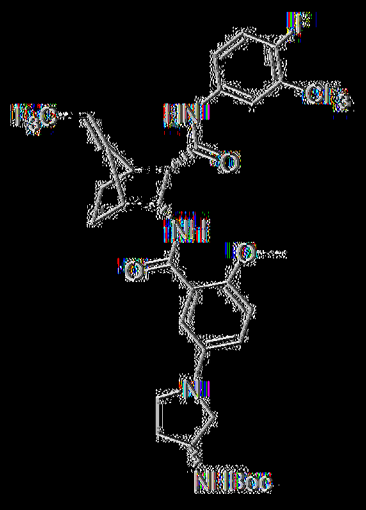
324		3'-{[(2R,3S,7Z)-7-[2-(3,3-二氟氮雜環丁烷-1-基)-2-側氧基亞乙基]-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-甲酸	720.3	(500 MHz, DMSO-d6) δ 10.46 (s, 1H), 9.75 (br d, J=7.3 Hz, 1H), 8.15 (br d, J=6.2 Hz, 1H), 8.11 (s, 1H), 8.02 (br d, J=7.2 Hz, 1H), 7.96 (br s, 1H), 7.83 - 7.76 (m, 1H), 7.72 (br d, J=8.7 Hz, 1H), 7.52 - 7.37 (m, 2H), 7.32 (d, J=8.7 Hz, 1H), 5.86 (s, 1H), 4.75 - 4.27 (m, 5H), 4.05 (s, 3H), 3.83 (br s, 1H), 3.24 (br dd, J=10.8, 4.2 Hz, 1H), 2.88 (br s, 1H), 2.13 - 2.01 (m, 1H), 1.90 (br t, J=8.5 Hz, 1H), 1.48 (br d, J=6.7 Hz, 2H)	2.29, C
326		3'-{[(2R,3S,7Z)-7-[(1-苯甲基-1H-1,2,3-三唑-4-基)亞甲基]-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-甲酸	758.1	(500 MHz, DMSO-d6) δ 10.77 (s, 1H), 9.95 (br d, J=7.0 Hz, 1H), 8.34 - 8.22 (m, 2H), 8.16 (br s, 1H), 8.02 (br d, J=7.6 Hz, 1H), 7.95 - 7.79 (m, 2H), 7.73 (br d, J=8.2 Hz, 1H), 7.50 (br t, J=9.8 Hz, 1H), 7.42 - 7.23 (m, 7H), 6.28 (s, 1H), 5.61 (s, 2H), 4.54 (br s, 1H), 3.59 (br s, 3H), 3.31 (br dd, J=10.7, 3.7 Hz, 1H), 2.94 (br s, 1H), 2.07 - 1.81 (m, 3H), 1.60 - 1.43 (m, 2H)	2.47, C

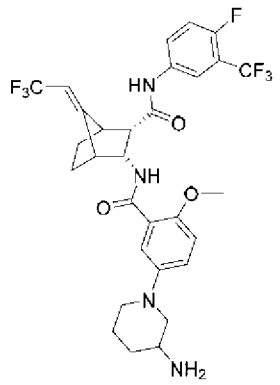
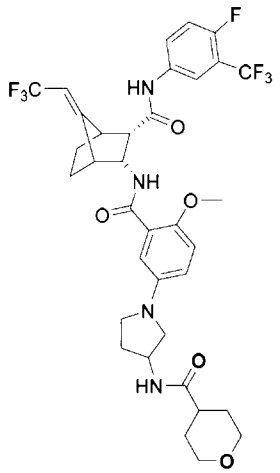
327		6-氟-3'-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-[(1-甲基-1H-1,2,3-三唑-4-基)亞甲基]雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-3-甲酸	682.3	(500 MHz, DMSO-d6) δ 10.64 (s, 1H), 9.96 (br d, J=7.0 Hz, 1H), 8.22 (br d, J=4.3 Hz, 1H), 8.13 (br s, 2H), 7.99 (br d, J=7.6 Hz, 1H), 7.89 (br s, 1H), 7.80 (br s, 1H), 7.72 (br d, J=9.5 Hz, 1H), 7.48 (br t, J=9.8 Hz, 1H), 7.38 - 7.21 (m, 2H), 6.29 (s, 1H), 4.59 - 4.45 (m, 1H), 4.05 (br d, J=7.9 Hz, 5H), 3.33 - 3.23 (m, 1H), 2.93 (br s, 1H), 2.03 - 1.84 (m, 2H)	2.33, C
328		4-(3-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)哌啡-2-甲酸甲酯	659.3	(500 MHz, DMSO-d6) δ 10.60 (s, 1H), 9.89 (br d, J=4.6 Hz, 1H), 8.20 (br d, J=4.9 Hz, 1H), 7.84 - 7.69 (m, 1H), 7.56 - 7.39 (m, 2H), 7.16 - 6.97 (m, 2H), 5.91 (br d, J=7.9 Hz, 1H), 4.54 - 4.40 (m, 1H), 3.96 - 3.86 (m, 3H), 3.86 - 3.76 (m, 1H), 3.68 (s, 2H), 3.32 - 2.92 (m, 4H), 2.92 - 2.78 (m, 2H), 2.00 - 1.91 (m, 1H), 1.88 (s, 1H), 1.84 (br t, J=8.5 Hz, 1H), 1.45 (br d, J=6.4 Hz, 2H)	2.05, B

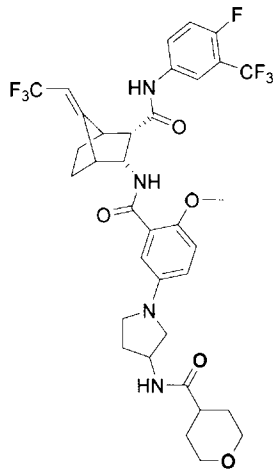
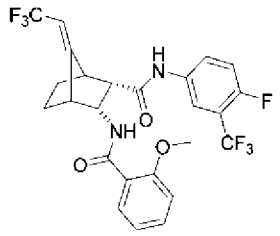
330		(2S,3R,4Z) 3-{5-[3-(苯甲基氧基)吡咯烷-1-基]-2-甲氧基苯甲醯胺基}-N-[4-氟-3-(三氟甲基)苯基]-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-甲醯胺	706.1	(500 MHz, DMSO-d6) δ 10.62 (s, 1H), 9.89 (d, J = 7.3 Hz, 1H), 8.24 (dd, J = 6.4, 2.4 Hz, 1H), 7.88 – 7.75 (m, 1H), 7.50 (t, J = 9.9 Hz, 1H), 7.37 – 7.32 (m, 3H), 7.30 – 7.24 (m, 1H), 7.16 (d, J = 3.1 Hz, 1H), 7.08 – 7.02 (m, 1H), 6.72 (dd, J = 8.9, 3.1 Hz, 1H), 5.94 (q, J = 7.9 Hz, 1H), 4.60 – 4.49 (m, 3H), 4.30 (br s, 1H), 3.96 – 3.82 (m, 3H), 3.51 – 3.39 (m, 1H), 3.33 – 3.20 (m, 2H), 2.99 (br s, 1H), 2.20 (d, J = 4.3 Hz, 1H), 2.15 – 2.07 (m, 2H), 2.08 – 1.85 (m, 3H), 1.49 (br d, J = 6.7 Hz, 2H), 1.36 (d, J = 7.6 Hz, 2H)	2.90, C

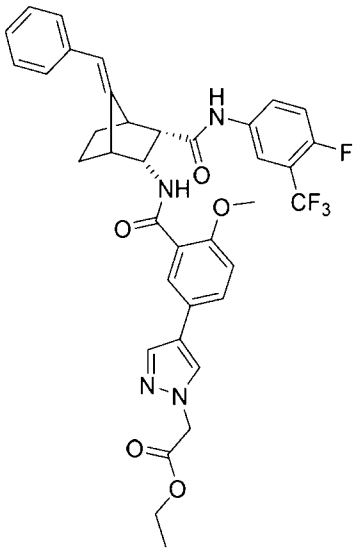
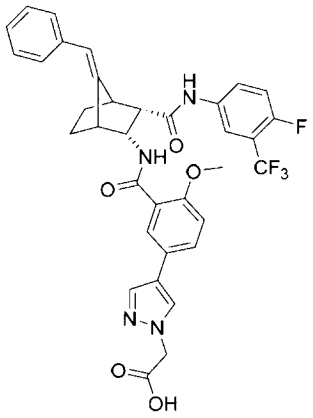
331	 其結構如	N-[1-(3-{[(2R,3S,4S)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-4-(2,2,2-三氟乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)哌啶-3-基]胺基甲酸苯甲酯	749.1	(500 MHz, DMSO-d6) δ 10.69 (s, 1H), 9.90 (d, J = 4.1 Hz, 1H), 8.29 – 8.21 (m, 1H), 7.96 (s, 1H), 7.88 – 7.74 (m, 1H), 7.64 (br d, J = 6.6 Hz, 1H), 7.50 (t, J = 9.7 Hz, 1H), 7.42 – 7.29 (m, 4H), 7.15 – 6.96 (m, 2H), 6.69 (br dd, J = 9.2, 2.7 Hz, 1H), 5.94 (q, J = 7.8 Hz, 1H), 5.03 (s, 2H), 4.61 – 4.47 (m, 1H), 4.25 – 4.13 (m, 1H), 3.97 – 3.87 (m, 3H), 3.37 – 3.15 (m, 2H), 3.12 – 2.97 (m, 2H), 2.90 (s, 2H), 2.74 (s, 2H), 2.26 – 2.17 (m, 1H), 2.04 – 1.79 (m, 2H), 1.57 – 1.44 (m, 2H)	2.65, C

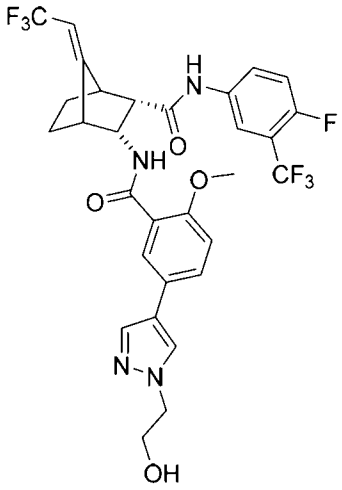
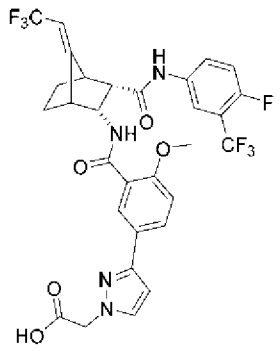
332		N-[1-(3-{[(2R,3S,7*)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)吡咯啶-3-基]胺基甲酸苯甲酯	648.9	(500 MHz, DMSO-d6) δ 10.72 (br s, 1H), 9.91 (br d, J = 6.8 Hz, 1H), 8.25 (br d, J = 4.5 Hz, 1H), 7.96 (s, 1H), 7.86 – 7.74 (m, 1H), 7.65 (br d, J = 6.1 Hz, 1H), 7.56 – 7.50 (m, 1H), 7.42 – 7.29 (m, 5H), 7.16 – 6.98 (m, 2H), 6.69 (br d, J = 7.7 Hz, 1H), 5.94 (br d, J = 8.0 Hz, 1H), 5.03 (s, 2H), 4.52 (br s, 1H), 4.24 – 4.12 (m, 1H), 3.90 (s, 3H), 3.11 – 2.95 (m, 2H), 2.90 (s, 2H), 2.74 (s, 2H), 2.19 (br dd, J = 12.5, 5.6 Hz, 1H), 2.06 – 1.84 (m, 3H), 1.49 (br d, J = 6.3 Hz, 2H)	2.64, C

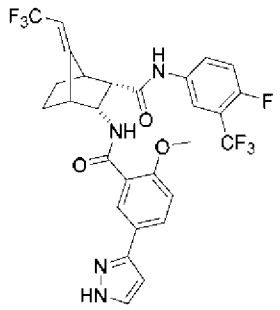
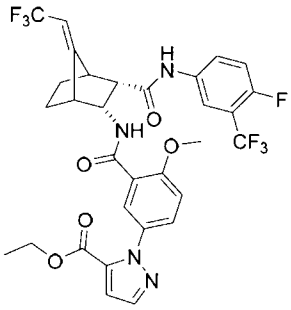
333		(2S,3R,'Z) N-[4-氟-3-(三氟甲基)苯基]-3-[5-(3-羥基吡咯啶-1-基)-2-甲氧基苯甲醯胺基]-7-(2,2,2-三氟乙基)雙環[2.2.1]庚烷-2-甲醯胺	616.03	(500 MHz, DMSO-d6) δ 10.56 (s, 1H), 9.81 (d, J = 6.7 Hz, 1H), 8.16 (dd, J = 6.4, 2.1 Hz, 1H), 7.78 – 7.64 (m, 1H), 7.43 (br t, J = 9.6 Hz, 1H), 7.09 – 6.94 (m, 2H), 6.60 (dd, J = 8.9, 3.1 Hz, 1H), 5.94 – 5.82 (m, 1H), 4.51 – 4.43 (m, 1H), 4.32 (br s, 1H), 4.05 – 3.92 (m, 1H), 3.82 (s, 3H), 3.27 – 3.10 (m, 2H), 2.97 – 2.89 (m, 2H), 2.83 (s, 1H), 2.67 (s, 1H), 2.02 – 1.87 (m, 2H), 1.87 – 1.75 (m, 3H), 1.42 (br d, J = 6.7 Hz, 2H)	2.33, C
334		N-[1-(3-{[(2R,3S,'Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)吡咯啶-3-基]胺基甲酸三級丁酯	715.29	(500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.81 (br d, J = 7.0 Hz, 1H), 8.22 – 8.09 (m, 1H), 7.81 – 7.65 (m, 1H), 7.43 (t, J = 9.8 Hz, 1H), 7.13 – 6.93 (m, 3H), 6.61 (dd, J = 9.0, 2.9 Hz, 1H), 5.87 (q, J = 7.6 Hz, 1H), 4.45 (ddd, J = 10.5, 6.6, 4.0 Hz, 1H), 4.11 – 4.00 (m, 1H), 3.83 (s, 3H), 3.42 – 3.24 (m, 2H), 3.16 (m, 2H), 2.96 – 2.88 (m, 2H), 2.08 (br d, J = 6.4 Hz, 1H), 2.00 – 1.90 (m, 1H), 1.88 – 1.77 (m, 2H), 1.41 (br d, J = 6.7 Hz, 2H), 1.33 (s, 10H)	2.76, C

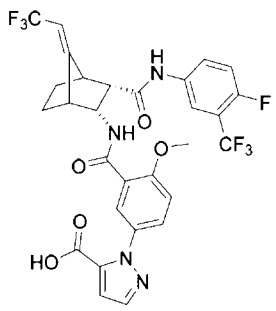
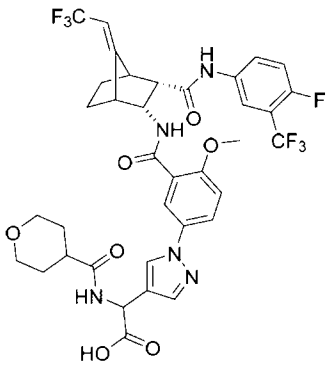
335		(2S,3R,7Z)-3-[5-(3-胺基哌啶-1-基)-2-甲氧基苯甲醯胺基]-N-[4-氟-3-(三氟甲基)苯基]-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-甲醯胺	628.9	(500 MHz, DMSO-d6) δ 10.68 (s, 1H), 9.93 (d, J=7.0 Hz, 1H), 8.24 (br d, J=4.0 Hz, 1H), 8.00 (br s, 2H), 7.84 - 7.68 (m, 1H), 7.58 (d, J=2.7 Hz, 1H), 7.50 (t, J=9.8 Hz, 1H), 7.19 - 7.06 (m, 3H), 5.93 (q, J=8.0 Hz, 1H), 4.57 - 4.43 (m, 1H), 3.94 (s, 3H), 3.30 - 3.16 (m, 2H), 2.99 (br s, 1H), 2.93 - 2.79 (m, 3H), 2.06 - 1.80 (m, 4H), 1.69 - 1.42 (m, 5H)	2.06, C
336	 MeOH/80% CO_2；流動條件：340 mL/min，100 巴， 40 ℃；偵測器波長：220 nm。異構物1，RT = 3.427 min，> 95% de	N-[1-(3-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)吡咯啶-3-基]嗯烷-4-甲醯胺	727.0	(500 MHz, DMSO-d6) δ 10.62 (s, 1H), 9.88 (br d, J=7.0 Hz, 1H), 8.29 - 8.16 (m, 1H), 8.07 (br d, J=6.7 Hz, 1H), 7.85 - 7.73 (m, 1H), 7.50 (br t, J=9.8 Hz, 1H), 7.16 - 6.98 (m, 2H), 6.76 - 6.67 (m, 1H), 5.93 (br d, J=7.9 Hz, 1H), 4.56 - 4.45 (m, 1H), 4.39 - 4.26 (m, 1H), 3.89 (s, 5H), 3.48 - 3.38 (m, 3H), 3.34 - 3.16 (m, 4H), 2.99 (br d, J=7.9 Hz, 2H), 2.41 - 2.32 (m, 1H), 2.17 (br s, 1H), 2.07 - 1.80 (m, 3H), 1.63 - 1.46 (m, 6H)。	2.41, C

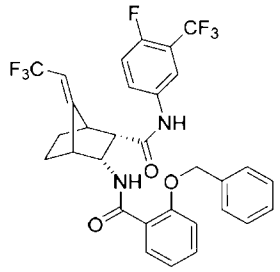
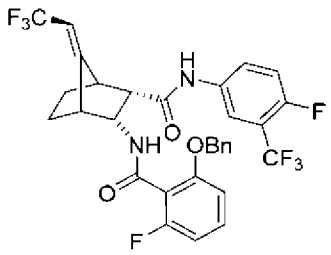
337	 MeOH/80% CO_2；流動條件：340 mL/min，100 巴， 40 ℃；偵測器波長：220 nm。異構物2，RT = 3.820 min，> 95% de	N-[1-(3-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)吡咯啶-3-基]噁烷-4-甲醯胺	727.1	(500 MHz, DMSO-d6) δ 10.65 (s, 1H), 9.90 (br d, J=6.7 Hz, 1H), 8.24 (br dd, J=6.1, 2.1 Hz, 1H), 8.09 (br d, J=7.0 Hz, 1H), 7.89 - 7.78 (m, 1H), 7.51 (br t, J=9.6 Hz, 1H), 7.14 (d, J=3.1 Hz, 1H), 7.06 (d, J=8.9 Hz, 1H), 6.71 (dd, J=8.9, 2.7 Hz, 1H), 5.94 (q, J=8.1 Hz, 1H), 4.53 (br t, J=10.7 Hz, 1H), 4.39 - 4.31 (m, 1H), 4.02 (br d, J=18.9 Hz, 1H), 3.99 - 3.75 (m, 6H), 3.33 - 3.19 (m, 3H), 3.10 - 2.97 (m, 2H), 2.44 - 2.29 (m, 1H), 2.19 (dq, J=12.9, 6.5 Hz, 1H), 2.11 - 1.96 (m, 1H), 1.94 - 1.83 (m, 2H), 1.69 - 1.38 (m, 8H)	2.43, C
338		(2S,3R,7Z)-N-[4-氟-3-(三氟甲基)苯基]-3-(2-甲氧基苯甲醯胺基)-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-甲醯胺	531.0	(500MHz, DMSO-d_6) δ 10.64 (s, 1H), 9.88 (d, *J*=6.9 Hz, 1H), 8.19 (d, *J*=4.8 Hz, 1H), 7.92 (d, *J*=7.7 Hz, 1H), 7.80 - 7.71 (m, 1H), 7.54 - 7.43 (m, 2H), 7.16 (d, *J*=8.3 Hz, 1H), 7.04 (t, *J*=7.5 Hz, 1H), 5.90 (q, *J*=8.0 Hz, 1H), 4.49 (br. s., 1H), 3.97 (s, 3H), 3.29 - 3.18 (m, 2H), 2.96 (br. s., 1H), 1.97 (t, *J*=9.2 Hz, 1H), 1.89 - 1.80 (m, 1H), 1.47 (d, *J*=6.6 Hz, 2H)	2.48, B

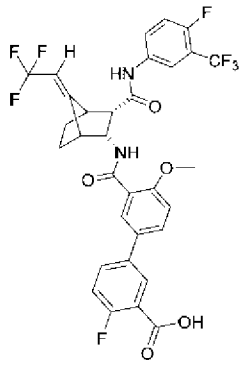
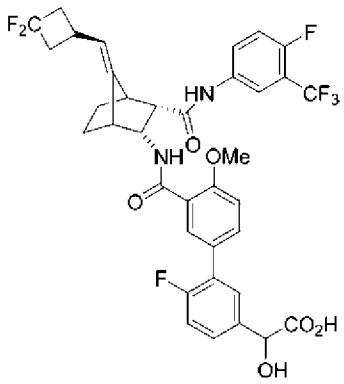
339		2-[4-(3-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(苯基亞甲基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-1H-吡唑-1-基]乙酸乙酯	691.4	(500MHz, DMSO-d_6) δ 10.49 (s, 1H), 9.87 (d, *J*=7.1 Hz, 1H), 8.23 - 8.16 (m, 1H), 8.08 (s, 2H), 7.81 (s, 2H), 7.67 (dd, *J*=8.5, 2.2 Hz, 1H), 7.45 (t, *J*=9.7 Hz, 1H), 7.37 (d, *J*=4.0 Hz, 4H), 7.29 - 7.21 (m, 1H), 7.18 (d, *J*=8.6 Hz, 1H), 6.38 (s, 1H), 5.03 (s, 2H), 4.55 (br. s., 1H), 4.22 - 4.11 (m, 2H), 4.00 (s, 3H), 2.93 (br. s., 1H), 2.02 - 1.84 (m, 2H), 1.53 (br. s., 2H), 1.26 - 1.15 (m, 3H)	2.64, B
340		2-[4-(3-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(苯基亞甲基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-1H-吡唑-1-基]乙酸	663.2	(500MHz, DMSO-d_6) δ 10.47 (s, 1H), 9.87 (d, *J*=7.2 Hz, 1H), 8.17 (d, *J*=6.4 Hz, 1H), 8.04 (d, *J*=18.2 Hz, 2H), 7.83 - 7.73 (m, 2H), 7.66 (dd, *J*=8.5, 2.0 Hz, 1H), 7.43 (s, 1H), 7.37 (d, *J*=4.2 Hz, 4H), 7.25 (d, *J*=4.3 Hz, 1H), 7.17 (d, *J*=8.7 Hz, 1H), 6.37 (s, 1H), 4.86 (s, 2H), 4.58 - 4.49 (m, 1H), 3.98 (s, 3H), 3.71 - 3.55 (m, 1H), 3.41 - 3.35 (m, 1H), 3.32 - 3.23 (m, 1H), 2.92 (br. s., 1H), 1.96 (d, *J*=9.8 Hz, 1H), 1.89 (d, *J*=13.6 Hz, 1H), 1.53 (br. s., 2H)	2.10, B

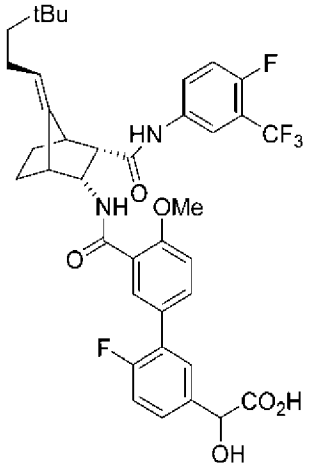
341		(2S,3R,7Z)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[1-(2-羥基乙基)-1H-吡唑-4-基]-2-甲氧基苯甲醯胺基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-甲醯胺	641.1	(500MHz, DMSO-d_6) δ 9.80 (d, *J*=7.0 Hz, 1H), 8.18 (d, *J*=4.1 Hz, 1H), 8.07 (d, *J*=2.3 Hz, 1H), 8.03 (s, 1H), 7.83 - 7.73 (m, 2H), 7.67 (dd, *J*=8.5, 2.1 Hz, 1H), 7.46 (t, *J*=9.8 Hz, 1H), 7.17 (d, *J*=8.6 Hz, 1H), 5.89 (m, 1H), 4.54 (br. s., 1H), 4.15 (t, *J*=5.6 Hz, 2H), 3.99 (s, 3H), 3.81 - 3.75 (m, 2H), 2.98 (d, *J*=5.0 Hz, 1H), 2.03 (t, *J*=8.9 Hz, 1H), 1.96 - 1.87 (m, 1H), 1.50 (d, *J*=7.3 Hz, 2H)	2.18, B
342		2-[3-(3-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-1H-吡唑-1-基]乙酸	655.4	(500MHz, DMSO-d_6) δ 10.66 (s, 1H), 9.97 - 9.91 (m, 1H), 8.37 (s, 1H), 8.28 - 8.20 (m, 1H), 7.93 - 7.86 (m, 1H), 7.84 - 7.76 (m, 1H), 7.74 (br. s., 1H), 7.55 - 7.44 (m, 1H), 7.21 (d, *J*=8.5 Hz, 1H), 6.65 (s, 1H), 5.94 (q, *J*=7.8 Hz, 1H), 4.92 (br. s., 2H), 4.53 (br. s., 1H), 4.02 (s, 3H), 2.99 (s, 2H), 2.01 - 1.86 (m, 2H), 1.49 (d, *J*=6.4 Hz, 2H), 1.23 (s, 2H)	1.89, B

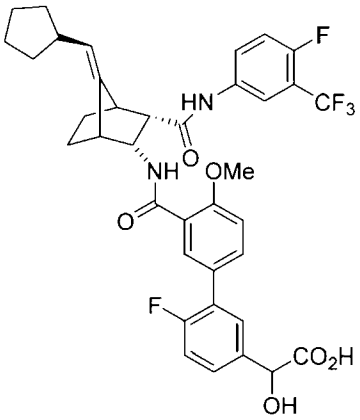
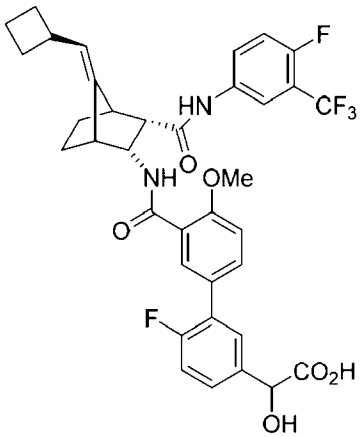
343		(2S,3R,7Z)-N-[4-氟-3-(三氟甲基)苯基]-3-[2-甲氧基-5-(1H-吡唑-3-基)苯甲醯胺基]-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-甲醯胺	597.1	(500MHz, DMSO-d_6) δ 10.64 (s, 1H), 9.99 - 9.89 (m, 1H), 8.40 - 8.35 (m, 1H), 8.26 - 8.20 (m, 1H), 7.97 - 7.87 (m, 1H), 7.83 - 7.72 (m, 2H), 7.54 - 7.45 (m, 1H), 7.26 - 7.17 (m, 1H), 6.67 - 6.58 (m, 1H), 5.98 - 5.90 (m, 1H), 4.59 - 4.49 (m, 1H), 3.41 - 3.14 (m, 3H), 3.02 - 2.87 (m, 2H), 2.04 - 1.85 (m, 2H), 1.49 (d, *J*=6.4 Hz, 2H), 1.16 (t, *J*=7.3 Hz, 1H)	2.38, B
344		1-(3-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-1H-吡唑-5-甲酸乙酯	669.1	(500MHz, DMSO-d_6) δ 10.05 (d, *J*=6.7 Hz, 1H), 8.58 (d, *J*=2.1 Hz, 1H), 8.42 (d, *J*=2.4 Hz, 1H), 8.24 (d, *J*=4.0 Hz, 1H), 8.01 (dd, *J*=8.8, 2.4 Hz, 1H), 7.79 (br. s., 1H), 7.50 (t, *J*=9.8 Hz, 1H), 7.37 (d, *J*=8.8 Hz, 1H), 6.98 (d, *J*=1.8 Hz, 1H), 5.94 (q, *J*=7.5 Hz, 1H), 4.54 (br. s., 1H), 4.33 (q, *J*=7.0 Hz, 2H), 4.06 (s, 3H), 3.35 - 3.22 (m, 1H), 3.00 (br. s., 1H), 2.02 - 1.84 (m, 2H), 1.50 (d, *J*=6.7 Hz, 2H), 1.37 - 1.27 (m, 3H)	2.69, B

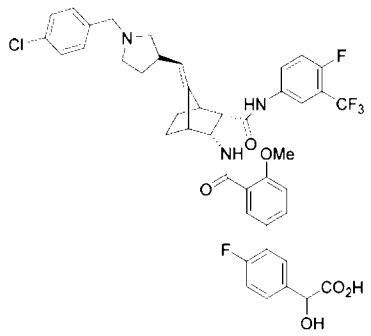
345		1-(3-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-1H-吡唑-5-甲酸	641.1	(500MHz, DMSO-d_6) δ 11.07 (br. s., 1H), 9.94 (d, *J*=6.7 Hz, 1H), 8.36 - 8.22 (m, 3H), 7.98 - 7.79 (m, 2H), 7.49 (t, *J*=9.6 Hz, 1H), 7.25 (d, *J*=9.2 Hz, 1H), 6.73 (s, 1H), 5.90 (q, *J*=7.8 Hz, 1H), 4.45 (br. s., 1H), 4.03 (s, 3H), 3.35 - 3.15 (m, 1H), 2.98 (br. s., 1H), 1.99 (t, *J*=9.2 Hz, 1H), 1.94 - 1.81 (m, 1H), 1.47 (d, *J*=6.7 Hz, 2H)	1.89, B
347		2-[1-(3-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-1H-吡唑-4-基]-2-[(噁烷-4-基)甲醯胺基]乙酸	782.4	(400MHz, CD_3OD) δ 10.35 (d, *J*=7.0 Hz, 1H), 10.25 (s, 1H), 8.35 (d, *J*=2.2 Hz, 1H), 8.24 - 8.14 (m, 2H), 7.89 (dd, *J*=8.7, 2.3 Hz, 1H), 7.81 - 7.72 (m, 2H), 7.38 - 7.27 (m, 2H), 5.79 (q, *J*=7.6 Hz, 1H), 5.56 (s, 1H), 4.67 (d, *J*=3.7 Hz, 1H), 4.15 (s, 3H), 4.05 - 3.95 (m, 2H), 3.53 - 3.41 (m, 3H), 3.32 - 3.23 (m, 2H), 2.96 (br. s., 1H), 2.72 - 2.56 (m, 1H), 2.20 (t, *J*=9.4 Hz, 1H), 2.10 - 2.02 (m, 1H), 1.89 - 1.56 (m, 6H), 1.44 - 1.36 (m, 1H)	1.03, D

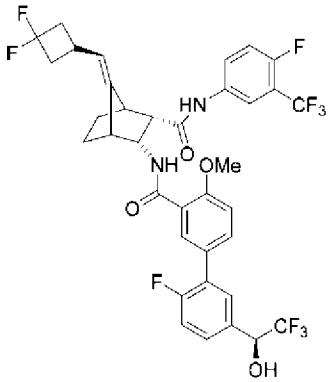
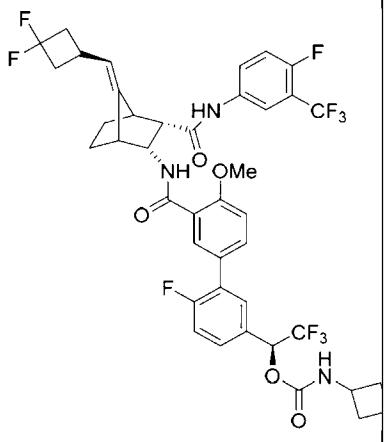
349		(2S,3R,7Z)-3-[2-(苯甲基氧基)苯甲醯胺基]-N-[4-氟-3-(三氟甲基)苯基]-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-甲醯胺	625.3	(500 MHz, DMSO-d6) δ 10.54 (s, 1H), 8.88 (d, J=7.5 Hz, 1H), 8.13 - 7.91 (m, 1H), 7.72 (dd, J=7.4, 4.8 Hz, 1H), 7.49 - 7.34 (m, 4H), 7.32 - 7.21 (m, 3H), 7.01 (d, J=8.5 Hz, 1H), 6.83 (t, J=8.7 Hz, 1H), 5.98 - 5.81 (m, 1H), 5.23 - 5.05 (m, 2H), 4.51 (d, J=1.7 Hz, 1H), 3.51 - 3.36 (m, 1H), 3.23 (dd, J=11.1, 3.9 Hz, 1H), 2.94 (t, J=3.9 Hz, 1H), 2.03 - 1.76 (m, 2H), 1.48 - 1.18 (m, 2H)	2.74, B
350		(2S,3R,7Z)-3-[2-(苯甲基氧基)-6-氟苯甲醯胺基]-N-[4-氟-3-(三氟甲基)苯基]-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-甲醯胺	625.33	(500 MHz, DMSO-d6) δ 10.54 (s, 1H), 8.88 (d, J=7.5 Hz, 1H), 8.13 - 7.91 (m, 1H), 7.72 (dd, J=7.4, 4.8 Hz, 1H), 7.49 - 7.34 (m, 4H), 7.32 - 7.21 (m, 3H), 7.01 (d, J=8.5 Hz, 1H), 6.83 (t, J=8.7 Hz, 1H), 5.98 - 5.81 (m, 1H), 5.23 - 5.05 (m, 2H), 4.51 (d, J=1.7 Hz, 1H), 3.51 - 3.36 (m, 1H), 3.23 (dd, J=11.1, 3.9 Hz, 1H), 2.94 (t, J=3.9 Hz, 1H), 2.03 - 1.76 (m, 2H), 1.48 - 1.18 (m, 2H)	2.33, B

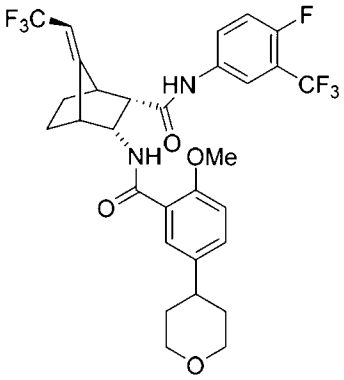
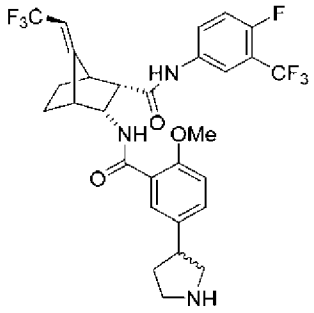
351		4-氟-3'-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-3-甲酸	669.2	(400 MHz, DMSO-d6) δ ppm 10.46 (s, 1H), 8.50 (d, *J* = 6.6 Hz, 1H), 8.13 (dd, *J* = 2.6, 6.5 Hz, 1H), 8.03 (dd, *J* = 2.6, 7.0 Hz, 1H), 7.91 - 7.70 (m, 4H), 7.47 (t, *J* = 9.9 Hz, 1H), 7.36 (dd, *J* = 8.7, 10.4 Hz, 1H), 7.24 (d, *J* = 8.6 Hz, 1H), 5.74 (q, *J* = 8.0 Hz, 1H), 4.71 - 4.61 (m, 1H), 3.91 (s, 3H), 3.25 - 3.22 (m, 1H), 2.79 (br s, 1H), 2.60 (d, *J* = 5.1 Hz, 1H), 2.01 - 1.92 (m, 1H), 1.81 - 1.64 (m, 2H), 1.61 - 1.48 (m, 1H)	1.89, D
353		2-(3'-{[(7Z)-7-[(3,3-二氟環丁基)亞甲基]-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2-羥基乙酸	721.14	(500 MHz, DMSO-d6) δ 10.44 (br s, 1H), 9.85 - 9.70 (m, 1H), 8.07 (br d, J=4.6 Hz, 1H), 7.97 (br d, J=8.2 Hz, 1H), 7.80 (s, 1H), 7.66 (br s, 1H), 7.57 - 7.48 (m, 1H), 7.35 (br dd, J=14.0, 5.2 Hz, 3H), 7.21 - 7.03 (m, 2H), 5.23 (br dd, J=16.0, 8.7 Hz, 1H), 4.71 (s, 1H), 4.26 (br s, 1H), 3.90 (s, 3H), 3.09 - 2.97 (m, 2H), 2.90 - 2.78 (m, 2H), 2.72 - 2.62 (m, 2H), 2.54 (br s, 1H), 2.28 (br d, J=5.8 Hz, 1H), 1.77 (s, 2H), 1.64 (br s, 1H), 1.26 (br s, 2H)	2.44, C

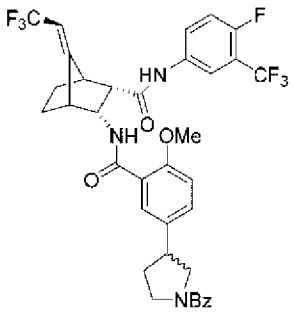
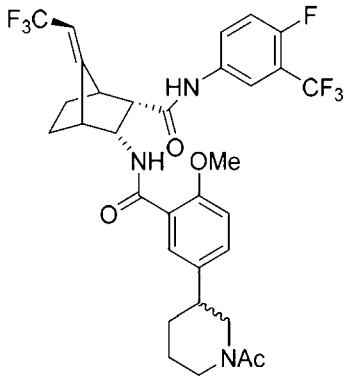
354		2-(3'-{[(7Z)-7-(4,4-二甲基亞戊基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2-羥基乙酸	715.04	(500 MHz, DMSO-d6) δ 10.47 (s, 1H), 9.73 (br d, J=7.0 Hz, 1H), 8.09 (br d, J=4.0 Hz, 1H), 7.95 (s, 1H), 7.68 (br s, 1H), 7.50 (br d, J=8.2 Hz, 1H), 7.39 - 7.29 (m, 2H), 7.22 (br d, J=4.9 Hz, 1H), 7.18 - 7.10 (m, 1H), 6.99 (dd, J=10.4, 8.9 Hz, 1H), 5.10 - 5.03 (m, 1H), 4.34 (s, 1H), 4.27 (br t, J=10.2 Hz, 1H), 3.90 (s, 3H), 3.07 - 3.00 (m, 1H), 2.94 - 2.89 (m, 1H), 2.50 (br s, 1H), 1.90 (br d, J=6.4 Hz, 2H), 1.81 - 1.56 (m, 2H), 1.52 (s, 1H), 1.28 - 1.04 (m, 5H), 0.77 (s, 9H)	2.76, C

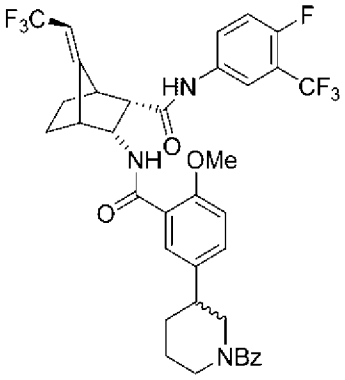
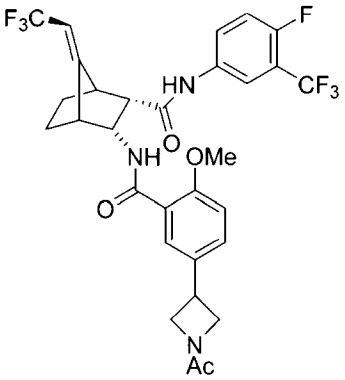
355		2-(3'-{[(7Z)-7-(環戊基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2-羥基乙酸	699.0	(500 MHz, DMSO-d6) δ 10.52 (s, 1H), 9.89 (br d, J=7.0 Hz, 1H), 8.19 (br d, J=4.3 Hz, 1H), 8.09 (s, 1H), 7.79 - 7.70 (m, 1H), 7.68 - 7.59 (m, 1H), 7.53 - 7.33 (m, 3H), 7.29 - 7.16 (m, 2H), 5.16 (d, J=8.9 Hz, 1H), 4.42 - 4.32 (m, 1H), 4.01 (s, 3H), 3.59 (br s, 1H), 3.12 (br dd, J=10.8, 4.1 Hz, 1H), 2.97 (br s, 1H), 2.68 (br s, 1H), 2.53 (s, 2H), 1.86 - 1.67 (m, 4H), 1.66 - 1.47 (m, 4H), 1.36 (br d, J=6.1 Hz, 2H), 1.19 (br s, 3H)	2.62, C
356		2-(3'-{[(7Z)-7-(環丁基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2-羥基乙酸	685.1	(500 MHz, DMSO-d6) δ 10.63 - 10.53 (m, 1H), 9.99 - 9.85 (m, 1H), 8.27 - 8.21 (m, 1H), 8.14 - 8.07 (m, 1H), 7.86 - 7.77 (m, 1H), 7.70 - 7.63 (m, 1H), 7.53 - 7.38 (m, 4H), 7.33 - 7.27 (m, 1H), 7.24 - 7.17 (m, 1H), 5.39 - 5.31 (m, 1H), 4.82 (s, 1H), 4.43 - 4.34 (m, 1H), 4.05 (s, 3H), 3.57 (br d, J=2.2 Hz, 1H), 3.21 - 3.06 (m, 1H), 2.21 - 2.05 (m, 3H), 1.92 - 1.66 (m, 8H), 1.37 (br s, 2H)	2.25, C

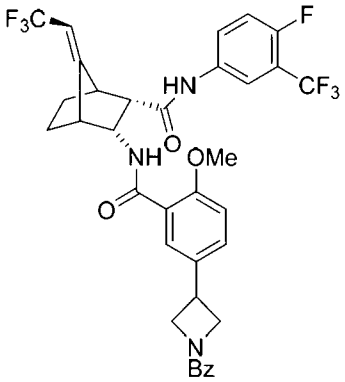
357		2-(3'-{[(7Z)-7-({1-[(4-氯苯基)甲基]吡咯啶-3-基}亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2-羥基乙酸	824.2	(500 MHz, DMSO-d6) δ 10.65 - 10.54 (m, 1H), 9.91 (br d, J=6.7 Hz, 1H), 8.25 (br d, J=5.8 Hz, 1H), 8.17 - 8.09 (m, 1H), 7.86 - 7.78 (m, 1H), 7.68 (br d, J=8.2 Hz, 1H), 7.57 - 7.46 (m, 2H), 7.45 - 7.35 (m, 5H), 7.33 - 7.19 (m, 2H), 5.25 (br d, J=8.5 Hz, 1H), 4.93 (br s, 1H), 4.41 (dt, J=7.3, 3.4 Hz, 1H), 4.05 (s, 3H), 3.74 - 3.66 (m, 1H), 3.23 - 3.12 (m, 1H), 3.04 - 2.94 (m, 2H), 2.82 (br t, J=8.5 Hz, 1H), 2.76 - 2.60 (m, 3H), 2.55 - 2.52 (m, 2H), 2.38 - 2.28 (m, 1H), 2.23 - 2.02 (m, 1H), 1.90 - 1.84 (m, 1H), 1.80 - 1.71 (m, 1H), 1.67 - 1.54 (m, 1H), 1.44 - 1.31 (m, 2H)	2.07, C

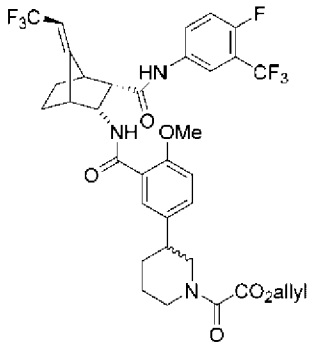
358		N-[(7Z)-7-[(3,3-二氟環丁基)亞甲基]-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]-2'-氟-4-甲氧基-5'-[(1S)-2,2,2-三氟-1-羥基乙基]-[1,1'-聯苯]-3-甲醯胺	745.2	(500 MHz, DMSO-d6) δ 10.57 (s, 1H), 9.94 (br d, J=7.1 Hz, 1H), 8.24 (br d, J=4.1 Hz, 1H), 8.13 (d, J=0.9 Hz, 1H), 7.89 - 7.78 (m, 1H), 7.70 (br d, J=8.4 Hz, 1H), 7.63 (br d, J=7.1 Hz, 1H), 7.57 - 7.44 (m, 2H), 7.39 - 7.29 (m, 2H), 5.40 (d, J=8.6 Hz, 1H), 5.28 (br d, J=6.8 Hz, 1H), 4.44 - 4.37 (m, 1H), 4.06 (s, 3H), 3.69 - 3.55 (m, 1H), 3.25 - 3.09 (m, 1H), 3.01 (br s, 1H), 2.98 - 2.79 (m, 3H), 2.77 (br s, 1H), 2.43 (br s, 2H), 1.87 (br s, 2H), 1.40 (br s, 2H)	2.75, C
359		N-環丁基胺基甲酸(1S)-1-(3'-{[(2R,3S,7Z)-7-[(3,3-二氟環丁基)亞甲基]-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2,2,2-三氟乙酯	842.2	(400 MHz, DMSO-d6) δ 10.56 (s, 1H), 9.94 (br d, J=7.0 Hz, 1H), 8.25 (dd, J=6.3, 2.3 Hz, 1H), 8.18 - 8.08 (m, 2H), 7.87 - 7.78 (m, 1H), 7.74 - 7.66 (m, 2H), 7.58 - 7.29 (m, 5H), 6.39 (q, J=7.3 Hz, 1H), 5.45 - 5.34 (m, 1H), 4.49 - 4.36 (m, 1H), 4.08 (s, 3H), 3.95 (br d, J=7.9 Hz, 1H), 3.24 - 2.68 (m, 7H), 2.47 (br d, J=2.0 Hz, 2H), 1.98 - 1.84 (m, 4H), 1.65 - 1.53 (m, 2H), 1.46 - 1.36 (m, 2H)	1.25, A

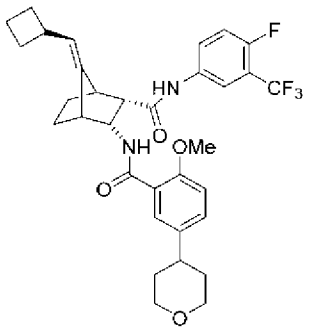
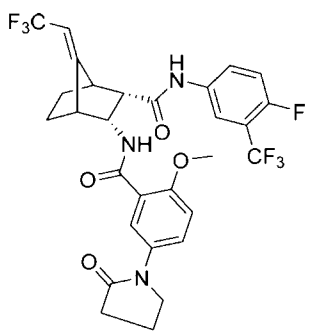
361		(7Z)-N-[4- 氟 -3-(三氟甲基)苯基]-3-[2- 甲 氧 基 -5-(喔烷-4-基)苯甲醯胺基]-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2- 甲醯胺	615.14	(500 MHz, DMSO-d6) δ 10.64 (s, 1H), 9.86 (br d, J=7.0 Hz, 1H), 8.24 (br d, J=5.5 Hz, 1H), 7.86 - 7.74 (m, 2H), 7.56 - 7.44 (m, 1H), 7.42 - 7.31 (m, 1H), 7.13 (br d, J=8.5 Hz, 1H), 5.94 (br d, J=7.6 Hz, 1H), 4.60 - 4.46 (m, 1H), 4.07 - 3.86 (m, 5H), 3.23 (br s, 1H), 2.99 (br s, 1H), 2.78 - 2.67 (m, 1H), 2.51 - 2.34 (m, 3H), 2.09 - 1.80 (m, 2H), 1.72 - 1.56 (m, 4H), 1.49 (br d, J=6.7 Hz, 2H)	2.64, C
362		(7Z)-N-[4- 氟 -3-(三氟甲基)苯基]-3-[2- 甲 氧 基 -5-(吡咯啶-3-基)苯甲醯胺基]-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-甲醯胺	600.1	(500 MHz, DMSO-d6) δ 9.89 (br d, J=6.4 Hz, 1H), 8.21 (br d, J=6.1 Hz, 1H), 7.85 (s, 1H), 7.81 - 7.71 (m, 1H), 7.55 - 7.40 (m, 2H), 7.15 (br d, J=8.5 Hz, 1H), 5.92 (q, J=8.2 Hz, 1H), 4.55 - 4.45 (m, 1H), 3.97 (s, 3H), 3.57 (br d, J=5.5 Hz, 2H), 3.46 - 3.38 (m, 1H), 3.31 - 3.19 (m, 3H), 3.12 - 3.03 (m, 1H), 2.98 (br s, 1H), 2.85 - 2.78 (m, 1H), 2.23 (br dd, J=7.2, 4.1 Hz, 1H), 2.02 - 1.93 (m, 1H), 1.87 - 1.72 (m, 3H), 1.54 - 1.43 (m, 2H)	2.09, C

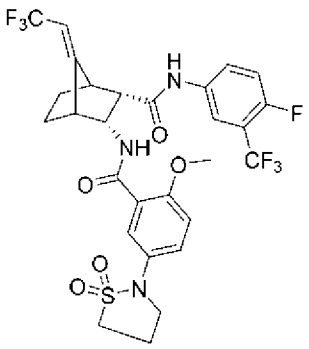
363		(7Z)-3-[5-(1-苯甲醯基吡咯啶-3-基)-2-甲氧基苯甲醯胺基]-N-[4-氟-3-(三氟甲基)苯基]-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-甲醯胺	704.4	(500 MHz, DMSO-d6) δ 9.87 (br dd, J=15.6, 6.7 Hz, 1H), 8.21 (br s, 1H), 7.80 - 7.76 (m, 1H), 7.58 - 7.39 (m, 7H), 7.19 - 7.07 (m, 1H), 5.96 - 5.87 (m, 1H), 4.56 - 4.43 (m, 1H), 3.97 (br d, J=16.2 Hz, 3H), 3.68 (br d, J=2.7 Hz, 1H), 3.47 (br s, 4H), 3.30 - 3.13 (m, 2H), 2.97 (br s, 1H), 2.73 (s, 1H), 2.27 (br d, J=5.5 Hz, 1H), 2.07 - 1.71 (m, 4H), 1.48 (br s, 2H)	2.56, C
364		(7Z)-3-[5-(1-乙醯基哌啶-3-基)-2-甲氧基苯甲醯胺基]-N-[4-氟-3-(三氟甲基)苯基]-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-甲醯胺	656.19	(500 MHz, DMSO-d6) δ 10.63 (s, 1H), 9.87 (br d, J=5.8 Hz, 1H), 8.23 (br d, J=6.1 Hz, 1H), 7.87 - 7.72 (m, 2H), 7.50 (br t, J=9.5 Hz, 1H), 7.39 (br d, J=8.5 Hz, 1H), 7.12 (br d, J=8.9 Hz, 1H), 5.94 (q, J=8.0 Hz, 1H), 4.51 (br d, J=11.3 Hz, 2H), 4.00 - 3.81 (m, 4H), 3.40 - 3.30 (m, 2H), 3.29 - 3.06 (m, 2H), 2.98 (br s, 1H), 2.82 - 2.72 (m, 1H), 2.66 - 2.54 (m, 1H), 2.09 - 1.96 (m, 4H), 1.91 - 1.83 (m, 1H), 1.80 - 1.68 (m, 2H), 1.63 - 1.46 (m, 3H)	2.34, C

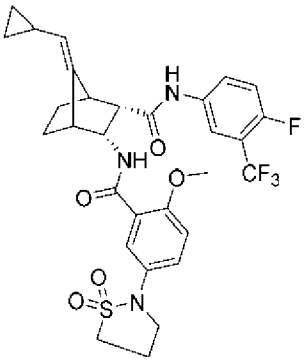
365		(7Z)-3-[5-(1-苯甲醯基哌啶-3-基)-2-甲氧基苯甲醯胺基]-N-[4-氟-3-(三氟甲基)苯基]-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-甲醯胺	718.44	(500 MHz, DMSO-d6) δ 10.63 (br s, 1H), 9.87 (br d, J=7.0 Hz, 1H), 8.27 - 8.17 (m, 1H), 7.89 - 7.72 (m, 2H), 7.55 - 7.36 (m, 7H), 7.12 (br d, J=8.5 Hz, 1H), 5.93 (br d, J=7.9 Hz, 1H), 4.57 - 4.45 (m, 1H), 3.97 (s, 3H), 3.48 - 3.38 (m, 2H), 3.29 - 3.18 (m, 1H), 2.98 (br s, 2H), 2.85 - 2.69 (m, 2H), 2.55 (s, 1H), 2.01 - 1.76 (m, 3H), 1.78 - 1.64 (m, 1H), 1.62 - 1.41 (m, 4H)	2.65, C
366		(7Z)-3-[5-(1-乙醯基氮雜環丁烷-3-基)-2-甲氧基苯甲醯胺基]-N-[4-氟-3-(三氟甲基)苯基]-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-甲醯胺	628.18	(500 MHz, DMSO-d6) δ 10.65 (s, 1H), 9.98 - 9.86 (m, 1H), 8.23 (br d, J=4.6 Hz, 1H), 8.00 - 7.87 (m, 1H), 7.85 - 7.74 (m, 1H), 7.57 - 7.44 (m, 2H), 7.18 (br d, J=8.9 Hz, 1H), 6.00 - 5.87 (m, 1H), 4.58 - 4.43 (m, 2H), 4.22 (t, J=9.0 Hz, 1H), 4.10 - 4.03 (m, 1H), 3.99 (s, 3H), 3.87 - 3.69 (m, 2H), 3.39 - 3.18 (m, 1H), 3.01 - 2.87 (m, 2H), 2.02 - 1.84 (m, 2H), 1.80 (d, J=2.1 Hz, 3H), 1.56 - 1.44 (m, 2H)	2.20, C

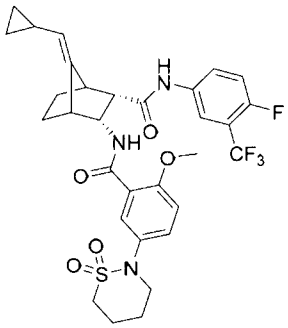
367		(7Z)-3-[5-(1-苯甲醯基氮雜環丁烷-3-基)-2-甲氧基苯甲醯胺基]-N-[4-氟-3-(三氟甲基)苯基]-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-甲醯胺	690.21	(500 MHz, DMSO-d6) δ 10.64 (s, 1H), 9.92 (br d, J=6.4 Hz, 1H), 8.23 (br d, J=5.5 Hz, 1H), 7.95 (br s, 1H), 7.81 - 7.72 (m, 2H), 7.69 (br d, J=7.3 Hz, 1H), 7.58 - 7.37 (m, 6H), 7.25 - 7.14 (m, 1H), 5.94 (q, J=7.8 Hz, 1H), 4.68 (br t, J=8.7 Hz, 1H), 4.54 - 4.42 (m, 2H), 4.34 - 4.24 (m, 1H), 4.00 (s, 4H), 3.23 (br d, J=1.8 Hz, 1H), 3.01 - 2.98 (m, 1H), 2.50 - 2.39 (m, 1H), 2.01 - 1.96 (m, 1H), 1.90 - 1.85 (m, 1H), 1.58 - 1.45 (m, 2H)	2.45, C

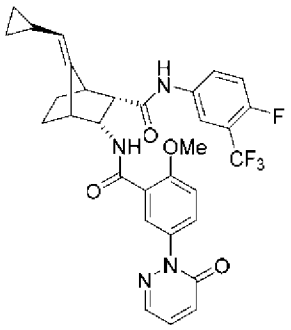
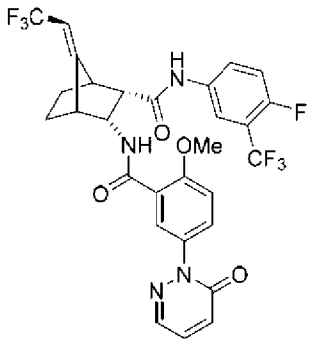
368		2-[3-(3-{[(7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)哌啶-1-基]-2-側氧基乙酸	686.2	(500 MHz, DMSO-d6) δ 10.80 - 10.58 (m, 1H), 9.94 - 9.74 (m, 1H), 8.24 (br d, J=6.4 Hz, 1H), 7.84 - 7.76 (m, 2H), 7.50 (br t, J=9.8 Hz, 1H), 7.36 (br d, J=5.8 Hz, 1H), 7.17 - 7.05 (m, 1H), 5.98 - 5.86 (m, 1H), 4.52 (br d, J=4.9 Hz, 1H), 4.38 - 4.20 (m, 1H), 4.00 - 3.94 (m, 3H), 3.82 - 3.70 (m, 1H), 3.22 (br s, 1H), 3.07 - 2.93 (m, 2H), 2.64 - 2.53 (m, 1H), 2.07 - 1.94 (m, 1H), 1.89 (br d, J=9.2 Hz, 2H), 1.76 - 1.59 (m, 2H), 1.51 - 1.31 (m, 4H), 1.19 - 0.93 (m, 1H)。	1.81, C

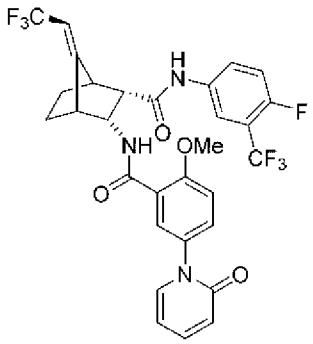
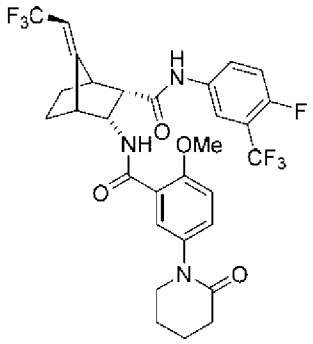
369		(7Z)-7-(環丁基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-[2-甲氧基-5-(噁烷-4-基)苯甲醯胺基]雙環[2.2.1]庚烷-2-甲醯胺	601.3	(500 MHz, DMSO-d6) δ 10.40 (s, 1H), 9.67 (br d, J=7.3 Hz, 1H), 8.08 (br d, J=5.2 Hz, 1H), 7.71 - 7.59 (m, 2H), 7.41 - 7.20 (m, 2H), 6.99 (br d, J=8.5 Hz, 1H), 5.24 (br d, J=8.2 Hz, 1H), 4.29 - 4.20 (m, 1H), 3.91 - 3.74 (m, 4H), 3.61 - 3.44 (m, 1H), 3.30 (br t, J=11.7 Hz, 2H), 3.12 - 2.88 (m, 2H), 2.81 (br s, 1H), 2.70 - 2.55 (m, 2H), 2.11 - 1.96 (m, 2H), 1.83 - 1.64 (m, 5H), 1.57 - 1.42 (m, 5H), 1.33 - 1.18 (m, 2H)	2.87, C
370		(2S,3R,7Z)-N-[4-氟-3-(三氟甲基)苯基]-3-[2-甲氧基-5-(2-側氧基吡咯啶-1-基)苯甲醯胺基]-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-甲醯胺	614.2	(500 MHz, DMSO-d_6) δ 10.65 (s, 1H), 9.91 (d, *J*=7.0 Hz, 1H), 8.25 - 8.11 (m, 1H), 8.09 (d, *J*=2.8 Hz, 1H), 7.75 (br dd, *J*=8.8, 2.7 Hz, 2H), 7.46 (t, *J*=9.7 Hz, 1H), 7.18 (d, *J*=9.1 Hz, 1H), 5.88 (q, *J*=7.7 Hz, 1H), 4.59 - 4.38 (m, 1H), 3.96 (s, 3H), 3.29 - 3.16 (m, 2H), 2.99 - 2.93 (m, 1H), 2.45 (t, *J*=8.0 Hz, 2H), 2.12 - 2.02 (m, 2H), 1.97 - 1.91 (m, 1H), 1.88 - 1.79 (m, 1H), 1.47 (br d, *J*=6.9 Hz, 2H)	2.36, C

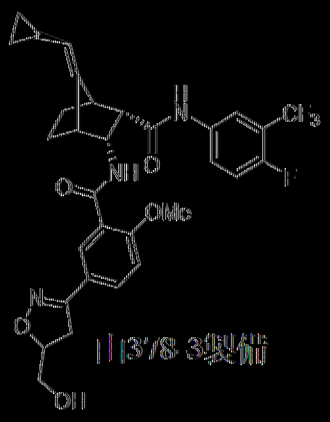
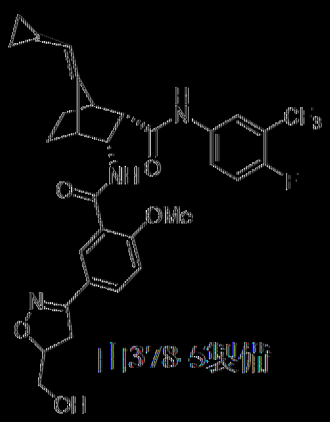
371		(2S,3R,7Z)-3-[5-(1,1-二側氧基-1λ⁶,2-噻唑啶-2-基)-2-甲氧基苯甲醯胺基]-N-[4-氟-3-(三氟甲基)苯基]-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-甲醯胺	650.2	(500 MHz, DMSO-d_6) δ 10.68 (s, 1H), 9.97 (br d, *J*=6.7 Hz, 1H), 8.20 (br d, *J*=4.0 Hz, 1H), 7.83 (d, *J*=2.7 Hz, 1H), 7.78 (br d, *J*=7.9 Hz, 1H), 7.48 (br t, *J*=9.8 Hz, 1H), 7.43 - 7.35 (m, 1H), 7.23 (d, *J*=9.2 Hz, 1H), 5.91 (q, *J*=7.9 Hz, 1H), 4.54 - 4.46 (m, 1H), 3.98 (s, 3H), 3.45 (t, *J*=7.6 Hz, 1H), 3.30 - 3.17 (m, 2H), 2.98 (br s, 1H), 2.40 (quin, *J*=6.9 Hz, 2H), 2.06 - 1.93 (m, 1H), 1.89 - 1.79 (m, 1H), 1.62 - 1.41 (m, 2H), 1.28 - 1.10 (m, 1H)	2.40, C

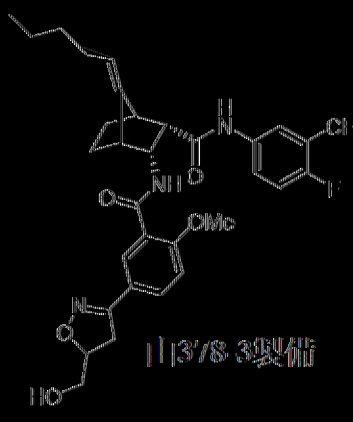
372		(2S,3R,7Z)-7-(環丙基亞甲基)-3-[5-(1,1-二側氧基-1λ⁶,2-噻唑啶-2-基)-2-甲氧基苯甲醯胺基]-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	622.1	(500 MHz, DMSO-d_6) δ 10.54 (s, 1H), 9.94 (br d, *J*=7.0 Hz, 1H), 8.24 (br d, *J*=4.6 Hz, 1H), 7.86 (d, *J*=3.1 Hz, 1H), 7.83 - 7.76 (m, 1H), 7.50 (br t, *J*=9.6 Hz, 1H), 7.37 (dd, *J*=8.7, 2.9 Hz, 1H), 7.24 (d, *J*=8.9 Hz, 1H), 4.70 (d, *J*=9.8 Hz, 1H), 4.45 (br t, *J*=10.4 Hz, 1H), 4.00 (s, 3H), 3.71 (br t, *J*=6.7 Hz, 1H), 3.60 - 3.41 (m, 1H), 3.45 - 3.29 (m, 1H), 3.17 (br dd, *J*=10.8, 3.8 Hz, 1H), 3.11 (br s, 1H), 2.73 (br s, 1H), 2.41 (quin, *J*=6.9 Hz, 2H), 1.94 - 1.81 (m, 1H), 1.82 - 1.73 (m, 1H), 1.60 - 1.47 (m, 1H), 1.46 - 1.32 (m, 2H), 0.90 - 0.63 (m, 2H), 0.37 (br s, 2H)	2.44, B

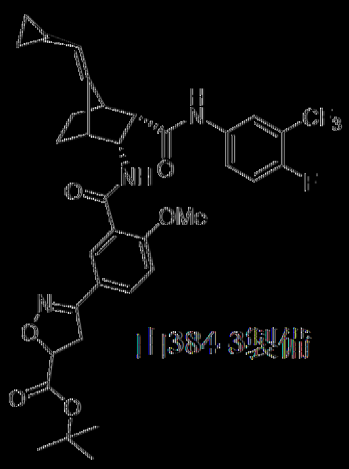
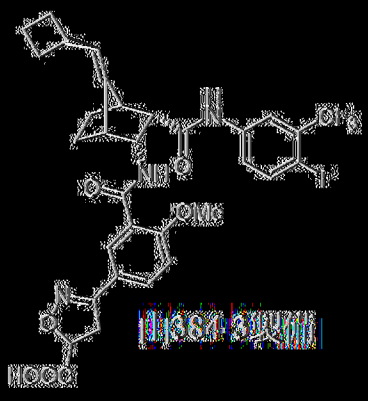
373		(2S,3R,7Z)-7-(環丙基亞甲基)-3-[5-(1,1-二側氧基-1λ⁶,2-噻咁烷-2-基)-2-甲氧基苯甲醯胺基]-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	636.3	(500 MHz, DMSO-d_6) δ 10.53 (s, 1H), 9.91 (d, *J*=7.0 Hz, 1H), 8.30 - 8.14 (m, 1H), 7.85 (d, *J*=2.7 Hz, 1H), 7.77 (br dd, *J*=8.4, 3.4 Hz, 1H), 7.47 (t, *J*=9.7 Hz, 1H), 7.43 (dd, *J*=8.8, 2.9 Hz, 1H), 7.19 (d, *J*=8.9 Hz, 1H), 4.68 (d, *J*=9.5 Hz, 1H), 4.50 - 4.31 (m, 1H), 4.00 (s, 3H), 3.79 - 3.64 (m, 2H), 3.34 - 3.22 (m, 2H), 3.14 (br dd, *J*=10.6, 4.1 Hz, 1H), 3.08 (br s, 1H), 2.71 (br s, 1H), 2.25 - 2.05 (m, 2H), 1.88 - 1.67 (m, 4H), 1.62 - 1.44 (m, 1H), 1.44 - 1.31 (m, 2H), 0.84 - 0.58 (m, 2H), 0.34 (br d, *J*=3.1 Hz, 2H)	2.51, B

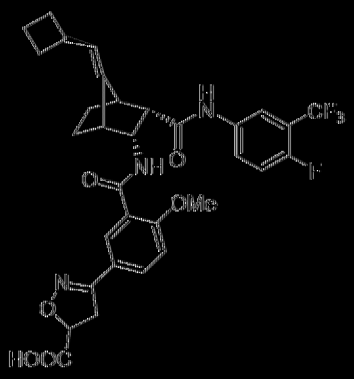
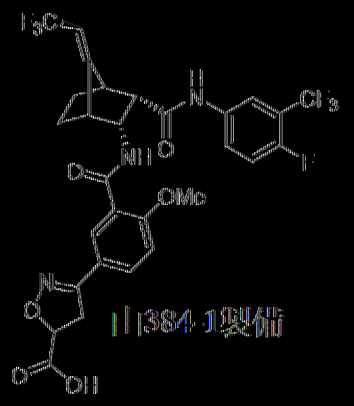
374		(2S,3R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-[2-甲氧基-5-(6-側氧基-1,6-二氫嗒吡-1-基)苯甲醯胺基]雙環[2.2.1]庚烷-2-甲醯胺	662.3	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.95 (br d, *J*=7.0 Hz, 1H), 8.20 (br d, *J*=4.6 Hz, 1H), 8.05 (dd, *J*=13.1, 2.4 Hz, 2H), 7.79 - 7.76 (m, 1H), 7.69 (dd, *J*=8.9, 2.7 Hz, 1H), 7.49 - 7.45 (m, 2H), 7.29 (d, *J*=8.9 Hz, 1H), 7.05 (dd, *J*=9.5, 1.2 Hz, 1H), 4.68 (d, *J*=9.8 Hz, 1H), 4.45 - 4.40 (m, 1H), 4.04 (s, 3H), 3.18 - 3.15 (m, 1H), 3.12 - 3.05 (m, 1H), 2.76 - 2.66 (m, 1H), 1.86 - 1.75 (m, 2H), 1.52 - 1.46 (m, 1H), 1.40 (br t, *J*=9.5 Hz, 2H), 0.77 - 0.68 (m, 2H), 0.36 - 0.29 (m, 2H)	2.38, C
375		(2S,3R,7Z)-N-[4-氟-3-(三氟甲基)苯基]-3-[2-甲氧基-5-(6-側氧基-1,6-二氫嗒吡-1-基)苯甲醯胺基]-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-甲醯胺	625.4	(500 MHz, DMSO-d6) δ 10.66 (s, 1H), 9.98 (br d, *J*=6.7 Hz, 1H), 8.21 (br d, *J*=4.3 Hz, 1H), 8.05 (dd, *J*=13.6, 2.6 Hz, 2H), 7.81 - 7.76 (m, 1H), 7.70 (dd, J=8.7, 2.6 Hz, 1H), 7.51 - 7.46 (m, 2H), 7.30 (d, *J*=8.9 Hz, 1H), 7.05 (br d, *J*=9.5 Hz, 1H), 5.92 (q, *J*=7.9 Hz, 1H), 4.54 - 4.48 (m, 1H), 4.05 (s, 3H), 3.29 - 3.23 (m, 1H), 3.01 - 2.93 (m, 1H), 1.97 - 1.83 (m, 3H), 1.52 - 1.44 (m, 2H)	2.42, B

376		(2S,3R,7Z)-N-[4-氟-3-(三氟甲基)苯基]-3-[2-甲氧基-5-(2-側氧基-1,2-二氫吡啶-1-基)苯甲醯胺基]-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-甲醯胺	624.1	(500 MHz, DMSO-d6) δ 10.67 (s, 1H), 10.00 (br d, *J*=6.7 Hz, 1H), 8.21 (br d, *J*=4.3 Hz, 1H), 7.85 (d, *J*=2.4 Hz, 1H), 7.79 (br d, *J*=8.5 Hz, 1H), 7.60 (br d, *J*=5.5 Hz, 1H), 7.55 - 7.46 (m, 3H), 7.31 (d, *J*=8.9 Hz, 1H), 6.47 (d, *J*=9.5 Hz, 1H), 6.32 (t, *J*=6.7 Hz, 1H), 5.92 (q, *J*=7.8 Hz, 1H), 4.50 (br t, *J*=10.7 Hz, 1H), 4.05 (s, 3H), 3.29 - 3.20 (m, 2H), 3.02 - 2.94 (m, 1H), 1.96 (br t, *J*=9.3 Hz, 1H), 1.90 - 1.84 (m, 1H), 1.52 - 1.44 (m, 2H)	2.40, B
377		(2S,3R,7Z)-N-[4-氟-3-(三氟甲基)苯基]-3-[2-甲氧基-5-(2-側氧基哌啶-1-基)苯甲醯胺基]-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-甲醯胺	628.1	(500 MHz, DMSO-d6) δ 10.64 (s, 1H), 9.90 (br d, *J*=7.3 Hz, 1H), 8.18 (br d, *J*=4.3 Hz, 1H), 7.79 - 7.72 (m, 2H), 7.47 (br t, *J*=9.8 Hz, 1H), 7.37 (dd, *J*=8.9, 2.4 Hz, 1H), 7.17 (d, *J*=8.9 Hz, 1H), 5.89 (q, *J*=7.9 Hz, 1H), 4.51 - 4.45 (m, 1H), 3.97 (s, 3H), 3.55 - 3.48 (m, 1H), 3.25 - 3.15 (m, 2H), 3.00 - 2.94 (m, 1H), 2.35 (br t, *J*=6.0 Hz, 2H), 2.00 - 1.93 (m, 1H), 1.87 - 1.78 (m, 5H), 1.51 - 1.42 (m, 2H)	2.40, B

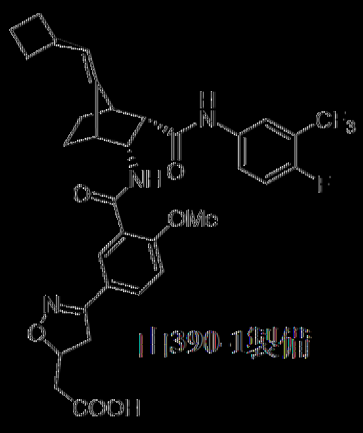
380	 使用3'/8-3製備	(2S,3R,1'S)-1'-(環丙基甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-[5-[5-(羥基甲基)-4,5-二氫-1,2-噁唑-3-基]-2-甲氧基苯甲醯胺基]雙環[2.2.1]庚烷-2-甲醯胺	602.3	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.92 (dd, J = 6.9, 3.8 Hz, 1H), 8.22 (s, 1H), 8.23 (d, J = 6.4 Hz, 1H), 1.82 – 1.76 (m, 2H), 1.49 (t, J = 9.8 Hz, 1H), 1.21 (d, J = 8.8 Hz, 1H), 5.09 – 4.97 (m, 1H), 4.75 – 4.64 (m, 2H), 4.44 (br s, 1H), 4.04 (s, 3H), 3.58 – 3.43 (m, 3H), 3.22 – 3.13 (m, 2H), 2.12 (br s, 1H), 1.92 – 1.73 (m, 2H), 1.61 – 1.46 (m, 1H), 1.41 (br s, 2H), 0.85 – 0.69 (m, 2H), 0.36 (br s, 2H)	2.32, C
381	 使用3'/8-5製備	(2S,3R,1'S)-1'-(環丙基甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-[5-[5-(羥基甲基)-4,5-二氫-1,2-噁唑-3-基]-2-甲氧基苯甲醯胺基]雙環[2.2.1]庚烷-2-甲醯胺	602.1	(500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.92 (br d, J = 7.3 Hz, 1H), 8.23 (s, 1H), 8.24 (d, J = 6.5 Hz, 1H), 1.80 (br d, J = 6.4 Hz, 2H), 1.50 (t, J = 9.8 Hz, 1H), 1.34 – 1.21 (m, 1H), 4.70 (br d, J = 9.5 Hz, 2H), 4.46 (br s, 1H), 4.05 (s, 3H), 3.51 (br s, 1H), 3.35 – 3.14 (m, 1H), 3.11 (br s, 1H), 2.13 (br s, 1H), 1.93 – 1.74 (m, 3H), 1.51 (br s, 1H), 1.42 (br s, 2H), 1.17 (br t, J = 7.5 Hz, 2H), 0.88 – 0.67 (m, 2H), 0.36 (br s, 2H)	2.38, C

382	 由3'S-4製備	(2S,3R,7Z) 7-(環丙基甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-[5-[5-(羥基甲基)-4,5-二氫-1,2-噁唑-3-基]-2-甲氧基苯甲醯胺基]雙環[2.2.1]庚烷-2-甲醯胺	602.1	(500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.91 (br d, J=7.3 Hz, 1H), 8.23 (br s, 2H), 7.89 – 7.75 (m, 2H), 7.49 (br t, J=9.9 Hz, 1H), 7.34 – 7.19 (m, 1H), 4.70 (br d, J=9.5 Hz, 2H), 4.46 (br s, 1H), 4.05 (s, 3H), 3.51 (br s, 1H), 3.33 – 3.14 (m, 2H), 3.11 (br s, 1H), 2.73 (br s, 1H), 1.91 – 1.72 (m, 3H), 1.51 (br s, 1H), 1.42 (br s, 2H), 1.17 (s, 1H), 0.88 – 0.68 (m, 2H), 0.36 (br s, 2H)	2.37, C
383	 由3'S-3製備	(2S,3R,7Z) N-[4-氟-3-(三氟甲基)苯基]-3-[5-[5-(羥基甲基)-4,5-二氫-1,2-噁唑-3-基]-2-甲氧基苯甲醯胺基]-7-亞戊基雙環[2.2.1]庚烷-2-甲醯胺	618.1	(500 MHz, DMSO-d6) δ 10.57 (s, 1H), 9.91 (dd, J=6.8, 3.7 Hz, 1H), 8.26 – 8.20 (m, 2H), 7.79 (br d, J=8.6 Hz, 2H), 7.49 (t, J=9.8 Hz, 1H), 7.27 (d, J=8.8 Hz, 1H), 5.23 (t, J=7.4 Hz, 1H), 4.71 – 4.66 (m, 1H), 4.39 (br s, 1H), 4.04 (s, 3H), 3.66 – 3.45 (m, 2H), 3.18 (br dd, J=16.5, 8.1 Hz, 2H), 2.97 (br s, 1H), 2.73 (br s, 1H), 2.14 – 2.01 (m, 2H), 1.93 – 1.80 (m, 1H), 1.80 – 1.61 (m, 1H), 1.44 – 1.29 (m, 6H), 0.99 – 0.83 (m, 3H)	2.62, B

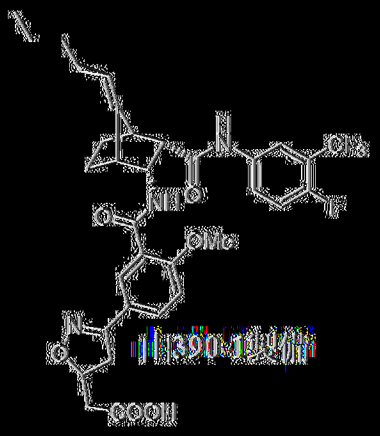
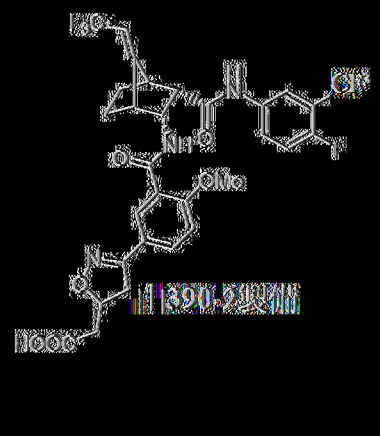
386	 使用384.3製備	3-(3-{[(2R,3S,7Z)-7-(環丙基甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-4,5-二氫-1,2-噁唑-5-甲酸三級丁酯	672.1	(500 MHz, DMSO-d6) δ 10.32 (s, 1H), 9.68 (d, J = 7.1 Hz, 1H), 8.01 – 7.95 (m, 2H), 7.62 – 7.52 (m, 2H), 7.24 (br t, J = 9.8 Hz, 1H), 7.04 (d, J = 8.8 Hz, 1H), 4.85 (dd, J = 11.7, 6.7 Hz, 1H), 4.44 (d, J = 9.6 Hz, 1H), 4.19 (br s, 1H), 3.80 (s, 3H), 3.49 (br dd, J = 17.2, 12.1 Hz, 1H), 3.35 – 3.23 (m, 3H), 2.97 – 2.88 (m, 1H), 2.86 (br s, 1H), 2.30 (s, 3H), 1.62 – 1.47 (m, 2H), 1.26 – 1.12 (m, 9H), 0.57 – 0.42 (m, 2H), 0.10 (br s, 2H)	2.71, B
387	 使用384.3製備	3-(3-{[(2R,3S,7Z)-7-(環丁基甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-4,5-二氫-1,2-噁唑-5-甲酸	630.3	(500 MHz, DMSO-d6) δ 10.75 – 10.65 (m, 1H), 9.95 – 9.89 (m, 1H), 8.31 – 8.21 (m, 2H), 7.88 – 7.73 (m, 2H), 7.54 – 7.44 (m, 1H), 7.31 – 7.26 (m, 1H), 5.42 – 5.34 (m, 1H), 4.90 – 4.76 (m, 1H), 4.44 – 4.32 (m, 1H), 4.07 (s, 3H), 3.23 – 3.06 (m, 2H), 3.01 – 2.93 (m, 1H), 2.78 – 2.67 (m, 1H), 2.23 – 2.11 (m, 2H), 2.25 – 2.08 (m, 3H), 1.96 – 1.66 (m, 5H), 1.44 – 1.30 (m, 2H)	2.09, B

388		3-(3-{[(2R,3S,7Z)-7-(環丁基甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-4,5-二氫-1,2-㗁唑-5-甲酸	630.1	(500 MHz, DMSO-d6) δ 10.56 (s, 1H), 9.91 (br s, 1H), 8.26 (br s, 1H), 7.82 (br s, 2H), 7.51 – 7.44 (m, 1H), 7.31 (s, 1H), 5.40 (br d, J= 8.5 Hz, 1H), 5.22 – 5.06 (m, 1H), 4.43 – 4.33 (m, 1H), 4.06 (s, 3H), 3.92 (s, 1H), 3.60 – 3.37 (m, 3H), 3.19 (br s, 2H), 2.73 (br s, 1H), 2.09 (s, 2H), 1.86 (br dd, J= 17.4, 7.6 Hz, 5H), 1.39 (br s, 2H)	2.12, C
389		3-(3-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-4,5-二氫-1,2-㗁唑-5-甲酸	644.1	(500 MHz, DMSO-d6) δ 10.70 (s, 1H), 9.97 (br d, J= 6.7 Hz, 1H), 8.24 (s, 1H), 8.23 (d, J= 5.8 Hz, 1H), 7.88 – 7.71 (m, 2H), 7.51 (t, J= 9.6 Hz, 1H), 7.29 (d, J= 8.9 Hz, 1H), 5.94 (q, J= 7.6 Hz, 1H), 5.13 (br dd, J= 11.3, 6.7 Hz, 1H), 4.52 (br s, 1H), 4.06 (s, 3H), 3.72 (br dd, J= 16.8, 11.9 Hz, 1H), 3.32 – 3.13 (m, 1H), 3.00 (s, 1H), 2.02 – 1.82 (m, 2H), 1.50 (br d, J= 5.5 Hz, 2H)	2.21, C

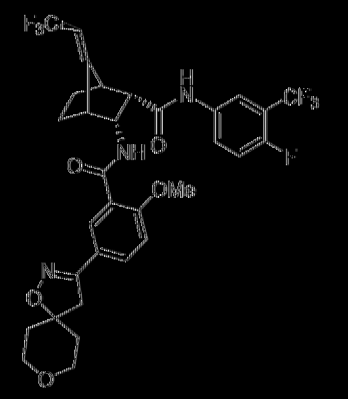
391	 由390.2製備	2-[3-(3-{[(2R,3S,7Z)-7-(環丙基甲基)-3-[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-4,5-二氫-1,2-噁唑-5-基]乙酸	630.3	(500 MHz, DMSO-d6) δ 10.56 (s, 1H), 9.93 (br d, J = 7.0 Hz, 1H), 8.24 (br s, 2H), 7.87 – 7.76 (m, 2H), 7.51 (br t, J = 9.6 Hz, 1H), 7.30 (br d, J = 8.9 Hz, 1H), 5.04 – 4.89 (m, 1H), 4.72 (br d, J = 9.8 Hz, 1H), 4.47 (br s, 1H), 4.07 (s, 3H), 3.19 (br d, J = 9.2 Hz, 2H), 3.13 (br s, 1H), 2.75 (br s, 1H), 2.71 – 2.61 (m, 2H), 2.58 – 2.55 (m, 2H), 1.94 – 1.73 (m, 2H), 1.52 (br s, 1H), 1.43 (br s, 2H), 0.84 – 0.66 (m, 2H), 0.38 (br s, 2H)	2.39, C

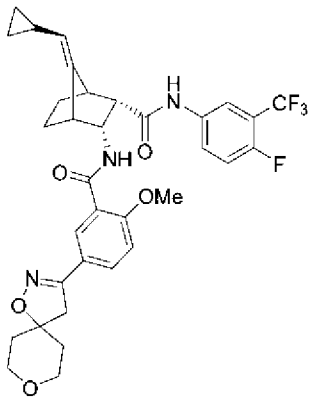
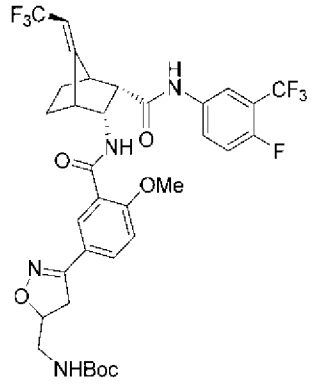
392	 使用390-1製備	2-[3-(3-{[(2R,3S,7Z)-7-(環丙基甲基)-3-[4-氟-3-(三氟甲基)苯基]胺甲醯基]雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-4,5-二氫-1,2-噁唑-5-基]乙酸	630.3	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.92 (br d, *J*= 7.0 Hz, 1H), 8.21 - 8.19 (m, 2H), 7.80 (br d, *J*= 9.2 Hz, 2H), 7.49 (t, *J*= 9.6 Hz, 1H), 7.28 (d, *J*= 8.9 Hz, 1H), 5.06 - 4.89 (m, 1H), 4.70 (d, *J*= 9.8 Hz, 1H), 4.46 (br s, 1H), 4.05 (s, 3H), 3.55 (br dd, *J*= 16.9, 10.5 Hz, 1H), 3.21 - 3.06 (m, 2H), 2.73 (br s, 1H), 2.68 - 2.59 (m, 2H), 2.49 - 2.28 (m, 1H), 1.92 - 1.72 (m, 2H), 1.63 - 1.46 (m, 1H), 1.46 - 1.35 (m, 2H), 0.87 - 0.68 (m, 2H), 0.36 (br s, 2H)	2.37, C
393	 使用390-1製備	2-[3-(3-{[(2R,3S,7Z)-7-(環丁基甲基)-3-[4-氟-3-(三氟甲基)苯基]胺甲醯基]雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-4,5-二氫-1,2-噁唑-5-基]乙酸	644.2	(500 MHz, DMSO-d6) δ 10.58 (s, 1H), 9.89 (d, *J*= 6.7 Hz, 1H), 8.24 - 8.18 (m, 2H), 7.78 (br d, *J*= 8.4 Hz, 2H), 7.48 (t, *J*= 9.7 Hz, 1H), 7.26 (d, *J*= 8.8 Hz, 1H), 5.36 (d, *J*= 8.3 Hz, 1H), 5.08 - 4.91 (m, 1H), 4.35 (br s, 1H), 4.03 (s, 3H), 3.58 (br s, 1H), 3.21 - 3.04 (m, 3H), 2.96 (br s, 1H), 2.70 (br s, 1H), 2.56 (s, 2H), 2.22 - 2.05 (m, 2H), 1.91 - 1.70 (m, 6H), 1.42 - 1.22 (m, 2H)	2.50, C

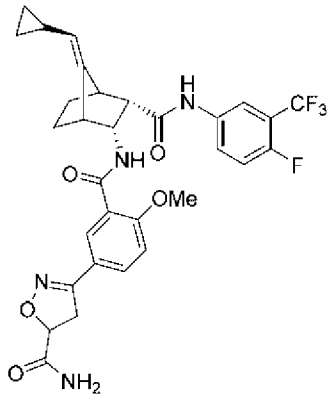
394	 [[390-3製備	2-[3-(3-{[(2R,3S,4Z)-1-(環丁基甲基)-3-[(4-氟-3-(三氟甲基)苯基)胺甲醯基]雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-4,5-二氫-1,2-噁唑-5-基]乙酸	644.3	(500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.88 (br d, *J* = 7.0 Hz, 1H), 8.25 – 8.19 (m, 2H), 7.79 (br d, *J* = 8.9 Hz, 2H), 7.49 (t, *J* = 9.9 Hz, 1H), 7.27 (d, *J* = 8.9 Hz, 1H), 5.38 (d, *J* = 8.5 Hz, 1H), 5.09 – 4.93 (m, 1H), 4.36 (br s, 1H), 4.04 (s, 3H), 3.55 (br dd, *J* = 17.1, 10.4 Hz, 1H), 3.24 – 3.04 (m, 2H), 2.97 (br s, 1H), 2.77 – 2.57 (m, 3H), 2.55 (bs, 2H), 2.16 (br d, *J* = 19.8 Hz, 2H), 1.92 – 1.71 (m, 4H), 1.48 – 1.27 (m, 2H)	2.55, C

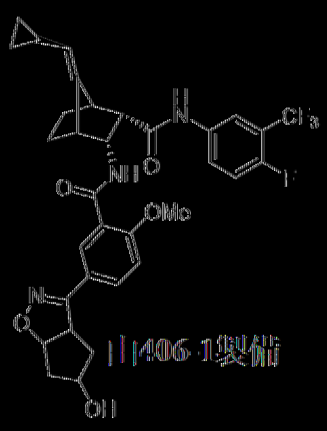
395		2-[3-({[(2R,3S,4Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-4-亞甲基雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-4,5-二氟-1,2-噁唑-5-基]乙酸	646.3	(500 MHz, DMSO-d6) δ 10.60 (s, 1H), 9.91 (br d, *J* = 7.1 Hz, 1H), 8.28 – 8.20 (m, 2H), 7.84 – 7.77 (m, 2H), 7.50 (t, *J* = 9.8 Hz, 1H), 7.27 (d, *J* = 8.8 Hz, 1H), 5.23 (t, *J* = 7.4 Hz, 1H), 5.08 – 4.90 (m, 1H), 4.46 – 4.35 (m, 1H), 4.05 (s, 3H), 3.54 (br dd, *J* = 16.6, 9.6 Hz, 1H), 3.23 – 3.11 (m, 2H), 2.98 (br s, 1H), 2.73 (br s, 1H), 2.61 (br d, *J* = 5.6 Hz, 2H), 2.13 – 2.01 (m, 3H), 1.92 – 1.80 (m, 1H), 1.80 – 1.64 (m, 1H), 1.43 – 1.24 (m, 6H), 0.91 (t, *J* = 7.0 Hz, 3H)	2.30, B
396		2-[3-({[(2R,3S,4Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-4-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-4,5-二氟-1,2-噁唑-5-基]乙酸	658.2	(500 MHz, DMSO-d6) δ 10.81 (br s, 1H), 10.10 (br s, 1H), 8.35 (br d, *J* = 12.8 Hz, 1H), 7.95 (br s, 1H), 7.65 (br d, *J* = 8.5 Hz, 1H), 7.53 – 7.37 (m, 1H), 6.07 (br d, *J* = 6.1 Hz, 1H), 5.11 (br s, 1H), 4.66 (br s, 2H), 4.18 (br s, 3H), 3.81 (br s, 1H), 3.38 (br s, 1H), 3.31 (br s, 1H), 3.13 (br s, 1H), 2.78 (br s, 2H), 2.09 (br s, 1H), 2.01 (br s, 1H), 1.64 (br s, 2H)	2.21, C

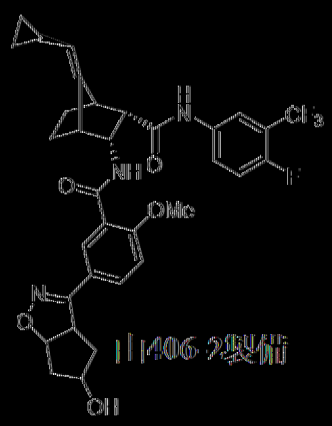
398	 中間體1製備	(2S,3R,7Z)-7-(環丙基甲基)-N-(4-氟-3-(三氟甲基)苯基)-3-羥基-15-(2-羥基乙基)-4,5-二氧-1,2-噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	616.3	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.91 (d, J = 7.0 Hz, 1H), 8.22 (s, 2H), 7.80 (br dd, J = 8.5, 2.1 Hz, 2H), 7.49 (t, J = 9.6 Hz, 1H), 7.28 (d, J = 8.9 Hz, 1H), 4.80 – 4.67 (m, 2H), 4.63 (t, J = 5.0 Hz, 1H), 4.46 (br s, 1H), 4.05 (s, 3H), 3.64 – 3.48 (m, 1H), 3.42 (br s, 1H), 3.20 – 3.01 (m, 3H), 2.91 (s, 1H), 2.79 – 2.68 (m, 2H), 2.58 – 2.54 (m, 2H), 1.89 – 1.69 (m, 4H), 1.60 – 1.46 (m, 1H), 1.42 (br s, 2H), 0.75 (br dd, J = 11.6, 8.5 Hz, 2H), 0.36 (br s, 2H)	2.35, C
399	 中間體2製備	(2S,3R,7Z)-7-(環丙基甲基)-N-(4-氟-3-(三氟甲基)苯基)-3-羥基-15-(2-羥基乙基)-4,5-二氧-1,2-噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	616.2	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.91 (br d, J = 7.0 Hz, 1H), 8.25 – 8.19 (m, 2H), 7.79 (br dd, J = 8.7, 2.0 Hz, 2H), 7.49 (t, J = 9.9 Hz, 1H), 7.28 (d, J = 8.9 Hz, 1H), 4.80 – 4.68 (m, 2H), 4.45 (br s, 1H), 4.05 (s, 3H), 3.55 (br t, J = 6.1 Hz, 1H), 3.21 – 3.01 (m, 3H), 2.73 (br s, 1H), 2.56 (s, 1H), 1.92 – 1.70 (m, 5H), 1.51 (br d, J = 4.3 Hz, 1H), 1.42 (br s, 2H), 0.86 – 0.69 (m, 2H), 0.36 (br s, 2H)	2.33, C

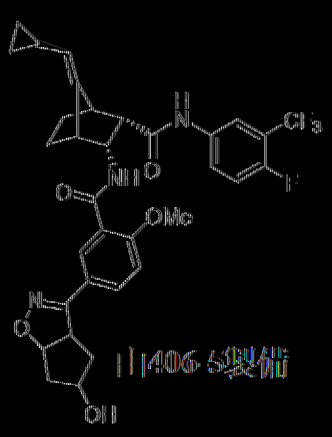
400	 同390-3製備	(2S,3R,7Z)-7-(環丁基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-[5-[5-(2-羥基乙基)-4,5-二氫-1,2-噁唑-3-基]-2-甲氧基苯甲醯胺基]雙環[2.2.1]庚烷-2-甲醯胺	630.3	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.88 (d, J= 7.2 Hz, 1H), 8.24 – 8.19 (m, 2H), 7.78 (br d, J= 8.4 Hz, 2H), 7.48 (br t, J= 9.9 Hz, 1H), 7.26 (d, J= 8.8 Hz, 1H), 5.37 (d, J= 8.4 Hz, 1H), 4.79 – 4.72 (m, 1H), 4.35 (br s, 1H), 4.03 (s, 3H), 3.53 (br s, 5H), 3.18 – 3.05 (m, 3H), 2.95 (br s, 1H), 2.70 (br s, 1H), 2.20 – 2.07 (m, 2H), 1.92 – 1.79 (m, 4H), 1.79 – 1.69 (m, 3H), 1.41 – 1.30 (m, 2H)	2.52, C
401		(2S,3R,7Z)-3-(5-{1,8-二氧雜-2-氮雜螺[4.5]癸-2-烯-3-基}-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-甲醯胺	670.1	(500 MHz, DMSO-d6) δ 9.96 (br d, J= 6.7 Hz, 1H), 8.28 – 8.19 (m, 2H), 7.82 (br dd, J= 8.5, 2.4 Hz, 2H), 7.52 (br t, J= 9.6 Hz, 1H), 7.29 (d, J= 8.5 Hz, 1H), 5.95 (q, J= 8.1 Hz, 1H), 4.53 (br s, 1H), 4.05 (s, 3H), 3.85 – 3.70 (m, 1H), 3.61 (br d, J= 6.1 Hz, 1H), 3.47 (br s, 1H), 3.32 – 3.18 (m, 2H), 3.01 (br s, 1H), 2.03 – 1.92 (m, 1H), 1.92 – 1.82 (m, 1H), 1.77 (br s, 5H), 1.51 (br d, J= 6.1 Hz, 3H)	2.48, C

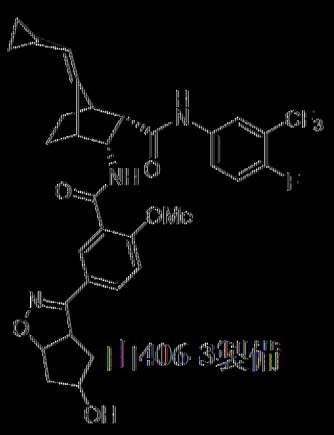
402		(2S,3R,7Z)-7-(環丙基亞甲基)-3-(5-{1,8-二氧雜-2-氮雜螺[4.5]癸-2-烯-3-基}-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	642.2	(500 MHz, DMSO-d_6) δ 10.55 (s, 1H), 9.90 (br d, *J*=7.0 Hz, 1H), 8.22 (br d, *J*=2.1 Hz, 2H), 7.80 (br dd, *J*=8.5, 2.1 Hz, 2H), 7.49 (t, *J*=9.9 Hz, 1H), 7.28 (d, *J*=8.9 Hz, 1H), 4.70 (d, *J*=9.5 Hz, 1H), 4.45 (br s, 1H), 4.05 (s, 3H), 3.91 - 3.71 (m, 2H), 3.60 (br d, *J*=4.9 Hz, 1H), 3.46 (br s, 1H), 3.25 (s, 1H), 3.17 (br dd, *J*=10.5, 4.1 Hz, 1H), 2.73 (br s, 1H), 2.56 (bs, 2H), 2.01 - 1.80 (m, 2H), 1.77 (br s, 4H), 1.51 (br d, *J*=4.9 Hz, 1H), 1.42 (br s, 2H), 0.88 - 0.67 (m, 2H), 0.36 (br s, 2H)	2.44, C
403		N-{[3-(3-{[(2R,3S,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-4,5-二氫-1,2-噁唑-5-基]甲基}胺基甲酸三級丁酯	729.3	(500 MHz, DMSO-d6) δ 10.69 (s, 1H), 9.97 (br d, *J*=6.7 Hz, 1H), 8.32 - 8.13 (m, 2H), 7.81 (br d, *J*=5.8 Hz, 2H), 7.51 (t, *J*=9.6 Hz, 1H), 7.29 (d, *J*=8.9 Hz, 1H), 7.05 (br s, 1H), 5.95 (q, *J*=7.8 Hz, 1H), 4.86 - 4.66 (m, 1H), 4.53 (br s, 1H), 4.05 (s, 3H), 3.48 - 3.36 (m, 1H), 3.33 - 3.12 (m, 3H), 2.02 - 1.80 (m, 2H), 1.50 (br d, *J*=6.7 Hz, 2H), 1.36 (s, 9H)	2.72, C

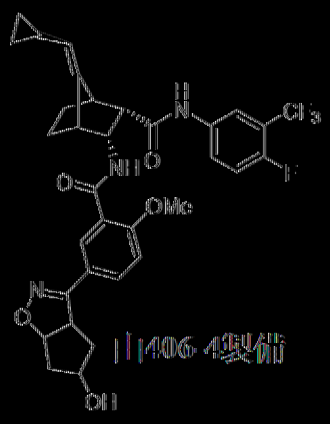
404		3-(3-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-4,5-二氫-1,2-噁唑-5-甲醯胺	615.2	(500 MHz, DMSO-d6) δ 10.58 (s, 1H), 9.93 (br d, *J*=7.0 Hz, 1H), 8.36 - 8.18 (m, 2H), 7.81 (br d, *J*=8.5 Hz, 2H), 7.66 (br s, 1H), 7.47 (br t, *J*=9.8 Hz, 1H), 7.40 (br s, 1H), 7.28 (d, *J*=8.5 Hz, 1H), 5.04 (dd, *J*=11.6, 6.4 Hz, 1H), 4.69 (d, *J*=9.5 Hz, 1H), 4.43 (br s, 1H), 4.04 (s, 3H), 3.51 (br d, *J*=7.0 Hz, 1H), 3.25 - 3.07 (m, 2H), 2.72 (br s, 1H), 2.05 (s, 1H), 1.93 - 1.72 (m, 2H), 1.69 (br s, 1H), 1.50 (br s, 1H), 1.41 (br s, 2H), 0.80 - 0.66 (m, 2H), 0.35 (br d, *J*=4.6 Hz, 2H)	2.24, B

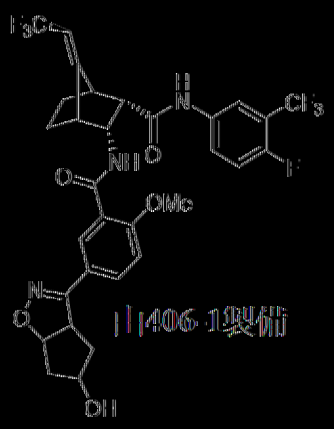
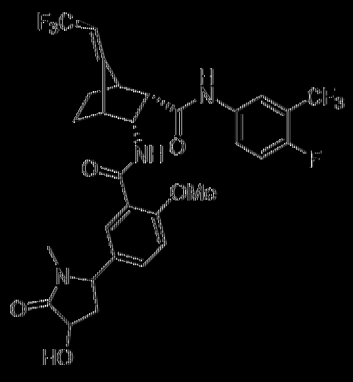
407		(2S,3R,7Z) 7 (環丙基亞甲基) N [4 氟 3 (三氟甲基) 苯基] 3 {5 [(5R) 5 羰基 3a,4,5,6,6a 六氫環戊并[d][1,2]噁唑 3 基] 2 甲氧基苯甲醯胺基}雙環[2.2.1]庚烷 2 甲醯胺	628.3	(500 MHz, DMSO d6) δ 10.56 (s, 1H), 9.92 (br d, J= 6.7 Hz, 1H), 8.25 (s, 1H), 8.25 (d, J= 5.2 Hz, 1H), 7.86 – 7.74 (m, 2H), 7.50 (t, J= 9.6 Hz, 1H), 7.28 (d, J= 8.5 Hz, 1H), 5.12 (br t, J= 7.2 Hz, 1H), 4.71 (d, J= 9.5 Hz, 1H), 4.46 (br d, J= 3.1 Hz, 2H), 4.18 – 4.02 (m, 4H), 3.29 – 3.14 (m, 1H), 3.12 (br s, 1H), 2.74 (br s, 1H), 2.18 – 2.02 (m, 2H), 1.94 – 1.72 (m, 4H), 1.52 (br d, J= 9.5 Hz, 1H), 1.43 (br s, 2H), 0.90 – 0.69 (m, 2H), 0.37 (br s, 2H)	2.34, C

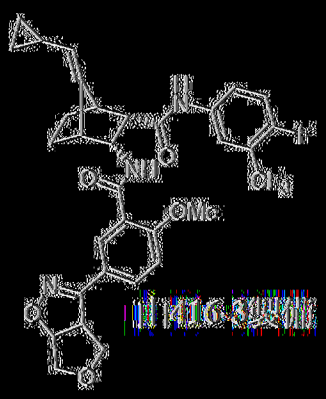
408		(2S,3R,7Z)-7-(環丙基甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-(5-{5-羥基-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	628.2	(500 MHz, DMSO-d6) δ 10.56 (s, 1H), 9.92 (d, J=7.0 Hz, 1H), 8.27 – 8.21 (m, 2H), 7.84 – 7.77 (m, 2H), 7.49 (t, J=9.8 Hz, 1H), 7.28 (d, J=8.5 Hz, 1H), 5.23 – 5.07 (m, 1H), 4.70 (d, J=9.8 Hz, 1H), 4.45 (br s, 1H), 4.22 (td, J=9.4, 4.1 Hz, 1H), 4.12 – 4.02 (m, 3H), 3.17 (br dd, J=10.5, 3.8 Hz, 1H), 3.11 (br s, 1H), 2.73 (br s, 1H), 2.01 – 1.97 (m, 1H), 1.96 – 1.89 (m, 2H), 1.87 – 1.77 (m, 3H), 1.64 – 1.46 (m, 1H), 1.42 (br s, 2H), 0.87 – 0.69 (m, 2H), 0.37 (br s, 2H)	2.23, C

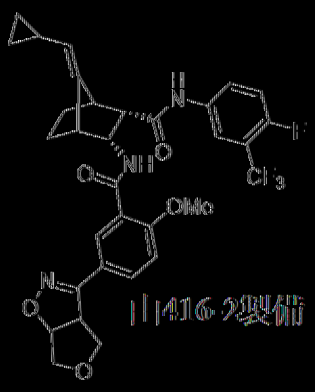
409		(2S,3R,7Z)-7-(環丙基甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-(5-{5-羥基-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	628.2	(500 MHz, DMSO-d6) δ 10.56 (s, 1H), 9.92 (br d, J = 6.7 Hz, 1H), 8.25 (s, 1H), 8.25 (d, J = 5.2 Hz, 1H), 7.86 – 7.74 (m, 2H), 7.50 (t, J = 9.6 Hz, 1H), 7.28 (d, J = 8.5 Hz, 1H), 5.12 (br t, J = 7.2 Hz, 1H), 4.71 (d, J = 9.5 Hz, 1H), 4.46 (br d, J = 3.1 Hz, 2H), 4.18 – 4.02 (m, 4H), 3.29 – 3.14 (m, 1H), 3.12 (br s, 1H), 2.74 (br s, 1H), 2.18 – 2.02 (m, 2H), 1.94 – 1.72 (m, 4H), 1.52 (br d, J = 9.5 Hz, 1H), 1.43 (br s, 2H), 0.90 – 0.69 (m, 2H), 0.37 (br s, 2H)	2.38, B

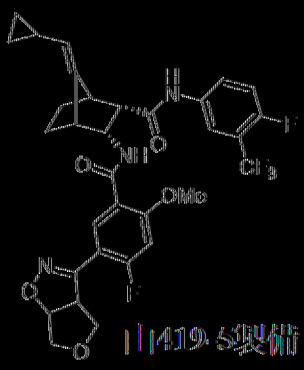
410	 由406.3製備	(2S,3R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-(5-{5-羥基-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	628.1	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.93 (d, J=7.0 Hz, 1H), 8.28 – 8.20 (m, 2H), 7.84 – 7.77 (m, 2H), 7.50 (t, J=9.8 Hz, 1H), 7.29 (d, J=8.5 Hz, 1H), 5.25 – 5.07 (m, 1H), 4.89 (d, J=4.0 Hz, 1H), 4.71 (d, J=9.5 Hz, 1H), 4.46 (br s, 1H), 4.35 – 4.17 (m, 1H), 4.11 (br d, J=5.2 Hz, 1H), 4.06 (s, 3H), 3.23 – 3.04 (m, 2H), 2.74 (br s, 1H), 2.01 – 1.78 (m, 5H), 1.53 (br d, J=4.6 Hz, 1H), 1.43 (br s, 2H), 0.90 – 0.69 (m, 2H), 0.37 (br s, 2H)	2.40, B

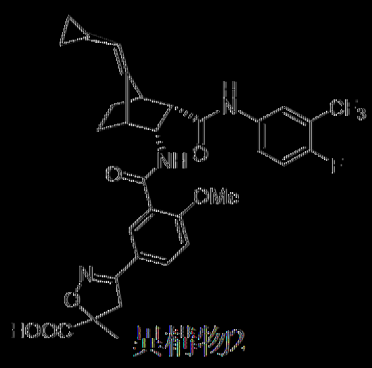
411	 同406-4製備	(2S,3R,7Z)-7-(環丙基甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-(5-{5-羥基-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	628.2	(500 MHz, DMSO-d6) δ 9.94 (br d, J=7.0 Hz, 1H), 8.24 (br d, J=2.1 Hz, 2H), 7.79 (br t, J=7.0 Hz, 2H), 7.49 (t, J=9.6 Hz, 1H), 7.27 (d, J=8.8 Hz, 1H), 5.11 (br t, J=7.4 Hz, 1H), 4.69 (d, J=9.6 Hz, 1H), 4.44 (br s, 1H), 4.03 (s, 3H), 3.57 - 3.47 (m, 2H), 3.29 - 3.13 (m, 1H), 3.11 (br s, 1H), 3.00 (s, 1H), 2.73 (br s, 1H), 2.09 (br dd, J=13.6, 5.5 Hz, 2H), 1.92 - 1.71 (m, 4H), 1.51 (br dd, J=8.8, 3.4 Hz, 1H), 1.42 (br s, 2H), 0.87 - 0.67 (m, 2H), 0.36 (br s, 2H)	2.32, C

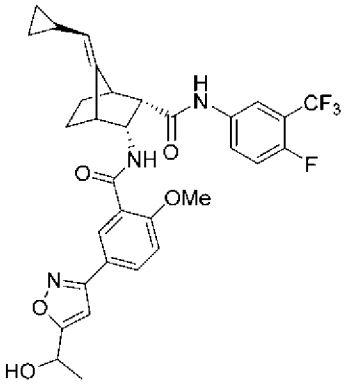
412		(2S,3R,7Z) 3-[5-[(3aS,5S,6aS)-5-羥基-3a(1H),4(1),5(1),6(1),6a(1H)-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基]-N-[4-氟-3-(三氟甲基)苯基]-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-甲醯胺	656.0	(500 MHz, DMSO-d6) δ 10.69 (s, 1H), 9.98 (br d, J= 6.3 Hz, 1H), 8.26 - 8.20 (m, 1H), 7.84 - 7.71 (m, 2H), 7.51 (t, J= 9.6 Hz, 1H), 7.28 (d, J= 8.8 Hz, 1H), 5.95 (q, J= 8.0 Hz, 1H), 5.20 - 5.09 (m, 1H), 4.95 (s, 1H), 4.52 (br s, 1H), 4.21 (dt, J= 9.2, 4.8 Hz, 1H), 4.03 (m, 3H), 3.47 (br s, 2H), 3.45 - 3.39 (m, 1H), 3.31 - 3.22 (m, 1H), 3.00 (br s, 1H), 2.02 - 1.85 (m, 2H), 1.79 (br d, J= 12.0 Hz, 1H), 1.50 (br d, J= 6.1 Hz, 2H)	2.29, C
415		(2S,3R,7Z) N-[4-氟-3-(三氟甲基)苯基]-3-[5-(4-羥基-1-甲基-5-側氧基吡咯啶-2-基)-2-甲氧基苯甲醯胺基]-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-甲醯胺	644.0	(500 MHz, DMSO-d6) δ 10.66 (s, 1H), 9.94 (t, J= 6.1 Hz, 1H), 8.32 - 8.11 (m, 1H), 7.89 (t, J= 2.6 Hz, 1H), 7.84 - 7.67 (m, 1H), 7.50 (t, J= 9.2 Hz, 1H), 7.45 (d, J= 8.3 Hz, 1H), 7.23 (d, J= 9.0 Hz, 1H), 5.93 (q, J= 7.5 Hz, 1H), 4.52 (br s, 1H), 4.41 (t, J= 7.5 Hz, 1H), 4.20 (t, J= 8.4 Hz, 1H), 4.06 (s, 3H), 3.32 - 3.13 (m, 1H), 2.99 (br s, 1H), 2.81 - 2.63 (m, 1H), 2.50 - 2.36 (m, 2H), 1.99 (br t, J= 9.3 Hz, 1H), 1.94 - 1.74 (m, 1H), 1.60 - 1.42 (m, 2H)	2.21, B

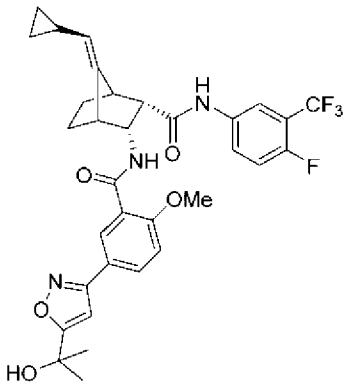
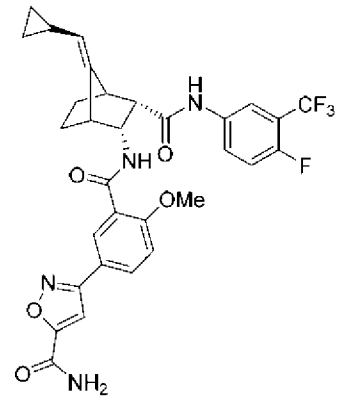
417		(2S,3R,7Z) 3 (5 {3aH,4H,6H,6aH 吡喃并[3,4 d][1,2]噁唑 3 基} 2 甲氧基苯甲醯胺基) 7 (環丙基亞甲基) N [4 氟 3 (三氟甲基)苯基]雙環[2.2.1]庚烷 2 甲醯胺	614.2	(500 MHz, DMSO d6) δ 10.70 10.42 (m, 1H), 9.93 (br d, J 7.3 Hz, 1H), 8.30 8.11 (m, 2H), 7.92 7.72 (m, 2H), 7.47 (br t, J 9.5 Hz, 1H), 7.28 (d, J 8.9 Hz, 1H), 5.35 (br dd, J 9.0, 3.2 Hz, 1H), 4.70 (br d, J 9.8 Hz, 1H), 4.48 (br t, J 7.9 Hz, 1H), 4.45 4.36 (m, 1H), 4.10 (br d, J 11.0 Hz, 1H), 4.04 (s, 3H), 3.89 (s, 1H), 3.71 (m, 3H), 3.24 3.06 (m, 2H), 2.72 (br d, J 3.7 Hz, 1H), 1.87 1.81 (m, 1H), 1.80 1.70 (m, 1H), 1.57 1.47 (m, 1H), 1.43 1.30 (m, 1H), 0.85 0.65 (m, 2H), 0.35 (br d, J 4.3 Hz, 2H)	2.50, B

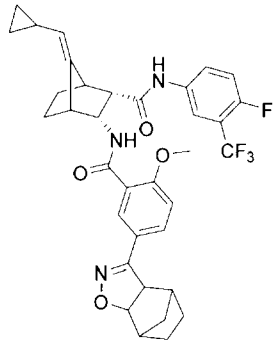
418	 以416-2製備	(2S,3R,7Z) 3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	614.3	(500 MHz, DMSO-d_6) δ 10.56 (s, 1H), 9.94 (br d, *J* = 7.0 Hz, 1H), 8.43 – 8.15 (m, 2H), 8.03 – 7.73 (m, 2H), 7.49 (br t, *J* = 9.8 Hz, 1H), 7.29 (d, *J* = 8.5 Hz, 1H), 5.36 (dd, *J* = 9.2, 3.4 Hz, 1H), 4.71 (br d, *J* = 9.8 Hz, 1H), 4.55 – 4.32 (m, 2H), 4.11 (br d, *J* = 11.0 Hz, 1H), 4.06 (s, 3H), 3.91 (br d, *J* = 9.5 Hz, 1H), 3.84 – 3.63 (m, 1H), 3.51 (br d, *J* = 3.1 Hz, 1H), 3.30 – 3.14 (m, 1H), 3.12 (br s, 1H), 2.73 (br s, 1H), 1.88 – 1.67 (m, 2H), 1.59 – 1.48 (m, 1H), 1.47 – 1.36 (m, 2H), 0.84 – 0.65 (m, 2H), 0.36 (br d, *J* = 2.1 Hz, 2H)	2.38, C

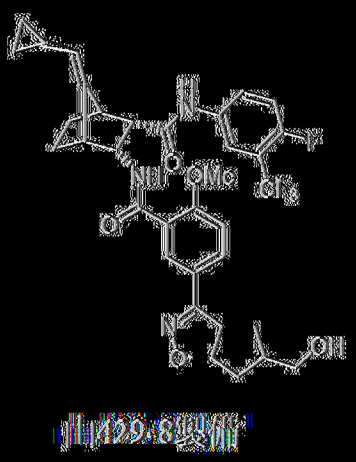
420	 由419.5製備	(2S,3R,4S)-3-(5-{3aH,4H,6H,6aH-吡喃并[3,4-d][1,2]㗁唑-3-基}-4-氟-2-甲氧基苯甲醯胺基)-4-(環丙基甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	632.3	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.88 (br d, J = 6.7 Hz, 1H), 8.35 (d, J = 8.9 Hz, 1H), 8.21 - 8.20 (m, 1H), 7.89 - 7.75 (m, 1H), 7.50 (br t, J = 9.8 Hz, 1H), 7.25 (d, J = 13.1 Hz, 1H), 5.35 (dd, J = 9.2, 3.4 Hz, 1H), 4.71 (d, J = 9.8 Hz, 1H), 4.53 - 4.39 (m, 2H), 4.12 (br d, J = 10.7 Hz, 1H), 4.07 (s, 3H), 3.91 (br d, J = 9.2 Hz, 1H), 3.75 (dd, J = 9.2, 7.0 Hz, 1H), 3.66 (dd, J = 10.7, 3.4 Hz, 1H), 3.23 - 3.14 (m, 1H), 3.11 (br s, 1H), 2.74 (br s, 1H), 1.91 - 1.81 (m, 1H), 1.80 - 1.72 (m, 1H), 1.51 (ddd, J = 12.8, 8.4, 4.4 Hz, 1H), 1.46 - 1.34 (m, 2H), 0.85 - 0.64 (m, 2H), 0.36 (br s, 2H)	2.55, B

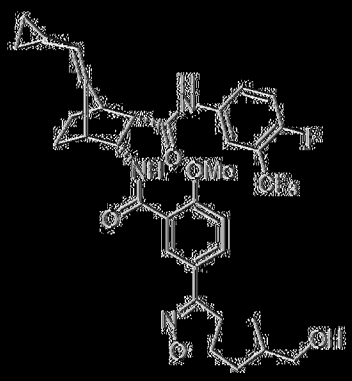
421	 異構物1	3-(3-{[(2R,3S,7Z)-7-(環丙基甲基)-3-[4-氟-3-(三氟甲基)苯基]胺甲醯基]雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-5-甲基-4,5-二氫-1,2-㗁唑-5-甲酸	630.2	(500 MHz, DMSO-d6) δ 10.61 - 10.56 (m, 1H), 9.95 - 9.87 (m, 1H), 8.26 - 8.20 (m, 2H), 7.86 - 7.74 (m, 3H), 7.54 - 7.44 (m, 2H), 7.32 - 7.23 (m, 1H), 4.73 - 4.69 (m, 1H), 4.50 - 4.41 (m, 1H), 4.05 (s, 3H), 3.80 - 3.70 (m, 2H), 3.21 - 3.09 (m, 2H), 3.03 - 3.02 (m, 1H), 2.71 - 2.70 (m, 1H), 1.87 - 1.71 (m, 2H), 1.51 (br s, 2H), 1.46 - 1.20 (m, 3H), 0.84 - 0.68 (m, 2H), 0.39 - 0.33 (m, 2H)	1.9, B
422	 異構物2	3-(3-{[(2R,3S,7Z)-7-(環丙基甲基)-3-[4-氟-3-(三氟甲基)苯基]胺甲醯基]雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-5-甲基-4,5-二氫-1,2-㗁唑-5-甲酸	630.2	(500 MHz, DMSO-d6) δ 10.61 - 10.56 (m, 1H), 9.95 - 9.87 (m, 1H), 8.26 - 8.20 (m, 2H), 7.86 - 7.74 (m, 3H), 7.54 - 7.44 (m, 2H), 7.32 - 7.23 (m, 1H), 4.73 - 4.69 (m, 1H), 4.50 - 4.41 (m, 1H), 4.05 (s, 3H), 3.80 - 3.70 (m, 2H), 3.21 - 3.09 (m, 2H), 3.03 - 3.02 (m, 1H), 2.71 - 2.70 (m, 1H), 1.87 - 1.71 (m, 3H), 1.51 (br s, 1H), 1.46 - 1.20 (m, 3H), 0.84 - 0.68 (m, 2H), 0.39 - 0.33 (m, 2H)	2.0, B

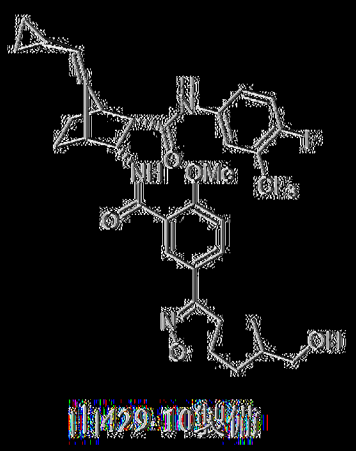
424		(2S,3R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(1-羥基乙基)-1,2-噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	614.1	(500 MHz, DMSO-d6) δ 10.57 (s, 1H), 9.94 (br d, *J*=7.0 Hz, 1H), 8.44 (d, *J*=2.1 Hz, 1H), 8.24 (br d, *J*=4.3 Hz, 1H), 8.00 (dd, *J*=8.5, 2.1 Hz, 1H), 7.81 (br d, *J*=8.5 Hz, 1H), 7.50 (br t, *J*=9.8 Hz, 1H), 7.34 (d, *J*=8.5 Hz, 1H), 6.86 (s, 1H), 5.05 - 4.84 (m, 1H), 4.71 (d, *J*=9.5 Hz, 1H), 4.48 (br s, 1H), 4.08 (s, 3H), 3.37 (br s, 1H), 3.27 - 3.15 (m, 1H), 3.13 (br s, 1H), 3.01 (s, 1H), 2.74 (br s, 1H), 1.97 - 1.75 (m, 2H), 1.57 - 1.37 (d, 3H), 1.25 (br s, 1H), 0.88 - 0.68 (m, 2H), 0.37 (br s, 2H)	2.6, B

425		(2S,3R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(2-羥基丙烷-2-基)-1,2-噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	628.3	(500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.93 (d, *J*=7.0 Hz, 1H), 8.42 (d, *J*=1.5 Hz, 1H), 8.22 (br d, *J*=4.3 Hz, 1H), 7.98 (dd, *J*=8.5, 1.7 Hz, 1H), 7.79 (br d, *J*=8.1 Hz, 1H), 7.48 (br t, *J*=9.7 Hz, 1H), 7.32 (d, *J*=8.6 Hz, 1H), 6.83 - 6.77 (m, 1H), 4.70 (d, *J*=9.5 Hz, 1H), 4.46 (br s, 1H), 4.06 (s, 3H), , 3.47 - 3.43 (m, 1H), 3.20 - 3.09 (m, 2H), 2.72 (br s, 1H), 1.92 - 1.74 (m, 2H), 1.51 (s, 6H), 1.42 (br s, 2H), 0.85 - 0.69 (m, 2H), 0.36 (br s, 2H)	2.66, B
426		3-(3-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-1,2-噁唑-5-甲醯胺	612.9	(500 MHz, DMSO-d6) δ 10.56 (s, 1H), 9.95 (br d, *J*=7.3 Hz, 1H), 8.48 - 8.39 (m, 2H), 8.19 (br d, *J*=4.3 Hz, 1H), 8.02 (br d, *J*=8.5 Hz, 1H), 8.00 (br d, *J*=7.9 Hz, 1H), 7.76 (br s, 1H), 7.57 - 7.42 (m, 2H), 7.35 (d, *J*=8.9 Hz, 1H), 4.69 (br d, *J*=9.5 Hz, 1H), 4.45 (br s, 1H), 4.06 (s, 3H), 3.22 - 3.05 (m, 2H), 2.72 (br s, 1H), 1.88 - 1.70 (m, 2H), 1.50 (br s, 2H), 1.42 (br s, 2H), 1.21 (br s, 1H), 0.86 - 0.65 (m, 2H), 0.35 (br d, *J*=4.3 Hz, 2H)	2.37, C

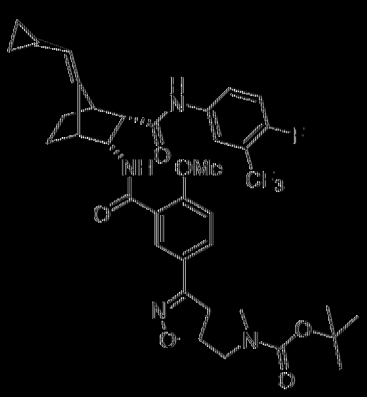
428		(1R,2S,3R,4R,Z)-7-(環丙基亞甲基)-*N*-(4-氟-3-(三氟甲基)苯基)-3-(5-(3a,4,5,6,7,7a-六氫-4,7-甲橋苯并[d]異噁唑-3-基)-2-甲氧基苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	638.2	(500 MHz, DMSO-d_6) δ 10.44 - 10.20 (m, 1H), 9.68 (br t, *J*=7.3 Hz, 1H), 8.34 - 7.88 (m, 2H), 7.80 - 7.45 (m, 2H), 7.26 (br t, *J*=9.8 Hz, 1H), 7.04 (d, *J*=8.9 Hz, 1H), 4.47 (br d, *J*=9.8 Hz, 1H), 4.35 (br d, *J*=8.2 Hz, 1H), 4.21 (br s, 1H), 3.82 (d, *J*=1.8 Hz, 3H), 3.43 (br dd, *J*=7.6, 4.6 Hz, 1H), 3.25 - 3.08 (m, 1H), 2.93 (br dd, *J*=11.0, 4.3 Hz, 1H), 2.88 (br s, 1H), 2.50 (br s, 1H), 2.13 (br d, *J*=8.5 Hz, 1H), 1.70 - 1.59 (m, 1H), 1.57 - 1.43 (m, 1H), 1.39 - 1.22 (m, 3H), 1.22 - 1.08 (m, 3H), 1.03 (br d, *J*=10.4 Hz, 1H), 0.90 (br d, *J*=10.1 Hz, 2H), 0.62 - 0.36 (m, 2H), 0.13 (br s, 2H)	2.84, B

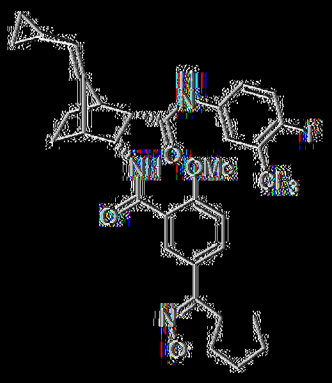
431		(2S,3R,7Z)-7-(環丙基甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-[5-[5-(羥基甲基)-3a,4,5,5a,6,6a-六氫環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基]雙環[2.2.1]庚烷-2-甲醯胺	642.2	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.91 (d, *J* = 7.2 Hz, 1H), 8.21 (d, *J* = 2.3 Hz, 1H), 8.19 (dd, *J* = 6.4, 2.4 Hz, 1H), 7.80 – 7.74 (m, 2H), 7.45 (t, *J* = 9.1 Hz, 1H), 7.26 (d, *J* = 8.8 Hz, 1H), 5.15 – 5.10 (m, 1H), 4.67 (d, *J* = 9.1 Hz, 1H), 4.45 – 4.39 (m, 1H), 4.07 (td, *J* = 9.6, 6.2 Hz, 1H), 4.02 (s, 3H), 3.28 (dt, *J* = 10.6, 5.3 Hz, 1H), 3.23 – 3.18 (m, 1H), 3.13 (br dd, *J* = 10.8, 4.1 Hz, 1H), 3.10 – 3.03 (m, 1H), 2.73 – 2.67 (m, 1H), 2.22 – 2.08 (m, 3H), 1.85 – 1.73 (m, 2H), 1.64 – 1.57 (m, 1H), 1.52 – 1.36 (m, 4H), 0.71 – 0.67 (m, 2H), 0.38 – 0.29 (m, 2H)	2.5, B

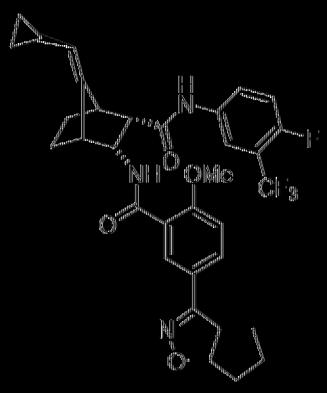
432		(2S,3R,7Z)-7-(環丙基甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-[5-[5-(羥基甲基)-3a,4,5,6,6a-五氫環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基]雙環[2.2.1]庚烷-2-甲醯胺	642.4	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.90 (br d, J=7.0 Hz, 1H), 8.24 - 8.21 (m, 1H), 8.21 - 8.17 (m, 1H), 7.80 - 7.75 (m, 2H), 7.46 (t, J=9.8 Hz, 1H), 7.26 (d, J=8.5 Hz, 1H), 5.15 - 5.10 (m, 1H), 4.68 (d, J=9.8 Hz, 1H), 4.42 (br t, J=10.1 Hz, 1H), 4.12 - 4.05 (m, 1H), 4.02 (s, 3H), 3.30 - 3.25 (m, 1H), 3.20 (dt, J=10.5, 5.4 Hz, 1H), 3.14 (br dd, J=11.0, 4.0 Hz, 1H), 3.11 - 3.03 (m, 1H), 2.73 - 2.66 (m, 1H), 2.22 - 2.09 (m, 3H), 1.84 - 1.73 (m, 2H), 1.65 - 1.58 (m, 1H), 1.51 - 1.36 (m, 4H), 0.71 - 0.68 (m, 2H), 0.37 - 0.30 (m, 2H)	2.41, B

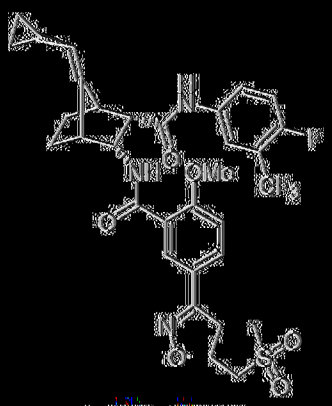
433		(2S,3R,7Z)-7-(環丙基甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-[5-[5-(羥基甲基)-3a,4,5,6,6a-五氫環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基]雙環[2.2.1]庚烷-2-甲醯胺	642.3	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.90 (d, J=7.2 Hz, 1H), 8.24 - 8.18 (m, 2H), 7.81 - 7.75 (m, 2H), 7.47 (t, J=9.1 Hz, 1H), 7.26 (d, J=8.8 Hz, 1H), 5.11 (dd, J=8.8, 5.1 Hz, 1H), 4.68 (d, J=9.5 Hz, 1H), 4.45 - 4.40 (m, 1H), 4.20 - 4.15 (m, 1H), 4.03 (s, 3H), 3.40 - 3.29 (m, 1H), 3.14 (dd, J=10.7, 4.1 Hz, 1H), 3.11 - 3.06 (m, 1H), 2.74 - 2.68 (m, 1H), 1.97 (br dd, J=13.6, 5.9 Hz, 1H), 1.93 - 1.71 (m, 5H), 1.68 - 1.60 (m, 1H), 1.57 - 1.46 (m, 2H), 1.45 - 1.37 (m, 2H), 0.78 - 0.68 (m, 2H), 0.38 - 0.30 (m, 2H)	2.42, B

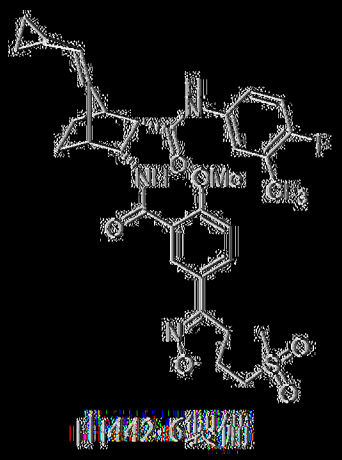
435	 中間體 434.4製備	3-(3-{[(2R,3S,7S)-7-(環丙基甲基)-3-[4-氟-3-(三氟甲基)苯基]胺甲醯基]雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-3aH,4H,5H,6H,6aH-吡咯并[3,4-d][1,2]噁唑-5-甲酸三級丁酯	713.1	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.91 (br d, J= 6.6 Hz, 1H), 8.22 - 8.18 (m, 2H), 7.80 - 7.75 (m, 2H), 7.46 (t, J= 9.8 Hz, 1H), 7.29 (d, J= 8.8 Hz, 1H), 5.25 (dd, J= 9.2, 4.8 Hz, 1H), 4.68 (d, J= 9.6 Hz, 1H), 4.46 - 4.39 (m, 2H), 4.04 (s, 3H), 3.80 - 3.70 (m, 1H), 3.18 - 3.12 (m, 1H), 3.11 - 3.07 (m, 1H), 2.74 - 2.69 (m, 1H), 1.86 - 1.74 (m, 2H), 1.50 (td, J= 8.7, 4.4 Hz, 1H), 1.43 - 1.22 (m, 12H), 0.77 - 0.68 (m, 2H), 0.37 - 0.31 (m, 2H)	2.8, C

436	 中間體436製備	3-(3-{[(2R,3S,7S)-7-(環丙基甲基)-3-[4-氟-3-(三氟甲基)苯基]胺甲醯基]雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-3a(1),4(1),5(1),6(1),6a(1)-吡咯并[3,4-d][1,2]噁唑-5-甲酸三級丁酯	713.1	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.91 (d, J = 7.1 Hz, 1H), 8.22 – 8.19 (m, 2H), 7.80 – 7.75 (m, 2H), 7.47 (t, J = 9.8 Hz, 1H), 7.29 (d, J = 8.9 Hz, 1H), 5.25 (dd, J = 9.2, 4.8 Hz, 1H), 4.68 (d, J = 9.6 Hz, 1H), 4.43 (br t, J = 10.3 Hz, 2H), 4.04 (s, 3H), 3.75 (br d, J = 12.8 Hz, 1H), 3.15 (dd, J = 10.6, 4.1 Hz, 1H), 3.10 – 3.08 (m, 1H), 2.71 (m, 1H), 1.84 – 1.74 (m, 2H), 1.49 (ddd, J = 12.9, 8.3, 4.4 Hz, 1H), 1.42 – 1.25 (m, 12H), 0.71 – 0.69 (m, 2H), 0.37 – 0.31 (m, 2H)	2.61, C

140	 [0389]製備	(2S,3R,7Z) 3 (5 {3aH,4H,5H,6H,6aH 環戊并[d][1,2]噁唑 3 基} 2 甲氧基苯甲醯胺基) 7 (環丙基甲基) N [4 氟 3 (三氟甲基)苯基]雙環[2.2.1]庚烷 2 甲醯胺	612.4	(500 MHz, DMSO d6) δ 10.52 (s, 1H), 9.88 (br d, J= 7.0 Hz, 1H), 8.22 – 8.18 (m, 2H), 7.80 – 7.75 (m, 2H), 7.46 (br t, J= 9.6 Hz, 1H), 7.25 (d, J= 8.5 Hz, 1H), 5.12 (br dd, J= 8.4, 4.7 Hz, 1H), 4.68 (d, J= 9.5 Hz, 1H), 4.45 – 4.39 (m, 1H), 4.14 (br t, J= 8.4 Hz, 1H), 4.02 (s, 3H), 3.14 (br dd, J= 10.8, 4.1 Hz, 1H), 3.11 – 3.06 (m, 1H), 2.73 – 2.68 (m, 1H), 1.94 (br dd, J= 13.3, 6.3 Hz, 1H), 1.88 – 1.81 (m, 2H), 1.78 – 1.72 (m, 2H), 1.67 (ddd, J= 19.4, 13.0, 6.1 Hz, 2H), 1.49 (dt, J= 8.4, 4.0 Hz, 1H), 1.43 – 1.34 (m, 2H), 1.32 – 1.24 (m, 1H), 0.71 – 0.69 (m, 2H), 0.37 – 0.30 (m, 2H)	2.72, B

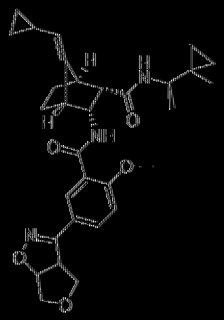
441	 中間体439.6製備	(2S,3R,4Z) 3-(5-{3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-4-(環丙基甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	612.3	(500 MHz, DMSO-d6) δ 10.52 (s, 1H), 9.89 (br d, *J*=7.0 Hz, 1H), 8.23 - 8.18 (m, 2H), 7.80 - 7.75 (m, 2H), 7.46 (br t, *J*=9.8 Hz, 1H), 7.25 (d, *J*=8.5 Hz, 1H), 5.12 (br dd, *J*=8.4, 4.7 Hz, 1H), 4.68 (br d, *J*=9.5 Hz, 1H), 4.45 - 4.40 (m, 1H), 4.14 (br t, *J*=9.0 Hz, 1H), 4.03 (s, 3H), 3.14 (br dd, *J*=10.8, 3.8 Hz, 1H), 3.10 - 3.08 (m, 1H), 2.73 - 2.68 (m, 1H), 1.94 (br dd, *J*=13.3, 6.0 Hz, 1H), 1.88 - 1.80 (m, 2H), 1.79 - 1.63 (m, 4H), 1.53 - 1.46 (m, 1H), 1.44 - 1.36 (m, 2H), 1.30 (qd, *J*=11.9, 5.5 Hz, 1H), 0.71 - 0.69 (m, 2H), 0.37 - 0.30 (m, 2H)	2.71, B

443		(2S,3R,7Z) 7 (環丙基亞甲基) 3 (5 {5,5 二側氧基 3aH,4H,6H,6aH 5λ⁶ 噻吩并[3,4 d][1,2] 噁唑 3 基} 2 甲氧基苯甲醯胺基) N [4 氟 3 (三氟甲基)苯基]雙環[2.2.1]庚烷 2 甲醯胺	662.2	(500 MHz, DMSO d6) δ 10.53 (s, 1H), 9.90 (br d, J = 7.0 Hz, 1H), 8.23 – 8.18 (m, 2H), 7.79 – 7.74 (m, 2H), 7.46 (br t, J = 9.8 Hz, 1H), 7.27 (d, J = 8.9 Hz, 1H), 5.43 – 5.38 (m, 1H), 4.77 – 4.72 (m, 1H), 4.68 (d, J = 9.5 Hz, 1H), 4.45 – 4.40 (m, 1H), 4.04 (s, 3H), 3.67 – 3.61 (m, 1H), 3.53 – 3.45 (m, 1H), 3.16 – 3.08 (m, 3H), 2.73 – 2.68 (m, 1H), 1.84 – 1.73 (m, 2H), 1.51 – 1.45 (m, 1H), 1.43 – 1.35 (m, 2H), 0.71 – 0.68 (m, 2H), 0.38 – 0.30 (m, 2H)	2.38, C

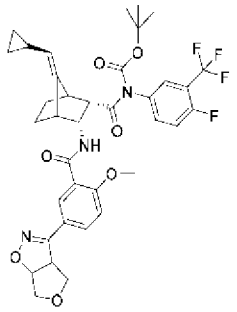
444		(2S,3R,7Z)-7-(環丙基亞甲基)-3-(5-{5,5-二側氧基-3aH,4H,6H,6aH-5λ⁶-噻吩并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	662.3	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.92 (br d, J = 7.3 Hz, 1H), 8.25 – 8.20 (m, 2H), 7.76 (br dd, J = 8.4, 2.0 Hz, 2H), 7.47 (br t, J = 9.8 Hz, 1H), 7.27 (d, J = 8.9 Hz, 1H), 5.40 (br dd, J = 8.9, 6.7 Hz, 1H), 4.75 (td, J = 10.1, 3.5 Hz, 1H), 4.68 (d, J = 9.5 Hz, 1H), 4.46 – 4.40 (m, 1H), 4.04 (s, 3H), 3.68 – 3.62 (m, 1H), 3.48 – 3.37 (m, 1H), 3.18 – 3.13 (m, 2H), 3.11 – 3.07 (m, 1H), 2.74 – 2.68 (m, 1H), 1.85 – 1.75 (m, 2H), 1.53 – 1.45 (m, 1H), 1.44 – 1.36 (m, 2H), 0.78 – 0.68 (m, 2H), 0.34 (br s, 2H)	2.38, C

|(0470)|

實例447



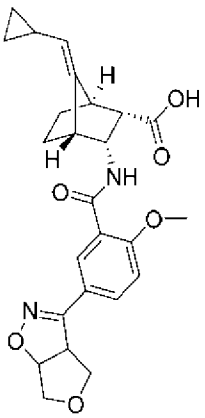
中間物447-1：



向(1R,2S,3R,4R,Z)-7-(環丙基亞甲基)-N-(4-氟-3-(三氟甲基)苯基)-3-(2-甲氧基-5-(3a,4,6,6a-四氫呋喃并[3,4-d]異噁唑-3-基)苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺(250 mg，0.407 mmol，**實例417**)於DCM (4.1 mL)中之溶液中添加Boc_2O (0.38 mL，1.6 mmol)、休尼格氏鹼(0.28 µl、1.6 mmol)及DMAP (25 mg，0.20 mmol)。攪拌反應混合物14 h，隨後真空濃縮。經由矽膠層析純化殘餘物，得到((1R,2S,3R,4R,Z)-7-(環丙基亞甲基)-3-(2-甲氧基-5-(3a,4,6,6a-四氫呋喃并[3,4-d]異噁唑-3-基)苯甲醯胺基)雙環[2.2.1]庚烷-2-羰基)(4-氟-3-(三氟甲基)苯基)胺基甲酸三級丁酯(242 mg，0.339 mmol，83.0%產率)。LC-MS RT: 1.20 min；MS (ESI) *m/z* 736 $(M+Na)^+$；方法E。

【0471】

中間物447-2：

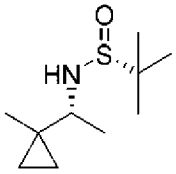


向**中間物447-1** (533 mg，0.747 mmol) 於THF (14mL)中之溶液中添加LiOH (1M水溶液) (3.7 mL，3.7 mmol)。3小時之後，將反應混合物用

水稀釋且用EtOAc萃取兩次。用1M NaOH再萃取有機層，隨後用1M HCl將水層酸化至約pH 1。濾出所沈澱之固體，接著用EtOAc萃取濾液兩次。將有機溶離份與固體合併且在減壓下濃縮，得到(1R,2S,3R,4R,Z)-7-(環丙基亞甲基)-3-(2-甲氧基-5-(3a,4,6,6a-四氫呋喃并[3,4-d]異噁唑-3-基)苯甲醯胺基)雙環[2.2.1]庚烷-2-甲酸**實例447-2** (294 mg，0.650 mmol，87.0%產率)。LC-MS RT:0.75 min；MS (ESI) *m/z* 453 $(M+H)^+$；方法E。

【0472】

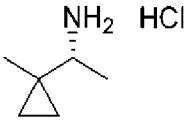
中間物447-3：



在兩個40 mL壓力小瓶中之每一者中，將1-(1-甲基環丙基)乙-1-酮(0.500 g，5.09 mmol)溶解於THF (10 ml)中。向此溶液中添加乙醇鈦(IV) (2.1 ml，10 mmol)及(R)-2-甲基丙烷-2-亞磺醯胺(0.617 g，5.09 mmol)。將反應混合物加熱至65℃持續14 h，隨後使其冷卻至室溫。將硼氫化鈉(1.54 g，40.8 mmol)於7 mL THF中之懸浮液冷卻至-50℃。將含有反應溶液之小瓶冷卻至-50℃。將反應溶液轉移至硼氫化鈉溶液中。在兩小時之後，用MeOH淬滅反應混合物。在氣體逸出停止之後，將反應混合物隨著攪拌倒入鹽水中。經由矽藻土過濾懸浮液，用EtOAc沖洗。在減壓下濃縮濾液。經由矽膠層析純化殘餘物，得到**中間物447-3** (982 mg，47%產率)。^{1}H NMR (400 MHz, $CDCl_3$) δ 3.22 (br s, 1H), 2.61 (qd, *J*=6.5, 3.2 Hz, 1H), 1.26 - 1.21 (m, 12H), 1.01 (s, 3H), 0.54 - 0.46 (m, 1H), 0.42 - 0.32 (m, 3H)。

【0473】

中間物447-4：



向**中間物447-3** (100 mg，0.492 mmol)於甲醇(0.49 mL)中之溶液中添加HCl (4M於二噁烷中) (0.12 mL，0.49 mmol)。2.75小時之後，真空濃縮反應混合物。將殘餘物用Et_2O進行音波處理且過濾。乾燥固體，得到(R)-1-(1-甲基環丙基)乙-1-胺HCl (60 mg，0.44 mmol，90%產率)。^1H NMR (400 MHz, CD_3OD) δ 2.66 - 2.52 (m, 1H), 1.38 - 1.27 (m, 3H), 1.09 (s, 3H), 0.65 - 0.55 (m, 1H), 0.55 - 0.41 (m, 3H)。

【0474】

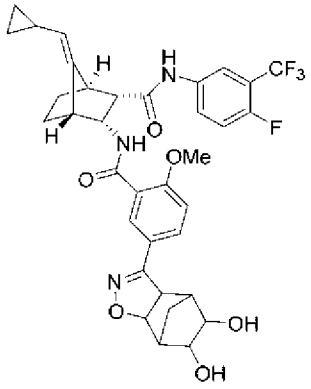
實例447：

向**中間物447-2** (20 mg，0.044 mmol)於DMF (0.5 mL)中之溶液中添加**中間物447-4** (24 mg，0.18 mmol)、HATU (22 mg，0.057 mmol)及休尼格氏鹼(0.046 mL，0.27 mmol)。1.5小時之後，用MeOH淬滅反應混合物。經由製備型HPLC純化殘餘物，得到**實例447** (15.2 mg，64.0%產率)。^1H NMR (400 MHz, DMSO-d_6) δ 10.07 (br d, *J*=6.7 Hz, 1H), 8.15 (d, *J*=2.4 Hz, 1H), 7.92 (d, *J*=8.6 Hz, 1H), 7.78 (dd, *J*=8.6, 2.4 Hz, 1H), 7.23 (d, *J*=8.8 Hz, 1H), 5.34 (dd, *J*=9.4, 3.5 Hz, 1H), 4.63 (d, *J*=9.4 Hz, 1H), 4.54 - 4.47 (m, 1H), 4.31 - 4.23 (m, 1H), 4.09 (d, *J*=10.9 Hz, 1H), 4.00 (s, 3H), 3.90 (d, *J*=10.0 Hz, 1H), 3.77 (dd, *J*=9.3, 6.7 Hz, 1H), 3.65 (dd, *J*=10.7, 3.6 Hz, 1H), 3.50 - 3.42 (m, 1H), 3.07 - 3.02 (m, 1H), 2.94 (dd, *J*=11.0, 4.0 Hz, 1H), 1.91 - 1.81 (m, 1H), 1.78 - 1.68 (m, 1H), 1.52 - 1.43 (m, 1H), 1.40 - 1.30 (m, 2H), 1.05 - 0.99 (m, 3H), 0.99 - 0.94 (m, 3H), 0.77 - 0.66 (m, 2H), 0.58 - 0.47 (m, 1H), 0.36 - 0.27 (m, 2H), 0.17

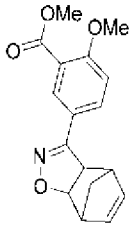
(br t, *J*=6.6 Hz, 2H)。LC-MS RT: 2.26 min；MS (ESI) *m/z* 534.3 $(M+H)^+$；方法B。

【0475】

實例448



中間物448-1：

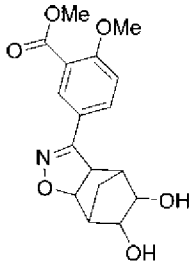


將(Z)-5-(氯(羥基亞胺基)甲基)-2-甲氧基苯甲酸甲酯(200 mg，0.821 mmol)及雙環[2.2.1庚-2,5-二烯(756 mg，8.21 mmol)溶解於DCM (5 mL)中。向溶液中添加TEA (1 mL)且在室溫下攪拌14h。將反應混合物用水(50 mL)淬滅且用EtOAc (2×25 mL)萃取，接著乾燥($MgSO_4$)，過濾且真空濃縮成油狀物。經由矽膠層析法純化殘餘物且用己烷/EtOAc溶離。單離含有純產物之溶離份且在減壓下濃縮成2-甲氧基-5-(3a,4,7,7a-四氫-4,7-甲橋苯并[d]異噁唑-3-基)苯甲酸甲酯**448-1** (240 mg，98%產率)。^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (d, J=2.3 Hz, 1H), 7.88 (dd, J=8.9, 2.3 Hz, 1H), 7.02 (d, J=8.7 Hz, 1H), 6.36 (dd, J=5.7, 3.0 Hz, 1H), 6.10 (dd, J=5.8, 3.2 Hz, 1H), 4.97 (dt, J=8.2, 1.2 Hz, 1H), 3.94 (s, 3H), 3.91 (s, 3H), 3.29 - 3.25 (m, 1H), 1.71 (d, J=9.5 Hz, 1H), 1.62 (dt, J=9.4, 1.5 Hz, 1H)。LCMS

m/z = 300.2 $(M+H)^+$。

【0476】

製備中間物同對掌性異構物**448-2**及**448-3**。

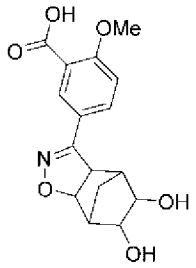


將中間物**448-1** (180 mg，0.60 mmol)攪拌成於t-BuOH (3 mL)中之漿液，且向溶液中添加*N*-甲基味啉氧化物(146 mg，1.20 mmol)，隨後添加OsO_4 (380 mg，0.060 mmol)。反應物立即變成黑色且在室溫下攪拌14h。將反應混合物用飽和亞硫酸鈉溶液(20 mL)淬滅，攪拌5 min且用EtOAc (2×25 mL)萃取，乾燥($MgSO_4$)，過濾且在減壓下蒸發成呈泡沫之5-(5,6-二羥基-3a,4,5,6,7,7a-六氫-4,7-甲橋苯并[d]異噁唑-3-基)-2-甲氧基苯甲酸甲酯(220 mg)。經由對掌性SFC將化合物分離成兩種同對掌性異構物**448-2**及**448-3**。製備型層析條件：儀器：Berger MG II (CTR-L409-PSFC1)管柱：Chiralpak IF，21 × 250 mm，5微米，移動相：30% MeOH / 70% CO_2，流動條件：45 mL/min，150巴， 40℃，偵測器波長：220 nm。注射詳情：1.0 mL ~200 mg/3mL於MeOH-CAN中。分析型層析條件：儀器：Shimadzu Nexera SFC (CTR-L410-SFC3)管柱：Chiralpak IF，4.6 × 100 mm，3微米。移動相：30% MeOH / 70% CO_2。流動條件：2.0 mL/min，150巴， 40℃。偵測器波長：220 nm。注射詳情：5 μL ~1mg/mL於MeOH中。將兩種同對掌性異構物單離成**448-2**異構物-1 >99% ee，RT=2.89 min (84 mg，49%產率)及**448-3**異構物-2 >99% ee，RT=6.03 min (78 mg，46%產率)。^1H NMR (500 MHz, $CDCl_3$) δ 8.07 -

8.04 (m, 1H), 7.89 - 7.87 (m, 1H), 7.05 - 7.00 (m, 1H), 4.67 - 4.59 (m, 1H), 3.96 (s, 3H), 3.93 (s, 3H), 3.91 - 3.83 (m, 1H), 3.52 - 3.41 (m, 1H), 2.64 - 2.58 (m, 1H), 2.52 - 2.49 (m, 1H), 1.89 - 1.82 (m, 1H), 1.50 - 1.44 (m, 1H)。LCMS m/z = 334.2 $(M+H)^+$。

【0477】

製備中間物**448-4**。



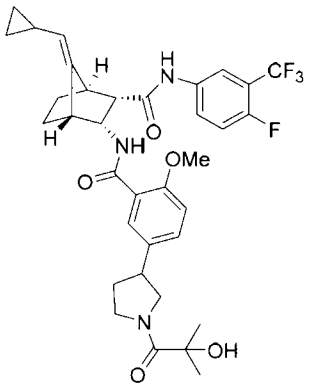
將5-(5,6-二羥基-3a,4,5,6,7,7a-六氫-4,7-甲橋苯并[d]異噁唑-3-基)-2-甲氧基苯甲酸甲酯**448-3** (> 99% ee)溶解於甲醇(3 mL)中，且向溶液中添加LiOH (20 mg，0.47 mmol)，隨後添加水(2 mL)。在室溫下攪拌反應混合物14 h，接著用水(25 mL)淬滅。將有機物用EtOAc (2×25 mL)萃取，乾燥($MgSO_4$)且真空蒸發，得到5-(5,6-二羥基-3a,4,5,6,7,7a-六氫-4,7-甲橋苯并[d]異噁唑-3-基)-2-甲氧基苯甲酸**448-4** (63 mg，84%產率)。LCMS m/z = 320.3 (M+H)。^{1}H NMR (500 MHz, CD_3OD) δ 8.17 - 8.12 (m, 1H), 7.90 (dd, J=8.7, 2.3 Hz, 1H), 7.23 (d, J=8.9 Hz, 1H), 4.81 - 4.61 (m, 1H), 3.97 (s, 3H), 3.92 (m. 1H), 3.78 - 3.75 (m, 1H), 3.71 - 3.58 (m, 1H), 2.45 (s, 1H), 2.35 (s, 1H), 1.84 (br d, J=11.1 Hz, 1H), 1.36 - 1.15 (m, 1H)。

【0478】 **實例448.** 中間物**448-4** (17 mg，0.050 mmol)係使用針對實例**378**所描述的得到(1R,2S,3R,4R,Z)-3-胺基-7-(環丙基亞甲基)-N-(4-氟-3-(三氟甲基)苯基)雙環[2.2.1]庚烷-2-甲醯胺中間物**166-2** (15 mg，0.050 mmol)之通用程序，使用BOP (10 mg，0.050 mmol)試劑及休尼格氏鹼

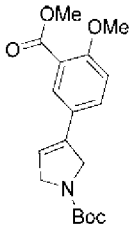
(0.1 mL)來製備。經由HPLC純化單離呈固體之**實例448** (18 mg，58%產率)。HPLC純度：98.3%；RT=2.35 min，[方法D]。LCMS m/z = 670.3 $(M+H)^+$。^1H NMR (500 MHz, CD_3OD) δ 8.41 - 8.36 (m, 1H), 8.16 (dd, J=6.6, 2.4 Hz, 1H), 7.91 (dd, J=8.7, 2.4 Hz, 1H), 7.84 - 7.74 (m, 1H), 7.32 - 7.22 (m, 2H), 4.85 - 4.82 (m, 1H), 4.79 - 4.70 (m, 1H), 4.67 - 4.51 (m, 1H), 4.14 (s, 3H), 3.92 (br d, J=6.9 Hz, 1H), 3.76 (d, J=5.6 Hz, 1H), 3.65 (d, J=8.1 Hz, 1H), 3.56 - 3.42 (m, 1H), 3.31 - 3.22 (m, 2H), 3.21 - 3.06 (m, 2H), 2.73 (br d, J=4.3 Hz, 1H), 2.45 (s, 1H), 2.35 (s, 1H), 2.06 - 1.97 (m, 1H), 1.97 - 1.91 (m, 1H), 1.83 (br d, J=11.1 Hz, 1H), 1.62 - 1.48 (m, 2H), 1.38 - 1.21 (m, 1H), 0.77 (br d, J=4.4 Hz, 2H), 0.37 (br s, 2H)。

【0479】

實例449



中間物449-1：

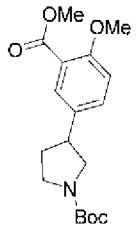


將含5-溴-2-甲氧基苯甲酸甲酯(2.0 g，8.2 mmol)及3-(4,4,5,5-四甲基-1,3,2-二氧雜硼雜環戊-2-基)-2,5-二氫-1H-吡咯1-甲酸三級丁酯(2.65 g，8.98 mmol)之二噁烷(55 mL)/水(10 mL)再次脫氣5 min，接著添加

$PdCl_2$(dppf)-CH_2Cl_2加合物(0.666 g，0.816 mmol)及K_3PO_4 (5.64 g，24.5 mmol)，且再次使反應混合物脫氣5 min，接著在密封管中在100℃攪拌漿液4 h。用EtOAc稀釋反應混合物，過濾固體，用過量EtOAc洗滌且收集濾液且在減壓下濃縮。藉由矽膠層析純化殘餘物，得到呈淡棕色固體之3-(4-甲氧基-3-(甲氧基羰基)苯基)-2,5-二氫-1H-吡咯-1-甲酸三級丁酯(2.2 g，6.60 mmol，81%產率)化合物。MS (ES): m/z = 234.2 [M+H-Boc]。

【0480】

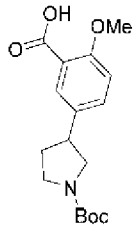
中間物449-2



在室溫下向**449-1** (2.2 g，6.6 mmol)於MeOH (100 mL)中之溶液中添加Pd-C (1.756 g，16.50 mmol)，且在氫氣氛圍下攪拌漿液12 h。經由矽藻土過濾反應混合物，用過量甲醇及THF洗滌矽藻土，收集濾液且在減壓下濃縮，得到呈淡棕色半固體之3-(4-甲氧基-3-(甲氧基羰基)苯基) 吡咯啶-1-甲酸三級丁酯(1.7 g，5.1 mmol，77%產率)。MS (ES): m/z = 353.2 [M+H_2O]。

【0481】

中間物449-3

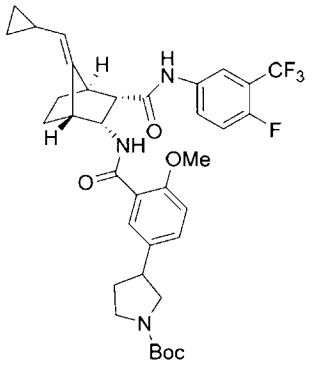


將含LiOH (1.43 g，59.6 mmol)之水(5.0 mL)添加至**449-2** (2.0 g，6.0 mmol)於甲醇(10 mL)、THF (10 mL)中之溶液中，在室溫下攪拌所得

反應混合物5h。真空蒸發揮發物且在高真空下乾燥。用冰水(10 mL)稀釋殘餘物，接著使用0.1M HCl酸化。形成固體且過濾，用水洗滌且在真空下乾燥，得到呈白色固體之5-(1-(三級丁氧基羰基)吡咯啶-3-基)-2-甲氧基苯甲酸(1.5 g，4.7 mmol，78%產率)化合物。MS (ES): m/z = 320.2 [M-H]。

【0482】

中間物449-4



在室溫下將HATU (206 mg，0.543 mmol)及TEA (0.38 mL，2.7 mmol)添加至**449-2** (349 mg，1.09 mmol)及**166-2** (200 mg，0.543 mmol)於DMF (30 mL)中之溶液中，攪拌反應混合物3 h。在減壓下移除揮發物且藉由矽膠層析純化殘餘物，得到呈灰白色固體之3-(3-(((1R,2R,3R,4R,Z)-7-(環丙基亞甲基)-3-((4-氟-3-(三氟甲基)苯基) 胺甲醯基)雙環[2.2.1]庚烷-2-基)胺甲醯基)-4-甲氧基苯基)吡咯啶-1-甲酸三級丁酯(190 mg)。對固體進行SFC純化：管柱名稱：Welk-01(R,R)(250*4.6)mm. 5μ，助溶劑；20%小瓶N°；LA8助溶劑名稱：0.2%氨/甲醇；注射量：30 μl，流動速率：4 ml/min，出口壓力：100巴，溫度：35℃，以分離非鏡像異構物。

【0483】 在SFC純化之後，收集溶離份，在減壓下濃縮且凍乾，以產生3-(3-(((1R,2R,3S,4R,Z)-7-(環丙基亞甲基)-3-((4-氟-3-(三氟甲基)苯

基)胺甲醯基)雙環[2.2.1]庚烷-2-基)胺甲醯基)-4-甲氧基苯基) 吡咯啶-1-甲酸三級丁酯。

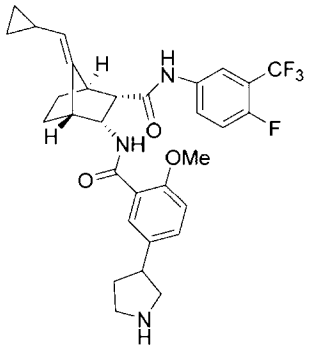
【0484】 峰 - 1，**449-4**，(55 mg，0.082 mmol，14%產率)，對掌性SFC RT - 9.9 min，^{1}H NMR (400MHz, DMSO-d6) δ ppm 10.50 (s, 1H), 9.82 (d, J=7.0 Hz, 1H), 8.22 (dd, J=2.5, 6.0 Hz, 1H), 7.82 (d, J=2.5 Hz, 2H), 7.48 (t, J=10.0 Hz, 1H), 7.43 (dd, J=2.5, 8.5 Hz, 1H), 7.14 (d, J=8.5 Hz, 1H), 6.88 (s, 1H), 4.69 (d, J=10.0 Hz, 1H), 3.97 (s, 3H), 3.68 (dd, J=7.5, 10.0 Hz, 1H), 3.49 - 3.36 (m, 5H), 3.31 - 3.21 (m, 5H), 3.20 - 3.05 (m, 4H), 2.73 - 2.69 (m, 1H), 2.19 (s, 3H), 1.86 (br d, J=10.5 Hz, 3H), 1.46 - 1.33 (m, 20H), 0.74 (br t, J=8.3 Hz, 2H), 0.35 (br d, J=2.5 Hz, 2H)；LCMS: RT = 1.565 min，MS (ES):m/z = 616.4 [M+H-tBu]方法B；呈白色固體之3-(3-(((1R,2R,3S,4R,Z)-7-(環丙基亞甲基)-3-((4-氟-3-(三氟甲基)苯基) 胺甲醯基)雙環[2.2.1]庚烷-2-基)胺甲醯基)-4-甲氧基苯基)吡咯啶-1-甲酸三級丁酯(55 mg，0.082 mmol，15%產率)。

【0485】 峰 - 2，(60 mg，0.089 mmol，16%產率)，對掌性SFC RT - 10.98 min，^{1}H NMR (400MHz, DMSO-d6) δ ppm 10.49 (s, 1H), 9.81 (d, J=7.0 Hz, 1H), 8.22 (dd, J=2.5, 6.5 Hz, 1H), 7.82 (d, J=2.5 Hz, 1H), 7.76 (br s, 1H), 7.48 (t, J=9.8 Hz, 1H), 7.42 (dd, J=2.5, 8.5 Hz, 1H), 7.13 (d, J=8.5 Hz, 1H), 4.68 (d, J=9.5 Hz, 1H), 4.44 (br s, 1H), 3.97 (s, 3H), 3.67 (dd, J=7.5, 10.0 Hz, 1H), 3.49 - 3.34 (m, 2H), 3.29 - 3.06 (m, 4H), 2.72 - 2.67 (m, 1H), 2.56 - 2.52 (m, 2H), 2.18 (s, 2H), 1.86 (br t, J=9.3 Hz, 2H), 1.76 (br s, 1H), 1.50 (br d, J=4.5 Hz, 1H), 1.45 - 1.33 (m, 17H), 0.74 (br t, J=9.0 Hz, 2H), 0.34 (br s, 2H)；LCMS: RT = 1.716 min，MS (ES):m/z

= 616.3 [M+H-tBu] 方法B。

【0486】

中間物449-5：



在0℃將TFA (0.16 mL，2.0 mmol)添加至**449-4** (55 mg，0.082 mmol)於DCM(5.0 mL)中之溶液中，隨後在室溫下攪拌反應混合物2 h。在減壓下移除揮發物且在真空下乾燥殘餘物，得到呈淡棕色半固體之(1R,2S,3R,4R,Z)-7-(環丙基亞甲基)-N-(4-氟-3-(三氟甲基)苯基)-3-(2-甲氧基-5-(吡咯啶-3-基)苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺(35 mg)，其不經進一步純化即用於下一步驟。MS (ES): m/z = 572.2 [M+H]。

【0487】

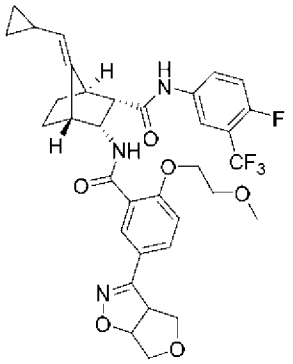
實例449

在室溫下將HATU (13 mg，0.035 mmol)、DIPEA (0.06 mL，0.04 mmol)添加至含**449-5** (20 mg，0.035 mmol)及2-羥基-2-甲基丙酸(3.6 mg，0.035 mmol)之DMF (2.0 mL)中。將反應混合物攪拌15h且藉由製備型逆相HPLC純化，得到呈白色固體之(1R,2S,3R,4R,Z)-7-(環丙基亞甲基)-N-(4-氟-3-(三氟甲基)苯基)-3-(5-(1-(2-羥基-2-甲基丙醯基)吡咯啶-3-基)-2-甲氧基苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺(13 mg，49%)。^{1}H NMR (400 MHz, DMSO-d6) δ ppm 10.48 (s, 1H), 9.83 (dd, *J* = 3.3, 6.7 Hz, 1H), 8.25 - 8.17 (m, 1H), 7.85 (br s, 1H), 7.77 (td, *J* = 3.6, 8.7 Hz,

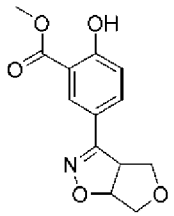
1H), 7.48 (t, *J*= 9.9 Hz, 1H), 7.43 (dd, *J* = 2.2, 8.6 Hz, 1H), 7.14 (dd, *J* = 1.8, 7.9 Hz, 1H), 5.19 - 5.12 (m, 1H), 4.68 (d, *J* = 9.5 Hz, 1H), 4.48 - 4.40 (m, 1H), 4.27 (br d, *J* =0.7 Hz, 1H), 4.08 (q, *J* = 5.5 Hz, 1H), 3.97 (s, 4H), 3.78 - 3.65 (m, 1H), 3.58 - 3.47 (m, 1H), 3.24 - 3.06 (m, 4H), 2.74 - 2.68 (m, 1H), 2.13 (br d, *J* = 0.7 Hz,1H), 1.93 - 1.72 (m, 3H), 1.53 - 1.36 (m, 3H), 1.32 - 1.26 (m, 7H), 0.80 - 0.65 (m, 2H), 0.35 (dd, *J* = 1.8, 4.8 Hz, 2H)。LCMS: RT = 2.465 min，MS (ES):*m/z* = 658.3 [M+H$^+$] 方法B。

【0488】

實例452



中間物452-1

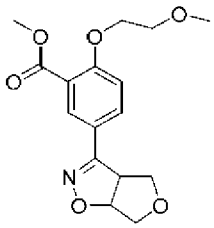


452-1 (0.13 g，0.49 mmol，49%產率)係以與實例**416**類似之方式，以5-甲醯基-2-甲氧基苯甲酸甲酯取代5-甲醯基-2-羥基苯甲酸甲酯來製備。^{1}H NMR (400 MHz, $CDCl_3$) δ 10.98 (s, 1H), 8.04 (d, *J*=2.2 Hz, 1H), 7.82 (dd, *J*=8.8, 2.2 Hz, 1H), 7.04 (d, *J*=8.8 Hz, 1H), 5.38 (dd, *J*=9.1, 3.9 Hz, 1H), 4.36 - 4.30 (m, 1H), 4.30 - 4.25 (m, 1H), 4.14 (dd, *J*=9.2, 1.3 Hz, 1H), 3.99 (s, 3H), 3.89 (dd, *J*=9.4, 6.7 Hz, 1H), 3.79 (dd, *J*=10.8, 3.7 Hz,

1H)。LCMS(ESI) *m/z*: 264 $(M+H)^+$。

【0489】

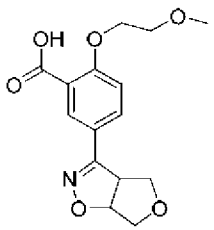
中間物452-2



向含**452-1** (0.1 g，0.4 mmol)之DMF (2 mL)中添加1-氯-2-甲氧基乙烷(72 mg，0.80 mmol)、K_2CO_3 (0.16 g，1.1 mmol)、KI (63 mg，0.38 mmol)且在60℃加熱反應混合物24h。用水(10 mL)及EtOAc (20 mL)分配反應混合物。用EtOAc (2×20 mL)萃取水層，將合併之有機層用鹽水(15 mL)洗滌且乾燥($MgSO_4$)，過濾且在減壓下濃縮。藉由正相矽膠層析純化殘餘物，得到呈澄清油狀物之**452-2** (62 mg，0.20 mmol，51%產率)。^1H NMR (500 MHz, $CDCl_3$) δ 7.99 (d, *J*=2.3 Hz, 1H), 7.87 (dd, *J*=8.8, 2.4 Hz, 1H), 7.07 (d, *J*=8.7 Hz, 1H), 5.39 (dd, *J*=9.2, 3.9 Hz, 1H), 4.37 - 4.32 (m, 1H), 4.32 - 4.28 (m, 1H), 4.28 - 4.24 (m, 2H), 4.16 (dd, *J*=9.4, 1.3 Hz, 1H), 3.93 - 3.92 (m, 3H), 3.91 - 3.87 (m, 1H), 3.84 (dd, *J*=5.3, 4.3 Hz, 2H), 3.80 (dd, *J*=10.8, 3.9 Hz, 1H), 3.50 (s, 3H)。LCMS(ESI) *m/z*: 322 $(M+H)^+$。

【0490】

中間物452-3



452-3 (41 mg，0.13 mmol，72%產率)係藉由如**378-3**中所描述水解

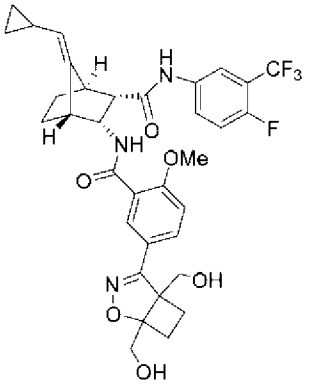
452-2來製備。^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23 - 8.07 (m, 2H), 7.20 - 7.07 (m, 1H), 5.42 (dd, *J*=9.2, 3.9 Hz, 1H), 5.32 (s, 1H), 4.46 - 4.39 (m, 2H), 4.36 - 4.30 (m, 2H), 4.14 (d, *J*=9.5 Hz, 1H), 3.93 - 3.88 (m, 1H), 3.85 - 3.82 (m, 2H), 3.78 (dd, *J*=10.9, 3.9 Hz, 1H), 3.49 (s, 3H)。

【0491】 **實例452**. 異構物混合物係藉由如實**例378**中所描述之BOP偶合，以中間物**378-3**及環丁基降冰片烷基中間物**369-1**取代環丙基降冰片烷基中間物**166-2**及中間物**452-3**來製備。使用對掌性SFC層析分離異構混合物。製備型層析條件：儀器：Waters 100 Prep SFC管柱：Chiral OD，30 × 250 mm，5微米，移動相：25% MeOH / 75% CO_2 (具有0.1% DEA)，流動條件：100 mL/min，偵測器波長：220 nm；分析方法：儀器：Shimadzu Nexera SFC，管柱Chiral OD，4.6 × 100 mm，5微米，移動相：25% MeOH / 75% CO_2 (具有0.1% DEA)，流動條件：2 mL/min，偵測器波長：220 nm，得到對掌性峰-1，實例**452** (9.3 mg，14 μmol，23%產率)，RT=2.92 min.，>95% de及峰-2 (9.3 mg，14 μmol，23%產率)，RT =3.6 min，>95% de。對於實例**452**：^{1}H NMR (500 MHz, DMSO-d6) δ 10.49 (s, 1H), 9.60 (br d, J=7.9 Hz, 1H), 8.37 - 8.10 (m, 2H), 7.86 - 7.68 (m, 2H), 7.47 (t, J=9.9 Hz, 1H), 7.32 (d, J=8.9 Hz, 1H), 5.35 (dd, J=9.2, 3.7 Hz, 1H), 4.71 (d, J=9.5 Hz, 1H), 4.61 - 4.47 (m, 2H), 4.43 (br d, J=4.0 Hz, 2H), 4.11 (d, J=10.7 Hz, 1H), 4.07 - 3.98 (m, 1H), 3.95 - 3.86 (m, 1H), 3.83 - 3.74 (m, 1H), 3.66 (dd, J=10.7, 3.4 Hz, 1H), 3.28 (s, 1H), 3.21 - 3.13 (m, 1H), 3.09 - 2.99 (m, 1H), 2.74 (br s, 1H), 2.52 (br s, 3H), 2.03 - 1.84 (m, 2H), 1.63 - 1.51 (m, 1H), 1.48 - 1.31 (m, 1H), 0.89 - 0.67 (m, 2H), 0.46 - 0.27 (m, 2H)。LCMS(ESI) *m/z*: 658.15 $(M+H)^+$。

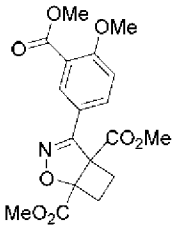
HPLC純度100%，滯留時間2.42 min。[方法C]

【0492】

實例461



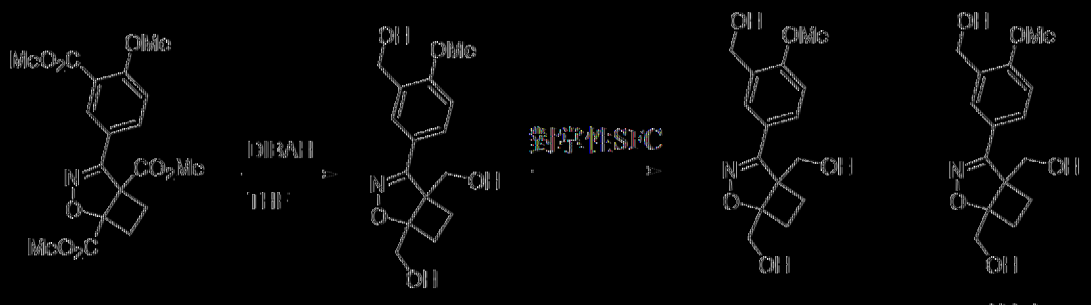
製備非鏡像異構中間物**461-1**。



非鏡像異構中間物**461-1** (200 mg，80%)係以如針對**實例378**所描述之類似方式，藉由使環丁-1-烯-1,2-二甲酸二甲酯與(Z)-5-(氯(羥基亞胺基)甲基)-2-甲氧基苯甲酸甲酯發生環化加成來製備。LCMS m/z = 378.2 (M+H)。^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (d, J=2.4 Hz, 1H), 7.75 (dd, J=8.9, 2.4 Hz, 1H), 7.00 (d, J=8.9 Hz, 1H), 3.96 (s, 3H), 3.92 (s, 3H), 3.87 (s, 3H), 3.68 (s, 3H), 3.21 - 3.09 (m, 1H), 2.79 - 2.67 (m, 1H), 2.62 - 2.52 (m, 2H)。

【0493】

製備同對掌性中間物**461-3及461-4**。



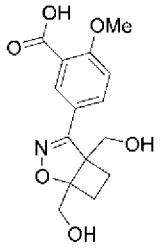
461-1 非鏡像異構混合物 | 461-2 非鏡像異構混合物 | 461-3 同對掌性峰-1 | 461-4 同對掌性峰-2

將非鏡像異構中間物461-1 (112 mg，0.29 mmol)溶解於THF (10 mL)中且向其中添加DIBAH (1M，2.08 mL，2.08 mmol)溶液。在室溫下攪拌反應混合物14 h且隨後用稀釋HCl (5 mL)淬滅，接著用EtOAc (2×25 mL)萃取有機物質。將合併之有機層乾燥($MgSO_4$)，過濾且在減壓下濃縮，得到呈油狀物之非鏡像異構物(4-(3-(羥基甲基)-4-甲氧基苯基)-2-氧雜-3-氮雜雙環[3.2.0]庚-3-烯-1,5-二基)二甲醇461-2 (100 mg，100%產率)。^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 - 7.49 (m, 2H), 6.92 - 6.86 (m, 1H), 4.73 - 4.60 (m, 2H), 3.90 (s, 3H), 3.88 (s, 3H), 3.74 - 3.65 (m, 1H), 3.05 - 2.82 (m, 1H), 2.54 - 2.32 (m, 2H), 2.19 - 1.97 (m, 2H), 1.95 - 1.37 (m, 1H), 1.33 - 0.84 (m, 1H)。LCMS m/z = 294.2 $(M+H)^+$。經由對掌性SFC條件以對掌性方式分離中間物461-2，得到同對掌性中間物461-3 (峰-1)及461-4 (峰-2)。製備型析條件：儀器：Berger MG II管柱：Chiralpak IC，21 × 250 mm，5微米，移動相：30%甲醇/ 70% CO_2，流動條件：45 mL/min，150巴， 40℃。偵測器波長：220 nm，注射詳情：0.5 mL ~55mg/mL於甲醇中。分析型析條件：儀器：Shimadzu Nexera SFC管柱：Chiralpak IC，4.6 × 100 mm，3微米，移動相：30%甲醇/ 70% CO_2，流動條件：2.0 mL/min，150巴， 40℃。偵測器波長：220 nm，注射詳情：5 μL ~1mg/mL於甲醇中。461-3同對掌性峰-1 (57 mg，

15%產率，> 99% ee，RT = 2.98 min)之分析資料；^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (s, 1H), 7.60 (d, J=8.4 Hz, 1H), 6.91 (d, J=8.7 Hz, 1H), 4.69 (br s, 2H), 4.05 (m, 2H), 3.91 (s, 3H), 3.81 (br s, 1H), 3.50 (s, 1H), 3.33 (br s, 1H), 2.56 (br s, 1H), 2.50 - 2.39 (m, 2H), 2.20 - 1.99 (m, 2H), 1.70 (br s, 1)。**461-4**同對掌性峰-2 (60 mg，60%產率，>99% ee，RT = 5.72 min)之分析資料。^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (s, 1H), 7.60 (d, J=8.4 Hz, 1H), 6.91 (d, J=8.5 Hz, 1H), 4.69 (d, J=6.3 Hz, 2H), 4.08 (m, 2H), 3.91 (s, 3H), 3.84 - 3.76 (m, 1H), 3.50 (d, J=4.7 Hz, 2H), 3.33 (br s, 1H), 2.56 (br t, J=6.5 Hz, 1H), 2.50 - 2.39 (m, 2H), 2.20 - 1.99 (m, 2H), 1.70 (s, 1H)。

【0494】

製備同對掌性異構物-1中間物**461-4**。



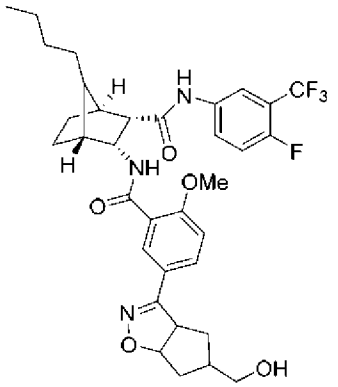
將同對掌性異構物-1中間物**461-2** (4-(3-(羥基甲基)-4-甲氧基苯基)-2-氧雜-3-氮雜雙環[3.2.0]庚-3-烯-1,5-二基)二甲醇(57 mg，0.19 mmol)溶解於無水DCM (10 mL)中且向溶液中添加經活化MnO_2 (847 mg，9.72 mmol)。在室溫下攪拌反應混合物14h。過濾反應混合物且真空濃縮成油狀物。將油狀物再溶解於tBuOH (5 mL)中且向溶液中添加$NaClO_2$ (37 mg，0.41 mmol)，隨後添加NaH_2PO_4水溶液(5 mL)以使pH約3且添加2-甲基丁烯(10 mmol)。在室溫下攪拌反應混合物6 h，接著用水(100 mL)淬滅且用EtOAc (2×25 mL)萃取。將合併之有機部分乾燥($MgSO_4$)，過濾且真

空蒸發，得到呈油狀物之異構物-1中間物**461-4** (50 mg，55%產率)。^{1}H NMR (500 MHz, CD_3OD) δ 8.15 (d, J=2.3 Hz, 1H), 7.88 (dd, J=8.8, 2.4 Hz, 1H), 7.17 (d, J=8.9 Hz, 1H), 4.79 - 4.58 (m, 4H), 3.97 (s, 3H), 3.95-3.88 (m, 2H), 3.51 - 3.34 (m, 2H), 2.63 - 1.96 (m, 2H)。LCMS m/z = 308.2 $(M+H)^+$。

【0495】 **實例461.** 如針對實例**378**所描述，使用BOP (6 mg，0.02 mmol)試劑及休尼格氏鹼(0.1 mL)使同對掌性異構物-1中間物**461-4** (4.3 mg，0.02 mmol)與中間物**166-2** (5.2 mg，0.02 mmol)偶合。在藉由逆相HPLC純化之後，以固體形式分離實例**461** (4.3 mg，45%產率)。HPLC純度：100%；RT= 2.43 min [方法D]。LCMS m/z = 658.33 $(M+H)^+$。^{1}H NMR (500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.93 (br d, J=7.0 Hz, 1H), 8.30 - 8.21 (m, 2H), 7.85 - 7.75 (m, 2H), 7.50 (br t, J=9.8 Hz, 1H), 7.27 (br d, J=8.9 Hz, 1H), 5.38 (br t, J=5.3 Hz, 1H), 4.85 - 4.67 (m, 2H), 4.45 (br s, 1H), 4.06 (s, 3H), 3.92 - 3.78 (m, 3H), 3.71 (br dd, J=11.9, 7.0 Hz, 1H), 3.38 (br s, 1H), 3.17 (br d, J=7.3 Hz,1H), 3.12 (br s, 1H), 2.74 (br s, 1H), 2.33 - 2.19 (m, 1H), 2.15 (br s, 3H), 2.09 (s, 1H), 1.93 (s, 1H), 1.89 - 1.68 (m, 2H), 1.52 (br d, J=8.5 Hz, 1H), 1.42 (br s, 2H), 0.87 - 0.67 (m, 2H), 0.36 (br s, 2H)

【0496】

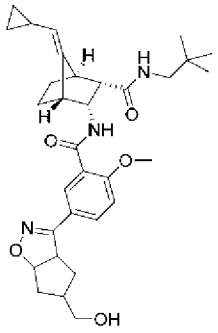
實例467



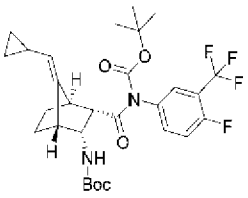
化合物**467**係如針對實例**378**所描述，藉由用催化性Pd/C (10%)還原**166-2** (6 mg，0.02 mmol)，隨後使所得(1S,2S,3R,4R)-3-胺基-7-丁基-N-(4-氟-3-(三氟甲基)苯基)雙環[2.2.1]庚烷-2-甲醯胺與**429-8** (4.72 mg，0.0200 mmol)及BOP (7.16 g，0.0200 mmol)以及休尼格氏鹼(0.1 mL)在DMF中偶合來製備。經由HPLC純化來純化殘餘物，以產生呈固體之**467** (0.7 mg，7%產率)。HPLC純度：100%；RT=2.72 min [方法C]。LCMS m/z = 645.94 (M+H)+。^{1}H NMR (500 MHz, DMSO-d_6) δ 10.64 (s, 1H), 8.37 (br d, *J*=7.3 Hz, 1H), 8.13 (br d, *J*=4.0 Hz, 1H), 7.94 (d, *J*=2.4 Hz, 1H), 7.87 (br s, 1H), 7.77 (br d, *J*=8.9 Hz, 1H), 7.50 (br t, *J*=9.6 Hz, 1H), 7.25 (d, *J*=8.9 Hz, 1H), 5.23 - 5.05 (m, 1H), 4.84 (br s, 1H), 4.23 (br t, *J*=9.2 Hz, 1H), 3.93 (s, 3H), 3.35 (br s, 1H), 2.77 - 2.54 (m, 2H), 2.43 - 2.27 (m, 2H), 2.17 - 1.95 (m, 2H), 1.95 - 1.86 (m, 1H), 1.80 (br d, *J*=12.8 Hz, 1H), 1.74 - 1.63 (m, 3H), 1.58 (br d, *J*=8.2 Hz, 1H), 1.54 - 1.44 (m, 2H), 1.36 (br d, *J*=6.7 Hz, 2H), 1.30 - 1.13 (m, 4H), 0.94 - 0.72 (m, 3H)

【0497】

實例453



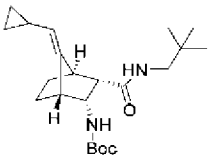
中間物453-1：



向(1R,2S,3R,4R,Z)-3-胺基-7-(環丙基亞甲基)-N-(4-氟-3-(三氟甲基)苯基)雙環[2.2.1]庚烷-2-甲醯胺**IV-2a** (33 mg，0.090 mmol)於DCM (0.9 mL)中之溶液中添加Boc_2O (0.10 mL，0.45 mmol)、休尼格氏鹼(78 µl，0.45 mmol)及DMAP (5.5 mg，0.045 mmol)。攪拌反應混合物14h，接著在減壓下濃縮且經由矽膠層析純化，得到((1R,2S,3R,4R,Z)-3-((三級丁氧基羰基)胺基)-7-(環丙基亞甲基)雙環[2.2.1]庚烷-2-羰基)(4-氟-3-(三氟甲基)苯基)胺基甲酸三級丁酯**中間物453-1** (43 mg，0.076 mmol，84%產率)。LC-MS RT: 1.37 min；MS (ESI) *m/z* 591 $(M+Na)^+$；方法A。

【0498】

中間物453-2：

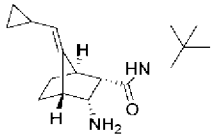


向((1R,2S,3R,4R,Z)-3-((三級丁氧基羰基)胺基)-7-(環丙基亞甲基)雙環[2.2.1]庚烷-2-羰基)(4-氟-3-(三氟甲基)苯基)胺基甲酸三級丁酯**中間物453-1** (43 mg，0.076 mmol)之溶液中添加2,2-二甲基丙烷-1-胺(26.4 mg，0.302 mmol)。攪拌反應混合物兩天，隨後真空濃縮且經由矽膠層析純

化，得到((1R,2R,3S,4R,Z)-7-(環丙基亞甲基)-3-(新戊基胺甲醯基)雙環[2.2.1]庚烷-2-基)胺基甲酸三級丁酯**中間物453-2** (20 mg，0.053 mmol，70%產率)。LC-MS RT: 1.19 min；MS (ESI) *m/z* 377 $(M+H)^+$；方法A。

【0499】

中間物453-3：



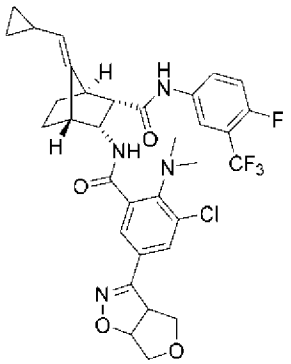
將((1R,2R,3S,4R,Z)-7-(環丙基亞甲基)-3-(新戊基胺甲醯基)雙環[2.2.1]庚烷-2-基)胺基甲酸三級丁酯(20 mg，0.053 mmol) **453-2**溶解於THF (0.4 mL)中。添加HCl (4M於二噁烷中) (0.13 mL，0.53 mmol)。在1小時之後，再添加0.3 mL 4M HCl/二噁烷。在2小時之後，真空濃縮反應混合物，隨後與DCM/己烷共沸，得到(1R,2S,3R,4R,Z)-3-胺基-7-(環丙基亞甲基)-N-新戊基雙環[2.2.1]庚烷-2-甲醯胺HCl**中間物453-3** (20 mg，0.064 mmol，120%產率)。LC-MS RT: 0.80 min；MS (ESI) *m/z* 277 $(M+H)^+$；方法A。

【0500】 **實例453**：向**429-8** (7.87 mg，0.0270 mmol)及中間物**453-3** (8.45 mg，0.0270 mmol)於DMF (0.4 mL)中之溶液中添加BOP (13 mg，0.030 mmol)及休尼格氏鹼(0.024 mL，0.14 mmol)。4小時之後，用MeOH稀釋反應混合物，經由針筒過濾器過濾且經由製備型逆相HPLC純化，得到**實例453** (7.4 mg，49%產率)。^{1}H NMR (500 MHz, DMSO-d_6) δ 9.96 (d, *J*=6.8 Hz, 1H), 8.16 (d, *J*=2.3 Hz, 1H), 7.96 (br t, *J*=6.2 Hz, 1H), 7.77 (dd, *J*=8.7, 2.3 Hz, 1H), 7.22 (d, *J*=8.7 Hz, 1H), 5.11 (dd, *J*=8.7, 5.2 Hz, 1H), 4.62 (d, *J*=9.5 Hz, 1H), 4.53 - 4.48 (m, 1H), 4.34 - 4.25 (m, 1H), 4.19 (br t, *J*=8.6 Hz, 1H), 3.99 (s, 3H), 3.06 - 2.97 (m, 3H), 2.79 (dd,

J=13.0, 5.7 Hz, 1H), 2.02 - 1.40 (m, 10H), 1.39 - 1.25 (m, 2H), 0.81 (s, 9H), 0.74 - 0.64 (m, 2H), 0.36 - 0.25 (m, 2H)。LC-MS RT: 2.23 min；MS (ESI) *m/z* 550.1 $(M+H)^+$；方法B。

【0501】

實例475



中間物475-1：製備2-(二甲基胺基)-5-甲醯基苯甲酸甲酯：

向2-氟-5-甲基苯甲酸甲酯(3.00 g，17.8 mmol)於CCl_4 (100 mL)中之溶液中添加*N*-溴代丁二醯亞胺(6.99 g，39.2 mmol)及過氧化苯甲醯(0.475 g，1.96 mmol)。在回流下加熱反應混合物14h。使反應混合物冷卻至室溫且藉由過濾移除丁二醯亞胺。在減壓下濃縮濾液，得到黃色液體，將其添加至二甲胺(40%水溶液) (90 mL，711 mmol)中，且將內容物緩慢加熱至56℃持續15 min，且接著排出熱量。將深橙色溶液倒入DCM (2×75 mL)中且分離各層。濃縮有機層且使用矽膠層析來純化，得到中間物**465-1** (2.2 g，56%產率)。MS (ESI) *m/z*: 208.2 (M+H)。

【0502】

中間物475-2：製備(E)-3-氯-2-(二甲基胺基)-5-(羥基亞胺基)甲基)苯甲酸甲酯：

向中間物**475-1** (2200 mg，10.62 mmol)於DCM (25 mL)中之溶液中添加TEA (1.48 mL，10.6 mmol)。隨後向此溶液中添加羥胺鹽酸鹽(885

mg，12.7 mmol)且在室溫下攪拌反應混合物過夜。隨後將反應混合物濃縮成固體且溶解於EtOAc中且用水洗滌。接著將有機層經$MgSO_4$乾燥且在真空下濃縮，得到中間物**475-2** (2.1 g，73%產率)。MS (ESI) *m/z*: 257.1 (M+H)。

【0503】 **中間物475-3**：製備(Z)-3-氯-5-(氯(羥基亞胺基)甲基)-2-(二甲基胺基)苯甲酸甲酯：向含中間物**475-2** (770 mg，3.00 mmol)之DMF (15 mL)中添加*N*-氯代丁二醯亞胺(441 mg，3.30 mmol)。在用水淬滅反應混合物之後，藉由過濾收集灰白色固體，將其真空乾燥，得到中間物**475-3** (480 mg，52%產率)。MS (ESI) *m/z*: 291.0 (M+H)。

【0504】 **475-4**：製備3-氯-2-(二甲基胺基)-5-(3a,4,6,6a-四氫呋喃并[3,4-d]異噁唑-3-基)苯甲酸甲酯：向含中間物**475-3** (1.13 g，3.88 mmol)及2,5-二氫呋喃(2.72 g，38.8 mmol)之DCM (12 mL)中添加TEA (1.62 mL，11.6 mmol)。在室溫下攪拌反應混合物14h，在真空下濃縮，且使用矽膠層析純化殘餘物，得到中間物**475-4** (440 mg，35%產率)。MS (ESI) *m/z*: 325.2 (M+H)。

【0505】

475-5：製備3-氯-2-(二甲基胺基)-5-(3a,4,6,6a-四氫呋喃并[3,4-d]異噁唑-3-基)苯甲酸：

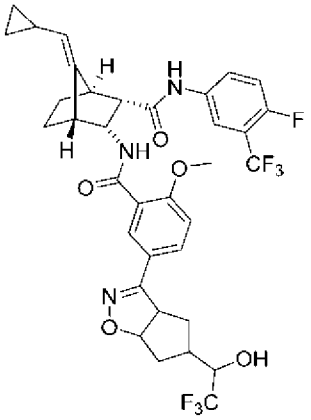
向中間物**475-4** (100 mg，0.308 mmol)於THF (3 mL)及水(1.000 mL)中之溶液中添加LiOH (0.462 mL，0.924 mmol)且在室溫下攪拌反應混合物2 h。在真空下濃縮反應混合物且不經進一步操作即用於下一步驟中。MS (ESI) *m/z*: 311.1 (M+H)。

【0506】 **實例475**：(1R,2S,3R,4R,Z)-3-(3-氯-2-(二甲基胺基)-5-

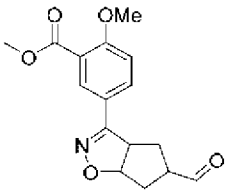
(3a,4,6,6a-四氫呋喃并[3,4-d]異噁唑-3-基)苯甲醯胺基)-N-(4-氟-3-(三氟甲基)苯基)-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-甲醯胺**475**係使用針對**378**所描述之通用程序，藉由使用環丙基降冰片烷基中間物**166-2** (75 mg，0.15 mmol)及中間物**475-5**來製備，得到**實例475** (經由逆相HPLC之第一溶離立體異構物，55mg，17%產率)。^{1}H NMR (500 MHz, DMSO-d_6) δ 10.45 (br d, *J*=5.2 Hz, 1H), 9.88 (br d, *J*=7.3 Hz, 1H), 8.12 (br d, *J*=4.6 Hz, 1H), 7.87 (s, 1H), 7.85 - 7.80 (m, 1H), 7.77 (br d, *J*=4.3 Hz, 2H), 7.45 (br t, *J*=9.8 Hz, 1H), 5.42 - 5.29 (m, 1H), 4.67 (br d, *J*=9.5 Hz, 1H), 4.55 - 4.37 (m, 2H), 4.09 (br dd, *J*=10.8, 5.0 Hz, 1H), 3.91 (br d, *J*=9.8 Hz, 1H), 3.70 - 3.57 (m, 2H), 3.15 (br d, *J*=11.0 Hz, 1H), 3.07 (br s, 1H), 2.82 (s, 6H), 2.72 (br s, 1H), 1.92 (br d, *J*=7.3 Hz, 2H), 1.60 - 1.47 (m, 1H), 1.42 (br d, *J*=18.3 Hz, 2H), 0.82 - 0.65 (m, 2H), 0.34 (br s, 2H)。MS (ESI) m/z = 661.0 (M+H)。HPLC純度：99%；滯留時間：2.96 min；方法B。

【0507】

實例489及530



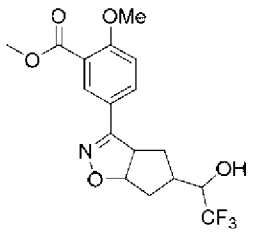
中間物489-1：



將戴斯-馬丁高碘烷(417 mg，0.983 mmol)添加至5-(5-(羥基甲基)-3a,5,6,6a-四氫-4H-環戊并[d]異噁唑-3-基)-2-甲氧基苯甲酸甲酯**429-8** (2.75 grams、9.01mmol)於DCM (90 mL)中之溶液。在3 h之後，將反應溶液轉移至分液漏斗中且依次用NH_4Cl溶液及鹽水洗滌，經硫酸鈉乾燥，過濾且在減壓下濃縮。藉由矽膠層析純化殘餘物，得到呈白色固體之5-(5-甲醯基-3a,5,6,6a-四氫-4H-環戊并[d]異噁唑-3-基)-2-甲氧基苯甲酸甲酯**489-1** (1.46公克，53%)。LC-MS RT = 0.97 min；(M+H) = 304.1；方法A。

【0508】

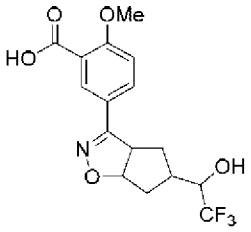
中間物489-2：



在氮氣氛圍下，向**489-1** (100 mg，0.330 mmol)於THF (3.3 mL)中之溶液中添加三甲基(三氟甲基)矽烷(188 mg，1.32 mmol)。將溶液冷卻至0℃且添加TBAF (0.40 mL，0.40 mmol)。10 min之後，使反應混合物升溫至室溫且攪拌14h。將反應物用MeOH淬滅，在減壓下濃縮於Celite®上，且藉由矽膠層析純化，得到2-甲氧基-5-(5-(2,2,2-三氟-1-羥基乙基)-3a,5,6,6a-四氫-4H-環戊并[d]異噁唑-3-基)苯甲酸甲酯**489-2** (82.2 mg，66.8%)。^1H NMR (500 MHz, $CDCl_3$) δ 8.05 - 8.01 (m, 1H), 7.84 (ddd, J=8.8, 4.7, 2.3 Hz, 1H), 7.04 - 6.98 (m, 1H), 5.24 - 5.17 (m, 1H), 4.08 (t, J=8.8 Hz, 1H), 3.94 (d, J=2.4 Hz, 3H), 3.89 (d, J=1.8 Hz, 3H), 2.38 - 2.23 (m, 2H), 2.10 - 1.96 (m, 2H), 1.89 - 1.81 (m, 1H)。LC-MS RT = 0.834 min；(M+H) = 374；方法C。

【0509】

中間物489-3：



將LiOH單水合物(27.0 mg，0.643 mmol)於H_2O (0.5 mL)中之溶液添加至含**489-2** (80 mg，0.214 mmol)之THF (2.1 mL)/MeOH(2.1 mL)。3 h之後，在減壓下濃縮反應混合物。將殘餘物懸浮於水中，用1.0M HCl溶液酸化，用EtOAc萃取，將萃取物用鹽水洗滌，經硫酸鈉乾燥，過濾且在減壓下濃縮。中間物**489-3** (71.7 mg，93%)不經進一步操作即繼續用於下一反應。LC-MS RT = 0.759 min；(M+H) = 360.0；方法C。

【0510】

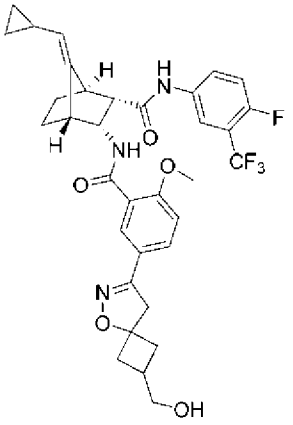
實例489係藉由使用DIEA (0.012 mL，0.068 mmol)及BOP (6.60 mg，0.015 mmol)使中間物**489-3** (3.95 mg，0.014 mmol)及溶解於無水DMF (2 mL)中之中間物**166-2** (5 mg，0.014 mmol)偶合來製備。3 h之後，將反應混合物過濾且藉由逆相製備型HPLC純化，得到(1R,2S,3R,4R,Z)-7-(環丙基亞甲基)-N-(4-氟-3-(三氟甲基)苯基)-3-(2-甲氧基-5-(5-(2,2,2-三氟-1-羥基乙基)-3a,5,6,6a-四氫-4H-環戊并[d]異噁唑-3-基)苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺**實例489** (52 mg，35%)作為第一溶離峰(RT = 10.87 min)。^{1}H NMR: (500 MHz, DMSO-d_6) δ 10.53 - 10.49 (m, 1H), 9.93 - 9.89 (m, 1H), 8.25 - 8.20 (m, 2H), 7.83 - 7.76 (m, 2H), 7.48 (t, *J*=9.8 Hz, 1H), 7.27 (d, *J*=8.9 Hz, 1H), 5.16 - 5.09 (m, 1H), 4.69 (d, *J*=9.5 Hz, 1H), 4.47 - 4.40 (m, 1H), 4.28 - 4.21 (m, 1H), 4.04 (s, 3H), 3.99 - 3.92 (m, 1H), 3.15 (dd, *J*=10.7, 4.1 Hz, 1H), 3.10 (br s, 1H),

2.74 - 2.68 (m, 1H), 2.06 - 1.96 (m, 2H), 1.94 - 1.87 (m, 1H), 1.86 - 1.72 (m, 4H), 1.54 - 1.35 (m, 3H), 0.78 - 0.69 (m, 2H), 0.38 - 0.31 (m, 2H)。LC-MS RT = 2.379 min；(M+H) = 710.4；方法C。

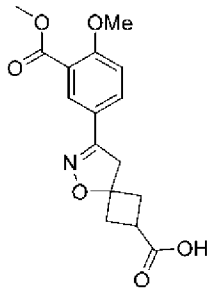
【0511】藉由**實例489**之逆相製備型HPLC單離**實例530** (25 mg，17%)作為第二溶離峰(11.52 min)。^{1}H NMR: (500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.92 (d, J=7.0 Hz, 1H), 8.27 - 8.21 (m, 2H), 7.84 - 7.77 (m, 2H), 7.49 (t, J=9.8 Hz, 1H), 7.28 (d, J=8.9 Hz, 1H), 5.15 (dd, J=8.9, 5.0 Hz, 1H), 4.70 (d, J=9.5 Hz, 1H), 4.45 (ddd, J=10.3, 6.4, 4.2 Hz, 1H), 4.25 (t, J=8.9 Hz, 1H), 4.05 (s, 3H), 3.99 - 3.92 (m, 1H), 3.17 (dd, J=10.8, 4.2 Hz, 1H), 3.11 (t, J=3.5 Hz, 1H), 2.73 (t, J=4.1 Hz, 1H), 2.04 - 1.89 (m, 3H), 1.86 - 1.76 (m, 4H), 1.54 - 1.47 (m, 1H), 1.45 - 1.38 (m, 2H), 0.79 - 0.70 (m, 2H), 0.39 - 0.33 (m, 2H)。LC-MS RT = 2.382 min；(M+H) = 710.4；方法C。

【0512】

實例511



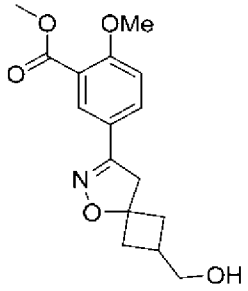
中間物511-1：



7-(4-甲氧基-3-(甲氧基羰基)苯基)-5-氧雜-6-氮雜螺[3.4]辛-6-烯-2-甲酸**511-1**係如針對中間物**378-2**所描述，以烯丙醇取代3-亞甲基環丁烷-1-甲酸來製備，得到呈茶色固體之**中間物511-1**(1 g，3 mmol，200%產率)，其不經純化即繼續用於下一步驟。LCMS(ESI) *m/z*: 320 $(M+H)^+$。

【0513】

中間物511-2：

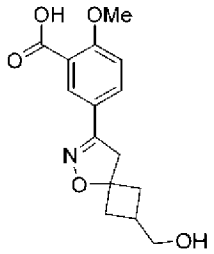


向含中間物**511-1** (0.6 g，2 mmol)之THF (15 mL)中添加$BH_3.Me_2S$ (1.4 mL，2.9 mmol)。在24h之後，再添加一當量之$BH_3.Me_2S$，且再過6h之後，用冰及1N HCl (10 mL)淬滅反應混合物，且用乙酸乙酯(3×30 mL)萃取水溶液。將合併之有機層用鹽水(15 mL)洗滌且乾燥($MgSO_4$)，過濾且在減壓下濃縮。藉由正相矽膠層析，用己烷/EtOAc溶離來純化殘餘物，得到呈白色固體之**中間物511-2** (170 mg，0.56 mmol，27%產率)。^1H NMR (500 MHz, $CDCl_3$) δ 8.05 - 7.93 (m, 1H), 7.90 - 7.82 (m, 1H), 7.06 - 6.97 (m, 1H), 3.97 - 3.93 (m, 3H), 3.90 (s, 3H), 3.70 (d, *J*=6.4 Hz, 2H), 2.73 - 2.65 (m, 2H), 2.62 - 2.54 (m, 1H), 2.52 - 2.44 (m, 1H), 2.40 - 2.31 (m, 1H), 2.22 - 2.14 (m, 2H), 1.87 (t, *J*=7.2 Hz, 1H)。LCMS(ESI)

m/z: 306.1 $(M+H)^+$。

【0514】

中間物511-3：



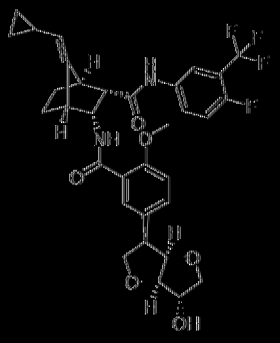
製備5-(2-(羥基甲基)-5-氧雜-6-氮雜螺[3.4]辛-6-烯-7-基)-2-甲氧基苯甲酸。中間物**511-3** (135 mg，0.460 mmol，83.0%產率)係藉由如**378-3**中所描述水解**511-2**來製備。^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (dd, *J*=5.2, 2.3 Hz, 1H), 8.18 - 8.12 (m, 1H), 7.14 (dd, *J*=8.8, 3.6 Hz, 1H), 4.15 (d, *J*=1.8 Hz, 3H), 3.73 (d, *J*=6.3 Hz, 2H), 3.48 (s, 1H), 3.42 (s, 1H), 2.55 - 2.42 (m, 1H), 2.43 - 2.33 (m, 3H), 2.27 - 2.15 (m, 3H)。LCMS(ESI) *m/z*: 291.2 $(M+H)^+$。

【0515】實例**511** (7.0 mg，11 μmol，40%產率)係藉由針對實例**452**所描述之程序，以中間物**452-3**取代中間物**511-3**來製備。^{1}H NMR (500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.91 (br d, J=7.0 Hz, 1H), 8.36 - 8.15 (m, 2H), 7.86 - 7.73 (m, 2H), 7.50 (t, J=9.8 Hz, 1H), 7.35 - 7.23 (m, 1H), 4.71 (d, J=9.5 Hz, 1H), 4.53 - 4.36 (m, 1H), 4.05 (s, 3H), 3.52 (s, 1H), 3.49 - 3.42 (m, 1H), 3.18 (br dd, J=10.7, 3.4 Hz, 1H), 3.12 (br s, 1H), 2.74 (br s, 1H), 2.49 - 2.40 (m, 1H), 2.38 - 2.31 (m, 1H), 2.30 - 2.21 (m, 1H), 2.15 - 2.09 (m, 2H), 2.08 (br s, 1H), 1.94 - 1.83 (m, 1H), 1.83 - 1.73 (m, 1H), 1.62 - 1.48 (m, 1H), 1.47 - 1.33 (m, 2H), 0.85 - 0.65 (m, 2H), 0.37 (br s, 2H)。LCMS(ESI) *m/z*: 642.91 $(M+H)^+$。HPLC純度100%，滯

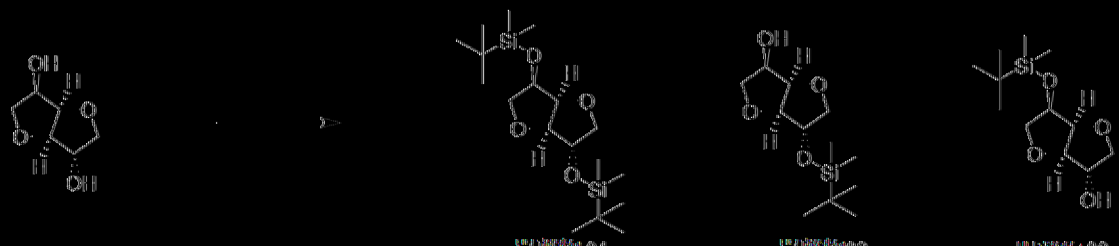
留時間2.42 min。[方法B]

[0516]

實例536



中間物536-1



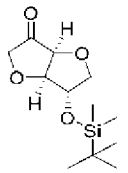
向1,6-脫水-D-葡萄糖醇(3.0 g，21 mmol)溶解於DCM(80 mL)中之溶液中添加咪唑(2.8 g，41 mmol)且冷卻至0℃。向此混合物中添加TBSCl(3.9 g，26 mmol)且使反應混合物升溫至室溫持續14h。用水洗滌反應混合物且在減壓下濃縮有機部分，接著藉由矽膠層析，利用直列光散射偵測來純化，得到中間物536-1、單離物02、(3R,3aR,6S,6aS)-6-((三級丁基二甲基矽基)氧基)六氫呋喃并[3,2-b]呋喃-3-醇(1.8 g，7.0 mmol，34%產率)。^{1}H NMR (400 MHz, $CDCl_3$) δ 4.70 – 4.58 (m, 1H), 4.39 – 4.23 (m, 3H), 3.97 – 3.82 (m, 3H), 3.55 (dd, *J* = 9.4, 6.1 Hz, 1H), 2.69 (d, *J* = 7.7 Hz, 1H), 0.97 – 0.84 (m, 9H), 0.13 (d, *J* = 2.0 Hz, 6H)

[0517] 將3，(3S,3aR,6R,6aS)-6-((三級丁基二甲基矽基)氧基)六氫呋喃并[3,2-b]呋喃-3-醇(0.92 g，3.5 mmol，17%產率)。^{1}H NMR (400 MHz, $CDCl_3$) δ 4.56 (t, *J* = 4.7 Hz, 1H), 4.41 (d, *J* = 4.4 Hz, 1H), 4.37 – 4.29

(m, 2H), 4.04 - 3.96 (m, 1H), 3.95 - 3.88 (m, 1H), 3.80 (dd, *J*=8.6, 5.9 Hz, 1H), 3.57 (dd, *J*=8.8, 6.8 Hz, 1H), 1.83 (d, *J*=5.3 Hz, 1H), 0.99 - 0.87 (m, 9H), 0.15 (d, *J*=5.7 Hz, 6H)。

【0518】

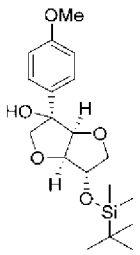
中間物536-2



向**536-1** (1.9 g，7.1 mmol)溶解於DCM(24 mL)中之溶液中添加戴斯-馬丁高碘烷(6.1 g，14 mmol)且攪拌反應混合物14h。使反應混合物分配於DCM與pH 7.4緩衝水溶液之間，且用DCM萃取。在減壓下濃縮合併之有機部分，隨後藉由矽膠層析，利用直列光散射偵測來純化，得到(3aS,6S,6aS)-6-((三級丁基二甲基矽基)氧基)四氫呋喃并[3,2-b]呋喃-3(2H)-酮(1.4 g，5.4 mmol，75%產率)。^{1}H NMR (500 MHz, $CDCL_3$) δ 4.63 (d, *J*=4.0 Hz, 1H), 4.46 (d, *J*=3.2 Hz, 1H), 4.31 (d, *J*=4.0 Hz, 1H), 4.12 (d, *J*=17.4 Hz, 1H), 4.02 (dd, *J*=9.5, 3.4 Hz, 1H), 3.95 - 3.89 (m, 2H), 0.94 - 0.88 (m, 9H), 0.12 (d, *J*=4.4 Hz, 6H)。

【0519】

中間物536-3

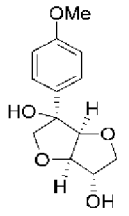


將**536-2** (1.4 g，5.4 mmol)溶解於THF (5.4 mL)中之溶液冷卻至0℃，添加(4-甲氧基苯基)溴化鎂(11 mL，5.4 mmol)且攪拌反應混合物

48h。將反應混合物用飽和NH_4Cl分配且用EtOAc萃取。在減壓下濃縮合併之有機層，接著經由矽膠層析純化，得到(3R,3aS,6S,6aS)-6-((三級丁基二甲基矽基)氧基)-3-(4-甲氧基苯基)六氫呋喃并[3,2-b]呋喃-3-醇(1.5 g，4.1 mmol，76%產率)：^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (d, *J*=8.9 Hz, 2H), 6.93 (d, *J*=8.9 Hz, 2H), 4.45 - 4.38 (m, 3H), 4.12 (d, *J*=9.3 Hz, 1H), 4.05 - 4.00 (m, 1H), 3.98 - 3.93 (m, 1H), 3.83 (s, 3H), 3.79 (d, *J*=9.3 Hz, 1H), 3.48 (s, 1H), 0.91 - 0.85 (m, 9H), 0.11 (d, *J*=3.1 Hz, 6H)。

【0520】

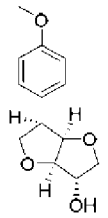
中間物536-4



向**536-3** (0.50 g，1.4 mmol)中添加1M TBAF/THF (1.4 mL，1.4 mmol)且攪拌反應混合物14h。將反應混合物用EtOAc稀釋，且依次用水及鹽水洗滌。將有機部分經Na_2SO_4乾燥，過濾且在減壓下濃縮，接著藉由矽膠層析純化，得到(3R,3aS,6S,6aR)-3-(4-甲氧基苯基)六氫呋喃并[3,2-b]呋喃-3,6-二醇(0.23 g，0.92 mmol，67%產率)。^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 - 7.43 (m, 2H), 6.99 - 6.89 (m, 2H), 4.55 (d, *J*=4.1 Hz, 1H), 4.52 - 4.45 (m, 2H), 4.14 - 4.01 (m, 3H), 3.88 - 3.78 (m, 4H), 3.40 (s, 1H)。

【0521】

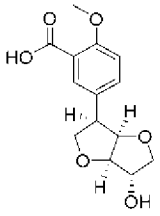
中間物536-5



向**536-4** (0.080 g，0.32 mmol)溶解於DCM (1 mL)中之溶液中添加三乙基矽烷(0.15 mL，0.95 mmol)及TFA (1 mL)，且攪拌反應混合物14h。在減壓下濃縮反應混合物，接著藉由矽膠層析純化，得到(3S,3aR,6R,6aR)-6-(4-甲氧基苯基)六氫呋喃并[3,2-b]呋喃-3-醇(0.050 g，0.21 mmol，67%產率)。^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, *J*=8.4 Hz, 2H), 6.90 (d, *J*=8.7 Hz, 2H), 4.84 (t, *J*=3.8 Hz, 1H), 4.60 (d, *J*=3.7 Hz, 1H), 4.43 - 4.38 (m, 1H), 4.23 (t, *J*=8.1 Hz, 1H), 4.02 (dd, *J*=10.1, 3.8 Hz, 1H), 3.91 - 3.83 (m, 2H), 3.82 (s, 3H), 3.41 (ddd, *J*=11.6, 7.8, 4.0 Hz, 1H)

【0522】

中間物536-6



向**536-5** (0.050 g，0.21 mmol)溶解於丙酮(2.1 mL)中之溶液中添加NBS (0.040 g，0.22 mmol)，隨後添加1滴1N HCl且攪拌14h。將反應混合物用EtOAc稀釋且用1M pH 7.4磷酸鹽緩衝液洗滌。在減壓下濃縮有機部分，接著藉由矽膠層析純化，得到(3S,3aR,6R,6aR)-6-(3-溴-4-甲氧基苯基)六氫呋喃并[3,2-b]呋喃-3-醇(定量)，其不經進一步操作即用於下一步驟中。

【0523】 向(3S,3aR,6R,6aR)-6-(3-溴-4-甲氧基苯基)六氫呋喃并

[3,2-b]呋喃-3-醇(0.090 g，0.21 mmol)溶解於DMF(2.6 mL)中之漿液中添加$Pd(OAc)_2$ (0.019 g，0.085 mmol)、1,3-雙(二苯基膦基)丙烷(0.035 g，0.085 mmol)、TEA (0.12 mL，0.85 mmol)及水(0.29 mL)。將反應混合物掩蓋於CO (100 psi)下且加熱至100℃持續14h。將反應混合物用EtOAc稀釋，用1 N HCl分配且用EtOAc萃取。在減壓下濃縮經合併之有機部分，接著不經進一步操作即以5-((3R,3aR,6S,6aR)-6-羥基六氫呋喃并[3,2-b]呋喃-3-基)-2-甲氧基苯甲酸(0.046 g，0.16 mmol，785產率，兩個步驟)用於下一步驟中。

【0524】

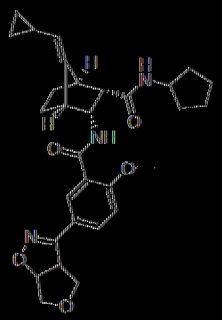
實例536

向**166-2** (0.060 g，0.16 mmol)溶解於ACN (3.3 mL)中之溶液中添加**536-6** (0.046 g，0.16 mmol)、DIEA (0.085 mL，0.49 mmol)及HATU (0.062 g，0.16 mmol)且攪拌反應混合物30 min。將反應混合物用甲醇稀釋且藉由製備型逆相HPLC純化，得到(1R,2S,3R,4R,Z)-7-(環丙基亞甲基)-N-(4-氟-3-(三氟甲基)苯基)-3-(5-((3R,3aR,6S,6aR)-6-羥基六氫呋喃并[3,2-b]呋喃-3-基)-2-甲氧基苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺(13 mg，0.021 mmol，13%產率)。^{1}H NMR (500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.84 (br d, J=7.0 Hz, 1H), 8.24 (br d, J=4.9 Hz, 1H), 7.88 (s, 1H), 7.83 - 7.71 (m, 1H), 7.50 (br t, J=9.5 Hz, 1H), 7.43 (br d, J=8.2 Hz, 1H), 7.12 (d, J=8.5 Hz, 1H), 5.26 (d, J=3.4 Hz, 1H), 4.76 - 4.61 (m, 2H), 4.52 - 4.39 (m, 2H), 4.17 - 4.06 (m, 2H), 3.99 (s, 3H), 3.81 (br dd, J=9.2, 3.1 Hz, 1H), 3.73 - 3.60 (m, 2H), 3.17 (br dd, J=10.8, 4.1 Hz, 1H), 3.10 (br s, 1H), 2.73 (br s, 1H), 1.91 - 1.84 (m, 1H), 1.83 - 1.71 (m, 1H), 1.51 (br dd,

J = 8.2, 4.6 Hz, 1H), 1.47 – 1.31 (m, 2H), 0.82 – 0.67 (m, 2H), 0.37 (br s, 2H)。LC-MS RT: 2.34 min；MS (ESI) *m/z* 631.2 $(M+H)^+$；方法A。

|0525|

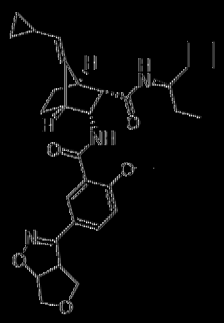
實例565



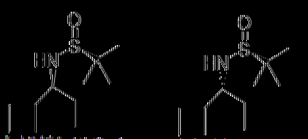
向中間物447-1 (20 mg，0.028 mmol)於DCM (0.5 mL)中之溶液中添加環戊胺(24 mg，0.28 mmol)。攪拌反應混合物14h，隨後在減壓下濃縮，溶解於MeOH中，且經由針筒過濾器過濾。經由製備型逆相HPLC純化殘餘物，得到實例565 (12.2 mg，84%)。^{1}H NMR (400 MHz, DMSO-d_6) δ 10.01 (d, *J* = 6.8 Hz, 1H), 8.15 (d, *J* = 2.4 Hz, 1H), 8.02 (d, *J* = 7.6 Hz, 1H), 7.79 (dd, *J* = 8.6, 2.4 Hz, 1H), 7.24 (d, *J* = 8.7 Hz, 1H), 5.34 (dd, *J* = 9.6, 3.2 Hz, 1H), 4.61 (d, *J* = 9.7 Hz, 1H), 4.50 (dd, *J* = 8.3, 6.6 Hz, 1H), 4.34 – 4.22 (m, 1H), 4.09 (d, *J* = 10.8 Hz, 1H), 4.02 (s, 4H), 3.90 (d, *J* = 9.3 Hz, 1H), 3.81 – 3.72 (m, 1H), 3.66 (dd, *J* = 10.6, 3.9 Hz, 1H), 3.09 – 3.01 (m, 1H), 2.88 (dd, *J* = 11.1, 4.4 Hz, 1H), 1.88 – 1.70 (m, 4H), 1.65 – 1.54 (m, 2H), 1.53 – 1.40 (m, 3H), 1.39 – 1.26 (m, 4H), 0.76 – 0.64 (m, 2H), 0.32 (br d, *J* = 3.5 Hz, 2H)。可能由於與溶劑峰重疊，一個質子在NMR中不可見。LC-MS RT: 2.14 min；MS (ESI) *m/z* 520.4 $(M+H)^+$；方法B。

|0526|

實例578



中間物578-1及578-2：



中間物578-1　　中間物578-2

在乾冰/內酮浴中冷卻(S,E)-N-(環丁基亞甲基)-2-甲基丙烷-2-亞磺醯胺(0.500 g，2.67 mmol)之溶液。逐滴添加溴化乙基鎂(3.6 M於2Me-THF中) (1.48 mL，5.34 mmol)，且使反應混合物升溫至室溫持續14h。將反應混合物用飽和氯化銨溶液淬滅且用DCM萃取兩次。在減壓下濃縮有機層。經由矽膠層析純化殘餘物，得到533 mg非鏡像異構物之混合物。經由製備型SFC在以下條件下分離非鏡像異構物：儀器：PIC Solution SFC Prep 200；管柱：Chiralpak AD-H，21 × 250 mm，5微米；移動相15%異丙醇-乙腈， 85% CO_2；流動速率：45 mL/min，150巴；管柱溫度：40 ℃。

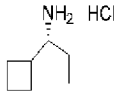
[0527] (S)-N-((S)-1-環丁基乙基)-2-甲基丙烷-2-亞磺醯胺中間物578-1峰1 RT: 6 min (70 mg，0.32 mmol，12%產率)。分析型SFC條件：儀器：Shimadzu Nexera SFC；管柱：Chiralpak AD-H，4.6 × 100 mm，3微米；移動相10%異丙醇-乙腈，90% CO_2；流動速率：42 mL/min，150巴；管柱溫度：40 ℃。RT: 2.09 min MS (ESI) *m/z* 218(M+H)$^+$

[0528] (S)-N-((R)-1-環丁基乙基)-2-甲基丙烷-2-亞磺醯胺中間物578-2峰2 RT: 8.7 min。(350 mg，1.61 mmol，60.3%產率)。分析型SFC

條件：儀器：Shimadzu Nexera SFC；管柱：Chiralpak AD-H，4.6 × 100 mm，3微米；移動相10%異丙醇-乙腈，90% CO_2；流動速率：42 mL/min，150巴；管柱溫度：40 ℃。RT: 2.26 min MS (ESI) *m/z* 218$(M+H)^+$。

【0529】

中間物578-3：



向**578-2** (350 mg，1.61 mmol)於MeOH(0.8 mL)中之溶液中添加HCl (4M於二噁烷中) (0.81 mL，3.2 mmol)。45分鐘之後，真空濃縮反應混合物。添加Et_2O，接著濾出固體且用Et_2O/己烷洗滌。收集固體且在真空下乾燥，得到(R)-1-環丁基丙烷-1-胺**578-3** (175 mg，1.55 mmol，96%產率)。^{1}H NMR (400 MHz, CD_3OD) δ 3.06 - 2.97 (m, 1H), 2.55 - 2.41 (m, 1H), 2.17 - 2.04 (m, 2H), 2.03 - 1.80 (m, 4H), 1.73 - 1.59 (m, 1H), 1.55 - 1.42 (m, 1H), 0.99 (t, *J*=7.6 Hz, 3H)。

【0530】

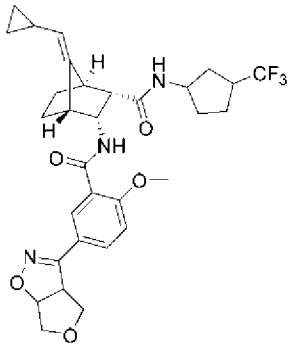
實例578

實例578 (4.8 mg，49%)係遵循針對**實例378**所給出之程序由**578-3**製備。^{1}H NMR (500 MHz, DMSO-d_6) δ 10.04 (d, *J*=6.8 Hz, 1H), 8.15 (d, *J*=2.4 Hz, 1H), 7.78 (dd, *J*=8.6, 2.4 Hz, 1H), 7.70 (br d, *J*=9.1 Hz, 1H), 7.23 (d, *J*=8.8 Hz, 1H), 5.33 (dd, *J*=9.2, 3.5 Hz, 1H), 4.62 (d, *J*=9.6 Hz, 1H), 4.49 (br t, *J*=7.9 Hz, 1H), 4.33 - 4.24 (m, 1H), 4.09 (d, *J*=10.7 Hz, 1H), 4.00 (s, 3H), 3.92 - 3.87 (m, 1H), 3.77 (dd, *J*=9.2, 6.7 Hz, 1H), 3.71 - 3.59 (m, 2H), 3.09 - 3.01 (m, 1H), 2.98 - 2.88 (m, 1H), 2.33 - 2.19 (m,

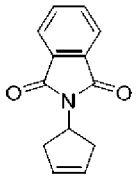
1H), 1.95 - 1.60 (m, 8H), 1.51 - 1.41 (m, 1H), 1.40 - 1.25 (m, 3H), 1.19 - 1.03 (m, 1H), 0.82 - 0.62 (m, 5H), 0.31 (dd, *J*=4.5, 2.2 Hz, 2H)。可能由於與溶劑峰重疊，一個質子在NMR中不可見。LC-MS RT: 2.58 min；MS (ESI) *m/z* 548.2 $(M+H)^+$；方法B。

【0531】

實例589及629：



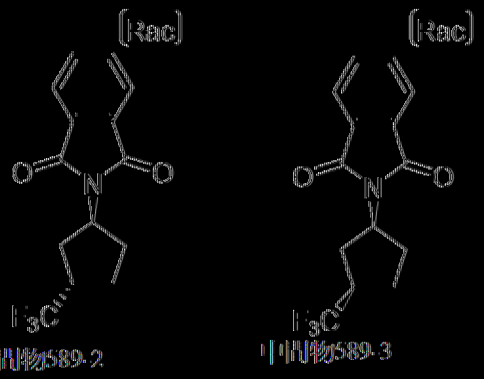
中間物589-1：



向異苯并呋喃-1,3-二酮(372 mg，2.51 mmol)及環戊-3-烯-1-胺HCl (300 mg，2.51 mmol)於甲苯(25 mL)中之懸浮液中添加休尼格氏鹼(0.44 mL，2.5 mmol)。將反應混合物加熱至120℃。大約5.5小時之後，在減壓下濃縮反應混合物。經由矽膠層析純化殘餘物，得到**中間物589-1** (369 mg，69%)。^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 - 7.80 (m, 2H), 7.76 - 7.67 (m, 2H), 5.81 (s, 2H), 5.02 (tt, *J*=9.6, 7.4 Hz, 1H), 2.93 - 2.82 (m, 2H), 2.74 - 2.63 (m, 2H)。

【0532】

中間物589-2及589-3：



中間物589-2　　中間物589-3

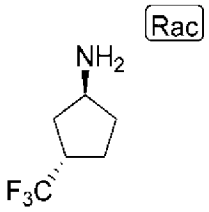
在四個壓力小瓶中之每一者中，使三氟甲烷磺酸鈉(234 mg，1.50 mmol)、9-均三甲苯基-10-甲基吖啶-10-鎓四氟硼酸鹽(15 mg，0.038 mmol)及rac-2-((1R,3R)-3-(三氟甲基)環戊基)異吲哚啉-1,3-二酮(273 mg，0.964 mmol)懸浮於$CHCl_3$ (3.4 mL)及三氟乙醇(0.38 mL)中。使氮氣鼓泡通過溶液，接著添加2-巰基苯甲酸甲酯(25 mg，0.15 mmol)，且使氮氣短暫鼓泡通過溶液。密封小瓶且用KSH 150B藍色Kessil生長燈(34W，λ最大值461 nm)照射48h。將反應混合物自光反應器移除且倒入$NaHCO_3$飽和水溶液中。用DCM萃取反應混合物三次。將有機層經硫酸鈉乾燥且真空濃縮。經由矽膠層析純化殘餘物。

[0533] 第一溶離峰為反式產物rac-2-((1R,3R)-3-(三氟甲基)環戊基)異吲哚啉-1,3-二酮中間物589-2 (273 mg，0.964 mmol，32.1%產率)。^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.77 – 7.68 (m, 2H), 4.88 – 4.72 (m, 1H), 3.22 – 3.06 (m, 1H), 2.37 (ddd, *J* = 14.0, 9.6, 6.9 Hz, 1H), 2.29 – 2.05 (m, 4H), 1.85 – 1.70 (m, 1H)

[0534] 第二溶離峰為順式產物中間物589-3 rac-2-((1R,3S)-3-(三氟甲基)環戊基)異吲哚啉-1,3-二酮(38 mg，0.134 mmol，4.47%產率)。^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 – 7.79 (m, 2H), 7.77 – 7.65 (m, 2H), 4.73 – 4.58 (m, 1H), 2.83 – 2.59 (m, 1H), 2.55 – 2.30 (m, 2H), 2.22 – 2.08 (m, 2H), 2.06 – 1.84 (m, 2H)。

【0535】

中間物589-4：



向**中間物589-2**於EtOH (1.8 mL)中之懸浮液中添加水合肼(29 µl，0.39 mmol)。將反應混合物加熱至75℃。大約30分鐘之後，添加1 mL EtOH。在2.5小時之後，使反應混合物冷卻，用EtOH稀釋且過濾。90 µL含4M HCl之二噁烷添加至濾液中且真空濃縮溶液。所得殘餘物含有約0.25 equiv之酞肼酮。使殘餘物懸浮於EtOH中且過濾。在減壓下濃縮濾液，得到**中間物589-4** rac-(1R,3R)-3-(三氟甲基)環戊-1-胺HCl (83 mg，0.44 mmol，120%產率)，其含有約0.1當量之酞肼酮。^{1}H NMR (400 MHz, CD_3OD) δ 3.74 - 3.65 (m, 1H), 3.06 - 2.91 (m, 1H), 2.29 - 2.09 (m, 3H), 2.00 - 1.87 (m, 1H), 1.85 - 1.64 (m, 2H)。

【0536】

實例629及589：

根據針對**實例565**所給出之程序製備**實例629及589**之非鏡像異構混合物。非鏡像異構物係經由製備型SFC在以下條件下分離：管柱：Chiral OD，30 × 250 mm，5微米；移動相：80% CO_2 /20% IPA (具有0.1%DEA)；流動速率：100 mL/min，120巴；管柱溫度：40℃。

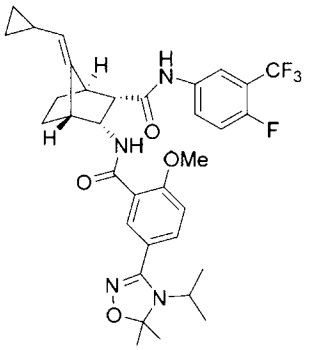
【0537】 第一溶離峰(RT=13.5 min)為**實例629** (0.8 mg，3.7%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 9.95 (br d, *J*=7.0 Hz, 1H), 8.17 (br d, *J*=2.1 Hz, 2H), 7.79 (br d, *J*=8.2 Hz, 1H), 7.29 - 7.20 (m, 1H), 5.34 (br dd, *J*=9.2, 3.1 Hz, 1H), 4.62 (br d, *J*=9.5 Hz, 1H), 4.50 (br t, *J*=7.8 Hz, 1H), 4.35 -

4.25 (m, 1H), 4.18 - 4.07 (m, 2H), 4.02 (s, 3H), 3.94 - 3.86 (m, 1H), 3.82 - 3.72 (m, 1H), 3.69 - 3.61 (m, 1H), 3.05 (br s, 1H), 2.98 - 2.82 (m, 2H), 2.04 - 1.40 (m, 9H), 1.39 - 1.26 (m, 2H), 0.76 - 0.65 (m, 2H), 0.32 (br d, *J*=2.4 Hz, 2H)。可能由於與經抑制之水峰重疊，一個質子在NMR中不可見。LC-MS RT: 2.30 min；MS (ESI) *m/z* 588.3 $(M+H)^+$；方法B。

【0538】 第二溶離峰(RT=16.0 min)為**實例589** (0.7 mg，3.4%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 9.95 (br d, *J*=7.3 Hz, 1H), 8.17 (br d, *J*=8.5 Hz, 2H), 7.79 (br d, *J*=8.5 Hz, 1H), 7.29 - 7.18 (m, 1H), 5.40 - 5.27 (m, 1H), 4.62 (br d, *J*=9.5 Hz, 1H), 4.54 - 4.45 (m, 1H), 4.35 - 4.25 (m, 1H), 4.16 - 4.06 (m, 2H), 4.02 (s, 3H), 3.90 (br d, *J*=5.8 Hz, 1H), 3.82 - 3.74 (m, 1H), 3.66 (br dd, *J*=7.0, 3.4 Hz, 1H), 3.08 - 3.02 (m, 1H), 2.98 - 2.83 (m, 2H), 2.02 - 1.41 (m, 9H), 1.40 - 1.26 (m, 2H), 0.76 - 0.66 (m, 2H), 0.32 (br d, *J*=3.7 Hz, 2H)。LC-MS RT: 2.23 min；MS (ESI) *m/z* 588.5 $(M+H)^+$；方法B。

【0539】

實例591



製備中間物**591-1**。5-(4-異丙基-5,5-二甲基-4,5-二氫-1,2,4-噁二唑-3-基)-2-甲氧基苯甲酸。藉由添加nBuLi (2.7M，2.3 mL，6.3 mmol)至冷卻至-78℃之二異丙胺(0.64 g，6.33 mmol)之THF (15 mL)溶液來產生LDA。冷攪拌反應混合物0.5 h且添加甲基-3-環戊烯甲酸鹽(0.4 g，3.0

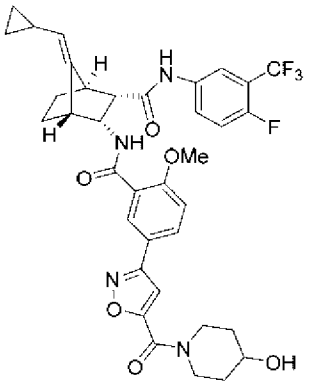
mmol)，隨後添加碘甲烷(0.2 mL，3.0 mmol)。將反應混合物低溫攪拌4 h且逐漸使其升溫至室溫持續14h。接著向反應混合物中添加(E)-5-(氯(羥基亞胺基)甲基)-2-甲氧基苯甲酸甲酯(1.05 g，4.32 mmol)，隨後添加TEA (1.4 mL，9.1 mmol)且在室溫下攪拌所得溶液14h。藉由添加稀釋HCl (1N，10 ml)淬滅反應物且用EtOAc (2×25 mL)萃取。將合併之有機部分乾燥($MgSO_4$)，過濾且在減壓下濃縮為油狀物。經由矽膠層析，使用己烷/EtOAc作為溶離劑純化該油狀物，得到呈固體之5-(4-異丙基-5,5-二甲基-4,5-二氫-1,2,4-噁二唑-3-基)-2-甲氧基苯甲酸甲酯中間物副產物(75 mg，8%產率)。將固體溶解於MeOH (2 mL)中且向該溶液中添加LiOH (10 mg. 0.24 mmol)及水(2 mL)。在室溫下攪拌反應混合物14h，接著在減壓下濃縮且用稀釋HCl (1N，5 mL)淬滅。將溶液轉移至分液漏斗中且用EtOAc (2×25 mL)萃取，將有機部分乾燥($MgSO_4$)，過濾且在減壓下濃縮為固體**591-1** (60 mg，85%產率)，其不經進一步操作即使用。^{1}H NMR (500 MHz, $CDCl_3$) δ 8.29 - 8.19 (m, 1H), 7.76 (dd, J=8.5, 2.3 Hz, 1H), 7.14 (d, J=8.3 Hz, 1H), 4.12 (s, 3H), 3.61 (spt, J=7.0 Hz, 1H), 1.63 (s, 6H), 1.84 - 0.82 (d, 6H)。LCMS m/z = 293.3 $(M+H)^+$。

【0540】 **實例591.** 如針對實例**378**中所描述使用BOP (13.62 mg，0.03 mmol)試劑及休尼格氏鹼(0.1 mL)使中間物**591-1** (9 mg，0.03 mmol)與**166-2** (11.34 mg，0.03 mmol)偶合，以在藉由製備型逆相HPLC純化之後得到呈固體之實例**591**(8.4 mg，41%產率)。HPLC純度：96.5%；RT= 2.67 min [方法B]。LCMS m/z = 643.18 $(M+H)^+$. ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.54 (s, 1H), 9.96 (br d, *J*=6.7 Hz, 1H), 8.23 (br d, *J*=4.0 Hz, 1H), 8.03 (d, *J*=2.1 Hz, 1H), 7.79 (br d, *J*=8.9 Hz, 1H), 7.61 (dd, *J*=8.5, 2.1 Hz, 1H), 7.49 (br t, *J*=9.8 Hz, 1H), 7.31 (d, *J*=8.5 Hz, 1H), 4.70

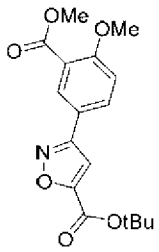
(d, *J*=9.5 Hz, 1H), 4.46 (br s, 1H), 4.07 (s, 3H), 3.68 - 3.48 (m, 1H), 3.41 (br s, 1H), 3.28 - 3.13 (m, 1H), 3.11 (br s, 1H), 2.73 (br s, 1H), 1.92 - 1.75 (m, 2H), 1.51 (s, 6H), 1.43 (br t, *J*=10.7 Hz, 2H), 1.06 (br d, *J*=6.7 Hz, 6H), 0.86 - 0.66 (m, 2H), 0.36 (br s, 2H)

【0541】

實例594



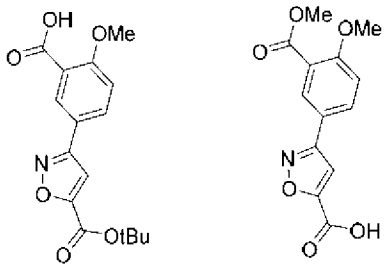
製備中間物**594-1**。



中間物**594-1** (434 mg，60.0%產率)係以如針對實例**378**所描述之類似方式，藉由如先前所描述將(Z)-5-(氯(羥基亞胺基)甲基)-2-甲氧基苯甲酸甲酯(530 mg，2.18 mol)與丙炔酸三級丁酯(274 mg，2.17 mmol)及TEA (2 mL)在DCM中進行環化加成來製備。LCMS m/z = 334.3 $(M+H)^+$。

【0542】

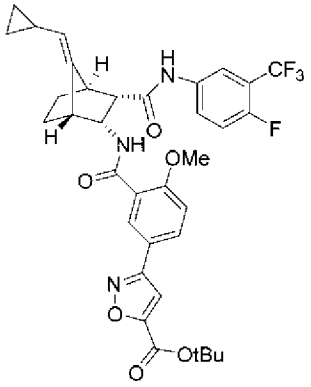
製備中間物**594-2**。



如實例378中先前所描述，使中間物**594-1** (100 mg，0.30 mmol)與LiOH (12 mg，0.35 mmol)一起在甲醇/水中水解，得到呈兩種產物之混合物形式之**594-2** (75 mg)。對於所需產物，LCMS m/z = 278.2 (M+H)。另一副產物為三級丁酯裂解為酸產物。粗混合物不經進一步操作即繼續用於下一步驟中。

【0543】

製備中間物**594-3**。



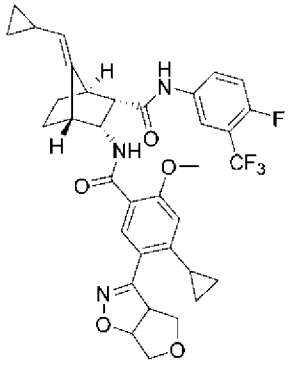
使中間物**594-2** (60 mg，0.22 mmol，作為混合物之部分)溶解於DMF (1 mL)中，且向其中添加4-OH-哌啶(22 mg，0.22 mmol)，隨後添加BOP (6 mg，0.22 mmol)試劑及休尼格氏鹼(0.1 mL)。在室溫下攪拌反應混合物14 h，用水(25 mL)淬滅且用EtOAc (2×25 mL)萃取。將合併之有機部分經燥且真空濃縮為油狀物。LCMS m/z = 361.2 (M+H)。將所得油狀物溶解於甲醇(1 mL)中且向其中添加LiOH (10 mg，0.2 mmol)，隨後添加水(1 mL)，且攪拌反應混合物14 h。將反應混合物用水(25 mL)稀釋且用EtOAc (2×25 mL)萃取。將合併之有機部分乾燥($MgSO_4$)且真空濃縮，得到呈油狀物之**594-3** (LCMS m/z = 347.3 (M+H))，其不經進一步純化即

用於下一步驟中。

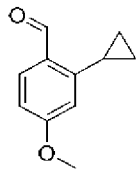
【0544】 **實例594.** 使用BOP (10 mg，0.02 mmol)試劑及休尼格氏鹼(0.1 mL)使中間物**594-3** (8 mg，0.02 mmol)與**166-2** (8.5 mg，0.020 mmol)偶合，以在以下條件下藉由製備型LC/MS純化之後得到呈固體之實例**594** (3.6 mg，22%產率)：管柱：XBridge C18，200 mm × 19 mm，5-μm粒子；移動相A：5:95 乙腈:水(具有0.05%三氟乙酸)；移動相B：95:5 乙腈:水(具有0.05%三氟乙酸)。HPLC純度：98.1%；RT= 2.30 min [方法B]。LCMS m/z = 697.01 $(M+H)^+$. ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.55 (s, 1H), 9.94 (br d, *J*=6.4 Hz, 1H), 9.26 - 9.19 (m, 1H), 8.27 (d, *J*=2.3 Hz, 1H), 8.22 (br d, *J*=4.6 Hz, 1H), 7.80 (br dd, *J*=8.6, 2.1 Hz, 2H), 7.48 (br t, *J*=9.7 Hz, 1H), 7.35 (d, *J*=8.8 Hz, 1H), 7.27 - 7.21 (bs, 1H), 7.17 - 7.13 (bs, 1H), 7.09 (bs, 1H)4.69 (d, *J*=9.5 Hz, 1H), 4.44 (br s, 1H), 4.06 (s, 3H), 3.67 (br s, 1H), 3.51 (m, 2H), 3.34 - 3.13 (m, 1H), 3.10 (br s, 1H), 2.80 - 2.63 (m, 1H), 1.83 (br d, *J*=9.8 Hz, 1H), 1.77 (br s, 2H), 1.50 (br s, 1H), 1.45 (br s, 1H), 1.41 (br s, 2H), 1.16 (t, *J*=7.3 Hz, 1H), 1.10 (br s, 1H), 0.86 - 0.68 (m, 2H), 0.35 (br s, 2H)

【0545】

實例626



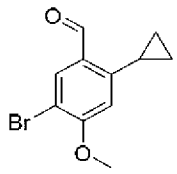
中間物626-1



製備2-環丙基-4-甲氧基苯甲醛。中間物**626-1** (0.30 g，1.9 mmol，84%產率)係以針對實例**12**描述之方式，以實例**11**及呋喃-3-基硼酸(boronic acid)取代2-溴-4-甲氧基苯甲醛及環丙基硼酸且以THF取代二噁烷來製備。^{1}H NMR (400 MHz, $CDCl_3$) δ 10.46 (s, 1H), 7.83 (d, *J*=8.6 Hz, 1H), 6.84 (dd, *J*=8.7, 2.5 Hz, 1H), 6.62 (d, *J*=2.4 Hz, 1H), 3.89 (s, 3H), 2.70 (tt, *J*=8.5, 5.4 Hz, 1H), 1.15 - 1.07 (m, 2H), 0.86 - 0.76 (m, 2H)。LCMS(ESI) *m/z*:177.1 $(M+H)^+$。

【0546】

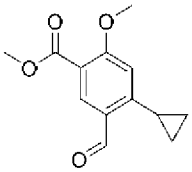
中間物626-2



製備5-溴-2-環丙基-4-甲氧基苯甲醛。向冷卻至0℃的含**626-1** (0.30 g，1.9 mmol)之MeOH (10 mL)中添加過溴化氫溴酸吡啶(0.60 g，1.9 mmol)。24 h之後，真空移除溶劑且藉由正相矽膠層析，用己烷/EtOAc溶離來純化殘餘物，得到呈白色固體之中間物**626-2** (0.31 g，1.2 mmol，65%產率)。^{1}H NMR (400 MHz, $CDCl_3$) δ 10.45 (s, 1H), 8.04 (s, 1H), 6.63 (s, 1H), 3.98 (s, 3H), 2.68 - 2.55 (m, 1H), 1.20 - 1.11 (m, 2H), 0.88 - 0.78 (m, 2H)。

【0547】

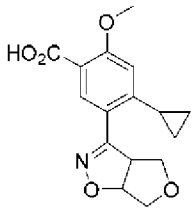
中間物626-3：



製備4-環丙基-5-甲醯基-2-甲氧基苯甲酸甲酯。除使用$PdOAc_2$、dppf及DMSO/MeOH之外，中間物**626-3** (0.16 g，0.70 mmol，58%產率)係以與中間物**323-1**類似之方式製備。^{1}H NMR (400 MHz, $CDCl_3$) δ 10.40 (s, 1H), 8.33 (s, 1H), 6.64 (s, 1H), 3.99 (s, 3H), 3.93 (s, 3H), 2.96 - 2.71 (m, 1H), 1.25 - 1.13 (m, 2H), 0.87 (dd, *J*=5.3, 1.8 Hz, 2H)。LCMS(ESI) *m/z*:235.2 $(M+H)^+$。

【0548】

中間物626-4：



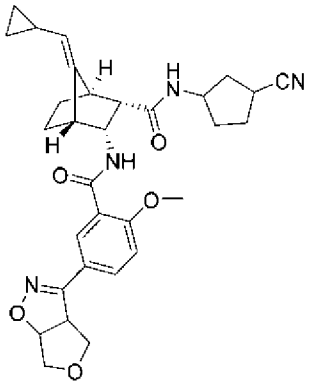
製備4-環丙基-2-甲氧基-5-(3a,4,6,6a-四氫呋喃并[3,4-d]異噁唑-3-基)苯甲酸。遵循針對實例**378**及實例**416**之通用程序，但以5-甲醯基-2-甲氧基苯甲酸甲酯取代**626-3**，得到**626-4** (46 mg，0.15 mmol，91%產率)。^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (s, 1H), 6.68 (s, 1H), 5.38 (dd, *J*=9.2, 3.7 Hz, 1H), 4.48 (t, *J*=7.5 Hz, 1H), 4.37 (d, *J*=10.6 Hz, 1H), 4.12 (s, 3H), 4.03 (d, *J*=9.5 Hz, 1H), 3.86 - 3.75 (m, 2H), 2.77 - 2.63 (m, 1H), 1.28 - 1.20 (m, 1H), 1.18 - 1.10 (m, 1H), 0.85 - 0.72 (m, 2H)。LCMS(ESI) *m/z*: 304.3 $(M+H)^+$。

【0549】 實例**626.** 非鏡像異構物之混合物係藉由如實**例378**中所描述之BOP偶合，以中間物**378 -3**及環丁基降冰片烷基中間物**369-1**取代環丙基降冰片烷基中間物**166-2**及中間物**626-4**來製備。使用以下將非鏡像異構物之混合物分離成個別異構物：對掌性SFC儀器：Waters 100 Prep SFC 管柱：Chiral AD，30 × 250 mm，5微米，移動相：25% MeOH / 75%

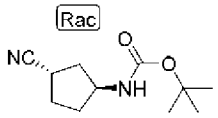
CO_2 (具有0.1% DEA)，流動條件：100 mL/min，偵測器波長：220 nm；分析方法：儀器：Shimadzu Nexera SFC，管柱Chiral AD，4.6 × 100 mm，5微米，移動相：25% MeOH / 75% CO_2 (具有0.1% DEA)，流動條件：2 mL/min，偵測器波長：220 nm，得到對掌性峰-1 (實例**626**) (8.2 mg，12 μmol，16%產率)，RT=2.6 min.，>95% de及對掌性峰-2 (8.1 mg，12 μmol，16%產率)，RT=3.3 min.，>95% de。對於實例**626**：^{1}H NMR (500 MHz, DMSO-d_6) δ 10.53 (s, 1H), 9.85 (br d, *J*=7.0 Hz, 1H), 8.31 - 8.18 (m, 1H), 7.90 (s, 1H), 7.82 - 7.74 (m, 1H), 7.48 (t, *J*=9.6 Hz, 1H), 6.68 (s, 1H), 5.32 (dd, *J*=9.0, 3.5 Hz, 1H), 4.69 (d, *J*=9.5 Hz, 1H), 4.56 (br t, *J*=7.6 Hz, 1H), 4.47 - 4.39 (m, 1H), 4.11 (br d, *J*=10.7 Hz, 1H), 4.04 (s, 3H), 3.76 (br d, *J*=8.9 Hz, 1H), 3.65 (br dd, *J*=10.5, 4.4 Hz, 1H), 3.48 (br s, 1H), 3.15 (br dd, *J*=10.8, 3.2 Hz, 1H), 3.09 (br s, 1H), 2.78 - 2.67 (m, 1H), 2.41 - 2.32 (m, 1H), 1.92 - 1.81 (m, 1H), 1.79 - 1.72 (m, 1H), 1.56 - 1.46 (m, 1H), 1.45 - 1.33 (m, 2H), 1.06 (br dd, *J*=8.7, 5.6 Hz, 1H), 1.02 - 0.94 (m, 1H), 0.93 - 0.87 (m, 1H), 0.87 - 0.81 (m, 1H), 0.79 - 0.67 (m, 2H), 0.35 (br s, 2H)。LCMS(ESI) *m/z*: 653.93 $(M+H)^+$。HPLC純度95%，滯留時間2.65 min。[方法C]。

【0550】

實例664及實例702



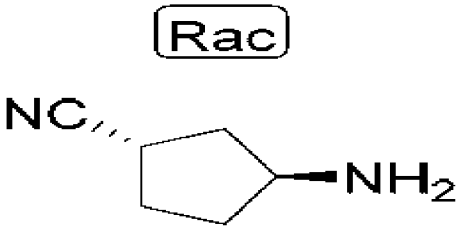
中間物664-1：



將rac-((1R,3S)-3-羥基環戊基)胺基甲酸三級丁酯(260 mg，1.29 mmol)溶解於DCM (15 mL)中。添加休尼格氏鹼(1.13 mL，6.46 mmol)及MsCl (0.101 mL，1.29 mmol)。2小時之後，真空濃縮反應混合物。用乙腈(20 mL)稀釋殘餘物，且添加氰化四丁基銨(347 mg，1.29 mmol)。1小時之後，真空濃縮反應混合物。經由矽膠層析純化殘餘物，得到**664-1** (135 mg，50%)。^{1}H NMR (400 MHz, $CDCl_3$) δ 4.48 (br d, *J*=4.3 Hz, 1H), 4.18 - 4.05 (m, 1H), 2.99 - 2.85 (m, 1H), 2.30 - 2.13 (m, 3H), 2.06 - 1.85 (m, 2H), 1.58 - 1.49 (m, 1H), 1.44 (s, 9H)。

【0551】

中間物664-2：



將rac-((1R,3R)-3-氰基環戊基)胺基甲酸三級丁酯(65 mg，0.31 mmol)溶解於DCM (1.9 mL)中。添加TFA (0.19 mL，2.5 mmol)。3小時之後，添加TFA (0.19 mL，2.5 mmol)。再過1.5小時之後，真空濃縮反應混合物，隨後與DCM及己烷共沸。獲得rac-(1R,3R)-3-胺基環戊烷-1-甲腈TFA (131 mg，0.584 mmol，189%產率)且不經進一步純化即繼續使用。^{1}H NMR (400 MHz, CD_3OD) δ 3.99 - 3.84 (m, 1H), 2.53 - 2.34 (m, 3H), 2.31 - 2.19 (m, 1H), 2.11 - 2.00 (m, 1H), 1.85 (dt, *J*=14.1, 7.0 Hz, 1H)。

【0552】

實例642及**實例702**：

實例642與**實例702**之混合物係根據針對實例**447**所描述之程序由**中間物642-2**製備。在以下條件下經由製備型逆相HPLC純化所得物質：管柱：XBridge C18, 200 mm × 19 mm, 5-μm粒子；移動相A：5:95乙腈:水(具有乙酸銨)；移動相B：95:5乙腈:水(具有乙酸銨)；梯度：在25% B下保持0分鐘，在30分鐘內25至70% B，隨後在100% B下保持0分鐘；流動速率：20 mL/min；管柱溫度：25℃。藉由MS信號觸發溶離份收集。合併含有所需產物之溶離份且經由離心蒸發乾燥。

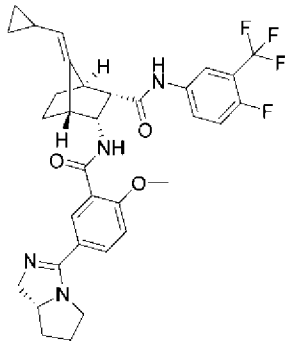
【0553】 峰1為**實例664** (6.3 mg，41%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 9.95 (br d, *J*=7.0 Hz, 1H), 8.21 - 8.14 (m, 2H), 7.79 (dd, *J*=8.5, 2.1 Hz, 1H), 7.24 (d, *J*=8.5 Hz, 1H), 5.34 (dd, *J*=9.0, 3.2 Hz, 1H), 4.61 (br d, *J*=9.5 Hz, 1H), 4.50 (br t, *J*=7.3 Hz, 1H), 4.27 (br dd, *J*=6.3, 4.1 Hz, 1H), 4.22 - 4.15 (m, 1H), 4.09 (br d, *J*=10.7 Hz, 1H), 4.02 (s, 3H), 3.90 (br d, *J*=9.2 Hz, 1H), 3.77 (br dd, *J*=9.2, 7.0 Hz, 1H), 3.67 - 3.60 (m, 1H), 3.13 - 3.01 (m, 2H), 2.86 (br dd, *J*=11.0, 4.3 Hz, 1H), 2.16 - 2.01 (m, 2H), 2.00 - 1.92 (m, 1H), 1.87 - 1.78 (m, 2H), 1.78 - 1.66 (m, 2H), 1.50 - 1.40 (m, 2H), 1.39 - 1.24 (m, 2H), 0.77 - 0.64 (m, 2H), 0.31 (br d, *J*=2.4 Hz, 2H)。可能由於與溶劑峰重疊，一個質子在NMR中不可見。LC-MS RT: 2.02 min；MS (ESI) *m/z* 545.2 $(M+H)^+$；方法B。

【0554】 峰2為**實例702** (5.1，32%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 9.97 (d, *J*=6.8 Hz, 1H), 8.20 - 8.12 (m, 2H), 7.79 (dd, *J*=8.6, 2.3 Hz, 1H), 7.25 (d, *J*=8.8 Hz, 1H), 5.33 (dd, *J*=9.2, 3.5 Hz, 1H), 4.61 (d, *J*=9.6 Hz, 1H), 4.49 (br t, *J*=7.8 Hz, 1H), 4.32 - 4.24 (m, 1H), 4.23 - 4.14 (m, 1H), 4.13 - 4.06 (m, 1H), 4.03 (s, 3H), 3.90 (br d, *J*=8.9 Hz, 1H), 3.77 (dd, *J*=9.4, 7.0 Hz, 1H), 3.65 (dd, *J*=10.7, 3.5 Hz, 1H), 3.12 - 3.01 (m,

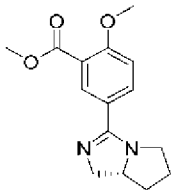
2H), 2.85 (dd, *J*=10.9, 4.2 Hz, 1H), 2.18 - 1.95 (m, 3H), 1.88 - 1.68 (m, 4H), 1.52 - 1.40 (m, 2H), 1.39 - 1.24 (m, 2H), 0.70 (quin, *J*=9.4 Hz, 2H), 0.40 - 0.21 (m, 2H)。可能由於與溶劑峰重疊，一個質子在NMR中不可見。LC-MS RT: 1.86 min；MS (ESI) *m/z* 545.2 $(M+H)^+$；方法B。

【0555】

實例699



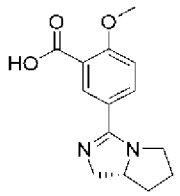
中間物699-1：



在冰浴中冷卻(R)-吡咯啶-2-基甲胺2 HCl (70.2 mg，0.406 mmol)於DCM(1.9 mL)中之溶液。添加休尼格氏鹼(0.14 mL，0.81 mmol)及5-甲醯基-2-甲氧基苯甲酸甲酯(75 mg，0.39 mmol)。使反應混合物升溫至室溫。1小時之後，添加NBS (72.2 mg，0.406 mmol)且攪拌反應混合物14h。在減壓下濃縮反應混合物。經由矽膠層析純化殘餘物，得到中間物**699-1** (49 mg，46%)。^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J*=2.0 Hz, 1H), 7.96 (dd, *J*=8.8, 2.0 Hz, 1H), 7.02 (d, *J*=8.7 Hz, 1H), 4.09 - 4.02 (m, 2H), 3.92 (s, 3H), 3.86 (s, 3H), 3.75 (q, *J*=9.4 Hz, 1H), 3.42 - 3.27 (m, 1H), 3.24 - 3.14 (m, 1H), 2.05 - 1.91 (m, 1H), 1.90 - 1.72 (m, 2H), 1.52 - 1.40 (m, 1H)。

【0556】

中間物699-2：

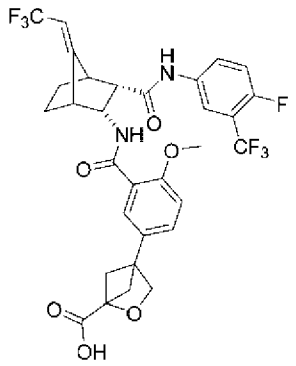


向**中間物699-1** (49 mg，0.18 mmol)於THF (1.9 mL)及MeOH (0.37 mL)中之溶液中添加LiOH (2M水溶液) (0.27 mL，0.54 mmol)。在4小時之後，將反應混合物用1M HCl酸化至pH 3且在減壓下濃縮，得到(R)-2-甲氧基-5-(5,6,7,7a-四氫-1H-吡咯并[1,2-c]咪唑-3-基)苯甲酸甲酯**中間物699-2** (49 mg，0.18 mmol)，其不經進一步純化即使用。

【0557】 **實例699**係藉由針對**實例378**所描述之通用程序由中間物**699-2**製備(3.8 mg，31%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 10.61 (s, 1H), 9.98 (d, *J*=6.8 Hz, 1H), 8.38 (d, *J*=2.4 Hz, 1H), 8.21 (dd, *J*=6.3, 2.2 Hz, 1H), 7.98 (dd, *J*=8.8, 2.4 Hz, 1H), 7.83 - 7.73 (m, 1H), 7.52 - 7.43 (m, 2H), 4.69 (d, *J*=9.6 Hz, 1H), 4.55 - 4.39 (m, 2H), 4.13 (s, 3H), 4.08 (t, *J*=11.5 Hz, 1H), 3.81 (dd, *J*=11.9, 7.1 Hz, 1H), 3.74 - 3.64 (m, 1H), 3.17 (dd, *J*=10.2, 4.9 Hz, 1H), 3.10 (br s, 1H), 2.73 (br s, 1H), 2.17 - 2.08 (m, 1H), 2.07 - 1.96 (m, 2H), 1.88 - 1.72 (m, 2H), 1.72 - 1.60 (m, 1H), 1.52 - 1.35 (m, 3H), 0.79 - 0.66 (m, 2H), 0.39 - 0.27 (m, 2H)。可能由於與經抑制之水峰重疊，一個質子在NMR中不可見。LC-MS RT: 2.20 min；MS (ESI) *m/z* 611.2 $(M+H)^+$；方法B。

【0558】

實例724



中間物724-1：製備5-溴-2-甲氧基苯甲酸三級丁酯：向5-溴-2-甲氧基苯甲酸(3.67 g，15.9 mmol)於THF (50 mL)中之溶液中添加Boc-酐(7.38 mL，31.8 mmol)及DMAP (0.194 g，1.59 mmol)。隨後向此混合物中添加*t*-BuOH (50 mL)且隨後在75℃加熱反應混合物14h。隨後在真空下濃縮反應混合物且對殘餘物進行矽膠層析，得到中間物**724-1** (4.1 g，81%產率)。^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (d, *J*=2.6 Hz, 1H), 7.52 (dd, *J*=8.9, 2.6 Hz, 1H), 6.85 (d, *J*=8.9 Hz, 1H), 3.88 (s, 3H), 1.61 - 1.57 (m, 9H)

【0559】 **中間物724-2**：製備5-(3-羥基丙-1-烯-2-基)-2-甲氧基苯甲酸三級丁酯：在氬氣下向丙-2-烯-1-醇(1.42 mL，20.9 mmol)及中間物**724-1** (1200 mg，4.18 mmol)於DMSO (3 mL)中之溶液中添加TEA (1.05 mL，7.52 mmol)及1,3-雙(二苯基膦基)丙烷(345 mg，0.836 mmol)。向反應混合物中添加$Pd(OAc)_2$ (94 mg，0.42 mmol)且用氬氣吹掃混合物10 min。隨後將反應混合物密封且在60℃攪拌14h。使反應混合物冷卻至室溫，用EtOAc稀釋且用鹽水洗滌有機部分。將有機部分經$MgSO_4$乾燥，過濾且使用矽膠層析純化，得到中間物**724-2** (222 mg，19.0%產率)。^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, *J*=2.4 Hz, 1H), 7.53 (dd, *J*=8.6, 2.5 Hz, 1H), 6.95 (d, *J*=8.7 Hz, 1H), 5.43 (d, *J*=0.8 Hz, 1H), 5.32 (q, *J*=1.2 Hz, 1H), 4.53 (d, *J*=5.3 Hz, 2H), 3.92 - 3.89 (s, 3H), 1.62 - 1.59 (m, 9H)

【0560】 **中間物724-3**：製備2-((2-(3-(三級丁氧基羰基)-4-甲氧基

苯基)烯丙基)氧基)丙二酸二甲酯：向中間物**724-2** (222 mg，0.840 mmol)於甲苯(5 mL)中之溶液中添加$Rh_2(OAc)_4$ (19 mg，0.042 mmol)。隨後用氮氣吹掃反應混合物，然後加熱至回流。隨後經約5分鐘向此回流溶液中添加2-重氮丙二酸二甲酯(133 mg，0.840 mmol)之甲苯(1 mL)。在繼續回流30分鐘之後，使反應混合物冷卻至室溫且在真空下濃縮。使用矽膠層析純化殘餘物，得到中間物**724-3** (192 mg，58.0%產率)。^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (d, *J*=2.4 Hz, 1H), 7.60 (dd, *J*=8.7, 2.4 Hz, 1H), 6.93 (d, *J*=8.7 Hz, 1H), 5.59 - 5.56 (m, 1H), 5.34 (d, *J*=0.9 Hz, 1H), 4.64 (s, 1H), 4.55 (d, *J*=0.8 Hz, 2H), 3.91 (s, 3H), 3.79 (s, 6H), 1.60 (s, 9H)。

【0561】 **中間物724-4**：製備2-((2-(3-(三級丁氧基羰基)-4-甲氧基苯基)烯丙基)氧基)-2-((二甲基胺基)甲基)丙二酸二甲酯：向中間物**724-3** (192 mg，0.487 mmol)於DCM(7 mL)中之溶液中添加埃申莫瑟氏鹽(Eschenmoser's salt) (135 mg，0.730 mmol)，隨後添加TEA(0.10 mL，0.73 mmol)。在室溫下攪拌反應混合物14h。使反應混合物冷卻至室溫且在真空下濃縮。使用矽膠層析純化殘餘物，得到中間物**724-4** (100 mg，45%產率)。MS (ESI) m/z = 452.5 (M+H)。

【0562】 **中間物724-5**：製備2-((2-(3-(三級丁氧基羰基)-4-甲氧基苯基)烯丙基)氧基)-3-甲氧基-2-(甲氧基羰基)-N,N,N-三甲基-3-側氧基丙烷-1-銨：向中間物**724-4** (100 mg，0.221 mmol)於丙酮(5 mL)中之溶液中添加碘甲烷(0.021 mL，0.33 mmol)且在室溫下攪拌反應混合物14h。在真空下濃縮反應混合物，得到中間物**724-5**，其不經進一步純化即使用(100 mg，87%產率)。MS (ESI) m/z = 466.5 (M+H)。

【0563】 **中間物724-6**：製備2-甲氧基-5-(3-((3-甲氧基-3-側氧基丙-1-烯-2-基)氧基)丙-1-烯-2-基)苯甲酸三級丁酯：向中間物**724-5** (100

mg，0.214 mmol)於DMSO (4 mL)中之溶液中添加NaOH (2M，0.13 mL，0.26 mmol)且在室溫下攪拌反應混合物3 h。在真空下濃縮反應混合物且使用矽膠層析純化，得到中間物**724-6** (50 mg，64%產率)。MS (ESI) m/z = 349.0 (M+H)。

【0564】 **中間物724-7**：製備4-(3-(三級丁氧基羰基)-4-甲氧基苯基)-2-氧雜雙環[2.1.1]己烷-1-甲酸甲酯：向中間物**724-6** (50 mg，0.14 mmol)於DMSO (30 mL)中之溶液中添加(Ir[dF(CF_3)ppy]$_2$(dtbpy))PF_6 (1.6 mg，1.4 μmol)且將反應混合物在N_2下脫氣三次。在藍色LED燈存在下攪拌反應混合物48h。用EtOAc稀釋反應混合物且用鹽水洗滌有機部分。將有機部分經$MgSO_4$乾燥，過濾且使用矽膠層析純化，得到中間物**724-7** (13 mg，23%產率)。^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, *J*=2.4 Hz, 1H), 7.45 (dd, *J*=8.6, 2.5 Hz, 1H), 6.93 (d, *J*=8.7 Hz, 1H), 5.28 (s, 1H), 5.07 (d, *J*=0.9 Hz, 1H), 3.90 (s, 3H), 3.86 (s, 3H), 3.04 - 2.98 (m, 2H), 2.88 - 2.79 (m, 2H), 1.62 - 1.59 (m, 9H)

【0565】 **中間物724-8**：製備2-甲氧基-5-(1-(甲氧基羰基)-2-氧雜雙環[2.1.1]己烷-4-基)苯甲酸TFA：向中間物**724-7** (13 mg，0.037 mmol)於DCM (0.8 mL)中之溶液中添加TFA (0.20 mL，2.6 mmol)且在室溫下攪拌反應混合物30 min。隨後真空濃縮反應混合物，得到中間物**724-8**，其不經進一步純化即使用(11 mg，95%產率)。MS (ESI) m/z = 293.2 (M+H)。

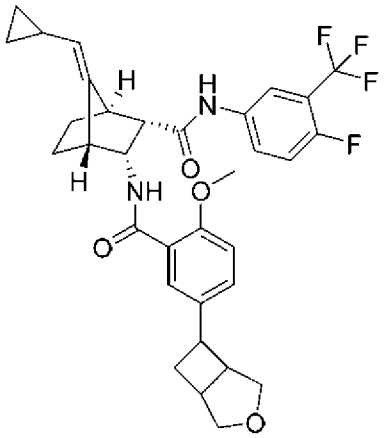
【0566】 **中間物724-9**：製備4-(3-(((1R,2R,3S,4R,Z)-3-((4-氟-3-(三氟甲基)苯基)胺甲醯基)-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基)胺甲醯基)-4-甲氧基苯基)-2-氧雜雙環[2.1.1]己烷-1-甲酸甲酯：中間物**724-9**係藉由針對**378**所描述之通用程序，藉由使用三氟甲基降冰片烷基中間物

170-2 (25 mg，0.049 mmol)及中間物**724-8**製備，得到中間物**724-9** (6 mg，20%產率)。MS (ESI) m/z = 671.1 (M+H)。

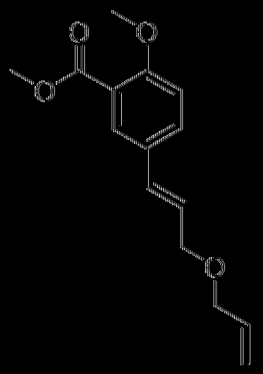
【0567】 **實例724**：藉由將中間物**724-9** (6 mg，9 μmol)溶解於THF (2 mL)及水(0.67 mL)中且添加LiOH (2 M，0.013 mL，0.027 mmol)來製備4-(3-(((1R,2R,3S,4R,Z)-3-((4-氟-3-(三氟甲基)苯基)胺甲醯基)-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基)胺甲醯基)-4-甲氧基苯基)-2-氧雜雙環[2.1.1]己烷-1-甲酸**724**。隨後在室溫下攪拌反應混合物2 h。真空濃縮反應混合物且使用逆相製備型HPLC純化，得到**724** (4.8 mg，75%產率)。^{1}H NMR (500 MHz, CD_3OD) δ 10.26 - 10.17 (m, 1H), 8.14 (dd, *J*=6.3, 2.6 Hz, 1H), 8.00 - 7.92 (m, 1H), 7.80 - 7.72 (m, 1H), 7.50 - 7.42 (m, 1H), 7.29 (t, *J*=9.6 Hz, 1H), 7.17 (d, *J*=8.5 Hz, 1H), 5.78 - 5.71 (m, 1H), 4.67 - 4.60 (m, 1H), 4.07 (s, 3H), 4.01 - 3.96 (m, 2H), 3.47 - 3.41 (m, 1H), 3.40 - 3.32 (m, 1H), 3.30 - 3.16 (m, 2H), 2.95 - 2.91 (m, 1H), 2.76 - 2.70 (m, 1H), 2.44 - 2.35 (m, 2H), 2.21 - 2.13 (m, 3H), 1.63 - 1.54 (m, 2H)。MS (ESI) m/z = 657.4 (M+H)。HPLC純度：92%；滯留時間：1.35 min；方法A。

【0568】

實例725-728



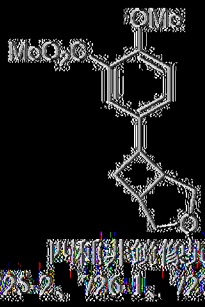
中間物725-1



將含(E)-5-(3-羥基丙-1-烯-1-基)-2-甲氧基苯甲酸甲酯(0.30 g，1.3 mmol)之DMF (14 mL)冷卻至0℃且用NaH (60%於礦物油中) (0.059 g，1.5 mmol)處理。15分鐘後，用烯丙基溴(0.13 mL，1.5 mmol)處理反應混合物且使溶液升溫至室溫持續14h。用飽和氯化銨溶液稀釋反應混合物且用EtOAc (2×)萃取。將有機部分合併，經硫酸鈉乾燥，過濾且在減壓下濃縮。藉由矽膠層析純化殘餘物，得到(E)-5-(3-(烯丙氧基)丙-1-烯-1-基)-2-甲氧基苯甲酸甲酯(0.20 g，0.76 mmol，57%產率)。MS (ESI) *m/z* 263.0 $(M+H)^+$。

[0569]

中間物725-2、726-1、727-1及728-1



向溶解於乙腈(75 mL)中之中間物725-1 (0.20 g，0.76 mmol)中添加(Ir[dF(CF3)ppy]2(dtbpy))PF6(9 mg，8 μmol)且用藍色LED照射溶液60 h。在減壓下濃縮反應混合物且藉由SFC使用兩個連續管柱純化殘餘物。第一管柱：(AS-3 250 × 4.6 mm ID，5 μm，溫度：環境溫度，流動速率：

2.0 mL/min，移動相：85/15 CO_2/MeOH)，然後是(AD 250 × 4.6 mm ID，5μm，溫度：環境溫度，流動速率：2.0 mL/min，移動相：90/10 CO_2/MeOH)，得到**726-2** (峰1：33 mg，0.13 mmol. 17%產率) MS (ESI) *m/z* 263.0 $(M+H)^+$, RT = 7.2 min，AD 250 × 4.6 mm ID，5μm，溫度：環境溫度，流動速率：2.0 mL/min，移動相：90/10 CO_2/MeOH ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, *J*=2.3 Hz, 1H), 7.34 (dd, *J*=8.5, 2.4 Hz, 1H), 6.94 (d, *J*=8.5 Hz, 1H), 4.02 - 3.96 (m, 2H), 3.90 (s, 3H), 3.89 (s, 3H), 3.65 - 3.60 (m, 1H), 3.53 - 3.50 (m, 1H), 3.23 - 3.17 (m, 1H), 3.01 - 2.93 (m, 2H), 2.31 - 2.22 (m, 1H), 2.21 - 2.13 (m, 1H)。

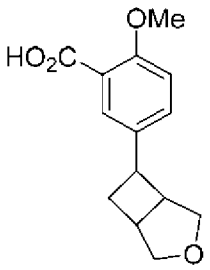
【0570】 **727-1** (峰2：20 mg，0.076 mmol. 10%產率) MS (ESI) *m/z* 263.0 $(M+H)^+$, RT = 13.2 min，A5-5 250 × 4.6 mm ID，5μm，溫度：環境溫度，流動速率：2.0 mL/min，移動相：85/15 CO_2/MeOH: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, *J*=2.4 Hz, 1H), 7.36 (dd, *J*=8.5, 2.4 Hz, 1H), 6.96 (d, *J*=8.7 Hz, 1H), 4.00 (dd, *J*=9.2, 7.6 Hz, 2H), 3.93 (s, 3H), 3.91 (s, 3H), 3.63 (dd, *J*=9.2, 5.4 Hz, 1H), 3.53 (dd, *J*=9.4, 4.0 Hz, 1H), 3.26 - 3.19 (m, 1H), 3.04 - 2.95 (m, 2H), 2.33 - 2.24 (m, 1H), 2.22 - 2.16 (m, 1H)。

【0571】 **728-1** (峰3：5.3 mg，0.020 mmol. 2.7%產率)，MS (ESI) *m/z* 263.0 $(M+H)^+$, RT = 6.11 min，AD 250 × 4.6 mm ID，5μm，溫度：環境溫度，流動速率：2.0 mL/min，移動相：90/10 CO_2/MeOH ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, *J*=2.3 Hz, 1H), 7.40 (dd, *J*=8.5, 2.2 Hz, 1H), 6.97 (d, *J*=8.7 Hz, 1H), 3.91 (s, 3H), 3.91 (s, 3H), 3.86 (d, *J*=9.0 Hz, 1H), 3.73 - 3.64 (m, 2H), 3.44 (dd, *J*=9.0, 4.4 Hz, 1H), 3.37 (dd, *J*=10.0, 6.6

Hz, 1H), 3.20 (q, *J*=7.5 Hz, 1H), 3.08 - 2.99 (m, 1H), 2.46 (dddd, *J*=12.3, 10.3, 8.2, 2.3 Hz, 1H), 2.13 (ddd, *J*=12.1, 9.6, 6.6 Hz, 1H)

【0572】

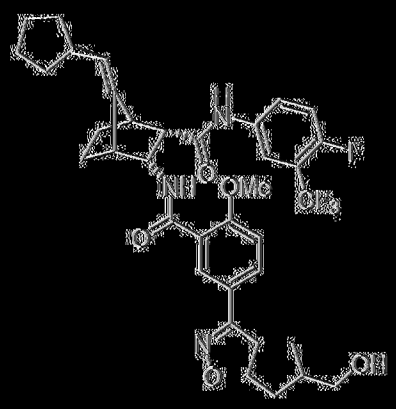
中間物725-3



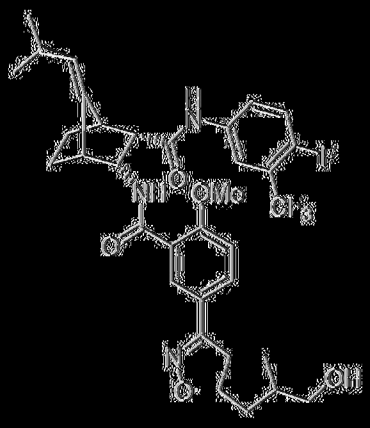
中間物**725-3**係藉由用於中間物**4-2**之通用程序由**725-2**製備。LC-MS RT: 0.77 min；MS (ESI) m/z 249.0 $(M+H)^+$；方法A。

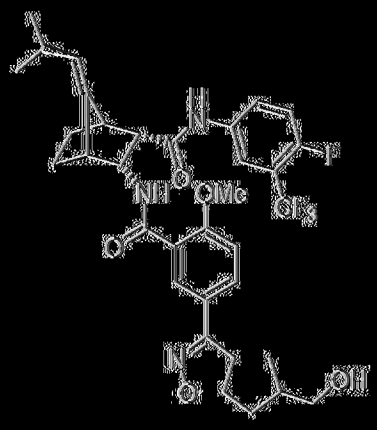
【0573】 **實例725**：根據**實例1**之通用程序由中間物**725-3**及**IV-2a**製備，得到(1R,2S,3R,4R,Z)-3-(5-(3-氧雜雙環[3.2.0]庚烷-6-基)-2-甲氧基苯甲醯胺基)-7-(環丙基亞甲基)-N-(4-氟-3-(三氟甲基)苯基)雙環[2.2.1]庚烷-2-甲醯胺(3.2 mg，10%產率)。^{1}H NMR (500 MHz, DMSO-d6) δ 10.49 (s, 1H), 9.81 (d, J=7.2 Hz, 1H), 8.23 (dd, J=6.6, 2.6 Hz, 1H), 7.84 (d, J=2.4 Hz, 1H), 7.78 (dt, J=8.5, 3.8 Hz, 1H), 7.49 (t, J=9.8 Hz, 1H), 7.41 (dd, J=8.5, 2.4 Hz, 1H), 7.13 (d, J=8.7 Hz, 1H), 4.69 (d, J=9.6 Hz, 1H), 4.49 - 4.41 (m, 1H), 3.97 (s, 3H), 3.91 - 3.84 (m, 2H), 3.48 (dd, J=9.2, 5.8 Hz, 1H), 3.39 (dd, J=9.2, 4.7 Hz, 1H), 3.15 (dd, J=10.7, 4.3 Hz, 1H), 3.13 - 3.06 (m, 2H), 3.00 - 2.90 (m, 1H), 2.89 - 2.83 (m, 1H), 2.72 (t, J=3.7 Hz, 1H), 2.16 (dt, J=12.3, 8.1 Hz, 1H), 2.09 - 2.01 (m, 1H), 1.87 (br t, J=8.7 Hz, 1H), 1.81 - 1.74 (m, 1H), 1.55 - 1.47 (m, 1H), 1.46 - 1.34 (m, 2H), 0.82 - 0.70 (m, 2H), 0.36 (dd, J=4.5, 2.5 Hz, 2H)。LC-MS RT: 2.7 min；MS (ESI) *m/z* 599.0 $(M+H)^+$；方法A。

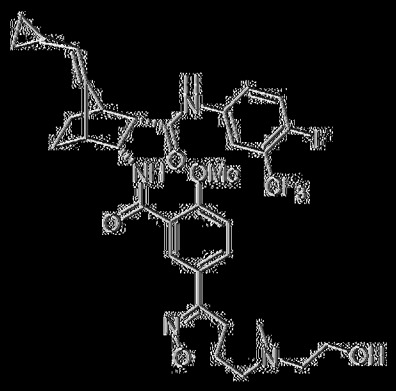
表3

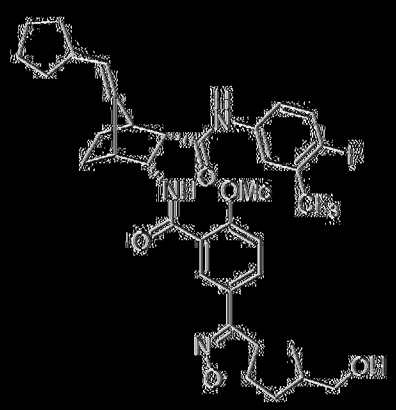
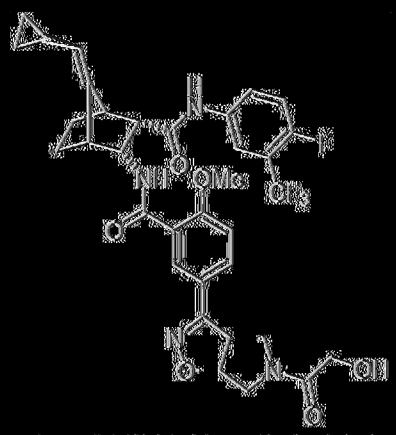
實例編號	結構	名稱	MS (ESI) (M+H)	^{1}H NMR	LC RT Meth. (min)
445	 中間體8雙鹽	(1R,2S,3R,4R,7Z)-7-(環戊基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(羥甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	670.6	(400 MHz, CD_3OD) δ 8.35 (d, J= 2.2 Hz, 1H), 8.18 (dd, J= 6.4, 2.6 Hz, 1H), 7.89 (dd, J= 8.8, 2.4 Hz, 1H), 7.81 - 7.73 (m, 1H), 7.30 (t, J= 9.6 Hz, 1H), 7.26 (d, J= 8.8 Hz, 1H), 5.24 - 5.18 (m, 2H), 4.56 - 4.48 (m, 1H), 4.23 (s, 1H), 4.14 (s, 3H), 3.60 - 3.48 (m, 2H), 3.34 (dt, J= 3.3, 1.7 Hz, 2H), 3.16 (dd, J= 10.7, 4.3 Hz, 1H), 3.12 (t, J= 3.6 Hz, 1H), 2.74 - 2.64 (m, 2H), 2.21 - 2.07 (m, 2H), 2.03 - 1.95 (m, 2H), 1.94 - 1.87 (m, 2H), 1.85 - 1.58 (m, 6H), 1.50 (br d, J= 2.9 Hz, 2H), 1.37 - 1.29 (m, 2H)	1.45, A

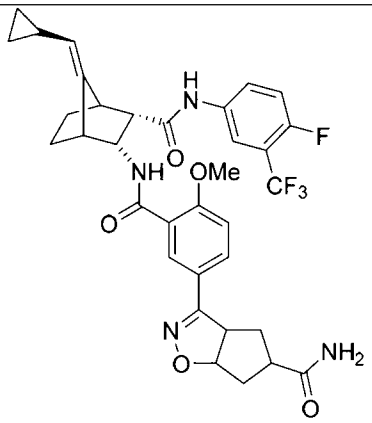
146		(1R,2S,3R,4R,7Z)-7-(環丁基甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-[5-[5-(羥甲基)-3a,4,4,5,6,6a-六氫-1H-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基]雙環[2.2.1]庚烷-2-甲醯胺	656.0	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.89 (br d, J = 7.0 Hz, 1H), 8.27 – 8.17 (m, 2H), 7.86 – 7.75 (m, 2H), 7.48 (br t, J = 9.8 Hz, 1H), 7.27 (d, J = 8.5 Hz, 1H), 5.38 (d, J = 8.2 Hz, 1H), 5.13 (br dd, J = 8.5, 5.5 Hz, 1H), 4.41 – 4.29 (m, 1H), 4.20 (br t, J = 8.9 Hz, 1H), 4.04 (s, 3H), 3.90 (s, 1H), 3.64 – 3.55 (m, 3H), 3.44 – 3.30 (m, 2H), 3.20 – 3.04 (m, 3H), 2.96 (br s, 1H), 2.71 (br s, 1H), 2.23 – 2.08 (m, 2H), 2.00 (br dd, J = 14.0, 6.1 Hz, 1H), 1.94 – 1.62 (m, 9H), 1.60 – 1.52 (m, 1H), 1.43 – 1.28 (m, 2H)	2.55, A

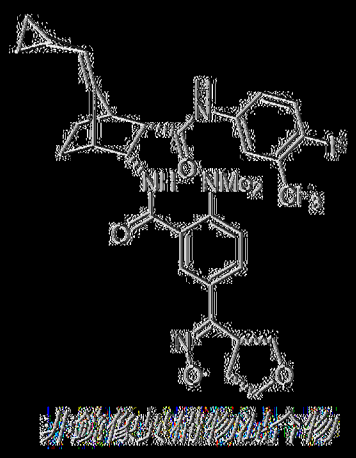
450		(1R,2S,3R,4R,7Z)-N-[4-氟-3-(三氟甲基)苯基]-3-[5-[5-(羥甲基)-3a,4,4a,5,6,6a-六氫環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基]-7-(2-甲基丙內基)雙環[2.2.1]庚烷-2-甲醯胺	644.6	(400 MHz, CD_3OD) δ 8.35 (dd, J = 2.2, 0.9 Hz, 1H), 8.18 (dd, J = 6.4, 2.6 Hz, 1H), 7.89 (dd, J = 8.6, 2.2 Hz, 1H), 7.81 – 7.74 (m, 1H), 7.30 (t, J = 9.6 Hz, 1H), 7.25 (d, J = 8.8 Hz, 1H), 5.36 – 5.13 (m, 2H), 4.52 (dt, J = 10.7, 2.0 Hz, 1H), 4.28 – 4.22 (m, 1H), 4.17 – 4.12 (m, 3H), 3.61 – 3.47 (m, 2H), 3.17 (dt, J = 10.6, 3.3 Hz, 1H), 3.14 – 3.09 (m, 1H), 2.72 (dt, J = 12.8, 3.9 Hz, 1H), 2.20 – 2.08 (m, 3H), 2.03 – 1.87 (m, 3H), 1.82 – 1.72 (m, 1H), 1.65 (ddd, J = 13.3, 11.4, 5.1 Hz, 1H), 1.55 – 1.39 (m, 3H), 1.11 – 0.94 (m, 5H)	1.44, A

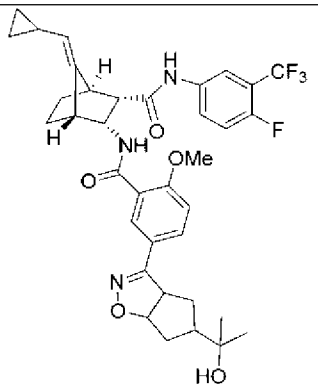
454	 請參考29-10製備	(1R,2S,3R,4R,7Z)-N-[4-氟-3-(三氟甲基)苯基]-3-[5-[5-(羥基甲基)-3a,4,4a,5,6,6a,7a-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基]-7-(2-甲基丙內基)雙環[2.2.1]庚烷-2-甲醯胺	644.6	(400 MHz, CD_3OD) δ 8.36 (dd, J = 2.3, 0.8 Hz, 1H), 8.18 (dd, J = 6.3, 2.5 Hz, 1H), 7.92 (dd, J = 8.8, 2.0 Hz, 1H), 7.78 (dt, J = 8.8, 3.4 Hz, 1H), 7.37 – 7.25 (m, 2H), 5.37 – 5.14 (m, 2H), 4.53 (dd, J = 10.7, 4.1 Hz, 1H), 4.20 – 4.10 (m, 4H), 3.54 – 3.41 (m, 2H), 3.22 – 3.11 (m, 2H), 2.74 (br dd, J = 13.0, 3.7 Hz, 1H), 2.44 – 2.27 (m, 3H), 2.21 – 2.12 (m, 1H), 2.09 – 2.01 (m, 1H), 1.99 – 1.77 (m, 2H), 1.65 (dt, J = 12.5, 6.0 Hz, 1H), 1.58 – 1.46 (m, 3H), 1.15 – 0.98 (m, 5H)	1.40, A

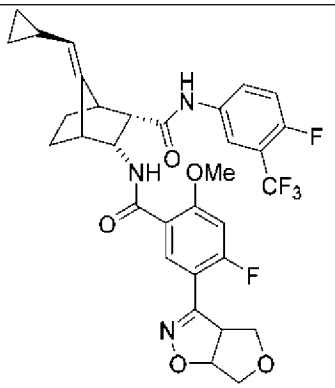
455	 由455之製備 1-[3-對掌性苯甲酸酯中間物(峰2；>99%ee；對掌性分析型RT: 8.259 min)製備製備型對掌性SFC條件：儀器：Jasco SFC Prep；管柱：Regis Whelk 01，21 × 250 mm，5微米；移動相：15% IPA / 85% CO_2；流動條件：45 mL/min，150 巴，40℃；偵測器波長：220 nm；注射詳情：0.5 mL ~50mg/mL於IPA中	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-[5-[5-(2-羥基乙基)-3a,4,4a,5,6,6a-六氫吡咯并[3,4-d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基]雙環[2.2.1]庚烷-2-甲醯胺	657.6	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.90 (br d, J=7.0 Hz, 1H), 8.26 (d, J=2.3 Hz, 1H), 8.23 (dd, J=6.5, 2.5 Hz, 1H), 7.83 (dd, J=8.5, 2.1 Hz, 1H), 7.77 (dt, J=8.5, 3.8 Hz, 1H), 7.48 (t, J=9.8 Hz, 1H), 7.30 (d, J=8.9 Hz, 1H), 5.45 (br d, J=4.9 Hz, 1H), 4.78 (br s, 1H), 4.69 (d, J=9.6 Hz, 1H), 4.43 (ddd, J=10.3, 6.5, 4.1 Hz, 1H), 4.05 (s, 3H), 3.98 (br d, J=11.0 Hz, 1H), 3.70 (br d, J=9.6 Hz, 1H), 3.65 (br s, 2H), 3.54 (br s, 2H), 3.23 (br s, 2H), 3.15 (dd, J=10.8, 4.2 Hz, 1H), 3.09 (t, J=3.5 Hz, 1H), 2.72 (t, J=3.6 Hz, 1H), 1.85-1.74 (m, 2H), 1.53-1.44 (m, 1H), 1.44-1.36 (m, 2H), 0.78-0.69 (m, 2H), 0.37-0.33 (m, 2H)	1.21, A

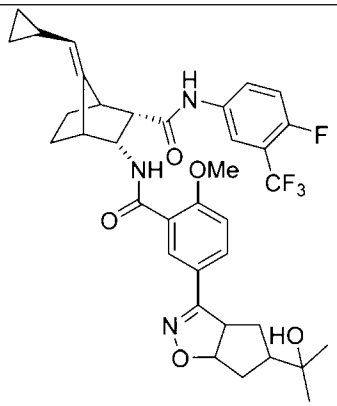
457	 由I429-10製備	(1R,2S,3R,4R,7Z)-7-(環戊基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-[5-[5-(羥基甲基)-3a,4,4a,5,6,6a,7a-環戊并[d][1,2]㗁唑-3-基]-2-甲氧基苯甲醯胺基]雙環[2.2.1]庚烷-2-甲醯胺	6/0.6	(400 MHz, CD_3OD) δ 8.36 (d, J= 2.4 Hz, 1H), 8.19 (dd, J= 6.2, 2.4 Hz, 1H), 7.90 (dd, J= 8.7, 2.3 Hz, 1H), 7.82 - 7.74 (m, 1H), 7.35 - 7.23 (m, 2H), 5.29 - 5.18 (m, 2H), 4.52 (dd, J= 10.6, 3.1 Hz, 1H), 4.15 - 4.13 (m, 4H), 3.54 - 3.40 (m, 2H), 3.22 - 3.10 (m, 2H), 2.76 - 2.67 (m, 2H), 2.43 - 2.25 (m, 3H), 1.94 - 1.80 (m, 4H), 1.76 - 1.59 (m, 5H), 1.50 (br s, 2H), 1.38 - 1.29 (m, 3H)	1.45, A
458	 由可對掌性苯甲酸酯中間物(峰2；>99%ee；對掌性分析程RT 5.036 min)製備；製備程對掌性SFC條件：儀器：Jasco SFC Prep；管柱：Regis Whelk-01，21 × 250 mm，5 微米；移動相：20% MeOH / 80% CO_2；流動條件：45 mL/min，150巴，40℃；偵測器波長：220 nm；注射詳情：0.5 mL ~52mg/mL於MeOH CAN中	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-[5-[5-(羥基乙醯基)-3a,4,4a,5,6,6a-吡咯并[3,4-d][1,2]㗁唑-3-基]-2-甲氧基苯甲醯胺基]雙環[2.2.1]庚烷-2-甲醯胺	6/2.0	(400 MHz, CD_3OD) δ 10.38 - 10.31 (m, 1H), 10.22 - 10.13 (m, 1H), 8.33 (dd, J= 16.4, 2.1 Hz, 1H), 8.24 - 8.16 (m, 1H), 7.96 - 7.88 (m, 1H), 7.82 - 7.75 (m, 1H), 7.36 - 7.27 (m, 2H), 5.47 - 5.35 (m, 1H), 4.80 - 4.73 (m, 1H), 4.64 - 4.42 (m, 2H), 4.29 - 4.13 (m, 5H), 4.12 - 3.87 (m, 3H), 3.80 - 3.68 (m, 2H), 3.27 - 3.16 (m, 2H), 2.75 (br s, 1H), 2.06 - 1.90 (m, 2H), 1.65 - 1.50 (m, 3H), 0.84 - 0.73 (m, 2H), 0.44 - 0.32 (m, 2H)	2.14, C

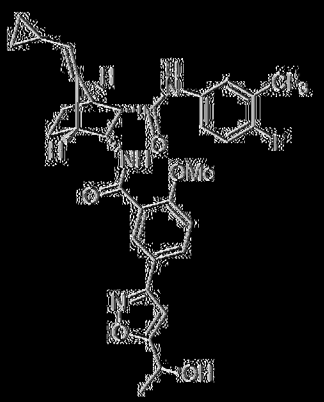
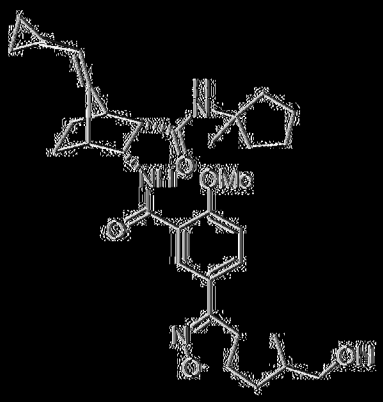
459	 由同對掌性苯甲酸酯中間物(峰2；>99%ee；對掌性分析型RT=2.742 min)製備；製備型對掌性SFC條件：儀器：Jasco SFC Prep：管柱：Chiralpak AS-H，30 × 250 mm，5微米；移動相：30% MeOH / 70% CO_2；流動條件：85 mL/min，150巴， 40℃；偵測器波長：220 nm；注射詳情：1.0 mL ~50mg/mLmg/mL於MeOH:TFA中	3-(3-{[(1R,2R,3S,4R,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-5-甲醯胺	655.5	(500 MHz, DMSO-d6) δ 10.55 - 10.51 (m, 1H), 9.92 - 9.88 (m, 1H), 8.31 - 8.26 (m, 1H), 8.25 - 8.20 (m, 1H), 7.84 - 7.77 (m, 2H), 7.49 (t, J=9.8 Hz, 1H), 7.29 - 7.25 (m, 1H), 4.70 (d, J=9.5 Hz, 1H), 4.61 - 4.57 (m, 1H), 4.47 - 4.43 (m, 1H), 4.04 (s, 3H), 3.95 (dd, J=12.0, 4.7 Hz, 1H), 3.86 - 3.81 (m, 2H), 3.59 (d, J=4.7 Hz, 2H), 3.17 (dd, J=10.7, 4.1 Hz, 1H), 3.11 (t, J=3.6 Hz, 1H), 2.73 (t, J=3.4 Hz, 1H), 1.87 - 1.76 (m, 2H), 1.54 - 1.47 (m, 1H), 1.46 - 1.37 (m, 2H), 0.80 - 0.70 (m, 2H), 0.39 - 0.33 (m, 2H)	2.14, A

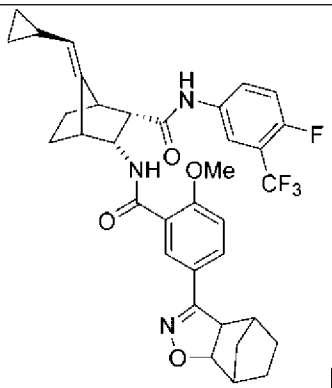
460		(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-吡喃并[3,4-d][1,2]噁唑-3-基}-2-(二甲基胺基)苯甲醯胺基)-7-(環丙基甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	626.9	(500 MHz, DMSO-d6) δ 10.48 (br d, J = 6.1 Hz, 1H), 9.93 (br d, J = 7.6 Hz, 1H), 8.19 (br s, 1H), 7.91 (dd, J = 16.8, 1.8 Hz, 1H), 7.75 (br s, 1H), 7.65 (t, J = 7.5 Hz, 1H), 7.46 (br t, J = 9.8 Hz, 1H), 7.20 (t, J = 8.5 Hz, 1H), 5.39 - 5.27 (m, 1H), 4.68 (br d, J = 9.8 Hz, 1H), 4.52 - 4.38 (m, 2H), 4.13 - 4.01 (m, 1H), 3.96 - 3.82 (m, 1H), 3.80 - 3.67 (m, 1H), 3.63 (br d, J = 10.7 Hz, 1H), 3.15 (br d, J = 10.1 Hz, 1H), 3.08 (br d, J = 4.3 Hz, 1H), 2.72 (s, 6H), 2.56 - 2.52 (m, 1H), 1.93 - 1.73 (m, 2H), 1.50 (br s, 1H), 1.45 (br s, 1H), 1.39 (br d, J = 11.3 Hz, 1H), 0.87 - 0.66 (m, 2H), 0.34 (br s, 2H)	2.58, B

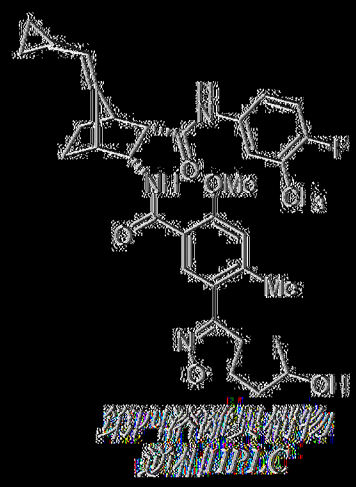
462	 由對掌性苯甲酸中間物製備。製備型層析條件：儀器：Berger MG II管柱：Chiralpak IC，30 × 250 mm，5微米，移動相：25%甲醇/75% CO_2，流動條件：70 mL/min，120巴， 40 ℃，偵測器波長：220 nm，注射詳情：0.5 mL ~75mg/mL於甲醇中。分析型層析條件：儀器：Shimadzu Nexera SFC管柱：Chiralpak IC，4.6 × 100 mm，3微米，移動相：25% MeOH / 75% CO_2，流動條件：2.0 mL/min，150巴， 40℃，偵測器波長：220 nm，注射詳情：5 µL ~1mg/mL於MeOH中。RT = 5.91 min 峰1	(1R,2S,3R,4R,Z)-7-(環丙基亞甲基)-N-(4-氟-3-(三氟甲基)苯基)-3-(5-(5-(2-羥基丙烷-2-基)-3a,5,6,6a-四氫-4H-環戊并[d]異噁唑-3-基)-2-甲氧基苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	670.4	(500 MHz, CD3OD) δ 8.34 (d, J=2.4 Hz, 1H), 8.19 - 8.14 (m, 1H), 7.87 (d, J=8.5 Hz, 1H), 7.80 - 7.73 (m, 1H), 7.28 (t, J=9.8 Hz, 1H), 7.24 (d, J=8.5 Hz, 1H), 5.17 (dd, J=8.7, 4.9 Hz, 1H), 4.72 (d, J=9.5 Hz, 1H), 4.57 (dd, J=10.6, 3.4 Hz, 1H), 4.13 (s, 3H), 3.33 (dt, J=3.3, 1.6 Hz, 1H), 3.25 - 3.14 (m, 2H), 2.72 (t, J=3.7 Hz, 1H), 2.11 - 2.06 (m, 1H), 2.03 - 1.90 (m, 4H), 1.88 - 1.77 (m, 2H), 1.60 - 1.46 (m, 3H), 1.16 (d, J=11.9 Hz, 6H), 0.82 - 0.68 (m, 2H), 0.42 - 0.28 (m, 2H)	2.53, C

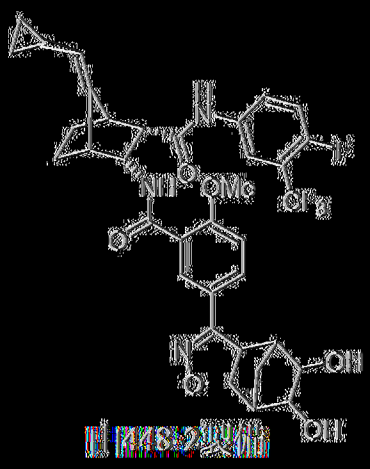
463	 由同對掌性甲酸酯中間物(峰-2，RT=5.46 min，>99% ee)製備-儀器：Jasco SFC管柱：Chiralpak IA，21 × 250 mm，5微米，移動相：20% MeOH / 80% CO_2，流動條件：45 mL/min，150巴， 40℃，偵測器波長：220 nm；分析方法：儀器：Shimadzu Nexera SFC，管柱 Chiralpak IA，4.6 × 100 mm，3微米，移動相：20% MeOH / 80% CO_2，流動條件：2 mL/min，150巴， 40℃，偵測器波長：220 nm，得到對掌性(峰-1，RT=1.69 min.，>99% ee) (峰-2，RT=5.46 min.，>99% ee)。	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-4-氟-2-甲氧基苯甲醯胺基)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	632.3	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.88 (br d, J=6.7 Hz, 1H), 8.35 (d, J=8.9 Hz, 1H), 8.27 - 8.20 (m, 1H), 7.89 - 7.75 (m, 1H), 7.50 (br t, J=9.8 Hz, 1H), 7.25 (d, J=13.1 Hz, 1H), 5.35 (dd, J=9.2, 3.4 Hz, 1H), 4.71 (d, J=9.8 Hz, 1H), 4.53 - 4.39 (m, 2H), 4.12 (br d, J=10.7 Hz, 1H), 4.07 (s, 3H), 3.91 (br d, J=9.2 Hz, 1H), 3.75 (dd, J=9.2, 7.0 Hz, 1H), 3.66 (dd, J=10.7, 3.4 Hz, 1H), 3.23 - 3.14 (m, 1H), 3.11 (br s, 1H), 2.74 (br s, 1H), 1.91 - 1.81 (m, 1H), 1.80 - 1.72 (m, 1H), 1.51 (ddd, J=12.8, 8.4, 4.4 Hz, 1H), 1.46 - 1.34 (m, 2H), 0.85 - 0.64 (m, 2H), 0.36 (br s, 2H)	2.55, B

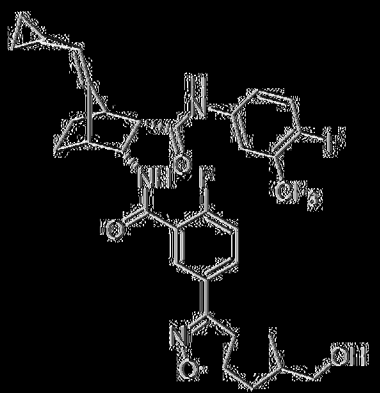
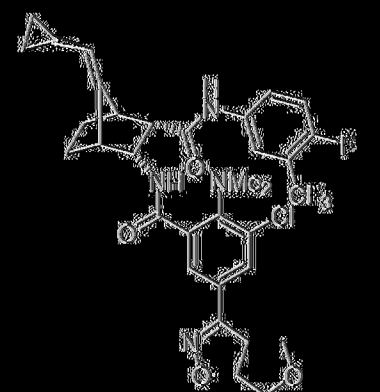
464	 由對掌性苯甲酸中間物製備。製備型層析條件：儀器：Berger MG II管柱：Chiralpak IC，30 × 250 mm，5微米，移動相：25%甲醇/75% CO_2，流動條件：70 mL/min，120巴， 40 ℃，偵測器波長：220 nm，注射詳情：0.5 mL ~75mg/mL於甲醇中。分析型層析條件：儀器：Shimadzu Nexera SFC管柱：Chiralpak IC，4.6 × 100 mm，3微米，移動相：25% MeOH / 75% CO_2，流動條件：2.0 mL/min，150巴， 40℃，偵測器波長：220 nm，注射詳情：5 µL ~1mg/mL於MeOH中。RT = 10.14 min 峰2	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(2-羥基丙烷-2-基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	670.4	(500 MHz, CD_3OD) δ 8.34 (d, J=2.4 Hz, 1H), 8.19 - 8.15 (m, 1H), 7.90 (dd, J=8.7, 2.4 Hz, 1H), 7.76 (d, J=8.3 Hz, 1H), 7.29 (t, J=9.3 Hz, 1H), 7.24 (d, J=8.6 Hz, 1H), 5.18 (dt, J=10.5, 7.0 Hz, 1H), 5.03 - 4.89 (m, 1H), 4.88 - 4.66 (m, 1H), 4.60 - 4.53 (m, 1H), 4.15 - 4.06 (s, 3H), 3.23 (t, J=3.8 Hz, 1H), 3.17 (dd, J=10.7, 4.1 Hz, 1H), 2.72 (t, J=3.8 Hz, 1H), 2.41 - 2.29 (m, 2H), 2.13 (tt, J=12.4, 6.3 Hz, 1H), 2.05 - 1.88 (m, 2H), 1.68 (td, J=12.8, 6.7 Hz, 1H), 1.61 - 1.48 (m, 4H), 1.18 (d, J=2.9 Hz, 6H), 0.81 - 0.71 (m, 2H), 0.40 - 0.31 (m, 2H)。	2.54, B

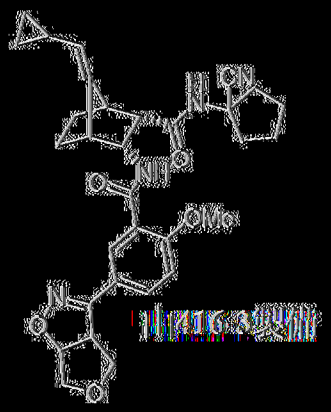
465	 來自(S)-2-丁炔醇	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-(4-氟-3-(三氟甲基)苯基)-3-(5-(5-((S)-1-羥基乙基)異噁唑-3-基)-2-甲氧基苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	614.2	(400 MHz, $CDCl_3$) δ 8.49 (d, J = 2.3 Hz, 1H), 8.14 (dd, J = 6.5, 2.5 Hz, 1H), 7.99 (dd, J = 8.6, 2.3 Hz, 1H), 7.75 (dt, J = 8.8, 3.4 Hz, 1H), 7.31 – 7.25 (m, 2H), 6.69 (d, J = 0.8 Hz, 1H), 5.00 – 4.93 (m, 1H), 4.83 (ss, 6H), 4.73 (d, J = 9.4 Hz, 1H), 4.57 (dd, J = 10.7, 3.0 Hz, 1H), 4.14 (s, 3H), 3.26 – 3.12 (m, 2H), 2.73 – 2.69 (m, 1H), 2.05 – 1.87 (m, 2H), 1.62 – 1.47 (d, 3H), 0.80 – 0.70 (m, 2H), 0.39 – 0.30 (m, 2H)	2.46, C
466	 [illegible]	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-3-{5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-N-(1-甲基環戊基)雙環[2.2.1]庚烷-2-甲醯胺	562.0	(500 MHz, DMSO-d6) δ 10.16 (d, J = 6.6 Hz, 1H), 8.19 (d, J = 2.3 Hz, 1H), 7.78 (dd, J = 8.7, 2.4 Hz, 1H), 7.73 (s, 1H), 7.23 (d, J = 8.8 Hz, 1H), 5.11 (dd, J = 8.6, 5.3 Hz, 1H), 4.60 (d, J = 9.5 Hz, 1H), 4.28 – 4.16 (m, 2H), 4.02 (s, 3H), 3.07 – 3.01 (m, 1H), 2.88 (dd, J = 10.9, 4.3 Hz, 1H), 2.03 – 1.41 (m, 17H), 1.31 (s, 5H), 0.77 – 0.63 (m, 2H), 0.31 (br d, J = 3.6 Hz, 2H)。可能由於與溶劑峰及/或經抑制之水峰重疊，兩個質子在NMR中不可見。	2.39, B

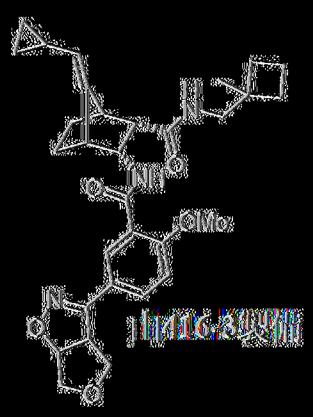
469	 由同對掌性苯甲酸酯中間物製備。峰1酯(RT=4.42 min.，>99% ee)中間物。儀器：Berger MG II管柱：Chiralcel OD-H，21 × 250 mm，5微米，移動相：7% MeOH / 93% CO_2，流動條件：45 mL/min，150巴，40℃，偵測器波長：220 nm；分析方法：儀器：Shimadzu Nexera SFC，管柱Chiralcel OD-H，4.6 × 100 mm，3微米，移動相：7% MeOH / 93% CO_2，流動條件：2 mL/min，150巴， 40℃，偵測器波長：220 nm，得到對掌性(峰-1，RT=4.42 min.，>99% ee)及對掌性(峰-2，RT=5.52 min.，>99% dee)。	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-(2-甲氧基-5-{3-氧雜-4-氮雜三環[5.2.1.0²,⁶]癸-4-烯-5-基}苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	638.0	(500 MHz, DMSO-d6) δ 10.77 - 10.47 (m, 1H), 9.91 (br d, J=7.0 Hz, 1H), 8.51 - 8.15 (m, 2H), 8.06 - 7.74 (m, 2H), 7.49 (br t, J=9.6 Hz, 1H), 7.28 (d, J=8.9 Hz, 1H), 4.71 (br d, J=9.5 Hz, 1H), 4.59 (br d, J=8.2 Hz, 1H), 4.48 - 4.41 (m, 1H), 4.05 (s, 3H), 3.52 (br s, 2H), 3.17 (br dd, J=10.5, 4.1 Hz, 1H), 3.11 (br s, 1H), 2.73 (br s, 1H), 2.47 (br s, 1H), 2.36 (br s, 1H), 1.91 - 1.80 (m, 1H), 1.80 - 1.69 (m, 1H), 1.61 - 1.48 (m, 2H), 1.45 - 1.31 (m, 3H), 1.25 (br s, 1H), 1.14 (br d, J=10.7 Hz, 2H), 0.92 - 0.67 (m, 2H), 0.36 (br s, 2H)	2.84, C

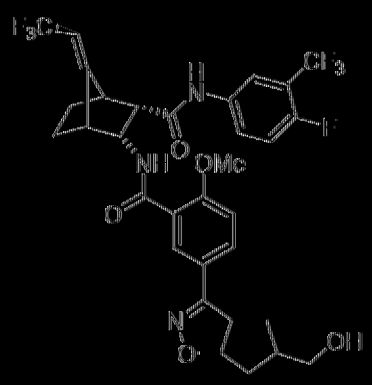
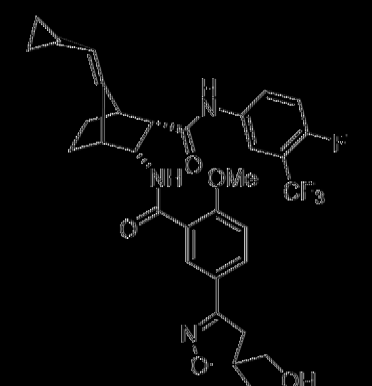
471		(1R,2S,3R,4R,7Z)-7-(環丙基甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-(5-{5-[(3aR,4R,5S,6R,6aR)-環戊并[d][1,2]噁唑-3-基]-2-甲氧基-4-甲基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	641.9	(500 MHz, DMSO-d6) δ 10.23 (br d, J=4.3 Hz, 1H), 9.64 (d, J=7.1 Hz, 1H), 7.95 (br d, J=4.8 Hz, 1H), 7.73 (s, 1H), 7.57 - 7.46 (m, 1H), 7.21 (br t, J=9.7 Hz, 1H), 6.90 (s, 1H), 4.91 - 4.75 (m, 1H), 4.43 (d, J=9.5 Hz, 1H), 4.25 - 4.10 (m, 1H), 3.99 (td, J=9.1, 3.0 Hz, 1H), 3.85 - 3.80 (m, 1H), 3.81 - 3.69 (m, 3H), 3.68 - 3.59 (m, 1H), 2.89 (br dd, J=10.6, 3.4 Hz, 1H), 2.83 (br s, 1H), 2.50 - 2.41 (m, 1H), 2.22 (s, 3H), 1.75 (br dd, J=13.9, 3.5 Hz, 1H), 1.68 - 1.55 (m, 3H), 1.52 - 1.47 (m, 1H), 1.46 - 1.35 (m, 1H), 1.30 - 1.19 (m, 1H), 1.18 - 1.05 (m, 2H), 0.59 - 0.35 (m, 2H), 0.25 - 0.01 (m, 2H)	2.52, B

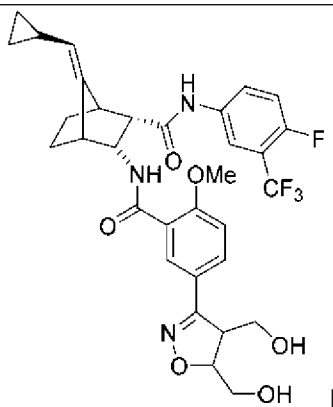
412	 中間體8-2製備	(1R,2S,3R,4R,7Z)-7-(環丙基甲基)-3-(5-{8,9-二羥基-3-氧雜-4-氮雜三環[5.2.1.0^{2,6}]癸-4-烯-5-基}-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	670.2	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.93 (br d, J=7.0 Hz, 1H), 8.36-8.21 (m, 2H), 7.99-7.77 (m, 2H), 7.49 (br t, J=9.8 Hz, 1H), 7.28 (br d, J=8.9 Hz, 1H), 4.96-4.75 (m, 1H), 4.70 (br d, J=9.8 Hz, 1H), 4.58 (br d, J=8.2 Hz, 1H), 4.45 (br s, 1H), 4.08 (s, 3H), 3.80 (br s, 1H), 3.67 (br d, J=4.0 Hz, 1H), 3.63 (br s, 1H), 3.32 (br s, 1H), 3.25-3.09 (m, 2H), 2.73 (br s, 1H), 2.31 (s, 1H), 2.17 (br s, 1H), 1.92 (s, 1H), 1.84 (br d, J=10.1 Hz, 1H), 1.78 (br s, 1H), 1.68 (br d, J=10.4 Hz, 1H), 1.52 (br s, 1H), 1.42 (br s, 2H), 1.11 (br d, J=10.1 Hz, 1H), 0.91-0.70 (m, 2H), 0.36 (br s, 2H)	2.38, C

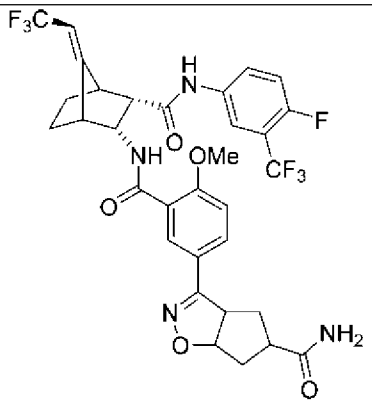
4'3	 由消對掌性苯甲酸酯中間物製備(峰3；100%ee；對掌性分析型RT 4.302 min)；製備型對掌性SFC條件：儀器：Berger MG II；管柱：Chiralpak AD-H，21 × 250 mm，5微米；移動相：20%MeOH / 80% CO_2；流動條件：45 mL/min，150巴，40℃；偵測器波長：220 nm；注射詳情：0.5 mL ~125mg/mL於MeOH:CAN中	(1R,2S,3R,4R,7'Z)-7'-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{2-氟-5-[5-(羥基甲基)-3a'H,4'H,5'H,6'H,6a'H-環戊并[d][1,2]噁唑-3'-基]苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	630.5	(500 MHz, DMSO-d6) δ 10.50 (s, 1H), 9.39 - 9.33 (m, 1H), 8.08 - 8.04 (m, 1H), 8.00 - 7.97 (m, 1H), 7.88 - 7.82 (m, 2H), 7.50 - 7.41 (m, 2H), 5.17 - 5.13 (m, 1H), 4.71 - 4.67 (m, 1H), 4.46 - 4.40 (m, 1H), 4.22 (t, J= 8.6 Hz, 1H), 3.40 - 3.30 (m, 2H), 3.16 (dd, J= 10.6, 4.2 Hz, 1H), 3.11 (t, J= 3.8 Hz, 1H), 2.75 - 2.72 (m, 1H), 1.99 (dd, J= 13.6, 5.8 Hz, 1H), 1.92 - 1.72 (m, 4H), 1.67 - 1.37 (m, 5H), 0.79 - 0.69 (m, 2H), 0.39 - 0.31 (m, 2H)	2.22, A
4'4	 製備型對掌性HPLC之後，將溶劑減壓蒸發得到	(1R,2S,3R,4R,7'Z)-3-(5'-{3a'H,4'H,6'H,6a'H-呋喃并[3,4-d][1,2]噁唑-3'-基}-3-氨基-2-(二甲基胺基)苯甲醯胺基)-7'-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	661.0	(500 MHz, DMSO-d6) δ 10.46 (s, 1H), 9.79 (br d, J= 7.6 Hz, 1H), 8.11 (br d, J= 6.9 Hz, 1H), 7.83 (d, J= 1.5 Hz, 1H), 7.80 - 7.73 (m, 2H), 7.44 (t, J= 9.8 Hz, 1H), 5.35 (dd, J= 9.0, 3.5 Hz, 1H), 4.68 (d, J= 9.5 Hz, 1H), 4.52 - 4.39 (m, 2H), 4.08 (d, J= 11.0 Hz, 1H), 3.95 - 3.87 (m, 1H), 3.68 - 3.56 (m, 2H), 3.21 - 3.11 (m, 1H), 3.07 (br s, 1H), 2.82 (s, 6H), 2.71 (br s, 1H), 1.96 - 1.83 (m, 2H), 1.56 - 1.47 (m, 1H), 1.42 (br d, J= 19.2 Hz, 2H), 0.79 - 0.67 (m, 2H), 0.34 (br s, 2H)	2.93, B

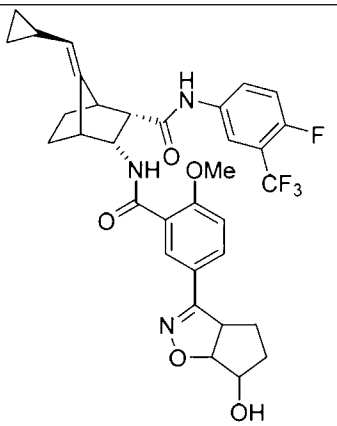
476		(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-N-(1-氰基環戊基)-7-(環丙基甲基)雙環[2.2.1]庚烷-2-甲醯胺	545.1	(500 MHz, DMSO-d6) δ 10.03 (br d, J=6.7 Hz, 1H), 8.69 (s, 1H), 8.20 (d, J=2.1 Hz, 1H), 7.79 (dd, J=8.7, 2.3 Hz, 1H), 7.25 (d, J=8.9 Hz, 1H), 5.34 (dd, J=9.3, 3.5 Hz, 1H), 4.63 (d, J=9.5 Hz, 1H), 4.49 (br t, J=7.6 Hz, 1H), 4.35-4.27 (m, 1H), 4.12-4.02 (m, 4H), 3.93-3.86 (m, 1H), 3.81-3.74 (m, 1H), 3.65 (dd, J=10.8, 3.5 Hz, 1H), 3.07 (br s, 1H), 2.96 (br dd, J=10.7, 4.0 Hz, 1H), 2.59 (br s, 1H), 2.16 (br d, J=4.3 Hz, 2H), 2.09-1.99 (m, 2H), 1.77-1.63 (m, 6H), 1.53-1.31 (m, 3H), 0.77-0.65 (m, 2H), 0.32 (br d, J=2.4 Hz, 2H)。	2.15, B

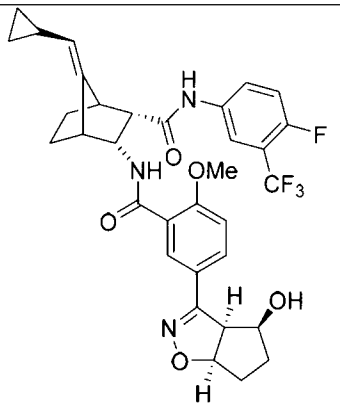
477		(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-[(1-甲基環丁基)甲基]雙環[2.2.1]庚烷-2-甲醯胺	534.0	(500 MHz, DMSO-d6) δ 9.98 (d, J=7.0 Hz, 1H), 8.16 (d, J=2.3 Hz, 1H), 8.05 (t, J=6.1 Hz, 1H), 7.78 (dd, J=8.7, 2.4 Hz, 1H), 7.23 (d, J=8.8 Hz, 1H), 5.34 (dd, J=9.2, 3.6 Hz, 1H), 4.63 (d, J=9.5 Hz, 1H), 4.50 (br t, J=7.9 Hz, 1H), 4.34-4.25 (m, 1H), 4.09 (d, J=10.7 Hz, 1H), 4.01 (s, 3H), 3.90 (d, J=9.5 Hz, 1H), 3.82-3.74 (m, 1H), 3.65 (dd, J=10.7, 3.6 Hz, 1H), 3.15 (dd, J=13.3, 6.4 Hz, 1H), 3.06-2.96 (m, 3H), 1.91-1.67 (m, 6H), 1.60-1.42 (m, 3H), 1.40-1.26 (m, 2H), 1.01 (s, 3H), 0.78-0.65 (m, 2H), 0.32 (dd, J=4.6, 2.1 Hz, 2H)。可能由於與溶劑峰重疊，一個質子不可見。	2.41, C

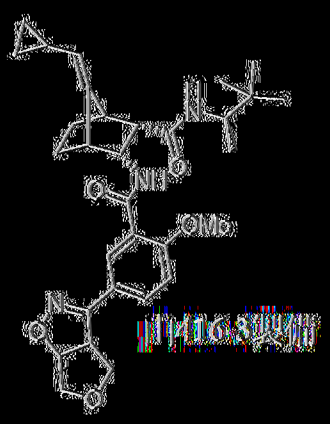
478	 中429.8製備	(1R,2S,3R,4R,7Z)-N-[4-氟-3-(三氟甲基)苯基]-3-[5-[5-(羥甲基)-3a,4,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基]-7-(2,2,2-三氟乙基)雙環[2.2.1]庚烷-2-甲醯胺	670.3	(400 MHz, CD_3OD) δ 10.32 - 10.26 (m, 1H), 8.34 (d, J= 2.2 Hz, 1H), 8.19 (dd, J= 6.3, 2.5 Hz, 1H), 7.92 (dd, J= 8.7, 2.3 Hz, 1H), 7.82 - 7.75 (m, 1H), 7.39 - 7.26 (m, 2H), 5.80 (q, J= 7.5 Hz, 1H), 5.23 (dd, J= 8.6, 5.1 Hz, 1H), 4.72 - 4.63 (m, 1H), 4.30 - 4.21 (m, 1H), 4.16 (s, 3H), 3.61 - 3.51 (m, 2H), 3.43 (br s, 1H), 3.28 (br dd, J= 10.8, 4.2 Hz, 1H), 2.97 (br s, 1H), 2.23 - 1.96 (m, 6H), 1.83 - 1.73 (m, 1H), 1.71 - 1.59 (m, 3H)	2.20, C
480	 峰-2，RT：3.12 min；製備型SFC條件：管柱/尺寸：Chiralpak IC (250 × 30) mm，5u, % CO_2: 50%助溶劑：50% 4M甲醇氨於MEOH中，總流速：140.0g/min，背壓：100巴，溫度：40℃，UV：238 nm。	(1R,2S,3R,4R)-7-(環丙基甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-[5-[5-(羥甲基)-4,5-二氫-1,2-噁唑-3-基]-2-甲氧基苯甲醯胺基]雙環[2.2.1]庚烷-2-甲醯胺	616.3	(500 MHz, DMSO-d6) δ 10.56 (s, 1H), 9.89 (d, J= 6.8 Hz, 1H), 8.22 (dd, J= 6.6, 2.7 Hz, 1H), 8.20 (d, J= 2.2 Hz, 1H), 7.84 - 7.77 (m, 1H),7.75 (dd, J= 8.7, 2.3 Hz, 1H), 7.48 (t, J= 9.8 Hz, 1H), 7.25 (d, J= 8.8 Hz, 1H), 5.14 - 5.01 (m, 1H), 4.69 (d, J= 9.3 Hz, 1H), 4.49 - 4.38 (m, 1H), 4.03(s, 4H), 3.16 (dd, J= 10.6, 4.3 Hz, 2H), 3.12 - 3.07 (m, 1H), 3.02 (d, J= 16.6 Hz, 1H), 2.75 - 2.69 (m, 1H), 1.88 - 1.72 (m, 3H), 1.55 - 1.35 (m, 4H),1.31 (s, 3H), 1.23 (s, 1H), 0.80 - 0.66 (m, 2H), 0.35 (dd, J= 4.5, 2.3 Hz, 2H)。	2.37, D

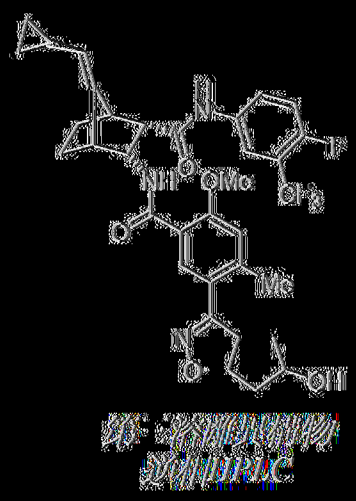
481	 由同對掌性苯甲酸酯中間物(峰2；>99%ee；對掌性分析型RT=6.217 min)製備；製備型對掌性SFC條件：儀器：PIC Solution SFC Prep-200：管柱：Chiralpak IF，21 × 250 mm，5微米：移動相：35% 甲醇/ 65% CO_2：流動條件：45 mL/min，150巴， 40℃；偵測器波長：220 nm；注射詳情：0.75 mL ~50mg/mL於MeOH-CAN中	(1R,2S,3R,4R,7Z)-3-{5-[4,5-雙(羥基甲基)-4,5-二氫-1,2-噁唑-3-基]-2-甲氧基苯甲醯胺基}-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	632.3	(500 MHz, DMSO-d6) δ 10.55 - 10.51 (m, 1H), 9.92 - 9.88 (m, 1H), 8.31 - 8.26 (m, 1H), 8.25 - 8.20 (m, 1H), 7.84 - 7.77 (m, 2H), 7.49 (t, J=9.8 Hz, 1H), 7.29 - 7.25 (m, 1H), 4.70 (d, J=9.5 Hz, 1H), 4.61 - 4.57 (m, 1H), 4.47 - 4.43 (m, 1H), 4.04 (s, 3H), 3.95 (dd, J=12.0, 4.7 Hz, 1H), 3.86 - 3.81 (m, 2H), 3.59 (d, J=4.7 Hz, 2H), 3.17 (dd, J=10.7, 4.1 Hz, 1H), 3.11 (t, J=3.6 Hz, 1H), 2.73 (t, J=3.4 Hz, 1H), 1.87 - 1.76 (m, 2H), 1.54 - 1.47 (m, 1H), 1.46 - 1.37 (m, 2H), 0.80 - 0.70 (m, 2H), 0.39 - 0.33 (m, 2H)	1.08, A

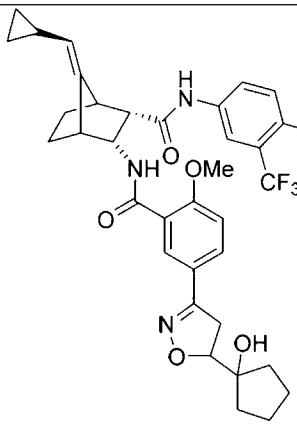
482	 由同對掌性苯甲酸酯中間物(峰2；>99%ee；對掌性分析型RT=2.742 min)製備；製備型對掌性SFC條件：儀器：Jasco SFC Prep：管柱：Chiralpak AS-H，30 × 250 mm，5微米；移動相：30% MeOH / 70% CO_2；流動條件：85 mL/min，150巴，40℃；偵測器波長：220 nm；注射詳情：1.0 mL ~50mg/mLmg/mL於MeOH:TFA中	3-(3-{[(1R,2R,3S,4R,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-5-甲醯胺	683.3	(500 MHz, DMSO-d6) δ 10.65 (s, 1H), 9.97 (d, J=6.9 Hz, 1H), 8.27 - 8.22 (m, 2H), 7.84 - 7.78 (m, 2H), 7.51 (t, J=9.8 Hz, 1H), 7.39 - 7.34 (m, 1H), 7.29 (d, J=8.9 Hz, 1H), 6.81 (br s, 1H), 5.99 - 5.92 (m, 1H), 5.16 (dd, J=8.5, 5.0 Hz, 1H), 4.55 - 4.48 (m, 1H), 4.28 (t, J=8.9 Hz, 1H), 4.05 (s, 3H), 3.31 - 3.23 (m, 2H), 3.02 - 2.97 (m, 1H), 2.58 - 2.53 (m, 1H), 2.13 - 1.85 (m, 6H), 1.50 (br d, J=6.7 Hz, 1H)	1.29

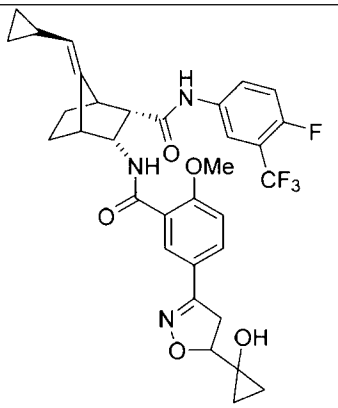
483	 藉由SFC分離之異構物，其中實例483為第四溶離異構物：儀器：Jasco SFC製備型管柱：Chiralpak IA，30 × 250 mm，5微米，移動相：15% MeOH / 85% CO_2，流動條件：85 mL/min，150巴， 40℃，偵測器波長：220 nm， 注射詳情：0.5 mL ~21mg/mL於甲醇中，分析型層析條件：儀器：Shimadzu Nexera SFC管柱：Chiralpak IA，4.6 × 100 mm，3微米，移動相：15% MeOH / 85% CO_2，流動條件：2.0 mL/min，150巴， 40℃，偵測器波長：220 nm，注射詳情：5 µL ~1mg/mL於MeOH中。峰-4 RT 6.83 min > 96.4% ee。	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-(5-{6-羥基-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	628.3	(500 MHz, DMSO-d6) δ 10.56 (s, 1H), 9.91 (br d, J=7.3 Hz, 1H), 8.28 - 8.15 (m, 2H), 7.81 (br d, J=8.5 Hz, 1H), 7.77 (br d, J=9.2 Hz, 1H), 7.47 (br t, J=9.6 Hz, 1H), 7.28 (br d, J=8.9 Hz, 1H), 4.80 (br d, J=8.9 Hz, 1H), 4.70 (d, J=9.8 Hz, 1H), 4.43 (br s, 1H), 4.24 (br t, J=8.5 Hz, 1H), 4.12 (br s, 1H), 4.04 (s, 3H), 3.68 (br s, 2H), 3.26 - 3.07 (m, 2H), 3.00 (s, 1H), 2.72 (br s, 1H), 2.20 (br s, 1H), 1.83 (br d, J=10.1 Hz, 1H), 1.77 (br d, J=9.8 Hz, 1H), 1.70 - 1.58 (m, 2H), 1.50 (br d, J=8.5 Hz, 1H), 1.41 (br s, 3H), 0.84 - 0.69 (m, 2H), 0.35 (br d, J=4.0 Hz, 2H)	2.45

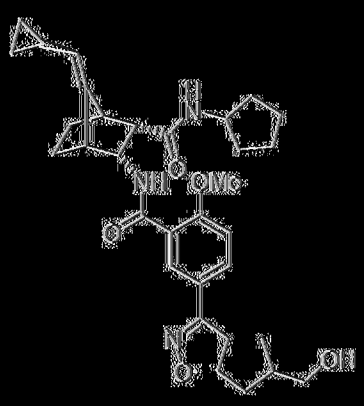
484	 由同對掌性苯甲酸酯中間物-峰1製備。層析條件：儀器：Berger MG II 管柱：Chiralpak IC，30 × 250 mm，5微米，移動相：25%甲醇/ 75% CO_2，流動條件：70 mL/min，120 巴， 40℃，偵測器波長：220 nm， 注射詳情：0.5 mL ~75mg/mL於甲醇中。分析型層析條件：儀器：Shimadzu Nexera SFC管柱：Chiralpak IC，4.6 × 100 mm，3微米，移動相：25% MeOH / 75% CO_2，流動條件：2.0 mL/min，150 巴， 40℃，偵測器波長：220 nm，注射詳情：5 μL ~1mg/mL於MeOH中(峰-1，RT 3.40 min.，> 99% ee)	(1R,2S,3R,4R,7Z)-3-{5-[(3aS,4S,6aR)-4-羥基-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	628.3	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.91 (br d, J=6.7 Hz, 1H), 8.23 (s, 1H), 8.23 (d, J=6.2 Hz, 1H), 7.79 (br d, J=8.5 Hz, 2H), 7.49 (br t, J=9.8 Hz, 1H), 7.28 (d, J=8.9 Hz, 1H), 4.97 (d, J=6.7 Hz, 1H), 4.82 (br dd, J=8.5, 4.6 Hz, 1H), 4.71 (br d, J=9.5 Hz, 1H), 4.45 (br s, 1H), 4.13 (br t, J=9.0 Hz, 1H), 4.05 (s, 3H), 3.47 (br s, 1H), 3.31 - 3.13 (m, 1H), 3.11 (br s, 1H), 2.73 (br s, 1H),1.93 - 1.76 (m, 3H), 1.76 - 1.66 (m, 1H), 1.62 - 1.47 (m, 2H), 1.43 (br s, 2H), 1.40 - 1.19 (m, 2H), 0.86 - 0.68 (m, 2H), 0.36 (br s, 2H)。	2.43

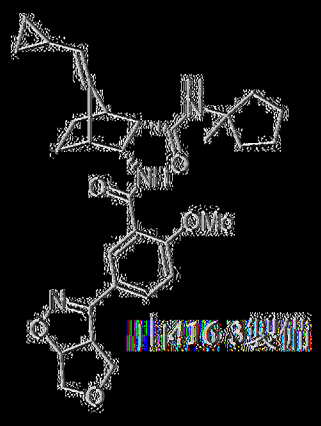
485		(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-[(2R)-3,3-二甲基丁烷-2-基]雙環[2.2.1]庚烷-2-甲醯胺	536.2	(500 MHz, DMSO-d6) δ 10.04 - 9.95 (m, 1H), 8.12 (d, J= 2.1 Hz, 1H), 7.80 - 7.71 (m, 2H), 7.25 - 7.21 (m, 1H), 5.33 (dd, J= 9.3, 3.2 Hz, 1H), 4.62 (d, J= 9.8 Hz, 1H), 4.48 (br t, J= 7.9 Hz, 1H), 4.30 - 4.21 (m, 1H), 4.09 (br d, J= 10.7 Hz, 1H), 4.00 (s, 3H), 3.92 - 3.86 (m, 1H), 3.80 - 3.61 (m, 2H), 3.07 - 3.02 (m, 1H), 3.01 - 2.94 (m, 1H), 1.88 - 1.80 (m, 1H), 1.77 - 1.67 (m, 1H), 1.51 - 1.41 (m, 1H), 1.38 - 1.24 (m, 2H), 0.96 - 0.89 (m, 3H), 0.83 (s, 9H), 0.76 - 0.64 (m, 2H), 0.30 (br d, J= 2.7 Hz, 2H)。可能由於與溶劑峰及/或經抑制之水峰重疊，兩個質子在NMR不可見。	2.46

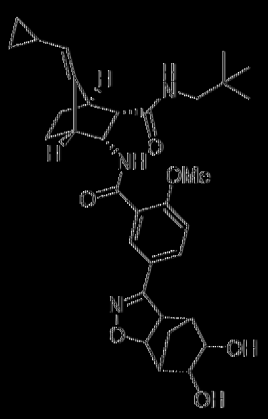
486		(1R,2S,3R,4R,7Z)-7-(環內基-[甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-(5-[5-羥基-3a,4,5,6,6a-五氫-1H-環戊并[d][1,2]噁唑-3-基]-2-甲氧基-4-甲基苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	641.9	(500 MHz, DMSO-d6) δ 10.70 - 10.36 (m, 1H), 10.01 - 9.69 (m, 1H), 8.25 (br d, J= 4.3 Hz, 1H), 8.02 (s, 1H), 7.80 (br d, J= 8.5 Hz, 1H), 7.50 (br t, J= 9.6 Hz, 1H), 7.23 - 7.06 (m, 1H), 5.07 (br t, J= 7.8 Hz, 1H), 4.70 (d, J= 9.8 Hz, 1H), 4.54 - 4.41 (m, 1H), 4.23 - 4.10 (m, 2H), 4.09 - 3.97 (m, 3H), 3.57 - 3.30 (m, 1H), 3.16 (br dd, J= 10.4, 4.0 Hz, 1H), 3.10 (br s, 1H), 2.78 - 2.68 (m, 1H), 2.49 (s, 3H), 2.15 - 2.04 (m, 1H), 2.00 - 1.90 (m, 2H), 1.87 - 1.80 (m, 1H), 1.80 - 1.72 (m, 1H), 1.64 - 1.56 (m, 1H), 1.55 - 1.46 (m, 1H), 1.46 - 1.31 (m, 2H), 0.87 - 0.65 (m, 2H), 0.51 - 0.21 (m, 2H)	2.54

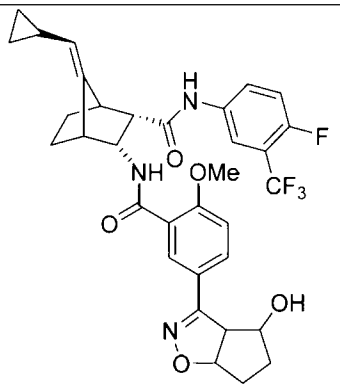
488	 由同對掌性苯甲酸酯製備。峰1-(RT=3.28 min.，>99% de) -儀器：Berger MG II管柱：Chiralpak IC，21 × 250 mm，5微米，移動相：30% MeOH / 70% CO_2，流動條件：45 mL/min，150巴， 40℃，偵測器波長：220 nm；分析方法：儀器：Shimadzu Nexera SFC，管柱ChiralpakIC，4.6 × 100 mm，3微米，移動相：30% MeOH / 70% CO_2，流動條件：2 mL/min，150巴， 40℃，偵測器波長：220 nm，得到對掌性(峰-1，RT=3.28 min.，>99% de)及對掌性(峰-2，RT=3.85 min.，>99% de)。	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(1-羥基環戊基)-4,5-二氫-1,2-噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	656.1	(500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.92 (br d, J=7.0 Hz, 1H), 8.24 (br s, 1H), 8.23 (br s, 1H), 7.80 (br d, J=1.8 Hz, 1H), 7.79 (br d, J=1.8 Hz, 1H), 7.53 - 7.47 (m, 1H), 7.28 (d, J=8.5 Hz, 1H), 4.71 (d, J=9.8 Hz, 1H), 4.60 (dd, J=11.0, 8.9 Hz, 1H), 4.48 - 4.41 (m, 1H), 4.06 (s, 3H), 3.60 - 3.21 (m, 1H), 3.17 (br dd, J=10.5, 4.1 Hz, 1H), 3.12 (br s, 1H), 2.74 (br s, 1H), 1.90 - 1.77 (m, 2H), 1.73 (br s, 2H), 1.64 - 1.49 (m, 7H), 1.45 - 1.37 (m, 2H), 0.76 (br dd, J=11.9, 8.9 Hz, 2H), 0.37 (br s, 2H)	2.65

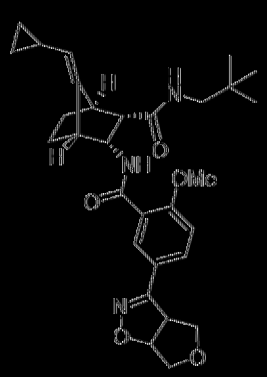
491	 由同對掌性苯甲酸酯中間物-峰2 (RT=6.88 min.，>97% ee)製備，所用儀器：Berger MG II管柱：Chiralpak IF，21 × 250 mm，5微米，移動相：30% MeOH/70% CO_2，流動條件：45 mL/min，150巴， 40℃，偵測器波長：220 nm；分析方法：儀器：Aurora Infinity SFC，管柱Chiralpak IF，4.6 × 250 mm，3微米，移動相：30% MeOH/70% CO_2，流動條件：2 mL/min，150巴， 40℃，偵測器波長：220 nm，得到對掌性(峰-1，RT=4.78 min.，>99% ee)及對掌性(峰-2，RT=6.88 min.，>97% ee)。	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(1-羥基環丙基)-4,5-二氫-1,2-噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	628.4	(500 MHz, DMSO-d6) δ 10.52 (s, 1H), 9.92 (d, J=7.2 Hz, 1H), 8.32 - 8.17 (m, 2H), 7.82 - 7.80 (m, 1H), 7.79 (d, J=2.3 Hz, 1H), 7.49 (t, J=9.8 Hz, 1H), 7.28 (d, J=8.7 Hz, 1H), 5.74 - 5.37 (m, 1H), 4.70 (d, J=9.6 Hz, 1H), 4.52 - 4.43 (m, 1H), 4.38 - 4.30 (m, 1H), 4.05 (s, 3H), 3.45 - 3.41 (m, 2H), 3.17 (dd, J=11.0, 4.1 Hz, 1H), 3.13 - 3.09 (m, 1H), 2.73 (t, J=3.6 Hz, 1H), 1.90 - 1.81 (m, 1H), 1.80 - 1.72 (m, 1H), 1.56 - 1.47 (m, 1H), 1.44 - 1.32 (m, 2H), 0.83 - 0.74 (m, 1H), 0.70 - 0.65 (m, 1H), 0.62 - 0.51 (m, 3H), 0.44 - 0.32 (m, 2H)	2.41, C

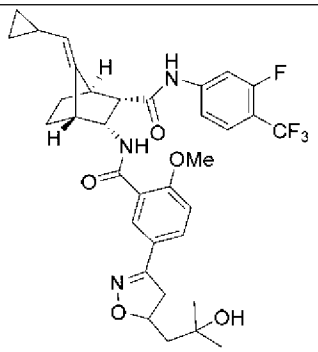
493	 [1429.8]雙鹽	(1R,2S,3R,4R,7Z)-N-環戊基-7-(環丙基甲基)-3-{5-[5-(羥基甲基)-3a,4,4,5,6,6,6a-七氫環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	548.2	(500 MHz, DMSO-d6) δ 10.01 (br d, J=6.7 Hz, 1H), 8.17 (d, J=1.8 Hz, 1H), 8.02 (br d, J=7.0 Hz, 1H), 7.79 (dd, J=8.5, 2.1 Hz, 1H), 7.23 (d, J=8.9 Hz, 1H), 5.11 (br dd, J=8.5, 5.2 Hz, 1H), 4.61 (d, J=9.5 Hz, 1H), 4.48 (br t, J=5.0 Hz, 1H), 4.30-4.23 (m, 1H), 4.20 (br t, J=8.9 Hz, 1H), 4.07-3.97 (m, 4H), 3.04 (br s, 1H), 2.88 (br dd, J=11.0, 4.3 Hz, 1H), 2.02-1.41 (m, 15H), 1.38-1.26 (m, 4H), 0.71 (quin, J=9.7 Hz, 2H), 0.32 (br s, 2H)。可能由於與溶劑峰及/或經抑制之水峰重疊，兩個質子在NMR中不可見。	2.19, B

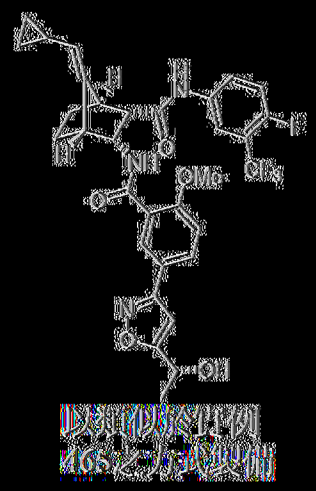
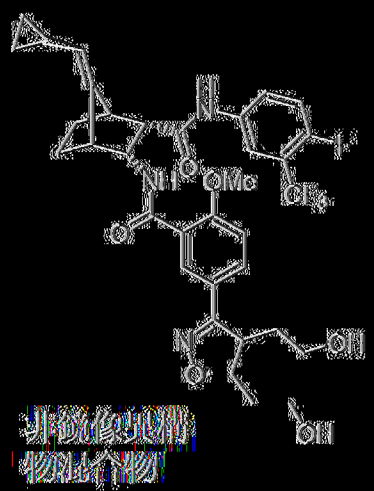
494		(1R,2S,3R,4R,7Z) 3 (5 {3aH,4H,6H,6aH 吠喃并[3,4 d][1,2]噁唑 3 基} 2 甲氧基苯甲醯胺基) 7 (環丙基甲基) N (1 甲基環戊基) 雙環[2.2.1]庚烷 2 甲醯胺	534.4	(500 MHz, DMSO d6) δ 10.17 (br d, J= 6.7 Hz, 1H), 8.17 (d, J= 1.8 Hz, 1H), 7.83 – 7.69 (m, 2H), 7.24 (d, J= 8.5 Hz, 1H), 5.33 (br dd, J= 9.3, 3.2 Hz, 1H), 4.60 (br d, J= 9.5 Hz, 1H), 4.48 (br t, J= 7.9 Hz, 1H), 4.30 – 4.20 (m, 1H), 4.09 (br d, J= 10.7 Hz, 1H), 4.02 (s, 3H), 3.92 – 3.83 (m, 1H), 3.82 – 3.72 (m, 1H), 3.65 (br dd, J= 10.8, 3.5 Hz, 1H), 3.03 (br s, 1H), 2.87 (br dd, J= 11.1, 4.1 Hz, 1H), 2.02 – 1.87 (m, 2H), 1.86 – 1.76 (m, 1H), 1.74 – 1.64 (m, 1H), 1.63 – 1.39 (m, 7H), 1.30 (s, 5H), 0.77 – 0.60 (m, 2H), 0.30 (br d, J= 2.1 Hz, 2H)。可能由於與溶劑峰重疊，一個質子不可見。	2.56, B

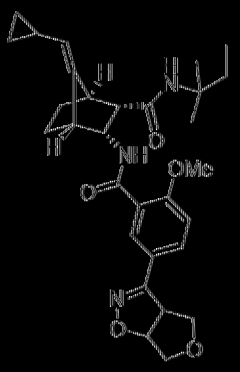
495	 I-448.3製備	(1R,2S,3R,4R,7Z)-7-(環丙基甲基)-3-(5-{8,9-二羥基-3-氧雜-4-氮雜三環[5.2.1.0^{2,6}]癸-4-烯-5-基}-2-甲氧基苯甲醯胺基)-N-(2,2-二甲基丙基)雙環[2.2.1]庚烷-2-甲醯胺	578.6	(500 MHz, DMSO-d6) δ 9.97 (br d, J = 7.0 Hz, 1H), 8.17 (d, J = 2.1 Hz, 1H), 7.97 (br t, J = 6.3 Hz, 1H), 7.80 (dd, J = 8.5, 1.8 Hz, 1H), 7.22 (d, J = 8.9 Hz, 1H), 4.79 (d, J = 5.2 Hz, 1H), 4.62 (br d, J = 9.5 Hz, 1H), 4.56 (br d, J = 8.9 Hz, 1H), 4.32 - 4.23 (m, 1H), 3.99 (s, 2H), 3.80 - 3.75 (m, 1H), 3.68 - 3.58 (m, 1H), 3.07 - 2.97 (m, 3H), 2.79 (br dd, J = 12.8, 5.8 Hz, 1H), 2.29 (s, 1H), 2.15 (s, 1H), 1.88 - 1.82 (m, 1H), 1.77 - 1.69 (m, 1H), 1.66 (br d, J = 11.3 Hz, 1H), 1.49 - 1.41 (m, 1H), 1.40 - 1.27 (m, 2H), 1.09 (br d, J = 10.4 Hz, 1H), 0.80 (s, 8H), 0.75 - 0.65 (m, 2H), 0.31 (br s, 2H)。可能由於與溶劑峰重疊，一個質子在NMR中不可見。	2.12, C

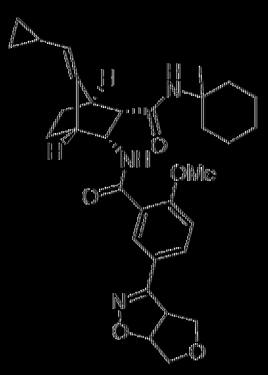
496	 由同對掌性苯甲酸酯中間物峰3製備：製備型層析條件：儀器：Berger MG II管柱：Chiralpak IC，30 × 250 mm，5微米，移動相：25%甲醇/75% CO_2，流動條件：70 mL/min，120 巴， 40℃，偵測器波長：220 nm，注射詳情：0.5 mL ~75mg/mL於甲醇中。分析型層析條件：儀器：Shimadzu Nexera SFC管柱：Chiralpak IC，4.6 × 100 mm，3微米，移動相：25% MeOH/75% CO_2，流動條件：2.0 mL/min，150 巴， 40℃，偵測器波長：220 nm，注射詳情：5 μL ~1mg/mL於MeOH中(峰-3，RT 4.93 min.，> 98% ee)	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-(5-{4-羥基-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	628.2	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.91 (br d, J=7.0 Hz, 1H), 8.33 (d, J=2.1 Hz, 1H), 8.23 (br d, J=4.6 Hz, 1H), 7.98 - 7.82 (m, 1H), 7.79 (br d, J=7.9 Hz, 1H), 7.49 (br t, J=9.6 Hz, 1H), 7.30 (d, J=8.5 Hz, 1H), 5.22 (br dd, J=8.2, 4.9 Hz, 1H), 4.71 (d, J=9.5 Hz, 1H), 4.45 (br s, 1H), 4.12 (br s, 1H), 4.06 (s, 3H), 4.01 - 3.83 (m, 1H), 3.57 - 3.39 (m, 1H), 3.24 - 3.08 (m, 2H), 2.85 - 2.63 (m, 1H), 2.15 (dt, J=13.0, 6.6 Hz, 1H), 1.94 (br dd, J=13.4, 6.4 Hz, 1H), 1.88 - 1.74 (m, 2H), 1.65 (br dd, J=13.0, 6.3 Hz, 1H), 1.56 - 1.37 (m, 4H), 0.88 - 0.68 (m, 2H), 0.36 (br s, 2H)	2.48, C

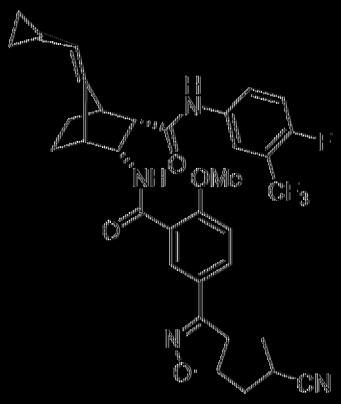
497	 中416.3製備	(1R,2S,3R,4R,7Z) 3 (5 {3aH,4H,6H,6aH 吠喃并[3,4 d][1,2]噁唑 3 基} 2 甲氧基苯甲醯胺基) 7 (環丙基甲基) N (2,2 二甲基丙基)雙環[2.2.1]庚烷 2 甲醯胺	534.4	(500 MHz, DMSO d6) δ 10.17 (br d, J= 6.7 Hz, 1H), 8.17 (d, J= 1.8 Hz, 1H), 7.83 – 7.69 (m, 2H), 7.24 (d, J= 8.5 Hz, 1H), 5.33 (br dd, J= 9.3, 3.2 Hz, 1H), 4.60 (br d, J= 9.5 Hz, 1H), 4.48 (br t, J= 7.9 Hz, 1H), 4.30 – 4.20 (m, 1H), 4.09 (br d, J= 10.7 Hz, 1H), 4.02 (s, 3H), 3.92 – 3.83 (m, 1H), 3.82 – 3.72 (m, 1H), 3.65 (br dd, J= 10.8, 3.5 Hz, 1H), 3.03 (br s, 1H), 2.87 (br dd, J= 11.1, 4.1 Hz, 1H), 2.02 – 1.87 (m, 2H), 1.86 – 1.76 (m, 1H), 1.74 – 1.64 (m, 1H), 1.63 – 1.39 (m, 7H), 1.30 (s, 5H), 0.77 – 0.60 (m, 2H), 0.30 (br d, J= 2.1 Hz, 2H)。可能由於與溶劑峰重疊，一個質子不可見。	2.56, B

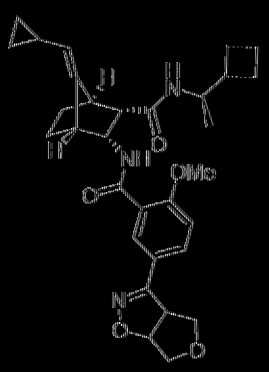
499	 由同對掌性苯甲酸峰2 (RT=7.92 min.，>99% ee)製備。所用儀器：PIC Solution SFC管柱：Chiralpak IC，21 × 250 mm，5微米，移動相：40% MeOH / 60% CO_2，流動條件：45 mL/min，150巴， 40℃，偵測器波長：220 nm；分析方法：儀器：Aurora Infinity SFC，管柱Chiralpak IC，4.6 × 250 mm，3微米，移動相：30% MeOH / 70% CO_2，流動條件：2 mL/min，150巴， 40℃，偵測器波長：220 nm，得到對掌性(峰-1，RT=5.75 min.，>99% ee)及對掌性(峰-2，RT=7.92 min.，>99% ee)。	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(2-羥基-2-甲基丙基)-4,5-二氫-1,2-噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	644.3	(500 MHz, DMSO-d6) δ 10.52 (s, 1H), 9.91 (d, J=7.2 Hz, 1H), 8.23 (dd, J=6.6, 2.6 Hz, 1H), 8.21 (d, J=2.4 Hz, 1H), 7.82 - 7.79 (m, 1H), 7.78 (d, J=2.4 Hz, 1H), 7.49 (t, J=9.8 Hz, 1H), 7.27 (d, J=8.9 Hz, 1H), 4.79 (tt, J=9.8, 6.1 Hz, 1H), 4.70 (d, J=9.6 Hz, 1H), 4.45 (ddd, J=10.2, 6.4, 4.1 Hz, 1H), 4.05 (s, 3H), 3.54 (d, J=10.2 Hz, 1H), 3.51 (d, J=10.2 Hz, 1H), 3.17 (dd, J=10.8, 4.2 Hz, 1H), 3.13 - 3.09 (m, 1H), 3.09 - 3.03 (m, 1H), 2.73 (t, J=3.5 Hz, 1H), 1.90 - 1.82 (m, 2H), 1.79 - 1.70 (m, 2H), 1.57 - 1.48 (m, 1H), 1.45 - 1.37 (m, 2H), 1.18 (s, 3H), 1.17 (s, 3H), 0.81 - 0.70 (m, 2H), 0.36 (dd, J=4.4, 2.6 Hz, 2H)	2.47, C

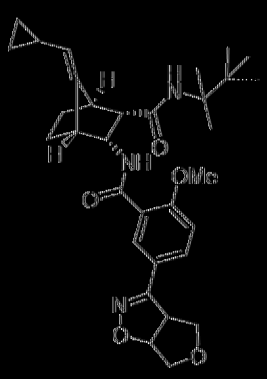
500	 以類似於製備例465之方式製備	(1R,2S,3R,4R,7Z)-7-(環丙基甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-(5-{5-[(1R)-1-羥基乙基]-1,2-噁唑-3-基}-2-甲氧基苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	614.2	(500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.94 (br d, J=7.0 Hz, 1H), 8.45 (d, J=1.8 Hz, 1H), 8.24 (br d, J=4.0 Hz, 1H), 8.00 (dd, J=8.4, 2.0 Hz, 1H), 7.81 (br d, J=9.5 Hz, 1H), 7.50 (t, J=9.8 Hz, 1H), 7.34 (d, J=8.9 Hz, 1H), 6.86 (s, 1H), 5.78 (d, J=5.5 Hz, 1H), 4.89 (br t, J=6.3 Hz, 1H), 4.72 (d, J=9.8 Hz, 1H), 4.48 (br s, 1H), 4.08 (s, 3H), 3.18 (br d, J=10.1 Hz, 1H), 3.13 (br s, 1H), 2.74 (br s, 1H), 1.93-1.75 (m, 2H), 1.56-1.38 (m, 5H), 0.88-0.69 (m, 2H), 0.37 (br s, 2H)	2.51, C
501	 非鏡像異構物混合物	(1R,2S,3R,4R,7Z)-3-{5-[4,5-雙(2-羥基乙基)-4,5-二氫-1,2-噁唑-3-基]-2-甲氧基苯甲醯胺基}-7-(環丙基甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	660.0	(500 MHz, DMSO-d6) δ 10.51 (s, 1H), 9.90 (t, J=6.9 Hz, 1H), 8.28-8.20 (m, 2H), 7.82-7.76 (m, 2H), 7.48 (t, J=9.8 Hz, 1H), 7.27 (d, J=8.7 Hz, 1H), 4.72-4.58 (m, 3H), 4.48-4.42 (m, 1H), 4.04 (d, J=2.0 Hz, 2H), 3.59 (br dd, J=6.8, 3.1 Hz, 1H), 3.54-3.46 (m, 5H), 3.18-3.09 (m, 2H), 2.75-2.69 (m, 1H), 1.86-1.56 (m, 6H), 1.55-1.46 (m, 2H), 1.45-1.36 (m, 2H), 0.79-0.69 (m, 2H), 0.39-0.31 (m, 2H)	2.12, C

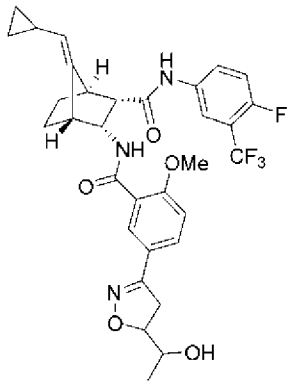
502	 I-416-3製備	(1R,2S,3R,4R,7′)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7′-(環丙基甲基)-N-(2-甲基丙烷-2-基)雙環[2.2.1]庚烷-2-甲醯胺	522.3	(500 MHz, DMSO-d6) δ 10.10 (br d, J=6.7 Hz, 1H), 8.19 (d, J=2.1 Hz, 1H), 7.79 (dd, J=8.5, 2.4 Hz, 1H), 7.48 (s, 1H), 7.24 (d, J=8.9 Hz, 1H), 5.34 (dd, J=8.9, 3.4 Hz, 1H), 4.60 (d, J=9.5 Hz, 1H), 4.50 (br t, J=7.6 Hz, 1H), 4.30-4.20 (m, 1H), 4.09 (br d, J=10.7 Hz, 1H), 4.03 (s, 3H), 3.93-3.86 (m, 1H), 3.82-3.73 (m, 1H), 3.66 (dd, J=10.7, 3.4 Hz, 1H), 3.03 (br s, 1H), 2.92 (br dd, J=10.5, 4.4 Hz, 1H), 1.91-1.82 (m, 1H), 1.76-1.55 (m, 3H), 1.50-1.40 (m, 1H), 1.38-1.26 (m, 2H), 1.19 (d, J=15.3 Hz, 6H), 0.78-0.64 (m, 5H), 0.31 (br d, J=3.7 Hz, 2H)。可能由於溶劑峰重疊，一個質子在 NMR 中不可見。	2.35, B

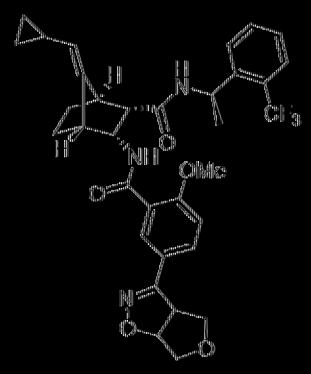
505	 中間體3	(1R,2S,3R,4R,7′′)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7′-(環丙基甲基)-N-(1-甲基環丙基)雙環[2.2.1]庚烷-2-甲醯胺	548.2	(500 MHz, DMSO-d6) δ 10.13 (br d, J= 6.7 Hz, 1H), 8.18 (d, J= 2.1 Hz, 1H), 7.78 (dd, J= 8.7, 2.0 Hz, 1H), 7.36 (s, 1H), 7.23 (d, J= 8.9 Hz, 1H), 5.34 (dd, J= 9.2, 3.4 Hz, 1H), 4.61 (d, J= 9.5 Hz, 1H), 4.50 (br t, J= 7.9 Hz, 1H), 4.31-4.20 (m, 1H), 4.09 (br d, J= 10.7 Hz, 1H), 4.01 (s, 3H), 3.92-3.85 (m, 1H), 3.80-3.73 (m, 1H), 3.65 (dd, J= 10.8, 3.5 Hz, 1H), 3.03 (br s, 1H), 2.98 (br dd, J= 10.8, 3.8 Hz, 1H), 2.12 (br d, J= 14.0 Hz, 1H), 2.02-1.93 (m, 1H), 1.91-1.83 (m, 1H), 1.77-1.65 (m, 1H), 1.51-1.09 (m, 14H), 0.78-0.64 (m, 2H), 0.31 (br d, J= 3.7 Hz, 2H)。可能由於與溶劑峰重疊，一個質子在 NMR 中不可見。	2.61, B

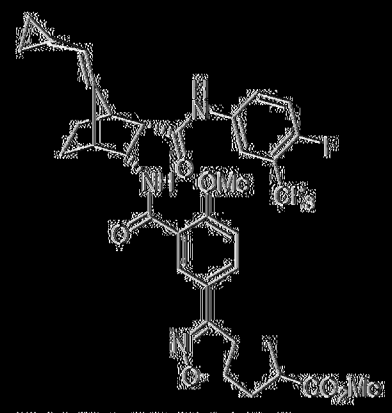
506	 非鏡像異構物混合物	(1R,2S,3R,4R,7′′)-3-(5-{5-氧代-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	637.1	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.92–9.87 (m, 1H), 8.25–8.19 (m, 2H), 7.78 (br d, J = 8.9 Hz, 2H), 7.47 (br t, J = 9.8 Hz, 1H), 7.21 (d, J = 8.9 Hz, 1H), 5.21–5.15 (m, 1H), 4.68 (br d, J = 9.5 Hz, 1H), 4.43 (br s, 1H), 4.38–4.29 (m, 1H), 4.03 (s, 3H), 3.18–3.12 (m, 1H), 3.09 (br s, 1H), 2.81 (tt, J = 12.1, 6.4 Hz, 1H), 2.71 (br s, 1H), 2.41 (br dd, J = 13.3, 5.6 Hz, 1H), 2.27–2.10 (m, 3H), 1.86–1.73 (m, 2H), 1.49 (br s, 1H), 1.44–1.35 (m, 2H), 0.79–0.68 (m, 2H), 0.39–0.30 (m, 2H)	.60, B

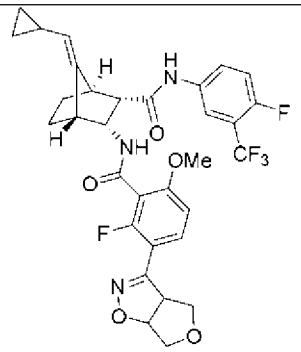
507	 中416.3製備	(1R,2S,3R,4R,7′′)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-N-[(1R)-1-環丁基乙基]-7-(環內基雙甲基)雙環[2.2.1]庚烷-2-甲醯胺	534.5	(500 MHz, DMSO-d6) δ 10.06 (d, J= 6.8 Hz, 1H), 8.14 (d, J= 2.3 Hz, 1H), 7.82 (br d, J= 8.6 Hz, 1H), 7.78 (dd, J= 8.7, 2.4 Hz, 1H), 7.23 (d, J= 8.8 Hz, 1H), 5.33 (dd, J= 9.2, 3.5 Hz, 1H), 4.61 (d, J= 9.5 Hz, 1H), 4.49 (br t, J= 7.9 Hz, 1H), 4.31-4.22 (m, 1H), 4.09 (d, J= 10.8 Hz, 1H), 4.01 (s, 3H), 3.89 (br d, J= 9.0 Hz, 1H), 3.85-3.73 (m, 2H), 3.65 (dd, J= 10.8, 3.6 Hz, 1H), 3.07-3.01 (m, 1H), 2.89 (dd, J= 10.8, 4.3 Hz, 1H), 2.26-2.17 (m, 1H), 1.95-1.80 (m, 3H), 1.80-1.59 (m, 5H), 1.51-1.41 (m, 1H), 1.40-1.26 (m, 2H), 0.88 (d, J= 6.6 Hz, 3H), 0.78-0.64 (m, 2H), 0.31 (dd, J= 4.4, 2.1 Hz, 2H)。可能由於與溶劑峰重疊，一個質子在NMR中不可見。	2.37, C

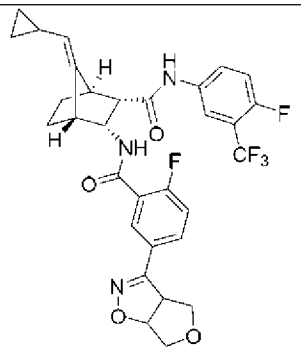
508	 I-416.3製備	(1R,2S,3R,4R,7′)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7′-(環丙基甲基)-N-(2,3,3-三甲基丁烷-2-基)雙環[2.2.1]庚烷-2-甲醯胺	550.0	(500 MHz, DMSO-d6) δ 10.14 (br d, J=6.7 Hz, 1H), 8.19 (d, J=2.1 Hz, 1H), 7.78 (br dd, J=8.7, 2.3 Hz, 1H), 7.23 (br d, J=8.9 Hz, 1H), 7.16 (s, 1H), 5.37-5.29 (m, 1H), 4.61 (br d, J=9.5 Hz, 1H), 4.54-4.44 (m, 1H), 4.24 (br d, J=5.5 Hz, 1H), 4.09 (br d, J=10.7 Hz, 1H), 4.01 (s, 3H), 3.89 (br d, J=8.5 Hz, 1H), 3.81-3.74 (m, 1H), 3.69-3.61 (m, 1H), 3.08-3.00 (m, 2H), 1.87 (br d, J=10.7 Hz, 1H), 1.74-1.64 (m, 1H), 1.50-1.41 (m, 1H), 1.32 (s, 5H), 1.25 (s, 3H), 0.89 (s, 9H), 0.76-0.64 (m, 2H), 0.30 (br s, 2H)。可能由於與溶劑峰重疊，一個質子在NMR中不可見。	2.33, B

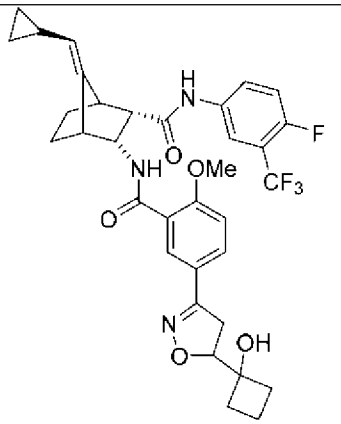
509	 由同對掌性苯甲酸中間物(峰2；86.6%de；對掌性分析型RT=9.186 min)製備；對掌性SFC純化條件；儀器：Berger MG II；管柱：Chiralpak IC，21 × 250 mm，5微米；移動相：20% MeOH / 80% CO_2；流動條件：45 mL/min，150巴， 40℃；偵測器波長：220 nm；注射詳情：0.5 mL ~35mg/mL於MeOH中	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(1-羥基乙基)-4,5-二氫-1,2-噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	616.4	(500 MHz, CD_3OD) δ 10.35 - 10.30 (m, 1H), 10.17 - 10.14 (m, 1H), 8.37 - 8.35 (m, 1H), 8.17 (dd, J=6.2, 2.7 Hz, 1H), 7.91 (dd, J=8.7, 2.4 Hz, 1H), 7.80 - 7.75 (m, 1H), 7.33 - 7.26 (m, 2H), 4.76 (d, J=9.5 Hz, 1H), 4.63 - 4.56 (m, 2H), 4.15 (s, 3H), 3.92 - 3.86 (m, 1H), 3.45 - 3.39 (m, 2H), 3.28 - 3.23 (m, 2H), 3.18 (dd, J=10.6, 3.9 Hz, 1H), 2.76 - 2.72 (m, 1H), 2.05 - 2.00 (m, 1H), 1.97 - 1.91 (m, 1H), 1.65 - 1.58 (m, 1H), 1.57 - 1.51 (m, 2H), 1.35 (t, J=7.3 Hz, 1H), 1.24 (s, 2H), 0.82 - 0.76 (m, 2H), 0.42 - 0.35 (m, 2H)	2.25, A

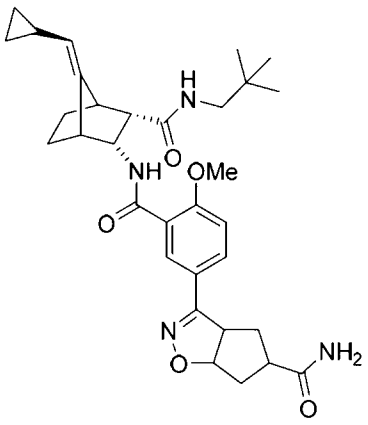
510	 由416-3製備	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-[(1R)-1-[2-(三氟甲基)苯基]乙基]雙環[2.2.1]庚烷-2-甲醯胺	623.9	(500 MHz, DMSO-d6) δ 9.83 (d, J=6.7 Hz, 1H), 8.74 (d, J=7.0 Hz, 1H), 8.14 (d, J=2.3 Hz, 1H), 7.72 (dd, J=8.7, 2.4 Hz, 1H), 7.61 (d, J=8.0 Hz, 2H), 7.49 (br t, J=7.6 Hz, 1H), 7.35-7.27 (m, 1H), 7.11-7.04 (m, 1H), 5.32 (dd, J=9.2, 3.5 Hz, 1H), 5.28-5.17 (m, 1H), 4.65 (d, J=9.5 Hz, 1H), 4.50-4.41 (m, 1H), 4.30-4.21 (m, 1H), 4.08 (d, J=10.8 Hz, 1H), 3.91-3.84 (m, 1H), 3.79-3.71 (m, 1H), 3.67-3.61 (m, 1H), 3.59-3.53 (m, 2H), 3.07-2.95 (m, 2H), 2.67-2.60 (m, 1H), 1.92-1.82 (m, 1H), 1.71-1.59 (m, 1H), 1.55-1.40 (m, 1H), 1.37-1.25 (m, 5H), 0.78-0.64 (m, 2H), 0.37-0.29 (m, 2H)。	2.43, A

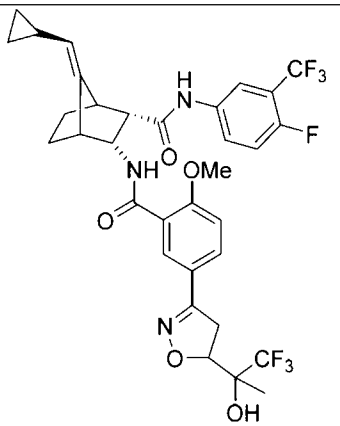
512	 非經修正結構物組合物	3-(3-{[(1R,2R,3S,4R,7Z)-7-(環丙基甲基)-3-[4-氟-3-(三氟甲基)苯甲醯基]雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-5-甲酸甲酯	669.9	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.92 (br d, J= 5.2 Hz, 1H), 8.27 - 8.20 (m, 2H), 7.80 (br t, J= 9.3 Hz, 2H), 7.49 (br t, J= 9.9 Hz, 1H), 7.29 (d, J= 8.5 Hz, 1H), 5.32 - 5.14 (m, 1H), 4.70 (br d, J= 9.2 Hz, 1H), 4.45 (br s, 1H), 4.31 (br s, 1H), 4.05 (s, 6H), 3.59 (s, 1H), 3.47 (br s, 1H), 3.17 (br dd, J= 10.4, 4.0 Hz, 1H), 3.11 (br s, 1H), 2.80 - 2.59 (m, 2H), 2.22 (br dd, J= 13.6, 6.0 Hz, 1H), 1.89 - 1.72 (m, 2H), 1.52 (br s, 1H), 1.42 (br s, 2H), 0.86 - 0.69 (m, 2H), 0.36 (br s, 2H)	2.60, C

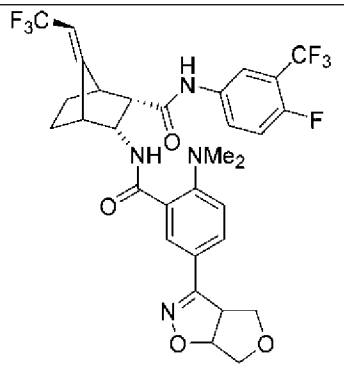
513	 經分離之異構物，其中實例513為峰1 (RT=6.74 min.，>95% de)：儀器：Waters 100 Prep SFC管柱：Chiral OD, 30 × 250 mm, 5微米，移動相：15% MeOH / 85% CO_2 (具有0.1% DEA)，流動條件：100 mL/min，偵測器波長：220 nm；分析方法：儀器：Shimadzu Nexera SFC，管柱Chiral OD，4.6 × 100 mm，5微米，移動相：15% MeOH / 85% CO_2 (具有0.1% DEA)，流動條件：2 mL/min，偵測器波長：220 nm，得到對掌性(峰-1，RT=6.74 min.，>95% de)及對掌性(峰-2，RT=8.25 min.，>95% de)。	(1R,2S,3R,4R,7Z)-3-(3-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-氟-6-甲氧基苯甲醯胺基)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	632.2	(500 MHz, DMSO-d6) δ 10.53 - 10.34 (m, 1H), 8.75 (br d, J=7.5 Hz, 1H), 8.07 (br d, J=6.3 Hz, 1H), 7.82 - 7.66 (m, 2H), 7.57 - 7.36 (m, 1H), 7.03 (d, J=9.0 Hz, 1H), 5.31 (dd, J=9.2, 3.4 Hz, 1H), 4.67 (d, J=9.8 Hz, 1H), 4.53 - 4.32 (m, 2H), 4.08 (br d, J=10.8 Hz, 1H), 3.84 (s, 1H), 3.80 - 3.67 (m, 3H), 3.65 - 3.55 (m, 2H), 3.50 - 3.31 (m, 1H), 3.18 - 3.05 (m, 2H), 2.70 (br s, 1H), 2.05 - 1.92 (m, 1H), 1.83 (br t, J=9.9 Hz, 1H), 1.47 - 1.31 (m, 2H), 0.81 - 0.66 (m, 2H), 0.47 - 0.25 (m, 2H)	2.33, B

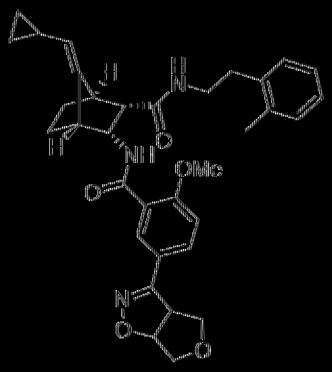
514	 由同對掌性苯甲酸酯中間物峰2 (RT=7.22 min，>99% ee)製備。所用儀器：Jasco SFC管柱：Chiralpak AD-H，21 × 250 mm，5微米，移動相：20% MeOH / 80% CO_2，流動條件：45 mL/min，150巴， 40℃，偵測器波長：220 nm；分析方法：儀器：Shimadzu Nexera SFC，管柱Chiralpak AD-H，4.6 × 100 mm，3微米，移動相：20% MeOH / 80% CO_2，流動條件：2 mL/min，150巴， 40℃，偵測器波長：240 nm，得到對掌性(峰-1，RT=1.99 min.，>99% ee)及對掌性(峰-2，RT=7.22 min.，>99% ee)。	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-氟苯甲醯胺基)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	602.3	(500 MHz, DMSO-d6) δ 10.52 (s, 1H), 9.35 (t, J=6.6 Hz, 1H), 8.06 (dd, J=7.1, 2.4 Hz, 1H), 8.02 (dd, J=6.5, 2.5 Hz, 1H), 7.88 (ddd, J=8.5, 4.7, 2.4 Hz, 1H), 7.86 - 7.77 (m, 1H), 7.57 - 7.39 (m, 2H), 5.39 (dd, J=9.2, 3.7 Hz, 1H), 4.71 (d, J=9.6 Hz, 1H), 4.58 - 4.50 (m, 1H), 4.46 - 4.38 (m, 1H), 4.11 (d, J=10.8 Hz, 1H), 3.99 - 3.91 (m, 1H), 3.77 - 3.72 (m, 2H), 3.69 - 3.62 (m, 1H), 3.26 - 3.16 (m, 1H), 3.13 (t, J=3.8 Hz, 1H), 2.75 (t, J=4.0 Hz, 1H), 1.89 - 1.81 (m, 1H), 1.80 - 1.67 (m, 1H), 1.60 - 1.48 (m, 1H), 1.45 - 1.34 (m, 1H), 0.86 - 0.65 (m, 2H), 0.45 - 0.25 (m, 2H)	2.48, C

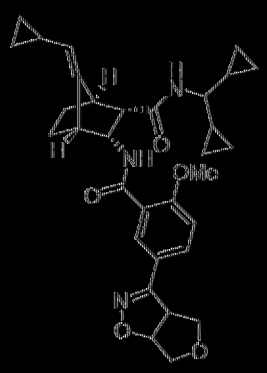
515	 由同對掌性苯甲酸酯中間物- 峰2 (RT=3.85 min，>99% ee)製備。所用儀器：Berger MG II管柱：Chiralcel OD-H, 21 × 250 mm，5微米，移動相：30% MeOH / 70% CO_2，流動條件：45 mL/min，150巴， 40℃，偵測器波長：220 nm；分析方法：儀器：Shimadzu Nexera SFC，管柱Chiralpak IC，4.6 × 100 mm，3微米，移動相：30% MeOH / 70% CO_2，流動條件：2 mL/min，150巴， 40℃，偵測器波長：220 nm，得到對掌性(峰-1，RT=3.29 min.，>99% ee)及對掌性(峰-2，RT=3.85 min.，>99% ee)。	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(1-羥基環丁基)-4,5-二氫-1,2-噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	642.2	(500 MHz, DMSO-d6) δ 10.53 - 10.34 (m, 1H), 8.75 (br d, J=7.5 Hz, 1H), 8.07 (br d, J=6.3 Hz, 1H), 7.82 - 7.66 (m, 2H), 7.57 - 7.36 (m, 1H), 7.03 (d, J=9.0 Hz, 1H), 5.31 (dd, J=9.2, 3.4 Hz, 1H), 4.67 (d, J=9.8 Hz, 1H), 4.53 - 4.32 (m, 2H), 4.08 (br d, J=10.8 Hz, 1H), 3.84 (s, 1H), 3.80 - 3.67 (m, 3H), 3.65 - 3.55 (m, 2H), 3.50 - 3.31 (m, 1H), 3.18 - 3.05 (m, 2H), 2.70 (br s, 1H), 2.05 - 1.92 (m, 1H), 1.83 (br t, J=9.9 Hz, 1H), 1.47 - 1.31 (m, 2H), 0.81 - 0.66 (m, 2H), 0.47 - 0.25 (m, 2H)	2.67, B

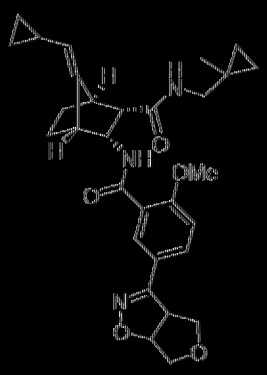
516	 由與實例459中相同之同對掌性苯甲酸酯製備	3-(3-{[(1R,2R,3S,4R,7Z)-7-(環丙基亞甲基)-3-[(2,2-二甲基丙基)胺甲醯基]雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-5-甲醯胺	563.0	(500 MHz, DMSO-d6) δ 9.95 (br d, J=6.7 Hz, 1H), 8.18 (d, J=2.1 Hz, 1H), 7.97 (br t, J=6.1 Hz, 1H), 7.77 (dd, J=8.5, 2.1 Hz, 1H), 7.37 (br s, 1H), 7.23 (d, J=8.9 Hz, 1H), 6.80 (br s, 1H), 5.15 (br dd, J=8.5, 4.9 Hz, 1H), 4.63 (d, J=9.2 Hz, 1H), 4.33 - 4.22 (m, 2H), 4.00 (s, 3H), 3.08 - 2.96 (m, 3H), 2.79 (br dd, J=13.0, 5.3 Hz, 1H), 2.13 - 1.83 (m, 5H), 1.77 - 1.68 (m, 1H), 1.53 - 1.41 (m, 1H), 1.39 - 1.27 (m, 2H), 0.81 (s, 9H), 0.75 - 0.63 (m, 2H), 0.32 (br s, 2H)。可能由於與溶劑峰重疊，兩個質子在 NMR 中不可見。	2.09, B

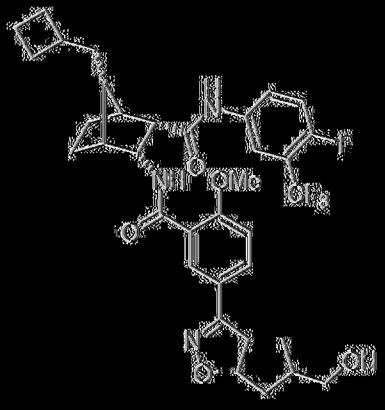
517	 由同對掌性苯甲酸酯中間物峰2製備。製備型層析條件：儀器：PIC Solution SFC Prep-200 (CTR-L409-PSFC2)管柱：Chiralpak IC，21 × 250 mm，5微米，移動相：10%甲醇/ 90% CO_2，流動條件：45 mL/min，150巴， 40℃，偵測器波長：220 nm，注射詳情：0.5 mL ~65mg/mL於甲醇中，分析型層析條件：儀器：Aurora Infinity SFC (CTR-L410-ASFC2)管柱：Chiralpak IC，4.6 × 250 mm，3微米，移動相：10%甲醇/ 90% CO_2，流動條件：2.0 mL/min，150巴， 40℃，偵測器波長：220 nm，注射詳情：15 μL ~1mg/mL於MeOH中。峰-2，RT 4.39 min.，> 98.5% ee。	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{2-甲氧基-5-[5-(1,1,1-三氟-2-羥基丙烷-2-基)-4,5-二氫-1,2-噁唑-3-基]苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	684.2	(500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.92 (d, J=7.1 Hz, 1H), 8.28 - 8.19 (m, 2H), 7.86 - 7.76 (m, 2H), 7.49 (t, J=9.7 Hz, 1H), 7.28 (d, J=8.8 Hz, 1H), 6.47 (s, 1H), 4.83 (dd, J=10.7, 8.4 Hz, 1H), 4.70 (d, J=9.6 Hz, 1H), 4.45 (br s, 1H), 4.05 (s, 3H), 3.59 - 3.37 (m, 1H), 3.17 (br dd, J=10.9, 4.0 Hz, 1H), 3.11 (br s, 1H), 2.73 (br s, 1H), 1.89 - 1.69 (m, 2H), 1.59 - 1.46 (m, 1H), 1.42 (br s, 2H), 1.30 (s, 3H), 0.83 - 0.67 (m, 2H), 0.36 (br s, 2H)	2.61, C

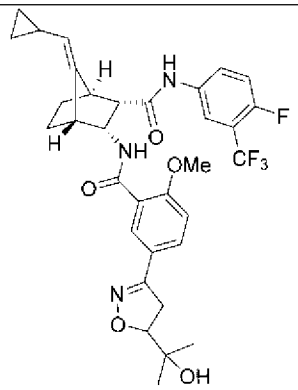
518	 藉由SFC分離之異構物，其中實例518為峰2 (RT=8.63 min，>95% ee)：所用儀器：Waters 100 Prep SFC管柱：Chiral AD，30 × 250 mm，5微米，移動相：20% MeOH / 80% CO_2 (具有0.1% DEA)，流動條件：100 mL/min，偵測器波長：220 nm；分析方法：儀器：Shimadzu Nexera SFC，管柱Chiral AD，4.6 × 100 mm，5微米，移動相：20% MeOH / 80% CO_2 (具有0.1% DEA)，流動條件：2 mL/min，偵測器波長：220 nm，得到對掌性(峰-1，RT=1.5 min.，>95% ee)及對掌性(峰-2，RT=3.25 min.，>95% ee)。	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-(二甲基胺基)苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-甲醯胺	655.0	(500 MHz, DMSO-d6) δ 10.05 (br d, J=7.3 Hz, 1H), 8.21 (br d, J=4.9 Hz, 1H), 7.91 (d, J=1.8 Hz, 1H), 7.76 (br s, 1H), 7.69 (br d, J=8.9 Hz, 1H), 7.48 (br t, J=9.6 Hz, 1H), 7.22 (d, J=8.5 Hz, 1H), 5.93 (q, J=7.9 Hz, 1H), 5.31 (br dd, J=9.0, 3.2 Hz, 1H), 4.54 (br s, 1H), 4.44 (br t, J=7.8 Hz, 1H), 4.07 (br d, J=10.7 Hz, 1H), 3.88 (br d, J=8.9 Hz, 1H), 3.79 - 3.67 (m, 1H), 3.63 (br dd, J=10.7, 3.4 Hz, 1H), 2.98 (br s, 1H), 2.71 (s, 6H), 2.57 - 2.52 (m, 2H), 2.04 - 1.86 (m, 2H), 1.49 (br s, 1H), 0.84 (br s, 2H)	2.50, B

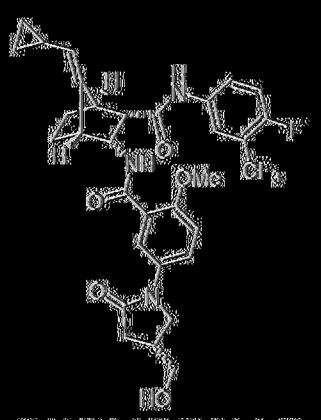
520	 中416.3製備	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-吡喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-[2-(2-甲基苯基)乙基]雙環[2.2.1]庚烷-2-甲醯胺	570.3	(500 MHz, DMSO-d6) δ 10.01 (br d, J= 6.7 Hz, 1H), 8.22 (br t, J= 5.5 Hz, 1H), 8.17 (d, J= 2.1 Hz, 1H), 7.79 (dd, J= 8.9, 2.1 Hz, 1H), 7.24 (d, J= 8.9 Hz, 1H), 7.14-7.00 (m, 4H), 5.33 (dd, J= 9.2, 3.4 Hz, 1H), 4.61 (d, J= 9.8 Hz, 1H), 4.50 (br t, J= 7.8 Hz, 1H), 4.32-4.24 (m, 1H), 4.09 (br d, J= 11.0 Hz, 1H), 4.03 (s, 3H), 3.93-3.86 (m, 1H), 3.77 (dd, J= 9.0, 6.9 Hz, 1H), 3.65 (dd, J= 10.8, 3.5 Hz, 1H), 3.25-3.14 (m, 1H), 3.07-3.00 (m, 1H), 2.90-2.83 (m, 1H), 2.70 (br t, J= 7.3 Hz, 2H), 2.27 (s, 3H), 1.82-1.67 (m, 2H), 1.45 (td, J= 8.4, 4.0 Hz, 1H), 1.39-1.22 (m, 2H), 0.77-0.62 (m, 2H), 0.32 (br d, J= 3.4 Hz, 2H)。可能由於與溶劑峰及/或經抑制之水峰重疊，兩個質子在NMR中不可見	2.49, C

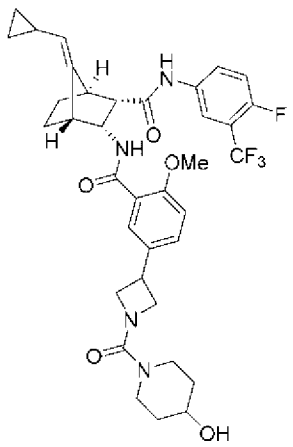
521	 I-416.3製備	(1R,2S,3R,4R,7*Z*)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基亞甲基)-N-(二環丙基甲基)雙環[2.2.1]庚烷-2-甲醯胺	546.0	(500 MHz, DMSO-d6) δ 9.96 (br d, J = 7.0 Hz, 1H), 8.16 (d, J = 2.1 Hz, 1H), 7.97 (br d, J = 8.9 Hz, 1H), 7.78 (dd, J = 8.7, 2.3 Hz, 1H), 7.23 (d, J = 8.5 Hz, 1H), 5.34 (dd, J = 9.0, 3.2 Hz, 1H), 4.63 (d, J = 9.5 Hz, 1H), 4.50 (br t, J = 7.9 Hz, 1H), 4.35 - 4.24 (m, 1H), 4.09 (br d, J = 10.4 Hz, 1H), 3.97 (s, 3H), 3.93 - 3.85 (m, 1H), 3.82 - 3.74 (m, 1H), 3.65 (dd, J = 11.0, 3.7 Hz, 1H), 3.07 - 2.95 (m, 2H), 2.91 (br dd, J = 10.7, 4.0 Hz, 1H), 1.91 - 1.80 (m, 1H), 1.77 - 1.68 (m, 1H), 1.54 - 1.41 (m, 1H), 1.33 (br s, 2H), 0.95 - 0.84 (m, 2H), 0.77 - 0.63 (m, 2H), 0.49 - 0.26 (m, 5H), 0.24 - 0.10 (m, 5H)。可能由於與溶劑峰重疊，一個質子在NMR中不可見。	2.28, B

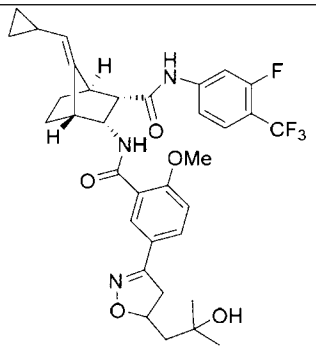
522	 中416.3製備	(1R,2S,3R,4R,7Z) 3 (5 {3aH,4H,6H,6aH 吡喃并[3,4 d][1,2]噁唑 3 基} 2 甲氧基苯甲醯胺基) 7 (環丙基甲基) N [(1 甲基環丙基)甲基] 雙環[2.2.1]庚烷 2 甲醯胺	520.1	(500 MHz, DMSO d6) δ 9.98 (br d, J= 6.7 Hz, 1H), 8.15 (s, 1H), 8.12 - 8.06 (m, 1H), 7.71 (br d, J= 8.5 Hz, 1H), 7.26 - 7.21 (m, 1H), 5.33 (br dd, J= 9.2, 3.1 Hz, 1H), 4.62 (br d, J= 9.5 Hz, 1H), 4.48 (br t, J= 7.9 Hz, 1H), 4.32 - 4.22 (m, 1H), 4.08 (br d, J= 11.0 Hz, 1H), 4.00 (s, 3H), 3.89 (br d, J= 8.9 Hz, 1H), 3.71 (br t, J= 8.1 Hz, 1H), 3.67 - 3.59 (m, 1H), 3.09 - 3.00 (m, 2H), 2.97 - 2.85 (m, 2H), 1.89 - 1.80 (m, 1H), 1.71 - 1.68 (m, 1H), 1.45 (br dd, J= 8.4, 4.4 Hz, 1H), 1.39 - 1.24 (m, 2H), 0.96 (s, 3H), 0.70 (quin, J= 9.7 Hz, 2H), 0.40 - 0.27 (m, 4H), 0.17 (s, 2H)。可能由於與溶劑峰重疊，一個質子在NMR中不可見。	2.18, B

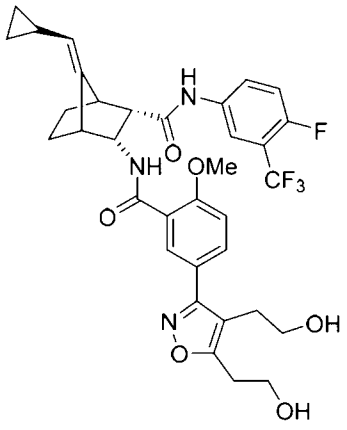
523	 中間體8製備之吲哚胺2,3-雙加氧酶抑制劑化合物	(1S,2S,3R,4R)-1'-(環丁基甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(溴基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	658.1	(500 MHz, DMSO-d6) δ 10.55 - 10.44 (m, 1H), 9.87 (d, J=1.0 Hz, 1H), 8.22 (br d, J=2.3 Hz, 2H), 7.78 (br dd, J=8.6, 2.4 Hz, 2H), 7.47 (br t, J=9.6 Hz, 1H), 7.26 (d, J=8.7 Hz, 1H), 5.11 (dd, J=8.7, 5.3 Hz, 1H), 4.65 - 4.46 (m, 1H), 4.42 (br s, 1H), 4.20 (br t, J=9.0 Hz, 1H), 4.12 - 3.95 (m, 3H), 3.55 - 3.36 (m, 1H), 3.10 (br dd, J=10.6, 4.1 Hz, 1H), 3.00 (s, 1H), 2.37 - 2.22 (m, 3H), 2.07 (ddd, J=11.5, 7.1, 3.5 Hz, 2H), 1.98 (br dd, J=13.5, 6.0 Hz, 1H), 1.93 - 1.72 (m, 5H), 1.70 - 1.49 (m, 6H), 1.49 - 1.33 (m, 4H)	2.16, C

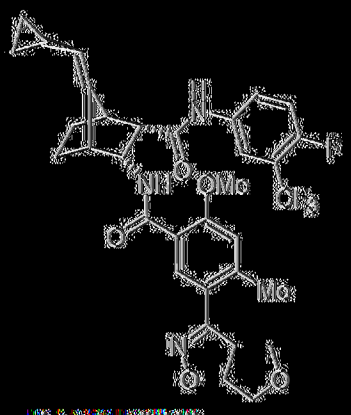
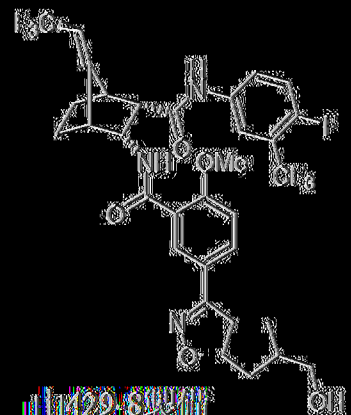
524	 由同對掌性苯甲酸-峰2 (RT=7.7 min.)製備。所用製備型層析條件：儀器：Berger MG II管柱：Chiralpak AD-H，21 × 250 mm，5微米，移動相：40% MeOH / 60% CO_2，流動條件：45 mL/min，150巴， 40℃，偵測器波長：220 nm，注射詳情：0.5 mL ~65mg/mL於甲醇中，分析型層析條件：儀器：Shimadzu Nexera SFC，管柱：Chiralpak AD-H，4.6 × 100 mm，3微米，移動相：35% MeOH / 65% CO_2，流動條件：2.0 mL/min，150巴， 40℃，偵測器波長：220 nm，注射詳情：5 μL ~1mg/mL於MeOH中；滯留時間：峰-1 = 5.51 min，峰-2 = 7.7 min。	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(2-羥基丙烷-2-基)-4,5-二氫-1,2-噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	630.1	(500 MHz, DMSO-d6) δ 10.70 - 10.46 (m, 1H), 9.92 (br d, J=7.0 Hz, 1H), 8.46 - 8.12 (m, 2H), 7.93 - 7.71 (m, 2H), 7.47 (br t, J=9.9 Hz, 1H), 7.27 (d, J=8.9 Hz, 1H), 4.69 (d, J=9.5 Hz, 1H), 4.52 - 4.25 (m, 2H), 4.03 (s, 2H), 3.71 - 3.54 (m, 4H), 3.37 - 3.22 (m, 1H), 3.15 (br dd, J=10.4, 4.0 Hz, 1H), 3.10 (br s, 1H), 2.72 (br s, 1H), 1.95 - 1.81 (m, 1H), 1.78 - 1.71 (m, 1H), 1.56 - 1.47 (m, 1H), 1.44 - 1.35 (m, 1H), 1.11 (br s, 3H), 1.10 (br s, 3H), 0.84 - 0.66 (m, 2H), 0.35 (br d, J=4.0 Hz, 2H)	2.46, B

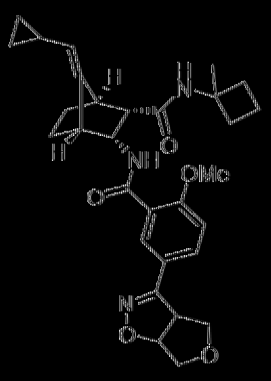
526	 非極性製備物純化條件	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-[5-[4-(羥基甲基)-2-側氧基吡咯啶-1-基]-2-甲氧基苯甲醯胺基]雙環[2.2.1]庚烷-2-甲醯胺	616.5	(500 MHz, DMSO-d6) δ 10.51 (s, 1H), 9.88 (dd, J=7.1, 3.6 Hz, 1H), 8.22 (br d, J=3.9 Hz, 1H), 8.18-8.06 (m, 1H), 7.87-7.70 (m, 2H), 7.48 (br t, J=9.7 Hz, 1H), 7.26-7.14 (m, 1H), 4.69 (d, J=9.6 Hz, 1H), 4.54-4.35 (m, 1H), 4.04-3.93 (m, 3H), 3.92-3.81 (m, 1H), 3.65-3.53 (m, 1H), 3.51-3.41 (m, 1H), 3.15 (br dd, J=11.0, 4.1 Hz, 1H), 3.09 (br s, 1H), 2.77-2.66 (m, 1H), 2.64-2.52 (m, 1H), 2.28 (dd, J=16.5, 5.1 Hz, 1H), 1.92-1.73 (m, 3H), 1.63-1.43 (m, 2H), 1.43-1.33 (m, 2H), 0.82-0.64 (m, 3H), 0.40-0.29 (m, 2H)	2.21, B

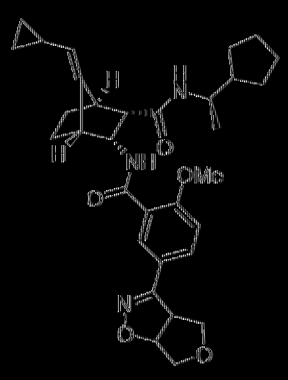
527		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[1-(4-羥基哌啶-1-羰基)氮雜環丁烷-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	685.2	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.86 (br d, J=7.0 Hz, 1H), 8.23 (br d, J=4.6 Hz, 1H), 7.92 (d, J=1.8 Hz, 1H), 7.84 - 7.70 (m, 1H), 7.53 - 7.43 (m, 2H), 7.17 (d, J=8.5 Hz, 1H), 4.70 (d, J=9.5 Hz, 1H), 4.53 - 4.39 (m, 1H), 4.33 - 4.20 (m, 2H), 3.99 (s, 3H), 3.88 - 3.72 (m, 2H), 3.70 - 3.52 (m, 2H), 3.16 (br dd, J=11.0, 4.0 Hz, 1H), 3.10 (br s, 1H), 2.92 (br t, J=10.1 Hz, 2H), 2.72 (br s, 1H), 1.92 - 1.83 (m, 1H), 1.82 - 1.75 (m, 1H), 1.74 - 1.66 (m, 2H), 1.56 - 1.35 (m, 3H), 1.34 - 1.18 (m, 2H), 0.82 - 0.67 (m, 2H), 0.36 (br s, 2H)	2.32, A

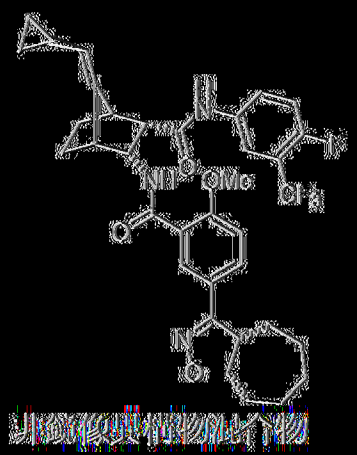
528	 藉由SFC分離之異構物，其中實例528為峰2 (RT=16.4 min，>95% ee)：所用儀器：Waters 100 Prep SFC管柱：Chiral OD，30 × 250 mm， 5微米，移動相：15% MeOH / 85% CO_2 (具有0.1% DEA)，流動條件：100 mL/min，偵測器波長：220 nm；分析方法：儀器：Shimadzu Nexera SFC，管柱Chiral OD，4.6 × 100 mm，5微米，移動相：15% MeOH / 85% CO_2 (具有0.1% DEA)，流動條件：2 mL/min，偵測器波長：220 nm，得到對掌性(峰-1，RT=13.9 min.，>95% ee)及對掌性(峰-2，RT=16.4 min.，>95% ee)。	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(2-羥基-2-甲基丙基)-4,5-二氫-1,2-噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	644.3	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.90 (d, J=7.0 Hz, 1H), 8.27 - 8.16 (m, 2H), 7.78 (br dd, J=8.6, 2.1 Hz, 2H), 7.48 (t, J=9.7 Hz, 1H), 7.26 (d, J=8.8 Hz, 1H), 4.86 - 4.76 (m, 1H), 4.69 (d, J=9.6 Hz, 1H), 4.52 - 4.39 (m, 2H), 4.04 (s, 3H), 3.22 - 3.13 (m, 1H), 3.11 - 3.00 (m, 2H), 2.72 (br d, J=3.3 Hz, 1H), 1.91 - 1.80 (m, 2H), 1.77 - 1.66 (m, 2H), 1.59 - 1.47 (m, 1H), 1.45 - 1.31 (m, 2H), 1.18 (s, 3H), 1.16 (s, 3H), 0.74 (br dd, J=11.5, 9.0 Hz, 2H), 0.35 (br d, J=1.7 Hz, 2H) 可能由於與溶劑峰重疊，一個質子在NMR中不可見	2.52, B

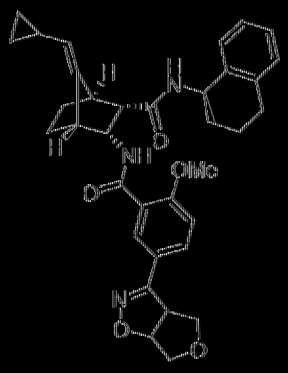
531		(1R,2S,3R,4R,7Z)-3-{5-[4,5-雙(2-羥基乙基)-1,2-噁唑-3-基]-2-甲氧基苯甲醯胺基}-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	658.1	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.93 (d, J=7.2 Hz, 1H), 8.41 (d, J=2.4 Hz, 1H), 8.23 (dd, J=6.4, 2.6 Hz, 1H), 7.96 (dd, J=8.7, 2.4 Hz, 1H), 7.80 (dt, J=8.4, 3.7 Hz, 1H), 7.49 (t, J=9.8 Hz, 1H), 7.35 - 7.30 (m, 1H), 6.83 (s, 1H), 4.73 - 4.68 (m, 1H), 4.47 (ddd, J=10.2, 6.4, 4.2 Hz, 1H), 4.07 (s, 3H), 3.77 (t, J=6.4 Hz, 2H), 3.53 - 3.46 (m, 4H), 3.17 (dd, J=10.7, 4.3 Hz, 1H), 3.12 (t, J=3.7 Hz, 1H), 3.05 (t, J=6.3 Hz, 2H), 2.73 (t, J=3.6 Hz, 1H), 1.88 - 1.78 (m, 2H), 1.55 - 1.48 (m, 1H), 1.47 - 1.38 (m, 2H), 0.80 - 0.71 (m, 2H), 0.40 - 0.33 (m, 2H)	2.25, A

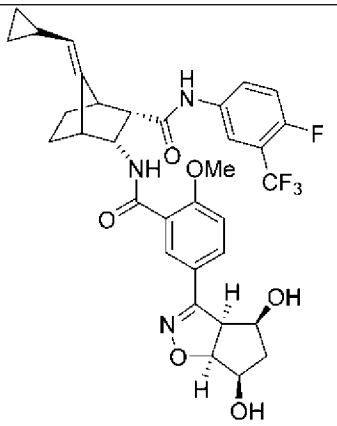
532	 曲線532之峰值	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基-4-甲基苯甲醯胺基)-7-(環丙基甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	628.2	(500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.88 (br d, J=7.0 Hz, 1H), 8.21 (br d, J=5.5 Hz, 1H), 7.95 (s, 1H), 7.85–7.68 (m, 1H), 7.48 (br t, J=9.3 Hz, 1H), 7.18 (s, 1H), 5.39–5.16 (m, 1H), 4.70 (br d, J=9.5 Hz, 1H), 4.52 (br t, J=7.8 Hz, 1H), 4.43 (br s, 1H), 4.18–3.94 (m, 3H), 3.91–3.87 (m, 1H), 3.80–3.74 (m, 1H), 3.73–3.69 (m, 1H), 3.61 (s, 1H), 3.58–3.55 (m, 1H), 3.21–3.12 (m, 1H), 3.09 (br s, 1H), 2.72 (br s, 1H), 2.60–2.54 (m, 1H), 1.90–1.81 (m, 1H), 1.80–1.70 (m, 1H), 1.56–1.46 (m, 1H), 1.44–1.32 (m, 2H), 0.83–0.61 (m, 2H), 0.35 (br s, 2H)可能由於與溶劑峰重疊，一個質子在NMR中不可見	2.60, C
533	 曲線429.8之峰值	(1R,2S,3R,4R,7Z)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-7-(2,2,2-三氟乙基)雙環[2.2.1]庚烷-2-甲醯胺	670.2	(500 MHz, DMSO-d6) δ 9.97 (br d, J=7.0 Hz, 1H), 8.23 (br d, J=2.2 Hz, 2H), 7.81 (br dd, J=8.5, 2.2 Hz, 2H), 7.54–7.48 (m, 1H), 7.28 (d, J=8.8 Hz, 1H), 5.97–5.91 (m, 1H), 5.16–5.11 (m, 1H), 4.53–4.49 (m, 1H), 4.14–4.07 (m, 1H), 4.04 (s, 3H), 3.43 (s, 3H), 3.31–3.20 (m, 2H), 2.23–2.10 (m, 3H), 1.98–1.85 (m, 2H), 1.78 (br s, 2H), 1.67–1.61 (m, 1H), 1.52–1.43 (m, 3H)	2.33, C

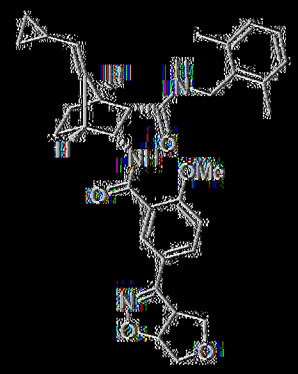
534	 中間體 39製備	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-(1-甲基環丁基)雙環[2.2.1]庚烷-2-甲醯胺	520.0	(500 MHz, DMSO-d6) δ 10.14 (d, J= 6.7 Hz, 1H), 8.19 (d, J= 2.4 Hz, 1H), 8.10 (s, 1H), 7.79 (dd, J= 8.6, 2.4 Hz, 1H), 7.24 (d, J= 8.8 Hz, 1H), 5.34 (dd, J= 9.3, 3.6 Hz, 1H), 4.60 (d, J= 9.5 Hz, 1H), 4.53 - 4.45 (m, 1H), 4.30 - 4.21 (m, 1H), 4.09 (d, J= 10.7 Hz, 1H), 4.02 (s, 3H), 3.90 (br d, J= 9.2 Hz, 1H), 3.78 (dd, J= 9.4, 7.0 Hz, 1H), 3.65 (dd, J= 10.9, 3.6 Hz, 1H), 3.04 (br s, 1H), 2.85 (dd, J= 10.9, 3.9 Hz, 1H), 2.29 - 2.15 (m, 2H), 1.97 - 1.81 (m, 3H), 1.79 - 1.65 (m, 3H), 1.52 - 1.41 (m, 1H), 1.40 - 1.27 (m, 5H), 0.77 - 0.65 (m, 2H), 0.38 - 0.26 (m, 2H)。可能由於溶劑峰重疊，一個質子在 NMR 中不可見。	2.33, C

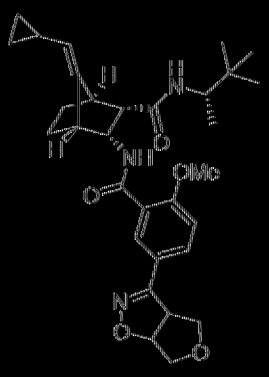
535	 中416-3製備	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-N-[(1R)-1-環戊基乙基]-7-(環丙基甲基)雙環[2.2.1]庚烷-2-甲醯胺	548.3	(500 MHz, DMSO-d6) δ 10.06 (d, J= 6.7 Hz, 1H), 8.14 (d, J= 2.3 Hz, 1H), 7.91 (br d, J= 8.7 Hz, 1H), 7.78 (dd, J= 8.7, 2.4 Hz, 1H), 7.23 (d, J= 8.8 Hz, 1H), 5.33 (dd, J= 9.3, 3.6 Hz, 1H), 4.62 (d, J= 9.6 Hz, 1H), 4.49 (br t, J= 7.8 Hz, 1H), 4.31-4.23 (m, 1H), 4.09 (d, J= 10.7 Hz, 1H), 4.00 (s, 3H), 3.90 (br d, J= 10.0 Hz, 1H), 3.77 (dd, J= 9.3, 6.9 Hz, 1H), 3.73-3.67 (m, 1H), 3.65 (dd, J= 10.8, 3.7 Hz, 1H), 3.07-3.02 (m, 1H), 2.89 (dd, J= 10.7, 4.2 Hz, 1H), 1.90-1.69 (m, 3H), 1.68-1.39 (m, 7H), 1.36-1.27 (m, 2H), 1.23-1.08 (m, 2H), 0.99 (d, J= 6.6 Hz, 3H), 0.77-0.64 (m, 2H), 0.36-0.24 (m, 2H)。可能由於與溶劑峰重疊，一個質子在NMR中不可見。	2.34, B

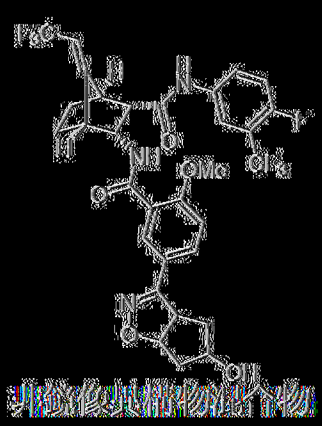
537		(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,5H,6H,7H,8H,9H,9aH-環辛並[d]吡唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	654.1	(500 MHz, DMSO-d6) δ 10.52 (s, 1H), 9.90 (dd, J = 7.0, 3.6 Hz, 1H), 8.26 - 8.20 (m, 2H), 7.78 (ddd, J = 8.6, 3.6, 2.4 Hz, 2H), 7.48 (t, J = 9.8 Hz, 1H), 7.27 (d, J = 8.8 Hz, 1H), 7.22 - 6.99 (m, 1H), 4.68 (d, J = 9.6 Hz, 1H), 4.47 - 4.37 (m, 2H), 4.06 - 4.02 (m, 3H), 3.66 - 3.59 (m, 1H), 2.72 (br s, 1H), 1.98 - 1.76 (m, 4H), 1.72 - 1.60 (m, 4H), 1.56 - 1.45 (m, 3H), 1.45 - 1.24 (m, 6H), 0.78 - 0.69 (m, 2H), 0.38 - 0.32 (m, 2H)	2.92, B

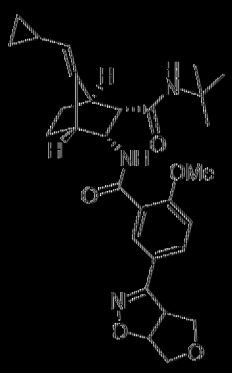
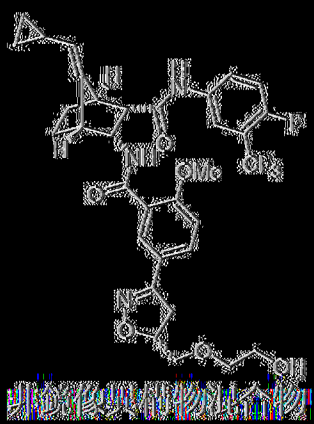
538	 中416-3製備	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-[(1R)-1,2,3,4-四氫萘-1-基]雙環[2.2.1]庚烷-2-甲醯胺	582.1	(500 MHz, DMSO-d6) δ 10.02 (br d, J=7.0 Hz, 1H), 8.46 (br d, J=8.5 Hz, 1H), 8.16 (d, J=2.1 Hz, 1H), 7.80 (dd, J=8.7, 2.3 Hz, 1H), 7.25 (d, J=8.9 Hz, 1H), 7.17 - 7.04 (m, 4H), 5.34 (br dd, J=9.0, 3.5 Hz, 1H), 5.02 (br d, J=5.5 Hz, 1H), 4.61 (br d, J=9.5 Hz, 1H), 4.50 (br t, J=7.8 Hz, 1H), 4.36 - 4.27 (m, 1H), 4.10 (br d, J=10.4 Hz, 1H), 4.02 (s, 3H), 3.91 (br d, J=9.5 Hz, 1H), 3.78 (br dd, J=9.2, 7.0 Hz, 1H), 3.66 (br dd, J=10.5, 3.5 Hz, 1H), 3.07 (br s, 1H), 2.96 (br dd, J=11.0, 3.7 Hz, 1H), 2.78 - 2.64 (m, 2H), 2.01 (br t, J=8.7 Hz, 1H), 1.91 - 1.77 (m, 3H), 1.74 - 1.57 (m, 2H), 1.53 - 1.34 (m, 3H), 0.71 (br t, J=8.4 Hz, 2H), 0.31 (br d, J=4.0 Hz, 2H)。可能由於與溶劑峰重疊，一個質子在NMR中不可見	2.47, B

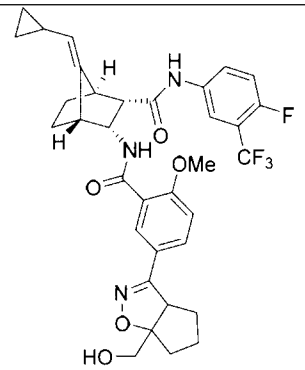
539	 由同對掌性苯甲酸酯中間物峰3製備。製備型層析條件：儀器：PIC Solution SFC Prep-200，管柱：Chiralpak IC，21 × 250 mm，5微米，移動相：10%甲醇/ 90% CO_2，流動條件：45 mL/min，150巴，40℃，偵測器波長：220 nm，注射詳情：0.5 mL ~65 mg/mL於甲醇中，分析型層析條件：儀器：Aurora Infinity SFC，管柱：Chiralpak IC，4.6 × 250 mm，3微米，移動相：10%甲醇/ 90% CO_2，流動條件：2.0 mL/min，150巴，40℃，偵測器波長：220 nm，注射詳情：15 μL ~1mg/mL於MeOH中。峰-3，RT 4.83 min.，> 99% ee。	(1R,2S,3R,4R,7Z)-3-{5-[(3aS,4S,6R,6aS)-4,6-二羥基-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	644.2	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.89 (br d, J=7.0 Hz, 1H), 8.27 (d, J=2.1 Hz, 1H), 8.20 (br d, J=4.0 Hz, 1H), 7.78 (d, J=8.1 Hz, 1H), 7.47 (br t, J=9.8 Hz, 1H), 7.19 (d, J=8.9 Hz, 1H), 4.78 (dd, J=8.4, 4.1 Hz, 1H), 4.70 (d, J=9.8 Hz, 1H), 4.43 (br s, 1H), 4.38 - 4.22 (m, 1H), 4.00 (s, 3H), 3.68 - 3.52 (m, 1H), 3.20 - 3.06 (m, 2H), 3.00 (s, 1H), 2.80 - 2.63 (m, 1H), 2.07 - 1.92 (m, 1H), 1.92 - 1.73 (m, 2H), 1.59 - 1.46 (m, 2H), 1.41 (br s, 2H), 0.86 - 0.68 (m, 2H), 0.35 (br d, J=3.7 Hz, 2H)	2.47, C

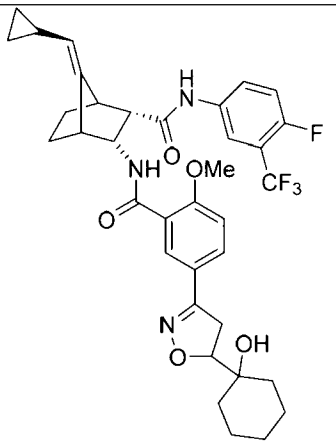
540	 中間體3	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-[(2,6-二甲基苯基)甲基]雙環[2.2.1]庚烷-2-甲醯胺	570.1	(500 MHz, DMSO-d6) δ 9.97 (d, J = 7.1 Hz, 1H), 8.17 (d, J = 2.3 Hz, 1H), 8.11 (br t, J = 4.8 Hz, 1H), 7.84 – 7.75 (m, 1H), 7.26 (d, J = 8.8 Hz, 1H), 7.08 – 7.01 (m, 1H), 7.01 – 6.92 (m, 2H), 5.34 (dd, J = 9.2, 3.4 Hz, 1H), 4.58 (d, J = 9.7 Hz, 1H), 4.50 (br t, J = 7.5 Hz, 1H), 4.32 – 4.25 (m, 3H), 4.10 (d, J = 10.6 Hz, 1H), 4.06 (s, 3H), 3.91 (br d, J = 9.4 Hz, 1H), 3.78 (dd, J = 9.2, 7.0 Hz, 1H), 3.66 (dd, J = 10.7, 3.5 Hz, 1H), 3.03 (br t, J = 3.9 Hz, 1H), 2.94 (dd, J = 10.5, 4.4 Hz, 1H), 2.25 (s, 6H), 1.97 – 1.86 (m, 1H), 1.82 – 1.70 (m, 1H), 1.51 – 1.27 (m, 3H), 0.76 – 0.64 (m, 2H), 0.35 – 0.23 (m, 2H)。可能由於與溶劑峰重疊，一個質子在NMR中不可見。	2.40, B

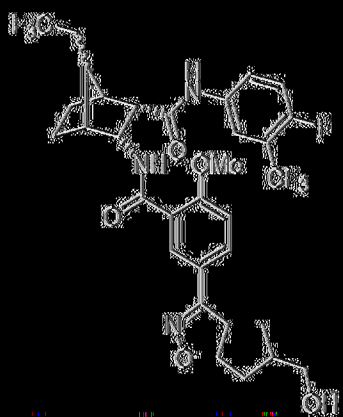
541	 H416.3製備	(1R,2S,3R,4R,7′)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7′-(環丙基甲基)-N-[(2S)-3,3-二甲基丁烷-2-基]雙環[2.2.1]庚烷-2-甲醯胺	536.3	(500 MHz, DMSO-d6) δ 9.95 (br d, J= 6.7 Hz, 1H), 8.15 (d, J= 1.8 Hz, 1H), 7.77 (dd, J= 8.5, 2.4 Hz, 1H), 7.70 (br d, J= 9.5 Hz, 1H), 7.22 (d, J= 8.9 Hz, 1H), 5.33 (dd, J= 9.5, 3.4 Hz, 1H), 4.61 (d, J= 9.5 Hz, 1H), 4.48 (br t, J= 7.5 Hz, 1H), 4.29 (br d, J= 3.1 Hz, 1H), 4.09 (d, J= 10.7 Hz, 1H), 4.00 (s, 3H), 3.93-3.87 (m, 1H), 3.80-3.59 (m, 2H), 3.03 (br s, 1H), 2.97 (br dd, J= 10.7, 3.7 Hz, 1H), 1.94-1.84 (m, 1H), 1.77-1.68 (m, 1H), 1.51-1.41 (m, 1H), 1.39-1.26 (m, 2H), 0.93 (d, J= 6.7 Hz, 3H), 0.76 (s, 9H), 0.73-0.64 (m, 2H), 0.31 (br d, J= 3.7 Hz, 2H)。可能由於溶劑峰及/或經抑制之水峰重疊，兩個質子在NMR中不可見。	2.33, C

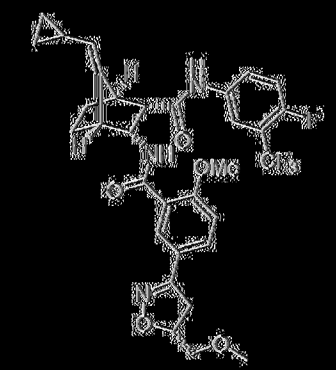
543	 中間產物結構	(1R,2S,3R,4R,7Z)-N-[4-氟-3-(三氟甲基)苯基]-3-(5-{5-甲基-3a,4,4a,5,6,6a-六氫環戊并[d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-甲醯胺	656.3	(500 MHz, DMSO-d6) δ 10.66 (s, 1H), 9.95 (br d, J= 6.9 Hz, 1H), 8.20 (br s, 2H), 7.79 (br dd, J= 8.5, 2.5 Hz, 2H), 7.50 (br t, J= 9.5 Hz, 1H), 7.35 - 7.08 (m, 1H), 6.09 - 5.72 (m, 1H), 5.27 - 5.02 (m, 1H), 4.68 - 4.44 (m, 1H), 4.25 - 4.07 (m, 2H), 4.04 (s, 3H), 3.70 - 3.61 (m, 1H), 3.33 (s, 1H), 3.05 - 2.89 (m, 1H), 2.21 - 2.06 (m, 1H), 2.01 - 1.84 (m, 4H), 1.81 - 1.68 (m, 1H), 1.59 - 1.38 (m, 2H)可能由於與溶劑峰重疊，一個質子在NMR中不可見	2.30, B

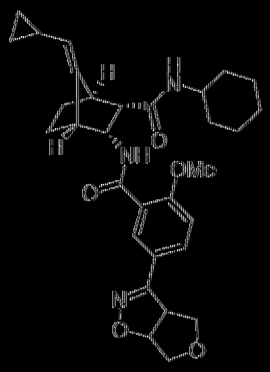
545	 中間體 3 製備	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-吡喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-N-三級丁基-7-(環丙基甲基)雙環[2.2.1]庚烷-2-甲醯胺	508.3	(500 MHz, DMSO-d6) δ 10.17 (d, J= 6.7 Hz, 1H), 8.18 (d, J= 2.2 Hz, 1H), 7.78 (dd, J= 8.7, 2.3 Hz, 1H), 7.65 (s, 1H), 7.24 (d, J= 8.8 Hz, 1H), 5.33 (dd, J= 9.2, 3.4 Hz, 1H), 4.59 (d, J= 9.5 Hz, 1H), 4.49 (br t, J= 7.1 Hz, 1H), 4.27-4.20 (m, 1H), 4.09 (d, J= 10.8 Hz, 1H), 4.03 (s, 3H), 3.89 (br d, J= 8.7 Hz, 1H), 3.77 (dd, J= 9.1, 7.0 Hz, 1H), 3.65 (br dd, J= 10.7, 3.8 Hz, 1H), 3.03 (br s, 1H), 2.86 (br dd, J= 10.8, 4.1 Hz, 1H), 2.53 (br s, 1H), 1.87-1.78 (m, 1H), 1.75-1.65 (m, 1H), 1.49-1.40 (m, 1H), 1.35-1.28 (m, 2H), 1.25 (s, 9H), 0.75-0.64 (m, 2H), 0.30 (br d, J= 2.6 Hz, 2H)。	2.27, B
546	 非經修飾物組合物	(1R,2S,3R,4R,7Z)-7-(環丙基甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-(5-{5-[(2-羥基乙氧基)甲基]-4,5-二氫-1,2-噁唑-3-基}-2-甲氧基苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	646.1	(500 MHz, DMSO-d6) δ 10.52 (s, 1H), 9.90 (br d, J= 7.2 Hz, 1H), 8.21 (br s, 2H), 7.81-7.76 (m, 2H), 7.48 (br t, J= 9.7 Hz, 1H), 7.29-7.24 (m, 1H), 4.84-4.77 (m, 1H), 4.69 (d, J= 9.6 Hz, 1H), 4.67-4.56 (m, 1H), 4.47-4.40 (m, 1H), 4.06-4.02 (m, 3H), 3.57-3.40 (m, 5H), 3.21-3.09 (m, 2H), 2.71 (br s, 1H), 1.86-1.74 (m, 2H), 1.53-1.37 (m, 3H), 0.79-0.68 (m, 2H), 0.41-0.29 (m, 2H)	2.39, B

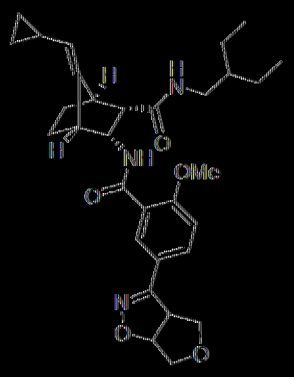
548	 由同對掌性苯甲酸中間物峰1製備。製備型層析條件：儀器：PIC Solution SFC Prep-200 (CTR-L409-PSFC2)管柱：Chiralpak IC, 21 × 250 mm，5微米，移動相：10%甲醇/ 90% CO_2，流動條件：45 mL/min，150巴， 40℃，偵測器波長：220 nm，注射詳情：0.5 mL ~65mg/mL於甲醇中，分析型層析條件：儀器：Aurora Infinity SFC (CTR-L410-ASFC2)管柱：Chiralpak IC, 4.6 × 250 mm，3微米，移動相：10%甲醇/ 90% CO_2，流動條件：2.0 mL/min，150巴， 40℃，偵測器波長：220 nm，注射詳情：15 μL ~1mg/mL於MeOH中。峰-1，RT 4.86 min.，> 99% ee。	(1R,2S,3R,4R,7Z)-3-{5-[6a-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	642.2	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.93 (br d, J=6.7 Hz, 1H), 8.24 (br s, 2H), 7.80 (br d, J=6.7 Hz, 2H), 7.50 (br t, J=10.2 Hz, 1H), 7.28 (br d, J=8.2 Hz, 2H), 5.06 (br s, 1H), 4.71 (br d, J=9.2 Hz, 1H), 4.46 (br s, 1H), 4.06 (s, 3H), 3.98 - 3.84 (m, 1H), 3.63 - 3.48 (m, 1H), 3.18 (br d, J=10.7 Hz, 1H), 3.12 (br s, 1H), 2.74 (br s, 1H), 1.96 (br s, 1H), 1.89 - 1.77 (m, 4H), 1.73 (br d, J=14.0 Hz, 2H), 1.52 (br s, 2H), 1.43 (br s, 3H), 0.91 - 0.70 (m, 2H), 0.37 (br s, 2H)	2.58, C

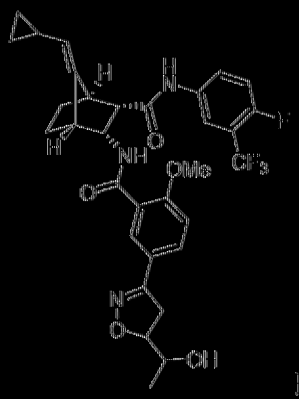
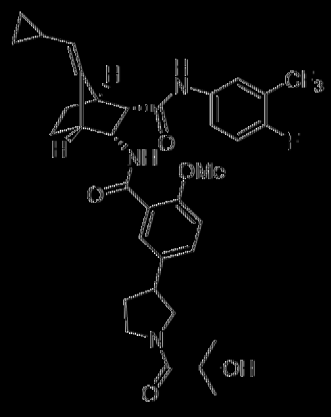
549	 經由SFC分離之異構物，其中實例549為峰2 (RT=2.72 min.，>99% de)。所用儀器：Berger MG II管柱：Chiralpak AD-H，21 × 250 mm，5微米，移動相：50% IPA-0.1% DEA/ 50% CO_2，流動條件：45 mL/min，150巴， 40℃，偵測器波長：220 nm；分析方法：儀器：Shimadzu Nexera SFC，管柱Chiralpak AD-H，4.6 × 100 mm，3微米，移動相：50% IPA0.1% DEA / 50% CO_2，流動條件：2 mL/min，150巴， 40℃，偵測器波長：220 nm，得到對掌性(峰-1，RT=1.15 min.，>99% de)及對掌性(峰-2，RT=2.72 min.，>99% de)。	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(1-羥基環己基)-4,5-二氫-1,2-噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	670.1	(500 MHz, DMSO-d6) δ 10.68 - 10.48 (m, 1H), 9.92 (d, J=7.0 Hz, 1H), 8.32 - 8.04 (m, 2H), 7.90 - 7.72 (m, 2H), 7.49 (t, J=9.7 Hz, 1H), 7.27 (d, J=8.9 Hz, 1H), 4.70 (d, J=9.5 Hz, 1H), 4.51 - 4.40 (m, 2H), 4.32 (s, 1H), 4.05 (s, 3H), 3.26 - 3.01 (m, 2H), 2.73 (br s, 1H), 1.95 - 1.74 (m, 2H), 1.66 - 1.50 (m, 5H), 1.42 (br d, J=5.2 Hz, 4H), 1.35 - 1.24 (m, 3H), 1.20 - 1.11 (m, 1H), 0.87 (q, J=7.1 Hz, 1H), 0.79 - 0.69 (m, 2H), 0.50 - 0.30 (m, 2H)可能由於與溶劑峰重疊，一個質子在NMR中不可見	2.74, C

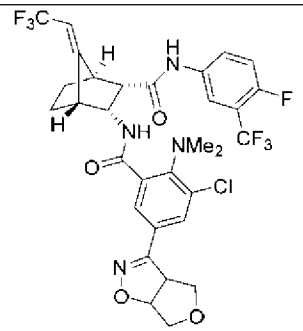
550	 中429.8雙鍵之順反異構物混合物	(1S,2S,3R,4R)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(羥基甲基)-3a,4,4a,5,6,6a-六氫環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-7-(2,2,2-三氟乙基)雙環[2.2.1]庚烷-2-甲醯胺	612.2	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.93 (br d, J=6.8 Hz, 1H), 8.29–8.18 (m, 2H), 7.86–7.74 (m, 2H), 7.49 (br t, J=9.8 Hz, 1H), 7.21 (d, J=8.8 Hz, 1H), 5.12 (dd, J=8.7, 5.2 Hz, 1H), 4.59–4.44 (m, 2H), 4.20 (br t, J=9.0 Hz, 1H), 4.10–3.99 (m, 3H), 3.38–3.31 (m, 1H), 3.25–3.15 (m, 1H), 2.49–2.43 (m, 1H), 2.39 (br dd, J=11.7, 6.4 Hz, 2H), 2.18 (br t, J=7.5 Hz, 1H), 1.99 (br dd, J=13.4, 5.6 Hz, 1H), 1.90 (td, J=11.8, 5.6 Hz, 1H), 1.77 (br dd, J=12.7, 6.0 Hz, 1H), 1.73–1.61 (m, 3H), 1.59–1.46 (m, 3H)	2.32, C

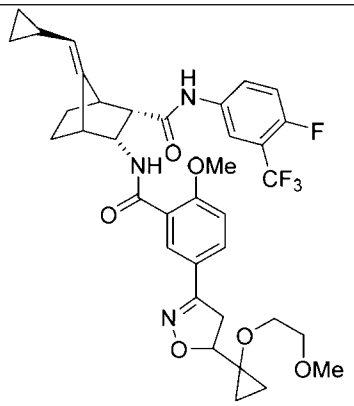
551	 非晶形雙鈉鹽之組合物	(1R,2S,3R,4R)-7-(環丙基甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-[2-甲氧基-5-[5-(甲氧基甲基)-4,5-二氫-1,2-噁唑-3-基]苯甲醯胺基]雙環[2.2.1]庚烷-2-甲醯胺	616.3	(400 MHz, DMSO-d6) δ 10.56 (s, 1H), 9.89 (d, J= 6.8 Hz, 1H), 8.22 (dd, J= 6.6, 2.1 Hz, 1H), 8.20 (d, J= 2.2 Hz, 1H), 7.84 - 7.77 (m, 1H), 7.75 (dd, J= 8.7, 2.3 Hz, 1H), 7.48 (t, J= 9.8 Hz, 1H), 7.25 (d, J= 8.8 Hz, 1H), 5.14 - 5.01 (m, 1H), 4.69 (d, J= 9.3 Hz, 1H), 4.49 - 4.38 (m, 1H), 4.03(s, 4H), 3.16 (dd, J= 10.6, 4.3 Hz, 2H), 3.12 - 3.07 (m, 1H), 3.02 (d, J= 16.6 Hz, 1H), 2.75 - 2.69 (m, 1H), 1.88 - 1.72 (m, 3H), 1.55 - 1.35 (m, 4H),1.31 (s, 3H), 1.23 (s, 1H), 0.80 - 0.66 (m, 2H), 0.35 (dd, J= 4.5, 2.3 Hz, 2H)。	2.37, D

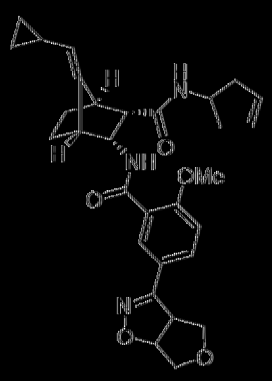
552	 由416.3製備	(1R,2S,3R,4R,7Z)-3-(5-{3a11,411,6H,6a H-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-N-環丙基-7-(環丙基甲基)雙環[2.2.1]庚烷-2-甲醯胺	534.4	(500 MHz, DMSO-d6) δ 9.97 (d, J=7.0 Hz, 1H), 8.20-8.08 (m, 1H), 7.98-7.90 (m, 1H), 7.85-7.76 (m, 1H), 7.23 (s, 1H), 5.34 (dd, J=9.2, 3.5 Hz, 1H), 4.64-4.58 (m, 1H), 4.50 (br t, J=8.1 Hz, 1H), 4.32-4.24 (m, 1H), 4.12-4.06 (m, 1H), 4.00 (s, 3H), 3.90 (br d, J=9.5 Hz, 1H), 3.80-3.73 (m, 1H), 3.65 (dd, J=10.9, 3.7 Hz, 1H), 3.60-3.52 (m, 1H), 3.08-3.00 (m, 1H), 2.88 (br dd, J=10.9, 4.0 Hz, 1H), 1.89-1.81 (m, 1H), 1.78-1.60 (m, 5H), 1.57-1.42 (m, 2H), 1.40-1.18 (m, 4H), 1.17-1.02 (m, 3H), 0.81-0.64 (m, 2H), 0.31 (dd, J=4.4, 2.3 Hz, 2H)。可能由於與溶劑峰重疊，一個質子在NMR中不可見。	2.38, C

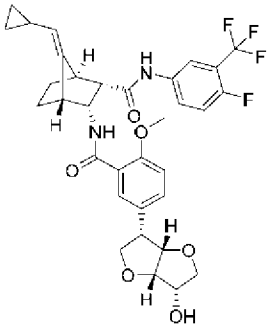
553	 I-416-3製備	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-(2-乙基丁基)雙環[2.2.1]庚烷-2-甲醯胺	536.0	(500 MHz, DMSO-d6) δ 10.01 (d, J = 7.0 Hz, 1H), 8.16 (d, J = 2.3 Hz, 1H), 8.00 – 7.95 (m, 1H), 7.78 (dd, J = 8.6, 2.4 Hz, 1H), 7.23 (d, J = 8.8 Hz, 1H), 5.34 (dd, J = 9.2, 3.6 Hz, 1H), 4.62 (d, J = 9.5 Hz, 1H), 4.50 (br t, J = 8.3 Hz, 1H), 4.33 – 4.24 (m, 1H), 4.09 (d, J = 10.7 Hz, 1H), 4.01 (s, 3H), 3.89 (br d, J = 9.1 Hz, 1H), 3.71 (dd, J = 9.3, 7.0 Hz, 1H), 3.65 (dd, J = 10.7, 3.7 Hz, 1H), 3.12 – 3.02 (m, 2H), 3.00 – 2.89 (m, 2H), 2.53 – 2.51 (m, 1H), 1.90 – 1.81 (m, 1H), 1.78 – 1.69 (m, 1H), 1.46 (tt, J = 12.9, 4.7 Hz, 1H), 1.39 – 1.14 (m, 7H), 0.79 (t, J = 7.4 Hz, 6H), 0.75 – 0.64 (m, 2H), 0.37 – 0.26 (m, 2H)。	2.43, C

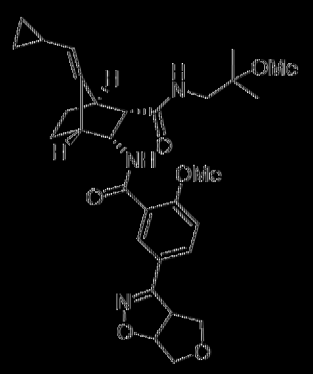
554	 H N H O NH OMe CF3 O N O OH H中間體製備；對掌性苯甲酸中間物(峰4；>99%de；對掌性分析型RT=12.821 min)製備；對掌性SFC純化條件；儀器：Berger MG II；管柱：Chiralpak IC，21 x 250 mm，5微米；移動相：20% MeOH / 80% CO_2；流動條件：45 mL/min，150巴，40℃；偵測器波長：220 nm；注射詳情：0.5 mL ~35mg/mL於MeOH中	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(1-羥基乙基)-4,5-二氫-1,2-噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	616.2	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.90 (d, J=7.1 Hz, 1H), 8.21 (br d, J=2.0 Hz, 2H), 7.78 (dd, J=8.6, 2.2 Hz, 2H), 7.47 (t, J=9.6 Hz, 1H), 7.26 (d, J=8.7 Hz, 1H), 4.94-4.88 (m, 1H), 4.68 (d, J=9.7 Hz, 1H), 4.51 (ddd, J=10.9, 8.2, 5.0 Hz, 1H), 4.46-4.40 (m, 1H), 4.06-4.00 (m, 3H), 3.73-3.65 (m, 1H), 3.20-3.08 (m, 2H), 2.74-2.69 (m, 1H), 1.87-1.74 (m, 2H), 1.54-1.36 (m, 3H), 1.11-1.05 (m, 3H), 0.78-0.68 (m, 2H), 0.38-0.30 (m, 2H)	2.41, B
555	 H N CF3 H O NH OMe O N O OH H中間體製備	(2S,3R)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[1-(2-羥基-2-甲基丙醯基)吡咯啶-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	658.3	(400MHz, DMSO-d6) δ 10.48 (s, 1H), 9.82 (d, J=7.1 Hz, 1H), 8.21 (dd, J=2.4, 6.4 Hz, 1H), 7.84 (br s, 1H), 7.81-7.69 (m, 1H), 7.47 (t,J=9.8 Hz, 1H), 7.44-7.34 (m, 1H), 7.14 (dd, J=2.4, 8.6 Hz, 1H), 5.18-5.12 (m, 1H), 4.68 (d, J=9.5 Hz, 1H), 4.48-4.40 (m, 1H), 4.32-4.04 (m,1H), 3.97 (s, 3H), 3.82-3.65 (m, 1H), 3.58-3.44 (m, 2H), 3.26-3.10 (m, 2H), 3.10-3.01 (m, 1H), 2.74-2.68 (m, 1H), 2.26-2.08 (m, 1H), 1.97-1.68 (m, 3H), 1.57-1.35 (m, 3H), 1.32-1.28 (m, 6H), 0.79-0.65 (m, 2H), 0.35 (dd, J=1.8, 4.3 Hz, 2H)	2.45, A

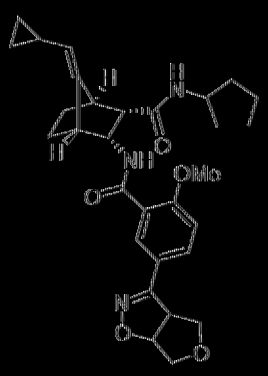
556	 藉由SFC分離之異構物，其中實例556為峰1 (RT=7.99 min，>95% ee)：所用儀器：Waters 100 Prep SFC管柱：Chiral AD，30 × 250 mm，5微米，移動相：15% IPA / 85% CO_2 (具有0.1% DEA)，流動條件：100 mL/min，偵測器波長：220 nm；分析方法：儀器：Shimadzu Nexera SFC，管柱Chiral AD，4.6 × 100 mm，5微米，移動相：15% IPA / 85% CO_2 (具有0.1% DEA)，流動條件：2 mL/min，偵測器波長：220 nm，得到對掌性(峰-1，RT=2.45 min.，>95% ee)及對掌性(峰-2，RT=3.41 min.，>95% ee)。	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-3-氯-2-(二甲基胺基)苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-甲醯胺	689.3	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.94 (br d, J=7.6 Hz, 1H), 8.13 (br d, J=4.3 Hz, 1H), 7.84 (d, J=1.5 Hz, 1H), 7.81 - 7.74 (m, 2H), 7.46 (t, J=9.8 Hz, 1H), 5.93 (q, J=7.7 Hz, 1H), 5.35 (dd, J=9.2, 3.4 Hz, 1H), 4.56 (br s, 1H), 4.50 - 4.36 (m, 1H), 4.08 (d, J=11.0 Hz, 1H), 3.95 - 3.85 (m, 1H), 3.69 - 3.57 (m, 2H), 3.25 (br d, J=4.6 Hz, 1H), 3.19 (br s, 1H), 2.98 (br s, 1H), 2.81 (s, 6H), 2.11 - 1.99 (m, 2H), 1.50 (br d, J=9.2 Hz, 2H)	2.87, B

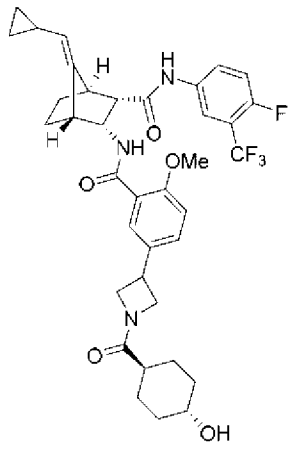
558	 由同對掌性苯甲酸峰2製備：儀器：Berger MG II管柱：Chiralpak IC，21 × 250 mm，5微米，移動相：25% MeOH / 75% CO_2，流動條件：45 mL/min，150巴， 40℃，偵測器波長：220 nm；分析方法：儀器：Shimadzu Nexera SFC，管柱Chiralpak IC，4.6 × 250 mm，3微米，移動相：25% MeOH / 75% CO_2，流動條件：2 mL/min，150巴， 40℃，偵測器波長：220 nm，得到(峰-1，RT=5.02 min.，>99% ee)及對掌性(峰-2，RT=6.46 min.，>99% ee)	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-(2-甲氧基-5-{5-[1-(2-甲氧基乙氧基)環丙基]-4,5-二氫-1,2-噁唑-3-基}苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	686.1	(500 MHz, DMSO-d6) δ 10.30 (s, 1H), 9.67 (br d, J=7.0 Hz, 1H), 8.16 - 7.85 (m, 2H), 7.75 - 7.50 (m, 2H), 7.24 (br t, J=9.8 Hz, 1H), 7.04 (d, J=8.9 Hz, 1H), 4.46 (d, J=9.5 Hz, 1H), 4.32 (br t, J=9.6 Hz, 1H), 4.21 (br t, J=10.2 Hz, 1H), 4.00 - 3.62 (m, 3H), 3.52 - 3.41 (m, 2H), 3.39 - 3.33 (m, 2H), 3.30 - 3.21 (m, 1H), 3.18 - 3.11 (m, 1H), 3.07 - 2.98 (m, 1H), 2.92 (br dd, J=10.1, 3.7 Hz, 1H), 2.90 - 2.82 (m, 3H), 2.48 (br s, 1H), 1.66 - 1.59 (m, 1H), 1.57 - 1.48 (m, 1H), 1.38 - 1.23 (m, 1H), 1.21 - 1.03 (m, 2H), 0.82 - 0.62 (m, 1H), 0.60 - 0.50 (m, 2H), 0.50 - 0.29 (m, 3H), 0.11 (br s, 2H)	2.54, C

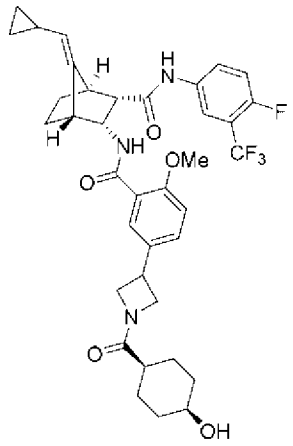
559	 中間體3製備	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-N-(環戊-3-烯-1-基)-7-(環丙基甲基)雙環[2.2.1]庚烷-2-甲醯胺	517.9	(500 MHz, DMSO-d6) δ 9.99 (d, J=7.0 Hz, 1H), 8.26 (br d, J=6.8 Hz, 1H), 8.15 (d, J=2.2 Hz, 1H), 7.79 (dd, J=8.7, 2.4 Hz, 1H), 7.24 (d, J=8.6 Hz, 1H), 5.74-5.61 (m, 2H), 5.33 (dd, J=9.1, 3.6 Hz, 1H), 4.60 (d, J=9.6 Hz, 1H), 4.49 (br t, J=7.9 Hz, 1H), 4.35-4.20 (m, 2H), 4.09 (d, J=10.5 Hz, 1H), 4.02 (s, 3H), 3.90 (br d, J=9.4 Hz, 1H), 3.81-3.73 (m, 1H), 3.65 (dd, J=10.8, 3.6 Hz, 1H), 3.03 (t, J=3.5 Hz, 1H), 2.88 (dd, J=10.8, 4.3 Hz, 1H), 2.67-2.56 (m, 2H), 2.11 (dt, J=15.3, 2.1 Hz, 2H), 1.89-1.80 (m, 1H), 1.76-1.66 (m, 1H), 1.50-1.40 (m, 1H), 1.33 (br t, J=10.6 Hz, 2H), 0.77-0.63 (m, 2H), 0.31 (br d, J=2.6 Hz, 2H)。可能由於與溶劑峰重疊，一個質子在NMR中不可見。	2.18, B

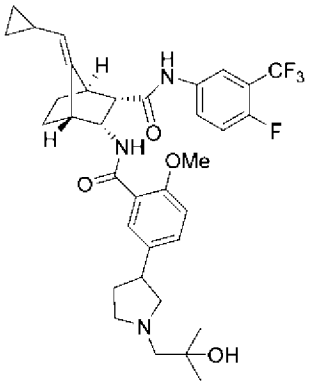
560		(1R,2S,3R,4R,7Z)-3-{5-[(3S,3aS,6S,6aS)-6-羥基-六氫呋喃并[3,2-b]呋喃-3-基]-2-甲氧基苯甲醯胺基}-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	631.3	(500 MHz, DMSO-d6) δ 10.52 (s, 1H), 9.84 (br d, J=7.0 Hz, 1H), 8.24 (br d, J=4.3 Hz, 1H), 7.86 (s, 1H), 7.82 - 7.76 (m, 1H), 7.49 (br t, J=9.8 Hz, 1H), 7.44 - 7.39 (m, 1H), 7.12 (d, J=8.9 Hz, 1H), 4.70 (br d, J=9.5 Hz, 1H), 4.57 (br t, J=4.0 Hz, 1H), 4.49 - 4.39 (m, 2H), 4.26 - 4.13 (m, 2H), 3.98 (s, 3H), 3.82 (br dd, J=11.4, 7.8 Hz, 1H), 3.74 (br t, J=7.3 Hz, 1H), 3.16 (br dd, J=10.7, 3.7 Hz, 1H), 3.10 (br s, 1H), 2.72 (br s, 1H), 1.91 - 1.83 (m, 1H), 1.82 - 1.73 (m, 1H), 1.59 - 1.47 (m, 1H), 1.45 - 1.34 (m, 2H), 0.84 - 0.66 (m, 2H), 0.42 - 0.32 (m, 2H)。	2.46, A

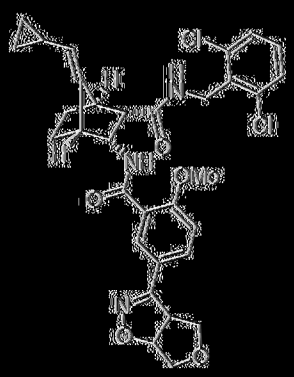
564	 中416.3製備	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-(2-甲氧基-2-甲基丙基)雙環[2.2.1]庚烷-2-甲醯胺	538.2	(500 MHz, DMSO-d6) δ 9.94 (br d, J= 6.7 Hz, 1H), 8.15 (d, J= 2.4 Hz, 1H), 7.95 (br t, J= 5.8 Hz, 1H), 7.78 (dd, J= 8.7, 2.3 Hz, 1H), 7.28 - 7.19 (m, 1H), 5.33 (dd, J= 9.2, 3.4 Hz, 1H), 4.62 (d, J= 9.5 Hz, 1H), 4.48 (br t, J= 7.5 Hz, 1H), 4.32 - 4.21 (m, 1H), 4.09 (br d, J= 11.0 Hz, 1H), 4.00 (s, 3H), 3.89 (br d, J= 8.9 Hz, 1H), 3.81 - 3.73 (m, 1H), 3.67 - 3.62 (m, 1H), 3.25 - 3.19 (m, 1H), 3.07 - 2.99 (m, 5H), 1.85 (br t, J= 9.5 Hz, 1H), 1.77 - 1.69 (m, 1H), 1.51 - 1.43 (m, 1H), 1.39 - 1.27 (m, 2H), 1.02 (d, J= 4.9 Hz, 6H), 0.77 - 0.64 (m, 2H), 0.31 (br s, 2H)。可能由於奧經抑制之水峰及/或溶劑峰重疊，兩個質子在NMR中不可見	2.07, C

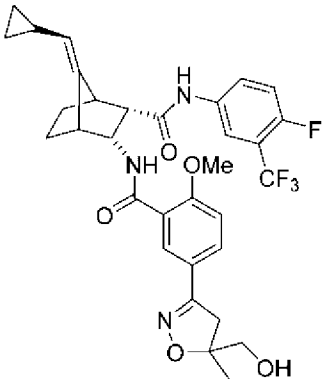
565	 中416.3製備	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-N-環戊基-7-(環丙基甲基)雙環[2.2.1]庚烷-2-甲醯胺	520.1	(400 MHz, DMSO-d6) δ 10.01 (d, J = 6.8 Hz, 1H), 8.15 (d, J = 2.4 Hz, 1H), 8.02 (d, J = 7.6 Hz, 1H), 7.79 (dd, J = 8.6, 2.4 Hz, 1H), 7.24 (d, J = 8.7 Hz, 1H), 5.34 (dd, J = 9.6, 3.2 Hz, 1H), 4.61 (d, J = 9.7 Hz, 1H), 4.50 (dd, J = 8.3, 6.6 Hz, 1H), 4.34 – 4.22 (m, 1H), 4.09 (d, J = 10.8 Hz, 1H), 4.02 (s, 4H), 3.90 (d, J = 9.3 Hz, 1H), 3.81 – 3.72 (m, 1H), 3.66 (dd, J = 10.6, 3.9 Hz, 1H), 3.09 – 3.01 (m, 1H), 2.88 (dd, J = 11.1, 4.4 Hz, 1H), 1.88 – 1.70 (m, 4H), 1.65 – 1.54 (m, 2H), 1.53 – 1.40 (m, 3H), 1.39 – 1.26 (m, 4H), 0.76 – 0.64 (m, 2H), 0.32 (br d, J = 3.5 Hz, 2H) 可能由於與溶劑峰重疊，一個質子在NMR中不可見。	2.23, B

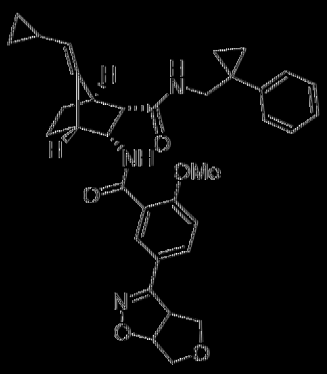
566		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-(2-甲氧基-5-{1-[(1r,4r)-4-羥基環己烷羰基]氮雜環丁烷-3-基}苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	684.1	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.87 (br d, J=7.0 Hz, 1H), 8.24 (br d, J=4.6 Hz, 1H), 7.93 (d, J=1.5 Hz, 1H), 7.83 - 7.74 (m, 1H), 7.53 - 7.43 (m, 2H), 7.19 (d, J=8.5 Hz, 1H), 4.71 (br d, J=9.8 Hz, 1H), 4.56 (br t, J=8.5 Hz, 1H), 4.46 (br dd, J=6.6, 3.2 Hz, 1H), 4.30 - 4.20 (m, 1H), 4.14 - 4.05 (m, 1H), 4.01 (s, 3H), 3.87 - 3.79 (m, 1H), 3.78 - 3.66 (m, 1H), 3.17 (br dd, J=10.2, 4.1 Hz, 1H), 3.10 (br s, 1H), 2.73 (br s, 1H), 2.24 - 2.12 (m, 1H), 1.96 - 1.76 (m, 4H), 1.74 - 1.63 (m, 2H), 1.51 (td, J=8.3, 3.5 Hz, 1H), 1.45 - 1.27 (m, 4H), 1.23 - 1.09 (m, 2H), 0.81 - 0.69 (m, 2H), 0.42 - 0.31 (m, 2H)	2.34, A

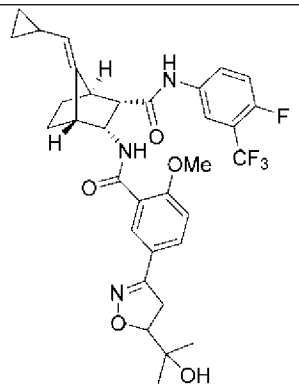
567		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-(2-甲氧基-5-{1-[(1s,4s)-4-羥基環己烷羰基]氮雜環丁烷-3-基}苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	684.3	(500 MHz, DMSO-d6) δ 10.52 (s, 1H), 9.86 (br d, J=7.3 Hz, 1H), 8.23 (br d, J=4.0 Hz, 1H), 7.92 (d, J=2.1 Hz, 1H), 7.81 - 7.72 (m, 1H), 7.56 - 7.42 (m, 2H), 7.18 (d, J=8.5 Hz, 1H), 4.70 (d, J=9.5 Hz, 1H), 4.55 (br t, J=8.5 Hz, 1H), 4.49 - 4.41 (m, 1H), 4.23 (br t, J=9.3 Hz, 1H), 4.14 - 4.05 (m, 1H), 4.00 (s, 3H), 3.87 - 3.71 (m, 3H), 3.16 (br dd, J=11.1, 3.8 Hz, 1H), 3.10 (br s, 1H), 2.73 (br s, 1H), 2.26 (br t, J=10.8 Hz, 1H), 1.92 - 1.72 (m, 4H), 1.67 (br dd, J=13.0, 2.9 Hz, 2H), 1.56 - 1.29 (m, 7H), 0.82 - 0.64 (m, 2H), 0.36 (br s, 2H)	2.41, A

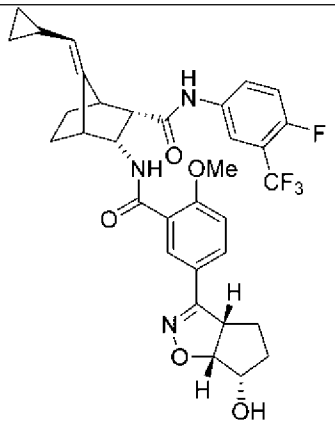
568	 由**449-4**製備	(2S,3R)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[1-(2-羥基-2-甲基丙基)吡咯啶-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	644.4	(400MHz, DMSO-d6) δ = 10.48 (s, 1H), 9.80 (d, J=7.1 Hz, 1H), 8.22 (dd, J=2.6, 6.7 Hz, 1H), 7.87 (d, J=2.4 Hz, 1H), 7.81 - 7.72 (m, 1H),7.47 (t, J=9.8 Hz, 1H), 7.42 (dd, J=2.3, 8.4 Hz, 1H), 7.10 (d, J=8.6 Hz, 1H), 4.68 (d, J=9.5 Hz, 1H), 4.50 - 4.35 (m, 1H), 3.96 (s, 4H), 3.18 - 3.12(m, 2H), 3.07 (br t, J=3.3 Hz, 1H), 2.70 (br t, J=3.1 Hz, 2H), 1.85 (br d, J=9.5 Hz, 1H), 1.80 - 1.62 (m, 2H), 1.54 - 1.45 (m, 1H), 1.42 - 1.33 (m,2H), 1.23 (s, 2H), 1.13 (br s, 7H), 0.80 - 0.66 (m, 2H), 0.35 (dd, J=2.1, 4.8 Hz, 2H)	2.32, A

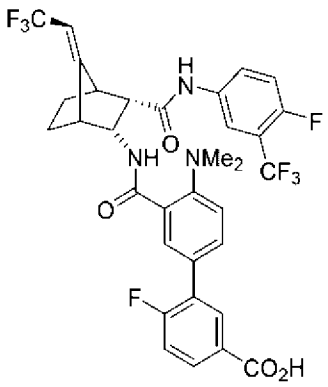
570	 [0016.3]製備	(1R,2S,3R,4R,7′′)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7′-(環丙基甲基)-N-[(2,6-二氯苯基)甲基]雙環[2.2.1]庚烷-2-甲醯胺	610.1	(500 MHz, DMSO-d6) δ 9.97 (br d, J=7.0 Hz, 1H), 8.37-8.32 (m, 1H), 8.17 (d, J=1.8 Hz, 1H), 7.79 (dd, J=8.7, 2.0 Hz, 1H), 7.44 (d, J=8.2 Hz, 2H), 7.36-7.29 (m, 1H), 7.25 (d, J=8.9 Hz, 1H), 5.34 (dd, J=9.3, 3.2 Hz, 1H), 4.61-4.45 (m, 4H), 4.33-4.23 (m, 1H), 4.09 (br d, J=10.7 Hz, 1H), 4.04 (s, 3H), 3.91 (br d, J=8.5 Hz, 1H), 3.81-3.74 (m, 1H), 3.65 (br dd, J=11.1, 3.2 Hz, 1H), 3.05-2.99 (m, 1H), 2.93 (br dd, J=10.8, 3.8 Hz, 1H), 1.88-1.79 (m, 1H), 1.76-1.68 (m, 1H), 1.49-1.40 (m, 1H), 1.38-1.21 (m, 2H), 0.74-0.63 (m, 2H), 0.29 (br s, 2H)。可能由於與溶劑峰重疊，一個質子在NMR中不可見。	2.40, B

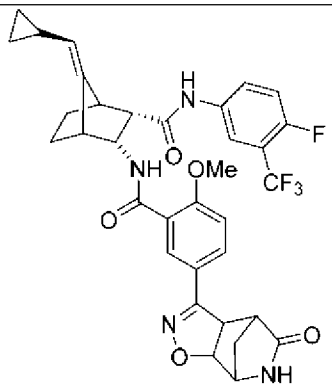
571	 峰1，RT = 2.11 min，製備型SFC條件：管柱/尺寸：Chiralpak IC (250 × 30) mm，5u, % CO_2: 50%助溶劑：50% 4M甲醇氨於MEOH中，總流速：140.0g/min，背壓：100巴，溫度：40℃，UV：238 nm。	(1R,2S,3R,4R)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(羥基甲基)-5-甲基-4,5-二氫-1,2-噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	616.3	(400 MHz, DMSO-d6) δ 10.56 (s, 1H), 9.89 (d, J=6.8 Hz, 1H), 8.22 (dd, J=6.6, 2.7 Hz, 1H), 8.20 (d, J=2.2 Hz, 1H), 7.84 - 7.77 (m, 1H),7.75 (dd, J=8.7, 2.3 Hz, 1H), 7.48 (t, J=9.8 Hz, 1H), 7.25 (d, J=8.8 Hz, 1H), 5.14 - 5.01 (m, 1H), 4.69 (d, J=9.3 Hz, 1H), 4.49 - 4.38 (m, 1H), 4.03(s, 4H), 3.16 (dd, J=10.6, 4.3 Hz, 2H), 3.12 - 3.07 (m, 1H), 3.02 (d, J=16.6 Hz, 1H), 2.75 - 2.69 (m, 1H), 1.88 - 1.72 (m, 3H), 1.55 - 1.35 (m, 4H),1.31 (s, 3H), 1.23 (s, 1H), 0.80 - 0.66 (m, 2H), 0.35 (dd, J=4.5, 2.3 Hz, 2H)。	2.37, D

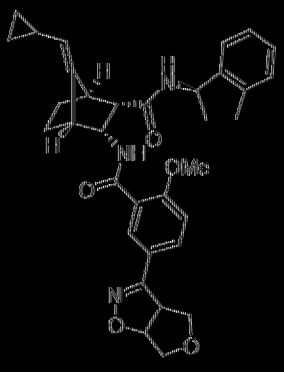
512	 中416-3製備	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-[(1-苯基環丙基)甲基]雙環[2.2.1]庚烷-2-甲醯胺	582.2	(500 MHz, DMSO-d6) δ 9.90 (d, J = 6.9 Hz, 1H), 8.15 (d, J = 2.4 Hz, 1H), 8.09 (br t, J = 5.8 Hz, 1H), 7.79 (dd, J = 8.6, 2.4 Hz, 1H), 7.29 - 7.20 (m, 3H), 7.19 - 7.13 (m, 2H), 7.09 - 7.01 (m, 1H), 5.33 (dd, J = 9.3, 3.4 Hz, 1H), 4.59 (d, J = 9.6 Hz, 1H), 4.49 (br t, J = 7.8 Hz, 1H), 4.27 - 4.19 (m, 1H), 4.09 (d, J = 10.7 Hz, 1H), 4.00 (s, 3H), 3.92 - 3.86 (m, 1H), 3.77 (dd, J = 9.3, 6.8 Hz, 1H), 3.65 (dd, J = 10.9, 3.6 Hz, 1H), 3.54 - 3.45 (m, 1H), 3.20 (dd, J = 13.6, 5.1 Hz, 1H), 3.00 (t, J = 4.0 Hz, 1H), 2.93 - 2.89 (m, 1H), 2.44 - 2.38 (m, 1H), 1.73 - 1.61 (m, 2H), 1.51 - 1.40 (m, 1H), 1.36 - 1.26 (m, 1H), 1.25 - 1.15 (m, 1H), 0.90 - 0.79 (m, 2H), 0.75 - 0.63 (m, 4H), 0.35 - 0.26 (m, 2H)。	2.42, C

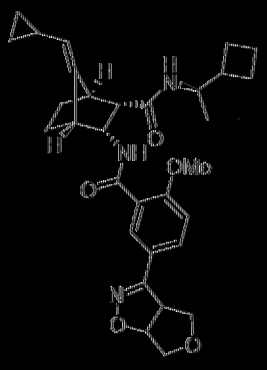
573	 由同對掌性苯甲酸峰1 (RT=5.51 min)製備， 製備型層析條件：儀器：Berger MG II，管柱：Chiralpak AD-H，21 × 250 mm，5微米，移動相：40% MeOH / 60% CO_2，流動條件：45 mL/min，150巴， 40℃，偵測器波長：220 nm，注射詳情：0.5 mL ~65mg/mL於甲醇中 分析型層析條件：儀器：Shimadzu Nexera SFC管柱：Chiralpak AD-H，4.6 × 100 mm，3微米，移動相：35% MeOH / 65% CO_2，流動條件：2.0 mL/min，150巴， 40℃，偵測器波長：220 nm，注射詳情：5 µL ~1mg/mL於MeOH中，滯留時間：峰-1 = 5.51 min，峰-2 = 7.7 min。	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(2-羥基丙烷-2-基)-4,5-二氫-1,2-噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	630.1	(500 MHz, DMSO-d6) δ 10.66 - 10.39 (m, 1H), 9.91 (br d, J=7.0 Hz, 1H), 8.33 - 8.10 (m, 2H), 7.79 (br d, J=6.7 Hz, 2H), 7.47 (br t, J=9.8 Hz, 1H), 7.27 (br d, J=8.9 Hz, 1H), 4.69 (br d, J=9.8 Hz, 1H), 4.48 - 4.29 (m, 2H), 4.03 (s, 2H), 3.73 - 3.58 (m, 2H), 3.47 - 3.27 (m, 1H), 3.21 - 3.13 (m, 1H), 3.10 (br s, 1H), 2.72 (br s, 1H), 1.88 - 1.81 (m, 1H), 1.79 - 1.70 (m, 1H), 1.60 - 1.48 (m, 1H), 1.46 - 1.29 (m, 2H), 1.25 - 0.90 (m, 6H), 0.83 - 0.65 (m, 2H), 0.49 - 0.20 (m, 2H) 可能由於與溶劑峰重疊，一個質子在NMR中不可見	2.45, B

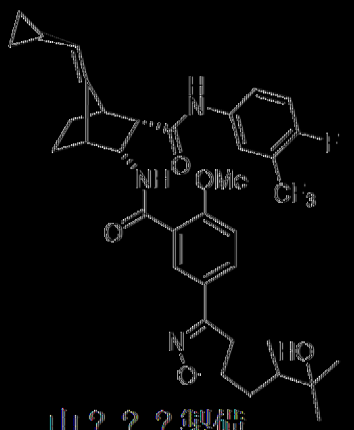
574	 如實例496中利用來自異構物分離之峰2製備。製備型層析條件：儀器：Jasco SFC Prep (CTR-L409-PSFC3)管柱：Chiralpak IA，30 × 250 mm，5微米，移動相：15% MeOH / 85% CO_2，流動條件：85 mL/min，150巴， 40℃，偵測器波長：220 nm，注射詳情：0.5 mL ~21mg/mL於甲醇中，分析型層析條件：儀器：Shimadzu Nexera SFC (CTR-L410-SFC3)管柱：Chiralpak IA，4.6 × 100 mm，3微米，移動相：15% MeOH / 85% CO_2，流動條件：2.0 mL/min，150巴， 40℃，偵測器波長：220 nm，注射詳情：5 μL ~1mg/mL於MeOH中。峰-2 RT 4.97 min > 99% ee。	(1R,2S,3R,4R,7Z)-3-{5-[(3aR,6S,6aS)-6-羥基-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	628.2	(500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.91 (br d, J=7.0 Hz, 1H), 8.28 - 8.17 (m, 2H), 7.80 (br d, J=8.9 Hz, 2H), 7.47 (br t, J=9.8 Hz, 1H), 7.27 (br d, J=8.5 Hz, 1H), 5.18 (br d, J=3.1 Hz, 1H), 4.80 (br d, J=9.2 Hz, 1H), 4.69 (br d, J=10.1 Hz, 1H), 4.44 (br s, 1H), 4.24 (br t, J=8.9 Hz, 1H), 4.12 (br s, 1H), 4.04 (s, 3H), 3.58 (br d, J=11.0 Hz, 2H), 3.22 - 3.13 (m, 3H), 3.10 (br s, 1H), 2.72 (br s, 1H), 2.20 (br s, 1H), 1.92 - 1.72 (m, 2H), 1.64 (br dd, J=11.9, 6.4 Hz, 2H), 1.51 (br s, 1H), 1.42 (br s, 1H), 0.81 - 0.66 (m, 2H), 0.35 (br s, 2H)	2.42, C

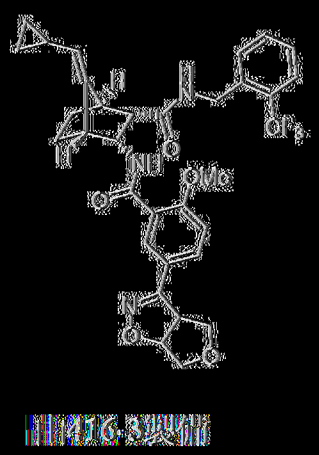
575		4'-(二甲基胺基)-6-氟-3'-{[(1R,2R,3S,4R,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-[1,1'-聯苯]-3-甲酸	680.0	(500 MHz, DMSO-d6) δ 10.58 (s, 1H), 10.42 (br d, J=7.9 Hz, 1H), 8.21 (br d, J=5.5 Hz, 1H), 8.00 (br d, J=7.6 Hz, 1H), 7.97 - 7.88 (m, 2H), 7.73 (br s, 1H), 7.64 (br d, J=7.9 Hz, 1H), 7.49 - 7.33 (m, 3H), 5.98 - 5.88 (m, 1H), 4.58 (br s, 1H), 2.97 (br s, 1H), 2.72 (s, 6H), 2.63 (br s, 1H), 2.14 - 2.02 (m, 1H), 2.00 - 1.86 (m, 1H), 1.50 (br s, 3H), 1.23 (br s, 1H)	2.22, B

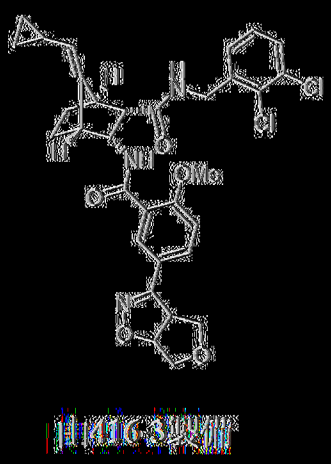
576	 經由SFC分離之異構物，其中實例576為峰1 (RT=3.1 min，>95% de)，所用儀器：Waters 100 Prep SFC管柱：Chiral AD，30 × 250 mm，5微米，移動相：25% MeOH / 75% CO_2 (具有0.1% DEA)，流動條件：100 mL/min，偵測器波長：220 nm；分析方法：儀器：Shimadzu Nexera SFC，管柱Chiral AD，4.6 × 100 mm，5微米，移動相：25% MeOH / 75% CO_2 (具有0.1% DEA)，流動條件：2 mL/min，偵測器波長：220 nm， 得到對掌性(峰-1，RT=3.1 min.，>95% de)及對掌性(峰-2，RT=4.75 min.，>95% de)。	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-(2-甲氧基-5-{8-側氧基-3-氧雜-4,9-二氮雜三環[5.2.1.0²,⁶]癸-4-烯-5-基}苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	653.1	(500 MHz, DMSO-d6) δ 10.67 - 10.47 (m, 1H), 10.10 - 9.83 (m, 1H), 8.26 (d, J=2.3 Hz, 1H), 8.21 (br dd, J=6.5, 2.4 Hz, 1H), 7.92 - 7.81 (m, 2H), 7.77 (br dd, J=8.1, 4.2 Hz, 1H), 7.47 (br t, J=9.7 Hz, 1H), 7.34 - 7.28 (m, 1H), 4.98 (br d, J=8.2 Hz, 1H), 4.69 (d, J=9.6 Hz, 1H), 4.49 - 4.40 (m, 1H), 4.25 (br d, J=8.2 Hz, 1H), 4.09 - 4.01 (m, 3H), 3.99 (br s, 1H), 3.22 - 3.04 (m, 2H), 2.82 - 2.66 (m, 1H), 2.66 - 2.59 (m, 1H), 1.93 - 1.80 (m, 2H), 1.81 - 1.72 (m, 1H), 1.56 - 1.49 (m, 1H), 1.48 - 1.35 (m, 3H), 0.83 - 0.63 (m, 2H), 0.34 (br s, 2H)	2.34, B

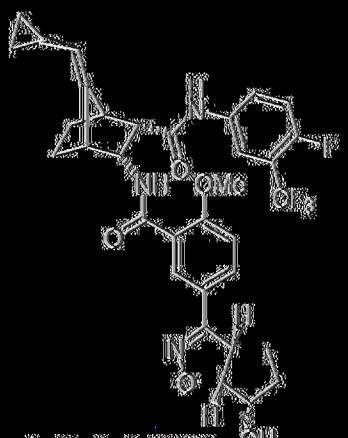
571	 中間體 3製備	(1R,2S,3R,4R,7Z) 3 (5 {3aH,4H,6H,6aH 吡喃并[3,4 d][1,2]噁唑 3 基} 2 甲氧基苯甲醯胺基) 7 (環丙基甲基) N [(1R) 2,3 二氫 1H 茚 1 基]雙環[2.2.1]庚烷 2 甲醯胺	568.3	(500 MHz, DMSO d6) δ 10.08 (d, J= 6.9 Hz, 1H), 8.47 (d, J= 8.2 Hz, 1H), 8.17 (d, J= 2.3 Hz, 1H), 7.79 (dd, J= 8.6, 2.4 Hz, 1H), 7.29 – 7.12 (m, 5H), 5.37 – 5.30 (m, 2H), 4.62 (d, J= 9.5 Hz, 1H), 4.50 (br t, J= 7.8 Hz, 1H), 4.36 – 4.26 (m, 1H), 4.09 (d, J= 10.9 Hz, 1H), 4.02 (s, 3H), 3.91 (br d, J= 9.1 Hz, 1H), 3.78 (dd, J= 9.2, 7.0 Hz, 1H), 3.65 (dd, J= 10.7, 3.6 Hz, 1H), 3.07 (br s, 1H), 2.96 (br dd, J= 10.9, 4.2 Hz, 1H), 2.92 – 2.86 (m, 1H), 2.81 – 2.73 (m, 1H), 2.61 – 2.55 (m, 1H), 2.41 – 2.31 (m, 1H), 2.01 – 1.93 (m, 1H), 1.84 – 1.68 (m, 2H), 1.51 – 1.35 (m, 3H), 0.77 – 0.63 (m, 2H), 0.37 – 0.24 (m, 2H)。	2.39, B

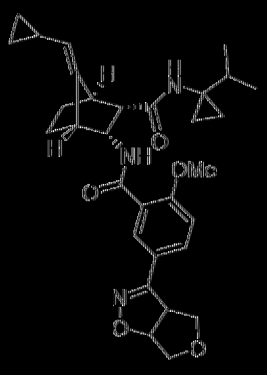
578	 中間體3製備	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-N-[(1R)-1-環丁基丙基]-7-(環丙基亞甲基)雙環[2.2.1]庚烷-2-甲醯胺	548.2	(500 MHz, DMSO-d6) δ 10.04 (d, J= 6.8 Hz, 1H), 8.15 (d, J= 2.4 Hz, 1H), 7.78 (dd, J= 8.6, 2.4 Hz, 1H), 7.70 (br d, J= 9.1 Hz, 1H), 7.23 (d, J= 8.8 Hz, 1H), 5.33 (dd, J= 9.2, 3.5 Hz, 1H), 4.62 (d, J= 9.6 Hz, 1H), 4.49 (br t, J= 7.9 Hz, 1H), 4.33 - 4.24 (m, 1H), 4.09 (d, J= 10.7 Hz, 1H), 4.00 (s, 3H), 3.92 - 3.87 (m, 1H), 3.77 (dd, J= 9.2, 6.7 Hz, 1H), 3.71 - 3.59 (m, 2H), 3.09 - 3.01 (m, 1H), 2.98 - 2.88 (m, 1H), 2.33 - 2.19 (m, 1H), 1.95 - 1.60 (m, 8H), 1.51 - 1.41 (m, 1H), 1.40 - 1.25 (m, 3H), 1.19 - 1.03 (m, 1H), 0.82 - 0.62 (m, 5H), 0.31 (dd, J= 4.5, 2.2 Hz, 2H)。可能由於與溶劑峰重疊，一個質子在NMR中不可見。	2.58, B

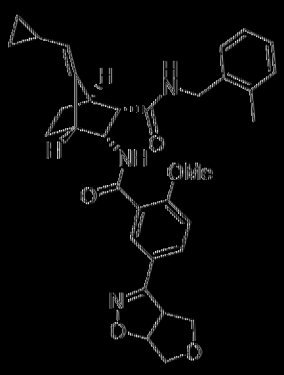
5'9	 中？？？製備 如實例4'9中精中在分離中隔離峰4製備。製備型析條件：儀器：Berger MG II 管柱：Chiralpak IC，30 × 250 mm，5微米，移動相：25%甲醇/ '75% CO_2，流動條件：'0 mL/min，120 巴， 40℃，偵測器波長：220 nm，注射詳情：0.5 mL ~'5mg/mL於甲醇中。分析型析條件：儀器：Shimadzu Nexera SFC管柱：Chiralpak IC，4.6 × 100 mm，3微米，移動相：25% MeOH / '75% CO_2，流動條件：2.0 mL/min，150 巴， 40℃，偵測器波長：220 nm，注射詳情：5 µL ~1mg/mL於MeOH中(峰 4，RT 11.45 min.，> 99% ee)	(1R,2S,3R,4R,'Z) '(環丙基亞甲基) N (4 氟 3 (三氟甲基)苯基 13 (5 (2 羥基丙烷 2 基) 3aH,4H,5H,6H,6aH 環戊并[d][1,2]噁唑 3 基] 2 甲氧基苯甲醯胺基}雙環[2.2.1]庚烷 2 甲醯胺	6'0.0	(500 MHz, DMSO d6) δ 10.56 (s, 1H), 9.93 (br d, J= '7.0 Hz, 1H), 8.2' 8.18 (m, 2H), '7.95 '7.'5 (m, 2H), '7.48 (br t, J= 9.6 Hz, 1H), '7.28 (d, J= 8.9 Hz, 1H), 5.18 5.06 (m, 1H), 4.'0 (br d, J= 9.5 Hz, 1H), 4.44 (br s, 1H), 4.05 (s, 3H), 3.21 3.06 (m, 3H), 2.'2 (br s, 1H), 2.20 (br dd, J= 12.5, 6.4 Hz, 2H), 1.98 (dt, J= 12.3, 5.9 Hz, 1H), 1.90 1.'1 (m, 2H), 1.65 1.46 (m, 2H), 1.46 1.33 (m, 3H), 1.11 1.00 (m, 6H), 0.8' 0.68 (m, 2H), 0.35 (br d, J= 3.' Hz, 2H)	2.50, C

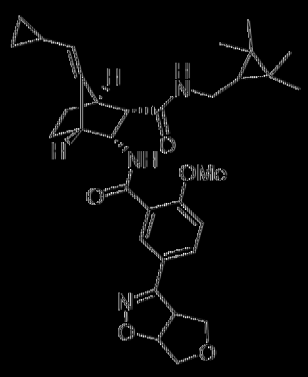
580		(1R,2S,3R,4R,7′)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7′-(環丙基甲基)-N-{[2-(三氟甲基)苯基]甲基}雙環[2.2.1]庚烷-2-甲醯胺	610.2	(500 MHz, DMSO-d6) δ 9.88 (d, J = 7.0 Hz, 1H), 8.74 (br t, J = 5.7 Hz, 1H), 8.17 (d, J = 2.2 Hz, 1H), 7.85 – 7.74 (m, 1H), 7.72 – 7.63 (m, 1H), 7.56 – 7.48 (m, 1H), 7.47 – 7.38 (m, 2H), 7.19 (d, J = 8.7 Hz, 1H), 5.33 (dd, J = 9.1, 3.5 Hz, 1H), 4.64 (d, J = 9.6 Hz, 1H), 4.51 – 4.45 (m, 3H), 4.38 – 4.30 (m, 1H), 4.09 (d, J = 10.7 Hz, 1H), 3.92 – 3.87 (m, 1H), 3.86 – 3.81 (m, 3H), 3.79 – 3.73 (m, 1H), 3.68 – 3.62 (m, 1H), 3.10 – 3.02 (m, 2H), 2.65 – 2.60 (m, 1H), 1.85 – 1.78 (m, 1H), 1.74 – 1.67 (m, 1H), 1.52 – 1.42 (m, 1H), 1.40 – 1.28 (m, 2H), 0.77 – 0.65 (m, 2H), 0.38 – 0.26 (m, 2H)。	2.37, B

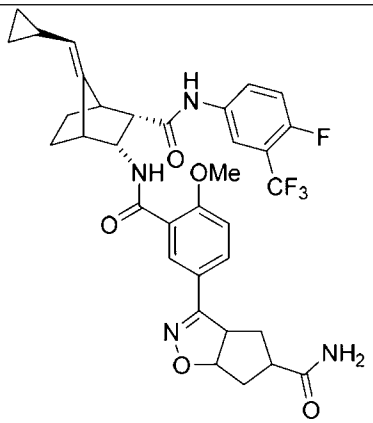
582	 由401G-3製備	(1R,2S,3R,4R,7′′)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7′-(環丙基甲基)-N-[(2,3-二氯苯基)甲基]雙環[2.2.1]庚烷-2-甲醯胺	610.2	(500 MHz, DMSO-d6) δ 9.86 (d, J = 7.0 Hz, 1H), 8.72 (br t, J = 5.9 Hz, 1H), 8.17 (d, J = 2.3 Hz, 1H), 7.78 (dd, J = 8.7, 2.4 Hz, 1H), 7.50 (br d, J = 7.7 Hz, 1H), 7.31 – 7.12 (m, 3H), 5.34 (dd, J = 9.1, 3.6 Hz, 1H), 4.64 (d, J = 9.5 Hz, 1H), 4.49 (br t, J = 7.7 Hz, 1H), 4.42 – 4.30 (m, 3H), 4.09 (d, J = 10.7 Hz, 1H), 3.95 – 3.85 (m, 4H), 3.81 – 3.74 (m, 1H), 3.65 (dd, J = 10.7, 3.4 Hz, 1H), 3.11 – 3.00 (m, 2H), 2.64 – 2.60 (m, 1H), 1.85 – 1.78 (m, 1H), 1.76 – 1.68 (m, 1H), 1.53 – 1.43 (m, 1H), 1.40 – 1.29 (m, 2H), 0.78 – 0.65 (m, 2H), 0.37 – 0.27 (m, 2H)。	2.32, B

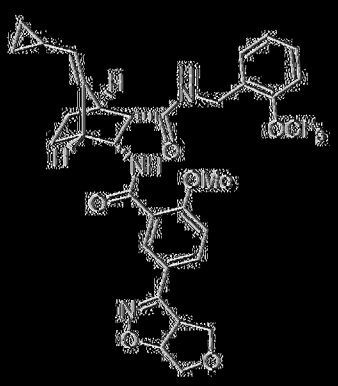
583	 如實例496中藉由HPLC分離峰2製備：製備型HPLC條件：儀器：Berger MG II；管柱：Chiralpak IC，30 × 250 mm，5微米，移動相：25% 甲醇/75% CO_2，流動條件：70 mL/min，120巴，40℃，偵測器波長：220 nm，注射詳情：0.5 mL ~75mg/mL於甲醇中。分析型HPLC條件：儀器：Shimadzu Nexera SFC；管柱：Chiralpak IC，4.6 × 100 mm，3微米，移動相：25% MeOH / 75% CO_2，流動條件：2.0 mL/min，150巴，40℃，偵測器波長：220 nm，注射詳情：5 μL ~1mg/mL於MeOH中(峰2，RT 4.38 min.，> 99% ee)	(1R,2S,3R,4R,7Z) 3-[5-[(3aR,6R,6aS) 6-羥基-3a,4,5,6,6a-環戊并[d][1,2]㗁唑-3-基]-2-甲氧基苯甲醯胺基]-7-(環丙基甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	628.2	(500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.92 (br d, J= 6.7 Hz, 1H), 8.30 - 8.17 (m, 2H), 7.79 (br d, J= 8.5 Hz, 2H), 7.49 (br t, J= 9.9 Hz, 1H), 7.28 (br d, J= 8.9 Hz, 1H), 4.95 (br d, J= 6.7 Hz, 1H), 4.81 (br dd, J= 8.2, 4.6 Hz, 1H), 4.70 (br d, J= 9.2 Hz, 1H), 4.45 (br s, 1H), 4.12 (br t, J= 8.5 Hz, 1H), 4.05 (s, 3H), 3.44 (br d, J= 9.8 Hz, 1H), 3.28 - 3.14 (m, 1H), 3.11 (br s, 1H), 2.73 (br s, 1H), 1.93 - 1.76 (m, 3H), 1.76 - 1.66 (m, 1H), 1.62 - 1.47 (m, 2H), 1.43 (br s, 1H), 1.40 - 1.24 (m, 1H), 0.84 - 0.68 (m, 2H), 0.36 (br s, 2H)	2.44, C

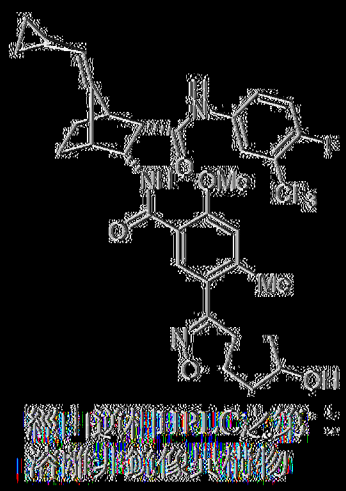
584	 I-416-3製備	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-(1-丙炔-2-基)環丙基]雙環[2.2.1]庚烷-2-甲醯胺	534.2	(500 MHz, DMSO-d6) δ 10.04 (br d, J=6.7 Hz, 1H), 8.17 (s, 2H), 7.79 (dd, J=8.4, 2.0 Hz, 1H), 7.24 (d, J=8.5 Hz, 1H), 5.34 (dd, J=9.2, 3.4 Hz, 1H), 4.60 (d, J=9.8 Hz, 1H), 4.50 (br t, J=7.9 Hz, 1H), 4.31-4.18 (m, 1H), 4.09 (br d, J=11.0 Hz, 1H), 4.03 (s, 3H), 3.92-3.87 (m, 1H), 3.80-3.73 (m, 1H), 3.65 (br dd, J=10.7, 3.7 Hz, 1H), 3.07-3.00 (m, 1H), 2.84 (br dd, J=11.0, 4.0 Hz, 1H), 1.86-1.76 (m, 1H), 1.74-1.65 (m, 1H), 1.50-1.39 (m, 2H), 1.32 (br s, 2H), 0.83 (br dd, J=18.6, 6.7 Hz, 6H), 0.75-0.64 (m, 2H), 0.63-0.45 (m, 4H), 0.31 (br s, 2H)。可能由於與溶劑峰重疊，一個質子不可見。	2.46, B

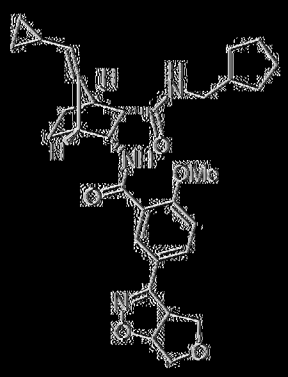
585	 I-416 3製備	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-[(2-甲氧苯基)甲基]雙環[2.2.1]庚烷-2-甲醯胺	556.1	(500 MHz, DMSO-d6) δ 9.94 (br d, J= 6.7 Hz, 1H), 8.48 (br t, J= 5.8 Hz, 1H), 8.16 (d, J= 1.8 Hz, 1H), 7.78 (dd, J= 8.9, 2.1 Hz, 1H), 7.21 (d, J= 8.9 Hz, 1H), 7.17 - 7.07 (m, 3H), 7.06 - 7.02 (m, 1H), 5.33 (dd, J= 9.0, 3.5 Hz, 1H), 4.62 (d, J= 9.5 Hz, 1H), 4.48 (br t, J= 7.6 Hz, 1H), 4.37 - 4.28 (m, 1H), 4.26 (br d, J= 5.8 Hz, 2H), 4.09 (br d, J= 10.7 Hz, 1H), 3.93 (s, 3H), 3.90 (br d, J= 9.5 Hz, 1H), 3.80 - 3.73 (m, 1H), 3.65 (dd, J= 10.8, 3.8 Hz, 1H), 3.04 (br s, 1H), 3.00 (br dd, J= 11.0, 4.3 Hz, 1H), 2.58 (br s, 1H), 2.23 (s, 3H), 1.92 - 1.81 (m, 1H), 1.78 - 1.69 (m, 1H), 1.53 - 1.42 (m, 1H), 1.40 - 1.27 (m, 2H), 0.77 - 0.64 (m, 2H), 0.32 (br d, J= 4.3 Hz, 2H)。	2.38, B

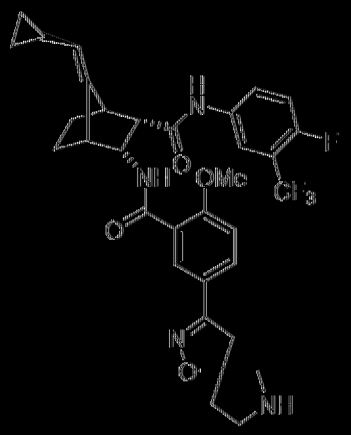
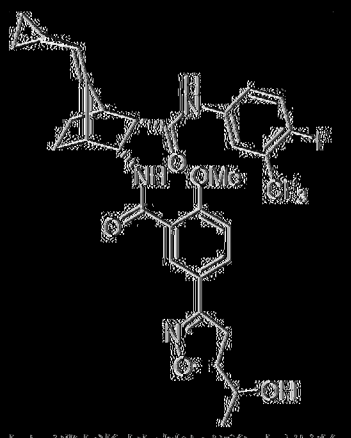
586	 中416-3製備	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-[(2,2,3,3-四甲基環丙基)甲基]雙環[2.2.1]庚烷-2-甲醯胺	562.4	(500 MHz, DMSO-d6) δ 10.00 (br d, J = 6.4 Hz, 1H), 8.15 (d, J = 2.1 Hz, 1H), 7.98 (br t, J = 4.9 Hz, 1H), 7.78 (dd, J = 8.5, 2.1 Hz, 1H), 7.23 (d, J = 8.9 Hz, 1H), 5.34 (dd, J = 9.0, 3.5 Hz, 1H), 4.63 (br d, J = 9.5 Hz, 1H), 4.50 (br t, J = 7.6 Hz, 1H), 4.34 - 4.24 (m, 1H), 4.09 (br d, J = 10.7 Hz, 1H), 4.01 (s, 3H), 3.93 - 3.86 (m, 1H), 3.81 - 3.73 (m, 1H), 3.65 (br dd, J = 10.7, 3.4 Hz, 1H), 3.15 - 2.99 (m, 2H), 2.95 (br dd, J = 11.0, 3.4 Hz, 1H), 1.91 - 1.82 (m, 1H), 1.79 - 1.71 (m, 1H), 1.52 - 1.41 (m, 1H), 1.41 - 1.26 (m, 2H), 1.00 (d, J = 3.4 Hz, 6H), 0.92 (d, J = 13.1 Hz, 6H), 0.78 - 0.66 (m, 2H), 0.38 - 0.24 (m, 3H)。可能由於與溶劑峰重疊，一個質子不可見。	2.55, C

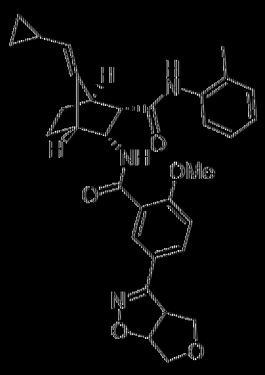
587	 由同對掌性苯甲酸酯中間物(峰1；100%ee；對掌性分析型RT=2.071 min)製備；製備型對掌性SFC條件：儀器：Jasco SFC Prep：管柱：Chiralpak AS-H，30 × 250 mm，5微米；移動相：30% MeOH / 70% CO_2；流動條件：85 mL/min，150巴， 40℃；偵測器波長：220 nm；注射詳情：1.0 mL ~50mg/mLmg/mL於MeOH:TFA中	3-(3-{[(1R,2R,3S,4R,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-5-甲醯胺	655.5	(500 MHz, DMSO-d6) δ 10.52 (s, 1H), 9.93 - 9.89 (m, 1H), 8.27 - 8.21 (m, 2H), 7.82 - 7.77 (m, 2H), 7.49 (t, J=9.8 Hz, 1H), 7.35 (br s, 1H), 7.27 (d, J=8.9 Hz, 1H), 6.80 (br s, 1H), 5.15 (dd, J=8.7, 5.0 Hz, 1H), 4.69 (d, J=9.6 Hz, 1H), 4.47 - 4.42 (m, 1H), 4.26 (t, J=9.0 Hz, 1H), 4.04 (s, 3H), 3.16 (dd, J=10.8, 4.2 Hz, 1H), 3.11 (t, J=3.7 Hz, 1H), 2.74 - 2.70 (m, 1H), 2.58 - 2.52 (m, 1H), 2.12 - 1.76 (m, 6H), 1.54 - 1.47 (m, 1H), 1.45 - 1.37 (m, 2H), 0.79 - 0.69 (m, 2H), 0.38 - 0.32 (m, 2H)	2.13, A

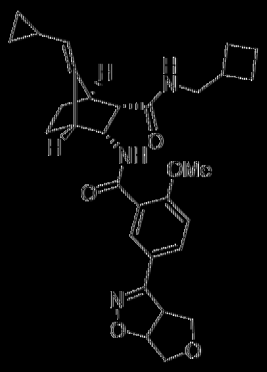
588	 重複6-3製備	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-{[2-(三氟甲氧基)苯基]甲基}雙環[2.2.1]庚烷-2-甲醯胺	626.1	(500 MHz, DMSO-d6) δ 9.91 (br d, J = 6.7 Hz, 1H), 8.65 (br t, J = 5.2 Hz, 1H), 8.18 (d, J = 1.5 Hz, 1H), 7.78 (dd, J = 8.5, 1.5 Hz, 1H), 7.38 - 7.30 (m, 3H), 7.28 - 7.23 (m, 1H), 7.20 (d, J = 8.9 Hz, 1H), 5.34 (br dd, J = 9.2, 3.4 Hz, 1H), 4.64 (br d, J = 9.5 Hz, 1H), 4.49 (br t, J = 7.8 Hz, 1H), 4.39 - 4.28 (m, 3H), 4.14 - 4.05 (m, 1H), 3.95 - 3.85 (m, 4H), 3.80 - 3.71 (m, 1H), 3.65 (br dd, J = 10.8, 3.5 Hz, 1H), 3.09 - 3.00 (m, 2H), 2.62 - 2.56 (m, 1H), 1.87 - 1.71 (m, 1H), 1.76 - 1.68 (m, 1H), 1.52 - 1.42 (m, 1H), 1.40 - 1.26 (m, 2H), 0.80 - 0.64 (m, 2H), 0.33 (br d, J = 4.3 Hz, 2H)。	2.44, B

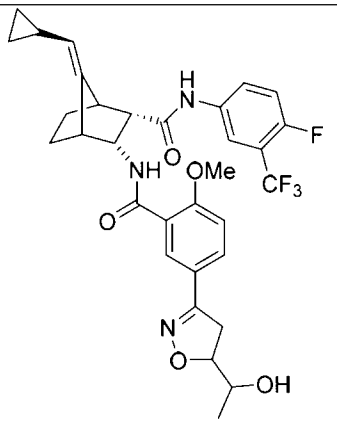
590		(1R,2S,3R,4R,7Z)-7-(環丙基甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-(5-{5-羥基-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基}-2-甲氧基-4-甲基苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	642.1	(500 MHz, DMSO-d6) δ 10.66 - 10.40 (m, 1H), 9.91 (br d, J=7.0 Hz, 1H), 8.24 (br d, J=4.3 Hz, 1H), 8.01 (s, 1H), 7.80 (dd, J=5.2, 2.7 Hz, 1H), 7.49 (br t, J=9.6 Hz, 1H), 7.17 (s, 1H), 5.15 - 5.05 (m, 1H), 4.70 (d, J=9.8 Hz, 1H), 4.51 - 4.38 (m, 1H), 4.25 (td, J=9.0, 3.7 Hz, 1H), 4.15 - 4.09 (m, 1H), 4.06 (s, 3H), 3.44 (br s, 1H), 3.16 (br dd, J=10.5, 4.4 Hz, 1H), 3.11 (br s, 1H), 2.77 - 2.68 (m, 1H), 2.50 (s, 3H), 2.07 - 1.98 (m, 1H), 1.94 - 1.82 (m, 3H), 1.82 - 1.75 (m, 1H), 1.75 - 1.65 (m, 1H), 1.57 - 1.48 (m, 1H), 1.45 - 1.31 (m, 2H), 0.75 (quin, J=9.3 Hz, 2H), 0.36 (br s, 2H)	2.52, B

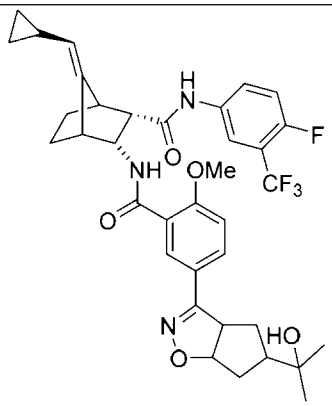
592	 中116a3製備	(1R,2S,3R,4R,7′)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-N-(環戊基甲基)-7-(環丙基甲基)雙環[2.2.1]庚烷-2-甲醯胺	534.0	(500 MHz, DMSO-d6) δ 9.96 (d, J = 6.8 Hz, 1H), 8.14 (d, J = 2.2 Hz, 1H), 8.08 (br t, J = 5.6 Hz, 1H), 7.78 (dd, J = 8.7, 2.3 Hz, 1H), 7.23 (d, J = 8.8 Hz, 1H), 5.33 (dd, J = 9.2, 3.6 Hz, 1H), 4.61 (d, J = 9.6 Hz, 1H), 4.49 (br t, J = 7.9 Hz, 1H), 4.33-4.22 (m, 1H), 4.09 (d, J = 10.6 Hz, 1H), 4.00 (s, 3H), 3.89 (br d, J = 8.6 Hz, 1H), 3.77 (dd, J = 9.2, 7.0 Hz, 1H), 3.65 (br dd, J = 10.8, 3.7 Hz, 1H), 3.09-3.00 (m, 2H), 3.00-2.86 (m, 2H), 1.99-1.89 (m, 1H), 1.86 (br t, J = 9.9 Hz, 1H), 1.78-1.69 (m, 1H), 1.66-1.54 (m, 2H), 1.53-1.26 (m, 7H), 1.18-1.06 (m, 2H), 0.77-0.64 (m, 2H), 0.31 (br d, J = 2.7 Hz, 2H)。可能由於與溶劑峰重疊，一個質子在NMR中不可見。	2.29, C

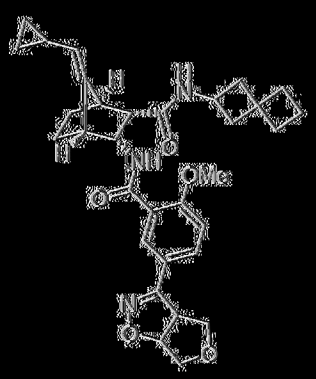
593	 非鏡像異構物混合物	(1R,2S,3R,4R,7*S*)-7-(環丙基甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-(2-甲氧基-5-{1-氧雜-2,7-二氮雜螺[4.4]壬-2-烯-3-基}苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	621.4	(500 MHz, DMSO-d6) δ 10.57 (s, 1H), 9.95–9.90 (m, 1H), 8.23 (br d, J= 2.4 Hz, 2H), 7.79 (dd, J= 8.7, 2.2 Hz, 2H), 7.49 (t, J= 9.8 Hz, 1H), 7.30 (d, J= 8.8 Hz, 1H), 4.69 (d, J= 9.5 Hz, 1H), 4.48–4.40 (m, 1H), 4.05 (s, 3H), 3.70–3.56 (m, 2H), 3.41 (s, 1H), 3.21–3.07 (m, 2H), 2.75–2.70 (m, 1H), 2.58–2.55 (m, 1H), 2.32–2.18 (m, 2H), 1.85–1.75 (m, 2H), 1.54–1.33 (m, 4H), 0.79–0.69 (m, 2H), 0.38–0.31 (m, 2H)	2.22, B
595	 甲磺酸掌性苯甲酸中間物(峰1；>99%de；對掌性分析型RT: 7.968 min)製備；對掌性SFC純化條件；儀器：Berger MG II；管柱：Chiralpak IC，21 × 250 mm，5微米；移動相：20% MeOH / 80% CO_2；流動條件：45 mL/min，150 巴，40°C；偵測器波長：220 nm；注射詳情：0.5 mL ~35mg/mL於MeOH中	(1R,2S,3R,4R,7*S*)-7-(環丙基甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(1-羥基乙基)-4,5-二氫-1,2-噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	616.2	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.89 (br d, J= 7.0 Hz, 1H), 8.22–8.17 (m, 2H), 7.80–7.74 (m, 2H), 7.49–7.43 (m, 1H), 7.25 (d, J= 8.9 Hz, 1H), 4.72–4.63 (m, 1H), 4.50–4.40 (m, 2H), 4.02 (s, 3H), 3.55–3.44 (m, 2H), 3.34–3.22 (m, 1H), 3.17–3.10 (m, 1H), 3.10–3.05 (m, 1H), 2.73–2.67 (m, 1H), 1.84–1.73 (m, 2H), 1.50–1.37 (m, 3H), 1.07 (d, J= 6.1 Hz, 3H), 0.78–0.69 (m, 2H), 0.37–0.30 (m, 2H)	2.41, B

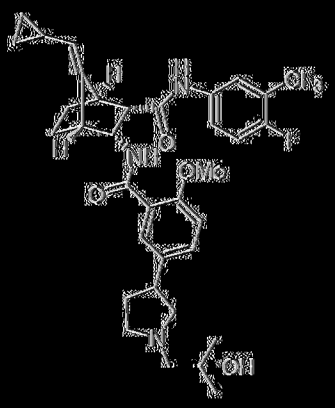
596	 中416-3製備	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-(2-甲基苯基)雙環[2.2.1]庚烷-2-甲醯胺	542.2	(500 MHz, DMSO-d6) δ 9.94 – 9.86 (m, 1H), 9.53 (s, 1H), 8.18 (d, J = 2.2 Hz, 1H), 7.78 (dd, J = 8.6, 2.4 Hz, 1H), 7.34 (d, J = 7.5 Hz, 1H), 7.21 – 7.21 (m, 2H), 7.19 – 7.15 (m, 1H), 7.14 – 7.09 (m, 1H), 5.34 (dd, J = 9.2, 3.4 Hz, 1H), 4.70 (d, J = 9.5 Hz, 1H), 4.52 – 4.46 (m, 1H), 4.45 – 4.37 (m, 1H), 4.10 (d, J = 10.7 Hz, 1H), 3.96 – 3.85 (m, 4H), 3.76 (dd, J = 9.2, 7.0 Hz, 1H), 3.65 (dd, J = 10.8, 3.8 Hz, 1H), 3.24 (dd, J = 10.9, 4.3 Hz, 1H), 3.09 (br s, 1H), 2.74 (br s, 1H), 1.92 (br d, J = 9.9 Hz, 1H), 1.81 – 1.72 (m, 1H), 1.52 – 1.45 (m, 4H), 1.45 – 1.36 (m, 2H), 0.78 – 0.66 (m, 2H), 0.39 – 0.29 (m, 2H)。	2.28, C

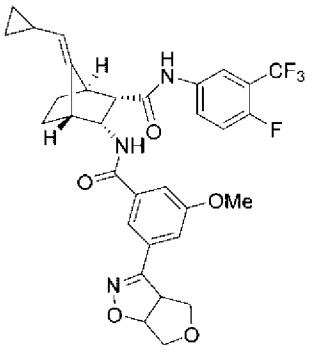
597	 中416-3製備	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-N-(環丁基甲基)-7-(環丙基甲基)雙環[2.2.1]庚烷-2-甲醯胺	520.0	(500 MHz, DMSO-d6) δ 9.98 (br d, J=7.0 Hz, 1H), 8.15 (d, J=2.1 Hz, 1H), 8.05 (br t, J=5.5 Hz, 1H), 7.78 (dd, J=8.7, 2.0 Hz, 1H), 7.23 (d, J=8.9 Hz, 1H), 5.33 (dd, J=9.3, 3.2 Hz, 1H), 4.61 (d, J=9.8 Hz, 1H), 4.49 (br t, J=7.8 Hz, 1H), 4.32-4.21 (m, 1H), 4.09 (br d, J=10.7 Hz, 1H), 4.01 (s, 3H), 3.89 (br d, J=9.5 Hz, 1H), 3.81-3.71 (m, 1H), 3.65 (dd, J=10.8, 3.5 Hz, 1H), 3.21-3.10 (m, 1H), 3.08-3.01 (m, 2H), 2.94-2.84 (m, 1H), 2.35 (dt, J=15.0, 7.8 Hz, 1H), 1.97-1.79 (m, 3H), 1.78-1.68 (m, 3H), 1.67-1.54 (m, 2H), 1.46 (dt, J=8.4, 4.0 Hz, 1H), 1.38-1.23 (m, 2H), 0.78-0.64 (m, 2H), 0.31 (br d, J=4.8 Hz, 2H)。可能由於與溶劑峰及/或經抑制之水峰重疊，兩個質子在NMR中不可見。	2.20, B

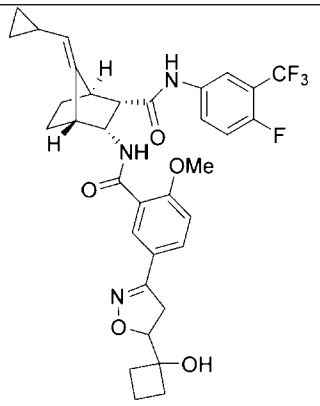
598	 由同對掌性苯甲酸酯中間物(峰3；94.8%de；對掌性分析型RT=9.925 min)製備；對掌性SFC純化條件；儀器：Berger MG II；管柱：Chiralpak IC，21 × 250 mm，5微米；移動相：20% MeOH / 80% CO_2；流動條件：45 mL/min，150巴，40℃；偵測器波長：220 nm；注射詳情：0.5 mL ~35mg/mL於MeOH中	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(1-羥基乙基)-4,5-二氫-1,2-噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	616.1	(500 MHz, DMSO-d6) δ 10.54 - 10.50 (m, 1H), 9.89 (d, J=7.1 Hz, 1H), 8.22 - 8.17 (m, 2H), 7.80 - 7.75 (m, 2H), 7.46 (br t, J=9.7 Hz, 1H), 7.25 (d, J=8.8 Hz, 1H), 4.68 (d, J=9.5 Hz, 1H), 4.50 (ddd, J=10.9, 8.3, 5.0 Hz, 1H), 4.42 (br t, J=9.9 Hz, 1H), 4.02 (s, 3H), 3.71 - 3.63 (m, 1H), 3.19 - 3.06 (m, 3H), 2.73 - 2.67 (m, 1H), 2.58 - 2.54 (m, 1H), 1.85 - 1.72 (m, 2H), 1.53 - 1.45 (m, 1H), 1.43 - 1.35 (m, 2H), 1.07 (d, J=6.4 Hz, 3H), 0.77 - 0.67 (m, 2H), 0.34 (br s, 2H)	2.38, C

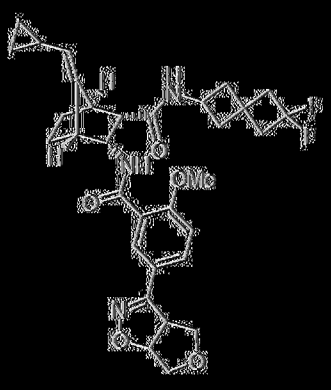
599	 如實例479中使用峰2製備：製備型層析條件：儀器：Berger MG II管柱：Chiralpak IC，30 × 250 mm，5微米，移動相：25%甲醇/ 75% CO_2， 流動條件：70 mL/min，120巴， 40℃，偵測器波長：220 nm，注射詳情：0.5 mL ~75mg/mL於甲醇中。分析型層析條件：儀器：Shimadzu Nexera SFC管柱：Chiralpak IC，4.6 × 100 mm，3微米，移動相：25% MeOH / 75% CO_2，流動條件：2.0 mL/min，150巴， 40℃，偵測器波長：220 nm，注射詳情：5 µL ~1mg/mL於MeOH中(峰-2，RT 7.44 min.，> 99% ee)	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(2-羥基丙烷-2-基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	670.0	(500 MHz, DMSO-d6) δ 10.56 (s, 1H), 9.93 (br d, J=7.0 Hz, 1H), 8.27 - 8.18 (m, 2H), 7.95 - 7.75 (m, 2H), 7.48 (br t, J=9.6 Hz, 1H), 7.28 (d, J=8.9 Hz, 1H), 5.18 - 5.06 (m, 1H), 4.70 (br d, J=9.5 Hz, 1H), 4.44 (br s, 1H), 4.05 (s, 3H), 3.21 - 3.06 (m, 3H), 2.72 (br s, 1H), 2.20 (br dd, J=12.5, 6.4 Hz, 2H), 1.98 (dt, J=12.3, 5.9 Hz, 1H), 1.90 - 1.71 (m, 2H), 1.65 - 1.46 (m, 2H), 1.46 - 1.33 (m, 3H), 1.11 - 1.00 (m, 6H), 0.87 - 0.68 (m, 2H), 0.35 (br d, J=3.7 Hz, 2H)	2.51, C

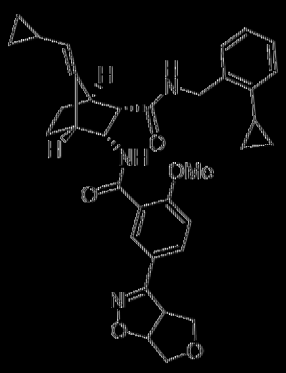
600	 申請16.8製備	(1R,2S,3R,4R,7Z) 3 (5 {3a11,411,611,6a H 呋喃并[3,4 d][1,2]噁唑 3 基} 2 甲氧基苯甲醯胺基) 7 (環丙基甲基) N {螺[3.3]庚烷 2 基} 雙環[2.2.1]庚烷 2 甲醯胺	5456.3	(500 MHz, DMSO d6) δ 9.95 (br d, J= 6.7 Hz, 1H), 8.24 (br d, J= 7.0 Hz, 1H), 8.14 (d, J= 2.1 Hz, 1H), 7.79 (dd, J= 8.7, 2.3 Hz, 1H), 7.24 (d, J= 8.9 Hz, 1H), 5.34 (br dd, J= 9.0, 3.5 Hz, 1H), 4.61 (br d, J= 9.2 Hz, 1H), 4.50 (br t, J= 7.8 Hz, 1H), 4.29 - 4.21 (m, 1H), 4.13 - 4.07 (m, 1H), 4.06 - 3.99 (m, 3H), 3.92 - 3.86 (m, 2H), 3.81 - 3.73 (m, 1H), 3.68 - 3.62 (m, 1H), 3.03 (br s, 1H), 2.83 (br dd, J= 11.6, 3.7 Hz, 1H), 2.31 - 2.19 (m, 2H), 1.98 (br t, J= 7.3 Hz, 2H), 1.90 - 1.69 (m, 6H), 1.49 - 1.41 (m, 1H), 1.36 - 1.15 (m, 3H), 0.88 - 0.76 (m, 1H), 0.75 - 0.64 (m, 2H), 0.32 (br d, J= 2.1 Hz, 2H)。	2.45, B

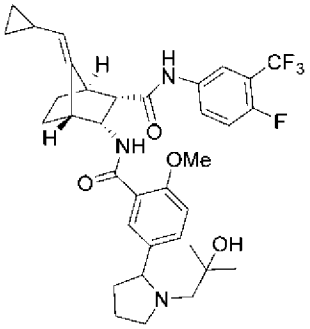
601	 [M+H]+ 644.4 觀測值	(2S,3R)-1-(環丙基甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[1-(2-羥基-2-甲基丙基)吡咯並[3,2-b]吡啶-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	644.4	(400MHz, DMSO-d6) δ = 10.48 (s, 1H), 9.78 (d, J= 6.8 Hz, 1H), 8.21 (dd, J= 2.6, 6.0 Hz, 1H), 7.85 (d, J= 2.4 Hz, 1H), 7.80 - 7.72 (m, 1H), 7.47 (t, J= 9.8 Hz, 1H), 7.42 (dd, J= 2.2, 8.3 Hz, 1H), 7.10 (d, J= 8.3 Hz, 1H), 4.68 (d, J= 9.5 Hz, 1H), 4.49 - 4.37 (m, 1H), 3.96 (s, 4H), 3.19 - 3.11 (m, 2H), 3.09 - 3.02 (m, 2H), 2.93 - 2.78 (m, 2H), 2.70 (br t, J= 3.1 Hz, 2H), 2.29 - 2.14 (m, 1H), 1.93 - 1.82 (m, 3H), 1.80 - 1.61 (m, 2H), 1.55 - 1.30 (m, 3H), 1.13 (s, 8H), 0.80 - 0.63 (m, 2H), 0.35 (dd, J= 2.0, 4.6 Hz, 2H)	2.32, A

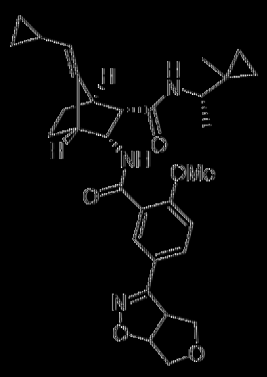
602	 經由SFC分離之異構物，其中實例602為峰2 (RT=2.76 min.， >99% de)-儀器：PIC Solution SFC管柱：Chiralpak AD-H，21 × 250 mm，5微米，移動相：30% IPA-0.1% DEA / 70% CO_2，流動條件：45 mL/min，150巴， 40℃，偵測器波長：220 nm；分析方法：儀器：Aurora Infinity SFC，管柱 Chiralpak IC， 4.6 × 250 mm，3微米，移動相：20% IPA-0.1% DEA / 80% CO_2，流動條件：2 mL/min，150巴， 40℃，偵測器波長：220 nm，得到對掌性(峰-1，RT=1.81 min.，>99% de)及對掌性(峰-2，RT=2.76 min.，>99% de)。	(1R,2S,3R,4R,7Z)-3-(3-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-5-甲氧基苯甲醯胺基)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	614.2	(500 MHz, DMSO-d6) δ 10.58 (s, 1H), 9.34 (br d, J=6.7 Hz, 1H), 8.18 - 8.05 (m, 1H), 7.84 - 7.78 (m, 1H), 7.60 (s, 1H), 7.50 (br t, J=9.8 Hz, 1H), 7.38 (s, 1H), 7.35 (s, 1H), 5.41 (dd, J=9.0, 3.2 Hz, 1H), 4.71 (d, J=9.2 Hz, 1H), 4.53 (br t, J=7.8 Hz, 1H), 4.45 - 4.36 (m, 1H), 4.13 (br d, J=10.7 Hz, 1H), 4.00 (br d, J=9.5 Hz, 1H), 3.86 (s, 2H), 3.82 - 3.75 (m, 1H), 3.67 (dd, J=10.8, 3.5 Hz, 1H), 3.19 (br dd, J=10.1, 3.4 Hz, 1H), 3.11 (br s, 1H), 2.77 (br s, 1H), 1.89 - 1.82 (m, 1H), 1.80 - 1.73 (m, 1H), 1.60 - 1.50 (m, 1H), 1.45 (br s, 2H), 0.82 - 0.70 (m, 2H), 0.37 (br s, 2H)可能由於與溶劑峰重疊，一個質子在NMR中不可見	2.51, B

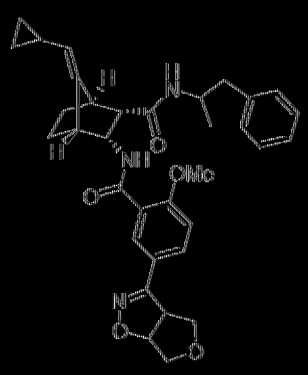
603	 由同對掌性苯甲酸酯峰1 (RT=3.28 min，>99% ee)製備，所用儀器：Berger MG II管柱：Chiralpak IC，21 × 250 mm，5微米，移動相：30% MeOH / 70% CO_2，流動條件：45 mL/min，150巴， 40℃，偵測器波長：220 nm；分析方法：儀器：Aurora Infinity SFC，管柱Chiralpak IC，4.6 × 250 mm，3微米，移動相：30% MeOH / 70% CO_2，流動條件：2 mL/min，150巴， 40℃，偵測器波長：220 nm，得到對掌性(峰-1，RT=3.28 min.，>99% ee)及對掌性(峰-2，RT=3.85 min.，>99% ee)。	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(1-羥基環丁基)-4,5-二氫-1,2-噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	642.3	(500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.91 (br d, J=7.3 Hz, 1H), 8.23 (br d, J=2.1 Hz, 2H), 7.84 - 7.74 (m, 2H), 7.49 (t, J=9.6 Hz, 1H), 7.27 (d, J=8.5 Hz, 1H), 5.26 (s, 1H), 4.79 - 4.65 (m, 2H), 4.50 - 4.39 (m, 1H), 4.05 (s, 3H), 3.38 (m, 1H), 3.22 - 3.15 (m, 1H), 3.13 - 3.08 (m, 1H), 2.73 (br s, 1H), 2.18 - 2.09 (m, 1H), 2.06 (br dd, J=7.8, 3.8 Hz, 1H), 2.02 - 1.90 (m, 2H), 1.88 - 1.83 (m, 1H), 1.81 - 1.77 (m, 1H), 1.75 - 1.66 (m, 1H), 1.64 - 1.57 (m, 1H), 1.55 - 1.47 (m, 1H), 1.47 - 1.31 (m, 2H), 0.75 (br dd, J=11.9, 8.9 Hz, 2H), 0.36 (br s, 2H)可能由於與溶劑峰重疊，一個質子在NMR中不可見	2.67, B

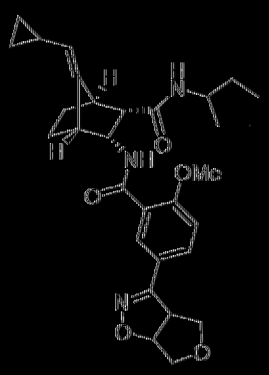
605		(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-{6,6-二氟螺[3.3]庚烷-2-基}雙環[2.2.1]庚烷-2-甲醯胺	582.2	(500 MHz, DMSO-d6) δ 9.94 (br d, J= 6.7 Hz, 1H), 8.33 (br d, J= 7.3 Hz, 1H), 8.14 (d, J= 1.8 Hz, 1H), 7.79 (br d, J= 8.5 Hz, 1H), 7.27-7.20 (m, 1H), 5.34 (br dd, J= 9.2, 3.1 Hz, 1H), 4.61 (br d, J= 9.8 Hz, 1H), 4.50 (br t, J= 8.1 Hz, 1H), 4.32-4.22 (m, 1H), 4.16-4.04 (m, 2H), 4.01 (s, 3H), 3.90 (br d, J= 9.2 Hz, 1H), 3.77 (br dd, J= 8.7, 7.5 Hz, 1H), 3.65 (br dd, J= 10.4, 3.4 Hz, 1H), 3.04 (br s, 1H), 2.84 (br dd, J= 10.8, 4.1 Hz, 1H), 2.63 (br t, J= 12.1 Hz, 2H), 2.42-2.28 (m, 2H), 2.06-1.91 (m, 2H), 1.81-1.67 (m, 2H), 1.51-1.40 (m, 1H), 1.38-1.22 (m, 2H), 0.78-0.64 (m, 2H), 0.31 (br s, 2H)。可能由於與經抑制之水峰及/或溶劑峰重疊，1個質子在NMR中不可見。	2.2.1, B

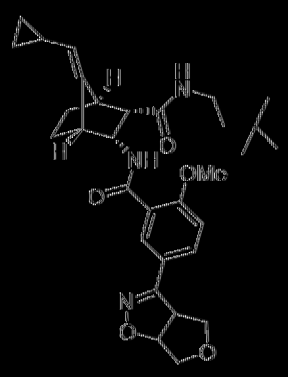
606	 中416.3製備	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-[(2-環丙基苯基)甲基]雙環[2.2.1]庚烷-2-甲醯胺	582.2	(500 MHz, DMSO-d6) δ 9.93 (br d, J=7.0 Hz, 1H), 8.53 (br t, J=5.3 Hz, 1H), 8.17 (d, J=2.4 Hz, 1H), 7.78 (dd, J=8.5, 2.1 Hz, 1H), 7.21 (d, J=8.9 Hz, 1H), 7.17–7.08 (m, 2H), 7.06–7.00 (m, 1H), 6.93 (d, J=7.3 Hz, 1H), 5.34 (dd, J=9.2, 3.1 Hz, 1H), 4.63 (d, J=9.5 Hz, 1H), 4.54–4.40 (m, 3H), 4.37–4.26 (m, 1H), 4.09 (d, J=10.7 Hz, 1H), 3.95–3.85 (m, 4H), 3.80–3.72 (m, 1H), 3.65 (dd, J=10.7, 3.4 Hz, 1H), 3.08–2.98 (m, 2H), 2.62–2.57 (m, 1H), 1.97–1.84 (m, 2H), 1.79–1.69 (m, 1H), 1.52–1.41 (m, 1H), 1.39–1.26 (m, 2H), 0.82 (br d, J=8.5 Hz, 2H), 0.75–0.64 (m, 2H), 0.63–0.51 (m, 2H), 0.32 (br d, J=4.3 Hz, 2H)。	2.43, C

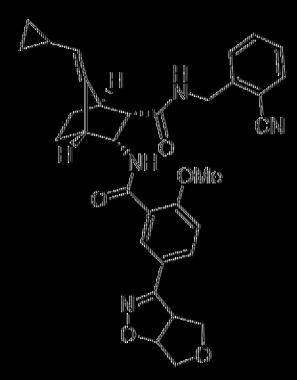
607	 由實例720製備	(2S,3R)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[1-(2-羥基-2-甲基丙基)吡咯啶-2-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	644.3	(400MHz, DMSO-d6) δ = 10.48 (s, 1H), 9.81 (d, J=6.8 Hz, 1H), 8.22 (dd, J=2.4, 6.6 Hz, 1H), 7.93 (d, J=1.7 Hz, 1H), 7.81 - 7.70 (m, 1H), 7.54 - 7.34 (m, 2H), 7.10 (d, J=8.6 Hz, 1H), 4.68 (d, J=9.5 Hz, 1H), 4.51 - 4.40 (m, 1H), 4.01 - 3.90 (m, 5H), 3.55 - 3.47 (m, 1H), 3.25 (br t, J=7.9 Hz, 1H), 3.18 - 3.10 (m, 2H), 3.09 - 3.04 (m, 1H), 2.73 - 2.68 (m, 1H), 2.29 - 2.21 (m, 2H), 2.06 - 1.95 (m, 2H), 1.89 - 1.69 (m, 4H), 1.55 - 1.32 (m, 5H), 1.00 (s, 3H), 0.87 (s, 3H), 0.79 - 0.65 (m, 2H), 0.35 (dd, J=2.0, 4.4 Hz, 2H)	2.67, A

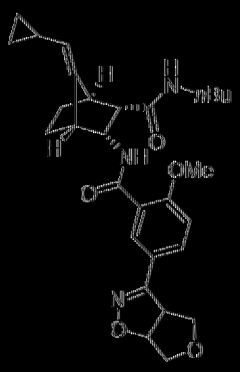
609	 中416-3製備	(1R,2S,3R,4R,7′)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7′-(環丙基甲基)-N-[(1S)-1-(1-甲基環丙基)乙基]雙環[2.2.1]庚烷-2-甲醯胺	534.2	(500 MHz, DMSO-d6) δ 10.07 (d, J= 6.9 Hz, 1H), 8.12 (d, J= 2.4 Hz, 1H), 7.93 (d, J= 8.5 Hz, 1H), 7.77 (dd, J= 8.7, 2.4 Hz, 1H), 7.22 (d, J= 8.8 Hz, 1H), 5.32 (dd, J= 9.2, 3.4 Hz, 1H), 4.62 (d, J= 9.5 Hz, 1H), 4.46 (br t, J= 8.0 Hz, 1H), 4.27-4.19 (m, 1H), 4.08 (d, J= 10.8 Hz, 1H), 3.97 (s, 3H), 3.88 (br d, J= 9.3 Hz, 1H), 3.76 (br dd, J= 9.3, 6.8 Hz, 1H), 3.49-3.38 (m, 1H), 3.06-2.99 (m, 1H), 2.92 (dd, J= 10.8, 4.2 Hz, 1H), 1.89-1.79 (m, 1H), 1.75-1.65 (m, 1H), 1.49-1.40 (m, 1H), 1.38-1.26 (m, 2H), 0.99 (d, J= 6.9 Hz, 3H), 0.95 (s, 3H), 0.76-0.64 (m, 2H), 0.54-0.46 (m, 1H), 0.37-0.24 (m, 3H), 0.21-0.10 (m, 2H)。可能由於與經抑制之水峰重疊，一個質子在NMR中不可見。	2.42, C

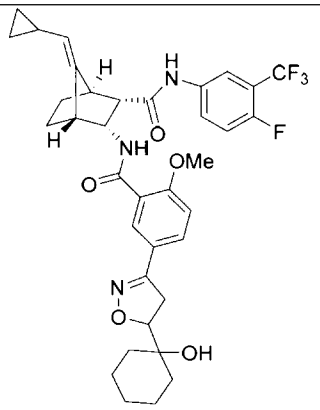
610	 中416-3製備	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-(2,3-二氟-4-甲基苯基)雙環[2.2.1]庚烷-2-甲醯胺	568.0	(500 MHz, DMSO-d6) δ 10.00 (br d, J= 6.7 Hz, 1H), 8.41 (br d, J= 6.7 Hz, 1H), 8.16 (s, 1H), 7.80 (dd, J= 8.7, 1.4 Hz, 1H), 7.26 (d, J= 8.9 Hz, 1H), 7.20 (br d, J= 6.4 Hz, 1H), 7.17 - 7.08 (m, 3H), 5.34 (dd, J= 9.2, 3.4 Hz, 1H), 4.59 (d, J= 9.5 Hz, 1H), 4.53 - 4.43 (m, 2H), 4.27 (br d, J= 4.0 Hz, 1H), 4.09 (br d, J= 11.0 Hz, 1H), 4.04 (s, 3H), 3.90 (br d, J= 9.5 Hz, 1H), 3.80 - 3.73 (m, 1H), 3.65 (br dd, J= 10.7, 3.4 Hz, 1H), 3.24 - 3.09 (m, 2H), 3.04 (br s, 1H), 2.88 (br dd, J= 10.7, 3.7 Hz, 1H), 2.72 (dt, J= 15.7, 6.2 Hz, 2H), 1.92 - 1.83 (m, 1H), 1.78 - 1.69 (m, 1H), 1.51 - 1.41 (m, 1H), 1.40 - 1.27 (m, 2H), 0.77 - 0.63 (m, 2H), 0.30 (br d, J= 2.4 Hz, 2H)。可能由於與溶劑峰重疊，一個質子在NMR中不可見	2.37, B

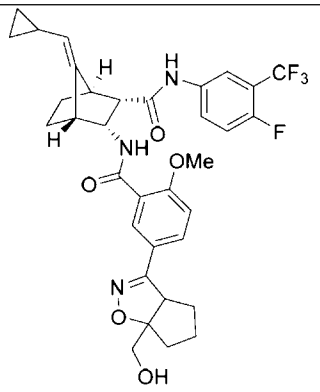
611	 H416.3製備	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-(戊烷-3-基)雙環[2.2.1]庚烷-2-甲醯胺	522.0	(500 MHz, DMSO-d6) δ 10.04 (br d, J = 6.7 Hz, 1H), 8.15 (d, J = 1.5 Hz, 1H), 7.81 - 7.70 (m, 2H), 7.23 (d, J = 8.9 Hz, 1H), 5.34 (dd, J = 9.2, 3.4 Hz, 1H), 4.62 (d, J = 9.5 Hz, 1H), 4.50 (br t, J = 7.8 Hz, 1H), 4.28 (br d, J = 4.3 Hz, 1H), 4.09 (br d, J = 10.7 Hz, 1H), 4.00 (s, 3H), 3.93 - 3.85 (m, 1H), 3.80 - 3.72 (m, 1H), 3.69 - 3.54 (m, 2H), 3.05 (br d, J = 2.7 Hz, 1H), 2.92 (br dd, J = 10.7, 4.0 Hz, 1H), 1.91 - 1.81 (m, 1H), 1.76 - 1.68 (m, 1H), 1.51 - 1.21 (m, 7H), 0.85 - 0.65 (m, 8H), 0.37 - 0.22 (m, 2H)。可能由於與溶劑峰重疊，一個質子在NMR中不可見。	2.32, B

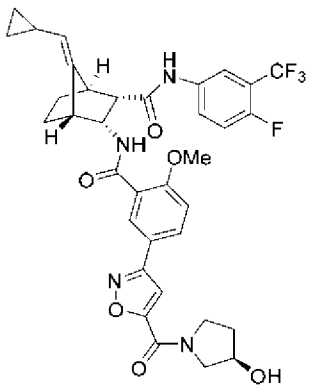
612	 中間體 3 製備	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-(3,3-二甲基丁基)雙環[2.2.1]庚烷-2-甲醯胺	536.3	(500 MHz, DMSO-d6) δ 9.98 (br d, J=7.0 Hz, 1H), 8.16 (d, J=2.1 Hz, 1H), 8.03 (br t, J=5.3 Hz, 1H), 7.79 (dd, J=8.5, 2.1 Hz, 1H), 7.24 (d, J=8.5 Hz, 1H), 5.34 (dd, J=9.0, 3.2 Hz, 1H), 4.61 (d, J=9.8 Hz, 1H), 4.49 (br t, J=7.9 Hz, 1H), 4.27 (br t, J=10.8 Hz, 1H), 4.09 (d, J=10.4 Hz, 1H), 4.02 (s, 3H), 3.92–3.86 (m, 1H), 3.77 (dd, J=9.0, 7.2 Hz, 1H), 3.65 (dd, J=10.7, 3.4 Hz, 1H), 3.11–3.01 (m, 2H), 2.86 (br dd, J=10.8, 3.8 Hz, 1H), 1.86 (br t, J=9.9 Hz, 1H), 1.78–1.68 (m, 1H), 1.46 (dtd, J=12.9, 8.4, 4.4 Hz, 1H), 1.39–1.24 (m, 4H), 0.86 (s, 9H), 0.75–0.63 (m, 2H), 0.32 (br d, J=3.7 Hz, 2H)。可能由於與溶劑峰重疊，一個質子在 NMR 中不可見。	2.38, C

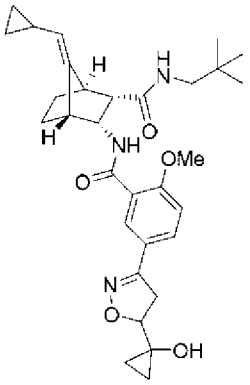
613	 I-416.3製備	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-N-[(2-氟苯基)甲基]-7-(羥亞胺甲基)雙環[2.2.1]庚烷-2-甲醯胺	561.2	(500 MHz, DMSO-d6) δ 9.91 (d, J = 7.0 Hz, 1H), 8.83 (br t, J = 5.9 Hz, 1H), 8.17 (d, J = 2.2 Hz, 1H), 7.84 – 7.73 (m, 2H), 7.57 (t, J = 7.9 Hz, 1H), 7.47 – 7.34 (m, 2H), 7.21 (d, J = 8.7 Hz, 1H), 5.34 (dd, J = 9.2, 3.6 Hz, 1H), 4.64 (d, J = 9.6 Hz, 1H), 4.55 – 4.38 (m, 3H), 4.33 (dt, J = 10.2, 5.0 Hz, 1H), 4.09 (d, J = 10.6 Hz, 1H), 3.90 (d, J = 0.7 Hz, 4H), 3.82 – 3.69 (m, 1H), 3.65 (dd, J = 10.7, 3.5 Hz, 1H), 3.10 – 2.98 (m, 2H), 2.68 – 2.60 (m, 1H), 1.86 – 1.65 (m, 2H), 1.55 – 1.43 (m, 1H), 1.39 – 1.20 (m, 2H), 0.78 – 0.60 (m, 2H), 0.40 – 0.24 (m, 2H)。	2.14, B

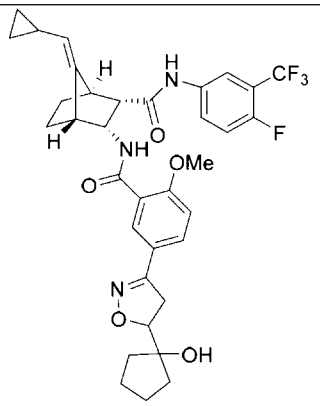
614	 由416-3製備	(1R,2S,3R,4R,7*Z*)-3-(5-{3a*H*,4*H*,6*H*,6a*H*-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-*N*-丁基-7-(環丙基甲基)雙環[2.2.1]庚烷-2-甲醯胺	508.0	(500 MHz, DMSO-d6) δ 9.98 (d, *J* = 6.7 Hz, 1H), 8.15 (d, *J* = 2.2 Hz, 1H), 8.04 (br t, *J* = 5.6 Hz, 1H), 7.78 (dd, *J* = 8.7, 2.3 Hz, 1H), 7.24 (d, *J* = 8.7 Hz, 1H), 5.34 (dd, *J* = 9.2, 3.5 Hz, 1H), 4.61 (d, *J* = 9.5 Hz, 1H), 4.50 (br t, *J* = 7.6 Hz, 1H), 4.32-4.23 (m, 1H), 4.09 (d, *J* = 10.8 Hz, 1H), 4.01 (s, 3H), 3.89 (br d, *J* = 9.3 Hz, 1H), 3.77 (dd, *J* = 9.2, 6.9 Hz, 1H), 3.65 (dd, *J* = 10.8, 3.6 Hz, 1H), 3.12-2.99 (m, 3H), 2.89 (dd, *J* = 10.9, 4.2 Hz, 1H), 1.89-1.81 (m, 1H), 1.79-1.70 (m, 1H), 1.51-1.42 (m, 1H), 1.41-1.29 (m, 1H), 1.29-1.19 (m, 1H), 0.82 (t, *J* = 7.3 Hz, 3H), 0.75-0.64 (m, 2H), 0.35-0.26 (m, 2H)。可能由於與經抑制之水峰重疊，一個質子在NMR中不可見。	2.23, B

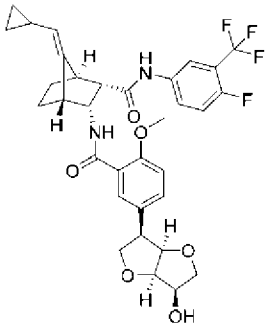
615	 藉由SFC分離之異構物，其中實例615為峰1 (RT=1.15 min，>99% de)， 儀器：Berger MG II管柱：Chiralpak AD-H，21 × 250 mm，5微米，移動相：50% IPA-0.1% DEA/ 50% CO_2，流動條件：45 mL/min，150巴， 40℃，偵測器波長：220 nm；分析方法：儀器：Shimadzu Nexera SFC，管柱Chiralpak AD-H, 4.6 × 100 mm，3微米，移動相：50% IPA0.1% DEA / 50% CO_2，流動條件：2 mL/min，150巴， 40℃，偵測器波長：220 nm，得到對掌性(峰-1，RT=1.15 min.，>99% de)及對掌性(峰-2，RT=2.72 min.，>99% de)。	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(1-羥基環己基)-4,5-二氫-1,2-噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	670.2	(500 MHz, DMSO-d6) δ 10.30 (s, 1H), 9.67 (br d, J=7.0 Hz, 1H), 8.04 - 7.96 (m, 2H), 7.60 - 7.53 (m, 2H), 7.25 (br t, J=9.9 Hz, 1H), 7.03 (d, J=8.9 Hz, 1H), 4.46 (d, J=9.2 Hz, 1H), 4.28 - 4.15 (m, 2H), 4.08 (s, 1H), 3.91 (br t, J=5.3 Hz, 1H), 3.86 - 3.73 (m, 3H), 2.93 (br dd, J=10.8, 4.4 Hz, 1H), 2.89 - 2.84 (m, 1H), 2.53 - 2.44 (m, 1H), 1.66 - 1.58 (m, 1H), 1.56 - 1.48 (m, 1H), 1.42 - 1.24 (m, 5H), 1.23 - 1.14 (m, 4H), 1.14 - 1.02 (m, 3H), 1.01 - 0.84 (m, 1H), 0.69 - 0.60 (m, 1H), 0.58 - 0.44 (m, 2H), 0.21 - 0.05 (m, 2H)	2.70, B

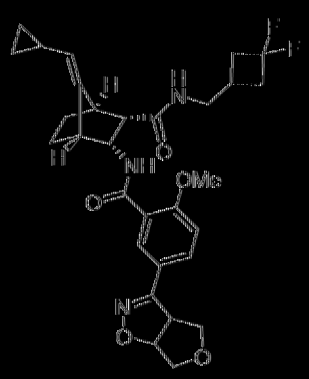
616	 由同對掌性苯甲酸中間物峰2製備。製備型層析條件：儀器：Berger MG II (CTR-L409-PSFC1)管柱：Chiralpak IC，30 × 250 mm，5微米，移動相：25%甲醇/ 75% CO_2，流動條件：70 mL/min，120巴，40℃，偵測器波長：220 nm，注射詳情：0.5 mL ~75mg/mL於甲醇中，分析型層析條件：儀器：Shimadzu Nexera SFC (CTR-L410-SFC3)管柱：Chiralpak IC，4.6 × 100 mm，3微米，移動相：25% MeOH / 75% CO_2，流動條件：2.0 mL/min，150巴，40℃，偵測器波長：220 nm，注射詳情：5 µL ~1mg/mL於MeOH中(峰-2，RT 4.97 min.，> 99% ee)	(1R,2S,3R,4R,7Z)-3-{5-[6a-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	642.1	(500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.88 (d, J=7.3 Hz, 1H), 8.22 (br d, J=2.2 Hz, 2H), 7.86 - 7.71 (m, 2H), 7.48 (t, J=9.9 Hz, 1H), 7.26 (d, J=8.7 Hz, 1H), 4.69 (d, J=9.6 Hz, 1H), 4.44 (br s, 1H), 4.04 (s, 3H), 3.89 (br d, J=6.6 Hz, 1H), 3.56 (br dd, J=11.6, 5.1 Hz, 1H), 3.16 (br dd, J=10.6, 4.0 Hz, 1H), 3.10 (br s, 1H), 2.89 (s, 1H), 2.79 - 2.67 (m, 2H), 1.97 - 1.88 (m, 6H), 1.87 - 1.72 (m, 4H), 1.68 (br s, 2H), 1.55 - 1.35 (m, 4H), 1.04 (d, J=6.1 Hz, 1H), 0.87 - 0.67 (m, 2H), 0.35 (br s, 2H)	2.65, C

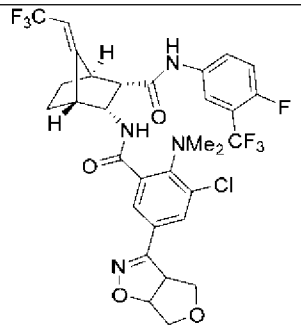
617		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-(5-{5-[(3R)-3-羥基吡咯啶-1-羰基]-1,2-噁唑-3-基}-2-甲氧基苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	682.9	(500 MHz, DMSO-d6) δ 10.29 (s, 1H), 9.67 (br d, J=6.6 Hz, 1H), 9.09 - 9.01 (m, 1H), 8.10 - 8.02 (m, 1H), 7.96 (br d, J=5.1 Hz, 1H), 7.61 - 7.47 (m, 2H), 7.22 (br t, J=9.7 Hz, 1H), 7.06 (dd, J=8.5, 7.0 Hz, 1H), 4.82 (br d, J=12.5 Hz, 1H), 4.43 (d, J=9.6 Hz, 1H), 4.19 (br s, 1H), 4.06 (br s, 1H), 3.95 (br d, J=2.6 Hz, 1H), 3.80 (s, 3H), 3.55 (br s, 1H), 3.37 - 3.25 (m, 2H), 3.19 - 3.08 (m, 1H), 2.97 - 2.87 (m, 1H), 2.85 (br s, 1H), 2.52 - 2.41 (m, 1H), 1.69 - 1.48 (m, 4H), 1.32 - 1.19 (m, 1H), 1.19 - 1.09 (m, 2H), 0.59 - 0.42 (m, 2H), 0.15 - 0.04 (m, 2H)	2.29, B

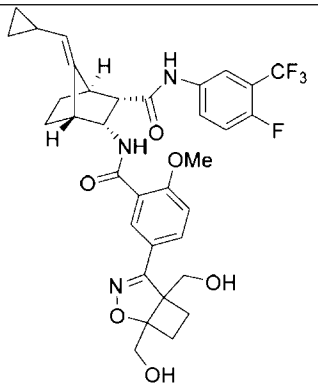
618	 由與實例491中相同之中間物製備	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-(2,2-二甲基丙基)-3-{5-[5-(1-羥基環丙基)-4,5-二氫-1,2-噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	536.0	(500 MHz, DMSO-d6) δ 9.96 (br d, J=6.7 Hz, 1H), 8.16 (d, J=1.8 Hz, 1H), 7.97 (br t, J=6.1 Hz, 1H), 7.77 (dd, J=8.4, 2.3 Hz, 1H), 7.22 (d, J=8.9 Hz, 1H), 5.62 (s, 1H), 4.63 (d, J=9.5 Hz, 1H), 4.39 - 4.23 (m, 2H), 4.03 - 3.94 (m, 3H), 3.02 (br dd, J=13.1, 7.3 Hz, 3H), 2.79 (br dd, J=12.8, 5.5 Hz, 1H), 1.90 - 1.81 (m, 1H), 1.78 - 1.68 (m, 1H), 1.51 - 1.42 (m, 1H), 1.38 - 1.25 (m, 2H), 0.81 (s, 9H), 0.74 - 0.64 (m, 3H), 0.62 - 0.52 (m, 3H), 0.31 (br d, J=1.8 Hz, 2H)。可能由於與溶劑峰及/或經抑制之水峰重疊，兩個質子在NMR中不可見。	2.33, B

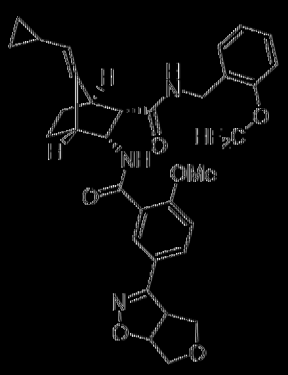
619	 由同對掌性苯甲酸酯峰2-(RT=3.85 min，>99% ee)製備，儀器：Berger MG II管柱：ChiralpakIC-H，21 × 250 mm， 5微米，移動相：30% MeOH / 70% CO_2，流動條件：45 mL/min，150巴， 40℃，偵測器波長：220 nm；分析方法：儀器：Shimadzu Nexera SFC，管柱 Chiralpak IC，4.6 × 100 mm，3微米，移動相：30% MeOH / 70% CO_2，流動條件：2 mL/min，150巴， 40℃，偵測器波長：220 nm，得到對掌性(峰-1，RT=3.28 min.，>99% ee)及對掌性(峰-2，RT=3.85 min.，>99% ee)。	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(1-羥基環戊基)-4,5-二氫-1,2-噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	656.1	(500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.92 (br d, J=7.0 Hz, 1H), 8.23 (br s, 2H), 7.84 - 7.80 (m, 1H), 7.79 (br s, 1H), 7.50 (br t, J=9.9 Hz, 1H), 7.28 (d, J=8.9 Hz, 1H), 4.71 (d, J=9.5 Hz, 1H), 4.63 - 4.57 (m, 1H), 4.51 - 4.43 (m, 1H), 4.11 - 4.00 (m, 3H), 3.45 - 3.36 (m, 1H), 3.29 (br dd, J=16.6, 8.1 Hz, 1H), 3.17 (br dd, J=10.7, 4.0 Hz, 1H), 3.12 (br s, 1H), 2.73 (br s, 1H), 1.92 - 1.82 (m, 1H), 1.82 - 1.76 (m, 1H), 1.73 (br s, 2H), 1.66 - 1.45 (m, 7H), 1.46 - 1.35 (m, 2H), 0.84 - 0.69 (m, 2H), 0.44 - 0.33 (m, 2H)可能由於與溶劑峰重疊，一個質子在NMR中不可見	2.65, C

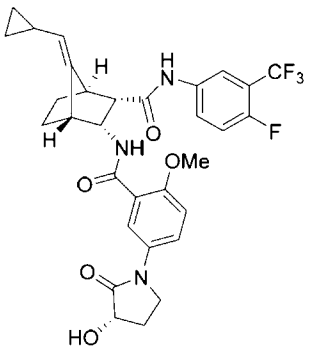
620		(1R,2S,3R,4R,7Z)-3-{5-[(3R,3aR,6R,6aR)-6-羥基-六氫呋喃并[3,2-b]呋喃-3-基]-2-甲氧基苯甲醯胺基}-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	631.5	(500 MHz, CD_3OD) δ 8.16 (dd, J=6.4, 2.6 Hz, 1H), 8.00 (d, J=2.4 Hz, 1H), 7.75 (dt, J=8.5, 3.6 Hz, 1H), 7.51 (dd, J=8.5, 2.4 Hz, 1H), 7.29 (t, J=9.8 Hz, 1H), 7.12 (d, J=8.5 Hz, 1H), 4.74 (d, J=9.3 Hz, 1H), 4.67 - 4.53 (m, 3H), 4.34 (td, J=6.8, 5.0 Hz, 1H), 4.26 (t, J=8.0 Hz, 1H), 4.07 (s, 3H), 4.01 (dd, J=11.6, 8.1 Hz, 1H), 3.87 (dd, J=8.8, 6.5 Hz, 1H), 3.63 (dd, J=8.8, 7.2 Hz, 1H), 3.53 - 3.44 (m, 2H), 3.22 (t, J=4.0 Hz, 1H), 3.19 - 3.11 (m, 1H), 2.72 (t, J=4.0 Hz, 1H), 2.06 - 2.00 (m, 1H), 1.97 - 1.89 (m, 1H), 1.64 - 1.44 (m, 3H), 0.83 - 0.67 (m, 2H), 0.44 - 0.27 (m, 2H)	2.33, B

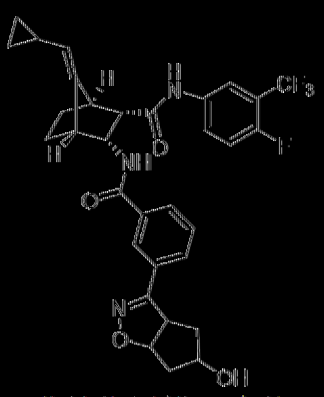
621	 中416.3製備	(1R,2S,3R,4R,7Z) 3 (5 {3aH,4H,6H,6aH 吡喃并[3,4 d][1,2]噁唑 3 基} 2 甲氧基苯甲醯胺基) 7 (環丙基甲基) N [(3,3 二氟環丁基)甲基]雙環[2.2.1]庚烷 2 甲醯胺	556.0	(500 MHz, DMSO d6) δ 9.95 (br d, J= 6.9 Hz, 1H), 8.24 (br t, J= 5.8 Hz, 1H), 8.17 (d, J= 2.4 Hz, 1H), 7.79 (dd, J= 8.6, 2.4 Hz, 1H), 7.24 (d, J= 8.7 Hz, 1H), 5.34 (dd, J= 9.2, 3.5 Hz, 1H), 4.63 (d, J= 9.5 Hz, 1H), 4.50 (br t, J= 8.1 Hz, 1H), 4.36 - 4.25 (m, 1H), 4.09 (d, J= 10.8 Hz, 1H), 4.01 (s, 3H), 3.90 (br d, J= 9.0 Hz, 1H), 3.81 - 3.74 (m, 1H), 3.65 (dd, J= 10.6, 3.6 Hz, 1H), 3.24 - 3.12 (m, 1H), 3.05 (br d, J= 3.6 Hz, 1H), 2.91 (br dd, J= 10.7, 4.1 Hz, 1H), 2.32 - 2.19 (m, 3H), 1.82 (br t, J= 9.2 Hz, 1H), 1.77 - 1.68 (m, 1H), 1.46 (ddd, J= 12.8, 8.1, 4.5 Hz, 1H), 1.39 - 1.27 (m, 2H), 0.77 - 0.64 (m, 2H), 0.32 (br dd, J= 4.2, 1.8 Hz, 2H)。可能由於溶劑峰及/或經抑制之水峰重疊，四個質子在NMR中不可見。	2.16, B

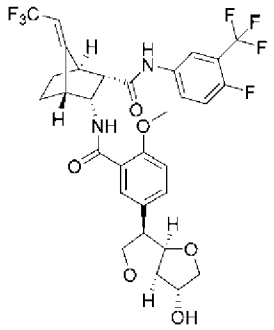
622	 藉由SFC分離之異構物，其中實例622為峰2 (RT=9.99 min.，>95% ee)：所用儀器：Waters 100 Prep SFC管柱：Chiral IC, 21 × 250 mm，5微米，移動相：25% MeOH / 75% CO_2 (具有0.1% DEA)，流動條件：60 mL/min，偵測器波長：220 nm；分析方法：儀器：Shimadzu Nexera SFC，管柱Chiral IC，4.6 × 150 mm，5微米，移動相：25% MeOH / 75% CO_2 (具有0.1% DEA)，流動條件：2 mL/min，偵測器波長：220 nm，得到對掌性(峰-1，RT=4.3 min.，>95% ee)及對掌性(峰-2，RT=5.1 min.，>95% ee)。	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-3-氯-2-(二甲基胺基)苯甲醯胺基)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	689.0	(500 MHz, DMSO-d_6) δ 10.56 (s, 1H), 10.02 (br d, *J*=7.6 Hz, 1H), 8.16 (br d, *J*=4.3 Hz, 1H), 7.88 (d, *J*=1.8 Hz, 1H), 7.84 - 7.74 (m, 2H), 7.48 (t, *J*=9.8 Hz, 1H), 5.95 (q, *J*=8.1 Hz, 1H), 5.37 (dd, *J*=9.2, 3.4 Hz, 1H), 4.59 (br s, 1H), 4.43 (br t, *J*=8.1 Hz, 1H), 4.11 (d, *J*=10.7 Hz, 1H), 3.93 (br d, *J*=11.3 Hz, 1H), 3.75 - 3.60 (m, 2H), 3.27 (br d, *J*=10.7 Hz, 1H), 3.21 (br s, 1H), 3.00 (br s, 1H), 2.83 (s, 6H), 2.20 - 2.01 (m, 2H), 1.52 (br s, 2H)	2.87, B

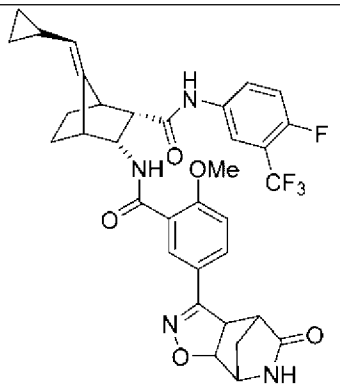
623	 在氧化成苯甲酸峰2之前由三醇製備：製備型層析條件：儀器：Berger MG II管柱：Chiralpak IC，30 × 250 mm，5微米，移動相：25%甲醇/ 75% CO_2，流動條件：70 mL/min，120巴，40℃，偵測器波長：220 nm， 注射詳情：0.5 mL ~75mg/mL於甲醇中。分析型層析條件：儀器：Shimadzu Nexera SFC管柱：Chiralpak IC，4.6 × 100 mm，3微米，移動相：25% MeOH / 75% CO_2，流動條件：2.0 mL/min，150巴，40℃，偵測器波長：220 nm，注射詳情：5 µL ~1mg/mL於MeOH中(峰-2，RT 5.72 min.，> 99% ee)	(1R,2S,3R,4R,7Z)-3-{5-[1,5- 雙(羥基甲基)-2-氧雜-3-氮雜雙環[3.2.0]庚-3-烯-4-基]-2-甲氧基苯甲醯胺基}-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	658.1	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.92 (br d, J=7.0 Hz, 1H), 8.23 (br s, 2H), 7.84 - 7.77 (m, 2H), 7.49 (t, J=9.8 Hz, 1H), 7.27 (d, J=8.9 Hz, 1H), 4.77 (br s, 1H), 4.70 (d, J=9.5 Hz, 1H), 4.44 (br s, 1H), 4.05 (s, 2H), 3.91 - 3.79 (m, 2H), 3.71 (br dd, J=11.7, 6.9 Hz, 1H), 3.40 (br s, 1H), 3.29 - 3.09 (m, 2H), 2.73 (br s, 1H), 2.42 - 2.20 (m, 1H), 2.18 - 2.11 (m, 2H), 2.08 (s, 1H), 1.94 - 1.73 (m, 2H), 1.52 (br d, J=4.3 Hz, 1H), 1.43 (br s, 2H), 0.92 - 0.70 (m, 2H), 0.36 (br s, 2H)	2.38, C

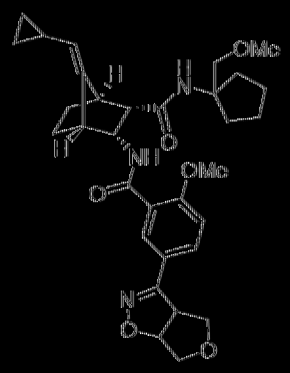
624	 中416.3製備	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-{[2-(二氟甲氧基)苯基]甲基}雙環[2.2.1]庚烷-2-甲醯胺	608.0	(500 MHz, DMSO-d6) δ 9.92 (d, J = 6.9 Hz, 1H), 8.58 (br t, J = 5.8 Hz, 1H), 8.16 (d, J = 2.3 Hz, 1H), 7.78 (dd, J = 8.7, 2.4 Hz, 1H), 7.36 - 7.07 (m, 5H), 7.03 (s, 1H), 5.33 (dd, J = 9.2, 3.4 Hz, 1H), 4.63 (d, J = 9.5 Hz, 1H), 4.48 (br t, J = 8.0 Hz, 1H), 4.38 - 4.25 (m, 3H), 4.09 (d, J = 10.6 Hz, 1H), 3.89 (s, 4H), 3.77 (dd, J = 9.3, 6.9 Hz, 1H), 3.66 - 3.60 (m, 1H), 3.06 - 2.96 (m, 2H), 2.62 - 2.58 (m, 1H), 1.82 (br t, J = 9.1 Hz, 1H), 1.77 - 1.67 (m, 1H), 1.52 - 1.43 (m, 1H), 1.39 - 1.28 (m, 2H), 0.78 - 0.65 (m, 2H), 0.38 - 0.27 (m, 2H)。	2.22, C

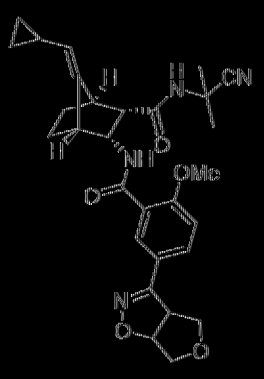
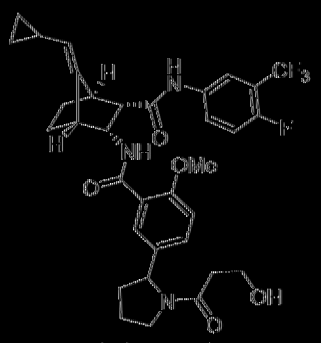
627		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[(3S)-3-羥基-2-側氧基吡咯啶-1-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	601.9	(500 MHz, DMSO-d_6) δ 10.50 (s, 1H), 9.87 (d, *J*=7.2 Hz, 1H), 8.21 (d, *J*=6.9 Hz, 1H), 8.16 (d, *J*=2.9 Hz, 1H), 7.86 - 7.74 (m, 2H), 7.47 (t, *J*=9.7 Hz, 1H), 7.20 (d, *J*=9.1 Hz, 1H), 4.68 (d, *J*=9.6 Hz, 1H), 4.51 - 4.37 (m, 1H), 4.28 (td, *J*=8.5, 5.9 Hz, 1H), 4.03 - 3.94 (m, 3H), 3.77 - 3.63 (m, 2H), 3.52 - 3.35 (m, 1H), 3.15 (br dd, *J*=10.8, 4.4 Hz, 1H), 3.09 (br s, 1H), 2.71 (br s, 1H), 2.43 - 2.34 (m, 1H), 1.90 - 1.73 (m, 3H), 1.49 (tt, *J*=8.7, 4.4 Hz, 1H), 1.43 - 1.34 (m, 2H), 0.82 - 0.66 (m, 2H), 0.41 - 0.29 (m, 2H)	2.27, B

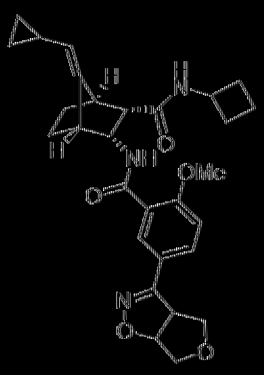
628	 非鏡像異構混合物	(1R,2S,3R,4R,7*S*)-7-(環丙基甲基)-*N*-[4-氟-3-(三氟甲基)苯基]-3-(3-{5-羥基-3a*H*,4*H*,5*H*,6*H*,6a*H*-環戊并[*d*][1,2]噁唑-3-基}苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	598.1	(500 MHz, DMSO-d6) δ 10.58 (br s, 1H), 9.51 - 9.26 (m, 1H), 8.10 - 7.99 (m, 2H), 7.96 - 7.78 (m, 3H), 7.68 - 7.58 (m, 1H), 7.50 (td, J= 9.7, 4.4 Hz, 1H), 5.25 - 5.13 (m, 1H), 4.72 (br d, J= 9.5 Hz, 1H), 4.52 - 4.36 (m, 1H), 4.34 - 4.23 (m, 1H), 4.20 - 4.07 (m, 1H), 3.43 - 3.33 (m, 1H), 3.25 - 3.17 (m, 1H), 3.12 (br s, 1H), 2.78 (br s, 1H), 2.18 - 2.06 (m, 1H), 2.05 - 1.99 (m, 1H), 1.98 - 1.90 (m, 1H), 1.89 - 1.80 (m, 2H), 1.80 - 1.70 (m, 1H), 1.59 - 1.51 (m, 1H), 1.50 - 1.38 (m, 2H), 0.83 - 0.69 (m, 2H), 0.38 (br s, 2H)	2.29, B

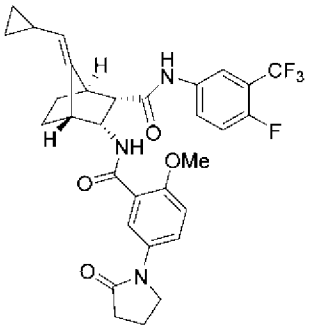
630		(1R,2S,3R,4R,7Z)-3-{5-[(3R,3aR,6S,6aR)-6-羥基-六氫呋喃并[3,2-b]呋喃-3-基]-2-甲氧基苯甲醯胺基}-N-[4-氟-3-(三氟甲基)苯基]-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-甲醯胺	259.2	(500 MHz, DMSO-d6) δ 10.65 (s, 1H), 9.91 (br d, J=7.0 Hz, 1H), 8.26 (br d, J=4.6 Hz, 1H), 7.89 (d, J=1.5 Hz, 1H), 7.84 - 7.75 (m, 1H), 7.52 (br t, J=9.8 Hz, 1H), 7.47 - 7.38 (m, 1H), 7.14 (d, J=8.5 Hz, 1H), 5.96 (q, J=7.9 Hz, 1H), 5.23 (d, J=4.0 Hz, 1H), 4.69 (t, J=3.7 Hz, 1H), 4.59 - 4.48 (m, 1H), 4.44 (br d, J=3.4 Hz, 1H), 4.21 - 4.07 (m, 2H), 3.99 (s, 3H), 3.82 (dd, J=9.5, 3.7 Hz, 1H), 3.74 - 3.62 (m, 2H), 3.33 - 3.20 (m, 2H), 3.00 (br s, 1H), 2.06 - 1.96 (m, 1H), 1.94 - 1.84 (m, 1H), 1.51 (br d, J=6.7 Hz, 2H)	2.31, A

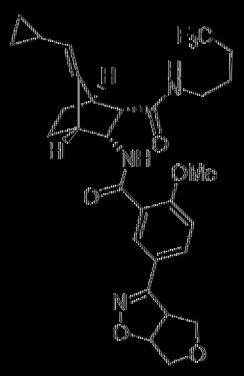
631	 藉由SFC分離之異構物，其中實例631為峰2 (RT=4.7 min.，>95% de)：-儀器：Waters 100 Prep SFC管柱：Chiral AD，30 × 250 mm，5微米，移動相：25% MeOH / 75% CO_2 (具有0.1% DEA)，流動條件：100 mL/min，偵測器波長：220 nm；分析方法：儀器：Shimadzu Nexera SFC，管柱Chiral AD，4.6 × 100 mm，5微米，移動相：25% MeOH / 75% CO_2 (具有0.1% DEA)，流動條件：2 mL/min，偵測器波長：220 nm，得到對掌性(峰-1，RT=3.2 min.，>95% de)及對掌性(峰-2，RT=4.7 min.，>95% de)。	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-(2-甲氧基-5-{8-側氧基-3-氧雜-4,9-二氮雜三環[5.2.1.0²,⁶]癸-4-烯-5-基}苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	653.1	(500 MHz, DMSO-d6) δ 10.65 - 10.48 (m, 1H), 9.91 (d, J=7.0 Hz, 1H), 8.28 (d, J=1.7 Hz, 1H), 8.24 - 8.15 (m, 1H), 7.90 (s, 1H), 7.85 (dd, J=8.6, 2.4 Hz, 1H), 7.80 - 7.74 (m, 1H), 7.48 (br t, J=9.7 Hz, 1H), 7.29 (d, J=8.8 Hz, 1H), 5.10 (br d, J=8.1 Hz, 1H), 4.69 (d, J=9.7 Hz, 1H), 4.48 - 4.38 (m, 1H), 4.27 (br d, J=8.0 Hz, 1H), 4.06 (br s, 1H), 4.04 (s, 3H), 3.20 - 3.13 (m, 1H), 3.10 (br s, 1H), 2.91 (s, 1H), 2.72 (br s, 1H), 1.90 (br d, J=10.4 Hz, 1H), 1.86 - 1.80 (m, 1H), 1.77 (br d, J=10.2 Hz, 1H), 1.59 (br d, J=10.6 Hz, 1H), 1.54 - 1.45 (m, 1H), 1.43 - 1.34 (m, 2H), 0.84 - 0.67 (m, 2H), 0.40 - 0.29 (m, 2H)	2.33, B

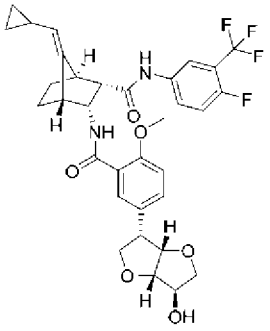
632	 中416-3製備	(1R,2S,3R,4R,7′)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-[1-(甲氧基甲基)環戊基]雙環[2.2.1]庚烷-2-甲醯胺	564.0	(500 MHz, DMSO-d6) δ 10.08 (br d, J=7.0 Hz, 1H), 8.18 (d, J=1.8 Hz, 1H), 7.78 (dd, J=8.5, 1.8 Hz, 1H), 7.67 (s, 1H), 7.24 (d, J=8.9 Hz, 1H), 5.33 (br dd, J=9.0, 3.2 Hz, 1H), 4.60 (br d, J=9.5 Hz, 1H), 4.48 (br t, J=7.8 Hz, 1H), 4.32-4.19 (m, 1H), 4.14-4.05 (m, 1H), 4.03 (s, 3H), 3.89 (br d, J=9.2 Hz, 1H), 3.81-3.73 (m, 1H), 3.65 (br dd, J=10.8, 3.2 Hz, 1H), 3.16 (s, 3H), 3.02 (br s, 1H), 2.91 (br dd, J=11.0, 4.0 Hz, 1H), 1.91-1.79 (m, 3H), 1.75-1.66 (m, 1H), 1.64-1.40 (m, 7H), 1.38-1.22 (m, 2H), 0.78-0.62 (m, 2H), 0.30 (br d, J=2.1 Hz, 2H)。可能由於觀察到抑制之水峰及/或溶劑峰重疊，3個質子在NMR中不可見。	2.36, B

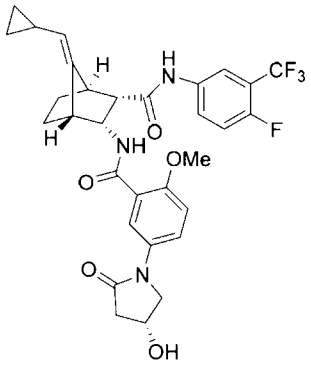
633	 中間體33製備	(1R,2S,3R,4R,7′Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-N-(1-氰基-1-甲基乙基)-7′-(環丙基亞甲基)雙環[2.2.1]庚烷-2-甲醯胺	519.2	(400 MHz, CD_3OD) δ 8.29 (d, J= 2.3 Hz, 1H), 7.91 - 7.84 (m, 1H), 7.26 (d, J= 9.0 Hz, 1H), 5.39 - 5.33 (m, 1H), 4.72 - 4.60 (m, 1H), 4.50 - 4.42 (m, 2H), 4.25 - 4.16 (m, 4H), 4.09 - 4.01 (m, 1H), 3.92 - 3.86 (m, 1H), 3.80 - 3.70 (m, 1H), 3.00 - 2.93 (m, 2H), 2.63 - 2.58 (m, 1H), 1.97 - 1.85 (m, 2H), 1.64 (d, J= 11.6 Hz, 6H), 1.55 - 1.23 (m, 3H), 0.75 - 0.68 (m, 2H), 0.38 - 0.27 (m,2H)	1.88, C
634	 中實例15製備	(2S,3R)-7′-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[1-(3-羥基丙醯基)吡咯啶-2-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	644.3	(400MHz, DMSO-d6) δ 9.91 - 9.76 (m, 1H), 8.21 (br d, J= 6.6 Hz, 1H), 7.80 - 7.66 (m, 2H), 7.47 (t, J= 9.8 Hz, 1H), 7.29 (ddd, J= 2.6, 8.6, 19.7 Hz, 1H), 7.20 - 7.00 (m, 1H), 5.13 - 4.94 (m, 1H), 4.68 (d, J= 9.5 Hz, 1H), 4.51 (t, J= 5.3 Hz, 1H), 4.47 - 4.39 (m, 1H), 4.37 (t, J= 5.4 Hz, 1H), 3.99 (s, 2H), 3.96 (s, 1H), 3.75 - 3.60 (m, 2H), 3.57 - 3.40 (m, 2H), 3.18 - 3.11 (m, 1H), 3.10 - 3.04 (m, 1H), 2.71 (br s, 1H), 2.42 - 2.16 (m, 2H), 1.93 - 1.64 (m, 5H), 1.54 - 1.32 (m, 3H), 0.80 - 0.67 (m, 2H), 0.41 - 0.29 (m, 2H)	2.34, A

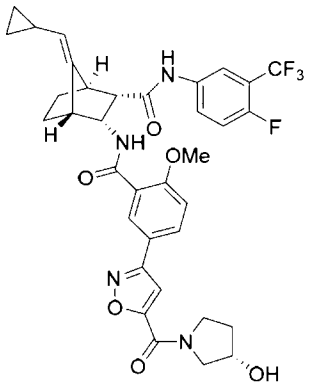
635	 416.3製備	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-N-環丁基-7-(環丙基亞甲基)雙環[2.2.1]庚烷-2-甲醯胺	506.3	(500 MHz, DMSO-d6) δ 9.98 (br dd, J=14.0, 6.7 Hz, 1H), 8.34 (br dd, J=14.0, 7.6 Hz, 1H), 8.16 (dd, J=14.0, 1.8 Hz, 1H), 7.85–7.74 (m, 1H), 7.25 (dd, J=14.0, 8.9 Hz, 1H), 5.40–5.28 (m, 1H), 4.62 (br dd, J=13.9, 9.6 Hz, 1H), 4.56–4.45 (m, 1H), 4.33–4.16 (m, 2H), 4.13–4.07 (m, 1H), 4.02 (d, J=14.0 Hz, 2H), 3.95–3.87 (m, 1H), 3.83–3.74 (m, 1H), 3.70–3.61 (m, 1H), 3.09–2.98 (m, 1H), 2.90–2.80 (m, 1H), 2.21–2.07 (m, 2H), 1.91–1.68 (m, 4H), 1.66–1.55 (m, 2H), 1.46 (ddd, J=12.9, 8.8, 4.3 Hz, 1H), 1.40–1.24 (m, 2H), 0.79–0.64 (m, 2H), 0.32 (br d, J=13.1 Hz, 2H)。	2.13, B

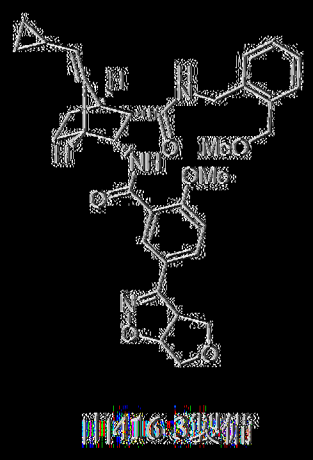
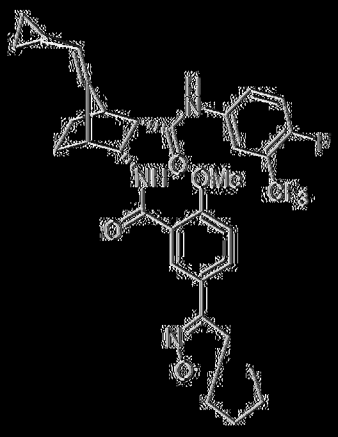
636		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-[2-甲氧基-5-(2-側氧基吡咯啶-1-基)苯甲醯胺基]雙環[2.2.1]庚烷-2-甲醯胺	586.3	(500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.89 (br d, J=7.0 Hz, 1H), 8.29 - 8.17 (m, 1H), 8.13 (d, J=3.1 Hz, 1H), 7.79 (br d, J=2.7 Hz, 1H), 7.77 (br d, J=2.7 Hz, 1H), 7.48 (br t, J=9.9 Hz, 1H), 7.20 (d, J=9.2 Hz, 1H), 4.70 (d, J=9.5 Hz, 1H), 4.45 (br d, J=6.1 Hz, 1H), 3.99 (s, 3H), 3.85 - 3.71 (m, 1H), 3.59 - 3.43 (m, 1H), 3.16 (br dd, J=11.3, 3.7 Hz, 1H), 3.10 (br s, 1H), 2.72 (br s, 1H), 2.48 (br t, J=8.1 Hz, 2H), 2.16 - 2.04 (m, 2H), 1.92 - 1.83 (m, 1H), 1.78 (br t, J=8.5 Hz, 1H), 1.59 - 1.50 (m, 1H), 1.46 - 1.33 (m, 2H), 0.87 - 0.67 (m, 2H), 0.36 (br d, J=3.1 Hz, 2H)	2.45, B

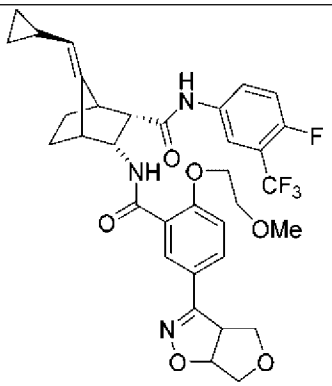
637	 H416-3製備	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-(4,4,4-三氟丁基)雙環[2.2.1]庚烷-2-甲醯胺	506.3	(500 MHz, DMSO-d6) δ 9.98 (br dd, J=14.0, 6.7 Hz, 1H), 8.34 (br dd, J=14.0, 7.6 Hz, 1H), 8.16 (dd, J=14.0, 1.8 Hz, 1H), 7.85–7.74 (m, 1H), 7.25 (dd, J=14.0, 8.9 Hz, 1H), 5.40–5.28 (m, 1H), 4.62 (br dd, J=13.9, 9.6 Hz, 1H), 4.56–4.45 (m, 1H), 4.33–4.16 (m, 2H), 4.13–4.07 (m, 1H), 4.02 (d, J=14.0 Hz, 2H), 3.95–3.87 (m, 1H), 3.83–3.74 (m, 1H), 3.70–3.61 (m, 1H), 3.09–2.98 (m, 1H), 2.90–2.80 (m, 1H), 2.21–2.07 (m, 2H), 1.91–1.68 (m, 4H), 1.66–1.55 (m, 2H), 1.46 (ddd, J=12.9, 8.8, 4.3 Hz, 1H), 1.40–1.24 (m, 2H), 0.79–0.64 (m, 2H), 0.32 (br d, J=13.1 Hz, 2H)。	2.13, B

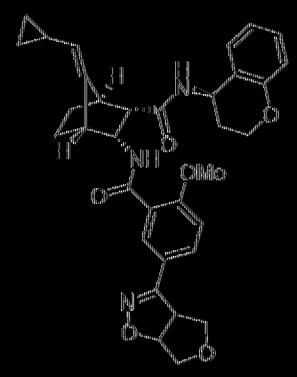
638		(1R,2S,3R,4R,7Z)-3-{5-[(3S,3aS,6R,6aS)-6-羥基-六氫呋喃并[3,2-b]呋喃-3-基]-2-甲氧基苯甲醯胺基}-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	631.1	(500 MHz, DMSO-d6) δ 10.52 (s, 1H), 9.83 (br d, J=7.0 Hz, 1H), 8.24 (br d, J=4.3 Hz, 1H), 7.86 (d, J=1.8 Hz, 1H), 7.83 - 7.74 (m, 1H), 7.49 (br t, J=9.8 Hz, 1H), 7.44 (dd, J=8.4, 1.7 Hz, 1H), 7.12 (d, J=8.5 Hz, 1H), 4.73 - 4.64 (m, 2H), 4.52 - 4.38 (m, 2H), 4.19 - 4.07 (m, 2H), 3.98 (s, 3H), 3.81 (dd, J=9.5, 3.7 Hz, 1H), 3.74 - 3.60 (m, 2H), 3.16 (br dd, J=10.5, 4.7 Hz, 1H), 3.10 (br s, 1H), 2.72 (br s, 1H), 1.91 - 1.83 (m, 1H), 1.82 - 1.72 (m, 1H), 1.61 - 1.48 (m, 1H), 1.47 - 1.34 (m, 2H), 0.80 - 0.69 (m, 2H), 0.36 (br s, 2H)	2.45, A

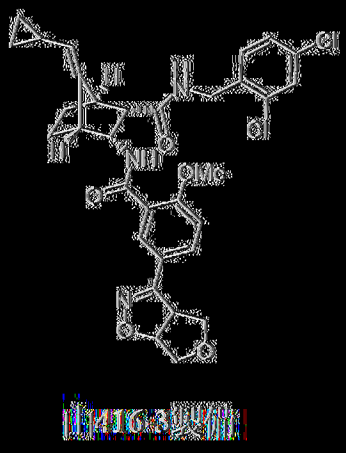
639		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[(4R)-4-羥基-2-側氧基吡咯啶-1-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	602.1	(500 MHz, DMSO-d6) δ 10.63 - 10.49 (m, 1H), 9.91 (br d, J=7.3 Hz, 1H), 8.30 - 8.20 (m, 1H), 8.16 (d, J=2.7 Hz, 1H), 7.89 - 7.72 (m, 2H), 7.50 (br t, J=9.6 Hz, 1H), 7.21 (d, J=8.9 Hz, 1H), 4.71 (d, J=9.5 Hz, 1H), 4.46 (br d, J=6.1 Hz, 1H), 4.40 (br s, 1H), 4.07 (dd, J=10.4, 5.2 Hz, 1H), 4.00 (s, 3H), 3.56 (br d, J=10.4 Hz, 1H), 3.17 (br dd, J=10.4, 4.0 Hz, 1H), 3.11 (br s, 1H), 2.80 (br d, J=6.1 Hz, 1H), 2.73 (br s, 1H), 2.35 - 2.26 (m, 1H), 1.98 - 1.84 (m, 2H), 1.82 - 1.70 (m, 1H), 1.60 - 1.49 (m, 1H), 1.47 - 1.34 (m, 2H), 0.89 - 0.65 (m, 2H), 0.37 (br s, 2H)	2.24, B

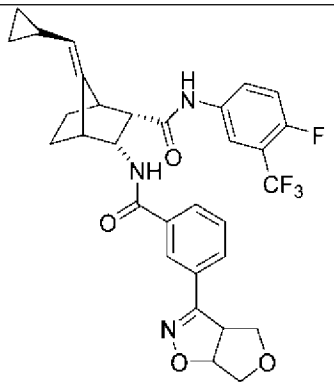
640		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-(5-{5-[(3S)-3-羥基吡咯啶-1-羰基]-1,2-噁唑-3-基}-2-甲氧基苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	682.9	(500 MHz, DMSO-d6) δ 10.31 (s, 1H), 9.69 (br d, J=6.7 Hz, 1H), 9.10 (d, J=18.9 Hz, 1H), 8.09 (s, 1H), 8.00 (br d, J=5.2 Hz, 1H), 7.63 - 7.52 (m, 2H), 7.33 (s, 1H), 7.25 (br t, J=9.6 Hz, 1H), 7.08 (dd, J=8.4, 6.6 Hz, 1H), 4.52 - 4.39 (m, 1H), 4.22 (br s, 1H), 4.08 (br s, 1H), 3.99 (br s, 1H), 3.83 (s, 3H), 3.67 (s, 1H), 3.35 - 3.12 (m, 1H), 2.97 - 2.83 (m, 2H), 2.54 - 2.45 (m, 1H), 1.73 - 1.50 (m, 4H), 1.42 - 1.24 (m, 2H), 1.24 - 1.06 (m, 2H), 0.58 - 0.40 (m, 2H), 0.12 (br s, 2H), 0.07 (br s, 2H)	2.28, C

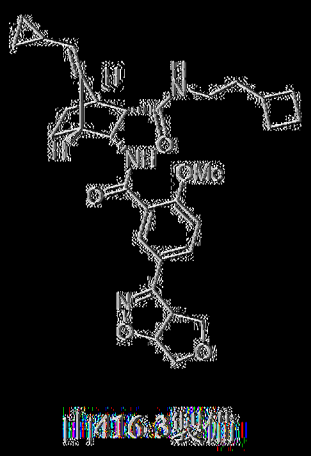
641		(1R,2S,3R,4R,7′S) 3 (5 {3aH,4H,6H,6aH 吡喃并[3,4 d][1,2]噁唑 3 基} 2 甲氧基苯甲醯胺基) 7 (環丙基甲基) N {[2 (甲氧基甲基)苯基]甲基} 雙環[2.2.1]庚烷 2 甲醯胺	586.3	(500 MHz, DMSO d6) δ 9.93 (br d, J=7.0 Hz, 1H), 8.55 8.47 (m, 1H), 8.13 (d, J=2.4 Hz, 1H), 7.77 (dd, J=8.5, 2.1 Hz, 1H), 7.27 (br d, J=6.7 Hz, 1H), 7.23 7.10 (m, 4H), 5.32 (dd, J=9.2, 3.4 Hz, 1H), 4.62 (d, J=9.5 Hz, 1H), 4.49 4.40 (m, 3H), 4.35 4.25 (m, 3H), 4.08 (d, J=10.7 Hz, 1H), 3.93 3.85 (m, 2H), 3.77 3.60 (m, 2H), 3.24 (s, 3H), 3.08 3.02 (m, 1H), 2.98 (br dd, J=10.5, 3.8 Hz, 1H), 2.60 2.56 (m, 1H), 1.88 1.79 (m, 1H), 1.75 1.67 (m, 1H), 1.51 1.40 (m, 1H), 1.39 1.25 (m, 2H), 0.78 0.60 (m, 2H), 0.37 0.22 (m, 2H)。可能由於與經抑制之水峰重疊，一個質子在NMR中不可見。	2.19, B
642		(1R,2S,3R,4R,7′S) 7 (環丙基甲基) N [4 氟 3 (三氟甲基)苯基] 3 (2 甲氧基 5 {1 氧雜 2 氮雜螺[4.4]壬 2 烯 3 基}苯甲醯胺基)雙環[2.2.1]庚烷 2 甲醯胺	626.1	(500 MHz, DMSO d6) δ 10.52 (s, 1H), 9.91 9.86 (m, 1H), 8.24 8.17 (m, 2H), 7.80 7.74 (m, 2H), 7.51 7.45 (m, 1H), 7.28 7.23 (m, 1H), 4.68 (d, J=9.7 Hz, 1H), 4.47 4.41 (m, 1H), 4.03 (s, 3H), 3.43 3.39 (m, 1H), 3.18 3.07 (m, 1H), 2.75 2.69 (m, 1H), 2.59 2.55 (m, 1H), 1.94 1.63 (m, 10H), 1.52 1.35 (m, 3H), 0.79 0.69 (m, 2H), 0.39 0.31 (m, 2H)	2.18, B

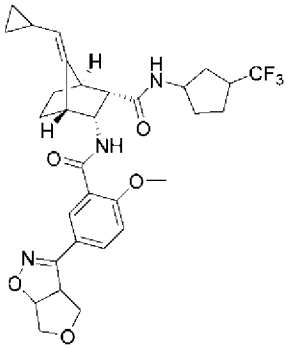
644	 藉由SFC分離之異構物，其中實例644為峰2 (RT=3.6 min，>95% de) -儀器：Waters 100 Prep SFC管柱：Chiral OD，30 × 250 mm，5微米，移動相：25% MeOH / 75% CO_2 (具有0.1% DEA)，流動條件：100 mL/min，偵測器波長：220 nm；分析方法：儀器：Shimadzu Nexera SFC，管柱Chiral OD，4.6 × 100 mm，5微米，移動相：25% MeOH / 75% CO_2 (具有0.1% DEA)，流動條件：2 mL/min，偵測器波長：220 nm，得到對掌性(峰-1，RT=2.92 min.，>95% de)及對掌性(峰-2，RT=3.6 min.，>95% de)。	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-(2-甲氧基乙氧基)苯甲醯胺基)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	658.2	(500 MHz, DMSO-d6) δ 10.49 (s, 1H), 9.63 (br d, J=7.6 Hz, 1H), 8.22 (d, J=2.4 Hz, 1H), 8.17 (br d, J=4.3 Hz, 1H), 7.82 - 7.72 (m, 2H), 7.48 (t, J=9.8 Hz, 1H), 7.33 (d, J=8.9 Hz, 1H), 5.36 (dd, J=9.2, 3.7 Hz, 1H), 4.76 - 4.68 (m, 1H), 4.58 - 4.48 (m, 2H), 4.48 - 4.40 (m, 2H), 4.12 (br d, J=10.7 Hz, 1H), 4.08 - 4.00 (m, 1H), 3.91 (br d, J=9.2 Hz, 1H), 3.82 - 3.76 (m, 1H), 3.68 (dd, J=10.7, 3.4 Hz, 1H), 3.41 - 3.34 (m, 1H), 3.17 (br dd, J=10.4, 3.7 Hz, 1H), 3.09 (br s, 1H), 2.75 (br s, 1H), 2.57 (s, 3H), 2.02 - 1.85 (m, 2H), 1.60 - 1.51 (m, 1H), 1.51 - 1.41 (m, 2H), 0.82 - 0.70 (m, 2H), 0.38 (br d, J=1.8 Hz, 2H)	2.42, C

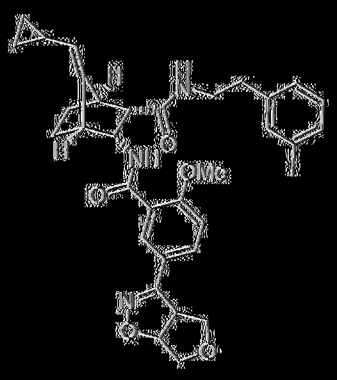
645	 I-416-3製備	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-[(4R)-3,4-二氫-2H-1-苯并哌喃-4-基]雙環[2.2.1]庚烷-2-甲醯胺	584.2	(500 MHz, DMSO-d6) δ 10.00 (br d, J=7.0 Hz, 1H), 8.58 (br d, J=8.2 Hz, 1H), 8.17 (d, J=2.4 Hz, 1H), 7.80 (dd, J=8.9, 2.1 Hz, 1H), 7.26 (d, J=8.5 Hz, 1H), 7.18-7.08 (m, 2H), 6.88 (t, J=7.2 Hz, 1H), 6.76 (d, J=8.2 Hz, 1H), 5.34 (dd, J=9.0, 3.5 Hz, 1H), 5.10-5.01 (m, 1H), 4.64-4.59 (m, 1H), 4.50 (br t, J=8.1 Hz, 1H), 4.34-4.28 (m, 1H), 4.19-4.12 (m, 2H), 4.10 (br d, J=10.7 Hz, 1H), 4.03 (s, 3H), 3.95-3.87 (m, 1H), 3.78 (dd, J=9.2, 7.0 Hz, 1H), 3.66 (dd, J=10.7, 3.7 Hz, 1H), 3.07 (br s, 1H), 2.95 (br dd, J=10.5, 3.8 Hz, 1H), 2.57-2.55 (m, 1H), 2.09-1.95 (m, 2H), 1.87-1.75 (m, 2H), 1.53-1.35 (m, 3H), 0.71 (br t, J=9.0 Hz, 2H), 0.31 (br d, J=4.0 Hz, 2H)。	2.2/1, C

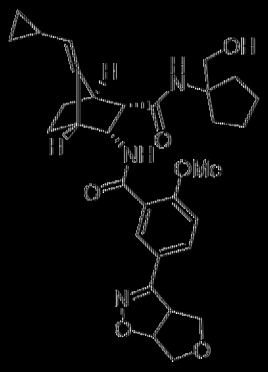
646		(1R,2S,3R,4R,7Z) 3 (5 {3aH,4H,6H,6aH 呋喃并[3,4 d][1,2]噁唑 3 基} 2 甲氧基苯甲醯胺基) 7 (環丙基甲基) N [(2,4 二氟苯基) 甲基] 雙環[2.2.1]庚烷 2 甲醯胺	610.2	(500 MHz, DMSO d6) δ 9.84 (d, J = 7.0 Hz, 1H), 8.68 (t, J = 5.8 Hz, 1H), 8.17 (d, J = 2.3 Hz, 1H), 7.78 (dd, J = 8.6, 2.4 Hz, 1H), 7.56 (d, J = 1.9 Hz, 1H), 7.31 – 7.25 (m, 2H), 7.21 – 7.18 (m, 1H), 5.34 (dd, J = 9.2, 3.4 Hz, 1H), 4.64 (d, J = 9.6 Hz, 1H), 4.48 (br t, J = 7.4 Hz, 1H), 4.39 – 4.28 (m, 3H), 4.09 (d, J = 10.6 Hz, 1H), 3.92 – 3.87 (m, 4H), 3.77 (dd, J = 9.2, 6.8 Hz, 1H), 3.65 (dd, J = 10.8, 3.7 Hz, 1H), 3.07 – 3.00 (m, 2H), 2.63 – 2.58 (m, 1H), 1.82 (br t, J = 9.1 Hz, 1H), 1.75 – 1.66 (m, 1H), 1.53 – 1.42 (m, 1H), 1.41 – 1.27 (m, 2H), 0.78 – 0.65 (m, 2H), 0.38 – 0.27 (m, 2H)。	2.43, C

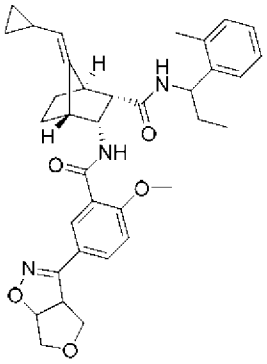
647	 由同對掌性酸中間物峰2 (RT=6.53 min.，>99% ee)製備：所用儀器：Berger MG II管柱：Chiralpak IA，21 × 250 mm，5微米，移動相：20% IPA / 80% CO_2，流動條件：45 mL/min，150巴，40℃，偵測器波長：220 nm；分析方法：儀器：Shimadzu Nexera SFC，管柱Chiralpak IA，4.6 × 100 mm，3微米，移動相：20% IPA / 80% CO_2，流動條件：2 mL/min，150巴，40℃，偵測器波長：220 nm，得到對掌性(峰-1，RT=2.55 min.，>99% ee)及對掌性(峰-2，RT=6.53 min.，>99% ee)。	(1R,2S,3R,4R,7Z)-3-(3-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}苯甲醯胺基)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	584.3	(500 MHz, DMSO-d6) δ 10.58 (s, 1H), 9.37 (br d, J=6.7 Hz, 1H), 8.05 (s, 2H), 7.86 (br dd, J=18.9, 7.3 Hz, 3H), 7.63 (t, J=7.8 Hz, 1H), 7.51 (t, J=9.8 Hz, 1H), 5.42 (dd, J=9.3, 3.5 Hz, 1H), 4.73 (d, J=9.8 Hz, 1H), 4.55 (br t, J=7.8 Hz, 1H), 4.48 - 4.39 (m, 1H), 4.15 (d, J=11.0 Hz, 1H), 4.01 (br d, J=9.5 Hz, 1H), 3.80 (dd, J=9.2, 7.0 Hz, 1H), 3.69 (dd, J=10.7, 3.4 Hz, 1H), 3.42 - 3.34 (m, 1H), 3.20 (br dd, J=10.5, 4.1 Hz, 1H), 3.13 (br s, 1H), 2.78 (br s, 1H), 1.91 - 1.85 (m, 1H), 1.80 - 1.74 (m, 1H), 1.54 (td, J=8.3, 3.8 Hz, 1H), 1.46 (br d, J=0.6 Hz, 1H), 0.84 - 0.70 (m, 2H), 0.38 (br d, J=1.5 Hz, 2H)	2.45, B

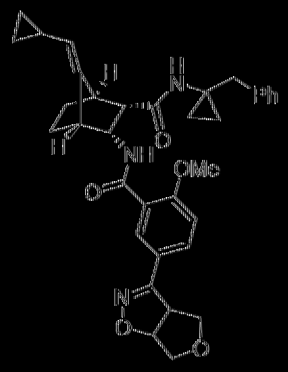
648	 中間體63製備	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-N-(2-環丁基乙基)-7-(環丙基甲基)雙環[2.2.1]庚烷-2-甲醯胺	534.2	(500 MHz, DMSO-d6) δ 9.96 (br d, J=6.7 Hz, 1H), 8.16 (d, J=2.1 Hz, 1H), 8.01 (br t, J=5.3 Hz, 1H), 7.79 (dd, J=8.5, 2.1 Hz, 1H), 7.24 (d, J=8.9 Hz, 1H), 5.34 (dd, J=9.2, 3.7 Hz, 1H), 4.61 (br d, J=9.5 Hz, 1H), 4.54-4.44 (m, 1H), 4.34-4.23 (m, 1H), 4.09 (br d, J=10.7 Hz, 1H), 4.02 (s, 3H), 3.89 (br d, J=9.2 Hz, 1H), 3.81-3.71 (m, 1H), 3.65 (br dd, J=10.7, 3.7 Hz, 1H), 3.08-2.93 (m, 3H), 2.87 (br dd, J=10.8, 4.1 Hz, 1H), 2.22 (quin, J=7.9 Hz, 1H), 2.03-1.90 (m, 2H), 1.86 (br t, J=9.2 Hz, 1H), 1.78-1.66 (m, 3H), 1.60-1.41 (m, 5H), 1.39-1.24 (m, 2H), 0.71 (quin, J=9.5 Hz, 2H), 0.31 (br s, 2H)。可能由於與經抑制之水峰重疊，一個質子在NMR中不可見。	2.40, B

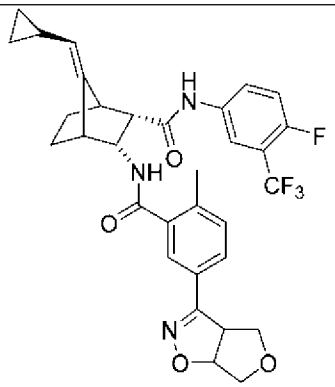
649	 與**實例589**中一樣由**589-3**製備	(1R,2S,3R,4R,Z)-7-(環丙基亞甲基)-3-(2-甲氧基-5-(3a,4,6,6a-四氫呋喃并[3,4-d]異噁唑-3-基)苯甲醯胺基)-N-(3-(三氟甲基)環戊基)雙環[2.2.1]庚烷-2-甲醯胺	588.4	(400 MHz, CD_3OD) δ 8.26 - 8.21 (m, 1H), 7.88 (dd, *J*=8.7, 2.3 Hz, 1H), 7.25 (d, *J*=8.7 Hz, 1H), 5.36 (dd, *J*=9.2, 3.6 Hz, 1H), 4.67 (d, *J*=9.3 Hz, 1H), 4.50 - 4.41 (m, 2H), 4.22 - 4.14 (m, 2H), 4.11 (s, 3H), 4.06 (d, *J*=9.2 Hz, 1H), 3.90 - 3.84 (m, 1H), 3.75 (dd, *J*=10.6, 3.8 Hz, 1H), 3.19 - 3.15 (m, 1H), 2.94 (dd, *J*=10.6, 4.7 Hz, 1H), 2.82 - 2.68 (m, 1H), 2.58 - 2.52 (m, 1H), 2.33 - 2.18 (m, 1H), 2.05 - 1.79 (m, 5H), 1.62 - 1.42 (m, 5H), 0.73 (br d, *J*=7.9 Hz, 2H), 0.39 - 0.24 (m, 2H)。	2.21, B

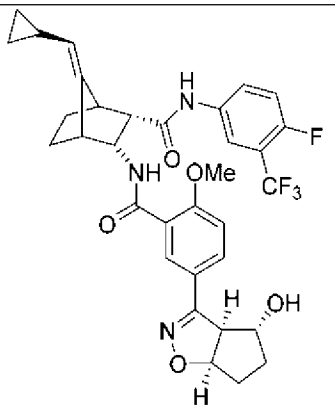
650	 中間體63製備	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-[2-(3-甲基苯基)乙基]雙環[2.2.1]庚烷-2-甲醯胺	570.4	(500 MHz, DMSO-d6) δ 9.99–9.91 (m, 1H), 8.20–8.11 (m, 2H), 7.78 (br dd, J= 8.7, 2.0 Hz, 1H), 7.24 (br d, J= 8.9 Hz, 1H), 7.17–7.06 (m, 1H), 7.01–6.90 (m, 3H), 5.33 (br dd, J= 9.2, 3.4 Hz, 1H), 4.60 (br d, J= 9.5 Hz, 1H), 4.49 (br t, J= 7.0 Hz, 1H), 4.27 (br t, J= 10.5 Hz, 1H), 4.09 (br d, J= 10.7 Hz, 1H), 4.02 (s, 3H), 3.89 (br d, J= 8.9 Hz, 1H), 3.81–3.71 (m, 1H), 3.68–3.59 (m, 1H), 3.03 (br s, 1H), 2.91–2.82 (m, 1H), 2.65 (br t, J= 6.9 Hz, 2H), 2.45 (br s, 1H), 2.22 (s, 3H), 1.80–1.65 (m, 2H), 1.53–1.40 (m, 1H), 1.37–1.18 (m, 2H), 0.77–0.61 (m, 2H), 0.31 (br s, 2H)。可能由於與溶劑峰及/或經抑制之水峰重疊，兩個質子在NMR中不可見。	2.41, C

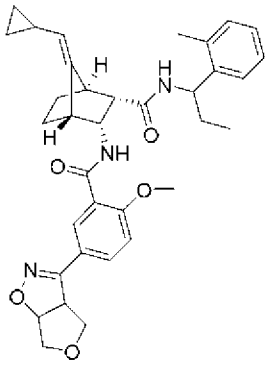
651	 H416.3製備	(1R,2S,3R,4R,7Z) 3 (5 {3aH,4H,6H,6aH 吡喃并[3,4 d][1,2]噁唑 3 基} 2 甲氧基苯甲醯胺基) 7 (環丙基甲基) N 甲 (羥基甲基)環戊基 1 雙環[2.2.1]庚烷 2 甲醯胺	550.3	(500 MHz, DMSO d6) δ 10.17 – 10.07 (m, 1H), 8.18 (br d, J= 2.1 Hz, 1H), 7.79 (br dd, J= 8.5, 2.1 Hz, 1H), 7.63 (s, 1H), 7.24 (br d, J= 8.9 Hz, 1H), 5.34 (br dd, J= 8.5, 2.4 Hz, 1H), 4.60 (br d, J= 9.2 Hz, 1H), 4.49 (br t, J= 7.8 Hz, 1H), 4.24 (br s, 1H), 4.09 (br d, J= 10.4 Hz, 1H), 4.02 (s, 3H), 3.90 (br d, J= 9.5 Hz, 1H), 3.78 (br t, J= 8.2 Hz, 1H), 3.65 (br dd, J= 10.4, 3.1 Hz, 1H), 3.51 (br d, J= 10.7 Hz, 1H), 3.03 (br s, 1H), 2.96 – 2.88 (m, 1H), 1.89 – 1.55 (m, 8H), 1.55 – 1.39 (m, 3H), 1.37 – 1.24 (m, 2H), 0.76 – 0.63 (m, 2H), 0.31 (br s, 2H)。可能由於與經抑制之水峰及/或溶劑峰重疊，兩個質子在NMR中不可見。	2.00, B

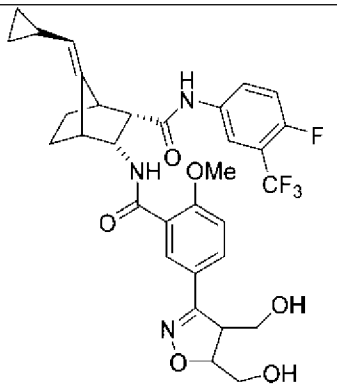
652	 由416-3製備， 經由製備型SFC在以下條件下分離非鏡像異構物：管柱：Chiral OJ，30 × 250 mm，5微米；移動相 85% CO_2 / 15% MeOH (具有0.1%DEA)；流動速率：120 mL/min，150巴；管柱溫度：40 ℃。 峰1 (RT=7.6 min)為**實例652**	(1R,2S,3R,4R,Z)-7-(環丙基亞甲基)-3-(2-甲氧基-5-(3a,4,6,6a-四氫呋喃并[3,4-d]異噁唑-3-基)苯甲醯胺基)-N-(1-(鄰甲苯基)丙基)雙環[2.2.1]庚烷-2-甲醯胺	584.0	(500 MHz, DMSO-d_6) δ 10.05 (br d, *J*=6.7 Hz, 1H), 8.49 (br d, *J*=7.9 Hz, 1H), 8.16 (d, *J*=2.1 Hz, 1H), 7.79 (dd, *J*=8.7, 2.3 Hz, 1H), 7.27 - 7.21 (m, 2H), 7.16 - 7.06 (m, 3H), 5.33 (dd, *J*=9.2, 3.4 Hz, 1H), 4.91 - 4.83 (m, 1H), 4.61 (d, *J*=9.5 Hz, 1H), 4.49 (br t, *J*=8.1 Hz, 1H), 4.33 - 4.26 (m, 1H), 4.09 (d, *J*=10.7 Hz, 1H), 4.02 (s, 3H), 3.92 - 3.86 (m, 1H), 3.81 - 3.74 (m, 1H), 3.65 (dd, *J*=10.7, 3.7 Hz, 1H), 3.04 - 2.96 (m, 2H), 2.35 (s, 3H), 1.65 - 1.54 (m, 3H), 1.49 - 1.38 (m, 2H), 1.31 - 1.20 (m, 1H), 1.18 - 1.07 (m, 1H), 0.80 (t, *J*=7.3 Hz, 3H), 0.75 - 0.64 (m, 2H), 0.35 - 0.23 (m, 2H)。可能由於與溶劑峰或經抑制之水峰重疊，一個質子不可見。	2.41, B

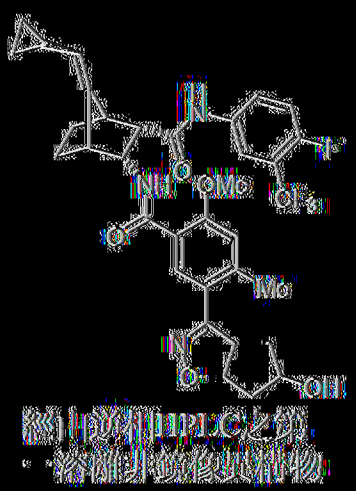
653	 中416-3製備	(1R,2S,3R,4R,7′′)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-N-(1-苯甲基環丙基)-7′-(環丙基甲基)雙環[2.2.1]庚烷-2-甲醯胺	582.0	(500 MHz, DMSO-d6) δ 9.98 (br d, J= 6.4 Hz, 1H), 8.21-8.12 (m, 2H), 7.80 (br dd, J= 8.5, 2.4 Hz, 1H), 7.27 (br d, J= 8.9 Hz, 1H), 7.24-7.19 (m, 2H), 7.18-7.10 (m, 3H), 5.36-5.31 (m, 1H), 4.56 (br d, J= 9.8 Hz, 1H), 4.53-4.46 (m, 1H), 4.23 (br s, 1H), 4.13-4.06 (m, 4H), 3.93-3.87 (m, 1H), 3.81-3.74 (m, 1H), 3.66 (br dd, J= 10.4, 2.7 Hz, 1H), 3.02 (br s, 1H), 2.94 (br d, J= 14.0 Hz, 1H), 2.78-2.70 (m, 2H), 2.37 (br s, 1H), 1.97-1.88 (m, 1H), 1.80-1.70 (m, 1H), 1.48-1.40 (m, 1H), 1.40-1.26 (m, 2H), 0.77-0.65 (m, 4H), 0.64-0.51 (m, 2H), 0.30 (br d, J= 0.9 Hz, 2H)。	2.30, B

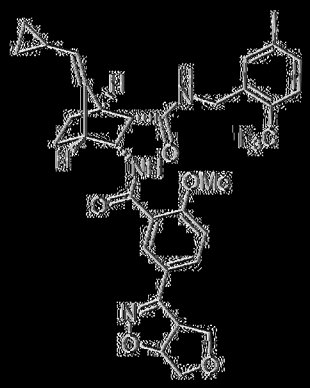
654	 藉由SFC分離之異構物，其中實例654為峰1 (RT=4.74 min.，>95% de)：儀器：Waters 100 Prep SFC管柱：Chiral OD，30 × 250 mm，5微米，移動相：15% MeOH / 85% CO_2 (具有0.1% DEA)，流動條件：100 mL/min，偵測器波長：220 nm；分析方法：儀器：Shimadzu Nexera SFC，管柱Chiral OD，4.6 × 100 mm，5微米，移動相：15% MeOH / 85% CO_2 (具有0.1% DEA)，流動條件：2 mL/min，偵測器波長：220 nm，得到對掌性(峰-1，RT=4.74 min.，>95% de)及對掌性(峰-2，RT=6.75 min.，>95% de)。	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲基苯甲醯胺基)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	597.9	(500 MHz, DMSO-d6) δ 10.62 - 10.32 (m, 1H), 8.72 (d, J=7.2 Hz, 1H), 8.03 (dd, J=6.3, 2.2 Hz, 1H), 7.81 - 7.76 (m, 1H), 7.64 (dd, J=8.0, 1.5 Hz, 1H), 7.62 (s, 1H), 7.44 (t, J=9.7 Hz, 1H), 7.34 (d, J=8.0 Hz, 1H), 5.34 (dd, J=9.1, 3.6 Hz, 1H), 4.68 (d, J=9.6 Hz, 1H), 4.48 - 4.37 (m, 3H), 4.09 (d, J=10.8 Hz, 1H), 3.95 (br d, J=9.8 Hz, 1H), 3.66 (dd, J=9.5, 7.0 Hz, 1H), 3.62 (dd, J=10.8, 3.7 Hz, 1H), 3.16 (br dd, J=10.6, 3.9 Hz, 1H), 3.09 (t, J=3.9 Hz, 1H), 2.72 (t, J=3.8 Hz, 1H), 2.01 - 1.88 (m, 1H), 1.86 - 1.73 (m, 1H), 1.59 - 1.51 (m, 1H), 1.48 - 1.44 (m, 1H), 1.42 - 1.36 (m, 1H), 0.78 - 0.69 (m, 3H), 0.35 (br d, J=2.9 Hz, 3H	2.43, B

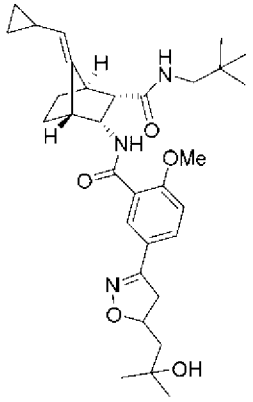
655	 由同對掌性苯甲酸酯中間物峰1製備：製備型層析條件：儀器：Jasco SFC Prep (CTR-L409-PSFC3)管柱：Chiralpak IA，30 × 250 mm，5微米，移動相：15% MeOH / 85% CO_2，流動條件：85 mL/min，150巴，40℃，偵測器波長：220 nm，注射詳情：0.5 mL ~21mg/mL於甲醇中，分析型層析條件：儀器：Shimadzu Nexera SFC (CTR-L410-SFC3)管柱：Chiralpak IA，4.6 × 100 mm，3微米，移動相：15% MeOH / 85% CO_2，流動條件：2.0 mL/min，150巴，40℃，偵測器波長：220 nm，注射詳情：5 μL ~1mg/mL於MeOH中。峰-1 RT 3.24 min > 99% ee。	(1R,2S,3R,4R,7Z)-3-{5-[(3aS,4R,6aR)-4-羥基-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	627.9	(500 MHz, DMSO-d6) δ 10.56 (s, 1H), 9.92 (br d, J=7.0 Hz, 1H), 8.36 - 8.28 (m, 1H), 8.22 (br d, J=3.7 Hz, 1H), 7.85 (d, J=8.2 Hz, 1H), 7.78 (br d, J=8.5 Hz, 1H), 7.48 (br t, J=9.8 Hz, 1H), 7.29 (d, J=8.9 Hz, 1H), 5.30 (d, J=2.7 Hz, 1H), 5.22 (br dd, J=8.5, 4.9 Hz, 1H), 4.70 (br d, J=9.5 Hz, 1H), 4.45 (br s, 1H), 4.12 (br s, 1H), 4.05 (s, 3H), 3.94 (br d, J=8.9 Hz, 1H), 3.69 - 3.50 (m, 2H), 3.20 - 3.09 (m, 3H), 2.73 (br s, 1H), 2.21 - 2.10 (m, 1H), 1.93 (br dd, J=13.4, 6.4 Hz, 1H), 1.88 - 1.73 (m, 2H), 1.66 (br dd, J=12.5, 6.1 Hz, 1H), 1.55 - 1.36 (m, 4H), 0.87 - 0.67 (m, 2H), 0.35 (br s, 2H)	2.44, C

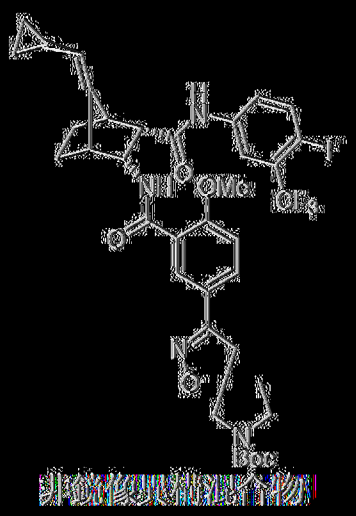
656	 由416-3製備。經由製備型SFC在以下條件下分離非鏡像異構物：管柱：Chiral OJ，30 × 250 mm，5微米；移動相 85% CO_2 / 15% MeOH (具有0.1%DEA)；流動速率：120 mL/min，150巴；管柱溫度：40 ℃。 峰2 (RT= 12.9 min)為**實例656**。	(1R,2S,3R,4R,Z)-7-(環丙基亞甲基)-3-(2-甲氧基-5-(3a,4,6,6a-四氫呋喃并[3,4-d]異噁唑-3-基)苯甲醯胺基)-N-(1-(鄰甲苯基)丙基)雙環[2.2.1]庚烷-2-甲醯胺	584.2	(500 MHz, DMSO-d_6) δ 9.96 (d, *J*=6.6 Hz, 1H), 8.49 (d, *J*=8.2 Hz, 1H), 8.10 (d, *J*=2.2 Hz, 1H), 7.73 (dd, *J*=8.7, 2.3 Hz, 1H), 7.23 (br d, *J*=7.2 Hz, 1H), 7.12 (d, *J*=8.8 Hz, 1H), 7.08 - 6.97 (m, 3H), 5.32 (dd, *J*=9.1, 3.6 Hz, 1H), 4.93 (q, *J*=7.5 Hz, 1H), 4.64 (d, *J*=9.5 Hz, 1H), 4.45 (br t, *J*=7.8 Hz, 1H), 4.28 - 4.19 (m, 1H), 4.08 (d, *J*=10.7 Hz, 1H), 3.91 - 3.83 (m, 1H), 3.74 (dd, *J*=9.2, 6.9 Hz, 1H), 3.70 (s, 3H), 3.64 (dd, *J*=10.8, 3.5 Hz, 1H), 3.04 (br s, 1H), 2.98 (dd, *J*=10.9, 4.3 Hz, 1H), 2.62 (br s, 1H), 2.31 (s, 3H), 1.89 - 1.82 (m, 1H), 1.72 - 1.66 (m, 1H), 1.63 - 1.55 (m, 2H), 1.46 (tt, *J*=12.7, 4.7 Hz, 1H), 1.39 - 1.28 (m, 2H), 0.87 (t, *J*=7.3 Hz, 3H), 0.76 - 0.65 (m, 2H), 0.32 (dd, *J*=4.3, 2.1 Hz, 2H)。	2.38, B

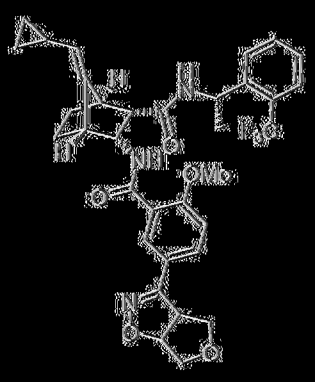
657	 由同對掌性苯甲酸酯中間物(峰1；>99%ee；對掌性分析型RT=3.383 min)製備；製備型對掌性SFC條件：儀器：PIC Solution SFC Prep-200:管柱：Chiralpak IF，21 × 250 mm，5微米：移動相：35%甲醇/ 65% CO_2：流動條件：45 mL/min，150巴，40℃；偵測器波長：220 nm；注射詳情：0.75 mL ~50mg/mL於MeOH-CAN中	(1R,2S,3R,4R,7Z)-3-{5-[4,5-雙(羥基甲基)-4,5-二氫-1,2-噁唑-3-基]-2-甲氧基苯甲醯胺基}-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	631.9	(500 MHz, DMSO-d6) δ 10.54 - 10.52 (m, 1H), 9.93 - 9.89 (m, 1H), 8.31 - 8.26 (m, 1H), 8.22 (dd, J=6.3, 2.1 Hz, 1H), 7.84 - 7.76 (m, 2H), 7.51 - 7.44 (m, 1H), 7.28 - 7.21 (m, 1H), 5.00 (t, J=5.6 Hz, 1H), 4.86 - 4.82 (m, 1H), 4.71 - 4.66 (m, 1H), 4.61 - 4.55 (m, 1H), 4.48 - 4.40 (m, 1H), 4.07 - 4.03 (m, 3H), 3.97 - 3.90 (m, 1H), 3.86 - 3.78 (m, 2H), 3.61 - 3.56 (m, 1H), 3.40 - 3.34 (m, 1H), 3.18 - 3.02 (m, 2H), 2.75 - 2.69 (m, 1H), 1.87 - 1.75 (m, 2H), 1.53 - 1.36 (m, 3H), 0.79 - 0.68 (m, 2H), 0.37 - 0.30 (m, 2H)	2.28, C

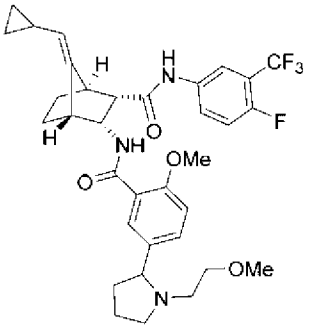
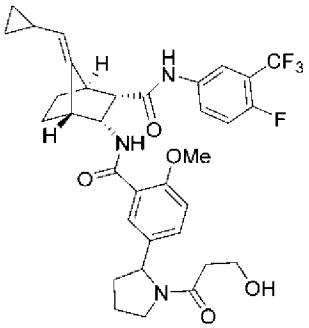
658	 藉由製備HPLC之管柱溶離步驟獲得之化合物	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-(5-{5-羥基-3a(1),4(1),5(1),6(1),6a(1)-環戊并[d][1,2]噁唑-3-基}-2-甲氧基-4-甲基苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	641.9	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 10.11 - 9.82 (m, 1H), 8.27 - 8.17 (m, 1H), 8.00 (s, 1H), 7.82 - 7.72 (m, 1H), 7.48 (br t, J= 9.6 Hz, 1H), 7.14 (s, 1H), 5.07 (br t, J= 8.2 Hz, 1H), 4.70 (d, J= 9.5 Hz, 1H), 4.47 - 4.38 (m, 1H), 4.21 - 4.12 (m, 2H), 4.12 - 3.91 (m, 3H), 3.62 - 3.44 (m, 1H), 3.15 (br dd, J= 10.8, 3.8 Hz, 1H), 3.10 (br s, 1H), 2.72 (br s, 1H), 2.48 (s, 2H), 2.14 - 2.02 (m, 1H), 1.99 - 1.90 (m, 2H), 1.88 - 1.82 (m, 1H), 1.80 - 1.74 (m, 1H), 1.62 (br d, J= 12.2 Hz, 1H), 1.54 - 1.47 (m, 1H), 1.45 - 1.32 (m, 2H), 0.78 - 0.65 (m, 2H), 0.42 - 0.27 (m, 2H) 可能由於與溶劑峰重疊，一個質子在NMR中不可見	2.47, B

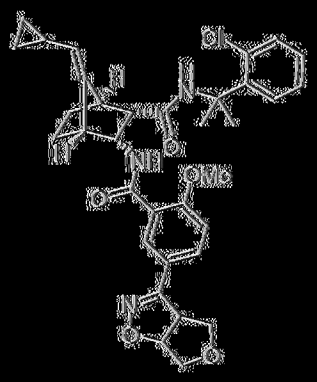
659	 請自行繪製	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-{[5-甲基-2-(三氟甲基)苯基]甲基}雙環[2.2.1]庚烷-2-甲醯胺	624.2	(500 MHz, DMSO-d6) δ 8.32 (br d, J=7.0 Hz, 2H), 7.86 (d, J=2.2 Hz, 1H), 7.79 - 7.72 (m, 1H), 7.57 (br d, J=7.5 Hz, 1H), 7.30 - 7.19 (m, 3H), 5.34 (br dd, J=8.7, 3.4 Hz, 1H), 4.49 (br d, J=8.9 Hz, 2H), 4.39 (br s, 2H), 4.09 (br d, J=10.9 Hz, 1H), 3.91 (s, 3H), 3.89 - 3.84 (m, 1H), 3.76 (br dd, J=9.2, 6.6 Hz, 1H), 3.65 (br dd, J=10.9, 3.5 Hz, 1H), 3.06 (br d, J=3.2 Hz, 1H), 2.99 (s, 1H), 2.95 - 2.87 (m, 1H), 2.38 - 2.30 (m, 3H), 1.84 - 1.74 (m, 1H), 1.64 - 1.42 (m,3H), 1.16 (t, J=7.2 Hz, 1H), 0.67 (br dd, J=8.2, 5.5 Hz, 2H), 0.25 (br dd, J=2.8, 1.7 Hz, 2H)。可能由於與溶劑峰重疊，一個質子在NMR中不可見	2.41, C

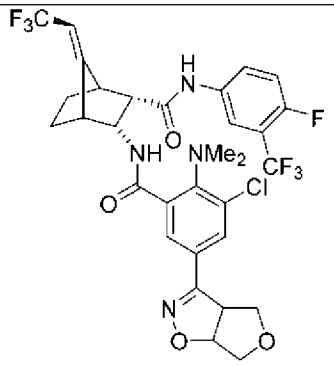
660	 由與實例499中相同之苯甲酸酯中間物製備	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-(2,2-二甲基丙基)-3-{5-[5-(2-羥基-2-甲基丙基)-4,5-二氫-1,2-噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	552.5	(500 MHz, DMSO-d6) δ 9.96 (br d, J=7.0 Hz, 1H), 8.14 (d, J=1.8 Hz, 1H), 7.97 (br t, J=6.1 Hz, 1H), 7.76 (dd, J=8.7, 2.0 Hz, 1H), 7.25 - 7.18 (m, 1H), 6.51 (s, 1H), 4.82 - 4.74 (m, 1H), 4.63 (d, J=9.8 Hz, 1H), 4.39 (s, 1H), 4.33 - 4.24 (m, 1H), 4.00 (s, 3H), 3.51 (br dd, J=16.8, 10.1 Hz, 1H), 3.10 - 2.97 (m, 3H), 2.79 (br dd, J=13.0, 5.6 Hz, 1H), 1.86 (br dd, J=13.6, 6.3 Hz, 2H), 1.73 (br dd, J=13.4, 6.4 Hz, 2H), 1.46 (dt, J=8.5, 4.3 Hz, 1H), 1.38 - 1.26 (m, 2H), 1.17 (d, J=6.7 Hz, 6H), 0.81 (s, 9H), 0.75 - 0.64 (m, 2H), 0.35 - 0.26 (m, 2H)。可能由於與溶劑峰重疊，一個質子在NMR中不可見。	2.28, C

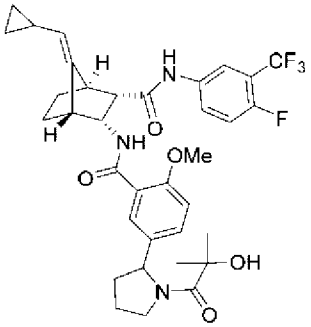
661	 非鏡像異構混合物	3-(3-{[(1R,2R,3S,4R)-7-(環丙基甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-1-氧雜-2,7-二氮雜螺[4.4]壬-2-烯-7-甲酸三級丁酯	725.1	(500 MHz, DMSO-d6) δ 10.52 (s, 1H), 9.89 (br d, J= 6.7 Hz, 1H), 8.24 - 8.18 (m, 2H), 7.77 (br d, J= 7.3 Hz, 2H), 7.48 (br t, J= 9.8 Hz, 1H), 7.27 (d, J= 8.5 Hz, 1H), 4.69 (d, J= 9.5 Hz, 1H), 4.47 - 4.40 (m, 1H), 4.04 (s, 3H), 3.54 - 3.44 (m, 1H), 3.10 (br s, 1H), 2.76 - 2.69 (m, 1H), 2.12 (br s, 2H), 1.87 - 1.74 (m, 2H), 1.41 (br d, J= 7.0 Hz, 9H), 0.78 - 0.69 (m, 2H), 0.39 - 0.31 (m, 2H)	2.76, B
662	由可對掌性苯甲酸酯中間物(峰2；96.5%cc；對掌性分析型RT= 3.602 min)製備；儀器：Jasco SFC Prep管柱：Chiralpak OJ-H，21 × 250 mm，5微米；移動相：5% IPA / 95% CO_2；流動條件：45 mL/min，150巴，40°C；偵測器波長：220 nm；注射詳情：0.5 mL ~35mg/mL於IPA CAN中	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	612.3	(500 MHz, DMSO-d6) δ 10.52 (s, 1H), 9.89 (br d, J= 7.0 Hz, 1H), 8.23 - 8.18 (m, 2H), 7.80 - 7.75 (m, 2H), 7.46 (br t, J= 9.8 Hz, 1H), 7.25 (d, J= 8.5 Hz, 1H), 5.12 (br dd, J= 8.4, 4.7 Hz, 1H), 4.68 (br d, J= 9.5 Hz, 1H), 4.45 - 4.40 (m, 1H), 4.14 (br t, J= 9.0 Hz, 1H), 4.03 (s, 3H), 3.14 (br dd, J= 10.8, 3.8 Hz, 1H), 3.10 - 3.08 (m, 1H), 2.73 - 2.68 (m, 1H), 1.94 (br dd, J= 13.3, 6.0 Hz, 1H), 1.88 - 1.80 (m, 2H), 1.79 - 1.63 (m, 4H), 1.53 - 1.46 (m, 1H), 1.44 - 1.36 (m, 2H), 1.30 (qd, J= 11.9, 5.5 Hz, 1H), 0.77 - 0.69 (m, 2H), 0.37 - 0.30 (m, 2H)。	2.71, B

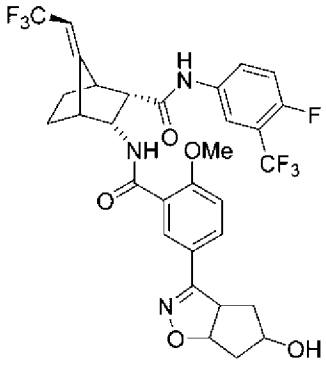
665	 中間體 3 製備	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-[(1S)-1-[2-(三氟甲基)苯基]乙基]雙環[2.2.1]庚烷-2-甲醯胺	624.2	(500 MHz, DMSO-d6) δ 9.83 (d, J = 6.8 Hz, 1H), 8.74 (br d, J = 6.6 Hz, 1H), 8.14 (d, J = 2.4 Hz, 1H), 7.77 – 7.68 (m, 1H), 7.61 (d, J = 8.0 Hz, 2H), 7.48 (t, J = 7.7 Hz, 1H), 7.34 – 7.25 (m, 1H), 7.08 (d, J = 8.6 Hz, 1H), 5.32 (dd, J = 9.2, 3.6 Hz, 1H), 5.27 – 5.15 (m, 1H), 4.65 (d, J = 9.4 Hz, 1H), 4.51 – 4.40 (m, 1H), 4.26 (ddd, J = 10.5, 6.1, 4.9 Hz, 1H), 4.08 (d, J = 10.7 Hz, 1H), 3.90 – 3.84 (m, 1H), 3.75 (dd, J = 9.4, 7.1 Hz, 1H), 3.67 – 3.62 (m, 1H), 3.60 – 3.52 (m, 3H), 3.07 – 3.02 (m, 1H), 3.02 – 2.96 (m, 1H), 2.65 – 2.60 (m, 1H), 1.90 – 1.82 (m, 1H), 1.68 – 1.61 (m, 1H), 1.51 – 1.40 (m, 1H), 1.37 – 1.27 (m, 5H), 0.76 – 0.64 (m, 2H), 0.39 – 0.25 (m, 2H)。	2.46, C

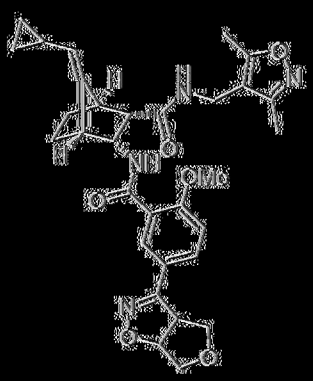
666	 由實例715製備	(2S,3R)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{2-甲氧基-5-[1-(2-甲氧基乙基)吡咯啶-2-基]苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	630.4	(400 MHz, DMSO-d6) δ = 10.49 (s, 1H), 9.90 - 9.72 (m, 1H), 8.22 (dd, J = 2.6, 6.4 Hz, 1H), 7.90 (br s, 1H), 7.77 (td, J = 3.9, 8.1 Hz, 1H), 7.54 - 7.37 (m, 2H), 7.13 (br d, J = 8.1 Hz, 1H), 4.69 (d, J = 9.6 Hz, 1H), 4.45 (tt, J = 3.6, 11.1 Hz, 1H), 4.11 (q, J = 5.2 Hz, 1H), 3.98 (s, 3H), 3.31 - 3.21 (m, 4H), 3.19 - 3.11 (m, 5H), 3.08 (br t, J = 3.8 Hz, 1H), 2.71 (t, J = 3.3 Hz, 1H), 2.29 - 1.99 (m, 3H), 1.94 - 1.67 (m, 4H), 1.58 - 1.33 (m, 4H), 0.82 - 0.65 (m, 2H), 0.35 (dd, J = 2.0, 4.6 Hz, 2H)	2.63, A
667	 由實例694製備	(2S,3R)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[1-(3-羥基丙醯基)吡咯啶-2-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	644.0	(400 MHz, DMSO-d6) δ = 10.48 (d, J = 1.0 Hz, 1H), 9.85 (dd, J = 7.5, 10.9 Hz, 1H), 8.25 - 8.18 (m, 1H), 7.81 - 7.68 (m, 2H), 7.48 (t, J = 9.9 Hz, 1H), 7.29 (ddd, J = 2.9, 8.6, 20.0 Hz, 1H), 7.20 - 7.03 (m, 1H), 5.14 - 4.96 (m, 2H), 4.68 (d, J = 9.5 Hz, 1H), 4.54 - 4.35 (m, 3H), 3.97 (d, J = 11.7 Hz, 3H), 3.73 - 3.47 (m, 4H), 3.16 - 3.04 (m, 3H), 2.74 - 2.68 (m, 1H), 2.40 - 2.32 (m, 1H), 1.90 - 1.66 (m, 5H), 1.55 - 1.29 (m, 3H), 0.79 - 0.65 (m, 2H), 0.35 (dd, J = 2.0, 4.4 Hz, 2H)。	2.33, A

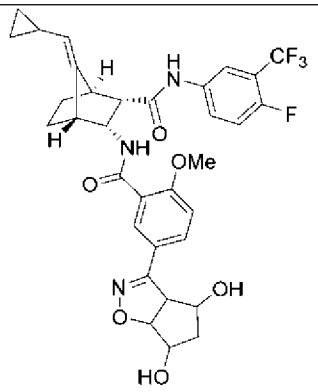
669	 [0416]製備	(1R,2S,3R,4R,7′Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-N-[2-(2-氯苯基)丙烷-2-基]-7-(環丙基甲基)雙環[2.2.1]庚烷-2-甲醯胺	604.2	(500 MHz, DMSO-d6) δ 9.92 (br d, J = 6.6 Hz, 1H), 8.42 (s, 1H), 8.17 (d, J = 2.2 Hz, 1H), 7.75 (dd, J = 8.7, 2.4 Hz, 1H), 7.51 (d, J = 8.0 Hz, 1H), 7.26 - 7.20 (m, 1H), 7.15 - 7.11 (m, 3H), 5.33 (dd, J = 9.2, 3.4 Hz, 1H), 4.62 (d, J = 9.5 Hz, 1H), 4.48 (br t, J = 7.8 Hz, 1H), 4.28 - 4.19 (m, 1H), 4.09 (d, J = 10.9 Hz, 1H), 3.89 (br d, J = 9.0 Hz, 1H), 3.77 (dd, J = 9.2, 7.0 Hz, 1H), 3.70 - 3.61 (m, 1H), 3.59 (s, 3H), 3.04 - 2.93 (m, 2H), 2.68 - 2.59 (m, 1H), 1.72 - 1.51 (m, 8H), 1.46 - 1.37 (m, 1H), 1.30 - 1.18 (m, 2H), 0.77 - 0.62 (m, 2H), 0.37 - 0.25 (m, 2H)。	2.39, C

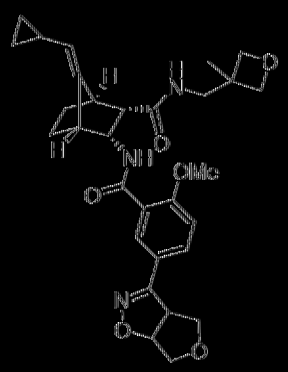
670	 藉由SFC分離之異構物，其中實例670為峰2 (RT=12.15 min，>95% ee)：所用儀器：Waters 100 Prep SFC管柱：Chiral AD，30 × 250 mm，5微米，移動相：15% IPA / 85% CO_2 (具有0.1% DEA)，流動條件：100 mL/min，偵測器波長：220 nm；分析方法：儀器：Shimadzu Nexera SFC，管柱Chiral AD，4.6 × 100 mm，5微米，移動相：15% IPA / 85% CO_2 (具有0.1% DEA)，流動條件：2 mL/min，偵測器波長：220 nm，得到對掌性(峰-1，RT=2.45 min.，>95% ee)及對掌性(峰-2，RT=3.41 min.，>95% ee)。	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-3-氯-2-(二甲基胺基)苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-甲醯胺	689.0	(500 MHz, DMSO-d_6) δ 10.54 (s, 1H), 10.00 (br d, *J*=7.6 Hz, 1H), 8.14 (br d, *J*=4.3 Hz, 1H), 7.86 (d, *J*=1.8 Hz, 1H), 7.82 - 7.72 (m, 2H), 7.46 (t, *J*=9.8 Hz, 1H), 5.93 (q, *J*=8.1 Hz, 1H), 5.35 (dd, *J*=9.2, 3.4 Hz, 1H), 4.57 (br s, 1H), 4.41 (br t, *J*=8.1 Hz, 1H), 4.09 (d, *J*=10.7 Hz, 1H), 3.91 (br d, *J*=11.3 Hz, 1H), 3.73 - 3.57 (m, 2H), 3.25 (br d, *J*=10.7 Hz, 1H), 3.19 (br s, 1H), 2.98 (br s, 1H), 2.81 (s, 6H), 2.18 - 1.99 (m, 2H), 1.50 (br s, 2H)	2.87, B

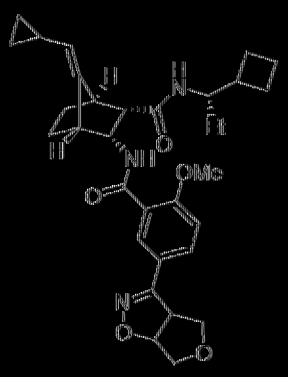
671	 由實例715製備	(2S,3R)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[1-(2-羥基-2-甲基丙醯基)吡咯啶-2-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	658.3	(400MHz, DMSO-d6) δ = 10.47 (s, 1H), 9.81 (br d, J=7.1 Hz, 1H), 8.21 (dd, J=2.6, 6.5 Hz, 1H), 7.77 (td, J=3.7, 8.7 Hz, 1H), 7.73 (d, J=2.2 Hz, 1H), 7.47 (t, J=9.8 Hz, 1H), 7.25 (dd, J=2.3, 8.7 Hz, 1H), 7.07 (d, J=8.6 Hz, 1H), 5.20 (s, 1H), 4.99 (dd, J=4.2, 7.8 Hz, 1H), 4.68 (d, J=9.5 Hz, 1H), 4.47 - 4.36 (m, 1H), 4.08 - 4.01 (m, 1H), 3.93 - 3.85 (m, 1H), 3.60 - 3.48 (m, 1H), 3.10 - 3.10 (m, 1H), 3.20 - 3.02 (m, 1H), 2.70 (brs, 1H), 2.22 - 2.09 (m, 1H), 1.92 - 1.70 (m, 4H), 1.62 - 1.44 (m, 2H), 1.43 - 1.35 (m, 2H), 1.30 (s, 3H), 1.28 - 1.18 (m, 3H), 0.80 - 0.65 (m, 2H), 0.39 - 0.27 (m, 2H)	2.49, A

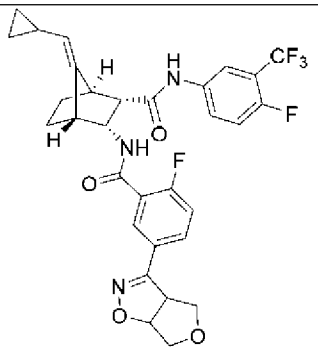
672	 藉由逆相HPLC與實例543分離之非鏡像異構物對	(1R,2S,3R,4R,7Z)-N-[4-氟-3-(三氟甲基)苯基]-3-(5-{5-羥基-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-甲醯胺	659.1	(500 MHz, DMSO-d6) δ 10.84 - 10.61 (m, 1H), 10.10 - 9.92 (m, 1H), 8.36 - 8.15 (m, 2H), 7.82 (br d, J=6.7 Hz, 2H), 7.53 (br t, J=9.8 Hz, 1H), 7.30 (br d, J=8.9 Hz, 1H), 6.07 - 5.88 (m, 1H), 5.25 - 5.04 (m, 1H), 4.62 - 4.43 (m, 1H), 4.21 - 4.11 (m, 1H), 4.11 - 3.89 (m, 3H), 3.50 - 3.19 (m, 1H), 3.02 (s, 2H), 2.11 (br dd, J=13.9, 5.6 Hz, 2H), 2.03 - 1.97 (m, 1H), 1.93 (br d, J=12.2 Hz, 2H), 1.87 - 1.81 (m, 1H), 1.81 - 1.72 (m, 1H), 1.62 - 1.44 (m, 2H)可能由於與溶劑峰重疊，一個質子在NMR中不可見	2.27, B

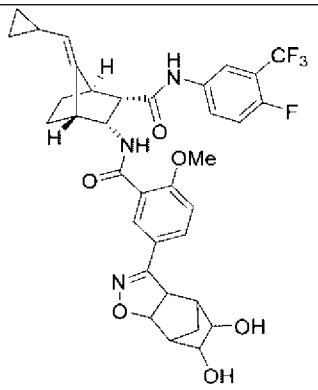
673	 [M+H]+ 563.3觀測值	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]㗁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-[(3,5-二甲基-1,2-㗁唑-4-基)甲基]雙環[2.2.1]庚烷-2-甲醯胺	561.3	(500 MHz, DMSO-d6) δ 10.00 (d, J = 7.0 Hz, 1H), 8.42 (br t, J = 5.4 Hz, 1H), 8.16 (d, J = 2.2 Hz, 1H), 7.79 (dd, J = 8.6, 2.2 Hz, 1H), 7.25 (d, J = 8.8 Hz, 1H), 5.34 (dd, J = 9.2, 3.4 Hz, 1H), 4.60 (d, J = 9.5 Hz, 1H), 4.49 (br t, J = 7.9 Hz, 1H), 4.33-4.23 (m, 1H), 4.11-3.95 (m, 5H), 3.90 (br d, J = 9.2 Hz, 1H), 3.80-3.73 (m, 1H), 3.65 (dd, J = 10.7, 3.7 Hz, 1H), 3.06-3.00 (m, 1H), 2.88 (br dd, J = 10.7, 4.3 Hz, 1H), 2.31 (s, 3H), 2.12 (s, 3H), 1.79-1.68 (m, 2H), 1.45 (ddq, J = 13.1, 8.6, 4.3 Hz, 1H), 1.38-1.23 (m, 2H), 0.79-0.62 (m, 2H), 0.30 (br d, J = 3.8 Hz, 2H)。可能由於與溶劑峰及/或經抑制之水峰重疊，兩個質子在NMR中不可見。	1.95, B

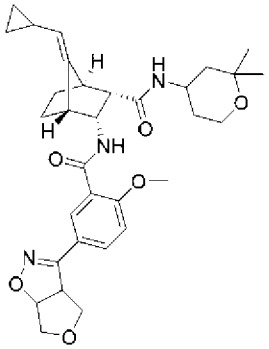
674	 由同對掌性苯甲酸酯中間物峰1製備。製備型層析條件：儀器：PIC Solution SFC Prep-200管柱：Chiralpak IC，30 × 250 mm，5微米，移動相：20% IPA / 80% CO_2，流動條件：90 mL/min，150巴，40℃，偵測器波長：270 nm，注射詳情：0.5 mL ~[樣本濃度]mg/mL於PA-CAN中，分析型層析條件：儀器：Shimadzu Nexera SFC管柱：Chiralpak IC，4.6 × 100 mm，3微米，移動相：10%異丙醇/ 90% CO2，流動條件：2.0 mL/min，150巴，40℃，偵測器波長：220 nm，注射詳情：5 μL ~1mg/mL於MeOH中。PK-1 RT = 4.69 min.，> 99% ee。	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-3-(5-{4,6-二羥基-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	644.3	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.89 (d, J=7.1 Hz, 1H), 8.41 - 8.35 (m, 1H), 8.21 (d, J=6.8 Hz, 1H), 7.87 (dd, J=8.7, 2.4 Hz, 1H), 7.77 (d, J=8.4 Hz, 1H), 7.47 (t, J=9.9 Hz, 1H), 7.27 (d, J=8.8 Hz, 1H), 5.26 (br d, J=5.7 Hz, 1H), 5.18 (br d, J=5.2 Hz, 1H), 4.94 (dd, J=10.0, 2.5 Hz, 1H), 4.68 (d, J=9.5 Hz, 1H), 4.43 (br s, 1H), 4.03 (s, 3H), 3.61 - 3.48 (bs, 2H), 3.18 - 3.07 (m, 2H), 2.79 - 2.63 (m, 1H), 1.87 - 1.66 (m, 4H), 1.50 (dt, J=8.8, 4.2 Hz, 1H), 1.45 - 1.34 (m, 2H), 0.80 - 0.67 (m, 2H), 0.34 (br s, 2H)	2.34, B

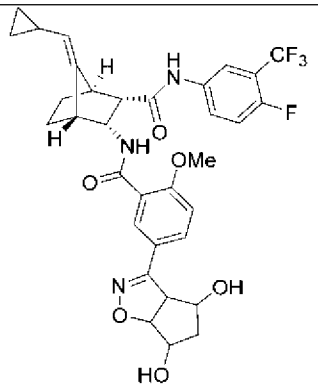
615	 中416-3製備	(1R,2S,3R,4R,7*Z*)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-[(3-甲基氧雜環丁烷-3-基)甲基]雙環[2.2.1]庚烷-2-甲醯胺	536.2	(500 MHz, DMSO-d6) δ 9.94 (br d, J= 6.7 Hz, 1H), 8.26 (br t, J= 6.0 Hz, 1H), 8.16 (d, J= 1.5 Hz, 1H), 7.81 - 7.75 (m, 1H), 7.24 (d, J= 8.5 Hz, 1H), 5.34 (dd, J= 9.2, 3.4 Hz, 1H), 4.63 (d, J= 9.5 Hz, 1H), 4.49 (br t, J= 7.9 Hz, 1H), 4.33 (br dd, J= 10.2, 6.0 Hz, 3H), 4.13 (t, J= 5.6 Hz, 2H), 4.09 (br d, J= 11.0 Hz, 1H), 4.01 (s, 3H), 3.89 (br d, J= 9.2 Hz, 1H), 3.80 - 3.74 (m, 1H), 3.65 (br dd, J= 10.4, 3.4 Hz, 1H), 3.05 (br s, 1H), 2.98 (br dd, J= 10.5, 3.8 Hz, 1H), 1.87 - 1.80 (m, 1H), 1.76 - 1.71 (m, 1H), 1.52 - 1.42 (m, 1H), 1.41 - 1.29 (m, 2H), 1.16 (s, 3H), 0.71 (quin, J= 9.5 Hz, 2H), 0.32 (br s, 2H)。可能由於與經抑制之水峰及/或溶劑峰重疊，三個質子在NMR中不可見。	1.89, C

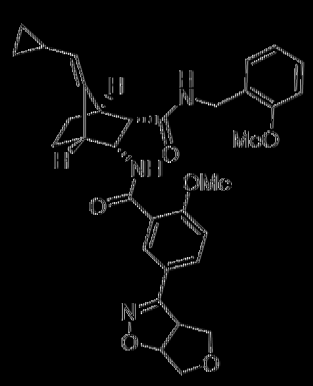
6/6	 中416-3製備	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-N-[(1S)-1-環丁基丙基]-7-(環丙基甲基)雙環[2.2.1]庚烷-2-甲醯胺	548.0	(500 MHz, DMSO-d6) δ 10.03 (br d, J=6.7 Hz, 1H), 8.15 (d, J=2.1 Hz, 1H), 7.77 (dd, J=8.5, 2.4 Hz, 1H), 7.71 (br d, J=9.2 Hz, 1H), 7.23 (d, J=8.9 Hz, 1H), 5.33 (dd, J=9.3, 3.5 Hz, 1H), 4.62 (d, J=9.5 Hz, 1H), 4.48 (br t, J=7.8 Hz, 1H), 4.28 (br t, J=10.2 Hz, 1H), 4.09 (d, J=10.7 Hz, 1H), 4.00 (s, 3H), 3.88 (br d, J=8.9 Hz, 1H), 3.79–3.74 (m, 1H), 3.71–3.62 (m, 1H), 3.49–3.39 (m, 1H), 3.04 (br s, 1H), 2.93 (br dd, J=10.8, 4.1 Hz, 1H), 2.27–2.19 (m, 1H), 1.92–1.80 (m, 2H), 1.78–1.57 (m, 6H), 1.49–1.27 (m, 4H), 1.16–1.09 (m, 1H), 0.77 (t, J=7.5 Hz, 3H), 0.74–0.64 (m, 2H), 0.31 (br d, J=2.1 Hz, 2H)。可能由於與溶劑峰重疊，一個質子在NMR中不可見。	2.54, B

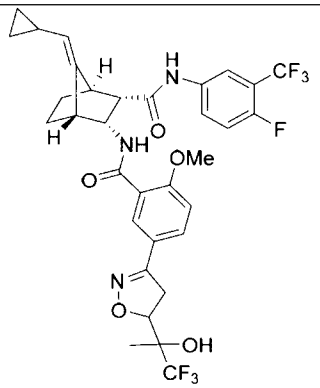
677	 由同對掌性苯甲酸酯中間物峰1 (RT=1.99 min.，>99% ee)製備；所用儀器：Jasco SFC管柱：Chiralpak AD-H，21 × 250 mm，5微米，移動相：20% MeOH / 80% CO_2，流動條件：45 mL/min，150巴，40℃，偵測器波長：220 nm；分析方法：儀器：Shimadzu Nexera SFC，管柱Chiralpak AD-H，4.6 × 100 mm，3微米，移動相：20% MeOH / 80% CO_2，流動條件：2 mL/min，150巴，40℃，偵測器波長：240 nm，得到對掌性(峰-1，RT=1.99 min.，>99% ee)及對掌性(峰-2，RT=7.22 min.，>99% ee)。	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-氟苯甲醯胺基)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	602.3	(500 MHz, DMSO-d6) δ 10.59 - 10.40 (m, 1H), 9.37 (t, J=6.6 Hz, 1H), 8.08 (dd, J=7.1, 2.4 Hz, 1H), 8.02 (dd, J=6.6, 2.6 Hz, 1H), 7.94 - 7.81 (m, 2H), 7.57 - 7.41 (m, 2H), 5.39 (dd, J=9.2, 3.6 Hz, 1H), 4.71 (d, J=9.6 Hz, 1H), 4.56 - 4.50 (m, 1H), 4.47 - 4.37 (m, 1H), 4.12 (d, J=10.8 Hz, 1H), 3.93 (br d, J=9.6 Hz, 2H), 3.76 - 3.71 (m, 1H), 3.66 (dd, J=10.8, 3.7 Hz, 1H), 3.17 (dd, J=10.8, 4.2 Hz, 1H), 3.13 (t, J=3.9 Hz, 1H), 2.75 (t, J=3.9 Hz, 1H), 1.89 - 1.82 (m, 1H), 1.80 - 1.71 (m, 1H), 1.58 - 1.47 (m, 1H), 1.46 - 1.41 (m, 1H), 0.88 - 0.69 (m, 2H), 0.46 - 0.29 (m, 2H)	2.48, C

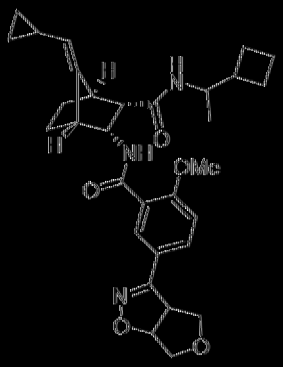
678	 由同對掌性苯甲酸酯中間物峰1製備。製備型層析條件：儀器：Berger MG II管柱：Chiralpak IF，21 × 250 mm，5微米，移動相：30% MeOH / 70% CO_2，流動條件：45 mL/min，150巴，40℃，偵測器波長：220 nm，注射詳情：1.0 mL ~200 mg/3mL於MeOH-CAN中，分析型層析條件：儀器：Shimadzu Nexera SFC管柱：Chiralpak IF，4.6 × 100 mm，3微米，移動相：30% MeOH / 70% CO_2，流動條件：2.0 mL/min，150巴，40℃， 偵測器波長：220 nm，注射詳情：5 μL ~1mg/mL於MeOH中。PK-1，RT = 2.81 min.，100% ee。	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-3-(5-{8,9-二羥基-3-氧雜-4-氮雜三環[5.2.1.0²,⁶]癸-4-烯-5-基}-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	670.3	(500 MHz, DMSO-d6) δ 10.56 (s, 1H), 9.94 (br d, J=7.0 Hz, 1H), 8.31 - 8.21 (m, 2H), 7.97 - 7.77 (m, 2H), 7.50 (br t, J=9.8 Hz, 1H), 7.29 (d, J=8.5 Hz, 1H), 4.79 (br dd, J=17.7, 4.9 Hz, 1H), 4.70 (br d, J=9.5 Hz, 1H), 4.58 (br d, J=8.2 Hz, 1H), 4.46 (br s, 1H), 4.06 (s, 3H), 3.79 (br s, 1H), 3.73 - 3.58 (m, 1H), 3.31 - 3.10 (m, 2H), 2.74 (br s, 1H), 2.31 (s, 1H), 2.17 (s, 1H), 1.95 - 1.74 (m, 2H), 1.68 (br d, J=10.7 Hz, 1H), 1.53 (br d, J=8.5 Hz, 1H), 1.43 (br s, 2H), 1.12 (br d, J=10.7 Hz, 1H), 0.90 - 0.69 (m, 2H), 0.36 (br s, 2H	3.09, C

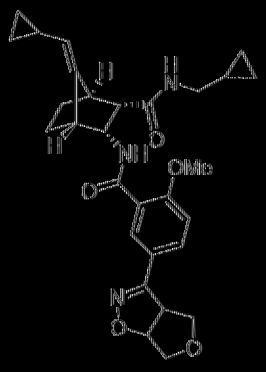
679	 由416-3製備，藉由逆相HPLC之第二溶離非鏡像異構物	(1R,2S,3R,4R,Z)-7-(環丙基亞甲基)-N-(2,2-二甲基四氫-2H-哌喃-4-基)-3-(2-甲氧基 -5-(3a,4,6,6a-四氫呋喃并[3,4-d]異噁唑-3-基)苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	564.0	1H NMR (500 MHz, DMSO-d6) δ 9.96 (br d, J=6.7 Hz, 1H), 8.14 (d, J=2.1 Hz, 1H), 7.99 (br d, J=7.3 Hz, 1H), 7.78 (dd, J=8.7, 2.3 Hz, 1H), 7.24 (br d, J=8.5 Hz, 1H), 5.34 (br dd, J=8.9, 3.1 Hz, 1H), 4.61 (br d, J=9.8 Hz, 1H), 4.49 (br t, J=7.8 Hz, 1H), 4.34 - 4.23 (m, 1H), 4.09 (br d, J=10.4 Hz, 1H), 4.01 (s, 3H), 3.97 - 3.87 (m, 2H), 3.82 - 3.74 (m, 1H), 3.68 - 3.52 (m, 2H), 3.04 (br s, 1H), 2.86 (br dd, J=10.7, 3.4 Hz, 1H), 1.88 - 1.79 (m, 1H), 1.77 - 1.59 (m, 3H), 1.51 - 1.27 (m, 3H), 1.25 - 1.18 (m, 1H), 1.17 (s, 3H), 1.14 - 1.06 (m, 4H), 0.76 - 0.64 (m, 2H), 0.32 (br d, J=2.1 Hz, 2H)。.	2.01, B

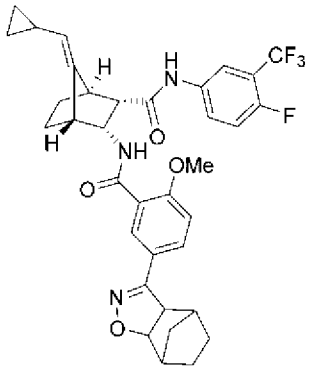
680	 由同對掌性苯甲酸酯中間物4製備；製備型層析條件：儀器：PIC Solution SFC Prep-200)管柱：Chiralpak IC，21 × 250 mm，5微米，移動相：15% IPA / 85% CO_2，流動條件：45 mL/min，150巴，40℃ ，偵測器波長：270 nm，注射詳情：0.5 mL ~[樣本濃度]mg/mL於IPA-CAN中，分析型層析條件：儀器：Shimadzu Nexera SFC管柱：Chiralpak IC，4.6 × 100 mm，3微米，移動相：10% 異丙醇/ 90% CO_2，流動條件：2.0 mL/min，150巴，40℃，偵測器波長：220 nm 注射詳情：5 μL ~1mg/mL於MeOH中。PK-4 RT = 7.18 min.，> 99% ee	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-3-(5-{4,6-二羥基-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	644.2	(500 MHz, DMSO-d6) δ 10.56 (s, 1H), 9.92 (br d, J=7.3 Hz, 1H), 8.25 (s, 1H), 8.20 (br d, J=4.9 Hz, 1H), 7.84 - 7.73 (m, 2H), 7.47 (br t, J=9.6 Hz, 1H), 7.19 (br d, J=8.9 Hz, 1H), 4.79 (br dd, J=8.1, 4.1 Hz, 1H), 4.70 (br d, J=9.8 Hz, 1H), 4.43 (br s, 1H), 4.39 - 4.23 (m, 1H), 4.02 (s, 3H), 3.82 - 3.65 (m, 1H), 3.32 - 3.11 (m, 1H), 3.09 (br s, 1H), 2.72 (br s, 1H), 2.13 - 1.92 (m, 1H), 1.89 - 1.69 (m, 2H), 1.64 - 1.46 (m, 2H), 1.41 (br s, 2H), 0.85 - 0.67 (m, 2H), 0.35 (br d, J=3.7 Hz, 2H)	2.24, B

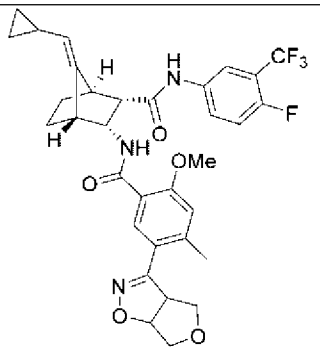
681	 中416.3製備	(1R,2S,3R,4R,7′)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7′-(環丙基甲基)-N-[(2-甲氧基苯基)甲基]雙環[2.2.1]庚烷-2-甲醯胺	572.1	(500 MHz, DMSO-d6) δ 9.94 (br d, J= 6.7 Hz, 1H), 8.42 (br t, J= 5.6 Hz, 1H), 8.16 (d, J= 1.8 Hz, 1H), 7.78 (dd, J= 8.7, 2.0 Hz, 1H), 7.24 - 7.16 (m, 2H), 7.12 (br d, J= 7.3 Hz, 1H), 6.95 (br d, J= 7.9 Hz, 1H), 6.78 (t, J= 7.3 Hz, 1H), 5.33 (br dd, J= 9.2, 3.1 Hz, 1H), 4.63 (br d, J= 9.8 Hz, 1H), 4.49 (br t, J= 7.8 Hz, 1H), 4.37 - 4.19 (m, 3H), 4.09 (br d, J= 10.7 Hz, 1H), 3.95 - 3.85 (m, 3H), 3.81 - 3.72 (m, 3H), 3.65 (br dd, J= 10.8, 3.5 Hz, 1H), 3.10 - 2.97 (m, 2H), 2.62 - 2.56 (m, 1H), 1.92 - 1.81 (m, 1H), 1.77 - 1.66 (m, 1H), 1.52 - 1.43 (m, 1H), 1.41 - 1.26 (m, 2H), 0.79 - 0.62 (m, 2H), 0.32 (br d, J= 4.3 Hz, 2H)。可能由於與溶劑峰或經抑制之水峰重疊，兩個質子在 NMR 中不可見。	2.23, B

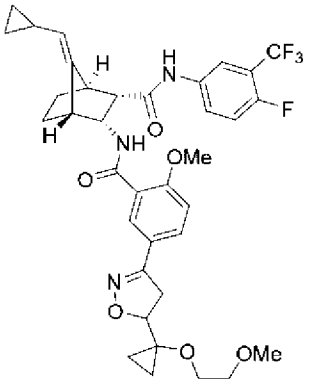
682	 由同對掌性苯甲酸酯中間物峰1製備。製備型層析條件：儀器：PIC Solution SFC Prep-200管柱：Chiralpak IC，21 × 250 mm，5微米，移動相：10%甲醇/ 90% CO_2，流動條件：45 mL/min，150巴，40℃ ，偵測器波長：220 nm，注射詳情：0.5 mL ~65mg/mL於甲醇中，分析型層析條件：儀器：Aurora Infinity SFC管柱：Chiralpak IC，4.6 × 250 mm，3微米，移動相：10% 甲醇/ 90% CO_2，流動條件：2.0 mL/min，150巴，40℃ ，偵測器波長：220 nm，注射詳情：15 μL ~1mg/mL於MeOH中。PK-1，RT = 3.07 min.，>99% ee。	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{2-甲氧基-5-[5-(1,1,1-三氟-2-羥基丙烷-2-基)-4,5-二氫-1,2-噁唑-3-基]苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	684.3	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.92 (d, J=7.0 Hz, 1H), 8.30 - 8.17 (m, 2H), 7.86 - 7.77 (m, 2H), 7.49 (t, J=9.7 Hz, 1H), 7.28 (d, J=8.8 Hz, 1H), 4.88 - 4.78 (m, 1H), 4.70 (d, J=9.6 Hz, 1H), 4.45 (br s, 1H), 4.05 (s, 3H), 3.51 (br t, J=10.0 Hz, 1H), 3.17 (br dd, J=11.2, 4.3 Hz, 1H), 3.11 (br s, 1H), 2.73 (br s, 1H), 1.89 - 1.69 (m, 2H), 1.50 (br dd, J=9.1, 4.3 Hz, 1H), 1.42 (br s, 2H), 1.30 (s, 3H), 0.81 - 0.66 (m, 2H), 0.36 (br s, 2H)	2.66, C

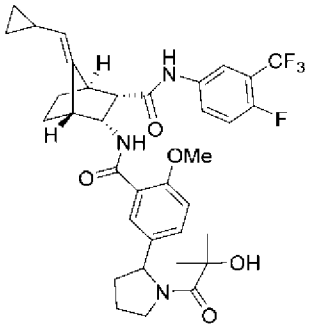
683	 由416-3製備 藉由逆相HPLC之第二溶離非鏡像異構物	(1R,2S,3R,4R,7*Z*)-3-(5-{3a*H*,4*H*,6*H*,6a*H*-呋喃并[3,4-*d*][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-*N*-(1-環丁基乙基)-7-(環丙基甲基)雙環[2.2.1]庚烷-2-甲醯胺	534.3	(500 MHz, DMSO-*d*6) δ 9.97 (br d, *J* = 6.7 Hz, 1H), 8.15 (br d, *J* = 2.1 Hz, 1H), 7.85 – 7.73 (m, 2H), 7.23 (br d, *J* = 8.5 Hz, 1H), 5.33 (br dd, *J* = 9.3, 3.2 Hz, 1H), 4.61 (br d, *J* = 9.5 Hz, 1H), 4.48 (br t, *J* = 7.8 Hz, 1H), 4.27 (br d, *J* = 5.2 Hz, 1H), 4.09 (br d, *J* = 11.0 Hz, 1H), 4.01 (s, 3H), 3.88 (br d, *J* = 9.5 Hz, 1H), 3.82 – 3.72 (m, 2H), 3.69 – 3.61 (m, 1H), 3.07 – 2.99 (m, 1H), 2.88 (br dd, *J* = 11.0, 3.7 Hz, 1H), 2.24 – 2.10 (m, 1H), 1.92 – 1.56 (m, 8H), 1.51 – 1.41 (m, 1H), 1.39 – 1.25 (m, 2H), 0.90 (br d, *J* = 6.7 Hz, 3H), 0.77 – 0.61 (m, 2H), 0.36 – 0.24 (m, 2H)。可能由於溶劑峰重疊，一個質子在 NMR 中不可見。	2.27, B

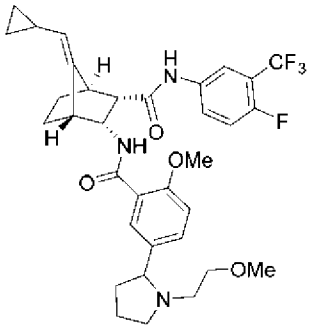
684	 由416-3製備	(1R,2S,3R,4R,7*S*)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]㗁唑-3-基}-2-甲氧基苯甲醯胺基)-N-(環丙基甲基)-7-(環丙基甲基)雙環[2.2.1]庚烷-2-甲醯胺	506.4	(500 MHz, DMSO-d6) δ 9.99 (br d, J= 6.7 Hz, 1H), 8.20-8.08 (m, 2H), 7.78 (dd, J= 8.5, 1.8 Hz, 1H), 7.23 (br d, J= 8.5 Hz, 1H), 5.33 (br dd, J= 8.9, 3.4 Hz, 1H), 4.62 (br d, J= 9.8 Hz, 1H), 4.49 (br t, J= 7.6 Hz, 1H), 4.32-4.23 (m, 1H), 4.14-4.05 (m, 1H), 4.00 (s, 3H), 3.89 (br d, J= 8.9 Hz, 1H), 3.77 (br t, J= 8.2 Hz, 1H), 3.69-3.60 (m, 1H), 3.04 (br s, 1H), 3.00-2.94 (m, 2H), 2.94-2.86 (m, 1H), 1.87-1.80 (m, 1H), 1.76-1.68 (m, 1H), 1.52-1.41 (m, 1H), 1.40-1.27 (m, 2H), 0.91-0.81 (m, 1H), 0.76-0.64 (m, 2H), 0.40-0.28 (m, 4H), 0.12 (br s, 2H)。可能由於與溶劑峰重疊，兩個質子不可見。	2.07, C

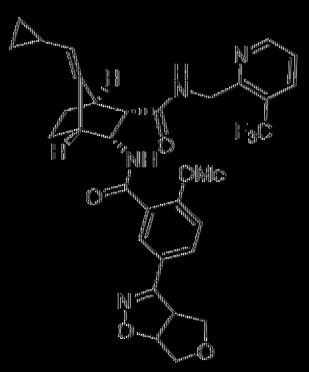
685	 由同對掌性苯甲酸酯中間物-峰2 (RT=5.52 min，>99% ee)製備：所用儀器：Berger MG II管柱：Chiralcel OD-H，21 × 250 mm，5微米，移動相：7% MeOH / 93% CO_2，流動條件：45 mL/min，150巴，40℃，偵測器波長：220 nm；分析方法：儀器：Shimadzu Nexera SFC，管柱Chiralcel OD-H，4.6 × 100 mm，3微米，移動相：7% MeOH / 93% CO_2，流動條件：2 mL/min，150巴，40℃，偵測器波長：220 nm，得到對掌性(峰-1，RT=4.42 min.，>99% ee)及對掌性(峰-2，RT=5.52 min.，>99% ee)。	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-(2-甲氧基-5-{3-氧雜-4-氮雜三環[5.2.1.0^{2,6}]癸-4-烯-5-基}苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	638.1	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.92 (br d, J=6.7 Hz, 1H), 8.25 (d, J=2.1 Hz, 1H), 8.23 (br d, J=4.6 Hz, 1H), 7.83 (dd, J=8.5, 2.1 Hz, 1H), 7.81 - 7.73 (m, 1H), 7.49 (br t, J=9.6 Hz, 1H), 7.28 (d, J=8.9 Hz, 1H), 4.70 (br d, J=9.5 Hz, 1H), 4.59 (br d, J=8.2 Hz, 1H), 4.51 - 4.40 (m, 1H), 4.05 (s, 3H), 3.66 (br d, J=8.2 Hz, 1H), 3.55 - 3.38 (m, 1H), 3.17 (br dd, J=10.7, 3.7 Hz, 1H), 3.12 (br d, J=3.4 Hz, 1H), 2.73 (br s, 1H), 2.47 (br d, J=0.6 Hz, 1H), 2.38 (br d, J=1.2 Hz, 1H), 1.90 - 1.83 (m, 1H), 1.82 - 1.73 (m, 1H), 1.62 - 1.47 (m, 3H), 1.46 - 1.40 (m, 2H), 1.27 (br d, J=10.4 Hz, 1H), 1.14 (br d, J=10.1 Hz, 2H), 0.85 - 0.68 (m, 2H), 0.36 (br s, 2H)	2.85, C

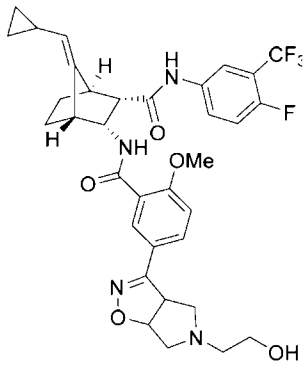
686	 藉由SFC分離之異構物，其中實例686為峰2 (RT=3.2 min.，>95% de)：儀器：Waters 100 Prep SFC管柱：Chiral OD，30 × 250 mm，5微米，移動相：30% MeOH / 70% CO_2 (具有0.1% DEA)，流動條件：100 mL/min，偵測器波長：220 nm；分析方法：儀器：Shimadzu Nexera SFC，管柱Chiral OD，4.6 × 100 mm，5微米，移動相：30% MeOH / 70% CO_2 (具有0.1% DEA)，流動條件：2 mL/min，偵測器波長：220 nm，得到對掌性(峰-1，RT=2.1 min.，>95% de)及對掌性(峰-2，RT=3.2 min.，>95% de)。	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基-4-甲基苯甲醯胺基)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	628.2	(500 MHz, DMSO-d6) δ 10.64 - 10.45 (m, 1H), 9.93 (br d, J=7.0 Hz, 1H), 8.22 (br d, J=4.6 Hz, 1H), 7.96 (s, 1H), 7.81 - 7.68 (m, 1H), 7.48 (br t, J=9.9 Hz, 1H), 7.18 (s, 1H), 5.36 - 5.14 (m, 1H), 4.70 (d, J=9.2 Hz, 1H), 4.56 - 4.47 (m, 1H), 4.47 - 4.39 (m, 1H), 4.11 (br d, J=10.4 Hz, 1H), 4.05 (s, 3H), 3.79 (br d, J=9.8 Hz, 1H), 3.74 - 3.68 (m, 1H), 3.64 (br s, 1H), 3.24 - 3.13 (m, 1H), 3.11 - 3.04 (m, 1H), 2.72 (br s, 1H), 2.48 (s, 3H), 1.98 - 1.82 (m, 1H), 1.79 - 1.68 (m, 1H), 1.61 - 1.49 (m, 1H), 1.46 - 1.30 (m, 2H), 0.86 - 0.60 (m, 2H), 0.35 (br d, J=3.1 Hz, 2H)	2.59, C

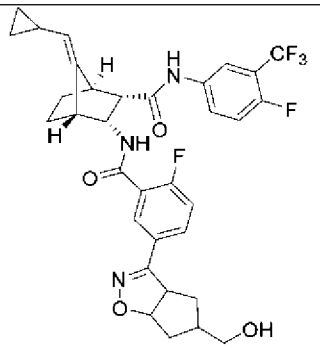
687	 由同對掌性苯甲酸中間物峰1 (RT=5.02 min.，>99% ee)製備-儀器：Berger MG II管柱：Chiralpak IC，21 × 250 mm，5微米，移動相：25% MeOH / 75% CO_2，流動條件：45 mL/min，150巴，40℃，偵測器波長：220 nm；分析方法：儀器：Shimadzu Nexera SFC，管柱Chiralpak IC，4.6 × 250 mm，3微米，移動相：25% MeOH / 75% CO_2，流動條件：2 mL/min，150巴，40℃，偵測器波長：220 nm，得到對掌性(峰-1，RT=5.02 min.，>99% ee)及對掌性(峰-2，RT=6.46 min.，>99% ee)。	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-(2-甲氧基-5-{5-[1-(2-甲氧基乙氧基)環丙基]-4,5-二氫-1,2-噁唑-3-基}苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	686.1	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.90 (d, J=7.2 Hz, 1H), 8.25 (d, J=2.3 Hz, 1H), 8.22 (dd, J=6.4, 2.3 Hz, 1H), 7.86 - 7.77 (m, 2H), 7.48 (t, J=9.7 Hz, 1H), 7.28 (d, J=8.8 Hz, 1H), 4.69 (d, J=9.7 Hz, 1H), 4.56 (dd, J=10.6, 8.5 Hz, 1H), 4.47 - 4.41 (m, 1H), 4.05 (s, 3H), 3.74 - 3.66 (m, 1H), 3.62 - 3.58 (m, 1H), 3.55 - 3.44 (m, 1H), 3.42 - 3.38 (m, 2H), 3.32 - 3.26 (m, 1H), 3.16 (dd, J=11.4, 4.1 Hz, 1H), 3.13 - 3.06 (m, 3H), 2.77 - 2.69 (m, 1H), 1.89 - 1.81 (m, 1H), 1.80 - 1.72 (m, 1H), 1.59 - 1.48 (m, 1H), 1.45 - 1.35 (m, 2H), 0.96 - 0.85 (m, 1H), 0.82 - 0.71 (m, 3H), 0.71 - 0.65 (m, 2H), 0.42 - 0.27 (m, 2H)可能由於與溶劑峰重疊，一個質子在NMR中不可見	2.64, C

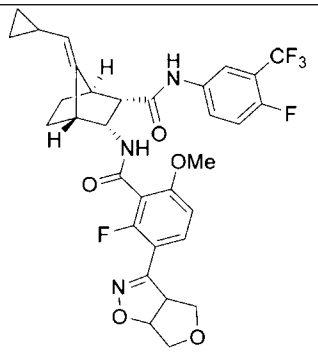
688	 由實例694製備	(2S,3R)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[1-(2-羥基-2-甲基丙醯基)吡咯啶-2-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	658.3	(400 MHz, DMSO-d6) δ = 10.47 (s, 1H), 9.80 (br d, J = 7.6 Hz, 1H), 8.21 (dd, J = 2.4, 6.6 Hz, 1H), 7.83 - 7.74 (m, 1H), 7.74 - 7.64 (m, 1H), 7.48 (d, J = 10.3 Hz, 1H), 7.23 (br d, J = 2.4 Hz, 1H), 7.07 (d, J = 8.6 Hz, 1H), 5.20 (s, 1H), 5.04 - 4.95 (m, 1H), 4.68 (d, J = 9.5 Hz, 1H), 4.49 - 4.37 (m, 1H), 4.07 - 3.99 (m, 1H), 3.96 (s, 3H), 3.91 - 3.82 (m, 1H), 3.58 - 3.49 (m, 1H), 3.20 - 3.10 (m, 2H), 3.07 (t, J = 4.2 Hz, 1H), 2.70 (t, J = 3.4 Hz, 1H), 2.21 - 2.08 (m, 1H), 1.90 - 1.70 (m, 4H), 1.62 - 1.46 (m, 2H), 1.44 - 1.35 (m, 2H), 1.29 (d, J = 14.9 Hz, 6H), 0.80 - 0.56 (m, 2H), 0.35 (dd, J = 2.2, 4.6 Hz, 2H)	2.47, A

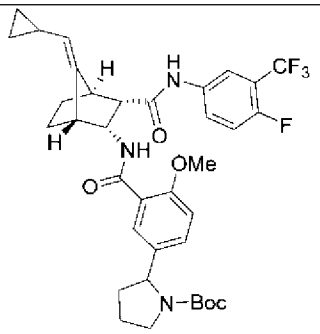
689	 由實例715製備	(2S,3R)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{2-甲氧基-5-[1-(2-甲氧基乙基)吡咯啶-2-基]苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	630.0	(400 MHz, DMSO-d6) δ = 10.48 (s, 1H), 9.85 - 9.73 (m, 1H), 8.21 (dd, J = 2.4, 6.6 Hz, 1H), 7.87 (br d, J = 0.7 Hz, 1H), 7.80 - 7.72 (m, 1H), 7.52 - 7.39 (m, 2H), 7.12 (br d, J = 9.0 Hz, 1H), 4.68 (d, J = 9.5 Hz, 1H), 4.49 - 4.39 (m, 1H), 3.97 (s, 3H), 3.26 - 3.22 (m, 1H), 3.18 - 3.10 (m, 4H), 3.08 (br d, J = 3.9 Hz, 1H), 2.70 (dt, J = 0.7, 3.1 Hz, 1H), 2.61 - 2.53 (m, 1H), 2.27 - 2.12 (m, 2H), 2.07 (s, 1H), 1.93 - 1.70 (m, 4H), 1.54 - 1.33 (m, 5H), 0.81 - 0.67 (m, 2H), 0.35 (dd, J = 2.2, 4.6 Hz, 2H)	2.63, A

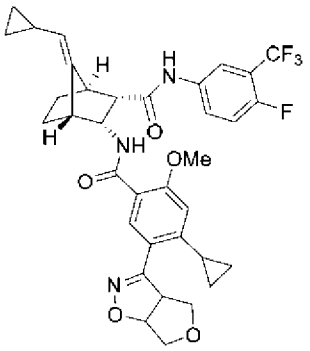
690	 中間體 3製備	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-{[3-(三氟甲基)吡啶-2-基]甲基}雙環[2.2.1]庚烷-2-甲醯胺	611.2	(500 MHz, DMSO-d6) δ 9.90 (br d, J= 6.7 Hz, 1H), 8.72-8.63 (m, 2H), 8.17-8.10 (m, 2H), 7.77 (dd, J= 8.5, 1.8 Hz, 1H), 7.47 (br dd, J= 6.9, 5.3 Hz, 1H), 7.18 (d, J= 8.9 Hz, 1H), 5.33 (dd, J= 9.2, 3.4 Hz, 1H), 4.63 (d, J= 9.8 Hz, 1H), 4.56 (br d, J= 4.6 Hz, 2H), 4.48 (br t, J= 8.1 Hz, 1H), 4.34-4.25 (m, 1H), 4.09 (br d, J= 10.7 Hz, 1H), 3.89 (br d, J= 9.2 Hz, 1H), 3.83 (s, 3H), 3.77 (br t, J= 8.1 Hz, 1H), 3.65 (br dd, J= 10.8, 3.2 Hz, 1H), 3.10-3.00 (m, 2H), 2.61 (br s, 1H), 1.81 (br t, J= 9.3 Hz, 1H), 1.74-1.62 (m, 1H), 1.53-1.40 (m, 1H), 1.31 (br s, 2H), 0.80-0.63 (m, 2H), 0.39-0.25 (m, 2H)。	2.14, B

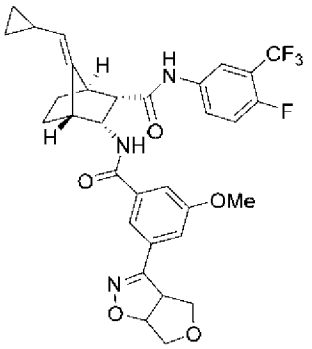
691	 由同對掌性苯甲酸酯中間物(峰1；>99%ee；對掌性分析型RT=6.621 min)製備；製備型對掌性SFC條件：儀器：Jasco SFC Prep；管柱：Regis Whelk-01，21 × 250 mm，5微米；移動相：15% IPA / 85% CO_2；流動條件：45 mL/min，150巴，40℃；偵測器波長：220 nm；注射詳情：0.5 mL ~50mg/mL於IPA中	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(2-羥基乙基)-3aH,4H,5H,6H,6aH-吡咯并[3,4-d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	657.6	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.97 (d, J=7.0 Hz, 1H), 8.30 (br s, 1H), 8.25 (dd, J=6.5, 2.5 Hz, 1H), 7.85 (dd, J=8.5, 2.0 Hz, 1H), 7.80 - 7.75 (m, 1H), 7.50 (t, J=9.7 Hz, 1H), 7.31 (d, J=8.9 Hz, 1H), 5.49 - 5.42 (m, 1H), 4.78 (br t, J=8.8 Hz, 1H), 4.70 (d, J=9.6 Hz, 1H), 4.47 - 4.41 (m, 1H), 4.07 (s, 3H), 3.98 (br d, J=11.9 Hz, 1H), 3.76 - 3.70 (m, 1H), 3.68 - 3.62 (m, 2H), 3.55 (br d, J=1.5 Hz, 2H), 3.23 (br s, 2H), 3.19 - 3.13 (m, 1H), 3.12 - 3.07 (m, 1H), 2.76 - 2.70 (m, 1H), 1.84 - 1.74 (m, 2H), 1.53 - 1.46 (m, 1H), 1.45 - 1.38 (m, 2H), 0.78 - 0.70 (m, 2H), 0.38 - 0.33 (m, 2H)	1.21, A

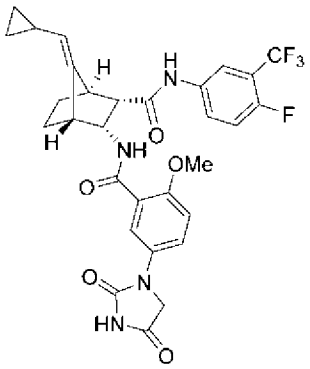
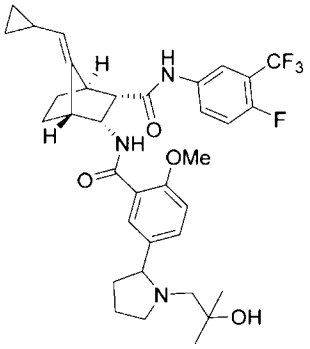
692	 由同對掌性苯甲酸酯中間物(峰2；83.4%ee；對掌性分析型RT=2.155 min)製備；製備型對掌性SFC條件：儀器：Berger MG II;管柱：Chiralpak AD-H，21 × 250 mm，5微米；移動相：20% MeOH / 80% CO_2；流動條件：45 mL/min，150巴，40℃；偵測器波長：220 nm；注射詳情：0.5 mL ~125mg/mL於MeOH:CAN中	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{2-氟-5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	630.4	(500 MHz, DMSO-d6) δ 10.51 (s, 1H), 9.37 (t, J=6.9 Hz, 1H), 8.08 - 8.04 (m, 1H), 8.00 (dd, J=6.5, 2.5 Hz, 1H), 7.88 - 7.83 (m, 2H), 7.51 - 7.42 (m, 2H), 5.20 - 5.14 (m, 1H), 4.69 (d, J=9.6 Hz, 1H), 4.47 - 4.41 (m, 1H), 4.10 (td, J=9.7, 6.3 Hz, 1H), 3.31 - 3.25 (m, 1H), 3.23 - 3.11 (m, 3H), 2.75 - 2.72 (m, 1H), 2.20 - 2.06 (m, 3H), 1.87 - 1.74 (m, 2H), 1.66 - 1.59 (m, 1H), 1.55 - 1.39 (m, 4H), 0.78 - 0.69 (m, 2H), 0.38 - 0.32 (m, 2H)	1.34, A

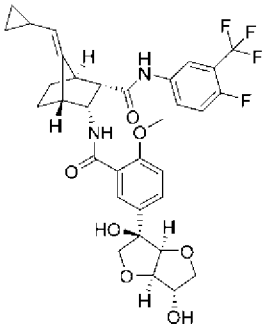
693	 經由SFC分離之異構物，其中實例693為峰2 (RT=8.3 min.，>95% de)；儀器：Waters 100 Prep SFC管柱：Chiral OD，30 × 250 mm，5微米，移動相：15% MeOH / 85% CO_2 (具有0.1% DEA)，流動條件：100 mL/min，偵測器波長：220 nm；分析方法：儀器：Shimadzu Nexera SFC，管柱Chiral OD，4.6 × 100 mm，5微米，移動相：15% MeOH / 85% CO_2 (具有0.1% DEA)，流動條件：2 mL/min，偵測器波長：220 nm，得到對掌性(峰-1，RT=6.75 min.，>95% de)及對掌性(峰-2，RT=8.3 min.，>95% de)。	(1R,2S,3R,4R,7Z)-3-(3-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-氟-6-甲氧基苯甲醯胺基)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	632.2	(500 MHz, DMSO-d6) δ 10.47 (s, 1H), 8.76 - 8.66 (m, 1H), 8.11 (br d, J=6.1 Hz, 1H), 7.84 - 7.70 (m, 2H), 7.46 (t, J=9.7 Hz, 1H), 7.02 (d, J=9.0 Hz, 1H), 5.30 (dd, J=9.3, 3.6 Hz, 1H), 4.67 (d, J=9.5 Hz, 1H), 4.54 - 4.43 (m, 1H), 4.37 - 4.28 (m, 1H), 4.08 (d, J=10.7 Hz, 1H), 3.92 (br d, J=9.6 Hz, 1H), 3.78 - 3.68 (m, 3H), 3.66 - 3.55 (m, 2H), 3.13 (br dd, J=10.8, 3.7 Hz, 1H), 3.05 (br s, 1H), 2.72 - 2.65 (m, 1H), 2.03 - 1.93 (m, 1H), 1.92 - 1.85 (m, 1H), 1.59 - 1.49 (m, 1H), 1.47 - 1.32 (m, 2H), 0.73 (quin, J=9.4 Hz, 2H), 0.43 - 0.27 (m, 2H)	2.32, B

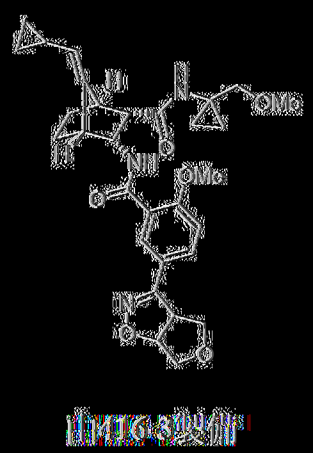
694	 峰1，RT = 3.54 min，製備型對掌性SFC純化條件：儀器詳情：品牌/型號：PIC – 175；製備型SFC條件：管柱/尺寸：Chiralpak IG (250 × 30)mm，5u，% CO_2: 75%，%助溶劑：25% 4M 甲醇氨於MEOH中，總流速：130.0 g/min，背壓：100巴，溫度：40℃，UV：240 nm。	2-(3-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)吡咯啶-1-甲酸三級丁酯	672.4	(400MHz, CD_3OD) δ ppm 8.21 - 8.05 (m, 1H), 7.88 - 7.81 (m, 1H), 7.76 - 7.69 (m, 1H), 7.35 - 7.22 (m, 2H), 7.16 - 7.08 (m, 1H), 4.80 - 4.74 (m, 1H), 4.74 - 4.67 (m, 1H), 4.60 - 4.49 (m, 1H), 4.08 - 4.01 (m, 3H), 3.68 - 3.49 (m, 3H), 3.23 - 3.09 (m, 2H), 2.74 - 2.64 (m, 1H), 2.44 - 2.22 (m, 1H), 2.09 - 1.96 (m, 1H), 1.96 - 1.73 (m, 4H), 1.63 - 1.38 (m, 7H), 1.15 (br s, 6H), 0.81 - 0.68 (m, 2H), 0.41 - 0.26 (m, 2H)。	1.61, C

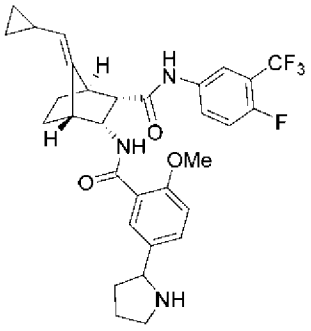
695	 藉由SFC分離之異構物，其中實例695為峰2 (RT=3.3 min.，>95% de)：-儀器：Waters 100 Prep SFC管柱：Chiral AD，30 × 250 mm，5微米，移動相：25% MeOH / 75% CO_2 (具有0.1% DEA)，流動條件：100 mL/min，偵測器波長：220 nm；分析方法：儀器：Shimadzu Nexera SFC，管柱Chiral AD，4.6 × 100 mm，5微米，移動相：25% MeOH / 75% CO_2 (具有0.1% DEA)，流動條件：2 mL/min，偵測器波長：220 nm，得到對掌性(峰-1，RT=2.6 min.，>95% de)及對掌(峰-2，RT=3.3 min.，>95% de)。	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-4-環丙基-2-甲氧基苯甲醯胺基)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	654.0	(500 MHz, DMSO-d6) δ 10.64 - 10.42 (m, 1H), 9.87 (br d, J=6.7 Hz, 1H), 8.33 - 8.11 (m, 1H), 7.92 (s, 1H), 7.83 - 7.72 (m, 1H), 7.48 (br t, J=9.8 Hz, 1H), 6.68 (s, 1H), 5.32 (dd, J=9.0, 3.5 Hz, 1H), 4.69 (d, J=9.5 Hz, 1H), 4.56 (br t, J=7.8 Hz, 1H), 4.48 - 4.40 (m, 1H), 4.11 (br d, J=11.0 Hz, 1H), 4.04 (s, 3H), 3.76 (br d, J=9.5 Hz, 1H), 3.70 - 3.61 (m, 1H), 3.51 - 3.42 (m, 1H), 3.15 (br dd, J=10.4, 4.0 Hz, 1H), 3.08 (br s, 1H), 2.72 (br s, 1H), 2.41 - 2.28 (m, 1H), 1.92 - 1.82 (m, 1H), 1.79 - 1.72 (m, 1H), 1.50 (br dd, J=8.4, 3.8 Hz, 1H), 1.41 (br s, 2H), 1.11 - 1.03 (m, 1H), 0.98 (dt, J=8.5, 4.6 Hz, 1H), 0.93 - 0.82 (m, 2H), 0.77 - 0.60 (m, 2H), 0.35 (br s, 2H)	2.63, C

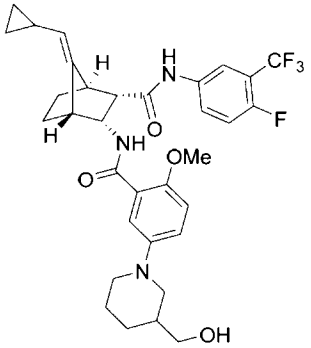
696	 藉由SFC分離之異構物，其中實例696為峰1 (RT=1.81 min，>99% de)，-儀器：PIC Solution SFC管柱：Chiralpak AD-H，21 × 250 mm，5微米，移動相：30% IPA-0.1% DEA / 70% CO_2，流動條件：45 mL/min，150巴，40℃，偵測器波長：220 nm；分析方法：儀器：Aurora Infinity SFC，管柱Chiralpak IC，4.6 × 250 mm，3微米，移動相：20% IPA-0.1% DEA / 80% CO_2，流動條件：2 mL/min，150巴，40℃，偵測器波長：220 nm，得到對掌性(峰-1，RT=1.81 min.，>99% de)及對掌性(峰-2，RT=2.76 min.，>99% de)。	(1R,2S,3R,4R,7Z)-3-(3-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-5-甲氧基苯甲醯胺基)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	614.2	(500 MHz, DMSO-d6) δ 10.69 - 10.53 (m, 1H), 9.39 (br d, J=6.7 Hz, 1H), 8.12 (br d, J=4.6 Hz, 1H), 7.87 - 7.79 (m, 1H), 7.60 (s, 1H), 7.49 (br t, J=9.6 Hz, 1H), 7.38 (s, 1H), 7.37 (s, 1H), 5.42 (dd, J=9.2, 3.1 Hz, 1H), 4.71 (d, J=9.5 Hz, 1H), 4.56 (br t, J=7.8 Hz, 1H), 4.47 - 4.37 (m, 1H), 4.14 (br d, J=10.7 Hz, 1H), 3.95 (br d, J=9.2 Hz, 1H), 3.86 (s, 3H), 3.74 (br dd, J=9.3, 6.9 Hz, 1H), 3.67 (dd, J=10.8, 3.5 Hz, 1H), 3.19 (br dd, J=10.5, 4.1 Hz, 1H), 3.10 (br s, 1H), 2.77 (br s, 1H), 1.91 - 1.83 (m, 1H), 1.79 - 1.73 (m, 1H), 1.59 - 1.49 (m, 1H), 1.45 (br s, 2H), 0.81 - 0.69 (m, 2H), 0.37 (br d, J=1.8 Hz, 2H) 可能由於與溶劑峰重疊，一個質子在NMR中不可見	2.51, B

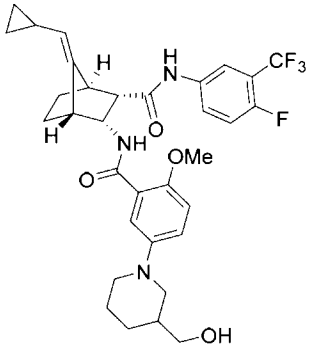
697		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-3-[5-(2,4-二側氧基咪唑啶-1-基)-2-甲氧基苯甲醯胺基]-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	601.3	(500 MHz, DMSO-d6) δ 8.28 - 8.15 (m, 1H), 7.90 - 7.76 (m, 1H), 7.69 (br dd, J=8.9, 2.7 Hz, 1H), 7.57 - 7.43 (m, 1H), 7.31 - 7.23 (m, 1H), 7.20 - 7.01 (m, 1H), 4.78 - 4.58 (m, 1H), 4.53 - 4.42 (m, 1H), 4.16 (br d, J=4.6 Hz, 1H), 4.05 - 3.96 (m, 1H), 3.22 - 3.03 (m, 1H), 2.82 (s, 3H), 2.78 - 2.64 (m, 1H), 1.93 - 1.66 (m, 3H), 1.59 - 1.24 (m, 4H), 0.84 - 0.67 (m, 2H), 0.42 - 0.25 (m, 2H)	2.31, B
698	 由實例703製備	(2S,3R)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[1-(2-羥基-2-甲基丙基)吡咯啶-2-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	644.0	(400 MHz, DMSO-d6) δ = 10.47 (s, 1H), 0.00 (d, J = 7.6 Hz, 1H), 8.24 - 8.11 (m, 1H), 7.87 (d, J = 2.2 Hz, 1H), 7.80 - 7.68 (m, 1H), 7.53 - 7.39 (m, 2H), 7.11 (d, J = 8.3 Hz, 1H), 4.68 (d, J = 9.8 Hz, 1H), 4.48 - 4.39 (m, 1H), 3.99 - 3.91 (m, 4H), 3.55 - 3.47 (m, 1H), 3.26 (s, 1H), 3.13 (dd, J = 4.2, 10.5 Hz, 1H), 3.07 (br t, J = 3.5 Hz, 1H), 2.70 (br s, 1H), 2.31 - 2.21 (m, 2H), 2.08 - 1.96 (m, 2H), 1.88 (s, 1H), 1.83 - 1.66 (m, 3H), 1.55 - 1.36 (m, 4H), 1.02 (s, 3H), 0.88 (s, 3H), 0.79 - 0.68 (m, 2H), 0.35 (dd, J = 2.2, 4.4 Hz, 2H)	2.67, A

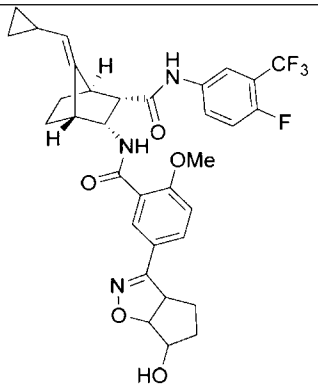
700		(1R,2S,3R,4R,7Z)-3-{5-[(3R,3aS,6S,6aR)-3,6-二羥基-六氫呋喃并[3,2-b]呋喃-3-基]-2-甲氧基苯甲醯胺基}-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	647.2	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.87 (br d, J=7.3 Hz, 1H), 8.23 (br d, J=4.9 Hz, 1H), 8.10 (d, J=2.4 Hz, 1H), 7.84 - 7.75 (m, 1H), 7.61 (dd, J=8.7, 2.3 Hz, 1H), 7.49 (br t, J=9.8 Hz, 1H), 7.19 (d, J=8.5 Hz, 1H), 4.71 (br d, J=9.8 Hz, 1H), 4.52 - 4.41 (m, 1H), 4.32 (br d, J=3.4 Hz, 1H), 4.24 - 4.12 (m, 2H), 4.01 (s, 3H), 3.97 - 3.90 (m, 1H), 3.89 - 3.78 (m, 2H), 3.70 (br d, J=8.9 Hz, 1H), 3.50 (br s, 1H), 3.17 (br dd, J=10.7, 4.0 Hz, 1H), 3.11 (br s, 1H), 2.73 (br s, 1H), 1.94 - 1.84 (m, 1H), 1.82 - 1.74 (m, 1H), 1.61 - 1.48 (m, 1H), 1.47 - 1.32 (m, 2H), 0.84 - 0.67 (m, 2H), 0.37 (br d, J=2.4 Hz, 2H)	2.28, A

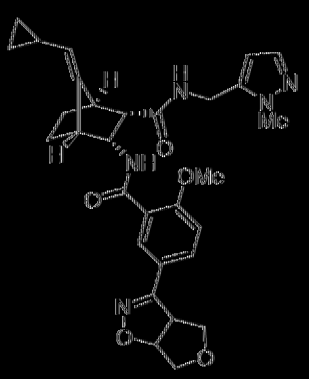
701	 由401.63製備	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]㗁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-{[1-(甲氧基甲基)環丙基]甲基}雙環[2.2.1]庚烷-2-甲醯胺	550.3	(500 MHz, DMSO-d6) δ 9.97 (br d, J=7.0 Hz, 1H), 8.14 (s, 1H), 8.05 (br t, J=5.2 Hz, 1H), 7.77 (dd, J=8.2, 1.2 Hz, 1H), 7.23 (d, J=8.5 Hz, 1H), 5.33 (br dd, J=9.3, 3.2 Hz, 1H), 4.62 (br d, J=9.5 Hz, 1H), 4.48 (br t, J=8.1 Hz, 1H), 4.28 (br t, J=10.4 Hz, 1H), 4.08 (br d, J=10.7 Hz, 1H), 4.00 (s, 3H), 3.89 (br d, J=9.2 Hz, 1H), 3.80-3.70 (m, 1H), 3.68-3.60 (m, 1H), 3.19-3.08 (m, 5H), 3.07-2.99 (m, 2H), 2.94 (br dd, J=10.5, 4.1 Hz, 1H), 1.87-1.80 (m, 1H), 1.77-1.69 (m, 1H), 1.50-1.41 (m, 1H), 1.38-1.26 (m, 2H), 0.76-0.64 (m, 2H), 0.46-0.35 (m, 2H), 0.30 (br s, 4H)。可能由於與經抑制之水峰重疊，一個質子在NMR中不可見。	2.02, B

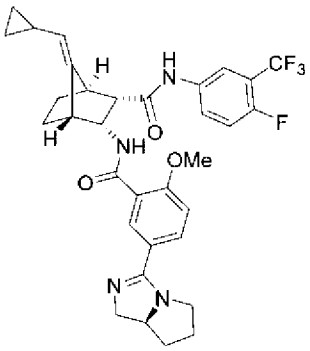
703	 由實例694製備	(2S,3R)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-[2-甲氧基-5-(吡咯啶-2-基)苯甲醯胺基]雙環[2.2.1]庚烷-2-甲醯胺	572.3	(400 MHz, DMSO-d6) δ = 10.52 (s, 1H), 9.86 (d, J = 7.3 Hz, 1H), 8.23 (dd, J = 2.4, 6.6 Hz, 1H), 8.02 (d, J = 2.4 Hz, 1H), 7.80 - 7.72 (m, 1H), 7.56 (dd, J = 2.6, 8.4 Hz, 1H), 7.51 - 7.43 (m, 1H), 7.21 (d, J = 8.6 Hz, 1H), 4.69 (d, J = 9.8 Hz, 1H), 4.49 - 4.40 (m, 1H), 4.39 - 4.32 (m, 1H), 4.00 (s, 3H), 3.20 - 3.11 (m, 4H), 3.08 (br t, J = 3.8 Hz, 1H), 2.74 - 2.69 (m, 1H), 2.29 - 2.17 (m, 1H), 2.02 - 1.72 (m, 6H), 1.55 - 1.33 (m, 4H), 0.83 - 0.62 (m, 2H), 0.35 (dd, J = 2.1, 4.5 Hz, 2H)	2.09, A

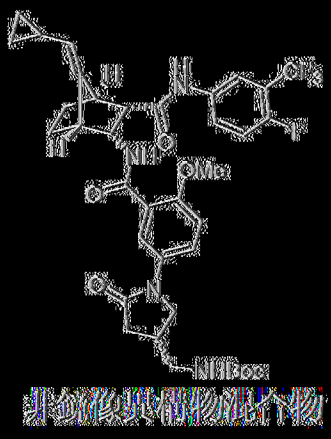
704	 峰 - 1 /異構物 - 1，SFC RT 4.7 min，儀器詳情：品牌/型號：Thar SFC-80，製備型SFC條件，管柱/尺寸：Chiralcel OD-H (250 × 30)mm，5u，% CO_2: 70%，%助溶劑：30% 4M 甲醇氨於MEOH中，總流速：80g/min，背壓：100 巴，溫度：35℃，UV：240，滯留時間(min)，峰-1：4.7，峰-2：8.0	(2S,3R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[3-(羥基甲基)哌啶-1-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	616.3	(400 MHz, DMSO-d6) δ 10.50 (s, 1H), 9.81 (d, J=7.3 Hz, 1H), 8.22 (dd, J=6.4, 2.7 Hz, 1H), 7.80 - 7.74 (m, 1H), 7.55 - 7.42 (m, 2H), 7.10 - 7.02 (m, 2H), 4.68 (d, J=9.3 Hz, 1H), 4.54 (t, J=5.5 Hz, 1H), 4.48 - 4.40 (m, 1H), 3.91 (s, 3H), 3.57 - 3.53 (m, 1H), 3.16 - 3.12 (m, 1H), 3.09 - 3.04 (m, 1H), 2.72 - 2.68 (m, 1H), 2.54 (s, 2H), 2.32 (dd, J=3.9, 2.0 Hz, 1H), 1.90 - 1.84 (m, 1H), 1.81 - 1.65 (m, 4H), 1.60 - 1.45 (m, 3H), 1.44 - 1.35 (m, 2H), 1.27 - 1.21 (m, 3H), 1.05 - 0.95 (m, 1H), 0.85 (br t, J=6.6 Hz, 1H), 0.73 (br t, J=8.6 Hz, 2H), 0.35 (dd, J=4.3, 1.6 Hz, 2H)	2.49, A

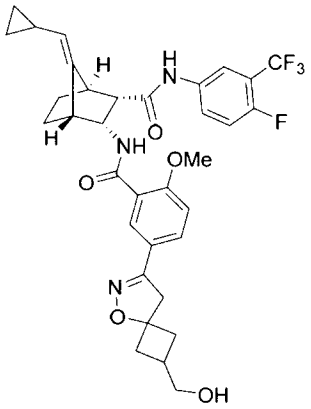
705	 峰 - 2 /異構物 - 2，SFC RT 8.0 min，儀器詳情：品牌/型號：Thar SFC-80，製備型SFC條件，管柱/尺寸：Chiralcel OD-H (250 × 30)mm,5u，% CO_2: 70%，%助溶劑：30% 4M甲醇氨於MEOH中，總流速：80g/min，背壓：100巴，溫度：35℃，UV: 240，滯留時間(min)，峰-1：4.7，峰-2：8.0	(2S,3R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[3-(羥基甲基)哌啶-1-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	616.3	(400 MHz, DMSO-d6) δ 10.49 (s, 1H), 9.84 - 9.76 (m, 1H), 8.21 (dd, J=6.2, 2.3 Hz, 1H), 7.83 - 7.71 (m, 1H), 7.52 (d, J=2.9 Hz, 1H), 7.47 (t, J=9.9 Hz, 1H), 7.12 - 6.97 (m, 2H), 4.68 (d, J=9.5 Hz, 1H), 4.54 (t, J=5.1 Hz, 1H), 4.48 - 4.40 (m, 1H), 3.91 (s, 3H), 3.55 - 3.50 (m, 1H), 3.17 - 3.12 (m, 1H), 3.07 (dd, J=4.4, 3.7 Hz, 1H), 2.72 - 2.68 (m, 1H), 2.54 (s, 1H), 2.35 - 2.31 (m, 1H), 1.91 - 1.84 (m, 1H), 1.80 - 1.65 (m, 4H), 1.62 - 1.33 (m, 5H), 1.28 - 1.19 (m, 3H), 1.02 (dt, J=9.3, 1.5 Hz, 1H), 0.79 - 0.68 (m, 2H), 0.42 - 0.26 (m, 2H	2.47, A

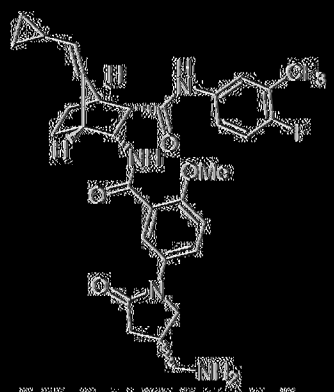
706	 由同對掌性苯甲酸酯中間物峰4製備。製備型層析條件：儀器：Berger MG II管柱：Chiralpak AD-H，21 × 250 mm，5微米，移動相：12% MeOH / 88% CO_2，流動條件：45 mL/min，150巴，40℃ ，偵測器波長：220 nm，注射詳情：0.5 mL ~35mg/mL於甲醇中，分析型層析條件：儀器：Shimadzu Nexera SFC管柱：Chiralpak AD-H，4.6 × 100 mm，3微米，移動相：12% MeOH / 88% CO_2，流動條件：2.0 mL/min，150巴，40℃，偵測器波長：220 nm， 注射詳情：5 μL ~1mg/mL於MeOH中。PK-4，RT = 7.80 min.，> 99% ee。	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-(5-{6-羥基-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	628.2	(500 MHz, DMSO-d_6) δ 10.70 (br s, 1H), 10.05 (br s, 1H), 8.42 (br s, 1H), 8.37 (br s, 1H), 7.95 (br s, 1H), 7.63 (br s, 1H), 7.35 (br d, *J*=8.2 Hz, 1H), 5.22 (br s, 1H), 4.84 (br d, *J*=9.8 Hz, 1H), 4.57 (br s, 1H), 4.23 (br d, *J*=9.2 Hz, 1H), 4.17 (br s, 3H), 3.75 - 3.67 (m, 1H), 3.64 (br d, *J*=6.4 Hz, 1H), 3.32 (br s, 1H), 3.25 (br s, 1H), 2.87 (br s, 1H), 2.68 (br d, *J*=18.3 Hz, 1H), 1.99 (br s, 2H), 1.93 (br s, 2H), 1.68 (br s, 1H), 1.56 (br s, 2H), 0.89 (br s, 2H), 0.50 (br s, 2H)	2.41, C

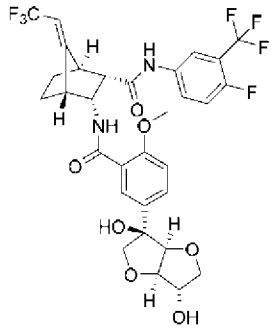
701	 H416.3製備	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-[(1-甲基-1H-吡唑-5-基)甲基]雙環[2.2.1]庚烷-2-甲醯胺	546.3	(500 MHz, DMSO-d6) δ 9.93 (d, J=7.0 Hz, 1H), 8.58 (br t, J=5.5 Hz, 1H), 8.16 (d, J=2.2 Hz, 1H), 7.79 (dd, J=8.6, 2.3 Hz, 1H), 7.24 (dd, J=5.2, 3.5 Hz, 2H), 6.08 (d, J=1.5 Hz, 1H), 5.34 (dd, J=9.2, 3.4 Hz, 1H), 4.62 (d, J=9.5 Hz, 1H), 4.49 (br t, J=7.9 Hz, 1H), 4.41-4.24 (m, 3H), 4.09 (d, J=10.6 Hz, 1H), 4.04-3.93 (m, 3H), 3.90 (br d, J=8.8 Hz, 1H), 3.71 (dd, J=9.5, 7.1 Hz, 1H), 3.72 (s, 3H), 3.65 (dd, J=10.7, 3.7 Hz, 1H), 3.09-3.01 (m, 1H), 2.96 (br dd, J=10.9, 4.1 Hz, 1H), 2.56 (br d, J=3.6 Hz, 1H), 1.87-1.69 (m, 2H), 1.53-1.41 (m, 1H), 1.41-1.21 (m, 2H), 0.71-0.65 (m, 2H), 0.32 (br d, J=4.3 Hz, 2H)。	1.78, B

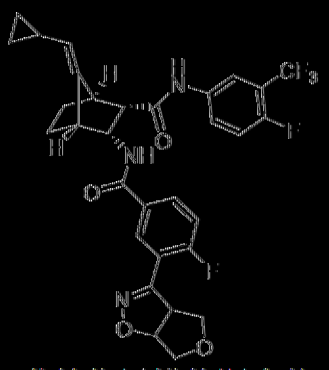
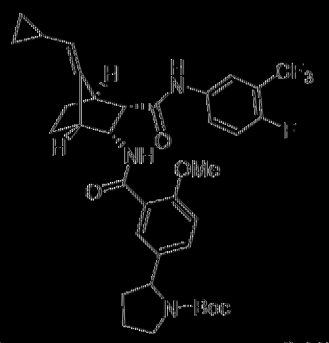
708		(1R,2S,3R,4R,7Z)-3-{5-[(7aS)-1H,5H,6H,7H,7aH-吡咯并[1,2-c]咪唑-3-基]-2-甲氧基苯甲醯胺基}-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	611.2	(500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.89 (br d, J=7.0 Hz, 1H), 8.30 (d, J=1.8 Hz, 1H), 8.20 (br d, J=4.3 Hz, 1H), 7.88 - 7.80 (m, 1H), 7.80 - 7.71 (m, 1H), 7.46 (br t, J=9.9 Hz, 1H), 7.24 (d, J=8.9 Hz, 1H), 4.67 (d, J=9.5 Hz, 1H), 4.51 - 4.37 (m, 1H), 4.11 - 4.00 (m, 3H), 3.96 - 3.82 (m, 2H), 3.25 - 3.18 (m, 1H), 3.17 - 3.11 (m, 1H), 3.10 - 2.98 (m, 2H), 2.74 - 2.67 (m, 1H), 1.95 - 1.81 (m, 4H) (與AcOH峰重疊), 1.79 - 1.58 (m, 3H), 1.53 - 1.26 (m, 4H), 0.79 - 0.65 (m, 2H), 0.33 (br s, 2H)。可能由於與溶劑峰重疊，一個質子在NMR中不可見。	2.21, B

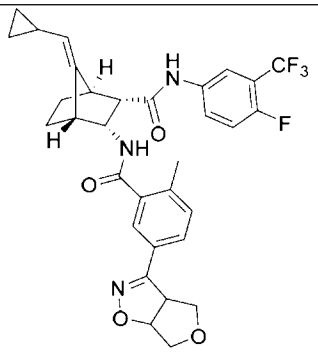
710	 非鏡像異構物混合物	N-{[1-(3-{[(1R,2R,3S,4R,7Z)-7-(羥亞胺甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-5-側氧基吡咯啶-3-基]甲基}胺基甲酸三級丁酯	712.9	(500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.89 (br dd, J= 13.9, 7.2 Hz, 1H), 8.23 (br s, 1H), 8.04 (br d, J= 3.1 Hz, 1H), 7.89 - 7.76 (m, 1H), 7.54 (br d, J= 8.5 Hz, 1H), 7.49 (br t, J= 9.8 Hz, 1H), 7.20 (br d, J= 8.5 Hz, 1H), 6.96 (br s, 1H), 4.70 (br d, J= 9.8 Hz, 1H), 4.45 (br d, J= 4.3 Hz, 1H), 4.25 (br s, 1H), 4.01 (s, 3H), 3.47 (br s, 1H), 3.16 (br dd, J= 10.7, 4.0 Hz, 1H), 3.09 (br d, J= 3.7 Hz, 1H), 3.00 - 2.88 (m, 1H), 2.72 (br s, 1H), 2.41 - 2.26 (m, 1H), 2.23 - 2.11 (m, 1H), 2.01 - 1.84 (m, 2H), 1.82 - 1.71 (m, 1H), 1.56 - 1.46 (m, 1H), 1.45 - 1.36 (m, 2H), 1.32 (s, 9H), 1.28 - 1.14 (m, 1H), 0.86 - 0.58 (m, 2H), 0.36 (br s, 2H)	2.50, B

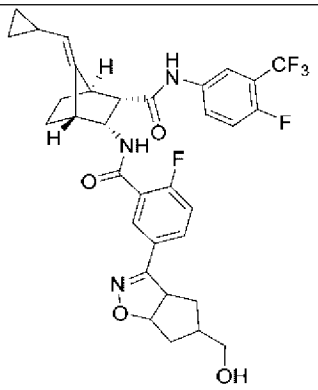
711	 經由逆相HPLC自實例511分離	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[2-(羥基甲基)-5-氧雜-6-氮雜螺[3.4]辛-6-烯-7-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	642.2	(500 MHz, DMSO-d6) δ 10.48 - 10.22 (m, 1H), 8.36 (br d, J=6.7 Hz, 1H), 8.14 (br d, J=4.0 Hz, 1H), 7.92 - 7.78 (m, 1H), 7.74 (br dd, J=8.5, 2.1 Hz, 1H), 7.47 (br t, J=9.8 Hz, 1H), 7.29 - 7.12 (m, 1H), 4.78 - 4.56 (m, 2H), 4.51 (d, J=9.5 Hz, 1H), 4.19 - 3.72 (m, 3H), 3.54 - 3.25 (m, 3H), 3.16 - 2.96 (m, 1H), 2.56 (br s, 1H), 2.47 - 2.40 (m, 2H), 2.39 - 2.29 (m, 1H), 2.28 - 2.22 (m, 1H), 2.15 - 2.07 (m, 2H), 1.89 - 1.80 (m, 1H), 1.71 - 1.58 (m, 2H), 1.54 - 1.42 (m, 2H), 0.80 - 0.60 (m, 2H), 0.40 - 0.24 (m, 2H)	2.36, B

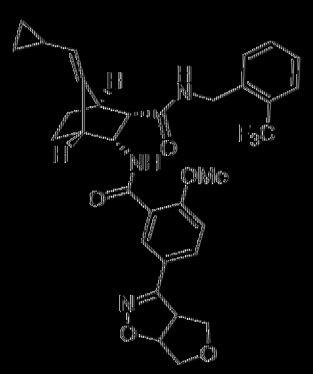
712	 非經修飾之結構之組合物	(1R,2S,3R,4R,7Z)-3-[5-[4-(胺基甲基)-2-側氧基吡咯啶-1-基]-2-甲氧基苯甲醯胺基]-7-(環丙基甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	615.3	(500 MHz, DMSO-d6) δ 10.56 (s, 1H), 10.04 – 9.79 (m, 1H), 8.41 – 8.17 (m, 1H), 8.12 – 7.96 (m, 1H), 7.99 – 7.83 (m, 1H), 7.88 – 7.74 (m, 1H), 7.61 – 7.42 (m, 2H), 7.35 – 7.08 (m, 1H), 4.69 (d, J= 9.7 Hz, 1H), 4.44 (br d, J= 2.0 Hz, 2H), 4.23 – 3.89 (m, 3H), 3.22 – 3.11 (m, 1H), 3.12 – 2.99 (m, 1H), 2.94 – 2.71 (m, 2H), 2.79 – 2.67 (m, 1H), 2.63 – 2.54 (m, 2H), 2.46 – 2.37 (m, 1H), 2.35 – 2.25 (m, 1H), 2.04 – 1.92 (m, 1H), 1.90 – 1.70 (m, 2H), 1.57 – 1.45 (m, 1H), 1.44 – 1.34 (m, 2H), 0.80 – 0.66 (m, 2H), 0.44 – 0.19 (m, 2H)	1.95, C

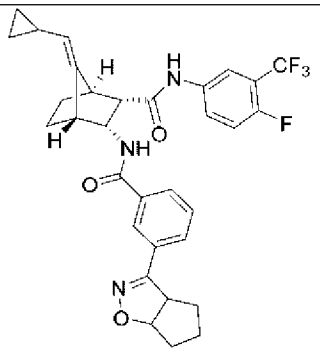
713		(1R,2S,3R,4R,7Z)-3-{5-[(3R,3aS,6S,6aR)-3,6-二羥基-六氫呋喃并[3,2-b]呋喃-3-基]-2-甲氧基苯甲醯胺基}-N-[4-氟-3-(三氟甲基)苯基]-7-(2,2,2-三氟亞乙基)雙環[2.2.1]庚烷-2-甲醯胺	674.8	(500 MHz, DMSO-d6) δ 10.68 (s, 1H), 9.92 (br d, J=6.7 Hz, 1H), 8.22 (br d, J=4.9 Hz, 1H), 8.08 (d, J=2.1 Hz, 1H), 7.86 - 7.76 (m, 1H), 7.62 (dd, J=8.5, 2.1 Hz, 1H), 7.50 (br t, J=9.9 Hz, 1H), 7.20 (d, J=8.9 Hz, 1H), 5.93 (q, J=8.1 Hz, 1H), 4.59 - 4.46 (m, 1H), 4.31 (br d, J=3.7 Hz, 1H), 4.25 - 4.14 (m, 2H), 4.00 (s, 3H), 3.94 (br dd, J=9.3, 3.2 Hz, 1H), 3.87 - 3.76 (m, 1H), 3.70 - 3.65 (m, 1H), 3.33 - 3.19 (m, 2H), 3.00 (br d, J=4.0 Hz, 1H), 2.00 (br t, J=9.9 Hz, 1H), 1.92 - 1.82 (m, 1H), 1.59 - 1.43 (m, 2H)	2.33, A

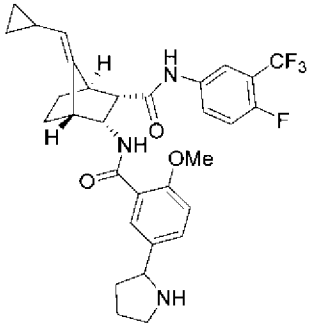
714	 非鏡像異構物混合物	(1R,2S,3R,4R,7Z)-3-(3-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-4-氟苯甲醯胺基)-7-(環丙基甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	602.1	(500 MHz, DMSO-d6) δ 10.64 - 10.37 (m, 1H), 9.33 (dd, J=14.8, 6.9 Hz, 1H), 8.14 (br d, J=5.5 Hz, 1H), 8.01 (br s, 1H), 7.94 - 7.84 (m, 1H), 7.82 (br s, 1H), 7.57 - 7.40 (m, 2H), 5.46 - 5.32 (m, 1H), 4.69 (d, J=9.5 Hz, 1H), 4.56 - 4.46 (m, 1H), 4.41 - 4.32 (m, 1H), 4.12 (br dd, J=10.8, 1.7 Hz, 1H), 3.96 - 3.88 (m, 1H), 3.78 - 3.69 (m, 1H), 3.65 (br dd, J=10.8, 3.6 Hz, 1H), 3.62 (br s, 1H), 3.16 (br dd, J=10.4, 3.4 Hz, 1H), 3.08 (br d, J=2.8 Hz, 1H), 1.91 - 1.80 (m, 1H), 1.79 - 1.63 (m, 1H), 1.53 - 1.32 (m, 3H), 0.73 (quin, J=9.9 Hz, 2H), 0.35 (br s, 2H)	2.50, C
715	 峰2，RT：5.48 min，製備型對掌性SFC純化條件：儀器詳情：品牌/型號：PIC 175；製備型SFC條件：管柱/尺寸：Chiralpak IG (250×30)mm，5u，% CO_2: 75%，%助溶劑：25% 4M甲醇氨於MEOH中，總流速：130.0 g/min，背壓：100巴，溫度：40℃，UV：240 nm。	2-(3-{[(2R,3S,7Z)-7-(環丙基甲基)-3-[4-氟-3-(三氟甲基)苯基胺甲醯基]雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)吡咯啶-1-甲酸三級丁酯	672.4	(400MHz, CD_3OD) δ ppm 8.18 - 8.12 (m, 1H), 7.89 - 7.84 (m, 1H), 7.71 - 7.70 (m, 1H), 7.37 - 7.24 (m, 2H), 7.16 - 7.08 (m, 1H), 4.82 - 4.74 (m, 1H), 4.74 - 4.68 (m, 1H), 4.59 - 4.52 (m, 1H), 4.09 - 4.03 (m, 3H), 3.99 - 3.96 (m, 1H), 3.68 - 3.49 (m, 2H), 3.23 - 3.16 (m, 1H), 3.17 - 3.10 (m, 2H), 2.74 - 2.66 (m, 1H), 2.41 - 2.26 (m, 1H), 2.08 - 1.71 (m, 6H), 1.60 - 1.35 (m, 7H), 1.24 - 1.07 (m, 7H), 0.80 - 0.71 (m, 2H), 0.41 - 0.29 (m, 2H)。	1.58, C

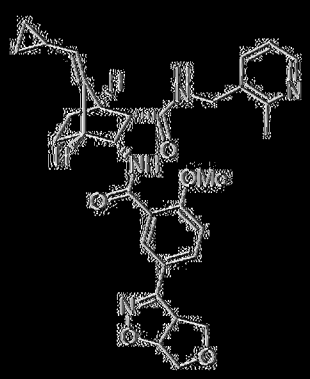
716	 實例716 (峰2)及實例654 (峰1)- 儀器：Waters 100 Prep SFC管柱：Chiral OD，30 × 250 mm，5微米，移動相：15% MeOH / 85% CO_2 (具有0.1% DEA)，流動條件：100 mL/min，偵測器波長：220 nm；分析方法：儀器：Shimadzu Nexera SFC，管柱Chiral OD，4.6 × 100 mm，5微米，移動相：15% MeOH / 85% CO_2 (具有0.1% DEA)，流動條件：2 mL/min，偵測器波長：220 nm，得到對掌性(峰-1，RT=4.7 min.，>95% de)及對掌性(峰-2，RT=6.7 min.，>95% de)。	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲基苯甲醯胺基)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	598.2	(500 MHz, DMSO-d6) δ 10.55 - 10.37 (m, 1H), 8.74 (d, J=7.2 Hz, 2H), 8.03 (br d, J=5.8 Hz, 1H), 7.86 - 7.78 (m, 1H), 7.66 - 7.60 (m, 3H), 7.45 (br t, J=9.8 Hz, 1H), 7.34 (d, J=7.9 Hz, 1H), 5.35 (dd, J=9.2, 3.4 Hz, 2H), 4.68 (d, J=9.5 Hz, 2H), 4.49 - 4.35 (m, 3H), 4.10 (d, J=10.6 Hz, 1H), 3.95 (br d, J=9.6 Hz, 1H), 3.74 - 3.59 (m, 2H), 3.15 (br dd, J=10.5, 4.4 Hz, 1H), 1.93 (br d, J=7.5 Hz, 1H), 1.85 - 1.76 (m, 1H), 1.52 (dt, J=8.2, 4.0 Hz, 2H), 1.47 - 1.45 (m, 1H), 1.41 - 1.34 (m, 1H), 0.81 - 0.65 (m, 2H), 0.48 - 0.24 (m, 2H)	2.44, B

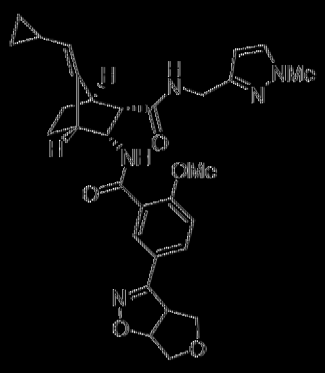
717	 由同對掌性苯甲酸酯中間物(峰1；100%ee；對掌性分析型RT=1.922 min)製備；製備型對掌性SFC條件：儀器：Berger MG II;管柱：Chiralpak AD-H，21 × 250 mm，5微米；移動相：20% MeOH / 80% CO_2；流動條件：45 mL/min，150巴，40℃；偵測器波長：220 nm；注射詳情：0.5 mL ~125mg/mL於MeOH:CAN中	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{2-氟-5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	630.3	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.35 (br t, J=6.7 Hz, 1H), 8.09 - 7.99 (m, 2H), 7.90 - 7.82 (m, 2H), 7.52 - 7.40 (m, 2H), 5.15 (dd, J=8.8, 5.3 Hz, 1H), 4.70 (d, J=9.6 Hz, 1H), 4.47 - 4.41 (m, 1H), 4.24 - 4.17 (m, 1H), 3.41 - 3.29 (m, 2H), 3.17 (dd, J=10.7, 4.1 Hz, 1H), 3.12 (t, J=3.7 Hz, 1H), 2.74 (t, J=3.7 Hz, 1H), 2.00 (br dd, J=13.7, 5.9 Hz, 1H), 1.94 - 1.81 (m, 2H), 1.80 - 1.74 (m, 2H), 1.65 - 1.40 (m, 5H), 0.78 - 0.69 (m, 2H), 0.38 - 0.32 (m, 2H)	1.35, A

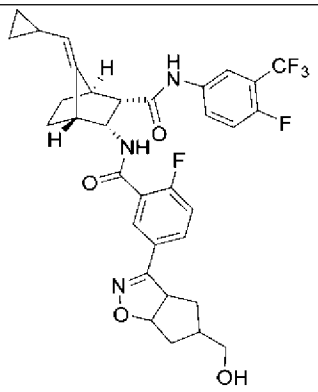
718	 I-416 2製備	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-{[2-(三氟甲基)苯基]甲基}雙環[2.2.1]庚烷-2-甲醯胺	610.2	(500 MHz, DMSO-d6) δ 9.89 (d, J = 7.0 Hz, 1H), 8.73 (br t, J = 5.8 Hz, 1H), 8.18 (br d, J = 1.2 Hz, 1H), 7.76 (dd, J = 8.7, 2.3 Hz, 1H), 7.71 – 7.65 (m, 1H), 7.54 – 7.46 (m, 1H), 7.46 – 7.36 (m, 2H), 7.18 (d, J = 8.7 Hz, 1H), 5.33 (dd, J = 9.2, 3.4 Hz, 1H), 4.64 (d, J = 9.5 Hz, 1H), 4.52 – 4.41 (m, 3H), 4.39 – 4.28 (m, 1H), 4.08 (d, J = 10.7 Hz, 1H), 3.92 – 3.87 (m, 1H), 3.86 – 3.79 (m, 3H), 3.78 – 3.72 (m, 1H), 3.66 – 3.61 (m, 1H), 3.09 – 3.01 (m, 2H), 2.67 – 2.60 (m, 1H), 1.86 – 1.77 (m, 1H), 1.75 – 1.64 (m, 1H), 1.55 – 1.42 (m, 1H), 1.39 – 1.27 (m, 2H), 0.75 – 0.63 (m, 2H), 0.41 – 0.22 (m, 2H)。	2.37, C

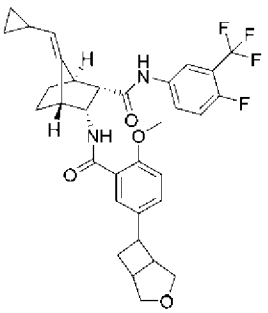
719	 由同對掌性苯甲酸中間物(峰-1，RT=2.55 min.，>99% ee)製備 –所用儀器：Berger MG II管柱：Chiralpak IA，21 × 250 mm，5微米，移動相：20% IPA / 80% CO_2，流動條件：45 mL/min，150巴，40℃，偵測器波長：220 nm；分析方法：儀器：Shimadzu Nexera SFC，管柱Chiralpak IA，4.6 × 100 mm，3微米，移動相：20% IPA / 80% CO_2，流動條件：2 mL/min，150巴，40℃，偵測器波長：220 nm，得到對掌性(峰-1，RT=2.55 min.，>99% ee)及對掌性(峰-2，RT=6.53 min.，>99% ee)。	(1R,2S,3R,4R,7Z)-3-(3-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}苯甲醯胺基)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	584.1	(500 MHz, DMSO-d6) δ 10.62 - 10.49 (m, 1H), 9.39 (br d, J=6.7 Hz, 1H), 8.15 - 7.97 (m, 2H), 7.91 - 7.74 (m, 3H), 7.61 (t, J=7.8 Hz, 1H), 7.48 (t, J=9.7 Hz, 1H), 5.41 (dd, J=9.3, 3.6 Hz, 1H), 4.87 - 4.67 (m, 1H), 4.59 - 4.51 (m, 1H), 4.46 - 4.37 (m, 1H), 4.13 (d, J=10.6 Hz, 1H), 3.94 (br d, J=9.3 Hz, 1H), 3.78 - 3.64 (m, 2H), 3.48 (br d, J=9.0 Hz, 1H), 3.43 - 3.39 (m, 1H), 3.18 (br dd, J=10.4, 4.0 Hz, 1H), 3.11 (br d, J=3.3 Hz, 1H), 2.76 (br s, 1H), 1.91 - 1.84 (m, 1H), 1.78 - 1.72 (m, 1H), 1.59 - 1.49 (m, 1H), 0.82 - 0.69 (m, 2H), 0.39 - 0.35 (m, 2H)	2.42, B

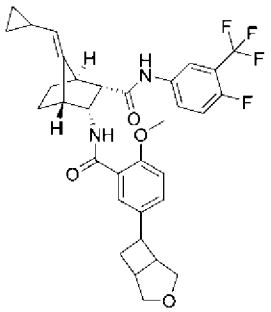
720	 由實例715製備	(2S,3R)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-[2-甲氧基-5-(吡咯啶-2-基)苯甲醯胺基]雙環[2.2.1]庚烷-2-甲醯胺	572.3	(400 MHz, DMSO-d6) δ = 10.54 (s, 1H), 9.91 (d, J = 7.1 Hz, 1H), 9.28 (br d, J = 5.6 Hz, 1H), 8.76 - 8.54 (m, 1H), 8.24 (dd, J = 2.6, 6.7 Hz, 1H), 8.07 (d, J = 2.7 Hz, 1H), 7.86 - 7.73 (m, 1H), 7.61 (dd, J = 2.4, 8.6 Hz, 1H), 7.49 (t, J = 9.8 Hz, 1H), 7.27 (d, J = 8.8 Hz, 1H), 4.69 (d, J = 9.8 Hz, 1H), 4.62 - 4.51 (m, 1H), 4.49 - 4.38 (m, 1H), 4.02 (s, 3H), 3.29 - 3.25 (m, 1H), 3.20 - 3.12 (m, 1H), 3.09 (t, J = 3.9 Hz, 1H), 2.72 (br s, 1H), 2.37 - 2.30 (m, 1H), 2.15 - 1.96 (m, 3H), 1.82 (br d, J = 9.3 Hz, 1H), 1.79 - 1.66 (m, 1H), 1.54 - 1.44 (m, 1H), 1.44 - 1.31 (m, 2H), 0.81 - 0.67 (m, 2H), 0.45 - 0.22 (m, 2H)	2.08, A

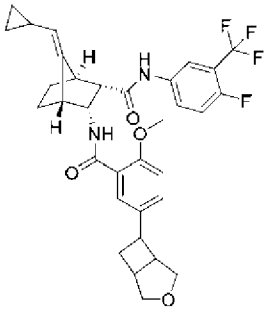
121	 由化合物製備	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-[(2-甲基吡啶-3-基)甲基]雙環[2.2.1]庚烷-2-甲醯胺	557.3	(500 MHz, DMSO-d6) δ 9.91 (d, J = 7.0 Hz, 1H), 8.64 - 8.55 (m, 1H), 8.27 (d, J = 4.7 Hz, 1H), 8.17 (d, J = 2.2 Hz, 1H), 7.78 (dd, J = 8.7, 2.3 Hz, 1H), 7.50 (d, J = 7.3 Hz, 1H), 7.21 (d, J = 8.8 Hz, 1H), 7.08 (dd, J = 7.6, 4.9 Hz, 1H), 5.34 (dd, J = 9.2, 3.5 Hz, 1H), 4.63 (d, J = 9.6 Hz, 1H), 4.49 (br t, J = 8.1 Hz, 1H), 4.38 - 4.24 (m, 3H), 4.09 (d, J = 10.6 Hz, 1H), 3.96 - 3.86 (m, 4H), 3.80 - 3.74 (m, 1H), 3.69 - 3.61 (m, 1H), 3.07 - 2.97 (m, 2H), 2.62 - 2.56 (m, 1H), 2.43 (s, 3H), 1.87 - 1.78 (m, 1H), 1.76 - 1.69 (m, 1H), 1.52 - 1.42 (m, 1H), 1.40 - 1.27 (m, 2H), 0.77 - 0.65 (m, 2H), 0.38 - 0.25 (m, 2H)。	1.90, B

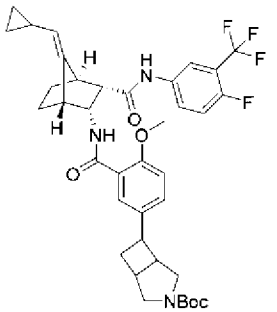
122	 中416-3製備	(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基甲基)-N-[(1-甲基-1H-吡唑-3-基)甲基]雙環[2.2.1]庚烷-2-甲醯胺	546.0	(500 MHz, DMSO-d6) δ 9.98 (d, J = 6.9 Hz, 1H), 8.47 (t, J = 5.8 Hz, 1H), 8.15 (d, J = 2.2 Hz, 1H), 7.79 (dd, J = 8.6, 2.4 Hz, 1H), 7.50 (d, J = 2.0 Hz, 1H), 7.23 (d, J = 8.8 Hz, 1H), 6.03 (d, J = 2.1 Hz, 1H), 5.33 (dd, J = 9.2, 3.5 Hz, 1H), 4.61 (d, J = 9.6 Hz, 1H), 4.48 (br t, J = 8.0 Hz, 1H), 4.32 – 4.26 (m, 1H), 4.25 – 4.16 (m, 2H), 4.09 (d, J = 10.8 Hz, 1H), 3.99 (s, 3H), 3.90 (br d, J = 9.2 Hz, 1H), 3.77 (dd, J = 9.4, 7.0 Hz, 1H), 3.73 (s, 3H), 3.65 (dd, J = 10.8, 3.7 Hz, 1H), 3.06 – 3.01 (m, 1H), 2.94 (dd, J = 10.7, 4.3 Hz, 1H), 1.91 – 1.80 (m, 1H), 1.78 – 1.67 (m, 1H), 1.52 – 1.41 (m, 1H), 1.39 – 1.25 (m, 2H), 0.78 – 0.63 (m, 2H), 0.38 – 0.22 (m, 2H)。可能由於與溶劑峰重疊，一個質子在NMR中不可見。	1.78, B

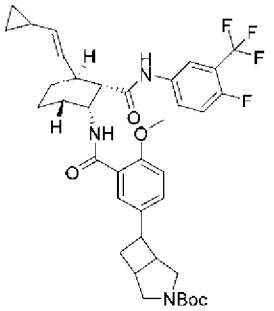
723	 由同對掌性苯甲酸酯中間物(峰4；100%ee；對掌性分析型RT=9.061 min)製備；製備型對掌性SFC條件：儀器：Berger MG II；管柱：Chiralpak AD-H，21 × 250 mm，5微米；移動相：20% MeOH / 80% CO_2；流動條件：45 mL/min，150巴，40℃；偵測器波長：220 nm；注射詳情：0.5 mL ~125mg/mL於MeOH:CAN中	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{2-氟-5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	630.3	(500 MHz, DMSO-d6) δ 10.52 (s, 1H), 9.38 (t, J=6.7 Hz, 1H), 8.08 (dd, J=7.2, 2.3 Hz, 1H), 8.00 (dd, J=6.4, 2.4 Hz, 1H), 7.89 - 7.83 (m, 2H), 7.51 - 7.43 (m, 2H), 5.21 - 5.15 (m, 1H), 4.73 - 4.68 (m, 1H), 4.47 - 4.42 (m, 1H), 4.14 (td, J=9.8, 6.3 Hz, 1H), 3.32 - 3.26 (m, 1H), 3.23 - 3.15 (m, 2H), 3.13 (t, J=3.7 Hz, 1H), 2.77 - 2.73 (m, 1H), 2.24 - 2.09 (m, 3H), 1.86 - 1.80 (m, 1H), 1.79 - 1.73 (m, 1H), 1.68 - 1.61 (m, 1H), 1.53 - 1.41 (m, 4H), 0.79 - 0.70 (m, 2H), 0.38 - 0.32 (m, 2H)	1.35, A

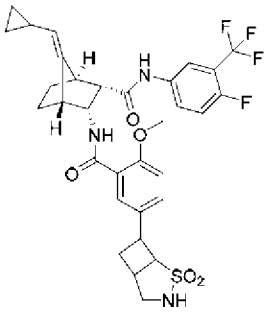
726	 由同對掌性苯甲酸酯中間物**726-1**製備	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-(2-甲氧基-5-{3-氧雜雙環[3.2.0]庚烷-6-基}苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	599.0	(500 MHz, DMSO-d6) δ 10.49 (s, 1H), 9.81 (d, J=7.2 Hz, 1H), 8.23 (dd, J=6.6, 2.6 Hz, 1H), 7.84 (d, J=2.4 Hz, 1H), 7.78 (dt, J=8.5, 3.8 Hz, 1H), 7.49 (t, J=9.8 Hz, 1H), 7.41 (dd, J=8.5, 2.4 Hz, 1H), 7.13 (d, J=8.7 Hz, 1H), 4.69 (d, J=9.6 Hz, 1H), 4.49 - 4.41 (m, 1H), 3.97 (s, 3H), 3.91 - 3.84 (m, 2H), 3.48 (dd, J=9.2, 5.8 Hz, 1H), 3.39 (dd, J=9.2, 4.7 Hz, 1H), 3.15 (dd, J=10.7, 4.3 Hz, 1H), 3.13 - 3.06 (m, 2H), 3.00 - 2.90 (m, 1H), 2.89 - 2.83 (m, 1H), 2.72 (t, J=3.7 Hz, 1H), 2.16 (dt, J=12.3, 8.1 Hz, 1H), 2.09 - 2.01 (m, 1H), 1.87 (br t, J=8.7 Hz, 1H), 1.81 - 1.74 (m, 1H), 1.55 - 1.47 (m, 1H), 1.46 - 1.34 (m, 2H), 0.82 - 0.70 (m, 2H), 0.36 (dd, J=4.5, 2.5 Hz, 2H)。	2.7, A

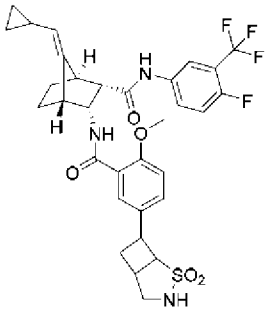
727	 由同對掌性苯甲酸酯中間物**727-1**製備	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-(2-甲氧基-5-{3-氧雜雙環[3.2.0]庚烷-6-基}苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	599.3	(500 MHz, DMSO-d6) δ 10.50 (s, 1H), 9.81 (d, J=7.2 Hz, 1H), 8.23 (dd, J=6.6, 2.6 Hz, 1H), 7.83 (d, J=2.4 Hz, 1H), 7.78 (dt, J=8.5, 3.8 Hz, 1H), 7.48 (t, J=9.8 Hz, 1H), 7.41 (dd, J=8.6, 2.4 Hz, 1H), 7.12 (d, J=8.5 Hz, 1H), 4.69 (d, J=9.6 Hz, 1H), 4.48 - 4.39 (m, 1H), 3.97 (s, 3H), 3.93 - 3.84 (m, 2H), 3.48 (dd, J=9.1, 5.7 Hz, 1H), 3.39 (dd, J=9.2, 4.8 Hz, 1H), 3.15 (dd, J=10.8, 4.3 Hz, 1H), 3.11 - 3.06 (m, 2H), 2.97 - 2.90 (m, 1H), 2.89 - 2.84 (m, 1H), 2.72 (t, J=3.6 Hz, 1H), 2.15 (dt, J=12.3, 8.1 Hz, 1H), 2.09 - 2.00 (m, 1H), 1.87 (br t, J=8.9 Hz, 1H), 1.82 - 1.73 (m, 1H), 1.56 - 1.47 (m, 1H), 1.46 - 1.33 (m, 2H), 0.81 - 0.69 (m, 2H), 0.36 (dd, J=4.5, 2.5 Hz, 2H)	2.7, A

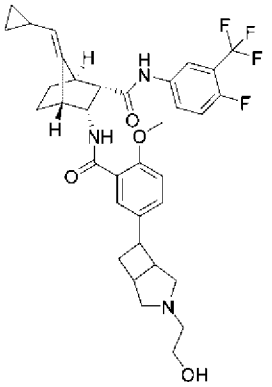
728	 由同對掌性苯甲酸酯中間物**728-1**製備	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-(2-甲氧基-5-{3-氧雜雙環[3.2.0]庚烷-6-基}苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	599.2	(500 MHz, DMSO-d6) δ 10.49 (s, 1H), 9.82 (d, J=7.3 Hz, 1H), 8.23 (dd, J=6.6, 2.4 Hz, 1H), 7.78 (dt, J=8.5, 3.8 Hz, 1H), 7.74 (d, J=2.3 Hz, 1H), 7.49 (t, J=9.8 Hz, 1H), 7.30 (dd, J=8.5, 2.3 Hz, 1H), 7.14 (d, J=8.5 Hz, 1H), 4.69 (d, J=9.6 Hz, 1H), 4.49 - 4.40 (m, 1H), 3.98 (s, 3H), 3.71 (d, J=9.0 Hz, 1H), 3.69 - 3.62 (m, 1H), 3.41 (d, J=9.9 Hz, 1H), 3.29 (dd, J=9.0, 4.4 Hz, 1H), 3.23 (dd, J=9.7, 6.6 Hz, 1H), 3.20 - 3.12 (m, 2H), 3.09 (t, J=3.9 Hz, 1H), 3.03 - 2.94 (m, 1H), 2.71 (t, J=3.8 Hz, 1H), 2.42 - 2.33 (m, 1H), 1.97 (ddd, J=11.8, 9.8, 6.6 Hz, 1H), 1.91 - 1.84 (m, 1H), 1.83 - 1.75 (m, 1H), 1.57 - 1.47 (m, 1H), 1.46 - 1.33 (m, 2H), 0.81 - 0.68 (m, 2H), 0.40 - 0.32 (m, 2H)。	2.72, A

729	 由同對掌性苯甲酸酯中間物(峰1；100%ee；對掌性分析型RT=5.14 min)製備；Chiralpak ID，4.6 × 100 mm，3微米，移動相：10%異丙醇/90% CO_2，流動條件：2.0 mL/min，150巴，40℃	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-(2-甲氧基-5-{3-氧雜雙環[3.2.0]庚烷-6-基}苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	599.0	(500 MHz, DMSO-d6) δ 10.49 (s, 1H), 9.83 (d, J=7.3 Hz, 1H), 8.23 (dd, J=6.5, 2.5 Hz, 1H), 7.78 (dt, J=8.8, 3.5 Hz, 1H), 7.74 (d, J=2.3 Hz, 1H), 7.48 (t, J=9.8 Hz, 1H), 7.30 (dd, J=8.5, 2.3 Hz, 1H), 7.14 (d, J=8.5 Hz, 1H), 4.69 (d, J=9.6 Hz, 1H), 4.49 - 4.41 (m, 1H), 3.98 (s, 3H), 3.72 (d, J=9.0 Hz, 1H), 3.66 (q, J=9.6 Hz, 1H), 3.41 (d, J=9.8 Hz, 1H), 3.29 (dd, J=8.9, 4.3 Hz, 1H), 3.23 (dd, J=9.6, 6.6 Hz, 1H), 3.19 - 3.12 (m, 2H), 3.08 (t, J=3.7 Hz, 1H), 3.02 - 2.94 (m, 1H), 2.71 (t, J=3.7 Hz, 1H), 2.38 (dddd, J=12.0, 10.1, 8.3, 2.1 Hz, 1H), 1.97 (ddd, J=11.7, 9.6, 6.8 Hz, 1H), 1.87 (br t, J=9.0 Hz, 1H), 1.82 - 1.77 (m, 1H), 1.55 - 1.46 (m, 1H), 1.45 - 1.34 (m, 2H), 0.82 - 0.67 (m, 2H), 0.36 (dd, J=4.6, 2.3 Hz, 2H)。	2.73, A

730	 由同對掌性苯甲酸酯中間物(峰2；100%ee；對掌性分析型RT=7.08 min)製備；Chiralpak ID，4.6 × 100 mm，3微米，移動相：10%異丙醇/90% CO_2，流動條件：2.0 mL/min，150巴，40℃	6-(3-{[(1R,2R,3S,4R,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-3-氮雜雙環[3.2.0]庚烷-3-甲酸三級丁酯	698.5	(500 MHz, $CDCl_3$-d) δ 9.41 (br d, J=7.3 Hz, 1H), 8.09 (br s, 1H), 7.98 (br s, 1H), 7.90 - 7.81 (m, 1H), 7.65 - 7.55 (m, 1H), 7.35 - 7.30 (m, 1H), 7.12 - 7.04 (m, 1H), 6.92 (br d, J=8.4 Hz, 1H), 4.89 - 4.80 (m, 1H), 4.65 (d, J=9.5 Hz, 1H), 3.99 (s, 3H), 3.80 - 3.60 (m, 2H), 3.47 (br d, J=7.6 Hz, 1H), 3.33 - 3.24 (m, 2H), 3.20 (t, J=3.9 Hz, 1H), 3.11 (dd, J=10.6, 3.1 Hz, 1H), 2.95 (br s, 2H), 2.74 (t, J=3.7 Hz, 1H), 2.39 - 2.28 (m, 1H), 2.24 - 2.15 (m, 2H), 1.93 - 1.84 (m, 1H), 1.57 - 1.45 (m, 10H), 0.80 - 0.73 (m, 2H), 0.39 - 0.32 (m, 2H)	2.96, A

731	 由同對掌性苯甲酸酯中間物(峰1；100%ee；對掌性分析型RT=3.13 min)製備；Chiral AD，4.6 × 100 mm，5微米，移動相：75% CO_2/25% IPA (具有0.1%DEA)，流動條件：2 mL/min	6-(3-{[(1R,2R,3S,4R,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-3-氮雜雙環[3.2.0]庚烷-3-甲酸三級丁酯	698.5	(500 MHz, $CDCl_3$-d) δ 9.41 (br d, J=8.1 Hz, 1H), 8.09 (br s, 1H), 7.98 (br s, 1H), 7.89 - 7.83 (m, 1H), 7.63 - 7.56 (m, 1H), 7.34 - 7.29 (m, 1H), 7.12 - 7.04 (m, 1H), 6.92 (d, J=8.4 Hz, 1H), 4.89 - 4.80 (m, 1H), 4.65 (d, J=9.6 Hz, 1H), 3.99 (s, 3H), 3.79 - 3.62 (m, 2H), 3.52 - 3.43 (m, 1H), 3.35 - 3.25 (m, 2H), 3.20 (t, J=3.9 Hz, 1H), 3.11 (dd, J=10.7, 3.4 Hz, 1H), 2.95 (br s, 2H), 2.74 (t, J=3.8 Hz, 1H), 2.36 - 2.28 (m, 1H), 2.23 - 2.14 (m, 2H), 1.91 - 1.84 (m, 1H), 1.56 - 1.44 (m, 10H), 0.79 - 0.73 (m, 2H), 0.40 - 0.32 (m, 2H)	2.96, A

732	 由同對掌性苯甲酸酯中間物(峰2；100%ee；對掌性分析型RT=4.10 min)製備；Chiral AD，4.6 × 100 mm，5微米，移動相：75% CO_2/25% IPA (具有0.1%DEA)，流動條件：2 mL/min	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-3-(5-{2,2-二側氧基-2λ⁶-硫雜-3-氮雜雙環[3.2.0]庚烷-7-基}-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	648.4	1H NMR (500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.89 (br d, J=7.0 Hz, 1H), 8.26 (br d, J=4.3 Hz, 1H), 7.90 - 7.74 (m, 2H), 7.57 - 7.39 (m, 3H), 7.21 (br d, J=8.2 Hz, 1H), 4.72 (br d, J=9.8 Hz, 1H), 4.54 - 4.39 (m, 1H), 4.02 (s, 3H), 3.87 - 3.76 (m, 1H), 3.72 (br t, J=6.6 Hz, 1H), 3.26 - 3.14 (m, 2H), 3.12 (br s, 1H), 2.74 (br s, 1H), 2.49 - 2.40 (m, 1H), 2.38 - 2.28 (m, 1H), 1.93 - 1.72 (m, 2H), 1.60 - 1.50 (m, 1H), 1.49 - 1.35 (m, 2H), 0.83 - 0.65 (m, 2H), 0.38 (br s, 2H)	2.47, A

733	 由同對掌性苯甲酸酯中間物(峰1；100%ee；對掌性分析型RT=4.32 min)製備；SFC (Chiral IA，4.6 × 100 mm)，3微米，移動相：15%異丙醇/ 85% CO_2，流動條件：2.0 mL/min，150巴，40℃	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-3-(5-{2,2-二側氧基-2λ⁶-硫雜-3-氮雜雙環[3.2.0]庚烷-7-基}-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	648.4	1H NMR (500 MHz, DMSO-d6) δ 10.52 (s, 1H), 9.86 (d, J=7.2 Hz, 1H), 8.22 (dd, J=6.7, 2.4 Hz, 1H), 7.82 (d, J=2.3 Hz, 1H), 7.80 - 7.73 (m, 1H), 7.54 - 7.41 (m, 3H), 7.18 (d, J=8.6 Hz, 1H), 4.69 (d, J=9.7 Hz, 1H), 4.52 - 4.37 (m, 1H), 3.99 (s, 3H), 3.83 - 3.74 (m, 1H), 3.70 (t, J=6.8 Hz, 1H), 3.23 - 3.12 (m, 2H), 3.09 (t, J=3.6 Hz, 1H), 2.76 - 2.68 (m, 1H), 2.45 - 2.37 (m, 1H), 2.36 - 2.26 (m, 1H), 1.89 - 1.82 (m, 1H), 1.81 - 1.72 (m, 1H), 1.58 - 1.46 (m, 1H), 1.45 - 1.32 (m, 2H), 0.85 - 0.64 (m, 2H), 0.41 - 0.28 (m, 2H)	2.47, A

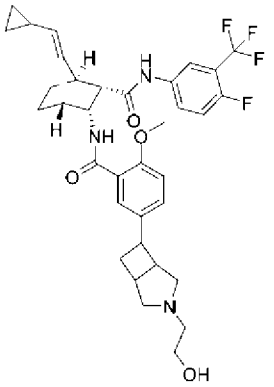
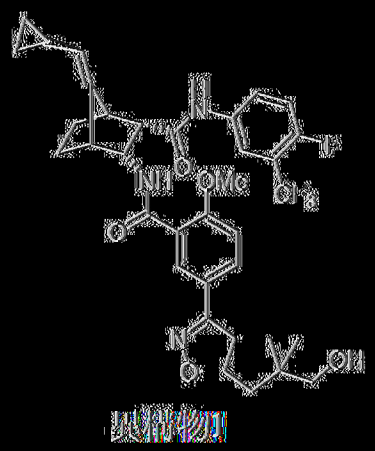
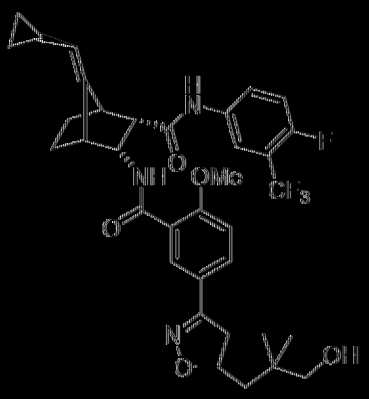
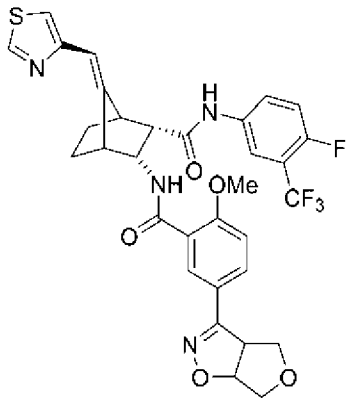
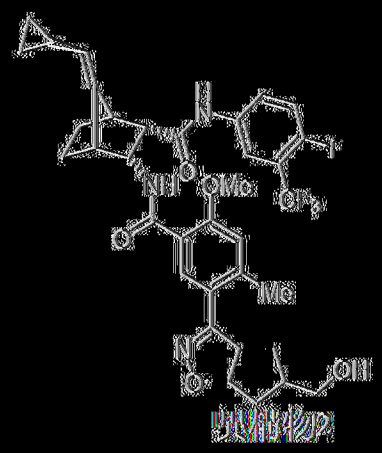
734	 由同對掌性苯甲酸酯中間物(峰2；100%ee；對掌性分析型RT=5.90 min)製備；SFC (Chiral IA，4.6×100 mm)，3微米，移動相：15%異丙醇/ 85% CO_2，流動條件：2.0 mL/min，150巴，40℃	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[3-(3-羥基丙基)-4-側氧基-3-氮雜雙環[3.2.0]庚烷-6-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	670.2	1H NMR (500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.86 (br d, J=7.3 Hz, 1H), 8.30 - 8.19 (m, 1H), 7.89 (s, 1H), 7.83 - 7.75 (m, 1H), 7.54 - 7.40 (m, 2H), 7.17 (d, J=8.5 Hz, 1H), 4.70 (d, J=9.5 Hz, 1H), 4.54 - 4.42 (m, 1H), 4.00 (s, 3H), 3.90 (br s, 1H), 3.69 (ddd, J=14.3, 9.9, 8.1 Hz, 1H), 3.30 - 3.22 (m, 1H), 3.21 - 3.12 (m, 2H), 3.11 (br s, 1H), 3.05 - 2.95 (m, 1H), 2.93 - 2.85 (m, 1H), 2.73 (br s, 1H), 2.43 - 2.29 (m, 2H), 1.94 - 1.85 (m, 1H), 1.80 (br dd, J=15.7, 6.0 Hz, 1H), 1.57 - 1.33 (m, 3H), 1.08 (br d, J=6.1 Hz, 3H), 0.83 - 0.68 (m, 2H), 0.36 (br s, 2H)	2.46, A

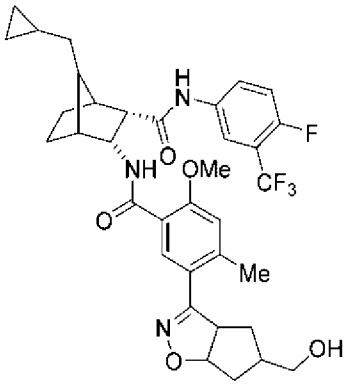
表4

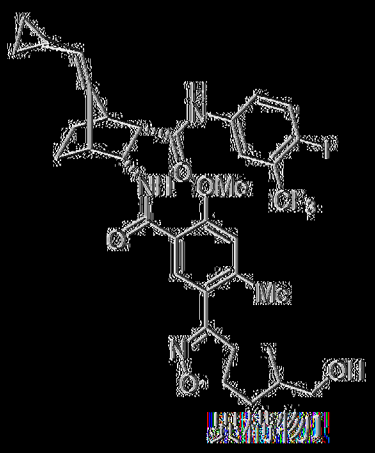
實例編號	結構	名稱	MS (ESI) (M+H)	^{1}H NMR	LC RT Meth. (min)
735	 異構物1	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(羥甲基)-5-甲基-3a,4,5,6,6a-四氫戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	656.2	(400 MHz, DMSO-d6) δ: 10.52 (s, 1H), 9.92 (d, J = 7.3 Hz, 1H), 8.27 - 8.17 (m, 2H), 7.79 (dd, J = 2.5, 8.8 Hz, 2H), 7.49 (t, J = 9.9 Hz, 1H), 7.26 (d, J = 8.8 Hz, 1H), 5.25 - 5.14 (m, 1H), 4.69 (d, J = 9.5 Hz, 1H), 4.63 - 4.54 (m, 1H), 4.49 - 4.38 (m, 1H), 4.30 - 4.17 (m, 1H), 4.04 (s, 3H), 3.20 - 3.07 (m, 4H), 2.72 (br d, J = 3.0 Hz, 1H), 1.87 - 1.73 (m, 5H), 1.66 (dd, J = 6.5, 13.0 Hz, 1H), 1.54 - 1.45 (m, 1H), 1.44 - 1.37 (m, 2H), 0.95 (s, 3H), 0.80 - 0.68 (m, 2H), 0.41 - 0.28 (m, 2H)	1.96, A

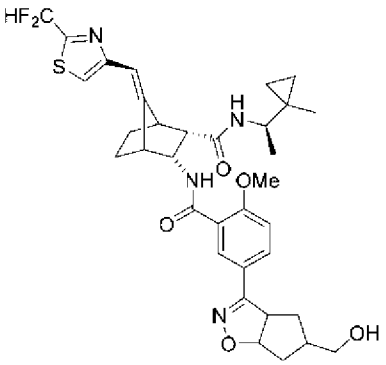
736	 異構物2	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(羥甲基)-5-甲基-3a,4,5,6,6a-四氫戊并[d][1,2]㗁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	656.2	(400 MHz, DMSO-d6) δ 10.52 (s, 1H), 9.92 (d, J = 7.3 Hz, 1H), 8.27 - 8.17 (m, 2H), 7.79 (dd, J = 2.5, 8.8 Hz, 2H), 7.49 (t, J = 9.9 Hz, 1H), 7.26 (d, J = 8.8 Hz, 1H), 5.25 - 5.14 (m, 1H), 4.69 (d, J = 9.5 Hz, 1H), 4.63 - 4.54 (m, 1H), 4.49 - 4.38 (m, 1H), 4.30 - 4.17 (m, 1H), 4.04 (s, 3H), 3.20 - 3.07 (m,4H), 2.72 (br d, J = 3.0 Hz, 1H), 1.87 - 1.73 (m, 5H), 1.66 (dd, J = 6.5, 13.0 Hz, 1H), 1.54 - 1.45 (m, 1H), 1.44 - 1.37 (m, 2H), 0.95 (s, 3H), 0.80 - 0.68 (m,2H), 0.41 - 0.28 (m, 2H)	2.38, A

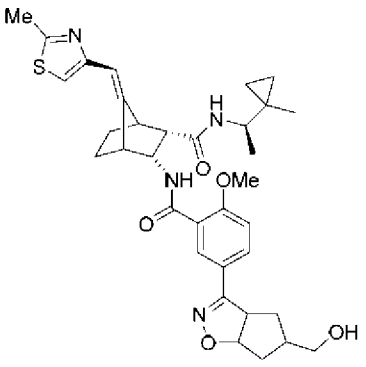
737		(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-[(1,3-噻唑-4-基)亞甲基]雙環[2.2.1]庚烷-2-甲醯胺	657.2	(400 MHz, DMSO-d6) δ = 10.60 (s, 1H), 9.90 (d, J = 7.1 Hz, 1H), 9.13 (d, J = 2.0 Hz, 1H), 8.25 (dd, J = 2.6, 6.5 Hz, 1H), 8.21 (d, J = 2.4 Hz, 1H), 7.87 - 7.74 (m, 2H), 7.58 (d, J = 2.2 Hz, 1H), 7.51 (t, J = 9.7 Hz, 1H), 7.29 (d, J = 8.8 Hz, 1H), 6.43 (s, 1H), 5.35 (dd, J = 3.7, 9.3 Hz, 1H), 4.56 - 4.47 (m, 2H), 4.10 (d, J = 10.8 Hz, 1H), 4.06 (s, 3H), 3.94 (br s, 1H), 3.90 (d, J = 8.3 Hz, 1H), 3.78 (dd, J = 6.8, 9.3 Hz, 1H), 3.66 (dd, J = 3.7, 10.8 Hz, 1H), 3.30 - 3.25 (m, 1H), 2.97 - 2.89 (m, 1H), 1.97 (br t, J = 8.8 Hz, 1H), 1.89 - 1.81 (m, 1H), 1.51 (br d, J = 6.6 Hz, 2H)	2.17.A

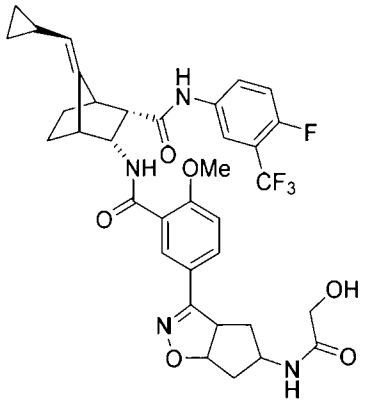
738	 實施例2	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(羥甲基)-3a,4,4a,5,6,6a-六氫環戊并[d][1,2]噁唑-3-基]-2-甲氧基-4-甲基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	656.2	(400 MHz, DMSO-d6) δ: 10.50 (s, 1H), 9.86 (d, J = 7.3 Hz, 1H), 8.23 (dd, J = 2.6, 6.4 Hz, 1H), 8.01 (s, 1H), 7.81 - 7.70 (m, 1H), 7.48 (t, J = 9.6 Hz, 1H), 7.15 (s, 1H), 5.06 (dd, J = 5.5, 9.0 Hz, 1H), 4.69 (d, J = 9.8 Hz, 1H), 4.51 - 4.37 (m, 2H), 4.23 (t, J = 9.5 Hz, 1H), 4.04 (s, 3H),3.39 (s, 1H), 3.15 (dd, J = 4.3, 10.8 Hz, 1H), 3.11 - 3.07 (m, 1H), 2.73 - 2.69 (m, 1H), 2.01 - 1.75 (m, 4H), 1.68 - 1.46 (m, 4H), 1.44 - 1.34 (m, 2H),0.73 (br t, J = 8.9 Hz, 2H), 0.35 (dd, J = 1.5, 4.8 Hz, 2H)	2.49, A

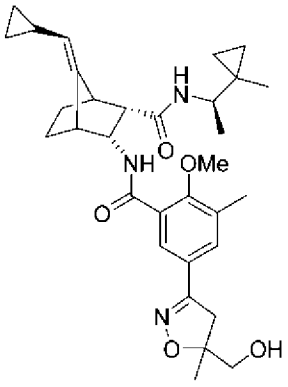
739		(1S,2S,3R,4R)-7-(環丙基甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基-4-甲基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	658.3	(400 MHz, DMSO-d6) δ = 10.48 (s, 1H), 9.76 (d, J = 7.0 Hz, 1H), 8.22 (dd, J = 2.4, 6.4 Hz, 1H), 8.00 (s, 1H), 7.84 - 7.74 (m, 1H), 7.48 (t,J = 9.8 Hz, 1H), 7.14 (s, 1H), 5.05 (dd, J = 5.5, 9.0 Hz, 1H), 4.68 - 4.56 (m, 1H), 4.47 (t, J = 5.3 Hz, 1H), 4.23 (t, J = 8.4 Hz, 1H), 4.03 (s, 3H), 3.39- 3.33 (m, 2H), 3.22 (dd, J = 3.8, 10.8 Hz, 1H), 2.48 (s, 3H), 2.38 (br d, J = 13.0 Hz, 2H), 2.03 - 1.83 (m, 3H), 1.80 - 1.71 (m, 1H), 1.67 - 1.47 (m,5H), 1.43 - 1.27 (m, 3H), 0.86 - 0.75 (m, 1H), 0.53 - 0.41 (m, 2H), 0.23 - 0.10 (m, 2H)	2.44, A

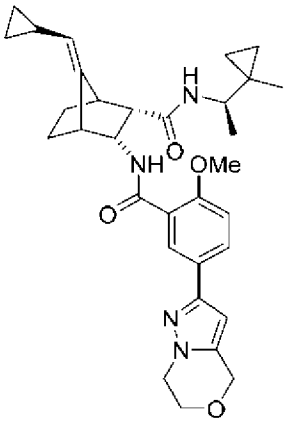
140	 中間物 1	(1R,2S,3R,4R,5S)-5-(環丙基甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(羥甲基)-3a,4,5,6,6a-四氫-1H-環戊并[d][1,2]噁唑-3-基]-2-甲氧基-4-甲基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	656.2	(400 MHz, DMSO-d6) δ: 10.50 (s, 1H), 9.85 (s, 1H), 8.23 (br d, J = 6.8 Hz, 1H), 8.04 (s, 1H), 7.82 - 7.72 (m, 1H), 7.53 - 7.42 (m, 1H), 7.16 (s, 1H), 5.13 - 5.02 (m, 1H), 4.69 (d, J = 10.0 Hz, 1H), 4.50 - 4.37 (m, 2H), 4.19 - 4.13 (m, 1H), 4.04 (s, 3H), 3.24 - 3.19 (m, 1H), 3.18 - 3.12(m, 1H), 3.12 - 3.05 (m, 1H), 2.71 (br d, J = 3.0 Hz, 1H), 2.17 - 2.04 (m, 2H), 1.86 - 1.80 (m, 1H), 1.80 - 1.71 (m, 1H), 1.66 - 1.58 (m, 1H), 1.54 -1.36 (m, 4H), 0.79 - 0.65 (m, 2H), 0.35 (br d, J = 2.8 Hz, 2H)	2.47, A

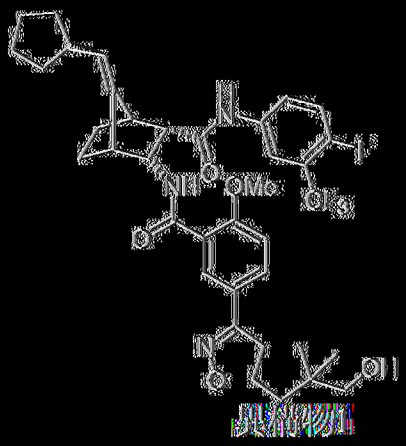
741		(1R,2S,3R,4R,7Z)-7-{[2-(二氟甲基)-1,3-噻唑-4-基]亞甲基}-3-{5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-N-[(1R)-1-(1-甲基環丙基)乙基]雙環[2.2.1]庚烷-2-甲醯胺	655.3	(400 MHz, DMSO-d6) δ ppm 10.08 (d, J=6.75 Hz, 1 H) 8.16 (d, J=2.50 Hz, 1 H) 8.02 (d, J=8.51 Hz, 1 H) 7.76 - 7.83 (m, 2 H) 7.20 - 7.51 (m, 2 H) 6.39 (s, 1 H) 5.12 (dd, J=8.88, 5.13 Hz, 1 H) 4.48 (t, J=5.25 Hz, 1 H) 4.37 (ddd, J=10.57, 4.25 Hz, 1 H) 4.16 - 4.26 (m, 1 H) 4.01 (s, 3 H) 3.74 (br s, 1 H) 3.46 - 3.53 (m, 1 H) 3.35 - 3.41 (m, 2 H) 3.08 (dd, J=10.88, 4.38 Hz, 1 H) 2.76 (br s, 1 H) 1.74 - 2.04 (m, 5 H) 1.61 - 1.71 (m, 1 H) 1.52 - 1.59 (m, 1 H) 1.46 (br d, J=5.25 Hz, 2 H) 1.04 (d, J=7.00 Hz, 3 H) 1.01 (s, 3 H) 0.51 - 0.59 (m, 1 H) 0.32 - 0.40 (m, 1 H) 0.16 - 0.25 (m, 2 H)	2.08, A

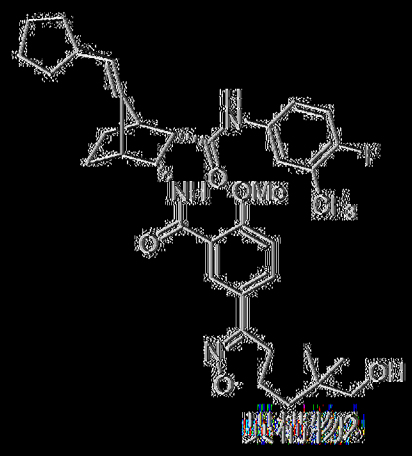
742		(1R,2S,3R,4R,7Z)-3-{5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-7-[(2-甲基-1,3-噻唑-4-基)亞甲基]-N-[(1R)-1-(1-甲基環丙基)乙基]雙環[2.2.1]庚烷-2-甲醯胺	619.2	(400 MHz, DMSO-d6) δ = 10.06 (d, J = 6.8 Hz, 1H), 8.16 (d, J = 2.3 Hz, 1H), 8.00 (d, J = 8.5 Hz, 1H), 7.80 (dd, J = 2.3, 8.8 Hz, 1H), 7.29 (s, 1H), 7.24 (d, J = 8.8 Hz, 1H), 6.26 (s, 1H), 5.12 (dd, J = 5.3, 8.8 Hz, 1H), 4.48 (t, J = 5.3 Hz, 1H), 4.35 (ddd, J = 4.1, 6.6, 10.8 Hz, 1H), 4.21 (t, J = 8.8 Hz, 1H), 4.01 (s, 3H), 3.79 (br s, 1H), 3.49 (dd, J = 7.0, 8.3 Hz, 1H), 3.42 - 3.35 (m, 2H), 3.05 (dd, J = 4.3, 11.0 Hz, 1H), 2.71 (br s, 1H), 2.67 (s, 3H), 2.04 - 1.86 (m, 3H), 1.85 - 1.74 (m, 2H), 1.72 - 1.53 (m, 2H), 1.43 (br d, J = 6.3 Hz, 2H), 1.04 (d, J = 6.8 Hz, 3H), 1.01 (s, 3H), 0.60 - 0.52 (m, 1H), 0.40 - 0.34 (m, 1H), 0.26 - 0.15 (m, 2H)	1.98, A

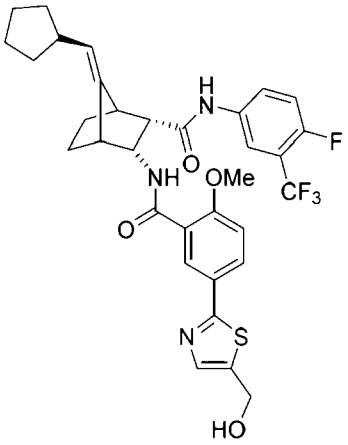
743		(2S,3R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(2-羥基乙醯胺基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	685.3	(400 MHz, DMSO-d6) δ = 10.51 (s, 1H), 9.91 (d, J = 7.0 Hz, 1H), 8.27 - 8.18 (m, 2H), 7.88 - 7.74 (m, 3H), 7.48 (t, J = 9.8 Hz, 1H), 7.27 (d, J = 8.8 Hz, 1H), 5.42 (br s, 1H), 5.11 (dd, J = 5.5, 9.0 Hz, 1H), 4.69 (d, J = 9.8 Hz, 1H), 4.48 - 4.38 (m, 1H), 4.25 (br t, J = 9.1 Hz, 1H), 4.04 (s, 4H), 3.75 (s, 2H), 3.16 (dd, J = 3.9, 10.6 Hz, 1H), 3.13 - 3.05 (m, 1H), 2.72 (br s, 1H), 2.13 - 2.07 (m, 1H), 2.00 - 1.74 (m, 5H), 1.56 - 1.34 (m, 3H), 0.80 - 0.62 (m, 2H), 0.35 (br d, J = 2.8 Hz, 2H)	2.27, A

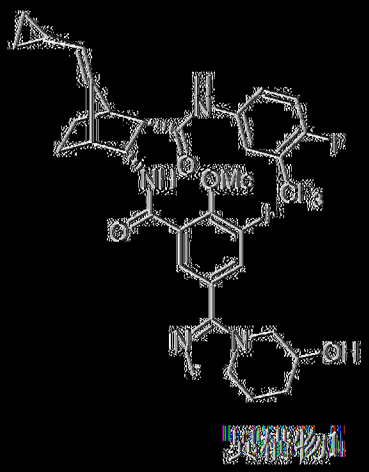
744		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-3-{3-氟-5-[5-(羥基甲基)-5-甲基-4,5-二氫-1,2-噁唑-3-基]-2-甲氧基苯甲醯胺基}-N-[(1R)-1-(1-甲基環丙基)乙基]雙環[2.2.1]庚烷-2-甲醯胺	554.3	(400 MHz, DMSO-d6) δ = 9.98 (d, J = 6.9 Hz, 1H), 7.98 (d, J = 8.6 Hz, 1H), 7.88 (s, 1H), 7.67 (dd, J = 2.2, 12.4 Hz, 1H), 5.09 (t, J = 5.9Hz, 1H), 4.65 (d, J = 9.5 Hz, 1H), 4.35 - 4.26 (m, 1H), 4.05 (d, J = 2.5 Hz, 3H), 3.49 - 3.38 (m, 3H), 3.11 - 3.00 (m, 2H), 2.96 (dd, J = 4.4, 11.0 Hz,1H), 2.55 (br s, 1H), 1.88 - 1.69 (m, 2H), 1.51 - 1.44 (m, 1H), 1.42 - 1.34 (m, 2H), 1.32 (s, 3H), 1.02 (d, J = 6.8 Hz, 3H), 0.98 (s, 3H), 0.78 - 0.61(m, 2H), 0.57 - 0.48 (m, 1H), 0.33 (br d, J = 3.5 Hz, 3H), 0.21 - 0.11 (m, 2H)	2.25, B

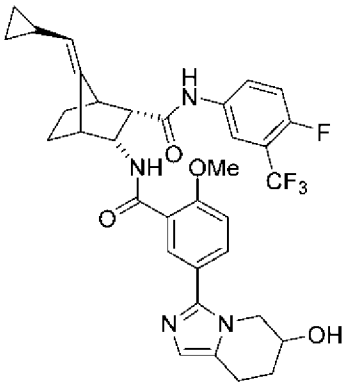
745		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-3-(2-甲氧基-5-{4H,6H,7H-吡唑并[3,2-c][1,4]噁吡-3-基}苯甲醯胺基)-N-[(1R)-1-(1-甲基環丙基)乙基]雙環[2.2.1]庚烷-2-甲醯胺	545.3	(400 MHz, DMSO-d6) δ = 10.02 (d, J = 6.9 Hz, 1H), 7.90 (d, J = 8.5 Hz, 1H), 7.81 (d, J = 2.5 Hz, 1H), 7.78 (s, 1H), 7.48 (dd, J = 2.4, 8.6Hz, 1H), 7.16 (d, J = 8.6 Hz, 1H), 4.98 (s, 2H), 4.64 (d, J = 9.5 Hz, 1H), 4.34 - 4.23 (m, 1H), 4.18 - 4.14 (m, 2H), 4.14 - 4.04 (m, 2H), 3.96 (s, 3H),3.47 (dd, J = 7.0, 8.4 Hz, 1H), 3.08 - 3.01 (m, 1H), 2.95 (dd, J = 4.4, 11.0 Hz, 1H), 1.93 - 1.84 (m, 1H), 1.81 - 1.72 (m, 1H), 1.54 - 1.44 (m, 1H),1.40 - 1.29 (m, 2H), 1.02 (d, J = 6.9 Hz, 3H), 0.98 (s, 3H), 0.77 - 0.63 (m, 2H), 0.58 - 0.50 (m, 1H), 0.41 - 0.29 (m, 3H), 0.23 - 0.11 (m, 2H)	2.26, B

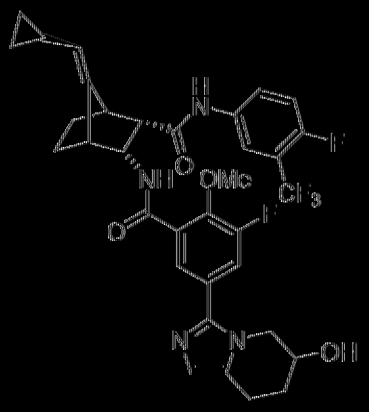
148		(1R,2S,3R,4R,5S)-5-(環戊基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(羥甲基)-5-甲基-3a,4,5,6,6a-四氫環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	684.3	(400 MHz, DMSO-d6) δ: 10.54 (br s, 1H), 9.88 (d, J = 7.1 Hz, 1H), 8.27 - 8.18 (m, 2H), 7.85 - 7.73 (m, 2H), 7.49 (t, J = 9.8 Hz, 1H), 7.27 (d, J = 8.8 Hz, 1H), 5.22 - 5.10 (m, 2H), 4.76 (br s, 1H), 4.43 - 4.36 (m, 1H), 4.17 (dt, J = 5.3, 9.5 Hz, 1H), 4.04 (s, 3H), 3.19 - 3.12 (m, 3H),3.00 (br s, 1H), 2.72 (br s, 1H), 2.59 (br d, J = 8.6 Hz, 1H), 2.20 - 2.04 (m, 2H), 1.88 - 1.73 (m, 4H), 1.69 - 1.50 (m, 6H), 1.44 - 1.16 (m, 6H), 0.91(s, 3H)	2.58, B

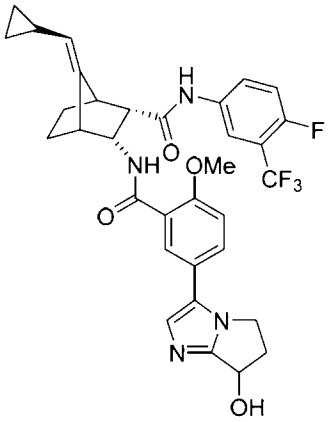
149		(1R,2S,3R,4R,7Z)-7-(環戊基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(羥甲基)-5-甲基-3a,4,5,6,6a-四氫環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	684.2	(400 MHz, DMSO-d6) δ 10.52 (s, 1H), 9.89 (d, J = 7.0 Hz, 1H), 8.26-8.17 (m, 2H), 7.86-7.74 (m, 2H), 7.49 (t, J = 9.8 Hz, 1H), 7.26(d, J = 8.9 Hz, 1H), 5.27-5.13 (m, 2H), 4.59 (br t, J = 5.3 Hz, 1H), 4.39 (ddd, J = 3.8, 6.6, 10.3 Hz, 1H), 4.28-4.21 (m, 1H), 4.04 (s, 3H), 3.19-3.13 (m, 3H), 3.01 (br s, 1H), 2.72 (br s, 1H), 2.63-2.55 (m, 2H), 1.87-1.72 (m, 8H), 1.69-1.49 (m, 7H), 1.43-1.13 (m, 5H), 0.96 (s, 3H)	2.58, B

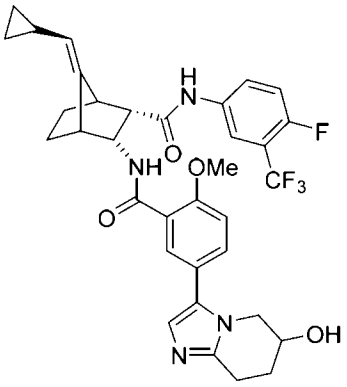
750		(1R,2S,3R,4R,7Z)-7-(環戊基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(羥基甲基)-1,3-噻唑-2-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	644.3	(400 MHz, DMSO-d6) δ = 10.52 (s, 1H), 9.87 (d, J = 7.1 Hz, 1H), 8.52 (d, J = 2.4 Hz, 1H), 8.25 (dd, J = 2.4, 6.4 Hz, 1H), 8.02 (dd, J =2.4, 8.6 Hz, 1H), 7.83 (s, 1H), 7.82 - 7.71 (m, 1H), 7.49 (t, J = 9.7 Hz, 1H), 7.24 (d, J = 8.8 Hz, 1H), 6.00 (s, 1H), 5.20 (d, J = 9.0 Hz, 1H), 4.45 -4.32 (m, 1H), 4.03 (s, 3H), 3.16 (dd, J = 3.8, 10.3 Hz, 1H), 3.02 (br s, 1H), 2.72 (br s, 1H), 2.65 - 2.55 (m, 1H), 1.90 - 1.73 (m, 4H), 1.70 - 1.50 (m,10H)	2.54, B

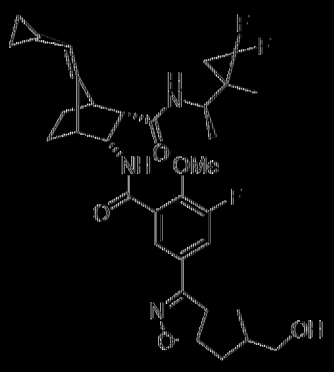
751	 實施例 1	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-(3-氟-5-{6-羥基-5H,6H,7H,8H-咪唑并[1,2-a]吡啶-3-基}-2-甲氧基苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺		651.2	(500 MHz, DMSO-d6) δ 10.60 - 10.50 (m, 1H), 9.76 - 9.66 (m, 1H), 8.15 - 8.07 (m, 1H), 7.85 - 7.79 (m, 1H), 7.76 - 7.61 (m, 1H), 7.51 (br d, J = 13.1 Hz, 1H), 7.51 - 7.44 (m, 1H), 7.03 (d, J = 3.4 Hz, 1H), 5.25 - 5.15 (m, 1H), 4.70 (d, J = 9.8 Hz, 1H), 4.52 - 4.42 (m, 1H), 4.21 - 4.14 (m, 1H), 4.09 (br d, J = 4.3 Hz, 1H), 4.06 (d, J = 1.5 Hz, 3H), 3.81 - 3.72 (m, 1H), 3.20 - 3.14 (m, 1H), 3.11 (br s, 1H), 2.95 - 2.85 (m, 1H), 2.82 - 2.76 (m, 1H), 2.76 - 2.71 (m, 1H), 1.92 (br d, J = 7.6 Hz, 2H), 1.87 - 1.78 (m, 2H), 1.55 - 1.38 (m, 3H), 0.80 - 0.69 (m, 2H), 0.36 (br d, J = 1.2 Hz, 2H)	2.08, C

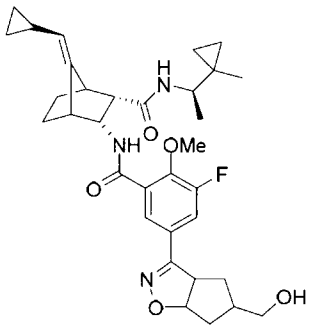
752		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-(5-{6-羥基-5H,6H,7H,8H-咪唑并[1,2-a]吡啶-3-基}-2-甲氧基苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	639.3	(500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.92 (br d, J=7.3 Hz, 1H), 8.24 (br d, J=4.9 Hz, 1H), 7.98 (d, J=2.1 Hz, 1H), 7.83 - 7.76 (m, 1H), 7.57 (dd, J=8.5, 2.1 Hz, 1H), 7.49 (t, J=9.9 Hz, 1H), 7.28 (d, J=8.9 Hz, 1H), 6.96 (s, 1H), 4.70 (d, J=9.5 Hz, 1H), 4.46 (br s, 1H), 4.15 (br s, 1H), 4.04 (s, 3H), 4.00 (br dd, J=12.2, 3.4 Hz, 1H), 3.73 (br dd, J=12.4, 4.7 Hz, 1H), 3.17 (br dd, J=10.5, 3.8 Hz, 1H), 3.11 (br s, 1H), 2.96 - 2.86 (m, 1H), 2.83 - 2.76 (m, 1H), 2.73 (br s, 1H), 2.01 - 1.90 (m, 2H), 1.89 - 1.75 (m, 2H), 1.59 - 1.48 (m, 1H), 1.47 - 1.34 (m, 2H), 0.80 - 0.69 (m, 2H), 0.36 (br s, 2H)	2.06, C

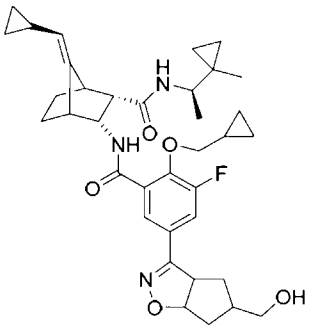
153	 異構物2	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-(3-氟-5-{6-羥基-5H,6H,7H,8H-咪唑并[1,2-a]吡啶-3-基}-2-甲氧基苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	657.2	(500 MHz, DMSO-d6) δ 10.57 (s, 1H), 9.74 (br d, J = 7.3 Hz, 1H), 8.11 (br d, J = 4.9 Hz, 1H), 7.89 – 7.79 (m, 1H), 7.71 (s, 1H), 7.65 (br d, J = 11.3 Hz, 1H), 7.48 (br t, J = 9.9 Hz, 1H), 7.42 (s, 1H), 4.70 (br d, J = 9.8 Hz, 1H), 4.53 – 4.41 (m, 1H), 4.23 (br s, 1H), 4.18 – 4.11 (m, 1H), 4.09 (s, 3H), 3.88 – 3.77 (m, 1H), 3.17 (br dd, J = 10.7, 4.3 Hz, 1H), 3.11 (br d, J = 3.4 Hz, 1H), 3.05 – 2.88 (m, 2H), 2.74 (br s, 1H), 1.97 (br d, J = 4.0 Hz, 2H), 1.88 – 1.76 (m, 2H), 1.58 – 1.35 (m, 3H), 0.74 (quin, J = 9.5 Hz, 2H), 0.36 (br d, J = 1.8 Hz, 2H)	2.13, C

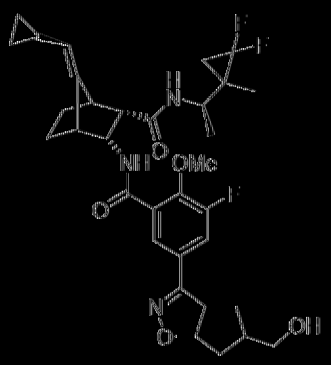
754		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-(5-{7-羥基-5H,6H,7H-吡咯并[1,2-a]咪唑-3-基}-2-甲氧基苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	625.3	(500 MHz, DMSO-d6) δ 10.52 (s, 1H), 9.92 (d, J=7.2 Hz, 1H), 8.23 (dd, J=6.4, 2.3 Hz, 1H), 8.11 (d, J=2.4 Hz, 1H), 7.87 - 7.75 (m, 1H), 7.70 (dd, J=8.6, 2.4 Hz, 1H), 7.48 (t, J=9.6 Hz, 1H), 7.30 - 7.18 (m, 2H), 5.61 (d, J=6.0 Hz, 1H), 4.90 (td, J=6.4, 3.2 Hz, 1H), 4.70 (d, J=9.6 Hz, 1H), 4.51 - 4.41 (m, 1H), 4.31 - 4.20 (m, 1H), 4.13 - 3.98 (m, 4H), 3.16 (dd, J=10.6, 4.0 Hz, 1H), 3.11 (br s, 1H), 2.85 (dq, J=14.1, 6.9 Hz, 1H), 2.73 (br s, 1H), 2.39 - 2.28 (m, 1H), 1.92 - 1.75 (m, 2H), 1.58 - 1.35 (m, 3H), 0.81 - 0.69 (m, 2H), 0.43 - 0.29 (m, 2H)	2.10, C

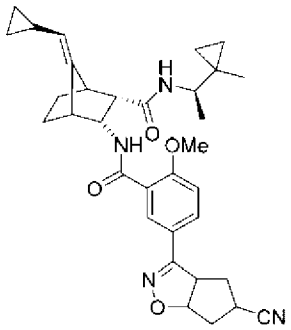
755		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-(5-{6-羥基-5H,6H,7H,8H-咪唑并[1,2-a]吡啶-3-基}-2-甲氧基苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	639.1	(500 MHz, DMSO-d6) δ 10.58 (br s, 1H), 9.94 (br d, J=7.0 Hz, 1H), 8.29 - 8.21 (m, 1H), 7.99 (d, J=1.8 Hz, 1H), 7.84 - 7.77 (m, 1H), 7.58 (dd, J=8.2, 1.8 Hz, 1H), 7.50 (br t, J=9.6 Hz, 1H), 7.28 (d, J=8.9 Hz, 1H), 6.94 (s, 1H), 4.71 (d, J=9.8 Hz, 1H), 4.52 - 4.41 (m, 1H), 4.17 (br s, 1H), 4.05 (s, 3H), 4.02 (br d, J=3.1 Hz, 1H), 3.71 (br dd, J=12.1, 4.7 Hz, 1H), 3.23 - 3.14 (m, 1H), 3.12 (br d, J=3.7 Hz, 1H), 2.96 - 2.86 (m, 1H), 2.82 - 2.75 (m, 1H), 2.74 (br s, 1H), 2.00 - 1.89 (m, 2H), 1.89 - 1.84 (m, 1H), 1.83 (s, 1H), 1.82 - 1.77 (m, 1H), 1.56 - 1.48 (m, 1H), 1.47 - 1.37 (m, 2H), 0.80 - 0.69 (m, 2H), 0.36 (br s, 2H)。	2.06, C

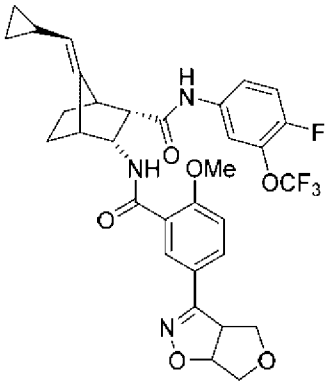
756	 異構物1	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[(1R)-1-(2,2-二氟-1-甲基環丙基)乙基]-3-{3-氟-5-[5-(羥甲基)-3a,4,5,6,6a-四氫-4,6-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	616.3	(500 MHz, DMSO-d6) δ 9.98 (br d, J= 6.6 Hz, 1H), 8.09 (br d, J= 8.5 Hz, 1H), 7.90 (br s, 1H), 7.68 (br dd, J= 12.6, 1.8 Hz, 1H), 5.15 (br dd, J= 8.2, 5.3 Hz, 1H), 4.63 (br d, J= 9.6 Hz, 1H), 4.31 - 4.22 (m, 1H), 4.19 - 4.15 (m, 1H), 4.07 - 3.99 (m, 3H), 3.84 - 3.72 (m, 1H), 3.42 - 3.29 (m, 2H), 3.04 (br s, 1H), 2.98 - 2.90 (m, 1H), 1.98 (br dd, J= 13.9, 5.4 Hz, 1H), 1.92 - 1.82 (m, 1H), 1.80 - 1.69 (m, 3H), 1.68 - 1.59 (m, 1H), 1.59 - 1.50 (m, 1H), 1.49 - 1.41 (m, 1H), 1.40 - 1.23 (m, 3H), 1.18 - 1.01 (m, 7H), 0.75 - 0.61 (m, 2H), 0.30 (br s, 2H)	2.25, C

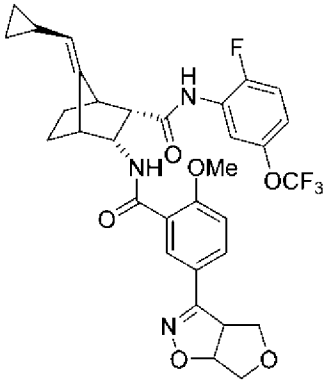
757		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-3-{3-氟-5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-N-[(1R)-1-(1-甲基環丙基)乙基]雙環[2.2.1]庚烷-2-甲醯胺	580.3	(500 MHz, DMSO-d6) δ 9.99 (br d, J=6.7 Hz, 1H), 7.98 (br d, J=8.5 Hz, 1H), 7.90 (s, 1H), 7.70 (dd, J=12.4, 1.7 Hz, 1H), 5.16 (dd, J=8.9, 5.2 Hz, 1H), 4.64 (d, J=9.5 Hz, 1H), 4.32 - 4.25 (m, 1H), 4.20 (br t, J=9.2 Hz, 1H), 4.04 (d, J=2.4 Hz, 3H), 3.49 - 3.41 (m, 1H), 3.06 (br s, 1H), 2.97 - 2.89 (m, 1H), 1.99 (br dd, J=13.7, 5.5 Hz, 1H), 1.94 - 1.73 (m, 4H), 1.69 - 1.60 (m, 1H), 1.59 - 1.50 (m, 1H), 1.46 (ddt, J=12.6, 8.5, 4.4 Hz, 1H), 1.41 - 1.29 (m, 2H), 1.01 (d, J=7.0 Hz, 3H), 0.97 (s, 3H), 0.77 - 0.65 (m, 2H), 0.55 - 0.47 (m, 1H), 0.32 (br d, J=3.4 Hz, 3H), 0.21 - 0.10 (m, 2H)	2.39, C

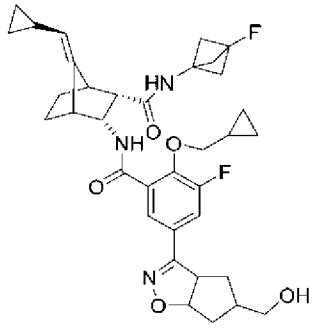
758		(1R,2S,3R,4R,7Z)-3-[2-(環丙基甲氧基)-3-氟-5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]苯甲醯胺基]-7-(環丙基亞甲基)-N-[(1R)-1-(1-甲基環丙基)乙基]雙環[2.2.1]庚烷-2-甲醯胺	620.3	(500 MHz, DMSO-d6) δ 9.94 - 9.82 (m, 1H), 7.99 (br d, J=8.5 Hz, 1H), 7.84 (s, 1H), 7.67 (br dd, J=12.5, 1.8 Hz, 1H), 5.15 (br dd, J=8.4, 5.0 Hz, 1H), 4.64 (d, J=9.5 Hz, 1H), 4.52 (br t, J=5.0 Hz, 1H), 4.33 - 4.26 (m, 1H), 4.20 (br t, J=9.0 Hz, 1H), 4.14 - 4.02 (m, 2H), 3.06 (br s, 1H), 2.94 (br dd, J=10.8, 4.1 Hz, 1H), 2.04 - 1.96 (m, 1H), 1.95 - 1.83 (m, 1H), 1.83 - 1.71 (m, 3H), 1.70 - 1.31 (m, 6H), 1.26 - 1.15 (m, 1H), 0.99 (d, J=7.0 Hz, 3H), 0.95 (s, 3H), 0.77 - 0.63 (m, 2H), 0.57 - 0.44 (m, 3H), 0.33 - 0.21 (m, 4H), 0.20 - 0.07 (m, 2H)	2.02, B

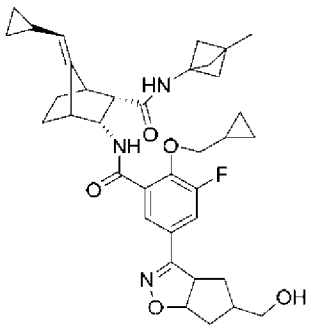
759	 異構物2	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[(1R)-1-(2,2-二氟-1-甲基環丙基)乙基]-3-{3-氟-5-[5-(羥甲基)-3a,4,5,6,6a-五氫-4,6-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	616.2	(500 MHz, DMSO-d6) δ 9.94 (d, J = 6.8 Hz, 1H), 8.33 (br d, J = 8.6 Hz, 1H), 7.91 (s, 1H), 7.74 - 7.66 (m, 1H), 5.16 (dd, J = 8.4, 5.3 Hz, 1H), 4.65 (d, J = 9.5 Hz, 1H), 4.36 - 4.27 (m, 1H), 4.20 (br t, J = 9.1 Hz, 1H), 4.06 - 4.02 (m, 3H), 3.87 (br t, J = 7.2 Hz, 1H), 3.06 (br s, 1H), 2.98 (dd, J = 10.8, 4.3 Hz, 1H), 2.57 (br d, J = 3.0 Hz, 1H), 1.99 (br dd, J = 13.5, 5.4 Hz, 1H), 1.88 (td, J = 11.5, 5.6 Hz, 1H), 1.81 - 1.70 (m, 3H), 1.69 - 1.61 (m, 1H), 1.58 - 1.44 (m, 3H), 1.43 - 1.33 (m, 2H), 1.23 - 1.15 (m, 1H), 1.13 - 1.05 (m, 6H), 0.72 (quin, J = 9.7 Hz, 2H), 0.32 (br s, 2H)	2.43, B

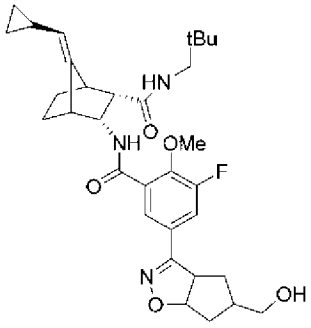
760		(1R,2S,3R,4R,7Z)-3-(5-{5-氰基-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基亞甲基)-N-[(1R)-1-(1-甲基環丙基)乙基]雙環[2.2.1]庚烷-2-甲醯胺	557.4	(500 MHz, DMSO-d6) δ 10.09 - 10.01 (m, 1H), 8.18 - 8.09 (m, 1H), 7.95 - 7.86 (m, 1H), 7.79 - 7.72 (m, 1H), 7.26 - 7.18 (m, 1H), 5.67 - 5.51 (m, 1H), 5.18 (br dd, J=8.3, 5.2 Hz, 1H), 4.63 (d, J=9.4 Hz, 1H), 4.35 (br t, J=8.8 Hz, 1H), 4.27 (dt, J=10.5, 5.3 Hz, 1H), 4.02 - 3.94 (m, 3H), 3.63 (t, J=6.6 Hz, 1H), 3.51 - 3.43 (m, 1H), 3.37 - 3.32 (m, 1H), 3.08 - 3.02 (m, 1H), 2.98 - 2.91 (m, 1H), 2.87 - 2.77 (m, 1H), 2.46 - 2.33 (m, 2H), 2.28 - 2.09 (m, 4H), 1.90 - 1.65 (m, 2H), 1.51 - 1.42 (m, 1H), 1.39 - 1.27 (m, 2H), 1.02 (br d, J=6.9 Hz, 3H), 0.97 (s, 3H), 0.75 - 0.66 (m, 1H), 0.58 - 0.47 (m, 1H), 0.35 - 0.29 (m, 2H), 0.21 - 0.11 (m, 2H)	2.32, C

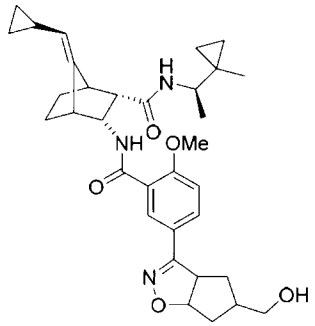
761		(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲氧基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	629.9	(500 MHz, DMSO-d6) δ 10.48 (s, 1H), 9.90 (br d, J=7.0 Hz, 1H), 8.20 (d, J=1.8 Hz, 1H), 8.01 (br d, J=6.1 Hz, 1H), 7.78 (dd, J=8.7, 2.0 Hz, 1H), 7.45 (br d, J=7.3 Hz, 2H), 7.26 (d, J=8.9 Hz, 1H), 5.33 (dd, J=9.3, 3.2 Hz, 1H), 4.67 (d, J=9.8 Hz, 1H), 4.50 - 4.44 (m, 1H), 4.43 - 4.37 (m, 1H), 4.08 (br d, J=10.7 Hz, 1H), 4.02 (s, 3H), 3.88 (br d, J=9.2 Hz, 1H), 3.80 - 3.74 (m, 1H), 3.16 - 3.10 (m, 1H), 3.08 (br s, 1H), 2.70 (br s, 1H), 1.85 - 1.72 (m, 2H), 1.53 - 1.34 (m, 3H), 0.78 - 0.66 (m, 2H), 0.33 (br d, J=2.4 Hz, 2H)。可能由於與經抑制之水峰重疊，一個質子不可見。	2.55, B

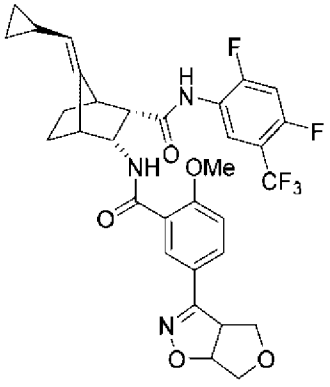
762		(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基亞甲基)-N-[2-氟-5-(三氟甲氧基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	630.1	(500 MHz, DMSO-d6) δ 10.19 (s, 1H), 9.81 (br d, J=7.0 Hz, 1H), 8.20 (d, J=2.1 Hz, 1H), 8.03 (br d, J=2.7 Hz, 1H), 7.78 (dd, J=8.7, 2.3 Hz, 1H), 7.39 (t, J=9.8 Hz, 1H), 7.25 (d, J=8.9 Hz, 1H), 7.20 - 7.14 (m, 1H), 5.33 (dd, J=9.2, 3.4 Hz, 1H), 4.68 (d, J=9.8 Hz, 1H), 4.51 - 4.44 (m, 1H), 4.44 - 4.36 (m, 1H), 4.08 (br d, J=10.7 Hz, 1H), 3.97 (s, 3H), 3.91 - 3.83 (m, 1H), 3.79 - 3.71 (m, 1H), 3.64 (br dd, J=11.0, 3.7 Hz, 1H), 3.34 (br dd, J=10.5, 3.5 Hz, 1H), 3.07 (br s, 1H), 2.72 (br s, 1H), 1.89 - 1.80 (m, 1H), 1.79 - 1.70 (m, 1H), 1.53 - 1.33 (m, 3H), 0.80 - 0.64 (m, 2H), 0.34 (br d, J=3.1 Hz, 2H)	2.55, C

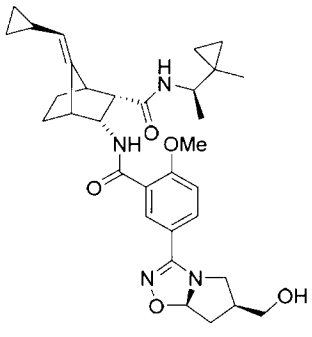
763		(1R,2S,3R,4R,7Z)-3-[2-(環丙基甲氧基)-3-氟-5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]苯甲醯胺基]-7-(環丙基亞甲基)-N-{3-氟雙環[1.1.1]戊烷-1-基}雙環[2.2.1]庚烷-2-甲醯胺	622.2	(500 MHz, DMSO-d6) δ 9.76 (d, J=7.0 Hz, 1H), 8.81 (s, 1H), 7.89 (s, 1H), 7.68 (dd, J=12.4, 1.6 Hz, 1H), 5.15 (dd, J=8.9, 5.0 Hz, 1H), 4.61 (d, J=9.6 Hz, 1H), 4.58 - 4.53 (m, 1H), 4.36 - 4.27 (m, 1H), 4.19 (br t, J=9.1 Hz, 2H), 4.16 - 4.11 (m, 1H), 3.07 - 3.01 (m, 1H), 2.91 - 2.84 (m, 1H), 2.55 (br s, 1H), 2.32 - 2.22 (m, 6H), 2.04 - 1.96 (m, 1H), 1.94 - 1.85 (m, 1H), 1.83 - 1.71 (m, 2H), 1.69 - 1.61 (m, 2H), 1.59 - 1.52 (m, 1H), 1.50 - 1.30 (m, 3H), 1.26 - 1.18 (m, 1H), 0.76 - 0.64 (m, 2H), 0.48 (br d, J=8.1 Hz, 2H), 0.36 - 0.18 (m, 4H)。可能由於與經抑制之水峰重疊，兩個質子在NMR中不可見。	2.37, B

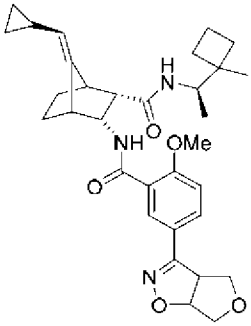
764		(1R,2S,3R,4R,7Z)-3-[2-(環丙基甲氧基)-3-氟-5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]苯甲醯胺基]-7-(環丙基亞甲基)-N-{3-甲基雙環[1.1.1]戊烷-1-基}雙環[2.2.1]庚烷-2-甲醯胺	618.2	(500 MHz, DMSO-d6) δ 9.88 (br d, J=6.7 Hz, 1H), 8.53 (s, 1H), 7.89 (s, 1H), 7.68 (br d, J=12.2 Hz, 1H), 5.15 (br dd, J=8.7, 5.0 Hz, 1H), 4.60 (d, J=9.5 Hz, 1H), 4.51 (br t, J=5.2 Hz, 1H), 4.32 - 4.25 (m, 1H), 4.20 (br t, J=9.2 Hz, 1H), 4.15 (br d, J=7.3 Hz, 2H), 3.04 (br s, 1H), 2.81 (br dd, J=10.8, 4.1 Hz, 1H), 1.99 (br dd, J=13.3, 6.0 Hz, 1H), 1.94 - 1.86 (m, 1H), 1.84 - 1.76 (m, 7H), 1.75 - 1.62 (m, 3H), 1.59 - 1.51 (m, 1H), 1.49 - 1.41 (m, 1H), 1.40 - 1.29 (m, 2H), 1.24 (br d, J=7.9 Hz, 1H), 1.17 (s, 3H), 0.76 - 0.65 (m, 2H), 0.51 - 0.44 (m, 2H), 0.36 - 0.22 (m, 4H)。可能由於與溶劑峰及/或經抑制之水峰重疊，三個質子在NMR中不可見。	2.55, C

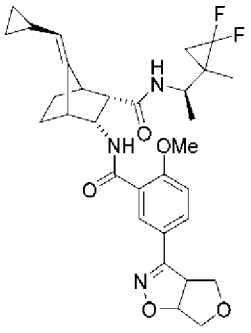
765		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-(2,2-二甲基丙基)-3-{3-氟-5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	568.3	(500 MHz, DMSO-d6) δ 9.87 (d, J=7.0 Hz, 1H), 8.01 (br t, J=6.1 Hz, 1H), 7.90 (s, 1H), 7.70 (dd, J=12.5, 2.1 Hz, 1H), 5.16 (dd, J=8.5, 5.2 Hz, 1H), 4.64 (d, J=9.5 Hz, 1H), 4.36 - 4.27 (m, 1H), 4.20 (br t, J=8.9 Hz, 1H), 4.06 (d, J=2.4 Hz, 3H), 3.09 - 3.00 (m, 2H), 2.74 (dd, J=13.1, 5.5 Hz, 1H), 2.56 (br s, 1H), 1.99 (br dd, J=13.9, 5.6 Hz, 1H), 1.93 - 1.73 (m, 4H), 1.70 - 1.51 (m, 2H), 1.50 - 1.43 (m, 1H), 1.42 - 1.29 (m, 2H), 0.81 (s, 8H), 0.76 - 0.64 (m, 2H), 0.32 (br d, J=2.7 Hz, 2H)。可能由於與溶劑峰及/或經抑制之水峰重疊，三個質子在NMR中不可見。	2.45, C

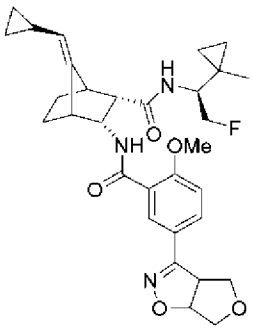
766		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-3-{5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-N-[(1R)-1-(1-甲基環丙基)乙基]雙環[2.2.1]庚烷-2-甲醯胺	561.9	(500 MHz, DMSO-d6) δ 10.06 (br d, J=6.4 Hz, 1H), 8.17 (d, J=2.1 Hz, 1H), 7.91 (br d, J=8.5 Hz, 1H), 7.78 (dd, J=8.7, 2.3 Hz, 1H), 7.22 (d, J=8.5 Hz, 1H), 5.13 (br dd, J=9.6, 6.6 Hz, 1H), 4.63 (d, J=9.5 Hz, 1H), 4.49 (t, J=5.2 Hz, 1H), 4.31 - 4.23 (m, 1H), 4.15 - 4.05 (m, 1H), 3.99 (s, 3H), 3.52 - 3.42 (m, 1H), 3.37 - 3.19 (m, 1H), 3.04 (br s, 1H), 2.94 (br dd, J=11.0, 4.0 Hz, 1H), 2.24 - 2.07 (m, 3H), 1.90 - 1.82 (m, 1H), 1.78 - 1.70 (m, 1H), 1.67 - 1.58 (m, 1H), 1.52 - 1.41 (m, 2H), 1.40 - 1.29 (m, 2H), 1.05 - 0.99 (m, 3H), 0.97 (s, 3H), 0.78 - 0.66 (m, 2H), 0.57 - 0.48 (m, 1H), 0.36 - 0.27 (m, 3H), 0.22 - 0.11 (m, 2H)。可能由於與溶劑峰及/或經抑制之水峰重疊，兩個質子在NMR中不可見。	2.17, B

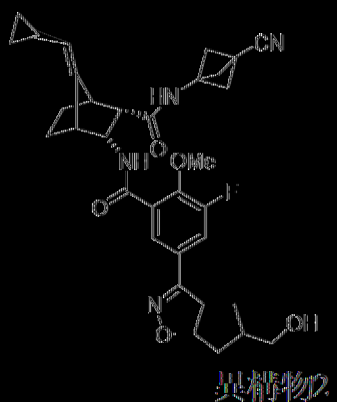
767		(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基亞甲基)-N-[2,4-二氟-5-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	632.1	(500 MHz, DMSO-d6) δ 10.24 (s, 1H), 9.78 (br d, J=7.3 Hz, 1H), 8.32 (br t, J=7.9 Hz, 1H), 8.20 (d, J=2.4 Hz, 1H), 7.78 (dd, J=8.7, 2.3 Hz, 1H), 7.70 (br t, J=10.5 Hz, 1H), 7.25 (d, J=8.9 Hz, 1H), 5.33 (dd, J=9.2, 3.7 Hz, 1H), 4.69 (d, J=9.5 Hz, 1H), 4.54 - 4.37 (m, 2H), 4.09 (d, J=10.7 Hz, 1H), 3.97 (s, 3H), 3.91 - 3.83 (m, 1H), 3.80 - 3.72 (m, 1H), 3.65 (dd, J=10.7, 3.7 Hz, 1H), 3.39 (br d, J=1.8 Hz, 1H), 3.08 (br d, J=3.7 Hz, 1H), 2.72 (br s, 1H), 1.87 - 1.80 (m, 1H), 1.79 - 1.71 (m, 1H), 1.53 - 1.34 (m, 3H), 0.81 - 0.64 (m, 2H), 0.34 (br d, J=3.4 Hz, 2H)	2.49, B

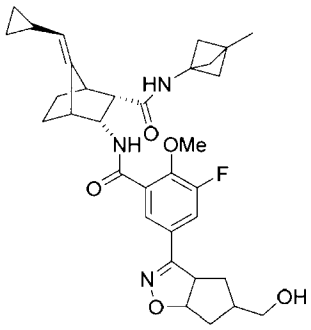
768		(1R,2S,3R,4R,7Z)-3-{5-[(6S,7aR)-6-(羥基甲基)-5H,6H,7H,7aH-吡咯并[1,2-d][1,2,4]噁二唑-3-基]-2-甲氧基苯甲醯胺基}-7-(環丙基亞甲基)-N-[(1R)-1-(1-甲基環丙基)乙基]雙環[2.2.1]庚烷-2-甲醯胺	563.2	(500 MHz, DMSO-d6) δ 10.18 - 10.02 (m, 1H), 8.19 (br d, J=11.0 Hz, 1H), 7.92 (br d, J=8.5 Hz, 1H), 7.78 (br d, J=8.5 Hz, 1H), 7.26 (br d, J=8.9 Hz, 1H), 5.85 - 5.72 (m, 1H), 4.63 (br d, J=9.5 Hz, 1H), 4.26 (br d, J=3.4 Hz, 1H), 4.01 (br d, J=3.1 Hz, 3H), 3.51 - 3.38 (m, 1H), 3.33 - 3.23 (m, 1H), 3.22 - 3.10 (m, 1H), 3.04 (br d, J=2.7 Hz, 1H), 2.98 - 2.84 (m, 2H), 2.32 - 1.71 (m, 6H), 1.54 - 1.41 (m, 1H), 1.38 - 1.28 (m, 2H), 1.01 (br d, J=6.7 Hz, 3H), 0.97 (s, 3H), 0.77 - 0.62 (m, 2H), 0.52 (br dd, J=6.4, 2.4 Hz, 1H), 0.37 - 0.27 (m, 2H), 0.22 - 0.07 (m, 2H)。可能由於與溶劑峰及/或經抑制之水峰重疊，兩個質子在NMR中不可見。	2.22, C

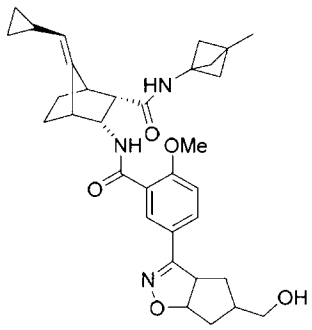
769		(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基亞甲基)-N-[(1R)-1-(1-甲基環丁基)乙基]雙環[2.2.1]庚烷-2-甲醯胺	548.3	(500 MHz, DMSO-d6) δ 10.05 (br d, J=6.7 Hz, 1H), 8.14 (d, J=2.4 Hz, 1H), 7.78 (dd, J=8.7, 2.0 Hz, 2H), 7.24 (d, J=8.9 Hz, 1H), 5.34 (dd, J=9.2, 3.4 Hz, 1H), 4.62 (d, J=9.5 Hz, 1H), 4.49 (br t, J=8.1 Hz, 1H), 4.27 (dt, J=10.2, 5.3 Hz, 1H), 4.09 (d, J=10.7 Hz, 1H), 4.01 (s, 3H), 3.99 - 3.92 (m, 1H), 3.90 (br d, J=10.1 Hz, 1H), 3.77 (dd, J=9.2, 7.0 Hz, 1H), 3.65 (dd, J=10.7, 3.7 Hz, 1H), 3.04 (br s, 1H), 2.98 (br dd, J=11.0, 4.3 Hz, 1H), 2.01 - 1.90 (m, 1H), 1.87 - 1.77 (m, 3H), 1.76 - 1.63 (m, 2H), 1.56 - 1.41 (m, 3H), 1.40 - 1.26 (m, 2H), 1.04 (s, 3H), 0.86 (d, J=6.7 Hz, 3H), 0.75 - 0.63 (m, 2H), 0.31 (br d, J=3.1 Hz, 2H)。可能由於與溶劑峰重疊，一個質子在NMR中不可見。	2.40, B

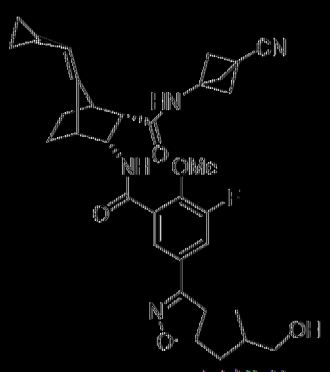
770		(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基亞甲基)-N-[(1R)-1-(2,2-二氟-1-甲基環丙基)乙基]雙環[2.2.1]庚烷-2-甲醯胺	570.2	(500 MHz, DMSO-d6) δ 10.06 (br d, J=6.4 Hz, 1H), 8.29 (br d, J=8.6 Hz, 1H), 8.15 (s, 1H), 7.78 (br d, J=8.5 Hz, 1H), 7.23 (d, J=8.1 Hz, 1H), 5.33 (br d, J=8.5 Hz, 1H), 4.63 (br d, J=9.8 Hz, 1H), 4.48 (br t, J=8.0 Hz, 1H), 4.32 - 4.23 (m, 1H), 4.09 (br d, J=10.5 Hz, 1H), 3.98 (s, 3H), 3.92 - 3.83 (m, 2H), 3.80 - 3.73 (m, 1H), 3.68 - 3.61 (m, 1H), 3.04 (br s, 1H), 2.96 (br dd, J=10.0, 3.2 Hz, 1H), 2.55 (br d, J=1.9 Hz, 1H), 1.79 - 1.65 (m, 2H), 1.57 - 1.44 (m, 2H), 1.34 (br d, J=2.9 Hz, 2H), 1.23 - 1.15 (m, 1H), 1.13 - 1.01 (m, 6H), 0.71 (quin, J=9.4 Hz, 2H), 0.31 (br s, 2H)	2.30, B

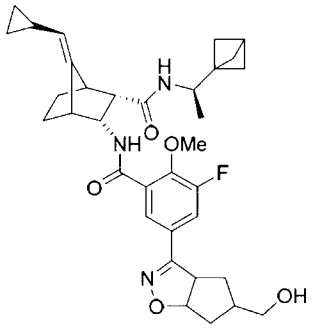
771		(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基亞甲基)-N-[(1S)-2-氟-1-(1-甲基環丙基)乙基]雙環[2.2.1]庚烷-2-甲醯胺	552.3	(500 MHz, DMSO-d6) δ 10.02 (br d, J=7.0 Hz, 1H), 8.21 (br d, J=8.5 Hz, 1H), 8.14 (d, J=2.4 Hz, 1H), 7.78 (dd, J=8.7, 2.3 Hz, 1H), 7.23 (d, J=8.9 Hz, 1H), 5.33 (dd, J=9.2, 3.7 Hz, 1H), 4.64 (d, J=9.5 Hz, 1H), 4.57 - 4.28 (m, 4H), 4.09 (d, J=10.7 Hz, 1H), 3.98 (s, 3H), 3.92 - 3.87 (m, 1H), 3.80 - 3.73 (m, 1H), 3.70 - 3.60 (m, 2H), 3.06 (br s, 1H), 3.01 (br dd, J=11.0, 4.6 Hz, 1H), 2.59 - 2.55 (m, 1H), 1.81 (br d, J=9.5 Hz, 1H), 1.77 - 1.67 (m, 1H), 1.53 - 1.42 (m, 1H), 1.40 - 1.29 (m, 2H), 0.99 (s, 3H), 0.79 - 0.65 (m, 2H), 0.59 - 0.50 (m, 1H), 0.50 - 0.41 (m, 1H), 0.36 - 0.29 (m, 2H), 0.27 (dt, J=9.2, 4.6 Hz, 1H), 0.17 (dt, J=8.6, 4.4 Hz, 1H)	2.16, B

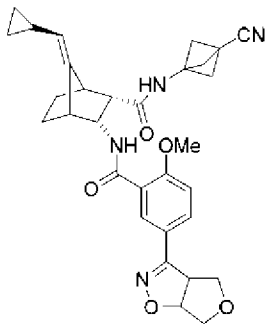
112	 異構物2	(2S,3R,7S)-N-{3-氟基雙環[1.1.1]戊烷-1-基}-7-(環丙基甲基)-3-{3-氟-5-[5-(羥基甲基)-3a,4,5,6,6a-五氫環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	589.1	(500 MHz, CD_3OD) δ 8.03 (dd, J= 2.2, 1.3 Hz, 1H), 7.10 (dd, J= 12.8, 2.2 Hz, 1H), 5.25 - 5.19 (m, 1H), 4.68 - 4.63 (m, 1H), 4.44 - 4.39 (m, 1H), 4.21 (d, J= 3.2 Hz, 4H), 3.58 - 3.50 (m, 1H), 2.87 - 2.83 (m, 1H), 2.56 - 2.49 (m, 8H), 2.19 - 2.14 (m, 1H), 2.11 - 2.05 (m, 1H), 1.99 - 1.92 (m, 1H), 1.86 - 1.82 (m, 2H), 1.79 - 1.71 (m, 1H), 1.67 - 1.60 (m, 1H), 1.56 - 1.42 (m, 3H), 0.75 - 0.70 (m, 2H), 0.36 - 0.28 (m, 2H)	2.11, C

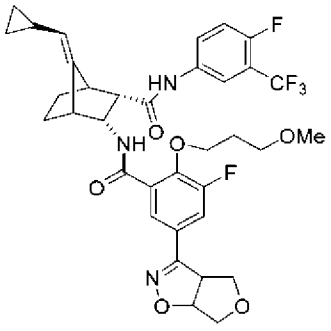
773		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-3-{3-氟-5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-N-{3-甲基雙環[1.1.1]戊烷-1-基}雙環[2.2.1]庚烷-2-甲醯胺	578.2	(500 MHz, DMSO-d6) δ 9.96 (br d, J=6.4 Hz, 1H), 8.55 (s, 1H), 7.94 (s, 1H), 7.71 (dd, J=12.5, 1.8 Hz, 1H), 5.16 (br dd, J=8.4, 5.3 Hz, 1H), 4.60 (d, J=9.5 Hz, 1H), 4.32 - 4.24 (m, 1H), 4.20 (br t, J=9.0 Hz, 1H), 4.08 (d, J=2.4 Hz, 3H), 3.43 - 3.31 (m, 1H), 3.03 (br s, 1H), 2.81 (br dd, J=10.2, 4.1 Hz, 1H), 2.05 - 1.95 (m, 1H), 1.94 - 1.59 (m, 11H), 1.59 - 1.50 (m, 1H), 1.48 - 1.40 (m, 1H), 1.39 - 1.26 (m, 2H), 1.17 (s, 3H), 0.76 - 0.61 (m, 2H), 0.37 - 0.24 (m, 2H)	2.36, B

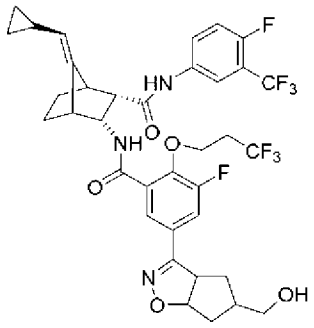
774		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-3-{5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-N-{3-甲基雙環[1.1.1]戊烷-1-基}雙環[2.2.1]庚烷-2-甲醯胺	560.3	(500 MHz, DMSO-d6) δ 10.13 (br d, J=6.7 Hz, 1H), 8.50 (s, 1H), 8.20 (d, J=2.1 Hz, 1H), 7.79 (dd, J=8.7, 2.3 Hz, 1H), 7.23 (d, J=8.9 Hz, 1H), 5.11 (dd, J=8.7, 5.3 Hz, 1H), 4.59 (d, J=9.8 Hz, 1H), 4.28 - 4.14 (m, 2H), 4.02 (s, 3H), 3.04 (br s, 1H), 2.80 (br dd, J=10.8, 4.1 Hz, 1H), 1.98 (br dd, J=13.3, 5.6 Hz, 1H), 1.94 - 1.87 (m, 1H), 1.85 (s, 6H), 1.80 - 1.70 (m, 2H), 1.70 - 1.60 (m, 2H), 1.58 - 1.50 (m, 1H), 1.48 - 1.40 (m, 1H), 1.37 - 1.25 (m, 2H), 1.18 (s, 3H), 0.77 - 0.64 (m, 2H), 0.37 - 0.26 (m, 2H)	2.19, C

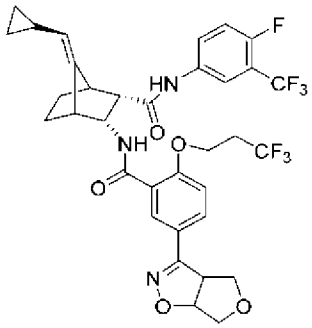
715	 異構物1	(1R,2S,3R,4R,7Z)-N-[3-氟基雙環[1.1.1]戊烷-1-基]-7-(環內基亞甲基)-3-[3-氟-5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]㗁唑-3-基]-2-甲氧基苯甲醯胺基]雙環[2.2.1]庚烷-2-甲醯胺	589.2	(500 MHz, DMSO-d6) δ 9.85 (br d, J= 6.7 Hz, 1H), 8.91 (br s, 1H), 7.96 (br s, 1H), 7.70 (br d, J= 12.2 Hz, 1H), 5.22 - 5.13 (m, 1H), 4.64 - 4.53 (m, 2H), 4.28 (br s, 1H), 4.09 (br s, 3H), 3.33 - 3.25 (m, 1H), 3.22 (br d, J= 5.5 Hz, 1H), 3.03 (br s, 1H), 2.88 - 2.78 (m, 1H), 2.49 - 2.43 (m, 6H), 2.26 - 2.08 (m, 3H), 1.74 - 1.59 (m, 3H), 1.52 - 1.40 (m, 2H), 1.40 - 1.28 (m, 2H), 0.77 - 0.63 (m, 2H), 0.31 (br s, 2H)	2.02, C

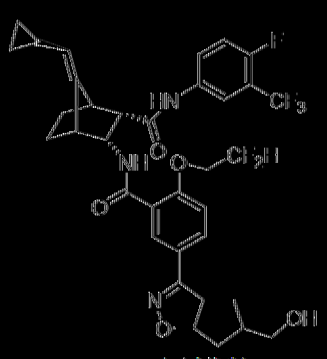
776		(1R,2S,3R,4R,7Z)-N-[(1R)-1-{雙環[1.1.1]戊烷-1-基}乙基]-7-(環丙基亞甲基)-3-{3-氟-5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	592.2	(500 MHz, DMSO-d6) δ 9.69 (br d, J=6.9 Hz, 1H), 7.72 - 7.60 (m, 2H), 7.45 (br dd, J=12.2, 1.3 Hz, 1H), 4.92 (br dd, J=8.7, 5.0 Hz, 1H), 4.39 (br d, J=9.5 Hz, 1H), 4.08 - 4.00 (m, 1H), 3.95 (br t, J=9.0 Hz, 1H), 3.82 - 3.76 (m, 3H), 3.64 - 3.58 (m, 1H), 3.18 - 3.06 (m, 2H), 2.81 (br s, 1H), 2.68 (br dd, J=10.6, 3.9 Hz, 1H), 2.19 (s, 1H), 1.81 - 1.72 (m, 1H), 1.67 - 1.48 (m, 4H), 1.45 - 1.37 (m, 1H), 1.37 - 1.26 (m, 7H), 1.25 - 1.17 (m, 1H), 1.16 - 1.06 (m, 2H), 0.67 (d, J=6.9 Hz, 3H), 0.52 - 0.40 (m, 2H), 0.07 (br d, J=2.4 Hz, 2H)	2.48, B

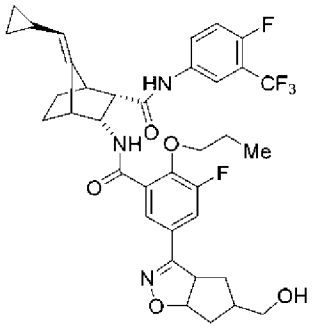
777		(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-N-{3-氰基雙環[1.1.1]戊烷-1-基}-7-(環丙基亞甲基)雙環[2.2.1]庚烷-2-甲醯胺	543.3	(500 MHz, DMSO-d6) δ 10.05 (br d, J=6.7 Hz, 1H), 8.89 (s, 1H), 8.21 (d, J=2.1 Hz, 1H), 7.81 (dd, J=8.7, 2.3 Hz, 1H), 7.27 (d, J=8.5 Hz, 1H), 5.35 (dd, J=9.2, 3.4 Hz, 1H), 4.62 (d, J=9.5 Hz, 1H), 4.51 (br t, J=8.1 Hz, 1H), 4.32 - 4.22 (m, 1H), 4.11 (d, J=10.4 Hz, 1H), 4.06 (s, 3H), 3.91 (br d, J=9.2 Hz, 1H), 3.79 (dd, J=9.3, 7.2 Hz, 1H), 3.67 (dd, J=10.5, 3.5 Hz, 1H), 3.06 (br s, 1H), 2.83 (br dd, J=10.8, 4.1 Hz, 1H), 2.54 (br s, 1H) (部分重疊DMSO), 2.52 - 2.50 (m, 6H) (部分重疊DMSO), 1.76 - 1.62 (m, 2H), 1.52 - 1.41 (m, 1H), 1.34 (br d, J=8.2 Hz, 2H), 0.79 - 0.65 (m, 2H), 0.33 (br d, J=4.3 Hz, 2H)	1.95, B

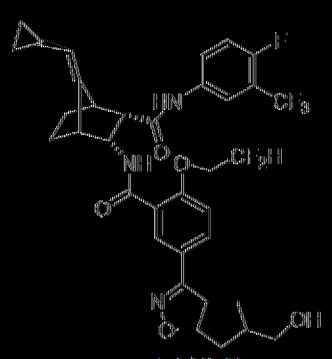
778		(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-3-氟-2-(3-甲氧基prop氧基)苯甲醯胺基)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	690.3	(500 MHz, DMSO-d6) δ 10.51 (s, 1H), 9.45 (d, J=7.0 Hz, 1H), 8.11 (dd, J=6.3, 2.3 Hz, 1H), 7.86 (s, 1H), 7.79 - 7.75 (m, 1H), 7.73 (dd, J=12.4, 2.0 Hz, 1H), 7.47 (t, J=9.6 Hz, 1H), 5.38 (dd, J=9.3, 3.5 Hz, 1H), 4.71 (d, J=9.5 Hz, 1H), 4.51 - 4.41 (m, 2H), 4.34 - 4.24 (m, 2H), 4.10 (d, J=11.0 Hz, 1H), 3.93 (br d, J=9.8 Hz, 1H), 3.72 (dd, J=9.3, 6.9 Hz, 1H), 3.64 (dd, J=10.8, 3.5 Hz, 1H), 3.47 - 3.30 (m, 1H), 3.17 (s, 2H), 3.12 (br s, 1H), 2.76 - 2.71 (m, 1H), 1.99 (qt, J=13.4, 6.8 Hz, 2H), 1.89 - 1.72 (m, 2H), 1.59 - 1.29 (m, 3H), 0.95 - 0.58 (m, 2H), 0.52 - 0.09 (m, 2H)	2.56, B

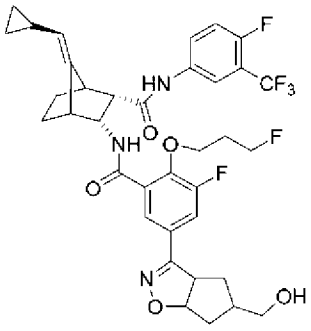
779		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{3-氟-5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-prop氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	688.3	(500 MHz, DMSO-d6) δ 10.57 - 10.47 (m, 1H), 9.61 - 9.44 (m, 1H), 8.24 - 8.11 (m, 1H), 7.89 (s, 1H), 7.80 - 7.74 (m, 1H), 7.71 - 7.64 (m, 1H), 7.47 (t, J=9.8 Hz, 1H), 5.31 - 5.12 (m, 1H), 4.71 (s, 1H), 4.52 (q, J=5.0 Hz, 1H), 4.46 (br t, J=10.2 Hz, 1H), 4.25 - 4.16 (m, 2H), 4.12 - 4.06 (m, 1H), 3.32 - 3.27 (m, 1H), 3.25 - 3.20 (m, 1H), 3.19 - 3.14 (m, 1H), 3.11 (br s, 1H), 2.73 (br s, 1H), 2.25 - 2.09 (m, 2H), 1.83 - 1.79 (m, 2H), 1.78 - 1.71 (m, 2H), 1.67 - 1.60 (m, 1H), 1.53 - 1.37 (m, 4H), 0.87 (t, J=7.4 Hz, 3H), 0.82 - 0.70 (m, 2H), 0.36 (br d, J=2.1 Hz, 2H) 一些質子因水抑制而被遮擋。	2.67, B

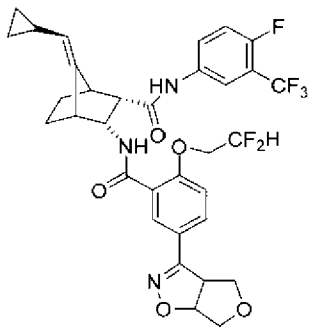
780		(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-(3,3,3-三氟prop氧基)苯甲醯胺基)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	696.0	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.59 (br d, J=7.0 Hz, 1H), 8.20 (d, J=2.1 Hz, 1H), 8.16 (dd, J=6.6, 2.0 Hz, 1H), 7.79 (dd, J=8.9, 2.1 Hz, 1H), 7.74 - 7.66 (m, 1H), 7.46 (t, J=9.9 Hz, 1H), 7.35 (d, J=8.9 Hz, 1H), 5.35 (dd, J=9.2, 3.4 Hz, 1H), 4.70 (d, J=9.5 Hz, 1H), 4.61 - 4.39 (m, 4H), 4.10 (br d, J=10.7 Hz, 1H), 3.92 - 3.85 (m, 1H), 3.82 - 3.75 (m, 1H), 3.66 (dd, J=11.0, 3.4 Hz, 1H), 3.35 (br s, 1H), 3.24 - 3.15 (m, 1H), 3.13 - 2.98 (m, 2H), 2.73 (br s, 1H), 1.87 - 1.72 (m, 2H), 1.50 (td, J=8.4, 4.3 Hz, 1H), 1.44 (br s, 2H), 0.84 - 0.66 (m, 2H), 0.36 (br s, 2H)	2.59, B

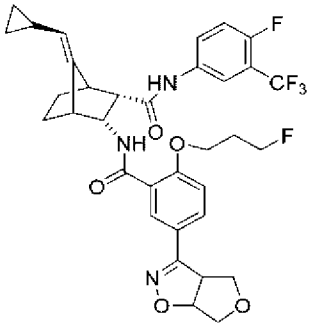
781	 中間物12	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-3-[2-(2,2-二氟乙氧基)-5-[5-(羥基甲基)-3a,4,4a,5,6,6a-六氫環戊并[d][1,2]噁唑-3-基]苯甲醯胺基]-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	692.3	(500 MHz, DMSO-d6) δ 10.59 - 10.47 (m, 1H), 9.57 (br d, J= 7.0 Hz, 1H), 8.20 (d, J= 2.1 Hz, 1H), 8.12 (br d, J= 4.3 Hz, 1H), 7.79 (dd, J= 8.7, 2.0 Hz, 1H), 7.75 - 7.67 (m, 1H), 7.47 (t, J= 9.6 Hz, 1H), 7.36 (d, J= 9.2 Hz, 1H), 6.88 - 6.43 (m, 1H), 5.13 (br dd, J= 8.5, 5.5 Hz, 1H), 4.70 (d, J= 9.5 Hz, 1H), 4.68 - 4.61 (m, 2H), 4.53 (t, J= 5.2 Hz, 1H), 4.50 - 4.45 (m, 1H), 4.21 (br t, J= 9.0 Hz, 1H), 3.49 - 3.31 (m, 1H), 3.16 (br dd, J= 11.0, 3.7 Hz, 1H), 3.09 (br s, 1H), 2.73 (br s, 1H), 2.04 - 1.94 (m, 1H), 1.92 - 1.81 (m, 2H), 1.79 - 1.71 (m, 1H), 1.69 - 1.61 (m, 1H), 1.58 - 1.45 (m, 2H), 1.44 - 1.35 (m, 2H), 0.93 - 0.59 (m, 2H), 0.42 - 0.20 (m, 2H)。 - 典質子因水抑制而被遮擋。	2.48, B

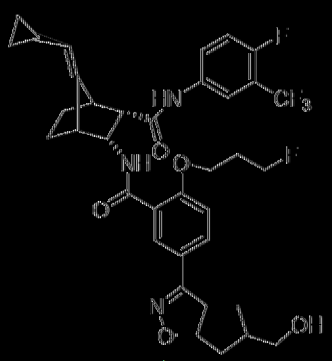
782		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{3-氟-5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-prop氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	688.3	(500 MHz, DMSO-d6) δ 10.52 (s, 1H), 9.49 (br d, J=7.6 Hz, 1H), 8.12 (br d, J=6.0 Hz, 1H), 7.87 (s, 1H), 7.77 - 7.71 (m, 1H), 7.68 (br d, J=12.7 Hz, 1H), 7.45 (br t, J=9.7 Hz, 1H), 5.15 (br dd, J=8.5, 5.1 Hz, 1H), 4.69 (br d, J=9.5 Hz, 1H), 4.61 (br d, J=3.2 Hz, 1H), 4.43 (br d, J=5.3 Hz, 1H), 4.27 - 4.11 (m, 3H), 3.41 - 3.28 (m, 1H), 3.18 - 3.14 (m, 1H), 3.10 (br s, 1H), 2.72 (br s, 1H), 1.99 (br dd, J=13.0, 5.4 Hz, 1H), 1.93 - 1.85 (m, 1H), 1.81 (br d, J=7.9 Hz, 2H), 1.78 - 1.68 (m, 3H), 1.67 - 1.61 (m, 1H), 1.59 - 1.54 (m, 1H), 1.50 - 1.37 (m, 3H), 0.85 (t, J=7.3 Hz, 3H), 0.77 - 0.67 (m, 2H), 0.34 (br d, J=3.1 Hz, 2H)。一些質子因水抑制而被遮擋。	2.67, B

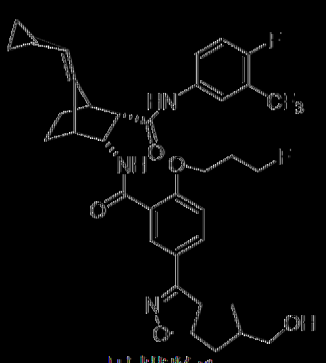
783	 異構物1	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-3-[2-(2,2-二氟乙氧基)-5-[5-(羥基甲基)-3a,4,4a,5,6,6a-六氫環戊并[d][1,2]噁唑-3-基]苯甲醯胺基]-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	692.2	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.57 (br d, J=7.2 Hz, 1H), 8.20 (d, J=2.2 Hz, 1H), 8.11 (br d, J=4.4 Hz, 1H), 7.85 - 7.75 (m, 1H), 7.71 (br dd, J=4.3, 3.0 Hz, 1H), 7.45 (br t, J=9.7 Hz, 1H), 7.35 (d, J=8.9 Hz, 1H), 6.62 (br t, J=54.9 Hz, 1H), 5.25 - 5.12 (m, 1H), 4.70 (s, 1H), 4.63 - 4.52 (m, 2H), 4.48 - 4.41 (m, 1H), 4.15 - 4.06 (m, 1H), 3.32 - 3.20 (m, 1H), 3.15 (br dd, J=10.6, 3.3 Hz, 1H), 3.09 (br s, 1H), 2.76 - 2.68 (m, 1H), 2.28 - 2.10 (m, 3H), 1.90 - 1.76 (m, 2H), 1.68 - 1.59 (m, 1H), 1.55 - 1.47 (m, 1H), 1.45 - 1.36 (m, 3H), 0.87 - 0.67 (m, 2H), 0.35 (br d, J=2.6 Hz, 2H)。*：典質子因水抑制而被遮擋。	2.41, B

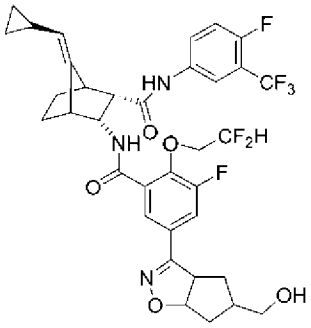
784		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-3-[3-氟-2-(3-氟prop氧基)-5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]苯甲醯胺基]-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	706.2	(500 MHz, DMSO-d6) δ 10.58 - 10.44 (m, 1H), 9.48 (d, J=7.1 Hz, 1H), 8.08 (br d, J=5.5 Hz, 1H), 7.85 (s, 1H), 7.78 - 7.72 (m, 1H), 7.71 - 7.67 (m, 1H), 7.45 (t, J=9.6 Hz, 1H), 5.15 (dd, J=8.6, 5.5 Hz, 1H), 4.69 (d, J=9.5 Hz, 1H), 4.64 - 4.57 (m, 2H), 4.52 (t, J=5.9 Hz, 1H), 4.43 (br d, J=5.2 Hz, 1H), 4.35 - 4.25 (m, 2H), 4.18 (br t, J=9.3 Hz, 1H), 3.43 - 3.30 (m, 1H), 3.19 - 3.14 (m, 1H), 3.11 (br s, 1H), 2.72 (br s, 1H), 2.25 - 2.14 (m, 1H), 2.15 - 2.09 (m, 1H), 2.04 - 1.96 (m, 1H), 1.93 - 1.84 (m, 1H), 1.81 - 1.73 (m, 3H), 1.68 - 1.61 (m, 1H), 1.59 - 1.54 (m, 1H), 1.53 - 1.48 (m, 1H), 1.46 - 1.38 (m, 1H), 0.81 - 0.65 (m, 2H), 0.47 - 0.30 (m, 2H)。一些質子因水抑制而被遮擋。	2.43, B

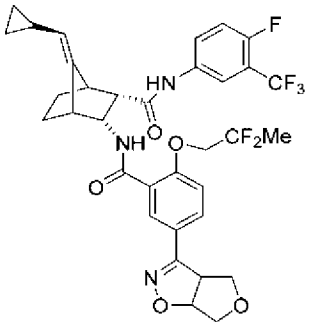
785		(1R,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-(2,2-二氟乙氧基)苯甲醯胺基)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	664.2	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.57 (br d, J=7.0 Hz, 1H), 8.18 (d, J=2.1 Hz, 1H), 8.15 - 8.10 (m, 1H), 7.79 (dd, J=8.5, 1.5 Hz, 1H), 7.75 - 7.69 (m, 1H), 7.46 (br t, J=9.8 Hz, 1H), 7.36 (d, J=8.5 Hz, 1H), 6.63 (br t, J=55.2 Hz, 1H), 5.35 (br dd, J=8.9, 3.4 Hz, 1H), 4.70 (br d, J=9.5 Hz, 1H), 4.66 - 4.58 (m, 2H), 4.54 - 4.44 (m, 2H), 4.10 (br d, J=10.4 Hz, 1H), 3.92 - 3.84 (m, 1H), 3.80 - 3.72 (m, 1H), 3.65 (br dd, J=10.7, 3.4 Hz, 1H), 3.16 (br dd, J=10.8, 3.5 Hz, 1H), 3.09 (br s, 1H), 2.73 (br s, 1H), 1.93 - 1.69 (m, 2H), 1.50 (td, J=8.7, 4.6 Hz, 1H), 1.47 - 1.31 (m, 2H), 0.85 - 0.61 (m, 2H), 0.47 - 0.21 (m, 2H)	2.45, B

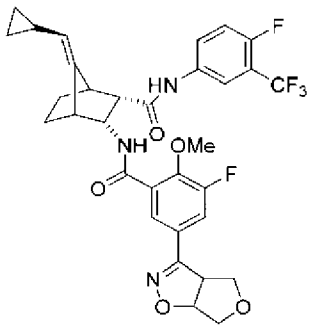
786		(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-(3-氟prop氧基)苯甲醯胺基)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	660.2	(500 MHz, DMSO-d6) δ 10.56 - 10.43 (m, 1H), 9.60 (br d, J=7.3 Hz, 1H), 8.18 (d, J=2.1 Hz, 1H), 8.14 (br d, J=4.6 Hz, 1H), 7.77 (dd, J=8.9, 2.1 Hz, 1H), 7.73 - 7.67 (m, 1H), 7.45 (br t, J=9.8 Hz, 1H), 7.31 (d, J=8.9 Hz, 1H), 5.34 (dd, J=8.9, 3.4 Hz, 1H), 4.76 - 4.67 (m, 2H), 4.65 - 4.57 (m, 1H), 4.53 - 4.46 (m, 2H), 4.42 - 4.35 (m, 1H), 4.09 (br d, J=11.0 Hz, 1H), 3.89 (br d, J=7.6 Hz, 1H), 3.81 - 3.73 (m, 1H), 3.65 (br dd, J=11.0, 3.1 Hz, 1H), 3.56 - 3.44 (m, 1H), 3.19 - 3.13 (m, 1H), 3.10 (br s, 1H), 2.72 (br s, 1H), 2.43 - 2.36 (m, 1H), 2.35 - 2.28 (m, 1H), 1.88 - 1.76 (m, 2H), 1.58 - 1.38 (m, 3H), 0.80 - 0.68 (m, 2H), 0.35 (br s, 2H)	2.48, B

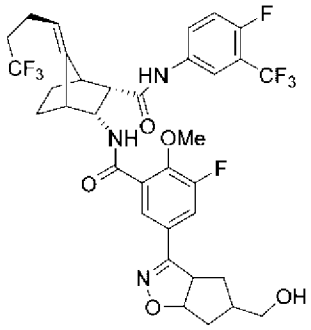
178	 其他物2	(1R,2S,3R,4R,17Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-[2-(3-氟 prop 氧基)-5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]苯甲醯胺基]雙環[2.2.1]庚烷-2-甲醯胺	688.4	(500 MHz, DMSO-d6) δ 10.56 - 10.45 (m, 1H), 9.58 (d, J=7.3 Hz, 1H), 8.16 (d, J=2.1 Hz, 1H), 8.12 (dd, J=6.5, 2.1 Hz, 1H), 7.76 (dd, J=8.7, 2.2 Hz, 1H), 7.71 - 7.66 (m, 1H), 7.43 (t, J=9.7 Hz, 1H), 7.30 (d, J=8.9 Hz, 1H), 5.11 (dd, J=8.7, 5.3 Hz, 1H), 4.72 - 4.67 (m, 2H), 4.63 (br d, J=6.7 Hz, 1H), 4.60 - 4.55 (m, 1H), 4.52 - 4.45 (m, 1H), 4.37 (br t, J=5.5 Hz, 2H), 4.17 (br t, J=8.8 Hz, 1H), 3.40 - 3.35 (m, 1H), 3.34 - 3.29 (m, 1H), 3.17 - 3.11 (m, 1H), 3.10 - 3.05 (m, 1H), 2.71 (br s, 1H), 2.39 - 2.33 (m, 1H), 2.31 - 2.25 (m, 1H), 2.02 - 1.98 (m, 1H), 1.97 - 1.94 (m, 1H), 1.92 - 1.86 (m, 1H), 1.81 (br d, J=7.9 Hz, 2H), 1.76 (br d, J=6.1 Hz, 1H), 1.73 (br s, 1H), 1.68 - 1.61 (m, 1H), 1.58 - 1.54 (m, 1H), 1.50 (br dd, J=10.6, 5.0 Hz, 1H), 0.82 - 0.66 (m, 2H), 0.34 (br d, J=4.0 Hz, 2H)	2.42, B

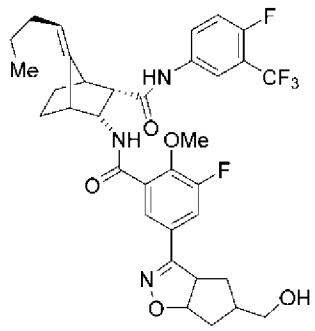
188	 異構物1	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-[2-(3-氟丙氧基)-5-[5-(羥甲基)-3a,4,4a,5,6,6a-六氫環戊并[d][1,2]噁唑-3-基]苯甲醯胺基]雙環[2.2.1]庚烷-2-甲醯胺	688.2	(500 MHz, DMSO-d6) δ 10.50 (s, 1H), 9.58 (br d, J=7.3 Hz, 1H), 8.20 (s, 1H), 8.14 (br d, J=5.3 Hz, 1H), 7.77 (br d, J=8.6 Hz, 1H), 7.73 (br dd, J=5.7, 3.0 Hz, 1H), 7.46 (t, J=9.9 Hz, 1H), 7.31 (d, J=8.7 Hz, 1H), 5.19 - 5.11 (m, 1H), 4.70 (br d, J=9.0 Hz, 2H), 4.64 - 4.58 (m, 1H), 4.53 - 4.47 (m, 2H), 4.39 (br s, 2H), 4.15 - 4.06 (m, 1H), 3.48 - 3.39 (m, 1H), 3.31 - 3.25 (m, 1H), 3.25 - 3.20 (m, 1H), 3.19 - 3.13 (m, 1H), 3.12 - 3.06 (m, 1H), 2.72 (br s, 1H), 2.42 - 2.36 (m, 1H), 2.35 - 2.29 (m, 1H), 2.22 - 2.08 (m, 3H), 1.88 - 1.79 (m, 2H), 1.67 - 1.60 (m, 1H), 1.55 - 1.49 (m, 1H), 1.47 - 1.41 (m, 2H), 0.83 - 0.69 (m, 2H), 0.36 (br s, 2H)	2.36, B

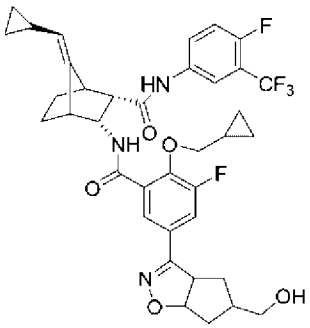
789		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-3-[2-(2,2-二氟乙氧基)-3-氟-5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]苯甲醯胺基]-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	710.2	(500 MHz, DMSO-d6) δ 10.50 (s, 1H), 9.31 (d, J=7.1 Hz, 1H), 8.05 (br d, J=4.3 Hz, 1H), 7.85 - 7.77 (m, 2H), 7.73 (br d, J=12.3 Hz, 1H), 7.46 (t, J=9.7 Hz, 1H), 6.51 - 6.16 (m, 1H), 5.17 (dd, J=8.6, 5.1 Hz, 1H), 4.70 (d, J=9.6 Hz, 1H), 4.55 - 4.46 (m, 2H), 4.45 - 4.37 (m, 1H), 4.20 (br t, J=8.9 Hz, 1H), 3.43 - 3.37 (m, 1H), 3.16 (br dd, J=10.6, 3.9 Hz, 1H), 3.11 (br s, 1H), 2.73 (br s, 1H), 1.99 (br dd, J=13.7, 5.6 Hz, 1H), 1.91 - 1.83 (m, 2H), 1.79 - 1.70 (m, 1H), 1.68 - 1.59 (m, 1H), 1.58 - 1.34 (m, 4H), 0.84 - 0.68 (m, 2H), 0.36 (br d, J=1.4 Hz, 2H)。一些質子因水抑制而被遮擋。	2.47, C

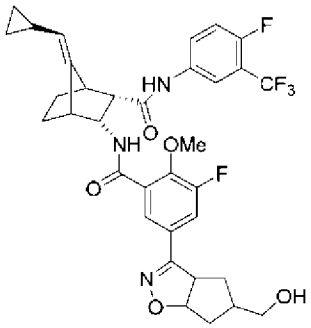
790		(2S,3R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-(2,2-二氟prop氧基)苯甲醯胺基)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	678.1	(500 MHz, DMSO-d6) δ 10.48 (s, 1H), 9.36 (d, J=7.4 Hz, 1H), 8.14 - 8.07 (m, 1H), 8.04 (d, J=2.3 Hz, 1H), 7.76 (dd, J=8.7, 2.2 Hz, 1H), 7.73 - 7.67 (m, 1H), 7.44 (t, J=9.6 Hz, 1H), 7.36 (d, J=8.9 Hz, 1H), 5.34 (dd, J=9.2, 3.4 Hz, 1H), 4.73 - 4.55 (m, 3H), 4.51 - 4.40 (m, 2H), 4.09 (d, J=10.8 Hz, 1H), 3.92 - 3.83 (m, 1H), 3.77 - 3.70 (m, 1H), 3.64 (br dd, J=10.8, 3.6 Hz, 1H), 3.14 (br dd, J=10.5, 3.9 Hz, 1H), 3.08 (br s, 1H), 2.71 (br s, 1H), 1.89 (br d, J=12.7 Hz, 1H), 1.83 - 1.69 (m, 4H), 1.50 (td, J=8.7, 4.3 Hz, 1H), 1.45 - 1.35 (m, 2H), 0.80 - 0.67 (m, 2H), 0.35 (br d, J=1.7 Hz, 2H)	2.43, C

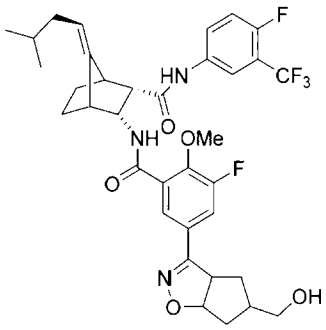
791		(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-3-氟-2-甲氧基苯甲醯胺基)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	632.3	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.69 (d, J=7.3 Hz, 1H), 8.17 - 8.06 (m, 1H), 7.95 (s, 1H), 7.81 (br dd, J=5.0, 3.6 Hz, 1H), 7.74 (dd, J=12.7, 1.6 Hz, 1H), 7.47 (t, J=9.7 Hz, 1H), 5.38 (dd, J=9.1, 3.5 Hz, 1H), 4.69 (d, J=9.5 Hz, 1H), 4.53 - 4.41 (m, 2H), 4.17 - 4.05 (m, 3H), 3.91 (br d, J=9.3 Hz, 1H), 3.73 (dd, J=9.3, 6.6 Hz, 1H), 3.64 (dd, J=10.8, 3.8 Hz, 1H), 3.16 (br dd, J=10.4, 4.1 Hz, 1H), 3.12 - 3.07 (m, 1H), 2.99 (s, 1H), 2.77 - 2.70 (m, 1H), 1.90 - 1.75 (m, 2H), 1.56 - 1.32 (m, 3H), 0.80 - 0.63 (m, 2H), 0.41 - 0.27 (m, 2H)	2.63, C

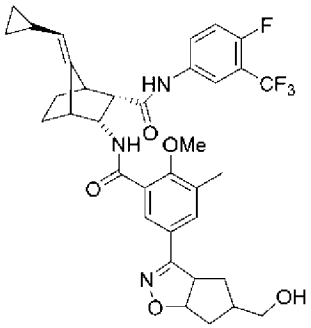
792		(1R,2S,3R,4R,7Z)-N-[4-氟-3-(三氟甲基)苯基]-3-{3-氟-5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-7-(4,4,4-三氟丁亞基)雙環[2.2.1]庚烷-2-甲醯胺	716.2	(500 MHz, DMSO-d6) δ 10.57 (s, 1H), 9.70 (br d, J=7.0 Hz, 1H), 8.12 (br d, J=4.3 Hz, 1H), 7.97 (s, 1H), 7.91 - 7.79 (m, 1H), 7.73 (dd, J=12.5, 1.8 Hz, 1H), 7.49 (br t, J=9.8 Hz, 1H), 5.29 (br t, J=7.2 Hz, 1H), 5.17 (br dd, J=8.5, 5.2 Hz, 1H), 4.51 (br t, J=5.0 Hz, 1H), 4.47 - 4.37 (m, 1H), 4.20 (br t, J=9.0 Hz, 1H), 4.09 (d, J=2.1 Hz, 3H), 3.18 (br dd, J=10.7, 4.0 Hz, 1H), 3.01 (br s, 1H), 2.77 (br s, 1H), 2.44 - 2.23 (m, 4H), 2.00 (br dd, J=13.6, 5.0 Hz, 1H), 1.94 - 1.72 (m, 4H), 1.70 - 1.51 (m, 2H), 1.48 - 1.34 (m, 2H)	2.50, C

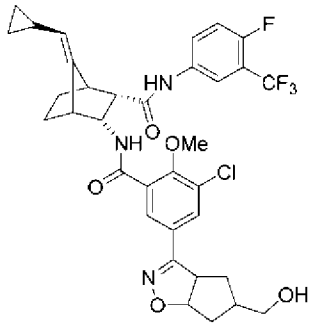
793		(1R,2S,3R,4R,7Z)-7-丁亞基-N-[4-氟-3-(三氟甲基)苯基]-3-{3-氟-5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	662.2	(500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.69 (br d, J=7.0 Hz, 1H), 8.16 - 8.06 (m, 1H), 7.95 (s, 1H), 7.85 - 7.77 (m, 1H), 7.71 (dd, J=12.7, 2.0 Hz, 1H), 7.47 (t, J=9.8 Hz, 1H), 5.24 (t, J=7.6 Hz, 1H), 5.16 (dd, J=8.7, 5.3 Hz, 1H), 4.60 (br t, J=5.3 Hz, 1H), 4.47 - 4.36 (m, 1H), 4.18 (br t, J=9.2 Hz, 1H), 4.08 (d, J=2.4 Hz, 3H), 3.41 - 3.27 (m, 1H), 3.17 (br dd, J=10.5, 4.1 Hz, 1H), 2.97 (br s, 1H), 2.74 (br s, 1H), 2.11 - 1.96 (m, 3H), 1.94 - 1.72 (m, 4H), 1.70 - 1.48 (m, 2H), 1.47 - 1.34 (m, 4H), 0.90 (t, J=7.3 Hz, 3H)	2.58, C

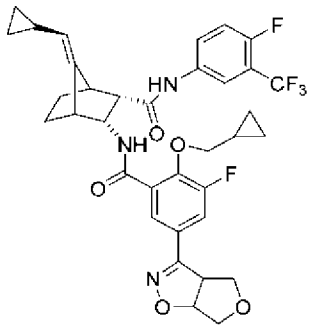
794		(1R,2S,3R,4R,7Z)-3-[2-(環丙基甲氧基)-3-氟-5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]苯甲醯胺基]-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	700.2	(500 MHz, DMSO-d6) δ 10.32 (s, 1H), 9.36 (d, J=7.3 Hz, 1H), 7.90 (dd, J=6.4, 2.1 Hz, 1H), 7.73 (s, 1H), 7.59 - 7.52 (m, 1H), 7.49 (dd, J=12.4, 2.0 Hz, 1H), 7.27 (br t, J=9.8 Hz, 1H), 4.96 (dd, J=8.5, 5.2 Hz, 1H), 4.55 - 4.46 (m, 1H), 4.27 (br t, J=10.5 Hz, 1H), 3.99 (br t, J=9.2 Hz, 1H), 3.93 (br d, J=6.1 Hz, 2H), 3.31 - 3.09 (m, 2H), 2.97 (br dd, J=10.1, 4.0 Hz, 1H), 2.91 (br d, J=4.0 Hz, 1H), 2.56 - 2.50 (m, 1H), 1.80 (br dd, J=13.4, 5.5 Hz, 1H), 1.74 - 1.53 (m, 4H), 1.52 - 1.16 (m, 6H), 1.08 - 0.97 (m, 1H), 0.61 - 0.47 (m, 2H), 0.29 - 0.09 (m, 4H), 0.07 - -0.07 (m, 2H)	2.59, C

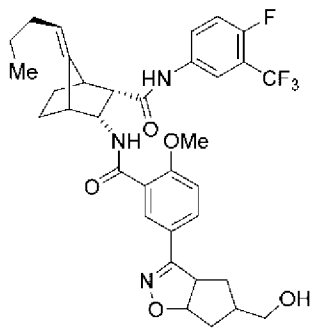
795		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{3-氟-5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	658.0	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.71 (d, J=7.1 Hz, 1H), 8.11 (br d, J=4.0 Hz, 1H), 7.97 (s, 1H), 7.88 - 7.77 (m, 1H), 7.72 (br d, J=12.3 Hz, 1H), 7.47 (t, J=9.8 Hz, 1H), 5.16 (dd, J=8.7, 5.1 Hz, 1H), 4.70 (d, J=9.5 Hz, 1H), 4.62 - 4.51 (m, 1H), 4.50 - 4.40 (m, 1H), 4.19 (br t, J=9.0 Hz, 1H), 4.09 (d, J=2.4 Hz, 3H), 3.16 (br dd, J=10.4, 4.3 Hz, 1H), 3.11 (br s, 1H), 2.73 (br s, 1H), 1.99 (br dd, J=13.7, 5.6 Hz, 1H), 1.94 - 1.73 (m, 4H), 1.70 - 1.33 (m, 5H), 0.81 - 0.68 (m, 2H), 0.35 (br d, J=2.5 Hz, 2H)	2.50, C

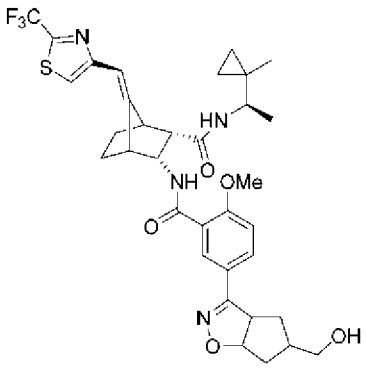
796		(1R,2S,3R,4R,7Z)-N-[4-氟-3-(三氟甲基)苯基]-3-{3-氟-5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-7-(3-甲基丁亞基)雙環[2.2.1]庚烷-2-甲醯胺	676.2	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.69 (d, J=7.3 Hz, 1H), 8.17 - 8.09 (m, 1H), 7.96 (s, 1H), 7.88 - 7.78 (m, 1H), 7.72 (dd, J=12.7, 2.0 Hz, 1H), 7.48 (t, J=9.6 Hz, 1H), 5.25 (t, J=7.6 Hz, 1H), 5.16 (dd, J=8.5, 5.2 Hz, 1H), 4.42 (br t, J=10.7 Hz, 1H), 4.19 (br t, J=9.2 Hz, 1H), 4.08 (d, J=2.4 Hz, 3H), 3.48 - 3.29 (m, 1H), 3.19 (br dd, J=10.5, 3.8 Hz, 1H), 2.96 (br s, 1H), 2.76 (br s, 1H), 2.04 - 1.93 (m, 3H), 1.92 - 1.82 (m, 2H), 1.82 - 1.72 (m, 2H), 1.70 - 1.51 (m, 3H), 1.48 - 1.33 (m, 2H), 0.91 (dd, J=11.0, 6.7 Hz, 6H)	2.67, C

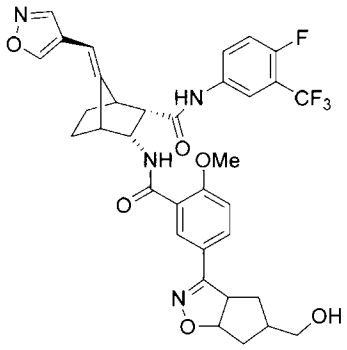
797		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基-3-甲基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	656.2	(500 MHz, DMSO-d6) δ 10.51 (s, 1H), 9.47 (br d, J=7.3 Hz, 1H), 8.05 (br d, J=4.3 Hz, 1H), 7.89 (d, J=1.8 Hz, 1H), 7.85 - 7.77 (m, 1H), 7.69 (s, 1H), 7.47 (t, J=9.9 Hz, 1H), 5.13 (dd, J=8.7, 5.3 Hz, 1H), 4.70 (d, J=9.8 Hz, 1H), 4.58 (t, J=5.2 Hz, 1H), 4.53 - 4.42 (m, 1H), 4.18 (br t, J=9.0 Hz, 1H), 3.74 (s, 3H), 3.42 - 3.25 (m, 1H), 3.16 (br dd, J=11.3, 4.3 Hz, 1H), 3.12 - 3.04 (m, 1H), 2.77 - 2.70 (m, 1H), 2.33 (s, 3H), 1.98 (br dd, J=14.0, 5.8 Hz, 1H), 1.93 - 1.72 (m, 4H), 1.69 - 1.58 (m, 1H), 1.58 - 1.31 (m, 4H), 0.82 - 0.67 (m, 2H), 0.36 (br d, J=3.7 Hz, 2H)	2.49, C

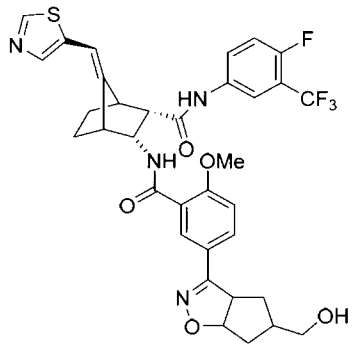
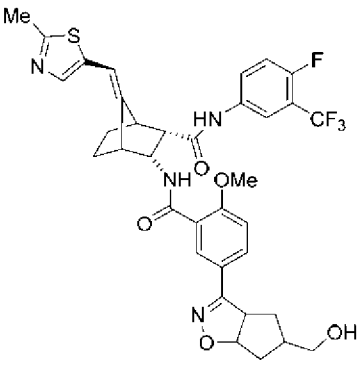
798		(1R,2S,3R,4R,7Z)-3-{3-氯-5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	676.4	(500 MHz, DMSO-d6) δ 10.52 (s, 1H), 9.55 (br d, J=7.3 Hz, 1H), 8.10 - 8.02 (m, 1H), 8.01 (d, J=2.1 Hz, 1H), 7.89 (d, J=2.1 Hz, 1H), 7.87 - 7.77 (m, 1H), 7.47 (br t, J=9.8 Hz, 1H), 5.17 (br dd, J=8.9, 5.2 Hz, 1H), 4.70 (d, J=9.5 Hz, 1H), 4.59 (br t, J=5.0 Hz, 1H), 4.52 - 4.40 (m, 1H), 4.26 - 4.17 (m, 1H), 3.88 (s, 3H), 3.42 - 3.28 (m, 1H), 3.17 (br dd, J=9.3, 5.0 Hz, 1H), 3.12 (br s, 1H), 2.74 (br s, 1H), 1.99 (br dd, J=13.1, 5.8 Hz, 1H), 1.93 - 1.73 (m, 4H), 1.69 - 1.35 (m, 5H), 1.04 (d, J=6.1 Hz, 1H), 0.83 - 0.66 (m, 2H), 0.36 (br d, J=2.4 Hz, 2H)	2.60, C

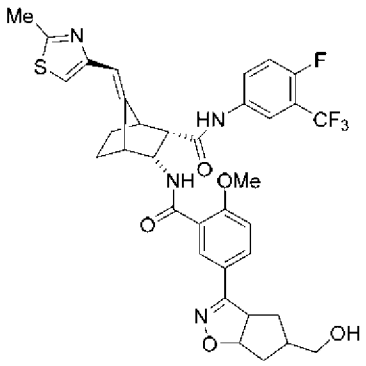
799		(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-(環丙基甲氧基)-3-氟苯甲醯胺基)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	672.1	(500 MHz, DMSO-d6) δ 10.30 (s, 1H), 9.32 (br d, J=7.3 Hz, 1H), 7.97 - 7.86 (m, 1H), 7.71 (s, 1H), 7.60 - 7.45 (m, 2H), 7.26 (t, J=9.6 Hz, 1H), 5.17 (dd, J=9.3, 3.5 Hz, 1H), 4.49 (d, J=9.8 Hz, 1H), 4.33 - 4.21 (m, 2H), 3.98 - 3.84 (m, 3H), 3.77 - 3.65 (m, 1H), 3.52 (dd, J=9.5, 7.0 Hz, 1H), 3.43 (dd, J=10.8, 3.5 Hz, 1H), 3.01 - 2.92 (m, 1H), 2.90 (br s, 1H), 2.52 (br s, 1H), 1.70 - 1.56 (m, 2H), 1.38 - 1.16 (m, 3H), 1.09 - 0.97 (m, 1H), 0.61 - 0.47 (m, 2H), 0.23 (ddd, J=16.6, 8.4, 4.9 Hz, 2H), 0.15 (br s, 2H), 0.08 - -0.05 (m, 2H)	2.71, C

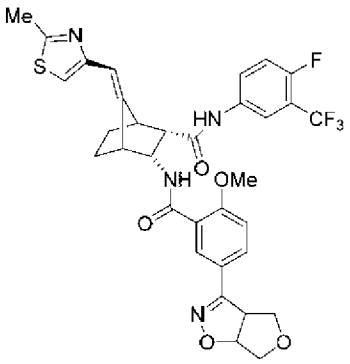
800		(1R,2S,3R,4R,7Z)-7-丁亞基-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	644.2	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.89 (br d, J=7.0 Hz, 1H), 8.20 (br d, J=2.1 Hz, 2H), 7.83 - 7.74 (m, 2H), 7.46 (t, J=9.6 Hz, 1H), 7.26 (d, J=8.9 Hz, 1H), 5.22 (t, J=7.5 Hz, 1H), 5.12 (dd, J=8.5, 4.9 Hz, 1H), 4.67 (t, J=5.2 Hz, 1H), 4.38 (br s, 1H), 4.18 (br t, J=9.2 Hz, 1H), 4.02 (s, 3H), 3.67 - 3.54 (m, 3H), 3.44 - 3.29 (m, 2H), 3.15 (br dd, J=11.4, 4.1 Hz, 1H), 2.96 (br s, 1H), 2.72 (br s, 1H), 2.09 - 1.94 (m, 2H), 1.93 - 1.80 (m, 1H), 1.80 - 1.71 (m, 1H), 1.70 - 1.48 (m, 2H), 1.44 - 1.31 (m, 4H), 0.89 (t, J=7.3 Hz, 3H)	2.54, C

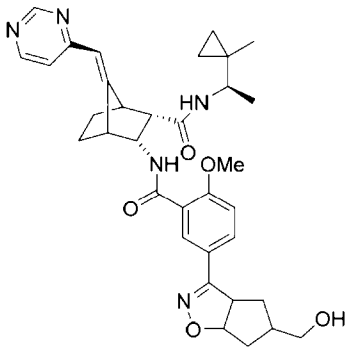
801		(1R,2S,3R,4R,7Z)-3-{5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-N-[(1R)-1-(1-甲基環丙基)乙基]-7-{[2-(三氟甲基)-1,3-噻唑-4-基]亞甲基}雙環[2.2.1]庚烷-2-甲醯胺	699.2	(400 MHz, DMSO-d6) δ = 10.63 (s, 1H), 10.04 (d, J = 6.8 Hz, 1H), 8.34 - 8.14 (m, 2H), 7.88 - 7.73 (m, 2H), 7.60 (s, 1H), 7.52 (t, J = 9.8 Hz, 1H), 7.29 (d, J = 8.8 Hz, 1H), 6.54 (s, 1H), 5.13 (dd, J = 5.1, 8.8 Hz, 1H), 4.56 - 4.43 (m, 2H), 4.27 - 4.17 (m, 1H), 4.06 (s, 3H), 3.31 - 3.26 (m, 1H), 2.95 (br d, J = 3.4 Hz, 1H), 2.66 (s, 3H), 1.99 (dd, J = 5.9, 13.7 Hz, 1H), 1.95 - 1.75 (m, 4H), 1.71 - 1.42 (m, 4H)	2.15, A

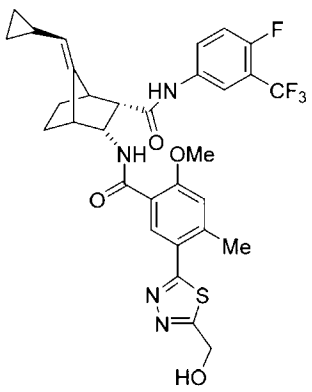
802		(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-[(1,2-噁唑-4-基)亞甲基]雙環[2.2.1]庚烷-2-甲醯胺	641.2	(400 MHz, DMSO-d6) δ = 10.68 - 10.54 (m, 1H), 9.97 (d, J = 7.3 Hz, 1H), 9.02 (s, 1H), 8.74 (s, 1H), 8.26 - 8.17 (m, 2H), 7.86 - 7.75 (m, 2H), 7.51 (t, J = 9.8 Hz, 1H), 7.29 (d, J = 8.8 Hz, 1H), 6.14 (s, 1H), 5.35 (dd, J = 3.5, 9.2 Hz, 1H), 4.50 (br t, J = 7.3 Hz, 2H), 4.10 (d, J = 10.8 Hz, 1H), 4.06 (s, 3H), 3.93 - 3.86 (m, 2H), 3.82 - 3.74 (m, 1H), 3.66 (dd, J = 3.8, 10.9 Hz, 1H), 3.30 - 3.23 (m, 2H), 2.94 (t, J = 3.3 Hz, 1H), 1.99 - 1.79 (m, 2H), 1.62 - 1.43 (m, 2H)	2.12, A

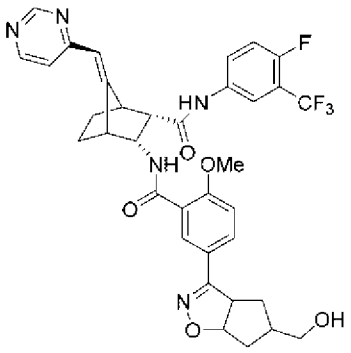
803		(1R,2S,3R,4R,7Z)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-7-[(1,3-噻唑-5-基)亞甲基]雙環[2.2.1]庚烷-2-甲醯胺	685.3	(400 MHz, CD_3OD) δ = 8.86 (s, 1H), 8.17 (d, J = 2.3 Hz, 1H), 8.06 (dd, J = 2.4, 6.4 Hz, 1H), 7.88 (dd, J = 2.3, 8.8 Hz, 1H), 7.83 - 7.76 (m, 2H), 7.32 - 7.21 (m, 2H), 6.51 (s, 1H), 5.19 (dd, J = 5.0, 8.5 Hz, 1H), 4.64 (t, J = 4.0 Hz, 1H), 4.56 (s, 1H), 4.23 (t, J = 8.8 Hz, 1H), 4.07 (s, 3H), 3.57 - 3.48 (m, 3H), 2.91 (d, J = 4.5 Hz, 1H), 2.56 (d, J = 4.8 Hz, 1H), 2.18 - 1.89 (m, 6H), 1.83 - 1.59 (m, 5H)	1.90, B
804		(1R,2S,3R,4R,7Z)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-7-[(2-甲基-1,3-噻唑-5-基)亞甲基]雙環[2.2.1]庚烷-2-甲醯胺	699.2	(400 MHz, DMSO-d6) δ = 10.63 (s, 1H), 10.04 (d, J = 6.8 Hz, 1H), 8.34 - 8.14 (m, 2H), 7.88 - 7.73 (m, 2H), 7.60 (s, 1H), 7.52 (t, J = 9.8 Hz, 1H), 7.29 (d, J = 8.8 Hz, 1H), 6.54 (s, 1H), 5.13 (dd, J = 5.1, 8.8 Hz, 1H), 4.56 - 4.43 (m, 2H), 4.27 - 4.17 (m, 1H), 4.06 (s, 3H), 3.31 - 3.26 (m, 1H), 2.95 (br d, J = 3.4 Hz, 1H), 2.66 (s, 3H), 1.99 (dd, J = 5.9, 13.7 Hz, 1H), 1.95 - 1.75 (m, 4H), 1.71 - 1.42 (m, 4H)	2.15, A

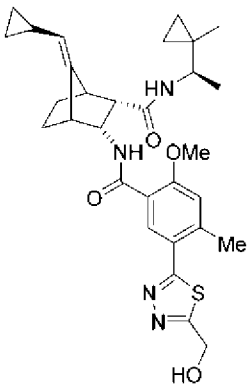
805		(1R,2S,3R,4R,7Z)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-7-[(2-甲基-1,3-噻唑-4-基)亞甲基]雙環[2.2.1]庚烷-2-甲醯胺	699.2	(400 MHz, DMSO-d6) δ ppm 10.54 - 10.66 (m, 1 H) 9.80 - 9.90 (m, 1 H) 8.17 - 8.26 (m, 1 H) 7.76 - 7.85 (m, 1 H) 7.45 - 7.54 (m, 1 H) 7.25 - 7.36 (m, 1 H) 6.29 - 6.34 (m, 1 H) 5.05 - 5.17 (m, 1 H) 4.40 - 4.59 (m, 1 H) 4.14 - 4.29 (m, 1 H) 4.01 - 4.09 (m, 1 H) 3.82 - 3.89 (m, 1 H) 2.85 - 2.94 (m, 1 H) 2.62 - 2.72 (m, 2 H) 2.28 - 2.36 (m, 1 H) 1.44 - 2.05 (m, 5 H)	3.42, E

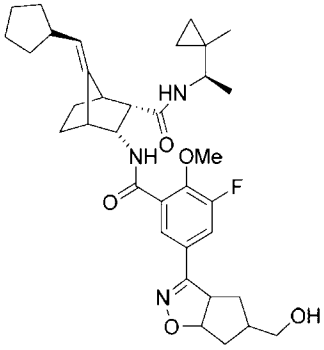
806		(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-[(2-甲基-1,3-噻唑-4-基)亞甲基]雙環[2.2.1]庚烷-2-甲醯胺	671.1	(400 MHz, DMSO-d6) δ = 10.59 (s, 1H), 9.87 (d, J = 7.3 Hz, 1H), 8.24 (dd, J = 2.7, 6.6 Hz, 1H), 8.21 (d, J = 2.4 Hz, 1H), 7.82 (qd, J = 2.4, 8.7 Hz, 2H), 7.50 (t, J = 9.7 Hz, 1H), 7.34 (s, 1H), 7.29 (d, J = 8.8 Hz, 1H), 6.32 (s, 1H), 5.35 (dd, J = 3.5, 9.2 Hz, 1H), 4.58 - 4.44 (m, 2H), 4.10 (d, J = 10.8 Hz, 1H), 4.06 (s, 3H), 3.90 (br d, J = 9.3 Hz, 2H), 3.77 (dd, J = 6.8, 9.3 Hz, 1H), 3.66 (dd, J = 3.7, 10.8 Hz, 1H), 3.27 (dd, J = 4.0, 10.6 Hz, 1H), 2.90 (br s, 1H), 2.68 (s, 3H), 2.02 - 1.93 (m, 1H), 1.90 - 1.81 (m, 1H), 1.58 - 1.44 (m, 2H)	2.25, A

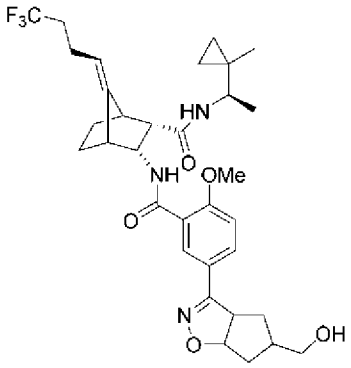
807		(1R,2S,3R,4R,7Z)-3-{5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-N-[(1R)-1-(1-甲基環丙基)乙基]-7-[(嘧啶-4-基)亞甲基]雙環[2.2.1]庚烷-2-甲醯胺	600.4	(400 MHz, DMSO-d6) δ 10.13 (d, J = 6.8 Hz, 1H), 9.13 (d, J = 0.8 Hz, 1H), 8.75 (d, J = 5.3 Hz, 1H), 8.16 (d, J = 2.4 Hz, 1H), 8.05 (d, J = 8.5 Hz, 1H), 7.81 (dd, J = 2.4, 8.6 Hz, 1H), 7.44 (dd, J = 1.2, 5.2 Hz, 1H), 7.24 (d, J = 8.9 Hz, 1H), 6.37 (s, 1H), 5.12 (dd, J = 5.1, 8.9 Hz, 1H), 4.49 (t, J = 5.3 Hz, 1H), 4.44 - 4.35 (m, 1H), 4.21 (t, J = 8.6 Hz, 1H), 4.06 - 3.94 (m, 4H), 3.50 (dd, J = 7.0, 8.4 Hz, 1H), 3.42 - 3.38 (m, 1H), 3.10 (dd, J = 4.2, 10.8 Hz, 1H), 2.81 (br s, 1H), 2.04 - 1.77 (m, 5H), 1.70 - 1.44 (m, 4H), 1.05 (d, J = 6.9 Hz, 3H), 1.01 (s, 3H), 0.63 - 0.52 (m, 1H), 0.43 - 0.32 (m, 1H), 0.26 - 0.15 (m, 2H)。	2.58, A

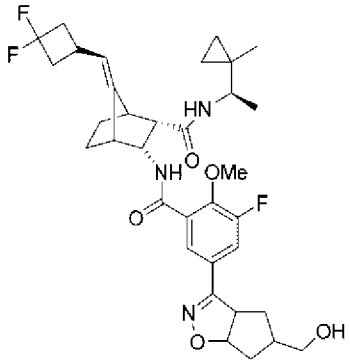
808		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(羥基甲基)-1,3,4-噻二唑-2-基]-2-甲氧基-4-甲基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	631.1	(400 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.93 (d, J = 7.1 Hz, 1H), 8.28 (s, 1H), 8.25 (dd, J = 2.4, 6.5 Hz, 1H), 7.88 - 7.67 (m, 1H), 7.50 (t, J = 9.8 Hz, 1H), 7.28 (s, 1H), 6.26 (t, J = 6.0 Hz, 1H), 4.90 (d, J = 5.9 Hz, 2H), 4.69 (d, J = 9.6 Hz, 1H), 4.50 - 4.38 (m, 1H), 4.09 (s, 3H), 3.21 - 3.13 (m, 1H), 3.11 (br s, 1H), 2.73 (br s, 1H), 2.59 (s, 3H), 1.92 - 1.72 (m, 2H), 1.55 - 1.30 (m, 3H), 0.83 - 0.61 (m, 2H), 0.35 (br d, J = 2.6 Hz, 2H)。	2.45, A

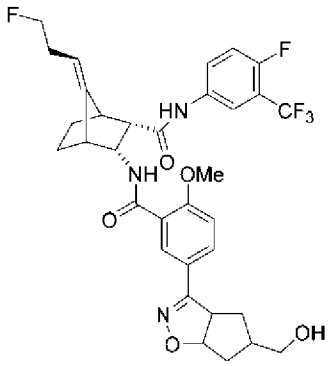
809		(1R,2S,3R,4R,7Z)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-7-[(嘧啶-4-基)亞甲基]雙環[2.2.1]庚烷-2-甲醯胺	680.2	(400 MHz, DMSO-d6) δ 10.62 (s, 1H), 9.14 (d, J = 1.0 Hz, 1H), 8.76 (d, J = 5.5 Hz, 1H), 8.33 - 8.13 (m, 2H), 7.87 - 7.75 (m, 2H), 7.56 - 7.43 (m, 2H), 7.28 (d, J = 8.8 Hz, 1H), 5.12 (dd, J = 5.4,8.9 Hz, 1H), 4.57 (ddd, J = 3.6, 6.6, 10.5 Hz, 1H), 4.48 (t, J = 5.3 Hz, 1H), 4.25 - 4.16 (m, 1H), 4.06 (s, 4H), 3.41 - 3.35 (m, 2H), 3.29 (br d, J = 4.3 Hz, 1H), 3.05 - 2.92 (m, 1H), 2.04 - 1.84 (m, 4H), 1.80 - 1.74 (m, 1H), 1.70 - 1.48 (m, 4H)	1.91, A

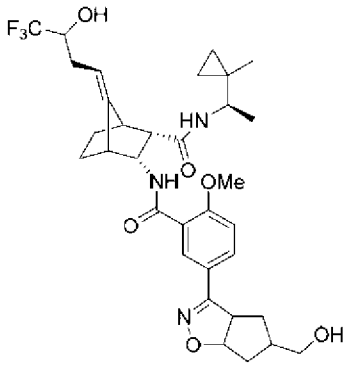
810		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-3-{5-[5-(羥基甲基)-1,3,4-噻二唑-2-基]-2-甲氧基-4-甲基苯甲醯胺基}-N-[(1R)-1-(1-甲基環丙基)乙基]雙環[2.2.1]庚烷-2-甲醯胺	551.2	(400 MHz, DMSO-d6) δ 10.11 (d, J = 6.8 Hz, 1H), 8.23 (s, 1H), 7.92 (d, J = 8.6 Hz, 1H), 7.23 (s, 1H), 6.24 (t, J = 5.9 Hz, 1H), 4.91 (d, J = 6.0 Hz, 2H), 4.64 (d, J = 9.5 Hz, 1H), 4.32 - 4.20 (m, 1H), 4.04 (s, 3H), 3.47 (dd, J = 6.9, 8.3 Hz, 1H), 3.09 - 3.02 (m, 1H), 2.96 (dd, J = 4.3, 11.0 Hz, 1H), 2.59 (s, 3H), 2.54 (br s, 1H), 1.91 - 1.83 (m, 1H), 1.74 (br s, 1H), 1.53 - 1.41 (m, 1H), 1.35 (br d, J = 2.8 Hz, 2H), 1.03 (d, J = 6.9 Hz, 3H), 0.99 (s, 3H), 0.72 (dt, J = 2.2, 8.3 Hz, 2H), 0.59 - 0.51 (m, 1H), 0.40 - 0.26 (m, 3H), 0.23 - 0.13 (m, 2H)。	2.17, A

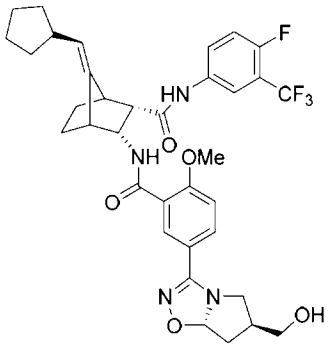
811		(1R,2S,3R,4R,7Z)-7-(環戊基亞甲基)-3-{3-氟-5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-N-[(1R)-1-(1-甲基環丙基)乙基]雙環[2.2.1]庚烷-2-甲醯胺	608.1	(500 MHz, DMSO-d6) δ 9.79 (d, J=6.7 Hz, 1H), 7.82 (br d, J=8.9 Hz, 1H), 7.73 (s, 1H), 7.55 (dd, J=12.4, 2.0 Hz, 1H), 5.03 - 4.93 (m, 2H), 4.13 - 3.99 (m, 2H), 3.88 (d, J=2.1 Hz, 3H), 2.83 - 2.77 (m, 2H), 2.44 - 2.40 (m, 1H), 1.87 - 1.80 (m, 1H), 1.78 - 1.54 (m, 7H), 1.53 - 1.33 (m, 7H), 1.25 - 1.15 (m, 2H), 1.13 - 1.03 (m, 2H), 0.89 - 0.78 (m, 6H), 0.35 (br dd, J=9.0, 3.8 Hz, 1H), 0.16 (br dd, J=9.0, 3.8 Hz, 1H), 0.06 - -0.07 (m, 2H) 一些質子因水抑制而被遮擋	2.70, C

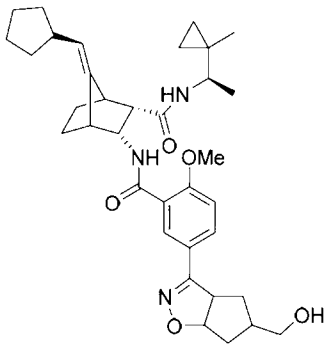
812		(1R,2S,3R,4R,7Z)-3-{5-[(3aS,5R,6aS)-5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-N-[(1R)-1-(1-甲基環丙基)乙基]-7-(4,4,4-三氟丁亞基)雙環[2.2.1]庚烷-2-甲醯胺	618.3	(500 MHz, DMSO-d6) δ 9.91 (d, J=6.7 Hz, 1H), 7.98 (d, J=2.1 Hz, 1H), 7.79 (br d, J=8.5 Hz, 1H), 7.62 (dd, J=8.5, 2.1 Hz, 1H), 7.05 (d, J=8.9 Hz, 1H), 5.04 (br t, J=6.9 Hz, 1H), 4.94 (dd, J=8.5, 5.2 Hz, 1H), 4.34 (br t, J=5.3 Hz, 1H), 4.12 - 3.98 (m, 2H), 3.81 (s, 3H), 2.81 - 2.73 (m, 2H), 2.39 (br s, 1H), 2.33 (br s, 3H), 2.22 - 2.07 (m, 4H), 1.81 (br dd, J=13.4, 5.5 Hz, 1H), 1.78 - 1.66 (m, 2H), 1.63 - 1.43 (m, 3H), 1.42 - 1.32 (m, 1H), 1.16 (br d, J=3.7 Hz, 2H), 0.91 - 0.83 (m, 3H), 0.81 (s, 3H), 0.36 (br dd, J=9.6, 3.5 Hz, 1H), 0.19 - 0.13 (m, 1H), 0.07 - -0.04 (m, 2H)	2.27, C

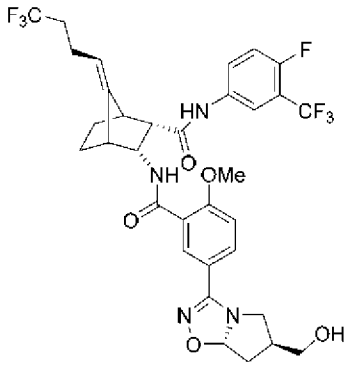
813		(1R,2S,3R,4R,7Z)-7-[(3,3-二氟環丁基)亞甲基]-3-{3-氟-5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-N-[(1R)-1-(1-甲基環丙基)乙基]雙環[2.2.1]庚烷-2-甲醯胺	630.4	(500 MHz, DMSO-d6) δ 9.82 (br d, J=6.7 Hz, 1H), 7.85 (br d, J=8.9 Hz, 1H), 7.73 (s, 1H), 7.54 (br d, J=12.2 Hz, 1H), 5.18 (d, J=8.5 Hz, 1H), 5.00 (br dd, J=8.7, 5.0 Hz, 1H), 4.39 (br t, J=4.9 Hz, 1H), 4.12 - 4.00 (m, 2H), 3.88 (s, 3H), 3.19 (br s, 1H), 2.85 - 2.58 (m, 5H), 2.42 (br s, 1H), 2.31 - 2.16 (m, 2H), 1.83 (br dd, J=13.1, 5.2 Hz, 1H), 1.77 - 1.34 (m, 7H), 1.19 (br d, J=1.8 Hz, 2H), 0.89 - 0.77 (m, 7H), 0.39 - 0.31 (m, 1H), 0.22 - 0.13 (m, 1H), 0.07 - -0.05 (m, 2H)	2.45, C

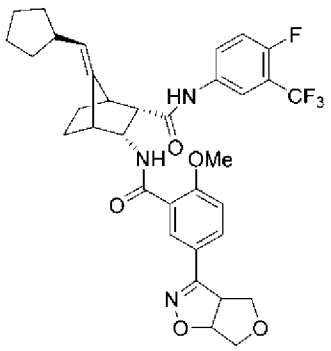
814		(1R,2S,3R,4R,7Z)-3-{5-[(3aS,6aS)-5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-N-[4-氟-3-(三氟甲基)苯基]-7-(3-氟亞丙基)雙環[2.2.1]庚烷-2-甲醯胺	647.9	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.88 (br d, J=7.0 Hz, 1H), 8.27 - 8.15 (m, 2H), 7.86 - 7.73 (m, 2H), 7.48 (t, J=9.6 Hz, 1H), 7.27 (d, J=8.9 Hz, 1H), 5.28 (t, J=7.3 Hz, 1H), 5.12 (dd, J=8.7, 5.0 Hz, 1H), 4.61 - 4.47 (m, 2H), 4.44 - 4.36 (m, 2H), 4.19 (br t, J=8.7 Hz, 1H), 4.04 (s, 3H), 3.46 - 3.31 (m, 2H), 3.20 - 3.15 (m, 1H), 3.00 (br s, 1H), 2.77 (br s, 1H), 2.49 - 2.37 (m, 2H), 1.99 (br dd, J=13.3, 5.3 Hz, 1H), 1.95 - 1.84 (m, 2H), 1.83 - 1.72 (m, 2H), 1.69 - 1.60 (m, 1H), 1.60 - 1.49 (m, 1H), 1.40 (br s, 2H)	2.21, C

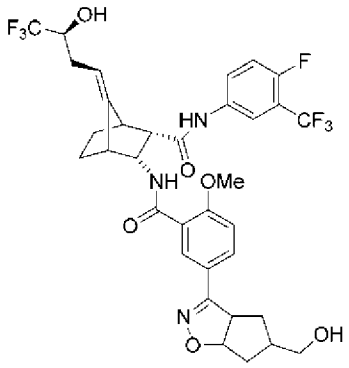
815		(1R,2S,3R,4R,7Z)-3-{5-[(3aS,5R,6aS)-5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-N-[(1R)-1-(1-甲基環丙基)乙基]-7-(4,4,4-三氟-3-羥基丁亞基)雙環[2.2.1]庚烷-2-甲醯胺	634.2	(500 MHz, DMSO-d6) δ 9.99 - 9.83 (m, 1H), 7.97 (d, J=2.1 Hz, 1H), 7.80 (br d, J=8.2 Hz, 1H), 7.62 (dd, J=8.5, 2.1 Hz, 1H), 7.05 (d, J=8.9 Hz, 1H), 6.08 (d, J=6.7 Hz, 1H), 5.08 (br t, J=7.3 Hz, 1H), 4.94 (br dd, J=8.7, 5.0 Hz, 1H), 4.11 - 3.97 (m, 2H), 3.84 - 3.76 (m, 3H), 3.36 - 3.25 (m, 1H), 3.23 - 3.10 (m, 1H), 2.81 - 2.65 (m, 3H), 2.43 - 2.39 (m, 1H), 2.26 - 2.17 (m, 1H), 2.09 (dt, J=14.6, 7.3 Hz, 1H), 1.81 (br dd, J=13.1, 5.5 Hz, 1H), 1.78 - 1.65 (m, 2H), 1.61 (br dd, J=12.7, 6.0 Hz, 1H), 1.56 - 1.43 (m, 2H), 1.40 - 1.31 (m, 1H), 1.24 - 1.10 (m, 2H), 0.99 (t, J=7.2 Hz, 2H), 0.87 - 0.66 (m, 6H), 0.41 - 0.32 (m, 1H), 0.20 - 0.11 (m, 1H), 0.04 - -0.09 (m, 2H)	2.09, C

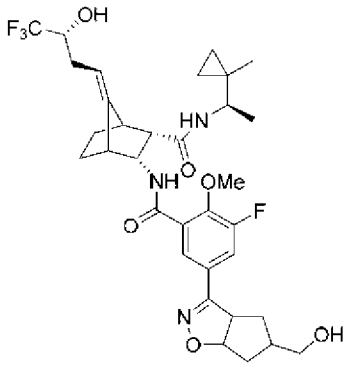
816		(1R,2S,3R,4R,7Z)-3-{5-[(6S,7aS)-6-(羥基甲基)-5H,6H,7H,7aH-吡咯并[1,2-d][1,2,4]噁二唑-3-基]-2-甲氧基苯甲醯胺基}-7-(環戊基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	671.3	(500 MHz, DMSO-d6) δ 10.54 (br s, 1H), 10.00 - 9.86 (m, 1H), 8.34 - 8.18 (m, 2H), 7.80 (br s, 2H), 7.59 - 7.46 (m, 1H), 7.37 - 7.29 (m, 1H), 5.91 - 5.71 (m, 1H), 5.19 (br d, J=8.9 Hz, 1H), 4.67 (br d, J=4.6 Hz, 1H), 4.48 - 4.32 (m, 1H), 4.16 - 3.95 (m, 3H), 3.22 - 3.11 (m, 1H), 3.05 - 2.99 (m, 1H), 2.94 - 2.85 (m, 1H), 2.77 - 2.69 (m, 1H), 2.36 - 2.24 (m, 1H), 2.21 - 2.11 (m, 1H), 2.10 - 2.02 (m, 1H), 2.01 - 1.90 (m, 1H), 1.90 - 1.72 (m, 4H), 1.69 - 1.52 (m, 4H), 1.48 - 1.34 (m, 2H), 1.34 - 1.12 (m, 2H) 一些質子因水抑制而被遮擋	2.65, C

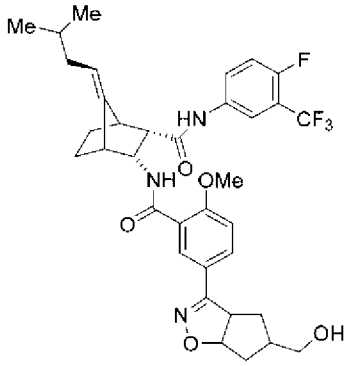
817		(1R,2S,3R,4R,7Z)-3-{5-[(3aS,5R,6aS)-5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-7-(環戊基亞甲基)-N-[(1R)-1-(1-甲基環丙基)乙基]雙環[2.2.1]庚烷-2-甲醯胺	590.3	(500 MHz, DMSO-d6) δ 9.86 (br d, J=6.7 Hz, 1H), 7.98 (d, J=2.1 Hz, 1H), 7.74 (br d, J=8.5 Hz, 1H), 7.61 (dd, J=8.7, 2.3 Hz, 1H), 7.05 (d, J=8.9 Hz, 1H), 5.01 - 4.87 (m, 2H), 4.09 - 3.96 (m, 2H), 3.81 (s, 3H), 3.32 - 3.24 (m, 1H), 2.77 (br d, J=5.5 Hz, 2H), 2.35 (br d, J=3.7 Hz, 1H), 2.33 (br s, 4H), 1.81 (br dd, J=13.1, 5.5 Hz, 1H), 1.78 - 1.42 (m, 9H), 1.42 - 1.33 (m, 3H), 1.19 - 1.01 (m, 4H), 0.87 - 0.75 (m, 6H), 0.39 - 0.31 (m, 1H), 0.19 - 0.11 (m, 1H), 0.06 - -0.07 (m, 2H)	2.48, C

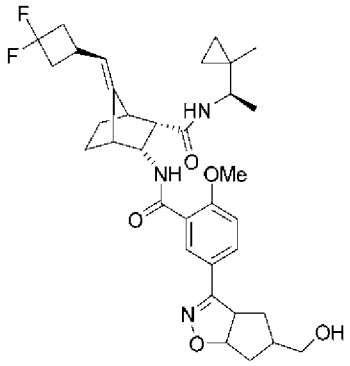
818		(1R,2S,3R,4R,7Z)-3-{5-[(6S,7aS)-6-(羥基甲基)-5H,6H,7H,7aH-吡咯并[1,2-d][1,2,4]噁二唑-3-基]-2-甲氧基苯甲醯胺基}-N-[4-氟-3-(三氟甲基)苯基]-7-(4,4,4-三氟丁亞基)雙環[2.2.1]庚烷-2-甲醯胺	699.2	(500 MHz, DMSO-d6) δ 10.73 - 10.51 (m, 1H), 10.00 - 9.83 (m, 1H), 8.25 (br d, J=16.8 Hz, 2H), 7.81 (br s, 2H), 7.58 - 7.46 (m, 1H), 7.32 (br d, J=8.9 Hz, 1H), 5.92 - 5.70 (m, 1H), 5.29 (br d, J=6.1 Hz, 1H), 4.49 - 4.36 (m, 1H), 4.07 (br s, 3H), 3.58 - 3.38 (m, 1H), 3.28 - 3.15 (m, 1H), 3.10 - 2.98 (m, 1H), 2.93 - 2.86 (m, 1H), 2.84 - 2.75 (m, 1H), 2.66 (br dd, J=5.2, 3.7 Hz, 1H), 2.47 - 2.25 (m, 5H), 2.22 - 2.01 (m, 2H), 2.01 - 1.70 (m, 4H), 1.41 (br s, 2H)	2.44, C

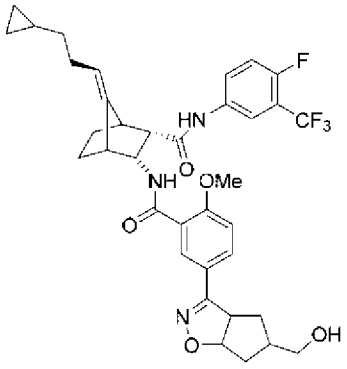
819		(1R,2S,3R,4R,7Z)-3-{5-[(3aR,6aR)-3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-7-(環戊基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	641.9	(500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.88 (br d, J=7.0 Hz, 1H), 8.26 - 8.17 (m, 2H), 7.87 - 7.72 (m, 2H), 7.47 (br t, J=9.9 Hz, 1H), 7.27 (d, J=8.5 Hz, 1H), 5.34 (dd, J=9.5, 3.4 Hz, 1H), 5.19 (d, J=8.5 Hz, 1H), 4.47 (br t, J=7.5 Hz, 1H), 4.43 - 4.32 (m, 1H), 4.19 - 4.08 (m, 1H), 4.03 (s, 3H), 3.97 - 3.85 (m, 1H), 3.77 (br dd, J=9.5, 7.0 Hz, 1H), 3.15 (td, J=10.6, 4.4 Hz, 2H), 2.99 (br s, 1H), 2.71 (br s, 1H), 2.62 - 2.56 (m, 1H), 1.92 - 1.69 (m, 4H), 1.65 - 1.51 (m, 4H), 1.45 - 1.35 (m, 2H), 1.29 - 1.16 (m, 2H)	2.66, C

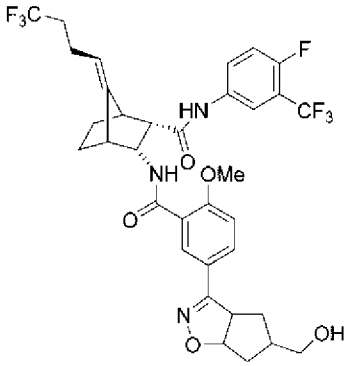
820		(1R,2S,3R,4R,7Z)-3-{5-[(3aS,5R,6aS)-5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-N-[4-氟-3-(三氟甲基)苯基]-7-(4,4,4-三氟-3-羥基丁亞基)雙環[2.2.1]庚烷-2-甲醯胺	714.2	(500 MHz, DMSO-d6) δ 10.56 (s, 1H), 9.86 (br d, J=6.9 Hz, 1H), 8.22 (br s, 2H), 7.86 - 7.75 (m, 2H), 7.49 (t, J=9.6 Hz, 1H), 7.27 (d, J=8.9 Hz, 1H), 6.27 (br d, J=6.6 Hz, 1H), 5.32 (t, J=7.0 Hz, 1H), 5.12 (dd, J=8.4, 5.2 Hz, 1H), 4.48 - 4.37 (m, 1H), 4.19 (br t, J=8.9 Hz, 1H), 4.04 (s, 3H), 4.02 - 3.92 (m, 1H), 2.98 (br s, 1H), 2.77 (br s, 1H), 2.51 (br s, 4H), 2.45 - 2.27 (m, 2H), 1.99 (br dd, J=13.6, 5.8 Hz, 1H), 1.95 - 1.84 (m, 2H), 1.82 - 1.71 (m, 2H), 1.68 - 1.51 (m, 2H), 1.45 - 1.35 (m, 2H)	2.27, C

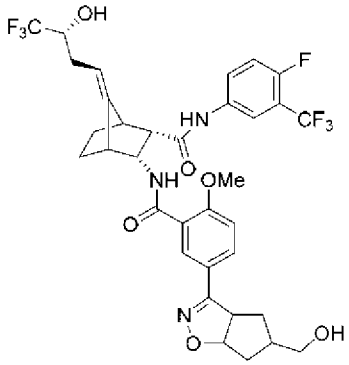
821		(1R,2S,3R,4R,7Z)-3-{3-氟-5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-N-[(1R)-1-(1-甲基環丙基)乙基]-7-(4,4,4-三氟-3-羥基丁亞基)雙環[2.2.1]庚烷-2-甲醯胺	652.2	(500 MHz, DMSO-d6) δ 9.82 (br d, J=6.6 Hz, 1H), 7.91 - 7.83 (m, 1H), 7.71 (br s, 1H), 7.53 (br d, J=12.4 Hz, 1H), 6.15 - 6.00 (m, 1H), 5.09 (br t, J=7.1 Hz, 1H), 5.02 - 4.96 (m, 1H), 4.63 (br d, J=8.4 Hz, 1H), 4.14 - 3.98 (m, 2H), 3.87 (s, 3H), 3.81 - 3.74 (m, 1H), 3.23 - 3.11 (m, 1H), 2.77 (br s, 1H), 2.34 (br s, 4H), 2.27 - 2.18 (m, 1H), 2.11 (s, 1H), 1.82 (br dd, J=13.2, 5.5 Hz, 1H), 1.77 - 1.53 (m, 4H), 1.51 - 1.32 (m, 2H), 1.28 - 1.13 (m, 2H), 0.89 - 0.70 (m, 6H), 0.38 - 0.31 (m, 1H), 0.16 (br d, J=4.3 Hz, 1H), 0.01 (br d, J=5.2 Hz, 2H)	2.16, C

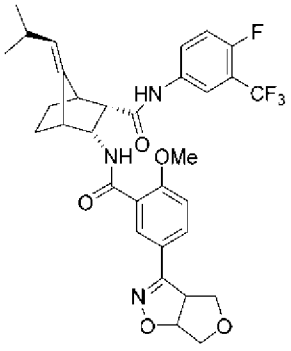
822		(1R,2S,3R,4R,7Z)-3-{5-[(3aS,6aS)-5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-N-[4-氟-3-(三氟甲基)苯基]-7-(3-甲基丁亞基)雙環[2.2.1]庚烷-2-甲醯胺	657.9	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.88 (br d, J=7.0 Hz, 1H), 8.20 (br d, J=2.1 Hz, 2H), 7.86 - 7.70 (m, 2H), 7.47 (br t, J=9.6 Hz, 1H), 7.26 (br d, J=8.8 Hz, 1H), 5.23 (br t, J=7.6 Hz, 1H), 5.12 (br dd, J=8.1, 5.0 Hz, 1H), 4.42 - 4.32 (m, 1H), 4.18 (br t, J=8.9 Hz, 1H), 4.02 (s, 3H), 3.16 (dd, J=10.7, 2.8 Hz, 1H), 2.94 (br s, 1H), 2.73 (br s, 1H), 2.51 (br s, 3H), 2.01 - 1.81 (m, 5H), 1.80 - 1.70 (m, 2H), 1.69 - 1.49 (m, 3H), 1.46 - 1.30 (m, 2H), 0.90 (br dd, J=12.3, 6.6 Hz, 6H)	2.66, C

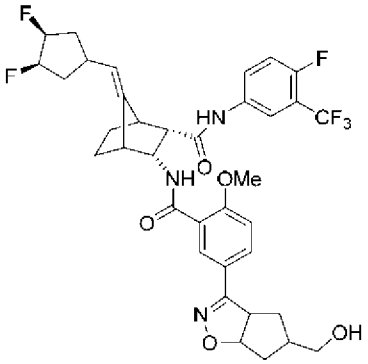
823		(1R,2S,3R,4R,7Z)-3-{5-[(3aS,5R,6aS)-5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-7-[(3,3-二氟環丁基)亞甲基]-N-[(1R)-1-(1-甲基環丙基)乙基]雙環[2.2.1]庚烷-2-甲醯胺	612.6	(500 MHz, DMSO-d6) δ 9.89 (br d, J=6.7 Hz, 1H), 7.97 (d, J=2.1 Hz, 1H), 7.77 (br d, J=8.5 Hz, 1H), 7.61 (dd, J=8.5, 1.8 Hz, 1H), 7.05 (d, J=8.5 Hz, 1H), 5.15 (d, J=8.2 Hz, 1H), 4.94 (br dd, J=8.5, 5.2 Hz, 1H), 4.12 - 3.95 (m, 2H), 3.81 (s, 3H), 2.85 - 2.71 (m, 3H), 2.69 - 2.55 (m, 2H), 2.33 (br s, 3H), 2.27 - 2.11 (m, 2H), 1.87 - 1.30 (m, 7H), 1.14 (br s, 2H), 0.95 - 0.63 (m, 6H), 0.42 - 0.31 (m, 1H), 0.20 - 0.08 (m, 1H), 0.06 - -0.12 (m, 2H) 由於水抑制而未觀測到一些質子	2.22, C

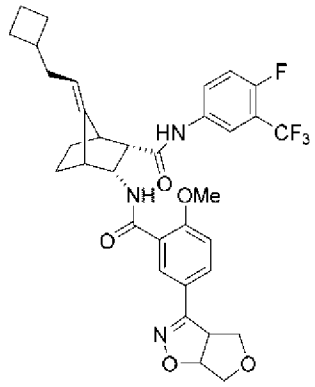
824		(1R,2S,3R,4R,7Z)-3-{5-[(3aS,6aS)-5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-7-(3-環丙基亞丙基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	670.0	(500 MHz, DMSO-d6) δ 10.51 (s, 1H), 9.85 (d, J=7.0 Hz, 1H), 8.18 (br s, 2H), 7.81 - 7.67 (m, 2H), 7.43 (t, J=9.7 Hz, 1H), 7.23 (d, J=8.8 Hz, 1H), 5.24 (t, J=7.5 Hz, 1H), 5.08 (dd, J=8.6, 5.2 Hz, 1H), 4.40 - 4.34 (m, 1H), 4.15 (br t, J=8.9 Hz, 1H), 3.99 (s, 3H), 3.39 - 3.22 (m, 2H), 3.12 (br dd, J=10.7, 4.1 Hz, 1H), 2.96 (br s, 1H), 2.69 (br s, 1H), 2.48 (s, 3H), 2.18 - 2.03 (m, 2H), 1.99 - 1.91 (m, 1H), 1.88 - 1.56 (m, 5H), 1.51 (td, J=12.5, 5.1 Hz, 1H), 1.40 - 1.30 (m, 2H), 1.29 - 1.16 (m, 2H), 0.72 - 0.64 (m, 1H), 0.49 - 0.33 (m, 2H)	2.56, C

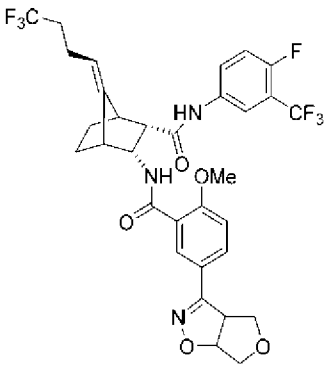
825		(1R,2S,3R,4R,7Z)-3-{5-[(3aS,6aS)-5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-N-[4-氟-3-(三氟甲基)苯基]-7-(4,4,4-三氟丁亞基)雙環[2.2.1]庚烷-2-甲醯胺	697.9	(500 MHz, DMSO-d6) δ 10.56 (s, 1H), 9.90 (d, J=7.0 Hz, 1H), 8.22 (br d, J=2.1 Hz, 2H), 7.85 - 7.73 (m, 2H), 7.48 (br t, J=9.7 Hz, 1H), 7.27 (d, J=8.8 Hz, 1H), 5.27 (br t, J=6.7 Hz, 1H), 5.12 (dd, J=8.6, 5.1 Hz, 1H), 4.41 (br t, J=10.0 Hz, 1H), 4.19 (br t, J=9.2 Hz, 1H), 4.03 (s, 3H), 3.16 (br dd, J=11.5, 3.5 Hz, 1H), 2.99 (br s, 1H), 2.75 (br s, 1H), 2.51 (br d, J=1.6 Hz, 3H), 2.44 - 2.27 (m, 4H), 1.98 (br dd, J=13.7, 5.8 Hz, 1H), 1.93 - 1.82 (m, 2H), 1.81 - 1.72 (m, 2H), 1.70 - 1.61 (m, 1H), 1.59 - 1.50 (m, 1H), 1.39 (br d, J=6.5 Hz, 2H)	2.44, C

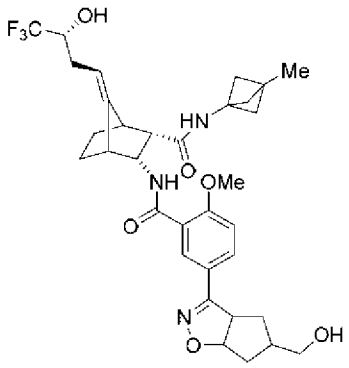
826		(1R,2S,3R,4R,7Z)-3-{5-[(3aS,5R,6aS)-5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-N-[4-氟-3-(三氟甲基)苯基]-7-(4,4,4-三氟-3-羥基丁亞基)雙環[2.2.1]庚烷-2-甲醯胺	714.2	(500 MHz, DMSO-d6) δ 10.57 (s, 1H), 9.90 (br d, J=7.3 Hz, 1H), 8.23 (br d, J=2.1 Hz, 2H), 7.81 (br dd, J=8.5, 1.8 Hz, 2H), 7.49 (t, J=9.9 Hz, 1H), 7.27 (d, J=8.9 Hz, 1H), 5.32 (br t, J=7.5 Hz, 1H), 5.12 (dd, J=8.5, 5.2 Hz, 1H), 4.48 - 4.38 (m, 1H), 4.20 (br t, J=9.0 Hz, 1H), 4.09 - 3.93 (m, 4H), 3.18 (br dd, J=11.0, 3.7 Hz, 1H), 2.99 (br d, J=7.0 Hz, 1H), 2.77 (br s, 1H), 2.51 (br s, 4H), 2.46 - 2.37 (m, 1H), 2.34 - 2.23 (m, 1H), 1.99 (br dd, J=13.7, 5.2 Hz, 1H), 1.93 - 1.83 (m, 2H), 1.82 - 1.72 (m, 2H), 1.70 - 1.62 (m, 1H), 1.59 - 1.51 (m, 1H), 1.45 - 1.35 (m, 2H)	2.21, C

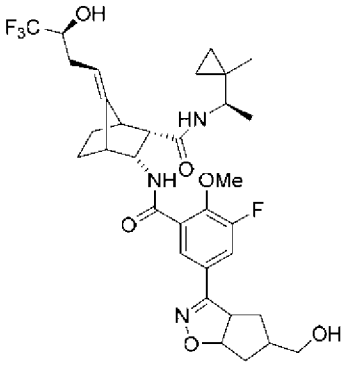
827		(1R,2S,3R,4R,7Z)-3-{5-[(3aR,6aR)-3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-N-[4-氟-3-(三氟甲基)苯基]-7-(2-甲基亞丙基)雙環[2.2.1]庚烷-2-甲醯胺	616.3	(500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.88 (br d, J=6.7 Hz, 1H), 8.28 - 8.17 (m, 2H), 7.86 - 7.74 (m, 2H), 7.48 (br t, J=9.8 Hz, 1H), 7.27 (d, J=8.9 Hz, 1H), 5.34 (dd, J=9.0, 3.5 Hz, 1H), 5.11 (d, J=8.9 Hz, 1H), 4.48 (br t, J=8.1 Hz, 1H), 4.41 - 4.33 (m, 1H), 4.10 (br d, J=10.7 Hz, 1H), 4.04 (s, 3H), 3.89 (br d, J=9.2 Hz, 1H), 3.77 (dd, J=9.3, 6.9 Hz, 1H), 3.70 - 3.62 (m, 1H), 3.20 - 3.13 (m, 1H), 2.99 (br s, 1H), 2.70 (br s, 1H), 2.49 - 2.40 (m, 1H), 1.91 - 1.70 (m, 2H), 1.49 - 1.32 (m, 2H), 1.09 - 0.93 (m, 6H)	2.64, C

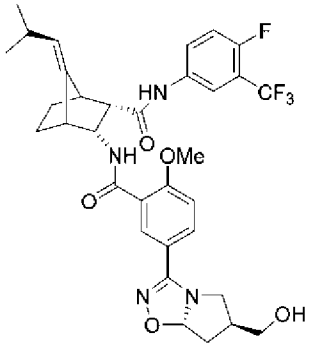
828		(1R,2S,3R,4R,7Z)-3-{5-[(3aS,5R,6aS)-5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-7-{[(3R,4S)-3,4-二氟環戊基]亞甲基}-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	706.3	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.90 (br d, J=6.7 Hz, 1H), 8.27 - 8.17 (m, 2H), 7.87 - 7.72 (m, 2H), 7.48 (t, J=9.8 Hz, 1H), 7.27 (d, J=8.9 Hz, 1H), 5.27 - 5.03 (m, 4H), 4.44 - 4.33 (m, 1H), 4.19 (br t, J=8.9 Hz, 1H), 4.03 (s, 3H), 3.42 - 3.30 (m, 1H), 3.23 - 3.10 (m, 2H), 2.98 (br s, 1H), 2.72 (br s, 1H), 2.52 (br s, 3H), 2.20 - 2.05 (m, 2H), 1.99 (br dd, J=13.3, 5.3 Hz, 1H), 1.93 - 1.81 (m, 2H), 1.78 - 1.62 (m, 4H), 1.60 - 1.50 (m, 1H), 1.44 - 1.33 (m, 2H)	2.36, C

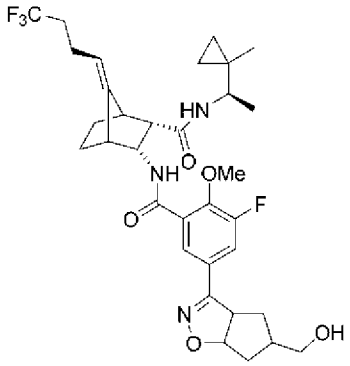
829		(1R,2S,3R,4R,7Z)-3-{5-[(3aR,6aR)-3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-7-(2-環丁基亞乙基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	642.2	(500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.89 (d, J=7.0 Hz, 1H), 8.31 - 8.14 (m, 2H), 7.86 - 7.72 (m, 2H), 7.48 (t, J=9.7 Hz, 1H), 7.27 (d, J=8.8 Hz, 1H), 5.34 (dd, J=9.0, 3.6 Hz, 1H), 5.17 (t, J=7.5 Hz, 1H), 4.49 (br t, J=8.3 Hz, 1H), 4.41 - 4.35 (m, 1H), 4.10 (d, J=10.6 Hz, 1H), 4.04 (s, 3H), 3.89 (br d, J=8.5 Hz, 1H), 3.77 (dd, J=9.3, 7.0 Hz, 1H), 3.66 (dd, J=10.7, 3.6 Hz, 1H), 3.15 (br dd, J=10.4, 4.1 Hz, 1H), 2.99 (br s, 1H), 2.72 (br s, 1H), 2.32 (quin, J=7.6 Hz, 1H), 2.14 (td, J=7.2, 2.6 Hz, 2H), 2.07 - 1.96 (m, 2H), 1.89 - 1.74 (m, 4H), 1.71 - 1.57 (m, 2H), 1.37 (br s, 2H)	2.74, C

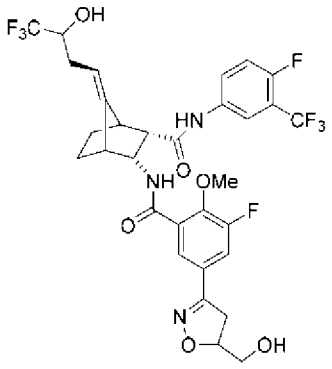
830		(1R,2S,3R,4R,7Z)-3-{5-[(3aR,6aR)-3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-N-[4-氟-3-(三氟甲基)苯基]-7-(4,4,4-三氟丁亞基)雙環[2.2.1]庚烷-2-甲醯胺	670.4	(500 MHz, DMSO-d6) δ 10.56 (s, 1H), 9.90 (br d, J=6.7 Hz, 1H), 8.30 - 8.14 (m, 2H), 7.87 - 7.70 (m, 2H), 7.49 (br t, J=9.6 Hz, 1H), 7.28 (d, J=8.9 Hz, 1H), 5.35 (dd, J=9.3, 3.5 Hz, 1H), 5.28 (br t, J=6.6 Hz, 1H), 4.50 (br t, J=7.9 Hz, 1H), 4.43 - 4.36 (m, 1H), 4.10 (br d, J=10.7 Hz, 1H), 4.05 (s, 3H), 3.90 (br d, J=8.9 Hz, 1H), 3.82 - 3.75 (m, 1H), 3.66 (dd, J=11.0, 3.4 Hz, 1H), 3.17 (br dd, J=10.7, 4.0 Hz, 1H), 3.00 (br s, 1H), 2.76 (br s, 1H), 2.44 - 2.22 (m, 4H), 1.93 - 1.70 (m, 2H), 1.48 - 1.28 (m, 2H)	2.45, C

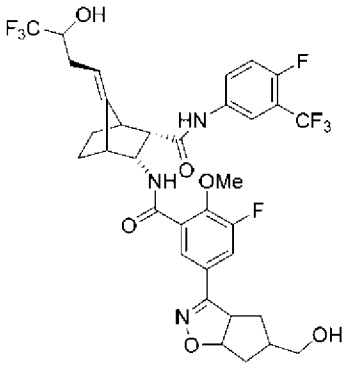
831		(1R,2S,3R,4R,7Z)-3-{5-[(3aS,5R,6aS)-5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-N-{3-甲基雙環[1.1.1]戊烷-1-基}-7-[(3R)-4,4,4-三氟-3-羥基丁亞基]雙環[2.2.1]庚烷-2-甲醯胺	632.3	(500 MHz, DMSO-d6) δ 10.16 (br d, J=6.7 Hz, 1H), 8.56 (s, 1H), 8.21 (d, J=1.5 Hz, 1H), 7.86 - 7.76 (m, 1H), 7.25 (d, J=8.9 Hz, 1H), 5.23 (br t, J=7.3 Hz, 1H), 5.13 (br dd, J=8.4, 5.3 Hz, 1H), 4.62 - 4.45 (m, 1H), 4.30 - 4.18 (m, 2H), 4.10 - 3.90 (m, 4H), 2.94 (br s, 1H), 2.84 (br dd, J=10.5, 4.4 Hz, 1H), 2.58 (br s, 1H), 2.52 (br s, 4H), 2.47 - 2.34 (m, 1H), 2.26 (dt, J=14.6, 7.6 Hz, 1H), 2.00 (br dd, J=13.4, 5.2 Hz, 1H), 1.92 - 1.75 (m, 8H), 1.74 - 1.53 (m, 3H), 1.33 (br s, 2H), 1.20 (s, 3H)	2.03, C

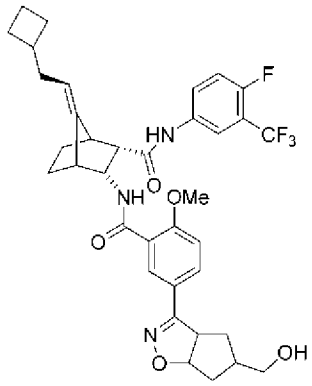
832		(1R,2S,3R,4R,7Z)-3-{3-氟-5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-N-[(1R)-1-(1-甲基環丙基)乙基]-7-(4,4,4-三氟-3-羥基丁亞基)雙環[2.2.1]庚烷-2-甲醯胺	652.3	(500 MHz, DMSO-d6) δ 9.82 (br d, J=6.6 Hz, 1H), 7.87 (br d, J=8.7 Hz, 1H), 7.72 (s, 1H), 7.53 (br d, J=12.5 Hz, 1H), 5.10 (br t, J=7.2 Hz, 1H), 5.00 (br dd, J=8.7, 5.3 Hz, 1H), 4.10 (br dd, J=10.1, 3.7 Hz, 1H), 4.06 - 3.97 (m, 1H), 3.87 (s, 3H), 3.80 (br dd, J=5.4, 4.1 Hz, 1H), 3.34 - 3.12 (m, 2H), 2.86 - 2.74 (m, 2H), 2.43 (br s, 1H), 2.35 - 2.31 (m, 2H), 2.25 - 2.05 (m, 2H), 1.84 (br dd, J=14.0, 5.7 Hz, 1H), 1.76 - 1.71 (m, 1H), 1.72 - 1.32 (m, 6H), 1.20 (br d, J=5.2 Hz, 2H), 0.92 - 0.68 (m, 6H), 0.34 (br dd, J=5.8, 2.9 Hz, 1H), 0.20 - 0.12 (m, 1H), 0.05 - -0.08 (m, 2H)	2.26, C

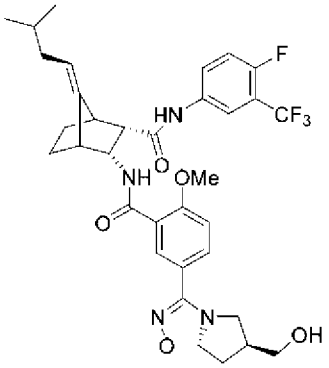
833		(1R,2S,3R,4R,7Z)-3-{5-[(6S,7aS)-6-(羥基甲基)-5H,6H,7H,7aH-吡咯并[1,2-d][1,2,4]噁二唑-3-基]-2-甲氧基苯甲醯胺基}-N-[4-氟-3-(三氟甲基)苯基]-7-(2-甲基亞丙基)雙環[2.2.1]庚烷-2-甲醯胺	645.3	(500 MHz, DMSO-d6) δ 9.99 - 9.84 (m, 1H), 8.29 - 8.18 (m, 2H), 7.82 - 7.74 (m, 2H), 7.47 (t, J=9.8 Hz, 1H), 7.30 (d, J=8.8 Hz, 1H), 5.83 - 5.76 (m, 1H), 5.10 (d, J=9.0 Hz, 1H), 4.43 - 4.35 (m, 1H), 4.11 - 4.00 (m, 3H), 3.38 - 3.24 (m, 2H), 3.22 - 3.10 (m, 2H), 2.98 (br s, 1H), 2.75 - 2.69 (m, 1H), 2.51 - 2.44 (m, 2H), 2.33 - 2.10 (m, 2H), 2.10 - 2.01 (m, 1H), 1.96 - 1.90 (m, 1H), 1.87 - 1.65 (m, 3H), 1.44 - 1.32 (m, 2H), 1.07 - 0.93 (m, 6H)	2.48, C

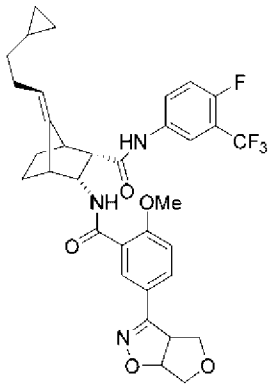
834		(1R,2S,3R,4R,7Z)-3-{3-氟-5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-N-[(1R)-1-(1-甲基環丙基)乙基]-7-(4,4,4-三氟丁亞基)雙環[2.2.1]庚烷-2-甲醯胺	636.2	(500 MHz, DMSO-d6) δ 9.84 (br d, J=6.7 Hz, 1H), 7.87 (br d, J=8.5 Hz, 1H), 7.73 (s, 1H), 7.54 (dd, J=12.5, 1.8 Hz, 1H), 5.11 - 4.96 (m, 2H), 4.14 - 3.97 (m, 2H), 3.88 (d, J=2.1 Hz, 3H), 3.26 - 3.09 (m, 1H), 2.91 - 2.74 (m, 2H), 2.42 (br s, 1H), 2.35 (br s, 3H), 2.25 - 2.06 (m, 4H), 1.84 (br dd, J=13.4, 5.5 Hz, 1H), 1.75 - 1.53 (m, 4H), 1.52 - 1.32 (m, 2H), 1.20 (br d, J=6.7 Hz, 2H), 0.92 - 0.72 (m, 6H), 0.34 (br dd, J=9.0, 3.5 Hz, 1H), 0.22 - 0.13 (m, 1H), 0.06 - -0.06 (m, 2H)	2.48, C

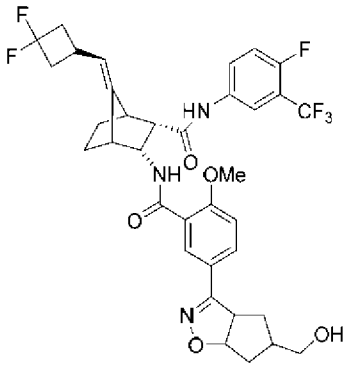
835		(1R,2S,3R,4R,7Z)-N-[4-氟-3-(三氟甲基)苯基]-3-{3-氟-5-[5-(羥基甲基)-4,5-二氫-1,2-噁唑-3-基]-2-甲氧基苯甲醯胺基}-7-(4,4,4-三氟-3-羥基丁亞基)雙環[2.2.1]庚烷-2-甲醯胺	692.2	(500 MHz, DMSO-d6) δ 10.64 - 10.49 (m, 1H), 9.68 (br d, J=7.3 Hz, 1H), 8.11 (br d, J=3.7 Hz, 1H), 7.93 (s, 1H), 7.86 - 7.78 (m, 1H), 7.70 (br d, J=12.5 Hz, 1H), 7.47 (br t, J=9.8 Hz, 1H), 5.32 (br t, J=7.2 Hz, 1H), 5.07 (s, 1H), 4.74 (br dd, J=10.7, 7.3 Hz, 1H), 4.44 (br d, J=5.5 Hz, 1H), 4.08 (d, J=2.1 Hz, 3H), 4.03 - 3.93 (m, 1H), 3.23 - 3.11 (m, 2H), 3.05 - 2.97 (m, 1H), 2.78 (br s, 1H), 2.52 (br s, 4H), 2.48 - 2.39 (m, 1H), 2.34 - 2.25 (m, 1H), 1.91 - 1.74 (m, 2H), 1.53 - 1.34 (m, 2H)	2.19, C

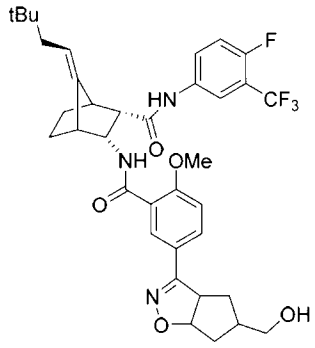
836		(1R,2S,3R,4R,7Z)-N-[4-氟-3-(三氟甲基)苯基]-3-{3-氟-5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-7-(4,4,4-三氟-3-羥基丁亞基)雙環[2.2.1]庚烷-2-甲醯胺	732.2	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.65 (br d, J=7.3 Hz, 1H), 8.11 (br d, J=5.9 Hz, 1H), 7.95 (s, 1H), 7.84 (br d, J=8.2 Hz, 1H), 7.72 (br d, J=12.4 Hz, 1H), 7.48 (br t, J=9.7 Hz, 1H), 6.27 (d, J=6.6 Hz, 1H), 5.32 (br t, J=7.2 Hz, 1H), 5.16 (br dd, J=8.2, 5.4 Hz, 1H), 4.57 - 4.38 (m, 2H), 4.19 (s, 1H), 4.08 (s, 3H), 4.03 - 3.92 (m, 1H), 3.18 (br dd, J=10.3, 3.5 Hz, 1H), 2.98 (br s, 1H), 2.78 (br s, 1H), 2.51 - 2.47 (m, 2H), 2.43 - 2.28 (m, 2H), 1.99 (br dd, J=14.0, 5.2 Hz, 1H), 1.94 - 1.84 (m, 2H), 1.84 - 1.73 (m, 2H), 1.71 - 1.51 (m, 2H), 1.47 - 1.33 (m, 2H)	2.31, C

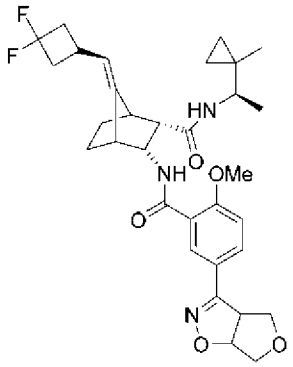
837		(1R,2S,3R,4R,7Z)-3-{5-[(3aS,6aS)-5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-7-(2-環丁基亞乙基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	670.3	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.89 (br d, J=7.2 Hz, 1H), 8.21 (br d, J=2.5 Hz, 2H), 7.92 - 7.73 (m, 2H), 7.47 (br t, J=9.5 Hz, 1H), 7.26 (d, J=8.9 Hz, 1H), 5.24 - 5.08 (m, 2H), 4.42 - 4.34 (m, 1H), 4.18 (br t, J=8.9 Hz, 1H), 4.03 (s, 3H), 3.38 - 3.29 (m, 1H), 3.18 - 3.10 (m, 1H), 2.98 (br d, J=3.6 Hz, 1H), 2.71 (br s, 1H), 2.31 (dt, J=15.1, 7.5 Hz, 1H), 2.21 - 2.10 (m, 3H), 2.04 - 1.91 (m, 3H), 1.85 - 1.72 (m, 5H), 1.67 - 1.61 (m, 2H), 1.60 - 1.50 (m, 1H), 1.43 - 1.28 (m, 5H)	2.61, C

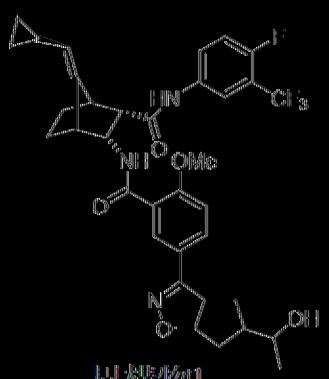
838		(1R,2S,3R,4R,7Z)-3-{5-[(6S,7aS)-6-(羥基甲基)-5H,6H,7H,7aH-吡咯并[1,2-d][1,2,4]噁二唑-3-基]-2-甲氧基苯甲醯胺基}-N-[4-氟-3-(三氟甲基)苯基]-7-(3-甲基丁亞基)雙環[2.2.1]庚烷-2-甲醯胺	659.2	(500 MHz, DMSO-d6) δ 10.63 (br s, 1H), 10.03 - 9.79 (m, 1H), 8.26 (br s, 2H), 7.96 - 7.77 (m, 2H), 7.56 - 7.45 (m, 1H), 7.36 - 7.24 (m, 1H), 5.94 - 5.75 (m, 1H), 5.39 - 5.21 (m, 1H), 4.40 (br d, J=4.3 Hz, 1H), 4.18 - 3.99 (m, 3H), 3.56 - 3.39 (m, 1H), 3.37 - 3.09 (m, 2H), 3.04 - 2.93 (m, 1H), 2.81 - 2.73 (m, 1H), 2.60 (br s, 1H), 2.38 - 2.15 (m, 2H), 2.10 - 1.71 (m, 7H), 1.69 - 1.56 (m, 1H), 1.48 - 1.29 (m, 2H), 1.07 - 0.83 (m, 6H)	2.62, C

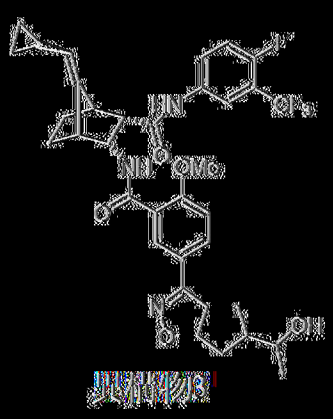
839		(1R,2S,3R,4R,7Z)-3-{5-[(3aR,6aR)-3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-7-(3-環丙基亞丙基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	642.4	(500 MHz, DMSO-d6) δ 10.51 (s, 1H), 9.85 (br d, J=7.3 Hz, 1H), 8.16 (br d, J=2.1 Hz, 2H), 7.85 - 7.70 (m, 2H), 7.52 - 7.39 (m, 1H), 7.24 (d, J=8.5 Hz, 1H), 5.30 (br dd, J=9.3, 3.2 Hz, 1H), 5.24 (br t, J=7.5 Hz, 1H), 4.48 - 4.41 (m, 1H), 4.37 - 4.30 (m, 1H), 4.06 (br d, J=11.0 Hz, 1H), 4.00 (s, 2H), 3.89 - 3.80 (m, 1H), 3.76 - 3.67 (m, 1H), 3.18 - 3.08 (m, 1H), 2.96 (br s, 1H), 2.69 (br s, 1H), 2.51 (s, 2H), 2.10 (br dd, J=7.2, 4.1 Hz, 2H), 1.85 - 1.65 (m, 2H), 1.42 - 1.32 (m, 2H), 1.27 - 1.15 (m, 2H), 0.73 - 0.63 (m, 1H), 0.50 - 0.33 (m, 2H), 0.01 (br d, J=4.0 Hz, 2H)	2.69, C

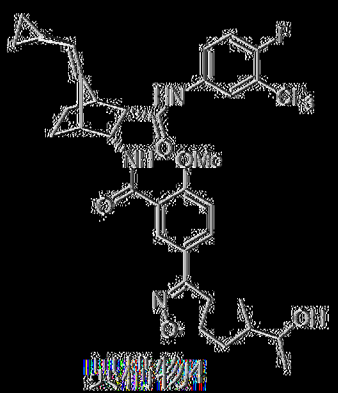
840		(1R,2S,3R,4R,7Z)-3-{5-[(3aS,6aS)-5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-7-[(3,3-二氟環丁基)亞甲基]-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	692.3	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.89 (br d, J=7.2 Hz, 1H), 8.22 (br s, 2H), 7.86 - 7.73 (m, 2H), 7.54 - 7.43 (m, 1H), 7.27 (d, J=8.8 Hz, 1H), 5.39 (br d, J=8.4 Hz, 1H), 5.12 (br dd, J=8.4, 5.3 Hz, 1H), 4.64 - 4.50 (m, 1H), 4.43 - 4.31 (m, 1H), 4.18 (br t, J=8.6 Hz, 1H), 4.03 (s, 3H), 3.43 - 3.27 (m, 1H), 3.16 (br dd, J=10.1, 3.4 Hz, 1H), 3.02 - 2.91 (m, 2H), 2.89 - 2.72 (m, 3H), 2.51 (br s, 2H), 2.47 - 2.33 (m, 2H), 1.99 (br s, 1H), 1.94 - 1.82 (m, 2H), 1.80 - 1.69 (m, 2H), 1.61 - 1.49 (m, 1H), 1.39 (br d, J=1.3 Hz, 2H)	2.42, C

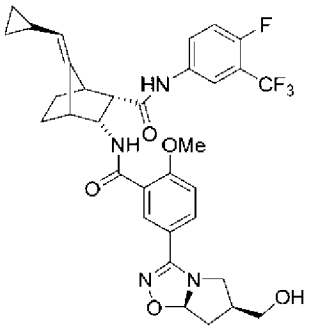
841		(1R,2S,3R,4R,7Z)-3-{5-[(3aS,6aS)-5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-7-(3,3-二甲基丁亞基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	672.2	(500 MHz, DMSO-d6) δ 10.40 (s, 1H), 9.73 (br d, J=7.0 Hz, 1H), 8.15 - 8.02 (m, 2H), 7.72 - 7.59 (m, 2H), 7.33 (br t, J=9.6 Hz, 1H), 7.11 (d, J=8.5 Hz, 1H), 5.13 (t, J=7.9 Hz, 1H), 4.96 (dd, J=8.4, 5.0 Hz, 1H), 4.33 (t, J=5.3 Hz, 1H), 4.25 (br s, 1H), 4.03 (br t, J=8.7 Hz, 1H), 3.88 (s, 3H), 3.06 - 2.98 (m, 1H), 2.82 (br d, J=17.7 Hz, 1H), 2.60 (br s, 1H), 2.35 (br s, 2H), 1.90 - 1.66 (m, 5H), 1.63 - 1.54 (m, 2H), 1.50 (br d, J=9.2 Hz, 1H), 1.40 (br d, J=3.4 Hz, 1H), 1.30 - 1.14 (m, 2H), 0.76 (s, 9H)	2.30, C

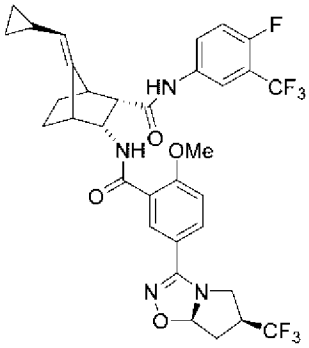
842		(1R,2S,3R,4R,7Z)-3-{5-[(3aR,6aR)-3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-7-[(3,3-二氟環丁基)亞甲基]-N-[(1R)-1-(1-甲基環丙基)乙基]雙環[2.2.1]庚烷-2-甲醯胺	584.3	(500 MHz, DMSO-d6) δ 9.89 (br d, J=6.7 Hz, 1H), 7.96 (d, J=2.1 Hz, 1H), 7.77 (br d, J=8.5 Hz, 1H), 7.61 (dd, J=8.7, 2.3 Hz, 1H), 7.05 (d, J=8.9 Hz, 1H), 5.21 - 5.11 (m, 2H), 4.31 (br t, J=7.6 Hz, 1H), 4.10 - 4.00 (m, 1H), 3.92 (br d, J=10.7 Hz, 1H), 3.81 (s, 3H), 3.74 - 3.66 (m, 1H), 3.60 (br dd, J=9.2, 7.3 Hz, 1H), 3.48 (br dd, J=10.5, 3.5 Hz, 1H), 2.73 - 2.51 (m, 3H), 2.39 (br s, 1H), 2.32 (br s, 4H), 2.28 - 2.15 (m, 2H), 1.75 - 1.66 (m, 1H), 1.58 - 1.48 (m, 1H), 1.23 - 1.05 (m, 2H), 0.89 - 0.78 (m, 5H), 0.43 - 0.32 (m, 1H), 0.24 - 0.10 (m, 1H), 0.00 (br t, J=7.3 Hz, 2H)	2.34, C

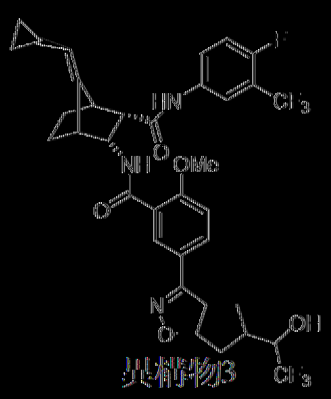
843	 異構物1	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(1-羥基乙基)-3a,4,4,5,5,6,6,6a-八氫環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	656.3	(500 MHz, DMSO-d6) δ 10.52 (s, 1H), 9.91 (br d, J = 7.3 Hz, 1H), 8.24 - 8.19 (m, 2H), 7.81 - 7.76 (m, 2H), 7.47 (t, J = 9.8 Hz, 1H), 7.26 (d, J = 8.5 Hz, 1H), 5.09 (br dd, J = 8.5, 4.9 Hz, 1H), 4.68 (d, J = 9.5 Hz, 1H), 4.47 - 4.42 (m, 1H), 4.17 (br t, J = 8.2 Hz, 1H), 4.03 (s, 3H), 3.18 - 3.13 (m, 1H), 3.09 (br s, 1H), 2.71 (br s, 1H), 2.54 (s, 2H), 1.90 - 1.81 (m, 3H), 1.79 - 1.74 (m, 1H), 1.72 - 1.64 (m, 2H), 1.60 - 1.46 (m, 2H), 1.45 - 1.34 (m, 2H), 1.01 (br d, J = 6.1 Hz, 3H), 0.78 - 0.68 (m, 2H), 0.34 (br s, 2H)	2.44, B

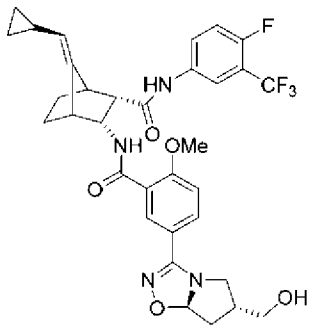
844		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(1-羥基乙基)-3a,4,4,5,5,6,6,6a-八氫環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	656.2	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.89 (br d, J = 7.0 Hz, 1H), 8.22 – 8.16 (m, 2H), 7.80 – 7.73 (m, 2H), 7.45 (t, J = 9.8 Hz, 1H), 7.25 (d, J = 8.5 Hz, 1H), 5.09 (dt, J = 10.1, 6.7 Hz, 1H), 4.68 (d, J = 9.5 Hz, 1H), 4.41 (br t, J = 10.4 Hz, 1H), 4.10 – 4.04 (m, 1H), 4.02 (s, 3H), 3.43 – 3.38 (m, 1H), 3.18 – 3.12 (m, 1H), 3.08 (br s, 1H), 2.70 (br s, 1H), 2.26 (dt, J = 12.8, 6.7 Hz, 1H), 2.17 – 2.10 (m, 1H), 1.91 – 1.72 (m, 3H), 1.56 – 1.45 (m, 2H), 1.43 – 1.33 (m, 2H), 1.32 – 1.24 (m, 1H), 0.96 (d, J = 6.1 Hz, 3H), 0.71 – 0.67 (m, 2H), 0.33 (br d, J = 3.4 Hz, 2H)	2.45, B

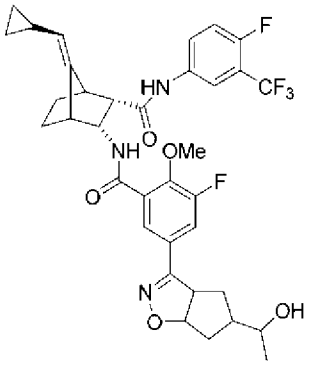
845		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(1-羥基乙基)-3a,4,4,5,5,6,6,6a-八氫環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	656.2	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.89 (br d, J = 7.0 Hz, 1H), 8.22 – 8.16 (m, 2H), 7.80 – 7.73 (m, 2H), 7.45 (t, J = 9.8 Hz, 1H), 7.25 (d, J = 8.5 Hz, 1H), 5.09 (dt, J = 10.1, 6.7 Hz, 1H), 4.68 (d, J = 9.5 Hz, 1H), 4.41 (br t, J = 10.4 Hz, 1H), 4.10 – 4.04 (m, 1H), 4.02 (s, 3H), 3.43 – 3.38 (m, 1H), 3.18 – 3.12 (m, 1H), 3.08 (br s, 1H), 2.70 (br s, 1H), 2.26 (dt, J = 12.8, 6.7 Hz, 1H), 2.17 – 2.10 (m, 1H), 1.91 – 1.72 (m, 3H), 1.56 – 1.45 (m, 2H), 1.43 – 1.33 (m, 2H), 1.32 – 1.24 (m, 1H), 0.96 (d, J = 6.1 Hz, 3H), 0.77 – 0.67 (m, 2H), 0.33 (br d, J = 3.4 Hz, 2H)	2.45, B

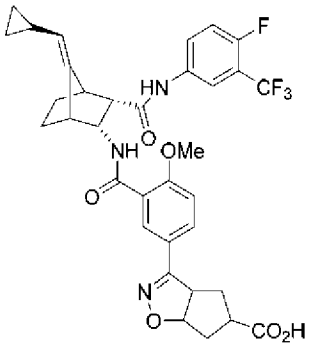
846		(1R,2S,3R,4R,7Z)-3-{5-[(6S,7aR)-6-(羥基甲基)-5H,6H,7H,7aH-吡咯并[1,2-d][1,2,4]噁二唑-3-基]-2-甲氧基苯甲醯胺基}-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	643.1	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.93 (br dd, J=17.4, 7.3 Hz, 1H), 8.27 - 8.21 (m, 1H), 8.19 (br s, 1H), 7.78 (br t, J=9.3 Hz, 2H), 7.46 (br t, J=9.6 Hz, 1H), 7.30 (d, J=8.5 Hz, 1H), 5.82 - 5.74 (m, 1H), 4.67 (br d, J=9.8 Hz, 1H), 4.42 (br s, 1H), 4.04 (s, 3H), 3.36 - 3.21 (m, 2H), 3.17 - 3.07 (m, 2H), 2.70 (br s, 1H), 2.32 - 2.19 (m, 1H), 2.18 - 2.07 (m, 1H), 2.06 - 2.00 (m, 1H), 1.97 - 1.89 (m, 1H), 1.85 - 1.74 (m, 2H), 1.52 - 1.36 (m, 3H), 0.80 - 0.67 (m, 2H), 0.38 - 0.30 (m, 2H)	2.39, B

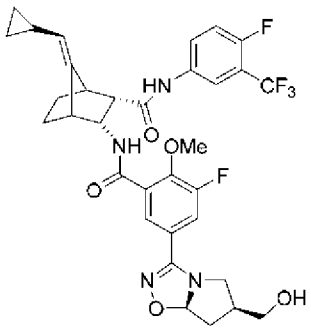
847		(1R,2S,3R,4R,7Z)-3-{5-[(6S,7aR)-6-(三氟甲基)-5H,6H,7H,7aH-吡咯并[1,2-d][1,2,4]噁二唑-3-基]-2-甲氧基苯甲醯胺基}-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	681.1	(500 MHz, DMSO-d6) δ 10.51 (s, 1H), 9.93 (br d, J=7.0 Hz, 1H), 8.23 - 8.19 (m, 2H), 7.81 - 7.74 (m, 2H), 7.47 (t, J=9.8 Hz, 1H), 7.32 (d, J=8.5 Hz, 1H), 5.93 (br t, J=4.6 Hz, 1H), 4.69 (d, J=9.8 Hz, 1H), 4.47 - 4.41 (m, 1H), 4.06 (s, 3H), 3.61 - 3.48 (m, 1H), 3.18 - 3.12 (m, 1H), 3.10 (br s, 1H), 2.72 (br s, 1H), 2.59 (ddd, J=14.5, 9.2, 6.0 Hz, 1H), 2.00 - 1.94 (m, 1H), 1.86 - 1.76 (m, 2H), 1.53 - 1.37 (m, 3H), 0.78 - 0.69 (m, 2H), 0.34 (br d, J=1.8 Hz, 2H)	2.68, B

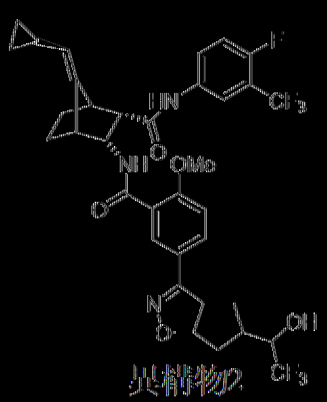
848	 見標物3	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{2-甲氧基-5-[5-(2,2,2-三氟-1-羥基乙基)-3a,4,5,6,6a-四氫戊并[d][1,2]噁唑-3-基]苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	710.2	(400 MHz, DMSO-d6) δ 10.51 (s, 1H), 9.91 (d, J = 7.0 Hz, 1H), 8.26 - 8.20 (m, 2H), 7.83 - 7.75 (m, 2H), 7.53 - 7.41 (m, 1H), 7.27 (d, J = 8.8 Hz, 1H), 6.50 (s, 1H), 6.21 (d, J = 6.7 Hz, 1H), 5.18 - 5.11 (m, 1H), 4.69 (d, J = 9.4 Hz, 1H), 4.50 - 4.39 (m, 1H), 4.16 - 4.07 (m, 1H), 4.04 (s, 3H), 3.97 - 3.86 (m, 1H), 3.19 - 3.06 (m, 2H), 2.72 (br s, 1H), 2.29 - 2.20 (m, 2H), 2.03 - 1.92 (m, 1H), 1.86 - 1.74 (m, 2H), 1.68 - 1.38 (m, 4H), 0.79 - 0.67 (m, 2H), 0.29 (s, 2H)	2.65, B

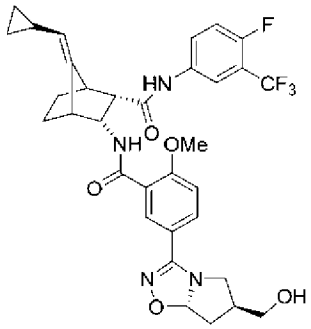
849		(1R,2S,3R,4R,7Z)-3-{5-[(6R,7aR)-6-(羥基甲基)-5H,6H,7H,7aH-吡咯并[1,2-d][1,2,4]噁二唑-3-基]-2-甲氧基苯甲醯胺基}-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	643.2	(500 MHz, DMSO-d6) δ 10.52 (s, 1H), 9.98 - 9.89 (m, 1H), 8.28 - 8.18 (m, 2H), 7.84 - 7.74 (m, 2H), 7.52 - 7.46 (m, 1H), 7.31 (d, J=8.7 Hz, 1H), 5.83 - 5.75 (m, 1H), 4.69 (d, J=9.6 Hz, 1H), 4.48 - 4.41 (m, 1H), 4.10 - 4.00 (m, 4H), 3.48 - 3.34 (m, 1H), 3.32 - 3.06 (m, 5H), 2.29 - 2.22 (m, 1H), 2.20 - 2.12 (m, 1H), 2.07 - 2.02 (m, 1H), 1.98 - 1.91 (m, 1H), 1.85 - 1.77 (m, 2H), 1.54 - 1.47 (m, 1H), 1.44 - 1.37 (m, 2H), 0.79 - 0.69 (m, 2H), 0.38 - 0.30 (m, 2H)	2.33, B

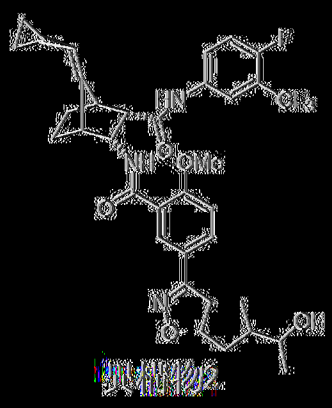
850		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{3-氟-5-[5-(1-羥基乙基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	674.3	(500 MHz, DMSO-d6) δ 10.52 (s, 1H), 9.70 (br d, J=7.3 Hz, 1H), 8.11 - 8.06 (m, 1H), 7.97 - 7.91 (m, 1H), 7.83 - 7.76 (m, 1H), 7.68 (br d, J=12.2 Hz, 1H), 7.45 (br t, J=9.8 Hz, 1H), 5.18 - 5.11 (m, 1H), 4.68 (br d, J=9.8 Hz, 1H), 4.47 - 4.39 (m, 1H), 4.10 - 4.00 (m, 4H), 3.62 - 3.49 (m, 1H), 3.45 - 3.34 (m, 1H), 3.17 - 3.06 (m, 2H), 2.75 - 2.68 (m, 1H), 2.28 (dt, J=13.4, 6.6 Hz, 1H), 2.18 - 2.10 (m, 1H), 1.91 - 1.74 (m, 3H), 1.56 - 1.36 (m, 4H), 1.31 - 1.22 (m, 1H), 0.97 (br d, J=6.1 Hz, 3H), 0.78 - 0.67 (m, 2H), 0.34 (br d, J=2.1 Hz, 2H)	2.49, B

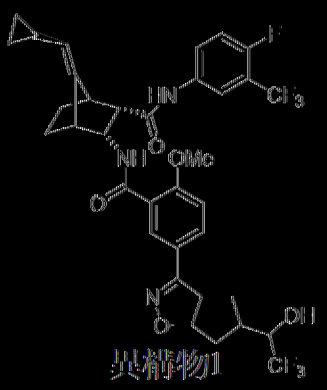
851		3-(3-{[(1R,2R,3S,4R,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-5-甲酸	656.1	(500 MHz, DMSO-d6) δ 10.52 (s, 1H), 9.90 (d, J=7.1 Hz, 1H), 8.24 - 8.20 (m, 2H), 7.81 - 7.76 (m, 2H), 7.47 (t, J=9.8 Hz, 1H), 7.27 (d, J=8.9 Hz, 1H), 5.16 (dd, J=8.4, 4.9 Hz, 1H), 4.69 (d, J=9.5 Hz, 1H), 4.46 - 4.41 (m, 1H), 4.29 (br t, J=8.5 Hz, 1H), 4.04 (s, 3H), 3.15 (br dd, J=10.6, 4.3 Hz, 1H), 3.10 (br s, 1H), 2.71 (br s, 1H), 2.18 (br dd, J=13.6, 6.3 Hz, 1H), 2.13 - 2.05 (m, 1H), 2.02 - 1.92 (m, 2H), 1.86 - 1.74 (m, 2H), 1.53 - 1.46 (m, 1H), 1.44 - 1.36 (m, 2H), 0.78 - 0.68 (m, 2H), 0.39 - 0.31 (m, 2H)	2.13, B

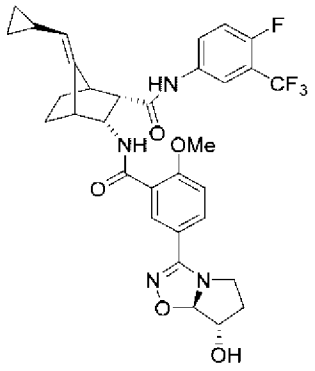
852		(1R,2S,3R,4R,7Z)-3-{5-[(6S,7aR)-6-(羥基甲基)-5H,6H,7H,7aH-吡咯并[1,2-d][1,2,4]噁二唑-3-基]-3-氟-2-甲氧基苯甲醯胺基}-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	661.3	(500 MHz, DMSO-d6) δ 10.56 - 10.49 (m, 1H), 9.79 - 9.69 (m, 1H), 8.15 - 8.08 (m, 1H), 8.04 - 7.97 (m, 1H), 7.87 - 7.78 (m, 1H), 7.69 (br d, J=12.2 Hz, 1H), 7.47 (t, J=9.7 Hz, 1H), 5.87 - 5.79 (m, 1H), 4.69 (d, J=9.7 Hz, 1H), 4.50 - 4.42 (m, 1H), 4.11 (d, J=2.1 Hz, 3H), 3.35 - 3.21 (m, 1H), 3.21 - 3.07 (m, 2H), 2.94 - 2.85 (m, 1H), 2.77 - 2.71 (m, 1H), 2.34 - 2.23 (m, 1H), 2.20 - 2.10 (m, 1H), 2.09 - 2.01 (m, 1H), 1.99 - 1.92 (m, 1H), 1.89 - 1.75 (m, 2H), 1.54 - 1.37 (m, 3H), 0.79 - 0.69 (m, 2H), 0.40 - 0.30 (m, 2H)	2.42, B

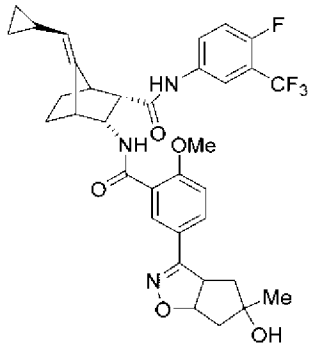
853	 共構物2	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{2-甲氧基-5-[5-(2,2,2-三氟-1-羥基乙基)-3a,4,5,6,6a-四氫-1,2-噁唑-3-基]苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	710.3	(400 MHz, DMSO-d6) δ 10.52 (s, 1H), 9.92 (d, J = 7.0 Hz, 1H), 8.26 - 8.21 (m, 2H), 7.84 - 7.76 (m, 2H), 7.49 (t, J = 9.7 Hz, 1H), 7.28 (d, J = 8.8 Hz, 1H), 6.21 (br d, J = 7.0 Hz, 1H), 5.14 (dd, J = 8.6, 4.9 Hz, 1H), 4.70 (d, J = 9.4 Hz, 1H), 4.48 - 4.41 (m, 1H), 4.25 (t, J = 8.2 Hz, 1H), 4.05 (s, 3H), 3.98 - 3.91 (m, 1H), 3.16 (dd, J = 10.7, 4.0 Hz, 1H), 3.13 - 3.09 (m, 1H), 2.72 (br s, 1H), 2.04 - 1.89 (m, 3H), 1.87 - 1.75 (m, 4H), 1.55 - 1.45 (m, 1H), 1.44 - 1.37 (m, 2H), 0.80 - 0.68 (m, 2H), 0.40 - 0.32 (m, 2H)	2.64, B

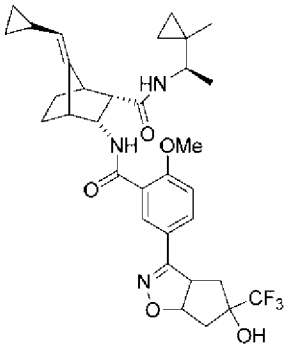
854		(1R,2S,3R,4R,7Z)-3-{5-[(6S,7aS)-6-(羥基甲基)-5H,6H,7H,7aH-吡咯并[1,2-d][1,2,4]噁二唑-3-基]-2-甲氧基苯甲醯胺基}-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	643.1	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.96 - 9.89 (m, 1H), 8.29 - 8.18 (m, 2H), 7.82 - 7.76 (m, 2H), 7.47 (br t, J=9.8 Hz, 1H), 7.30 (d, J=8.9 Hz, 1H), 5.83 - 5.75 (m, 1H), 4.68 (br d, J=9.5 Hz, 1H), 4.43 (br s, 1H), 4.05 (s, 3H), 3.52 - 3.42 (m, 1H), 3.35 - 3.25 (m, 1H), 3.19 - 3.07 (m, 2H), 2.93 - 2.84 (m, 1H), 2.71 (br s, 1H), 2.32 - 2.21 (m, 1H), 2.18 - 2.09 (m, 1H), 2.07 - 2.00 (m, 1H), 1.98 - 1.90 (m, 1H), 1.86 - 1.74 (m, 2H), 1.53 - 1.36 (m, 3H), 0.79 - 0.68 (m, 2H), 0.38 - 0.27 (m, 2H)	2.39, B

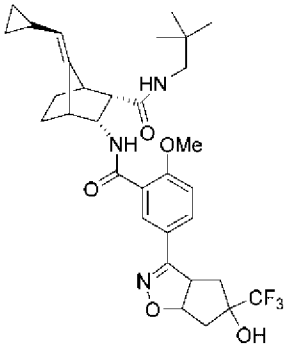
855	 興結構2	(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(1-羥基乙基)-3a,4,4,5,5,6,6,6a-八氫環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	656.2	(500 MHz, DMSO-d6) δ 10.55 - 10.51 (m, 1H), 9.91 (br d, J=7.0 Hz, 1H), 8.26 - 8.20 (m, 2H), 7.82 - 7.76 (m, 2H), 7.48 (t, J=9.6 Hz, 1H), 7.26 (d, J=8.9 Hz, 1H), 5.11 (dt, J=10.3, 6.4 Hz, 1H), 4.69 (d, J=9.5 Hz, 1H), 4.43 (br t, J=10.5 Hz, 1H), 4.10 - 4.05 (m, 1H), 4.04 (s, 3H), 3.93 - 3.86 (m, 1H), 3.15 (br dd, J=10.5, 4.1 Hz, 1H), 3.10 (br s, 1H), 2.72 (br s, 1H), 2.31 - 2.24 (m, 1H), 2.13 (dt, J=13.0, 6.4 Hz, 1H), 1.93 - 1.74 (m, 3H), 1.53 - 1.36 (m, 5H), 1.05 - 0.98 (m, 3H), 0.79 - 0.68 (m, 2H), 0.35 (br d, J=4.2 Hz, 2H)	2.44, B

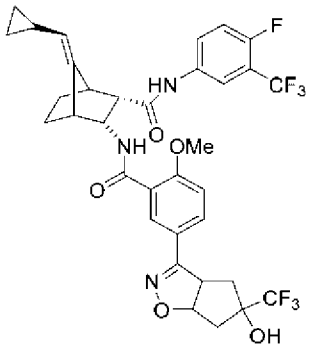
856	 異構物1	(1R,2S,3R,4R,7*)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{2-甲氧基-5-[5-(2,2,2-三氟-1-羥基乙基)-3a*H*,4*H*,5*H*,6*H*,6a*H*-環戊并[*d*][1,2]噁唑-3-基]苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	*m*/*z* 710.3	(400 MHz, DMSO-d6) δ 10.54 - 10.47 (m, 1H), 9.95 - 9.87 (m, 1H), 8.27 - 8.17 (m, 2H), 7.85 - 7.74 (m, 2H), 7.54 - 7.42 (m, 1H), 7.35 - 7.23 (m, 1H), 6.51 (br s, 1H), 6.28 - 6.21 (m, 1H), 5.16 - 5.09 (m, 1H), 4.70 (d, J= 9.4 Hz, 1H), 4.48 - 4.41 (m, 1H), 4.26 (t, J= 8.7 Hz, 1H), 4.05 (s, 3H), 4.00 - 3.92 (m, 1H), 3.16 (dd, J= 10.7, 4.4 Hz, 1H), 3.13 - 3.07 (m, 1H), 2.75 - 2.69 (m, 1H), 2.07 - 1.96 (m, 2H), 1.92 - 1.72 (m, 5H), 1.54 - 1.46 (m, 1H), 0.80 - 0.68 (m, 2H), 0.39 - 0.30 (m, 2H)	2.59, B

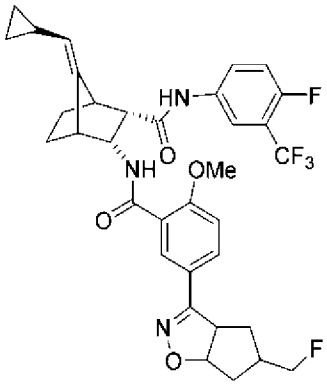
857		(1R,2S,3R,4R,7Z)-3-{5-[(7S,7aR)-7-羥基-5H,6H,7H,7aH-吡咯并[1,2-d][1,2,4]噁二唑-3-基]-2-甲氧基苯甲醯胺基}-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	629.2	(500 MHz, DMSO-d6) δ 10.52 (s, 1H), 9.89 (br d, J=7.3 Hz, 1H), 8.27 - 8.18 (m, 2H), 7.78 (br dd, J=8.5, 2.4 Hz, 2H), 7.47 (t, J=9.8 Hz, 1H), 7.31 (d, J=8.9 Hz, 1H), 5.42 (s, 1H), 4.72 - 4.66 (m, 1H), 4.47 - 4.40 (m, 1H), 4.19 - 4.12 (m, 1H), 4.05 (s, 3H), 3.23 - 3.07 (m, 2H), 2.74 - 2.68 (m, 1H), 1.87 - 1.75 (m, 2H), 1.72 - 1.62 (m, 2H), 1.54 - 1.34 (m, 3H), 0.79 - 0.68 (m, 2H), 0.34 (br s, 2H)	2.40, B

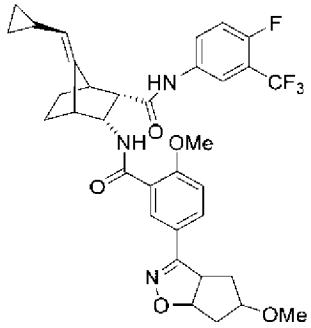
858		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-(5-{5-羥基-5-甲基-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	642.3	(400 MHz, DMSO-d6) δ = 10.55 (s, 1H), 9.90 (d, J = 7.0 Hz, 1H), 8.30 - 8.15 (m, 2H), 7.85 - 7.70 (m, 2H), 7.49 (t, J = 9.8 Hz, 1H), 7.26(d, J = 8.8 Hz, 1H), 5.20 - 5.02 (m, 1H), 4.70 (d, J = 9.6 Hz, 1H), 4.45 (ddd, J = 4.1, 6.7, 10.3 Hz, 1H), 4.26 (s, 1H), 4.16 (dt, J = 3.5, 9.6 Hz, 1H),4.04 (s, 3H), 3.17 (dd, J = 4.1, 10.8 Hz, 1H), 3.11 (br s, 1H), 2.73 (br s, 1H), 2.04 - 1.90 (m, 3H), 1.87 - 1.71 (m, 3H), 1.55 - 1.34 (m, 3H), 1.20 (s,3H), 0.81 - 0.65 (m, 2H), 0.36 (dd, J = 1.9, 4.3 Hz, 2H)	2.35, A

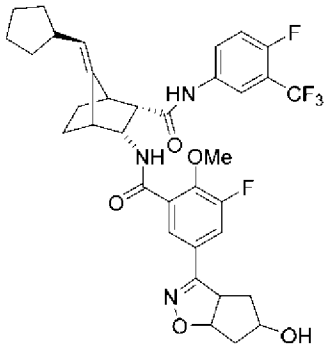
859		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-3-{5-[5-羥基-5-(三氟甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-N-[(1R)-1-(1-甲基環丙基)乙基]雙環[2.2.1]庚烷-2-甲醯胺	616.3	(400 MHz, DMSO-d6) δ = 10.05 (d, J = 6.8 Hz, 1H), 8.15 (d, J = 2.4 Hz, 1H), 7.92 (d, J = 8.5 Hz, 1H), 7.77 (dd, J = 2.4, 8.6 Hz, 1H), 7.23 (d, J = 8.8 Hz, 1H), 5.93 (s, 1H), 5.27 (br dd, J = 6.6, 9.0 Hz, 1H), 4.64 (d, J = 9.5 Hz, 1H), 4.40 (br t, J = 9.3 Hz, 1H), 4.32 - 4.23 (m, 1H), 3.99 (s, 3H), 3.47 (dd, J = 6.9, 8.4 Hz, 1H), 3.08 - 3.03 (m, 1H), 2.95 (dd, J = 4.3, 10.8 Hz, 1H), 2.32 - 2.18 (m, 3H), 2.00 (br d, J = 14.0 Hz, 1H), 1.85 (br d, J = 10.1 Hz, 1H), 1.78 - 1.71 (m, 1H), 1.47 (td, J = 4.3, 9.0 Hz, 1H), 1.35 (br s, 2H), 1.02 (d, J = 6.9 Hz, 3H), 0.98 (s, 3H), 0.72 (qd, J = 8.5, 10.4 Hz, 2H), 0.53 (br dd, J = 3.7, 8.7 Hz, 1H), 0.39 - 0.26 (m, 3H), 0.23 - 0.12 (m, 2H)	2.31, A

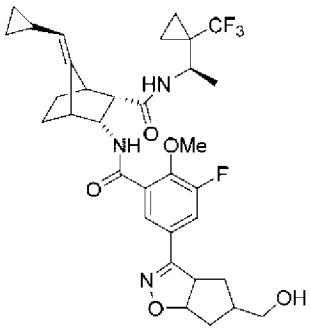
862		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-(2,2-二甲基丙基)-3-{5-[5-羥基-5-(三氟甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	604.2	(400 MHz, DMSO-d6) δ = 9.95 (d, J = 6.3 Hz, 1H), 8.16 (d, J = 2.5 Hz, 1H), 7.98 - 7.93 (m, 1H), 7.76 (dd, J = 2.4, 8.9 Hz, 1H), 7.23 (d, J= 8.8 Hz, 1H), 5.92 (s, 1H), 5.29 - 5.22 (m, 1H), 4.63 (d, J = 9.8 Hz, 1H), 4.44 - 4.37 (m, 1H), 4.29 (s, 1H), 4.00 (s, 3H), 3.06 - 2.98 (m, 3H), 2.78(br d, J = 5.0 Hz, 1H), 2.30 - 2.21 (m, 3H), 2.02 - 1.95 (m, 1H), 1.90 - 1.82 (m, 1H), 1.77 - 1.70 (m, 1H), 1.51 - 1.45 (m, 1H), 1.34 (br d, J = 1.3 Hz,2H), 0.88 - 0.77 (m, 10H), 0.75 - 0.68 (m, 2H), 0.32 (br d, J = 2.8 Hz, 2H)	2.21, A

864		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-羥基-5-(三氟甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	696.3	(400 MHz, DMSO-d6) δ = 10.0 (d, J = 4.4 Hz, 1H), 9.90 (d, 1H), 8.26 - 8.17 (m, 2H), 7.77 (dd, J = 2.5, 8.5 Hz, 2H), 7.45 (t, J = 9.8 Hz, 1H), 7.26 (d, J = 9.0 Hz, 1H), 5.99 (s, 1H), 5.28 - 5.23 (m, 1H), 4.68 (d, J = 9.5 Hz, 1H), 4.46 - 4.28 (m, 3H), 4.02 (s, 5H), 3.91 - 3.77 (m, 3H), 3.16 - 3.07 (m, 2H), 2.72 - 2.68 (m, 1H), 2.32 - 2.16 (m, 4H), 1.95 (br d, J = 14.1 Hz, 1H), 1.86 - 1.69 (m, 2H), 1.63 (s, 6H), 1.53 - 1.43 (m, 2H), 1.40 (br s, 2H), 1.33 (s, 3H), 0.72 (br t, J = 8.0 Hz, 2H), 0.33 (br d, J = 4.5 Hz, 2H)	2.87, C

866		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(氟甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	644.3	(400 MHz, DMSO-d6) δ = 10.52 (s, 1H), 9.90 (d, J = 7.0 Hz, 1H), 8.27 - 8.20 (m, 2H), 7.85 - 7.75 (m, 2H), 7.55 - 7.44 (m, 2H), 7.28 (d, J= 8.8 Hz, 1H), 7.10 (s, 1H), 5.19 - 5.12 (m, 1H), 4.70 (d, J = 9.8 Hz, 1H), 4.48 (br d, J = 5.8 Hz, 2H), 4.36 (d, J = 5.0 Hz, 1H), 4.31 - 4.23 (m, 1H),4.05 (s, 4H), 3.18 - 3.14 (m, 1H), 3.12 - 3.09 (m, 1H), 2.72 (br d, J = 3.0 Hz, 1H), 2.17 - 2.03 (m, 3H), 1.87 - 1.61 (m, 10H), 1.54 - 1.48 (m, 2H),1.42 (br dd, J = 3.1, 5.1 Hz, 2H), 1.36 (s, 3H), 1.31 - 1.14 (m, 13H), 0.95 - 0.83 (m, 3H), 0.75 (br t, J = 8.9 Hz, 2H), 0.40 - 0.31 (m, 2H)	2.64, A

867		(2S,3R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-(2-甲氧基-5-{5-甲氧基-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基}苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	642.2	(400 MHz, DMSO-d6) δ = 10.51 (s, 1H), 9.89 (d, J = 7.0 Hz, 1H), 8.28 - 8.12 (m, 2H), 7.83 - 7.67 (m, 2H), 7.48 (t, J = 9.9 Hz, 1H), 7.27 (d, J = 8.8 Hz, 1H), 5.13 (ddd, J = 2.8, 6.1, 9.4 Hz, 1H), 4.69 (d, J = 9.8 Hz, 1H), 4.49 - 4.37 (m, 1H), 4.22 (dt, J = 4.3, 9.6 Hz, 1H), 4.04 (s, 3H), 3.83 - 3.73 (m, 1H), 3.22 - 3.12 (m, 4H), 3.10 (t, J = 3.8 Hz, 1H), 2.75 - 2.69 (m, 1H), 2.13 - 1.94 (m, 3H), 1.92 - 1.71 (m, 3H), 1.54 - 1.31 (m, 3H), 0.81 - 0.64 (m, 2H), 0.35 (dd, J = 2.1, 4.6 Hz, 2H)	2.50, A

868		(1R,2S,3R,4R,7Z)-7-(環戊基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-(3-氟-5-{5-羥基-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)雙環[2.2.1]庚烷-2-甲醯胺	674.2	(400 MHz, DMSO-d6) δ ppm 10.52 (s, 1H), 9.68 (d, J = 7.0 Hz, 1H), 8.12 (dd, J = 2.8, 6.5 Hz, 1H), 7.94 (dd, J = 1.0, 2.0 Hz, 1H), 7.88 - 7.77 (m, 1H), 7.71 (dd, J = 2.3, 12.5 Hz, 1H), 7.48 (t, J = 9.9 Hz, 1H), 5.24 - 5.15 (m, 2H), 4.85 (d, J = 4.3 Hz, 1H), 4.47 - 4.37 (m, 1H), 4.20 (dt, J = 4.0, 9.3 Hz, 1H), 4.09 (d, J = 2.8 Hz, 4H), 3.22 - 3.13 (m, 1H), 3.00 (br s, 1H), 2.73 (br s, 1H), 2.64 - 2.56 (m, 1H), 2.04 - 1.73 (m, 8H), 1.72 - 1.53 (m, 4H), 1.47 - 1.37 (m, 2H), 1.35 - 1.21 (m, 2H)	2.61, A

869		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-3-{3-氟-5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-N-[(1R)-1-[1-(三氟甲基)環丙基]乙基]雙環[2.2.1]庚烷-2-甲醯胺	634.2	(500 MHz, DMSO-d6) δ 9.63 (br d, J=7.0 Hz, 1H), 7.92 (br d, J=8.5 Hz, 1H), 7.68 (s, 1H), 7.52 - 7.40 (m, 1H), 4.92 (br dd, J=8.5, 4.9 Hz, 1H), 4.41 (d, J=9.5 Hz, 1H), 4.27 (t, J=5.2 Hz, 1H), 4.16 - 4.03 (m, 1H), 3.97 (br t, J=9.2 Hz, 1H), 3.93 - 3.84 (m, 1H), 3.82 (d, J=2.1 Hz, 3H), 2.86 - 2.67 (m, 3H), 1.76 (br dd, J=13.6, 5.6 Hz, 1H), 1.65 (td, J=11.4, 5.8 Hz, 1H), 1.59 - 1.47 (m, 3H), 1.46 - 1.37 (m, 1H), 1.37 - 1.28 (m, 1H), 1.27 - 1.18 (m, 1H), 1.18 - 1.05 (m, 2H), 0.87 (br d, J=7.0 Hz, 3H), 0.73 (br d, J=9.8 Hz, 1H), 0.68 - 0.57 (m, 2H), 0.55 - 0.40 (m, 3H), 0.09 (br d, J=3.4 Hz, 2H)	2.39, C

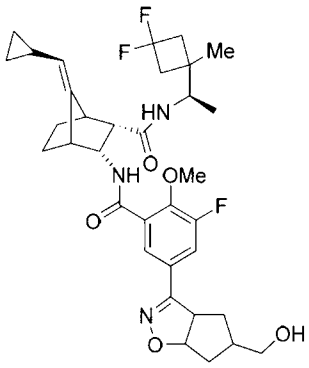
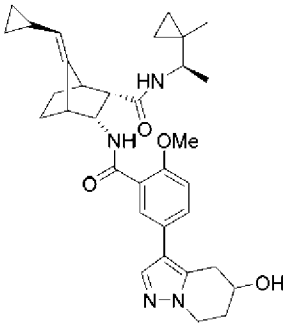
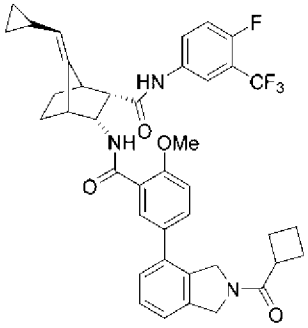
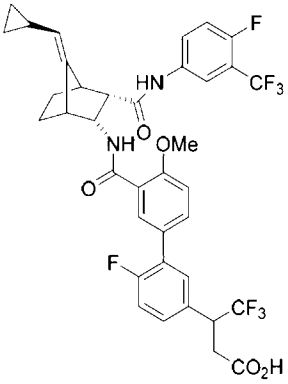
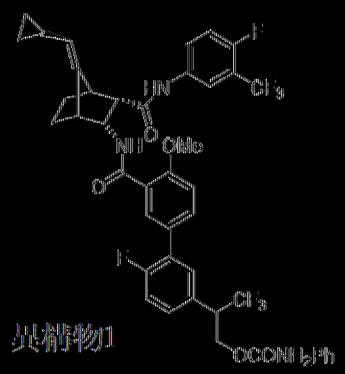
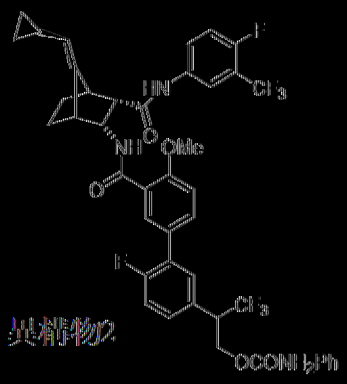
870		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[(1R)-1-(3,3-二氟-1-甲基環丁基)乙基]-3-{3-氟-5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	630.2	(500 MHz, DMSO-d6) δ 9.66 (br d, J=7.0 Hz, 1H), 7.88 (br d, J=9.2 Hz, 1H), 7.68 (s, 1H), 7.48 (br dd, J=12.5, 1.8 Hz, 1H), 4.93 (br dd, J=8.5, 5.2 Hz, 1H), 4.41 (d, J=9.5 Hz, 1H), 4.17 - 4.03 (m, 1H), 3.97 (br t, J=8.7 Hz, 1H), 3.86 - 3.71 (m, 3H), 3.66 (s, 1H), 2.84 (br s, 1H), 2.75 (br dd, J=10.8, 4.1 Hz, 1H), 2.44 - 2.33 (m, 1H), 2.24 - 2.11 (m, 2H), 2.03 - 1.80 (m, 3H), 1.76 (br dd, J=13.6, 5.3 Hz, 1H), 1.65 (td, J=11.7, 5.5 Hz, 1H), 1.59 - 1.47 (m, 3H), 1.45 - 1.28 (m, 2H), 1.27 - 1.04 (m, 4H), 0.90 (s, 3H), 0.69 (d, J=7.0 Hz, 3H), 0.55 - 0.41 (m, 2H), 0.09 (br d, J=4.0 Hz, 2H)	2.36, C

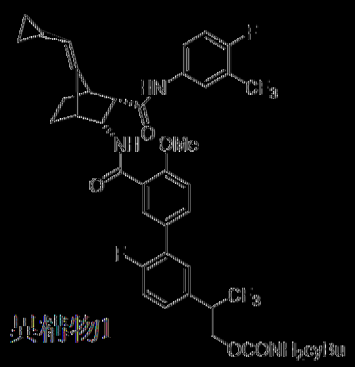
表5					
實例編號	**結構**	**名稱**	**MS (ESI) (M+H)**	**^{1}H NMR**	**LC RT Meth. (min)**
871		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-3-(5-{5-羥基-4H,5H,6H,7H-吡唑并[1,5-a]吡啶-3-基}-2-甲氧基苯甲醯胺基)-N-[(1S)-1-(1-甲基環丙基)乙基]雙環[2.2.1]庚烷-2-甲醯胺	559.3	(400 MHz, DMSO-d6) δ = 10.03 (d, J = 6.6 Hz, 1H), 7.93 (d, J = 2.0 Hz, 1H), 7.90 (d, J = 8.6 Hz, 1H), 7.66 (s, 1H), 7.54 (dd, J = 2.4, 8.6 Hz, 1H), 7.16 (d, J = 8.6 Hz, 1H), 5.10 (dd, J = 3.4, 5.9 Hz, 1H), 4.64 (d, J = 9.6 Hz, 1H), 4.35 - 4.25 (m, 1H), 4.23 - 4.05 (m, 3H), 3.96 (s, 3H),3.52 - 3.44 (m, 1H), 3.13 - 3.01 (m, 2H), 2.95 (dd, J = 4.4, 10.9 Hz, 1H), 2.80 (dd, J = 5.6, 16.3 Hz, 1H), 2.14 - 1.97 (m, 2H), 1.88 (br d, J = 10.4 Hz, 1H), 1.81 - 1.72 (m, 1H), 1.53 - 1.43 (m, 1H), 1.35 (br s, 2H), 1.02 (d, J = 6.9 Hz, 3H), 0.98 (s, 3H), 0.79 - 0.63 (m, 2H), 0.53 (br dd, J = 3.8,8.7 Hz, 1H), 0.40 - 0.25 (m, 3H), 0.23 - 0.09 (m, 2H)	2.05, A

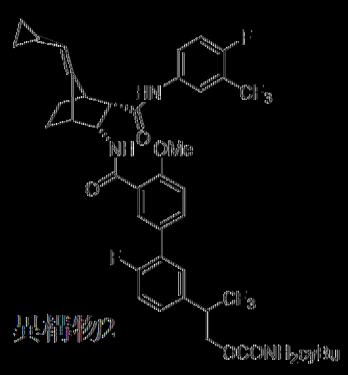
872		(2S,3R,7Z)-3-[5-(2-環丁烷羰基-2,3-二氫-1H-異吲哚-4-基)-2-甲氧基苯甲醯胺基]-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	702.5	(500 MHz, DMSO-d6) δ 10.60 - 10.43 (m, 1H), 10.00 - 9.84 (m, 1H), 8.21 (br d, J=4.4 Hz, 1H), 8.00 (dd, J=13.8, 2.3 Hz, 1H), 7.77 (br dd, J=7.9, 3.7 Hz, 1H), 7.74 - 7.62 (m, 1H), 7.47 (br t, J=9.8 Hz, 1H), 7.43 - 7.38 (m, 1H), 7.36 - 7.30 (m, 1H), 7.30 - 7.23 (m, 2H), 4.77 (br s, 2H), 4.71 - 4.60 (m, 3H), 4.55 - 4.33 (m, 1H), 4.05 (s, 3H), 3.47 - 3.24 (m, 1H), 3.24 - 3.12 (m, 1H), 3.14 - 3.03 (m, 1H), 2.79 - 2.62 (m, 1H), 2.24 - 2.15 (m, 2H), 2.11 - 2.03 (m, 1H), 1.99 - 1.85 (m, 2H), 1.84 - 1.69 (m, 2H), 1.62 - 1.48 (m, 1H), 1.45 - 1.32 (m, 2H), 0.78 - 0.64 (m, 2H), 0.47 - 0.12 (m, 2H), 一個H隱藏於水/溶劑峰下	2.83, C

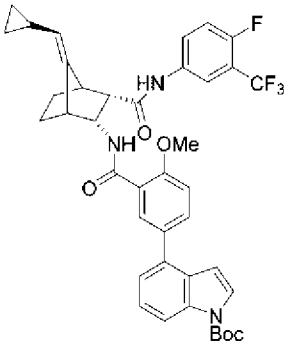
873		3-(3'-{[(1R,2R,3S,4R,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-4,4,4-三氟丁酸	737.1	(500 MHz, DMSO-d6) δ 10.63 - 10.50 (m, 1H), 9.92 (d, J=7.0 Hz, 1H), 8.22 (dd, J=6.2, 2.2 Hz, 1H), 8.11 (s, 1H), 7.88 - 7.77 (m, 1H), 7.69 (br d, J=8.6 Hz, 1H), 7.56 (br s, 1H), 7.50 - 7.40 (m, 2H), 7.35 - 7.23 (m, 2H), 4.69 (d, J=9.5 Hz, 1H), 4.50 - 4.38 (m, 1H), 4.23 - 4.09 (m, 1H), 4.05 (s, 3H), 3.25 - 3.15 (m, 1H), 3.11 (br s, 1H), 3.01 - 2.89 (m, 2H), 2.76 - 2.66 (m, 1H), 1.88 - 1.73 (m, 2H), 1.57 - 1.48 (m, 1H), 1.45 - 1.34 (m, 2H), 0.86 - 0.64 (m, 2H), 0.41 - 0.25 (m, 2H), 一個H隱藏於水/溶劑峰下	2.32, A

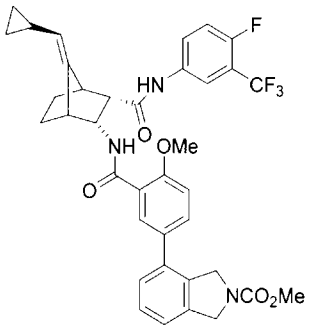
875	 共結物1	N-苯基胺基甲酸2-(3'-{[(1R,2R,3S,4R,7s)-7-(環丙基甲基)-3-{[4-氟-3-(三氟甲基)苯基胺甲醯基]雙環[2.2.1]庚烷-2-基胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-3,3,3-三氟丙酯	828.0	(500 MHz, DMSO-d6) δ 10.57 - 10.49 (m, 1H), 9.92 (d, J=7.1 Hz, 1H), 9.69 (br s, 1H), 8.23 (dd, J=6.4, 2.4 Hz, 1H), 8.14 (s, 1H), 7.89 - 7.77 (m, 1H), 7.70 (br d, J=8.9 Hz, 1H), 7.65 (br d, J=7.0 Hz, 1H), 7.58 - 7.52 (m, 1H), 7.51 - 7.45 (m, 2H), 7.42 (br s, 2H), 7.39 - 7.33 (m, 1H), 7.30 (d, J=8.8 Hz, 1H), 7.25 (br t, J=7.8 Hz, 2H), 6.99 (t, J=7.3 Hz, 1H), 4.76 - 4.68 (m, 2H), 4.62 - 4.55 (m, 1H), 4.49 - 4.44 (m, 1H), 4.34 - 4.26 (m, 1H), 4.05 (s, 3H), 3.17 (br dd, J=10.3, 3.9 Hz, 1H), 3.12 - 3.08 (m, 1H), 1.91 - 1.84 (m, 1H), 1.83 - 1.77 (m, 1H), 1.54 - 1.49 (m, 1H), 1.46 - 1.38 (m, 2H), 0.78 - 0.70 (m, 2H), 0.41 - 0.33 (m, 2H)	2.96, A

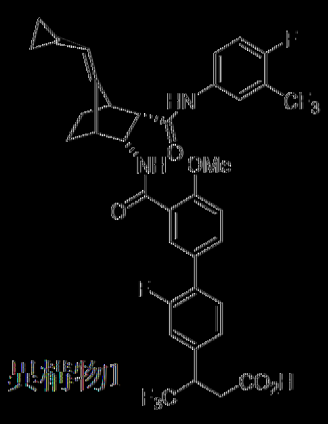
876	 異構物2	N-苯胺基甲酸2-(3'-{[(1R,2R,3S,4R,7S)-7-(環丙基甲基)-3-[4-氟-3-(三氟甲基)苯基胺甲醯基]雙環[2.2.1]庚烷-2-基胺甲醯基]-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-3,3,3-三氟丙酯	828.0	(500 MHz, DMSO-d6) δ 10.29 (s, 1H), 9.67 (d, J = 7.2 Hz, 1H), 9.45 (br s, 1H), 7.99 (dd, J = 6.4, 2.4 Hz, 1H), 7.90 (s, 1H), 7.55 (br dd, J = 8.4, 3.6 Hz, 1H), 7.45 (br d, J = 8.9 Hz, 1H), 7.42 – 7.39 (m, 1H), 7.32 – 7.28 (m, 1H), 7.26 – 7.22 (m, 1H), 7.17 (br d, J = 1.2 Hz, 1H), 7.14 – 7.11 (m, 1H), 7.06 (d, J = 8.7 Hz, 1H), 7.01 (br t, J = 7.7 Hz, 2H), 6.74 (t, J = 7.4 Hz, 1H), 4.51 – 4.47 (m, 1H), 4.45 (d, J = 9.2 Hz, 1H), 4.34 (dd, J = 11.7, 7.2 Hz, 1H), 4.25 – 4.19 (m, 1H), 4.10 – 4.01 (m, 1H), 3.88 – 3.75 (m, 3H), 3.17 – 3.13 (m, 1H), 2.96 – 2.90 (m, 1H), 2.86 (br s, 1H), 2.48 (br d, J = 3.9 Hz, 1H), 1.66 – 1.60 (m, 1H), 1.58 – 1.53 (m, 1H), 1.30 – 1.23 (m, 1H), 1.20 – 1.12 (m, 2H), 0.54 – 0.45 (m, 2H), 0.14 – 0.05 (m, 2H)	2.96, A

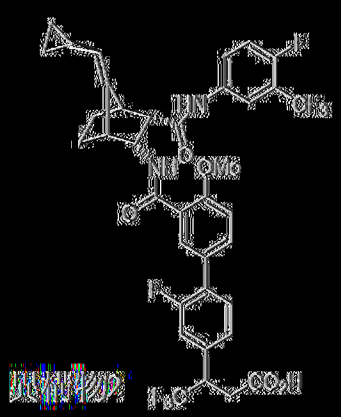
878	 異構物1	N-環丁基胺基甲酸 2-(3'-{[(1R,2R,3S,4R,7r)-7-(環丙基甲基)-3-[4-氟-3-(三氟甲基)苯基胺甲醯基]雙環[2.2.1]庚烷-2-基胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-3,3,3-三氟丙酯	806.2	(500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.93 (br d, J= 6.9 Hz, 1H), 8.29 - 8.21 (m, 1H), 8.14 (s, 1H), 7.80 (br dd, J= 4.5, 3.4 Hz, 1H), 7.70 (br d, J= 8.4 Hz, 1H), 7.63 - 7.59 (m, 1H), 7.55 - 7.50 (m, 1H), 7.49 - 7.45 (m, 2H), 7.38 - 7.35 (m, 1H), 7.32 (d, J= 8.8 Hz, 1H), 4.70 (d, J= 9.5 Hz, 1H), 4.60 - 4.52 (m, 1H), 4.50 - 4.46 (m, 1H), 4.43 - 4.39 (m, 1H), 4.22 - 4.16 (m, 1H), 4.06 (s, 3H), 3.94 - 3.88 (m, 1H), 3.17 (br dd, J= 11.2, 4.2 Hz, 1H), 3.12 (br s, 1H), 2.73 (br s, 1H), 2.11 - 2.03 (m, 2H), 1.86 (br d, J= 8.5 Hz, 2H), 1.83 - 1.78 (m, 1H), 1.57 - 1.49 (m, 2H), 1.46 - 1.38 (m, 2H), 0.80 - 0.71 (m, 2H), 0.39 - 0.31 (m, 2H)	2.84, A

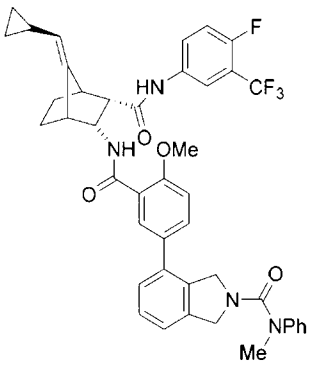
879	 共構物2	N-環丁基胺基甲酸 2-(3'-{[(1R,2R,3S,4R,7Z)-7-(環丙基甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-3,3,3-三氟丙酯	806.0	(500 MHz, DMSO-d6) δ 10.29 (s, 1H), 9.68 (d, J=7.2 Hz, 1H), 7.99 (dd, J=6.4, 2.3 Hz, 1H), 7.89 (s, 1H), 7.60 - 7.51 (m, 1H), 7.46 (br d, J=9.3 Hz, 1H), 7.35 (br d, J=7.1 Hz, 1H), 7.29 (br d, J=8.0 Hz, 1H), 7.23 (br d, J=9.5 Hz, 2H), 7.16 - 7.09 (m, 1H), 7.08 (d, J=8.7 Hz, 1H), 4.46 (d, J=9.5 Hz, 1H), 4.35 - 4.27 (m, 1H), 4.26 - 4.21 (m, 1H), 4.20 - 4.13 (m, 1H), 4.00 - 3.92 (m, 1H), 3.82 (s, 3H), 2.93 (br dd, J=10.6, 4.0 Hz, 1H), 2.87 (br s, 1H), 2.49 (br s, 1H), 1.83 (br dd, J=6.0, 2.2 Hz, 2H), 1.62 (br d, J=8.5 Hz, 2H), 1.60 - 1.52 (m, 2H), 1.35 - 1.25 (m, 3H), 1.20 - 1.13 (m, 2H), 0.50 (quin, J=9.3 Hz, 2H), 0.11 (br d, J=2.0 Hz, 2H),	2.84, A

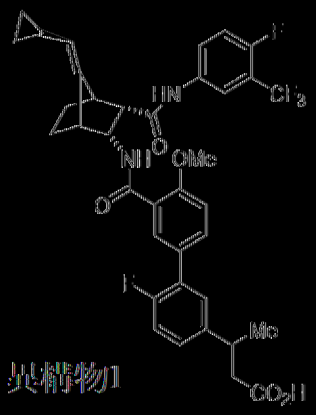
880		4-(3-{[(1R,2R,3S,4R,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-1H-吲哚-1-甲酸三級丁酯	718.5	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.93 (d, J=7.3 Hz, 1H), 8.22 (dd, J=6.4, 2.1 Hz, 1H), 8.17 (d, J=2.4 Hz, 1H), 8.09 (d, J=8.5 Hz, 1H), 7.81 - 7.77 (m, 1H), 7.74 - 7.70 (m, 2H), 7.47 (t, J=9.7 Hz, 1H), 7.40 (d, J=8.1 Hz, 1H), 7.34 (d, J=8.7 Hz, 1H), 7.28 (d, J=7.4 Hz, 1H), 6.68 (d, J=3.8 Hz, 1H), 4.69 (d, J=9.5 Hz, 1H), 4.53 - 4.44 (m, 1H), 4.06 (s, 3H), 3.16 (dd, J=10.7, 4.6 Hz, 1H), 3.13 - 3.09 (m, 1H), 2.76 - 2.69 (m, 1H), 1.93 - 1.86 (m, 1H), 1.85 - 1.79 (m, 1H), 1.64 (s, 9H), 1.58 - 1.48 (m, 1H), 1.42 (br s, 2H), 0.81 - 0.66 (m, 2H), 0.38 - 0.32 (m, 2H	3.18, A

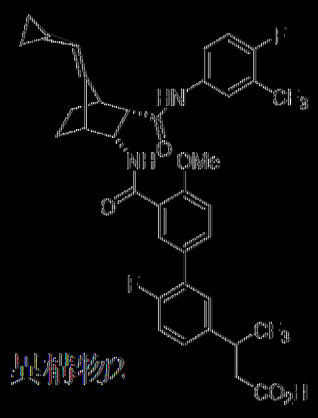
881		4-(3-{[(2R,3S,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-2,3-二氫-1H-異吲哚-2-甲酸甲酯	678.1	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.93 (br d, J=6.3 Hz, 1H), 8.23 (dd, J=6.6, 2.4 Hz, 1H), 8.02 (dd, J=12.6, 2.1 Hz, 1H), 7.90 - 7.76 (m, 1H), 7.72 - 7.63 (m, 1H), 7.48 (t, J=9.7 Hz, 1H), 7.44 - 7.39 (m, 1H), 7.37 - 7.33 (m, 1H), 7.32 - 7.27 (m, 2H), 7.26 - 7.02 (m, 2H), 4.81 - 4.62 (m, 5H), 4.53 - 4.40 (m, 1H), 4.06 (s, 3H), 3.65 (d, J=14.3 Hz, 2H), 3.24 - 3.13 (m, 1H), 3.11 (br d, J=3.0 Hz, 1H), 1.96 - 1.86 (m, 1H), 1.82 (br t, J=8.2 Hz, 1H), 1.61 - 1.50 (m, 1H), 1.43 (br t, J=11.7 Hz, 2H), 0.74 (br dd, J=10.4, 9.2 Hz, 2H), 0.41 - 0.27 (m, 2H)	2.75, C

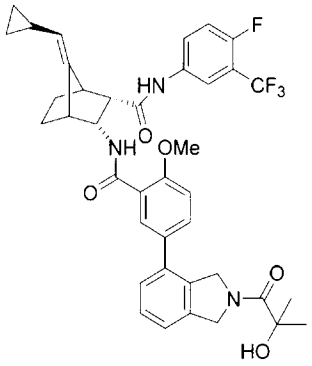
883	 異構物1	3-(3'-{[(1R,2R,3S,4R,7A)-7-(環丙基甲基)-3-[4-氟-3-(三氟甲基)苯基胺甲醯基]雙環[2.2.1]庚烷-2-基胺甲醯基}-2-氟-4'-甲氧基-[1,1'-聯苯]-4-基)-4,4,4-三氟丁酸	773.1	(500 MHz, DMSO-d6) δ 10.61 - 10.52 (m, 1H), 9.91 (d, J= 7.1 Hz, 1H), 8.23 (dd, J= 6.6, 2.4 Hz, 1H), 8.14 (s, 1H), 7.89 - 7.79 (m, 1H), 7.70 (br d, J= 8.6 Hz, 1H), 7.54 - 7.45 (m, 2H), 7.39 (s, 1H), 7.33 - 7.24 (m, 2H), 4.69 (d, J= 9.7 Hz, 1H), 4.55 - 4.42 (m, 1H), 4.21 - 4.10 (m, 1H), 4.05 (s, 3H), 3.90 (s, 1H), 3.24 - 3.14 (m, 2H), 3.11 (br s, 1H), 2.76 - 2.66 (m, 1H), 1.84 - 1.71 (m, 1H), 1.51 (qd, J= 8.6, 4.9 Hz, 1H), 1.46 - 1.38 (m, 2H), 0.86 - 0.70 (m, 2H), 0.35 (br s, 2H),	2.31, A

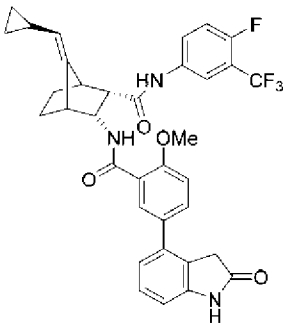
884		3-(3'-{[(1R,2R,3S,4R,7S)-7-(環丙基甲基)-3-[4-氟-3-(三氟甲基)苯基胺甲醯基]雙環[2.2.1]庚烷-2-基胺甲醯基}-2-氟-4'-甲氧基-[1,1'-聯苯]-4-基)-4,4,4-三氟丁酸	737.1	(500 MHz, DMSO-d6) δ 10.58 (s, 1H), 9.91 (d, J = 7.2 Hz, 1H), 8.24 (dd, J = 6.4, 2.2 Hz, 1H), 8.14 (s, 1H), 7.88 – 7.79 (m, 1H), 7.70 (br d, J = 8.9 Hz, 1H), 7.55 – 7.45 (m, 2H), 7.38 (br d, J = 11.5 Hz, 1H), 7.33 – 7.25 (m, 2H), 4.69 (d, J = 9.6 Hz, 1H), 4.52 – 4.40 (m, 1H), 4.18 – 4.09 (m, 1H), 4.05 (s, 3H), 3.90 (s, 1H), 3.13 – 3.09 (m, 1H), 2.73 (br d, J = 6.7 Hz, 1H), 1.89 – 1.79 (m, 2H), 1.56 – 1.48 (m, 1H), 1.46 – 1.38 (m, 2H), 0.83 – 0.68 (m, 2H), 0.35 (br d, J = 2.4 Hz, 2H	2.31, A

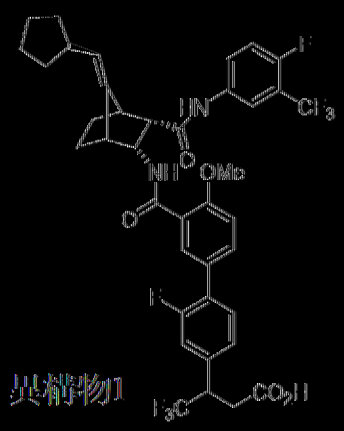
886		4-(3-{[(1R,2R,3S,4R,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-4-甲氧基苯基)-N-甲基-N-苯基-2,3-二氫-1H-異吲哚-2-甲醯胺	753.0	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.90 (d, J=7.1 Hz, 1H), 8.24 (dd, J=6.2, 2.6 Hz, 1H), 7.94 (d, J=2.4 Hz, 1H), 7.80 (dt, J=7.9, 3.9 Hz, 1H), 7.54 - 7.46 (m, 2H), 7.38 - 7.33 (m, 2H), 7.32 - 7.29 (m, 1H), 7.26 - 7.23 (m, 2H), 7.21 (s, 1H), 7.18 - 7.13 (m, 2H), 4.71 (d, J=9.5 Hz, 1H), 4.50 (br d, J=5.7 Hz, 2H), 4.33 (s, 2H), 4.05 (s, 3H), 3.51 - 3.40 (m, 1H), 3.14 (s, 3H), 2.73 (br s, 1H), 1.93 - 1.88 (m, 1H), 1.88 - 1.82 (m, 1H), 1.56 - 1.50 (m, 1H), 1.44 - 1.37 (m, 2H), 1.26 - 1.20 (m, 2H), 0.76 - 0.65 (m, 2H), 0.44 - 0.32 (m, 2H), 一個H隱藏於水/溶劑峰下	2.77, A

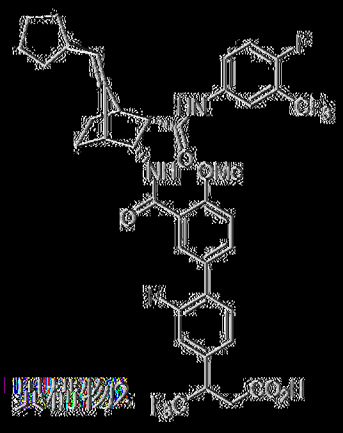
887	 共結物1	3-(3'-{[(1R,2R,3S,4R,7Z)-7-(環丙基甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)丁酸	683.4	(500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.92 (d, J = 7.2 Hz, 1H), 8.23 (dd, J = 6.4, 2.3 Hz, 1H), 8.12 (s, 1H), 7.83 – 7.75 (m, 1H), 7.69 (br d, J = 9.2 Hz, 1H), 7.48 (t, J = 9.1 Hz, 1H), 7.39 – 7.34 (m, 1H), 7.30 (d, J = 8.8 Hz, 1H), 7.28 – 7.26 (m, 1H), 7.24 – 7.18 (m, 1H), 4.70 (d, J = 9.5 Hz, 1H), 4.51 – 4.44 (m, 1H), 4.05 (s, 3H), 3.21 (br d, J = 7.0 Hz, 1H), 3.12 (br s, 1H), 2.73 (br d, J = 4.4 Hz, 1H), 1.89 – 1.73 (m, 2H), 1.57 – 1.48 (m, 1H), 1.45 – 1.35 (m, 2H), 1.25 (d, J = 6.9 Hz, 3H), 0.84 – 0.68 (m, 2H), 0.35 (br d, J = 2.0 Hz, 2H), 四個H隱藏於水/溶劑峰下	2.42, A

888	 異構物2	3-(3'-{[(1R,2R,3S,4R,7S)-7-(環丙基甲基)-3-[4-氟-3-(三氟甲基)苯基胺甲醯基]雙環[2.2.1]庚烷-2-基胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)丙酸	683.1	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.92 (d, J = 7.2 Hz, 1H), 8.23 (dd, J = 6.6, 2.4 Hz, 1H), 8.12 (s, 1H), 7.90 – 7.77 (m, 1H), 7.69 (br d, J = 8.8 Hz, 1H), 7.48 (t, J = 9.8 Hz, 1H), 7.36 (dd, J = 7.7, 2.0 Hz, 1H), 7.32 – 7.28 (m, 1H), 7.27 (br dd, J = 4.8, 2.2 Hz, 1H), 7.23 – 7.17 (m, 1H), 4.70 (d, J = 9.6 Hz, 1H), 4.55 – 4.41 (m, 1H), 4.05 (s, 3H), 3.24 – 3.19 (m, 1H), 3.19 – 3.14 (m, 1H), 3.11 (br s, 1H), 2.73 (br s, 1H), 1.90 – 1.85 (m, 1H), 1.83 – 1.77 (m, 1H), 1.56 – 1.48 (m, 1H), 1.45 – 1.37 (m, 2H), 1.30 – 1.21 (m, 3H), 0.81 – 0.70 (m, 2H), 0.44 – 0.31 (m, 2H), 3個OH隱藏於水/溶劑峰下	2.40, A

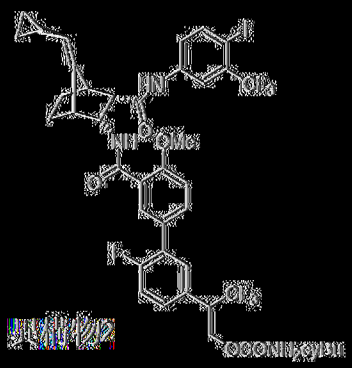
889		(2S,3R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[2-(2-羥基-2-甲基丙醯基)-2,3-二氫-1H-異吲哚-4-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	706.1	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 10.01 - 9.87 (m, 1H), 8.24 (dd, J=6.3, 2.3 Hz, 1H), 8.04 (dd, J=14.9, 2.3 Hz, 1H), 7.86 - 7.75 (m, 1H), 7.70 - 7.61 (m, 1H), 7.57 - 7.47 (m, 1H), 7.43 - 7.33 (m, 2H), 7.32 - 7.24 (m, 2H), 5.36 (s, 1H), 5.19 (br d, J=9.5 Hz, 2H), 4.79 - 4.66 (m, 3H), 4.53 - 4.35 (m, 1H), 4.07 (s, 3H), 3.17 (br dd, J=10.9, 3.7 Hz, 1H), 3.14 - 3.04 (m, 1H), 2.73 (s ,1H), 1.95 - 1.76 (m, 2H), 1.56 - 1.48 (m, 1H), 1.47 - 1.40 (m, 2H), 1.35 (s, 3H), 1.32 (s, 3H), 0.89 - 0.58 (m, 2H), 0.35 (br dd, J=3.9, 2.6 Hz, 2H)	2.63, A

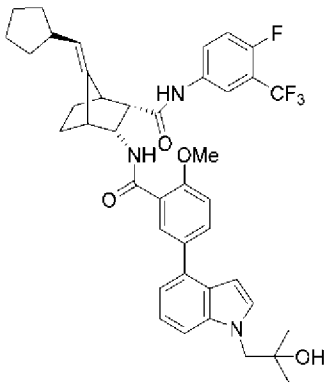
890		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-[2-甲氧基-5-(2-側氧基-2,3-二氫-1H-indol-4-基)苯甲醯胺基]雙環[2.2.1]庚烷-2-甲醯胺	634.0	(500 MHz, DMSO-d6) δ 10.54 (s, 1H), 10.00 - 9.80 (m, 1H), 8.24 (dd, J=6.4, 2.4 Hz, 1H), 8.09 (d, J=2.4 Hz, 1H), 7.87 - 7.78 (m, 1H), 7.76 - 7.70 (m, 1H), 7.49 (t, J=9.6 Hz, 1H), 7.36 - 7.20 (m, 2H), 7.00 (d, J=7.6 Hz, 1H), 6.82 (d, J=7.7 Hz, 1H), 4.70 (d, J=9.5 Hz, 1H), 4.55 - 4.43 (m, 1H), 4.05 (s, 3H), 3.56 (s, 1H), 3.17 (br dd, J=10.9, 3.9 Hz, 1H), 3.11 (br s, 1H), 2.73 (br d, J=3.7 Hz, 1H), 1.97 - 1.86 (m, 1H), 1.84 - 1.74 (m, 1H), 1.58 - 1.48 (m, 1H), 1.45 - 1.34 (m, 2H), 0.74 (quin, J=10.0 Hz, 2H), 0.45 - 0.29 (m, 2H)，兩個H隱藏於水/溶劑峰下	2.50, A

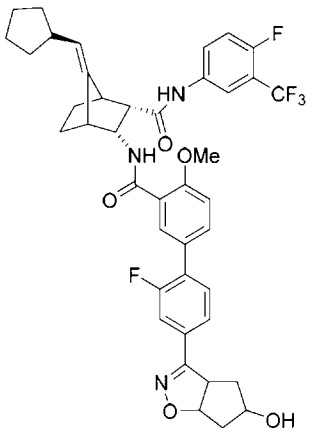
891		3-(3'-{[(1R,2R,3S,4R,7s)-7-(環戊基甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-2-氟-4'-甲氧基-[1,1'-聯苯]-4-基)-4,4,4-三氟丁酸	765.1	(500 MHz, DMSO-d6) δ 10.52 (s, 1H), 9.88 (d, J = 7.2 Hz, 1H), 8.24 (dd, J = 6.4, 2.3 Hz, 1H), 8.15 (s, 1H), 7.88 - 7.76 (m, 1H), 7.72 (br d, J = 8.5 Hz, 1H), 7.64 - 7.52 (m, 1H), 7.50 - 7.43 (m, 2H), 7.37 (br d, J = 8.3 Hz, 1H), 7.30 (s, 1H), 5.19 (d, J = 8.8 Hz, 1H), 4.51 - 4.35 (m, 1H), 4.29 - 4.10 (m, 1H), 4.06 (s, 3H), 3.10 - 2.96 (m, 3H), 2.66 - 2.57 (m, 2H), 1.93 - 1.86 (m, 2H), 1.85 - 1.82 (m, 2H), 1.81 - 1.73 (m, 3H), 1.65 (br dd, J = 7.0, 3.6 Hz, 2H), 1.58 (br d, J = 5.3 Hz, 2H), 1.43 - 1.38 (m, 2H), 1.29 - 1.25 (m, 1H)	2.25, A

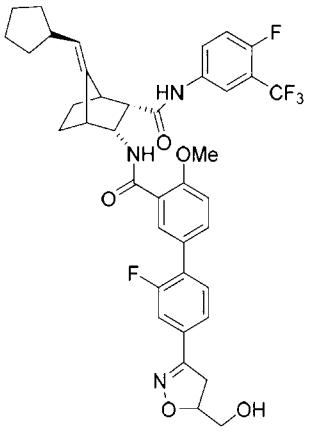
892		3-(3'-{[(1R,2R,3S,4R,7S)-7-(環戊基甲基)-3-[4-氟-3-(三氟甲基)苯基胺甲醯基]雙環[2.2.1]庚烷-2-基胺甲醯基]-2-氟-4'-甲氧基-[1,1'-聯苯]-4-基)-4,4,4-三氟丁酸	765.5	(500 MHz, DMSO-d6) δ 10.62 (s, 1H), 9.88 (d, J = 7.2 Hz, 1H), 8.25 (dd, J = 6.5, 2.3 Hz, 1H), 8.14 (s, 1H), 7.89 – 7.79 (m, 1H), 7.71 (br d, J = 8.2 Hz, 1H), 7.60 – 7.48 (m, 1H), 7.49 – 7.45 (m, 1H), 7.42 (br d, J = 11.7 Hz, 1H), 7.35 (br d, J = 7.6 Hz, 1H), 7.30 (d, J = 8.8 Hz, 1H), 5.19 (d, J = 8.9 Hz, 1H), 4.45 – 4.39 (m, 1H), 4.24 – 4.06 (m，3H？水抑制？), 2.85 (q, J = 7.3 Hz, 2H), 2.71 – 2.68 (m, 1H), 2.66 – 2.59 (m, 1H), 1.96 – 1.85 (m, 1H), 1.85 – 1.74 (m, 3H), 1.72 – 1.64 (m, 2H), 1.61 – 1.52 (m, 2H), 1.48 – 1.36 (m, 2H), 1.36 – 1.21 (m, 3H), 1.12 (t, J = 7.2 Hz, 3H)	2.53, A

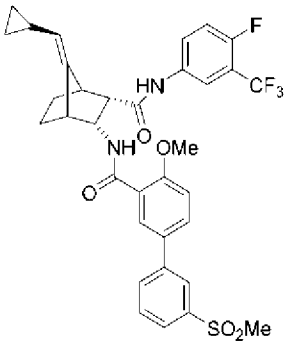
893	 異構物1	N-環丁基胺基甲酸 2-(3'-{[(1R,2R,3S,4R,7Z)-7-(羥基甲基)-3-[4-氟-3-(三氟甲基)苯基胺甲醯基]雙環[2.2.1]庚烷-2-基胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-3,3,3-三氟丙基酯	834.1	(500 MHz, DMSO-d6) δ 10.58 - 10.49 (m, 1H), 9.90 (d, J=7.0 Hz, 1H), 8.25 (dd, J=6.3, 2.1 Hz, 1H), 8.14 (s, 1H), 7.87 - 7.78 (m, 1H), 7.70 (br d, J=8.2 Hz, 1H), 7.62 - 7.58 (m, 1H), 7.53 (br d, J=7.9 Hz, 1H), 7.48 (br d, J=9.5 Hz, 2H), 7.36 (br d, J=10.2 Hz, 1H), 7.34 - 7.29 (m, 1H), 5.20 (d, J=8.9 Hz, 1H), 4.59 - 4.51 (m, 1H), 4.42 (br dd, J=11.0, 7.3 Hz, 2H), 4.23 - 4.16 (m, 1H), 4.06 (s, 3H), 3.97 - 3.91 (m, 1H), 3.17 (dd, J=10.4, 3.8 Hz, 1H), 3.01 (br s, 1H), 2.72 (br s, 1H), 2.64 - 2.57 (m, 1H), 2.13 - 2.04 (m, 2H), 1.91 - 1.82 (m, 3H), 1.81 - 1.73 (m, 2H), 1.70 - 1.62 (m, 2H), 1.60 - 1.47 (m, 3H), 1.43 - 1.37 (m, 2H), 1.32 - 1.20 (m, 2H), 一個H隱藏於水/溶劑峰下	3.20, A

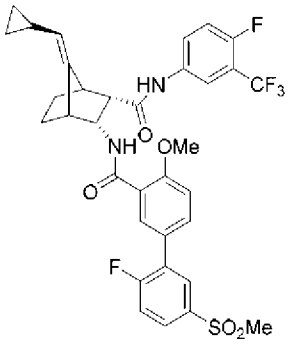
894		N-[[2-[3-[[(1R,2R,3S,4R,7S)-7-(環戊基甲基)-3-[4-氟-3-(三氟甲基)苯基甲醯基]雙環[2.2.1]庚烷-2-基]胺甲醯基]-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基]-3,3,3-三氟丙基]磺醯基]胺甲酸銨鹽	834.1	(500 MHz, DMSO-d6) δ 10.65 - 10.48 (m, 1H), 9.90 (d, J= 7.2 Hz, 1H), 8.25 (dd, J= 6.4, 2.5 Hz, 1H), 8.14 (s, 1H), 7.84 - 7.75 (m, 1H), 7.70 (br d, J= 9.0 Hz, 1H), 7.60 (br s, 1H), 7.54 (br d, J= 7.9 Hz, 1H), 7.50 - 7.46 (m, 2H), 7.36 (br d, J= 10.3 Hz, 1H), 7.32 (d, J= 8.9 Hz, 1H), 5.20 (d, J= 8.9 Hz, 1H), 4.60 - 4.49 (m, 1H), 4.47 - 4.38 (m, 2H), 4.26 - 4.15 (m, 1H), 4.06 (s, 3H), 3.97 - 3.89 (m, 1H), 3.17 (dd, J= 10.5, 4.3 Hz, 1H), 3.01 (br s, 1H), 2.72 (br s, 1H), 2.63 - 2.57 (m, 1H), 2.15 - 2.05 (m, 2H), 1.94 - 1.82 (m, 4H), 1.81 - 1.72 (m, 2H), 1.71 - 1.63 (m, 2H), 1.60 - 1.48 (m, 4H), 1.46 - 1.37 (m, 2H), 1.33 - 1.21 (m, 2H)	3.21, A

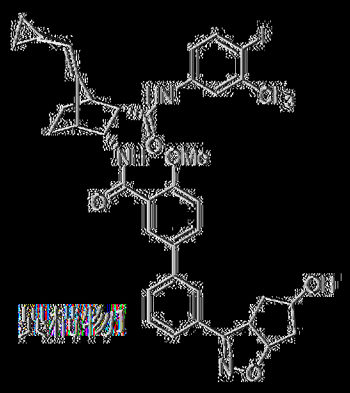
895		(2S,3R,7Z)-7-(環戊基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[1-(2-羥基-2-甲基丙基)-1H-indol-4-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	718.0	(500 MHz, DMSO-d6) δ 10.63 - 10.45 (m, 1H), 9.91 (d, J=7.0 Hz, 1H), 8.30 (d, J=2.4 Hz, 1H), 8.25 (dd, J=6.6, 2.4 Hz, 1H), 7.84 - 7.76 (m, 2H), 7.54 (d, J=8.2 Hz, 1H), 7.49 (t, J=9.7 Hz, 1H), 7.41 (d, J=3.1 Hz, 1H), 7.32 (d, J=8.8 Hz, 1H), 7.19 (t, J=7.8 Hz, 1H), 7.05 (d, J=7.1 Hz, 1H), 6.50 (d, J=3.1 Hz, 1H), 5.20 (d, J=8.9 Hz, 1H), 4.50 - 4.39 (m, 1H), 4.11 (s, 2H), 4.07 (s, 3H), 3.17 (dd, J=10.8, 4.1 Hz, 1H), 3.02 (br s, 1H), 2.72 (br s, 1H), 2.66 - 2.58 (m, 1H), 1.92 (br t, J=8.7 Hz, 1H), 1.87 - 1.81 (m, 2H), 1.79 - 1.75 (m, 1H), 1.70 - 1.63 (m, 2H), 1.61 - 1.54 (m, 2H), 1.45 - 1.38 (m, 2H), 1.34 - 1.22 (m, 2H), 1.12 (s, 6H), 一個H隱藏於水/溶劑峰下	3.07, C

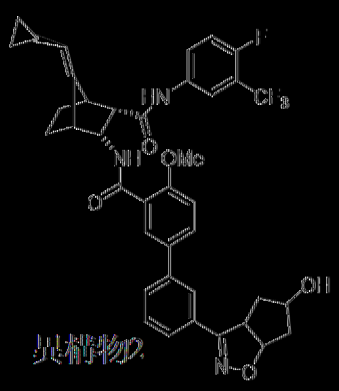
896		N-[(2R,3S,7Z)-7-(環戊基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]-2'-氟-4'-{5-羥基-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基}-4-甲氧基-[1,1'-聯苯]-3-甲醯胺	857.1	(500 MHz, DMSO-d6) δ 10.52 (s, 1H), 9.96 - 9.84 (m, 1H), 8.24 (br d, J=5.8 Hz, 1H), 8.18 (br s, 1H), 7.87 - 7.77 (m, 1H), 7.74 (br d, J=8.9 Hz, 1H), 7.66 - 7.53 (m, 3H), 7.50 - 7.42 (m, 1H), 7.32 (d, J=8.9 Hz, 1H), 5.33 - 5.14 (m, 2H), 4.49 - 4.39 (m, 1H), 4.26 (td, J=9.4, 3.7 Hz, 1H), 4.20 - 4.10 (m, 2H), 4.06 (s, 3H), 3.44 - 3.32 (m, 1H), 3.16 (br dd, J=10.9, 3.7 Hz, 1H), 3.00 (br d, J=4.5 Hz, 1H), 2.72 (br s, 1H), 2.64 - 2.57 (m, 1H), 2.18 - 2.07 (m, 1H), 2.04 - 1.94 (m, 1H), 1.89 - 1.71 (m, 5H), 1.70 - 1.61 (m, 2H), 1.58 - 1.52 (m, 2H), 1.44 - 1.37 (m, 2H), 1.31 - 1.20 (m, 2H)	3.26, A

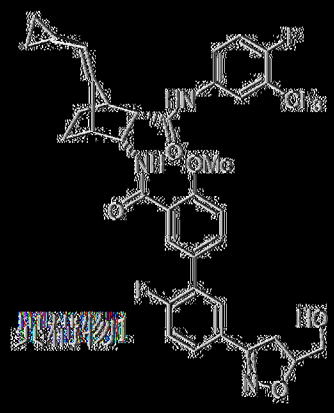
897		N-[(2R,3S,7Z)-7-(環戊基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]-2'-氟-4'-[5-(羥基甲基)-4,5-二氫-1,2-噁唑-3-基]-4-甲氧基-[1,1'-聯苯]-3-甲醯胺	724.6	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.89 (d, J=7.0 Hz, 1H), 8.25 (dd, J=6.6, 2.4 Hz, 1H), 8.18 - 8.12 (m, 1H), 7.80 (br dd, J=9.0, 3.0 Hz, 1H), 7.74 (br d, J=8.7 Hz, 1H), 7.64 - 7.54 (m, 3H), 7.49 (t, J=9.7 Hz, 1H), 7.32 (d, J=8.9 Hz, 1H), 5.19 (d, J=8.6 Hz, 1H), 5.02 (t, J=5.8 Hz, 1H), 4.77 (qd, J=7.7, 4.3 Hz, 1H), 4.50 - 4.32 (m, 1H), 4.06 (s, 3H), 3.61 - 3.52 (m, 2H), 3.50 - 3.37 (m, 1H), 3.29 - 3.13 (m, 1H), 3.06 - 2.94 (m, 1H), 2.72 (br s, 1H), 2.61 (s, 2H), 1.89 - 1.74 (m, 4H), 1.70 - 1.62 (m, 2H), 1.59 - 1.48 (m, 2H), 1.45 - 1.35 (m, 2H), 1.32 - 1.17 (m, 2H)	2.81, A

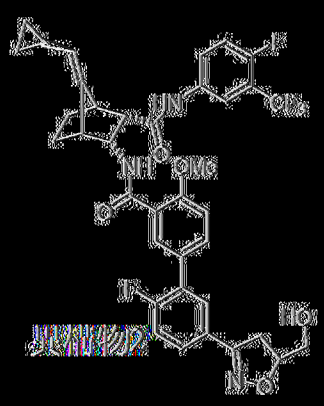
898		N-[(1R,2R,3S,4R,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]-3'-甲磺醯基-4-甲氧基-[1,1'-聯苯]-3-甲醯胺	657.2	(500 MHz, DMSO-d6) δ 10.65 - 10.47 (m, 1H), 10.04 - 9.89 (m, 1H), 8.32 - 8.28 (m, 1H), 8.25 - 8.21 (m, 1H), 8.14 - 8.10 (m, 1H), 8.04 - 7.99 (m, 1H), 7.96 - 7.87 (m, 1H), 7.77 - 7.71 (m, 1H), 7.52 - 7.46 (m, 1H), 7.38 - 7.31 (m, 1H), 4.75 - 4.67 (m, 1H), 4.53 - 4.44 (m, 1H), 4.09 - 4.01 (m, 1H), 3.33 - 3.26 (m, 1H), 3.20 - 3.09 (m, 1H), 2.57 - 2.53 (m, 32H), 1.92 - 1.75 (m, 1H), 1.56 - 1.36 (m, 1H), 0.81 - 0.68 (m, 1H), 0.40 - 0.30 (m, 1H)	2.56, C

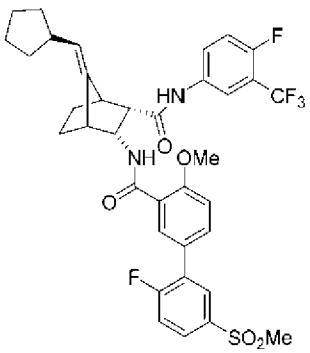
899		N-[(1R,2R,3S,4R,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]-2'-氟-5'-甲磺醯基-4-甲氧基-[1,1'-聯苯]-3-甲醯胺	675.1	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.93 (br d, J=7.3 Hz, 1H), 8.26 - 8.12 (m, 2H), 8.02 (br d, J=5.1 Hz, 1H), 7.99 - 7.89 (m, 1H), 7.79 (br d, J=6.3 Hz, 2H), 7.60 (br t, J=9.5 Hz, 1H), 7.47 (br t, J=9.6 Hz, 1H), 7.35 (br d, J=8.6 Hz, 1H), 4.69 (br d, J=9.6 Hz, 1H), 4.45 (br s, 1H), 4.06 (s, 3H), 3.15 (br d, J=7.6 Hz, 1H), 3.10 (br s, 1H), 2.72 (br s, 1H), 1.89 - 1.68 (m, 2H), 1.49 (br s, 1H), 1.41 (br s, 2H), 0.84 - 0.66 (m, 2H), 0.34 (br s, 2H)	2.61, C

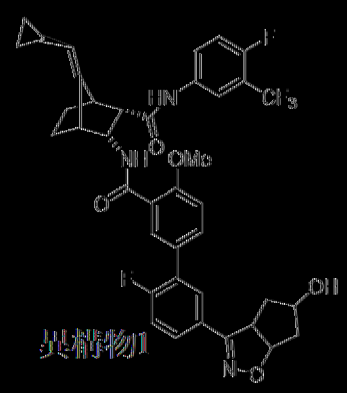
901		N-[(1R,2R,3S,4R,7S)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]-3'-{5-羥基-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基}-4-甲氧基-[1,1'-聯苯]-3-甲醯胺	704.2	(500 MHz, DMSO-d6) δ 10.32 (s, 1H), 9.68 (d, J = 7.2 Hz, 1H), 8.06 – 7.92 (m, 1H), 7.65 – 7.52 (m, 2H), 7.54 (m, 1H), 7.45 (br d, J = 7.6 Hz, 1H), 7.38 (d, J = 7.6 Hz, 1H), 7.32 – 7.20 (m, 1H), 7.06 (d, J = 8.8 Hz, 1H), 4.94 (td, J = 6.2, 3.2 Hz, 1H), 4.45 (d, J = 9.7 Hz, 1H), 4.23 (br s, 1H), 4.07 (td, J = 9.5, 4.2 Hz, 1H), 3.95 – 3.84 (m, 1H), 3.81 (s, 3H), 2.93 (br dd, J = 10.5, 4.3 Hz, 1H), 2.87 (br s, 1H), 2.48 (br s, 1H), 1.78 – 1.55 (m, 4H), 1.51 (s, 1H), 1.26 (br dd, J = 8.8, 4.2 Hz, 1H), 1.21 – 0.98 (m, 2H), 0.49 (br dd, J = 12.6, 8.9 Hz, 2H), 0.10 (br s, 2H)	2.61, A

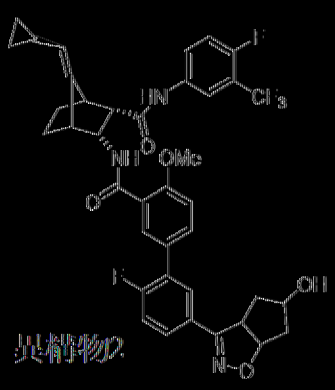
902	 異構物2	N-[(1R,2R,3S,4R,7s)-7-(環丙基甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]-3'-{5-氧基-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基}-4-甲氧基-[1,1'-聯苯]-3-甲醯胺	704.3	(500 MHz, DMSO-d6) δ 9.94 (d, J = 7.0 Hz, 1H), 8.25 (br d, J = 2.4 Hz, 2H), 7.87 – 7.79 (m, 3H), 7.68 (br d, J = 8.0 Hz, 1H), 7.64 (d, J = 7.9 Hz, 1H), 7.56 – 7.52 (m, 1H), 7.49 (t, J = 9.9 Hz, 1H), 7.32 (d, J = 8.7 Hz, 1H), 5.18 – 5.13 (m, 1H), 4.70 (d, J = 9.6 Hz, 1H), 4.48 (br s, 1H), 4.24 – 4.15 (m, 2H), 4.06 (s, 3H), 3.91 (s, 1H), 3.20 – 3.17 (m, 1H), 3.13 (br s, 1H), 2.74 (br s, 1H), 2.17 – 2.09 (m, 2H), 1.95 – 1.79 (m, 4H), 1.51 (br dd, J = 8.9, 4.5 Hz, 1H), 1.47 – 1.38 (m, 2H), 0.75 (br dd, J = 12.7, 8.9 Hz, 2H), 0.36 (br s, 2H)	2.57, A

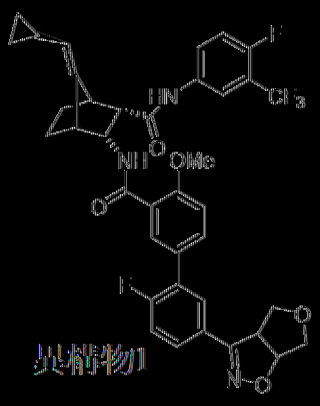
905		N-[(1R,2R,3S,4R,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]-2'-氟-5'-[5-(羥基甲基)-4,5-二氫-1,2-噁唑-3-基]-4'-甲氧基-[1,1'-聯苯]-3-甲醯胺	696.2	(500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.93 (d, J = 7.2 Hz, 1H), 8.24 (dd, J = 6.4, 2.5 Hz, 1H), 8.16 (s, 1H), 7.82 – 7.68 (m, 4H), 7.49 (t, J = 9.8 Hz, 1H), 7.43 – 7.38 (m, 1H), 7.33 (d, J = 8.7 Hz, 1H), 4.76 – 4.68 (m, 2H), 4.47 (br t, J = 10.6 Hz, 1H), 4.07 (s, 3H), 3.55 – 3.49 (m, 1H), 3.17 (dd, J = 10.4, 4.3 Hz, 1H), 3.12 (br s, 1H), 2.73 (br s, 1H), 1.90 – 1.78 (m, 2H), 1.54 – 1.37 (m, 3H), 0.74 (quin, J = 10.1 Hz, 2H), 0.38 – 0.33 (m, 2H)	2.61, A

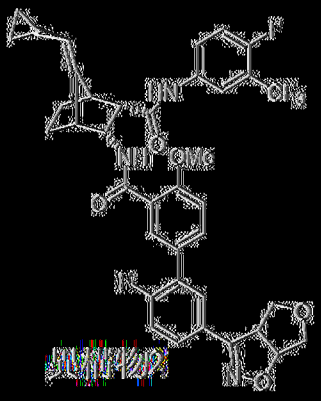
906		N-[(1R,2R,3S,4R,7Z)-7-(環丙基亞甲基)-3-[4-氟-3-(三氟甲基)苯基]胺甲醯基]雙環[2.2.1]庚烷-2-基]-2'-氟-5'-[5-(羥基甲基)-4,5-二氫-1,2-噁唑-3-基]-4-甲氧基-[1,1'-聯苯]-3-甲醯胺	696.1	(500 MHz, DMSO-d6) δ 10.29 (s, 1H), 9.69 (d, J = 11.4 Hz, 1H), 8.00 (d, J = 6.7 Hz, 1H), 7.92 (s, 1H), 7.58 – 7.45 (m, 3H), 7.25 (t, J = 9.7 Hz, 1H), 7.17 (dd, J = 10.5, 8.7 Hz, 1H), 7.09 (d, J = 8.8 Hz, 1H), 4.77 (t, J = 5.7 Hz, 1H), 4.52 – 4.44 (m, 1H), 4.23 (br s, 1H), 3.83 (s, 3H), 3.29 (q, J = 5.0 Hz, 1H), 2.95 – 2.87 (m, 1H), 2.49 (br s, 1H), 1.66 – 1.55 (m, 1H), 1.30 – 1.21 (m, 1H), 1.21 – 1.14 (m, 1H), 0.55 – 0.46 (m, 1H), 0.12 (br s, 1H)	2.5%, C

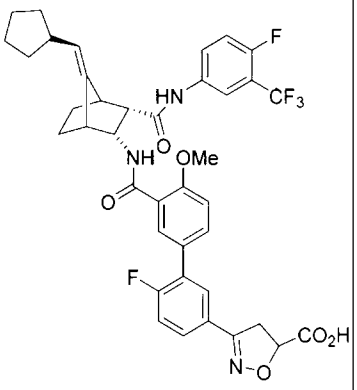
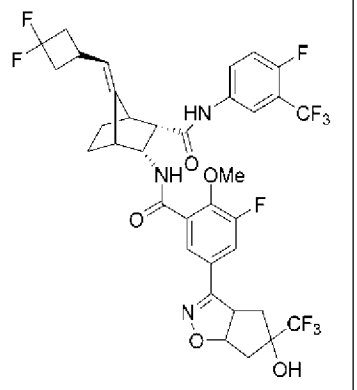
907		N-[(1R,2R,3S,4R,7Z)-7-(環戊基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]-2'-氟-5'-甲磺醯基-4-甲氧基-[1,1'-聯苯]-3-甲醯胺	703.2	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.91 (d, J=7.2 Hz, 1H), 8.24 (dd, J=6.4, 2.3 Hz, 1H), 8.19 (s, 1H), 8.04 (dd, J=7.2, 2.3 Hz, 1H), 7.97 (d, J=8.2 Hz, 1H), 7.82 - 7.77 (m, 2H), 7.61 (t, J=9.0 Hz, 1H), 7.49 (t, J=9.8 Hz, 1H), 7.36 (d, J=8.8 Hz, 1H), 5.20 (d, J=8.9 Hz, 1H), 4.42 (br t, J=10.5 Hz, 1H), 4.07 (s, 3H), 3.30 (s, 1H), 3.17 (dd, J=10.7, 4.0 Hz, 1H), 3.02 (br s, 1H), 2.72 (br s, 1H), 2.63 - 2.57 (m, 1H), 2.55 (s, 3H), 1.90 - 1.74 (m, 5H), 1.68 - 1.54 (m, 2H), 1.40 (br s, 2H), 1.31 - 1.23 (m, 2H)	2.83, C

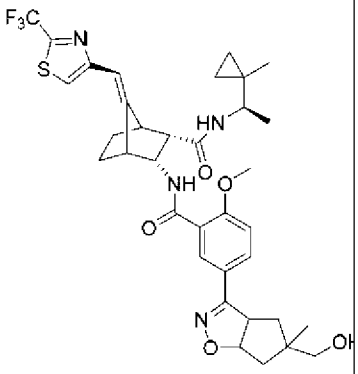
908		N-[(1R,2R,3S,4R,7Z)-7-(環丙基亞甲基)-3-[4-氟-3-(三氟甲基)苯基]胺甲醯基]雙環[2.2.1]庚烷-2-基]-2'-氟-5'-[5-氧雜-3a,4,4a,5,6,6a,7a-七氫-4,6-環戊并[d][1,2]噁唑-3-基]-4-甲氧基-[1,1'-聯苯]-3-甲醯胺	722.5	(500 MHz, DMSO-d6) δ 9.69 (d, J = 7.2 Hz, 1H), 7.99 (d, J = 6.7 Hz, 1H), 7.91 (s, 1H), 7.56 (d, J = 8.0 Hz, 1H), 7.51 – 7.43 (m, 2H), 7.24 (t, J = 9.7 Hz, 1H), 7.16 (t, J = 9.5 Hz, 1H), 7.09 (d, J = 8.7 Hz, 1H), 4.96 – 4.91 (m, 1H), 4.45 (d, J = 9.5 Hz, 1H), 4.25 – 4.20 (m, 1H), 4.06 (td, J = 9.4, 4.0 Hz, 1H), 3.89 – 3.85 (m, 1H), 3.82 (s, 3H), 2.93 (br dd, J = 10.6, 4.1 Hz, 1H), 2.87 (br s, 1H), 2.49 (br s, 1H), 1.78 – 1.55 (m, 5H), 1.29 – 1.15 (m, 2H), 0.54 – 0.45 (m, 2H), 0.13 – 0.09 (m, 2H)	2.61, C

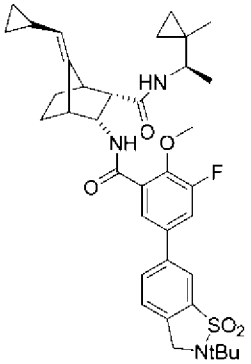
909	 異構物2	N-[(1R,2R,3S,4R,7Z)-7-(環丙基亞甲基)-3-[4-氟-3-(三氟甲基)苯基]胺甲醯基]雙環[2.2.1]庚烷-2-基]-2-氟-5-[5-羥基-3a,4,5,6,6a-四氫-4,6-環戊并[d][1,2]噁唑-3-基]-4-甲氧基-[1,1'-聯苯]-3-甲醯胺		722.6	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.94 (d, J = 7.2 Hz, 1H), 8.24 (dd, J = 6.5, 2.4 Hz, 1H), 8.15 (s, 1H), 7.82 – 7.78 (m, 1H), 7.75 – 7.67 (m, 3H), 7.49 (t, J = 9.7 Hz, 1H), 7.41 (t, J = 9.0 Hz, 1H), 7.34 (d, J = 8.7 Hz, 1H), 5.17 – 5.13 (m, 1H), 4.70 (d, J = 9.7 Hz, 1H), 4.47 (br s, 1H), 4.22 – 4.15 (m, 2H), 4.07 (s, 3H), 3.17 (dd, J = 10.5, 4.4 Hz, 1H), 3.12 (br s, 1H), 2.73 (br s, 1H), 2.14 – 2.07 (m, 2H), 1.94 – 1.78 (m, 4H), 1.51 (br dd, J = 8.7, 4.2 Hz, 1H), 1.46 – 1.39 (m, 2H), 0.79 – 0.70 (m, 2H), 0.35 (br d, J = 2.5 Hz, 2H)	2.59, A

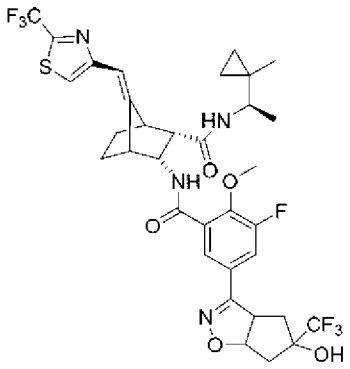
910	 見結物I	5'-{3aH,4H,6H,6aH-吡喃并[3,4-d][1,2]噁唑-3-基}-N-[(1R,2R,3S,4R,7Z)-7-(環丙基亞甲基)-3-[4-氟-3-(三氟甲基)苯基胺甲醯基]雙環[2.2.1]庚烷-2-基]-2'-氟-4'-甲氧基-[1,1'-聯苯]-3-甲醯胺	'08.1	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.92 (d, J = '7.3 Hz, 1H), 8.24 (dd, J = 6.3, 2.4 Hz, 1H), 8.15 (s, 1H), '7.81 - '7.'0 (m, 4H), '7.49 (t, J = 9.8 Hz, 1H), '7.42 (t, J = 8.8 Hz, 1H), '7.33 (d, J = 8.8 Hz, 1H), 5.39 (dd, J = 9.2, 3.'7 Hz, 1H), 4.'0 (d, J = 9.5 Hz, 1H), 4.58 (br t, J = '7.'7 Hz, 1H), 4.50 - 4.45 (m, 1H), 4.13 - 4.11 (m, 1H), 4.0'7 (s, 3H), 3.98 (br d, J = 9.5 Hz, 1H), 3.'7'7 (dd, J = 9.4, '7.0 Hz, 1H), 3.6'7 (dd, J = 10.'7, 3.5 Hz, 1H), 3.19 - 3.10 (m, 2H), 2.'73 (br s, 1H), 1.90 - 1.'79 (m, 2H), 1.54 - 1.45 (m, 1H), 1.45 - 1.38 (m, 2H), 0.'74 (quin, J = 10.1 Hz, 2H), 0.38 - 0.33 (m, 2H)	2.'5, C

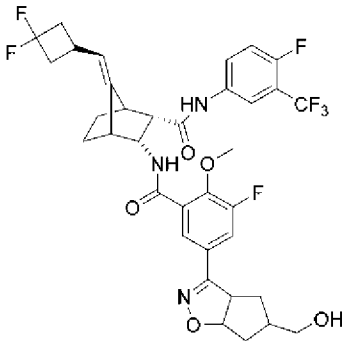
911		5'-{3aH,4H,6H,6aH-吡喃并[3,4-d][1,2]噁唑-3-基}-N-[(1R,2R,3S,4R,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]-2'-氟-4'-甲氧基-[1,1'-聯苯]-3-甲醯胺	708.4	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.92 (d, J = 7.3 Hz, 1H), 8.24 (dd, J = 6.3, 2.4 Hz, 1H), 8.15 (s, 1H), 7.81 – 7.70 (m, 4H), 7.49 (t, J = 9.8 Hz, 1H), 7.42 (t, J = 8.8 Hz, 1H), 7.33 (d, J = 8.8 Hz, 1H), 5.39 (dd, J = 9.2, 3.7 Hz, 1H), 4.70 (d, J = 9.5 Hz, 1H), 4.58 (br t, J = 7.1 Hz, 1H), 4.50 – 4.45 (m, 1H), 4.13 – 4.11 (m, 1H), 4.07 (s, 3H), 3.98 (br d, J = 9.5 Hz, 1H), 3.71 (dd, J = 9.4, 7.0 Hz, 1H), 3.67 (dd, J = 10.7, 3.5 Hz, 1H), 3.19 – 3.10 (m, 2H), 2.73 (br s, 1H), 1.90 – 1.79 (m, 2H), 1.54 – 1.45 (m, 1H), 1.45 – 1.38 (m, 2H), 0.74 (quin, J = 10.1 Hz, 2H), 0.38 – 0.33 (m, 2H)	2.69, A

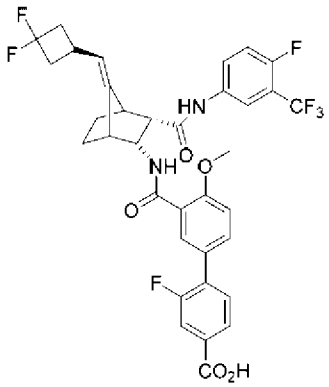
913		3-(3'-{[(1R,2R,3S,4R,7Z)-7-(環戊基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-4,5-二氫-1,2-噁唑-5-甲酸	738.4	(500 MHz, DMSO-d6) δ 10.58 (s, 1H), 9.89 (br d, J=6.9 Hz, 1H), 8.26 - 8.20 (m, 1H), 8.16 (s, 1H), 7.82 - 7.70 (m, 3H), 7.48 (t, J=9.8 Hz, 1H), 7.40 (t, J=9.0 Hz, 1H), 7.32 (d, J=8.7 Hz, 1H), 5.19 (d, J=8.9 Hz, 1H), 5.08 - 5.03 (m, 1H), 4.41 (br s, 1H), 4.06 (s, 3H), 3.19 - 3.15 (m, 1H), 3.01 (br s, 1H), 2.72 (br s, 1H), 1.92 - 1.86 (m, 1H), 1.86 - 1.71 (m, 3H), 1.70 - 1.50 (m, 4H), 1.39 (br s, 2H), 1.32 - 1.19 (m, 2H)	2.38, A
914		(1R,2S,3R,4R,7Z)-7-[(3,3-二氟環丁基)亞甲基]-N-[4-氟-3-(三氟甲基)苯基]-3-{3-氟-5-[5-羥基-5-(三氟甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	764.2	(DMSO-d6, 400 MHz) δ 10.5-10.6 (m, 1H), 9.7-9.7 (m, 1H), 8.1-8.2 (m, 1H), 7.9-8.0 (m, 1H), 7.8-7.9 (m, 1H), 7.7-7.8 (m, 1H), 7.4-7.5 (m, 1H), 5.9-6.0 (m, 1H), 5.4-5.4 (m, 1H), 5.3-5.4 (m, 1H), 4.3-4.4 (m, 2H), 4.0-4.1 (m, 3 H), 3.1-3.2 (m, 1H), 2.6-3.0 (m, 8H), 2.4-2.5 (m, 1H), 2.2-2.3 (m, 2H), 1.9-2.1 (m, 1H), 1.8-1.9 (m, 2H), 1.3-1.5 (m, 2H)	2.50, B

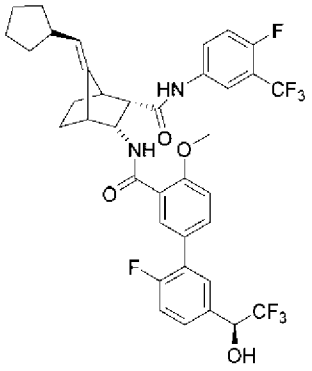
915		(1R,2S,3R,4R,7Z)-3-{5-[5-(羥基甲基)-5-甲基-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-N-[(1R)-1-(1-甲基環丙基)乙基]-7-{[2-(三氟甲基)-1,3-噻唑-4-基]亞甲基}雙環[2.2.1]庚烷-2-甲醯胺	687.3	(400 MHz, DMSO-d6) δ = 10.11 (d, J = 6.8 Hz, 1H), 8.14 (d, J = 2.4 Hz, 1H), 8.04 (d, J = 8.6 Hz, 1H), 7.97 (s, 1H), 7.79 (dd, J = 2.4, 8.6 Hz, 1H), 7.24 (d, J = 8.9 Hz, 1H), 6.43 (s, 1H), 5.30 - 5.09 (m, 1H), 4.59 (t, J = 5.3 Hz, 1H), 4.37 (ddd, J = 4.4, 6.5, 10.4 Hz, 1H), 4.25 (dt, J = 6.6, 9.8 Hz, 1H), 4.01 (s, 3H), 3.70 (br s, 1H), 3.53 - 3.48 (m, 1H), 3.21 - 3.12 (m, 2H), 3.09 (dd, J = 4.4, 10.9 Hz, 1H), 2.78 (br s, 1H), 2.06 - 1.96 (m, 1H), 1.92 - 1.76 (m, 4H), 1.66 (dd, J = 6.5, 12.9 Hz, 1H), 1.47 (br d, J = 6.0 Hz, 2H), 1.04 (d, J = 6.9 Hz, 3H), 1.01 (s, 3H), 0.96 (s, 3H), 0.63 - 0.50 (m, 1H), 0.40 - 0.29 (m, 1H), 0.25 - 0.10 (m, 2H)	2.36, B

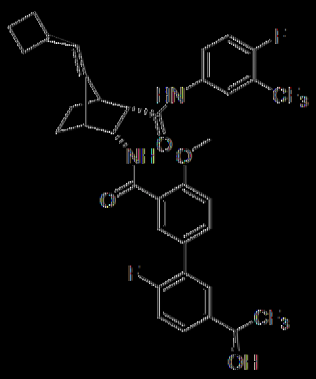
916		(1R,2S,3R,4R,7Z)-3-[5-(2-三級丁基-1,1-二側氧基-2,3-二氫-1λ⁶,2-苯并噻唑-6-基)-3-氟-2-甲氧基苯甲醯胺基]-7-(環丙基亞甲基)-N-[(1R)-1-(1-甲基環丙基)乙基]雙環[2.2.1]庚烷-2-甲醯胺	664.3	(400 MHz, DMSO-d6) δ 9.98 (d, J = 6.9 Hz, 1H), 8.06 (d, J = 1.1 Hz, 1H), 8.04 - 7.87 (m, 4H), 7.66 (d, J = 8.3 Hz, 1H), 4.66 (d, J = 9.5 Hz, 1H), 4.59 (s, 2H), 4.38 - 4.29 (m, 1H), 4.05 (d, J = 2.3 Hz, 3H), 3.50 - 3.45 (m, 1H), 3.11 - 3.04 (m, 1H), 2.98 (dd, J = 4.4, 10.9 Hz, 1H), 2.59 - 2.54 (m, 1H), 1.93 - 1.72 (m, 2H), 1.54 - 1.30 (m, 12H), 1.02 (d, J = 6.9 Hz, 3H), 0.98 (s, 3H), 0.80 - 0.66 (m, 2H), 0.58 - 0.47 (m, 1H), 0.41 - 0.27 (m, 3H), 0.24 - 0.08 (m, 2H)。	2.69, A

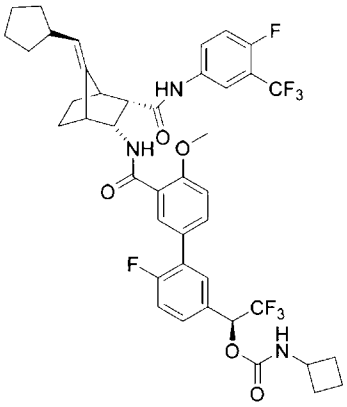
917		(1R,2S,3R,4R,7Z)-3-{3-氟-5-[5-羥基-5-(三氟甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-N-[(1R)-1-(1-甲基環丙基)乙基]-7-{[2-(三氟甲基)-1,3-噻唑-5-基]亞甲基}雙環[2.2.1]庚烷-2-甲醯胺	745.2	(400 MHz, DMSO-d6) δ 10.15 (d, J = 6.5 Hz, 1H), 8.13 (d, J = 9.0 Hz, 1H), 8.09 (s, 1H), 7.94 - 7.87 (m, 1H), 7.71 (dd, J = 2.3, 12.5 Hz, 1H), 6.67 (s, 1H), 5.92 (s, 1H), 5.31 (dd, J = 6.3, 9.5 Hz, 1H), 4.54 - 4.27 (m, 2H), 4.06 (d, J = 2.5 Hz, 3H), 3.48 (dd, J = 7.0, 8.8 Hz, 1H), 3.12 (dd, J = 4.4, 11.1 Hz, 1H), 2.85 (br d, J = 2.5 Hz, 1H), 2.32 - 2.18 (m, 3H), 2.00 (br d, J = 14.0 Hz, 1H), 1.96 - 1.84 (m, 2H), 1.58 - 1.44 (m, 2H), 1.04 (d, J = 7.0 Hz, 3H), 1.00 (s, 3H), 0.58 - 0.49 (m, 1H), 0.40 - 0.31 (m, 1H), 0.28 - 0.11 (m, 2H)。	2.56, A

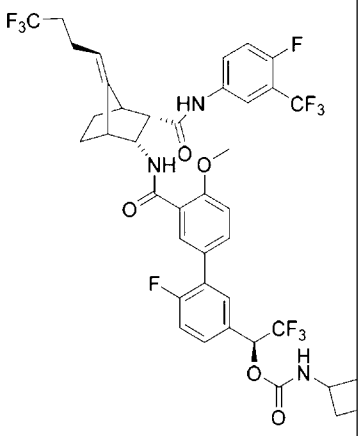
918		(1R,2S,3R,4R,7Z)-7-[(3,3-二氟環丁基)亞甲基]-N-[4-氟-3-(三氟甲基)苯基]-3-{3-氟-5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	710.2	(500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.69 (d, J=7.2 Hz, 1H), 8.11 (dd, J=6.3, 2.1 Hz, 1H), 7.96 (s, 1H), 7.86 - 7.81 (m, 1H), 7.72 (dd, J=12.6, 1.9 Hz, 1H), 7.48 (t, J=9.8 Hz, 1H), 5.40 (d, J=8.5 Hz, 1H), 5.16 (dd, J=8.7, 5.1 Hz, 1H), 4.51 (t, J=5.1 Hz, 1H), 4.45 - 4.36 (m, 1H), 4.19 (br t, J=8.6 Hz, 1H), 4.08 (s, 1H), 4.09 (s, 2H), 3.17 (dd, J=10.4, 4.3 Hz, 1H), 3.05 - 2.99 (m, 1H), 2.97 - 2.79 (m, 3H), 2.78 - 2.73 (m, 1H), 2.47 - 2.36 (m, 2H), 1.99 (br dd, J=13.3, 5.8 Hz, 1H), 1.93 - 1.73 (m, 4H), 1.68 - 1.51 (m, 2H), 1.41 (br d, J=4.6 Hz, 2H), 由於水抑制未觀測到兩個質子	2.54, C

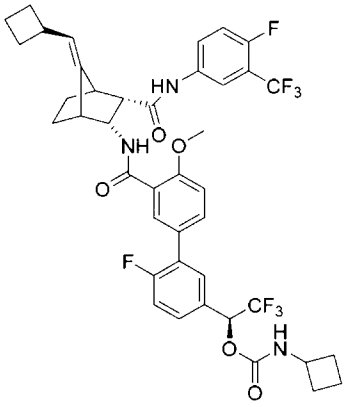
919		3'-{[(1R,2R,3S,4R,7Z)-7-[(3,3-二氟環丁基)亞甲基]-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-2-氟-4'-甲氧基-[1,1'-聯苯]-4-甲酸	691.2	(500 MHz, DMSO-d6) δ 10.60 - 10.52 (m, 1H), 9.90 (br d, J=7.2 Hz, 1H), 8.24 - 8.11 (m, 2H), 7.84 (br d, J=8.1 Hz, 1H), 7.79 - 7.68 (m, 3H), 7.62 (br t, J=8.0 Hz, 1H), 7.51 - 7.42 (m, 1H), 7.32 (br d, J=8.8 Hz, 1H), 5.38 (br d, J=8.5 Hz, 1H), 4.43 - 4.35 (m, 1H), 4.04 (s, 3H), 3.62 (br s, 3H), 3.19 - 3.11 (m, 1H), 2.99 (br s, 1H), 2.96 - 2.90 (m, 1H), 2.75 (br s, 1H), 2.46 - 2.33 (m, 2H), 1.94 - 1.74 (m, 2H), 1.45 - 1.32 (m, 2H)	2.18, C

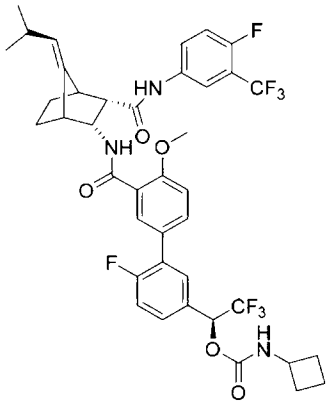
920		N-[(1R,2R,3S,4R,7Z)-7-(環戊基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]-2'-氟-4-甲氧基-5'-[(1S)-2,2,2-三氟-1-羥基乙基]-[1,1'-聯苯]-3-甲醯胺	723.2	(500 MHz, DMSO-d6) δ 10.57 - 10.49 (m, 1H), 9.91 (d, J=7.2 Hz, 1H), 8.22 (dd, J=6.2, 2.2 Hz, 1H), 8.12 (s, 1H), 7.82 - 7.75 (m, 1H), 7.70 (br d, J=8.6 Hz, 1H), 7.61 (br d, J=7.6 Hz, 1H), 7.56 - 7.43 (m, 2H), 7.38 - 7.28 (m, 2H), 7.03 (d, J=5.6 Hz, 1H), 5.30 - 5.22 (m, 1H), 5.18 (s, 1H), 4.46 - 4.37 (m, 1H), 4.05 (s, 3H), 3.15 (dd, J=10.5, 4.3 Hz, 1H), 3.00 (br s, 1H), 2.71 (br s, 1H), 2.64 - 2.57 (m, 1H), 1.92 - 1.70 (m, 4H), 1.67 - 1.49 (m, 4H), 1.46 - 1.34 (m, 2H), 1.29 - 1.19 (m, 2H)	3.00, C

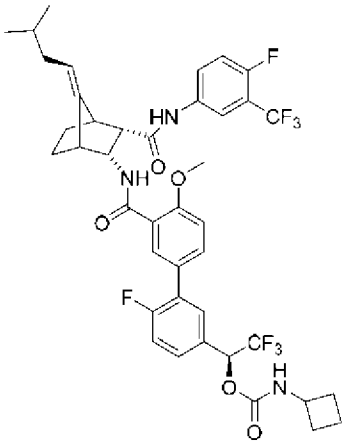
921		N-[(1R,2R,3S,4R,7S)-7-(環丁基甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]-2'-氟-4'-甲氧基-5'-[(1S)-2,2,2-三氟-1-羥基乙基][1,1'-聯苯]-3-甲醯胺	709.1	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.90 (d, J = 7.1 Hz, 1H), 8.21 (br d, J = 4.2 Hz, 1H), 8.12 (s, 1H), 7.82 – 7.75 (m, 1H), 7.69 (br d, J = 8.5 Hz, 1H), 7.62 (br d, J = 7.2 Hz, 1H), 7.53 – 7.43 (m, 2H), 7.38 – 7.28 (m, 2H), 5.37 (d, J = 8.5 Hz, 1H), 5.29 – 5.21 (m, 1H), 4.43 – 4.32 (m, 1H), 4.04 (s, 3H), 3.22 – 3.04 (m, 2H), 2.96 (br s, 1H), 2.70 (br s, 1H), 2.20 – 2.07 (m, 2H), 1.95 – 1.67 (m, 7H), 1.48 – 1.29 (m, 2H) 質子由於溶膠而缺失	2.92, C

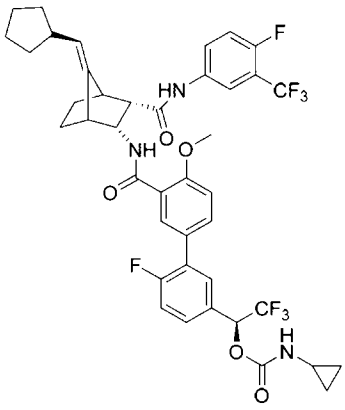
922		N-環丁基胺基甲酸 (1S)-1-(3'-{[(2R,3S,7Z)-7-(環戊基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2,2,2-三氟乙酯	820.1	(500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.91 (br d, J=7.1 Hz, 1H), 8.28 - 8.19 (m, 1H), 8.17 - 8.05 (m, 2H), 7.81 - 7.75 (m, 1H), 7.67 (br dd, J=18.3, 7.9 Hz, 2H), 7.54 (br dd, J=3.5, 2.3 Hz, 1H), 7.49 - 7.36 (m, 2H), 7.32 (d, J=8.6 Hz, 1H), 6.42 - 6.26 (m, 1H), 5.19 (d, J=8.9 Hz, 1H), 4.48 - 4.37 (m, 1H), 4.04 (s, 3H), 3.96 - 3.85 (m, 1H), 3.15 (br dd, J=10.8, 3.7 Hz, 1H), 2.99 (br s, 1H), 2.71 (br s, 1H), 2.64 - 2.57 (m, 1H), 2.27 - 2.03 (m, 2H), 1.98 - 1.74 (m, 6H), 1.67 - 1.47 (m, 6H), 1.46 - 1.35 (m, 2H), 1.29 - 1.17 (m, 2H)	3.26, C

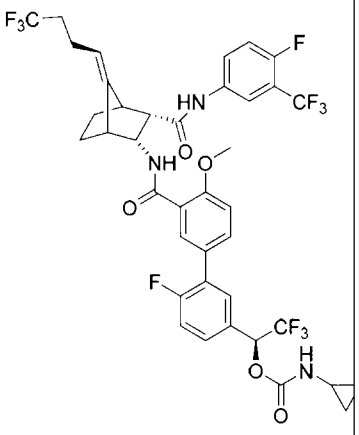
923		N-環丁基胺基甲酸 (1S)-2,2,2- 三氟 -1-(6- 氟 -3'-{[(2R,3S,7Z)-3-{[4- 氟 -3-(三氟甲基)苯基]胺甲醯基 }-7-(4,4,4- 三氟丁亞基)雙環[2.2.1]庚烷-2-基]胺甲醯基 }-4'- 甲氧基 -[1,1'- 聯苯]-3-基)乙酯	848.0	(500 MHz, DMSO-d6) δ 10.56 (s, 1H), 9.93 (br d, J=7.2 Hz, 1H), 8.28 - 8.19 (m, 1H), 8.16 - 8.08 (m, 2H), 7.83 - 7.77 (m, 1H), 7.70 - 7.62 (m, 2H), 7.54 (br s, 1H), 7.48 - 7.37 (m, 2H), 7.33 (d, J=8.7 Hz, 1H), 6.41 - 6.31 (m, 1H), 5.27 (br t, J=7.1 Hz, 1H), 4.51 - 4.39 (m, 1H), 4.05 (s, 3H), 3.98 - 3.86 (m, 1H), 3.16 (br dd, J=10.3, 3.6 Hz, 1H), 3.00 (br s, 1H), 2.75 (br s, 1H), 2.44 - 2.27 (m, 4H), 2.24 - 2.04 (m, 2H), 1.98 - 1.84 (m, 3H), 1.81 - 1.71 (m, 1H), 1.70 - 1.50 (m, 2H), 1.45 - 1.35 (m, 2H)	3.08, C

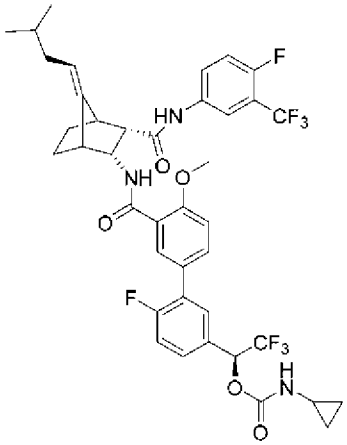
924		N-環丁基胺基甲酸 (1S)-1-(3'-{[(2R,3S,7Z)-7-(環丁基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2,2,2-三氟乙酯	806.0	(500 MHz, DMSO-d6) δ 11.95 - 11.95 (m, 1H), 10.53 (s, 1H), 9.91 (br d, J=6.9 Hz, 1H), 8.29 - 8.22 (m, 1H), 8.16 - 8.10 (m, 2H), 7.85 - 7.77 (m, 1H), 7.69 (br t, J=9.1 Hz, 2H), 7.54 (br dd, J=2.9, 2.0 Hz, 1H), 7.52 - 7.39 (m, 2H), 7.35 - 7.26 (m, 1H), 6.39 - 6.28 (m, 1H), 5.38 (d, J=8.3 Hz, 1H), 4.42 - 4.34 (m, 1H), 4.06 (s, 3H), 3.98 - 3.91 (m, 1H), 3.14 - 3.06 (m, 1H), 2.97 (br s, 1H), 2.72 (br d, J=2.7 Hz, 1H), 2.23 - 2.08 (m, 4H), 1.97 - 1.75 (m, 8H), 1.70 - 1.51 (m, 2H), 1.45 - 1.31 (m, 2H)	3.19, C

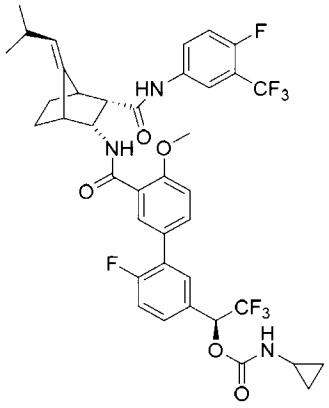
925		N-環丁基胺基甲酸 (1S)-2,2,2- 三氟 -1-(6- 氟 -3'-{[(2R,3S,7Z)-3-{[4- 氟 -3-(三氟甲基)苯基]胺甲醯基}-7-(2- 甲基亞丙基) 雙環 [2.2.1] 庚烷 -2- 基] 胺甲醯基 }-4'- 甲氧基 -[1,1'- 聯苯]-3- 基)乙酯	794.1	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.91 (br d, J=6.9 Hz, 1H), 8.23 (br d, J=4.1 Hz, 1H), 8.16 - 8.08 (m, 2H), 7.80 - 7.76 (m, 1H), 7.68 (br dd, J=13.7, 8.3 Hz, 2H), 7.55 (br dd, J=6.1, 2.7 Hz, 1H), 7.50 - 7.39 (m, 2H), 7.33 (d, J=8.8 Hz, 1H), 6.35 (br d, J=6.9 Hz, 1H), 5.11 (d, J=8.9 Hz, 1H), 4.46 - 4.38 (m, 1H), 4.05 (s, 3H), 3.95 - 3.85 (m, 1H), 3.16 (dd, J=10.9, 3.9 Hz, 1H), 2.99 (s, 1H), 2.70 (br s, 1H), 2.48 - 2.41 (m, 1H), 2.21 - 2.04 (m, 2H), 1.98 - 1.84 (m, 3H), 1.81 - 1.74 (m, 1H), 1.64 - 1.52 (m, 2H), 1.45 - 1.35 (m, 2H), 1.07 - 0.93 (m, 6H)	3.15. C

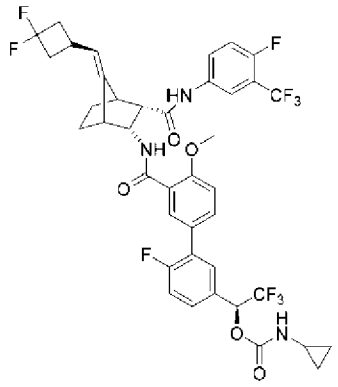
926		N-環丁基胺基甲酸 (1S)-2,2,2- 三氟 -1-(6- 氟 -3'-{[(2R,3S,7Z)-3-{[4- 氟 -3-(三氟甲基)苯基]胺甲醯基}-7-(3- 甲基丁亞基)雙環[2.2.1] 庚烷 -2-基]胺甲醯基}-4'- 甲氧基 -[1,1'-聯苯]-3-基)乙酯	808.0	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.92 (br d, J=7.0 Hz, 1H), 8.28 - 8.22 (m, 1H), 8.16 - 8.09 (m, 2H), 7.85 - 7.76 (m, 1H), 7.69 (br dd, J=13.9, 8.1 Hz, 2H), 7.54 (br s, 1H), 7.50 - 7.38 (m, 2H), 7.33 (d, J=8.8 Hz, 1H), 6.41 - 6.26 (m, 1H), 5.24 (t, J=7.6 Hz, 1H), 4.45 - 4.39 (m, 1H), 4.05 (s, 3H), 3.96 - 3.89 (m, 1H), 3.18 (br dd, J=10.7, 3.7 Hz, 1H), 2.96 (br s, 1H), 2.74 (br s, 1H), 2.20 - 2.04 (m, 2H), 1.99 - 1.84 (m, 5H), 1.80 - 1.72 (m, 1H), 1.67 - 1.53 (m, 3H), 1.46 - 1.33 (m, 2H), 0.91 (dd, J=12.3, 6.6 Hz, 6H)	3.23, C

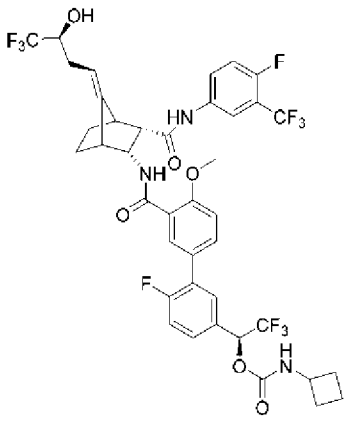
927		N-環丙基胺基甲酸 (1S)-1-(3'-{[(1R,2R,3S,4R,7Z)-7-(環戊基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2,2,2-三氟乙酯	806.4	(500 MHz, DMSO-d6) δ 10.30 (s, 1H), 9.68 (br d, J=6.9 Hz, 1H), 8.04 - 7.95 (m, 1H), 7.89 (s, 1H), 7.77 (br s, 1H), 7.58 - 7.52 (m, 1H), 7.45 (br d, J=1.1 Hz, 2H), 7.30 (br s, 1H), 7.27 - 7.14 (m, 2H), 7.09 (d, J=8.8 Hz, 1H), 6.14 (br d, J=7.5 Hz, 1H), 4.95 (d, J=8.9 Hz, 1H), 4.24 - 4.10 (m, 1H), 3.82 (s, 3H), 2.92 (br dd, J=10.4, 4.2 Hz, 1H), 2.78 - 2.76 (m, 1H), 2.75 - 2.72 (m, 1H), 2.48 (br s, 1H), 2.35 (br d, J=8.6 Hz, 1H), 1.66 - 1.50 (m, 4H), 1.46 - 1.25 (m, 4H), 1.15 (br d, J=3.0 Hz, 2H), 1.03 (td, J=8.0, 3.9 Hz, 2H), 0.41 - 0.30 (m, 2H), 0.25 - 0.12 (m, 2H)	3.06, C

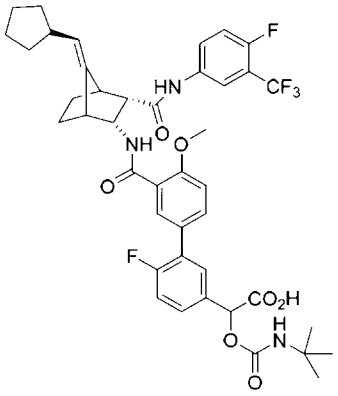
928		N-環丙基胺基甲酸 (1S)-2,2,2- 三氟 -1-(6- 氟 -3'-{[(1R,2R,3S,4R,7Z)-3-{[4- 氟 -3-(三氟甲基)苯基]胺甲醯基 }-7-(4,4,4-三氟丁亞基)雙環[2.2.1]庚烷-2-基]胺甲醯基 }-4'- 甲氧基 -[1,1'-聯苯]-3-基) 乙酯	834.2	(500 MHz, DMSO-d6) δ 10.38 - 10.30 (m, 1H), 9.70 (br d, J=7.0 Hz, 1H), 8.04 - 7.99 (m, 1H), 7.90 (s, 1H), 7.78 (br d, J=2.2 Hz, 1H), 7.57 (br dd, J=8.6, 3.3 Hz, 1H), 7.46 (br t, J=9.6 Hz, 2H), 7.35 - 7.30 (m, 1H), 7.28 - 7.17 (m, 2H), 7.10 (d, J=8.8 Hz, 1H), 6.22 - 6.12 (m, 1H), 5.05 (br t, J=6.7 Hz, 1H), 4.20 (ddd, J=10.3, 6.8, 3.9 Hz, 1H), 3.83 (s, 3H), 3.01 - 2.91 (m, 1H), 2.78 (br s, 1H), 2.53 (br s, 1H), 2.20 - 2.02 (m, 4H), 1.72 - 1.50 (m, 2H), 1.22 - 1.11 (m, 2H), 0.81 (d, J=6.0 Hz, 1H), 0.40 - 0.30 (m, 2H), 0.25 - 0.14 (m, 2H)	2.84, C

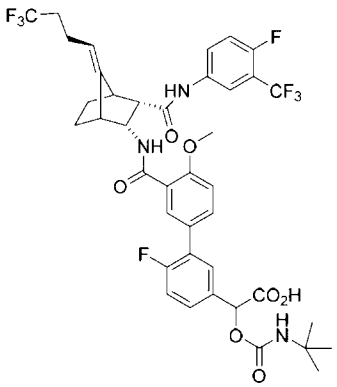
929		N-環丙基胺基甲酸 (1S)-2,2,2- 三氟 -1-(6- 氟 -3'-{[(1R,2R,3S,4R,7Z)-3-{[4- 氟 -3-(三氟甲基)苯基]胺甲醯基}-7-(3-甲基丁亞基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'- 甲氧基 -[1,1'-聯苯]-3-基)乙酯	794.2	(500 MHz, DMSO-d6) δ 10.35 (s, 1H), 9.70 (br d, J=7.1 Hz, 1H), 8.07 - 8.00 (m, 1H), 7.91 (s, 1H), 7.79 (br d, J=2.4 Hz, 1H), 7.57 (dt, J=7.8, 3.9 Hz, 1H), 7.50 - 7.42 (m, 2H), 7.31 (br d, J=3.4 Hz, 1H), 7.29 - 7.18 (m, 2H), 7.10 (d, J=8.8 Hz, 1H), 6.17 (br d, J=6.3 Hz, 1H), 5.02 (t, J=7.7 Hz, 1H), 4.26 - 4.16 (m, 1H), 3.83 (s, 3H), 2.97 (dd, J=10.8, 4.1 Hz, 1H), 2.74 (br s, 1H), 2.52 (t, J=3.4 Hz, 1H), 1.80 - 1.71 (m, 2H), 1.70 - 1.54 (m, 2H), 1.47 - 1.35 (m, 1H), 1.25 - 1.12 (m, 2H), 0.69 (dd, J=12.3, 6.6 Hz, 6H), 0.36 (br d, J=3.2 Hz, 2H), 0.23 - 0.12 (m, 2H) 質子由於水抑制而缺失	3.00, C

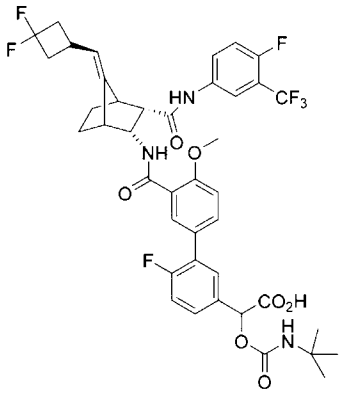
930		N-環丙基胺基甲酸 (1S)-2,2,2- 三氟 -1-(6- 氟 -3'-{[(1R,2R,3S,4R,7Z)-3-{[4- 氟 -3-(三氟甲基)苯基]胺甲醯基}-7-(2-甲基亞丙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'- 甲氧基 -[1,1'-聯苯]-3-基)乙酯	780.1	(500 MHz, DMSO-d6) δ 10.35 (s, 1H), 9.73 (br d, J=6.9 Hz, 1H), 8.10 - 8.02 (m, 1H), 7.95 (s, 1H), 7.83 (br d, J=2.7 Hz, 1H), 7.64 - 7.57 (m, 1H), 7.55 - 7.48 (m, 2H), 7.36 (br s, 1H), 7.32 - 7.20 (m, 2H), 7.15 (d, J=8.8 Hz, 1H), 6.21 (br d, J=6.6 Hz, 1H), 4.93 (d, J=9.0 Hz, 1H), 4.24 (ddd, J=10.7, 7.2, 3.8 Hz, 1H), 3.88 (s, 3H), 2.99 (dd, J=10.8, 4.1 Hz, 1H), 2.83 - 2.80 (m, 1H), 2.52 (br s, 1H), 2.28 (br s, 1H), 1.76 - 1.58 (m, 2H), 1.21 (br d, J=7.6 Hz, 2H), 0.86 - 0.77 (m, 6H), 0.44 - 0.35 (m, 2H), 0.28 - 0.17 (m, 2H) 質子由於水抑制而缺失	2.93, C

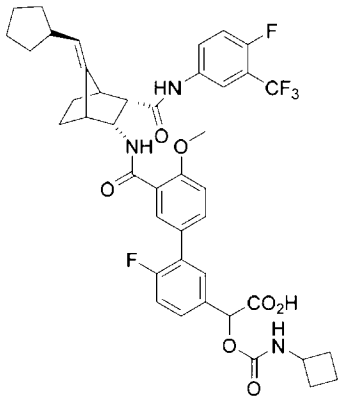
931		N-環丙基胺基甲酸 (1S)-1-(3'-{[(1R,2R,3S,4R,7Z)-7-[(3,3-二氟環丁基)亞甲基]-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2,2,2-三氟乙酯	828.2	(500 MHz, DMSO-d6) δ 10.32 (s, 1H), 9.70 (br d, J=6.9 Hz, 1H), 8.04 - 7.98 (m, 1H), 7.90 (s, 1H), 7.79 (br d, J=2.1 Hz, 1H), 7.56 (br dd, J=8.1, 3.3 Hz, 1H), 7.46 (br t, J=9.0 Hz, 2H), 7.35 - 7.17 (m, 3H), 7.11 (d, J=8.6 Hz, 1H), 6.23 - 6.10 (m, 1H), 5.17 (d, J=8.5 Hz, 1H), 4.24 - 4.14 (m, 1H), 3.83 (s, 3H), 2.99 - 2.93 (m, 1H), 2.78 (br s, 1H), 2.74 - 2.58 (m, 3H), 2.54 (br s, 1H), 2.25 - 2.13 (m, 2H), 1.72 - 1.51 (m, 2H), 1.24 - 1.11 (m, 2H), 0.45 - 0.31 (m, 2H), 0.24 - 0.12 (m, 2H) 質子由於水抑制而缺失	2.82, C

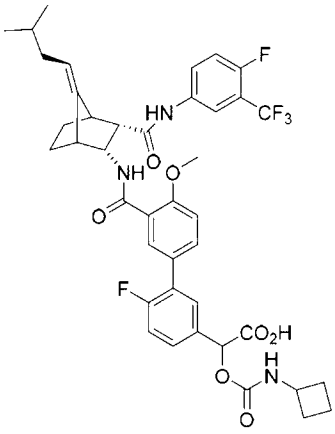
932		N-環丁基胺基甲酸 (1S)-2,2,2- 三氟 -1-(6- 氟 -3'-{[(1R,2R,3S,4R,7Z)-3-{[4- 氟 -3-(三氟甲基)苯基]胺甲醯基 }-7-[(3R)-4,4,4- 三氟 -3- 羥基丁亞基]雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'- 甲氧基 -[1,1'-聯苯]-3-基)乙酯	864.0	(500 MHz, DMSO-d6) δ 10.59 (s, 1H), 9.93 (br d, J=7.1 Hz, 1H), 8.29 - 8.22 (m, 1H), 8.17 - 8.09 (m, 2H), 7.83 - 7.78 (m, 1H), 7.69 (br t, J=9.0 Hz, 2H), 7.59 - 7.30 (m, 4H), 6.43 - 6.31 (m, 1H), 5.32 (t, J=7.3 Hz, 1H), 4.50 - 4.38 (m, 1H), 4.07 (s, 3H), 4.01 - 3.93 (m, 2H), 3.44 - 3.32 (m, 1H), 3.19 (dd, J=10.8, 4.2 Hz, 1H), 3.00 (br s, 1H), 2.78 (br s, 1H), 2.46 - 2.40 (m, 1H), 2.30 (dt, J=14.7, 7.4 Hz, 1H), 2.19 - 2.05 (m, 2H), 1.96 - 1.82 (m, 3H), 1.78 (br d, J=7.6 Hz, 1H), 1.65 - 1.52 (m, 2H), 1.42 (br d, J=5.8 Hz, 2H)	2.77, C

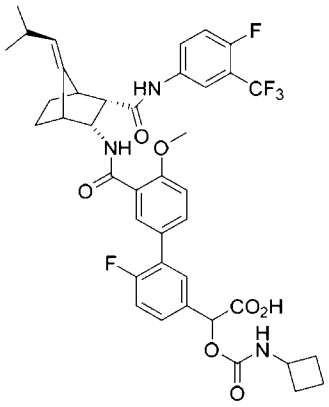
933		2-[(三級丁基胺甲醯基)氧基]-2-(3'-{[(1R,2R,3S,4R,7Z)-7-(環戊基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)乙酸	798.2	(500 MHz, DMSO-d6) δ 10.33 (s, 1H), 9.68 (d, J=7.2 Hz, 1H), 8.01 (dd, J=6.4, 2.4 Hz, 1H), 7.88 (s, 1H), 7.56 (br dd, J=8.4, 3.6 Hz, 1H), 7.43 (br d, J=8.7 Hz, 1H), 7.39 - 7.32 (m, 1H), 7.28 - 7.19 (m, 2H), 7.09 - 7.01 (m, 2H), 6.88 (br d, J=2.7 Hz, 1H), 5.43 (s, 1H), 4.95 (d, J=8.9 Hz, 1H), 4.23 - 4.10 (m, 1H), 3.81 (s, 3H), 3.66 (s, 1H), 2.93 (dd, J=10.5, 4.3 Hz, 1H), 2.82 - 2.74 (m, 1H), 2.48 (br s, 1H), 2.42 - 2.33 (m, 1H), 1.65 - 1.50 (m, 4H), 1.45 - 1.38 (m, 2H), 1.32 (br dd, J=7.3, 5.1 Hz, 2H), 1.14 (br d, J=2.6 Hz, 2H), 1.07 - 1.01 (m, 2H), 0.99 - 0.93 (m, 9H)	2.91, C

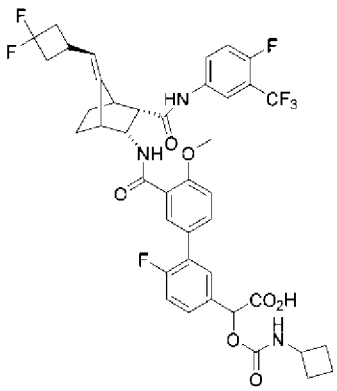
934		2-[(三級丁基胺甲醯基)氧基]-2-(6-氟-3'-{[(1R,2R,3S,4R,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(4,4,4-三氟丁亞基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-3-基)乙酸	826.2	(500 MHz, DMSO-d6) δ 10.67 - 10.53 (m, 1H), 9.94 (br d, J=7.2 Hz, 1H), 8.26 (dd, J=6.6, 2.4 Hz, 1H), 8.13 (s, 1H), 7.82 (br dd, J=8.2, 3.5 Hz, 1H), 7.69 (br d, J=8.2 Hz, 1H), 7.60 (br d, J=7.7 Hz, 1H), 7.52 - 7.42 (m, 2H), 7.37 - 7.29 (m, 2H), 7.20 (br d, J=1.6 Hz, 1H), 5.72 (s, 1H), 5.28 (t, J=6.7 Hz, 1H), 4.50 - 4.31 (m, 1H), 4.06 (s, 3H), 3.19 (dd, J=10.3, 4.1 Hz, 1H), 3.05 - 2.96 (m, 1H), 2.77 (br s, 1H), 2.43 - 2.23 (m, 5H), 1.96 - 1.71 (m, 2H), 1.47 - 1.35 (m, 2H), 1.23 (s, 9H)	2.73, C

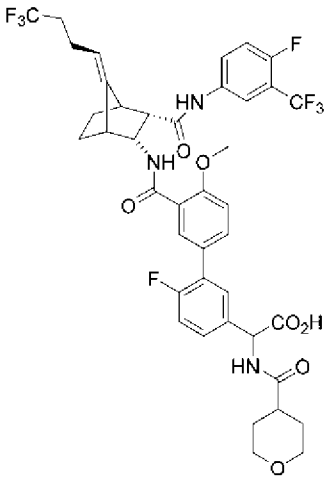
935		2-[(三級丁基胺甲醯基)氧基]-2-(3'-{[(1R,2R,3S,4R,7Z)-7-[(3,3-二氟環丁基)亞甲基]-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)乙酸	820.1	(500 MHz, DMSO-d6) δ 10.59 (s, 1H), 9.94 (br d, J=7.2 Hz, 1H), 8.25 (dd, J=6.4, 2.1 Hz, 1H), 8.13 (s, 1H), 7.88 - 7.79 (m, 1H), 7.69 (br d, J=8.5 Hz, 1H), 7.61 (br d, J=7.2 Hz, 1H), 7.53 - 7.45 (m, 2H), 7.38 - 7.31 (m, 2H), 7.20 (br s, 1H), 5.72 (s, 1H), 5.40 (d, J=8.5 Hz, 1H), 4.48 - 4.33 (m, 1H), 4.06 (s, 3H), 3.19 (dd, J=10.9, 3.3 Hz, 1H), 3.02 (br s, 1H), 2.98 - 2.81 (m, 3H), 2.77 (br s, 1H), 2.48 - 2.38 (m, 2H), 1.92 - 1.76 (m, 2H), 1.51 - 1.36 (m, 2H), 1.23 (s, 10H)	2.71, C

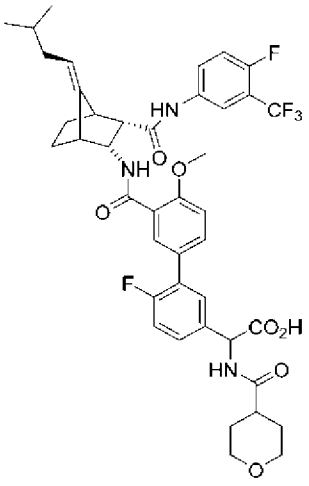
936		2-[(環丁基胺甲醯基)氧基]-2-(3'-{[(1R,2R,3S,4R,7Z)-7-(環戊基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)乙酸	796.3	(500 MHz, DMSO-d6) δ 10.59 (s, 1H), 9.93 (br d, J=6.9 Hz, 1H), 8.25 (dd, J=6.4, 2.1 Hz, 1H), 8.13 (s, 1H), 7.80 (br dd, J=7.9, 3.5 Hz, 1H), 7.67 (br d, J=6.9 Hz, 2H), 7.57 (br d, J=6.9 Hz, 1H), 7.51 - 7.42 (m, 2H), 7.33 - 7.26 (m, 2H), 5.69 (s, 1H), 5.19 (d, J=8.8 Hz, 1H), 4.47 - 4.36 (m, 1H), 4.06 (s, 3H), 4.01 - 3.93 (m, 1H), 3.25 - 3.17 (m, 1H), 3.11 - 3.03 (m, 1H), 2.72 (br s, 1H), 2.60 (br d, J=8.4 Hz, 1H), 2.18 - 2.07 (m, 2H), 1.96 - 1.76 (m, 6H), 1.66 - 1.51 (m, 6H), 1.44 - 1.35 (m, 2H), 1.34 - 1.25 (m, 2H)	2.87, C

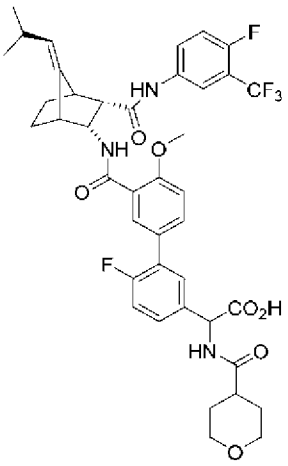
937		(2S)-2-[(環丁基胺甲醯基)氧基]-2-(6-氟-3'-{[(1R,2R,3S,4R,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(3-甲基丁亞基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-3-基)乙酸	784.1	(500 MHz, DMSO-d6) δ 10.35 (s, 1H), 9.70 (br d, J=7.2 Hz, 1H), 8.03 (dd, J=6.3, 2.5 Hz, 1H), 7.89 (s, 1H), 7.58 (br dd, J=8.7, 3.8 Hz, 1H), 7.47 (br dd, J=15.1, 8.1 Hz, 2H), 7.34 (br d, J=7.0 Hz, 1H), 7.29 - 7.19 (m, 2H), 7.13 - 7.00 (m, 2H), 5.48 (s, 1H), 5.01 (t, J=7.6 Hz, 1H), 4.25 - 4.11 (m, 1H), 3.83 (s, 3H), 3.76 - 3.70 (m, 1H), 2.96 (dd, J=11.0, 4.4 Hz, 1H), 2.78 - 2.69 (m, 1H), 2.52 (t, J=3.4 Hz, 1H), 1.99 - 1.85 (m, 2H), 1.77 - 1.57 (m, 6H), 1.41 - 1.27 (m, 3H), 1.23 - 1.10 (m, 2H), 0.69 (dd, J=12.3, 6.6 Hz, 6H)	2.84, C

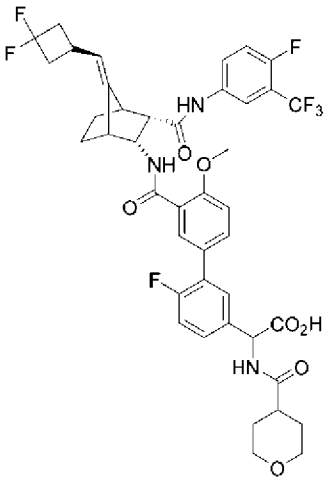
938		2-[(環丁基胺甲醯基)氧基]-2-(6-氟-3'-{[(1R,2R,3S,4R,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2-甲基亞丙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-3-基)乙酸	770.4	(500 MHz, DMSO-d6) δ 10.51 (s, 1H), 9.88 (br d, J=7.2 Hz, 1H), 8.20 (dd, J=6.9, 2.0 Hz, 1H), 8.08 (s, 1H), 7.82 - 7.73 (m, 2H), 7.64 (br d, J=8.9 Hz, 1H), 7.54 (br s, 1H), 7.50 - 7.39 (m, 2H), 7.38 - 7.25 (m, 2H), 7.20 - 7.00 (m, 1H), 5.73 (s, 1H), 5.07 (d, J=9.0 Hz, 1H), 4.44 - 4.28 (m, 1H), 4.01 (s, 3H), 3.94 - 3.87 (m, 1H), 3.12 (br dd, J=7.1, 3.9 Hz, 1H), 2.99 - 2.94 (m, 1H), 2.66 (br s, 1H), 2.15 - 2.04 (m, 2H), 1.97 - 1.80 (m, 3H), 1.79 - 1.71 (m, 1H), 1.58 - 1.49 (m, 2H), 1.35 (br d, J=7.2 Hz, 2H), 1.02 - 0.93 (m, 6H)	2.76, C

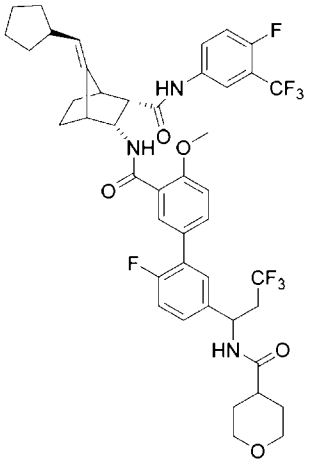
939		2-[(環丁基胺甲醯基)氧基]-2-(3'-{[(1R,2R,3S,4R,7Z)-7-[(3,3-二氟環丁基)亞甲基]-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)乙酸	818.2	(500 MHz, DMSO-d6) δ 10.57 (s, 1H), 9.94 (br d, J=6.9 Hz, 1H), 8.32 - 8.19 (m, 1H), 8.12 (s, 1H), 7.85 - 7.77 (m, 2H), 7.69 (br d, J=8.7 Hz, 1H), 7.59 (br d, J=7.3 Hz, 1H), 7.51 - 7.46 (m, 2H), 7.37 - 7.28 (m, 2H), 5.76 (s, 1H), 5.40 (d, J=8.5 Hz, 1H), 4.50 - 4.37 (m, 1H), 4.06 (s, 3H), 4.00 - 3.93 (m, 1H), 3.18 (dd, J=10.4, 4.4 Hz, 1H), 3.02 (br s, 1H), 2.97 - 2.71 (m, 4H), 2.48 - 2.31 (m, 2H), 2.20 - 2.10 (m, 2H), 2.01 - 1.74 (m, 4H), 1.67 - 1.54 (m, 2H), 1.40 (br d, J=1.8 Hz, 2H)	2.67, C

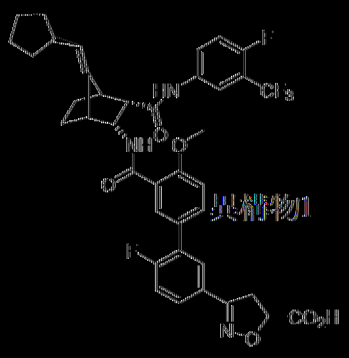
940		2-(6-氟-3'-{[(1R,2R,3S,4R,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(4,4,4-三氟丁亞基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-3-基)-2-[(噁烷-4-基)甲醯胺基]乙酸	838.2	(500 MHz, DMSO-d6) δ 10.56 (s, 1H), 9.94 (br d, J=7.1 Hz, 1H), 8.33 - 8.20 (m, 2H), 8.13 (br s, 1H), 7.80 (br dd, J=5.0, 3.4 Hz, 1H), 7.69 - 7.64 (m, 1H), 7.54 - 7.46 (m, 2H), 7.41 - 7.27 (m, 2H), 7.22 - 7.14 (m, 1H), 5.27 (br t, J=5.8 Hz, 2H), 4.48 - 4.37 (m, 1H), 4.04 (s, 3H), 3.83 (br dd, J=10.6, 3.1 Hz, 2H), 3.32 - 3.25 (m, 1H), 3.17 (br dd, J=10.7, 3.7 Hz, 1H), 3.02 - 2.95 (m, 1H), 2.75 (br s, 1H), 2.59 - 2.56 (m, 1H), 2.40 - 2.26 (m, 4H), 1.93 - 1.76 (m, 3H), 1.64 - 1.49 (m, 4H), 1.47 - 1.36 (m, 2H)	2.49, C

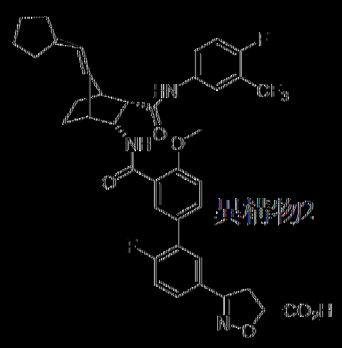
941		2-(6- 氟 -3'-{[(1R,2R,3S,4R,7Z)-3-{[4- 氟 -3-(三氟甲基)苯基]胺甲醯基}-7-(3-甲基丁亞基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'- 甲氧基 -[1,1'-聯苯]-3- 基)-2-[(噁烷 -4- 基)甲醯胺基]乙酸	798.2	(500 MHz, DMSO-d6) δ 10.57 (s, 1H), 9.92 (d, J=6.9 Hz, 1H), 8.46 - 8.34 (m, 1H), 8.26 (dd, J=6.5, 2.3 Hz, 1H), 8.15 (s, 1H), 7.81 (br dd, J=8.4, 3.5 Hz, 1H), 7.68 (br d, J=8.8 Hz, 1H), 7.55 - 7.45 (m, 2H), 7.37 (br d, J=2.8 Hz, 1H), 7.31 (d, J=8.7 Hz, 1H), 7.27 - 7.21 (m, 1H), 5.33 - 5.11 (m, 2H), 4.51 - 4.34 (m, 1H), 4.06 (s, 3H), 3.88 - 3.79 (m, 2H), 3.34 - 3.26 (m, 1H), 3.19 (dd, J=10.8, 4.7 Hz, 1H), 3.01 - 2.93 (m, 1H), 2.81 - 2.73 (m, 1H), 2.61 - 2.57 (m, 1H), 2.02 - 1.93 (m, 2H), 1.91 - 1.84 (m, 1H), 1.81 - 1.73 (m, 1H), 1.70 - 1.49 (m, 6H), 1.44 - 1.29 (m, 2H), 0.92 (dd, J=12.3, 6.6 Hz, 6H)	2.64, C

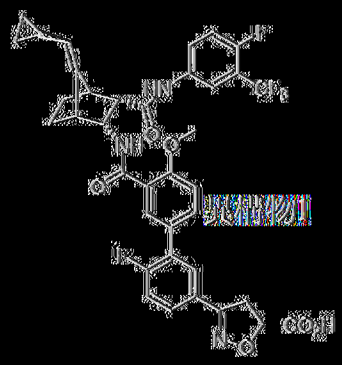
942		2-(6-氟-3'-{[(1R,2R,3S,4R,7Z)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}-7-(2-甲基亞丙基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-4'-甲氧基-[1,1'-聯苯]-3-基)-2-[(噁烷-4-基)甲醯胺基]乙酸	784.2	(500 MHz, DMSO-d6) δ 10.36 - 10.27 (m, 1H), 9.69 (d, J=7.1 Hz, 1H), 8.36 (br d, J=7.6 Hz, 1H), 8.02 (dd, J=6.4, 2.3 Hz, 1H), 7.92 (s, 1H), 7.65 - 7.54 (m, 1H), 7.47 (br d, J=8.4 Hz, 1H), 7.34 - 7.16 (m, 3H), 7.13 - 7.02 (m, 2H), 5.16 (br d, J=7.4 Hz, 1H), 4.89 (d, J=8.9 Hz, 1H), 4.27 - 4.12 (m, 1H), 3.83 (s, 3H), 3.66 - 3.57 (m, 2H), 3.12 - 3.02 (m, 1H), 2.95 (dd, J=10.8, 3.9 Hz, 1H), 2.78 (br s, 1H), 2.48 (br s, 1H), 2.36 - 2.33 (m, 1H), 2.26 - 2.20 (m, 1H), 1.73 - 1.51 (m, 2H), 1.44 - 1.28 (m, 4H), 1.22 - 1.10 (m, 2H), 0.84 - 0.74 (m, 6H) 質子由於水抑制而缺失	2.55, C

943		2-(3'-{[(1R,2R,3S,4R,7Z)-7-[(3,3-二氟環丁基)亞甲基]-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2-[(噁烷-4-基)甲醯胺基]乙酸	832.0	(500 MHz, DMSO-d6) δ 10.56 (s, 1H), 9.93 (br d, J=6.9 Hz, 1H), 8.44 (br s, 1H), 8.30 - 8.20 (m, 1H), 8.14 (br s, 1H), 7.87 - 7.76 (m, 1H), 7.68 (br d, J=8.0 Hz, 1H), 7.54 - 7.46 (m, 2H), 7.38 (br d, J=2.7 Hz, 1H), 7.36 - 7.23 (m, 2H), 5.39 (d, J=8.5 Hz, 1H), 5.30 (br d, J=5.8 Hz, 1H), 4.48 - 4.34 (m, 1H), 4.05 (s, 3H), 3.88 - 3.80 (m, 2H), 3.33 - 3.25 (m, 1H), 3.21 (s, 1H), 2.96 - 2.73 (m, 4H), 2.46 - 2.36 (m, 2H), 1.92 - 1.67 (m, 3H), 1.67 - 1.51 (m, 4H), 1.44 - 1.31 (m, 2H) 質子由於水抑制而缺失	2.47, C

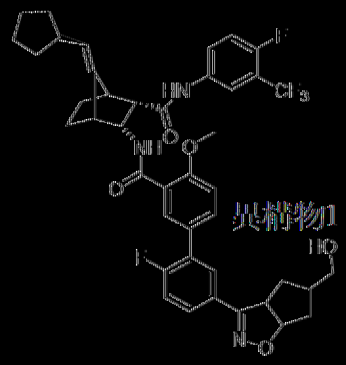
944		N-[1-(3'-{[(1R,2R,3S,4R,7Z)-7-(環戊基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-3,3,3-三氟丙基]噁烷-4-甲醯胺	848.2	(500 MHz, DMSO-d6) δ 10.56 (s, 1H), 9.90 (br d, J=7.0 Hz, 1H), 8.50 (d, J=8.5 Hz, 1H), 8.27 - 8.23 (m, 1H), 8.15 (s, 1H), 7.82 - 7.77 (m, 1H), 7.71 (br d, J=8.9 Hz, 1H), 7.56 - 7.52 (m, 1H), 7.49 (t, J=9.8 Hz, 1H), 7.39 - 7.35 (m, 1H), 7.32 - 7.25 (m, 2H), 5.28 - 5.22 (m, 1H), 5.19 (d, J=8.8 Hz, 1H), 4.44 - 4.38 (m, 1H), 4.05 (s, 3H), 3.84 (br t, J=9.6 Hz, 2H), 3.19 - 3.15 (m, 1H), 3.01 (br s, 1H), 2.81 - 2.75 (m, 2H), 2.73 (br d, J=4.6 Hz, 1H), 2.64 - 2.57 (m, 1H), 1.87 - 1.75 (m, 4H), 1.67 - 1.54 (m, 9H), 1.39 (br d, J=2.5 Hz, 2H), 1.31 - 1.20 (m, 4H)	2.84, C

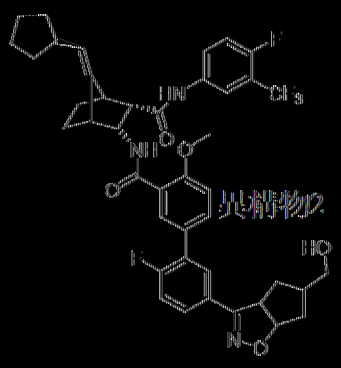
945		3-(3'-{[(1R,2R,3S,4R,7S)-7-(環戊基甲基)-3-{[4-氟-3-(三氟甲基)苯基]甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-4,5-二氫-1,2-噁唑-5-甲酸	738.1	(500 MHz, DMSO-d6) δ 10.59 (s, 1H), 9.89 (d, J = 7.0 Hz, 1H), 8.24 (dd, J = 6.3, 2.4 Hz, 1H), 8.15 (s, 1H), 7.82 – 7.77 (m, 1H), 7.76 – 7.69 (m, 3H), 7.47 (t, J = 9.8 Hz, 1H), 7.39 (dd, J = 10.3, 8.7 Hz, 1H), 7.31 (d, J = 8.8 Hz, 1H), 5.19 – 5.15 (m, 1H), 5.03 – 4.99 (m, 1H), 4.43 – 4.38 (m, 1H), 4.05 (s, 3H), 3.18 – 3.13 (m, 1H), 3.02 – 2.98 (m, 1H), 2.71 (br s, 1H), 2.62 – 2.55 (m, 1H), 1.91 – 1.85 (m, 1H), 1.84 – 1.73 (m, 3H), 1.67 – 1.59 (m, 2H), 1.59 – 1.51 (m, 2H), 1.43 – 1.35 (m, 2H), 1.30 – 1.19 (m, 2H)	2.42, C

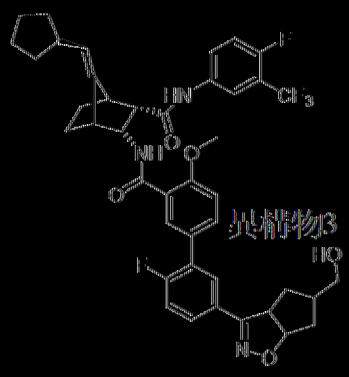
946		3-(3'-{[(1R,2R,3S,4R,7A)-7-(環戊基亞甲基)-3-[4-氟-3-(三氟甲基)苯基胺甲醯基]雙環[2.2.1]庚烷-2-基胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-4,5-二氫-1,2-噁唑-5-甲酸	'38.2	(500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.89 (br d, J= '1.2 Hz, 1H), 8.26 - 8.23 (m, 1H), 8.1' - 8.14 (m, 1H), '7.82 - '7.'1 (m, 4H), '7.48 (t, J= 9.'1 Hz, 1H), '7.41 (t, J= 9.5 Hz, 1H), '7.33 - '7.29 (m, 1H), 5.21 - 5.14 (m, 2H), 4.44 - 4.38 (m, 1H), 4.05 (s, 3H), 3.81 - 3.'2 (m, 1H), 3.'0 - 3.61 (m, 1H), 3.18 - 3.13 (m, 1H), 3.02 - 2.98 (m, 1H), 2.'1 (br s, 1H), 2.63 - 2.56 (m, 1H), 1.91 - 1.'3 (m, 4H), 1.69 - 1.60 (m, 2H), 1.60 - 1.51 (m, 2H), 1.43 - 1.35 (m, 2H), 1.32 - 1.20 (m, 2H)	2.42, C

941		3-(3'-{[(1R,2R,3S,4R,7Z)-7-(環丙基甲基)-3-[4-氟-3-(三氟甲基)苯基胺甲醯基]雙環[2.2.1]庚烷-2-基胺甲醯基]-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-4,5-二氫-1,2-噁唑-5-甲酸	710.1	(500 MHz, DMSO-d6) δ 10.57 - 10.53 (m, 1H), 9.92 (d, J = 7.1 Hz, 1H), 8.25 - 8.19 (m, 1H), 8.15 (s, 1H), 7.80 - 7.70 (m, 4H), 7.47 (t, J = 9.7 Hz, 1H), 7.40 (dd, J = 10.4, 8.7 Hz, 1H), 7.31 (d, J = 8.7 Hz, 1H), 5.15 - 5.08 (m, 1H), 4.68 (d, J = 9.6 Hz, 1H), 4.50 - 4.41 (m, 1H), 4.08 - 4.03 (m, 3H), 3.77 - 3.69 (m, 1H), 3.19 - 3.08 (m, 2H), 2.74 - 2.69 (m, 1H), 1.89 - 1.75 (m, 2H), 1.54 - 1.34 (m, 3H), 0.78 - 0.65 (m, 2H), 0.38 - 0.29 (m, 2H)	2.19, C

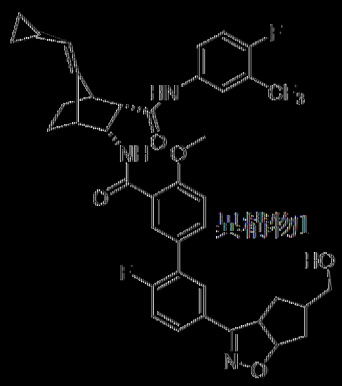
948	 異構物2	3-(3'-{[(1R,2R,3S,4R,7s)-7-(環丙基甲基)-3-[4-氟-3-(三氟甲基)苯基胺甲醯基]雙環[2.2.1]庚烷-2-基胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-4,5-二氫-1,2-噁唑-5-甲酸	'10.2	(500 MHz, DMSO-d6) δ 10.59 - 10.54 (m, 1H), 9.91 (d, J= 7.2 Hz, 1H), 8.25 - 8.20 (m, 1H), 8.14 (s, 1H), 7.82 - 7.67 (m, 4H), 7.50 - 7.43 (m, 1H), 7.39 (dd, J= 10.4, 8.7 Hz, 1H), 7.32 - 7.29 (m, 1H), 5.07 - 5.00 (m, 1H), 4.69 - 4.65 (m, 1H), 4.48 - 4.42 (m, 1H), 4.08 - 4.02 (m, 3H), 3.72 - 3.52 (m, 1H), 3.19 - 3.14 (m, 1H), 3.13 - 3.07 (m, 1H), 2.73 - 2.69 (m, 1H), 1.92 - 1.75 (m, 2H), 1.53 - 1.35 (m, 3H), 0.78 - 0.67 (m, 2H), 0.38 - 0.29 (m, 2H)	2.19, C

949		N-[(1R,2R,3S,4R,7S)-7-(環戊基甲基)-3-[4-氟-3-(三氟甲基)苯基]胺甲醯基]雙環[2.2.1]庚烷-2-基]-2-氟-5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-4-甲氧基-[1,1'-聯苯]-3-甲醯胺	764.5	(500 MHz, DMSO-d6) δ 10.52 (s, 1H), 9.89 (d, J = 7.0 Hz, 1H), 8.24 (dd, J = 6.6, 2.4 Hz, 1H), 8.14 (s, 1H), 7.80 – 7.68 (m, 4H), 7.48 (t, J = 9.8 Hz, 1H), 7.40 (dd, J = 10.4, 8.7 Hz, 1H), 5.20 – 5.13 (m, 2H), 4.43 – 4.38 (m, 1H), 4.28 (t, J = 8.9 Hz, 1H), 4.06 (s, 3H), 3.16 (dd, J = 10.7, 4.2 Hz, 1H), 3.00 (br d, J = 5.5 Hz, 1H), 2.71 (br s, 1H), 2.63 – 2.56 (m, 1H), 2.02 – 1.74 (m, 8H), 1.70 – 1.62 (m, 3H), 1.57 (td, J = 12.5, 5.1 Hz, 3H), 1.42 – 1.36 (m, 2H), 1.31 – 1.21 (m, 3H)	2.51, C

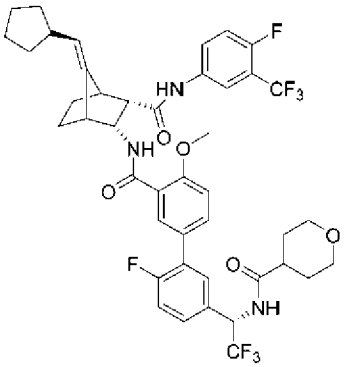
950		N-[(1R,2R,3S,4R,7Z)-7-(環戊基亞甲基)-3-[4-氟-3-(三氟甲基)苯基]胺甲醯基雙環[2.2.1]庚烷-2-基]-2-氟-5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]㗁唑-3-基]-4-甲氧基-[1,1'-聯苯]-3-甲醯胺	764.2	(500 MHz, DMSO-d6) δ 10.53 - 10.51 (m, 1H), 9.89 (d, J= 7.1 Hz, 1H), 8.25 - 8.21 (m, 1H), 8.14 (s, 1H), 7.80 - 7.68 (m, 4H), 7.47 (t, J= 9.7 Hz, 1H), 7.40 (dd, J= 10.5, 8.7 Hz, 1H), 7.34 - 7.30 (m, 1H), 5.21 - 5.15 (m, 2H), 4.40 (ddd, J= 10.4, 6.7, 4.2 Hz, 1H), 4.21 - 4.14 (m, 1H), 4.05 (s, 3H), 3.30 - 3.21 (m, 1H), 3.16 (dd, J= 10.6, 4.4 Hz, 1H), 3.02 - 2.98 (m, 1H), 2.71 (br s, 1H), 2.63 - 2.56 (m, 1H), 2.25 - 2.10 (m, 3H), 1.91 - 1.86 (m, 1H), 1.84 - 1.73 (m, 3H), 1.68 - 1.60 (m, 3H), 1.59 - 1.53 (m, 2H), 1.52 - 1.46 (m, 1H), 1.43 - 1.35 (m, 2H), 1.31 - 1.21 (m, 2H)	2.50, C

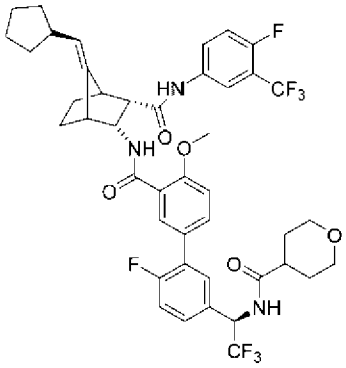
951		N-[(1R,2R,3S,4R,7Z)-7-(環戊基亞甲基)-3-[4-氟-3-(三氟甲基)苯基]胺甲醯基雙環[2.2.1]庚烷-2-基]-2-氟-5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-4-甲氧基-[1,1'-聯苯]-3-甲醯胺	764.2	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.92 - 9.87 (m, 1H), 8.26 - 8.22 (m, 1H), 8.16 - 8.13 (m, 1H), 7.81 - 7.77 (m, 1H), 7.76 - 7.69 (m, 3H), 7.48 (t, J= 9.8 Hz, 1H), 7.43 - 7.37 (m, 1H), 7.34 - 7.30 (m, 1H), 5.20 - 5.15 (m, 2H), 4.54 - 4.50 (m, 1H), 4.44 - 4.38 (m, 1H), 4.21 - 4.15 (m, 1H), 4.06 (s, 3H), 3.32 - 3.21 (m, 1H), 3.16 (dd, J= 10.7, 4.1 Hz, 1H), 3.02 - 2.98 (m, 1H), 2.71 (br s, 1H), 2.63 - 2.56 (m, 1H), 2.26 - 2.09 (m, 3H), 1.91 - 1.73 (m, 4H), 1.68 - 1.61 (m, 3H), 1.60 - 1.52 (m, 2H), 1.49 (dt, J= 12.8, 6.4 Hz, 1H), 1.43 - 1.34 (m, 2H), 1.32 - 1.20 (m, 2H)	2.49, C

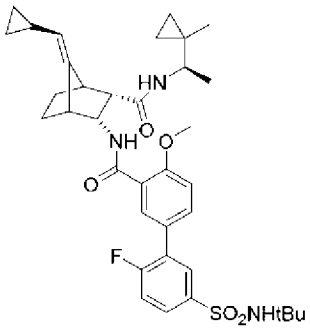
952		N-[(1R,2R,3S,4R,7Z)-7-(環戊基亞甲基)-3-[4-氟-3-(三氟甲基)苯基]胺甲醯基雙環[2.2.1]庚烷-2-基]-2-氟-5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]㗁唑-3-基]-4-甲氧基-[1,1'-聯苯]-3-甲醯胺	764.5	(500 MHz, DMSO-d6) δ 10.54 - 10.51 (m, 1H), 9.89 (d, J=7.2 Hz, 1H), 8.26 - 8.21 (m, 1H), 8.15 - 8.12 (m, 1H), 7.81 - 7.76 (m, 1H), 7.75 - 7.68 (m, 3H), 7.48 (t, J=9.8 Hz, 1H), 7.43 - 7.37 (m, 1H), 7.34 - 7.29 (m, 1H), 5.20 - 5.13 (m, 2H), 4.49 (t, J=5.3 Hz, 1H), 4.44 - 4.38 (m, 1H), 4.28 (t, J=8.8 Hz, 1H), 4.06 (s, 3H), 3.16 (dd, J=10.5, 4.1 Hz, 1H), 3.02 - 2.98 (m, 1H), 2.71 (br s, 1H), 2.63 - 2.56 (m, 1H), 2.03 - 1.75 (m, 7H), 1.70 - 1.61 (m, 3H), 1.60 - 1.52 (m, 3H), 1.41 - 1.36 (m, 2H), 1.32 - 1.20 (m, 2H)	2.86, C

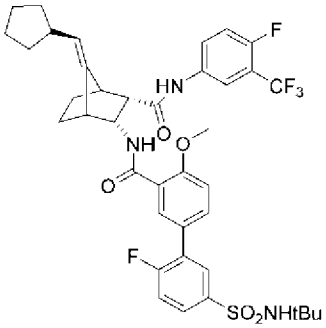
953		N-[(1R,2R,3S,4R,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]-2-氟-5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-4-甲氧基-[1,1'-聯苯]-3-甲醯胺	736.2	(500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.93 (d, J = 7.1 Hz, 1H), 8.23 (dd, J = 6.4, 2.6 Hz, 1H), 8.15 (s, 1H), 7.81 – 7.68 (m, 4H), 7.48 (t, J = 9.7 Hz, 1H), 7.40 (dd, J = 10.4, 8.7 Hz, 1H), 7.33 (d, J = 8.7 Hz, 1H), 5.21 – 5.14 (m, 1H), 4.69 (d, J = 9.6 Hz, 1H), 4.52 (t, J = 5.3 Hz, 1H), 4.46 (br t, J = 10.8 Hz, 1H), 4.18 (td, J = 9.5, 6.1 Hz, 1H), 4.06 (s, 3H), 3.32 – 3.21 (m, 1H), 3.17 (dd, J = 10.8, 4.1 Hz, 1H), 3.13 – 3.09 (m, 1H), 2.74 – 2.70 (m, 1H), 2.27 – 2.09 (m, 3H), 1.91 – 1.78 (m, 2H), 1.68 – 1.62 (m, 1H), 1.54 – 1.37 (m, 4H), 0.78 – 0.69 (m, 2H), 0.38 – 0.32 (m, 2H)	2.26, C

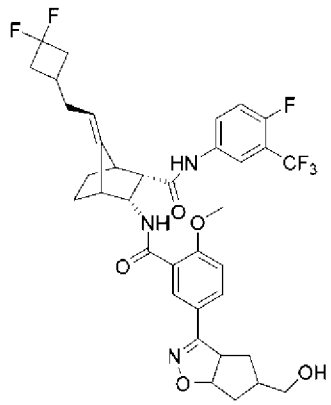
954	 異構物2	N-[(1R,2R,3S,4R,7S)-7-(環丙基甲基)-3-[4-氟-3-(三氟甲基)苯基]胺甲醯基]雙環[2.2.1]庚烷-2-基]-2-氟-5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-4-甲氧基-[1,1'-聯苯]-3-甲醯胺		736.2	(500 MHz, DMSO-d6) δ 10.54 - 10.50 (m, 1H), 9.95 - 9.90 (m, 1H), 8.23 (dd, J= 6.4, 2.6 Hz, 1H), 8.14 (s, 1H), 7.81 - 7.77 (m, 1H), 7.76 - 7.68 (m, 3H), 7.48 (t, J= 9.7 Hz, 1H), 7.40 (dd, J= 10.5, 8.6 Hz, 1H), 7.32 (d, J= 8.8 Hz, 1H), 5.20 - 5.14 (m, 1H), 4.69 (d, J= 9.6 Hz, 1H), 4.51 (t, J= 5.2 Hz, 1H), 4.49 - 4.44 (m, 1H), 4.18 (td, J= 9.7, 6.3 Hz, 1H), 4.06 (s, 3H), 3.32 - 3.21 (m, 1H), 3.16 (dd, J= 10.9, 4.1 Hz, 1H), 3.13 - 3.08 (m, 1H), 2.74 - 2.70 (m, 1H), 2.26 - 2.09 (m, 3H), 1.89 - 1.77 (m, 2H), 1.68 - 1.61 (m, 1H), 1.53 - 1.37 (m, 4H), 0.78 - 0.67 (m, 2H), 0.38 - 0.30 (m, 2H)	2.26, C

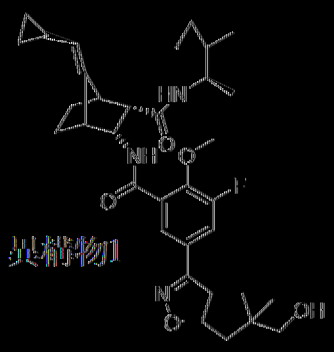
955		N-[(1S)-1-(3'-{[(1R,2R,3S,4R,7Z)-7-(環戊基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2,2,2-三氟乙基]喏烷-4-甲醯胺	834.6	(500 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.90 (d, J=7.0 Hz, 1H), 9.11 (d, J=9.8 Hz, 1H), 8.25 (dd, J=6.4, 2.3 Hz, 1H), 8.15 (s, 1H), 7.79 (br d, J=7.7 Hz, 2H), 7.70 (br d, J=8.6 Hz, 1H), 7.62 - 7.56 (m, 1H), 7.48 (t, J=9.7 Hz, 1H), 7.39 - 7.30 (m, 2H), 5.93 - 5.83 (m, 1H), 5.19 (d, J=8.9 Hz, 1H), 4.43 - 4.37 (m, 1H), 4.05 (s, 3H), 3.90 - 3.82 (m, 2H), 3.21 - 3.12 (m, 1H), 3.02 - 2.97 (m, 1H), 2.75 - 2.68 (m, 1H), 2.64 - 2.55 (m, 2H), 1.90 - 1.73 (m, 4H), 1.68 - 1.51 (m, 9H), 1.43 - 1.34 (m, 2H), 1.31 - 1.17 (m, 3H)	2.94, C

956		N-[(1R)-1-(3'-{[(1R,2R,3S,4R,7Z)-7-(環戊基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2,2,2-三氟乙基]喏烷-4-甲醯胺	834.3	(500 MHz, DMSO-d6) δ 10.60 - 10.55 (m, 1H), 9.90 (d, J=6.9 Hz, 1H), 9.12 (d, J=9.6 Hz, 1H), 8.25 (dd, J=6.6, 2.4 Hz, 1H), 8.15 (s, 1H), 7.82 - 7.76 (m, 2H), 7.71 (br d, J=8.6 Hz, 1H), 7.61 - 7.56 (m, 1H), 7.48 (t, J=9.7 Hz, 1H), 7.40 - 7.30 (m, 2H), 5.92 - 5.83 (m, 1H), 5.22 - 5.15 (m, 1H), 4.43 - 4.37 (m, 1H), 4.05 (s, 3H), 3.90 - 3.84 (m, 2H), 3.20 - 3.13 (m, 1H), 3.03 - 2.96 (m, 1H), 2.75 - 2.69 (m, 1H), 2.65 - 2.56 (m, 2H), 1.87 - 1.72 (m, 4H), 1.68 - 1.51 (m, 9H), 1.42 - 1.34 (m, 2H), 1.31 - 1.21 (m, 3H)	2.95, C

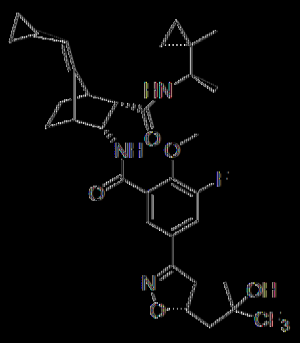
957		5'-(三級丁基胺磺醯基)-N-[(1R,2R,3S,4R,7Z)-7-(環丙基亞甲基)-3-{[(1R)-1-(1-甲基環丙基)乙基]胺甲醯基}雙環[2.2.1]庚烷-2-基]-2'-氟-4-甲氧基-[1,1'-聯苯]-3-甲醯胺	652.2	(400 MHz, DMSO-d6) δ 10.13 (d, J = 6.9 Hz, 1H), 8.11 (d, J = 1.5 Hz, 1H), 7.99 (dd, J = 2.4, 7.3 Hz, 1H), 7.92 (d, J = 8.8 Hz, 1H), 7.84(ddd, J = 2.4, 4.5, 8.5 Hz, 1H), 7.74 (td, J = 1.9, 8.7 Hz, 1H), 7.63 (s, 1H), 7.52 (dd, J = 8.6, 10.6 Hz, 1H), 7.32 (d, J = 8.8 Hz, 1H), 4.64 (d, J = 9.5Hz, 1H), 4.34 - 4.23 (m, 1H), 4.03 (s, 3H), 3.48 (dd, J = 6.9, 8.3 Hz, 1H), 3.07 (br s, 1H), 2.97 (dd, J = 4.1, 10.9 Hz, 1H), 2.54 (br s, 1H), 1.95 - 1.83 (m, 1H), 1.82 - 1.70 (m, 1H), 1.53 - 1.43 (m, 1H), 1.36 (br s, 2H), 1.12 (s, 9H), 1.03 (d, J = 6.9 Hz, 3H), 0.99 (s, 3H), 0.72 (dt, J = 2.3, 8.2 Hz,2H), 0.61 - 0.49 (m, 1H), 0.43 - 0.26 (m, 3H), 0.25 - 0.11 (m, 2H)	2.64, A

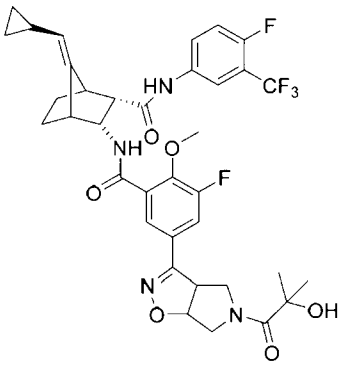
958		5'-(三級丁基胺磺醯基)-N-[(1R,2R,3S,4R,7Z)-7-(環戊基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]-2'-氟-4-甲氧基-[1,1'-聯苯]-3-甲醯胺	760.3	(400 MHz, DMSO-d6) δ 10.52 (s, 1H), 9.92 (d, J = 7.1 Hz, 1H), 8.24 (dd, J = 2.4, 6.4 Hz, 1H), 8.16 (s, 1H), 7.98 (dd, J = 2.3, 7.4 Hz, 1H), 7.89 - 7.67 (m, 3H), 7.63 (s, 1H), 7.56 - 7.42 (m, 2H), 7.36 (d, J = 8.8 Hz, 1H), 5.20 (d, J = 9.0 Hz, 1H), 4.47 - 4.29 (m, 1H), 4.07 (s, 3H), 3.19- 3.06 (m, 1H), 3.01 (br s, 1H), 2.72 (br s, 1H), 2.65 - 2.57 (m, 1H), 1.92 - 1.72 (m, 4H), 1.69 - 1.49 (m, 4H), 1.46 - 1.36 (m, 2H), 1.34 - 1.18 (m,2H), 1.12 (s, 9H)	2.93, A

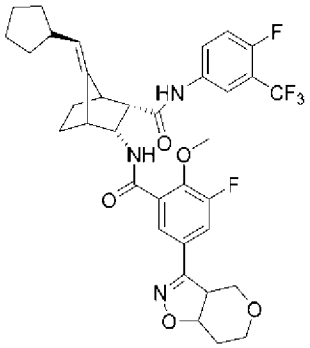
959		(1R,2S,3R,4R,7Z)-7-[2-(3,3-二氟環丁基)亞乙基]-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	706.5	(400 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.91 (d, J = 7.1 Hz, 1H), 8.29 - 8.15 (m, 2H), 7.85 - 7.70 (m, 2H), 7.49 (t, J = 9.8 Hz, 1H), 7.27(d, J = 8.8 Hz, 1H), 5.22 (t, J = 7.5 Hz, 1H), 5.12 (dd, J = 5.1, 8.7 Hz, 1H), 4.56 - 4.34 (m, 2H), 4.20 (t, J = 8.8 Hz, 1H), 4.04 (s, 3H), 3.40 (br d, J =5.8 Hz, 1H), 3.18 (br dd, J = 4.2, 6.4 Hz, 1H), 3.00 (br s, 1H), 2.78 - 2.73 (m, 1H), 2.70 - 2.63 (m, 2H), 2.32 - 2.14 (m, 5H), 2.02 - 1.73 (m, 5H),1.70 - 1.54 (m, 2H), 1.39 (br s, 2H)	2.44, A

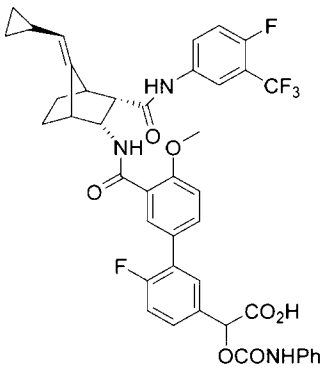
960	 異構物1	(1R,2S,3R,4R,7Z)-7-(環丙基甲基)-3-{3-氟-5-[5-(羥基甲基)-5-甲基-3a,4,5,6,6a-五氫-4,6-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-N-[(1R)-1-(1-甲基環丙基)乙基]雙環[2.2.1]庚烷-2-甲醯胺	706.5	(400 MHz, DMSO-d6) δ 10.55 (s, 1H), 9.91 (d, J = 7.1 Hz, 1H), 8.29 - 8.15 (m, 2H), 7.85 - 7.70 (m, 2H), 7.49 (t, J = 9.8 Hz, 1H), 7.27(d, J = 8.8 Hz, 1H), 5.22 (t, J = 7.5 Hz, 1H), 5.12 (dd, J = 5.1, 8.7 Hz, 1H), 4.56 - 4.34 (m, 2H), 4.20 (t, J = 8.8 Hz, 1H), 4.04 (s, 3H), 3.40 (br d, J = 5.8 Hz, 1H), 3.18 (br dd, J = 4.2, 6.4 Hz, 1H), 3.00 (br s, 1H), 2.78 - 2.73 (m, 1H), 2.70 - 2.63 (m, 2H), 2.32 - 2.14 (m, 5H), 2.02 - 1.73 (m, 5H),1.70 - 1.54 (m, 2H), 1.39 (br s, 2H)	2.44, A

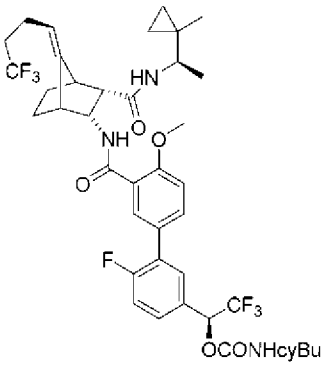
961	 共精物2	(1R,2S,3R,4R,7Z)-7-(環丙基甲基)-3-{3-氟-5-[5-(羥基甲基)-5-甲基-3a,4,5,6,6a-五氫環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-N-[(1R)-1-(1-甲基環丙基)乙基]雙環[2.2.1]庚烷-2-甲醯胺	594.3	(400 MHz, DMSO-d6) δ 10.00 (d, J = 6.8 Hz, 1H), 7.99 (d, J = 8.8 Hz, 1H), 7.93 – 7.83 (m, 1H), 7.69 (dd, J = 2.3, 12.5 Hz, 1H), 5.33 – 5.19 (m, 1H), 4.73 – 4.51 (m, 2H), 4.34 – 4.15 (m, 2H), 4.05 (d, J = 2.6 Hz, 3H), 3.46 (dd, J = 7.0, 8.4 Hz, 1H), 3.18 – 3.12 (m, 2H), 3.07 (br s, 1H), 2.96 (dd, J = 4.3, 10.8 Hz, 1H), 2.55 (br d, J = 3.8 Hz, 1H), 1.93 – 1.72 (m, 5H), 1.71 – 1.62 (m, 1H), 1.53 – 1.31 (m, 3H), 1.02 (d, J = 6.9 Hz, 3H), 0.97 (d, J = 8.8 Hz, 6H), 0.81 – 0.65 (m, 2H), 0.59 – 0.47 (m, 1H), 0.42 – 0.27 (m, 3H), 0.25 – 0.08 (m, 2H)	2.38, A

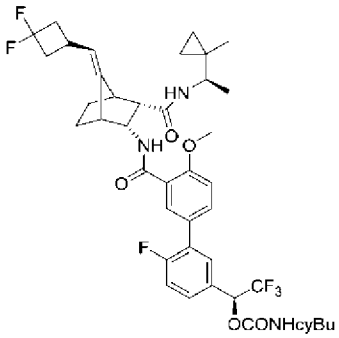
962		(1R,2S,3R,4R,7Z)-7-(環丙基甲亞基)-3-{3-氟-5-[5-羥基-5-(三氟甲基)-3a,4,5,6,6a-五氫環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}-N-[(1R)-1-(1-甲基環丙基)乙基]雙環[2.2.1]庚烷-2-甲醯胺	711.2	(400 MHz, DMSO-d6) δ 10.52 (s, 1H), 9.75 (br d, J = 6.9 Hz, 1H), 8.12 (dd, J = 2.4, 6.3 Hz, 1H), 7.99 (br s, 1H), 7.89 - 7.80 (m, 1H), 7.78 (br d, J = 12.5 Hz, 1H), 7.48 (t, J = 9.8 Hz, 1H), 5.33 (br s, 2H), 4.71 - 4.30 (m, 4H), 3.97 - 3.43 (m, 2H), 3.17 (dd, J = 4.3, 10.9 Hz, 1H), 3.13 - 3.03 (m, 1H), 2.74 (br s, 1H), 1.82 (br d, J = 8.5 Hz, 2H), 1.57 - 1.32 (m, 3H), 1.24 (br s, 6H), 0.83 - 0.65 (m, 2H), 0.50 - 0.26 (m, 2H)	2.40, A

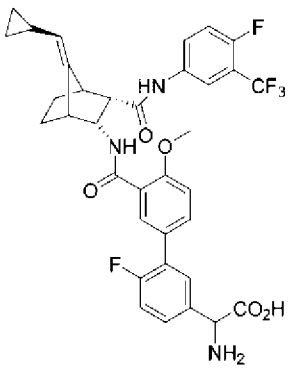
963		(1R,2S,3R,4R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{3-氟-5-[5-(2-羥基-2-甲基丙醯基)-3aH,4H,5H,6H,6aH-吡咯并[3,4-d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	634.2	(400 MHz, DMSO-d6) δ = 9.97 (d, J = 6.8 Hz, 1H), 8.00 (d, J = 8.8 Hz, 1H), 7.91 - 7.81 (m, 1H), 7.70 (dd, J = 2.1, 12.5 Hz, 1H), 5.93 (s,1H), 5.31 (dd, J = 6.4, 9.1 Hz, 1H), 4.65 (d, J = 9.6 Hz, 1H), 4.41 (br t, J = 9.4 Hz, 1H), 4.34 - 4.20 (m, 1H), 4.04 (d, J = 2.4 Hz, 3H), 3.50 - 3.42(m, 1H), 3.07 (t, J = 3.3 Hz, 1H), 2.96 (dd, J = 4.3, 10.9 Hz, 1H), 2.58 - 2.55 (m, 1H), 2.31 - 2.17 (m, 3H), 2.02 (br d, J = 14.0 Hz, 1H), 1.87 - 1.72(m, 2H), 1.55 - 1.28 (m, 3H), 1.07 - 0.93 (m, 6H), 0.80 - 0.63 (m, 2H), 0.51 (br dd, J = 4.0, 8.9 Hz, 1H), 0.43 - 0.26 (m, 3H), 0.24 - 0.05 (m, 2H)	2.43, A

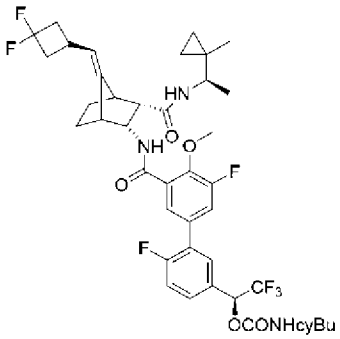
964		(1R,2S,3R,4R,7Z)-3-(5-{3aH,4H,6H,7H,7aH-哌喃o[3,4-d][1,2]噁唑-3-基}-3-氟-2-甲氧基苯甲醯胺基)-7-(環戊基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	700.2	(400 MHz, DMSO-d6) δ 10.54 (s, 1H), 10.06 (br d, J = 6.8 Hz, 1H), 8.73 - 8.49 (m, 2H), 8.24 (dd, J = 2.4, 6.6 Hz, 1H), 7.88 - 7.71 (m,1H), 7.50 (t, J = 9.8 Hz, 1H), 5.31 (br d, J = 6.3 Hz, 2H), 4.71 (d, J = 9.5 Hz, 1H), 4.60 - 4.25 (m, 2H), 4.15 (s, 3H), 3.95 - 3.38 (m, 2H), 3.18 (dd, J= 4.4, 10.5 Hz, 1H), 3.12 (br s, 1H), 2.74 (br s, 1H), 1.89 - 1.66 (m, 2H), 1.57 - 1.35 (m, 3H), 1.32 - 0.97 (m, 6H), 0.84 - 0.66 (m, 2H), 0.47 - 0.26(m, 2H)	2.30, A

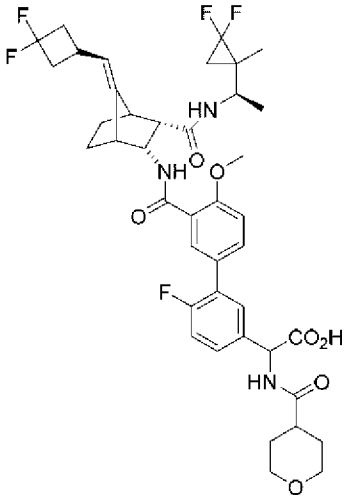
965		2-(3'-{[(1R,2R,3S,4R,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2-[(苯基胺甲醯基)氧基]乙酸	790.1	(400 MHz, $CDCl_3$) δ 9.73 (br d, J=8.0 Hz, 1H), 8.11 (br s, 1H), 8.07 (s, 1H), 7.96 (dd, J=6.2, 2.5 Hz, 1H), 7.93 (br s, 1H), 7.64 - 7.54 (m, 2H), 7.44 (dt, J=8.7, 3.4 Hz, 1H), 7.37 - 7.29 (m, 3H), 7.19 (t, J=7.9 Hz, 2H), 7.11 - 6.94 (m, 4H), 6.13 (s, 1H), 4.79 - 4.66 (m, 1H), 4.60 (d, J=9.5 Hz, 1H), 4.04 (s, 3H), 3.19 (t, J=3.8 Hz, 1H), 3.05 (dd, J=10.7, 3.9 Hz, 1H), 2.67 (t, J=3.8 Hz, 1H), 2.23 - 2.07 (m, 1H), 1.97 - 1.82 (m, 1H), 1.71 - 1.51 (m, 2H), 1.46 (qd, J=8.6, 4.6 Hz, 1H), 0.82 - 0.63 (m, 2H), 0.40 - 0.26 (m, 2H)	2.22, A

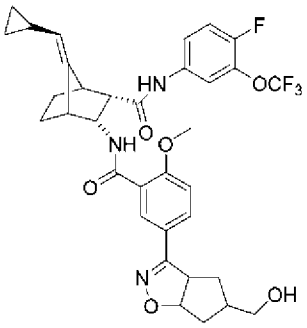
966		N-環丁基胺基甲酸 (1S)-2,2,2- 三氟-1-(6-氟-4'-甲氧基-3'-{[(1R,2R,3S,4R,7Z)-3-{[(1R)-1-(1-甲基環丙基)乙基]胺甲醯基}-7-(4,4,4- 三氟丁亞基)雙環[2.2.1]庚烷-2-基]胺甲醯基}-[1,1'-聯苯]-3-基)乙酯	768.4	(500 MHz, DMSO-d6) δ 9.95 (br d, J=6.6 Hz, 1H), 7.97 (br d, J=7.7 Hz, 1H), 7.90 (s, 1H), 7.84 - 7.76 (m, 1H), 7.51 (br d, J=6.5 Hz, 2H), 7.37 (br d, J=8.7 Hz, 1H), 7.30 - 7.21 (m, 1H), 7.12 (br d, J=8.8 Hz, 1H), 6.28 - 6.12 (m, 1H), 5.05 (br t, J=6.9 Hz, 1H), 4.16 - 4.04 (m, 1H), 3.84 (s, 3H), 3.80 - 3.69 (m, 1H), 3.24 (br d, J=6.6 Hz, 1H), 2.83 - 2.78 (m, 1H), 2.21 - 2.06 (m, 4H), 2.00 - 1.87 (m, 2H), 1.73 (dt, J=19.7, 9.7 Hz, 3H), 1.46 - 1.34 (m, 2H), 1.22 - 1.11 (m, 2H), 0.91 - 0.78 (m, 6H), 0.43 - 0.33 (m, 1H), 0.20 - 0.12 (m, 1H), 0.07 - -0.07 (m, 2H)	2.86, C

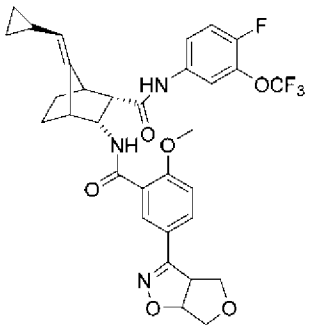
967		N-環丁基胺基甲酸 (1S)-1-(3'-{[(1R,2R,3S,4R,7Z)-7-[(3,3-二氟環丁基)亞甲基]-3-{[(1R)-1-(1-甲基環丙基)乙基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2,2,2-三氟乙酯	762.2	(500 MHz, DMSO-d6) δ 9.95 (br d, J=6.9 Hz, 1H), 7.97 (d, J=7.9 Hz, 1H), 7.89 (s, 1H), 7.79 (d, J=8.7 Hz, 1H), 7.55 - 7.47 (m, 2H), 7.41 - 7.33 (m, 1H), 7.30 - 7.21 (m, 1H), 7.12 (d, J=8.7 Hz, 1H), 6.17 (br d, J=7.2 Hz, 1H), 5.16 (d, J=8.3 Hz, 1H), 4.13 - 3.99 (m, 1H), 3.84 (s, 3H), 2.85 - 2.57 (m, 5H), 2.41 (br s, 1H), 2.29 - 2.12 (m, 2H), 2.02 - 1.86 (m, 2H), 1.82 - 1.67 (m, 3H), 1.63 - 1.51 (m, 1H), 1.48 - 1.35 (m, 2H), 1.17 (br s, 2H), 0.85 (d, J=6.9 Hz, 3H), 0.81 (s, 3H), 0.36 (br dd, J=9.3, 4.1 Hz, 1H), 0.20 - 0.13 (m, 1H), 0.07 - -0.04 (m, 2H)	2.93, C

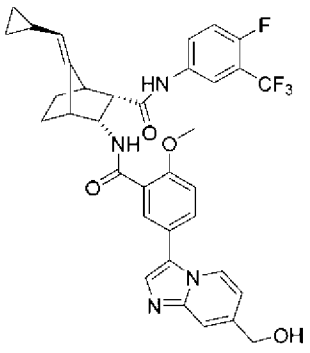
969		2-胺基-2-(3'-{[(1R,3S,4R,7Z)-7-(環丙基亞甲基)-3-{[4-氟-3-(三氟甲基)苯基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)乙酸	670.2	(500 MHz, DMSO-d6) δ 10.61 (s, 1H), 9.96 (br d, J=7.0 Hz, 1H), 8.23 (dd, J=6.4, 2.3 Hz, 1H), 8.17 (s, 1H), 7.85 - 7.75 (m, 1H), 7.73 - 7.62 (m, 2H), 7.53 - 7.43 (m, 2H), 7.42 - 7.29 (m, 2H), 5.02 (s, 1H), 4.69 (d, J=9.6 Hz, 1H), 4.52 - 4.41 (m, 1H), 4.05 (s, 3H), 3.17 (br dd, J=10.9, 3.9 Hz, 1H), 3.10 (br s, 1H), 2.72 (br s, 1H), 1.90 - 1.75 (m, 2H), 1.54 - 1.35 (m, 3H), 0.80 - 0.67 (m, 2H), 0.34 (br d, J=3.2 Hz, 2H)	2.14, C

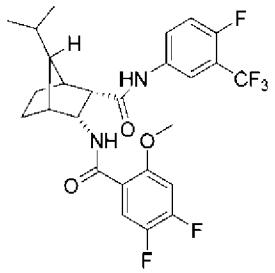
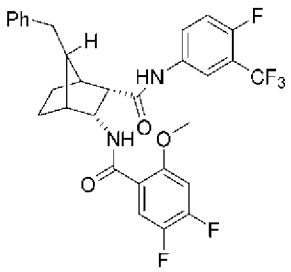
970		N-環丁基胺基甲酸 (1S)-1-(3'-{[(1R,2R,3S,4R,7Z)-7-[(3,3-二氟環丁基)亞甲基]-3-{[(1R)-1-(1-甲基環丙基)乙基]胺甲醯基}雙環[2.2.1]庚烷-2-基]胺甲醯基}-5',6-二氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2,2,2-三氟乙酯	780.1	(500 MHz, DMSO-d6) δ 9.85 (br d, J=6.8 Hz, 1H), 7.98 (d, J=7.8 Hz, 1H), 7.85 (d, J=8.9 Hz, 1H), 7.66 (s, 1H), 7.56 (br d, J=6.6 Hz, 1H), 7.50 (br d, J=12.1 Hz, 1H), 7.43 (br s, 1H), 7.29 (dd, J=10.3, 8.7 Hz, 1H), 6.20 (q, J=7.0 Hz, 1H), 5.18 (d, J=8.5 Hz, 1H), 4.19 - 4.04 (m, 1H), 3.90 (d, J=2.1 Hz, 3H), 3.83 - 3.71 (m, 1H), 2.86 - 2.57 (m, 5H), 2.43 (br s, 1H), 2.31 - 2.16 (m, 2H), 2.05 - 1.88 (m, 2H), 1.83 - 1.66 (m, 3H), 1.65 - 1.56 (m, 1H), 1.49 - 1.34 (m, 2H), 1.20 (br d, J=6.3 Hz, 2H), 0.91 - 0.77 (m, 6H), 0.36 (br dd, J=9.3, 3.9 Hz, 1H), 0.22 - 0.12 (m, 1H), 0.08 - -0.05 (m, 2H) 由於水抑制而缺失1個質子	2.97, C

971		2-(3'-{[(1R,2R,3S,4R,7Z)-3-{[(1R)-1-(2,2-二氟-1-甲基環丙基)乙基]胺甲醯基}-7-[(3,3-二氟環丁基)亞甲基]雙環[2.2.1]庚烷-2-基]胺甲醯基}-6-氟-4'-甲氧基-[1,1'-聯苯]-3-基)-2-[(噁烷-4-基)甲醯胺基]乙酸	788.2	(500 MHz, DMSO-d6) δ 10.09 (d, J=6.8 Hz, 1H), 8.60 (br d, J=7.5 Hz, 1H), 8.31 (br d, J=8.4 Hz, 1H), 8.11 (s, 1H), 7.69 (br d, J=8.7 Hz, 1H), 7.58 - 7.51 (m, 1H), 7.45 - 7.38 (m, 1H), 7.35 - 7.26 (m, 2H), 5.40 (br d, J=7.3 Hz, 1H), 5.35 (d, J=8.4 Hz, 1H), 4.35 - 4.22 (m, 1H), 4.01 (s, 3H), 3.94 - 3.80 (m, 3H), 3.04 - 2.95 (m, 2H), 2.94 - 2.76 (m, 3H), 2.62 (br s, 1H), 2.47 - 2.33 (m, 2H), 1.86 - 1.71 (m, 2H), 1.68 - 1.51 (m, 5H), 1.35 (br d, J=0.6 Hz, 2H), 1.26 - 1.18 (m, 1H), 1.13 (s, 3H), 1.10 (d, J=6.9 Hz, 3H) 由於水抑制而缺失4個質子	2.36, C

972		(2S,3R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲氧基)苯基]-3-{5-[5-(羥基甲基)-3aH,4H,5H,6H,6aH-環戊并[d][1,2]噁唑-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	658.2	(500 MHz, DMSO-d6) δ 10.48 (s, 1H), 9.90 (br d, J=7.2 Hz, 1H), 8.23 (d, J=2.3 Hz, 1H), 8.03 (br d, J=6.8 Hz, 1H), 7.79 (dd, J=8.7, 2.3 Hz, 1H), 7.52 - 7.41 (m, 2H), 7.26 (d, J=8.8 Hz, 1H), 5.11 (dd, J=8.9, 5.0 Hz, 1H), 4.68 (d, J=9.5 Hz, 1H), 4.51 (t, J=5.3 Hz, 1H), 4.47 - 4.36 (m, 1H), 4.25 - 4.15 (m, 1H), 4.02 (s, 3H), 3.14 (br dd, J=11.0, 4.2 Hz, 1H), 3.09 (br s, 1H), 2.71 (br s, 1H), 1.98 (br dd, J=13.5, 5.3 Hz, 1H), 1.93 - 1.71 (m, 4H), 1.71 - 1.60 (m, 1H), 1.59 - 1.45 (m, 2H), 1.46 - 1.36 (m, 2H), 0.82 - 0.64 (m, 2H), 0.40 - 0.28 (m, 2H)	2.46, C

973		(2S,3R,7Z)-3-(5-{3aH,4H,6H,6aH-呋喃并[3,4-d][1,2]噁唑-3-基}-2-甲氧基苯甲醯胺基)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲氧基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	630.1	(500 MHz, DMSO-d6) δ 10.49 (s, 1H), 9.90 (d, J=7.1 Hz, 1H), 8.28 - 8.15 (m, 1H), 8.04 (br d, J=6.1 Hz, 1H), 7.79 (dd, J=8.6, 2.3 Hz, 1H), 7.51 - 7.42 (m, 2H), 7.30 - 7.22 (m, 1H), 5.34 (dd, J=9.2, 3.4 Hz, 1H), 4.69 (d, J=9.7 Hz, 1H), 4.49 (br t, J=7.7 Hz, 1H), 4.46 - 4.39 (m, 1H), 4.09 (d, J=10.5 Hz, 1H), 4.03 (s, 2H), 4.06 - 4.00 (m, 1H), 3.89 (br d, J=9.2 Hz, 1H), 3.77 (dd, J=9.1, 7.1 Hz, 1H), 3.65 (dd, J=10.5, 3.5 Hz, 1H), 3.15 (dd, J=10.8, 4.2 Hz, 1H), 3.10 (br s, 1H), 2.71 (br s, 1H), 1.87 - 1.69 (m, 2H), 1.49 (td, J=8.4, 4.1 Hz, 1H), 1.44 - 1.32 (m, 2H), 0.80 - 0.66 (m, 2H), 0.34 (br d, J=2.5 Hz, 2H)	2.47, C

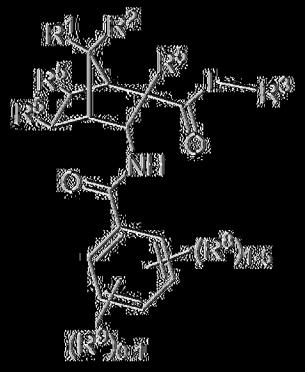
974		(2S,3R,7Z)-7-(環丙基亞甲基)-N-[4-氟-3-(三氟甲基)苯基]-3-{5-[7-(羥基甲基)咪唑并[1,2-a]吡啶-3-基]-2-甲氧基苯甲醯胺基}雙環[2.2.1]庚烷-2-甲醯胺	649.5	(500 MHz, DMSO-d6) δ 10.54 (s, 1H), 9.95 (d, J=7.2 Hz, 1H), 8.37 (d, J=7.0 Hz, 1H), 8.24 - 8.19 (m, 1H), 8.13 (d, J=2.3 Hz, 1H), 7.81 - 7.74 (m, 2H), 7.65 (s, 1H), 7.51 (s, 1H), 7.47 (t, J=9.7 Hz, 1H), 7.37 (d, J=8.7 Hz, 1H), 6.94 - 6.87 (m, 1H), 4.69 (d, J=9.5 Hz, 1H), 4.56 (br d, J=5.3 Hz, 2H), 4.46 (br dd, J=6.4, 2.8 Hz, 1H), 4.07 (s, 3H), 3.16 (br dd, J=10.8, 3.7 Hz, 1H), 3.10 (br s, 1H), 2.72 (br s, 1H), 1.89 - 1.77 (m, 2H), 1.56 - 1.46 (m, 1H), 1.46 - 1.37 (m, 2H), 0.78 - 0.67 (m, 2H), 0.34 (br d, J=2.1 Hz, 2H)	2.10, C

975		(1R,2R,3S,4S)-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]-7-丙烷-2-基)雙環[2.2.1]庚烷-2-甲醯胺	529.2	(500 MHz, 氯仿-d) δ 9.58 (br d, J=7.7 Hz, 1H), 8.12 (s, 1H), 8.07 - 7.98 (m, 2H), 7.55 (dt, J=8.7, 3.4 Hz, 1H), 7.11 (t, J=9.4 Hz, 1H), 6.79 (dd, J=11.6, 6.3 Hz, 1H), 4.70 - 4.53 (m, 1H), 4.01 (s, 3H), 2.95 (dd, J=11.0, 3.9 Hz, 1H), 2.48 - 2.39 (m, 2H), 2.01 - 1.94 (m, 1H), 1.71 - 1.61 (m, 1H), 1.55 - 1.50 (m, 2H), 1.36 (br d, J=10.2 Hz, 1H), 1.26 (br d, J=1.9 Hz, 1H), 0.85 (d, J=6.3 Hz, 6H)	1.24, C
976		(2S,3R)-7-苯甲基-3-(4,5-二氟-2-甲氧基苯甲醯胺基)-N-[4-氟-3-(三氟甲基)苯基]雙環[2.2.1]庚烷-2-甲醯胺	577.2	(400 MHz, 氯仿-d) δ 9.59 - 9.47 (m, 1H), 8.07 - 7.99 (m, 1H), 7.93 (dd, J=6.2, 2.6 Hz, 1H), 7.65 (s, 1H), 7.49 - 7.44 (m, 1H), 7.33 - 7.29 (m, 2H), 7.18 - 7.06 (m, 5H), 6.76 (dd, J=11.4, 6.2 Hz, 1H), 4.64 (ddd, J=11.1, 7.4, 4.0 Hz, 1H), 3.98 (s, 3H), 2.93 (dd, J=10.8, 3.7 Hz, 1H), 2.76 - 2.64 (m, 2H), 2.46 (br s, 1H), 2.37 (br s, 1H), 2.32 (br s, 1H), 2.15 - 2.09 (m, 2H), 2.04 (br s, 1H) 自混合物報導之主要非鏡像異構物	1.24, C

【發明申請專利範圍】

【請求項1】

一種式(I)化合物：



(I)

或其醫藥學上可接受之鹽，其中：

L為O或NH；

R^1為經0至1個芳基或C_{3-6}環烷基取代基取代之C_{1-3}烷基；

R^2為H；其限制條件為，當R^1為經0個芳基或C_{3-6}環烷基取代之C_{1-3}烷基時，R^9為不存在；

或R^1及R^2組合為CR^6R^7或NOC$_{1-4}$烷基，其中「=」為雙鍵；

或R^1及R^2與該兩者所連接之碳原子一起形成經0至1芳基取代基取代之二氧戊環基；

R^3為經0至5個鹵基、CN、OH或OC$_{1-3}$烷基取代基取代之C_{1-8}烷基、經0至5個R^4取代之$(CR^dR^d)_n$-C_{3-10}碳環基或包含1至4個選自O、S(=O)$_p$、N及NR^{4c}之雜原子且經0至5個R^4取代之$(CR^dR^d)_n$-3員至12員雜環基；

R^4為鹵基、CN、OH、SF_5、S(=O)$_pR^c$、經0至5個鹵基、OH或OC$_{1-4}$烷基取代基取代之C_{1-4}烷基、經0至5個鹵基取代基取代之OC$_{1-4}$烷基、經0至5個R^c取代之$(CR^dR^d)_n$-C_{3-10}碳環基或包含1至4個選自O、

$S(=O)_p$、N及NR^{4c}之雜原子且經0至5個R^e取代之-$(CR^dR^d)_n$-4員至6員雜環基；

R^{4c}為H、C_{1-4}烷基或-$S(=O)_2CF_3$；

各R^5為H、鹵基、-OH、經0至5個鹵基取代基取代之C_{1-4}烷基、或經0至5個鹵基取代基取代之-OC_{1-4}烷基；

R^6為H、鹵基、CN、經0至3個R^{6a}取代之C_{1-7}烷基、經0至3個R^{6a}取代之C_{2-7}烯基、經0至3個R^{6a}取代之C_{2-7}炔基、-$C(=O)OR^{6b}$、-$C(=O)NR^{6b}R^{6b}$、經0至5個R^{14}取代之-$(CH_2)_n$-C_{3-10}碳環基、或包含1至4個選自O、$S(=O)_p$、N或NR^{14a}之雜原子且經0至5個R^{14}取代之3員至12員雜環基；

R^{6a}為鹵基、-OH、-OC_{1-4}烷基、C_{1-4}烷基、芳基、或經0至4個鹵基取代基取代之C_{3-6}環烷基；

R^{6b}為H、經0至1個芳基取代基取代之C_{1-4}烷基、或經0至4個鹵基取代基取代之C_{3-6}環烷基；

R^7為H或C_{1-4}烷基；

或R^6及R^7與該兩者所連接之碳原子一起形成環戊二烯基、二氫茚基或茚基；

R^8為H、鹵基、CN、-NR^7R^7、經0至5個鹵基或-OH取代基取代之C_{1-4}烷基、或經0至5個鹵基取代之-OC_{1-4}烷基、-OH、C_{3-6}環烷基、芳基、包含1至4個選自O、$S(=O)_p$及N之雜原子的4員至9員雜環基、或經0至1個-OC_{1-3}烷基取代基取代之-OC_{1-4}烷基；

R^9為經0至3個R^{10}及0至2個R^{11}取代之芳基、或包含1至5個選自O、$S(=O)_p$、N及NR^{11a}之雜原子且經0至3個R^{10}及0至2個R^{11}取代之3員至12員

雜環基；

R^{10}為鹵基、CN、C_{1-4}烷基、=O、-OH或-OC_{1-4}烷基；

R^{11}為經0至4個R^{12}及0至2個R^{13}取代之C_{1-4}烷基、-OR^b、-NR^aR^a、-$NR^aC(=O)R^b$、-$NR^aC(=O)OR^b$、-$NR^aC(=O)NR^aR^a$、-$NR^aS(=O)_pR^c$、-$C(=O)R^b$、-$C(=O)OR^b$、-$C(=O)NR^aR^a$、-$C(=O)NR^aS(=O)_pR^c$、-$OC(=O)R^b$、-$S(=O)_pR^c$、-$S(=O)_pNR^aR^a$、經0至5個R^e取代之C_{3-6}碳環基、或包含1至4個選自O、$S(=O)_p$、N及NR^{15}之雜原子且經0至5個R^e取代之3員至12員雜環基；

R^{11a}為H、經0至4個R^{11b}取代之C_{1-5}烷基、-$C(=O)R^b$、-$C(=O)OR^b$、-$C(=O)NR^aR^a$、經0至5個R^e取代之C_{3-6}環烷基、經0至5個R^e取代之芳基、包含1至4個選自O、$S(=O)_p$、N及NR^{15}之雜原子且經0至5個R^e取代之4員至6員雜環基；

R^{11b}為鹵基、-OH、-C(=O)OH、-$C(=O)OC_{1-4}$烷基或芳基；

R^{12}為鹵基、-$C(=O)OR^b$、-$C(=O)NR^aR^a$、-$C(=O)NR^aOR^b$、或經0至3個鹵基或-OH取代基取代之C_{1-4}烷基、或C_{3-6}環烷基；

R^{13}為-OR^b、-NR^aR^a、-$NR^aC(=O)R^b$、-$NR^aC(=O)OR^b$、-$NR^aC(=O)NR^aR^a$、-$NR^aS(=O)_pR^c$、-$NR^aS(=O)_pNR^aR^a$、-$OC(=O)NR^aR^a$、-$OC(=O)NR^aOR^b$、-$S(=O)_pNR^aR^a$、-$S(=O)_pR^c$、經0至3個R^e取代之-$(CH_2)_n$-C_{3-10}碳環基、或包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至3個R^e取代之-$(CH_2)_n$-3員至12員雜環基；

R^{14}為鹵基、CN、經0至3個鹵基取代基取代之C_{1-4}烷基、經0至3個鹵基取代基取代之-OC_{1-4}烷基、-$(CH_2)_n$-NR^aR^a、經0至3個R^e取代之-$(CH_2)_n$-芳基、經0至3個R^e取代之-O-芳基、或包含1至4個選自O、$S(=O)_p$及N之

雜原子且經0至3個R^e取代之-$(CH_2)_n$-3員至12員雜環基；

R^{14a}為H、C(=O)C_{1-4}烷基或經以下取代之C_{1-3}烷基：0至3個Si(C_{1-3}烷基)$_3$或經0至2個鹵基取代基取代之芳基；

R^{15}為H、C_{1-4}烷基或芳基；

R^a為H、-OC_{1-6}烷基、經0至5個R^e取代之C_{1-6}烷基、經0至5個R^e取代之C_{2-6}烯基、經0至5個R^e取代之C_{2-6}炔基、經0至5個R^e取代之-$(CH_2)_n$-C_{3-10}碳環基、或包含1至4個選自O、S(=O)$_p$及N之雜原子且經0至5個R^e取代之-$(CH_2)_n$-3員至12員雜環基；或R^a及R^a與該兩者所連接之氮原子一起形成包含1至4個選自O、S(=O)$_p$及N之雜原子且經0至5個R^e取代之3員至12員雜環基；

R^b為H、經0至5個R^e取代之C_{1-6}烷基、經0至5個R^e取代之C_{2-6}烯基、經0至5個R^e取代之C_{2-6}炔基、經0至5個R^e取代之-$(CH_2)_n$-C_{3-10}碳環基、或包含1至4個選自O、S(=O)$_p$及N之雜原子且經0至5個R^e取代之-$(CH_2)_n$-3員至12員雜環基；

R^c為經0至5個R^e取代之C_{1-6}烷基、經0至5個R^e取代之C_{2-6}烯基、經0至5個R^e取代之C_{2-6}炔基、經0至5個R^e取代之C_{3-6}碳環基、或包含1至4個選自O、S(=O)$_p$及N之雜原子且經0至5個R^e取代之3員至12員雜環基；

R^d為H、C_{1-4}烷基或C_{3-6}環烷基；

R^e為鹵基、CN、NO_2、=O、經0至5個R^g取代之C_{1-6}烷基、經0至5個R^g取代之C_{2-6}烯基、經0至5個R^g取代之C_{2-6}炔基、經0至5個R^g取代之-$(CH_2)_n$-C_{3-10}碳環基、包含1至4個選自O、S(=O)$_p$及N之雜原子且經0至5個R^g取代之-$(CH_2)_n$-3員至12員雜環基、-$(CH_2)_n$OR^f、-C(=O)OR^f、-C(=O)N$R^f R^f$、-NR^fC(=O)R^f、-S(=O)$_p R^f$、-S(=O)$_p$N$R^f R^f$、-

$NR^fS(=O)_pR^f$、$-NR^fC(=O)OR^f$、$-OC(=O)NR^fR^f$或$-(CH_2)_nNR^fR^f$；

R^f為H、經0至2個-OH或$-OC_{1-4}$烷基取代基取代之C_{1-6}烷基、C_{3-6}環烷基、芳基、或包含1至4個選自O、$S(=O)_p$及N之雜原子的3員至12員雜環基；或R^f及R^f與該兩者所連接之氮原子一起形成包含1至4個選自O、$S(=O)_p$及N之雜原子的3員至12員雜環基；

R^g為鹵基、CN、-OH、C_{1-6}烷基、C_{3-6}環烷基或芳基；

n為0、1、2或3；及

p為0、1或2。

【請求項2】

如請求項1之化合物或其醫藥學上可接受之鹽，其中：

R^3為經0至4個鹵基或-OH取代基取代之C_{1-6}烷基、經0至4個R^4取代之$-(CHR^d)_{0-1}-C_{3-6}$環烷基、經0至4個R^4取代之C_{6-9}螺環烷基、經0至4個R^4取代之C_{6-10}雙環碳環基、或包含1至2個選自O、$S(=O)_p$、N及NR^{4c}之雜原子且經0至4個R^4取代之3員至6員雜環基；及

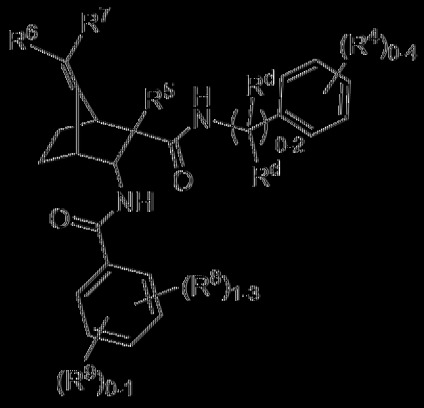
R^4為鹵基或經0至4個鹵基取代基取代之C_{1-3}烷基；

R^{4c}為H或C_{1-4}烷基；及

R^d為C_{1-3}烷基。

【請求項3】

如請求項1之化合物，其具有式(II)：



(II)

或其醫藥學上可接受之鹽，其中：

R^4為鹵基、經0至4個鹵基取代基取代之-S(=O)$_p$C$_{1-4}$烷基、經0至4個鹵基取代基取代之C$_{1-4}$烷基、或經0至4個鹵基取代基取代之-OC$_{1-4}$烷基；

R^5為H或鹵基；

R^6為鹵基、CN、經0至3個R^{6a}取代之C$_{1-7}$烷基、 經0至3個R^{6a}取代之C$_{2-7}$烯基、經0至3個R^{6a}取代之C$_{2-7}$炔基、C(=O)OR^{6b}、-C(=O)N$R^{6b}R^{6b}$、經0至3個R^{14}取代之C$_{3-6}$環烷基、經0至3個R^{14}取代之C$_{3-6}$環烯基、經0至3個R^{14}取代之芳基、或包含1至3個選自O、S(=O)$_p$、N及NR^{14a}之雜原子且經0至3個R^{14}取代之4員至6員雜環基；

R^{6a}為鹵基、-OH、C$_{3-6}$環烷基或芳基；

R^{6b}為H、經0至1個芳基取代基取代之C$_{1-4}$烷基、或經0至4個鹵基取代基取代之C$_{3-6}$環烷基；

R^7為H或C$_{1-3}$烷基；

R^8為鹵基、CN、-N(C$_{1-2}$烷基)$_2$、經0至5個鹵基或-OH取代基取代之C$_{1-4}$烷基、或經0至4個鹵基、-OH、芳基或-OC$_{1-4}$烷基取代基取代之-OC$_{1-4}$烷基；

R^9為經0至3個R^{10}及0至2個R^{11}取代之芳基、或包含1至4個選自O、S(=O)$_p$、N及NR^{11a}之雜原子且經0至3個R^{10}及0至1個R^{11}取代之3員至12員

雜環基；

R^{10}為鹵基、CN、C_{1-4}烷基、=O、-OH或-OC_{1-4}烷基；

R^{11}為經0至3個R^{12}及0至1個R^{13}取代之C_{1-4}烷基、-OR^b、-NR^aR^a、-$NR^aC(=O)R^b$、-$NR^aC(=O)OR^b$、-$NR^aC(=O)NR^aR^a$、-$NR^aS(=O)_pR^c$、-$C(=O)R^b$、-$C(=O)OR^b$、-$C(=O)NR^aR^a$、-$C(=O)NR^aS(=O)_pR^c$、-$OC(=O)R^b$、-$S(=O)_pR^c$、-$S(=O)_pNR^aR^a$、經0至5個R^e取代之C_{3-6}環烷基、包含1至4個選自O、$S(=O)_p$、N及NR^{15}之雜原子且經0至5個R^e取代之4員至12員雜環基；

R^{11a}為H、經0至2個R^{11b}取代之C_{1-4}烷基、-$C(=O)R^b$、-$C(=O)OR^b$、-$C(=O)NR^aR^a$、經0至5個R^e取代之C_{3-6}環烷基、包含1至4個選自O、$S(=O)_p$、N及NR^{15}之雜原子且經0至5個R^e取代之4員至6員雜環基；

R^{11b}為-OH、-C(=O)OH或芳基；

R^{12}為鹵基、-$C(=O)OR^b$、-$C(=O)NHR^a$、-$C(=O)NHOR^b$、或經0至3個鹵基或-OH取代基取代之C_{1-4}烷基；

R^{13}為-OR^b、-NR^aR^a、-$NR^aC(=O)R^b$、-$NR^aC(=O)OR^b$、-$NR^aS(=O)_pR^c$、-$NR^aS(=O)_pNR^aR^a$、-$OC(=O)NR^aR^a$、-$OC(=O)NR^aOR^b$、-$S(=O)_pNR^aR^a$或-$S(=O)_pR^c$；

R^{14}為鹵基、CN、經0至3個鹵基取代基取代之C_{1-4}烷基、經0至3個鹵基取代基取代之-OC_{1-4}烷基、-$(CH_2)_{0-3}$-NR^aR^a、經0至3個R^e取代之-$(CH_2)_{0-3}$-芳基、經0至3個R^e取代之-O-芳基、或包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至3個R^e取代之-$(CH_2)_{0-2}$-3員至12員雜環基；

R^{14a}為H、$C(=O)C_{1-4}$烷基或經以下取代之C_{1-3}烷基：0至3個經0至2個鹵基取代基取代之芳基；

R^{15}為H、C_{1-3}烷基或芳基；

R^a為H、經0至5個R^e取代之C_{1-5}烷基、經0至5個R^e取代之C_{2-5}烯基、經0至5個R^e取代之C_{2-5}炔基、經0至5個R^e取代之-$(CH_2)_n$-C_{3-10}碳環基、或包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至5個R^e取代之-$(CH_2)_n$-3員至12員雜環基；或R^a及R^a與該兩者所連接之氮原子一起形成包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至5個R^e取代之3員至12員雜環基；

R^b為H、經0至5個R^e取代之C_{1-5}烷基、經0至5個R^e取代之C_{2-5}烯基、經0至5個R^e取代之C_{2-5}炔基、經0至5個R^e取代之-$(CH_2)_n$-C_{3-10}碳環基、或包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至5個R^e取代之-$(CH_2)_n$-3員至12員雜環基；

R^c為經0至5個R^e取代之C_{1-5}烷基、經0至5個R^e取代之C_{2-5}烯基、經0至5個R^e取代之C_{2-5}炔基、經0至5個R^e取代之C_{3-6}碳環基、或包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至5個R^e取代之3員至12員雜環基；

R^d為H或C_{1-4}烷基；

R^e為鹵基、CN、=O、經0至5個R^g取代之C_{1-6}烷基、經0至5個R^g取代之C_{2-6}烯基、經0至5個R^g取代之C_{2-6}炔基、經0至4個R^g取代之-$(CH_2)_n$-C_{3-6}環烷基、經0至4個R^g取代之-$(CH_2)_n$-芳基、包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至4個R^g取代之-$(CH_2)_n$-4員至6員雜環基、-$(CH_2)_n$$OR^f$、-$C(=O)OR^f$、-$C(=O)NR^fR^f$、-$NR^fC(=O)R^f$、-$S(=O)_pR^f$、-$NR^fC(=O)OR^f$、-$OC(=O)NR^fR^f$或-$(CH_2)_n$$NR^fR^f$；

R^f為H、C_{1-5}烷基、C_{3-6}環烷基或芳基；或R^f及R^f與該兩者所連接之氮原子一起形成雜環基；

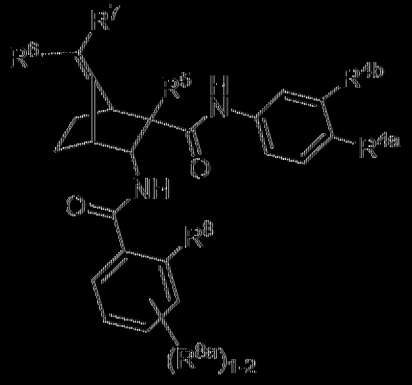
R^g為鹵基、CN、-OH、C_{1-5}烷基、C_{3-6}環烷基或芳基；

n為0、1、2或3；及

p為0、1或2。

|(請求項4)|

如請求項1之化合物，其具有式(III)：



(III)

或其醫藥學上可接受之鹽，其中：

R^{4a}為鹵基；

R^{4b}為經0至4個鹵基取代基取代之C_{1-4}烷基；

R^5為H或F；

R^6為鹵基、經0至3個R^{6a}取代之C_{1-4}烷基、經0至1個苯基或-OH取代基取代之C_{2-4}烯基、-C(=O)OR^{6b}、C(=O)NHR^{6b}、經0至3個R^{14}取代之C_{3-6}環烷基、經0至3個R^{14}取代之C_{3-6}環烯基、經0至3個R^{14}取代之苯基、萘基、或包含1至3個選自O、S、N及NR^{14a}之雜原子且經0至3個R^{14}取代之5員至6員雜環基；

R^{6a}為鹵基、-OH、C_{3-6}環烷基或苯基；

R^{6b}為H或C_{1-4}烷基；

R^7為H或C_{1-3}烷基；

或R^6及R^7與該兩者所連接之碳原子一起形成環戊烯基、二氫茚基或茚基；

R^8為-N(C_{1-4}烷基)$_2$或經0至1個-OC_{1-4}烷基取代基取代之-OC_{1-4}烷基；

R^{8a}為鹵基；

R^{14}為鹵基、CN、經0至3個鹵基取代基取代之C_{1-4}烷基、經0至3個鹵基取代基取代之-OC_{1-4}烷基、-$(CH_2)_{0-2}$-NR^aR^a、經0至3個R^e取代之-$(CH_2)_{0-2}$-芳基、經0至3個R^e取代之-O-芳基、或包含1至4個選自O、S(=O)$_p$及N之雜原子且經0至3個R^e取代之-$(CH_2)_{0-2}$-3員至12員雜環基；

R^{14a}為H、C(=O)C_{1-3}烷基或經以下取代之C_{1-3}烷基：0至3個經0至2個鹵基取代基取代之芳基；

R^a為H、經0至5個R^e取代之C_{1-6}烷基、經0至5個R^e取代之-$(CH_2)_n$-苯基、或包含1至4個選自O、S(=O)$_p$及N之雜原子且經0至5個R^e取代之-$(CH_2)_n$-3員至12員雜環基；或R^a及R^a與該兩者所連接之氮原子一起形成包含1至4個選自O、S(=O)$_p$及N之雜原子且經0至5個R^e取代之3員至12員雜環基；

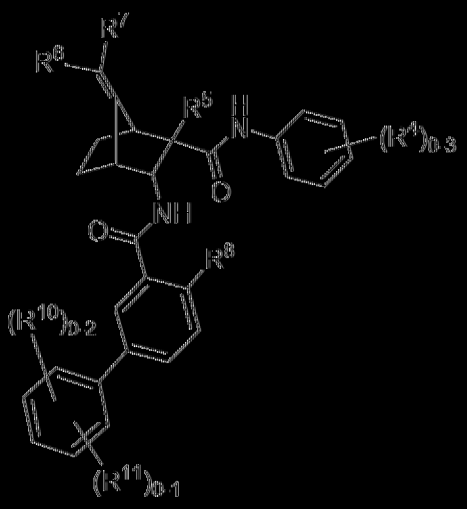
R^b為H、經0至5個R^e取代之C_{1-6}烷基、經0至5個R^e取代之-$(CH_2)_{0-1}$-苯基、或包含1至4個選自O、S(=O)$_p$及N之雜原子且經0至5個R^e取代之-$(CH_2)_n$-3員至12員雜環基；

R^e為鹵基、CN、NO_2、=O、C_{1-6}烷基或C(=O)OH；及

n為0、1、2或3。

【請求項5】

如請求項3之化合物，其具有式(IV)：



(IV)

或其醫藥學上可接受之鹽，其中：

R^4為鹵基、經0至3個鹵基取代基取代之C_{1-4}烷基或經0至3個鹵基取代基取代之-OC_{1-4}烷基；

R^5為H或F；

R^6為鹵基、CN、經0至3個R^{6a}取代之C_{1-6}烷基、經0至3個R^{6a}取代之C_{2-6}烯基、經0至3個R^{6a}取代之C_{2-6}炔基、-C(=O)OR^{6b}、-C(=O)$NR^{6b}R^{6b}$、經0至3個R^{14}取代之C_{3-6}環烷基、經0至3個R^{14}取代之C_{3-6}環烯基、經0至3個R^{14}取代之苯基、或包含1至3個選自O、S(=O)$_p$、N及NR^{14a}之雜原子且經0至3個R^{14}取代之5員至6員雜芳基；

R^{6a}為鹵基、C_{3-6}環烷基或苯基；

R^{6b}為H、經0至1個芳基取代基取代之C_{1-3}烷基、或經0至4個鹵基取代基取代之C_{3-6}環烷基；

R^7為H或C_{1-2}烷基；

R^8為經0至4個鹵基、-OH、芳基或-OC_{1-4}烷基取代基取代之-OC_{1-4}烷基；

R^{10}為鹵基、CN、C_{1-3}烷基、-OH或-OC_{1-4}烷基；

R^{11}為經0至2個R^{12}及0至1個R^{13}取代之C_{1-4}烷基、$-OR^b$、$-NR^aR^a$、$-NR^aC(=O)R^b$、$-NR^aC(=O)NR^aR^a$、$-NR^aS(=O)_pR^c$、$-C(=O)R^b$、$-C(=O)OR^b$、$-C(=O)NR^aR^a$、$-C(=O)NR^aS(=O)_pR^c$、$-OC(=O)R^b$、$-S(=O)_pR^c$、$-S(=O)_pNR^aR^a$、C_{3-6}環烷基、包含1至4個選自O、$S(=O)_p$、N及NR^{15}之雜原子且經0至4個R^e取代之4員至9員雜環基；

R^{12}為鹵基、$-C(=O)OR^b$、$-C(=O)NHR^a$、$-C(=O)NHOR^b$、或經0至3個鹵基或-OH取代基取代之C_{1-4}烷基；

R^{13}為$-OR^b$、$-NR^aR^a$、$-NR^aC(=O)R^b$、$-NR^aC(=O)OR^b$、$-NR^aS(=O)_pR^c$、$-NR^aS(=O)_pNR^aR^a$、$-OC(=O)NR^aR^a$、$-OC(=O)NR^aOR^b$、$-S(=O)_pNR^aR^a$或$-S(=O)_pR^c$；

R^{14}為鹵基、CN、經0至3個鹵基取代基取代之C_{1-4}烷基、經0至3個鹵基取代基取代之$-OC_{1-4}$烷基、$-(CH_2)_{0-2}-NR^aR^a$、經0至3個R^e取代之$-(CH_2)_{0-2}-$芳基、經0至3個R^e取代之-O-芳基、或包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至3個R^e取代之$-(CH_2)_{0-2}-$3員至12員雜環基；

R^{14a}為H、$C(=O)C_{1-3}$烷基、經以下取代之C_{1-3}烷基：0至2個經0至2個鹵基取代基取代之芳基；

R^{15}為H、C_{1-2}烷基或苯基；

R^a為H、經0至4取代之C_{1-5}烷基、經0至4個R^e取代之C_{2-5}烯基、經0至4個R^e取代之C_{2-5}炔基、經0至4個R^e取代之$-(CH_2)_n-C_{3-10}$碳環基、或包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至4個R^e取代之$-(CH_2)_n-$3員至12員雜環基；或R^a及R^a與該兩者所連接之氮原子一起形成包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至4個R^e取代之3員至12員雜環基；

R^b為H、經0至4個R^e取代之C_{1-5}烷基、經0至4個R^e取代之C_{2-5}烯基、經

0至4個R^e取代之C_{2-5}炔基、經0至4個R^e取代之-$(CH_2)_n$-C_{3-10}碳環基、或包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至4個R^e取代之-$(CH_2)_n$-3員至12員雜環基；

R^c為經0至4個R^e取代之C_{1-5}烷基、經0至4個R^e取代之C_{2-5}烯基、經0至4個R^e取代之C_{2-5}炔基、C_{3-6}碳環基、或包含1至4個選自O、$S(=O)_p$及N之雜原子之3員至12員雜環基；

R^e為鹵基、CN、NO_2、=O、經0至5個R^g取代之C_{1-6}烷基、經0至5個R^g取代之C_{2-6}烯基、經0至5個R^g取代之C_{2-6}炔基、-$(CH_2)_n$-C_{3-6}環烷基、-$(CH_2)_n$-芳基、包含1至4個選自O、$S(=O)_p$及N之雜原子的-$(CH_2)_n$-4員至6員雜環基、-$(CH_2)_n$$OR^f$、$S(=O)_pR^f$、$C(=O)NR^fR^f$、$C(=O)OR^f$、$NR^fC(=O)R^f$、$S(=O)_pNR^fR^f$、$NR^fS(=O)_pR^f$、$NR^fC(=O)OR^f$、$OC(=O)NR^fR^f$或-$(CH_2)_n$$NR^fR^f$；

R^f為H、C_{1-6}烷基、C_{3-6}環烷基或芳基；或R^f及R^f與該兩者所連接之氮原子一起形成雜環基；

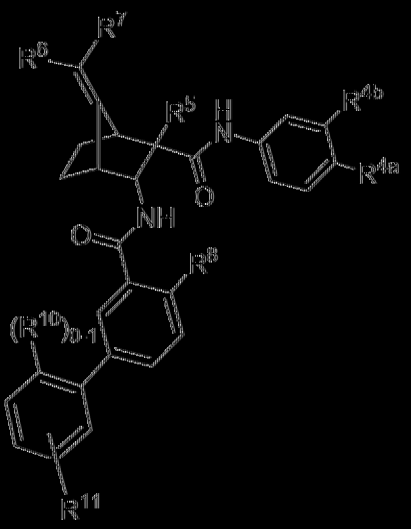
R^g為鹵基、CN、-OH、C_{1-5}烷基、C_{3-6}環烷基或芳基；

n為0、1、2或3；及

p為0、1或2。

【請求項6】

如請求項5之化合物，其具有式(V)：



(V)

或其醫藥學上可接受之鹽，其中：

R^{4a}為鹵其或C_{1-2}烷其；

R^{4b}為經0至4個鹵其取代其取代之C_{1-4}烷其；

R^5為H或F；

R^6為鹵其、CN、經0至3個R^{6a}取代之C_{1-4}烷其、經0至3個R^{6a}取代之C_{2-4}烯其、$-C(=O)OR^{6b}$、$C(=O)NR^{6b}R^{6b}$、經0至3個R^{14}取代之C_{3-6}環烷其、經0至3個R^{14}取代之苯其、或包含1至3個選自O、$S(=O)_p$、N及NR^{14a}之雜原子且經0至3個R^{14}取代之5員至6員雜芳其；

R^{6a}為鹵其、-OH、C_{3-6}環烷其或苯其；

R^{6b}為H、經0至1個芳其取代其取代之C_{1-3}烷其或C_{3-6}環烷其；

R^7為H或C_{1-2}烷其；

R^8為經0至4個鹵其、-OH、$-OC_{1-4}$烷其或芳其取代其取代之$-OC_{1-4}$烷其；

R^{10}為鹵其或C_{1-3}烷其；

R^{11}為經0至2個R^{12}及0至1個R^{13}取代之C_{1-4}烷其、-OH、$-OC_{1-4}$烷其、$-NR^aC(=O)R^b$、$-NR^aC(=O)NR^aR^a$、$-NR^aS(=O)_pR^c$、$-C(=O)R^b$、

$-C(=O)OR^b$ 、 $-C(=O)NR^aR^a$ 、 $-C(=O)NR^aS(=O)_pR^c$ 、 $-OC(=O)R^b$ 、 $-S(=O)_pR^c$、$-S(=O)_pNR^aR^a$、C_{3-6}環烷基、包含1至4個選自O、$S(=O)_p$、N及NR^{15}之雜原子且經0至3個R^e取代之4員至9員雜環基；

R^{12}為鹵基、$-C(=O)OR^b$、$-C(=O)NHR^a$、$-C(=O)NHOR^b$、或經0至3個鹵基或-OH取代基取代之C_{1-4}烷基；

R^{13} 為 $-OR^b$ 、 $-NR^aR^a$ 、 $-NR^aC(=O)R^b$ 、 $-NR^aC(=O)OR^b$ 、 $-NR^aS(=O)_pR^c$、$-NR^aS(=O)_pNR^aR^a$、$-OC(=O)NR^aR^a$或$-OC(=O)NR^aOR^b$；

R^{14}為鹵基、CN、經0至3個鹵基取代基取代之C_{1-4}烷基、經0至3個鹵基取代基取代之$-OC_{1-4}$烷基、$-(CH_2)_{0-2}-NR^aR^a$、經0至3個R^e取代之$-(CH_2)_{0-1}-$芳基、經0至3個R^e取代之-O-芳基、或包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至3個R^e取代之$-(CH_2)_{0-1}-$3員至9員雜環基；

R^{14a}為H、$C(=O)C_{1-3}$烷基、經以下取代之C_{1-3}烷基：0至1個經0至2個鹵基取代基取代之芳基；

R^{15}為H、C_{1-2}烷基或苯基；

R^a為H、經0至5個R^e取代之C_{1-4}烷基、經0至5個R^e取代之C_{2-4}烯基、經0至5個R^e取代之C_{2-4}炔基、經0至5個R^e取代之$-(CH_2)_n-C_{3-10}$碳環基、或包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至5個R^e取代之$-(CH_2)_n-$3員至12員雜環基；或R^a及R^a與該兩者所連接之氮原子一起形成包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至5個R^e取代之3員至9員雜環基；

R^b為H、經0至5個R^e取代之C_{1-4}烷基、經0至5個R^e取代之C_{2-4}烯基、經0至5個R^e取代之C_{2-4}炔基、經0至5個R^e取代之$-(CH_2)_n-C_{3-10}$碳環基、或包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至5個R^e取代之$-(CH_2)_n-$3員至12員雜環基；

R^c為經0至5個R^e取代之C_{1-4}烷基、經0至5個R^e取代之C_{2-4}烯基、經0至5個R^e取代之C_{2-4}炔基、C_{3-6}碳環基、或包含1至4個選自O、$S(=O)_p$及N之雜原子之3員至9員雜環基；

R^e為鹵基、CN、=O、經0至5個R^g取代之C_{1-6}烷基、經0至5個R^g取代之C_{2-6}烯基、經0至5個R^g取代之C_{2-6}炔基、$-(CH_2)_n-C_{3-6}$環烷基、$-(CH_2)_n-$芳基、包含1至4個選自O、$S(=O)_p$及N之雜原子的$-(CH_2)_n-$4員至6員雜環基、$-(CH_2)_nOR^f$、$S(=O)_pR^f$、$C(=O)NR^fR^f$、$C(=O)OR^f$、$NR^fC(=O)R^f$、$S(=O)_pNR^fR^f$、$NR^fS(=O)_pR^f$、$NR^fC(=O)OR^f$、$OC(=O)NR^fR^f$或$-(CH_2)_nNR^fR^f$；

R^f為H、C_{1-6}烷基、C_{3-6}環烷基或芳基；或R^f及R^f與該兩者所連接之氮原子一起形成雜環基；

R^g為鹵基、CN、-OH、C_{1-6}烷基、C_{3-6}環烷基或芳基；

n為0、1、2或3；及

p為0、1或2。

【請求項7】

如請求項6之化合物或其醫藥學上可接受之鹽，其中：

R^{4a}為鹵基；

R^{4b}為CF_3；

R^6為經0至3個鹵基取代基取代之C_{1-4}烷基或經0至3個鹵基取代基取代之C_{3-6}環烷基；

R^8為$-OC_{1-4}$烷基；

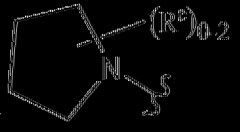
R^{10}為F；

R^{11}為-OH、$-OC_{1-4}$烷基、$-NR^aC(=O)R^b$、$-NR^aS(=O)_pR^c$、

C(=O)OR^b、C(=O)NR^{a}R^a、C(=O)NR^{a}S(=O)$_p$R^c、包含1至4個選自O、S(=O)$_p$、N及NR^{15}之雜原子且經0至5個R^{e}取代之4員至9員雜環基；

R^{15}為H或C$_{1-2}$烷基；

R^{a}為H或經0至5個R^{e}取代之C$_{1-4}$烷基，

或R^{a}及R^{a}一起為  ；

R^{b}為H或經0至5個R^{e}取代之C$_{1-4}$烷基；

R^{c}為經0至5個R^{e}取代之C$_{1-3}$烷基或C$_{3-6}$碳環基；

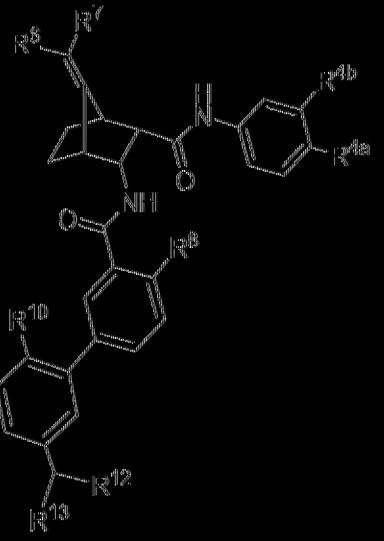
R^{e}為鹵基、=O、經0至5個R^{g}取代之C$_{1-4}$烷基、C(=O)OH、-OR^{f}或-NR^{f}R^f；及

R^{f}為H及C$_{1-6}$烷基；或R^{f}及R^{f}與該兩者所連接之氮原子一起形成雜環基；及

R^{g}為鹵基。

|請求項8|

如請求項6之化合物，其具有式(VI)：



(VI)

或其醫藥學上可接受之鹽，其中：

R^{4a}為鹵基；

R^{4b}為CF_3；

R^6為經0至3個鹵基取代基取代之C_{1-4}烷基或經0至3個鹵基取代基取代之C_{3-6}環烷基；

R^7為H；

R^8為經0至1個芳基取代基取代之-OC_{1-4}烷基；

R^{10}為鹵基；

R^{12}為-C(=O)OH、-C(=O)OC_{1-4}烷基、-C(=O)NHC_{1-4}烷基、-C(=O)$NHOC_{1-3}$烷基、或經0至3個鹵基取代基取代之C_{1-3}烷基；

R^{13}為$-OR^b$、$-NR^aR^a$、$-NR^aC(=O)R^b$、$-NR^aC(=O)OR^b$、$-NR^aS(=O)_pR^c$、$-NR^aS(=O)_pNR^aR^a$、$-OC(=O)NR^aR^a$或$-OC(=O)NR^aOR^b$；

R^a為H、經0至5個鹵基取代基取代之C_{1-4}烷基、經0至4個R^e取代之苯基、經0至4個R^e取代之C_{3-10}環烷基、經0至4個R^e取代之螺環烷基、或包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至4個R^e取代之3員至9員雜環基；或R^a及R^a與該兩者所連接之氮原子一起形成包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至4個R^e取代之3員至12員雜環基；

R^b為H、經0至5個R^e取代之C_{1-4}烷基、經0至4個鹵基取代基取代之-$(CH_2)_n$-苯基、經0至4個鹵基取代基取代之C_{3-6}環烷基、或包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至4個R^e取代之3員至12員雜環基；

R^c為經0至4個R^e取代之C_{1-4}烷基，

R^e為鹵基、CN、=O、經0至5個R^g取代之C_{1-5}烷基、C_{3-6}環烷基、芳基、包含1至4個選自O、$S(=O)_p$及N之雜原子之4員至6員雜環基、或-OR^f；

R^f為H、C_{1-4}烷基、C_{3-6}環烷基或芳基；

R^g為鹵基；

n為0或1；及

p為0、1或2。

[請求項9]

如請求項8之化合物或其醫藥學上可接受之鹽，其中：

R^{4a}為F

R^{4b}為CF_3；

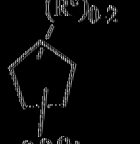
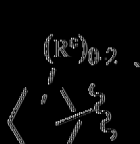
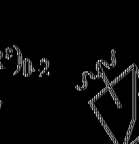
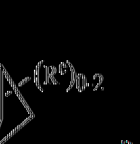
R^6為CF_3或C_{3-6}環烷基；

R^8為-OCH_3或-OCH_2-苯基；

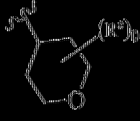
R^{10}為F；

R^{12}為-C(=O)OH、-C(=O)OC_{1-4}烷基、-C(=O)NHC_{1-4}烷基、-C(=O)$NHOC_{1-3}$烷基、CH_3、CHF_2或CF_3；

R^{13}為-OH、-NR^aR^a、-$NHC(=O)R^b$、-$NHS(=O)_pC_{1-4}$烷基、-$OC(=O)NR^aR^a$或-$OC(=O)NHOC_{1-4}$烷基；

R^a為H、經0至4個F取代基取代之C_{1-4}烷基、  、  、  、  、  、  、  或  ；

或R^a及R^a一起為  ，

R^b為H、經0至5個R^c取代之C_{1-4}烷基、苯基，或  ；及

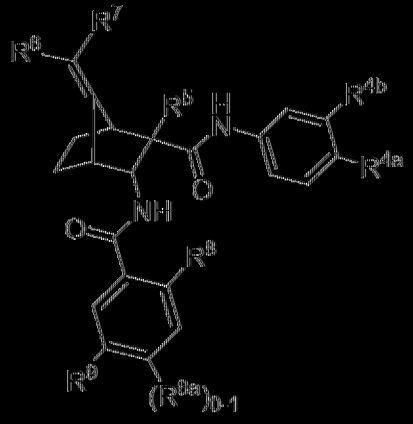
R^c為鹵基、=O、芳基、包含1至4個選自O、S(=O)$_p$及N之雜原子的4

員至6員雜環基或-OR^{1}；及

R^{1}為H、C$_{1-3}$烷基、C$_{3-6}$環烷基或苯基。

[請求項10]

如請求項3之化合物，其具有式(VII)：



(VII)

或其醫藥學上可接受之鹽，其中：

R^{4a}為鹵基；

R^{4b}為經0至3個鹵基取代基取代之C$_{1-4}$烷基或經0至3個鹵基取代基取代之-OC$_{1-4}$烷基；

R^{5}為H或F；

R^{6}為鹵基、CN、經0至3個R^{6a}取代之C$_{1-6}$烷基、經0至3個R^{6a}取代之C$_{2-6}$烯基、經0至3個R^{6a}取代之C$_{2-6}$炔基、經0至3個R^{14}取代之C$_{3-6}$環烷基、0至3個R^{14}經取代之C$_{3-6}$環烯基、經0至3個R^{14}取代之苯基、或包含1至3個選自O、S(=O)$_{p}$、N及NR^{14a}之雜原子且經0至3個R^{14}取代之5員至6員雜芳基；

R^{6a}為鹵基、C$_{3-6}$環烷基或苯基；

R^{7}為H或C$_{1-2}$烷基；

R^{8}為鹵基、CN或經0至4個鹵基、-OH或-OC$_{1-4}$烷基取代基取代之-

OC_{1-4}烷基；

R^{8a}為鹵基或CN；

R^{9}為包含1至4個選自O、$S(=O)_p$、N及NR^{11a}之雜原子且經0至3個R^{10}及0至1個R^{11}取代之3員至12員雜環基；

R^{10}為鹵基、CN、C_{1-3}烷基、=O、-OH或-OC_{1-3}烷基；

R^{11}為經0至1個R^{12}及0至1個R^{13}取代之C_{1-3}烷基、-OR^b、-NR^aR^a、-$NR^aC(=O)R^b$、-$NR^aC(=O)OR^b$、-$NR^aC(=O)NR^aR^a$、-$NR^aS(=O)_pR^c$、-$C(=O)R^b$、-$C(=O)OR^b$、-$C(=O)NR^aR^a$、-$C(=O)NR^aS(=O)_pR^c$、-$OC(=O)R^b$、-$S(=O)_pR^c$、-$S(=O)_pNR^aR^a$、經0至5個R^e取代之C_{3-6}環烷基、包含1至4個選自O、$S(=O)_p$、N及NR^{15}之雜原子且經0至4個R^e取代之4員至6員雜環基；

R^{11a}為H、經0至2個R^{11b}取代之C_{1-4}烷基、-$C(=O)R^b$、-$C(=O)OR^b$、-$C(=O)NR^aR^a$、C_{3-6}環烷基、包含1至4個選自O、$S(=O)_p$、N及NR^{15}之雜原子且經0至4個R^e取代之4員至6員雜環基；

R^{11b}為-OH、-C(=O)OH或芳基；

R^{12}為-$C(=O)OR^b$、-$C(=O)NHR^a$、-$C(=O)NHOR^b$或經0至3個鹵基或-OH取代基取代之C_{1-4}烷基；

R^{13}為-OR^b、-NR^aR^a、-$NR^aC(=O)R^b$、-$NR^aC(=O)OR^b$、-$NR^aS(=O)_pR^c$、-$NR^aS(=O)_pNR^aR^a$、-$OC(=O)NR^aR^a$、-$S(=O)_pNR^aR^a$或-$S(=O)_pR^c$；

R^{14}為鹵基、CN、經0至3個鹵基取代基取代之C_{1-4}烷基、經0至3個鹵基取代基取代之-OC_{1-4}烷基、-$(CH_2)_{0-2}$-NR^aR^a、經0至3個R^e取代之-$(CH_2)_{0-2}$-芳基、經0至3個R^e取代之-O-芳基、或包含1至4個選自O、

$S(=O)_p$及N之雜原子且經0至3個R^e取代之-$(CH_2)_{0-2}$-3員至12員雜環基；

R^{14a}為H、$C(=O)C_{1-3}$烷基或經以下取代之C_{1-3}烷基：0至2個經0至2個鹵基取代基取代之芳基；

R^{15}為H、C_{1-2}烷基或苯基；

R^a為H、經0至4取代之C_{1-5}烷基、經0至4個R^e取代之C_{2-5}烯基、經0至4個R^e取代之C_{2-5}炔基、經0至4個R^e取代之-$(CH_2)_n$-C_{3-10}碳環基、或包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至4個R^e取代之-$(CH_2)_n$-3員至12員雜環基；或R^a及R^a與該兩者所連接之氮原子一起形成包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至4個R^e取代之3員至12員雜環基；

R^b為H、經0至4個R^e取代之C_{1-5}烷基、經0至4個R^e取代之C_{2-5}烯基、經0至4個R^e取代之C_{2-5}炔基、經0至4個R^e取代之-$(CH_2)_n$-C_{3-10}碳環基、或包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至4個R^e取代之-$(CH_2)_n$-3員至12員雜環基；

R^c為經0至4個R^e取代之C_{1-5}烷基、經0至4個R^e取代之C_{2-5}烯基、經0至4個R^e取代之C_{2-5}炔基、C_{3-6}碳環基、或包含1至4個選自O、$S(=O)_p$及N之雜原子之3員至12員雜環基；

R^e為鹵基、CN、=O、經0至4個R^g取代之C_{1-6}烷基、經0至4個R^g取代之C_{2-6}烯基、經0至4個R^g取代之C_{2-6}炔基、經0至4個R^g取代之-$(CH_2)_n$-C_{3-6}環烷基、經0至4個R^g取代之-$(CH_2)_n$-芳基、包含1至4個選自O、$S(=O)_p$及N之雜原子且經0至4個R^g取代之-$(CH_2)_n$-4員至6員雜環基、-$(CH_2)_nOR^f$、$C(=O)OR^f$、$C(=O)NR^fR^f$、$NR^fC(=O)R^f$、$S(=O)_pR^f$、$NR^fS(=O)_pR^f$、$NR^fC(=O)OR^f$、$OC(=O)NR^fR^f$或-$(CH_2)_nNR^fR^f$；

R^f為H、C_{1-6}烷基、C_{3-6}環烷基或芳基；

R^8為鹵基、CN、-OH、C_{1-4}烷基、C_{3-6}環烷基或苯基；

n為0、1、2或3；及

p為0、1或2。

[請求項11]

如請求項10之化合物或其醫藥學上可接受之鹽，其中：

R^{4a}為鹵基；

R^{4b}為經0至3個鹵基取代基取代之C_{1-4}烷基；

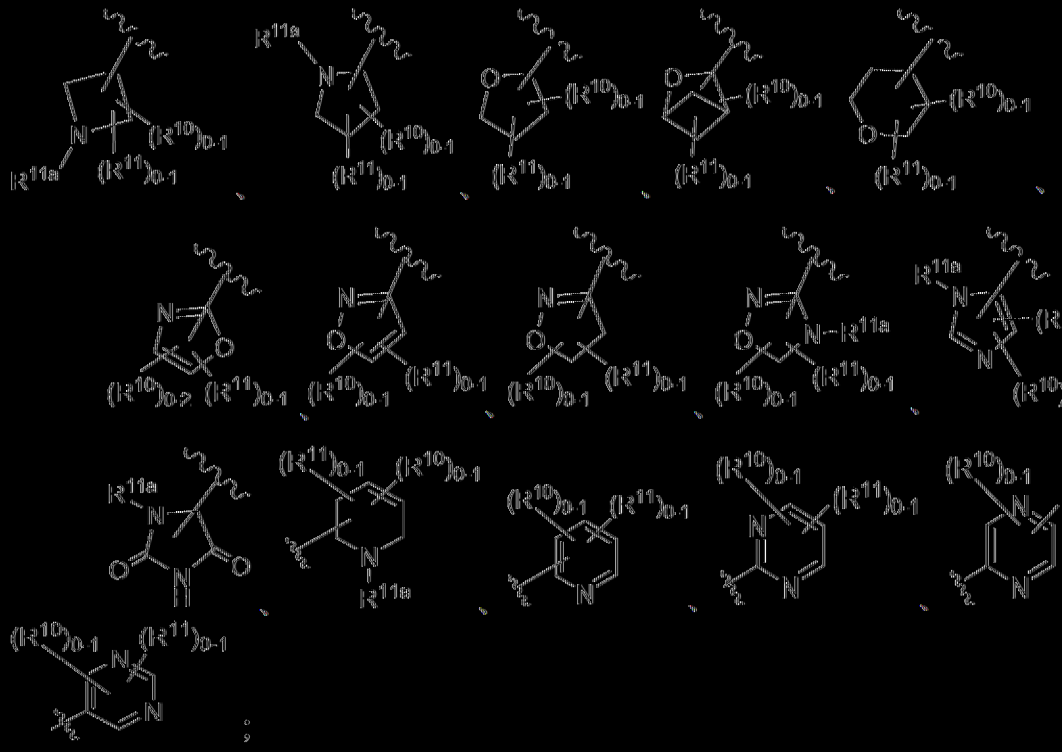
R^5為H；

R^6為經0至2個F取代基取代之C_{1-2}烷基或C_{3-6}環烷基；

R^8為-OC_{1-3}烷基；

R^{8a}為F或CN；

R^9為



；

R^{10}為鹵基、CN、C_{1-2}烷基、=O、-OH或-OC_{1-2}烷基；

R^{11}為經0至1個R^{12}及0至1個R^{13}取代之C_{1-3}烷基、-OR^b、-NR^aR^a、-

$NR^aC(=O)R^b$、$-C(=O)R^b$、$-C(=O)OR^b$、$-C(=O)NR^aR^a$或經0至5個R^e取代之C_{3-6}環烷基；

R^{11a}為H、$-C(=O)R^b$、$-C(=O)NR^aR^a$或經0至1個R^{11b}取代之C_{1-4}烷基；

R^{11b}為-OH或芳基；

R^{12}為$-C(=O)OR^b$、$-C(=O)NHR^a$、$-C(=O)NHOR^b$或經0至2個鹵基或-OH取代基取代之C_{1-4}烷基；

R^{13}為-OH、經0至2個-OH取代基取代之$-OC_{1-4}$烷基、或$-S(=O)_2C_{1-4}$烷基；

R^a為H或C_{1-4}烷基，或R^a及R^a與該兩者所連接之氮原子一起形成經0至4個R^e取代之3員至9員雜環基；

R^b為H、經0至1個R^e取代之C_{1-4}烷基或經0至1個R^e取代之C_{3-6}環烷基；

R^e為$-OR^f$；及

R^f為H或C_{1-4}烷基。

【請求項12】

如請求項11之化合物或其醫藥學上可接受之鹽，其中：

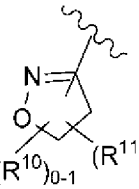
R^{4a}為鹵基；

R^{4b}為CF_3；

R^5為H；

R^6為CF_3或C_{3-6}環丙基；

R^8為$-OC_{1-3}$烷基；

R^9為  ；

R^{10}為C_{1-2}烷基、-OH或-OC_{1-2}烷基；

R^{11}為經0至1個R^{12}及0至1個R^{13}取代之C_{1-3}烷基、-C(=O)OR^b或-C(=O)NR^aR^a；

R^{12}為-C(=O)OR^b；

R^{13}為-OH；

R^a為H或C_{1-4}烷基；及

R^b為H或C_{1-4}烷基。

【請求項13】

如請求項10之化合物或其醫藥學上可接受之鹽，其中：

R^{4a}為鹵基；

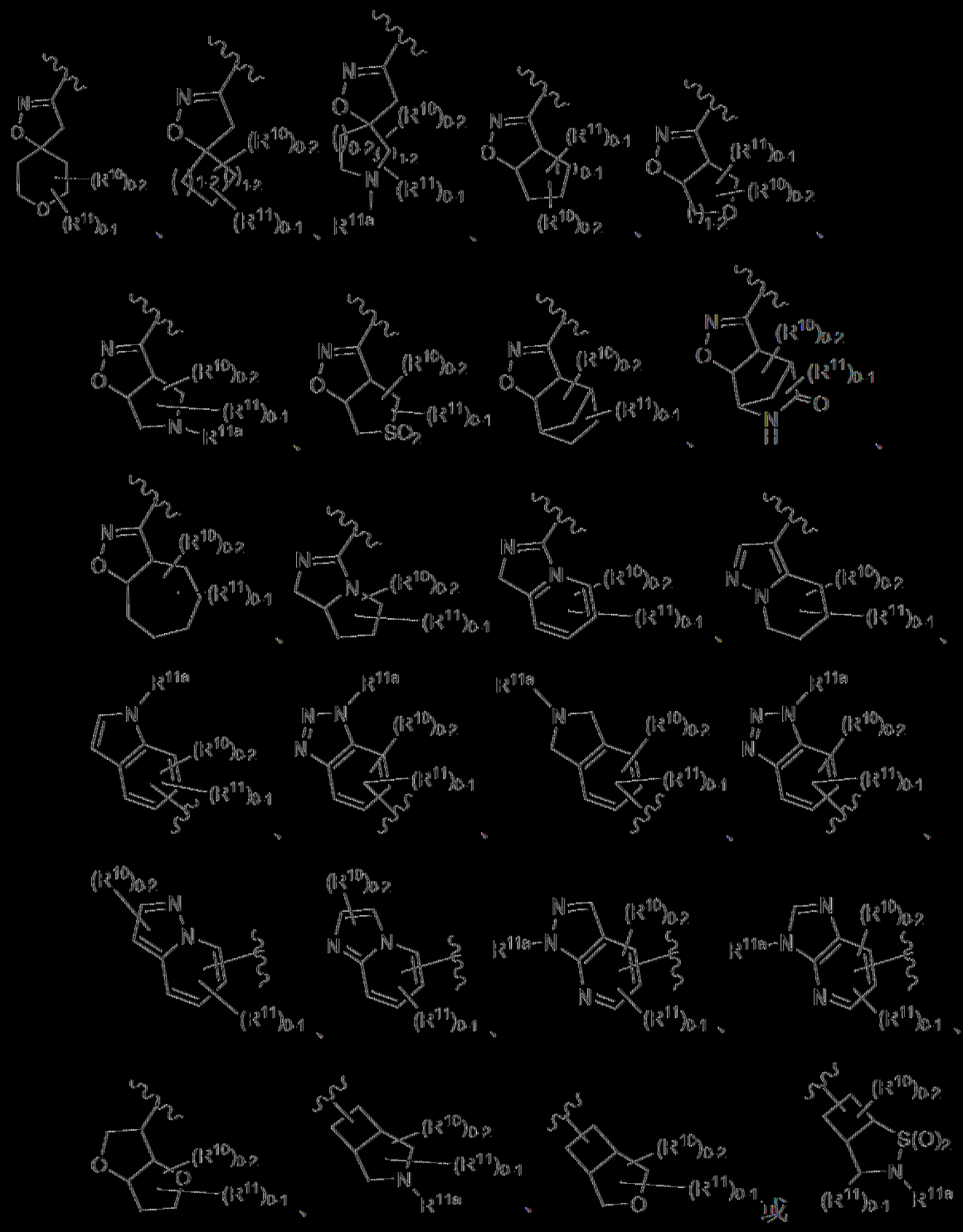
R^{4b}為經0至3個鹵基取代基取代之C_{1-4}烷基；

R^5為H；

R^6為經0至3個F取代基取代之C_{1-3}烷基或C_{3-6}環烷基；

R^8為-OC_{1-3}烷基；

R^9為



。

R^{10}為鹵素、C_{1-3}烷基、-OH或-OC_{1-3}烷基；

R^{11}為經0至1個R^{12}及0至1個R^{13}取代之C_{1-3}烷基；

R^{11a}為H、經0至2個R^{11b}取代之C_{1-4}烷基或-C(=O)OC_{1-4}烷基；

R^{11b}為-OH、-C(=O)OH或芳基；

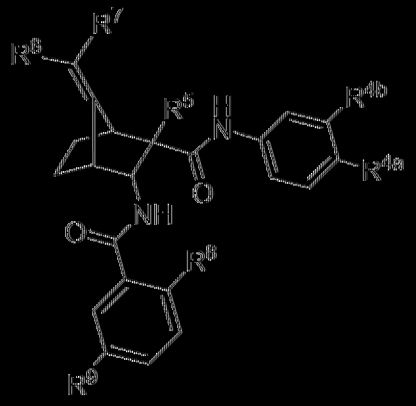
R^{12}為-C(=O)OR^b或經0至3個鹵基取代基取代之C_{1-3}烷基；

R^{13}為-OH；及

R^b為H或C_{1-4}烷基。

[請求項14]

如請求項3之化合物，其具有式(VIII)：



(VIII)

或其醫藥學上可接受之鹽，其中：

R^{4a}為鹵基；

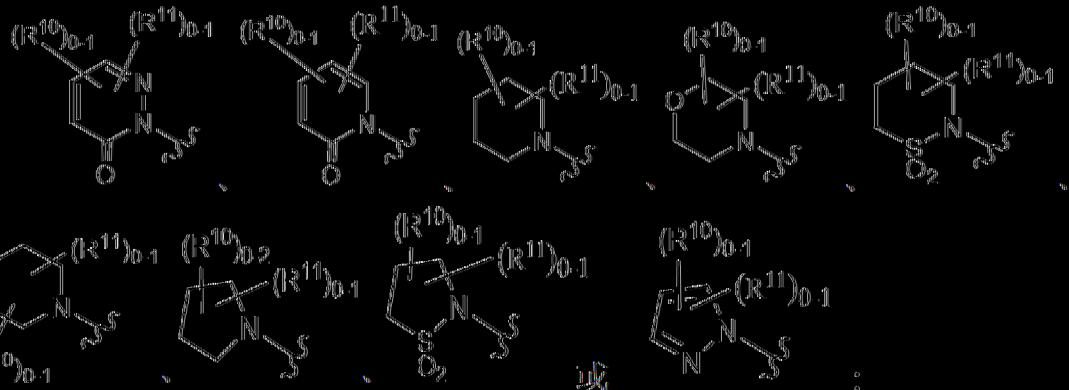
R^{4b}為經0至4個鹵基取代基取代之C_{1-4}烷基；

R^6為經0至2個F取代基取代之C_{1-2}烷基、C_{3-6}環烷基或芳基；

R^7為H；

R^8為-OC_{1-3}烷基；

R^9為



R^{10}為鹵基、CN、C_{1-4}烷基、=O、-OH或-OC_{1-4}烷基；

R^{11}為經0至1個R^{12}及0至1個R^{13}取代之C_{1-2}烷基、-NR^aR^a、-$NR^aC(=O)R^b$、-$NR^aC(=O)OR^b$或-$C(=O)OR^b$；

R^{12}為-$C(=O)OR^b$、-$C(=O)NHR^a$、-$C(=O)NHOR^b$或經0至3個鹵基或-OH取代基取代之C_{1-4}烷基；

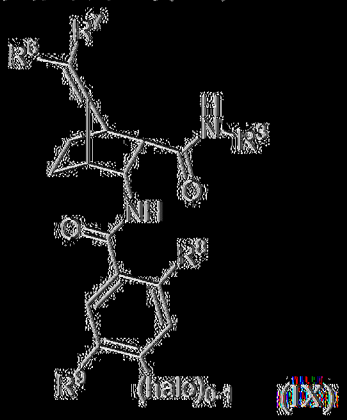
R^{13}為-OH或-$NR^aC(=O)R^b$；

R^a為H或C_{1-4}烷基；及

R^b為H、C_{1-4}烷基、或包含1至4個選自O、$S(=O)_p$及N之雜原子的3員至9員雜環基。

[請求項15]

如請求項1之化合物，其具有式(IX)：



或其醫藥學上可接受之鹽，其中：

R^3為C_{1-5}烷基、CF_3、經0至4個R^4取代之-$(CR^dR^d)_{0-1}$-C_{3-6}環烷基或經0至4個R^4取代之苯基；

R^4為鹵基、CN、CH_3或CF_3；

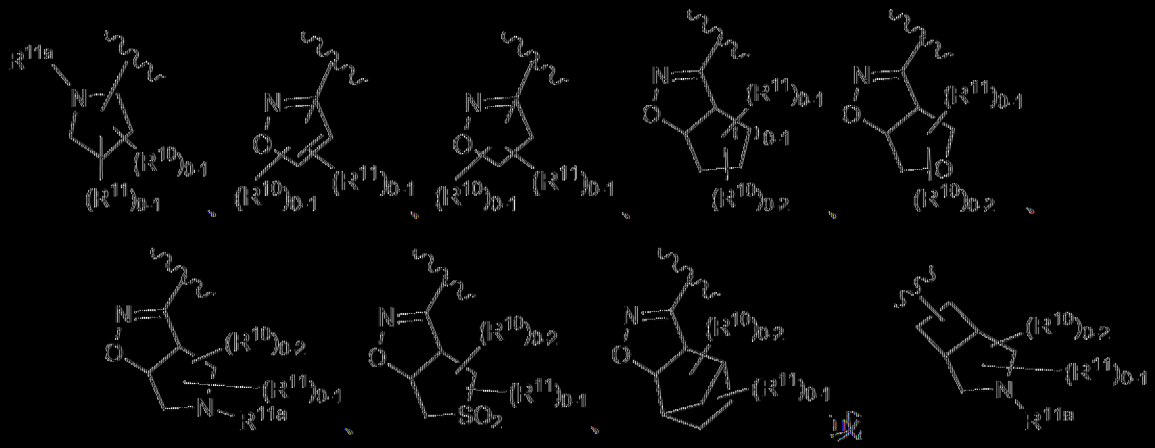
R^6為C_{1-6}烷基、CF_3或經0至2個F取代基取代之C_{3-6}環烷基；

R^7為H；

R^8為鹵基、-$N(C_{1-3}$烷基$)_2$、經0至1個-OC_{1-4}烷基取代基取代之-OC_{1-3}烷

其；

R^9為



；

R^{10}為鹵其、C_{1-4}烷其、-OH或-OC_{1-4}烷其；

R^{11}為經0至2個R^{12}及0至2個R^{13}取代之C_{1-4}烷其、-C(=O)OR^b、-C(=O)NR^aR^a或經0至2個R^c取代之C_{3-6}環烷其；

R^{11a}為H、經0至2個R^{11b}取代之C_{1-4}烷其、-C(=O)R^b或-C(=O)OC_{1-4}烷其；

R^{11b}為-OH；

R^{12}為經0至3個鹵其取代其取代之C_{1-3}烷其或-C(=O)OR^b；

R^{13}為-OH；

R^a為H或C_{1-3}烷其；

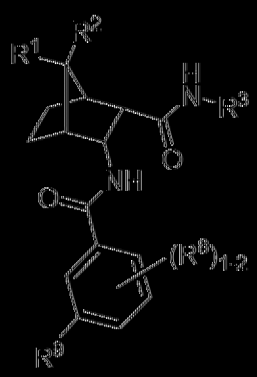
R^b為H或經0至1個R^c取代之C_{1-4}烷其；

R^c為-OR^f；及

R^f為H或C_{1-6}烷其。

[請求項16]

如請求項1之化合物，其具有式(X)：



(X)

或其醫藥學上可接受之鹽，其中：

R^1為經C_{3-6}環烷基取代基取代之C_{1-2}烷基；

R^2為H；

或R^1及R^2經組合為-CR^6R^7；

R^3為經0至5個鹵基、CN或-OC_{1-3}烷基取代基取代之C_{1-6}烷基、經0至5個R^4取代之-$(CHR^d)_n$-C_{3-10}碳環基、或包含1至3個選自O、S、N之雜原子且經0至3個R^4取代之5員至6員雜芳基；

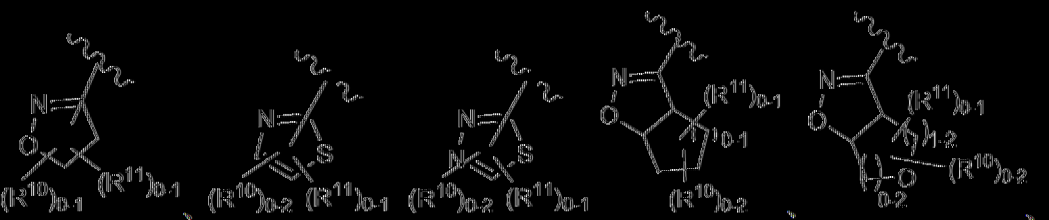
R^4為鹵基、$S(=O)_2CF_3$、CN或經0至5個鹵基取代基取代之C_{1-4}烷基；

R^6為鹵基、經0至3個R^{6a}取代之C_{1-5}烷基、經0至3個R^{14}取代之C_{3-6}環烷基或包含1至3個選自O、S及N之雜原子且經0至3個R^{14}取代之5員至6員雜環基；

R^{6a}為鹵基、-OH或C_{3-6}環烷基；

R^7為H；

R^8為H、鹵基、CN、C_{1-4}烷基或經0至5個鹵基、-OH、C_{3-6}環烷基或-OC_{1-4}烷基取代基取代之-OC_{1-4}烷基；

R^9 為  、、、、、  ；

R^{10}為鹵基、CN、C_{1-4}烷基或-OH；

R^{11}為經0至3個R^{12}及0至1個R^{13}取代之C_{1-3}烷基、-OR^b、-$NHC(=O)R^b$或-$C(=O)OR^b$；

R^{12}為鹵基；

R^{13}為-OR^b或C_{3-6}碳環基；

R^{14}為鹵基、CN或經0至3個鹵基取代基取代之C_{1-4}烷基；

R^b為H或經0至5個R^c取代之C_{1-3}烷基；

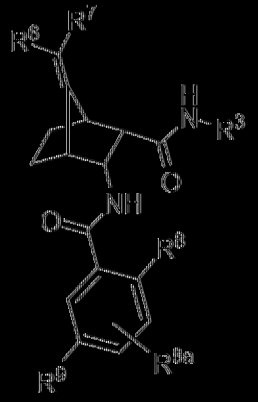
R^d為H或C_{1-4}烷基；

R^c為-OH；及

n為0或1。

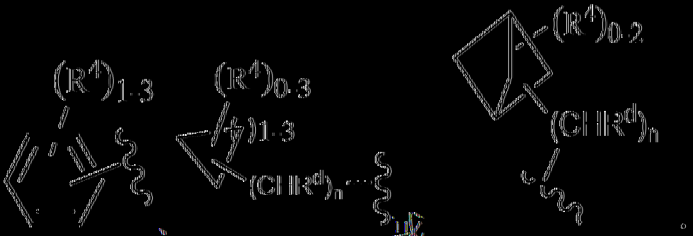
[請求項17]

如請求項16之化合物，其具有式(XI)：



(XI)

或其醫藥學上可接受之鹽，其中：

R^3為C_{1-5}烷基或  ；

R^4為鹵基、CN、-S(=O)$_2$$CF_3$、經0至5個鹵基取代基取代之$C_{1-4}$烷基；

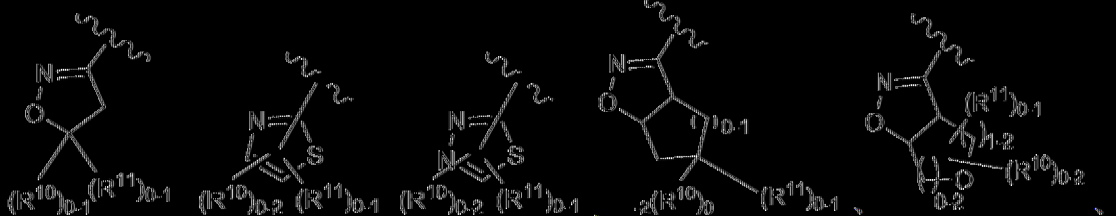
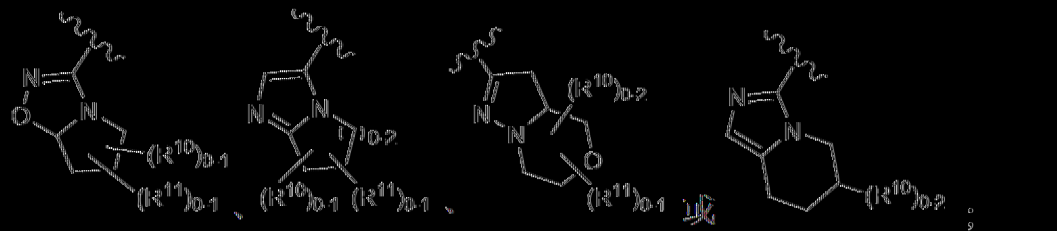
R^6為經0至2個R^{6a}取代之C_{1-5}烷基、經0至2個R^{14}取代之C_{3-6}環烷基、或包含1至3個選自O、S及N之雜原子且經0至2個R^{14}取代之5員至6員雜環基；

R^{6a}為鹵基、-OH或C_{3-6}環烷基；

R^7為H；

R^8為經0至5個鹵基、-OH、C_{3-6}環烷基或-OC_{1-3}烷基取代基取代之-OC_{1-3}烷基；

R^{8a}為H、鹵基、CN或C_{1-3}烷基；

R^9為  、  ；

R^{10}為鹵基、CN、C_{1-4}烷基或-OH；

R^{11}為經0至3個R^{12}及0至1個R^{13}取代之C_{1-3}烷基、-OR^b、-NHC(=O)R^b或-C(=O)OR^b；

R^{12}為鹵基；

R^{13}為-OR^b或C_{3-6}碳環基；

R^{14}為鹵基或經0至3個鹵基取代基取代之C_{1-4}烷基；

R^b為H或經0至5個R^e取代之C_{1-3}烷基；

R^d為H或C_{1-2}烷基；及

n為0或1。

【請求項18】

一種醫藥組合物，其包含如請求項1之化合物或其醫藥學上可接受之鹽及醫藥學上可接受之載劑。

【請求項19】

一種用於治療鬆弛素相關疾病之方法，其包含向有需要患者投與治療有效量之如請求項18之醫藥組合物。

【請求項20】

如請求項19之方法，其中該疾病係選自由以下組成之群：心絞痛、不穩定型心絞痛、心肌梗塞、心臟衰竭、急性冠狀動脈疾病、急性心臟衰竭、慢性心臟衰竭及心臟醫源性損傷。

【請求項21】

如請求項20之方法，其中該疾病為心臟衰竭。

【請求項22】

如請求項19之方法，其中該疾病為纖維化。