

發明專利說明書

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壹、發明名稱：(中文/英文)

作為週期素依賴性激酶抑制劑之新穎吡唑并嘧啶

NOVEL PYRAZOLOPYRIMIDINES AS CYCLIN DEPENDENT
KINASE INHIBITORS

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8.印度	INDIA
10.香港	HONG KONG
17.南韓	KOREA

肆、聲明事項：

☐ 本案係符合專利法第二十條第一項 ☐ 第一款但書或 ☐ 第二款但書規定之期間，其日期為： 年 月 日。

☒ 本案申請前已向下列國家（地區）申請專利：

1.美國； 2002 年 09 月 04 日； 60/408,027

2.美國； 2002 年 10 月 29 日； 60/421,959

3.

4.

5.

☒ 主張國際優先權(專利法第二十四條)：

【格式請依：受理國家（地區）；申請日；申請案號數 順序註記】

1.美國； 2002 年 09 月 04 日； 60/408,027

2.美國； 2002 年 10 月 29 日； 60/421,959

3.

4.

5.

☐ 主張國內優先權(專利法第二十五條之一)：

【格式請依：申請日；申請案號數 順序註記】

1.

2.

☐ 主張專利法第二十六條微生物：

☐ 國內微生物 【格式請依：寄存機構；日期；號碼 順序註記】

☐ 國外微生物 【格式請依：寄存國名；機構；日期；號碼 順序註記】

☐ 熟習該項技術者易於獲得，不須寄存。

玖、發明說明：

【發明所屬之技術領域】

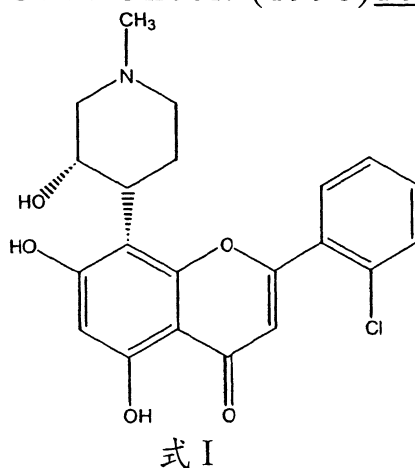
本發明有關可作為蛋白質激酶抑制劑(例如週期素依賴性激酶、有絲分裂原活化之蛋白質激酶(MAPK/ERK)、醣原合成酶激酶3(GSK3 β)等之抑制劑)之吡唑并[1,5-a]嘧啶化合物、含此化合物之醫藥組合物、及使用此化合物或醫藥組合物治療例如癌症、發炎、關節炎、病毒疾病、神經退化疾病如阿茲海默氏(Alzheimer's)疾病、心臟血管疾病及真菌疾病之治療方法。本申請案主張2002年9月4日申請之美國專利臨時申請號60/408,027及2002年10月29日申請之申請號60/421,959之優先權。

【先前技術】

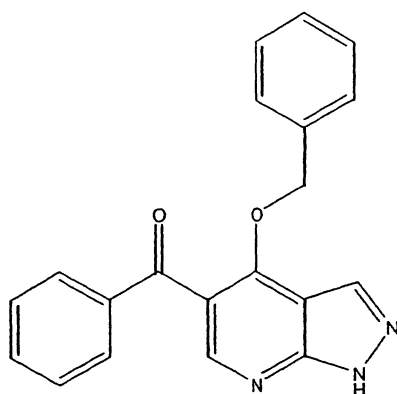
蛋白質激酶抑制劑包含激酶例如週期素依賴性激酶(CDKs)、有絲分裂原活化之蛋白質激酶(MAPK/ERK)、醣原合成酶激酶3(GSK3 β)等之抑制劑。蛋白質激酶抑制劑係描述於，例如M. Hale等人於WO 02/22610 A1及Y. Mettey等人於J. Med. Chem.,(2003) 46 222-236。週期素依賴性激酶為絲胺酸/蘇胺酸蛋白質激酶，其為細胞週期及細胞增殖背後之驅動力。個別CDK's如CDK1、CDK2、CDK3、CDK4、CDK5、CDK6及CDK7、CDK8及類似物在細胞週期漸進中扮演不同角色且可歸類為G1、S或G2M期酵素。非控制之增殖作用為癌細胞之檢驗印記且在許多重要實心瘤中高頻率發生CDK功能錯調節。CDK2及CDK4由於其活性在廣泛種類之人類癌症中經常錯調節而特別受到注意。CDK2活性對細胞週期

由G1期漸進至S期而言為必須者，且CDK2為G1檢核點之重要成分之一。檢核點作用為維持細胞週期事件之適當順序且使細胞對傷害或對增殖訊號反應，同時在癌細胞中喪失適當之檢核點控制造成腫瘤形成。該CDK2路徑以腫瘤抑制劑功能(如p52、RB及p27)及癌基因活化作用(週期素E)之程度影響腫瘤形成。許多報導已證明CDK2之輔活化劑(週期素E)及抑制劑(p27)兩者分別於乳癌、結腸炎、非小細胞肺癌、胃癌、前列腺癌、膀胱癌、非-荷葛金氏(non-Hodgkin's)淋巴瘤、卵巢癌及其他癌症中過度表現或表現不足。它們的改變表現已顯示與增加之CDK2活性量及不良之總存活率有關。此觀察使CDK2及其調節路徑為近年來發展之必要標的，數種腺苷5'-三磷酸酯(ATP)競爭性小有機分子以及肽已於文獻中報導可作為有潛力治療癌症之CDK抑制劑。US 6,413,974第1欄第23行-第15欄第10行提供對各種CDKs及其與各種癌症關聯性之良好描述。

CDK抑制劑為已知。例如黃素比多醇(flavopiridol)(式I)為目前經歷人類臨床試驗之非選擇性CDK抑制劑。A.M. Sanderowicz等人, J. Clin. Oncol. (1998)16, 2986-2999。



其他已知之 CDKs 之抑制劑包含例如歐樂姆辛 (olomoucine)(J Vesely 等人, Eur. J. Biochem., (1994)224, 771-786) 及羅可維汀 (roscovitine)(I. Meijer 等人, Eur. J. Biochem., (1997)243, 527- 536)。US 6,107,305 描述某種吡唑并 [3,4-b] 吡啶化合物為 CDK 抑制劑。該 '305 專利之例舉化合物具有式 II：



式 II

K. S. Kim 等人, J. Med. Chem. 45(2002) 3905-3927 及 WO 02/10162 揭示某種胺基噻唑化合物為 CDK 抑制劑。

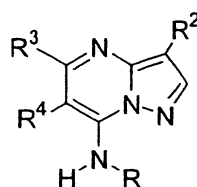
吡唑并嘧啶為已知。例如 WO 92/18504、WO 02/50079、WO 95/35298、WO 02/40485、EP 94304104.6、EP 0628559(相當於 US 專利 5,602,136; 5,602,137 及 5,571,813)、US 6,383,790、Chem. Pharm. Bull., (1999)47, 928、J. Med. Chem., (1977)20, 296、J. Med. Chem., (1976)19, 517 及 Chem. Pharm. Bull., (1962)10 620 揭示各種吡唑并嘧啶。

仍需要一種新穎化合物、調配物、治療方法以治療與 CDKs 有關之疾病及失調。因此，本發明之目的係提供一種可用以治療或預防或舒緩此疾病及失調之化合物。

【發明內容】

許多具體例中，本發明提供作為週期素依賴性激酶之抑制劑之新一類吡啶并[1,5-a]嘓啶化合物、製備此化合物之方法、含一或多種此化合物之醫藥組合物、製備包括一或多種此化合物之醫藥調配物之方法、及使用此化合物或醫藥組合物治療、預防、抑制或舒緩與CDKs有關之一或多種疾病之方法。

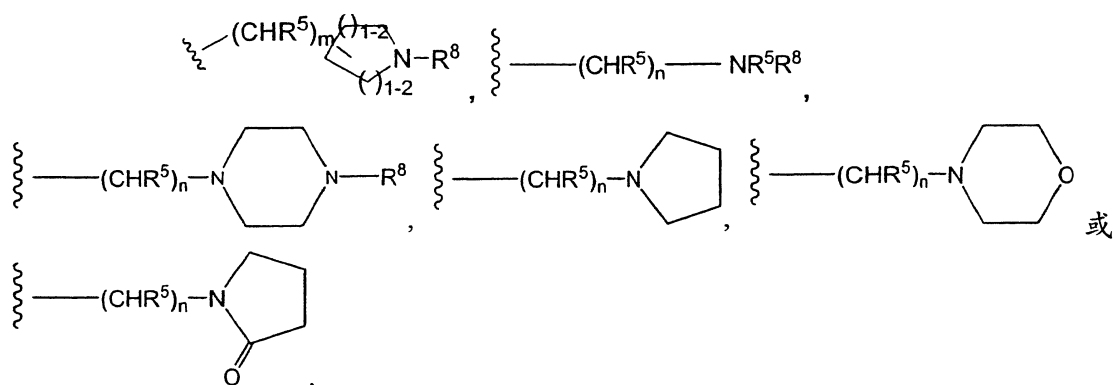
一方面，本發明揭示一種化合物、或該化合物之醫藥可接受性鹽或溶劑化物，該化合物具有式III所示通式：



式 III

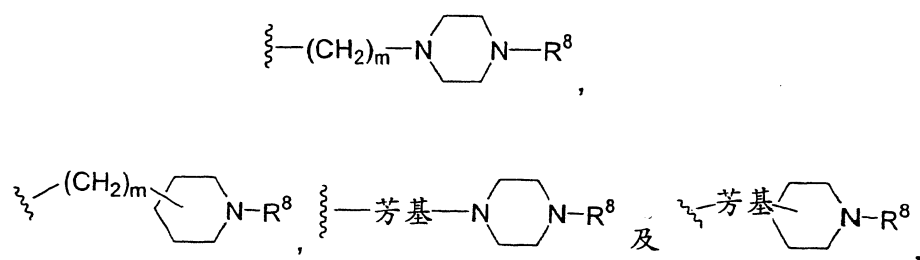
其中：

R為H、烷基、烯基、炔基、芳基烷基、芳基烯基、環烷基、環烷基烷基、烯基烷基、炔基烷基、雜環基、雜環基烷基、雜芳基烷基(包含該雜芳基之N-氧離子)、 $-(CHR^5)_n$ -芳基、 $-(CHR^5)_n$ -雜芳基、



其中該烷基、烯基、炔基、芳基、環烷基、雜環基及雜芳基各可為未經取代或視情況經一或多個可相同或不同之基團取代，各基團獨立選自下列所組成之組群：鹵素、烷基、芳基、環烷基、雜環基烷基、 CF_3 、 OCF_3 、 CN 、 $-\text{OR}^5$ 、 $-\text{NR}^5\text{R}^{10}$ 、 $-\text{C}(\text{R}^4\text{R}^5)_p-\text{R}^9$ 、 $-\text{N}(\text{R}^5)\text{Boc}$ 、 $-(\text{CR}^4\text{R}^5)_p\text{OR}^5$ 、 $-\text{C}(\text{O}_2)\text{R}^5$ 、 $-\text{C}(\text{O})\text{R}^5$ 、 $-\text{C}(\text{O})\text{NR}^5\text{R}^{10}$ 、 $-\text{SO}_3\text{H}$ 、 $-\text{SR}^{10}$ 、 $-\text{S}(\text{O}_2)\text{R}^7$ 、 $-\text{S}(\text{O}_2)\text{NR}^5\text{R}^{10}$ 、 $-\text{N}(\text{R}^5)\text{S}(\text{O}_2)\text{R}^7$ 、 $-\text{N}(\text{R}^5)\text{C}(\text{O})\text{R}^7$ 及 $-\text{N}(\text{R}^5)\text{C}(\text{O})\text{NR}^5\text{R}^{10}$ ；

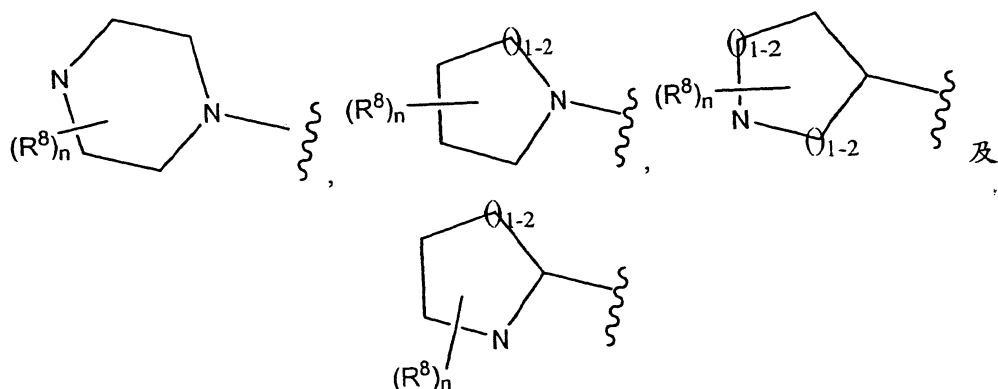
R^2 係選自由 R^9 、烷基、烯基、炔基、 CF_3 、雜環基、雜環基烷基、鹵素、鹵烷基、芳基、芳基烷基、雜芳基烷基、炔基烷基、環烷基、雜芳基、經1-6個 R^9 基取代之烷基(該 R^9 基可相同或不同且各 R^9 基係獨立選自後述所列之 R^9)、經1-3個可相同或不同之芳基或雜芳基(獨立選自苯基、吡啶基、噻吩基、呋喃基及噻唑基)取代之芳基、與芳基或雜芳基稠合之芳基、經1-3個可相同或不同之芳基或雜芳基(獨立選自苯基、吡啶基、噻吩基、呋喃基及噻唑基)取代之芳基、與芳基或雜芳基稠合之雜芳基、



其中 R^2 之上述定義中該一或多個芳基及/或一或多個雜芳基可為未經取代或視情況經一或多個基團取代，該基團可相同或不同且獨立選自由鹵素、 $-\text{CN}$ 、 $-\text{OR}^5$ 、 SR^5 、 $-\text{S}(\text{O}_2)\text{R}^6$ 、

$-\text{S}(\text{O}_2)\text{NR}^5\text{R}^6$ 、 $-\text{NR}^5\text{R}^6$ 、 $-\text{C}(\text{O})\text{NR}^5\text{R}^6$ 、 CF_3 、烷基、芳基及 OCF_3 所組成之組群；

R^3 係選自由下列所組成之組群： H 、鹵素、 $-\text{NR}^5\text{R}^6$ 、 $-\text{OR}^6$ 、 $-\text{SR}^6$ 、 $-\text{C}(\text{O})\text{N}(\text{R}^5\text{R}^6)$ 、烷基、炔基、環烷基、芳基、芳基烷基、雜環基、雜環基烷基、雜芳基及雜芳基烷基、



其中 R^3 之該烷基、環烷基、芳基、芳基烷基、雜環基、雜環基烷基、雜芳基及雜芳基烷基及對上述 R^3 剛顯示之結構之雜環基團各可經或視情況可獨立經一或多個可相同或不同之基團取代，各基團獨立選自由下列所組成之組群：鹵素、烷基、芳基、環烷基、 CF_3 、 CN 、 $-\text{OCF}_3$ 、 $-(\text{CR}^4\text{R}^5)_p\text{OR}^5$ 、 $-\text{OR}^5$ 、 $-\text{NR}^5\text{R}^6$ 、 $-(\text{CR}^4\text{R}^5)_p\text{NR}^5\text{R}^6$ 、 $-\text{C}(\text{O}_2)\text{R}^5$ 、 $-\text{C}(\text{O})\text{R}^5$ 、 $-\text{C}(\text{O})\text{NR}^5\text{R}^6$ 、 $-\text{SR}^6$ 、 $-\text{S}(\text{O}_2)\text{R}^6$ 、 $-\text{S}(\text{O}_2)\text{NR}^5\text{R}^6$ 、 $-\text{N}(\text{R}^5)\text{S}(\text{O}_2)\text{R}^7$ 、 $-\text{N}(\text{R}^5)\text{C}(\text{O})\text{R}^7$ 及 $-\text{N}(\text{R}^5)\text{C}(\text{O})\text{NR}^5\text{R}^6$ ；但條件為與雜環基環上之氮原子相鄰之碳原子不帶有 $-\text{OR}^5$ 基；

R^4 為 H 、鹵基或烷基；

R^5 為 H 、烷基、芳基或環烷基；

R^6 係選自由 H 、烷基、烯基、芳基、芳基烷基、芳基烯基、環烷基、雜環基、雜環基烷基、雜芳基及雜芳基烷基所組

成之組群，其中該烷基、芳基、芳基烷基、環烷基、雜環基、雜環基烷基、雜芳基及雜芳基烷基各可為未經取代或視情況經一或多個可相同或不同之基團取代，各基團獨立選自下列所組成之組群：鹵素、烷基、芳基、環烷基、雜環基烷基、 CF_3 、 OCF_3 、 CN 、 $-\text{OR}^5$ 、 $-\text{NR}^5\text{R}^{10}$ 、 $-\text{C}(\text{R}^4\text{R}^5)_p-\text{R}^9$ 、 $-\text{N}(\text{R}^5)\text{Boc}$ 、 $-(\text{CR}^4\text{R}^5)_p\text{OR}^5$ 、 $-\text{C}(\text{O}_2)\text{R}^5$ 、 $-\text{C}(\text{O})\text{R}^5$ 、 $-\text{C}(\text{O})\text{NR}^5\text{R}^{10}$ 、 $-\text{SO}_3\text{H}$ 、 $-\text{SR}^{10}$ 、 $-\text{S}(\text{O}_2)\text{R}^7$ 、 $-\text{S}(\text{O}_2)\text{NR}^5\text{R}^{10}$ 、 $-\text{N}(\text{R}^5)\text{S}(\text{O}_2)\text{R}^7$ 、 $-\text{N}(\text{R}^5)\text{C}(\text{O})\text{R}^7$ 及 $-\text{N}(\text{R}^5)\text{C}(\text{O})\text{NR}^5\text{R}^{10}$ ；

R^{10} 係選自由H、烷基、芳基、芳基烷基、環烷基、雜環基、雜環基烷基、雜芳基及雜芳基烷基所組成之組群，其中該烷基、芳基、芳基烷基、環烷基、雜環基、雜環基烷基、雜芳基及雜芳基烷基各可為未經取代或視情況經一或多個可相同或不同之基團取代，各基團獨立選自下列所組成之組群：鹵素、烷基、芳基、環烷基、雜環基烷基、 CF_3 、 OCF_3 、 CN 、 $-\text{OR}^5$ 、 $-\text{NR}^4\text{R}^5$ 、 $-\text{C}(\text{R}^4\text{R}^5)_p-\text{R}^9$ 、 $-\text{N}(\text{R}^5)\text{Boc}$ 、 $-(\text{CR}^4\text{R}^5)_p\text{OR}^5$ 、 $-\text{C}(\text{O}_2)\text{R}^5$ 、 $-\text{C}(\text{O})\text{NR}^4\text{R}^5$ 、 $-\text{C}(\text{O})\text{R}^5$ 、 $-\text{SO}_3\text{H}$ 、 $-\text{SR}^5$ 、 $-\text{S}(\text{O}_2)\text{R}^7$ 、 $-\text{S}(\text{O}_2)\text{NR}^4\text{R}^5$ 、 $-\text{N}(\text{R}^5)\text{S}(\text{O}_2)\text{R}^7$ 、 $-\text{N}(\text{R}^5)\text{C}(\text{O})\text{R}^7$ 及 $-\text{N}(\text{R}^5)\text{C}(\text{O})\text{NR}^4\text{R}^5$ ；

或視情況(i)基團 $-\text{NR}^5\text{R}^{10}$ 中之 R^5 及 R^{10} 或(ii)基團 $-\text{NR}^5\text{R}^6$ 中之 R^5 及 R^6 可一起形成環烷基或雜環基基團，該環烷基或雜環烷基基團各為未經取代或視情況獨立經一或多個 R^9 基取代；

R^7 係選自由烷基、環烷基、芳基、芳基烯基、雜芳基、芳基烷基、雜芳基烷基、雜芳基烯基及雜環基所組成之組

群，其中該烷基、環烷基、雜芳基烷基、芳基、雜芳基及芳基烷基各可為未經取代或視情況獨立經一或多個可相同或不同之基團取代，各基團獨立選自下列所組成之組群：鹵素、烷基、芳基、環烷基、 CF_3 、 OCF_3 、 CN 、 $-\text{OR}^5$ 、 $-\text{NR}^5\text{R}^{10}$ 、 $-\text{CH}_2\text{OR}^5$ 、 $-\text{C}(\text{O}_2)\text{R}^5$ 、 $-\text{C}(\text{O})\text{NR}^5\text{R}^{10}$ 、 $-\text{C}(\text{O})\text{R}^5$ 、 $-\text{SR}^{10}$ 、 $-\text{S}(\text{O}_2)\text{R}^{10}$ 、 $-\text{S}(\text{O}_2)\text{NR}^5\text{R}^{10}$ 、 $-\text{N}(\text{R}^5)\text{S}(\text{O}_2)\text{R}^{10}$ 、 $-\text{N}(\text{R}^5)\text{C}(\text{O})\text{R}^{10}$ 及 $-\text{N}(\text{R}^5)\text{C}(\text{O})\text{NR}^5\text{R}^{10}$ ；

R^8 係選自由 R^6 、 $-\text{OR}^6$ 、 $-\text{C}(\text{O})\text{NR}^5\text{R}^{10}$ 、 $-\text{S}(\text{O}_2)\text{NR}^5\text{R}^{10}$ 、 $-\text{C}(\text{O})\text{R}^7$ 、 $-\text{C}(=\text{N}-\text{CN})-\text{NH}_2$ 、 $-\text{C}(=\text{NH})-\text{NHR}^5$ 、雜環基及 $-\text{S}(\text{O}_2)\text{R}^7$ 所組成之組群；

R^9 係選自由鹵素、 $-\text{CN}$ 、 $-\text{NR}^5\text{R}^{10}$ 、 $-\text{C}(\text{O}_2)\text{R}^6$ 、 $-\text{C}(\text{O})\text{NR}^5\text{R}^{10}$ 、 $-\text{OR}^6$ 、 $-\text{SR}^6$ 、 $-\text{S}(\text{O}_2)\text{R}^7$ 、 $-\text{S}(\text{O}_2)\text{NR}^5\text{R}^{10}$ 、 $-\text{N}(\text{R}^5)\text{S}(\text{O}_2)\text{R}^7$ 、 $-\text{N}(\text{R}^5)\text{C}(\text{O})\text{R}^7$ 及 $-\text{N}(\text{R}^5)\text{C}(\text{O})\text{NR}^5\text{R}^{10}$ 所組成之組群；

m 為0至4；

n 為1至4；及

p 為1至4；

但條件為當 R^2 為苯基，則 R^3 不為烷基、炔基或鹵素，且當 R^2 為芳基， R 不為

$$\begin{array}{c} \text{~} \\ \text{~} \\ \text{~} \end{array} \text{---} (\text{CHR}^5)_n \text{---} \text{NR}^5\text{R}^8$$

，且又當 R 為芳基烷基時，該芳基烷基之芳基上任何雜芳基取代基含有至少三個雜原子。

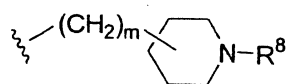
式III化合物可作為蛋白酶激酶抑制劑且可用以治療及預防增殖性疾病例如癌症、發炎及關節炎。其亦可用於治療神經退化疾病如阿茲海默氏(Alzheimer's)疾病、心臟血管疾

病、病毒疾病及真菌疾病。

【實施方式】

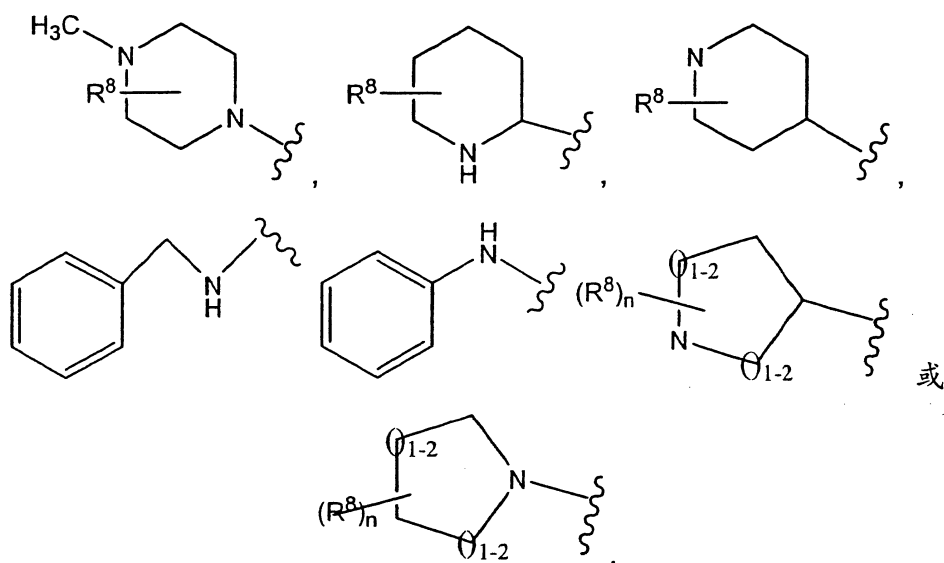
一具體例中，本發明揭示由結構式III所示之吡啶并[1,5-a]嘧啶化合物，或其醫藥可接受性鹽或溶劑化物，其中各種基團如前述定義。

另一具體例中，R為 $-(CHR^5)_n$ -芳基、 $-(CHR^5)_n$ -雜芳基、 $-(CHR^5)_n$ -雜芳基(該雜芳基為經額外之相同或不同之雜芳基取代)、 $-(CHR^5)_n$ -雜環基(該雜環基為經額外之相同或不同之雜環基取代)、或



另一具體例中， R^2 為鹵素、 CF_3 、CN、低碳烷基、經 $-OR^6$ 取代之烷基、炔基、芳基、雜芳基或雜環基。

另一具體例中， R^3 為H、低碳烷基、芳基、雜芳基、環烷基、 $-NR^5R^6$ 、



其中上述 R^3 剛述及之該烷基、芳基、雜芳基、環烷基及雜環基結構視情況經一或多個可相同或不同之基團取代，各基團獨立選自下列所組成之組群：鹵素、 CF_3 、 OCF_3 、低碳烷基、 CN 、 $-C(O)R^5$ 、 $-S(O_2)R^5$ 、 $-C(=NH)-NH_2$ 、 $-C(=CN)-NH_2$ 、羥基烷基、烷氧基羰基、 $-SR^5$ 及 OR^5 ，但條件為與雜環基環上之氮原子相鄰之碳原子不帶有 $-OR^5$ 基。

另一具體例中， R^4 為H或低碳烷基。

另一具體例中， R^5 為H、低碳烷基或環烷基。

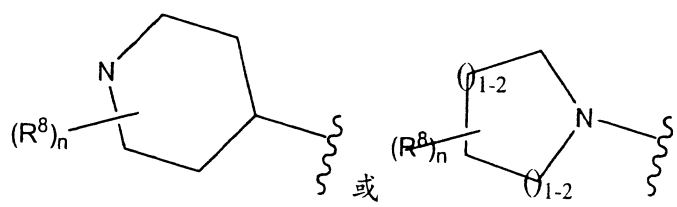
另一具體例中， n 為1至2。

又一具體例中， R 為 $-(CHR^5)_n$ -芳基、 $-(CHR^5)_n$ -雜芳基。

又一具體例中， R^2 為鹵素、 CF_3 、 CN 、低碳烷基、炔基或經 $-OR^6$ 取代之烷基。

又一具體例中， R^2 為低碳烷基、炔基或Br。

又一具體例中， R^3 為H、低碳烷基、芳基、



其中上述 R^3 剛述及之該烷基、芳基及雜環基視情況經一或多個可相同或不同之基團取代，各基團獨立選自下列所組成之組群：鹵素、 CF_3 、低碳烷基、羥基烷基、烷氧基、 $-S(O_2)R^5$

及CN。

又一具體例中， R^4 為H。

又一具體例中， R^5 為H、乙基、環丙基、環丁基、環戊基或環己基。

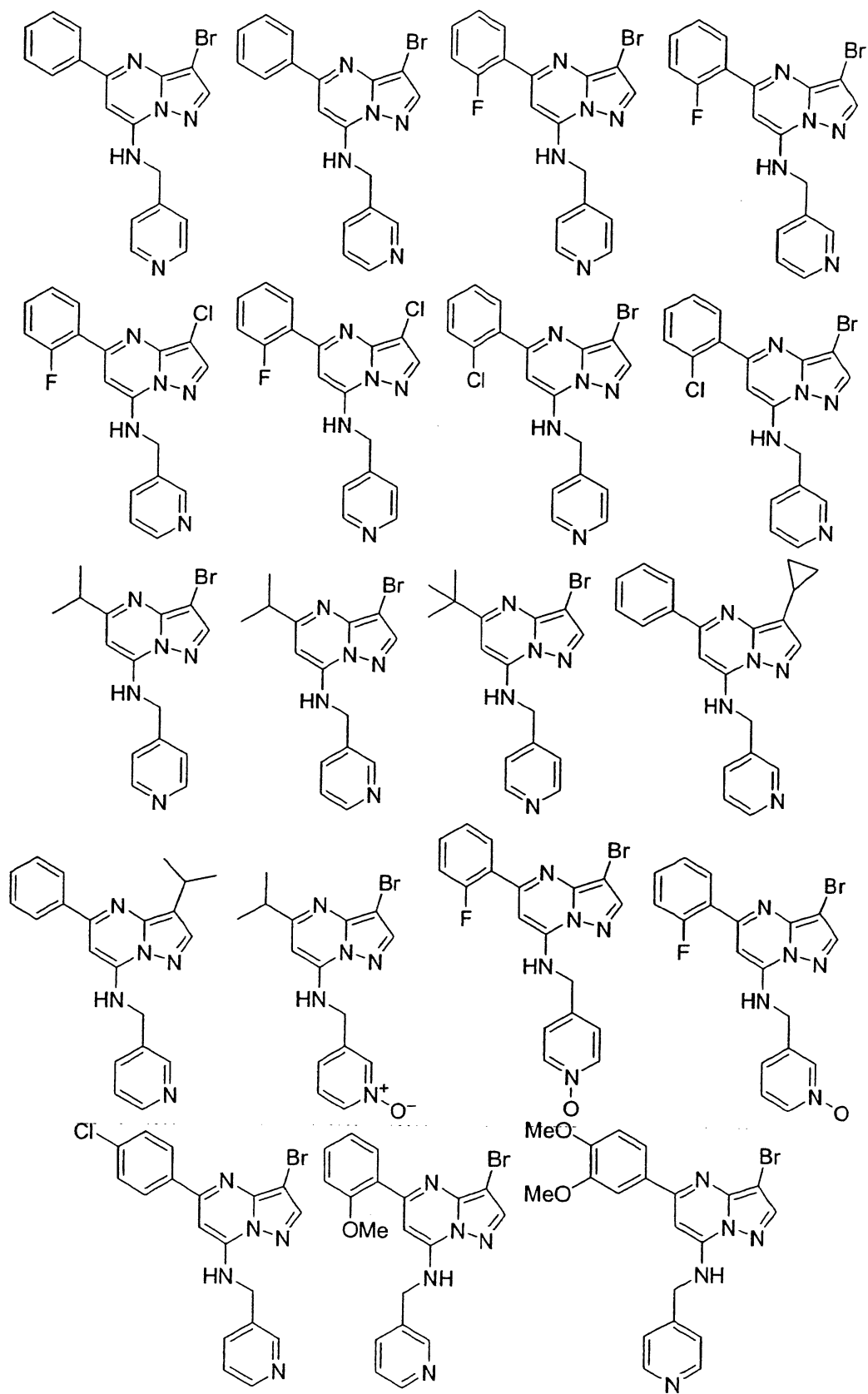
又一具體例中， R^8 為烷基或羥基烷基。

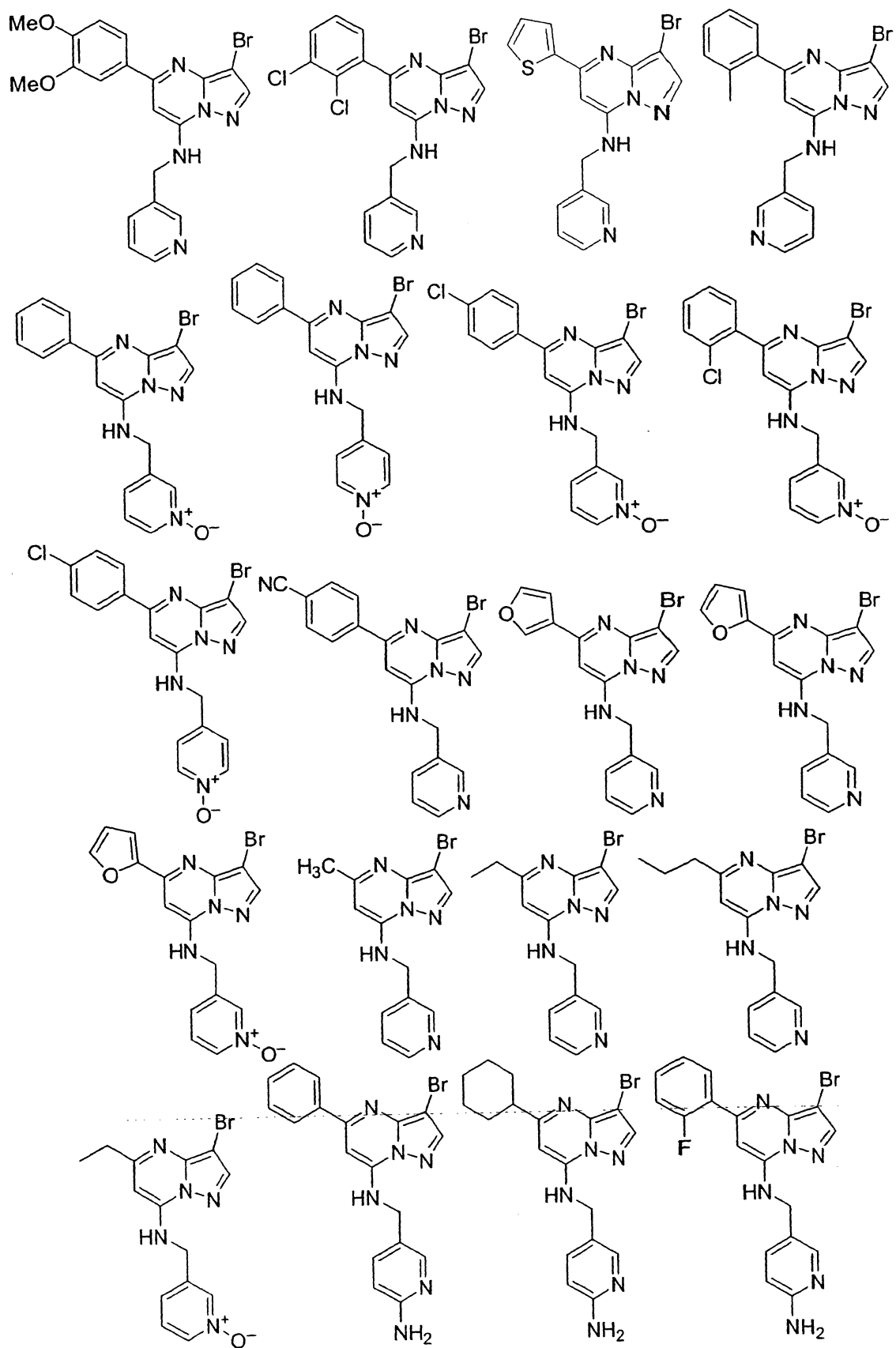
又一具體例中，n為1。

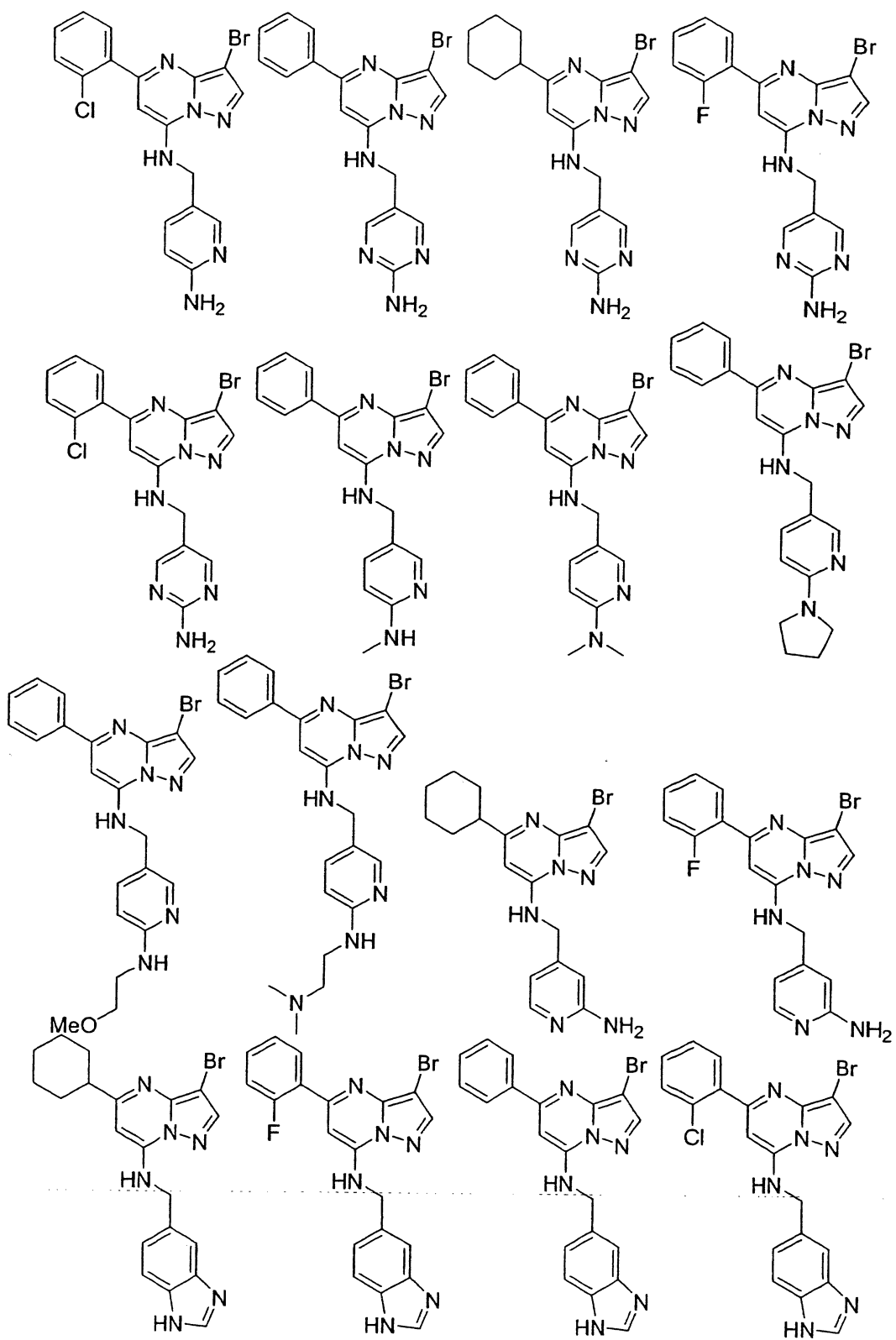
又一具體例中，p為1或2。

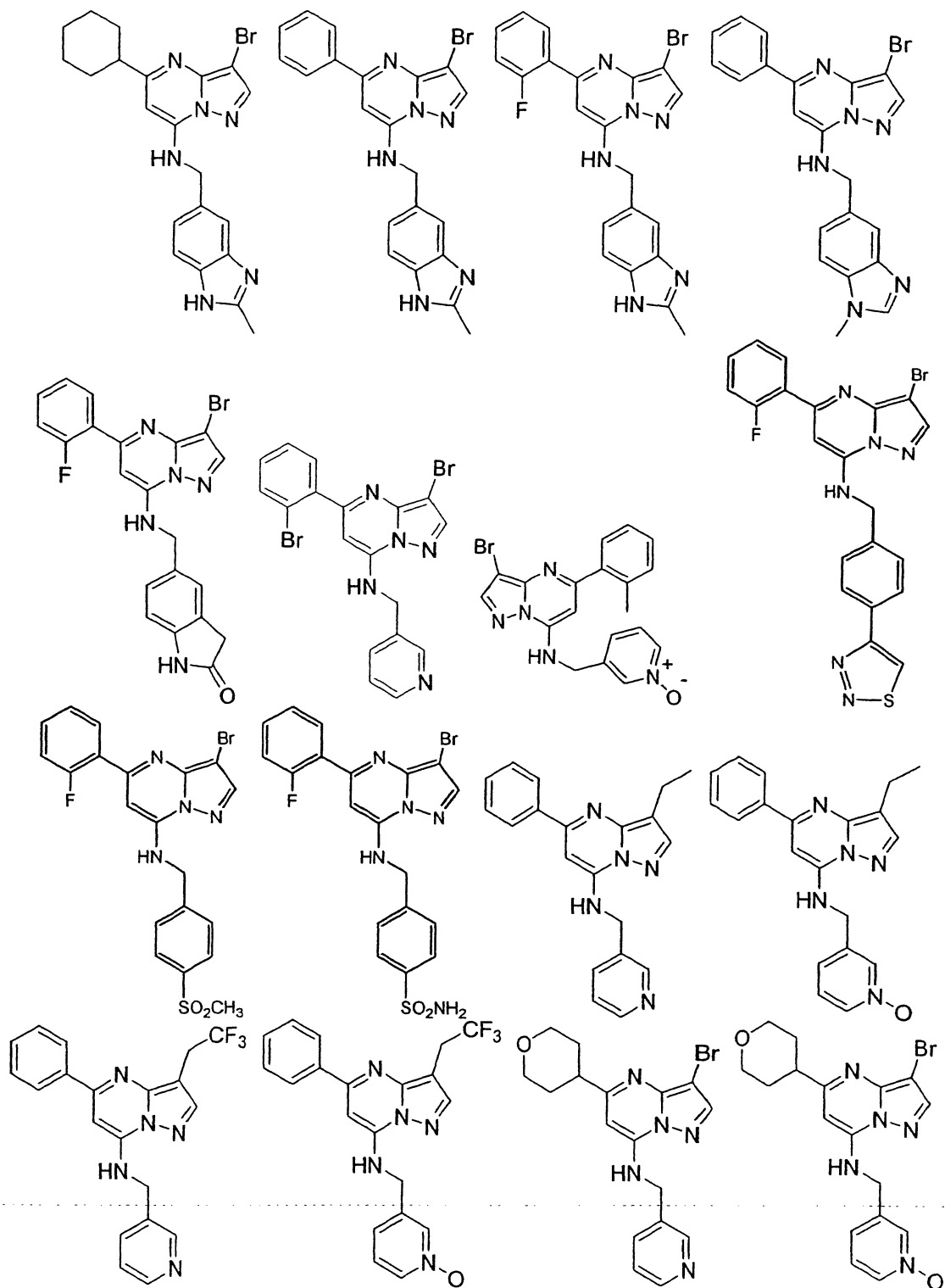
又一具體例揭示表1所示之本發明化合物展現CDK2抑制活性約0.0001 μM 至大於約5 μM 。該分析方法述於後文(下文之第333頁)。

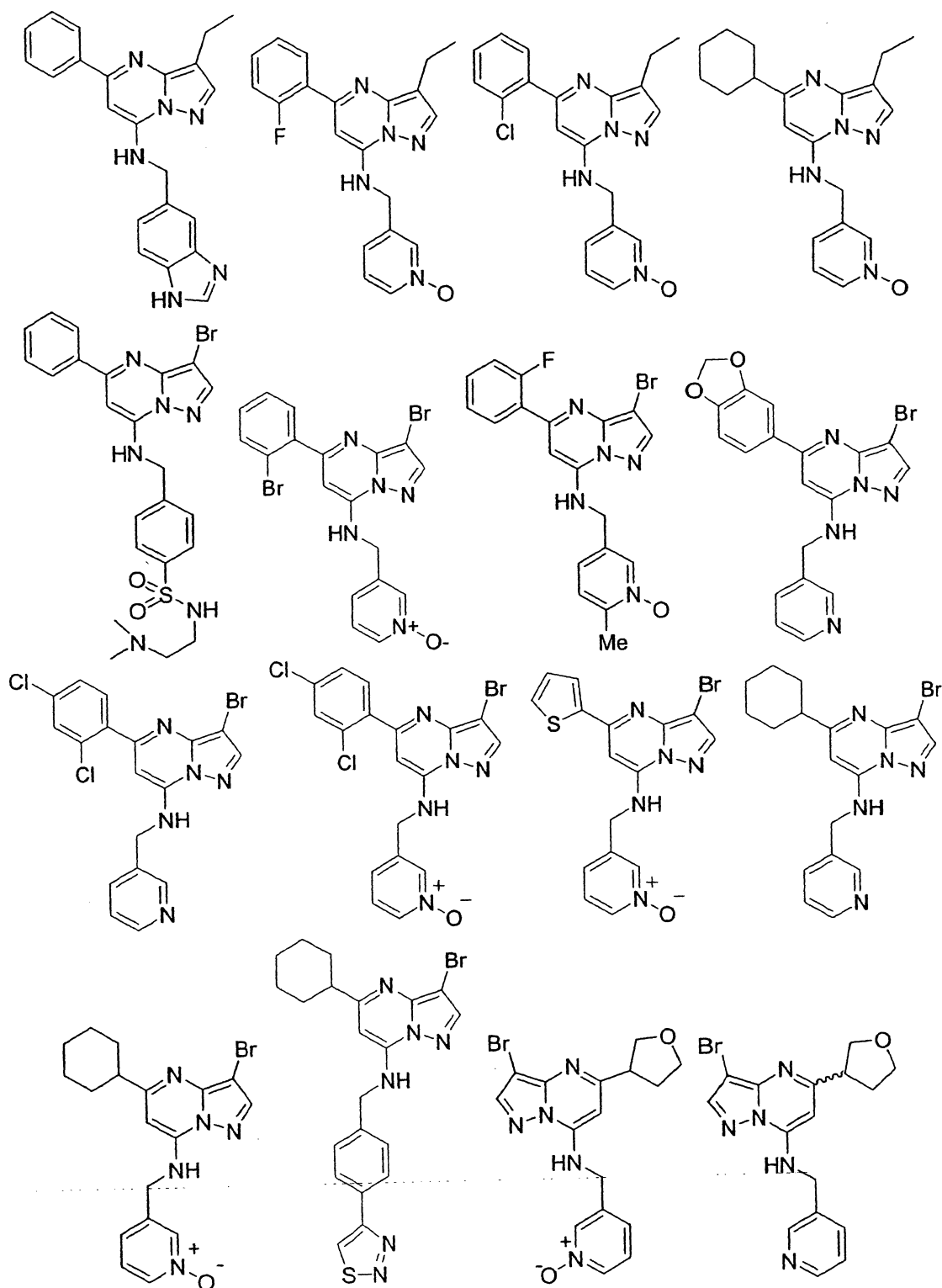
表 1

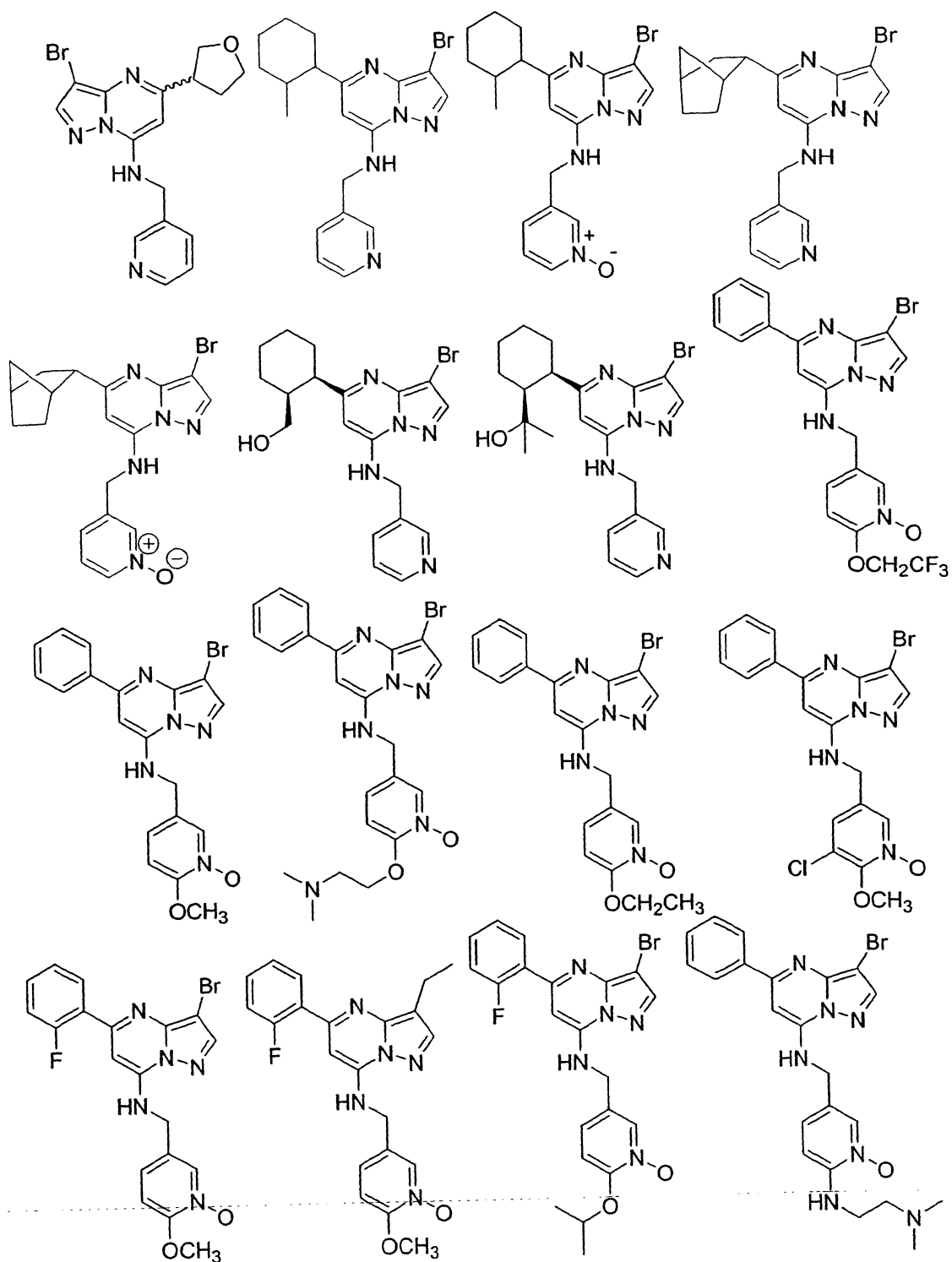


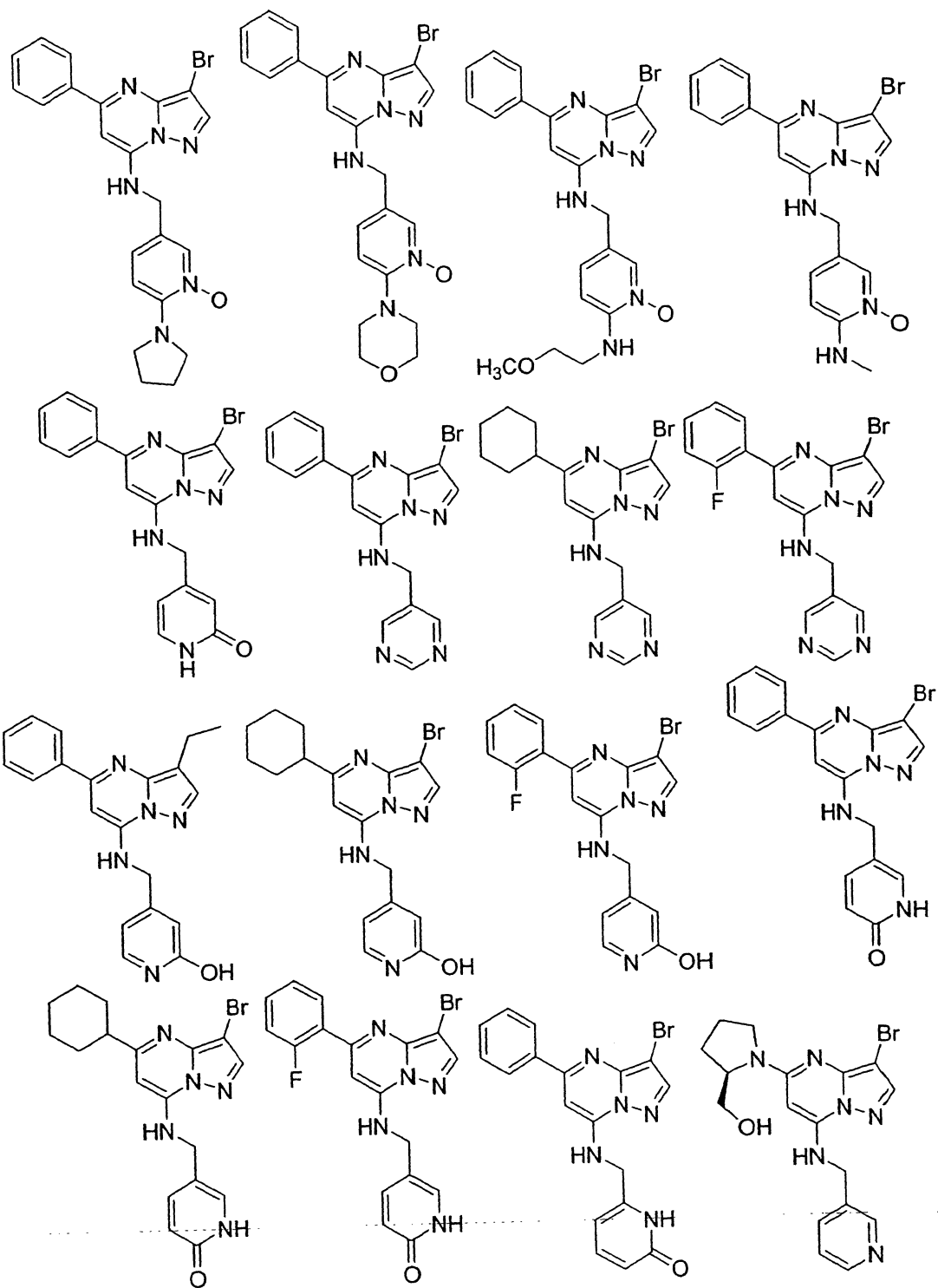


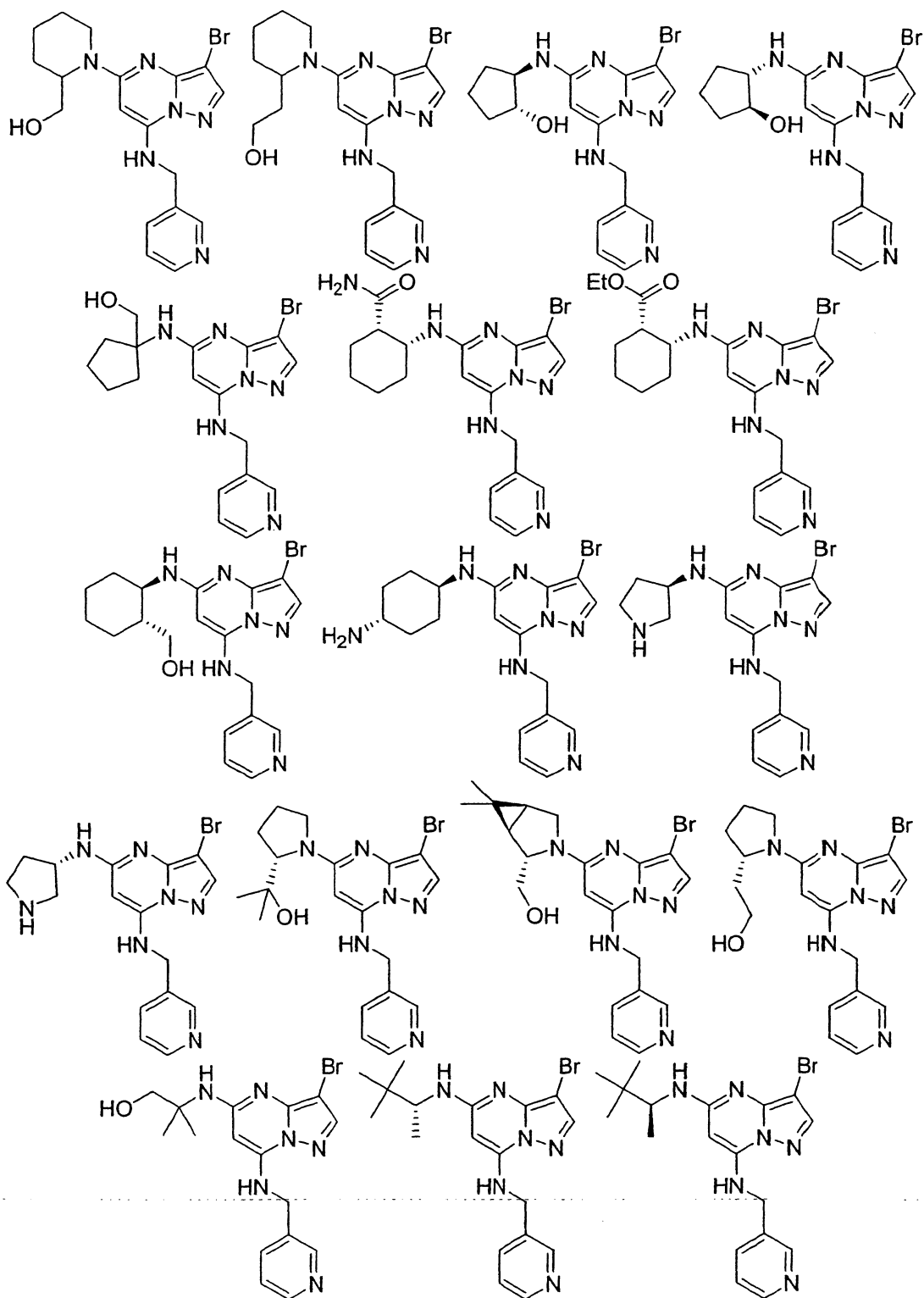


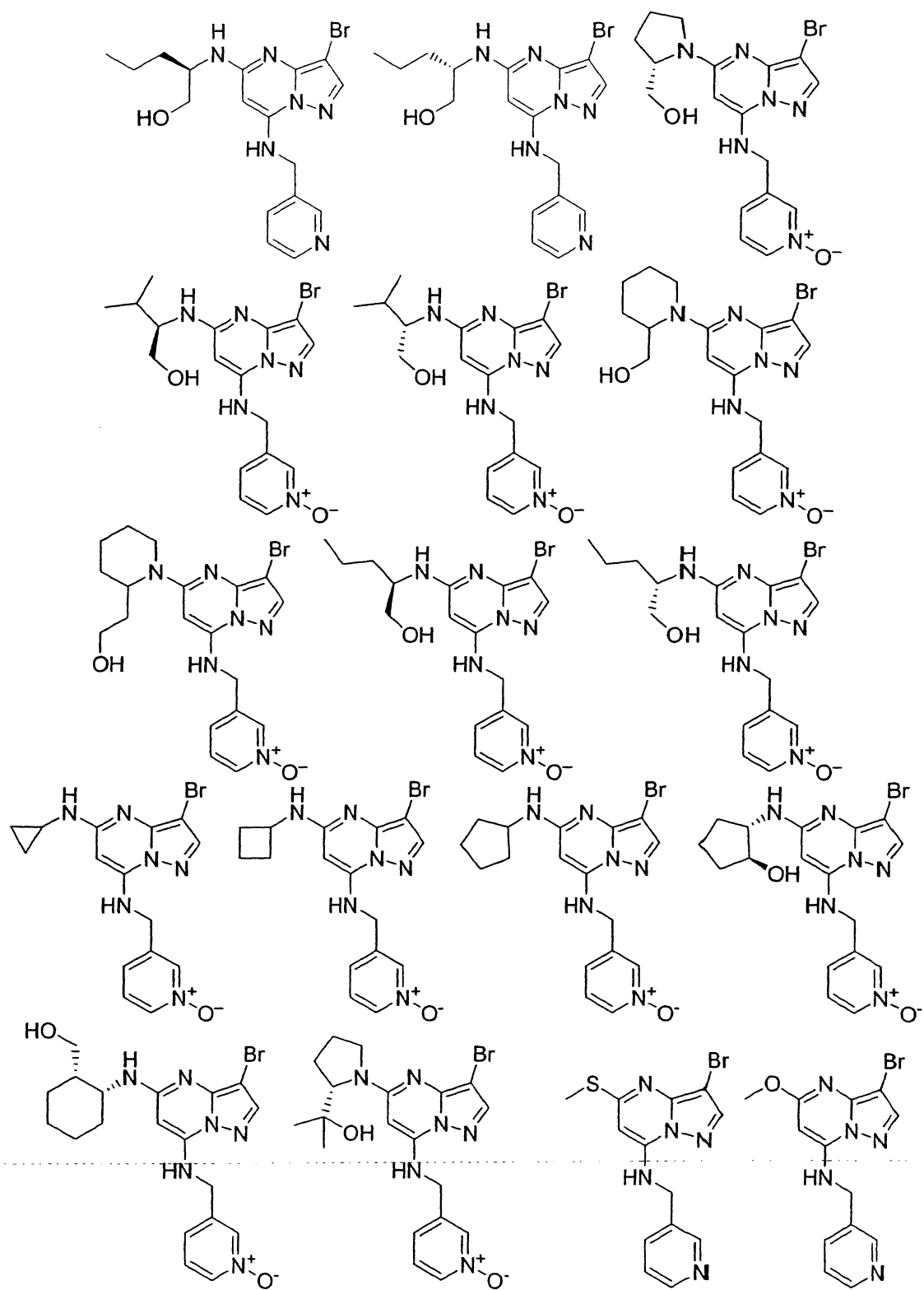


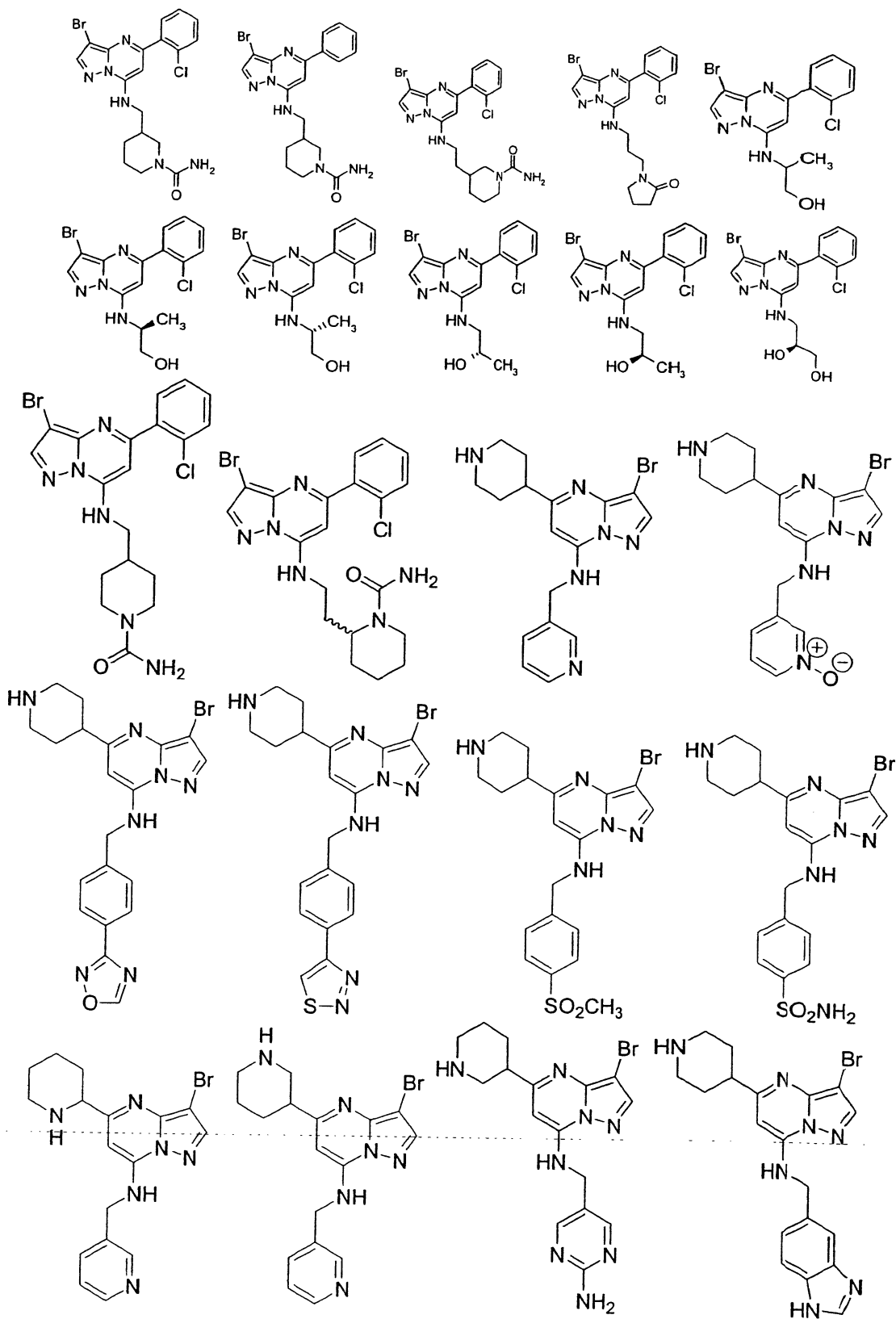


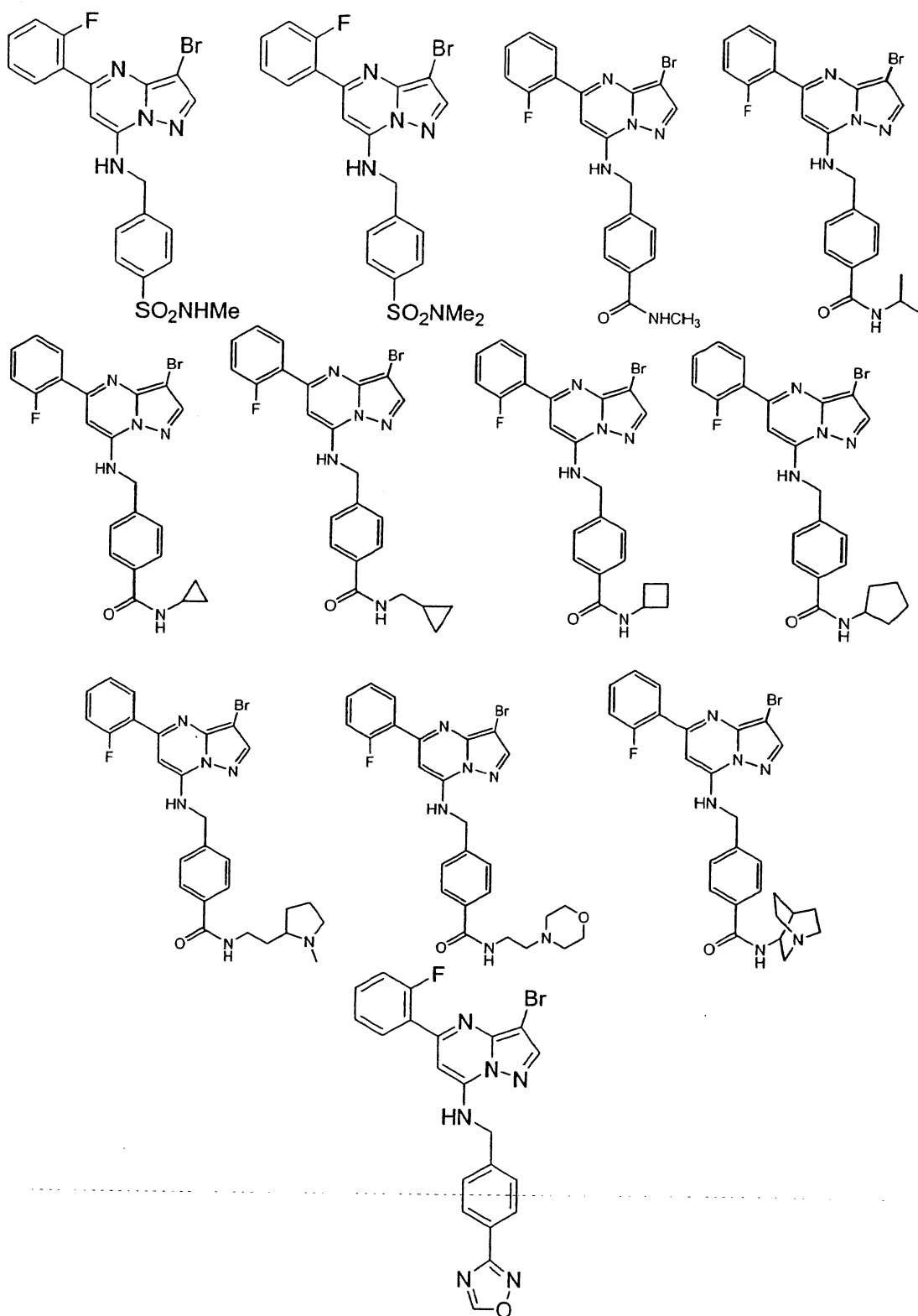


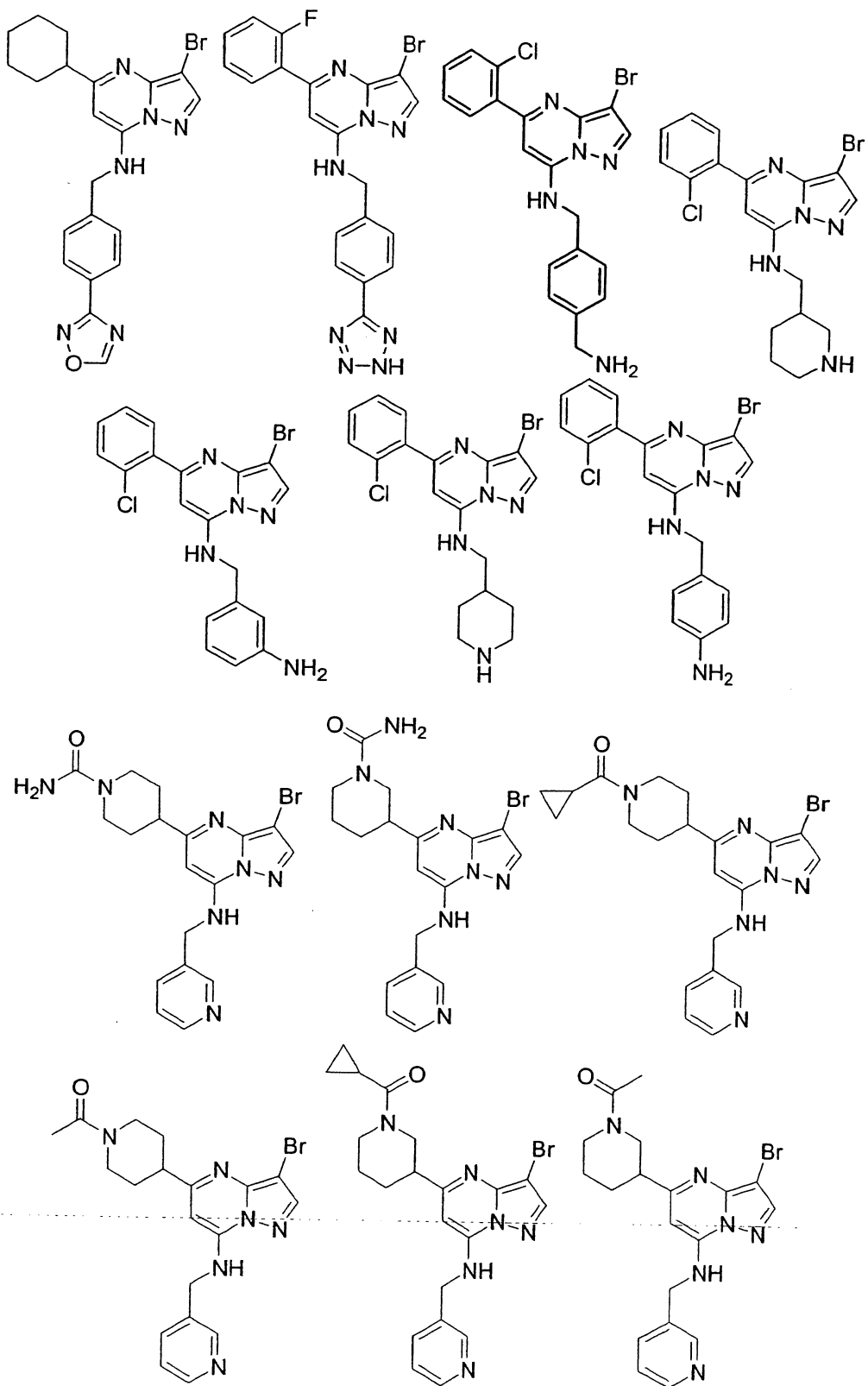


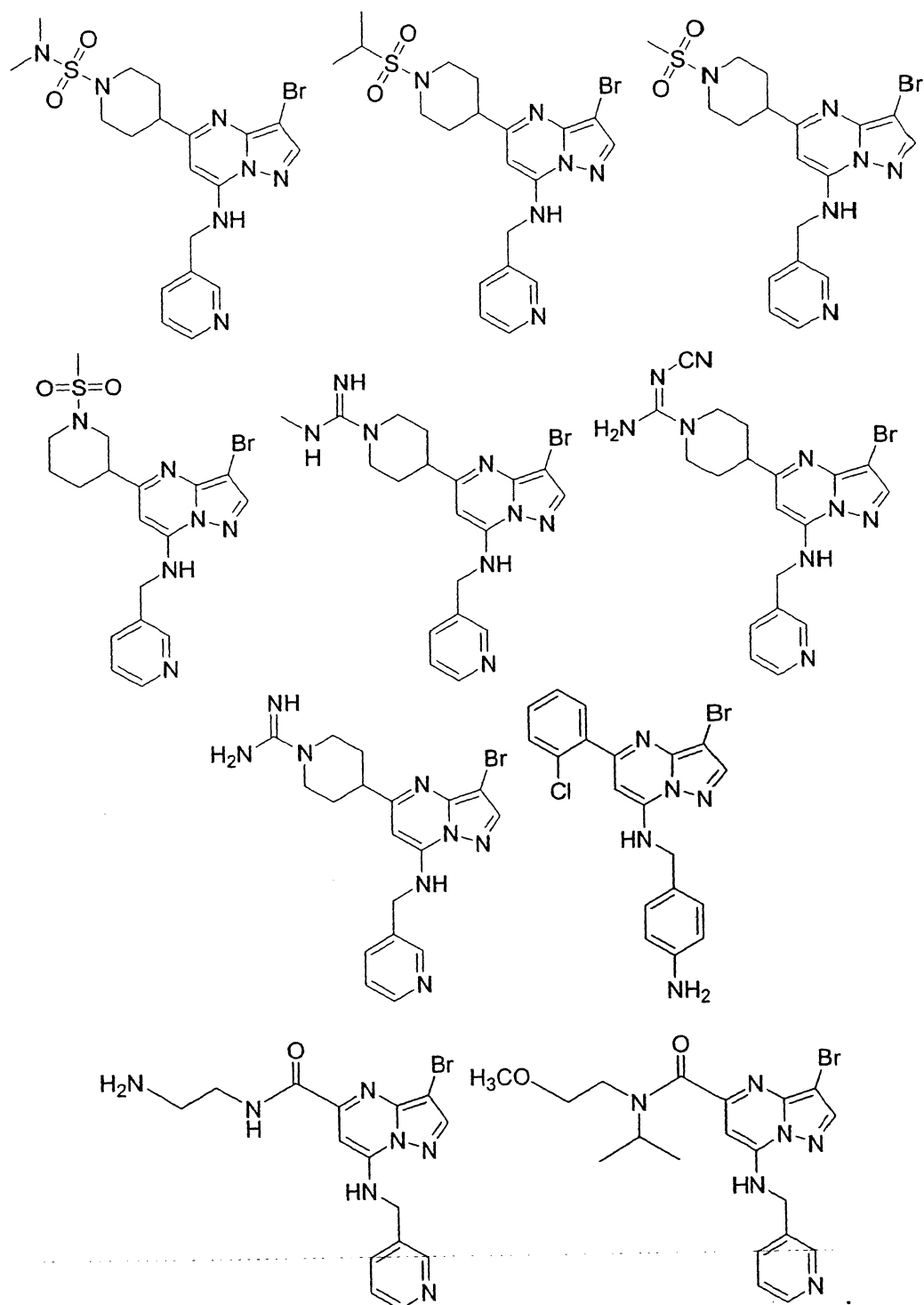




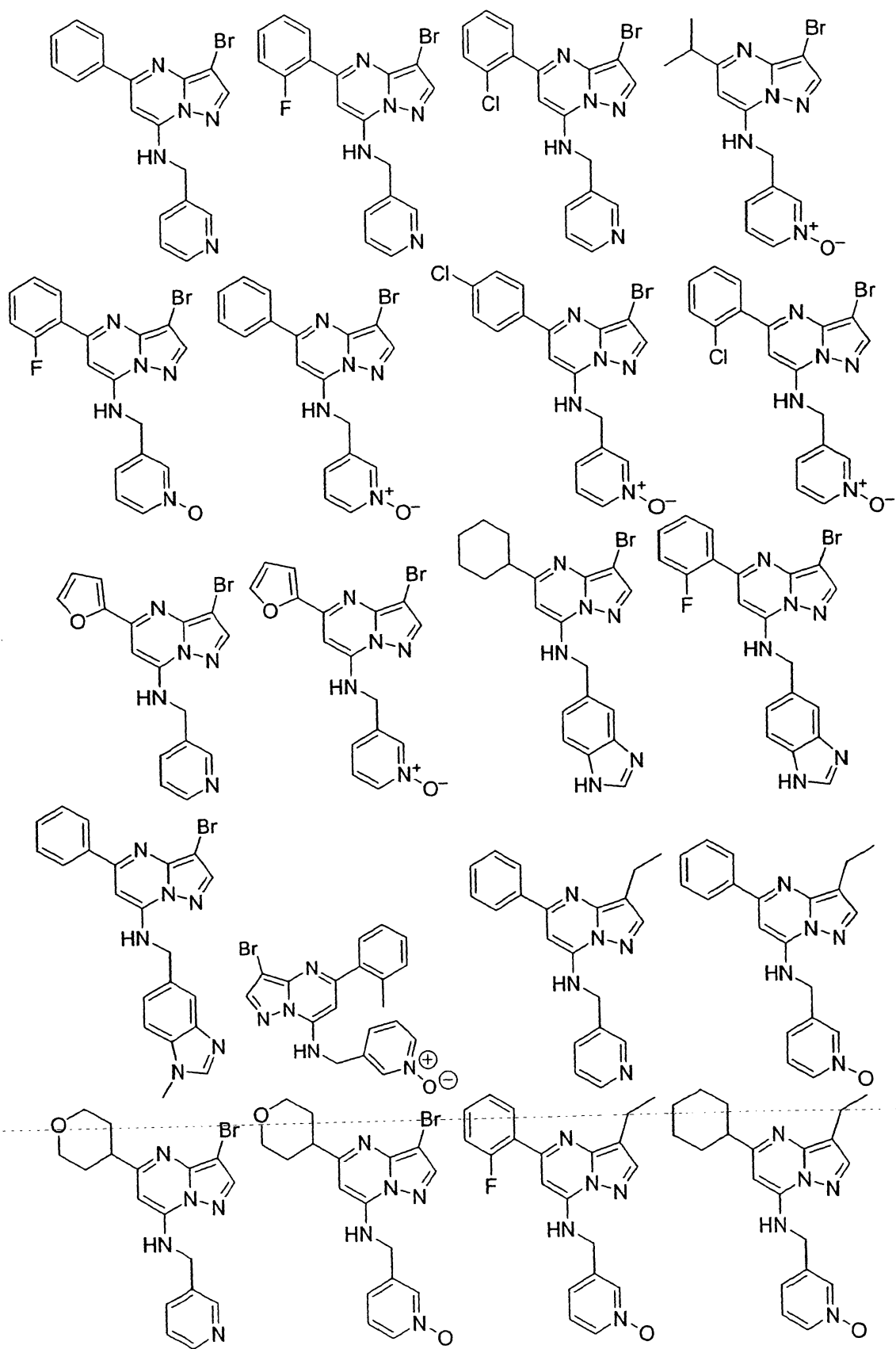


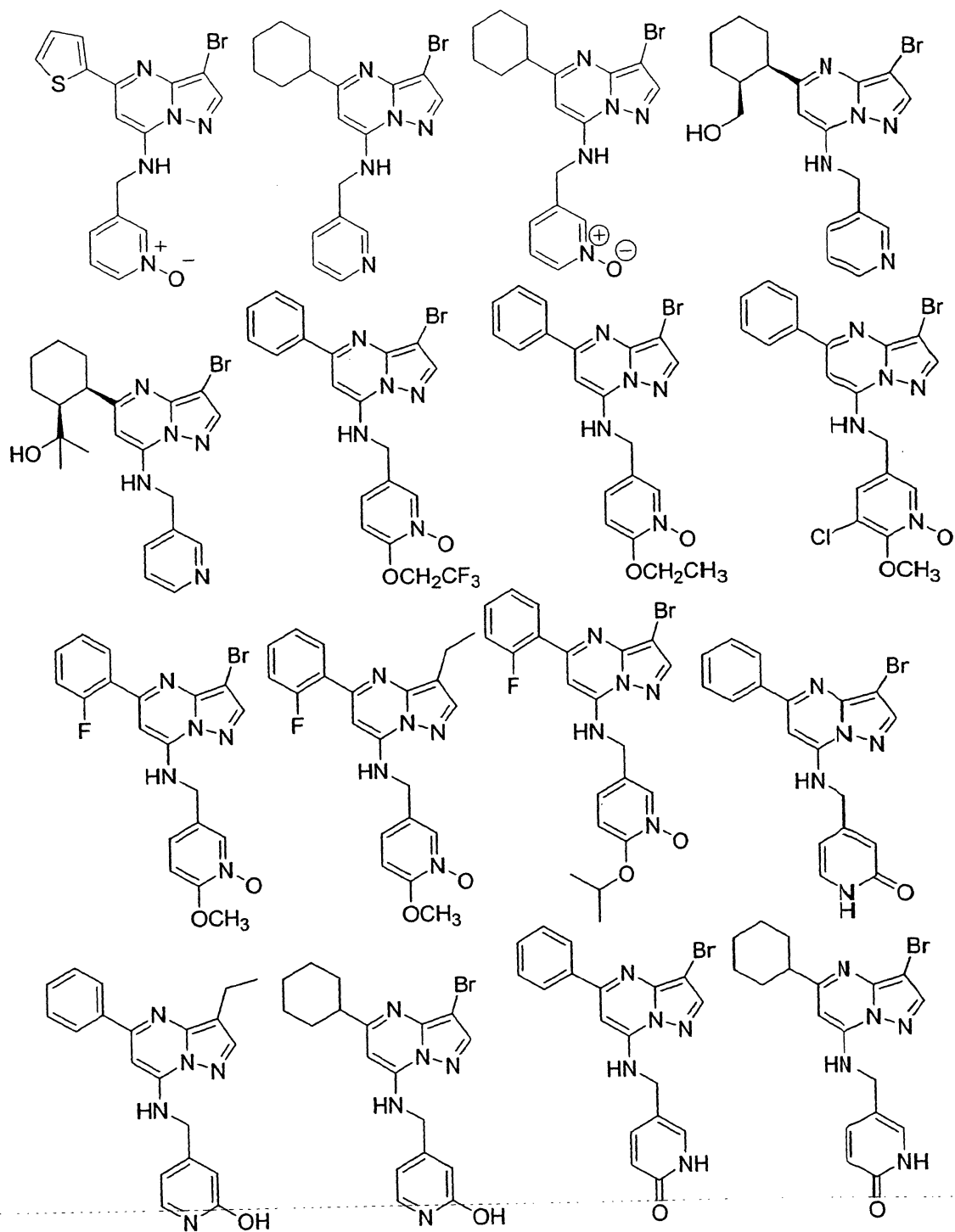


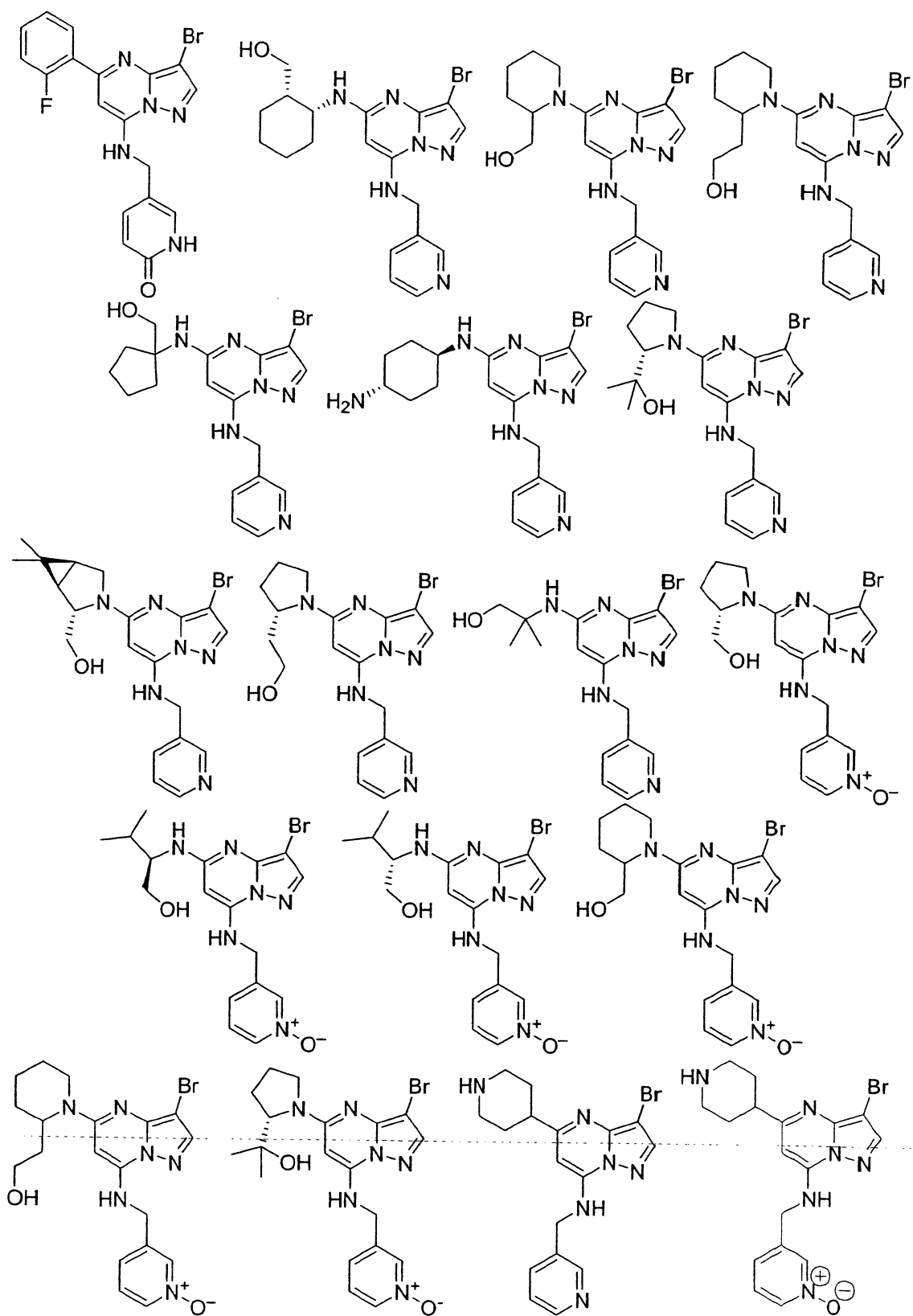


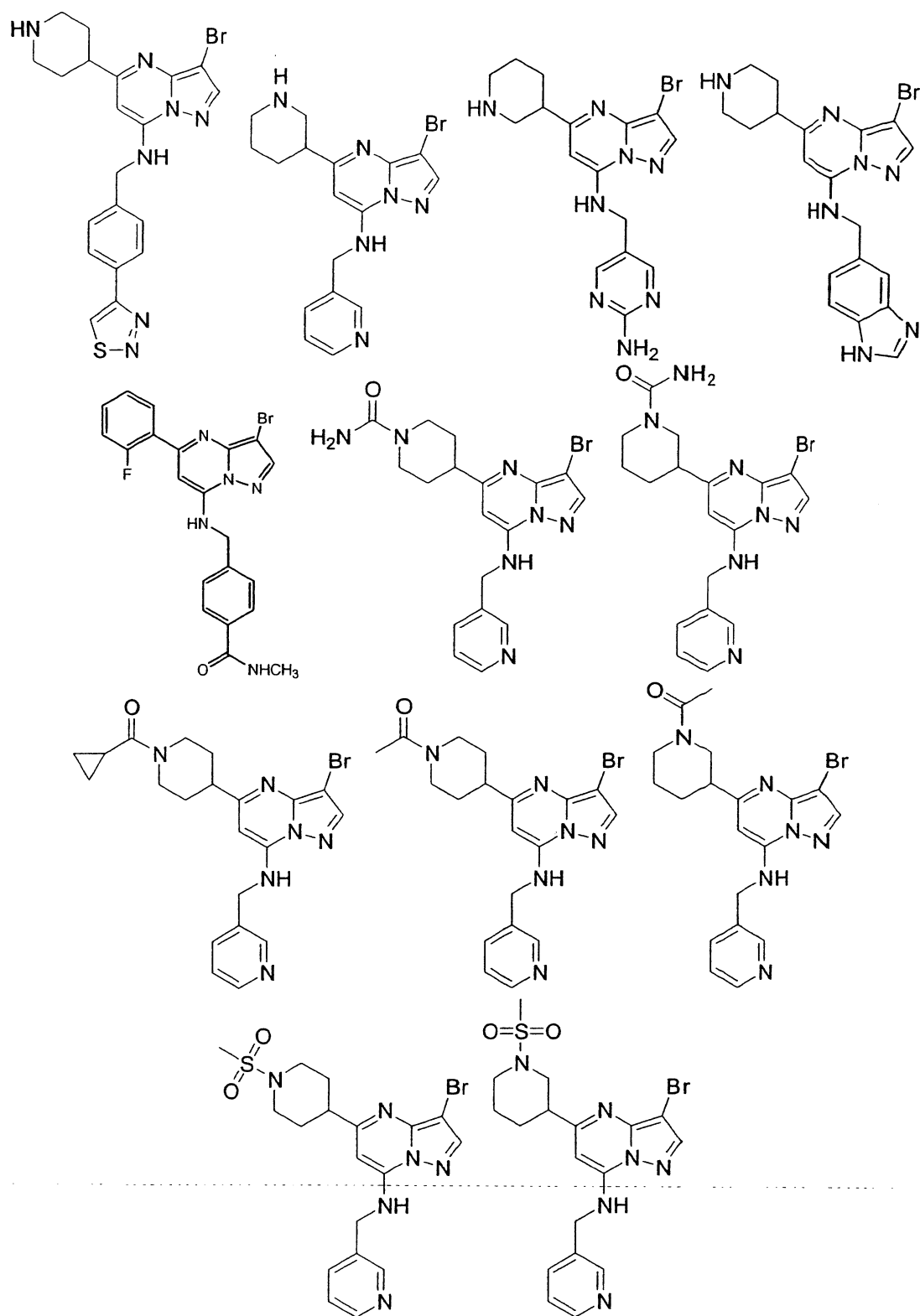


本發明另一具體例揭示下列化合物，其展現CDK2抑制活性約0.0001 μM 至約0.5 μM ：

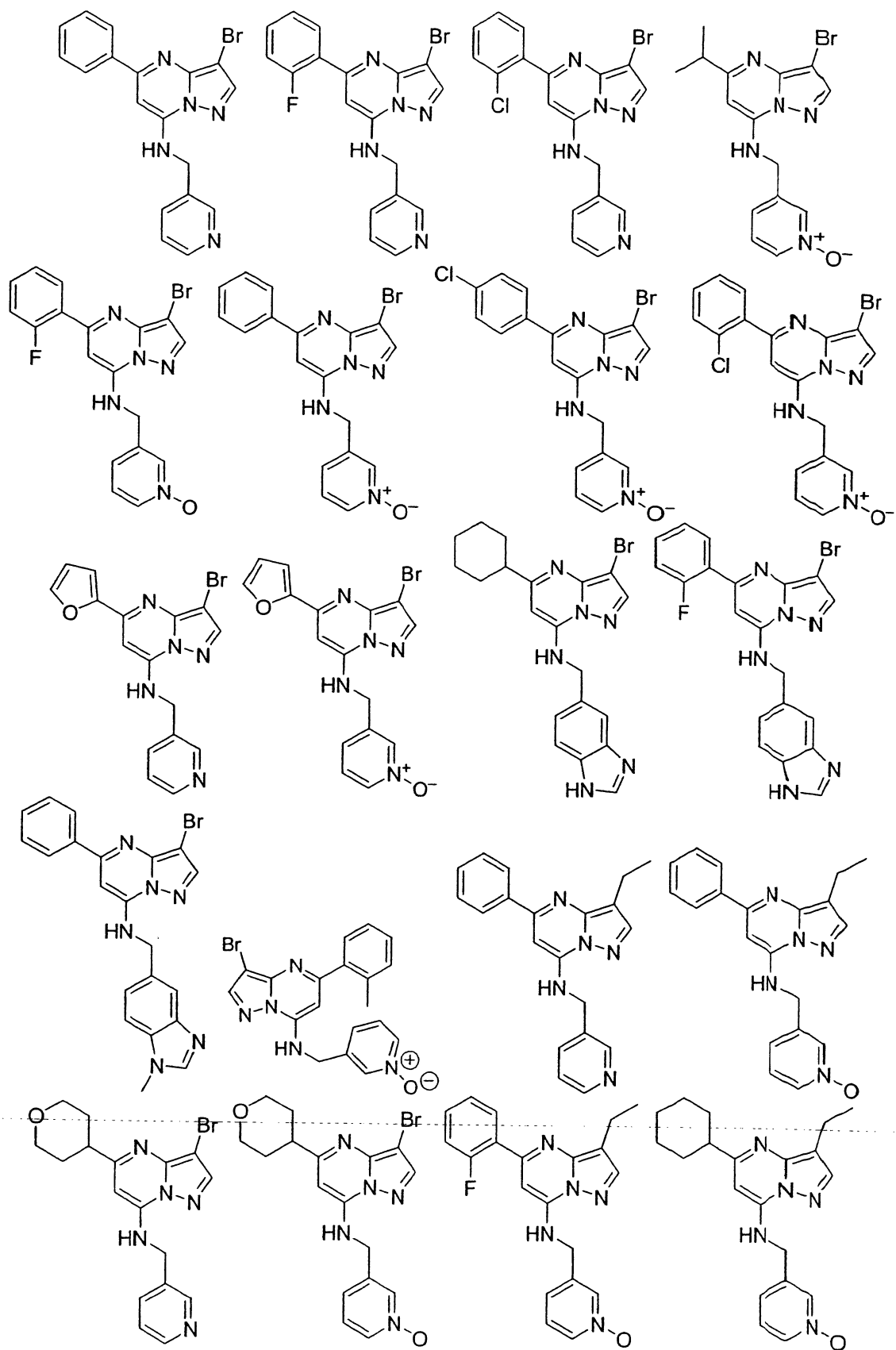


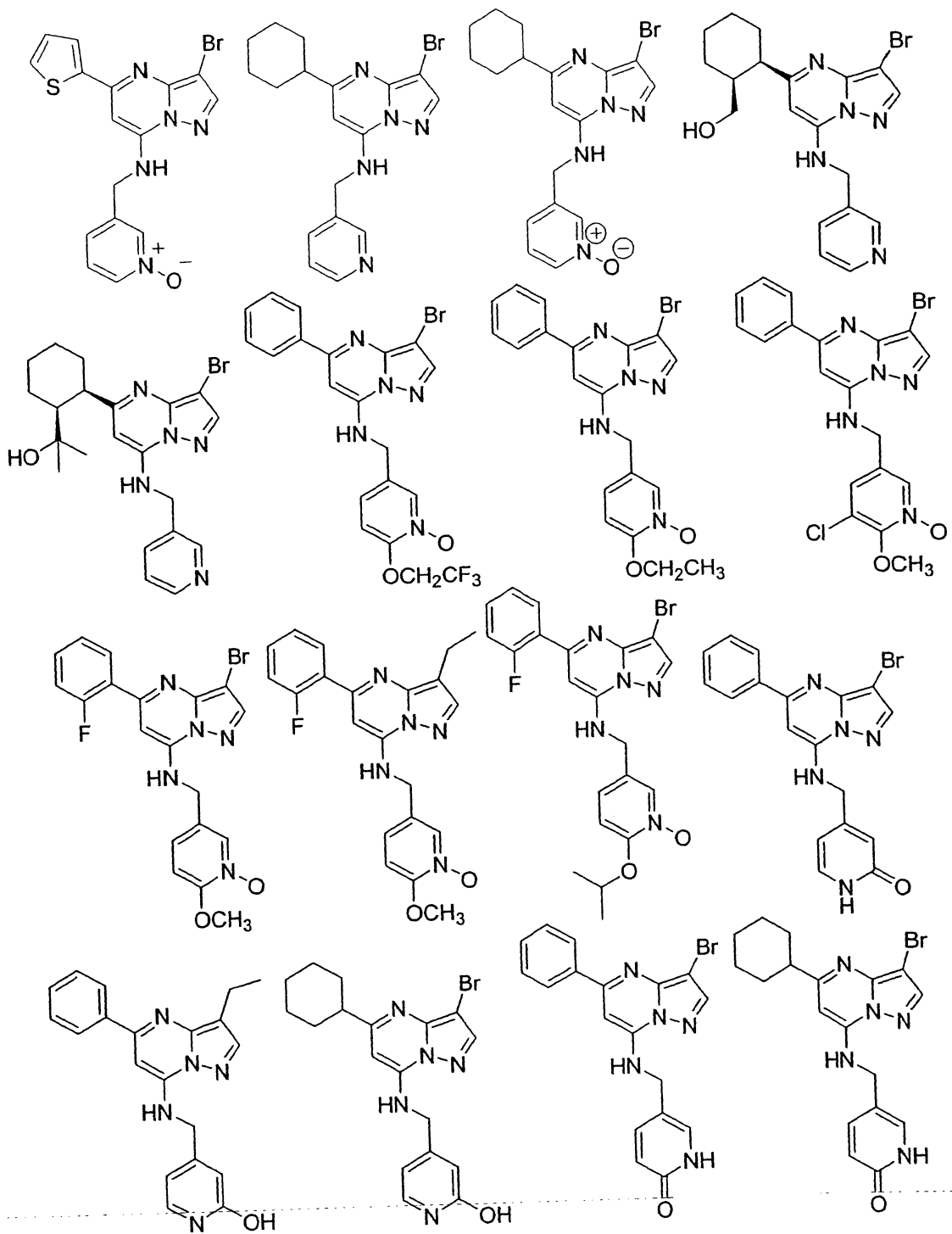


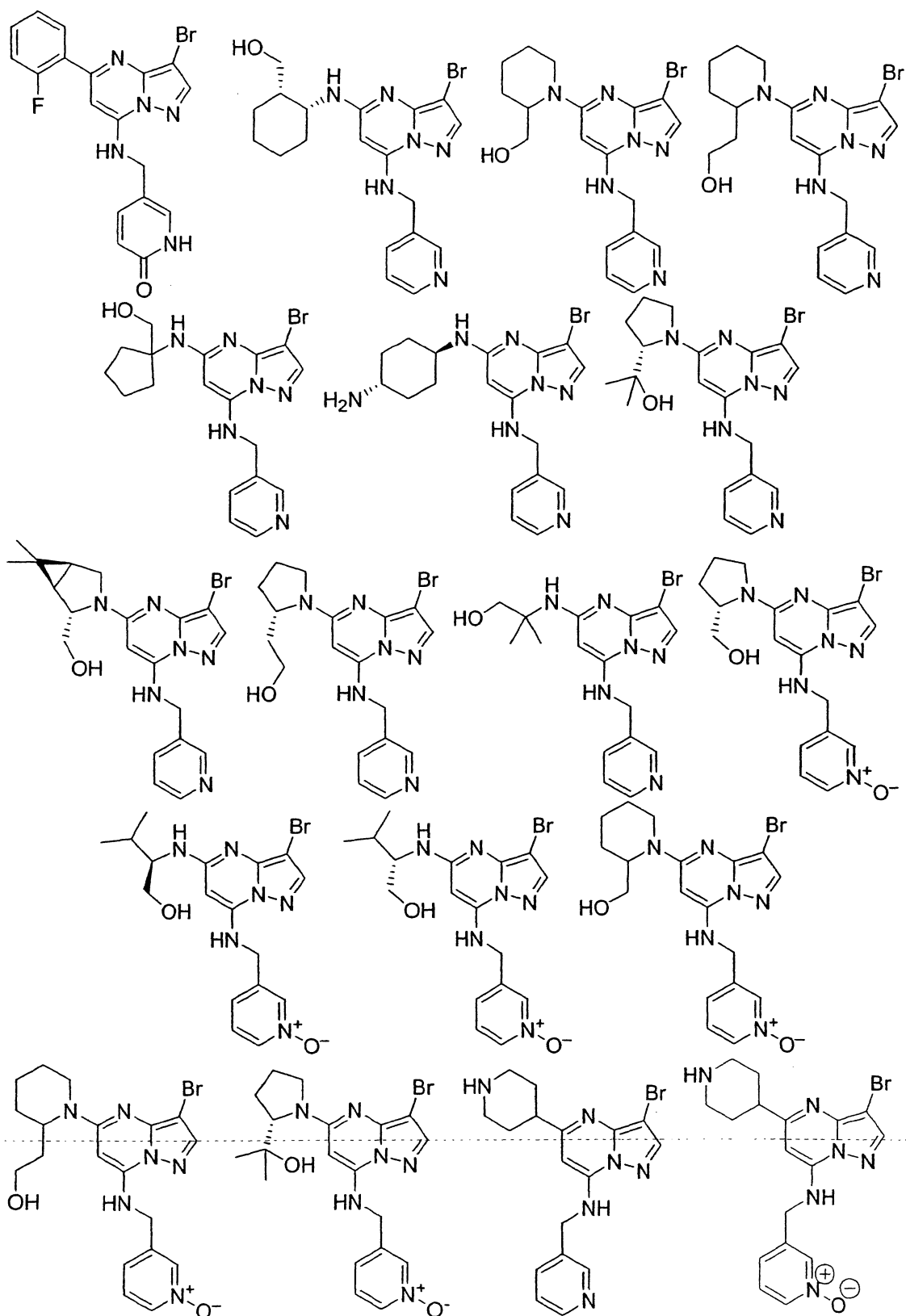


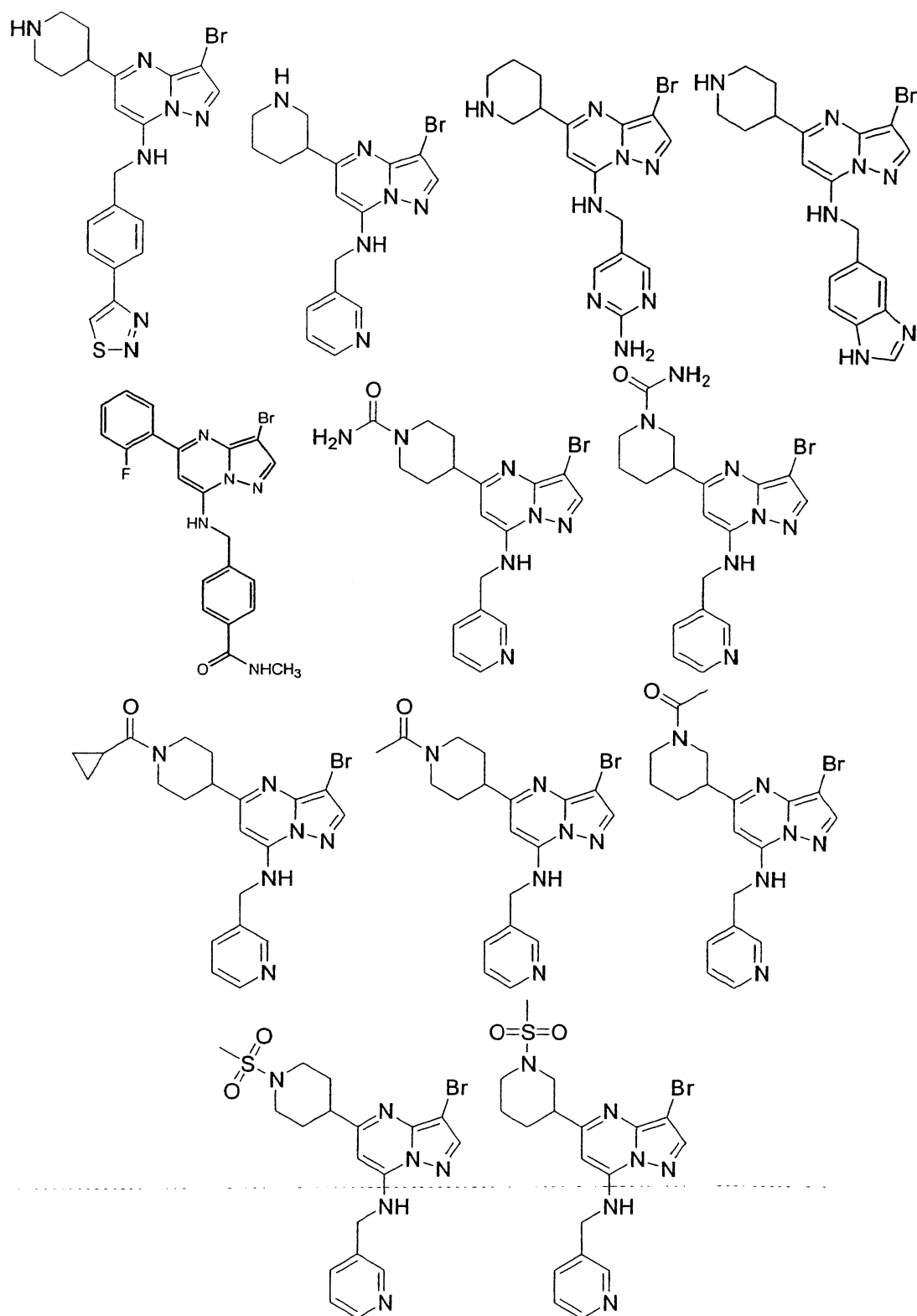


本發明另一具體例揭示下列化合物，其展現CDK2抑制活性約0.0001 μM 至約0.1 μM ：









上述及整個揭示中所用之下列名詞除非另有說明，否則應了解為具有下列意義：

"病患"包含人類及動物。

"哺乳類"意指人類及其他哺乳類動物。

"烷基"意指可為直鏈或分支且在鏈中包括約1至約20個碳原子之脂族烴基。較佳之烷基在鏈中含約1至約12個碳原子。更佳之烷基在鏈中含約1至約6個碳原子。分支意指一或多個低碳烷基如甲基、乙基或丙基鍵結至直鏈烷基鏈上。"低碳烷基"意指鏈中含約1至約6個碳原子且可為直鏈或分支之基。"經取代烷基"意指該烷基可經一或多個可相同或不同之取代基取代，各取代基係獨立選自鹵基、烷基、芳基、環烷基、氰基、羥基、烷氧基、烷硫基、胺基、-NH(烷基)、-NH(環烷基)、-N(烷基)₂、羧基及-C(O)O-烷基所組成之組群。適宜烷基之非限制性實例包含甲基、乙基、正丙基、異丙基及第三丁基。

"炔基"意指含至少一個碳-碳參鍵且可為直鏈或分支且在鏈中包括約2至約15個碳原子之脂族烴基。較佳之炔基在鏈中具有約2至約12個碳原子；且更好鏈中含約2至約4個碳原子。分支意指一或多個低碳烷基如甲基、乙基或丙基鍵結至直鏈炔基鏈上。"低碳炔基"意指鏈中約2至約6個碳原子且可為直鏈或分支之基。適宜炔基之非限制性實例包含乙炔基、丙炔基、2-丁炔基及3-甲基丁炔基。"經取代炔基"意指炔基可經一或多個可相同或不同之取代基取代，各取代基係獨立選自烷基、芳基及環烷基所組成之組群。

"芳基"意指包括約6至約14個碳原子、較好約6至約10個碳原子之芳族單環或多環系統。該芳基可視情況經一或多

個可相同或不同且如本文定義之"環系統取代基"所取代。
適宜芳基之非限制性實例包含苯基及萘基。

"雜芳基"意指包括約5至約14個環原子、較好約5至約10個環原子且其中一或多個環原子為非碳之元素例如氮、氧或硫之單獨或組合狀況之芳族單環或多環系統。較好雜芳基含約5至約6個環原子。該"雜芳基"可視情況經一或多個可相同或不同且如本文定義之"環系統取代基"取代。雜芳基命名前之字首氮雜、氧雜或硫雜分別意指存在有至少一個氮、氧或硫原子作為環原子。雜芳基之氮原子可視情況氧化成對應之N-氧化物。適宜雜芳基之非限制性實例包含吡啶基、吡嗪基、呋喃基、噻吩基、嘧啶基、吡啶酮基(包含N-取代之吡啶酮基)、異喹啉基、異噻啉基、喹啉基、噻啉基、吡啉基、呋咕基、吡咯基、三唑基、1,2,4-噻二唑基、吡嗪基、噻嗪基、喹啉基、呋喃基、氧雜吡啶基、咪唑并[1,2-a]吡啶基、咪唑并[2,1-b]噻啉基、苯并呋咕基、吡啶基、氮雜吡啶基、苯并咪唑基、苯并噻吩基、喹啉基、咪唑基、噻吩并吡啶基、喹啉基、噻吩并嘧啶基、吡咯并吡啶基、咪唑并吡啶基、異喹啉基、苯并氮雜吡啶基、1,2,4-三唑基、苯并噻啉基等。該"雜芳基"一詞亦代表部分飽和之雜芳基基團，如四氫異喹啉基、四氫喹啉基等。

"芳烷基"或"芳基烷基"意指芳基-烷基-，其中芳基及烷基如前述。較佳之芳烷基包括低碳烷基。適宜芳烷基之非限制實例包含苄基、2-苯乙基及萘基甲基。經由烷基與母基團鍵結。

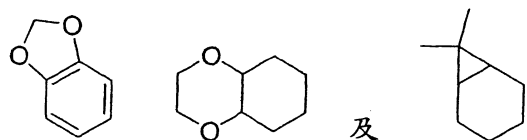
"烷基芳基"意指烷基-芳基-，其中烷基及芳基如前述。較佳之烷基芳基包括低碳烷基。適宜烷基芳基之非限制實例為甲苯基。經由芳基與母基團鍵結。

"環烷基"意指包括約3至約10個碳原子，較好約5至約10個碳原子之非芳族單-或多環系統。較佳之環烷基環含有約5至約7個環原子。環烷基可視情況經一或多個"環系統取代基"取代，其可相同或不同且如前述定義。適宜單環環烷基之非限制實例包含環丙基、環戊基、環己基、環庚基等。適宜多環環烷基之非限制實例包含1-十氫萘基、原冰片基、金剛烷基等以及部分飽和之物種例如茛滿基、四氫萘基等。

"鹵素"意指氟、氯、溴或碘。較佳為氟、氯及溴。

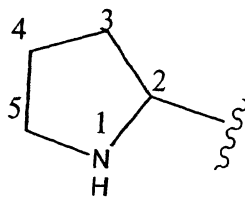
"環系統取代基"意指附接至芳族或非芳族環系統之取代基，其可置換在例如環系統所提供之氮上。環系統取代基可相同或不同，各獨立選自由烷基、烯基、炔基、芳基、雜芳基、芳烷基、烷基芳基、雜芳烷基、雜芳基烯基、雜芳基炔基、烷基雜芳基、羥基、羥基烷基、烷氧基、芳氧基、芳烷基、醯基、芳醯基、鹵基、硝基、氰基、羧基、烷氧基羰基、芳氧基羰基、芳烷基羰基、烷基磺醯基、芳基磺醯基、雜芳基磺醯基、烷硫基、芳硫基、雜芳硫基、芳烷基硫基、雜芳烷基硫基、環烷基、雜環基、 $-C(=N-CN)-NH_2$ 、 $-C(=NH)-NH_2$ 、 $-C(=NH)-NH(\text{烷基})$ 、 Y_1Y_2N- 、 $Y_1Y_2N-\text{烷基}-$ 、 $Y_1Y_2NC(O)-$ 、 $Y_1Y_2NSO_2-$ 及 $-SO_2NY_1Y_2$ 所組成之組群，其中 Y_1 及 Y_2 可相同或不同且獨立選自由氫、烷基、芳基、環烷

基及芳烷基所組成之組群。"環系統取代基"亦可意指同時置換環系統中兩相鄰碳原子上之兩個可提供氫(各碳上一個H)之單一基團。此基團實例為亞甲二氧基、伸乙二氧基、 $-\text{C}(\text{CH}_3)_2-$ 及形成基團之基例如：



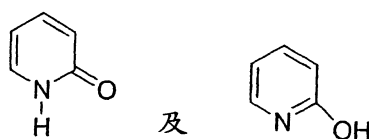
"雜環基"意指包括約3至約10個環原子，較好約5至約10個環原子之非芳族飽和單環或多環系統，其中環系統中一或多個原子為碳以外之元素，例如氮、氧或硫(單獨或組合)。環系統中不存在相鄰氧及/或硫原子。較佳之雜環基含有約5至約6個環原子。雜環基名稱之字首氮雜、氧雜或硫雜分別意指至少存在有氮、氧或硫原子作為環原子。雜環基環中任何-NH可以經保護方式存在例如-N(Boc)、-N(CBz)、-N(Tos)基等；此經保護基團亦視為本發明之一部分。該雜環基可視情況經一或多個"環系統取代基"取代，其可相同或不同且如本文定義。雜環基之氮或硫原子可視情況氧化成對應之N-氧化物、S-氧化物或S,S-二氧化物。適宜單環雜環基環之非限制實例包含哌啶基、吡咯啶基、哌嗪基、嗎啉基、硫嗎啉基、噻唑啶基、1,4-二氧環己基、四氫呋喃基、四氫噻吩基、內醯胺、內酯等。

需注意本發明之含雜原子之環系統中，在相鄰於N、O或S之碳原子上無羥基且在相鄰其他雜原子之碳上無N或S基。因此，例如，下列環中：



-OH基不直接鍵結至標記為2及5之碳上。

亦需注意例如下列基團之互變體：



在本發明某些具體例中視為相等。

"炔基烷基"意指炔基-烷基-，其中炔基及烷基如前述。較佳之炔基含有低碳炔基及低碳烷基。經由烷基鍵結至母基團上。適宜炔基烷基之非限制實例包含炔丙基甲基。

"雜芳烷基"意指雜芳基-烷基-，其中該雜芳基及烷基如前述。較佳之雜芳烷基含有低碳烷基。適宜芳烷基之非限制實例包含吡啶基甲基及喹啉-3-基甲基。經烷基鍵結至母基團上。

"羥基烷基"意指HO-烷基-，其中烷基如前述。較佳之羥基烷基含低碳烷基。適宜羥基烷基之非限制實例包含羥基甲基及2-羥基乙基。

"鹽基"意指H-C(O)-、烷基-C(O)-或環烷基-C(O)-基，其中各種基如前述。經由該羰基鍵結至母基團。較佳之鹽基含低碳烷基。適宜鹽基之非限制實例包含甲鹽基、乙鹽基及丙鹽基。

"芳醯基"意指芳基-C(O)-基，其中芳基如前述。經由該羰基鍵結至母基團。適宜芳醯基之非限制實例包含苯甲醯基及1-萘甲醯基。

"烷氧基"意指烷基-O-基，其中烷基如前述。適宜烷氧基之非限制實例包含甲氧基、乙氧基、正丙氧基、異丙氧基及正丁氧基。係經該醚氧鍵結至母基團。

"芳氧基"意指芳基-O-基，其中芳基如前述。適宜芳氧基之非限制實例包含苯氧基及萘氧基。係經由該醚氧鍵結至母基團。

"芳烷氧基"意指芳烷基-O-基，其中芳烷基如前述。適宜芳烷氧基之非限制實例包含苄氧基及1-或2-萘基甲氧基。係經由醚氧鍵結至母基團。

"烷硫基"意指烷基-S-基，其中烷基如前述。適宜烷硫基之非限制實例包含甲硫基及乙硫基。係經由該硫鍵結至母基團。

"芳硫基"意指芳基-S-基，其中芳基如前述。適宜芳硫基之非限制實例包含苯硫基及萘硫基。係經由該硫鍵結至母基團。

"芳烷硫基"意指芳烷基-S-基，其中芳烷基如前述。適宜芳硫基之非限制實例為苄硫基。係經由該硫鍵結至母基團。

"烷氧基羰基"意指烷基-O-CO-基。適宜烷氧基羰基之非限制實例包含甲氧基羰基及乙氧基羰基。係經由該羰基鍵結至母基團。

"芳氧基羰基"意指芳基-O-C(O)-基。適宜芳氧基羰基之非

限制實例包含苯氧基羰基及萘氧基羰基。係經由該羰基鍵結至母基團。

"芳烷氧基羰基"意指芳烷基-O-C(O)-基。適宜芳烷氧基羰基之非限制實例為苄氧基羰基。係經由該羰基鍵結至母基團。

"烷基磺醯基"意指烷基-S(O₂)-基。較佳之基為其中烷基為低碳烷基者。係經由該磺醯基鍵結至母基團。

"芳基磺醯基"意指芳基-S(O₂)-基。係經由該磺醯基鍵結至母基團。

"經取代"意指在所指定之原子上之一或多個氫經選自所示基置換，但在既有環境下不超過所指定原子之正常價數，且該取代產生穩定化合物。適宜取代基及/或變數之組合若可導致穩定化合物則均可行。"安定化合物"或"安定結構"意指化合物充分穩定而可自反應混合物單離至可用程度之純度並調配成有效之治療劑。

"視情況經取代"意指經特定基、殘基或基團之視情況取代。

對化合物所述之"經單離"或"呈單離態"代表該化合物自合成製程或自天然來源或其組合中單離後之物理狀態。對化合物所述之"經純化"或"呈純化態"代表該化合物自純化製程或自本文所述製程或本技藝悉知製程獲得足夠純度以藉本文所述或本技藝已知標準分析技術特徵化之物理狀態。

需了解說明書、反應圖、實例及表中之具未滿足價數之

任何雜原子係假設具有氫原子以滿足該價數。

當化合物中之官能基稱為"經保護"時，此意指該基為經改質態以在化合物進行反應時，排除在所保護位置上不需要之副反應。適宜保護基將可由熟知本技藝者所了解且可參考標準教科書如 T. W. Greene 等人, 有機合成之保護基 (1991), Wiley, 紐約。

當任何變數(如芳基、雜環基， R^2 等)在任何構成或式 III 中出現一次以上時，其各次出現之定義在每一次其他出現時各有其獨立之定義。

本文所用之"組合物"欲包含包括特定量之特定成分之產品，以及直接或間接源自組合特定量之特定成分之任何產物。

本發明化合物之前藥及溶劑化物亦包含於本文。本文所用之"前藥"代表為藥物前驅物且在對個體投藥後經代謝或化學過程歷經化學轉換產生式 III 化合物或其鹽及/或溶劑化物之化合物。前藥之討論見於 T. Higuchi 及 V. Stella, A.C.S. 研討會系列之作為新穎遞送系統之前藥 (1987)¹⁴ 及藥物設計中之生物可逆載劑, (1987) Edward B. Roche 編輯，美國醫藥協會及派拉蒙出版社，兩者均併於本文供參考。

"溶劑化物"意指本發明化合物與一或多種溶劑分子之物理結合。此物理結合包含變化程度之離子及共價鍵結，包含氫鍵。某些例中，溶劑化物在例如一或多種溶劑分子併入結晶固體之晶格時，將可單離。"溶劑化物"包含溶液相及可單離溶劑化物兩者。適宜溶劑化物之非限制實例包含

乙醇鹽、甲醇鹽等。"水合物"為其中溶劑分子為 H_2O 之溶劑化物。

"有效量"或"治療有效量"意欲描述本發明化合物或組合物有效抑制CDK(s)且因此可產生所需治療、舒緩、抑制或預防效果之量。

式III化合物可形成鹽，其亦在本發明範圍內。有關本文之式III化合物應了解有關其鹽類，除非另有說明。本文所用之"鹽(類)"代表與無機及/或有機酸形成之酸性鹽以及與無機及/或有機鹼形成之鹼性鹽。此外，當式III化合物同時含有鹼性基團如(但不限於)吡啶或咪唑及酸性基團如(但不限於)羧酸時，可形成兩性離子("內鹽")且包含在本文所用之"鹽(類)"名詞中。以醫藥可接受性(亦即非毒性生理可接受)鹽較佳，但亦可使用其他鹽。式III化合物之鹽可例如藉式III化合物與某量之酸或鹼，例如等當量之酸或鹼，在介質如其中鹽可沉澱之介質中或在水性介質中反應，接著凍乾而形成。

例舉之酸加成鹽包含乙酸鹽、抗壞血酸鹽、苯甲酸鹽、苯磺酸鹽、硫酸氫鹽、硼酸鹽、丁酸鹽、檸檬酸鹽、樟腦酸鹽、樟腦磺酸鹽、反丁烯二酸鹽、鹽酸鹽、氫溴酸鹽、氫碘酸鹽、乳酸鹽、順丁烯二酸鹽、甲烷磺酸鹽、萘磺酸鹽、硝酸鹽、草酸鹽、磷酸鹽、丙酸鹽、水楊酸鹽、丁二酸鹽、硫酸鹽、酒石酸鹽、硫代氰酸鹽、甲苯磺酸鹽等。此外，一般被視為適合自鹼性醫藥化合物形成醫藥可接受性鹽之酸討論於例如S. Berge等人，醫藥科學期刊(1977)

66(1) 1-19 ; P. Gould, 國際醫藥期刊 (1986)33 201-217 ; Anderson等人, 醫藥化學實務 (1996), 學院出版社, 紐約 ; 及橘皮書 (食品藥物管理局, 華盛頓 D.C. 之網站)。該等揭示併入本文供參考。

例舉之鹼性鹽包含銨鹽、鹼金屬鹽如鈉、鋰及鉀鹽、鹼土金屬鹽如鈣及鎂鹽、與有機鹼 (例如有機胺) 如二環己基胺、第三丁基胺之鹽、及與胺基酸如精胺酸、離胺酸等之鹽。鹼性含氮基可以例如低碳烷基鹵 (如甲基、乙基及丁基氯化物、溴化物及碘化物)、硫酸二烷酯 (如硫酸二甲酯、二乙酯及二丁酯)、長鏈鹵化物 (如癸基、月桂基及硬脂基氯化物、溴化物及碘化物)、芳烷基鹵化物 (如苄基及苯乙基溴化物) 等予以四級化。

所有此酸鹽及鹼鹽欲在本發明範圍內之醫藥可接受性鹽且所有酸及鹼鹽被視為均等於游離態之本發明目的之對應化合物。

式 III 化合物及其鹽、溶劑化物及前藥可存在為其互變體 (例如 鹽胺或亞胺基醚)。所有此互變態在本文中為本發明之一部分。

本化合物 (包含該化合物之鹽、溶劑化物及前藥以及前藥之鹽及溶劑化物) 之所有立體異構物 (例如幾何異構物、光學異構物等) 例如因各種取代基之不對稱碳而存在之異構物 (包含對映異構物, 其甚至可在無不對稱碳時亦存在)、旋轉異構物、拓撲異構物及非對映異構物均在本發明範圍內, 如同位置異構物 (如 4-吡啶基及 3-吡啶基)。本發明化合物之

個別立體異構物可為例如實質上不含其他異構物或可與例如消旋異構物或與所有其他或其他所選擇之立體異構物混合。本發明之對掌中心可具有如IUPAC 1974命名法所定義之S或R組態。使用"鹽"、"溶劑化物"、"前藥"等名詞欲同等地應用於本發明化合物之對映異構物、立體異構物、旋轉異構物、互變體、位置異構物、消旋物或前藥之鹽、溶劑化物及前藥。

本發明化合物具有藥理性質；尤其，式III化合物可能為蛋白質激酶之抑制劑，如週期素依賴性激酶、有絲分裂原活化之蛋白質激酶(MAPK/ERK)、醣原合成酶激酶3(GSK3 β)等之抑制劑。週期素依賴性激酶(CDKs)包含例如CDC2(CDK1)、CDK2、CDK4、CDK5、CDK6、CDK7及CDK8。式III之新穎化合物預期可用於治療增殖性疾病如癌症、自動免疫疾病、病毒疾病、真菌疾病、神經學/神經退化失調、關節炎、發炎、抗-增殖(如眼睛視網膜病)、神經元、禿髮及心臟血管疾病。該等疾病及失調許多列於前面引述之U.S. 6,413,974，其揭示併於本文供參考。

更詳言之，式III化合物可用於治療各種癌症，包含(但不限於)下列：癌瘤包含(但不限於)膀胱癌、乳癌、結腸癌、腎癌、肝癌、肺癌(包含小細胞肺癌)、食道癌、膽囊癌、卵巢癌、胰癌、胃癌、頸癌、甲狀腺癌、前列腺癌及皮膚癌(包

霍金氏(Hodgkins)淋巴瘤、非霍金氏淋巴瘤、髮細胞淋巴瘤及布克特氏(Burkett's)淋巴瘤；

骨髓系之造血腫瘤，包含急性及慢性骨髓性白血癌、骨髓發育不良徵候群及前骨髓細胞白血癌；

間葉源腫瘤，包含纖維肉瘤及橫紋肌肉瘤；

中樞及末梢神經系統之腫瘤，包含星細胞瘤、神經母細胞瘤、神經膠瘤及神經鞘瘤；及

其他腫瘤，包含黑色瘤、精細胞瘤、畸胎瘤、骨肉瘤、外生性色素頸瘤、keratoctanthoma、甲狀腺卵胞癌及卡波西氏(Kaposi's)肉瘤。

由於CDKs一般在調節細胞增殖上之主要角色，因此抑制劑可作為可逆之制細胞劑，其可用於治療具有異常細胞增殖特徵之任何疾病，如良性前列腺肥大、家族性腺瘤息肉病、神經纖維瘤、動脈硬化、肺纖維化、關節炎、牛皮癬、絲球體腎炎、血管造型術或血管手術後之再阻塞、肥大癥形成、發炎性腸疾病、移植排斥、內毒素休克及真菌感染。

式III化合物亦可用於治療阿茲海默氏疾病，如最近發現CDK5與腦脊髓(tau)蛋白質之磷醯化有關所教示(生物化學期刊(1995)117, 741-749)。

式III化合物可誘發或抑制細胞凋亡。細胞凋亡反應為各種人類疾病之異常現象。式III化合物作為細胞凋亡之調節劑將可用以治療癌症(包含但不限於前述類型者)、病毒感染(包含但不限於疱疹病毒、痘病毒、非洲淋巴細胞瘤病毒、Sindbis病毒及腺病毒)、預防HIV-感染之個體之AIDS發展、

自動免疫疾病(包含但不限于全身性狼瘡、紅斑、自動免疫調節之絲球體腎炎、風濕性關節炎、牛皮癬、發炎性腸疾病及自動免疫糖尿病)、神經退化疾病(包含但不限于阿茲海默氏疾病、AIDS-相關痴呆、帕金森氏(Parkinson's)疾病、肌萎縮性側索硬化、色素性視網膜癌、脊肌肉萎縮及小腦退化)、脊髓發育不良徵候群、成血不全性貧血、與心肌梗塞有關之缺血性損傷，中風及再灌注損傷、節律不整、動脈硬化、毒素誘發或酒精相關性肝疾病、血液學疾病(包含但不限于慢性貧血及成血不全性貧血)、肌肉骨骼系統之退化疾病(包含但不限于骨質疏鬆症及關節炎)、阿斯匹靈敏感性鼻竇炎、囊腫纖維化、多發性硬化、腎疾病及癌疼痛。

式III化合物作為CDKs抑制劑可調節細胞RNA及DNA合成量。該等藥劑因此可用於治療病毒感染(包含但不限于HIV、人類乳頭狀瘤病毒、疱疹病毒、痘病毒、非洲淋巴瘤病毒、Sindbis病毒及腺病毒)。

式III化合物亦可用於化學預防癌症。化學預防定義為藉阻斷起始之突變事件或藉阻斷已被傷害之惡性瘤細胞前之發展而抑制侵入性癌發展或抑制腫瘤復發。

式III化合物亦可用以抑制腫瘤血管形成及遷移。

式III化合物亦可作為其他蛋白質激酶如蛋白質激酶C、her2、raf1、MEK1、MAP激酶、EGF受體、PDGF受體、IGF受體、PI3激酶、weel激酶、Src、Abl之抑制劑且因此可有效治療與其他蛋白質激酶有關之疾病。

本發明另一目的係治療患有受CDKs調節之疾病或病況

之哺乳類(如人類)之方法，係對該哺乳類投與治療有效量之至少一種式III化合物或該化合物之醫藥可接受性鹽或溶劑化物。

式III化合物之較佳劑量約0.001至500毫克/公斤體重/天。特佳之劑量約0.01至25毫克/公斤體重/天之式III化合物或該化合物之醫藥可接受性鹽或溶劑化物。

本發明化合物亦可與一或多種抗癌療法如放射療法及/或一或多種抗癌劑組合(一起或依序投予)投藥，該抗癌劑係選自制細胞劑、細胞毒素劑(例如但不限於DNA相互作用藥劑(如順氯胺鉑或多索鹵賓(doxorubicin)))；坦烷(taxanes)(如坦羅特(taxotere)、坦醇(taxol))；拓樸異構酶II抑制劑(如依托塞(etoposide))；拓樸異構酶I抑制劑(如艾諾泰肯(irinotecan)(或CPT-11)、肯托斯塔(camptostar)或托譜泰肯(topotecan))；小管相互作用劑(如帕克利坦(paclitaxel)、多塞坦(docetaxel)或艾譜塞酮(epothilones))；荷爾蒙劑(如坦墨希分(tamoxifen))；胸腺嘧啶脫氧核苷酸合成酶抑制劑(如5-氟尿嘧啶)；抗-代謝劑(如胺甲喋呤(methotrexate))；烷化劑(如泰默醯胺(temozolomide)(TEMODARTM購自Schering-Plough公司，Kenilworth，紐澤西州)、環磷醯胺)；法呢基蛋白質轉移酶抑制劑(如SARASARTM(4-[2-[4-[(11R)-3,10-二溴-8-氯-6,11-二氫-5H-苯并[5,6]環庚并[1,2-b]吡啶-11-基]-1-哌啶基]-2-氧代乙基]-1-哌啶羧醯胺)或SCH 66336購自Schering-Plough公司，Kenilworth，紐澤西州)、替普法尼(tipifarnib)(Zarnestra®或R115777，購自Janssen醫藥公司)、

L778,123 (法呢基蛋白質轉移酶抑制劑，購自Merck公司，白宮區，紐澤西州)、BMS 214662 (法呢基蛋白質轉移酶抑制劑，購自Bristol-Myers Squibb醫藥公司，Princeton，紐澤西州)；訊號傳導抑制劑(如愛利沙(Iressa) (購自Astra Zeneca醫藥公司，英國)、塔希瓦(Tarceva) (EGFR激酶抑制劑)、對EGFR之抗體(如C225)、GLEEVECTM (C-abl激酶抑制劑，購自Novartis醫藥公司，East Hanover，紐澤西州)；干擾素如干擾酮(intron) (購自Schering-Plough公司)、Peg-干擾酮(Peg-Intron)(購自Schering-Plough公司)；荷爾蒙治療組合；芳族酶組合；ara-C、阿霉素(adriamycin)、胞色烷(cytosan)及葛希塔賓(gemcitabine)。

其他抗癌劑(亦稱為抗贅瘤劑)，包含(但不限於)尿嘧啶氮芥、氮芥(Chlormethine)、艾法鹽胺(Ifosfamide)、美法倫(Melphalan)、苯丁酸氮芥(Chlorambucil)、柏溴烷(Pipobroman)、曲他胺(Triethylenemelamine)、三伸乙基硫代磷鹽胺(Triethylenethiophosphoramine)、馬利蘭(Busulfan)、卡默斯汀(Carmustine)、羅姆斯汀(Lomustine)、斯特唑辛(Streptozocin)、達卡貝啖(Dacarbazine)、氟索利啶(Floxuridine)、塞塔賓(Cytarabine)、6-氫硫基嘌呤、6-硫代胍、磷酸氟達賓(Fludarabine phosphate)、喙利鉑(oxaliplatin)、雷可瓦寧(leucovirin)、喙利鉑(ELOXATINTM，購自Sanofi-Synthelabo 醫藥公司，法國)、分妥斯達汀(Pentostatine)、長春鹼、長春新鹼、長春地辛(Vindesine)、平陽黴素(Bleomycin)、更生黴素(Dactinomycin)、柔紅黴素

(Daunorubicin)、多索鹵賓(Doxorubicin)、艾比鹵賓(Epirubicin)、艾達鹵賓(Idarubicin)、光輝黴素(Mithramycin)、去氧助間型黴素(Deoxycoformycin)、絲裂黴素-C(Mitomycin-C)、L-門冬醯胺酶、替尼泊(Teniposide) 17 α -乙炔基雌二醇、己烯雌酚、睪酮、潑尼松(Prednisone)、氟甲睪酮(Fluoxymesterone)、多莫斯坦酮丙酸鹽(Dromostanolone propionate)、睪內酯(Testolactone)、甲地孕酮乙酸鹽(Megestrolacetate)、甲基潑尼松、甲基睪丸酮、強的松(Prednisolone)、鼻浪花(Triamcinolone)、氯烯雌醚(Chlorotrianisene)、羥孕酮(Hydroxyprogesterone)、胺鹵米特(Aminoglutethimide)、雌莫斯汀(Estramustine)、甲羥孕酮乙酸鹽(Medroxyprogesteroneacetate)、利普胺(Leuprolide)、福特胺(Flutamide)、托瑞米分(Toremifene)、高瑞林(goserelin)、順氯胺鉑、碳胺鉑(Carboplatin)、羥基尿素、胺沙林(Amsacrine)、普卡貝吡(Procarbazine)、米多坦(Mitotane)、米托山酮(Mitoxantrone)、左米梭(Levamisole)、納瓦賓(Navelbene)、胺斯塔唑(Anastrozole)、雷塔唑(Letrozole)、卡配烯塔賓(Capecitabine)、雷羅色分(Reloxafine)、多羅塞分(Droxifene)或六甲蜜胺。

若調配為固定劑量，此組合產物利用本文所述劑量範圍內之本發明化合物及其他在其劑量範圍內之醫藥活性劑。例如，CDC2抑制劑歐樂姆辛(olomucine)已發現與已知之細胞毒素劑在誘發細胞凋亡中有相乘作用(細胞科學期刊(1995)108, 2897)。式III化合物與已知抗癌劑或細胞毒素劑

當不適合調配在一起時，可依序投藥。本發明不限於依序投藥；式III化合物可在已知抗癌劑或細胞毒素劑投藥前後投藥。例如，週期素依賴性激酶抑制劑黃素比多醇(flavopiridol)之細胞毒素活性受抗癌劑投藥順序之影響。Cancer Research, (1997) 57, 3375。此技術為熟知本技藝者以及參予之醫師所悉知。

據此，本發明一目的係包含組合物，其包括某量之至少一種式III化合物或其醫藥可接受性鹽或溶劑化物及某量之一或多種抗癌療法及選自上述之抗癌劑，其中化合物/治療之量導致所需之治療效果。

本發明化合物之醫藥性質可藉數種藥理分析確認。後述此例舉之藥理分析已利用本發明化合物及其鹽進行。

本發明又有關醫藥組合物，其包括至少一種式III化合物或該化合物之醫藥可接受性鹽或溶劑化物及至少一種醫藥可接受性載劑。

就自本發明所述化合物製備醫藥組合物而言，惰性之醫藥可接受性載劑可為固體或液體。固體劑型包含粉劑、錠劑、可分散顆粒劑、膠囊、藥囊及栓劑。該粉劑及錠劑可包括約5至約95%活性成分。適宜之固體載劑為本技藝已知，例如碳酸鎂、硬脂酸鎂、滑石、糖或乳糖。錠劑、粉劑、藥囊及膠囊可使用為適合經口投藥之固體劑型。醫藥可接受性載劑及製造各種組合物之方法實例可見於A. Gennaro(編輯),雷明頓藥理科學第18版,(1990), Mack出版公司, Easton,賓州。

液態製劑包含溶液、懸浮液及乳液。實例可述及水或水-丙二醇溶液用以非經腸道注射或添加甜味劑及霧濁劑供口服溶液、懸浮液及乳液。液態製劑亦可包含鼻內投藥之溶液。

適用於吸入之氣溶膠製劑可包含溶液及粉劑固體，其可與醫藥可接受性載劑如惰性壓縮氣體如氮氣組合。

亦包含固態製劑，其在欲使用前才轉化成液體劑型供口服或非經腸道投藥。此液態劑型包含溶液、懸浮液及乳液。

本發明化合物亦可經皮遞送。該經皮組合物可製成乳霜、乳劑、氣溶膠及/或乳液且可包含於基質或儲存形式之經皮貼片中，如本領域就本目的所習知者。

本發明化合物亦可經皮下遞送。

較好該化合物口服投藥。

較好，該醫藥組合物呈單位劑型。此劑型中，該製劑次分成含適當量活性成分之式一大小劑型，如達到所需目的之有效量。

單位製劑中活性化合物之量可自約1毫克至約100毫克，較好約1毫克至約50毫克，更好自約1毫克至約25毫克之間變化或調整，依據特定用途而定。

所用確實劑量可視病患需求及欲治療病況之嚴重度而定。對特定狀況決定適當劑量療程在本領域熟知範圍內。為便利起見，總日劑量可分成數次且如所需在一天內分次投藥。

本發明化合物及/或其醫藥可接受性鹽之投藥量及次數

將可依據臨床醫師考慮如病患年齡、病況及大小以及欲治療病徵嚴重性等因素而調整。對口服投藥之典型推薦日劑量可自約1毫克/天至約500毫克/天間之範圍，較好1毫克/天至200毫克/天，分兩次至四次投藥。

本發明另一目的係包括醫藥有效量之至少一種式III化合物或該化合物之醫藥可接受性鹽或溶劑化物及醫藥可接受性載劑、載體或稀釋劑之套組。

本發明另一目的係包括有效量之至少一種式III化合物或該化合物之醫藥可接受性鹽或溶劑化物及至少一種上述抗癌療法及/或抗癌劑之套組，其中該兩或多種成分之量導致所需治療效果。

本文揭示之發明由下列製劑及實例加以舉例，但非用以限制本發明。其他機制路徑及類似結構將為本技藝者所悉知。

當提出NMR數據時，在Varian VXR-200(200 MHz, ^1H)、Varian Gemini-300(300 MHz)或XL-400(400 MHz)上獲得 ^1H 光譜並以自 Me_4Si 之下磁場ppm數表示，括弧內為質子數、多重峰及偶合常數(赫茲，Hz)。當報導LC/MS數據時，使用應用生物系統API-100質譜儀及島津SCL-10A LC管柱進行分析：Altech鉑C18，3微米，33毫米x7毫米ID；梯度流速：0分鐘-10% CH_3CN 、5分鐘-95% CH_3CN 、7分鐘-95% CH_3CN 、7.5分鐘-10% CH_3CN 、9分鐘-停止。提供駐留時間及所觀察之母離子。

下列溶劑及試劑可藉其縮寫表示於括弧內：

薄層層析：TLC

二氯甲烷： CH_2Cl_2

乙酸乙酯：AcOEt或EtOAc

甲醇：MeOH

三氟乙酸：TFA

三乙胺： Et_3N 或TEA

丁氧基羰基：n-Boc或Boc

核磁共振分光計：NMR

液體層析質譜儀：LCMS

高解析質譜儀：HRMS

毫升：mL

毫莫耳：mmol

微升： μl

克：g

毫克：mg

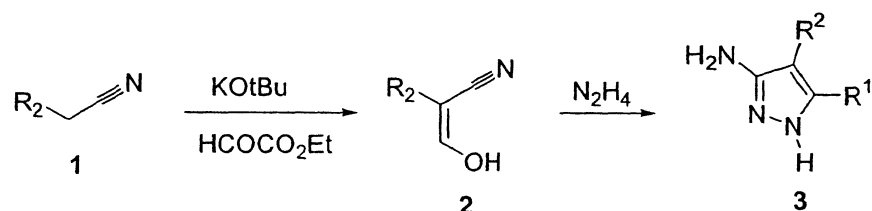
室溫或rt(周圍)：約 25°C

二甲氧基乙烷：DME。

實例

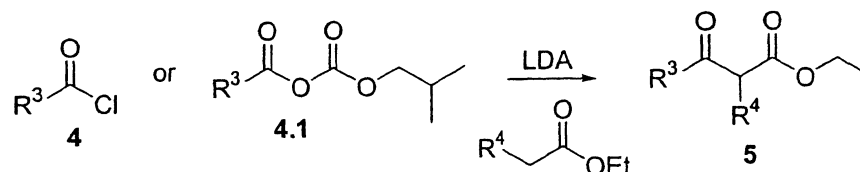
通常本發明所述化合物可經下述反應圖1之一般路徑製備。以第三丁醇鉀及甲酸乙酯處理起始物腈，獲得中間物烯醇2，其以聯胺處理獲得所需3-胺基吡唑。

反應圖1



號數3之化合物與號數5之適當官能基化酮酯縮合獲得吡啶酮6，如反應圖3所示。此一般路徑中所用之酮基酯為市售或可如反應圖2所說明般製得。

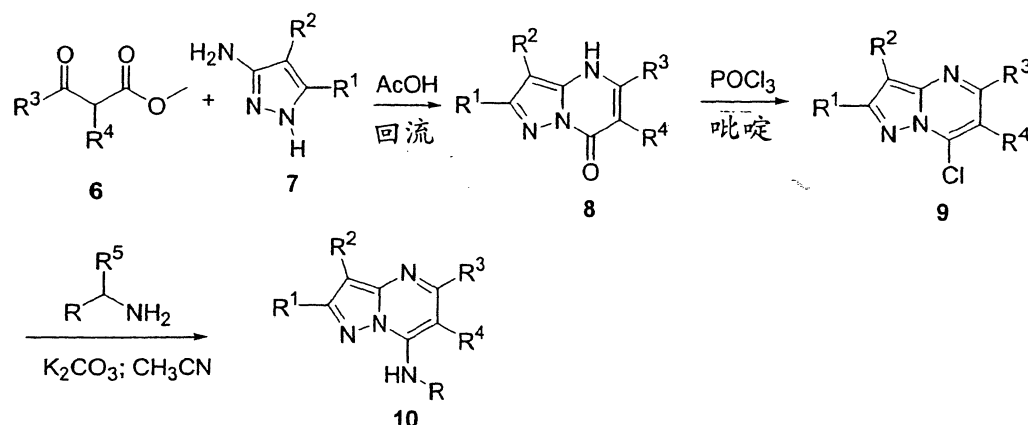
反應圖2



號數9之氯化物可藉POCl₃處理吡啶酮8而製備。當R²等於H，此位置之取代對號數9之化合物而言，可能藉親電子性鹵化、醯化及各種其他親電子性芳族取代作用進行。

N7-胺基官能基之併入可經由號數9之化合物與適當胺反應而置換該氯化物，如反應圖3所示。

反應圖3



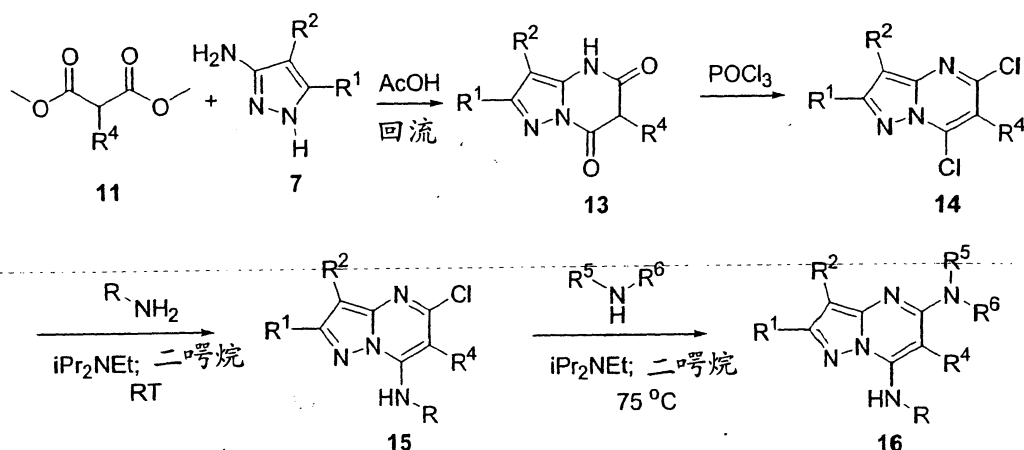
號數7之化合物與號數11之適當官能基化丙二酸酯縮合獲得吡啶酮13，如反應圖4所示。

號數14之氯化物可藉POCl₃處理吡啶酮13而製備。當R²為H，此位置之取代對號數9之化合物而言，可能藉親電子性

鹵化、醢化及各種其他親電子性芳族取代作用進行。

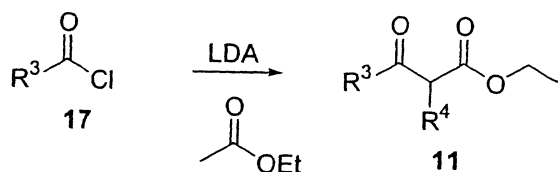
N7-胺基官能基之併入可經由號數14之氯化物經立體選擇性置換反應完成。N5-胺基官能基之併入係藉由在較高溫添加適當胺。

反應圖 4



或者，號數7之胺基吡唑與如反應圖5所示般製備之適當官能基化之酮基酯縮合，獲得號數13之化合物，如反應圖4所示。

反應圖 5

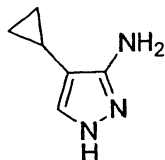


號數14之氯化物可藉POCl₃處理吡啶酮13而製備。當R²為H，此位置之取代對號數14之化合物而言，可能藉親電子性鹵化、醢化及各種其他親電子性芳族取代作用進行。

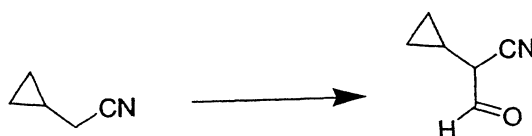
N7-胺基官能基之併入可經由號數15之氯化物經立體選擇性置換反應完成。

製備例：

製備例 1：

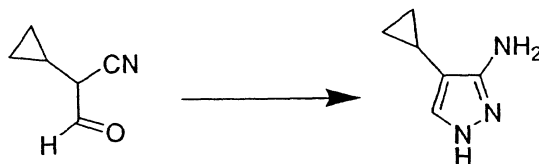


步驟 A：



依循德國專利 DE 19834047 A1 第 19 頁之程序。於 KOtBu (6.17 克, 0.055 莫耳) 之無水 THF (40 毫升) 溶液中, 滴加環丙基乙腈 (2.0 克, 0.025 毫莫耳) 及甲酸乙酯 (4.07 克, 0.055 莫耳) 之無水 THF (4 毫升) 溶液。立即形成沉澱。此混合物攪拌 12 小時。在真空下濃縮且殘留物與 Et₂O (50 毫升) 攪拌。傾析且所得殘留物以 Et₂O (2x50 毫升) 洗滌且真空自殘留物移除 Et₂O。殘留物溶於冷卻之 H₂O (20 毫升) 中並以 12 N HCl 調整至 pH 4-5。混合物以 CH₂Cl₂ (2x50 毫升) 萃取。合併有機層, 以 MgSO₄ 脫水並真空濃縮獲得褐色液體之醛。

步驟 B：



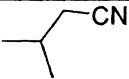
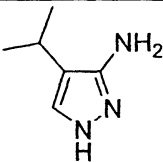
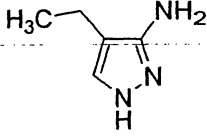
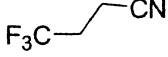
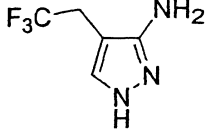
製備例 1 步驟 A 之產物 (2.12 克, 0.0195 莫耳)、NH₂NH₂·H₂O (1.95 克, 0.039 莫耳) 及 1.8 克 (0.029 莫耳) 冰醋酸 (1.8 克, 0.029 莫耳) 溶於 EtOH (10 毫升) 中。回流 6 小時並真空濃縮。殘留

物於CH₂Cl₂ (150毫升)中攪拌且pH以1 N NaOH調整至9。有機層以食鹽水洗滌，以MgSO₄脫水並真空濃縮，獲得蠟質橘色固體產物。

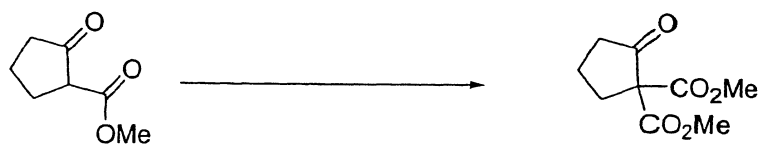
製備例 2-3.10

基本上同製備例1所述程序，僅以表2欄2所示之腈替代，獲得表2欄3之化合物：

表 2

製備例	欄2	欄3
2		
3		
3.10		

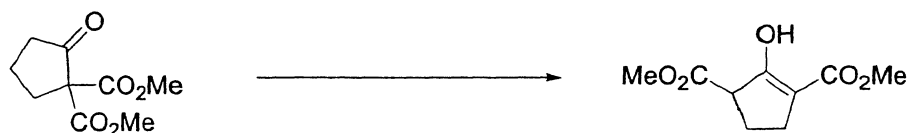
製備例 4



2-碳甲氧基環戊酮(6.6毫升，0.05莫耳)之THF(15毫升)滴加至NaH(60%礦油中，4克，1.0莫耳)之THF(100毫升)在0-10℃激烈攪拌溶液中。冒泡停止時，反應混合物在相同溫度以ClCOOMe(7.8毫升，0.1莫耳)於THF(15毫升)中處理。所

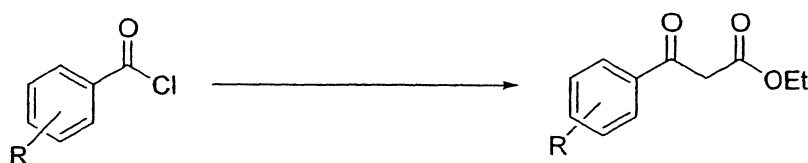
得灰白色懸浮液在室溫攪拌30分鐘並回流30分鐘。反應藉TLC追蹤起始物之消失。反應混合物小心以水驟冷並於漏斗中分配於乙酸乙酯及飽和氯化銨溶液之間。搖晃及分離後，有機層以食鹽水洗滌及以無水硫酸鈉脫水。移除溶劑且殘留物藉快速層析純化，以5%接著10%乙酸乙酯之己烷溶離。獲得9.4克無色油，94%產率。 $^1\text{H NMR}(\text{CDCl}_3)$ δ 3.90(s, 3H), 3.73(s, 3H), 2.65(m, 4H), 1.98(m, 2H)。

製備例 5



於二異丙基醯胺鋰之THF溶液(2.0 N, 0.04莫耳)中在-65℃滴加2,2-二碳甲氧基環戊酮(4克, 0.02莫耳)之THF(60毫升)。所得反應混合物在相同溫度攪拌後，添加氯甲酸甲酯(1.54毫升, 0.02莫耳)。反應混合物攪拌1小時並倒入含些許冰之飽和氯化銨溶液中。溶液以乙醚萃取3次且合併之醚層以硫酸鈉脫水。真空移除溶劑且殘留物藉快速層析純化，以30%增加至50%乙酸乙酯之己烷溶離。獲得2.3克黃色油產率58%。 $^1\text{H NMR}(\text{CDCl}_3)$ δ 3.77(s, 6H), 3.32(t, 1H), 3.60- 3.10(m, 4H)。

製備例 6：

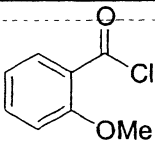
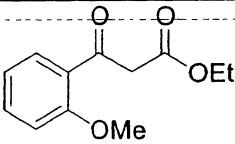
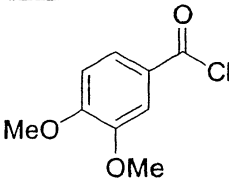
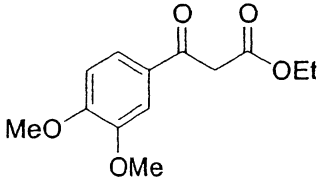
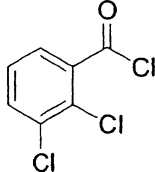
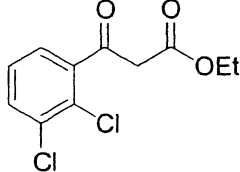


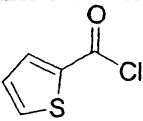
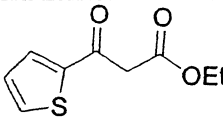
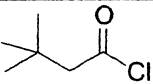
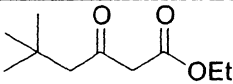
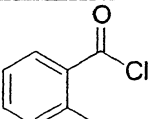
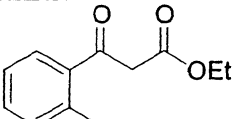
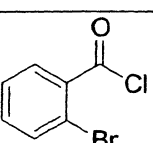
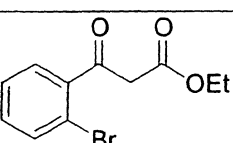
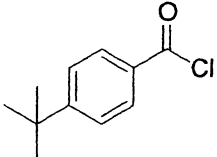
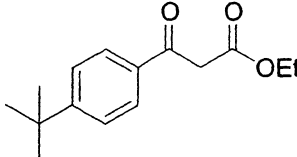
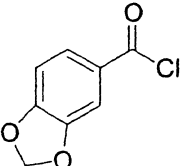
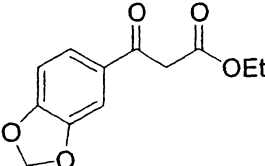
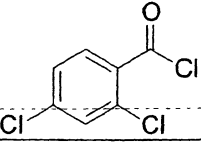
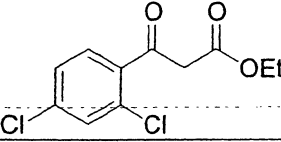
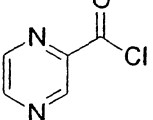
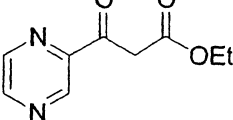
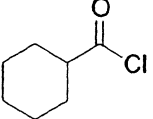
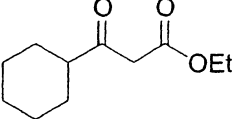
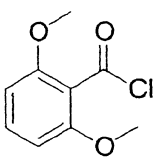
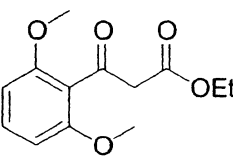
此反應如(K.O. Olsen,有機化學期刊(1987) 52, 4531-4536)所述般進行。因此，於二異丙基醯胺鋰之THF攪拌溶液中在-65至-70℃滴加剛蒸餾之乙酸乙酯。所得溶液攪拌30分鐘且以THF溶液添加醯氯。反應混合物在-65至-70℃攪拌30分鐘接著藉添加1 N HCl溶液終止。所得兩相混合物溫至周圍溫度。所得混合物以EtOAc(100毫升)稀釋且收集有機層。水層以EtOAc(100毫升)萃取。合併有機層，以食鹽水洗滌，脫水(Na_2SO_4)並真空濃縮，獲得粗製 β -酮基酯，其用於隨後縮合反應。

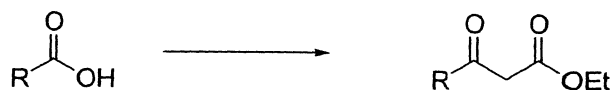
製備例 7-19：

基本上同製備例6所述程序，僅以表3欄2所示之醯氯替代，獲得表3欄3之 β -酮基酯：

表 3

製備例	欄2	欄3	數據
7			LCMS: $\text{MH}^+ = 223$
8			LCMS: $\text{MH}^+ = 253$
9			LCMS: $\text{MH}^+ = 261$

10			MH ⁺ = 199
11			
12			
13			LCMS: MH ⁺ = 271
14			產率=定量 MH ⁺ = 249
15			產率=定量 MH ⁺ = 237
16			產率=定量 MH ⁺ = 262
17			產率= 48 MH ⁺ = 195
18			產率= 99 MH ⁺ = 199
19			產率= 77% ¹ H NMR (CDCl ₃) δ 7.42(t, 1H), 6.68(d, 2H), 4.29(q, 2H), 3.97(d, 2H), 3.95(s, 3H), 1.38(t, 3H).

製備例 20

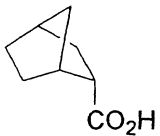
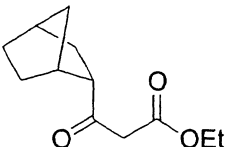
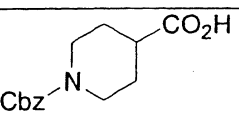
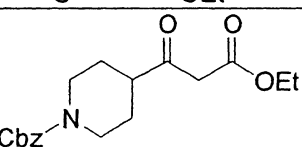
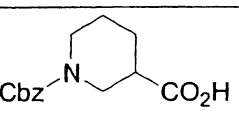
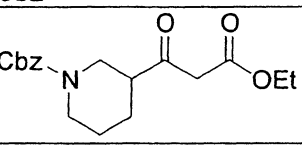
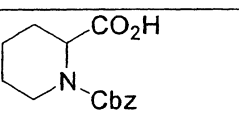
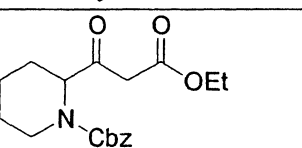
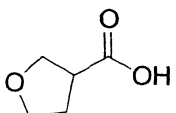
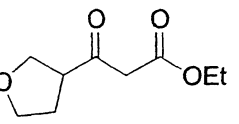
於酸之 THF 溶液中添加 Et_3N ，接著在 -20 至 -30°C 添加 氯 甲 酸 異 丁 酯。混合物在 -20 至 -30°C 攪拌 30 分鐘後，在 氫 氣 中 濾 除 三 乙 胺 鹽 酸 鹽，且 濾 液 添 加 至 -65 至 -70°C 之 LDA-EtOAc 反應 混 合 物 (如 方 法 A 所 述 般 製 備) 中。添 加 1 N HCl 後，接 著 例 行 操 作 反 應 混 合 物 並 蒸 發 溶 劑，單 離 粗 製 之 β -酮 基 酯。該 粗 製 物 質 用 於 隨 後 縮 合 反 應。

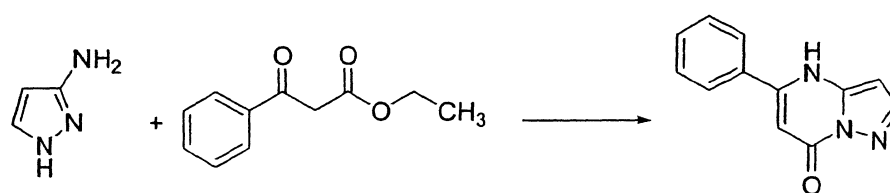
製備例 21-28：

基本上同製備例 20 所述相同條件，僅以表 4 欄 2 所示之羧酸替代，獲得表 4 欄 3 之化合物：

表 4

製備例	欄2	欄3	數據
21			產率 = 99% $\text{MH}^+ = 213$
22			產率 = 70% $\text{MH}^+ = 275$
23			產率 = 定量 $\text{MH}^+ = 213$

24			產率=定量 MH ⁺ =211
25			產率= 99 MH ⁺ = 334
26			產率= 99 MH ⁺ = 334
27			產率= 99 MH ⁺ = 334
28			產率= 77% ¹ H NMR (CDCl ₃) δ 4.21(q, 2H), 3.95(d, 2H), 3.93-3.79(m, 4H), 3.52(s, 2H), 2.65(m, 1H), 1.25(t, 3H), 1.23-1.2(m, 2H).

製備例 29

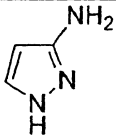
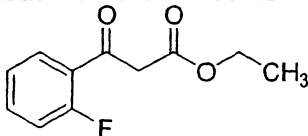
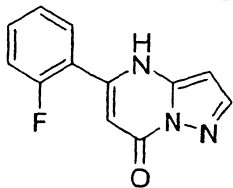
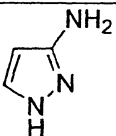
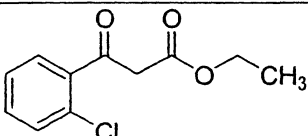
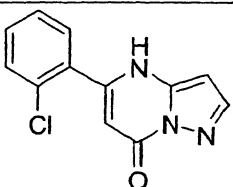
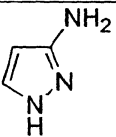
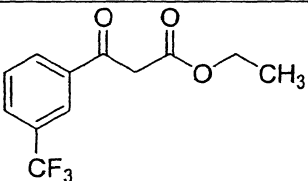
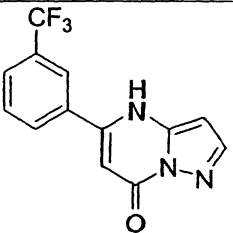
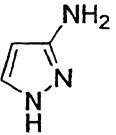
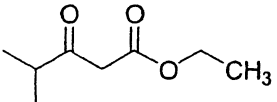
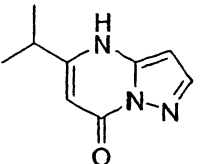
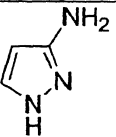
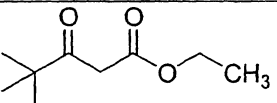
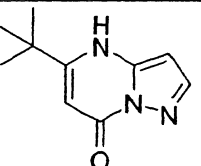
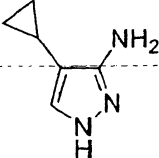
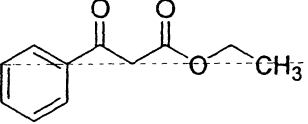
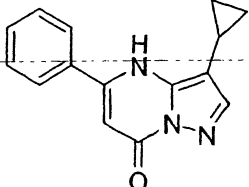
3-氨基吡啶(2.0克，24.07毫莫耳)及苯甲醯基乙酸乙酯(4.58毫升，1.1當量)之AcOH(15毫升)溶液回流加熱3小時。反應混合物冷卻至室溫並真空濃縮。所得固體以EtOAc稀釋並過濾獲得白色固體(2.04克，40%產率)。

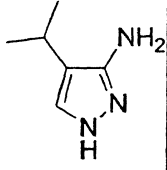
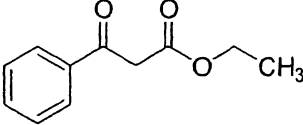
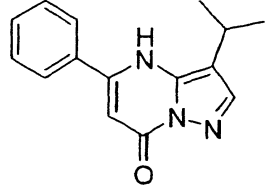
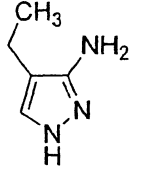
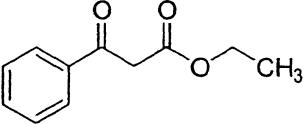
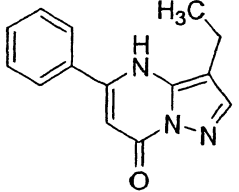
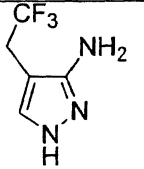
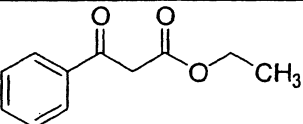
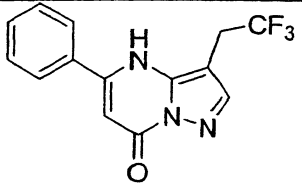
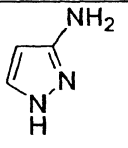
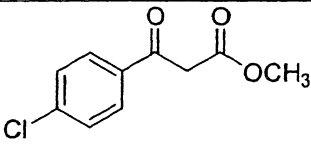
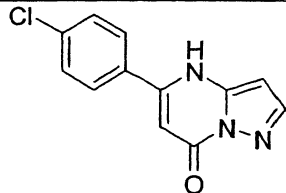
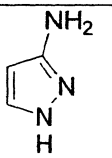
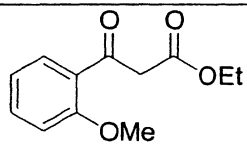
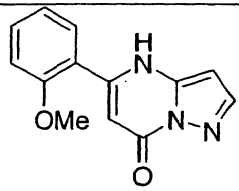
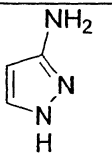
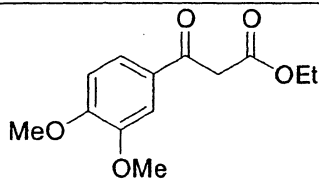
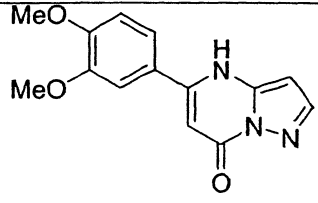
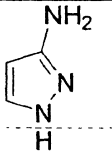
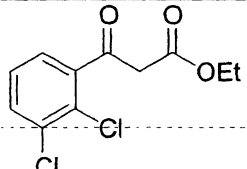
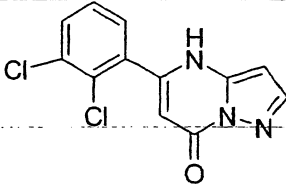
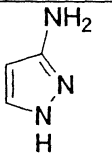
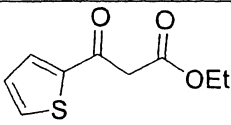
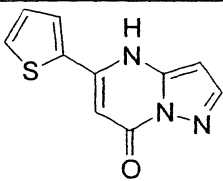
製備例 30-73

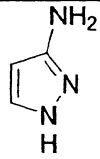
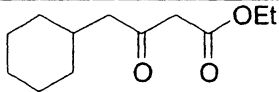
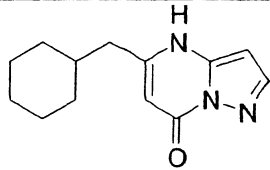
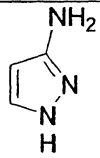
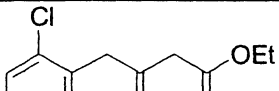
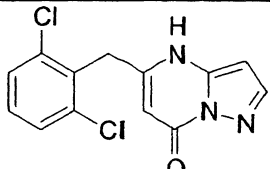
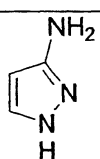
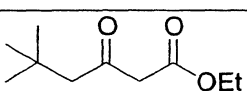
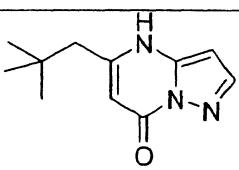
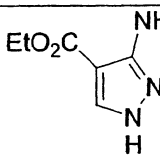
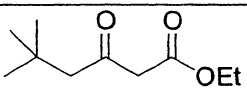
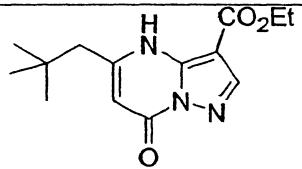
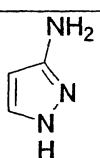
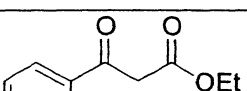
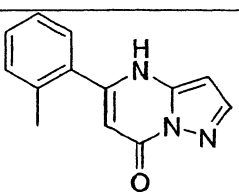
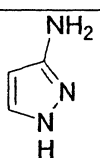
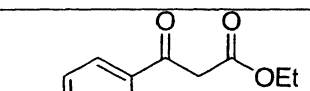
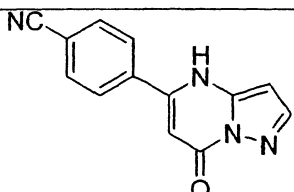
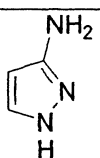
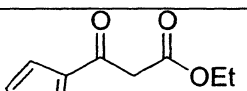
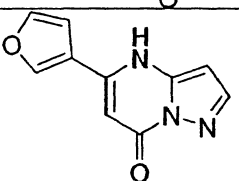
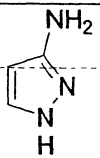
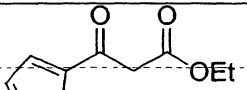
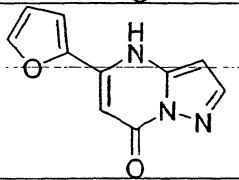
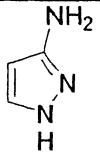
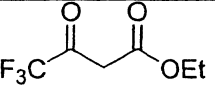
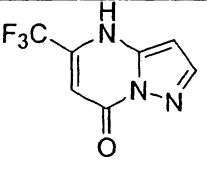
基本上同製備例29所述相同程序，僅以表5欄2所示之胺

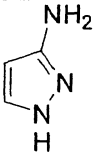
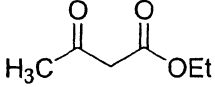
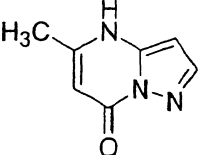
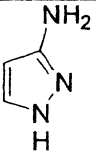
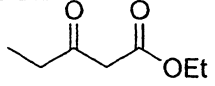
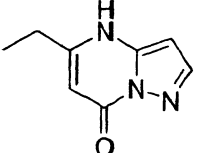
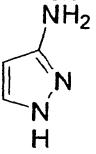
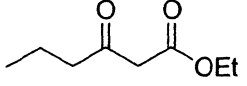
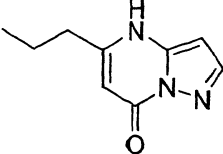
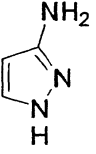
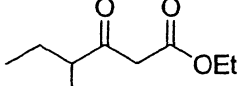
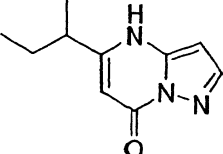
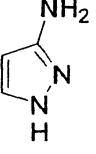
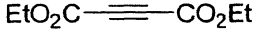
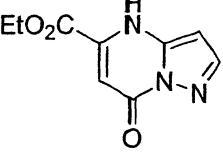
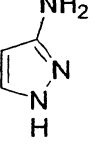
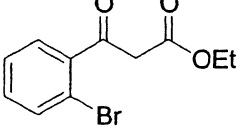
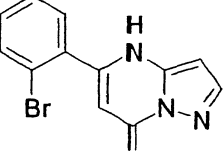
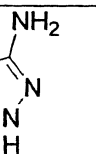
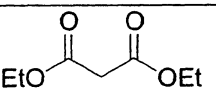
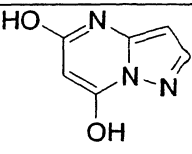
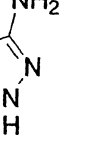
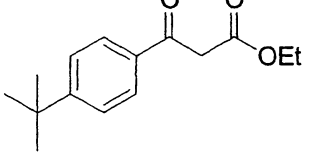
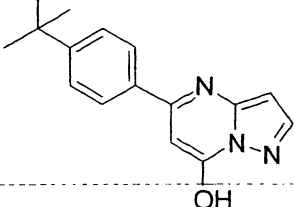
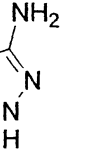
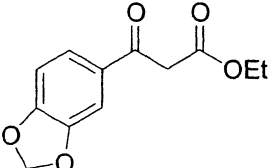
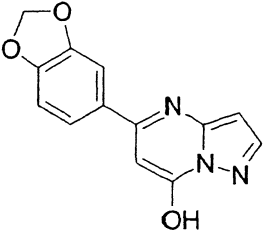
基吡唑及表5欄3所示之酯替代，獲得表5欄4之化合物：

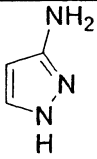
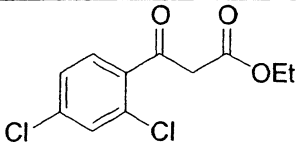
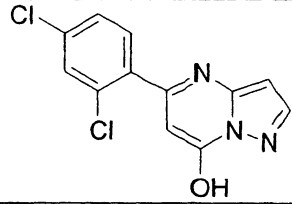
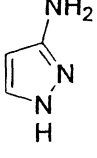
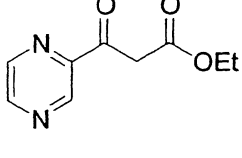
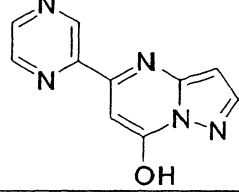
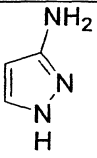
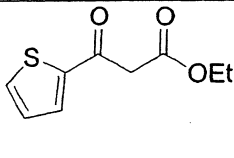
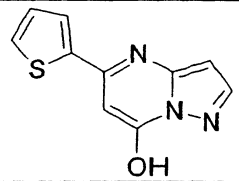
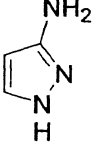
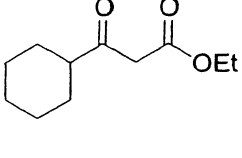
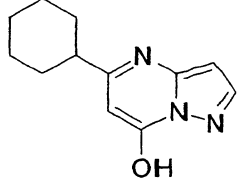
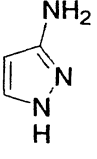
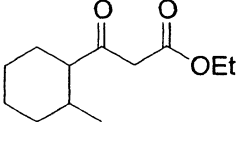
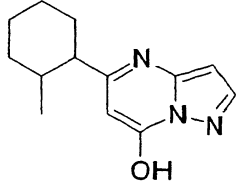
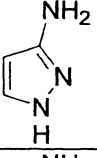
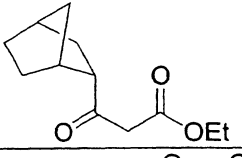
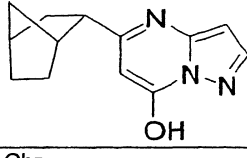
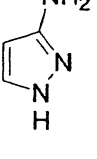
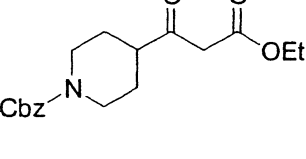
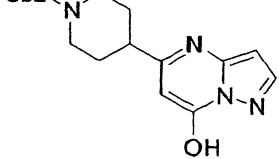
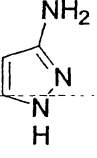
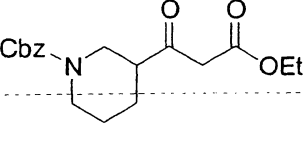
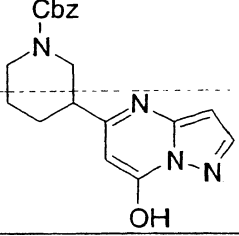
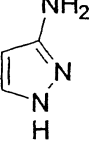
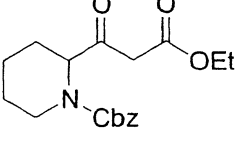
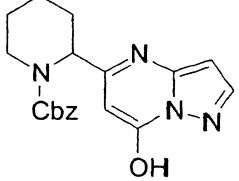
表 5

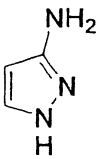
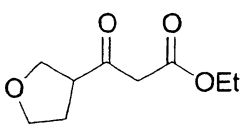
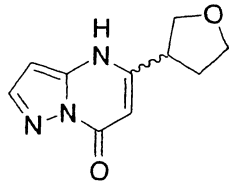
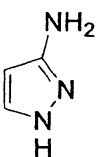
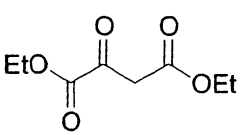
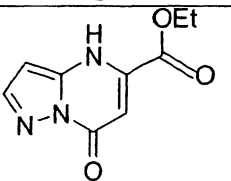
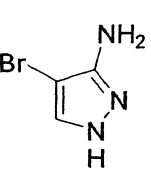
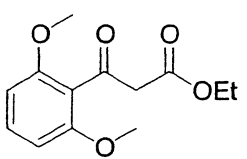
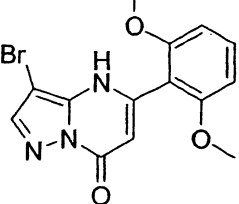
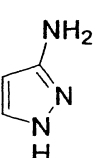
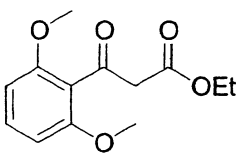
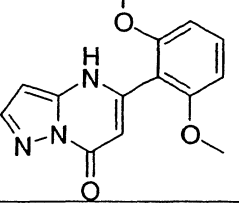
製備例	欄2	欄3	欄4	數據
30				
31				
32				
33				
34				
35				

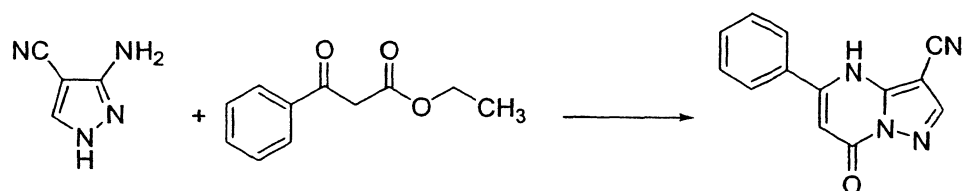
36				
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37.10				
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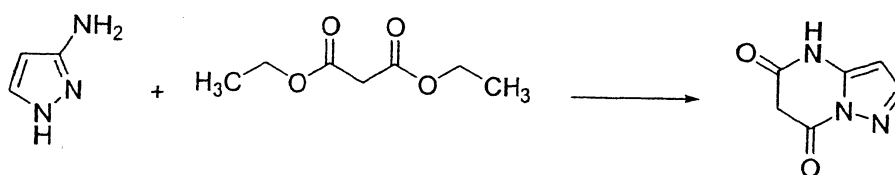
52				
53				
54				
55				
56				
57				
58				産率= 68 MH ⁺ = 152
59				産率= 46 MH ⁺ = 268
60				産率= 63 MH ⁺ = 255

61				產率= 80 MH ⁺ = 280
62				產率= 72 MH ⁺ = 214
63				產率= 51 MH ⁺ = 218
64				產率= 82 MH ⁺ = 218
65				產率= 39 MH ⁺ = 232
66				產率= 30 MH ⁺ = 230
67				產率= 80 MH ⁺ = 353
68				產率= 49 MH ⁺ = 353
69				產率= 42 MH ⁺ = 353

70				
71				
72				
73				

製備例 74：

苯甲醯基乙酸乙酯(1.76毫升，1.1當量)及3-氨基-4-氰基吡啶(1.0克，9.25毫莫耳)之AcOH(5.0毫升)及H₂O(10毫升)溶液回流加熱72小時。所得溶液冷卻至室溫，真空濃縮，並以EtOAc稀釋。過濾所得沉澱，以EtOAc洗滌且真空乾燥(0.47克，21%產率)。

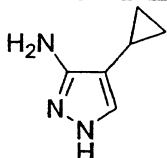
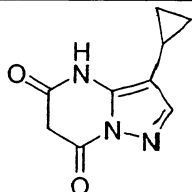
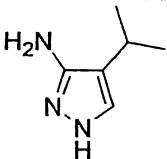
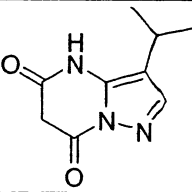
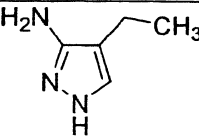
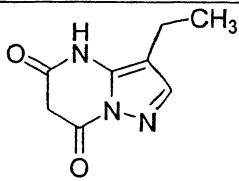
製備例 75：

依循 US 專利 3,907,799 之程序。鈉(2.3克, 2當量)逐次添加至 EtOH(150 毫升)中。當鈉完全溶解時, 添加 3-胺基吡唑(4.2 克, 0.05 莫耳)及丙二酸二乙酯(8.7 克, 1.1 當量)且所得溶液加熱回流 3 小時。所得懸浮液冷卻至室溫並過濾。濾餅以 EtOH(100 毫升)洗滌並溶於水(250 毫升)中。所得溶液於冰浴中冷卻且 pH 以濃 HCl 調整至 1-2。過濾所得懸浮液, 並以水(100 毫升)洗滌及真空乾燥獲得白色固體(4.75 克, 63% 產率)。

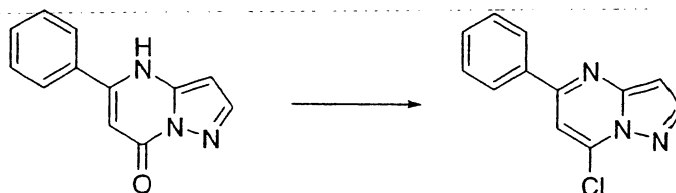
製備例 76-78:

基本上同製備例 75 所述相同程序, 僅以表 6 欄 2 所示之化合物替代, 獲得表 6 欄 3 之化合物:

表 6

製備例	欄2	欄3
76		
77		
78		

製備例 79:

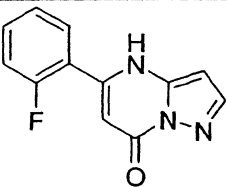
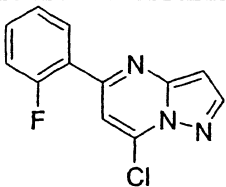
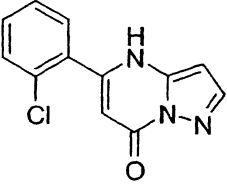
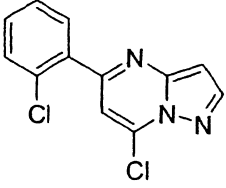
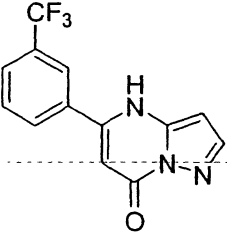
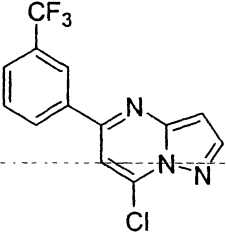
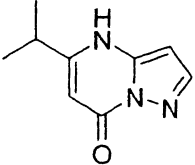
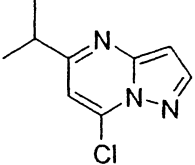


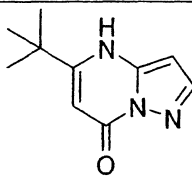
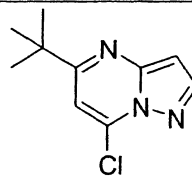
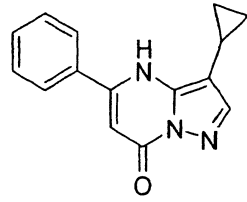
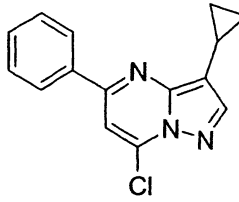
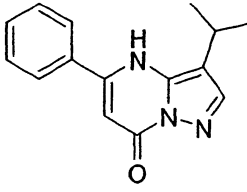
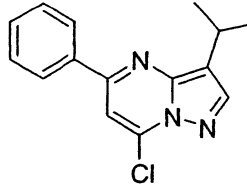
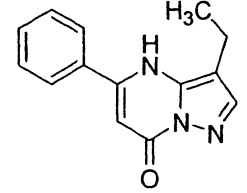
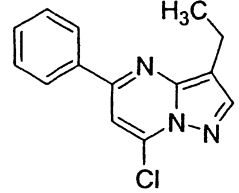
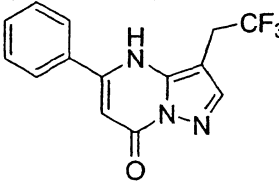
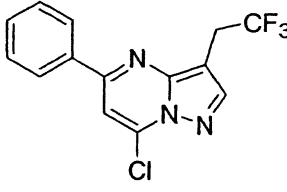
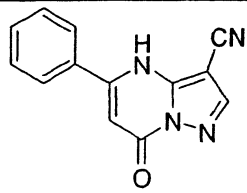
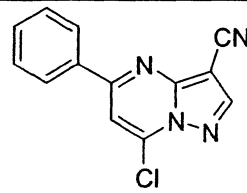
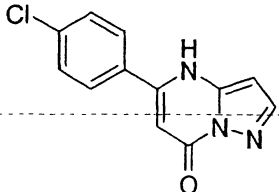
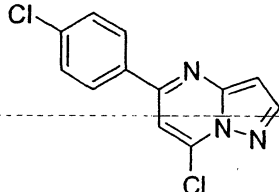
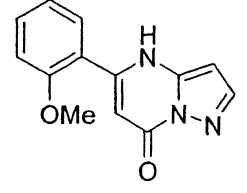
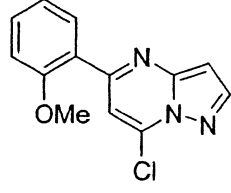
製備例29所製備之化合物(1.0克，4.73毫莫耳)之 POCl_3 (5毫升)及吡啶(0.25毫升)溶液在室溫攪拌3天。所得漿液以 Et_2O 稀釋，過濾且固體殘留物以 Et_2O 洗滌。合併之 Et_2O 洗液冷卻至 0°C 並以冰處理。當發生激烈反應，所得混合物以 H_2O 稀釋，分離且水層以 Et_2O 萃取。合併之有機相以 H_2O 及飽和 NaCl 洗滌，以 Na_2SO_4 脫水，過濾及濃縮，獲得淡黃色固體(0.86克，79%產率)。LCMS: $\text{MH}^+ = 230$ 。

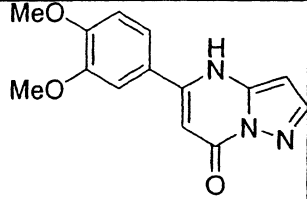
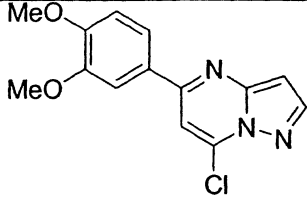
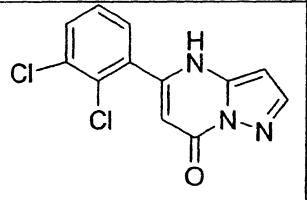
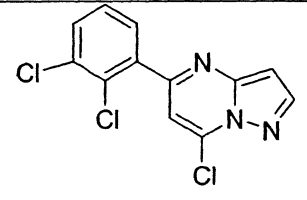
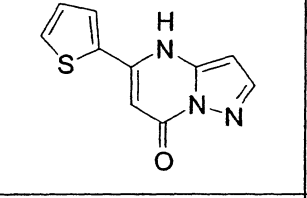
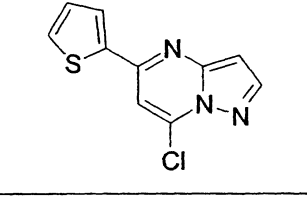
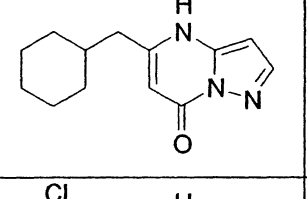
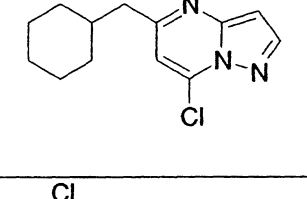
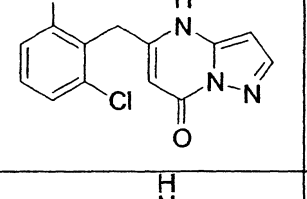
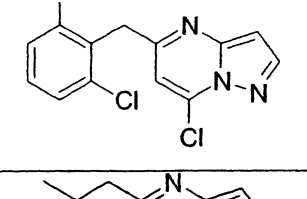
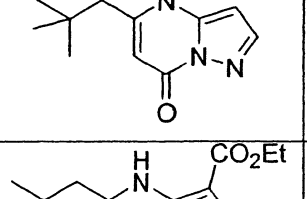
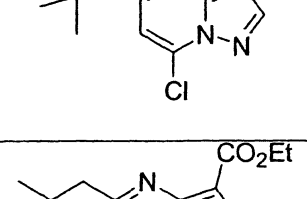
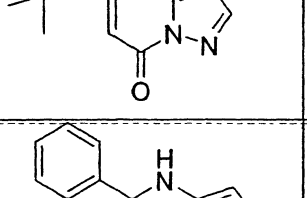
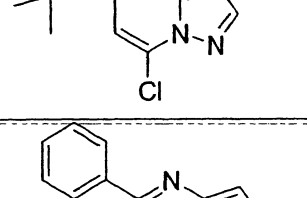
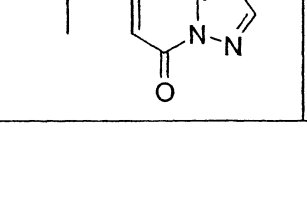
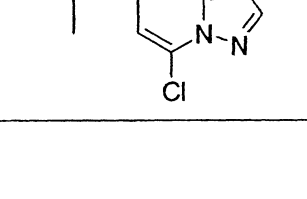
製備例80-122：

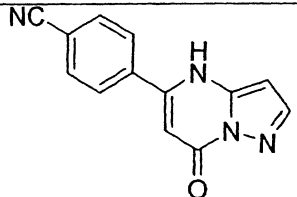
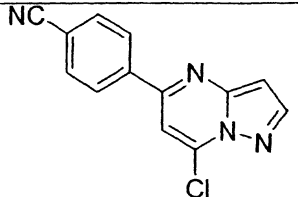
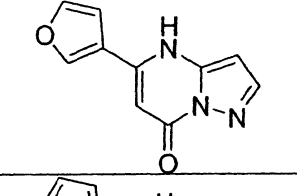
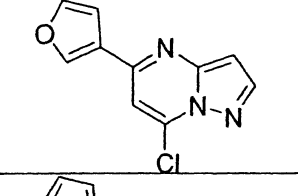
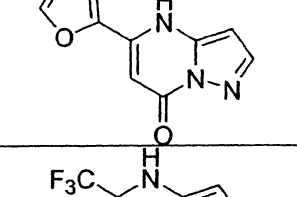
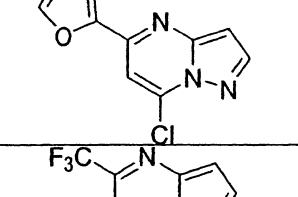
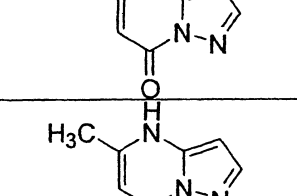
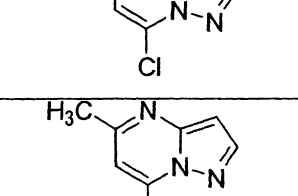
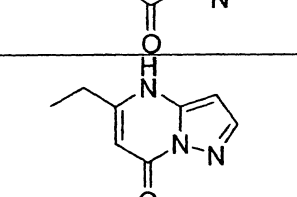
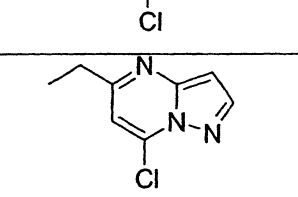
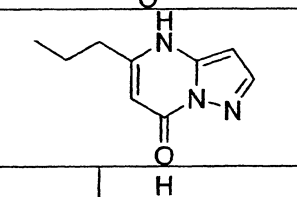
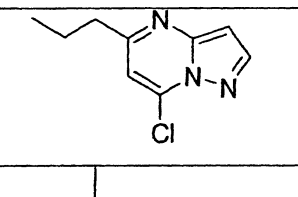
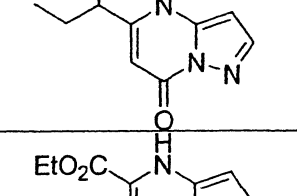
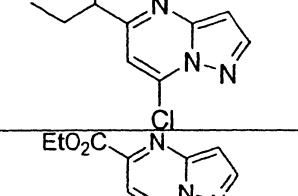
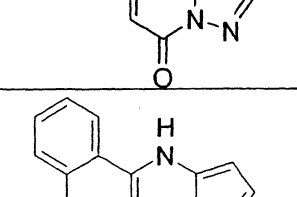
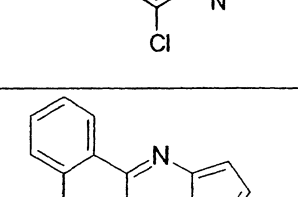
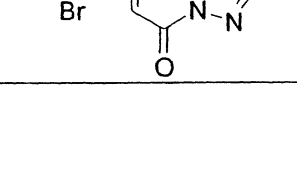
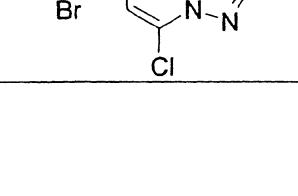
基本上同製備例79所述相同程序，僅以表7欄2所示之化合物替代，獲得表7欄3之化合物：

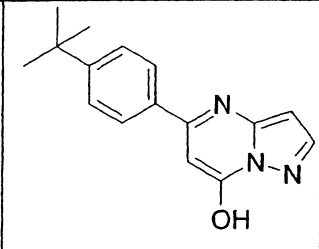
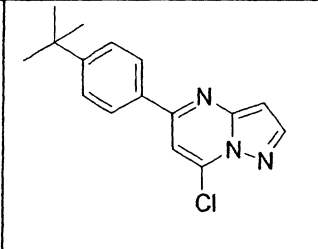
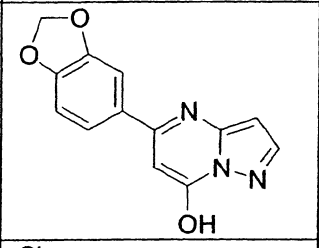
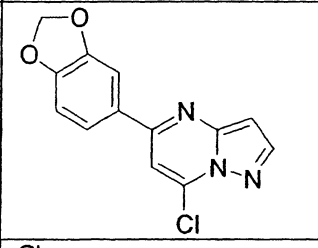
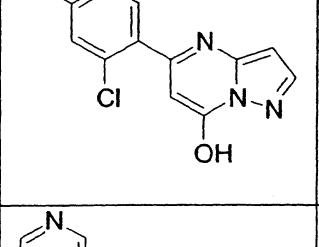
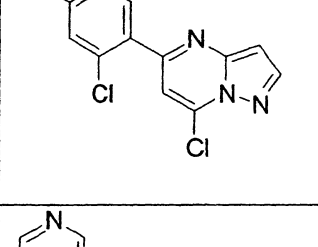
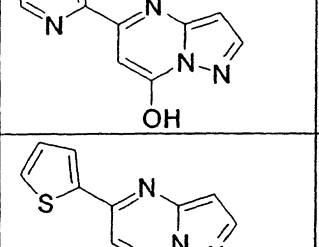
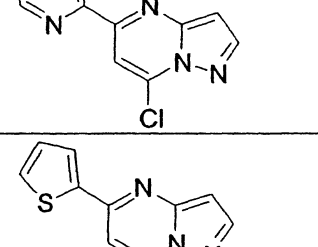
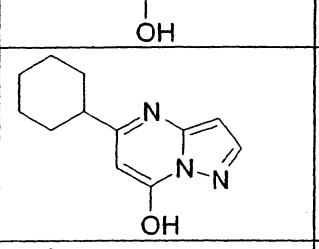
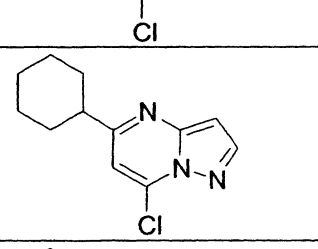
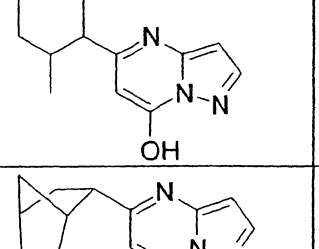
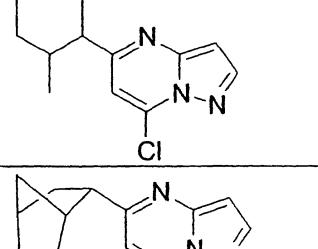
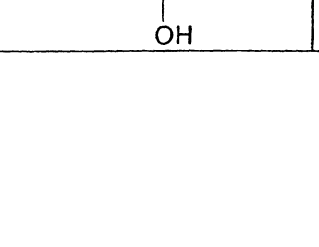
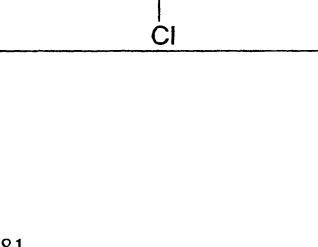
表 7

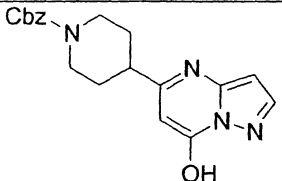
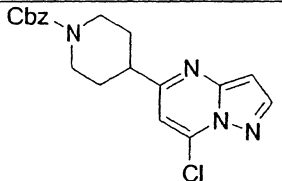
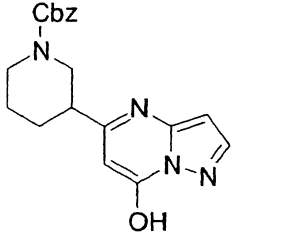
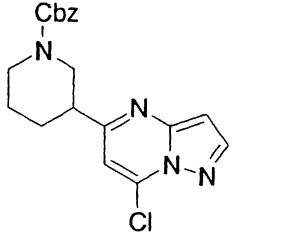
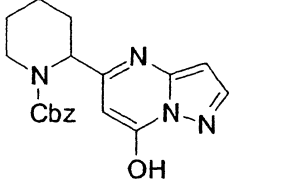
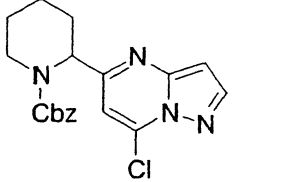
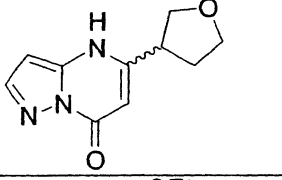
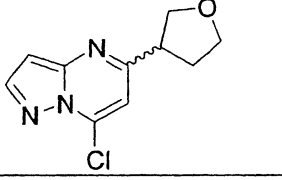
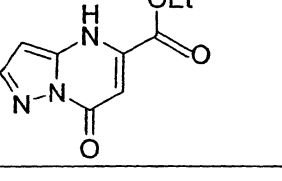
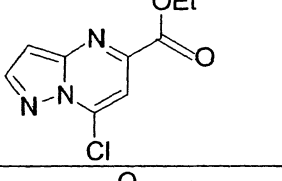
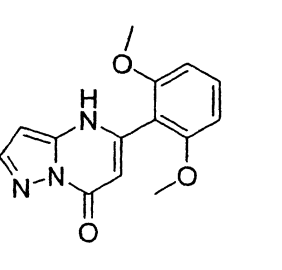
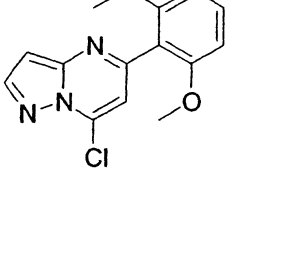
製備例	欄2	欄3	數據
80			MS: $\text{MH}^+ = 248$
81			
82			MS: $\text{MH}^+ = 298$
83			MS: $\text{MH}^+ = 196$

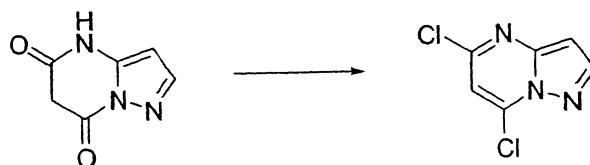
84			MS: $MH^+ = 210$
85			
86			MS: $MH^+ = 272$
87			
87.10			
88			MS: $MH^+ = 255$
89			
90			產率 = 65% MS: $MH^+ = 260$

91			產率= 35% MS: MH ⁺ = 290
92			產率= 32% MS: MH ⁺ = 298
93			產率= 45% MS: MH ⁺ = 236
94			產率= 100% LCMS: MH ⁺ = 250
95			產率= 88% MS: MH ⁺ = 314
96			產率= 43% MS: MH ⁺ = 223
97			產率= 30% MS: MH ⁺ = 295
98			產率= 98% MS: MH ⁺ = 244

99			
100			
101			
102			
103			
104			
105			
106			
107			45% 產率; MS: MH ⁺ =226
108			MS: MH ⁺ = 308

109			產率=定量 MH ⁺ = 286
110			產率= 50 MH ⁺ = 272
111			產率= 85 MH ⁺ = 299
112			產率= 97 MH ⁺ = 231
113			產率= 45 MH ⁺ = 236
114			產率=定量 MH ⁺ = 236
115			產率= 57 MH ⁺ = 250
116			產率= 89 MH ⁺ = 248

117			產率= 96 MH ⁺ =371
118			產率= 99 MH ⁺ =371
119			產率= 50 MH ⁺ =371
120			產率=57% LCMS: MH ⁺ =224
121			產率=34% LCMS: MH ⁺ =226
122			產率=100% ¹ H NMR (CDCl ₃) δ 8.53(d, 1H), 7.66(t, 1H), 7.51(s, 1H), 7.45(d, 1H), 6.84(d, 2H).

製備例 123

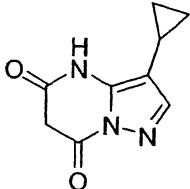
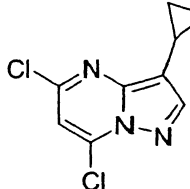
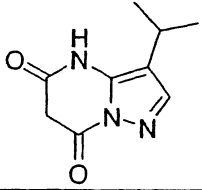
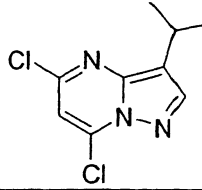
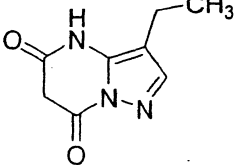
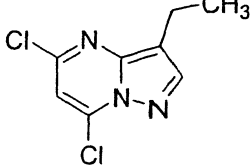
POCl₃(62毫升)在氮氣下冷卻至5℃及添加二甲基苯胺(11.4克, 2.8當量)及製備例75製備之化合物(4.75克, 0.032

莫耳)。反應混合物溫至60℃並攪拌隔夜。反應混合物冷卻至30℃並減壓蒸除POCl₃。殘留物溶於CH₂Cl₂(300毫升)並倒入冰上。攪拌15分鐘後，混合物之pH以固體NaHCO₃調整至7-8。分離層且有機層以H₂O(3x200毫升)洗滌，以MgSO₄脫水，過濾並濃縮。粗產物藉快速層析純化使用50:50 CH₂Cl₂:己烷溶液作為溶離液，溶離該二甲基苯胺。溶離液接著改變成75:25 CH₂Cl₂:己烷以溶離所需產物(4.58克，77%產率)。MS：MH⁺=188。

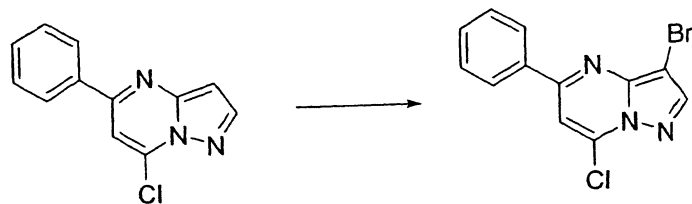
製備例 124-126：

基本上同製備例123所述相同程序，僅以表8欄2所示之化合物替代，獲得表8欄3之化合物：

表 8

製備例	欄2	欄3
124		
125		
126		

製備例 127：



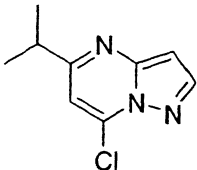
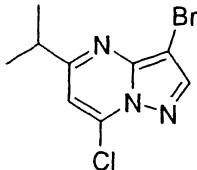
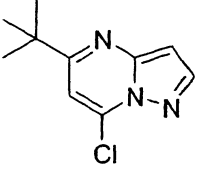
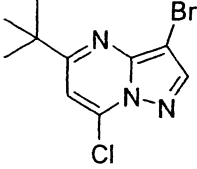
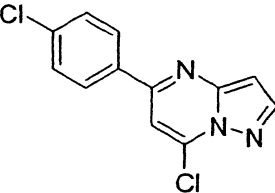
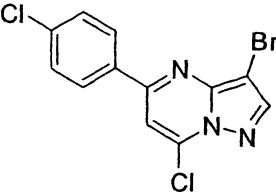
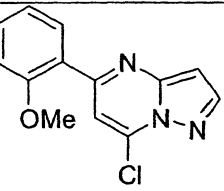
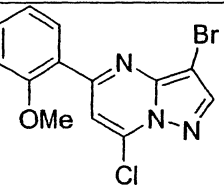
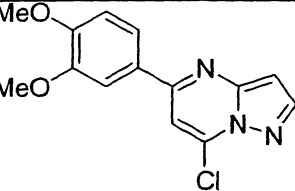
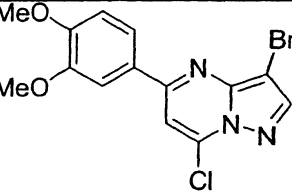
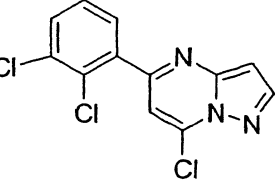
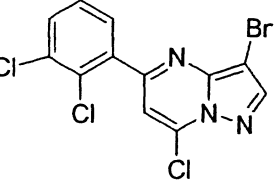
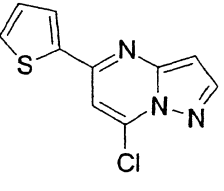
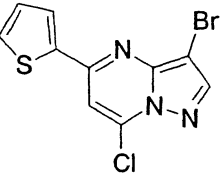
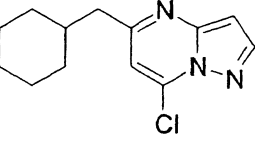
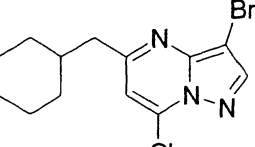
製備例 79 所製備之化合物 (0.10 克, 0.435 毫莫耳) 之 CH_3CN (3 毫升) 溶液以 NBS (0.085 克, 1.1 當量) 處理。反應混合物在室溫攪拌 1 小時且減壓濃縮。粗產物藉快速層析純化使用 20% EtOAc 之己烷溶液作為溶離液 (0.13 克, 100% 產率)。LCMS: $\text{MH}^+ = 308$ 。

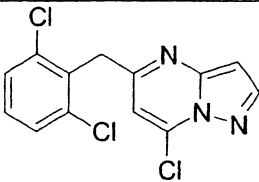
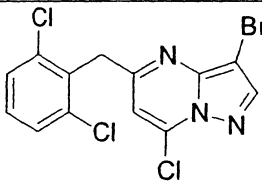
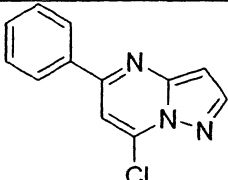
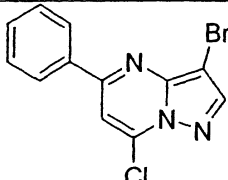
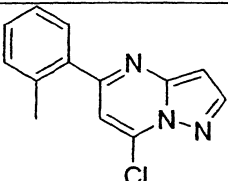
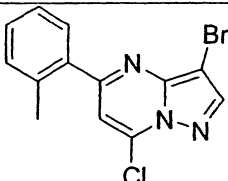
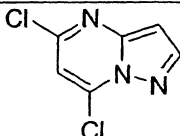
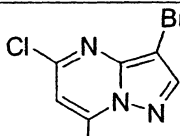
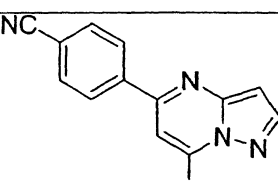
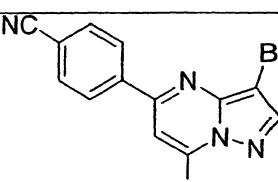
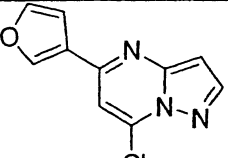
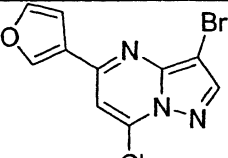
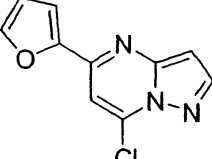
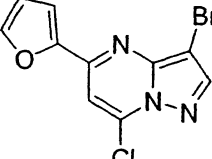
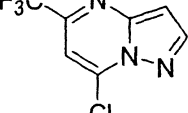
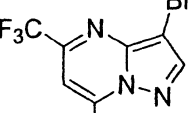
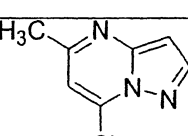
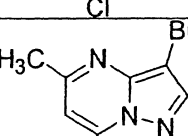
製備例 128-164:

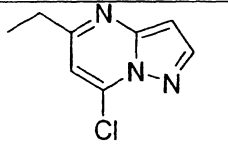
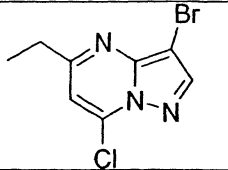
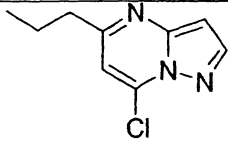
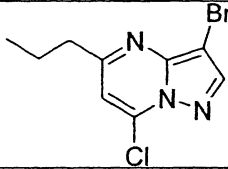
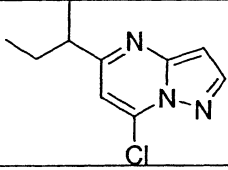
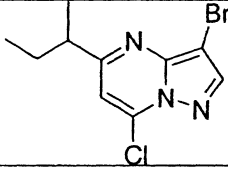
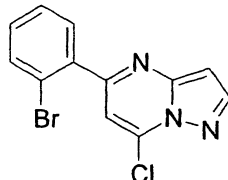
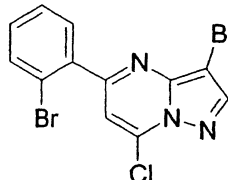
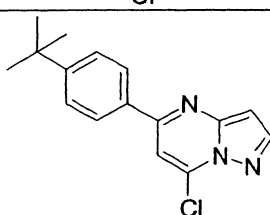
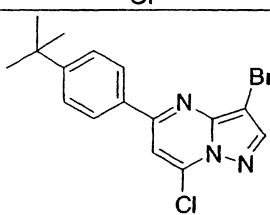
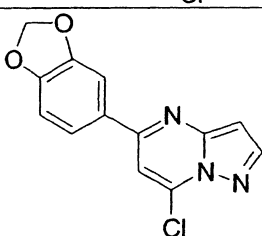
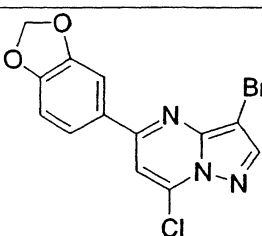
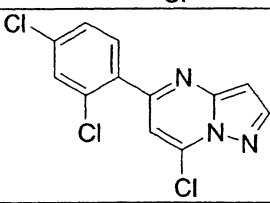
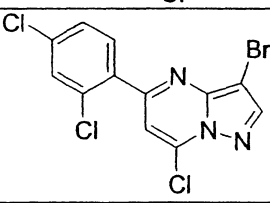
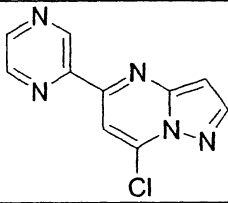
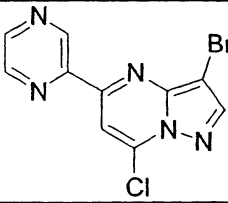
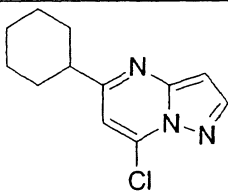
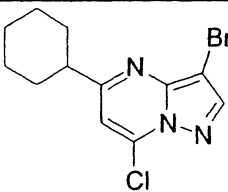
基本上同製備例 127 所述相同程序, 僅以表 9 欄 2 所示之化合物替代, 獲得表 9 欄 3 之化合物:

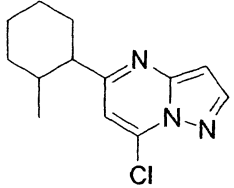
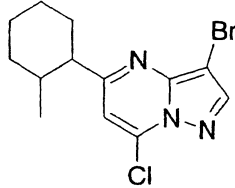
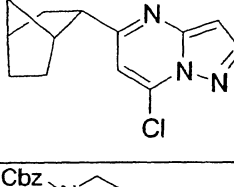
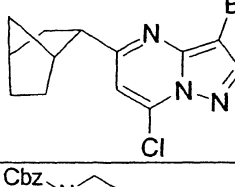
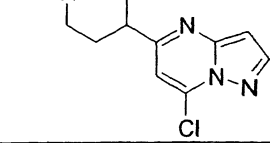
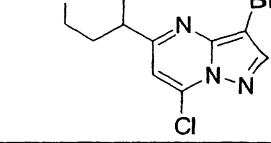
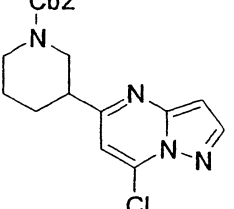
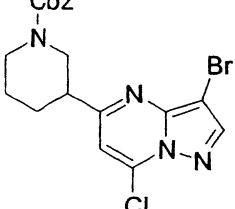
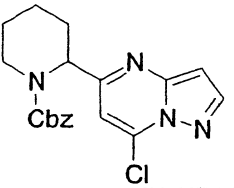
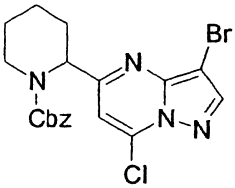
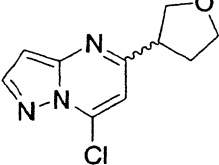
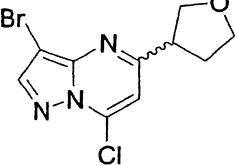
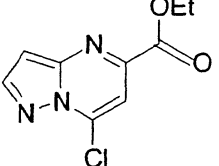
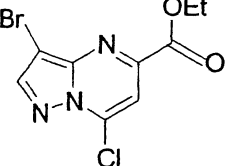
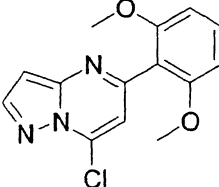
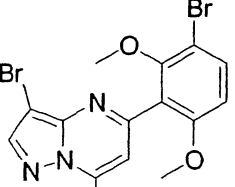
表 9

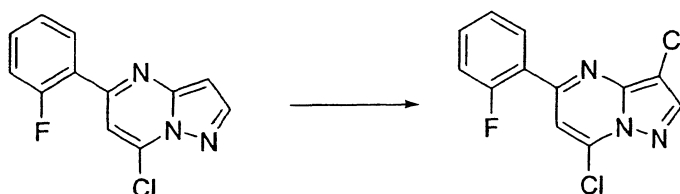
製備例	欄2	欄3	數據
128			MS: $\text{MH}^+ = 326$
129			MS: $\text{MH}^+ = 342$
130			MS: $\text{MH}^+ = 376$

131			MS: MH ⁺ =274
132			MS: MH ⁺ =288
133			
134			產率= 75% MS: MH ⁺ = 338
135			產率= 52% MS: MH ⁺ = 368
136			產率= 87% MS: MH ⁺ = 376
137			產率= 100% MS: MH ⁺ = 316
138			產率= 92% MS: MH ⁺ = 330

139			產率= 82% MS: MH ⁺ = 395
140			產率=88% MS: MH ⁺ =308
141			產率=100% MS: MH ⁺ =322
142			MH ⁺ =266
143			
144			
145			
146			
147			

148			
149			
150			
151			LCMS: MH ⁺ = 386
152			產率=定量 MH ⁺ = 364
153			產率=定量 MH ⁺ = 353
154			產率= 95 MH ⁺ = 378
155			產率= 77 MH ⁺ = 311
156			產率=定量 MH ⁺ = 314

157			產率= 99 MH ⁺ =328
158			產率= 98 MH ⁺ =326
159			產率= 99 MH ⁺ =449
160			產率= 95 MH ⁺ =449
161			產率= 72 MH ⁺ =449
162			產率=98% LCMS: MH ⁺ =302
163			產率=95% LCMS: MH ⁺ =305
164			產率=50% ¹ H NMR (CDCl ₃) δ 8.36(s, 1H), 7.72(d, 1H), 7.20(s, 1H), 6.82(d, 1H), 3.99(s, 3H), 3.90(s, 3H);

製備例 165：

製備例 80 所製備之化合物 (0.3 克，1.2 毫莫耳) 之 CH_3CN (15 毫升) 溶液以 NCS (0.18 克，1.1 當量) 處理且所得溶液加熱回流 4 小時。添加其他 NCS (0.032 克，0.2 當量) 且所得溶液回流攪拌隔夜。反應混合物冷卻至室溫，真空濃縮且殘留物藉快速層析使用 20% EtOAc 之己烷溶液作為溶離液純化 (0.28 克，83% 產率)。LCMS: $\text{MH}^+ = 282$ 。

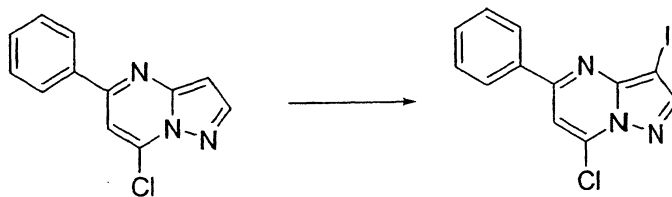
製備例 166-167：

基本上同製備例 165 所述相同程序，僅以表 10 欄 2 所示之化合物替代，獲得表 10 欄 3 之化合物：

表 10

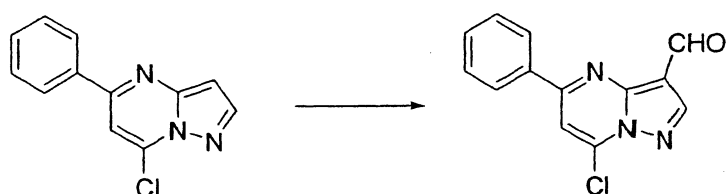
製備例	欄2	欄3	數據
166			產率 = 82% LCMS: $\text{MH}^+ = 286$
167			

製備例 167.10：



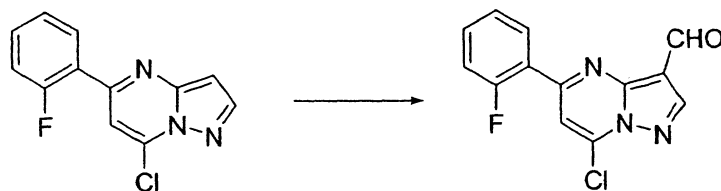
基本上同製備例165所述相同程序，僅替代N-碘丁二醯亞胺，獲得上述化合物。

製備例168：



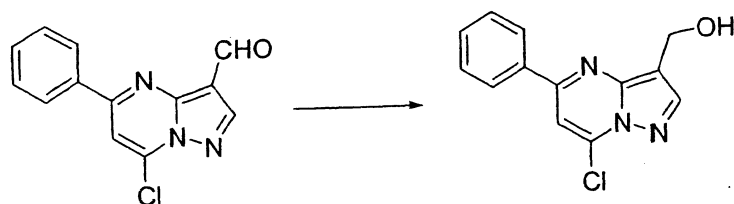
於製備例79之化合物(1.0克，4.35毫莫耳)之DMF(6毫升)溶液中添加POCl₃(1.24毫升，3.05當量)且所得混合物在室溫攪拌隔夜。反應混合物冷卻至0℃並藉添加冰捕捉過量之POCl₃。所得溶液以1 N NaOH中和，以H₂O稀釋並以CH₂Cl₂萃取。合併之有機層以Na₂SO₄脫水，過濾並真空濃縮。粗產物藉快速層析純化使用5% MeOH之CH₂Cl₂溶液作為溶離液(0.95克，85%產率)。LCMS: MH⁺=258。

製備例169：



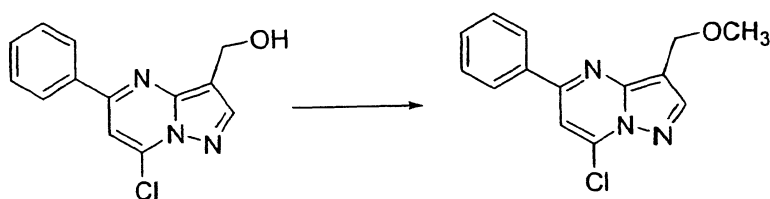
基本上同製備例168所述相同程序，僅替代製備例80中製備之化合物，獲得上述化合物(0.45克，40%產率)。

製備例170：



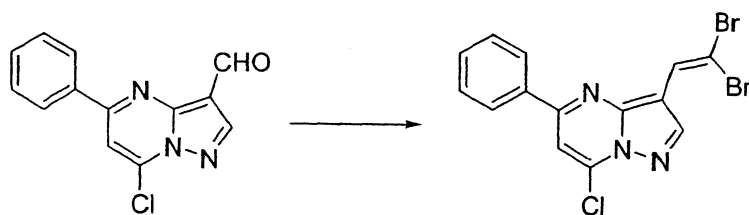
於製備例169之產物(0.25克，0.97毫莫耳)之THF溶液中添加NaBH₄(0.041克，1.1當量)且所得溶液在室溫攪拌隔夜。反應混合物藉添加H₂O驟冷並以CH₂Cl₂萃取。合併之有機層以Na₂SO₄脫水，過濾並減壓濃縮。粗產物藉快速層析純化使用60:40之己烷:EtOAc混合物作為溶離液(0.17克，69%產率)。MS: MH⁺=260。

製備例171：



製備例170之化合物(0.12克，0.462毫莫耳)、硫酸二甲酯(0.088毫升，2.0當量)、50% NaOH(0.26毫升)及催化量之Bu₄NBr之CH₂Cl₂(4毫升)之溶液在室溫攪拌隔夜。反應混合物以H₂O稀釋並以CH₂Cl₂萃取。合併之有機物以Na₂SO₄脫水，過濾並減壓濃縮。粗產物藉快速層析使用30% EtOAc之己烷溶液作為溶離液(0.062克，48%產率)。

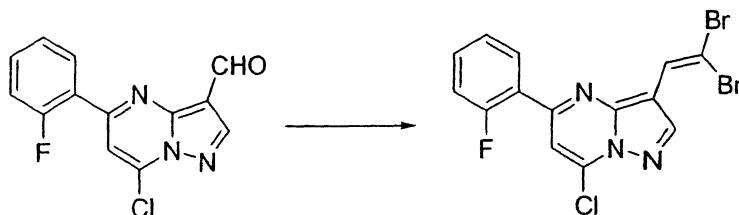
製備例172：



於PPh₃(4.07克，4.0當量)及CBr₄(2.57克，2.0當量)之

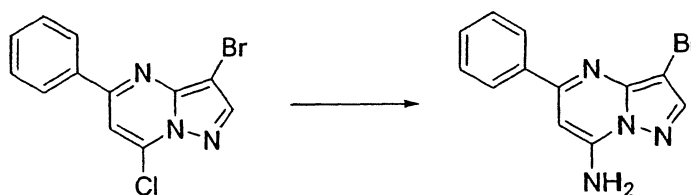
CH_2Cl_2 (75 毫升)之 0°C 溶液中添加製備例 168 之化合物 (1.0 克, 3.88 毫莫耳)。所得溶液在 0°C 攪拌 1 小時並減壓濃縮。殘留物藉快速層析使用 20% EtOAc 之己烷溶液作為溶離液純化 (1.07 克, 67% 產率)。

製備例 173：



基本上同製備例 172 所述相同程序，僅替代製備例 169 中製備之化合物，獲得上述化合物 (0.5 克, 70% 產率)。

製備例 174：

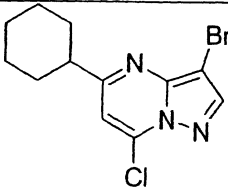
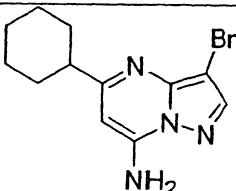
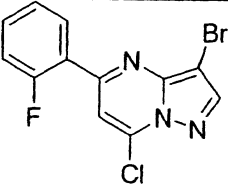
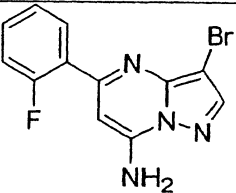
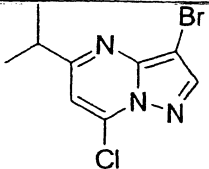
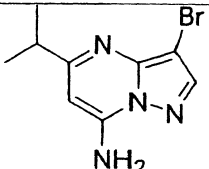
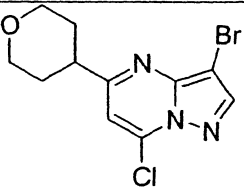
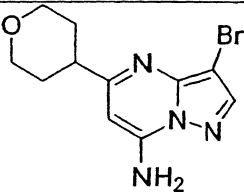
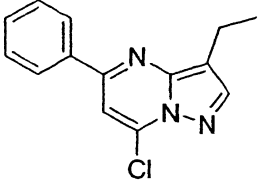
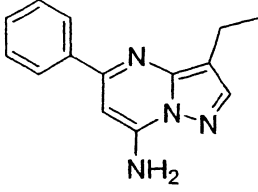
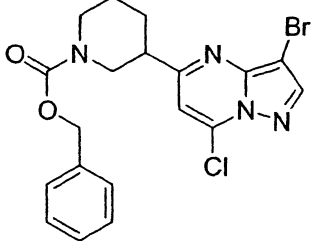
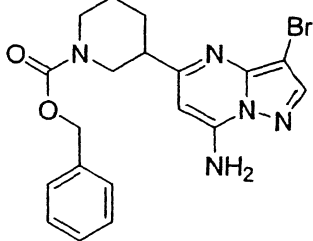


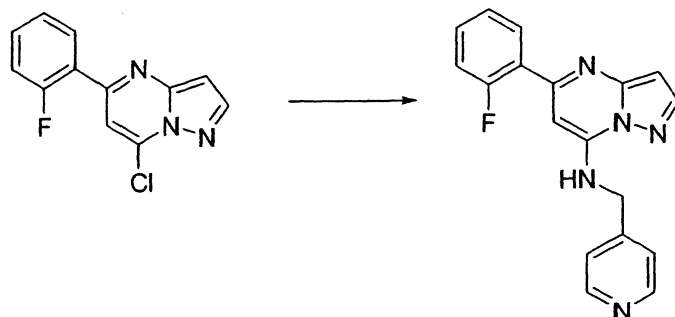
製備例 127 所製備之化合物 (3.08 克, 10.0 毫莫耳)、2.0 M NH_3 之 2-丙醇 (50 毫升, 100.0 毫莫耳) 及 37% NH_3 水溶液 (10.0 毫升) 在密閉壓力容器中在 50°C 攪拌 1 天。蒸發溶劑且粗產物藉快速層析使用 3 : 1 CH_2Cl_2 : EtOAc 作為溶離液純化。獲得淡黃色固體 (2.30 克, 80%)。LCMS : $\text{M}^+ = 289$ 。

製備例 175-180：

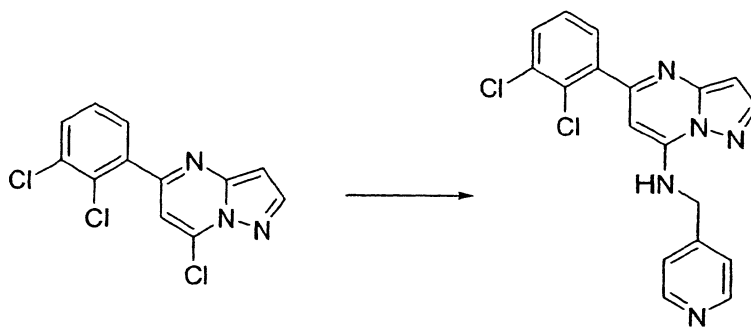
基本上同製備例 174 所述相同程序，僅以表 11 欄 2 所示之化合物替代，獲得表 11 欄 3 之化合物：

表 11

製備例	欄2	欄3
175		
176		
177		
178		
179		
180		

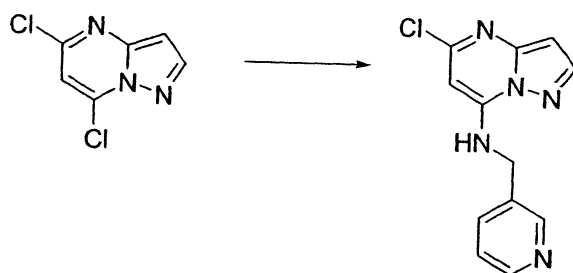
製備例 181：

製備例 80 製備之化合物 (0.3 克，1.2 毫莫耳)、 K_2CO_3 (0.33 克，2 當量) 及 4-胺基甲基吡啶 (0.13 毫升，1.1 當量) 回流隔夜。反應混合物冷卻至室溫並減壓濃縮。殘留物以 H_2O 稀釋及以 CH_2Cl_2 萃取。合併之有機層以 Na_2SO_4 脫水，過濾並濃縮。粗產物藉快速層析純化使用 5% (10% NH_4OH 之 $MeOH$) 溶液之 CH_2Cl_2 作為溶離液 (0.051 克，40% 產率)。LCMS: $MH^+ = 320$ 。

製備例 182：

基本上同製備例 181 所述相同程序，僅替代製備例 92 中製備之化合物，獲得上述化合物。LCMS: $MH^+ = 370$ 。

製備例 183：

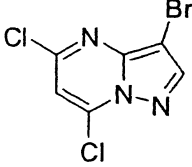
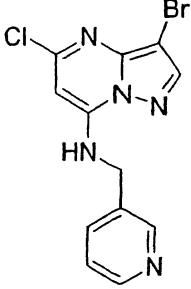
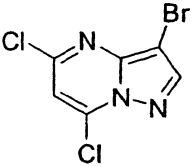
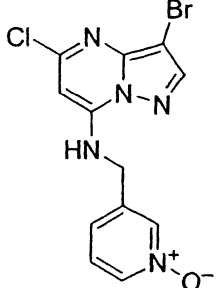
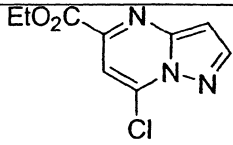
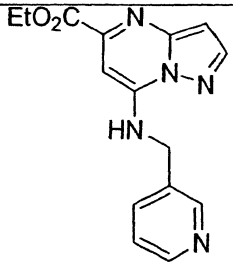
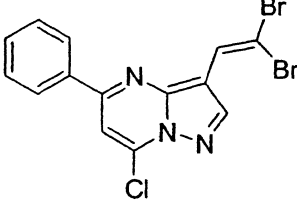
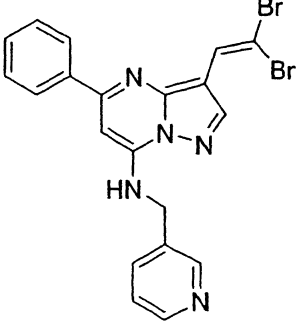
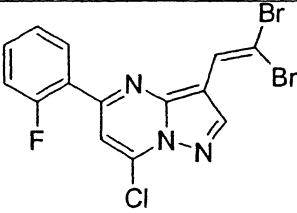
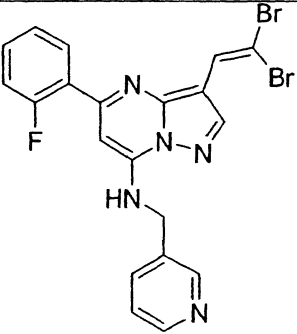


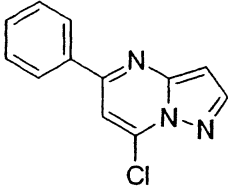
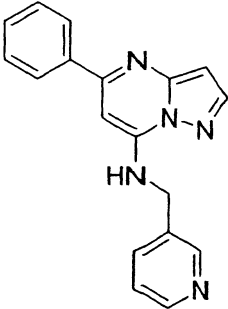
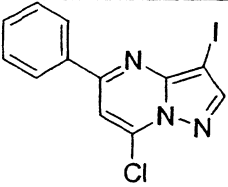
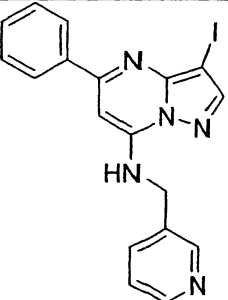
製備例123中製備之化合物(0.25克，1.3毫莫耳)之二噁烷(5毫升)溶液中添加 $i\text{Pr}_2\text{NEt}$ (0.47毫升，2.0當量)及3-胺基甲基吡啶(0.15毫升，1.1當量)。所得溶液在室溫攪拌72小時。反應混合物以 H_2O 稀釋並以 EtOAc 萃取。合併之有機相以 H_2O 及飽和 NaCl 洗滌，以 Na_2SO_4 脫水，過濾並真空濃縮。粗產物藉快速層析純化使用5% MeOH 之 CH_2Cl_2 溶液作為溶離液(0.29克，83%產率)。LCMS: $\text{MH}^+=260$ 。

製備例184-187：

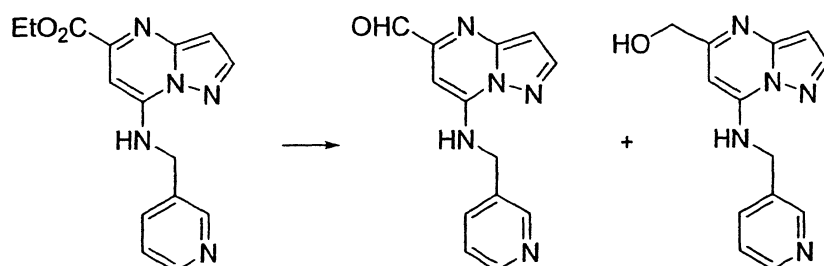
基本上同製備例183所述相同程序，僅以表12欄2所示之化合物替代，獲得表12欄3之化合物。

表 12

製備例	欄2	欄3
184		
184.1		
185		
186		
187		

187.1		
187.11		

製備例 188 及製備例 189：



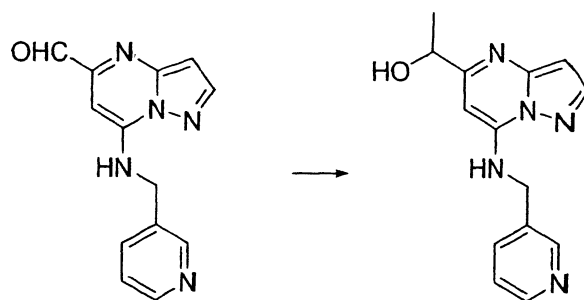
製備例 185 製備之化合物(1.18 克，3.98 毫莫耳)之 THF(35 毫升)溶液中，在 -78°C 滴加 LAH(4.78 毫升，1 M 於 Et_2O ，1.0 當量)。反應混合物在 -78°C 攪拌 3 小時，期間又滴加 LAH(2.0 毫升，1 M 於 Et_2O ，0.42 當量)。反應混合物又攪拌 1.25 小時且藉添加飽和 Na_2SO_4 (8.5 毫升)驟冷。反應混合物以 EtOAc (23 毫升)、 H_2O (2 毫升)及 CH_3OH (50 毫升)稀釋。所得漿液經矽藻土栓柱過濾。矽藻土以 CH_3OH 洗滌且濾液以 Na_2SO_4 脫水，過濾並濃縮。產物藉快速層析使用 $\text{CH}_2\text{Cl}_2:\text{CH}_3\text{OH}$ (93:7) 溶液作為溶離液，獲得第一溶離產物之醛及第二溶離產物

之醇。

製備例 188：(醛)：0.4 克，39%產率。MS:MH⁺=254。

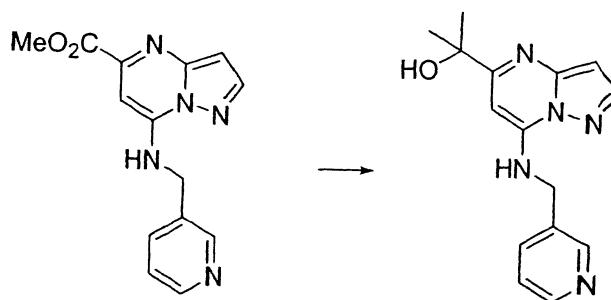
製備例 189：(醇)：0.25 克，24%產率。MS:MH⁺=256。

製備例 190：



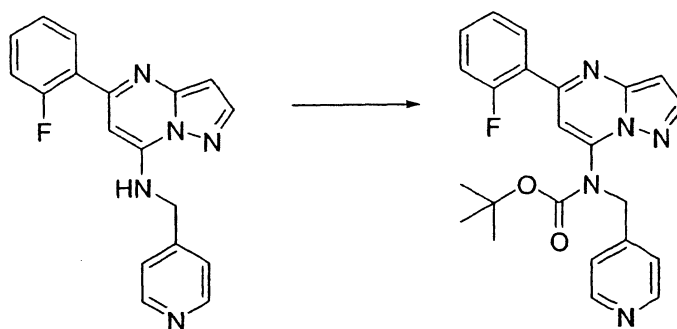
於製備例 188 製備之產物 (0.075 克，0.30 毫莫耳) 之 THF (2.0 毫升) 溶液中，在 0℃ 滴加 CH₃MgBr (0.3 毫升，3.0 M 之 Et₂O 溶液，3.0 當量)。所得溶液在 0℃ 又攪拌 1.5 小時，溫至室溫並攪拌隔夜。又添加 CH₃MgBr (0.15 毫升，3.0 M 於 Et₂O，1 當量) 且所得溶液又攪拌 1.5 小時。反應混合物冷卻至 0℃ 並藉添加飽和 NH₄Cl 驟冷。所得溶液以 CH₂Cl₂ 及 H₂O 稀釋並以 CH₂Cl₂ 萃取。合併之有機層以飽和 NaCl 洗滌並以 Na₂SO₄ 脫水，過濾並濃縮。粗產物藉快速層析使用 CH₂Cl₂:CH₃OH (90:10) 溶液作為溶離液純化 (0.048 克，60% 產率)。MS:MH⁺=270。

製備例 191：



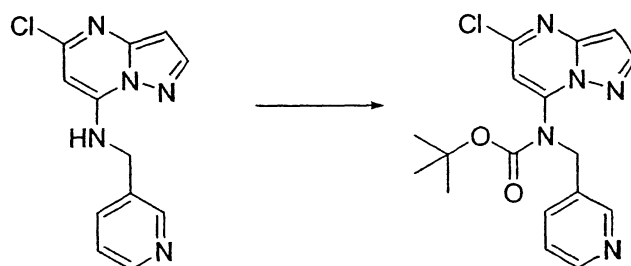
基本上同製備例190所述相同程序，僅替代製備例185中製備之化合物並使用過量MeMgBr(5當量)，製備上述化合物。

製備例192：



製備例181製備之化合物(0.29克，0.91毫莫耳)、 BOC_2O (0.22克，1.1當量)及DMAP(0.13克，1.1當量)於二噁烷(10毫升)中在室溫攪拌3天。添加額外 BOC_2O (0.10克，0.5當量)且反應混合物攪拌4小時。反應混合物真空濃縮，以飽和 NaHCO_3 (15毫升)稀釋並以 CH_2Cl_2 (2x100毫升)萃取。合併之有機層以 Na_2SO_4 脫水，過濾並減壓濃縮。粗產物藉快速層析純化使用5%(10% NH_4OH 之MeOH)溶液之 CH_2Cl_2 作為溶離液(0.35克，91%產率)。LCMS: $\text{MH}^+=420$ 。

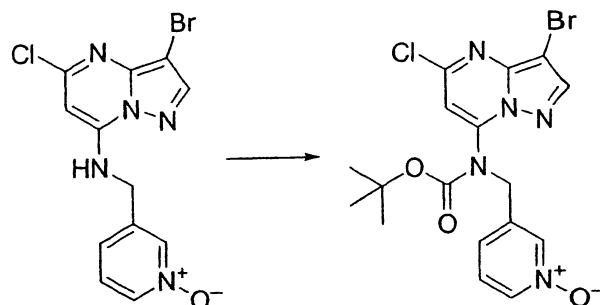
製備例193：



基本上同製備例192所述相同程序，僅替代製備例183中

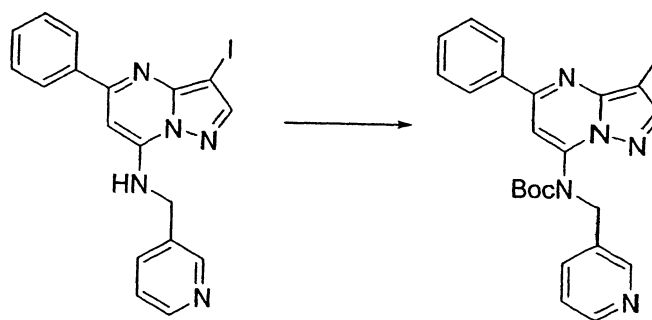
製備之化合物，製備上述化合物。MS:MH⁺=360。

製備例 193.10：



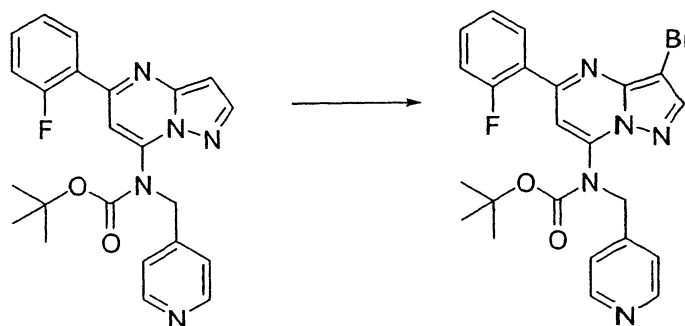
基本上同製備例 192 所述相同程序，僅替代製備例 184.1 中製備之化合物，製備上述化合物。MS:MH⁺=454。

製備例 194：



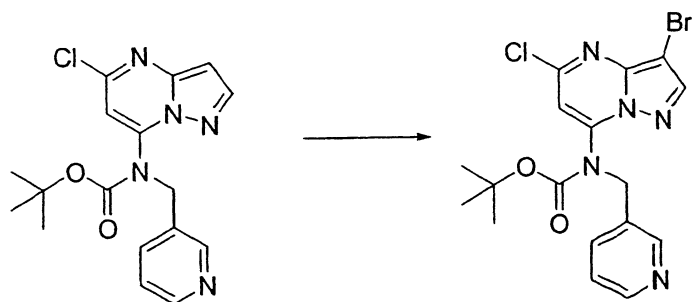
基本上同製備例 192 所述相同程序，僅替代製備例 187.11 中製備之化合物，製備上述化合物 (0.223 克，88% 產率)。
MS:MH⁺=528。

製備例 195：



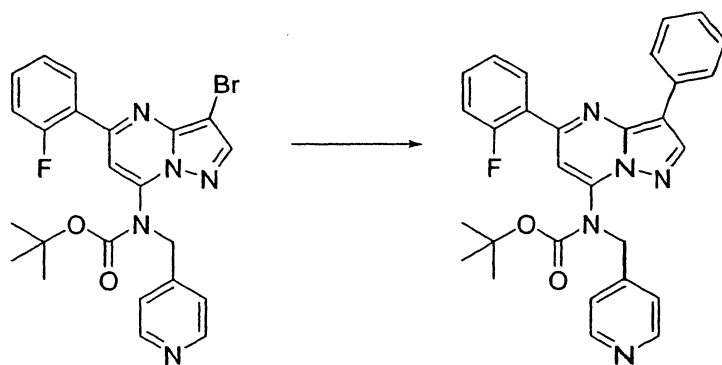
基本上同製備例127所述相同程序，僅替代製備例192中製備之化合物，製備上述化合物(0.38克，95%產率)。LCMS: $MH^+ = 498$ 。

製備例196：



基本上同製備例195所述相同程序，僅替代製備例193中製備之化合物，製備上述化合物(0.3克，83%產率)。MS: $MH^+ = 438$ 。

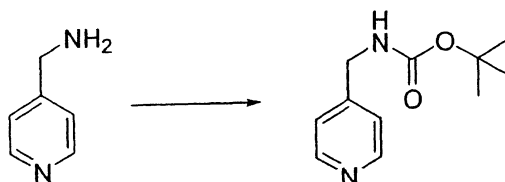
製備例197：



製備例195所製備之化合物(0.15克，0.3毫莫耳)、苯基硼酸(0.073克，2.0當量)、 K_3PO_4 (0.19克，3.0當量)及 $Pd(PPh_3)_4$ (0.017克，5莫耳%)之溶液於DME(16毫升)及 H_2O (4毫升)中回流加熱7小時。所得溶液冷卻至室溫，以 H_2O (10毫升)稀釋並以 CH_2Cl_2 (3x50毫升)萃取。合併之有機層以 Na_2SO_4 脫水，過濾並濃縮。粗產物藉快速層析純化使用2.5%(10%

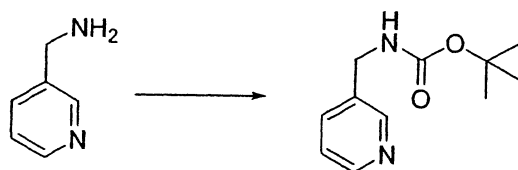
NH_4OH 之 MeOH)之 CH_2Cl_2 溶液作為溶離液(0.16克，100%產率)。

製備例 198：



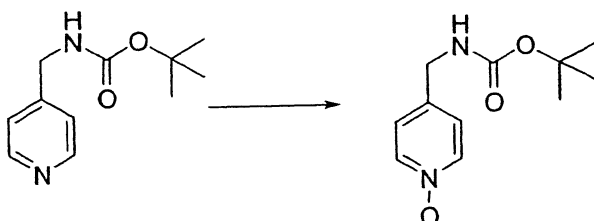
於4-胺基甲基吡啶(1.41毫升，13.87毫莫耳)之 CH_2Cl_2 (50毫升)溶液中添加 BOC_2O (3.3克，1.1當量)及TEA且所得溶液在室溫攪拌2小時。反應混合物以 H_2O (50毫升)稀釋並以 CH_2Cl_2 萃取。合併之有機層以 Na_2SO_4 脫水，過濾並減壓濃縮。粗產物藉快速層析純化使用5%(10% NH_4OH 之 MeOH)之 CH_2Cl_2 溶液作為溶離液，獲得黃色固體(2.62克，91%產率)。LCMS: $\text{MH}^+=209$ 。

製備例 199：



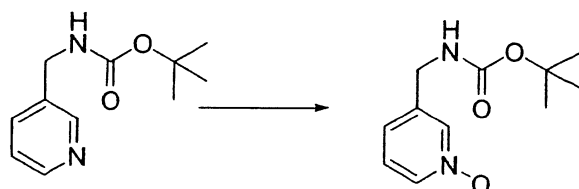
基本上同製備例198所述相同程序，僅替代3-胺基甲基吡啶，製備上述化合物，黃色油(2.66克，92%產率)。LCMS: $\text{MH}^+=209$ 。

製備例 200：



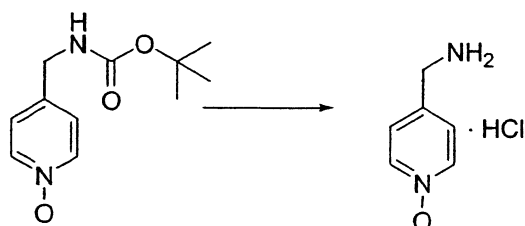
於製備例 198 所製備之化合物 (0.20 克, 0.96 毫莫耳) 之 CH_2Cl_2 (5 毫升) 溶液中, 在 0°C 添加 m-CPBA (0.17 克, 1.0 當量) 且所得溶液在 0°C 攪拌 2 小時並儲存在 4°C 隔夜, 期間反應混合物溫至室溫並攪拌 3 小時。反應混合物以 H_2O 稀釋並以 CH_2Cl_2 萃取。合併之有機層以 Na_2SO_4 脫水, 過濾並濃縮。粗產物藉快速層析純化使用 10% (10% NH_4OH 之 MeOH) 溶液作為溶離液。LCMS: $\text{MH}^+ = 255$ 。

製備例 201:



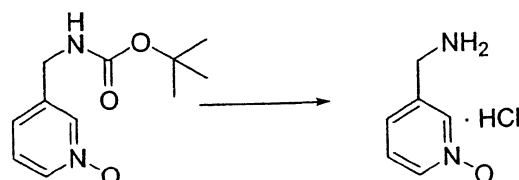
oxone (58.6 克) 之 H_2O (250 毫升) 溶液滴加至製備例 199 所製備之化合物 (27 克, 0.13 莫耳) 及 NaHCO_3 (21.8 克, 2.0 當量) 之 MeOH (200 毫升) 及 H_2O (250 毫升) 溶液中。所得溶液在室溫攪拌隔夜。反應混合物以 CH_2Cl_2 (500 毫升) 稀釋並過濾。分離層且水層以 CH_2Cl_2 萃取。合併之有機層以 Na_2SO_4 脫水, 過濾並減壓濃縮, 獲得白色固體 (21.0 克, 72% 產率)。MS: $\text{MH}^+ = 255$ 。

製備例 202:



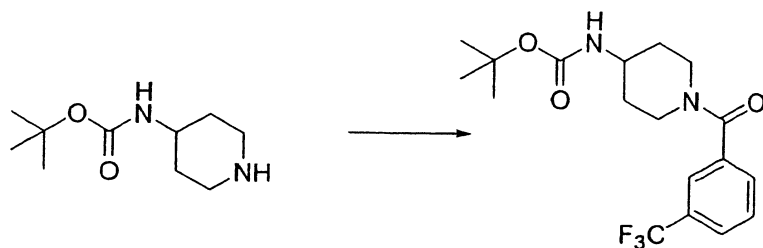
製備例 200 所製備之化合物 (0.29 克, 1.29 毫莫耳) 於 4 M HCl 之二噁烷 (0.97 毫升) 中在室溫攪拌 2 小時。反應混合物真空濃縮且未經進一步純化使用。LCMS: $MH^+ = 125$ 。

製備例 203:



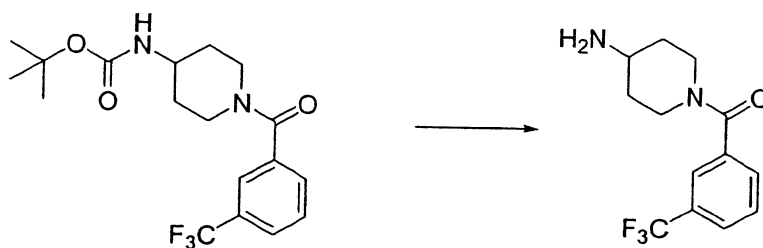
基本上同製備例 202 所述相同程序, 僅替代製備例 201 所製備之化合物, 製備上述化合物。LCMS: $MH^+ = 125$ 。

製備例 204:



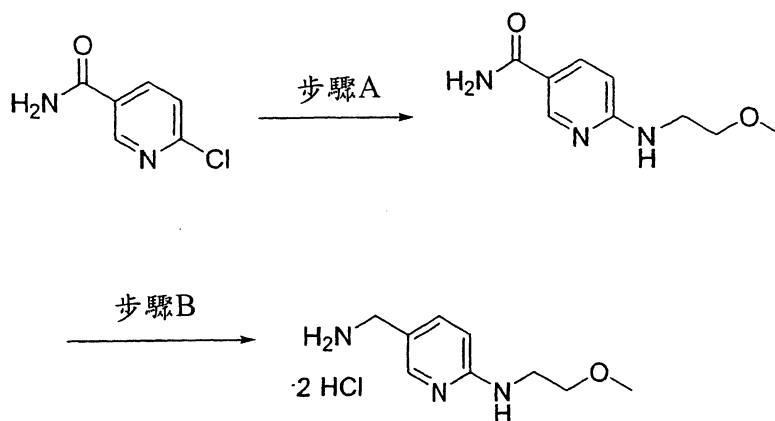
於 4-N-第三丁氧羰基胺基哌啶 (0.8 克, 4.0 毫莫耳) 之 CH_2Cl_2 (10 毫升) 中, 在 $0^\circ C$ 添加 TEA (1.40 毫升, 2.5 當量) 及 3-三氟甲基苯甲醯氯 (1.05 克, 1.25 當量)。所得溶液攪拌 15 分鐘並溫至室溫及攪拌 3 小時。反應混合物以 CH_2Cl_2 稀釋並以 5% Na_2CO_3 (2x100 毫升) 洗滌。有機層以 Na_2SO_4 脫水, 過濾並濃縮獲得淡黃色固體 (定量粗產率)。

製備例 205:



於製備例 204 所製備之化合物 (1.0 克, 2.76 毫莫耳) 之 CH_2Cl_2 (15 毫升) 溶液中, 在 0°C 添加 TFA (8 毫升) 且所得溶液在 0°C 攪拌 30 分鐘及在室溫攪拌 1 小時。反應混合物倒入 Na_2CO_3 (40 克) 中並添加 H_2O (400 毫升) 且所得混合物以 CH_2Cl_2 萃取。合併之有機層以 Na_2SO_4 脫水, 過濾並減壓濃縮。粗產物藉快速層析使用 20% (7 N NH_3 之 MeOH) 溶液之 CH_2Cl_2 作為溶離液純化 (0.6 克, 82% 產率)。

製備例 206:



步驟 A:

於 6-氯菸鹼醯胺 (1 克, 6.39 毫莫耳) 之異戊醇 (15 毫升) 溶液中在 rt 添加 Na_2CO_3 (0.81 克, 7.67 毫莫耳) 接著添加甲氧基甲基胺 (0.67 毫升, 7.67 毫莫耳)。混合物在 130°C 加熱 16 小時, 冷卻至 rt 且經中度玻璃熔料之過濾器過濾。所得濾液減壓濃縮且所得固體以 Et_2O (2x10 毫升) 分散。粗固體置入高真空中獲得 1.2 克 (96%) 淡黃色固體。M+H=196。

步驟 B:

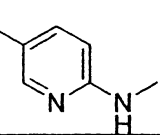
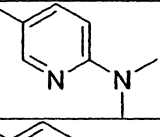
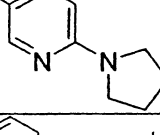
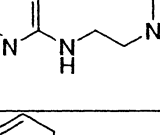
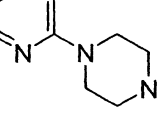
製備例 206 步驟 A 之醯胺 (1.2 克, 6.12 毫莫耳) 之 THF (5 毫升)

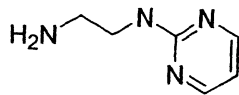
溶液中，在 0℃ 以 10 分鐘內滴加 $\text{BH}_3\text{-THF}$ 溶液 (43 毫升，43 毫莫耳)。所得溶液溫至 rt 並攪拌 14 小時。混合物冷卻至 0℃ 並依序以 6 M HCl (35 毫升)、水 (30 毫升) 及 MeOH (150 毫升) 處理。混合物攪拌 8 小時並減壓濃縮。粗殘留物以 MeOH 分散，減壓濃縮且置入高真空中，獲得 1.6 克 (82%) 白色固體，為二鹽酸鹽。 $\text{M}+\text{H}$ (游離鹼) = 182.0。此物質以粗製使用與 7-Cl 加成物偶合。

製備例 207-211：

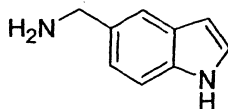
基本上同製備例 206 所述相同程序，僅利用表 13 欄 2 所示之胺，製備表 13 欄 3 之化合物：

表 13

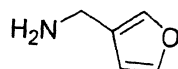
製備例	欄2(胺)	欄3(胺)	數據 $\text{M}+\text{H}$ (游離鹼)
207	$\text{H}_2\text{N}-$	$\text{H}_2\text{N}-$ 2 HCl 	$\text{M}+\text{H} = 138$
208	$\text{HN}-$	$\text{H}_2\text{N}-$ 2 HCl 	$\text{M}+\text{H} = 152$
209		$\text{H}_2\text{N}-$ 2 HCl 	$\text{M}+\text{H} = 178$
210	$\text{H}_2\text{N}-\text{CH}_2\text{CH}_2\text{N}-$	$\text{H}_2\text{N}-$ 3 HCl 	$\text{M}+\text{H} = 195$
211		$\text{H}_2\text{N}-$ 3 HCl 	$\text{M}+\text{H} = 207$

製備例 212：

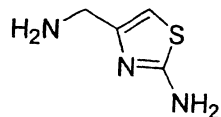
依據 WO 91/18904 所述之方法製備上述化合物。

製備例 213：

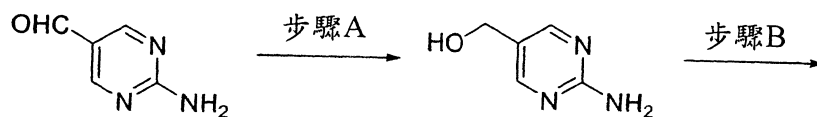
依據 US 6,180,627 B1 所述之方法製備上述化合物。

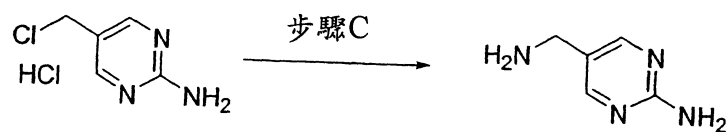
製備例 214：

該已知之胺係如醫藥化學期刊(2001), 44, 4505-4508 所述
般製備。

製備例 215：

該已知之胺係如醫藥化學期刊(1997), 40, 3726-3733 所述
般製備。

製備例 216：

步驟 A：

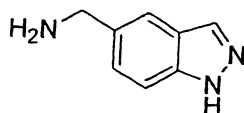
醛(50克，0.41莫耳)[WO 0232893]之MeOH(300毫升)溶液冷卻至0°C並小心以NaBH₄(20克，0.53莫耳，分6批次)以20分鐘內處理。反應接著溫至20°C並攪拌4小時。混合物再冷卻至0°C，小心以飽和NH₄Cl溶液驟冷並濃縮。快速層析(5-10% 7 N NH₃-MeOH/CH₂Cl₂)獲得淡黃色固體之一級醇(31克，62%)。

步驟 B：

得自製備例216步驟A之醇(31克，0.25莫耳)於CH₂Cl₂(500毫升)之漿液冷卻至0°C並緩慢以SOCl₂(55毫升，0.74莫耳，歷時30分鐘)處理。反應接著在20°C攪拌隔夜。物質濃縮，於丙酮中成漿液接著過濾。所得灰褐色固體於真空中乾燥隔夜(38.4克，52%，HCl鹽)。

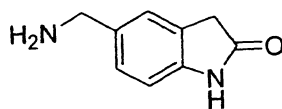
步驟 C：

於15毫升壓力管中饋入攪拌棒，添加得自製備例216步驟B之氯化物(150毫克，0.83毫莫耳)接著添加7 M NH₃/MeOH(10毫升)。所得溶液在rt攪拌48小時，隨後混合物減壓濃縮獲得淡黃色固體(0.146克，83%)。M+H(游離鹼)=140。

製備例 217：

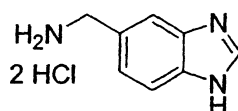
依據 WO 00/26210 所述之方法製備上述化合物。

製備例 218：



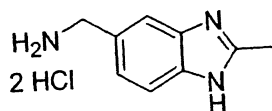
依據 WO 99/10325 所述方法製備上述化合物。

製備例 219：



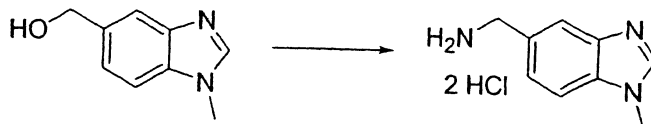
依據 WO 02/64211 所述方法製備已知之胺二鹽酸鹽。

製備例 220：



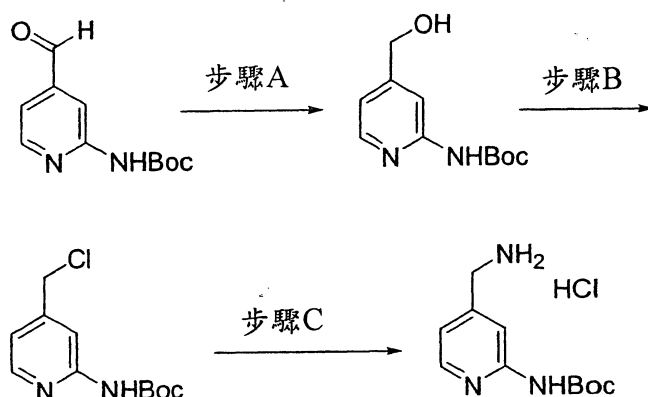
依據 WO 02/64211 所述方法製備上述化合物。

製備例 221：



依據 WO 00/37473 製備已知之一級醇並以類似製備例 220 之方式依據 WO 02/064211 轉化成所需之胺二鹽酸鹽。

製備例 222：

步驟 A：

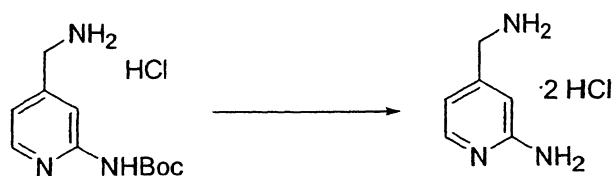
於醛(WO 02/32893)(0.46克，2.07毫莫耳)之MeOH/THF(2毫升/2毫升)溶液中，在0°C一次添加NaBH₄(94毫克，2.48毫莫耳)。所得混合物在rt攪拌12小時並以飽和NH₄Cl水溶液(3毫升)稀釋。混合物減壓濃縮且所得水層以CH₂Cl₂(3x5毫升)萃取。合併有機層，以食鹽水(1x5毫升)洗滌，脫水(Na₂SO₄)並過濾。有機層減壓濃縮獲得417毫克(90%產率)之白色固體。M+H=225。

步驟 B：

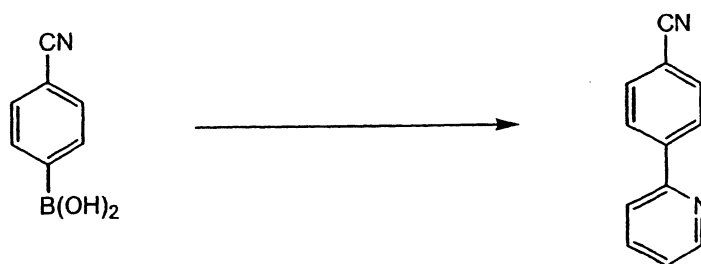
得自製備例222步驟A之粗製醇(0.4克，1.78毫莫耳)之CH₂Cl₂(4毫升)中添加SOCl₂(0.65毫升，8.91毫莫耳)且混合物在rt攪拌2小時。混合物減壓濃縮獲得407毫克(94%)淡黃色固體。M+H=243。粗產物未經進一步純化即使用。

步驟 C：

得自製備例222步驟B之粗製氯化物(0.33克，1.36毫莫耳)溶液之壓力管中饋入7 M NH₃/MeOH(35毫升)且混合物攪拌72小時。混合物減壓濃縮獲得257毫克(85%)黃色半固體。M+H(游離鹼)=224。

製備例 223：

於圓底瓶中饋入得自製備例 222 所得之胺鹽酸鹽 (0.24 克，1.1 毫莫耳) 及攪拌棒，添加 4 N HCl/二噁烷 (10 毫升)。所得溶液在 rt 攪拌 12 小時，減壓濃縮並以 CH_2Cl_2 (3x5 毫升) 分散。粗產物過濾，以 Et_2O (2x5 毫升) 洗滌並在高真空下乾燥獲得 0.19 克 (91%)，為二鹽酸鹽。M+H (游離鹼)=124。

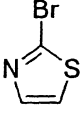
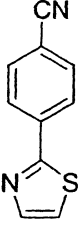
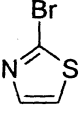
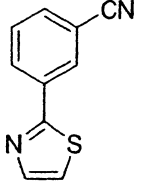
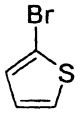
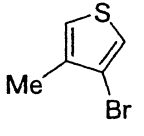
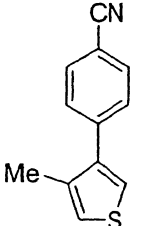
製備例 224：

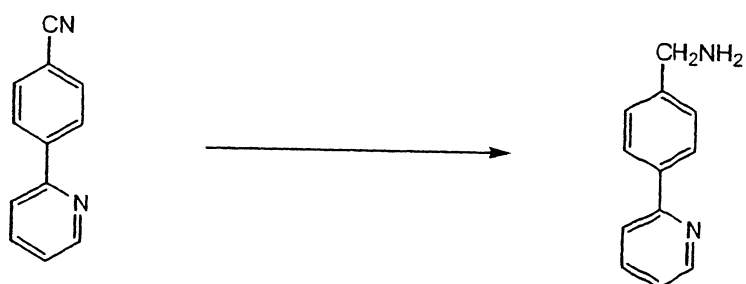
$\text{Pd}(\text{PPh}_3)_4$ (0.404 克，0.35 毫莫耳) 添加至 4-氰基苯硼酸 (1.029 克，7 毫莫耳) 及 2-溴吡啶 (1.11 克，7 毫莫耳) 之 75 毫升乙腈脫氣溶液中。於反應混合物中添加 0.4 M 碳酸鈉溶液 (35 毫升) 且所得溶液在 90°C 及 Ar 下攪拌 24 小時 (反應過程以 TLC 追蹤)。反應混合物冷卻並分離水層。含產物及用過之觸媒之有機層與矽膠 (15 克) 混合並濃縮至乾。藉管柱層析單離 4-(2-吡啶基)-苄腈 (0.850 克，68%)。LCMS: $\text{MH}^+ = 181$; ^1H NMR (CDCl_3) δ 8.85 (d, 1H), 8.7 (dd, 1H), 7.9 (dd, 1H), 7.75 (d, 2H), 7.7 (d, 2H), 7.4 (dd, 1H)。

製備例 225-228：

基本上依循製備例 224 所述程序，僅以表 14 欄 2 之溴化物替代，製備表 14 欄 3 之化合物。

表 14

製備例	欄2	欄3	欄4
225			產率= 70% LCMS: $MH^+ = 187$
226			產率= 60% LCMS: $MH^+ = 187$
227			產率= 70% LCMS: $MH^+ = 186$
228			產率= 70% LCMS: $MH^+ = 200$

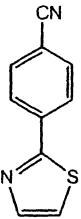
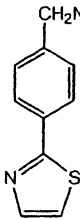
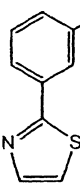
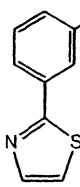
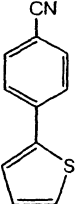
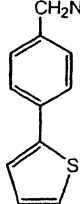
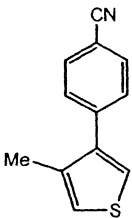
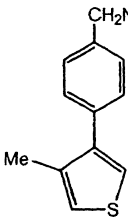
製備例 229：

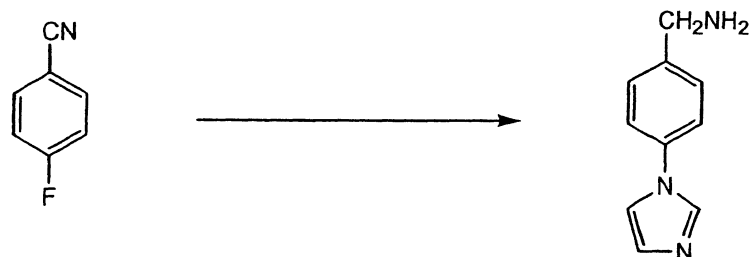
BH₃-THF溶液(1 M, 24毫升, 5當量)緩慢添加至4-(2-吡啶基)-苄腈(0.85克, 4.72毫莫耳)之無水THF(25毫升)在Ar中攪拌之溶液中, 且所得溶液回流約12小時。溶液使用冰水冷卻至0°C。滴加甲醇(15毫升)至冷卻之反應混合物中並攪拌1小時以破壞過量之BH₃。緩慢添加HCl-甲醇(1 M, 10毫升)至反應混合物中並回流5小時。濃縮溶液至乾且殘留物溶於25毫升水中並以乙醚萃取以移除任何未反應之物質。水溶液以固體碳酸鉀中和至pH 10-11。所形成之游離胺以乙醚萃取, 以碳酸鉀脫水(0.45克, 50%)。LCMS: MH⁺=185; ¹H NMR (CDCl₃)δ 8.85 (d, 1H), 8.7 (dd, 1H), 7.9 (dd, 1H), 7.75 (d, 2H), 7.7 (d, 2H), 7.4 (dd, 1H), 3.7 (t, 2H), 1.7 (t, 2H)。

製備例 230-233：

基本上依循製備例 229 所述程序, 製備表 15 欄 3 之化合物。

表 15

製備例	欄2	欄3	欄4
230			產率= 60% LCMS: MH ⁺ = 191
231			產率= 60% LCMS: MH ⁺ = 191
232			產率= 70% LCMS: MH ⁺ = 190
233			產率= 70% LCMS: MH ⁺ = 204

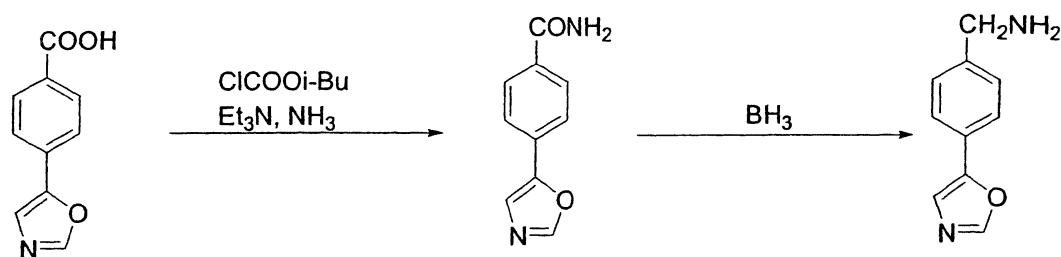
製備例 234：步驟 A：

4-氟苄腈(3克，25毫莫耳)及咪唑基鈉(2.48克，27.5毫莫耳)於DMF(50毫升)中之混合物在80℃及Ar下攪拌12小時。反應過程藉TLC追蹤。反應混合物真空濃縮且殘留物以50毫升水稀釋並攪拌。水性混合物以EtOAc(2x50毫升)萃取。合併之EtOAc萃取液以無水MgSO₄脫水，濃縮且藉管柱層析單離4-(1-咪唑基)-苄腈(3.6克，78%)。LCMS: MH⁺=170; ¹H NMR (CDCl₃) δ 8.0 (s, 1H), 7.5 (d, 2H), 7.4 (m, 3H), 7.3 (d, 1H)。

步驟 B：

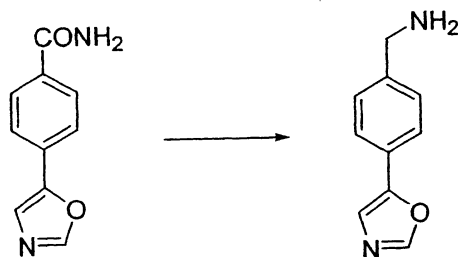
4-(1-咪唑基)-苄腈(1克，5.92毫莫耳)溶於無水THF(10毫升)並在室溫滴加至LAH-THF(1M於THF，18毫升)攪拌溶液中。反應混合物在Ar中回流2小時且反應過程以TLC追蹤。混合物冷卻至0℃並藉滴加飽和Na₂SO₄-H₂O溶液驟冷。混合物攪拌1小時並過濾移除鋰鹽。濾液以無水MgSO₄脫水並濃縮獲得4-(1-咪唑基)-苄胺(0.8克，80%)。LCMS: MH⁺=174。

製備例 235：



4-(5-噁唑基)苯甲酸(1.0克，5.46毫莫耳)及 Et_3N (552毫克，5.46毫莫耳)之25毫升THF中之混合物冷卻至 0°C 並滴加 ClCOOi-Bu (745毫克，5.46毫莫耳)。添加完成後，反應混合物又攪拌5分鐘接著添加 NH_4OH 水溶液(0.63毫升，28%溶液，10.46毫莫耳)。攪拌隔夜後，蒸發溶劑，殘留物置入水中並鹼化至pH9。過濾沉澱之固體，以水洗滌並以 P_2O_5 於真空乾燥器中乾燥，獲得500毫克(48%) 4-(5-噁唑基)-苄醯胺： ^1H NMR(DMSO-d_6) δ 8.50(s,1H), 8.20-7.80 (m,5H)。

製備例 236：



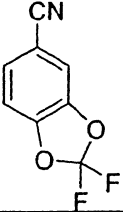
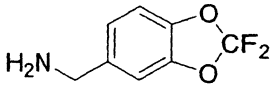
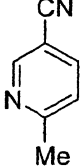
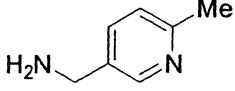
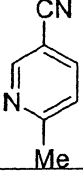
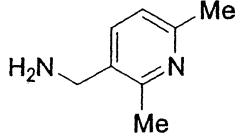
4-(5-噁唑基)-苄醯胺(500毫克，2.657毫莫耳)之10毫升無水THF懸浮液冷卻至 0°C 並添加10毫升1 M $\text{BH}_3\cdot\text{THF}$ (10.00毫莫耳)。內容物回流隔夜且藉滴加甲醇破壞過量硼烷。蒸發溶劑且殘留物以甲醇 HCl 處理分解胺-硼烷錯合物。蒸發甲醇後，殘留物置入水中，鹼化至pH10且產物萃取入DCM中。DCM層脫水(K_2CO_3)且移除溶劑獲得150毫克(32%)4-(5-噁唑基)苄胺： ^1H NMR (CDCl_3) δ 7.90 (s, 1H), 7.60 (d, 2H),

7.40 (d, 2H), 7.30 (s, 1H), 3.90 (s, 2H)。

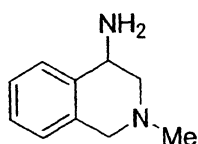
製備例 237-239：

基本上同上述相同程序，使用表16欄3所示之方法使表16欄2之化合物還原，獲得表16欄4所示之胺。

表 16

製備例	欄2	欄3	欄4	數據
237		BH ₃		¹ H NMR (CDCl ₃) δ 7.15-6.90 (m, 3H), 3.85 (s, 2H), 1.45 (s, 2H)
238		H ₂		¹ H NMR (CDCl ₃) δ 8.40(s, 1H), 7.55 (dd, 1H), 7.10 (d, 1H), 3.85 (s, 2H), 2.50 (s, 3H), 1.70 (bs, 2 H)
239		BH ₃		

製備例 240：

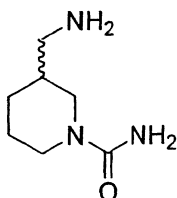


藉文獻程序(PCT國際申請案 WO 0105783)製備：¹H NMR (CDCl₃)δ 7.35 (d, 1H), 7.24-7.10 (m, 2H), 7.02 (d, 1H), 3.95 (t, 1H), 3.70 (d, 1H), 3.37 (d, 1H), 2.65 (m, 2H), 2.45 (s, 3H),

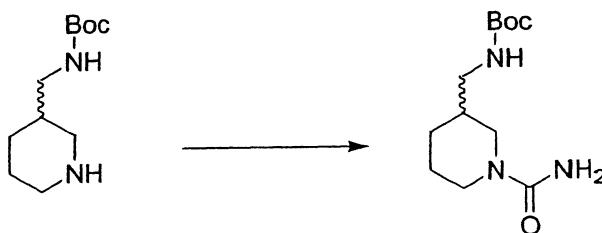
1.90 (bs, 2H)。

製備例 241：

3-(胺基甲基)哌啶-1-羧醯胺



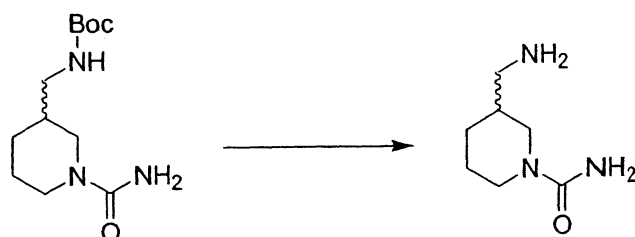
A.3-(第三丁氧羰基胺基甲基)哌啶-1-羧醯胺



3(R/S)-(第三丁氧羰基胺基甲基)哌啶(3克，14.0毫莫耳)溶於無水二氯甲烷(50毫升)並添加異氰酸三甲基矽烷酯(9.68克，11.4毫升，84.0毫莫耳)。混合物在氫氣及25℃下攪拌68小時。添加額外之異氰酸三甲基矽烷酯(4.84克，5.7毫升，42.0毫莫耳)且混合物在25℃總共攪拌90小時。混合物蒸發至乾且在矽膠管柱(30x5公分)上層析使用2%(10%濃氫氧化銨之甲醇)-二氯甲烷作為溶離液，獲得3-(第三丁氧羰基胺基甲基)哌啶-1-羧醯胺(3.05克，85%)：FABMS: m/z 258.1 (MH^+); HRFABMS: m/z 258.1816 (MH^+)。對 $C_{12}H_{24}O_3N_3$ 計算值： m/z 258.1818; δ_H ($CDCl_3$) 1.22(1H, m, CH_2), 1.42 (9H, s, $-COOC(CH_3)_3$), 1.48 (1H, m, CH_2), 1.67 (2H, m, CH_2), 1.78 (1H, m, CH), 2.80 (1H, m, CH_2), 2.99 (3H, m, CH_2), 3.59 (1H,

m, CH₂), 3.69 (1H, m, CH₂), 4.76 (2H, bm, CONH₂)及4.98 ppm (1H, bm, NH); δ_c (CDCl₃)CH₃:28.5, 28.5, 28.5; CH₂:24.0, 28.3, 43.2, 45.1, 47.8; CH: 36.5; C: 79.4, 156.3, 158.5。

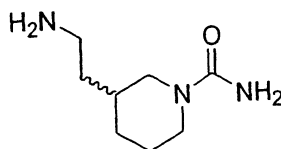
B.3-(胺基甲基)哌啶-1-羧醯胺



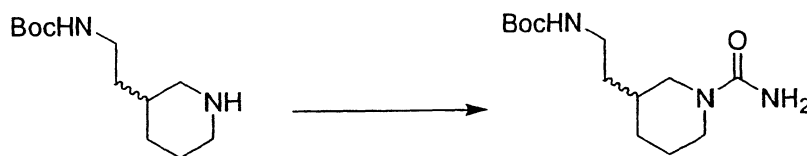
3-(第三丁氧羰基胺基甲基)哌啶-1-羧醯胺(150毫克, 0.583毫莫耳)(上述製備例241步驟A製備)溶於甲醇(3毫升)。添加10%濃硫酸之1,4-二噁烷(7.9毫升)且混合物在25℃攪拌1小時。混合物以甲醇稀釋並添加BioRad AG1-X8樹脂(OH⁻態)直至pH為鹼性。濾除樹脂,以甲醇洗滌,蒸發至乾且在矽膠管柱(15x2公分)上層析使用二氯甲烷接著15%(10%濃氫氧化銨之甲醇)-二氯甲烷作為溶離液,獲得3-(胺基甲基)哌啶-1-羧醯胺(80毫克, 87%): FABMS: m/z 158.1 (MH⁺); HRFABMS: m/z 158.1294 (MH⁺)。對C₇H₁₆N₃O計算值: m/z 158.1293; δ_H (CDCl₃+drop CD₃OD) 1.20 (1H, m, CH₂), 1.48 (1H, m, CH₂), 1.60 (1H, m, CH), 1.68 (1H, m, CH₂), 1.83 (1H, m, CH₂), 2.64 (bm, 2H, -CH₂NH₂), 2.82 (1H, m, CH₂), 3.02 (1H, m, CH₂), 2.98 (2H, m, CH₂), 3.70 (1H, m, -CH₂NH₂), 3.78 (1H, m, -CH₂NH₂)及5.24 ppm (1H, bs, NH); δ_c (CDCl₃+drop CD₃OD) CH₂:24.1, 28.6, 44.0, 44.8, 47.9; CH: 38.3; C:159.0。

製備例 242：

3-(2-氨基乙基)哌啶-1-羧醯胺



A.3-(2-第三丁氧羰基氨基乙基)哌啶-1-羧醯胺



3-(2-第三丁氧羰基氨基乙基)哌啶(500毫克，2.19毫莫耳)溶於無水二氯甲烷(10毫升)並添加異氰酸三甲基矽烷酯(2.96毫升，21.9毫莫耳)。混合物在氫氣及25℃下攪拌3.35小時。混合物以二氯甲烷稀釋並以飽和碳酸氫鈉水溶液洗滌。有機層脫水(MgSO₄)，過濾，蒸發至乾並在矽膠管柱(15x5公分)上層析使用5%(10%濃氫氧化銨之甲醇)-二氯甲烷作為溶離液，獲得3-(2-第三丁氧羰基氨基乙基)哌啶-1-羧醯胺(417.7毫克，70%)：FABMS: m/z 272.0 (MH⁺)；HRFABMS: m/z 272.1979 (MH⁺)。對C₁₃H₂₆O₃計算值：m/z 272.1974；δ_H (CDCl₃) 1.16 (1H, m, CH₂), 1.30-1.60 (5H, m, CH/CH₂), 1.46 (9H, s, -COOC(CH₃)₃), 1.68 (1H, m, CH₂), 1.84 (1H, m, CH₂), 2.54 (1H, dd, CH₂), 2.73 (1H, m, CH₂), 3.08 (1H, m, CH₂), 3.42 (1H, m, CH₂), 4.02 (1H, m, CH₂), 4.10 (1H, m, CH₂), 4.84 (1H, m, NH)及4.96 ppm (2H, bm, CONH₂)；

δ_c (CDCl₃) CH₃: 28.5, 28.5, 28.5; CH₂: 25.2, 31.7, 34.9, 37.3, 44.6, 50.3; CH: 32.9; C: 79.5, 156.4, 158.2。

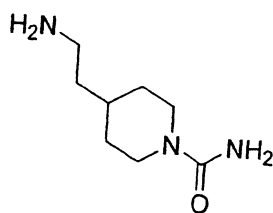
B.3-(2-氨基乙基)哌啶-1-羧醯胺



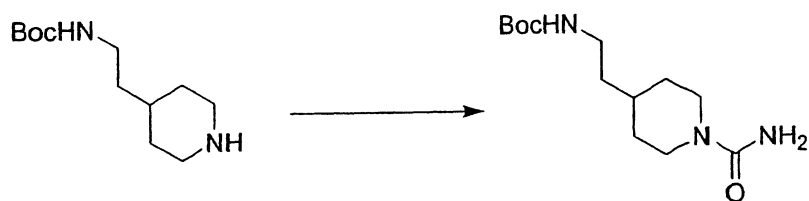
3-(2-第三丁氧羰基氨基乙基)哌啶-1-羧醯胺(392.7毫克, 1.45毫莫耳)(上述製備例242步驟A製備)溶於甲醇(7.5毫升)並添加10%濃硫酸之1,4-二噁烷(19.5毫升)且混合物在25℃攪拌1.25小時。混合物以甲醇稀釋並添加BioRad AG1-X8樹脂(OH⁻態)直至pH為鹼性。濾除樹脂, 以甲醇洗滌, 蒸發至乾且在矽膠管柱(30x2.5公分)上層析使用15%(10%濃氫氧化銨之甲醇)-二氯甲烷作為溶離液, 獲得3-(2-氨基乙基)哌啶-1-羧醯胺(233毫克, 94%): FABMS: m/z 172.1 (MH⁺); HRFABMS: m/z 172.1444 (MH⁺)。對C₈H₁₈N₃O計算值: m/z 172.1450; δ_H (CDCl₃+3% CD₃OD) 1.14 (1H, m, CH₂), 1.40 (2H, m, CH₂), 1.49 (1H, m, CH), 1.58 (1H, m, CH₂), 1.69 (1H, m, CH₂), 1.85 (1H, m, CH₂), 2.55 (1H, m, CH₂), 2.67 (5H, m, CH₂/NH₂), 2.76 (1H, bm, CH₂), 2.84 (1H, m, CH₂)及3.82 ppm (2H, m, CONH₂); δ_c (CDCl₃+3% CD₃OD) CH₂: 24.8, 30.9, 36.6, 38.9, 44.9, 50.0; CH: 33.4。

製備例243:

4-(2-氨基乙基)哌啶-1-羧醯胺

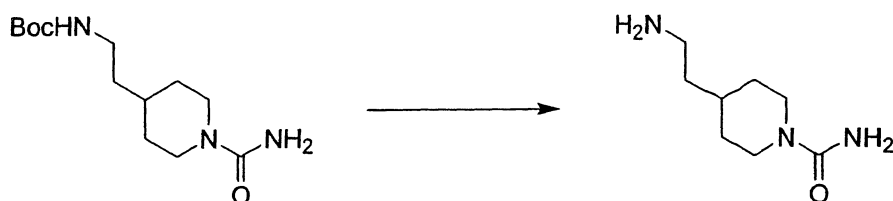


A.4-(2-第三丁氧羰基氨基乙基)哌啶-1-羧醯胺



4-(2-第三丁氧羰基氨基乙基)哌啶(500毫克，2.19毫莫耳)溶於無水二氯甲烷(10毫升)並添加異氰酸三甲基矽烷酯(2.96毫升，21.9毫莫耳)。混合物在氫氣及25°C下攪拌3.25小時。混合物以二氯甲烷稀釋並以飽和碳酸氫鈉水溶液洗滌。有機層脫水(MgSO₄)，過濾，蒸發至乾並在矽膠管柱(15x5公分)上層析使用5%(10%濃氫氧化銨之甲醇)-二氯甲烷作為溶離液，獲得4-(2-第三丁氧羰基氨基乙基)哌啶-1-羧醯胺(308.2毫克，52%)：FABMS: m/z 272.0 (MH⁺)；HRFABMS: m/z 272.1965 (MH⁺)。對C₁₃H₂₆O₃N₃計算值： m/z 272.1974； δ_H (CDCl₃) 1.20 (2H, m, CH₂), 1.47 (9H, s, -COOC(CH₃)₃), 1.45-1.55 (3H, m, CH/CH₂), 1.75 (2H, m, CH₂), 2.82 (2H, m, CH₂), 3.19 (2H, m, CH₂), 3.96 (2H, m, CH₂), 4.64 (2H, m, CH₂)及4.70 ppm (1H, bm, NH)； δ_C (CDCl₃) CH₃: 28.5, 28.5, 28.5；CH₂: 31.8, 31.8, 36.7, 38.0, 44.5, 44.5；CH: 33.4；C: 79.2, 156.7, 158.1。

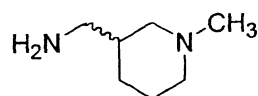
B.4-(2-胺基乙基)哌啶-1-羧醯胺



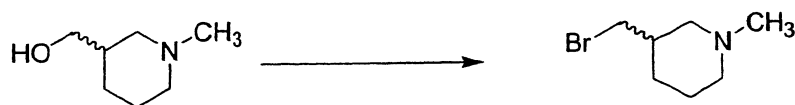
4-(2-第三丁氧羰基胺基乙基)哌啶-1-羧醯胺(283.3毫克, 1.04毫莫耳)(上述製備例243步驟A製備)溶於甲醇(5.4毫升)並添加10%濃硫酸之1,4-二噁烷(14.2毫升)且混合物在25℃攪拌1.25小時。混合物以甲醇稀釋並添加BioRad AG1-X8樹脂(OH⁻態)直至pH為鹼性。濾除樹脂, 以甲醇洗滌, 蒸發至乾且在矽膠管柱(30x2.5公分)上層析使用15%(10%濃氫氧化銨之甲醇)-二氯甲烷作為溶離液, 獲得4-(2-胺基乙基)哌啶-1-羧醯胺(170毫克, 95%): FABMS: m/z 172.1 (MH^+); HRFABMS: m/z 172.1442。對C₈H₁₈N₃O計算值: m/z 172.1450; δ_H (CDCl₃+3% CD₃OD) 1.16 (2H, m, CH₂), 1.43 (2H, m, CH₂), 1.52 (1H, m, CH), 1.70 (2H, m, CH₂), 2.70-2.85 (8H, m, CH₂)及3.92 ppm (2H, m, CONH₂); δ_C (CDCl₃+3% CD₃OD) CH₂: 31.9, 31.9, 39.0, 39.7, 44.4, 44.4; CH: 33.5; C: 158.7。

製備例244:

3-(胺基甲基)-1-甲基哌啶

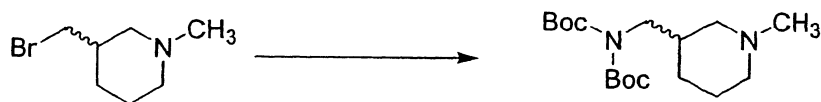


A.3-(溴甲基)-1-甲基哌啶



3-(羥基甲基)-1-甲基哌啶(2克, 15.5毫莫耳)溶於無水乙腈(32毫升)並添加無水吡啶(2.02毫升, 24.8毫莫耳)且溶液冷卻至0℃。在0℃添加二溴三苯基磷烷(8.49克, 20.2毫莫耳)且混合物溫至25℃並攪拌94小時。混合物蒸發至乾且殘留物在矽膠管柱(30x5公分)上層析使用梯度溶離以二氯甲烷、35%乙醚之二氯甲烷及5-10%甲醇之二氯甲烷作為溶離液, 獲得3-(溴甲基)-1-甲基哌啶(3.13克, 100%): FABMS: m/z 192.1 (MH^+); δ_H ($CDCl_3$) 1.52 (1H, m, CH_2), 1.99 (2H, m, CH_2), 2.43 (1H, m, CH_2), 2.75 (2H, m, CH_2), 2.82 (1H, m, CH), 2.86/2.88 (3H, s, NCH_3), 3.42/3.49 (2H, dd, $-CH_2Br$)及3.56 ppm (2H, m, CH_2); δ_C ($CDCl_3$) CH_3 :44.3; CH_2 : 22.1, 26.6, 35.4, 54.8, 58.2; CH: 34.6。

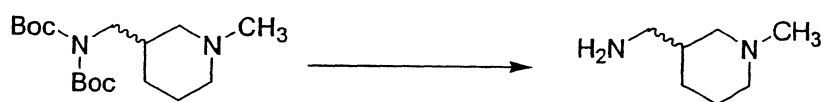
B.3-(二-第三丁氧羰基氨基甲基)-1-甲基哌啶



3-(溴甲基)-1-甲基哌啶(1.5克, 7.81毫莫耳)(得自上述製備例224步驟A)及二羧酸二-第三丁酯(1.697克, 7.81毫莫耳)溶於無水乙腈(25毫升)。添加碳酸鉍(5.1克, 15.6毫莫耳)及碘化鋰(52毫克, 0.391毫莫耳)且混合物在70℃攪拌20小

時。混合物蒸發至乾且殘留物分配於二氯甲烷及飽和碳酸氫鈉水溶液之間。有機層脫水(MgSO_4)，過濾並蒸發至乾，殘留物在矽膠管柱(30x5公分)上層析使用3%甲醇之二氯甲烷作為溶離液，獲得3-(二-第三丁氧羰基氨基甲基)-1-甲基哌啶(1.331克，52%)：FABMS: m/z 329.2 (MH^+)；HRFABMS: m/z 329.2438 (MH^+)。對 $\text{C}_{17}\text{H}_{33}\text{N}_2\text{O}_4$ 計算值: m/z 329.2440; δ_{H} (CDCl_3) 1.10 (1H, m, CH_2), 1.54 (18H, s, $-\text{COOC}(\text{CH}_3)_3$), 1.86 (2H, m, CH_2), 2.01 (1H, m, CH_2), 2.19 (1H, m, CH), 2.34 (2H, bm, CH_2), 2.59 (3H, $-\text{NCH}_3$), 3.19 (2H, m, CH_2) 及 3.52/3.52 ppm (2H, $-\text{CH}_2\text{N}-$); δ_{C} (CDCl_3) CH_3 : 28.5, 28.5, 28.5, 28.5, 28.5, 28.5, 47.2; CH_2 : 25.4, 28.3, 50.4, 56.8, 60.8; CH: 37.2; C: 83.0, 83.0, 153.5, 153.5。

C.3-(氨基甲基)-1-甲基哌啶

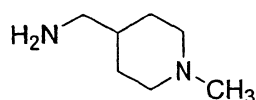


3-(二-第三丁氧羰基氨基甲基)-1-甲基哌啶(500毫克，1.52毫莫耳)(上述製備例224步驟B所製備)溶於甲醇(7.5毫升)並添加10% (v/v)濃硫酸之1,4-二噁烷(19.75毫升)。溶液在25°C攪拌0.5小時。添加甲醇(300毫升)，接著添加BioRad AG1-X8樹脂(OH^- 態)直至pH約10。濾除樹脂並以甲醇(2x200毫升)洗滌。合併之溶離液蒸發至乾且殘留物在矽膠管柱(30x2.5公分)上層析，使用10%(10%濃氫氧化銨之甲醇)-二氯甲烷作為溶離液，獲得3-(氨基甲基)-1-甲基哌啶(69.2毫

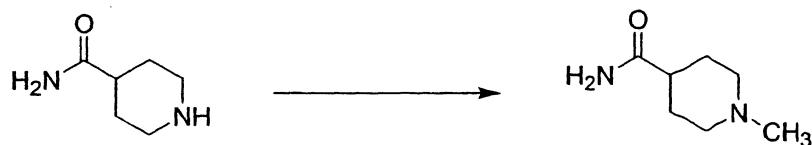
克，35%)：FABMS: m/z 129.1 (MH^+); HRFABMS: m/z 129.1392 (MH^+)。對 $C_7H_{17}N_2$ 計算值: m/z 129.1392; δ_H ($CDCl_3$) 0.90 (2H, m, CH_2), 1.65 (2H, m, CH_2), 1.72 (1H, m, CH), 1.79 (1H, m, CH_2), 1.91 (1H, m, CH_2), 2.30 (3H, s, $-NCH_3$), 2.64 (2H, m, CH_2), 2.82 (1H, m, $-\underline{CH_2}NH_2$) 及 2.92 ppm (1H, m, $-\underline{CH_2}NH_2$); δ_C ($CDCl_3$) CH_3 : 46.7; CH_2 : 25.2, 28.0, 46.3, 56.4, 60.3; CH: 39.9。

製備例 245：

4-(胺基甲基)-1-甲基哌啶



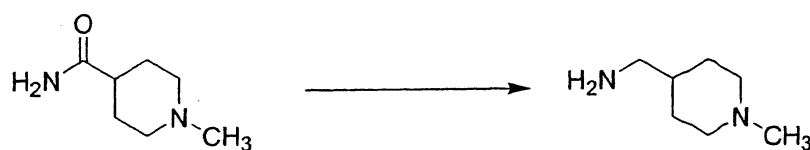
A.1-甲基異哌啶鹽胺



異哌啶鹽胺(10克，78.0毫莫耳)溶於蒸餾水(100毫升)並添加37%甲醛水溶液(7.6毫升，等於2.81克HCHO，93.6毫莫耳)。在氫氣下添加濕的10% Pd-C(8湯匙)且混合物在25°C及50 psi氫化43小時。經矽藻土濾除觸媒且後者以水及甲醇洗滌。合併之濾液蒸發至乾且殘留物在矽膠管柱(60x5公分)上層析使用8%-10%-20% (10%濃氫氧化銨之甲醇)-二氯甲烷作為溶離液，獲得1-甲基異哌啶鹽胺(7.15克，64%)：FABMS: m/z 143.1 (MH^+); HRFABMS: m/z 143.1184 (MH^+)。

對 $C_7H_{15}N_2O$ 計算值: m/z 143.1184; δ_H (d_6 -DMSO) 1.50/1.57 (4H, m, CH_2), 1.76/1.94 (4H, m, CH_2), 2.10 (3H, s, $-NCH_3$), 2.72 (1H, m, CH) 及 6.68/7.18 ppm (2H, m, $CONH_2$); δ_C (d_6 -DMSO) CH_3 : 41.2; CH_2 : 28.5, 28.5, 54.9, 54.9; CH: 46.2; C: 176.7。

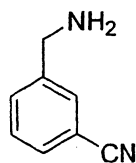
B.4-(胺基甲基)-1-甲基哌啶



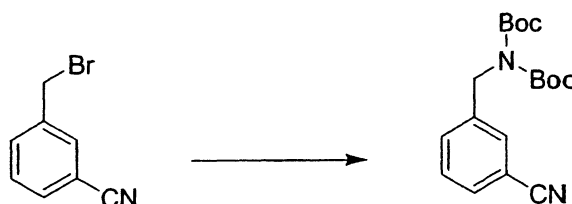
1-甲基異哌啶醯胺(6.75克, 47.5毫莫耳)(上述製備例245步驟A製備)溶於無水THF(350毫升)且所得混合物在 $0^{\circ}C$ 及氮氣下逐次添加至氫化鋰鋁(1.8克, 47.5毫莫耳)之無水THF(100毫升)攪拌漿液中。混合物在 $0^{\circ}C$ 攪拌30分鐘接著在 $66^{\circ}C$ 及氮氣下加熱25小時。於攪拌混合物中在 $0^{\circ}C$ 滴加蒸餾水(1.88毫升), 接著添加20%氫氧化鈉水溶液(1.42毫升)接著添加蒸餾水(6.75毫升)且混合物攪拌15分鐘。混合物過濾且固體以THF及二氯甲烷洗滌。合併之濾液蒸發至乾並在矽膠管柱(30x5公分)上層析使用15%-20%(10%濃氫氧化銨之甲醇)-二氯甲烷作為溶離液, 獲得4-(胺基甲基)-1-甲基哌啶(0.678克, 11%): FABMS: m/z 129.1 (MH^+); HRFABMS: m/z 129.1389 (MH^+)。對 $C_7H_{17}N_2$ 計算值: m/z 129.1392; δ_H (d_6 -DMSO): 2.08 ppm (3H, s, $-NCH_3$); δ_C (d_6 -DMSO): CH_3 : 在DMSO峰內; CH_2 : 29.6, 29.6, 46.7, 55.2, 55.2; CH: 46.2。

製備例246:

3-(胺基甲基)苄腈

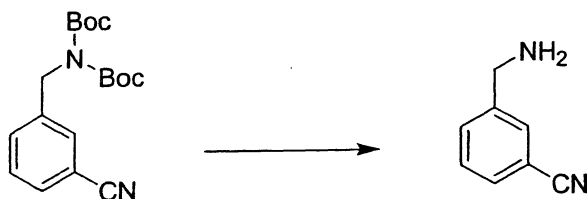


A.3-(二-第三丁氧羰基胺基甲基)苄腈



3-(溴甲基)苄腈(5克, 25.5毫莫耳)及二羧酸二-第三丁基亞胺基酯(5.54克, 25.5毫莫耳)溶於無水THF(50毫升)及添加碳酸鉍(16.62克, 25.5毫莫耳)及碘化鋰(170.5毫克, 1.275毫莫耳)。混合物在70℃攪拌22小時且反應如上述製備例89步驟B所述般操作。殘留物在矽膠管柱(60x5公分)上層析使用5%乙酸乙酯之己烷作為溶離液, 獲得3-(二-第三丁氧羰基胺基甲基)苄腈(7.39克, 87%): FABMS: m/z 333.2 (MH^+); HRFABMS: m/z 333.1815 (MH^+)。對 $C_{18}H_{25}N_2O_4$ 計算值: m/z 333.1814; δ_H ($CDCl_3$) 1.52 (18H, s, $-COOC(CH_3)_3$), 4.84 (2H, s, CH_2), 7.48 (1H, m, Ar-H), 7.60 (2H, m, Ar-H)及7.65 ppm (1H, m, Ar-H); δ_C ($CDCl_3$) CH_3 : 28.1, 28.1, 28.1, 28.1, 28.1, 28.1; CH_2 : 48.4; CH: 129.2, 131.0, 131.0, 131.9; C: 83.2, 83.2, 112.5, 118.8, 140.1, 152.5, 152.5。

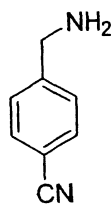
B.3-(胺基甲基)苄腈



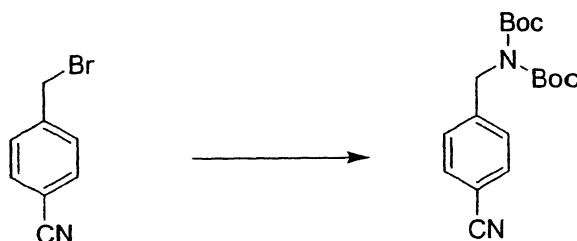
3-(二-第三丁氧羰基氨基甲基)苄腈(2克, 6.0毫莫耳)(上述製備例246步驟A製備)溶於甲醇(30毫升)並添加10% (v/v) (10%濃硫酸之1,4-二噁烷)(79毫升)。溶液在25℃攪拌0.25小時並如上述製備例89步驟C所述般操作。殘留物在矽膠管柱(15x5公分)上層析使用3% (10%濃氫氧化銨之甲醇)-二氯甲烷作為溶離液, 獲得標題化合物(651.4毫克, 82%) : FABMS: m/z 133.1 (MH^+); HRFABMS: m/z 133.0762 (MH^+)。對 $C_8H_9N_2$ 計算值: m/z 133.0766; δ_H ($CDCl_3$) 2.57 (2H, s, $-CH_2NH_2$), 3.92 (2H, s, $-CH_2NH_2$), 7.46 (1H, m, Ar-H), 7.57 (2H, m, Ar-H)及7.64 ppm (1H, m, Ar-H); δ_C ($CDCl_3$) CH_2 : 45.2; CH: 129.4, 130.7, 130.7, 131.8; C: 112.4, 118.8, 143.8。

製備例 247:

4-(氨基甲基)苄腈

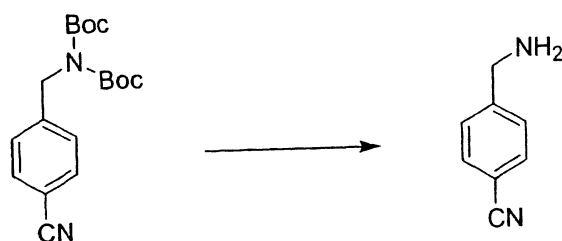


A.4-(二-第三丁氧羰基氨基甲基)苄腈



4-(溴甲基)苄腈(5克, 25.5毫莫耳)及二羧酸二-第三丁基亞胺基酯(5.54克, 25.5毫莫耳)溶於無水THF(50毫升)及添加碳酸鉍(16.62克, 25.5毫莫耳)及碘化鋰(170.5毫克, 1.275毫莫耳)。混合物在70℃攪拌23小時且反應如上述製備例224步驟B所述般操作。殘留物在矽膠管柱(50x5公分)上層析使用5%乙酸乙酯之己烷作為溶離液, 獲得4-(二-第三丁氧羰基胺基甲基)苄腈(7.07克, 83%): FABMS: m/z 333.2 (MH^+); HRFABMS: m/z 333.1816 (MH^+)。對 $C_{18}H_{25}N_2O_4$ 計算值: m/z 333.1814; δ_H ($CDCl_3$) 1.45 (18H, s, $-COOC(CH_3)_3$), 4.81 (2H, s, CH_2), 7.37 (2H, d, Ar-H)及7.62 ppm (2H, d, Ar-H); δ_C ($CDCl_3$) CH_3 : 28.1, 28.1, 28.1, 28.1, 28.1, 28.1; CH_2 : 49.2; CH: 127.8, 127.8, 132.3, 132.3; C: 83.2, 83.2, 111.1, 118.9, 144.1, 152.4, 152.4。

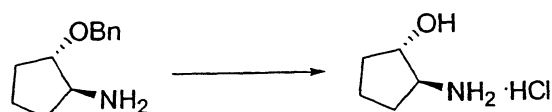
B.4-(胺基甲基)苄腈



4-(二-第三丁氧羰基胺基甲基)苄腈(2克, 6.0毫莫耳)(上述製備例247步驟A製備)溶於TFA(4毫升)且溶液在25℃攪拌0.25小時。反應混合物以二氯甲烷稀釋並以1 N氫氧化鈉萃取。有機層脫水($MgSO_4$), 過濾並蒸發至乾。殘留物在矽膠管柱(15x5公分)上層析使用3% (10%濃氫氧化銨之甲醇)-二氯甲烷作為溶離液, 獲得4-(胺基甲基)苄腈(108毫克,

68%) : FABMS: m/z 133.1 (MH^+); HRFABMS: m/z 133.0764 (MH^+)。對 $C_8H_9N_2$ 計算值: m/z 133.0766; δ_H ($CDCl_3$) 2.04 (2H, s, $-CH_2NH_2$), 3.89 (2H, s, $-CH_2NH_2$), 7.40 (2H, d, Ar-H) 及 7.59 ppm (2H, d, Ar-H); δ_C ($CDCl_3$) CH_2 : 45.7; CH: 127.8, 127.8, 132.4, 132.4; C: 110.6, 118.9, 148.0。

製備例 248 :



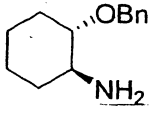
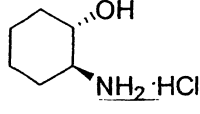
於(1S,2S)-2-苄氧基環戊基胺(1.5克, 7.84毫莫耳)之MeOH (50毫升)溶液中, 在rt添加10% Pd/C(50%濕重, 1.0克)接著滴加濃HCl(0.7毫升)。混合物在 H_2 汽球下攪拌14小時並經矽藻土墊濾除觸媒。矽藻土墊以MeOH(2x10毫升)洗滌且所得濾液減壓濃縮獲得0.97克(90%)黃色半固體; $M+H$ (游離鹼)=102。

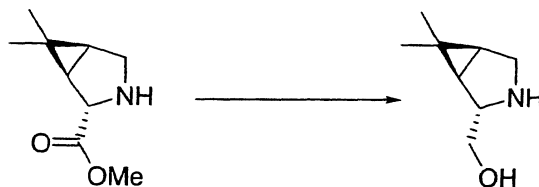
製備例 249-251

類似製備例248之方式, 使苄基保護之環烷基胺(欄2)轉化成所需胺基環烷醇鹽酸鹽衍生物(欄3), 如表17所示。

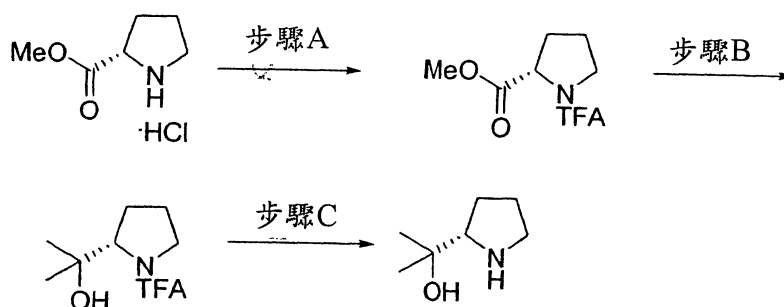
表 17

製備例	欄2 (胺)	欄3 (斷裂方法)	數據 $M+2$
249			$M+H=102$ (游離鹼)
250			$M+H=116$ (游離鹼)

251			M+H=116 (游離鹼)
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製備例 252

於酯(依據有機化學期刊(1999), 64, 330)(0.5克, 2.43毫莫耳)之THF(8毫升)溶液中, 在0°C一次添加LiAlH₄(0.37克, 9.74毫莫耳)。所得混合物回流加熱12小時並冷卻至0°C。混合物依序以H₂O(1毫升)、1 M NaOH(1毫升)及H₂O(3毫升)處理。於混合物中添加CH₂Cl₂(10毫升), 其激烈攪拌30分鐘。混合物經矽藻土墊過濾並以CH₂Cl₂(3x5毫升)溫和洗滌。所得濾液減壓濃縮獲得0.41克(85%)黃色/橘色固體。M+H=142。

製備例 253步驟 A:

於L-脯胺酸甲酯鹽酸鹽(0.50克, 3.0毫莫耳)之CH₂Cl₂(15毫升)溶液中, 在0°C添加Et₃N(1.1毫升, 7.55毫莫耳)接著添

加 TFAA (0.56 毫升, 3.92 毫莫耳)。混合物在 rt 攪拌 12 小時並添加 1 N HCl (25 毫升)。分離層且有機層依序以飽和 NaHCO_3 水溶液 (1x25 毫升) 及食鹽水 (1x25 毫升) 洗滌。有機層脫水 (Na_2SO_4)，過濾並減壓濃縮獲得 0.72 克 (100%) 黃色油。M+H=226。粗物質未經純化用於步驟 B。

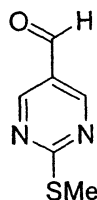
步驟 B：

於製備例 253 步驟 A 製備之化合物 (0.68 克, 3.0 毫莫耳) 之 THF (20 毫升) 溶液中，在 0°C 以 10 分鐘滴加 MeMgI (5.1 毫升, 3.0 M 於 Et_2O)。所得溶液在 rt 攪拌 16 小時，該時混合物藉添加飽和 NH_4Cl 水溶液驟冷。混合物濃縮至乾且所得殘留物與 EtOAc (100 毫升) 攪拌 45 分鐘並過濾。濾液減壓濃縮獲得 0.68 克 (100%) 黃色/橘色油。M+H=226。粗物質未經純化用於步驟 C。

步驟 C：

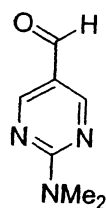
於製備例 253 步驟 B 製備之化合物 (0.68 克, 3.0 毫莫耳) 之 MeOH (5 毫升) 溶液中，添加 KOH (0.68 克, 12.1 毫莫耳) 之 MeOH (5 毫升) 溶液。混合物回流攪拌 12 小時及在 rt 攪拌 72 小時，隨後混合物濃縮至乾。粗殘留物懸浮於 EtOAc (50 毫升) 中並激烈攪拌 30 分鐘且過濾。重複此程序 2 次以上且所得濾液減壓濃縮獲得 128 毫克 (33%) 褐紅色/橘色油。M+H=130。此物質未經純化用於隨後偶合步驟。

製備例 254：



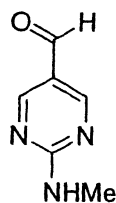
依據 Gupton(雜環化學期刊(1991), 28,1281)之程序製備此醛。

製備例 255



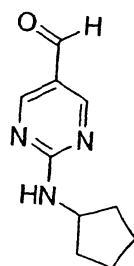
使用製備例 254之醛，利用 Gupton(雜環化學期刊(1991), 28,1281)之程序製備標題醛。

製備例 256



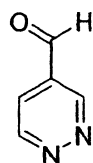
依據 Ragan 等人，Synlett(2000), 8, 1172-1174之程序製備標題醛。

製備例 257



已知之環戊基胍鹽酸鹽(有機通訊(2003), 5, 1369-1372)在 Ragan (Synlett (2000), 8, 1172-1174)之條件下反應，獲得標題醛。

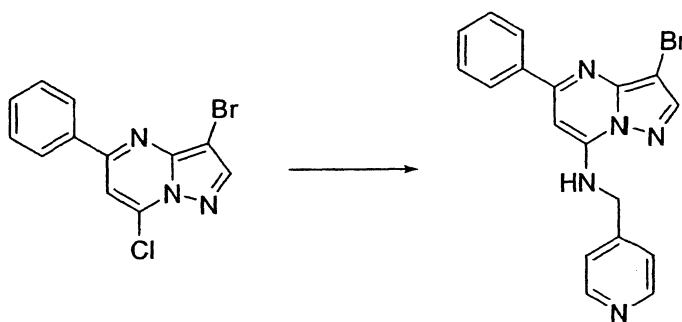
製備例 258



依據已知文獻 *Monatshefte für Chemie* (1973), 104, 1372-1382 製備標題化合物。

實例

實例 1：

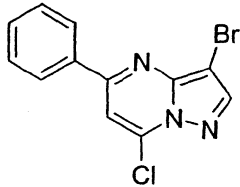
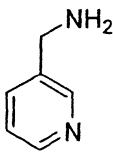
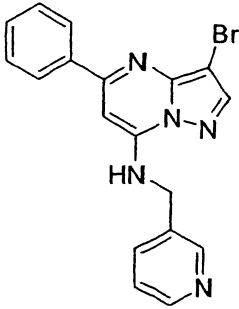
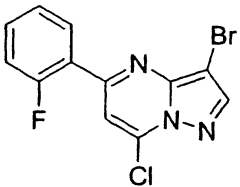
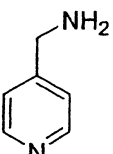
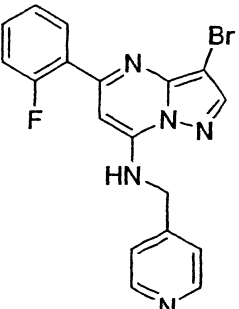
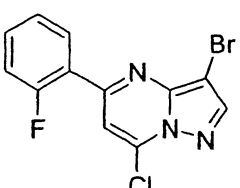
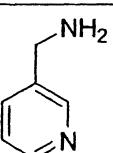
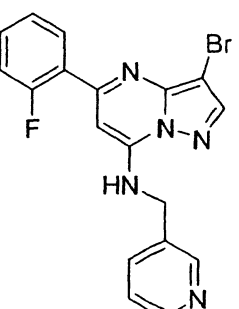


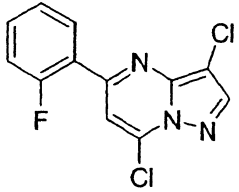
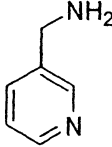
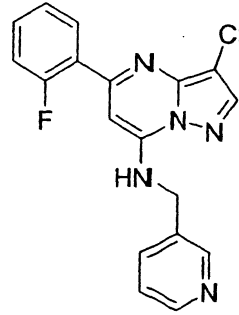
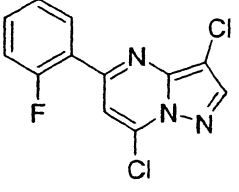
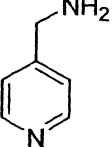
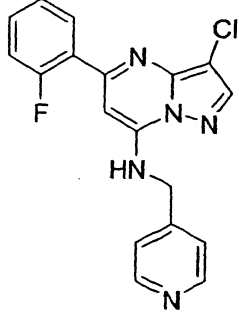
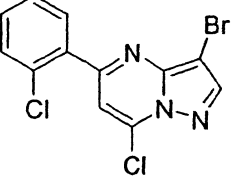
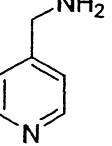
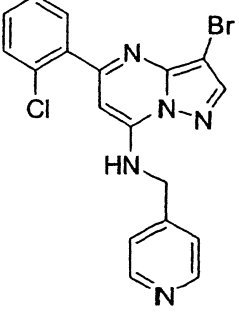
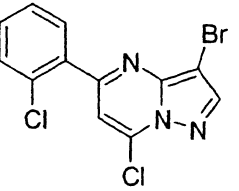
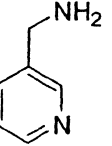
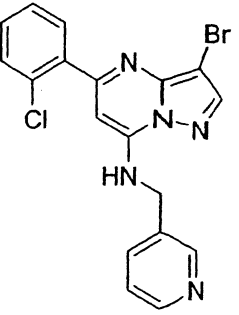
製備例 127 之產物 (0.27 克，0.875 毫莫耳)、4-胺基甲基吡啶 (0.12 克，1.3 當量) 及 K_2CO_3 (0.24 克，2 當量) 之 CH_3CN (5 毫升) 溶液在室溫攪拌 48 小時。反應混合物以 H_2O 稀釋及以 CH_2Cl_2 萃取。合併之有機層以 Na_2SO_4 脫水，過濾並濃縮。粗產物藉快速層析純化使用 4% MeOH 之 CH_2Cl_2 溶液作為溶離液 (0.28 克，93% 產率)。LCMS: $MH^+ = 380$ ； $mp = > 205^\circ C$ (分解)。

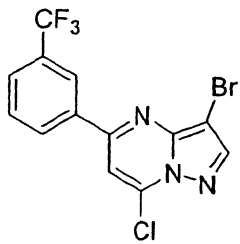
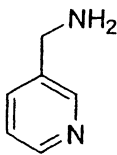
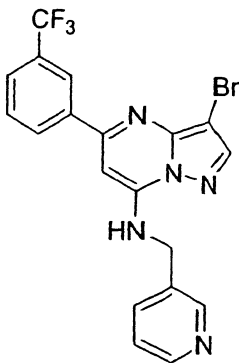
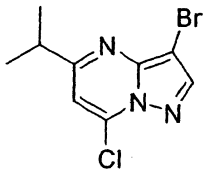
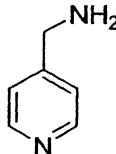
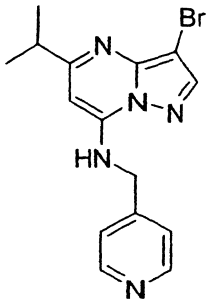
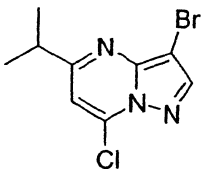
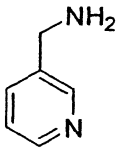
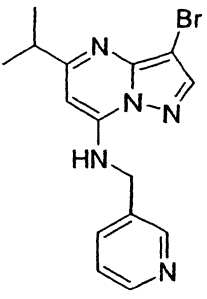
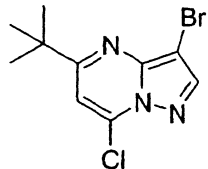
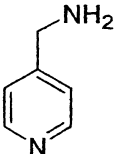
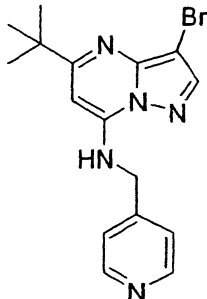
實例 2-210：

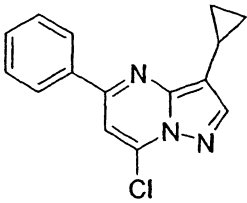
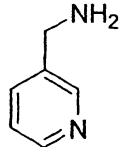
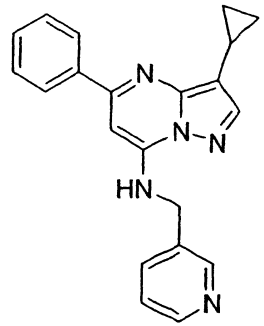
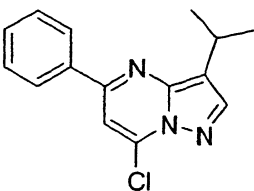
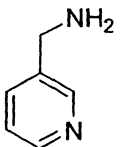
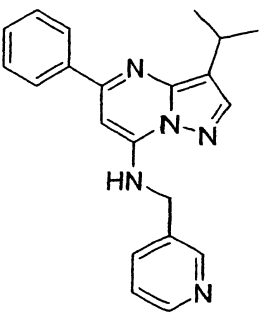
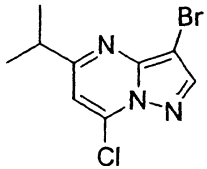
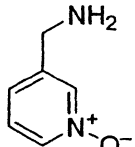
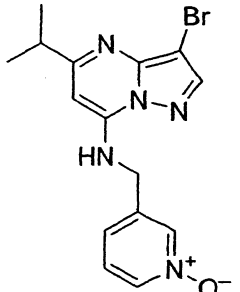
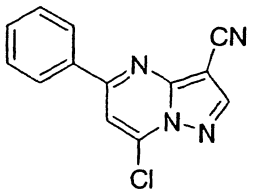
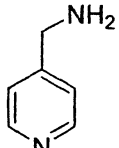
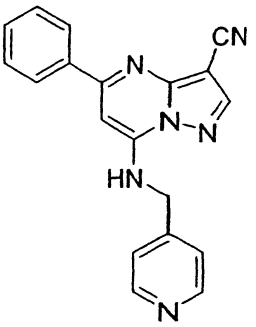
基本上依循實例 1 所述之相同程序，僅替代表 18 欄 2 所示之氯化物及表 18 欄 3 所示之胺，製備表 18 欄 4 所示之化合物。

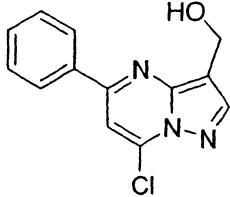
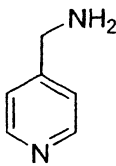
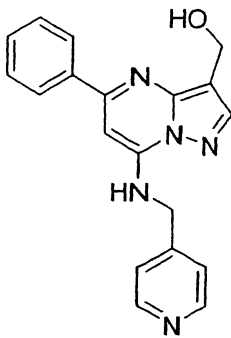
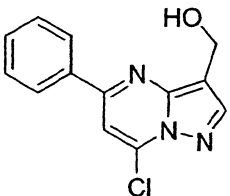
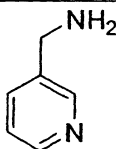
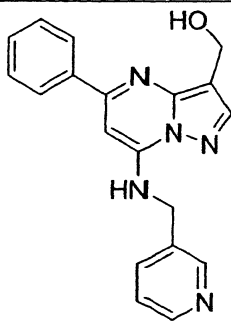
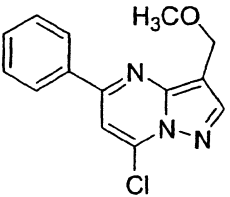
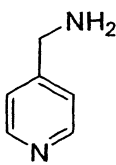
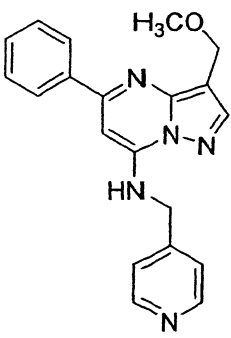
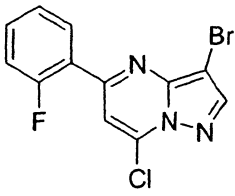
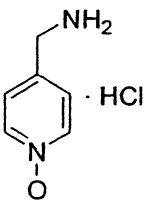
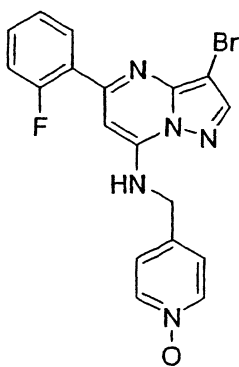
表 18

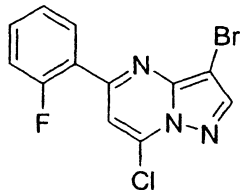
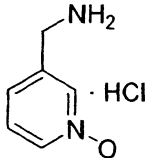
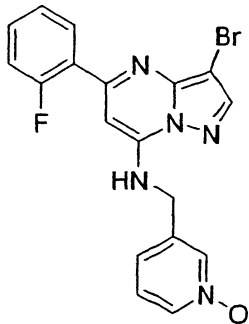
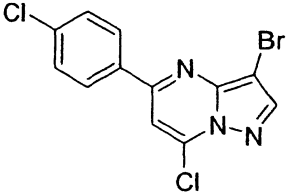
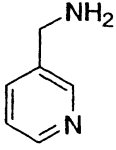
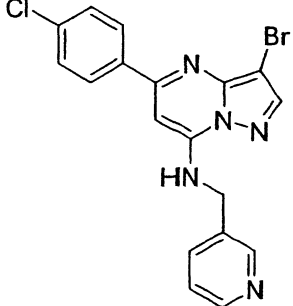
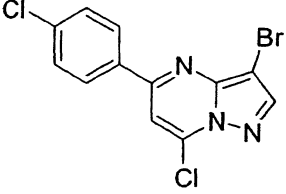
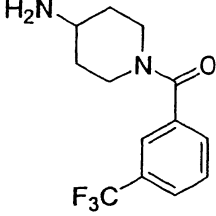
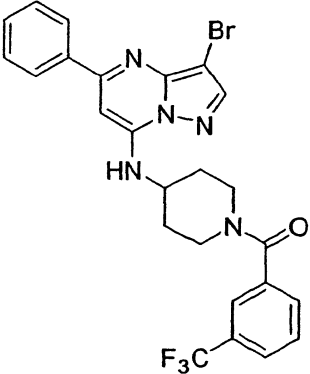
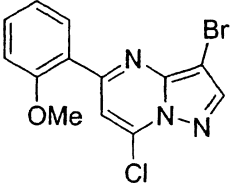
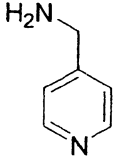
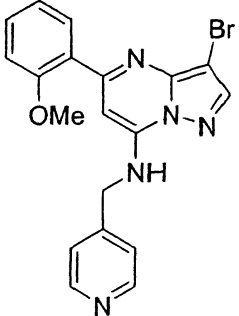
實例	欄2	欄3	欄4	數據
2				LCMS: MH ⁺ = 380; mp=175- 176°C
3				LCMS: MH ⁺ = 398; mp= 156- 157°C
4				LCMS: MH ⁺ = 398; mp= 45-49°C

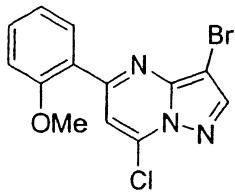
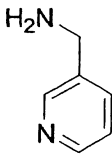
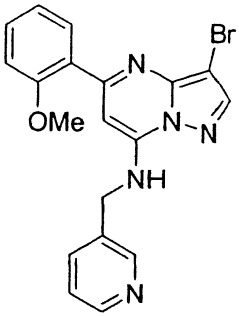
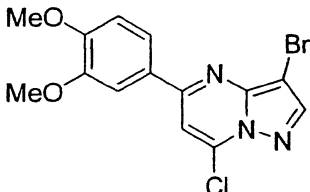
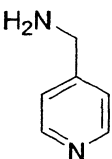
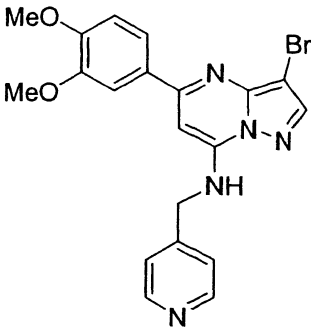
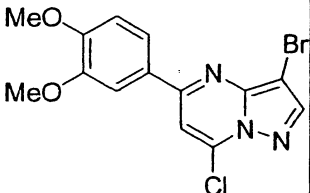
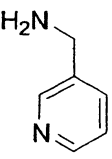
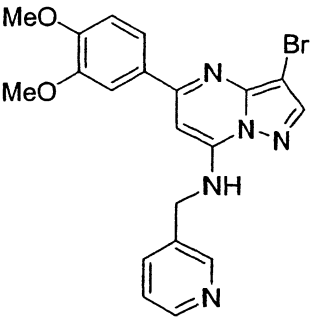
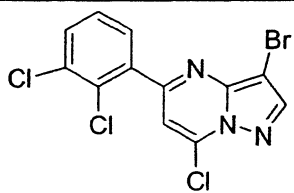
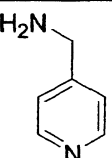
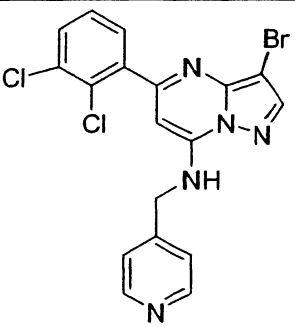
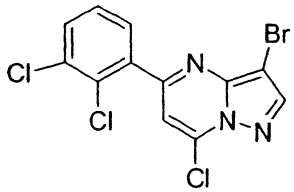
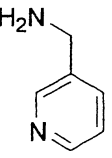
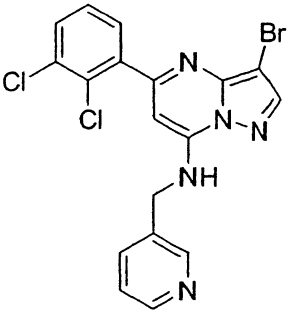
5				LCMS: MH ⁺ = 354; mp= 43-46°C
6				LCMS: MH ⁺ = 354; mp= 149- 150°C
7				LCMS: MH ⁺ = 414; mp= 86-92°C
8				LCMS: MH ⁺ = 414; mp= 185- 186°C

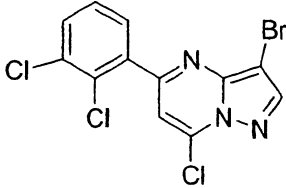
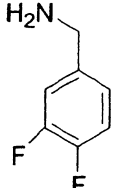
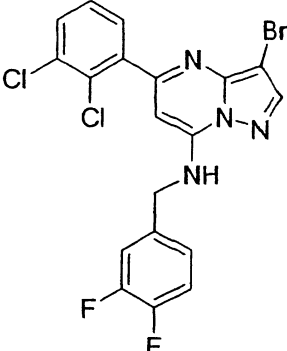
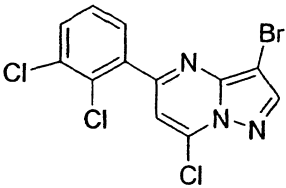
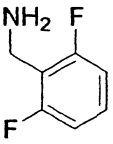
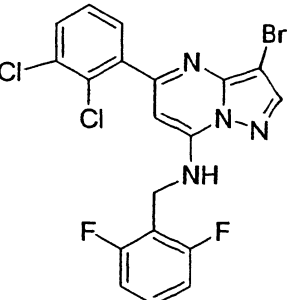
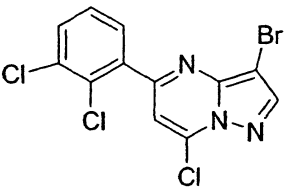
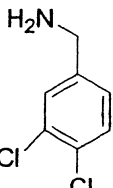
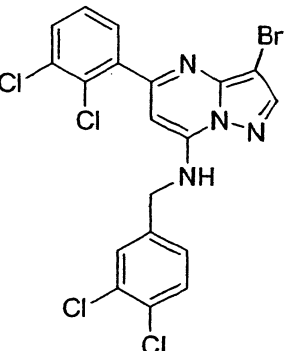
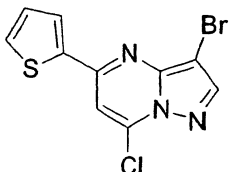
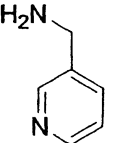
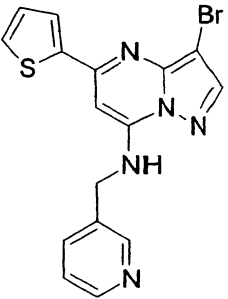
9				LCMS: MH ⁺ = 448; mp= 167- 168°C
10				LCMS: MH ⁺ = 346; mp= 57-58°C
11				LCMS: MH ⁺ = 347; mp=122. 9-125.3 °C
12				LCMS: MH ⁺ = 360; mp= 127- 128°C

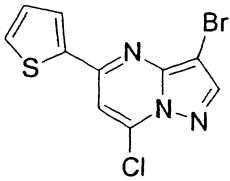
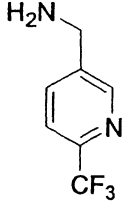
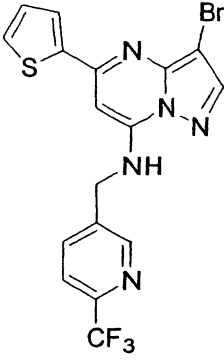
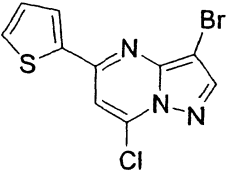
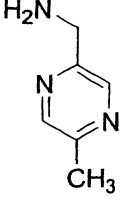
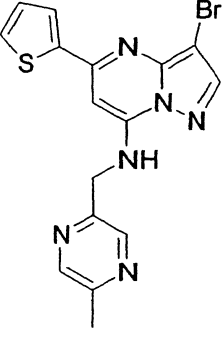
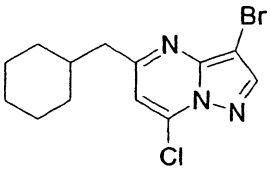
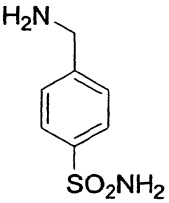
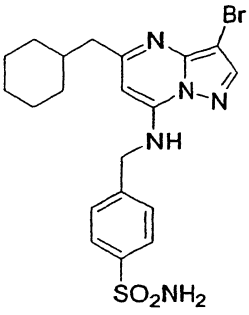
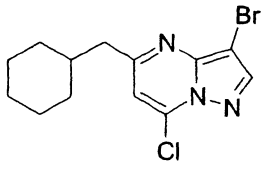
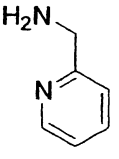
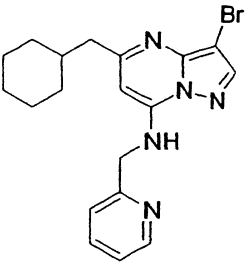
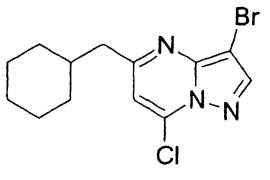
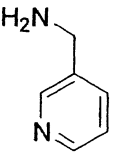
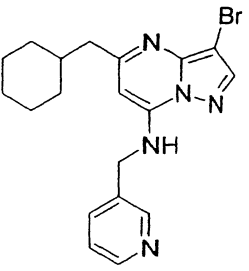
13				LCMS: MH ⁺ = 342; mp= 133- 135°C
14				LCMS: MH ⁺ = 344; mp= 152- 155°C
15				LCMS: MH ⁺ = 362; mp= 164- 167°C
16				LCMS: MH ⁺ = 327; mp= 146- 155°C

17				LCMS: MH ⁺ = 332; mp= 71-82°C
17. 1				MS: MH ⁺ = 332.
18				LCMS: MH ⁺ = 346; mp= 58-65°C
19				LCMS: MH ⁺ = 414; mp= 211- 213°C

20				LCMS: MH ⁺ = 414; mp= 194- 197°C
21				MS: MH ⁺ = 414 m.p. 211 - 216°C
22				LCMS: MH ⁺ = 544; mp= 104- 107°C
23				產率= 83% LCMS: MH ⁺ = 410.

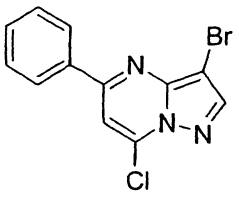
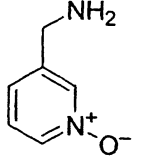
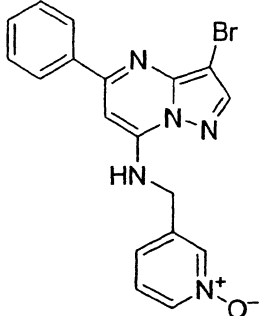
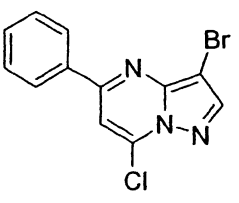
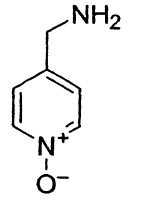
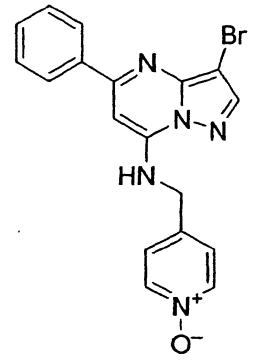
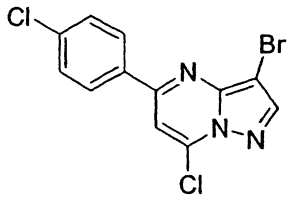
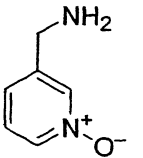
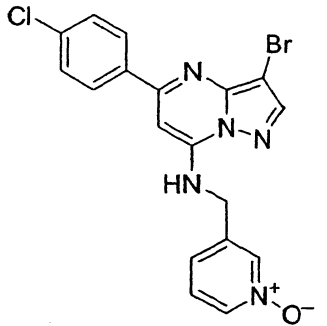
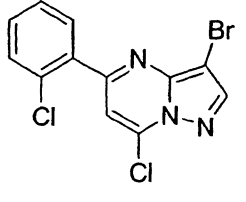
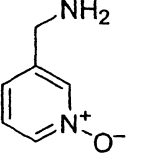
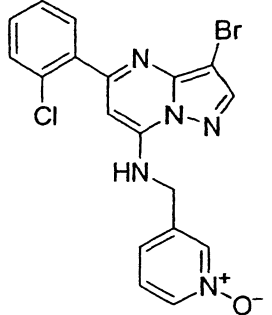
24				產率= 84% LCMS: MH ⁺ = 410.
25				產率= 96% LCMS: MH ⁺ = 440.
26				產率= 99% LCMS: MH ⁺ = 440.
27				產率= 89% LCMS: MH ⁺ = 448.
28				產率= 78% LCMS: MH ⁺ = 448.

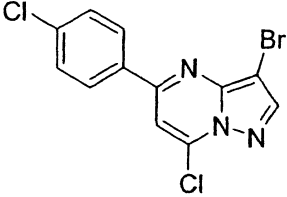
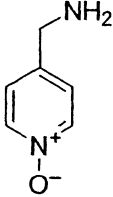
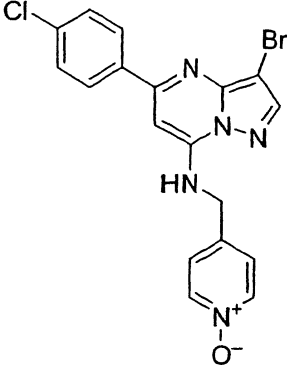
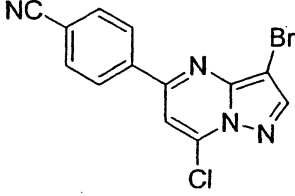
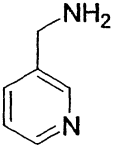
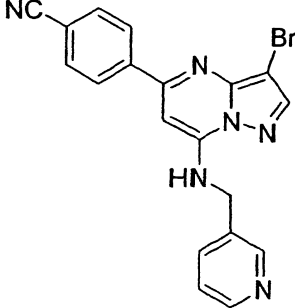
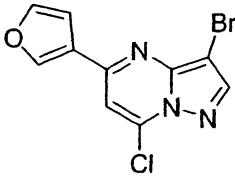
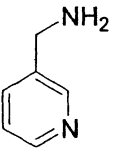
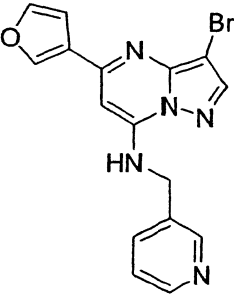
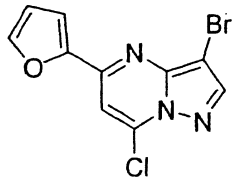
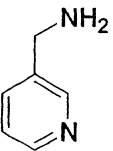
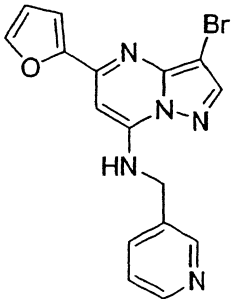
30				產率= 96% LCMS: MH ⁺ = 483.
31				產率= 35% LCMS: MH ⁺ = 483.
32				產率= 77% LCMS: MH ⁺ = 515.
33				產率= 100% m.p. 179°C LCMS: MH ⁺ = 388

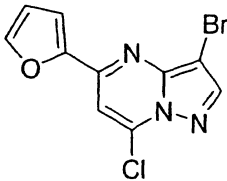
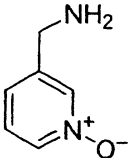
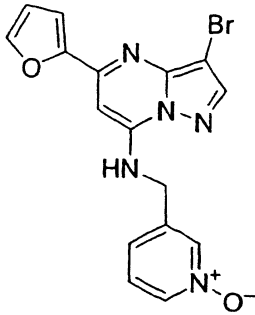
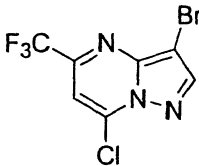
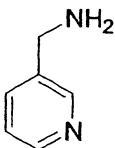
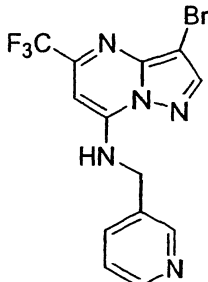
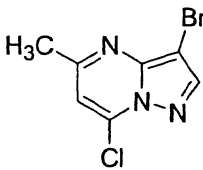
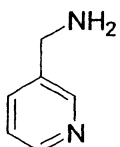
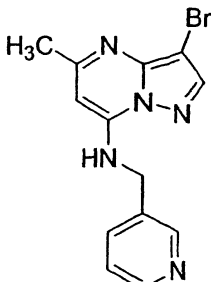
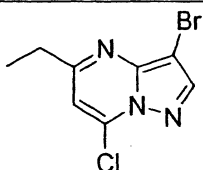
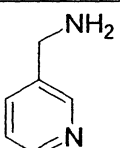
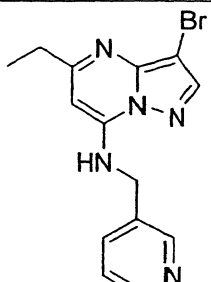
34				產率= 99% m.p. 186°C LCMS: MH ⁺ = 456
35				產率= 98% m.p. 181°C LCMS: MH ⁺ = 401
36				產率= 63% m.p. 192°C LCMS: MH ⁺ = 480
37				產率= 75% m.p. 126 - 127°C LCMS: MH ⁺ = 400
38				產率= 94% m.p. 132 - 133°C LCMS: MH ⁺ = 400

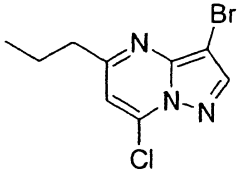
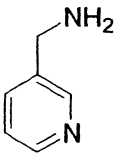
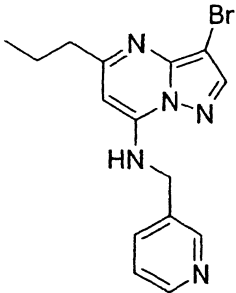
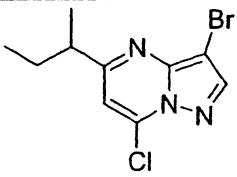
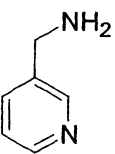
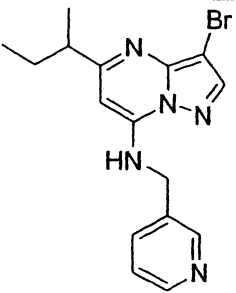
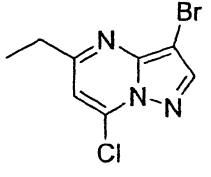
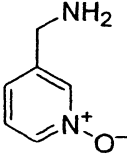
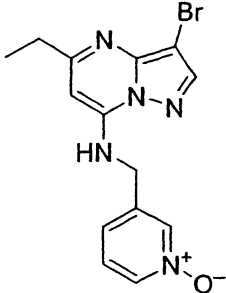
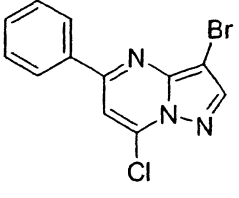
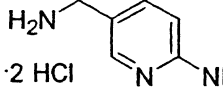
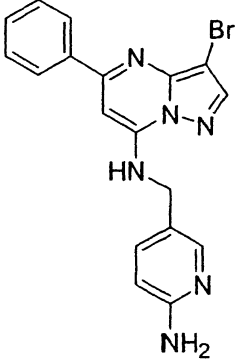
39				産率= 95% m.p. 121 - 122°C LCMS: MH ⁺ = 400
40				産率= 98% LCMS: MH ⁺ = 460
41				産率= 87% m.p. 170 - 171°C LCMS: MH ⁺ = 464
42				産率= 84% m.p. 216 - 217°C LCMS: MH ⁺ = 464
43				産率= 96% m.p. 214°C LCMS: MH ⁺ = 464

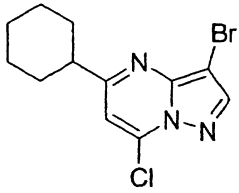
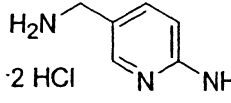
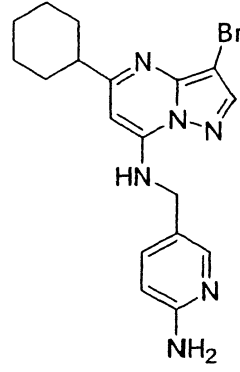
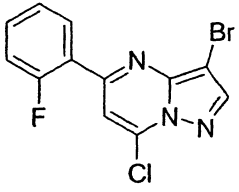
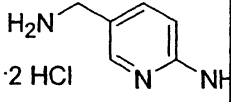
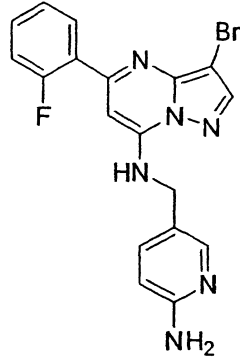
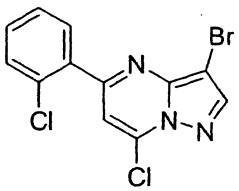
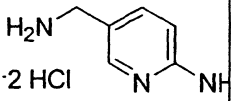
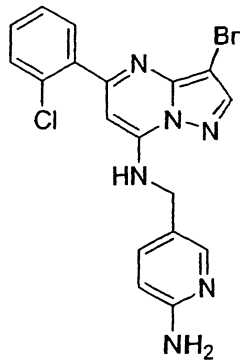
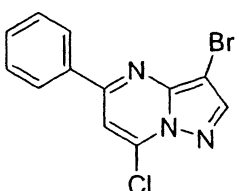
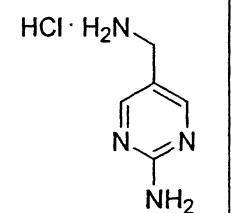
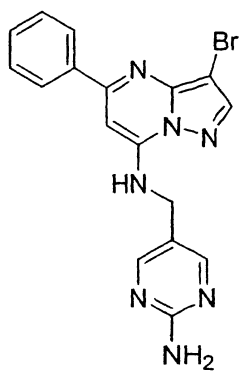
44				產率=95% m.p. 158°C LCMS: MH ⁺ =522
45				產率=90% LCMS: MH ⁺ =278
46				產率=100% ; LCMS: MH ⁺ =394
47				LCMS: MH ⁺ =473 m.p. 84 - 87°C

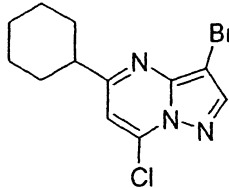
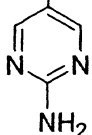
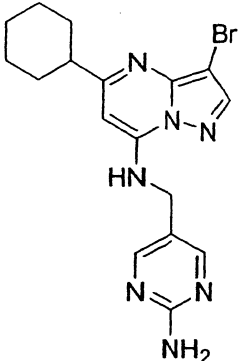
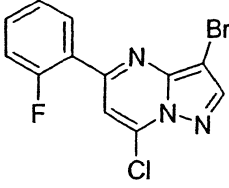
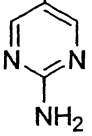
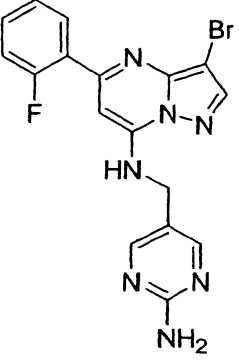
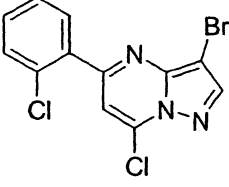
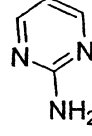
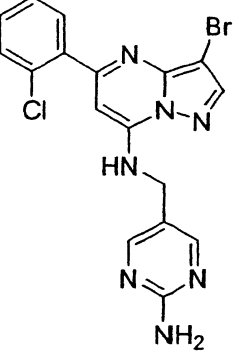
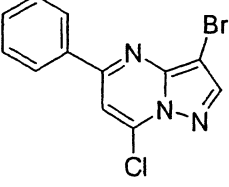
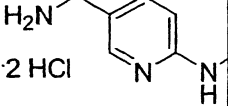
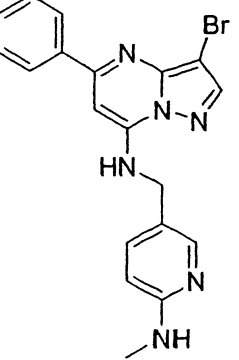
48				MS: MH ⁺ = 396 m.p. 91.5 – 93.3°C
49				MS: MH ⁺ = 396 m.p. 196 – 199°C
50				MS: MH ⁺ = 430 m.p. 242 – 244°C
51				MS: MH ⁺ = 430 m.p. 218°C

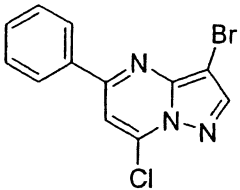
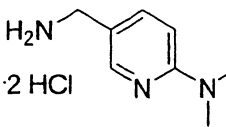
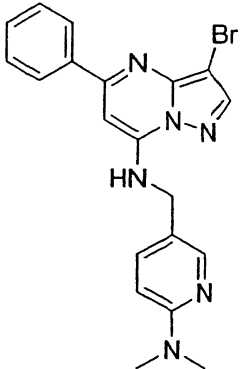
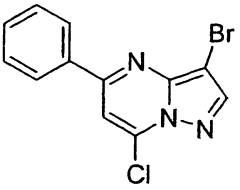
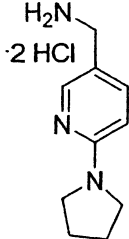
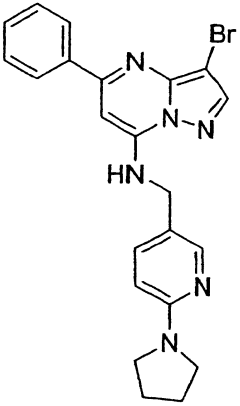
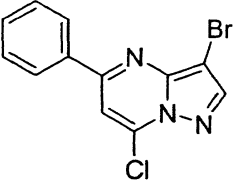
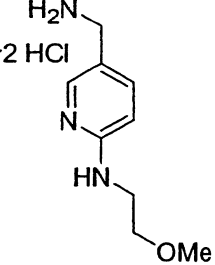
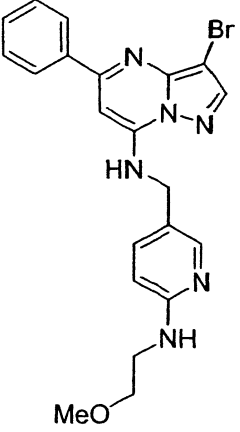
52				MS: MH ⁺ = 430 m.p. 230 – 233°C
54				MS: MH ⁺ = 405 m.p. 185 – 188°C
55				MS: MH ⁺ = 370 m.p. 229 – 232°C
56				MS: MH ⁺ = 370 m.p. 85 – 90°C

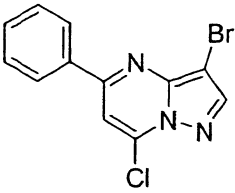
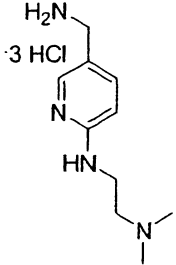
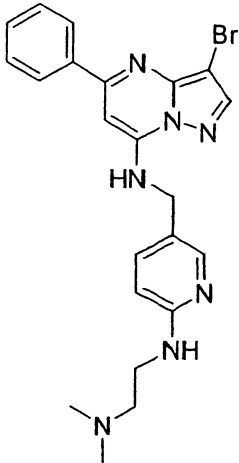
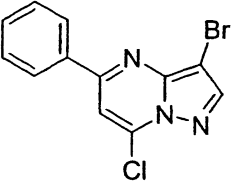
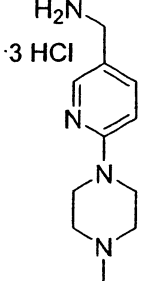
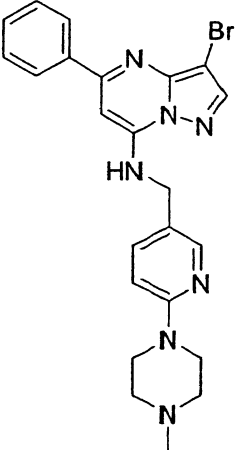
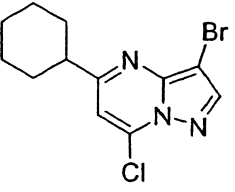
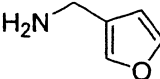
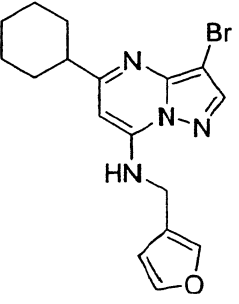
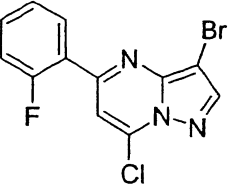
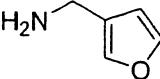
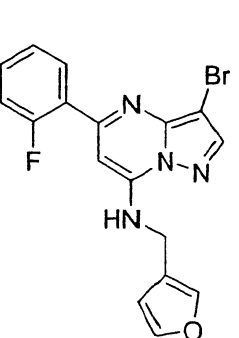
57				MS: MH ⁺ = 386 m.p. 227 - 230°C
58				MS: MH ⁺ = 372 m.p. 212 - 215°C
59				MS: MH ⁺ = 318 m.p. 169 - 171°C
60				MS: MH ⁺ = 332 m.p. 170 - 173°C

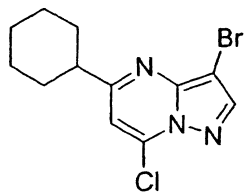
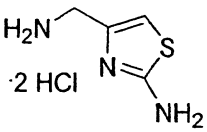
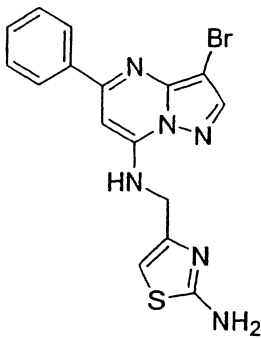
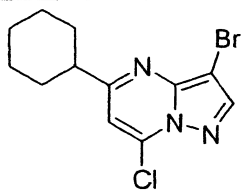
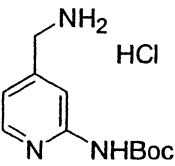
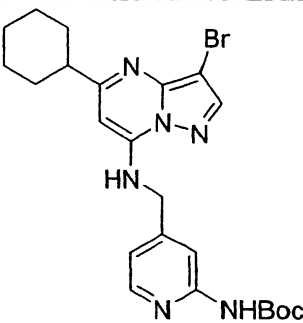
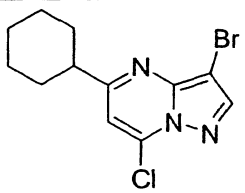
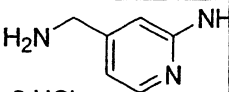
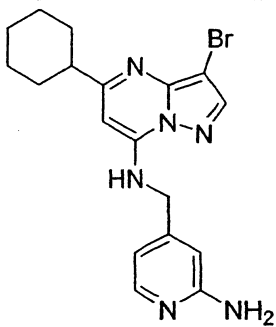
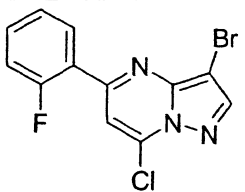
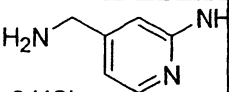
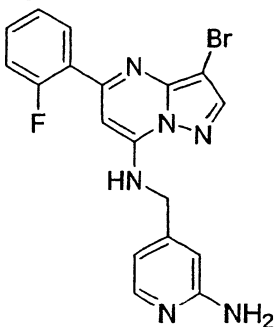
61				MS: MH ⁺ = 346 m.p. 156 – 159°C
62				MS: MH ⁺ = 360 m.p. 114 – 116°C
63				MS: MH ⁺ = 348 m.p. 197 – 200°C
64				1. mp = 230-232 2. M+H = 396

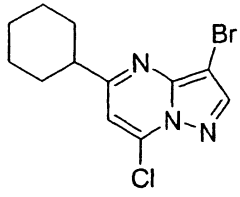
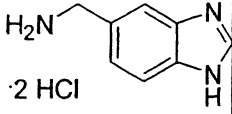
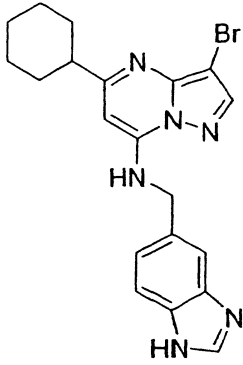
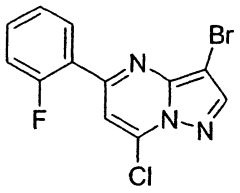
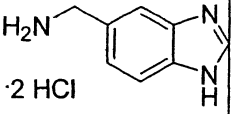
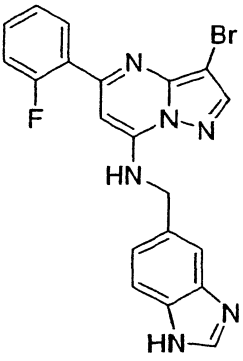
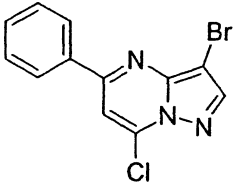
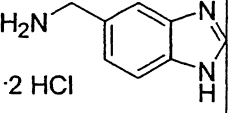
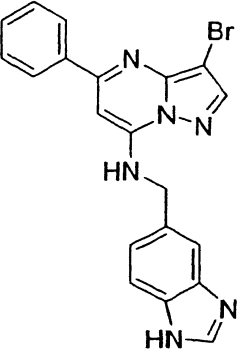
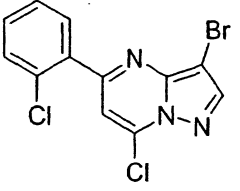
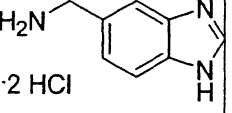
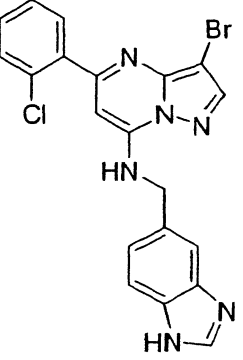
65				1. mp = 205-207 2. M+H = 402
66				1. mp = 220-223 2. M+H = 414
67				1. mp = 191-193 2. M+H = 431
68				1. mp = 235-237 2. M+H = 397

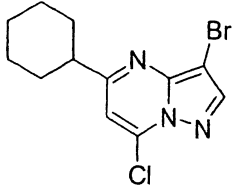
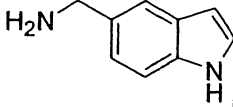
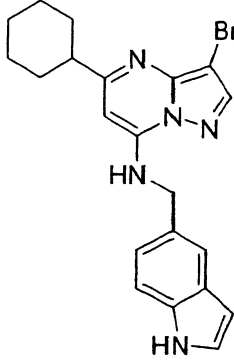
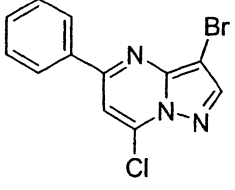
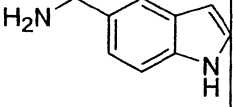
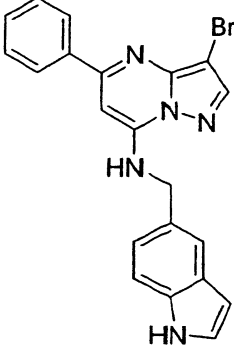
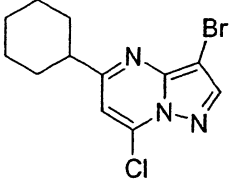
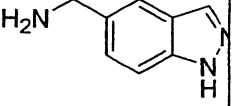
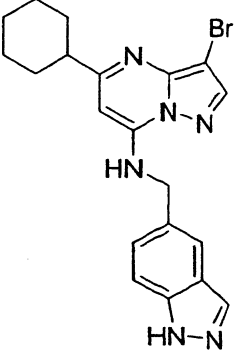
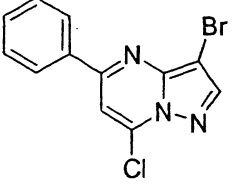
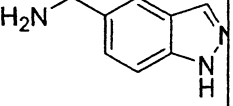
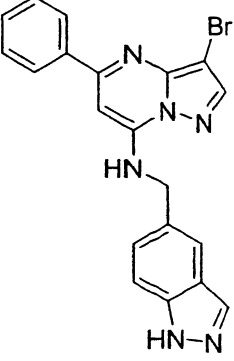
69		$\text{HCl} \cdot \text{H}_2\text{N}$ 		1. mp = >250 2. M+H = 403
70		$\text{HCl} \cdot \text{H}_2\text{N}$ 		1. mp = 230-232 2. M+H = 415
71		$2\text{HCl} \cdot \text{H}_2\text{N}$ 		1. mp = 235-238 2. M+H = 431
72		H_2N $\cdot 2\text{HCl}$ 		1. mp = 186-188 2. M+H = 410

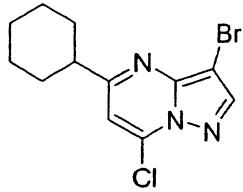
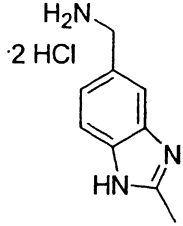
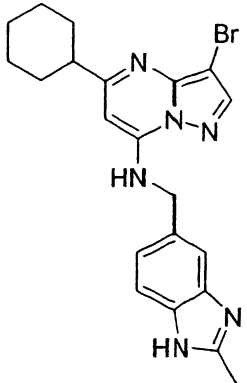
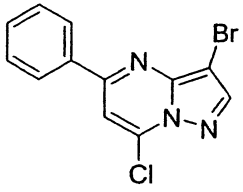
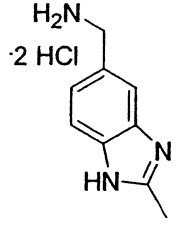
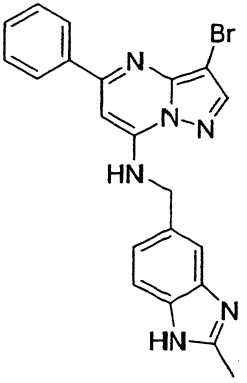
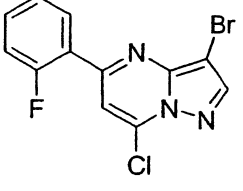
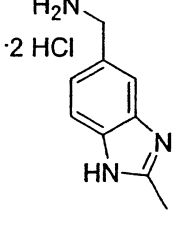
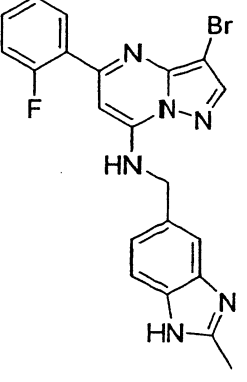
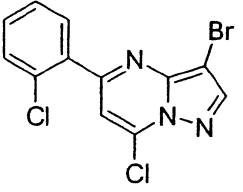
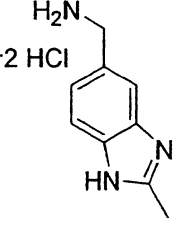
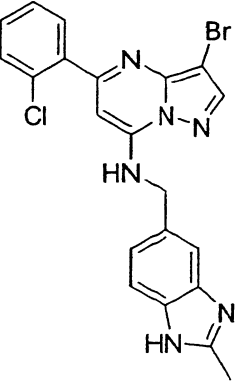
73				1. mp = 136-138 2. M+H = 424
74				1. mp = 192-195 2. M+H = 450
75				1. mp = 88-90 2. M+H = 454

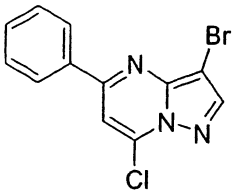
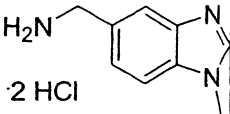
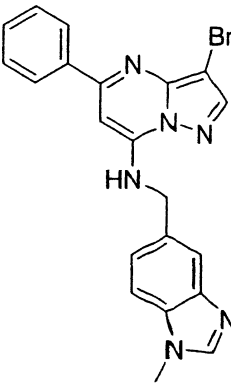
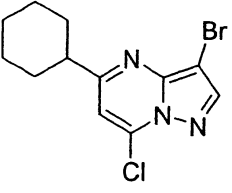
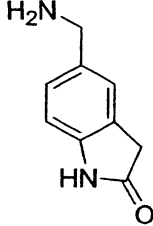
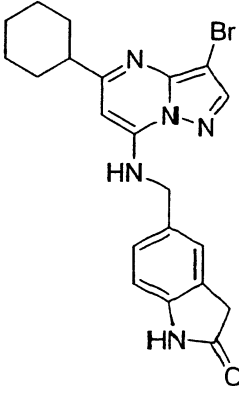
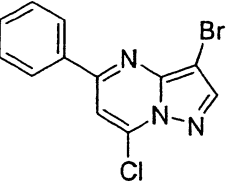
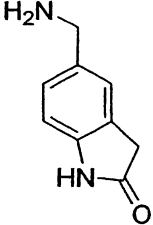
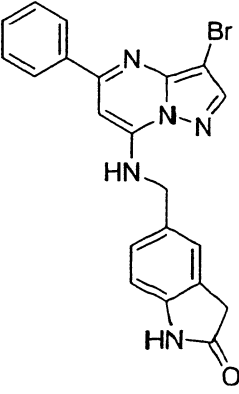
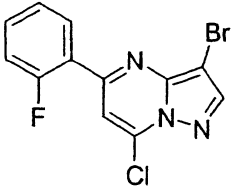
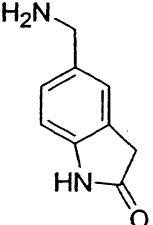
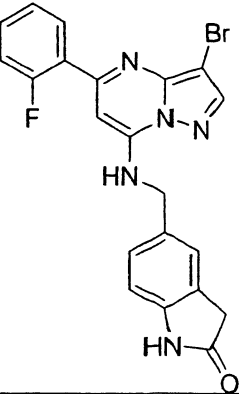
76				1. mp = 230-232 2. M+H = 467
77				1. mp = 131-133 2. M+H = 479
78				1. mp = 85-88 2. M+H = 376
79				1. mp = 131-133 2. M+H = 388

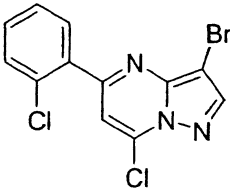
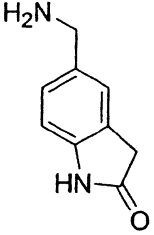
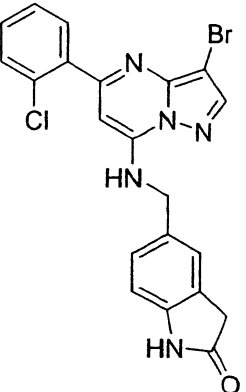
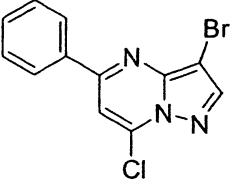
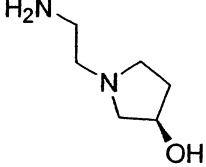
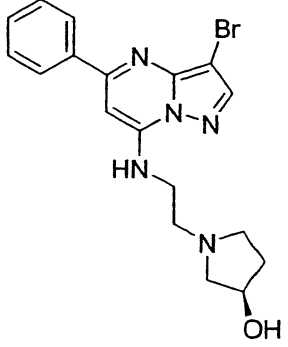
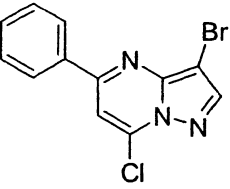
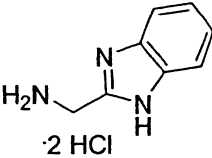
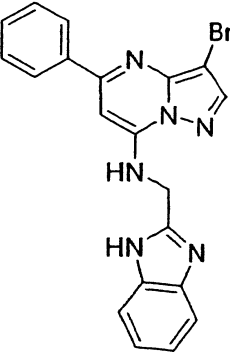
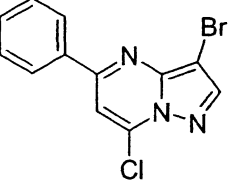
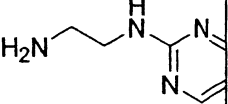
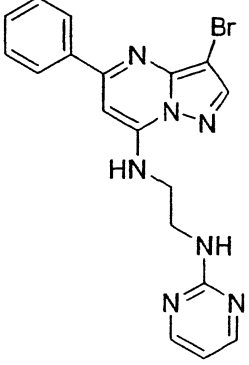
80		 · 2 HCl		1. mp = 206-208 2. M+H = 408
81		 HCl		1. mp = 108-110 2. M+H = 502
82		 · 2 HCl		1. mp = 83-85 2. M+H = 402
83		 · 2 HCl		1. mp = 220 2. M+H = 414

84		 · 2 HCl		1. mp = 154-156 2. M+H = 426
85		 · 2 HCl		1. mp = 152-153 2. M+H = 438
86		 · 2 HCl		1. mp = 159-161 2. M+H = 420
87		 · 2 HCl		1. mp = >220 2. M+H = 455

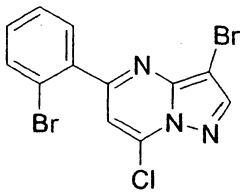
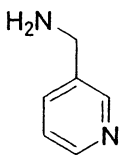
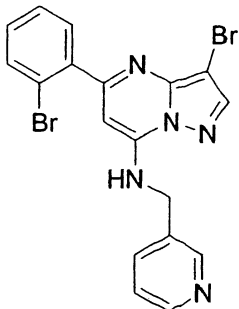
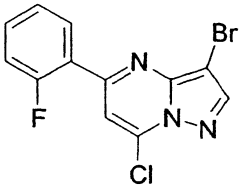
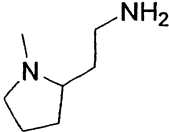
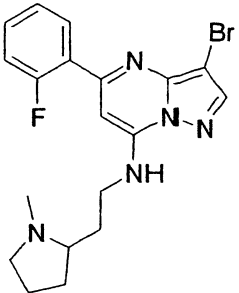
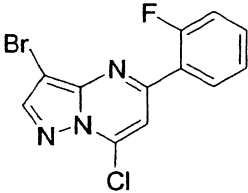
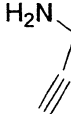
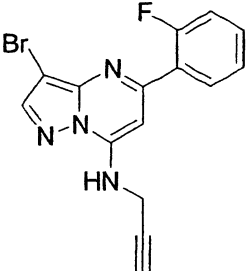
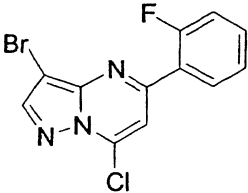
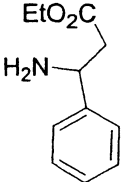
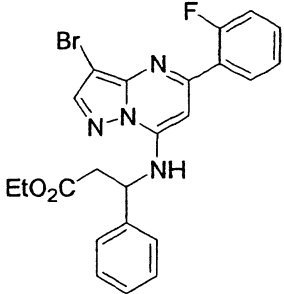
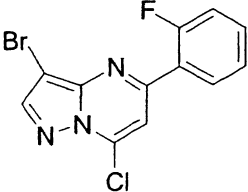
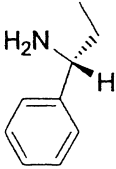
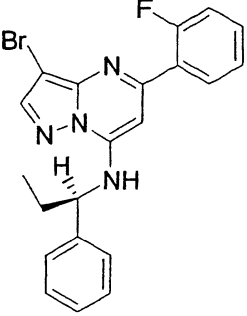
88				1. mp = 223-225 2. M+H = 425
89				1. mp = 199-201 2. M+H = 419
90				1. mp = 184-186 2. M+H = 426
91				1. mp = 196-198 2. M+H = 420

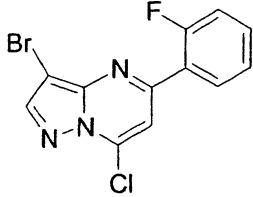
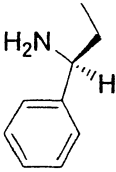
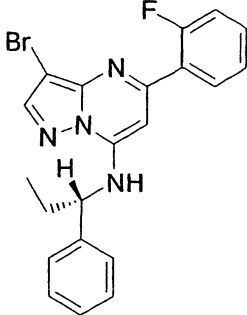
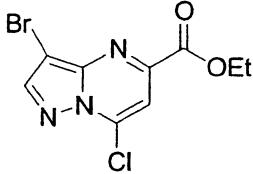
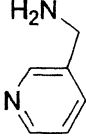
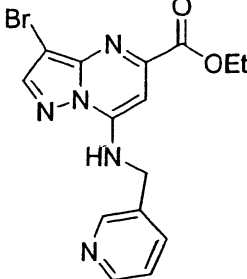
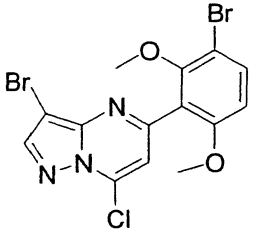
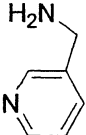
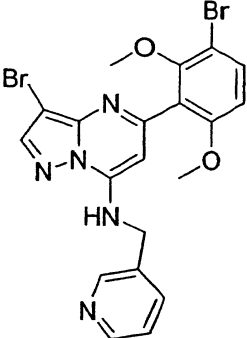
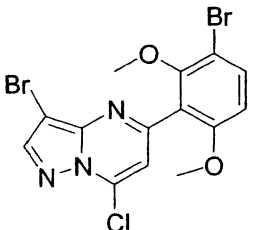
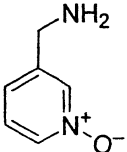
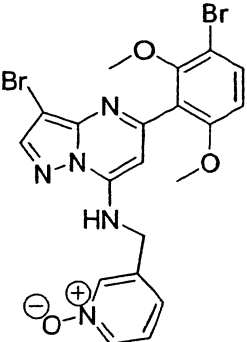
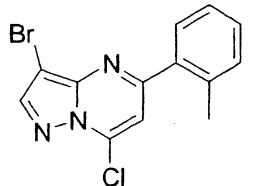
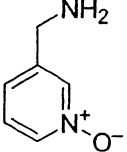
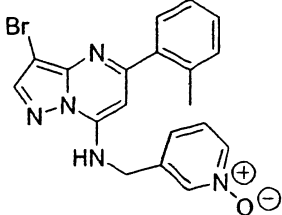
92				1. mp = 156-159 2. M+H = 440
93				1. mp = 173-176 2. M+H = 434
94				1. mp = 173-175 2. M+H = 452
95				1. mp = 174-176 2. M+H = 469

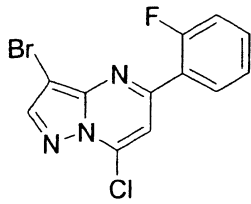
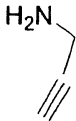
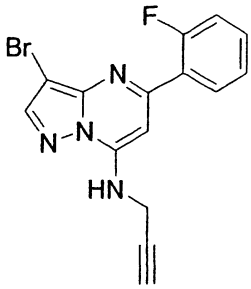
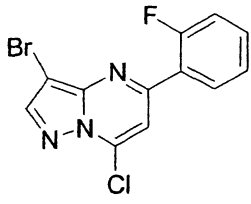
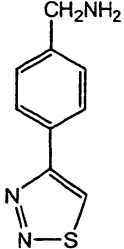
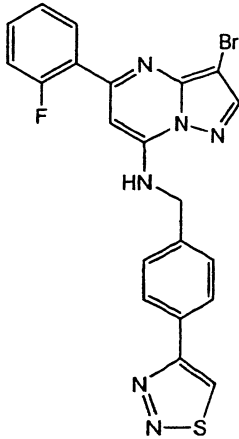
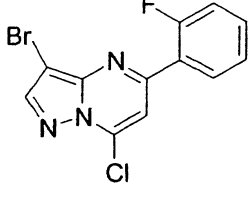
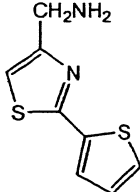
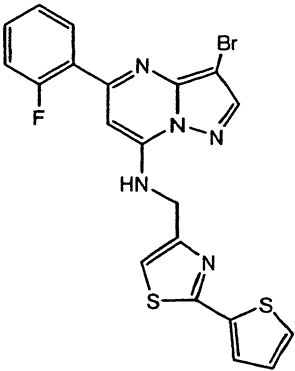
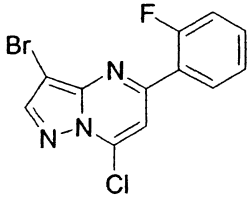
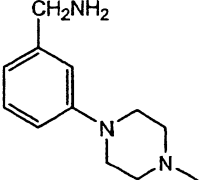
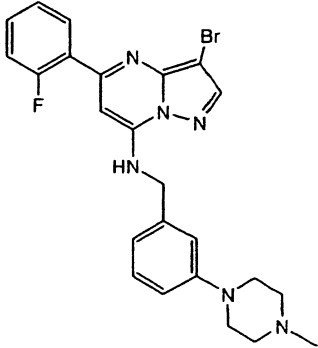
96		 · 2 HCl		1. mp = 230-234 2. M+H = 434
97				1. mp = 191-193 2. M+H = 441
98				1. mp = 202-205 2. M+H = 434
99				1. mp = 209-212 2. M+H = 453

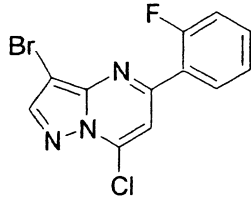
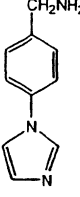
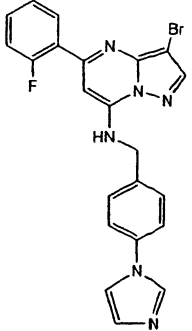
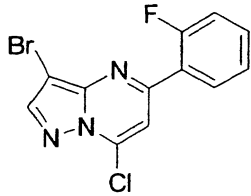
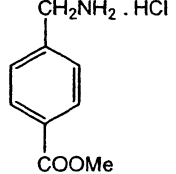
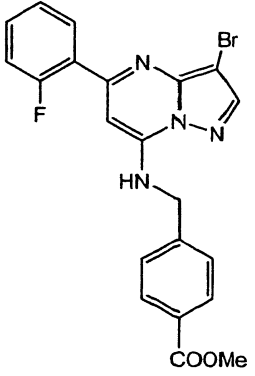
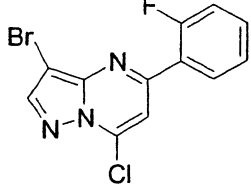
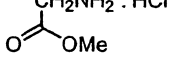
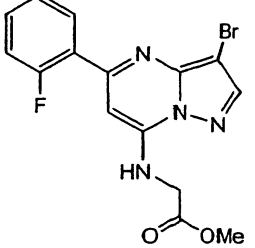
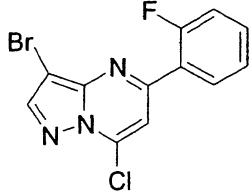
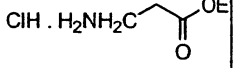
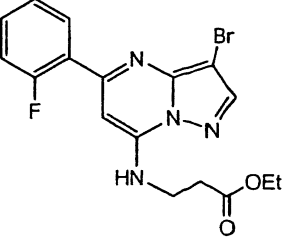
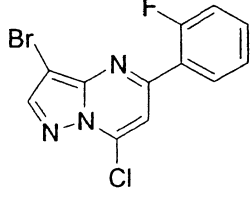
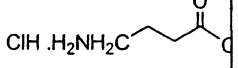
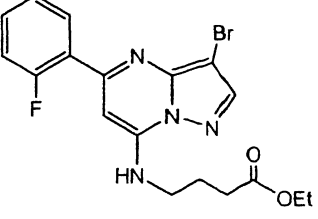
100				1. mp = 219-221 2. M+H = 469
101				1. mp = 64-66 2. M+H = 403
102				1. mp = 168-170 2. M+H = 420
103				1. mp = 213-216 2. M+H = 411

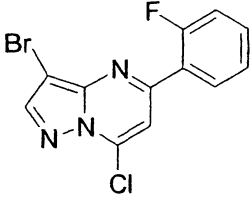
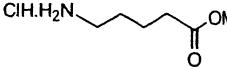
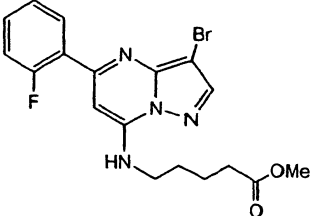
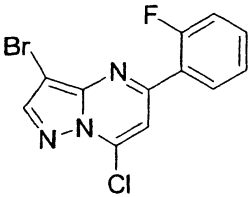
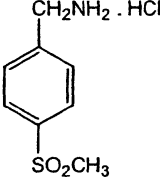
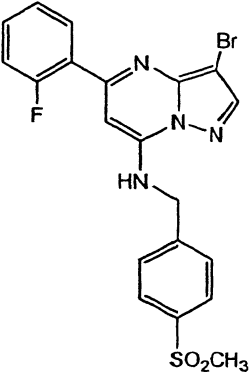
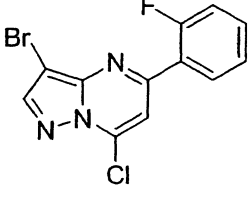
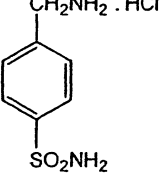
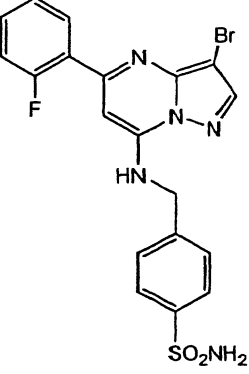
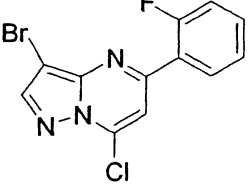
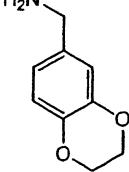
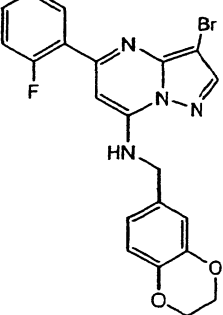
104				1. mp = 98-100 2. M+H = 561
105				1. mp 70-72 2. M+H = 608
106				1. mp 168-170 2. M+H = 538
107				1. mp 189-191 2. M+H = 592

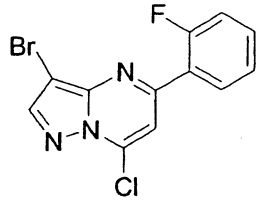
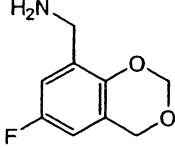
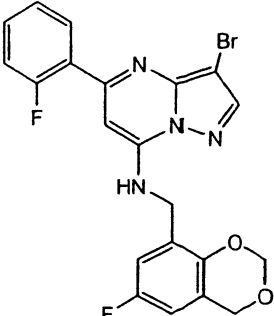
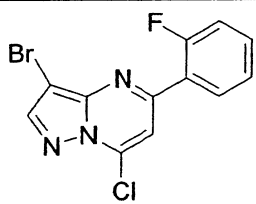
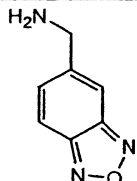
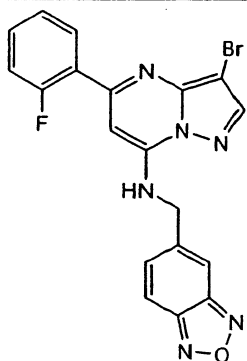
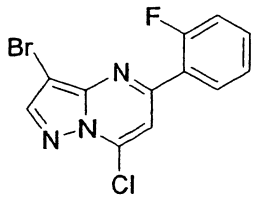
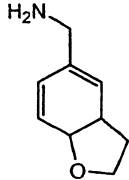
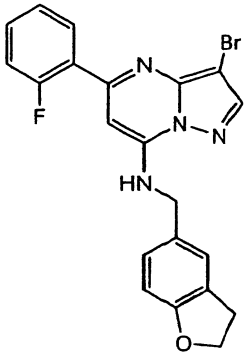
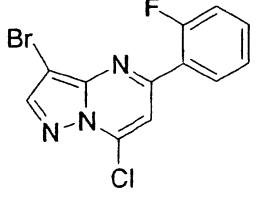
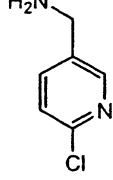
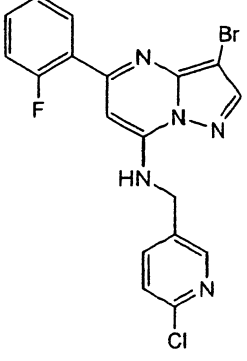
108				LCMS: MH ⁺ = 458;
109				產率= 89 LCMS: MH ⁺ = 418 m. p. = 131-132 °C
110				產率=95% LCMS: MH ⁺ = 347
111				產率=91% 3H); LCMS: MH ⁺ = 484
112				產率=87% LCMS: MH ⁺ = 427

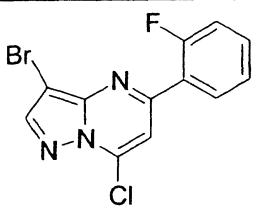
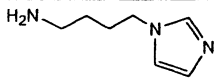
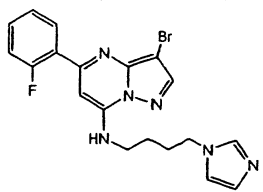
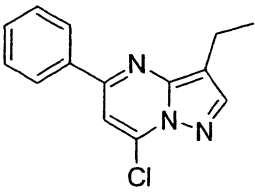
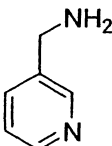
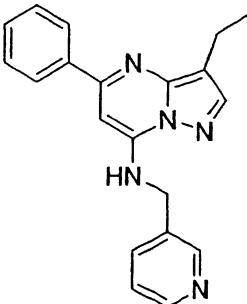
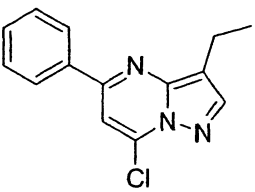
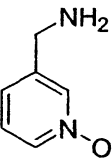
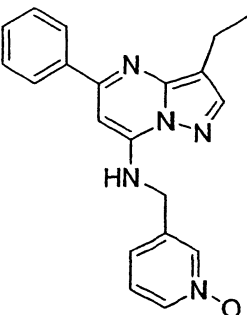
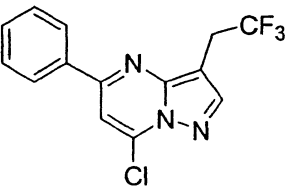
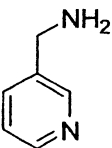
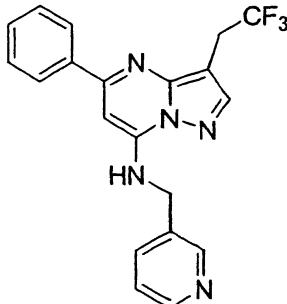
113				產率=80% LCMS: MH ⁺ = 427
114				產率=91% LCMS: MH ⁺ = 378
115				產率=92% , 3H); LCMS: MH ⁺ =520
116				產率= 98% LCMS: MH ⁺ =536
117				產率=82% LCMS: MH ⁺ =410

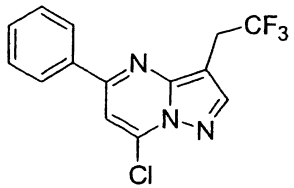
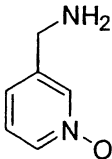
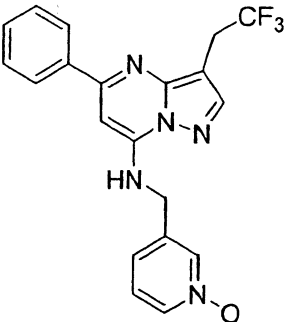
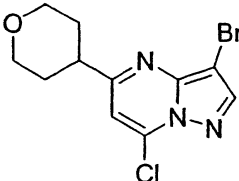
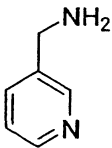
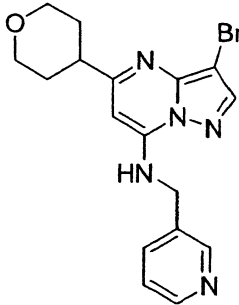
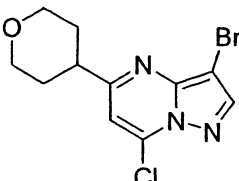
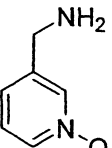
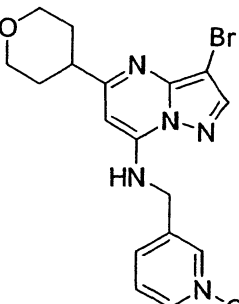
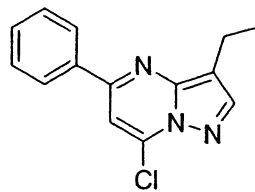
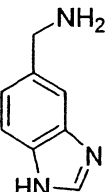
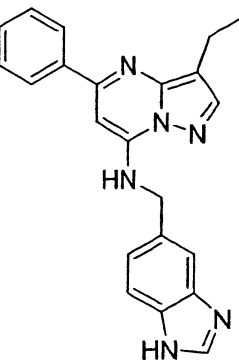
118				產率=95% LCMS: MH ⁺ = 347
121				產率=65% LCMS: MH ⁺ = 481.02
126				產率=71% MH ⁺ = 486
127				產率=71% MH ⁺ = 495.1

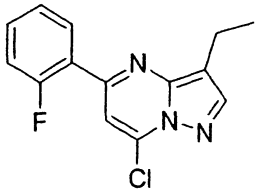
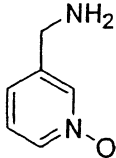
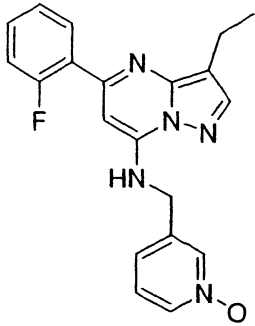
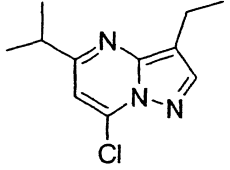
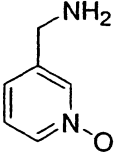
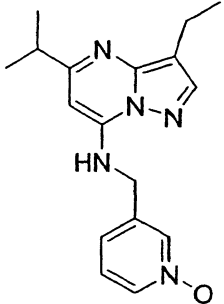
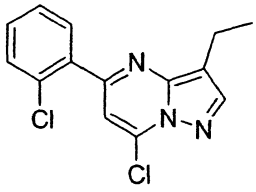
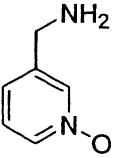
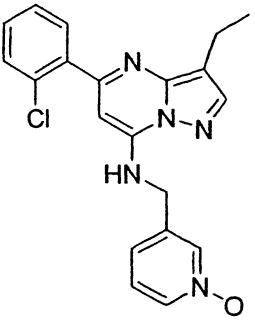
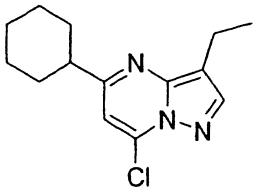
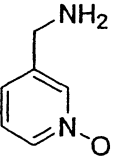
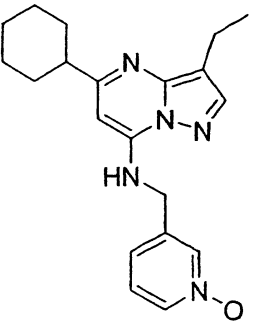
128				産率=55% MH ⁺ = 463
129				産率=77% LCMS: MH ⁺ = 455
130				¹ H NMR (Yield = 75%) LCMS: MH ⁺ = 379
131				産率=75% LCMS: MH ⁺ = 407
132				産率=75% LCMS: MH ⁺ = 421

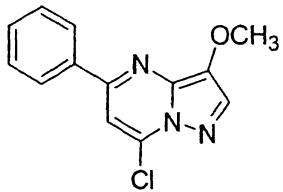
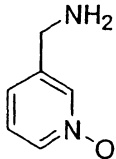
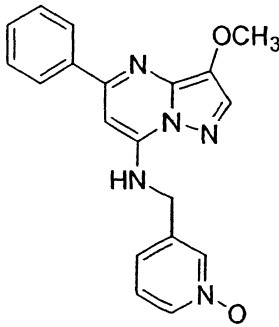
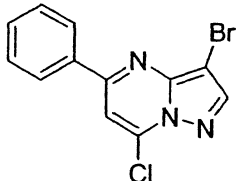
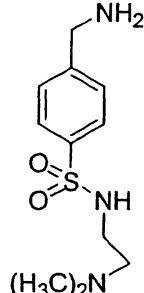
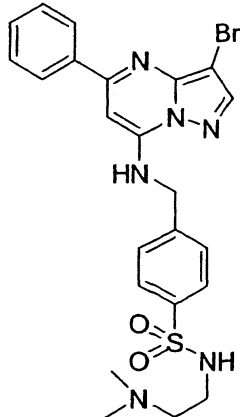
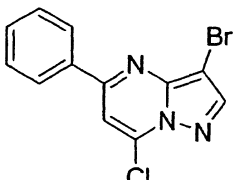
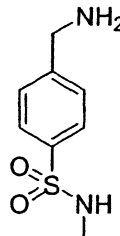
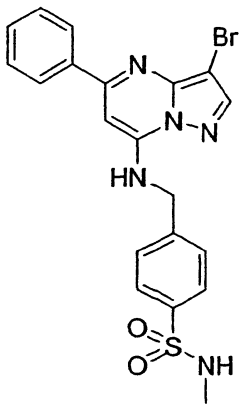
133				產率= 70% LCMS: MH ⁺ = 421
134				產率= 78% LCMS: MH ⁺ = 475
135				產率= 75% LCMS: MH ⁺ = 476
136				產率= 65% LCMS: MH ⁺ = 455

137				產率= 55% LCMS: MH ⁺ = 473)
138				產率= 60% LCMS: MH ⁺ = 439
139				產率= 65% LCMS: MH ⁺ = 441
140				產率= 80% LCMS: MH ⁺ = 432

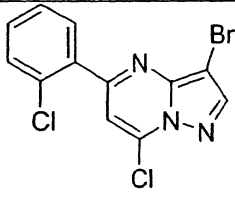
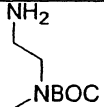
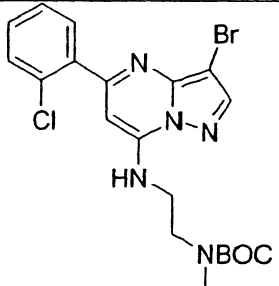
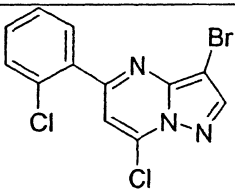
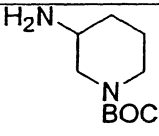
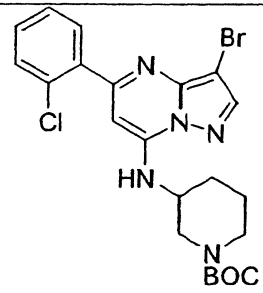
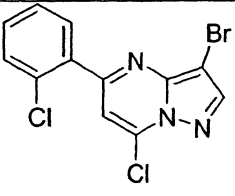
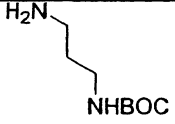
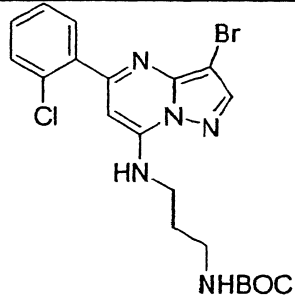
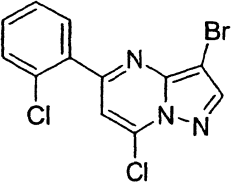
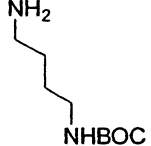
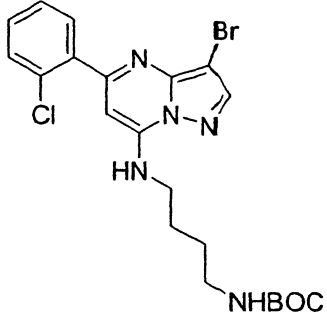
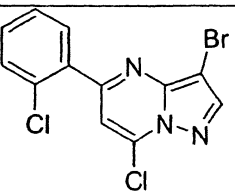
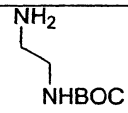
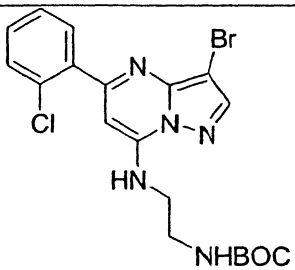
141				產率= 60% LCMS: MH ⁺ = 429
142				LCMS: MH ⁺ =330 ; mp=109- 111°C
143				LCMS: MH ⁺ =346 ; mp=186- 188°C
144				LCMS: MH ⁺ =384 ; mp=148- 150°C

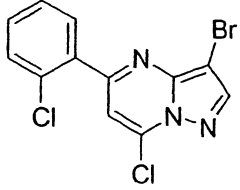
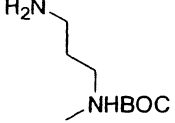
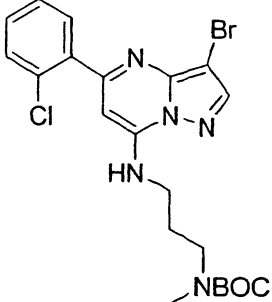
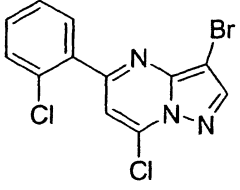
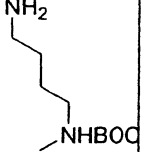
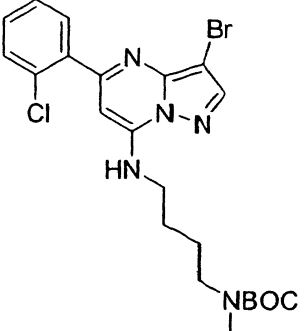
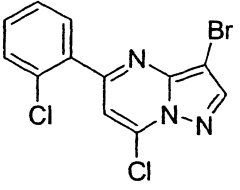
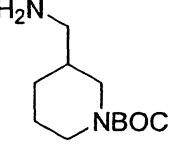
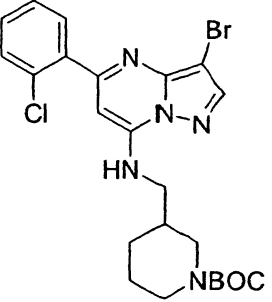
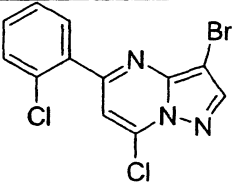
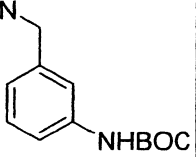
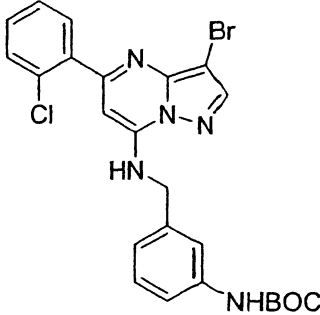
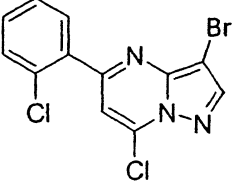
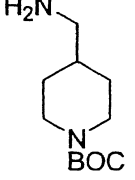
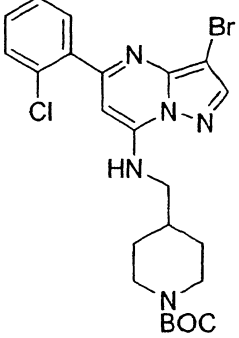
145				LCMS: MH ⁺ =400 ; mp=186-188°C
146				LCMS: M2H ⁺ =390; mp=192-194°C
147				LCMS: M ⁺ =404; mp=220-222°C
148				LCMS: MH ⁺ =369 ; mp>230°C

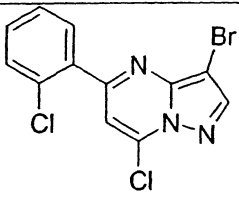
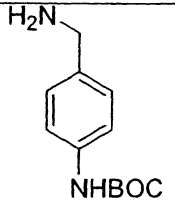
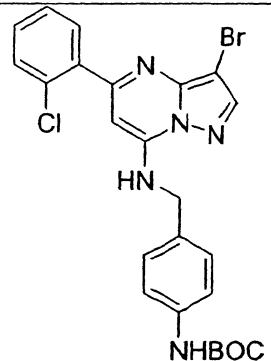
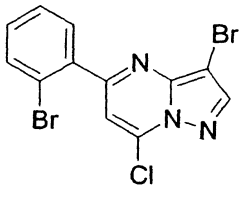
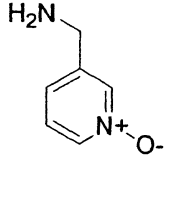
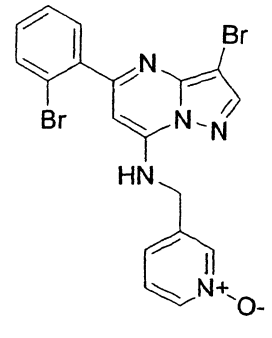
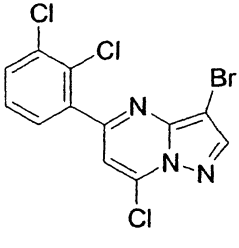
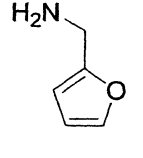
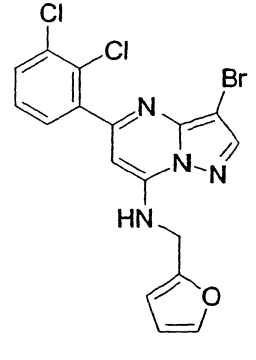
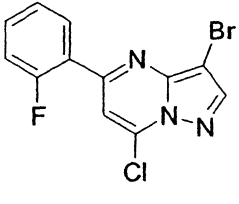
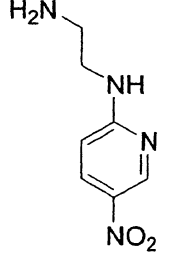
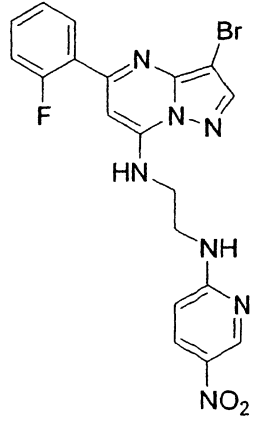
149				LCMS: MH ⁺ =364 ; mp=186-188°C
150				LCMS: MH ⁺ =312 ; mp=138-140°C
151				LCMS: M ⁺ =380; mp=172-174°C
152				LCMS: MH ⁺ =352 ; mp=201-203°C

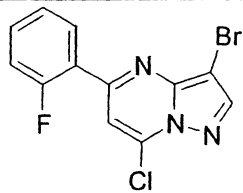
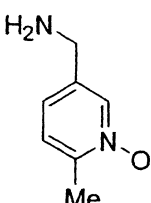
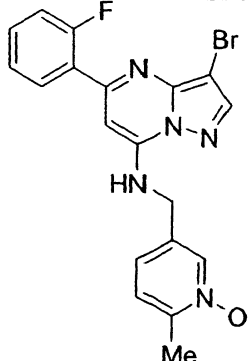
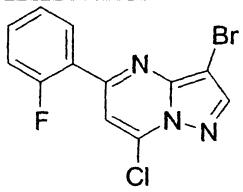
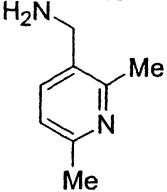
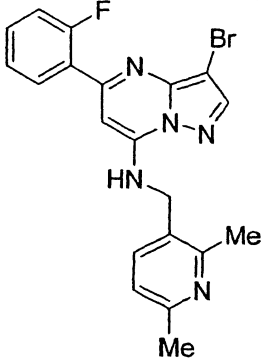
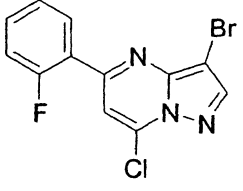
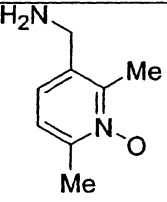
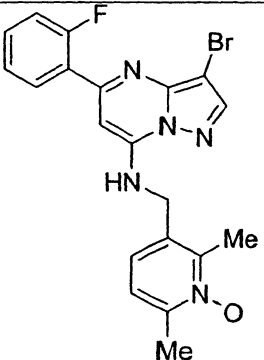
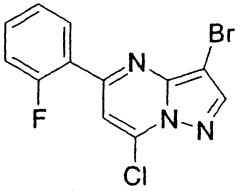
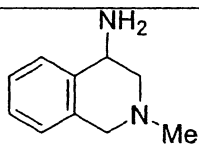
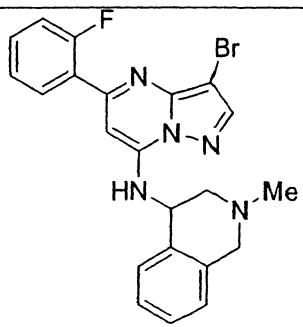
153				LCMS: M ⁺ H ⁺ =348 ; mp=166-168°C
154				LCMS: M ⁺ H ⁺ =531 ; mp=78-80°C
155				LCMS: M ⁺ H ⁺ =474 ; mp=161-163°C

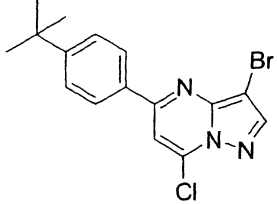
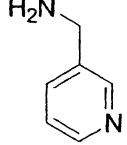
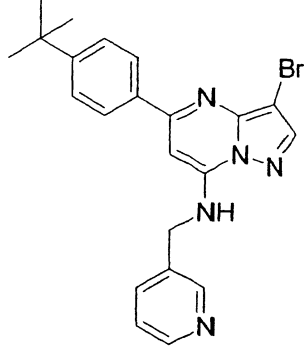
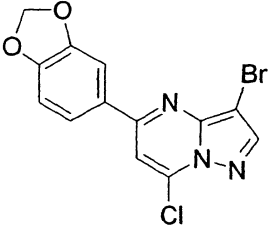
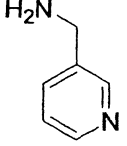
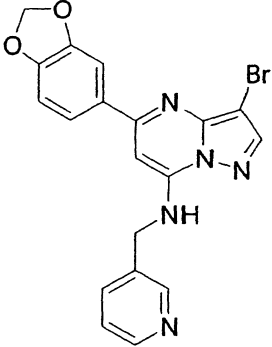
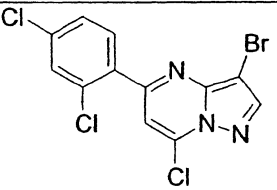
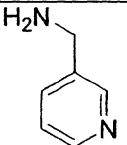
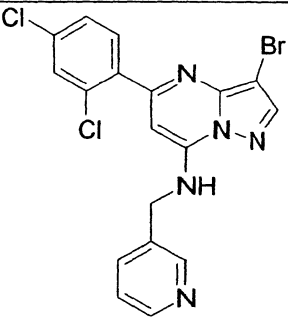
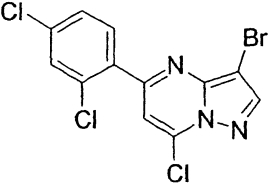
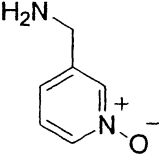
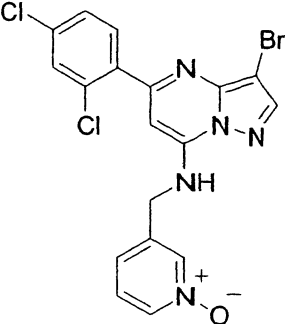
156				LCMS: M ⁺ =444; mp=48-51°C
157				MH ⁺ = 542.1
158				MH ⁺ = 520.1
159				MH ⁺ = 542.1

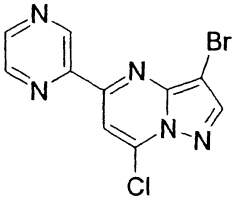
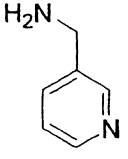
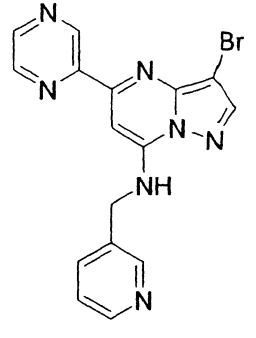
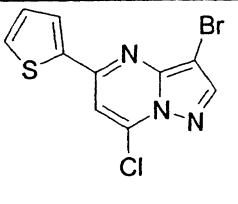
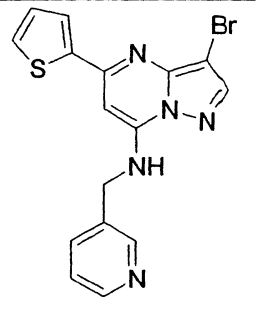
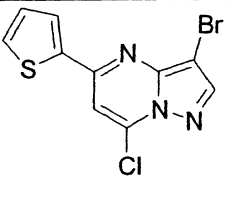
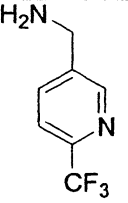
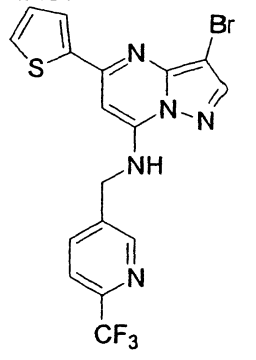
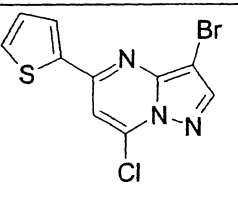
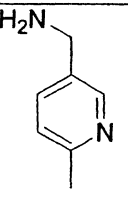
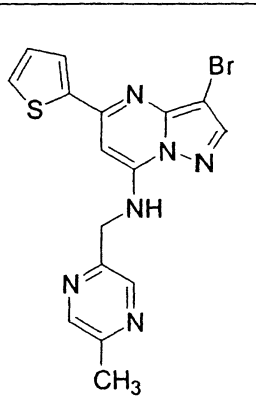
160				$MH^+ = 480.1$
161				$MH^+ = 506.1$
162				$MH^+ = 480.1$
163				$MH^+ = 494.1$
164				$MH^+ = 466.1$

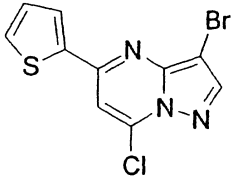
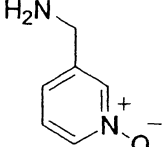
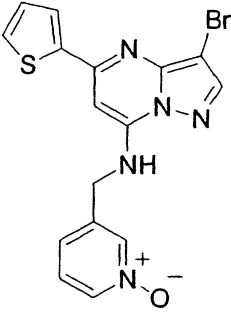
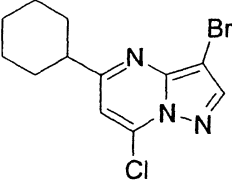
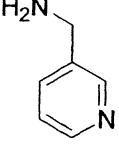
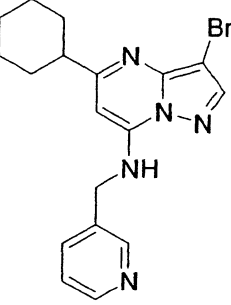
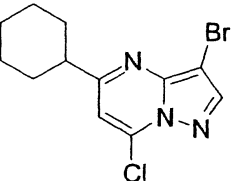
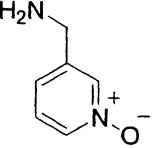
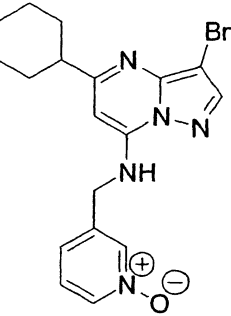
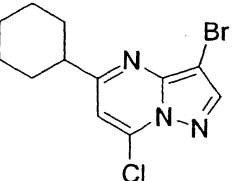
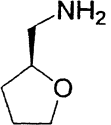
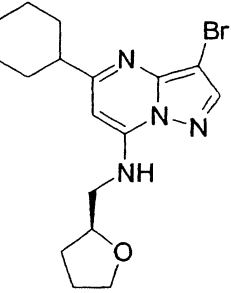
165				$MH^+ = 494.1$
166				$MH^+ = 508.1$
167				$MH^+ = 520.1$
168				$MH^+ = 528.1$
169				$MH^+ = 520.1$

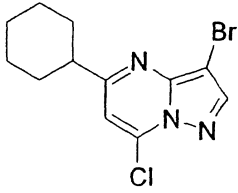
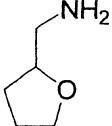
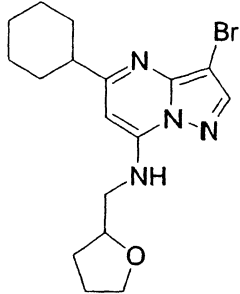
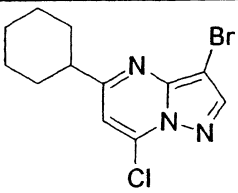
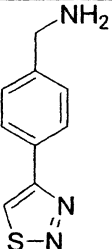
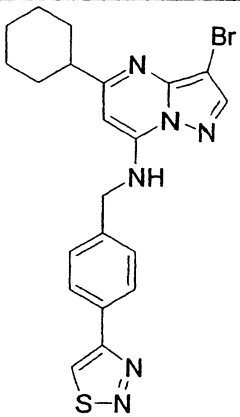
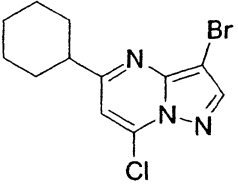
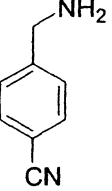
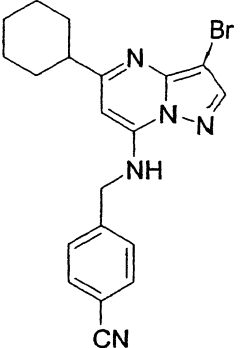
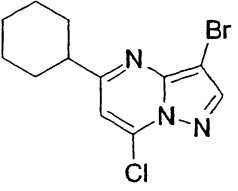
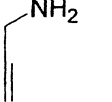
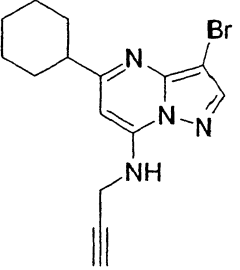
170				MH ⁺ = 528.1
171				LCMS: MH ⁺ = 474;
172				LCMS: MH ⁺ = 437;
173				LCMS: MH ⁺ = 472;

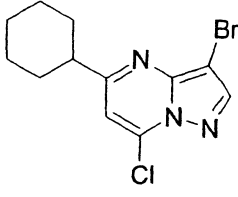
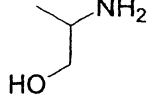
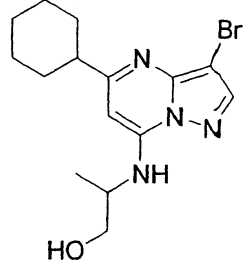
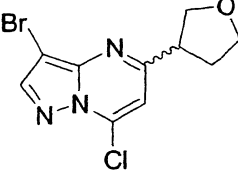
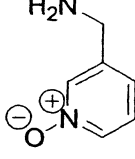
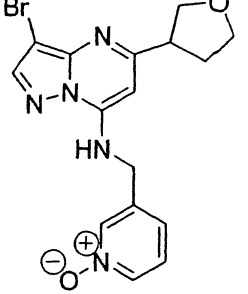
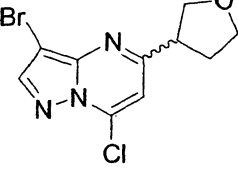
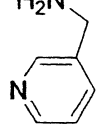
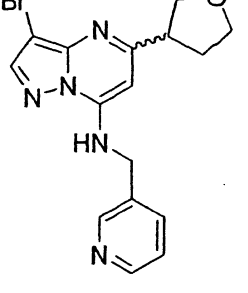
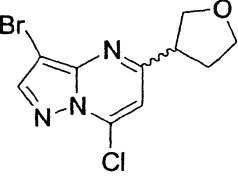
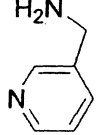
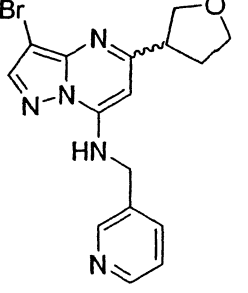
174				LCMS: MH ⁺ = 428.1
175				LCMS: MH ⁺ = 426.2
176				LCMS: MH ⁺ = 442.0
177				LCMS: MH ⁺ = 452.0

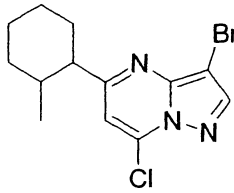
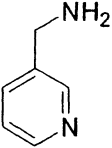
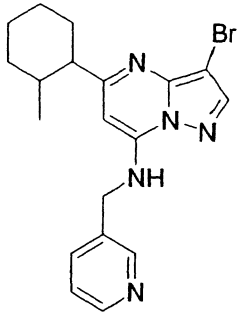
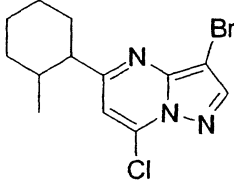
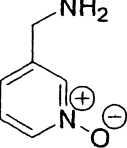
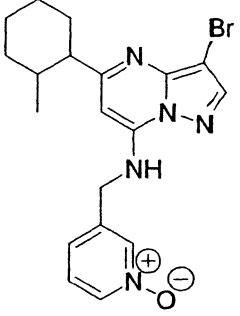
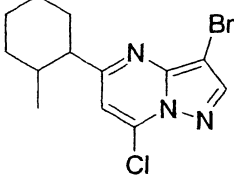
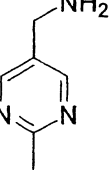
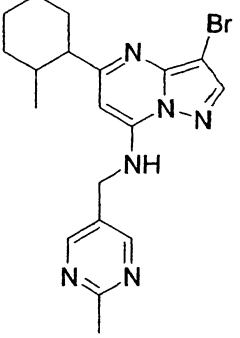
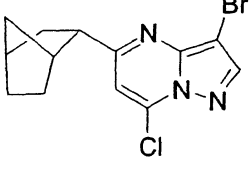
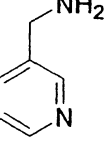
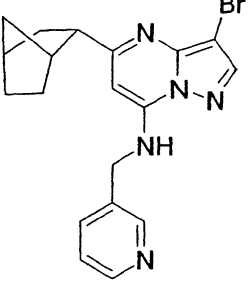
178				產率=90 MH ⁺ =436 m. pt. = 89.1 °C
179				MH ⁺ =424 m. pt. = 188.2 °C
180				MH ⁺ =448 m. pt. = 211.3 °C
181				產率=定量 MH ⁺ =464

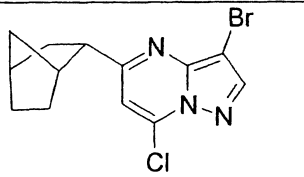
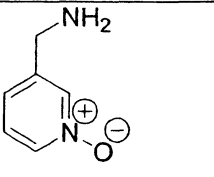
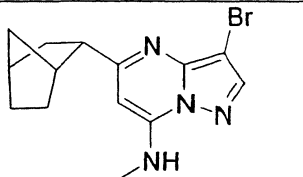
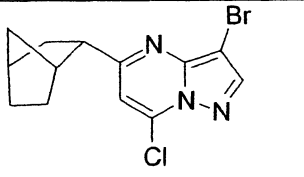
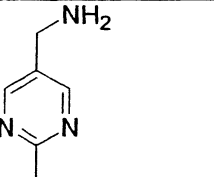
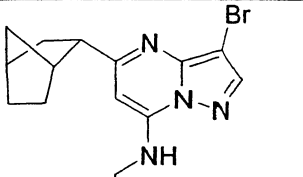
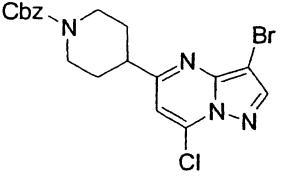
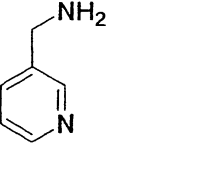
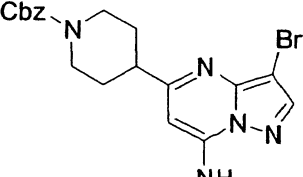
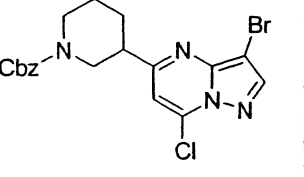
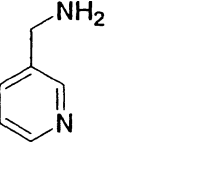
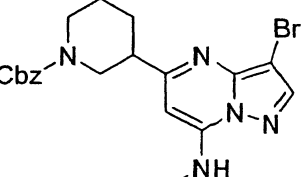
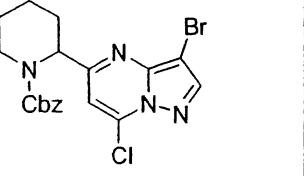
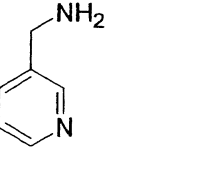
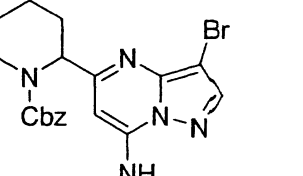
182				MH ⁺ = 382 m. pt. = 185.8 °C
183				MH ⁺ = 387 m. pt. = 181 – 182 °C
184				MH ⁺ = 453
185				MH ⁺ = 401 m. pt. = 178.3 °C

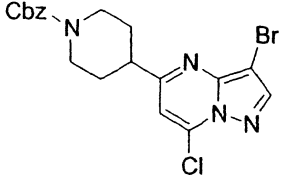
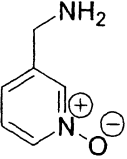
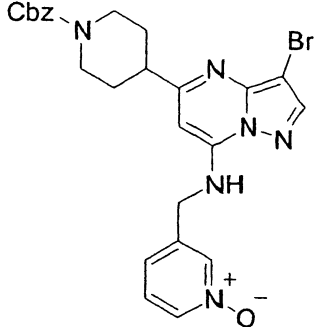
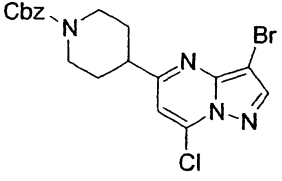
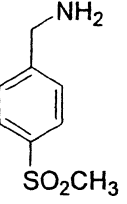
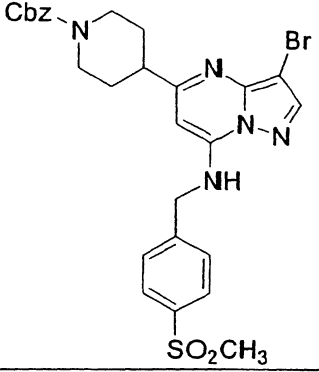
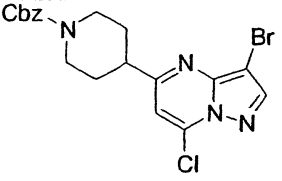
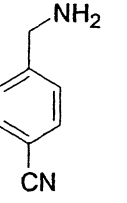
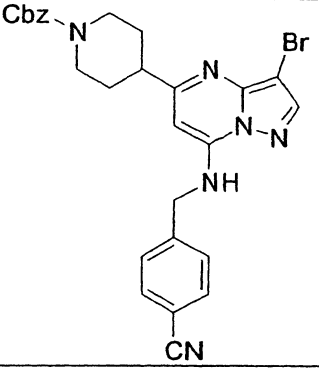
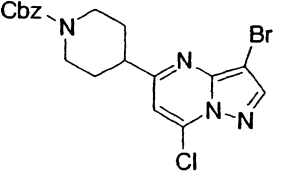
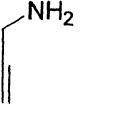
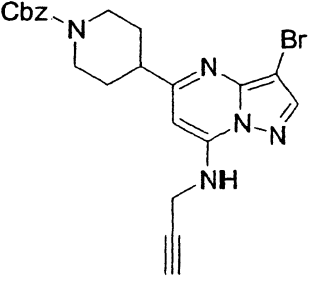
186				MH ⁺ = 402
187				産率 = 91 MH ⁺ = 386 m. pt. = 148.3 °C
188				産率 = 65 MH ⁺ = 402 m. pt. = 174.5 °C
189				MH ⁺ = 379 m. pt. = 82 – 83 °C

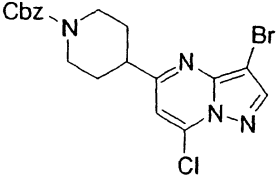
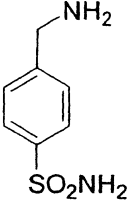
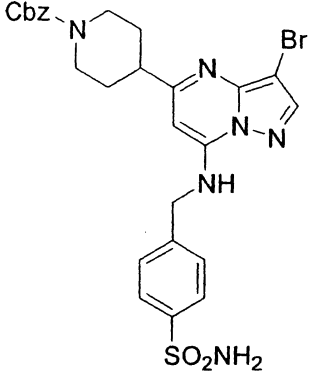
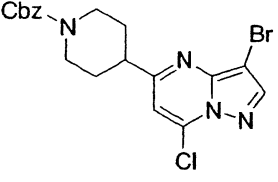
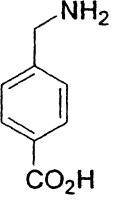
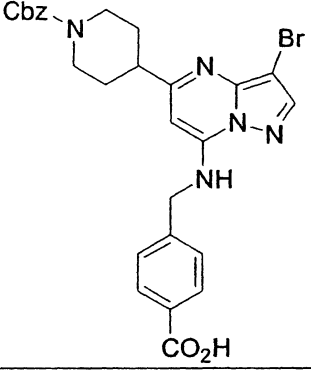
190				MH ⁺ = 379 m. pt. = 50.7 °C
191				產率 = 89 MH ⁺ = 469 m. pt. = 186.7 °C
192				產率 = 93 MH ⁺ = 410 m. pt. = 86.7 °C
193				產率 = 76 MH ⁺ = 333 m. pt. = 120.3 °C

194				產率=86 MH ⁺ =353 m. pt.=188.9 °C
195				產率=11% LCMS:374 MH ⁺ =390
196				產率=88% LCMS:374 MH ⁺ =346
197				產率=88% LCMS:374 MH ⁺ =346

198				產率 = MH ⁺ = 400 m. pt. = 111.5 – 112.2 °C
199				MH ⁺ = 416
200				MH ⁺ = 415
201				MH ⁺ = 398 m.p. = 156.5 °C

202				MH ⁺ = 414 m.p. = 89.5 °C
203				MH ⁺ = 413
204				產率= 86 MH ⁺ = 521 m.p. = 79.9 °C
204 .10				
204 .11				產率= 87 MH ⁺ = 521 m.p. = 128.6 °C

205				產率= 99 MH ⁺ = 537 m.p. = 83.5 °C
206				產率= 94 MH ⁺ = 598 m.p. = 110.8 °C
207				產率= 定量 MH ⁺ = 545
208				產率= 96 MH ⁺ = 468 m.p. = 69.2 °C

209				MH ⁺ = 498 m.p. = 226.5 °C
210				MH ⁺ = 564 m.p. = 174.2 °C

對所選擇之實例之額外數據如下：

實例 23: ¹H NMR (CD₃OD) δ 8.63 (d, J=5.7 Hz, 2H), 8.18 (s, 1H), 7.81 (dd, J=8.1 Hz, 2.1 Hz, 1H), 7.58 (d, J=6.0 Hz, 2H), 7.48 (m, 1H), 7.15-7.10 (m, 2H), 6.50 (s, 1H), 4.86 (s, 2H), 3.70 (s, 3H)

實例 24: ¹H NMR (CDCl₃) δ 8.82 (s, 1H), 8.73 (d, J=4.2 Hz, 1H), 8.11 (s, 1H), 8.06 (dd, J=7.8 Hz, 1.8 Hz, 1H), 7.91 (d, J=8.1 Hz, 1H), 7.53-7.47 (m, 2H), 7.20 (m, 1H), 7.08 (d, J=8.1 Hz, 1H), 6.75 (s, 1H), 4.81 (d, J=4.5 Hz, 2H), 3.86 (s, 3H)

實例 25: ¹H NMR (CDCl₃) δ 8.75 (d, J=5.7 Hz, 2H), 8.12 (s, 1H), 7.81 (d, J=2.1 Hz, 1H), 7.53 (dd, J=8.4, 2.1 Hz, 1H), 7.45 (d, J=6.0 Hz, 2H), 6.96 (t, J=6.0 Hz, 2H), 6.33 (s, 1H), 4.85 (d, J=6.0 Hz, 2H), 4.09 (s, 3H), 4.03 (s, 3H)

實例 26: ^1H NMR (CDCl_3) δ 8.82 (s, 1H), 8.72 (s, 1H), 8.09 (m, 1H), 7.87-7.83 (m, 2H), 7.60 (m, 1H), 7.45 (m, 1H), 7.03 (d, $J=8.4$ Hz, 1H), 6.87 (s, 1H), 6.43 (s, 1H), 4.83 (d, $J=4.5$ Hz, 2H), 4.11 (s, 3H), 4.04 (s, 3H)

實例 27: ^1H NMR (CDCl_3) δ 8.75 (d, $J=4.5$ Hz, 2H), 8.19 (s, 1H), 7.63 (d, $J=7.8$ Hz, 2H), 7.44-7.40 (m, 3H), 7.07 (m, 1H), 6.26 (s, 1H), 4.83 (d, $J=5.1$ Hz, 2H)

實例 28: ^1H NMR (CDCl_3) δ 8.86 (s, 1H), 8.74 (m, 1H), 8.17 (s, 1H), 7.97 (m, 1H), 7.66-7.63 (m, 2H), 7.62 (m, 1H), 7.41 (m, 1H), 7.07 (m, 1H), 6.35 (s, 1H), 4.87 (d, $J=6.0$ Hz, 2H)

實例 30: ^1H NMR (CDCl_3) δ 8.16 (s, 1H), 7.66-7.62 (m, 2H), 7.41 (m, 1H), 7.33-7.22 (m, 3H), 6.96 (t, $J=6.0$ Hz, 1H), 6.33 (s, 1H), 4.73 (d, $J=6.0$ Hz, 2H)

實例 31: ^1H NMR (CDCl_3) δ 8.13 (s, 1H), 7.66 (d, $J=7.8$ Hz, 2H), 7.45-7.40 (m, 2H), 7.10-7.04 (m, 2H), 6.93 (t, $J=6.6$ Hz, 1H), 6.60 (s, 1H), 4.84 (d, $J=6.6$ Hz, 2H)

實例 32: ^1H NMR (CDCl_3) δ 8.16 (s, 1H), 7.66-7.62 (m, 2H), 7.57-7.55 (m, 2H), 7.41 (t, $J=7.8$ Hz, 1H), 7.31 (dd, $J=7.8$, 1.8 Hz, 1H), 6.99 (t, $J=6.0$ Hz, 1H), 6.32 (s, 1H), 4.73 (d, $J=6.0$ Hz, 2H)

實例 40: ^1H NMR (CDCl_3) δ 8.01 (s, 1H), 7.31-7.24 (d, $J=8.2$ Hz, 1H), 6.72-6.64 (br t, $J=5.4$ Hz, 1H), 6.62-6.52 (m, 2H), 6.05-6.01 (s, 1H), 5.56-4.64 (d, $J=6.0$ Hz, 2H), 4.03-3.93 (s, 3H), 3.94-3.86 (s, 3H), 2.79-2.70 (d, $J=8.1$ Hz, 2H), 2.02-

1.66 (m, 6H), 1.43-1.22 (m, 3H), 1.20-1.02 (m, 2H)

實例 45: ^1H NMR (CDCl_3) δ 8.73 (d, 2H), 8.54 (s, 1H), 7.41 (d, 2H), 7.02 (br, 1H), 5.90 (s, 1H), 4.80 (s, 2H), 4.48 (q, 2H), 2.75 (s, 2H), 1.50 (t, 2H), 1.06 (s, 9H);

實例 46: ^1H NMR (CDCl_3) δ 8.79 (s, 1H), 8.72 (d, 1H), 8.14 (s, 1H), 7.84 (d, 1H), 7.54-7.33 (m, 4H), 6.97 (t, 1H), 6.18 (s, 1H), 4.79 (d, 2H), 2.47 (s, 3H)

實例 108: ^1H NMR (CDCl_3) δ 8.79 (s, 1H), 8.72 (d, $J=3.0$ Hz, 1H), 8.16 (s, 1H), 7.84 (d, $J=7.8$ Hz, 1H), 7.74 (d, $J=7.5$ Hz, 2H), 7.55-7.35 (m, 3H), 6.92 (t, $J=6.3$ Hz, 1H), 6.42 (s, 1H), 4.81 (d, $J=6.3$ Hz, 2H)

實例 110: ^1H NMR (CDCl_3) δ 8.18 (t, 1H), 8.03 (s, 1H), 7.44 (m, 1H), 7.30 (t, 1H), 7.17 (q, 1H), 6.66 (s, 1H), 6.56 (br, 1H), 4.28 (d, 2H), 2.38 (s, 1H)

實例 111: ^1H NMR (CDCl_3) δ 8.72 (br, 1H), 8.59 (d, 1H), 8.11 (d, 2H), 8.06 (s, 1H), 7.73 (d, 1H), 7.44 (d, 1H), 7.42-7.21 (m, 3H), 7.07 (q, 1H), 6.39 (d, 1H), 5.21 (q, 1H), 4.16 (q, 2H), 3.08 (d, 2H), 1.22 (t, 3H)

實例 112: ^1H NMR (CDCl_3) δ 8.22 (t, 1H), 8.15 (s, 1H), 7.51-7.33 (m, 7H), 7.21 (q, 1H), 6.82 (d, 1H), 6.51 (s, 1H), 4.68 (q, 1H), 2.18 (m, 2H), 1.17 (t, 3H)

實例 113: ^1H NMR (CDCl_3) δ 8.22 (t, 1H), 8.14 (s, 1H), 7.51-7.33 (m, 7H), 7.21 (q, 1H), 6.82 (d, 1H), 6.51 (s, 1H), 4.68 (q, 1H), 2.18 (m, 2H), 1.17 (t, 3H)

實例 114: ^1H NMR (CDCl_3) δ 8.81 (s, 1H), 8.75 (d, 1H), 8.21 (s, 1H), 7.84 (d, 1H), 7.47 (q, 1H), 6.96 (s, 1H), 6.94 (t, 1H), 4.85 (d, 2H), 4.60 (q, 2H), 1.58 (t, 3H)

實例 115: ^1H NMR (CDCl_3) δ 8.77 (s, 1H), 8.72 (d, 1H), 8.14 (s, 1H), 7.83 (d, 1H), 7.65 (d, 1H), 7.44 (q, 1H), 7.80 (t, 1H), 7.6 (d, 1H), 6.18 (s, 1H), 4.75 (d, 2H), 3.91 (s, 3H), 3.81 (s, 3H)

實例 116: ^1H NMR (CDCl_3) δ 8.67 (s, 1H), 8.55 (d, 1H), 8.50 (s, 1H), 7.92 (d, 1H), 7.90 (d, 1H), 7.78 (t, 1H), 7.10 (d, 1H), 6.97 (s, 1H), 5.11 (s, 2H), 3.77 (s, 6H)

實例 117: ^1H NMR (CDCl_3) δ 8.38 (s, 1H), 8.30 (d, 1H), 8.17 (s, 1H), 7.52-7.37 (m, 6H), 6.97 (t, 1H), 6.13 (s, 1H), 4.77 (d, 2H), 2.50 (s, 3H)

實例 118: ^1H NMR (CDCl_3) δ 8.18 (t, 1H), 8.03 (s, 1H), 7.44 (m, 1H), 7.30 (t, 1H), 7.17 (q, 1H), 6.66 (s, 1H), 6.56 (br, 1H), 4.28 (d, 2H), 2.38 (s, 1H);

實例 121: ^1H NMR (CDCl_3) δ 8.6 (s, 1H), 8.15 (dt, 1H), 8.1 (s, 1H), 8.0 (d, 2H), 7.5 (d, 2H), 7.4 (dd, 1H), 7.2 (d, 1H), 7.15 (dd, 1H), 6.8 (t, 1H), 6.6 (s, 1H), 4.75 (d, 2H)。

實例 126: ^1H NMR (CDCl_3) δ 8.15 (dt, 1H), 8.0 (s, 1H), 7.5 (d, 1H), 7.42-7.35 (m, 2H), 7.3-7.2 (m, 2H), 7.15 (dd, 1H), 7.1 (dd, 1H), 7.0 (t, 1H), 6.6 (s, 1H), 4.8 (d, 2H)。

實例 127: ^1H NMR (CDCl_3) δ 8.2 (dt, 1H), 8.0 (s, 1H), 7.4 (dd, 1H), 7.3-7.25 (m, 3H), 7.1 (dd, 1H), 6.9-6.85 (m, 2H), 6.7 (t,

1H), 6.6 (s, 1H), 4.6 (d, 2H), 3.2 (m, 4H), 2.6 (m, 4H), 2.3 (s, 3H)

實例 128: ^1H NMR (CDCl_3) δ 8.15 (dt, 1H), 8.1 (s, 1H), 8.0 (d, 2H), 7.5 (d, 2H), 7.4 (m, 2H), 7.25 (d, 1H), 7.2 (s, 1H), 7.15 (dd, 1H), 7.0 (s, 1H), 6.8 (t, 1H), 6.6 (s, 1H), 4.75 (d, 2H)。

實例 129: ^1H NMR (CDCl_3) δ 8.15 (dt, 1H), 8.05 (s, 1H), 8.0 (d, 2H), 7.5 (d, 2H), 7.4 (m, 1H), 7.3 (dd, 1H), 7.15 (dd, 1H), 6.9 (t, 1H), 6.5 (s, 1H), 4.75 (d, 2H), 3.85 (s, 3H)

實例 130: ^1H NMR (CDCl_3) δ 8.2 (dt, 1H), 8.0 (s, 1H), 7.4 (dd, 1H), 7.3 (dd, 1H), 7.15 (dd, 1H), 6.8 (t, 1H), 6.4 (s, 1H), 4.2 (d, 2H), 3.8 (s, 3H)。

實例 131: ^1H NMR (CDCl_3) δ 8.2 (dt, 1H), 8.0 (s, 1H), 7.4-7.15 (m, 3H), 6.7 (t, 1H), 4.2 (q, 2H), 3.8 (dt, 2H), 2.8 (t, 2H), 1.2 (t, 3H)

實例 132: ^1H NMR (CDCl_3) δ 8.2 (dt, 1H), 8.0 (s, 1H), 7.4-7.15 (m, 3H), 6.7 (t, 1H), 4.2 (q, 2H), 3.8 (dt, 2H), 2.8 (t, 2H), 2.05 (m, 2H), 1.2 (t, 3H)

實例 133: ^1H NMR (CDCl_3) δ 8.15 (dt, 1H), 8.0 (s, 1H), 7.4 (m, 1H), 7.3 (dd, 1H), 7.2 (dd, 1H), 6.5 (s, 1H), 6.4 (t, 1H), 3.7 (s, 3H), 3.5 (dd, 2H), 2.4 (t, 2H), 1.8 (m, 4H)

實例 134: ^1H NMR (CDCl_3) δ 8.15 (dt, 1H), 8.0 (s, 1H), 7.95 (d, 2H), 7.6 (d, 2H), 7.4 (m, 1H), 7.25 (dd, 1H), 7.1 (dd, 1H), 6.9 (t, 1H), 6.5 (s, 1H), 4.8 (d, 2H), 3.0 (s, 3H)

實例 135: ^1H NMR ($\text{DMSO } d_6$) δ 9.1 (bs, 2H), 8.4 (s, 1H), 8.0

(t, 1H), 7.85 (d, 2H), 7.7 (d, 2H), 7.6 (m, 1H), 7.4 (m, 2H), 6.6 (s, 1H), 4.8 (bs, 2H)

實例 136: ^1H NMR (CDCl_3) δ 8.2 (dt, 1H), 8.0 (s, 1H), 7.4 (m, 1H), 7.25 (dd, 1H), 7.15 (dd, 1H), 6.9 (m, 3H), 6.7 (t, 1H), 6.5 (s, 1H), 4.5 (d, 2H), 4.2 (s, 4H)

實例 137: ^1H NMR (CDCl_3) δ 8.2 (dt, 1H), 8.0 (s, 1H), 7.4 (m, 1H), 7.3 (dd, 1H), 7.2 (dd, 1H), 6.9 (dd, 1H), 6.8 (t, 1H), 6.7 (m, 1H), 6.6 (s, 1H), 5.3 (s, 2H), 4.85 (s, 2H), 4.6 (d, 2H)。

實例 138: ^1H NMR (CDCl_3) δ 8.2 (dt, 1H), 8.0 (s, 1H), 7.9 (d, 1H), 7.8 (d, 1H), 7.4 (m, 2H), 7.3 (dd, 1H), 7.1 (dd, 1H), 6.9 (t, 1H), 6.6 (s, 1H), 4.8 (d, 2H)

實例 139: ^1H NMR (CDCl_3) δ 8.2 (dt, 1H), 8.0 (s, 1H), 7.4 (m, 1H), 7.3 (m, 2H), 7.2 (dd, 1H), 7.1 (dd, 1H), 6.8 (d, 1H), 6.7 (t, 1H), 6.6 (s, 1H), 4.6 (m, 4H), 3.2 (t, 2H)

實例 140: ^1H NMR (CDCl_3) δ 8.45 (s, 1H), 8.2 (dt, 1H), 8.0 (s, 1H), 7.7 (dd, 1H), 7.4-7.3 (m, 3H), 7.15 (dd, 1H), 6.8 (t, 1H), 6.6 (s, 1H), 4.7 (d, 2H)

實例 141: ^1H NMR (CDCl_3) δ 8.2 (dt, 1H), 8.0 (s, 1H), 7.45-7.1 (m, 7H), 6.6 (s, 1H), 4.4 (dt, 2H), 2.6 (t, 2H), 1.8 (m, 2H), 1.4 (m, 2H)

實例 171: ^1H NMR (CD_3OD) δ 8.41 (s, 1H), 8.25 (d, $J=6.3$ Hz, 1H), 8.15 (s, 1H), 7.67 (d, $J=7.8$ Hz, 2H), 7.55-7.48 (m, 2H), 7.45 (dd, $J=7.5, 1.2$ Hz, 1H), 7.34 (dd, $J=7.5, 1.8$ Hz, 1H), 6.28 (s, 1H), 4.79 (s, 2H)。

實例 172: ^1H NMR (CDCl_3) δ 8.64 (s, 1H), 7.68-7.64 (m, 2H), 7.52 (m, 1H), 7.43 (t, $J=7.8$ Hz, 1H), 6.89 (t, $J=6.0$ Hz, 1H), 6.51 (s, 1H), 6.48 (m, 2H), 4.74 (d, $J=6.0$ Hz, 2H)。

實例 173: ^1H NMR ($\text{DMSO}-d_6$) δ 8.86 (s, 1H), 8.46 (s, 1H), 8.32-8.28 (m, 2H), 7.97 (m, 1H), 7.87 (m, 1H), 7.52 (m, 1H), 7.35-7.24 (m, 2H), 6.57 (s, 1H), 6.46 (m, 1H), 3.65 (m, 4H)。

實例 174: ^1H NMR (CDCl_3) d 8.37 (s, 1H), 8.16 (t, $J=7.5$ Hz, 1H), 7.45-7.35 (m, 1H), 7.32-7.20 (m, 3H), 7.17-7.07 (m, 1H), 6.92 (t, $J=6$ Hz, 1H), 6.48 (s, 1H), 4.65 (d, 2H), 2.50 (s, 3H)。

實例 175: ^1H NMR (CDCl_3)d 8.16 (t, $J=9$ Hz, 1H), 8.00 (s, 1H), 7.49 (d, $J=9$ Hz, 1H), 7.46-7.36 (m, 1H), 7.18-7.08 (m, 1H), 7.00 (d, $J=9$ Hz, 1H), 6.62-6.50 (m, 2H), 2.60 (s, 3H), 2.55 (s, 3H)。

實例 176: ^1H NMR (CDCl_3)d 8.15 (t, $J=9$ Hz, 1H), 8.00 (s, 1H), 7.45-7.35 (m, 1H), 7.32-7.20 (m, 1H), 7.20-7.05 (m, 3H), 6.80 (t, 1H), 6.50 (s, 1H), 4.65 (d, 2H), 2.65 (s, 3H), 2.50 (s, 3H)。

實例 177: ^1H NMR (CDCl_3)d 8.20 (t, 1H), 7.90 (s, 1H), 7.50-7.05 (m, 8H), 6.80 (s, 1H), 5.05-4.90 (m, 2H), 3.80 (d, 1H), 3.45 (d, 1H), 3.00 (dd, 1H), 2.90 (dd, 1H), 2.50 (s, 3H)。

實例 181: ^1H NMR (300 MHz, CDCl_3) δ 8.41 (s, 1H), 8.28-8.23 (d, 1H), 8.15 (s, 1H), 7.69-7.60 (d, 1H), 7.62-7.50 (m, 3H), 7.50-7.47 (dd, 1H), 6.35 (s, 1H), 5.36 (s, 1H), 4.80 (s, 2H)。

實例 184: ^1H NMR (300 MHz, CDCl_3) δ 8.96-8.90 (s, 1H), 8.08 (s, 1H), 8.04 (d, 1H), 7.72 (d, 1H), 7.70-7.61 (dd, 1H), 7.24-

7.20 (dd, 1H), 6.92-6.84 (t, 1H), 6.36 (s, 1H), 4.96-4.89 (d, 2H)。

實例 186: ^1H NMR (300 MHz, CDCl_3) δ 8.96-8.90 (s, 1H), 8.08 (s, 1H), 8.44 (s, 1H), 8.27-8.24 (d, 1H), 8.02 (s, 1H), 7.78-7.76 (d, 1H), 7.73-7.70 (d, 1H), 7.58-7.51 (m, 2H), 7.13-7.08 (dd, 1H), 5.51 (s, 2H)。

實例 195: ^1H NMR (CD_3OD) δ 8.40 (s, 1H), 8.27 (d, 1H), 8.03 (s, 1H), 7.75-7.50 (m, 2H), 6.10 (s, 1H), 4.76 (s, 2H), 4.05 (m, 2H), 3.88 (m, 2H), 3.52 (m, 1H), 2.33 (m, 1H), 2.20 (m, 1H)。

實例 196: ^1H NMR (CD_3OD) δ 8.73 (d, 1H), 8.58 (q, 1H), 8.12 (s, 1H), 8.00 (d, 1H), 7.54 (q, 1H), 6.19 (s, 1H), 4.86 (s, 2H), 4.22-4.08 (m, 2H), 4.03-3.93 (m, 2H), 3.63 (m, 1H), 2.50-2.39 (m, 1H), 2.32-2.21 (m, 1H)。

實例 197: ^1H NMR (CD_3OD) δ 8.73 (d, 1H), 8.58 (q, 1H), 8.12 (s, 1H), 8.00 (d, 1H), 7.54 (q, 1H), 6.19 (s, 1H), 4.86 (s, 2H), 4.22-4.08 (m, 2H), 4.03-3.93 (m, 2H), 3.63 (m, 1H), 2.50-2.39 (m, 1H), 2.32-2.21 (m, 1H)。

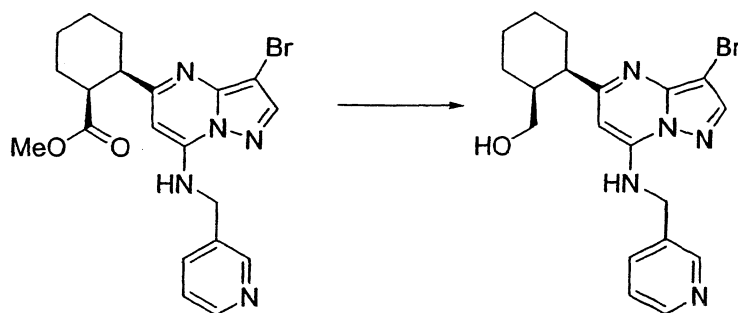
實例 199: ^1H NMR (300 MHz, CDCl_3) δ 8.29 (s, 1H), 8.15 (br s, 1H), 7.95 (s, 1H), 7.28 (d, 1H), 7.05-6.95 (appt t, 1H), 5.70 (s, 1H), 4.62 (d, 2H), 2.90 (m, 1H), 2.30 (m, 1H), 1.9-1.2 (m, 8H), 0.65 (d, 3H)。

實例 200: ^1H NMR (300 MHz, CDCl_3) δ 8.71 (s, 2H), 8.00 (s, 1H), 6.13 (s, 1H), 3.59 (s, 2H), 3.01-2.58 (m, 1H), 2.51-2.45 (m, 1H), 2.44-2.30 (m, 1H), 2.20 (s, 3H), 2.09-1.95 (m, 2H),

1.85-1.70 (m, 2H), 0.80-0.76 (d, 3H)。

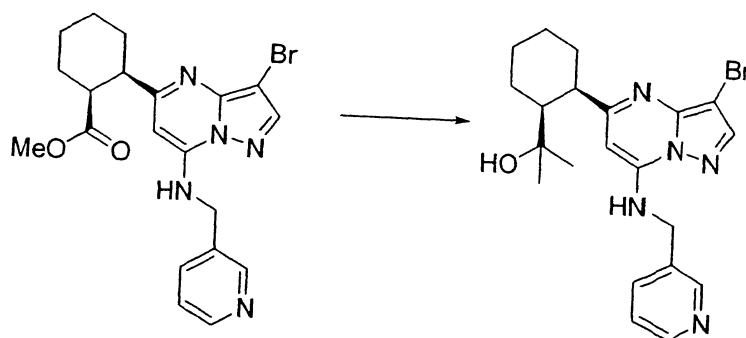
實例 203: ^1H NMR (300 MHz, CDCl_3) δ 8.10 (s, 1H), 8.08 (s, 1H), 6.27 (s, 2H), 4.95 (s, 2H), 3.00-2.90 (dd, 2H), 2.60 (m, 2H), 2.48 (br s, 1H), 2.39 (s, 3h), 2.25 (m, 1H), 1.95-1.70 (m, 3H)。

實例 211:



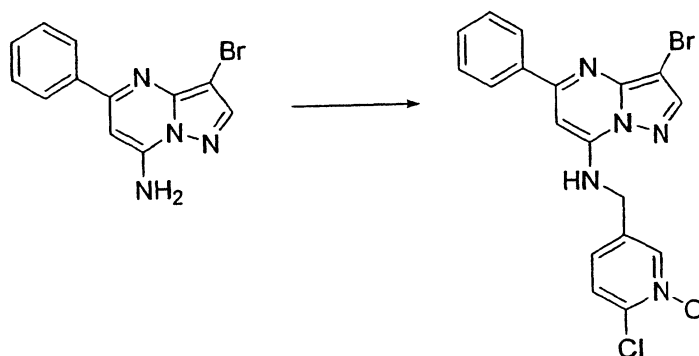
於實例 156 製備之化合物 (100 毫克，0.23 毫莫耳) 之無水 THF (4 毫升) 溶液中，在 0°C 及 N_2 下添加 LiAlH_4 (1.0 M 於 THF，0.110 毫升，0.110 毫莫耳)。混合物在 0°C 攪拌 1 小時，溫至 25°C ，接著添加額外之 LiAlH_4 (1.0 M 於 THF，0.400 毫升)，混合物攪拌 20 分鐘接著以 MeOH (2.0 毫升) 驟冷。蒸發溶劑且粗產物藉快速層析使用 10:1 CH_2Cl_2 :MeOH 作為溶離液純化。獲得白色固體 (46 毫克，49%)。LCMS: $\text{M}^+ = 416$ 。Mp = $71-72^\circ\text{C}$ 。

實例 212:



於實例 156 製備之化合物 (70 毫克, 0.16 毫莫耳) 之無水 THF (3 毫升) 溶液中在 N_2 下添加 MeMgBr (3.0 M 於 Et_2O , 1.10 毫升, 3.20 毫莫耳)。混合物在 $25^\circ C$ 攪拌 45 分鐘接著以飽和 NH_4Cl 水溶液 (5.0 毫升) 驟冷。混合物倒入飽和 NH_4Cl 水溶液 (30 毫升) 中並以 CH_2Cl_2 (3x20 毫升) 萃取。萃取液以 Na_2SO_4 脫水並過濾。蒸發溶劑且粗產物藉快速層析使用 20:1 CH_2Cl_2 :MeOH 作為溶離液純化。獲得白色固體 (25 毫克, 36%)。LCMS: $M^+ = 444$ 。Mp = $76-80^\circ C$ 。

實例 213：



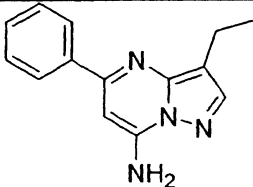
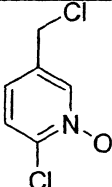
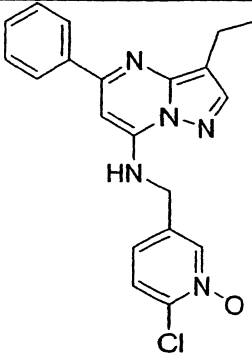
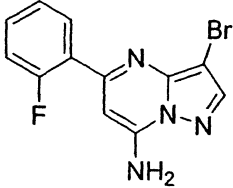
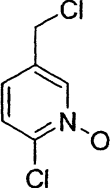
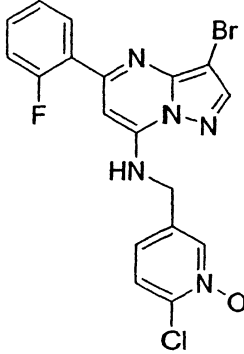
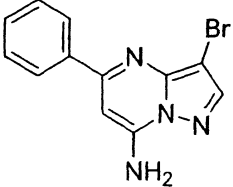
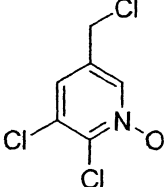
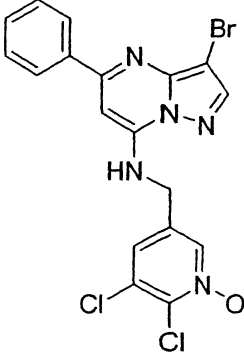
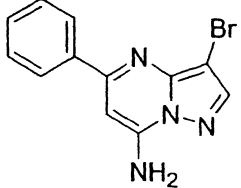
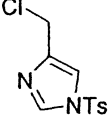
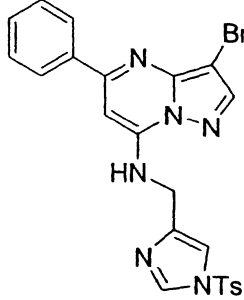
無水 DMF (40 毫升) 在 N_2 下添加至製備例 174 製備之化合物 (2.50 克, 8.65 毫莫耳) 及 60% NaH 之礦油 (346 毫克, 8.65 毫莫耳) 中。混合物在 $25^\circ C$ 攪拌 1 小時, 接著緩慢添加 2-氯-5-氯甲基吡啶 N-氧化物 (1.54 克, 8.65 毫莫耳) 之無水 DMF (20 毫升)。混合物在 $25^\circ C$ 攪拌 18 小時, 蒸發溶劑且粗產物藉快速層析使用 30:1 CH_2Cl_2 : MeOH 作為溶離液純化。所得固體藉 50 毫升 1:1 EtOAc: 己烷分散。獲得淡黃色固體 (1.25 克, 34%)。LCMS: $MH^+ = 432$ 。Mp = $224-226^\circ C$ 。

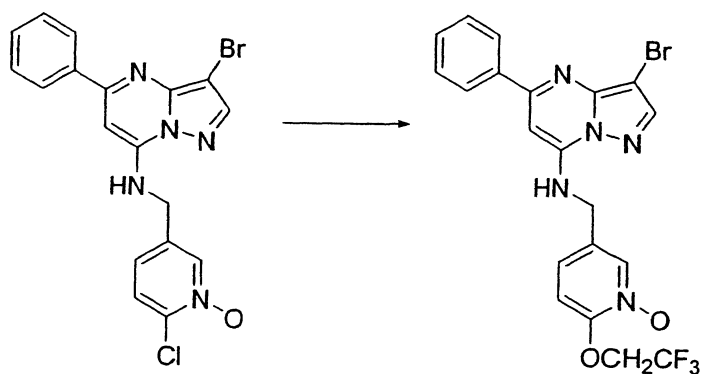
實例 214-217：

基本上依循實例 213 所述之相同程序, 組合表 19 欄 2 所示

之化合物及表19欄3所示之化合物，製備表19欄4所示之化合物。

表 19

實例	欄2	欄3	欄4	數據
214				LCMS: MH ⁺ =380; mp=°C
215				LCMS: MH ⁺ =450; mp=218-222°C
216				LCMS: MH ⁺ =466; mp=126-128°C
217				LCMS: M ⁺ =523

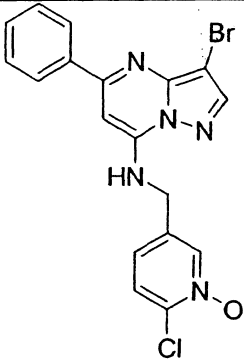
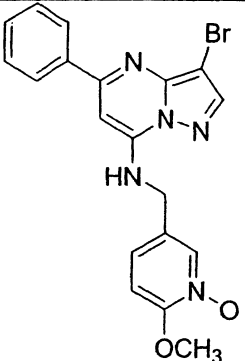
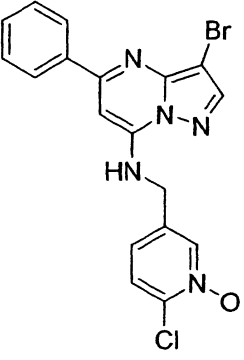
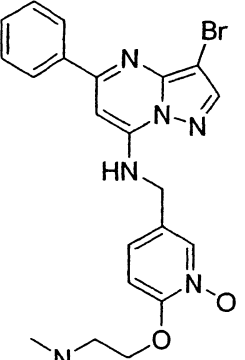
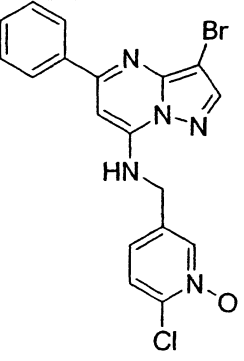
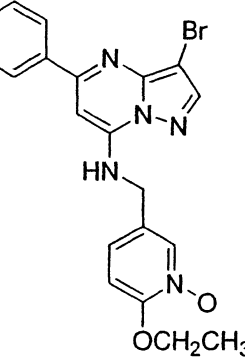
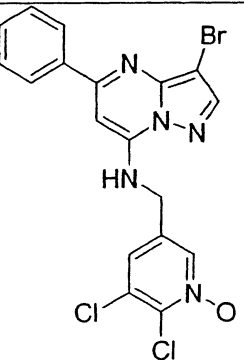
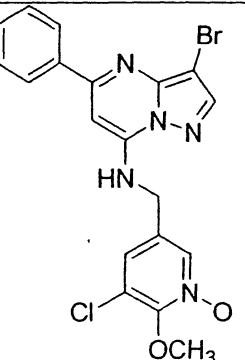
實例 218：

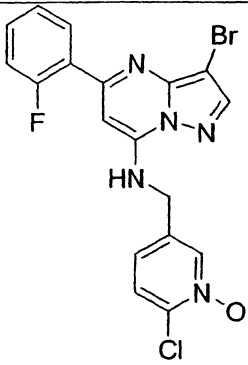
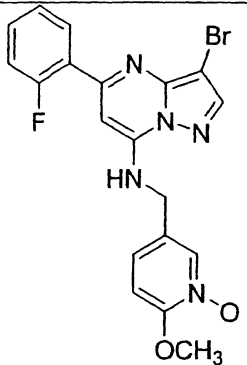
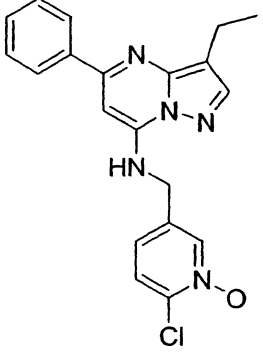
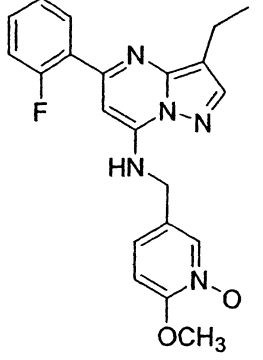
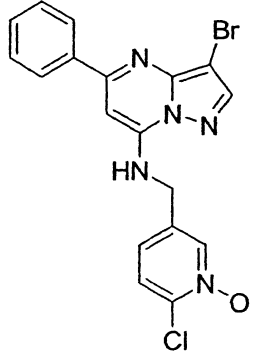
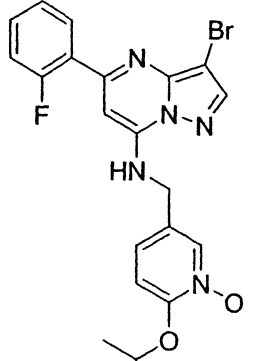
CF₃CH₂OH(3.0 毫升)在 N₂ 下添加至 60% NaH 之礦油 (40 毫克，1.0 毫莫耳) 中，混合物攪拌 20 分鐘接著添加實例 213 製備之產物 (50 毫克，0.12 毫莫耳)。混合物回流 20 小時，蒸發溶劑，且殘留物藉快速層析使用 20:1 CH₂Cl₂:MeOH 作為溶離液純化，獲得淡黃色固體 (35 毫克，61%)。LCMS: M₂H⁺ = 496。Mp = 208-210°C。

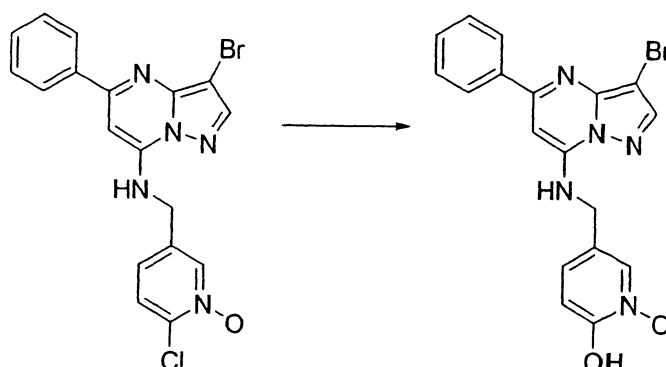
實例 219-225：

基本上依循實例 218 所述之相同程序，組合表 20 欄 1 所示之化合物及適當醇，製備表 20 欄 2 所示之化合物。

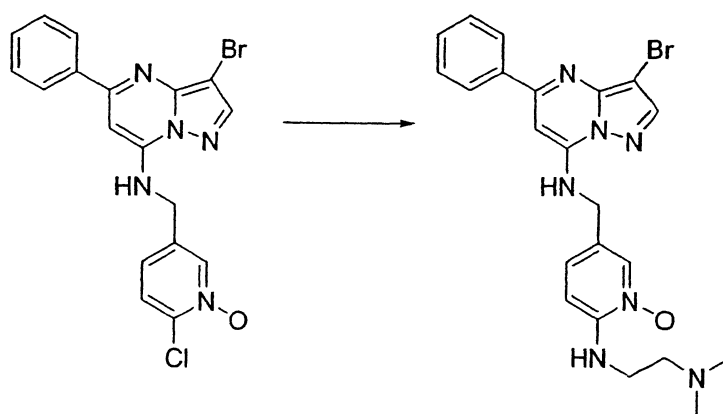
表 20

實例	欄1	欄2	數據
219			LCMS: M ⁺ =426; mp=126-128°C
220			LCMS: M ⁺ =483; mp=89-91°C
221			LCMS: M2H ⁺ =442 ; mp=112-114°C
222			LCMS: MH ⁺ =462; mp=121-123°C

223			LCMS: MH ⁺ =444; mp=112-114°C
224			LCMS: M ⁺ =376; mp=°C
225			LCMS: MH ⁺ =; mp=°C

實例 226：

實例 213 所製備之產物(100 毫克，0.23 毫莫耳)及 KOH(95 毫克，1.70 毫莫耳)之 1,2-二甲氧基乙烷(3 毫升)及 H₂O(1.5 毫升)之混合物在 N₂ 下回流 20 小時，以乙酸(0.30 毫升)驟冷，且蒸發溶劑。殘留物懸浮於 H₂O(15 毫升)中，過濾且固體以 H₂O(15 毫升)及 Et₂O(10 毫升)洗滌。接著與 CH₂Cl₂(2 毫升)及 Et₂O(2 毫升)混合並過濾。Et₂O (5 毫升)添加至濾液中且混合物靜置隔夜。固體藉過濾移除，以 Et₂O 洗滌接著溶於 MeOH(5 毫升)。溶液予以過濾且自濾液蒸發溶劑。獲得灰白色固體(5 毫克，5%)。LCMS:M⁺=412。Mp=206-208℃。

實例 227：

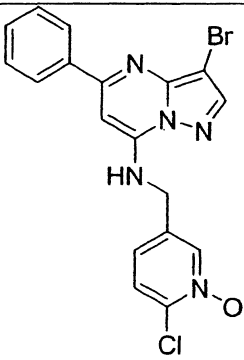
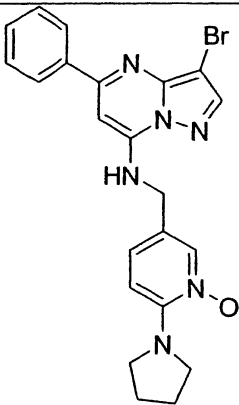
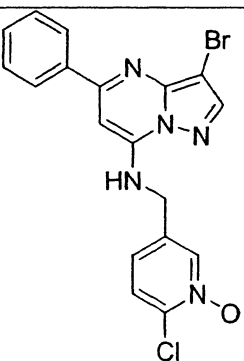
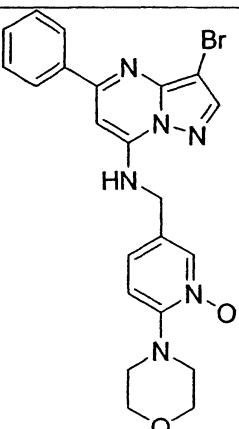
實例 213 製備之產物(129 毫克，0.30 毫莫耳)、N,N-二甲基

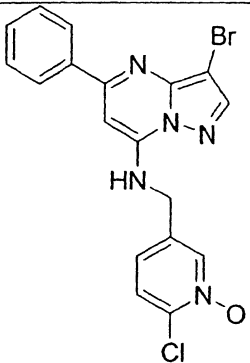
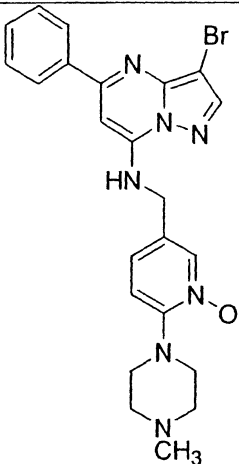
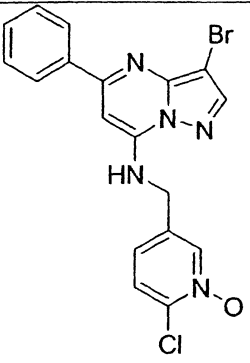
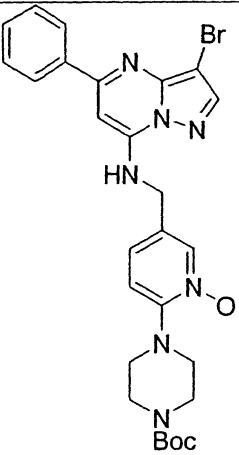
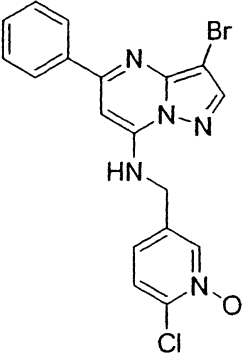
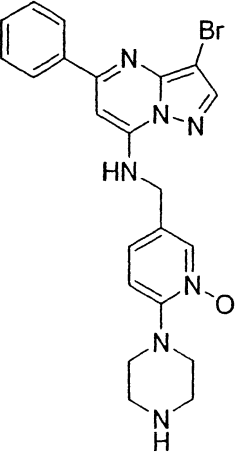
伸乙二胺(0.165毫升, 1.50毫莫耳)及二異丙基乙基胺(0.10毫升)之無水N-甲基吡咯啉酮(1.0毫升)之混合物在100°C攪拌24小時。蒸發溶劑且殘留物藉快速層析使用20:1 CH₂Cl₂: 7 N NH₃之MeOH作為溶離液純化, 獲得淡黃色固體(110毫克, 76%)。LCMS:M⁺=482。Mp=76-78°C。

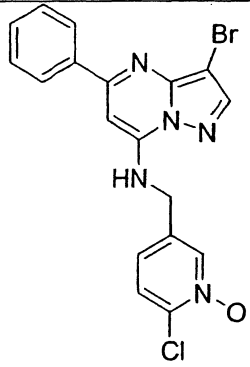
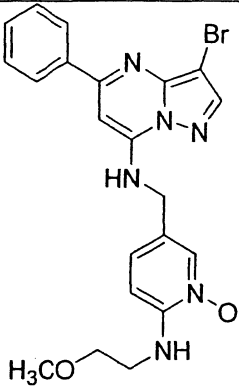
實例 228-233：

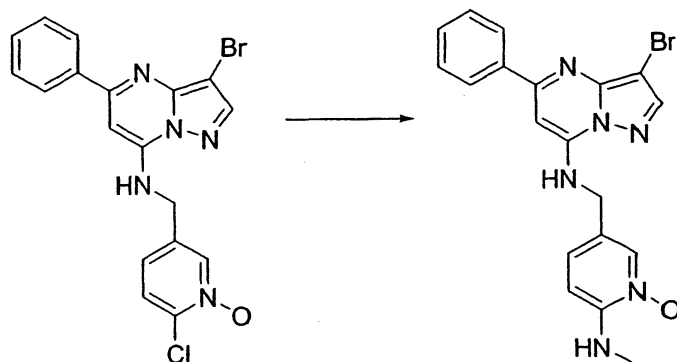
基本上依循實例227所述之相同程序, 組合表21欄1所示之化合物及適當胺, 製備表21欄2所示之化合物。

表 21

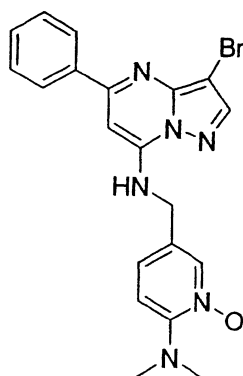
實例	欄1	欄2	數據
228			LCMS: M ₂ H ⁺ =467 ; mp126-128°C
229			LCMS: M ⁺ =481; mp=128-130°C

230			LCMS: $M^+=494$; mp=108-110°C
231			LCMS: $M2H^+=482$; mp=129-133°C
232			LCMS: $M2H^+=482$; mp=124-126°C

233			LCMS: $M2H^+ = 471$; mp=88-90°C
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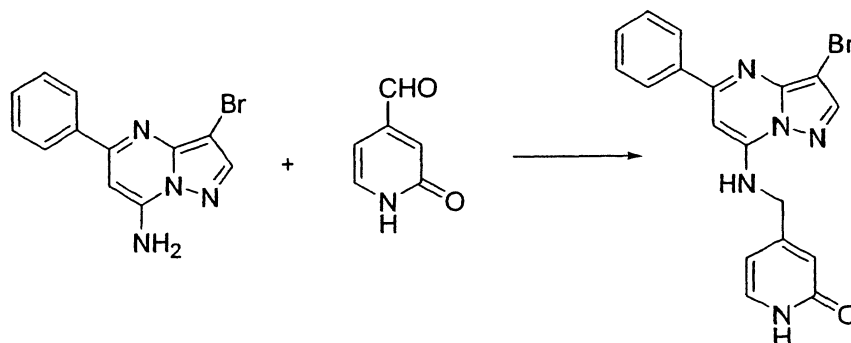
實例 234：

實例 213 製備之產物 (80 毫克, 0.19 毫莫耳) 及 2.0 M 甲基胺之 THF 之混合物在密閉壓力容器中在 50°C 攪拌 72 小時。蒸發溶劑且殘留物藉快速層析使用 10:1 CH_2Cl_2 :MeOH 作為溶離液純化, 獲得淡黃色固體 (40 毫克, 51%)。LCMS: $M2H^+ = 427$ 。Mp=217-219°C。

實例 235：

基本上如實例 234 所述相同程序，製備上述所示之化合物。LCMS: $M2H^+ = 441$ 。Mp = 98-101°C。

實例 236：

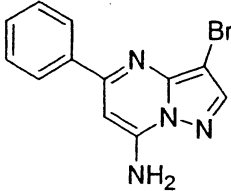
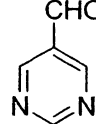
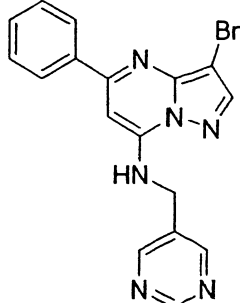
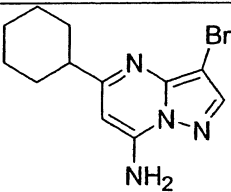
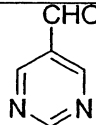
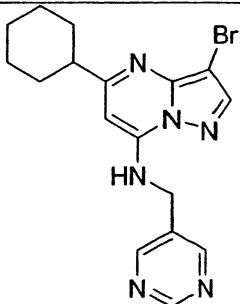
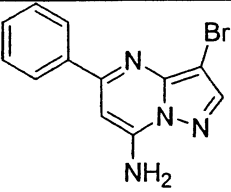
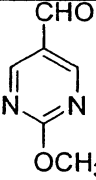
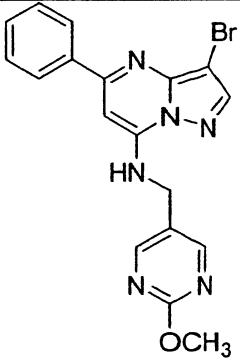
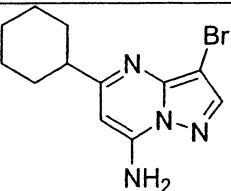
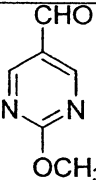
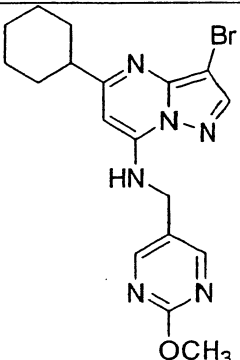


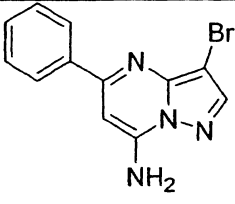
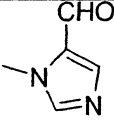
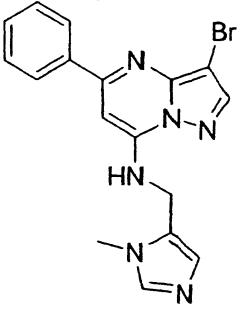
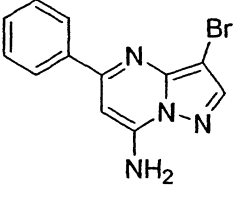
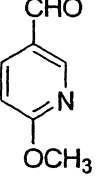
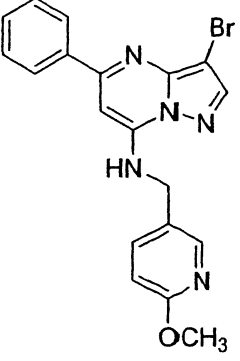
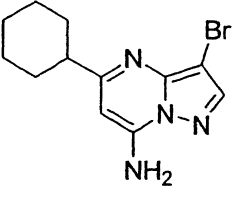
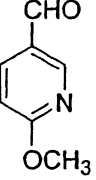
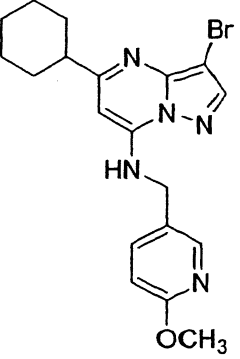
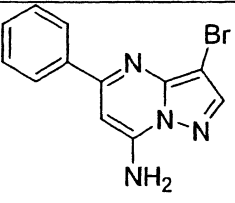
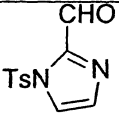
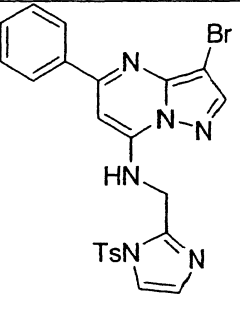
製備例 174 製備之化合物 (140 毫克，0.48 毫莫耳) 及醛 (71 毫克，0.58 毫莫耳) 在無水 THF (4 毫升) 中在 50°C 及 N_2 下攪拌。添加 $Ti(OiPr)_4$ (0.574 毫升，1.92 毫莫耳)，混合物在 50°C 攪拌 3 小時並冷卻至 25°C。添加 $NaBH_3CN$ (181 毫克，2.88 毫莫耳)，混合物又攪拌 2 小時接著倒入 10% Na_2CO_3 水溶液 (100 毫升) 並以 CH_2Cl_2 (3x50 毫升) 萃取。合併之萃取液以 Na_2SO_4 脫水，過濾且蒸發溶劑。殘留物藉快速層析使用 15:1 CH_2Cl_2 :MeOH 作為溶離液純化，獲得淡黃色固體 (40 毫克，21%)。LCMS: $MH^+ = 398$ 。Mp > 230°C。

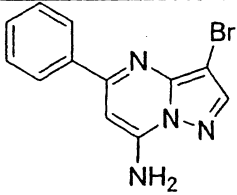
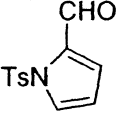
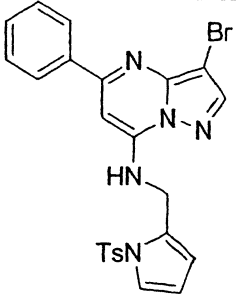
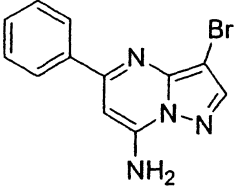
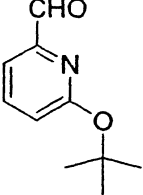
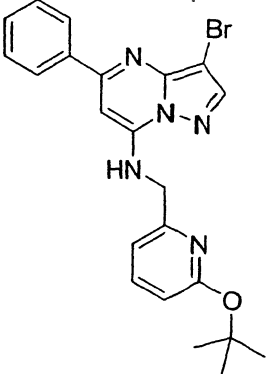
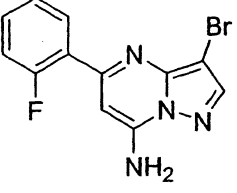
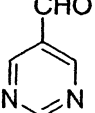
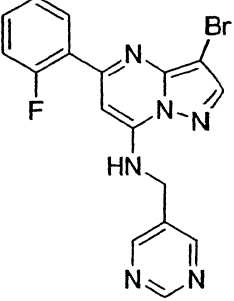
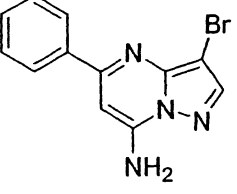
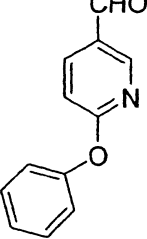
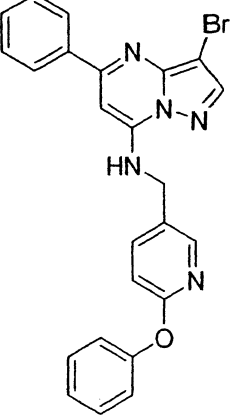
實例 237-256：

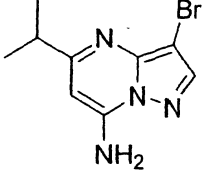
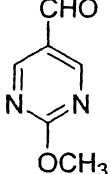
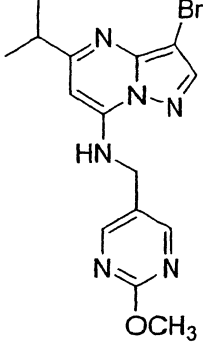
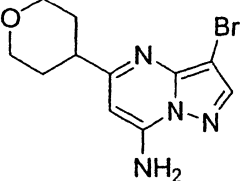
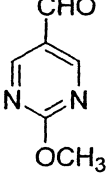
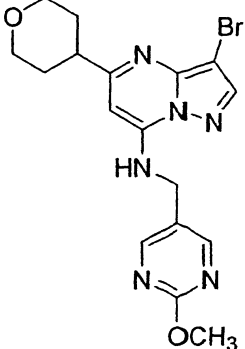
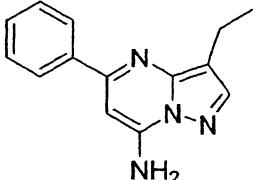
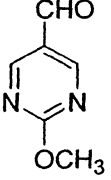
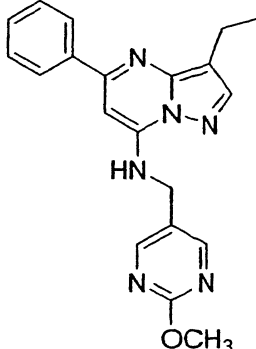
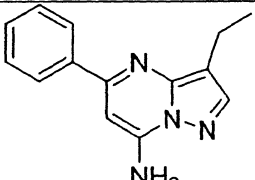
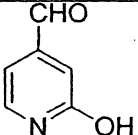
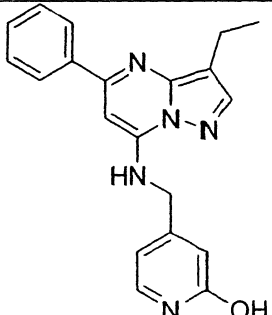
基本上如實例 236 所述相同程序組合表 22 欄 2 及 3 所示之化合物，製備表 22 欄 4 所示之化合物。

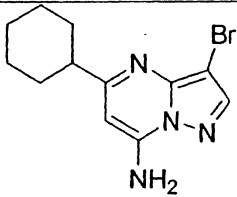
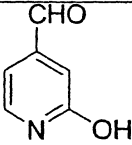
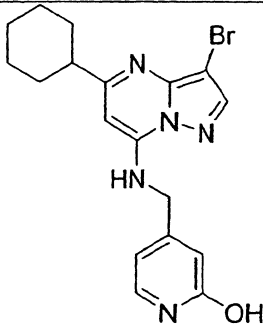
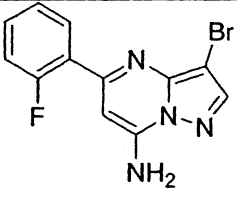
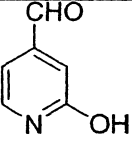
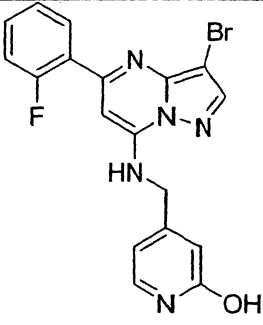
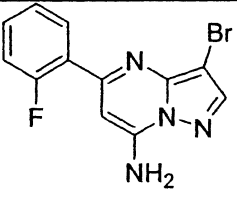
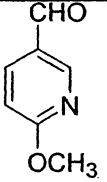
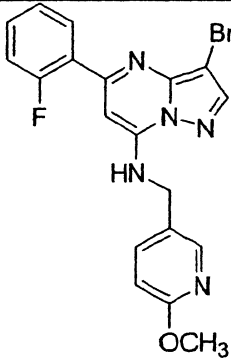
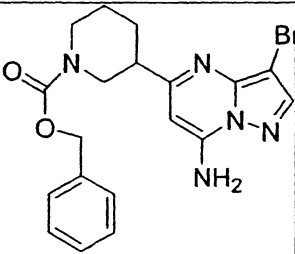
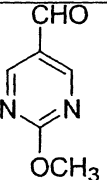
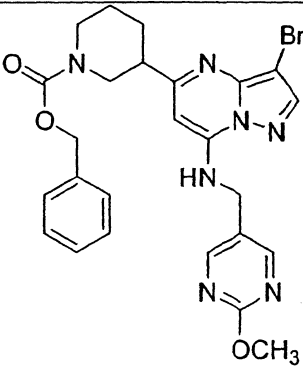
表 22

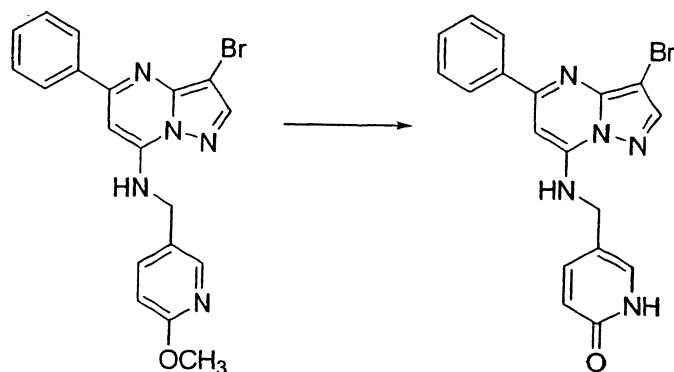
實例	欄2	欄3	欄4	數據
237				LCMS: M ⁺ =381; mp>200°C
238				LCMS: M ⁺ =387; mp=°C
239				LCMS: MH ⁺ =413; mp=157-159°C
240				LCMS: M2H ⁺ =419 ; mp=77-79°C

241				LCMS: $M2H^+ = 385$; mp=214-216°C
242				LCMS: $MH^+ =$; mp=°C
243				LCMS: $M^+ = 416$; mp=80-82°C
244				

245				
246				LCMS: M ⁺ =452; mp=54-56°C
247				LCMS: MH ⁺ = 401; mp>200°C
248				LCMS: M2H ⁺ = 474; mp>200.0. °C dec.

249				LCMS: MH ⁺ = 377; mp= 65-67°C
250				LCMS: M2H ⁺ =421; mp=87-93°C
251				LCMS: MH ⁺ =361; mp>225°C
252				LCMS: MH ⁺ =346; mp=270-271°C

253				LCMS: MH ⁺ =402; mp=250-255°C
254				LCMS: MH ⁺ =416; mp=210-215°C
255				LCMS: MH ⁺ =428; mp=145°C
256				LCMS: MH ⁺ =; mp=°C

實例 257：

實例 242 製備之化合物 (100 毫克，0.24 毫莫耳)、濃 HCl 水溶液 (1.0 毫升) 及乙酸 (2.0 毫升) 之混合物在 100°C 及 N₂ 下攪拌 2 小時，接著倒入 Na₂CO₃ (15 克) 上並以 1:1 丙酮:CH₂Cl₂ (3x30 毫升) 萃取。合併之萃取液經過濾且蒸發溶劑。殘留物藉快速層析使用 10:1 CH₂Cl₂:MeOH 作為溶離液純化，獲得淡黃色固體 (36 毫克，37%)。LCMS: M₂H⁺=398。

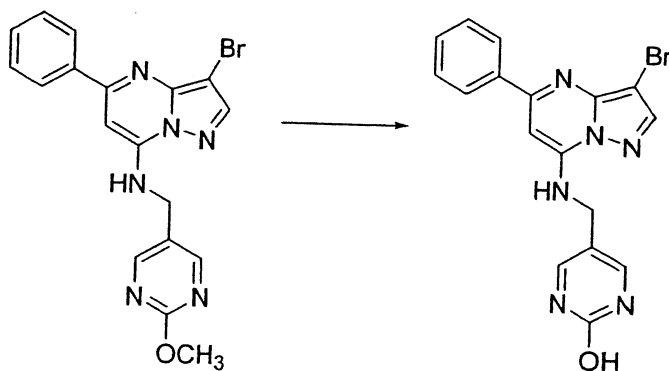
實例 258-260：

基本上如實例 257 所述相同程序自表 23 欄 1 之化合物起始，製備表 23 欄 2 所示之化合物。

表 23

實例	欄1	欄2	數據
258			LCMS: M ⁺ =402; mp=229- 231°C

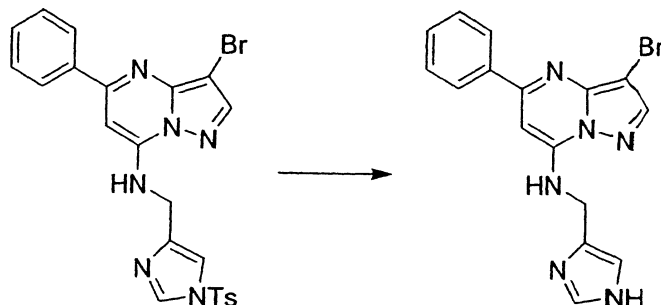
259			LCMS: MH ⁺ =416; mp=215-218°C
260			LCMS: M2H ⁺ =398 ; mp>230°C

實例 261：

於實例 239 製備之化合物 (41 毫克，0.10 毫莫耳) 之 CH_2Cl_2 攪拌溶液中，在 -78°C 添加 1.0 M BBr_3 (0.30 毫升，0.30 毫莫耳) 之 CH_2Cl_2 。混合物在 -78°C 攪拌 5 分鐘接著在 24°C 攪拌 3 小時，接著添加 MeOH (2.0 毫升) 且混合物攪拌 10 分鐘。蒸發溶劑且殘留物藉快速層析使用 5:1:0.1 CH_2Cl_2 : MeOH :濃 NH_4OH 作為溶離液純化，獲得白色固體 (39 毫克，99%)。

LCMS: $M^+ = 397$ 。Mp $> 230^\circ\text{C}$ 。

實例 262：



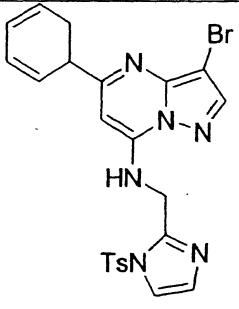
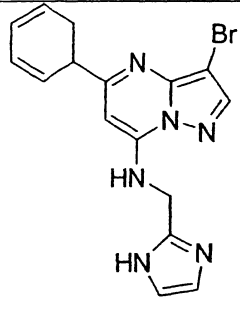
實例 217 製備之產物 (40 毫克，0.077 毫莫耳) 及 5.0 M NaOH 水溶液 (0.8 毫升) 之 MeOH (3.0 毫升) 中之混合物在 N_2 回流 1 小時。添加 NaHCO_3 (700 毫克)，蒸發溶劑且殘留物藉快速層析使用 10:1:0.1 CH_2Cl_2 :MeOH:濃 NH_4OH 作為溶離液純化，獲得白色固體 (10 毫克，35%)。LCMS: $M2H^+ = 371$ 。Mp = $237-239^\circ\text{C}$ 。

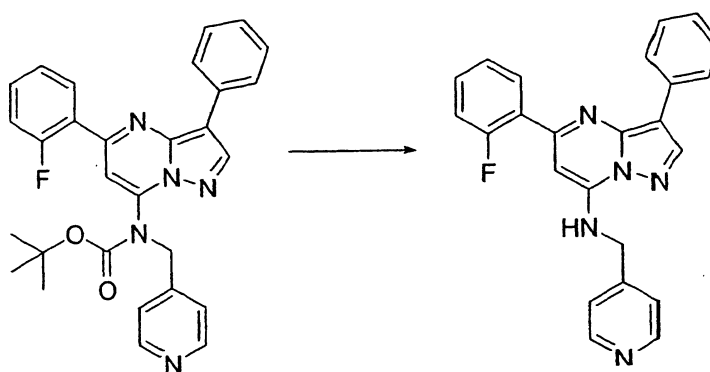
實例 263-264：

基本上如實例 262 所述相同程序自表 24 欄 1 之化合物起始，製備表 24 欄 2 所示之化合物。

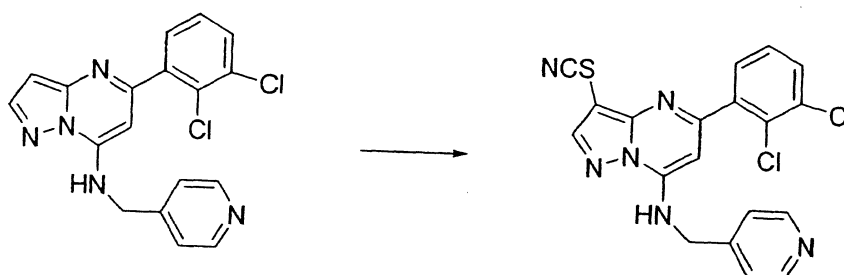
表 24

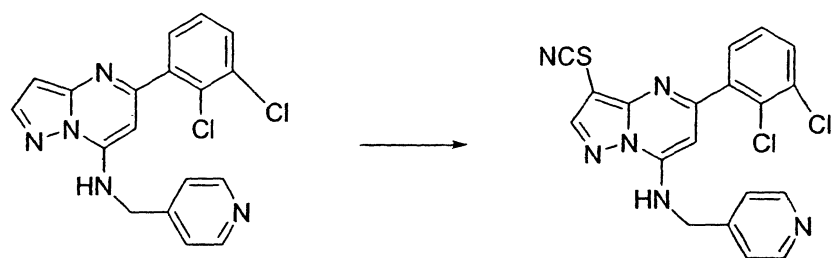
實例	欄1	欄2	數據
263			LCMS: $M2H^+ = 370$; mp = $166-168^\circ\text{C}$

264			LCMS: M2H ⁺ =371 ; mp=180-182°C
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實例 265：

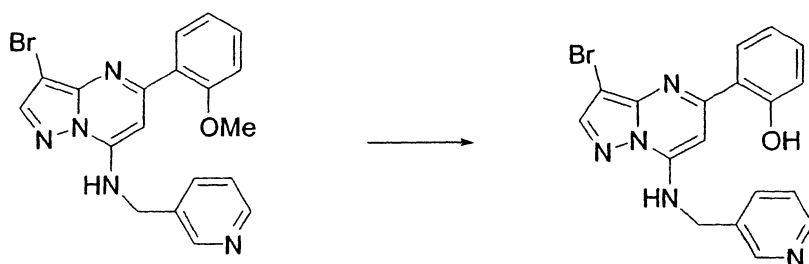
TFA(0.5 毫升)在 0°C 添加至製備例 197 所製備之化合物 (0.08 克, 0.16 毫莫耳)之 CH₂Cl₂(2.0 毫升)溶液中且所得溶液攪拌 2.5 小時並在 4°C 儲存隔夜, 該時又添加 TFA(0.5 毫升)。所得溶液攪拌 4 小時並真空濃縮。殘留物以 1 N NaOH 中和並以 CH₂Cl₂ 萃取。合併之有機物以 Na₂SO₄ 脫水, 過濾並減壓濃縮。粗產物藉快速層析使用 2.5%(10% NH₄OH 之 MeOH)之 CH₂Cl₂ 溶液作為溶離液純化 (0.009 克, 15% 產率)。LCMS: MH⁺=396, mp=53-54°C。

實例 266：



製備例182製備之化合物(26毫克, 0.070毫莫耳)及硫代氰酸鉀(13毫克, 0.14毫莫耳)之MeOH(1毫升)溶液於冷水浴中冷卻。於其中滴加溴(22毫克, 0.14毫莫耳)之MeOH(0.7毫升)溶液。所得反應混合物在室溫攪拌4小時且減壓移除揮發物。殘留物懸浮於小量之CH₂Cl₂中。濾除溴化鉀且濾液之pH藉添加氨水調整pH至約7。減壓濃縮且殘留油藉製備性薄層層析使用15% MeOH之CH₂Cl₂作為溶離液純化(26毫克, 87%產率)。¹H NMR (CDCl₃) δ 8.75 (d, J=4.2 Hz, 2H), 8.38 (s, 1H), 7.68-7.64 (m, 2H), 7.46-7.39 (m, 3H), 7.22 (t, J=6.3 Hz, 1H), 6.43 (s, 1H), 4.84 (d, J=6.3 Hz, 2H); LCMS: MH⁺=427。

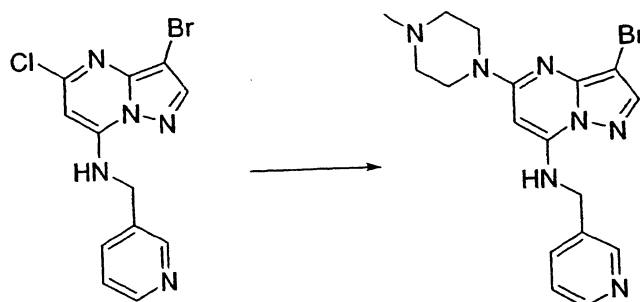
實例267：



三溴化硼(1 M於CH₂Cl₂, 0.60毫升, 0.60毫莫耳)在氫氣中滴加至實例24製備之化合物(50毫克, 0.12毫莫耳)之CH₂Cl₂(1.5毫升)冰冷卻攪拌溶液中。所得反應混合物在0°C攪拌30分鐘, 溫至室溫並攪拌隔夜。混合物藉添加小量水驟冷並

以 CH_2Cl_2 萃取。有機層以硫酸鎂脫水並真空濃縮(45毫克，94%產率)。 ^1H NMR (CD_3OD) δ 9.16 (s, 1H), 8.95 (s, 1H), 8.88 (d, $J=8.1$ Hz, 1H), 8.24 (t, $J=6.9$ Hz, 1H), 8.18 (s, 1H), 7.95 (d, $J=7.8$ Hz, 1H), 7.40 (t, $J=7.8$ Hz, 1H), 7.00-6.96 (m, 2H), 6.86 (s, 1H), 5.28 (s, 2H); LCMS: $\text{MH}^+=396$ 。

實例 268：

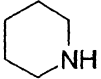
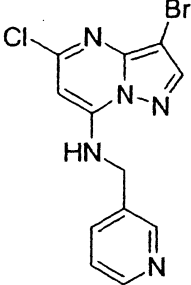
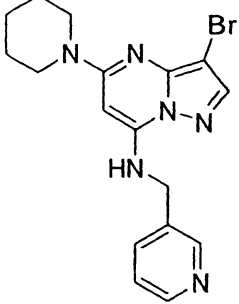
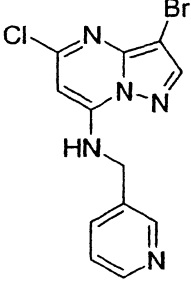
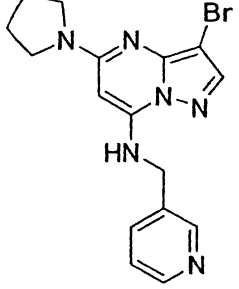
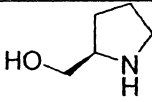
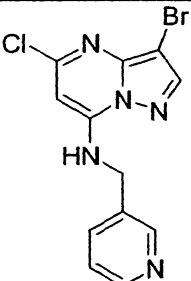
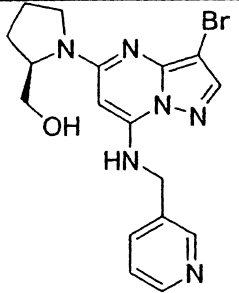
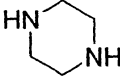
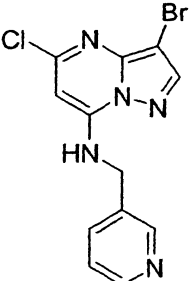
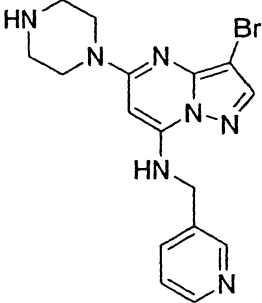


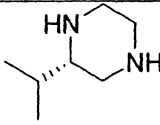
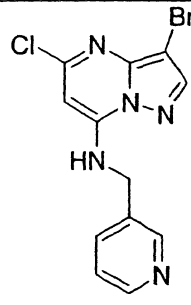
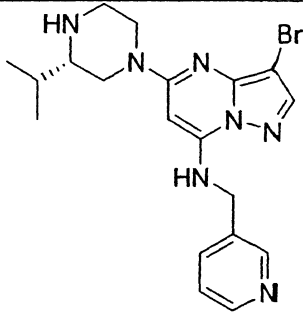
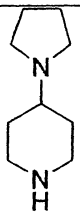
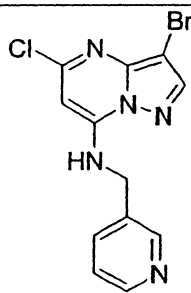
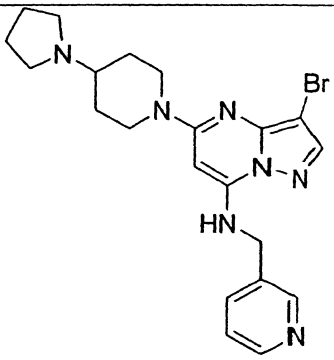
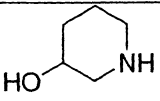
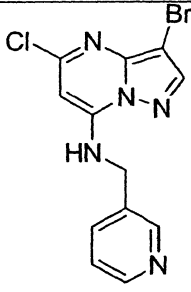
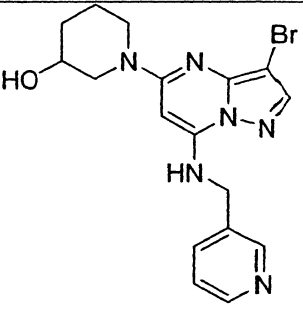
製備例 184 製備之化合物(0.05克，0.15毫莫耳)、N-甲基哌啶(20微升，1.2當量)及 iPr_2Et (52微升，2.0當量)之二噁烷(1毫升)溶液加熱至 70°C 隔夜。反應混合物冷卻至室溫並以 H_2O 及飽和 NaHCO_3 稀釋。所得混合物以 CH_2Cl_2 萃取且合併之有機層以 Na_2SO_4 脫水，過濾並減壓濃縮。粗產物藉製備性 TLC 使用 5%(10% NH_4OH 之 MeOH) 之 CH_2Cl_2 溶液作為溶離液純化(0.028克，47%產率)。MS: $\text{MH}^+=402$ 。mp= 210°C (分解)。

實例 269-275：

基本上如實例 268 所述相同程序僅替代表 25 欄 2 之胺及表 25 欄 3 之氯化物，製備表 25 欄 4 所示之化合物。

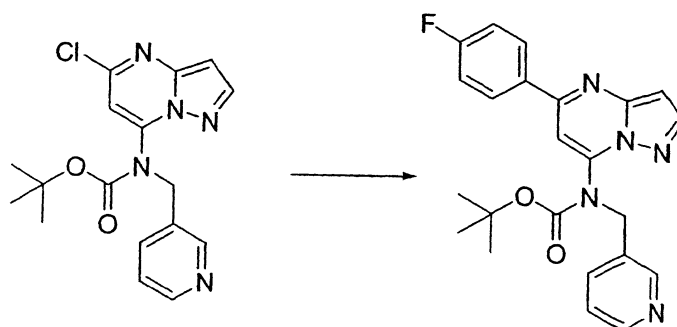
表 25

實例	欄2	欄3	欄4	數據
269				MS: $MH^+ = 387$ m.p. 182 – 183 °C
270				MS: $MH^+ = 373$ m.p. 190 – 191 °C
271				MS: $MH^+ = 403$ m.p. 227 – 230 °C
272				MS: $MH^+ = 388$ m.p. 198 – 201 °C

273				MS: $MH^+ = 430$ m.p. 100-103 °C
274				MS: $MH^+ = 456$ m.p. 175 – 178 °C
275				MS: $MH^+ = 403$ m.p. 218 °C

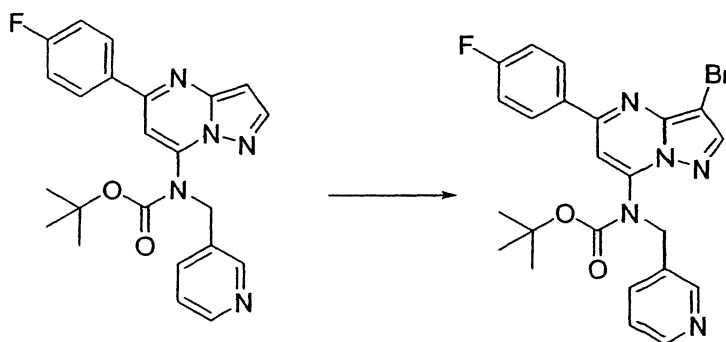
實例 276：

步驟 A：



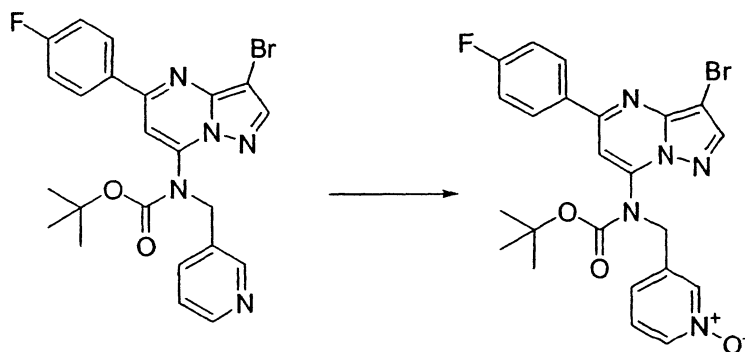
溴化4-氟苯基鎂(0.68毫升, 1.2當量)添加至製備例193製備之化合物(0.20克, 0.55毫莫耳)及PdCl₂(dppf)₂(0.037克, 10毫莫耳%)之THF中且所得溶液在室溫攪拌72小時。反應混合物以飽和NH₄Cl稀釋並以EtOAc萃取。合併之有機層以飽和NaCl洗滌, 以Na₂SO₄脫水, 過濾並濃縮。粗產物藉快速層析使用純EtOAc作為溶離液純化(0.15克, 65%產率)。MS: MH⁺=420。

步驟B:

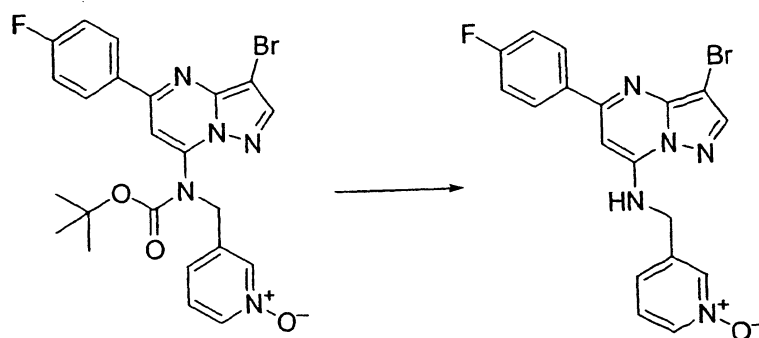


基本上如製備例127所述相同程序, 僅替代製備例276步驟A製備之化合物, 製備上述化合物(0.17克, 94%產率)。

步驟C:

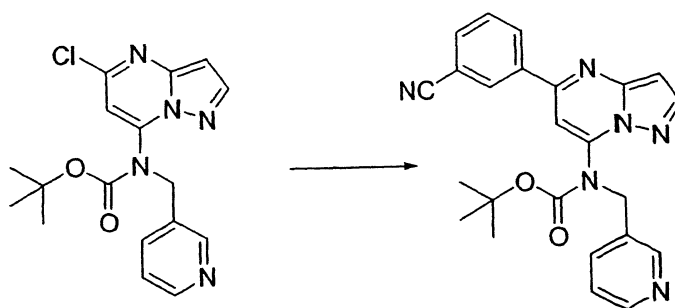


基本上如製備例200所述相同程序, 僅替代製備例276步驟B製備之化合物, 製備上述化合物(0.1克, 100%產率)。

步驟 D：

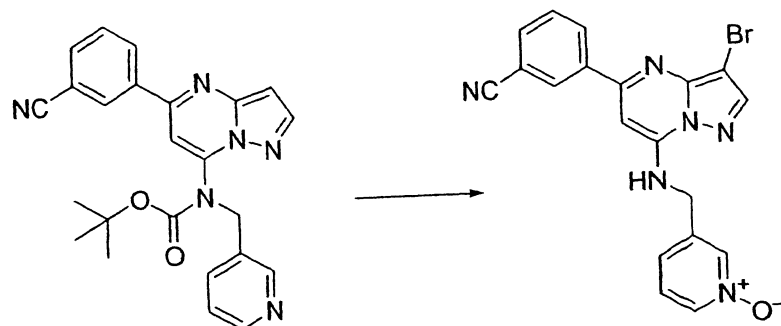
基本上如製備例265所述相同程序，僅替代製備例276步驟C製備之化合物，製備上述化合物(0.049克，62%產率)。

MS: $MH^+ = 414$; mp=110-115°C。

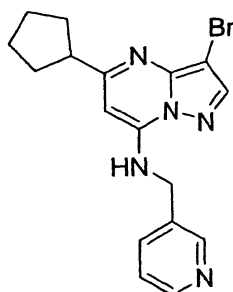
實例 277：步驟 A：

$Pd(PPh_3)_4$ (0.065克，10莫耳%)添加至碘化3-氰基苯基鋅(2.2毫升，0.5 M於THF，2當量)及製備例193製備之化合物(0.2克，0.56毫莫耳)之DMF(2.0毫升)中且所得溶液加熱至80°C歷時144小時。反應混合物冷卻至室溫，以飽和 NH_4Cl 稀釋並以EtOAc萃取。合併之有機層以 H_2O 及食鹽水洗滌，以 Na_2SO_4 脫水，過濾並減壓濃縮。粗產物藉快速層析使用純EtOAc溶液作為溶離液純化(0.07克，29%產率)。MS: $MH^+ =$

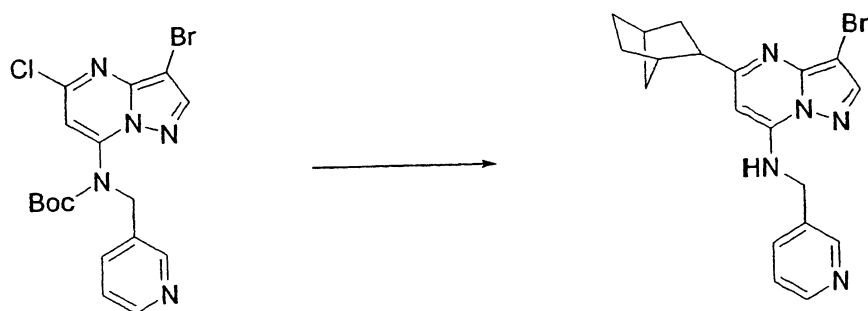
427。

步驟B至步驟D：

基本上如實例276步驟B至步驟D所述之相同程序，製備上述化合物(0.023克，53%產率)。MS:MH⁺=421；mp=230°C (分解)。

實例278：

基本上如實例276所述相同程序，僅步驟A中替代適當溴化環丙基鎂，製備該化合物。MS:MH⁺=372；mp=96-98°C。

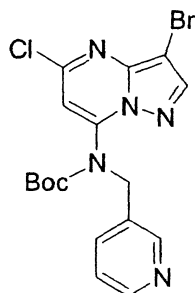
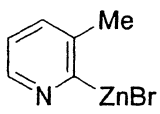
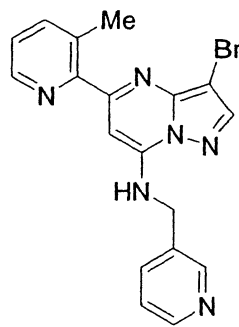
實例279：

以類似有機化學期刊(1999), 453所述程序進行鈀-催化之鋅交互偶合反應。氯吡啶并嘓啶(200毫克, 0.458毫莫耳)、 $\text{Pd}(\text{PPh}_3)_4$ (53毫克, 0.046毫莫耳)及溴化挂-2-原冰片基鋅(0.5 M於THF, 0.95毫升, 0.47毫莫耳)之DMF(2毫升)溶液在 100°C (油浴溫度)回流隔夜。反應混合物藉半飽和之 NH_4Cl 驟冷並以 CH_2Cl_2 萃取。有機相以 MgSO_4 脫水並減壓濃縮。殘留物藉快速層析使用50% EtOAc之己烷作為溶離液純化。所得之N-Boc-保護之產物(121毫克, 53%產率, LCMS: $\text{MH}^+=498$)及TFA(1毫升)之 CH_2Cl_2 (2毫升)溶液在室溫攪拌2小時。減壓移除揮發物。殘留物溶於 CH_2Cl_2 , 以飽和 NaHCO_3 中和並以 CH_2Cl_2 萃取。有機相以 MgSO_4 脫水且真空濃縮(96毫克, 99%產率)。LCMS: $\text{MH}^+=398$; ^1H NMR (CDCl_3) δ 8.78 (s, 1H), 8.71 (d, $J=4.2$ Hz, 1H), 8.04 (d, $J=3.9$ Hz, 1H), 7.80 (d, $J=7.8$ Hz, 1H), 7.44 (m, 1H), 6.73 (m, 1H), 5.98 (d, $J=7.5$ Hz, 1H), 4.74 (d, $J=5.4$ Hz, 2H), 3.40-1.00 (m, 11H)。

實例 280-294：

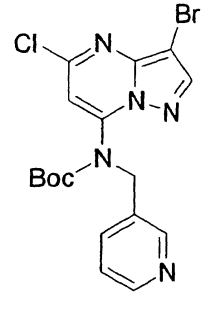
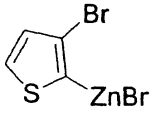
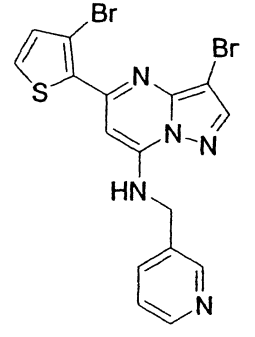
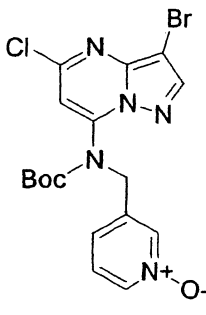
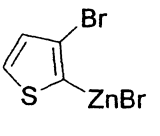
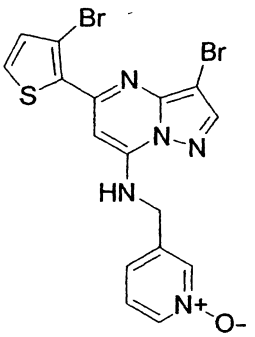
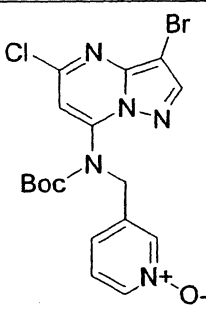
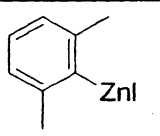
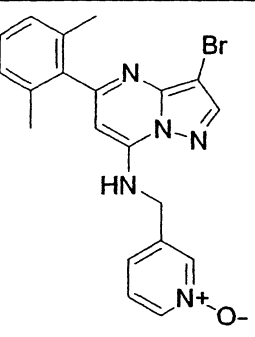
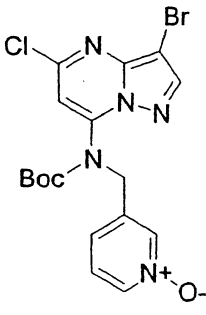
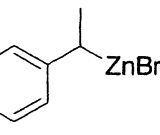
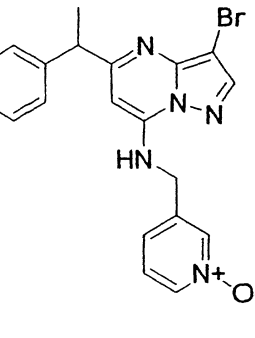
基本上如實例 279所述相同程序僅替代表 26 欄 2 之氯化物及表 26 欄 3 之有機鋅試劑，製備表 26 欄 4 所示之化合物。

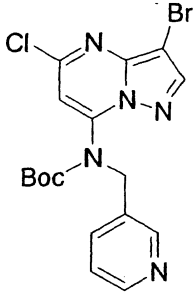
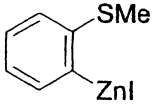
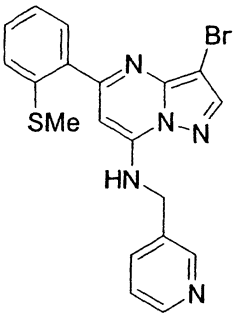
表 26

實例	欄2	欄3	欄4	數據
280				LCMS: $\text{MH}^+ = 395$

281				LCMS: $MH^+ = 400$
282				LCMS: $MH^+ = 412$
283				LCMS: $MH^+ = 452$
284				LCMS: $MH^+ = 422$

285				LCMS: $MH^+ = 408$
286				LCMS: $MH^+ = 404$
287				LCMS: $MH^+ = 404$
288				LCMS: $MH^+ = 408$
289				LCMS: $MH^+ = 386$

290				LCMS: $MH^+ = 464$
291				LCMS: $MH^+ = 480$
292				LCMS: $MH^+ = 424$
293				LCMS: $MH^+ = 424$

294				LCMS: MH ⁺ = 426
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所選擇之化合物其他數據如下：

實例 280: ¹H NMR (CDCl₃)δ 8.65 (s, 1H), 8.57 (d, J=4.2 Hz, 1H), 8.50 (d, J=4.5 Hz, 1H), 8.01 (s, 1H), 7.69 (d, J=7.5 Hz, 1H), 7.61 (d, J=7.8 Hz, 1H), 7.31-7.22 (m, 2H), 6.77 (m, 2H), 4.71 (d, J=5.4 Hz, 2H), 2.68 (s, 3H)。

實例 281: ¹H NMR (CDCl₃)δ 8.80 (s, 1H), 8.72 (d, J=4.8 Hz, 1H), 8.08 (s, 1H), 7.85-7.40 (m, 3H), 7.02 (d, J=5.1 Hz, 1H), 6.90 (t, J=6.0 Hz, 1H), 6.29 (s, 1H), 4.79 (d, J=6.0 Hz, 2H), 2.61 (s, 3H)。

實例 282: ¹H NMR (CDCl₃)δ 8.67 (s, 1H), 8.61 (d, J=3.9 Hz, 1H), 8.03 (s, 1H), 7.72-7.31 (m, 3H), 7.22-7.00 (m, 2H), 6.81 (t, J=6.0 Hz, 1H), 6.03 (s, 1H), 4.68 (d, J=6.0 Hz, 2H), 2.28 (s, 3H)。

實例 283: ¹H NMR (CDCl₃)δ 8.68 (s, 1H), 8.63 (d, J=4.0 Hz, 1H), 8.00 (s, 1H), 7.80-7.72 (m, 2H), 7.54-7.47 (m, 3H), 7.35 (m, 1H), 6.74 (t, J=6.0 Hz, 1H), 6.19 (s, 1H), 4.67 (d, J=6.0 Hz, 2H), 4.21 (q, J=7.2 Hz, 2H), 1.13 (t, J=7.2 Hz, 3H)。

實例 284: ^1H NMR (CDCl_3) δ 7.97 (s, 1H), 7.65 (d, $J=7.2$ Hz, 1H), 7.33-7.15 (m, 5H), 6.73 (t, $J=5.4$ Hz, 1H), 5.99 (s, 1H), 4.61 (d, $J=5.4$ Hz, 2H), 3.09 (sept, $J=6.9$ Hz, 1H), 1.11 (d, $J=6.9$ Hz, 6H)。

實例 285: ^1H NMR (CDCl_3) δ 8.56-8.55 (m, 2H), 7.94 (s, 1H), 7.54 (m, 1H), 7.30-7.22 (m, 6H), 6.59 (t, $J=5.7$ Hz, 1H), 5.66 (s, 1H), 4.47 (d, $J=5.7$ Hz, 2H), 4.26 (q, $J=7.2$ Hz, 1H), 1.68 (d, $J=7.2$ Hz, 3H)。

實例 286: ^1H NMR (CDCl_3) δ 8.67 (m, 2H), 7.94 (s, 1H), 7.69 (d, $J=7.8$ Hz, 1H), 7.34 (m, 1H), 6.63 (t, $J=5.7$ Hz, 1H), 5.87 (s, 1H), 4.62 (d, $J=5.7$ Hz, 2H), 3.64 (s, 3H), 3.13 (m, 2H), 2.82 (m, 1H), 1.22 (m, 3H)。

實例 287: ^1H NMR (CDCl_3) δ 8.66 (m, 2H), 7.94 (s, 1H), 7.68 (d, $J=7.8$ Hz, 1H), 7.34 (m, 1H), 6.62 (t, $J=6.0$ Hz, 1H), 5.87 (s, 1H), 4.62 (d, $J=6.0$ Hz, 2H), 3.64 (s, 3H), 3.13 (m, 2H), 2.81 (m, 1H), 1.22 (m, 3H)。

實例 288: ^1H NMR (CDCl_3) δ 8.64 (s, 1H), 8.60 (d, $J=3.6$ Hz, 1H), 8.04 (s, 1H), 7.68 (m, 1H), 7.31 (m, 1H), 7.16 (m, 1H), 7.07-7.05 (m, 2H), 6.80 (t, $J=6.3$ Hz, 1H), 5.93 (s, 1H), 4.64 (d, $J=6.3$ Hz, 2H), 2.08 (s, 6H)。

實例 289: ^1H NMR (CDCl_3) δ 8.72 (s, 1H), 8.62 (d, $J=4.8$ Hz, 1H), 7.99-7.97 (m, 2H), 7.73-7.69 (m, 2H), 7.40-7.33 (m, 2H), 6.67 (t, $J=6.0$ Hz, 1H), 6.29 (s, 1H), 4.71 (d, $J=6.0$ Hz, 2H)。

實例 290: ^1H NMR (CDCl_3) δ 8.73 (s, 1H), 8.62 (d, $J=4.5$ Hz,

1H), 8.01 (s, 1H), 7.76 (m, 1H), 7.41 (d, J=5.1 Hz, 1H), 7.34 (dd, J=8.1, 5.1 Hz, 1H), 7.05 (d, J=5.1 Hz, 1H), 7.01 (s, 1H), 6.79 (t, J=6.0 Hz, 1H), 4.74 (d, J=6.0 Hz, 2H)。

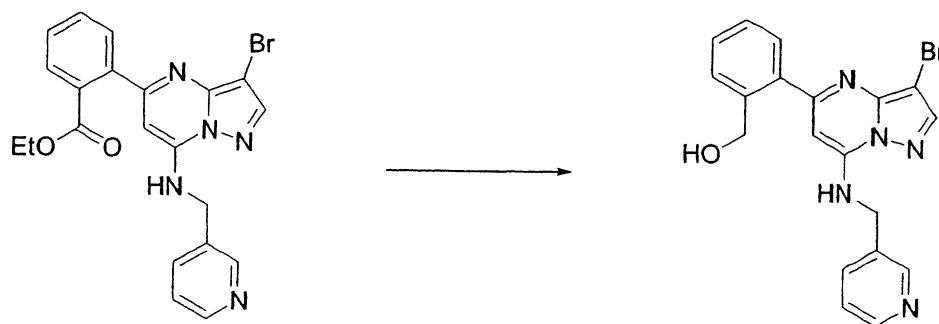
實例 291: ^1H NMR (DMSO- d_6) δ 9.12 (s, 1H), 8.40 (s, 1H), 8.33 (s, 1H), 8.13 (m, 1H), 7.82 (d, J=5.1 Hz, 1H), 7.40-7.39 (m, 2H), 7.22 (d, J=5.1 Hz, 1H), 6.86 (s, 1H), 4.86 (s, 2H)。

實例 292: ^1H NMR (CDCl_3) δ 8.23 (s, 1H), 8.16 (d, J=6.0 Hz, 1H), 8.06 (s, 1H), 7.31-7.05 (m, 5H), 6.86 (m, 1H), 5.87 (s, 1H), 4.62 (d, J=6.3 Hz, 2H), 2.09 (s, 6H)。

實例 293: ^1H NMR (CDCl_3) δ 8.14 (s, 1H), 8.12 (d, J=6.3 Hz, 1H), 7.94 (s, 1H), 7.29-7.16 (m, 6H), 7.07 (m, 1H), 6.78 (t, J=6.0 Hz, 1H), 5.54 (s, 1H), 4.44 (d, J=6.0 Hz, 2H), 4.24 (t, J=7.2 Hz, 1H), 1.68 (d, J=7.2 Hz, 3H)。

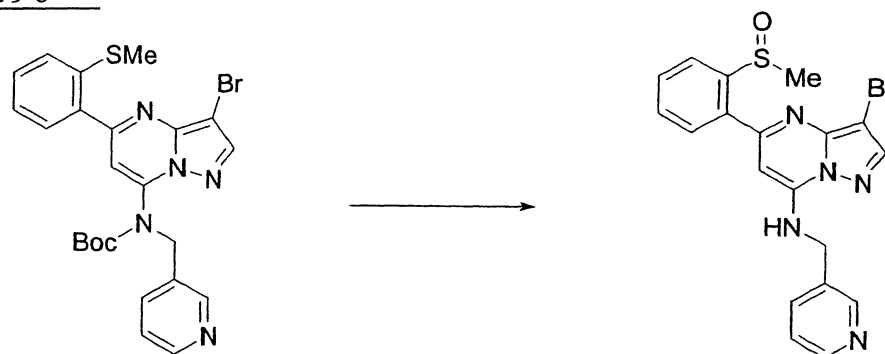
實例 294: ^1H NMR (CDCl_3) δ 8.67 (s, 1H), 8.59 (d, J=4.8 Hz, 1H), 8.01 (s, 1H), 7.71 (m, 1H), 7.52 (dd, J=7.8, 1.8 Hz, 1H), 7.40-7.19 (m, 4H), 6.78 (t, J=6.0 Hz, 1H), 6.32 (s, 1H), 4.67 (d, J=6.0 Hz, 2H), 2.38 (s, 3H)。

實例 295 :



於氫化鋰鋁(10毫克, 0.26毫莫耳)之無水THF(2毫升)懸浮液中, 在0℃滴加實例283製備之化合物(20毫克, 0.044毫莫耳)之無水THF(2毫升)溶液。所得混合物回流1小時並在室溫攪拌隔夜, 以稀硫酸中和並以EtOAc萃取。有機相以MgSO₄脫水並減壓濃縮。粗產物藉製備性薄層層析使用5% MeOH之EtOAc溶液作為溶離液純化(15毫克, 83%產率)。LCMS:MH⁺= 410; ¹H NMR (CDCl₃)δ 8.69 (s, 1H), 8.61 (d, J=3.9 Hz, 1H), 8.05 (d, J=2.1 Hz, 1H), 7.74 (d, J=7.8 Hz, 1H), 7.52-7.31 (m, 5H), 6.97 (t, J=6.3 Hz, 1H), 6.55 (d, J=2.7 Hz, 1H), 6.20 (s, 1H), 4.71 (d, J=6.3 Hz, 2H), 4.52 (s, 2H)。

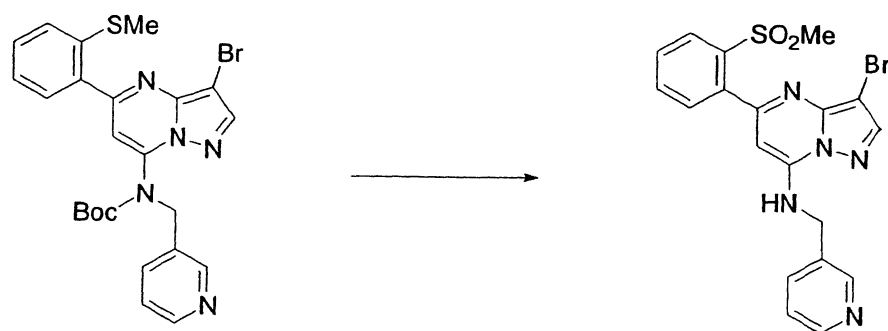
實例 296 :



於實例294製備之N-Boc-保護之化合物(45毫克, 0.085毫莫耳)之CH₂Cl₂(4毫升)在-50℃之溶液中, 添加m-CPBA(18毫克, 0.10毫莫耳)。在-50℃攪拌1小時後, 添加更多m-CPBA(4毫克, 0.02毫莫耳)。混合物又攪拌2小時後, 以CH₂Cl₂(20毫升)稀釋並以飽和NaHCO₃(20毫升)洗滌。有機相以MgSO₄脫水並減壓濃縮。殘留物藉製備性薄層層析使用2.5% MeOH之CH₂Cl₂溶液作為溶離液純化。所得N-Boc-保護之產物(37毫克, 80%產率, LCMS:MH⁺=542)及TFA(1毫升)之

CH₂Cl₂(2毫升)溶液在室溫攪拌2小時。減壓移除揮發物。殘留物溶於CH₂Cl₂，以飽和NaHCO₃中和且以CH₂Cl₂萃取。有機相以MgSO₄脫水且減壓濃縮。粗產物藉製備性薄層層析使用5% MeOH之EtOAc溶液作為溶離液純化(26毫克，89%產率)。LCMS:MH⁺=442; ¹H NMR (CDCl₃)δ 8.71 (s, 1H), 8.64 (d, J=3.9 Hz, 1H), 8.41 (m, 1H), 8.03 (s, 1H), 7.75-7.54 (m, 4H), 7.36 (dd, J=8.1, 5.1 Hz, 1H), 6.81 (t, J=6.0 Hz, 1H), 6.34 (s, 1H), 4.74 (d, J=6.0 Hz, 2H), 3.25 (s, 3H)。

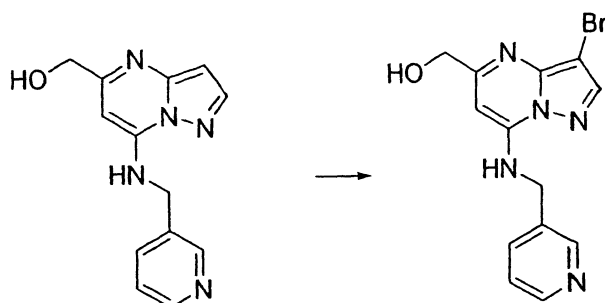
實例 297：



於實例 294 製備之 N-Boc-保護之化合物(56毫克，0.11毫莫耳)之CH₂Cl₂(4毫升)在0℃之溶液中，添加 m-CPBA(42毫克，0.24毫莫耳)。在室溫攪拌2小時後，添加更多 m-CPBA(13毫克，0.075毫莫耳)。混合物在室溫攪拌隔夜，以CH₂Cl₂ (20毫升)稀釋並以飽和NaHCO₃(20毫升)洗滌。有機相以MgSO₄脫水並減壓濃縮。殘留物藉製備性薄層層析使用2.5% MeOH之EtOAc溶液作為溶離液純化。所得 N-Boc-保護之產物(29毫克，49%產率，LCMS:MH⁺ =558)及TFA(1毫升)之CH₂Cl₂(2毫升)溶液在室溫攪拌2小時。減壓移除揮發物。殘留物溶於CH₂Cl₂，以飽和NaHCO₃中和且以CH₂Cl₂萃取。有

機相以 MgSO_4 脫水且減壓濃縮。粗產物藉製備性薄層層析使用 2.5% MeOH 之 EtOAc 溶液作為溶離液純化 (21 毫克, 90% 產率)。LCMS: $\text{MH}^+ = 458$; $^1\text{H NMR}$ (CDCl_3) δ 8.64 (s, 2H), 8.20 (m, 1H), 8.01 (s, 1H), 7.73-7.60 (m, 3H), 7.46 (m, 1H), 7.35 (s, 1H), 6.82 (t, $J=5.9$ Hz, 1H), 6.17 (s, 1H), 4.65 (d, $J=5.7$ Hz, 2H), 3.60 (s, 3H)。

實例 298



基本上藉製備例 127 所述相同程序，僅替代製備例 189 所製備之化合物，製備上述化合物。MS: $\text{MH}^+ = 334$; mp = 170-173 $^{\circ}\text{C}$ 。

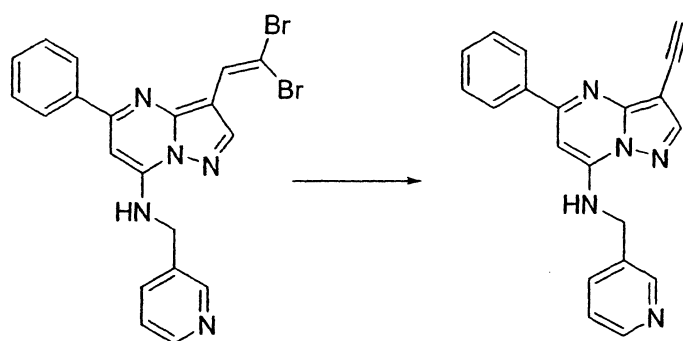
實例 299-300：

基本上藉實例 298 所述相同程序，僅替代表 27 欄 2 所示之化合物，製備表 27 欄 3 所示之化合物：

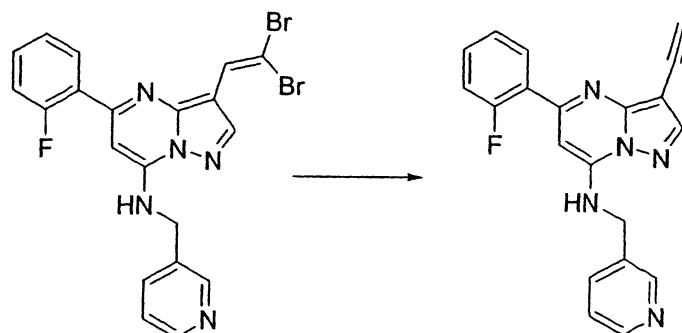
表 27

實例	欄2	欄3	數據
299			MS: $\text{MH}^+ = 348$ m.p. = 73 - 83 $^{\circ}\text{C}$

300			MS: $MH^+ = 362$ m.p. = 165 – 175 °C
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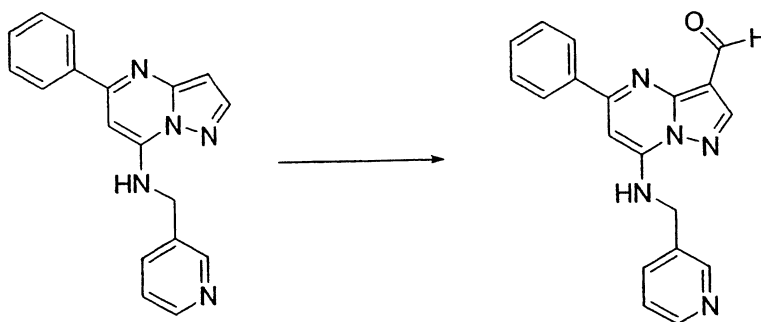
實例 301：

於製備例186製備之化合物(0.1克，0.21毫莫耳)之THF(4.0毫升)在 -78°C 之溶液中，在 -78°C 添加nBuLi(0.57毫升，2.16 M於己烷，5.0當量)。反應混合物在 -78°C 攪拌2小時，以 H_2O 驟冷，溫至室溫，並以EtOAc萃取。合併之有機相以 Na_2SO_4 脫水，過濾並減壓濃縮。粗產物藉製備性TLC使用2.5% (10% NH_4OH 之 CH_3OH)溶液之 CH_2Cl_2 作為溶離液純化(0.013克，20%產率)。MS: $MH^+ = 326$ ；mp= $71-72^{\circ}\text{C}$ 。

實例 302

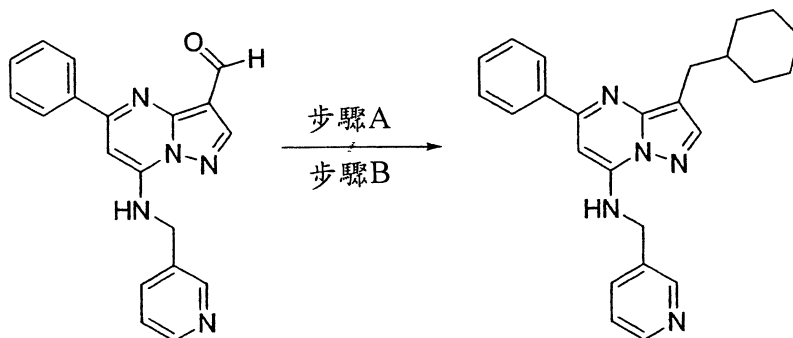
基本上藉製備例301所述相同程序，僅替代製備例187所製備之化合物，製備上述化合物(0.049克，68%產率)。MS: $MH^+ = 344$ ；mp=69-71℃。

實例 303：



於製備例187.1之3-H加成物(0.70克，2.32毫莫耳)之DMF(4.2毫升)之0℃溶液中，滴加POCl₃(0.67毫升，7.2毫莫耳)。混合物在室溫攪拌14小時，冷卻至0℃，並藉添加冰驟冷。小心添加1 N NaOH以調整pH至8且混合物以CH₂Cl₂(3x25毫升)萃取。合併有機層，脫水(Na₂SO₄)，過濾並減壓濃縮。粗產物自EtOAc再結晶獲得0.43克(56%)黃色固體。mp=181-183℃；M+H=330。

實例 304：



步驟 A：

於得自實例303之醛(100毫克，0.30毫莫耳)於THF(1毫升)之0°C溶液中，歷時5分鐘滴加溴化環己基鎂(0.46毫升，2.0 M之Et₂O)。所得混合物在0°C攪拌2小時並在室溫攪拌12小時。混合物冷卻至0°C且以飽和NH₄Cl(3毫升)及CH₂Cl₂(5毫升)處理。分離層且水層以CH₂Cl₂(2x5毫升)萃取。合併有機層，以食鹽水(1x5毫升)洗滌，脫水(Na₂SO₄)，過濾並減壓濃縮，獲得110毫克(89%)淡黃色半固體。M+H=414。此物質未經純化用於步驟B。

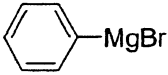
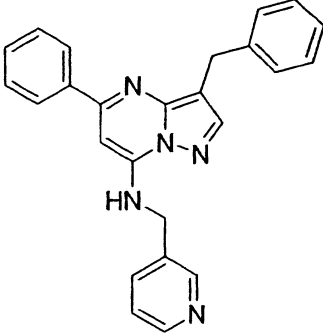
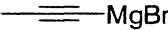
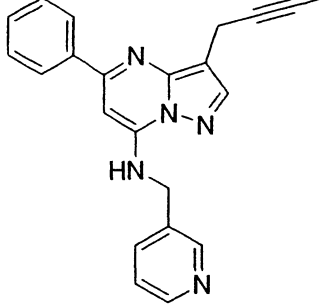
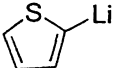
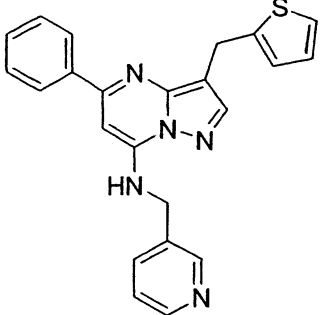
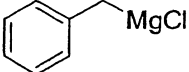
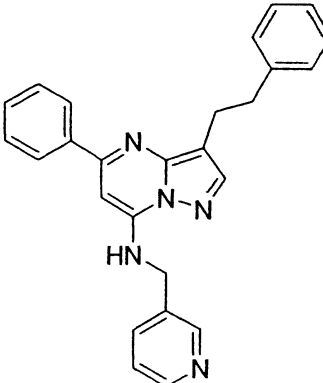
步驟B：

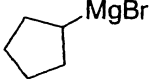
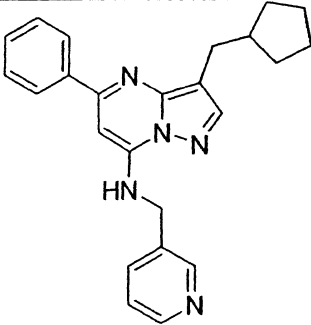
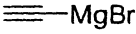
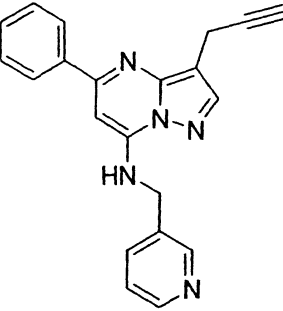
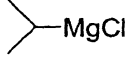
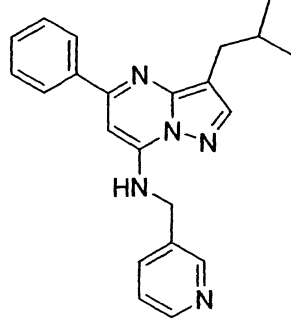
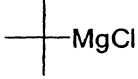
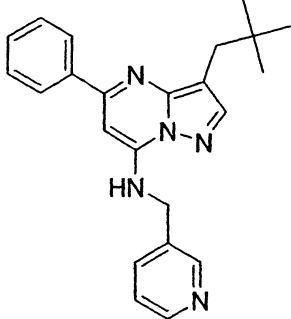
於醇(53毫克，0.13毫莫耳)之CH₂Cl₂(0.5毫升)之0°C溶液中，添加Et₃SiH(24微升，0.15毫莫耳)接著添加TFA(24微升，0.30毫莫耳)。混合物在0°C攪拌2小時並在室溫攪拌2小時，隨後添加額外部分之Et₃SiH(24微升，0.15毫莫耳)及TFA(24微升，0.30毫莫耳)且混合物在室溫攪拌3小時(直至藉TLC發現完成)。混合物減壓濃縮且粗製殘留物分配於CH₂Cl₂(5毫升)及飽和NaHCO₃水溶液(2.5毫升)之間。分離層且水層以CH₂Cl₂(2x5毫升)萃取。合併有機層，以食鹽水(1x5毫升)洗滌，脫水(Na₂SO₄)，過濾並減壓濃縮。粗產物藉製備性TLC(8x1000 mM)純化以CH₂Cl₂/MeOH(22:1)溶離，獲得29毫克(56%)黃色半固體。M+H=398。

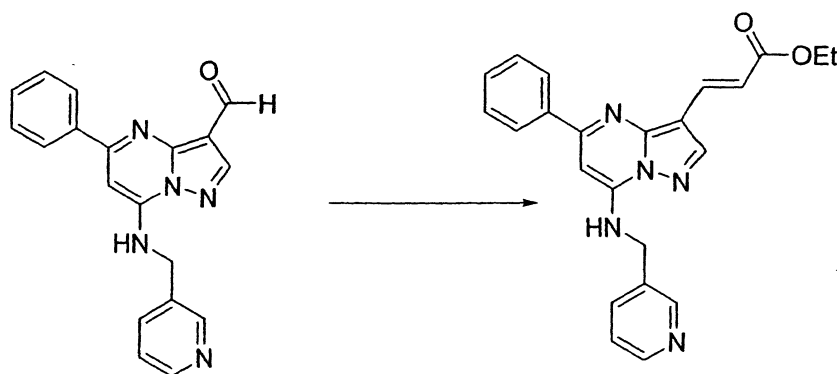
實例305-312：

基本上如實例304所述之相同程序，利用實例303之醛並替代表28欄2所示之格林納或有機鋰試劑，製備表28欄3所示之化合物：

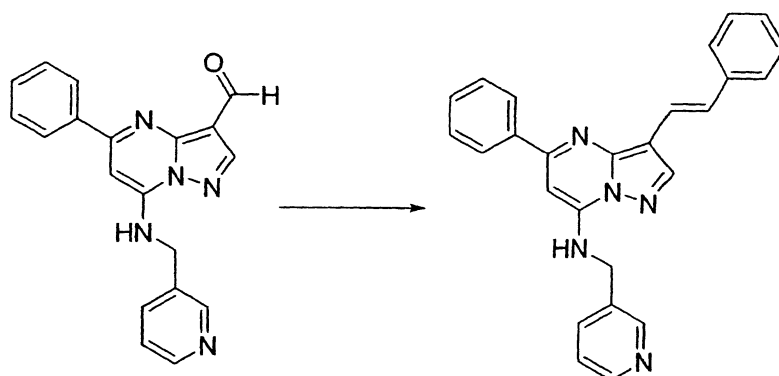
表 28

實例	欄2 (Organometallic)	欄3 (最終結構)	數據 1. mp (°C) 2. M+H
305			1. 黃色油 2. M+H = 392
306			1. 紅色油 2. M+H = 353
307			1. 紅色油 2. M+H = 398
308			1. 黃色油 2. M+H = 406

309			1. 黃色半固體 2. M+H = 384
310			1. 半固體 2. M+H = 340
311			1. mp = 141-143 2. M+H = 358
312			1. mp = 148-150 2. M+H = 372

實例 313：

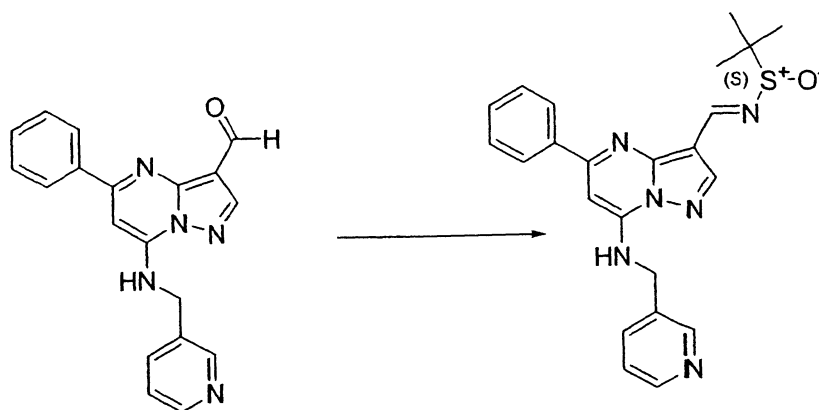
於得自實例 303 之醛 (81 毫克，0.25 毫莫耳) 於苯 (2.5 毫升) 之溶液中，一次添加碳乙氧基亞甲基三苯基磷烷 (0.12 克，0.33 毫莫耳)。混合物在回流加熱 24 小時，冷卻至室溫並減壓濃縮。混合物以 CH_2Cl_2 (5 毫升) 稀釋，添加食鹽水 (2 毫升) 並分離層。水層以 CH_2Cl_2 (2x4 毫升) 萃取。合併有機層，脫水 (Na_2SO_4)，過濾並減壓濃縮。粗產物藉製備性 TLC (8x1000 μM) 純化以 $\text{CH}_2\text{Cl}_2/\text{MeOH}$ (20:1) 溶離，獲得 98 毫克 (100%) 白色固體。mp 151-153°C； $\text{M}+\text{H}=400$ 。

實例 314：

於含苄基三苯基磷溴化物 (0.59 克，1.37 毫莫耳) 之 THF (3 毫升) 混合物中添加 NaH (55 毫克，1.37 毫莫耳)，且使混合物攪拌 30 分鐘。一次添加實例 303 之醛 (0.15 克，0.46 毫莫耳)，

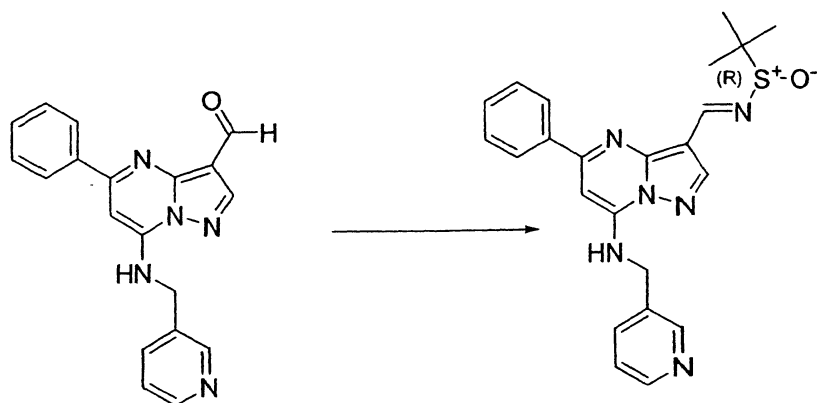
且使混合物回流加熱36小時。混合物冷卻至室溫且減壓濃縮。混合物以 CH_2Cl_2 (5毫升)稀釋，添加食鹽水(2毫升)，且使層分離。水層以 CH_2Cl_2 (2x4毫升)萃取。合併有機層，脫水(Na_2SO_4)、過濾且減壓濃縮。粗產物以製備性TLC($8 \times 1000 \mu\text{M}$)以 $\text{CH}_2\text{Cl}_2/\text{MeOH}$ (20 : 1)溶離純化，獲得58毫克(32%)黃色固體。mp 138-141°C; $\text{M}+\text{H} = 404$ 。

實例 315：



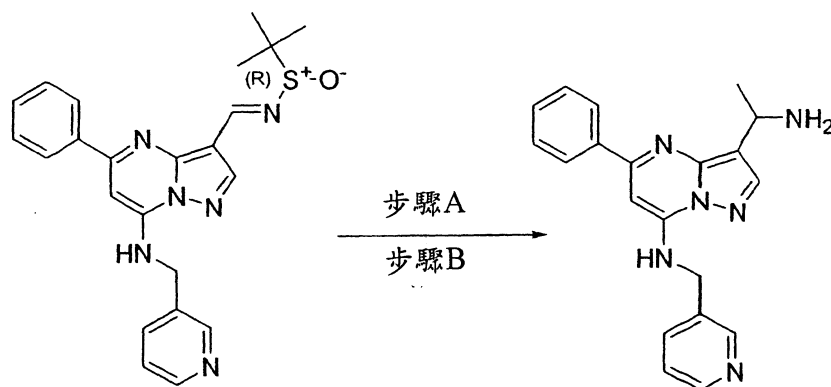
於含實例 303 之醛(0.20 克, 0.60 毫莫耳)之 THF(3 毫升)溶液中滴加 $\text{Ti}(\text{i-OPr})_4$ (0.36 毫升, 1.21 毫莫耳)，接著添加 (S)-(-)-2-甲基-2-丙烷亞磺醯胺(74 毫克, 0.61 毫莫耳)。所得混合物回流攪拌 18 小時，冷卻至室溫，且以食鹽水(2 毫升)驟冷。混合物經矽藻土墊過濾，以 EtOAc(2x2 毫升)洗滌。使層分離且水層以 EtOAc(2x4 毫升)萃取。合併有機層，脫水(Na_2SO_4)、過濾且減壓濃縮。粗產物以製備性 TLC($8 \times 1000 \mu\text{M}$)經 $\text{CH}_2\text{Cl}_2/\text{MeOH}$ (20 : 1)溶離純化，獲得 0.21 克(80%)黃色固體。mp 108-110°C; $\text{M}+\text{H} = 433$ 。

實例 316：



如實例315之相同方式製備，但以(R)-(-)-2-甲基-2-丙烷亞磺醯胺替代，獲得0.25克(94%)黃色固體。mp 107-109°C; M+H = 433。

實例 317：



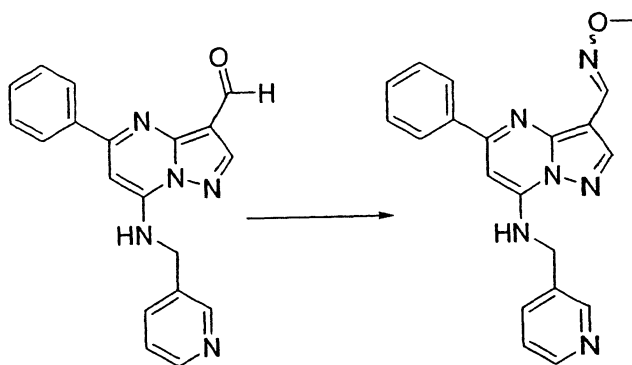
步驟 A：

在-40°C下，於含實例316之亞磺亞胺(50毫克，0.12毫莫耳)之CH₂Cl₂(2.5毫升)溶液中滴加MeMgBr(96毫升，0.29毫莫耳)。混合物於-40°C攪拌5小時及在室溫攪拌12小時。添加額外部分之MeMgBr(96毫升，0.29毫莫耳)，且混合物攪拌12小時。添加飽和NH₄Cl水溶液(2毫升)，且以EtOAc(3x4毫升)萃取混合物。合併有機層，脫水(Na₂SO₄)、過濾且減壓濃縮，獲得30毫克(58%)粗殘留物。該物質未經純化用於下一步驟中。

步驟 B：

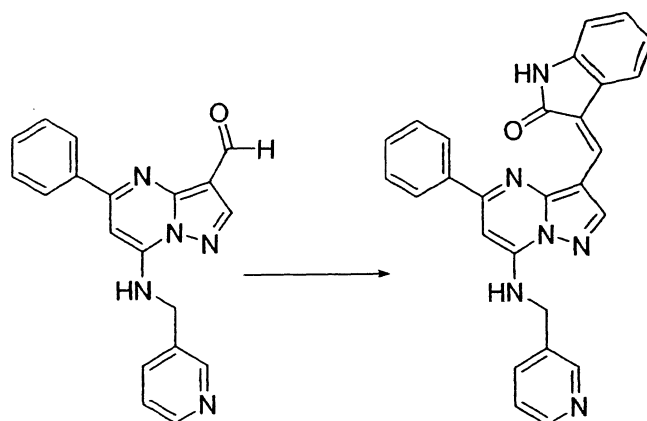
含步驟A之粗物質(30毫克, 0.067毫莫耳)之MeOH(2毫升)中添加濃HCl(2毫升)。混合物在室溫攪拌12小時, 且使混合物濃縮至乾。粗物質分配於CH₂Cl₂(3毫升)及飽和NaHCO₃水溶液(2毫升)中, 且使層分離。水層以CH₂Cl₂(2x3毫升)萃取, 且合併有機層。有機層經脫水(Na₂SO₄)、過濾且減壓濃縮, 獲得6毫克(24%)淡黃色固態標題化合物。mp 100-102°C; M+H = 345。

實例 318:



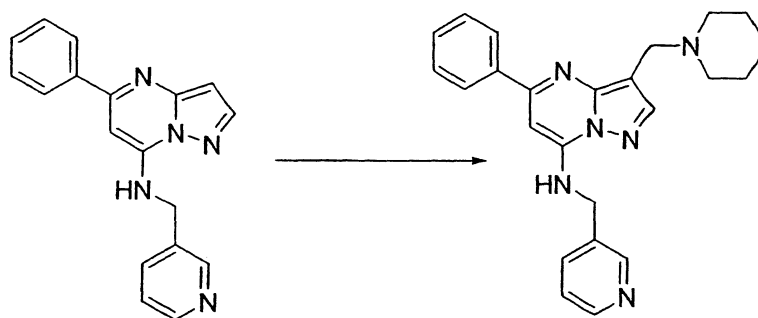
在室溫下於含實例300之醛(75毫克, 0.23毫莫耳)之THF/CH₂Cl₂ (5毫升/1毫升)溶液中添加MeONH₂·HCl(38毫克, 0.46毫莫耳), 接著滴加吡啶(46微升, 0.57毫莫耳)。混合物在室溫攪拌72小時, 隨後使混合物濃縮至乾。粗物質分配於CH₂Cl₂(3毫升)及飽和NaHCO₃水溶液(2毫升)中, 且使層分離。水層以CH₂Cl₂(2x3毫升)萃取, 且合併有機層。有機層經脫水(Na₂SO₄)、過濾且減壓濃縮。粗產物以製備性TLC(3x1000 μM)經CH₂Cl₂/MeOH(22:1)溶離純化, 獲得90毫克(100%)淡黃色固體。mp 173-175°C; M+H=359。

實例 319:



於含實例303醛(60毫克，0.18毫莫耳)之EtOH(2.5毫升)溶液中添加氧雜吡啶(48毫克，0.37毫莫耳)，接著添加吡啶(3滴)。混合物回流加熱14小時，且使混合物冷卻至室溫。過濾所得沉澱物且以冷EtOH(2x2毫升)洗滌。產物於高度真空中乾燥，獲得81毫克(100%)橘色/棕色固態標題化合物。mp 182-185°C；M+H = 445。

實例320：



於含製備例187.10之3-H類似物(106毫克，0.35毫莫耳)之AcOH(2毫升)溶液中添加37%甲醛水溶液(1.5毫升，1.40毫莫耳)，接著添加吡啶(100微升，0.37毫莫耳)。所得混合物於室溫攪拌24小時，且減壓移除AcOH。混合物以水(2毫升)稀釋且以2 M NaOH中和至pH=8。水層以CH₂Cl₂(3x7毫升)萃取且合併有機層。有機層以食鹽水(1x4毫升)洗滌，脫水

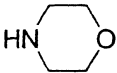
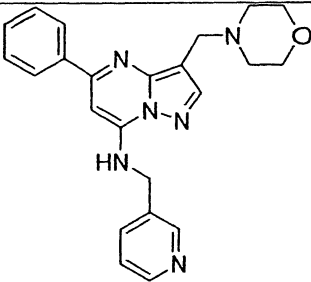
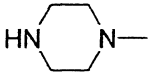
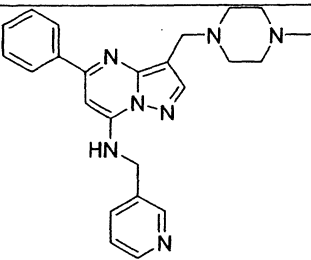
(Na₂SO₄)、過濾且減壓濃縮，獲得96毫克(69%)灰白色固體。

mp 88-90°C ; M+H 399 。

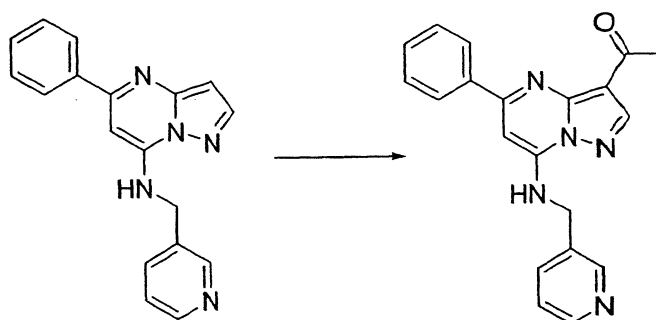
實例 321-322 :

基本上與前述實例320相似之程序，僅以表29欄2之胺替代並使用製備例187.10之3-H加成物，製備表29欄3之化合物。

表 29

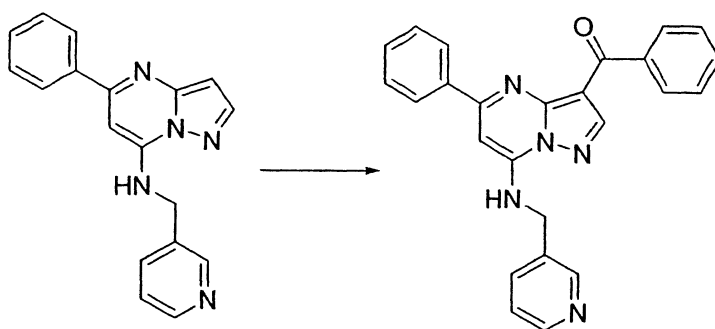
實例	欄2 (胺)	欄3 (最終結構)	數據 1. mp (°C) 2. M+H
321			1. mp = 178-180 2. M+H = 401
			
322			1. mp = 102-104 2. M+H = 414

實例 323 :



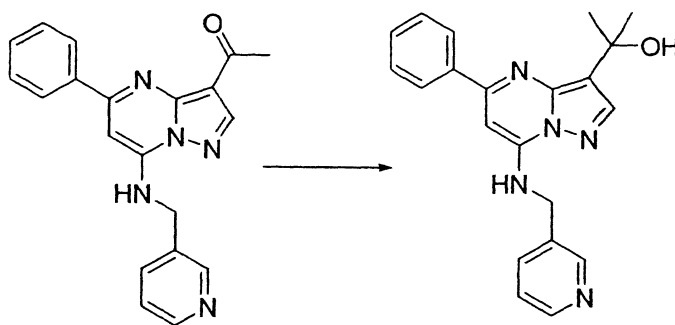
在室溫下，於含製備例187.10之3-H類似物(113毫克，0.38毫莫耳)之 CH_2Cl_2 (5毫升)溶液中添加 AlCl_3 (215毫克，1.61毫莫耳)，接著添加 AcCl (100毫升，1.40毫莫耳)。混合物回流加熱12小時，且冷卻至室溫。混合物再以3 M HCl (3毫升)處理，接著以飽和 NaHCO_3 水溶液處理(直到 $\text{pH}=8$)。使層分離且以 CH_2Cl_2 (2x5毫升)萃取水層。合併有機層，脫水(Na_2SO_4)、過濾且減壓濃縮。粗產物以製備性TLC(8x1000 mM)經 $\text{CH}_2\text{Cl}_2/\text{MeOH}$ (20:1)溶離純化，獲得68毫克(52%)白色固體。mp 220-221°C； $\text{M}+\text{H} = 344$ 。

實例 324：



利用實例323所述之方法，但使用苯甲醯氯，以產率61%製備白色固態標題化合物。mp 172-175°C； $\text{M}+\text{H} = 406$ 。

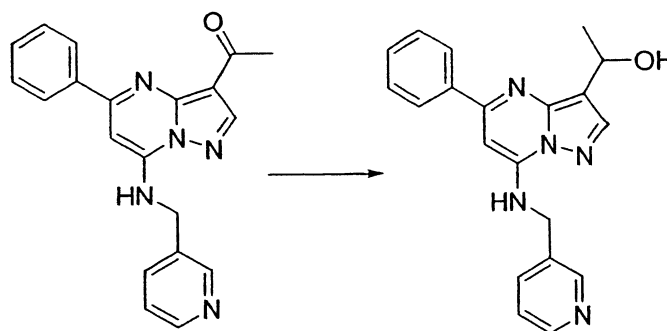
實例 325：



在0°C下於含實例323之酮(100毫克，0.29毫莫耳)之

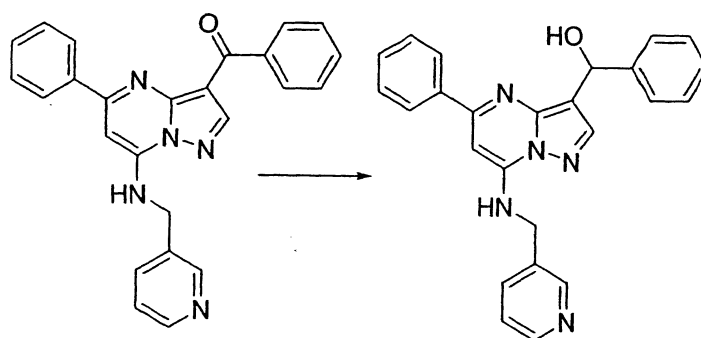
CH₂Cl₂(2.5 毫升)溶液中滴加 MeMgBr(0.35 毫升, Et₂O 中 3.0 M)。所得混合物在室溫攪拌 18 小時, 且添加飽和 NH₄Cl 水溶液(2 毫升)小心終止反應, 及添加 CH₂Cl₂(2 毫升)。使層分離且以 CH₂Cl₂(2x4 毫升)萃取水層。合併有機層, 脫水(Na₂SO₄)、過濾且減壓濃縮。粗產物以製備性 TLC(8x1000 μM)經 CH₂Cl₂/MeOH(10:1)溶離純化, 獲得 68 毫克(52%)黃色固體。mp 160-162°C; M+H = 360。

實例 326:



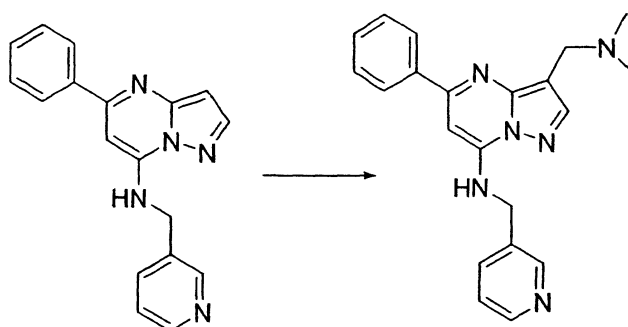
在 0°C 下, 於含實例 323 之酮(84 毫克, 0.24 毫莫耳)之 MeOH/THF (1:1, 合計 2 毫升)溶液中一次添加 NaBH₄(12 毫克, 0.30 毫莫耳)。所得混合物在室溫攪拌 18 小時, 隨後添加額外部分之 NaBH₄(12 毫克, 0.30 毫莫耳)。混合物在室溫攪拌 12 小時, 隨後以冰使混合物驟冷, 接著添加 1 M NaOH 調整 pH=9。混合物以 CH₂Cl₂(5 毫升)稀釋。使層分離且以 CH₂Cl₂(2x4 毫升)萃取水層。合併有機層, 脫水(Na₂SO₄)且減壓濃縮。粗產物以製備性 TLC(8x1000 μM)經 CH₂Cl₂/MeOH(10:1)溶離純化, 獲得 25 毫克(30%)黃色固體。mp 148-150°C; M+H = 346。

實例 327:



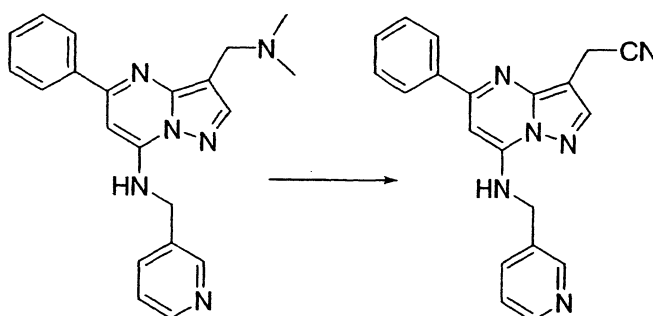
使用與實例326相同之程序，將酮(84毫克，0.21毫莫耳)轉化成53毫克(62%)淡黃色固體。mp 78-80°C；M+H = 408。

實例 328：



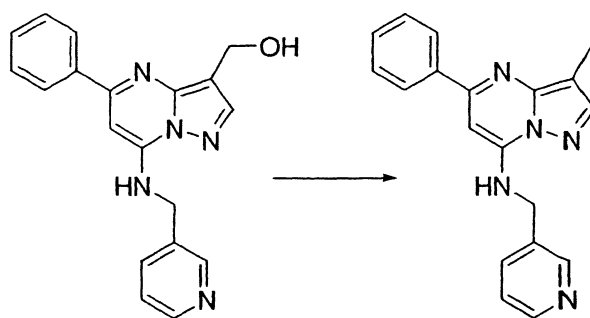
於含製備例187.10之3-H加成物(1.3克，4.31毫莫耳)之CH₂Cl₂(50毫升)溶液中添加 Eschenmoser's 鹽(0.79克，4.31毫莫耳)，接著滴加TFA(0.56毫升，7.33毫莫耳)。混合物在室溫攪拌48小時且以CH₂Cl₂(250毫升)稀釋。有機層以飽和NaHCO₃水溶液(2x125毫升)洗滌，獲得1.41克(92%)黃色固體。mp 231-233°C；M+H = 359。

實例 329：



在加壓管中，於含實例328之三級胺加成物(100毫克，0.28毫莫耳)之50%DMF水溶液(5毫升)溶液中添加 KCN(0.15克，2.32毫莫耳)。將管密封且在100°C加熱96小時。混合物冷卻至室溫且以EtOAc(25毫升)稀釋。有機層以食鹽水(1x5毫升)及水(1x5毫升)洗滌。有機層經脫水(Na_2SO_4)、過濾且減壓濃縮。粗產物以製備性TLC(4x1000 μM)經EtOAc溶離純化，獲得21毫克(30%)棕色固體。mp 152-155°C; $\text{M}+\text{H} = 341$ 。

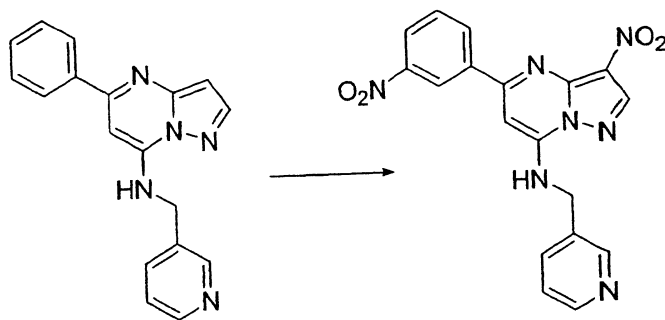
實例330：



在0°C下，於含實例17.10之醇(45毫克，0.14毫莫耳)之 CH_2Cl_2 (0.7毫升)溶液中添加 Et_3SiH (26微升，0.16毫莫耳)，接著添加TFA(25微升，0.33毫莫耳)。混合物在0°C攪拌2小時，且在室溫攪拌2小時，隨後添加額外部分之 Et_3SiH (26微升，0.16毫莫耳)及TFA(25微升，0.33毫莫耳)，且使混合物在室溫攪拌4小時(以TLC偵測直到反應完全)。減壓濃縮混合物，將粗產物分配在 CH_2Cl_2 (3毫升)及飽和 NaHCO_3 水溶液(1.5毫升)中。使層分離且以 CH_2Cl_2 (2x4毫升)萃取水層。合併有機層，以食鹽水(1x5毫升)洗滌，脫水(Na_2SO_4)、過濾且減壓濃縮。粗產物以製備性TLC(4x1000 mM)經 CH_2Cl_2 /

MeOH (20:1)溶離純化，獲得21毫克(48%)黃色固體。mp 146-148°C；M+H = 316。

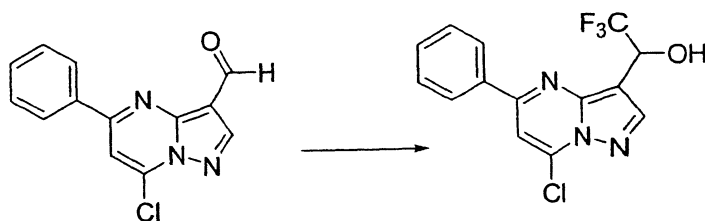
實例 331：



在0°C下，於含製備例187.10之3-H加成物(90毫克，0.30毫莫耳)之濃H₂SO₄(2毫升)溶液中滴加發煙HNO₃(30微升，0.72毫莫耳)。所得混合物在0°C攪拌1小時，隨後將冰(約1克)添加於混合物中。收集所得沉澱物，以水(2x2毫升)及CH₂Cl₂(2x2毫升)洗滌。粗產物在高度真空下乾燥，獲得67毫克(60%)黃/橘色固態單硫酸鹽。mp 250°C；M+H(游離鹼)=392。

實例 332：

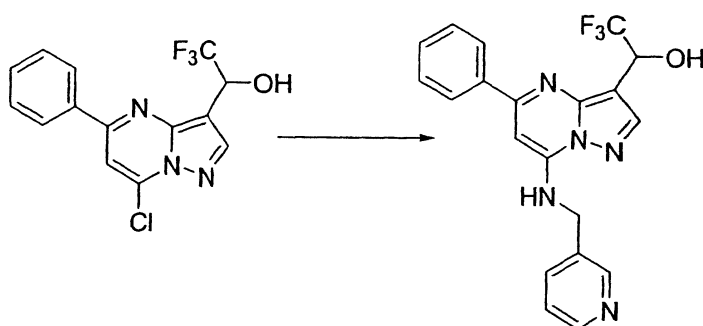
步驟 A：



在0°C下於含實例168之醛(0.10克，0.39毫莫耳)之THF(2.5毫升)溶液中添加CF₃TMS(64毫升，0.43毫莫耳)，接著添加CsF(10毫克)。所得混合物在0°C攪拌2小時，且在室溫攪拌2

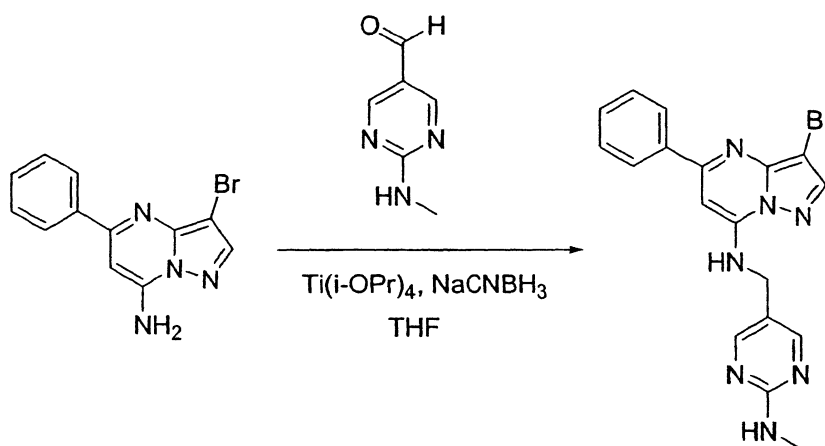
小時。添加 1 M HCl(5 毫升)，且混合物以 CH_2Cl_2 (10 毫升) 稀釋。使層分離，以 CH_2Cl_2 (2x10 毫升) 萃取水層，且合併有機層。有機層以食鹽水(1x10 毫升)洗滌，脫水(Na_2SO_4)、過濾且減壓濃縮，獲得 127 毫克(99%)黃色半固體。M+H=328。粗產物未經進一步純化用於下一步驟中。

步驟 B：



利用實例 1 中所列之一般程序，使實例 332 步驟 A 之 7-Cl 加成物(127 毫克，0.39 毫莫耳)與 3-(胺基甲基)吡啶(73 微升，0.43 毫莫耳)反應，獲得 80 毫克(51%)淡黃色固態標題化合物。mp 68-72°C；M+H = 400。

實例 333：



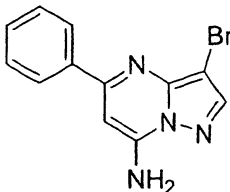
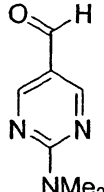
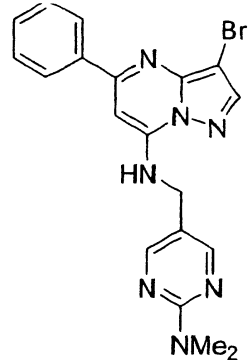
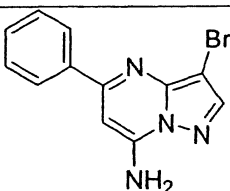
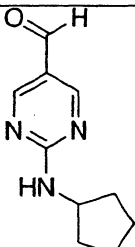
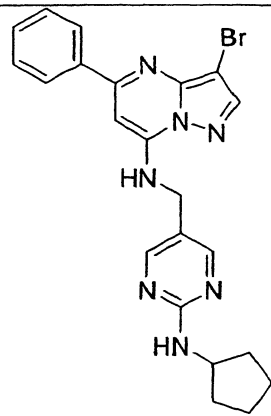
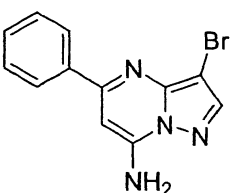
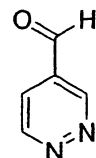
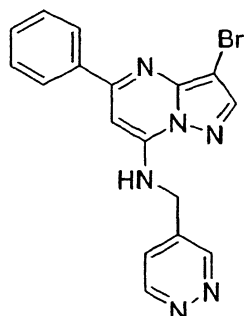
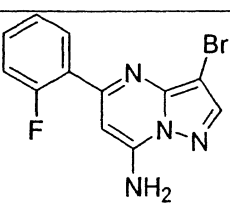
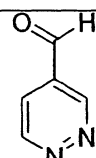
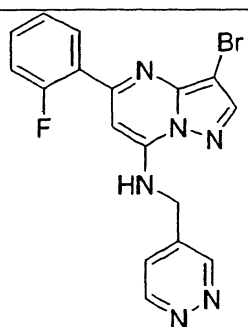
在室溫下於含製備例 174 之苯胺(200 毫克，0.69 毫莫耳)之

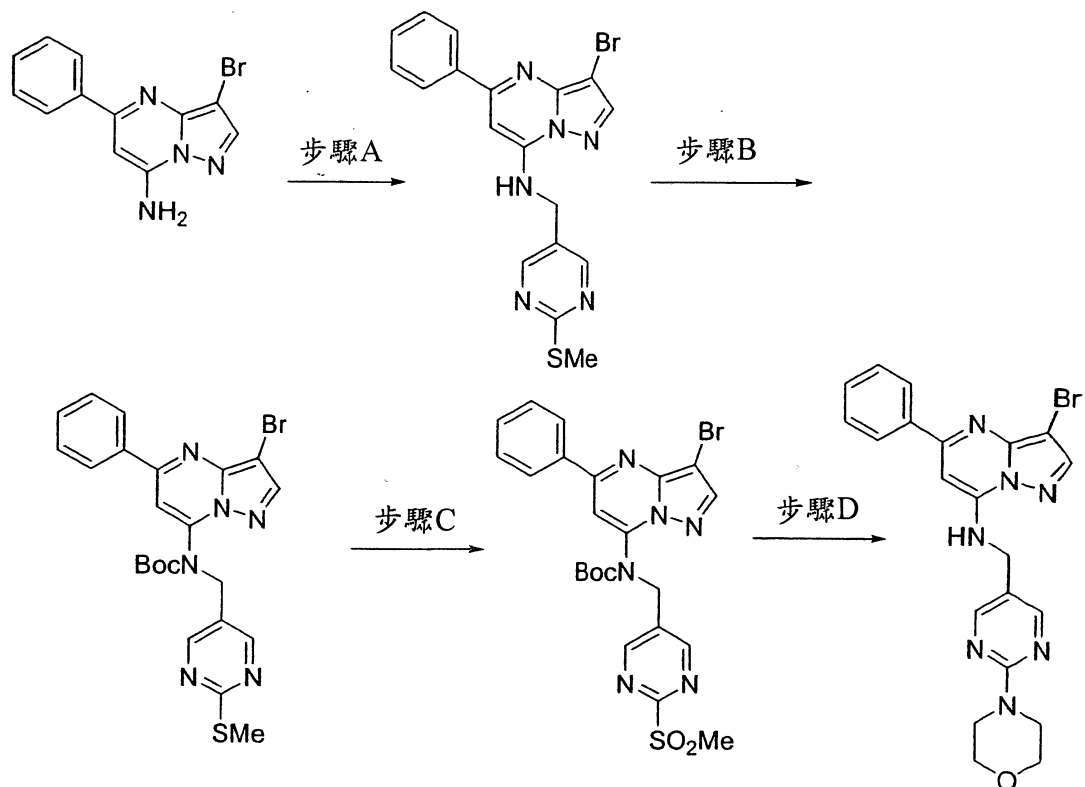
THF(6毫升)溶液中添加製備例256之醛(114毫克，0.83毫莫耳)，接著滴加 $\text{Ti}(\text{i-OPr})_4$ (0.82毫升，2.77毫莫耳)。混合物回流攪拌4小時且冷卻至室溫。添加 NaCNBH_3 (347毫克，5.53毫莫耳)，且混合物在室溫攪拌2小時。使混合物冷卻至 0°C ，以1 M NaOH (4毫升)及食鹽水(1毫升)處理，攪拌30分鐘。混合物以 CH_2Cl_2 (3x10毫升)萃取，合併有機層。有機層以食鹽水(1x7毫升)洗滌，脫水(Na_2SO_4)、過濾且減壓濃縮。粗產物以製備性薄層層析(8x1000 μM 板)經 $\text{CH}_2\text{Cl}_2/\text{MeOH}$ (25:1)溶離純化，獲得89毫克(31%)黃色固態標題化合物。
 $\text{mp } 210\text{-}213^\circ\text{C}$ ； $\text{M}+\text{H} = 411$ 。

實例 334-337：

基本上與實例333所示相同程序，僅使用表30欄2所示之苯胺及表30欄3所示之醛，製備表30欄4所示之化合物：

表 30

實例	欄2 (苯胺)	欄3 i(醛)	欄4 (最終結構)	數據 1. mp (°C) 2. M+H
334				1. mp = 85-87 2. M+H = 425
335				1. mp = 160-162 2. M+H = 451
336				1. mp = 117-119 2. M+H = 382
337				1. mp = 171-175 2. M+H = 400

實例 338：步驟 A：

在實例333所述之反應條件下，使苯胺(0.20克，0.69毫莫耳)與醛(0.13克，0.83毫莫耳)反應，獲得70毫克(23%)黃色固態硫代甲基衍生物。M+H=428。

步驟 B：

於含實例338步驟A之硫代甲基衍生物(60毫克，0.14毫莫耳)之二噁烷(2毫升)溶液中添加Boc₂O(61毫克，0.28毫莫耳)，接著添加DMAP(21毫克，0.17毫莫耳)。混合物在室溫攪拌14小時且減壓濃縮。粗產物以製備性薄層層析(6x1000 μM板)經己烷/EtOAc (4:1)溶離純化，獲得61毫克(83%)黃色固態標題化合物。M+H=528。

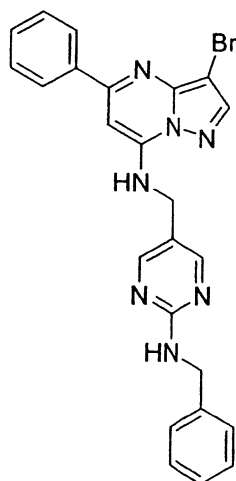
步驟 C：

於含實例338步驟B之硫代甲基衍生物(41毫克，0.078毫莫耳)之 CH_2Cl_2 (2毫升)溶液中一次添加MCPBA(33毫克，0.19毫莫耳)。所得混合物在室溫攪拌3小時，混合物以 CH_2Cl_2 (5毫升)及飽和 NaHCO_3 水溶液(2.5毫升)稀釋。使層分離且以 CH_2Cl_2 (2x5毫升)萃取水層，合併有機層。有機層經脫水(Na_2SO_4)、過濾且減壓濃縮，獲得40毫克(92%)淡黃色固態磺加成物。 $\text{M}+\text{H}=560$ 。

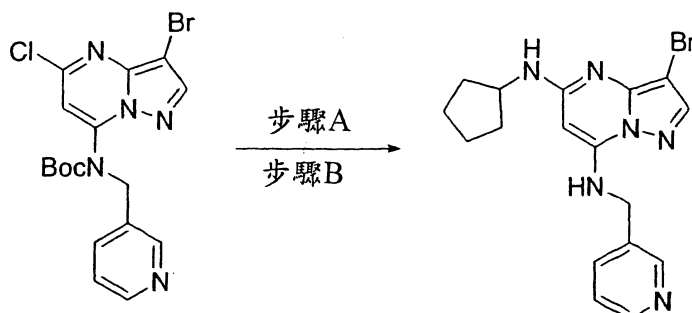
步驟D：

於瓶中加入實例338步驟C之磺(75毫克，0.13毫莫耳)及攪拌棒，且添加嗎啉(2毫升，22毫莫耳)。混合物回流加熱12小時，冷卻至室溫且在高度真空中濃縮至乾。粗產物以製備性薄層層析(6x1000 μM 板)經 $\text{CH}_2\text{Cl}_2/\text{MeOH}$ (40:1)溶離純化，獲得41毫克(68%)黃色固體標題化合物。 $\text{mp } 209-210^\circ\text{C}$ ； $\text{M}+\text{H}=466$ 。

實例339：



如實例338所示般製備標題化合物，但使用苄基胺，獲得12毫克(70%)白色固體。 $\text{mp } 194-196^\circ\text{C}$ ； $\text{M}+\text{H}=487$ 。

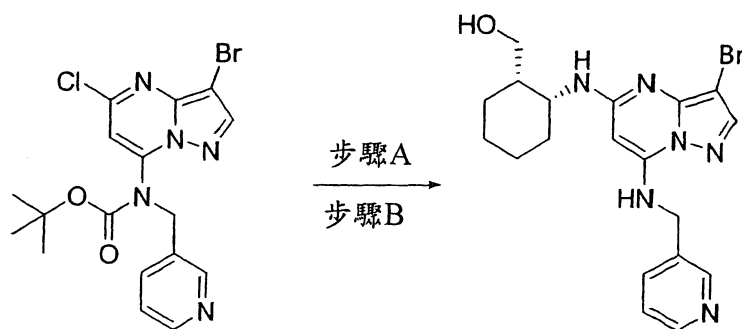
實例 340：步驟 A：

在室溫下，於含 5-氯加成物 (0.15 克，0.34 毫莫耳) 之二噁烷 / DIPEA (2.5 毫升 / 1.0 毫升) 溶液中滴加環戊胺 (0.041 微升，0.41 毫莫耳)。所得溶液回流攪拌 16 小時，冷卻至室溫，且以製備性薄層層析 (8x1000 μ M) 經 CH_2Cl_2 / MeOH (25:1) 溶離純化，獲得 148 毫克 (89%) 黃色油狀物。M+H=489。

步驟 B：以 TFA 移除第三丁氧羰基保護基

在室溫下於含實例 340 步驟 A 製備之化合物 (135 毫克，0.28 毫莫耳) 之 CH_2Cl_2 (2 毫升) 溶液中滴加 TFA (0.54 毫升，7.0 毫莫耳)。所得溶液在室溫攪拌 18 小時且減壓濃縮。粗物質溶於 CH_2Cl_2 (5 毫升) 中，且以飽和 NaHCO_3 水溶液 (2x2 毫升) 及食鹽水 (1x2 毫升) 依序洗滌有機層。有機層經脫水 (Na_2SO_4)、過濾且減壓濃縮。粗物質以製備性薄層層析 (8x1000 μ M) 經 CH_2Cl_2 / MeOH (20:1) 溶離純化，獲得 105 毫克 (97%) 白色固體。mp 120-122°C；M+H = 389。

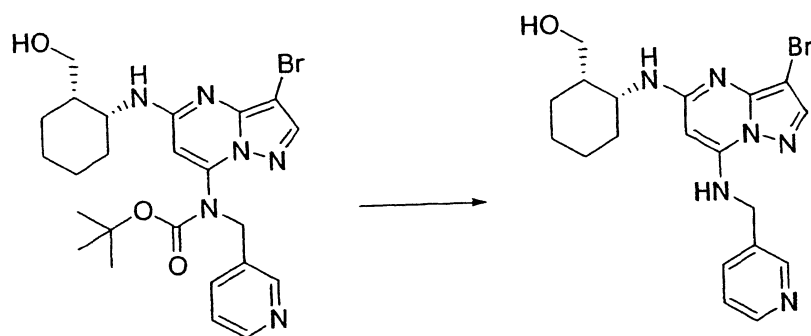
實例 341：



步驟 A：

基本上與實例340所示相同之程序，僅替代適當之胺，製備上述化合物。MS： MH^+ =431。

步驟 B：以 KOH 移除第三丁氧羰基保護基



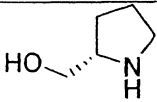
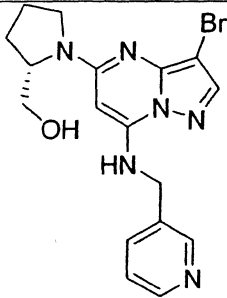
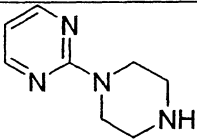
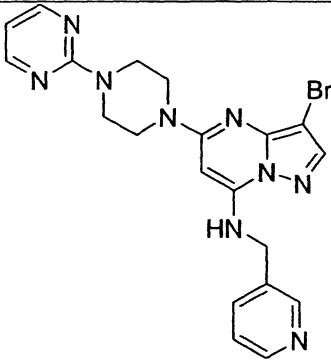
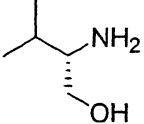
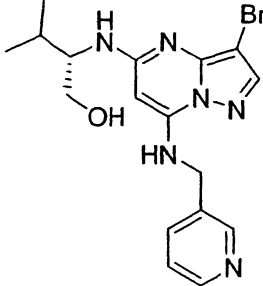
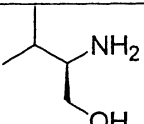
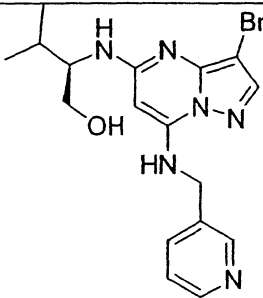
於含實例341步驟A製備之化合物(0.14克，0.26毫莫耳)之 EtOH:H₂O(3毫升，2:1)混合物中一次添加 KOH(0.29克，20當量)。所得溶液回流攪拌14小時，冷卻至室溫且減壓濃縮。殘留物置於CH₂Cl₂(5毫升)中，且以飽和NaHCO₃(2毫升)稀釋。使層分離且以CH₂Cl₂(2x4毫升)萃取水層。合併之有機層以食鹽水洗滌，以Na₂SO₄脫水，經過濾且減壓濃縮。粗產物以製備性TLC(8x1000 μM)經5% MeOH/CH₂Cl₂溶液溶離純化(0.066克，59%產率)。MS: MH^+ = 432；mp = 219-221°C。

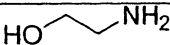
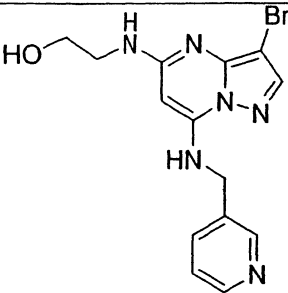
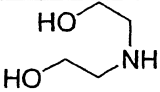
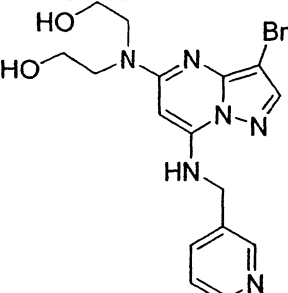
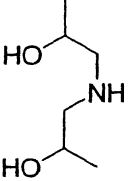
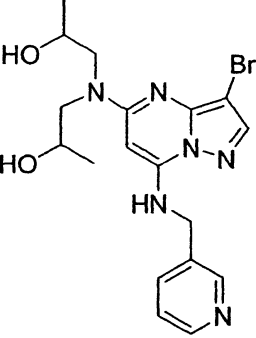
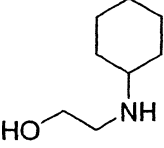
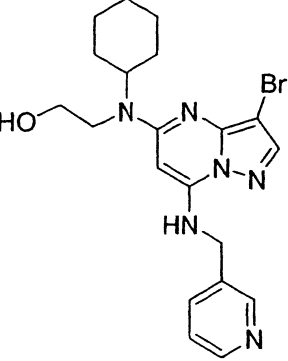
實例 342-397：

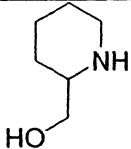
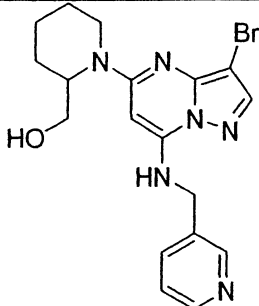
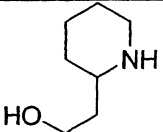
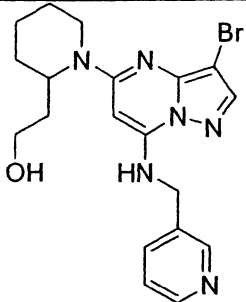
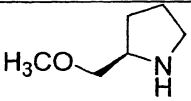
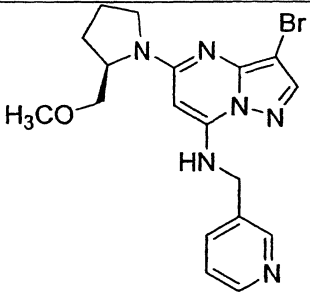
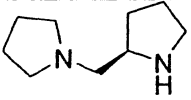
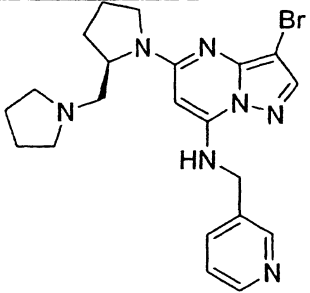
基本上與實例340相同之程序，僅替代表31欄2之氯化

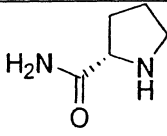
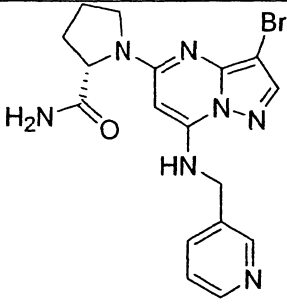
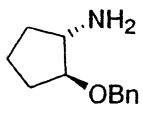
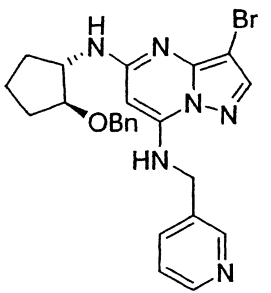
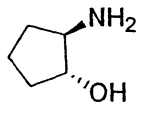
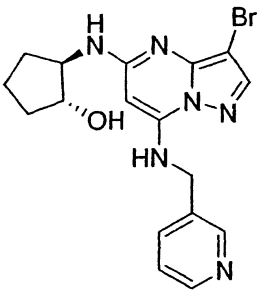
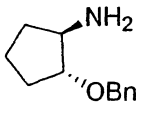
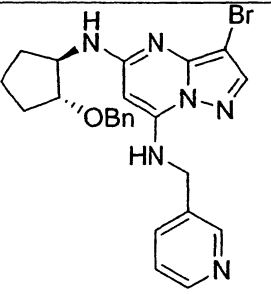
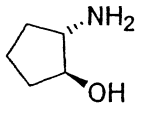
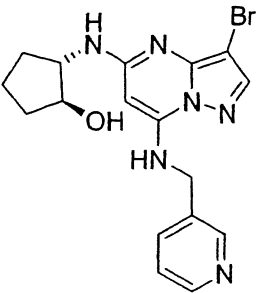
物，且藉表31欄3所示之方法移除第三丁氧羰基保護基，製備表31欄4所示之化合物。

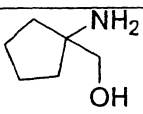
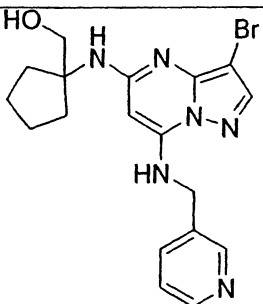
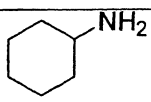
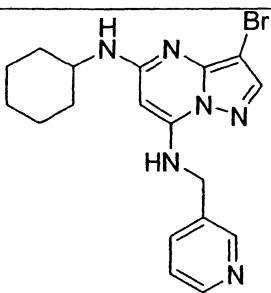
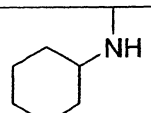
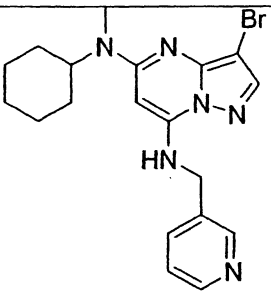
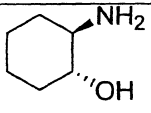
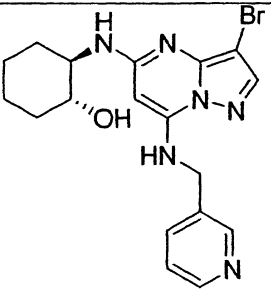
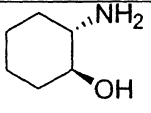
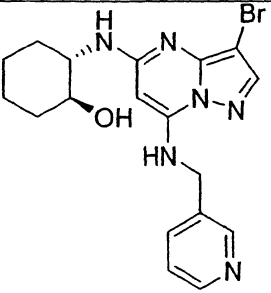
表 31

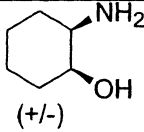
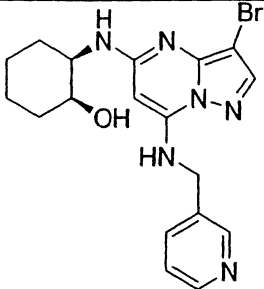
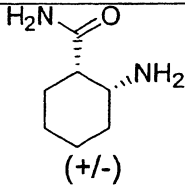
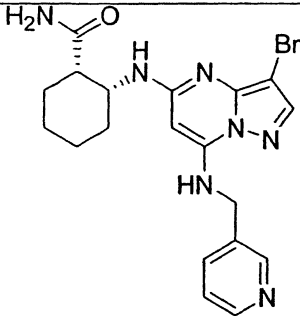
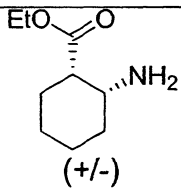
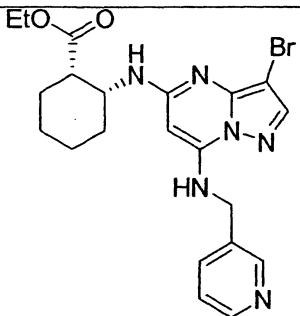
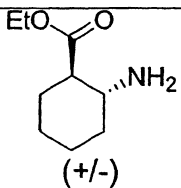
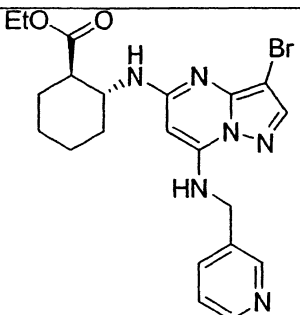
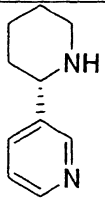
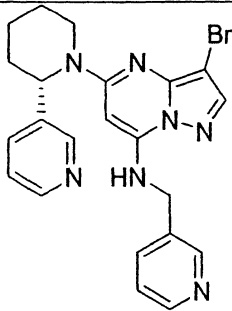
實例	欄2	欄3	欄4	數據
342		HCl		MS: MH ⁺ = 403 m.p. 151 – 157 °C
343		HCl		MS: MH ⁺ = 466 m.p. 212 – 217 °C
344		HCl		MS: MH ⁺ = 405 m.p. 53 – 58 °C
345		HCl		MS: MH ⁺ = 405 m.p. 63 – 69 °C

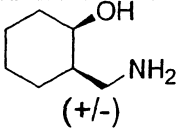
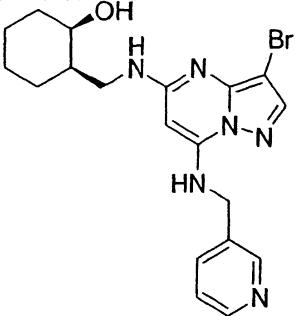
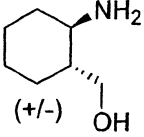
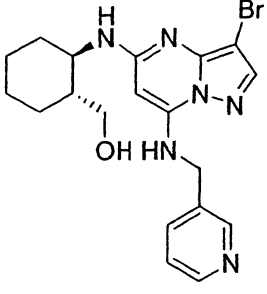
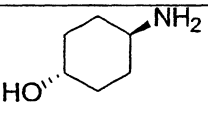
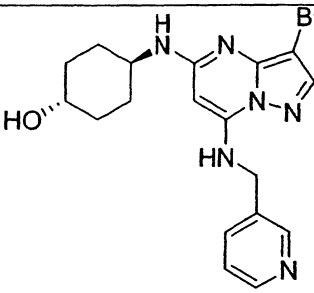
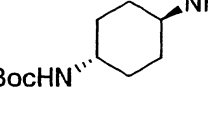
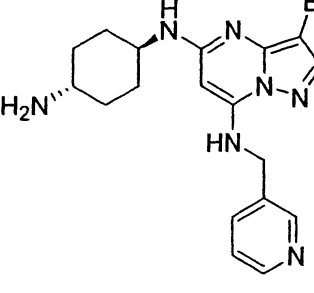
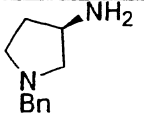
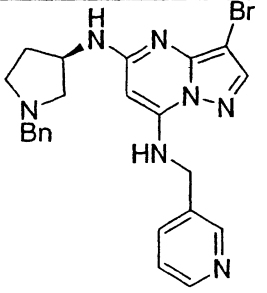
346		HCl		MS: $MH^+ = 363$ m.p. 170 – 171 °C
347		HCl		MS: $MH^+ = 407$ m.p. 148 – 151 °C
348		HCl		MS: $MH^+ = 435$ m.p. 56 – 59 °C
349		HCl		MS: $MH^+ = 445$ m.p. 66 – 68 °C

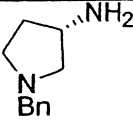
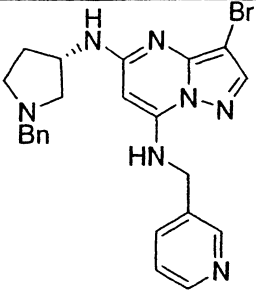
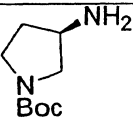
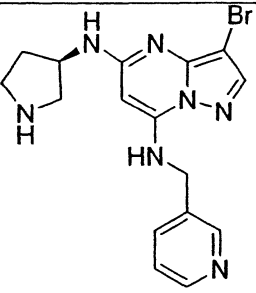
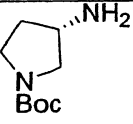
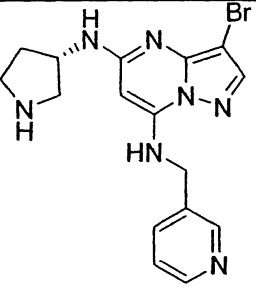
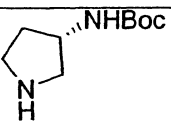
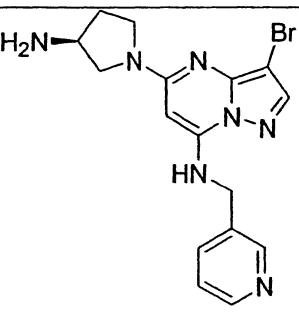
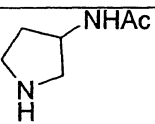
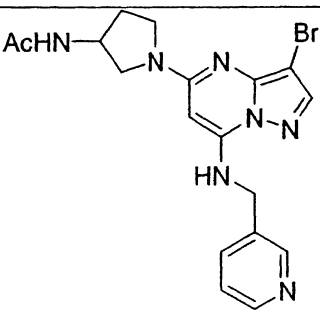
350		KOH		MS: MH^+ = 417 m.p. 149 – 151 °C
351		KOH		MS: MH^+ = 431 m.p. 111 – 114 °C
352		KOH		MS: MH^+ = 417 m.p. 53 – 58 °C
353		KOH		MS: MH^+ = 456 m.p. 186 – 189 °C

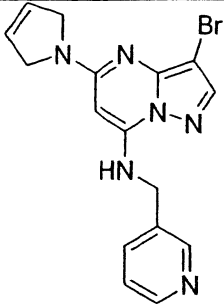
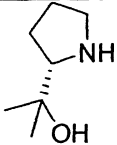
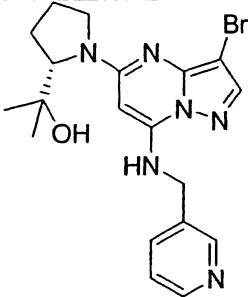
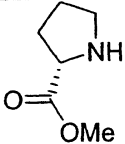
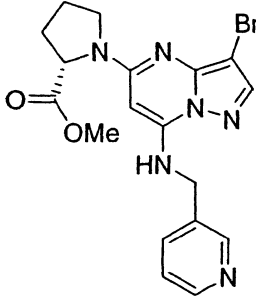
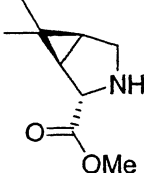
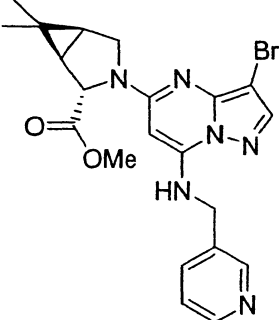
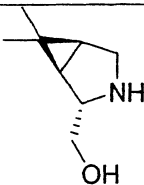
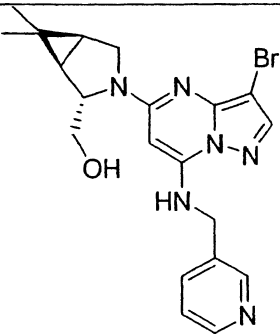
354		KOH		MS: $MH^+ = 416$ m.p. 210 – 213 °C
355		TFA		1. mp = 68-70 2. $M+H = 494$
356		KOH		1. mp = 181-183 2. $M+H = 404$
357		TFA		1. mp = 69-71 2. $M+H = 494$
358		KOH		1. mp = 182-184 2. $M+H = 404$

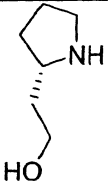
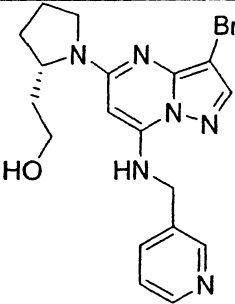
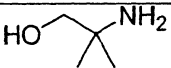
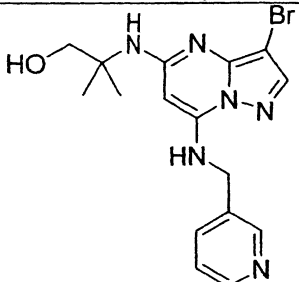
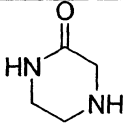
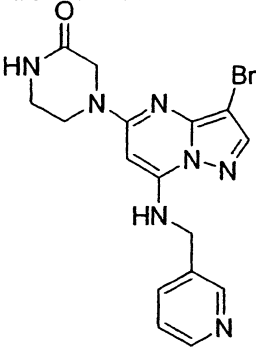
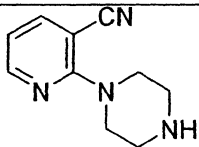
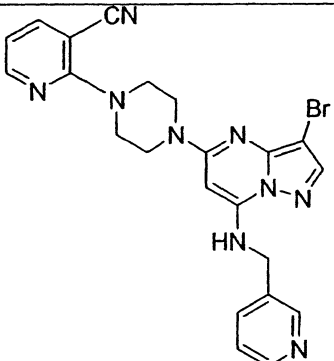
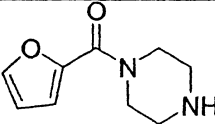
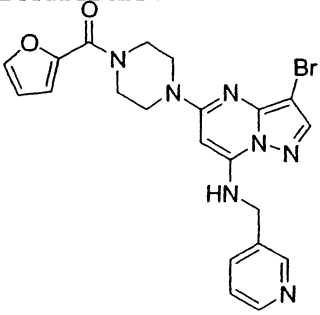
359		KOH		1. mp = 202-204 2. M+H = 418
360		TFA		1. mp = 160-162 2. M+H = 402
361		TFA		1. mp = 151-153 2. M+H = 416
362		KOH		1. mp = 140-143 2. M+H = 418
363		KOH		1. mp = 139-142 2. M+H = 418

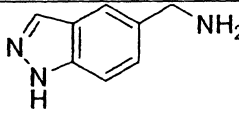
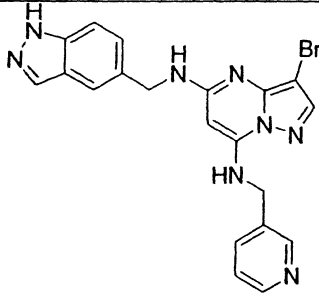
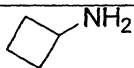
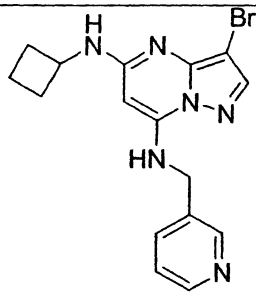
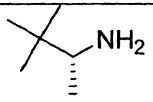
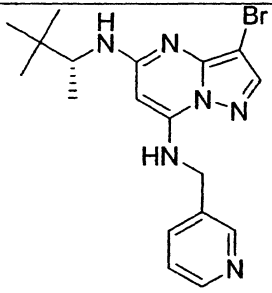
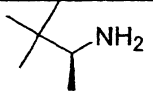
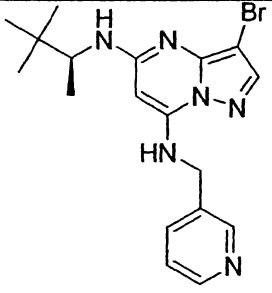
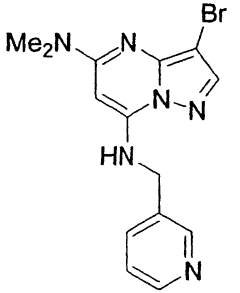
364	 (+/-)	KOH		1. mp = 115-117 2. M+H = 418
366	 (+/-)	TFA		1. mp = 102-104 2. M+H = 445
367	 (+/-)	TFA		1. mp = 118-120 2. M+H = 474
368	 (+/-)	TFA		1. mp = 106-108 2. M+H = 474
369		TFA		1. mp = 160-161 2. M+H = 464

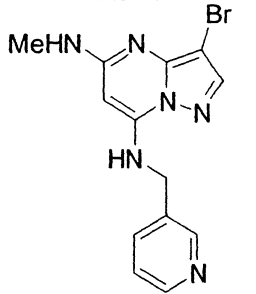
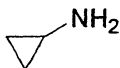
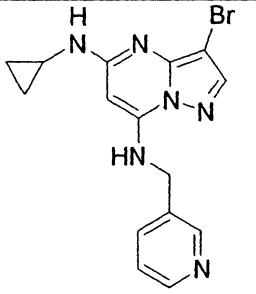
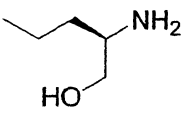
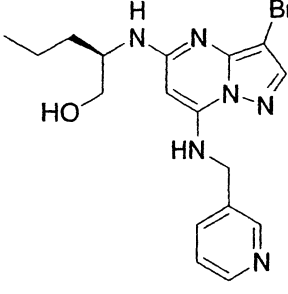
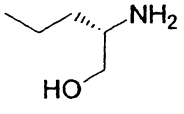
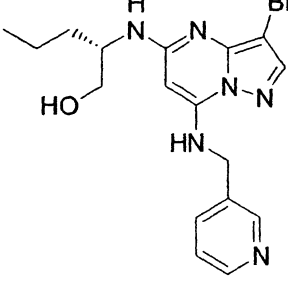
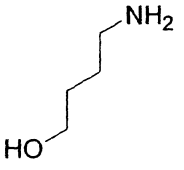
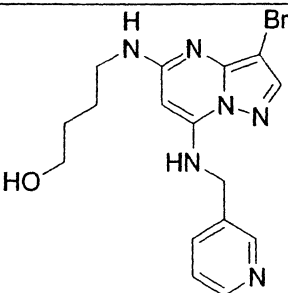
370	 (+/-)	TFA		1. mp = 93-95 2. M+H = 432
371	 (+/-)	KOH		1. mp = 108-110 2. M+H = 432
372		KOH		1. mp = 180-182 2. M+H = 418
373	 BocHN	TFA		1. mp = 169-170 2. M+H = 417
374		TFA		1. mp = 77-79 2. M+H = 479

375		TFA		1. mp = 76-79 2. M+H = 479
376		TFA		1. mp = 105-107 2. M+H = 389
377		TFA		1. mp = 105-107 2. M+H = 389
378		TFA		1. mp = 130-133 2. M+H = 389
379		TFA		1. mp = 132-135 2. M+H = 431

380		TFA		1. mp = 135-137 2. M+H = 372
381		KOH		1. mp = 78-82 2. M+H = 432
382		TFA		1. mp = 101-103 2. M+H = 432
383		TFA		1. mp = 92-95 2. M+H = 472
384		TFA		1. mp = 107-111 2. M+H = 444

384. 10		TFA		1. mp = 2. M+H = 417
384. 11		TFA		1. mp = 210-212 2. M+H = 391
385		TFA		1. mp = 122-124 2. M+H = 403
386		TFA		1. mp = 186-188 2. M+H = 491
387		TFA		1. mp = 173-175 2. M+H = 483

388		TFA		1. mp = 167-169 2. M+H = 450
389		TFA		1. mp = 90-92 2. M+H = 374
390		TFA		1. mp = 113-115 2. M+H = 404
391		TFA		1. mp = 114-116 2. M+H = 404
392	HNMe ₂	TFA		LCMS: MH ⁺ = 347;

393	<chem>H2NMe</chem>	TFA		LCMS: $MH^+ = 333$;
394		TFA		LCMS: $MH^+ = 359$;
395		TFA		LCMS: $MH^+ = 405$;
396		TFA		LCMS: $MH^+ = 405$;
397		TFA		LCMS: $MH^+ = 391$;

選用實例之額外數據列於下列：

實例 392: ^1H NMR (DMSO-d_6) δ 8.65 (s, 1H), 8.46 (d, $J=3.3$ Hz, 1H), 8.21 (t, $J=6.6$ Hz, 1H), 7.90 (s, 1H), 7.80 (d, $J=7.8$ Hz, 1H), 7.35 (dd, $J=7.8, 4.8$ Hz, 1H), 5.46 (s, 1H), 4.61 (d, $J=6.9$ Hz, 2H), 3.01 (s, 6H)。

實例 393: ^1H NMR (CDCl_3) δ 8.65 (s, 1H), 8.60 (d, $J=4.8$ Hz, 1H), 7.76 (s, 1H), 7.70 (m, 1H), 7.32 (dd, $J=8.1, 4.8$ Hz, 1H), 6.43 (t, $J=6.0$ Hz, 1H), 5.08 (s, 1H), 4.80 (m, 1H), 4.56 (d, $J=6.0$ Hz, 2H), 2.96 (d, $J=5.1$ Hz, 3H)。

實例 394: ^1H NMR (CDCl_3) δ 8.68 (s, 1H), 8.60 (d, $J=4.8$ Hz, 1H), 7.76 (s, 1H), 7.72 (m, 1H), 7.32 (dd, $J=7.8, 5.4$ Hz, 1H), 6.55 (t, $J=5.7$ Hz, 1H), 5.53 (s, 1H), 5.35 (s, 1H), 4.62 (d, $J=5.7$ Hz, 2H), 2.49 (m, 1H), 0.75 (m, 2H), 0.51 (m, 2H)。

實例 395: ^1H NMR (CDCl_3) δ 8.65 (s, 1H), 8.60 (d, $J=4.0$ Hz, 1H), 7.75 (s, 1H), 7.69 (m, 1H), 7.33 (dd, $J=8.1, 5.1$ Hz, 1H), 6.45 (t, $J=6.0$ Hz, 1H), 5.07 (s, 1H), 4.69 (m, 1H), 4.54 (d, $J=6.0$ Hz, 2H), 3.98 (m, 1H), 3.79 (dd, $J=10.8, 2.4$ Hz, 1H), 3.59 (dd, $J=11.1, 7.2$ Hz, 1H), 1.59-1.36 (m, 4H), 0.94 (t, $J=6.9$ Hz, 3H)。

實例 396: ^1H NMR (CDCl_3) δ 8.60 (s, 1H), 8.56 (d, $J=4.2$ Hz, 1H), 7.73 (s, 1H), 7.66 (m, 1H), 7.31 (dd, $J=7.8, 4.8$ Hz, 1H), 6.51 (t, $J=6.0$ Hz, 1H), 5.05 (s, 1H), 4.86 (d, $J=6.6$ Hz, 1H), 4.50 (d, $J=6.0$ Hz, 2H), 3.94 (m, 1H), 3.78 (dd, $J=11.1, 2.4$ Hz, 1H), 3.57 (dd, $J=11.1, 7.2$ Hz, 1H), 1.57-1.34 (m, 4H), 0.91 (t,

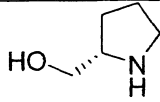
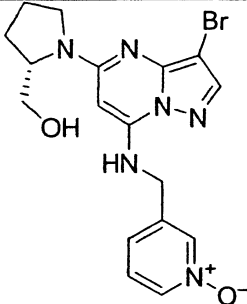
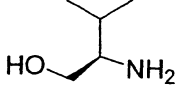
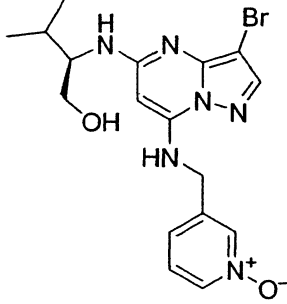
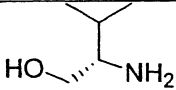
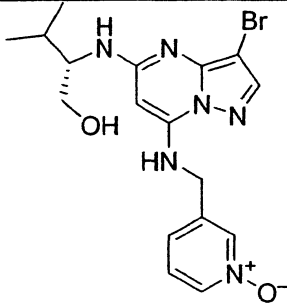
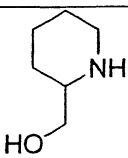
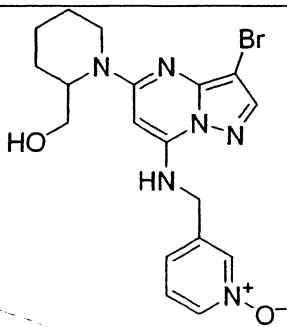
J=7.2 Hz, 3H)。

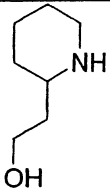
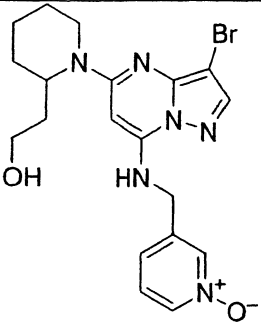
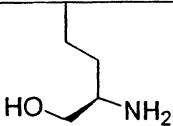
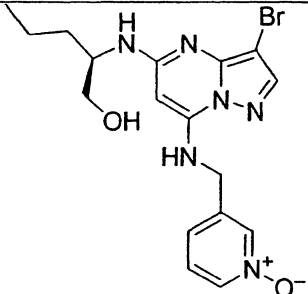
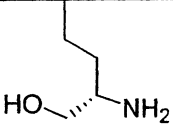
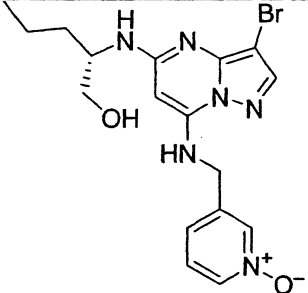
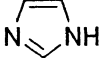
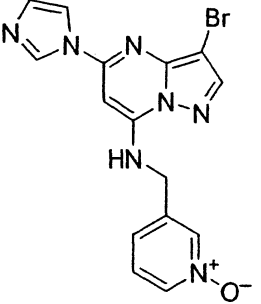
實例 397: ^1H NMR (CDCl_3) δ 8.65 (s, 1H), 8.59 (d, J=4.5 Hz, 1H), 7.75 (s, 1H), 7.69 (m, 1H), 7.31 (m, 1H), 6.43 (t, J=6.0 Hz, 1H), 5.06 (s, 1H), 4.88 (m, 1H), 4.55 (d, J=6.0 Hz, 2H), 3.70 (m, 2H), 3.38 (m, 2H), 1.79-1.61 (m, 4H)。

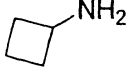
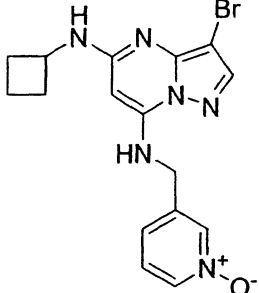
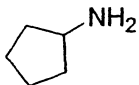
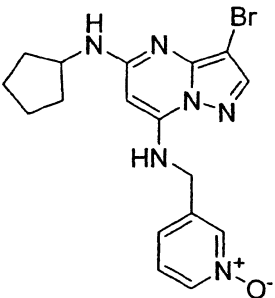
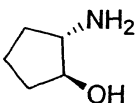
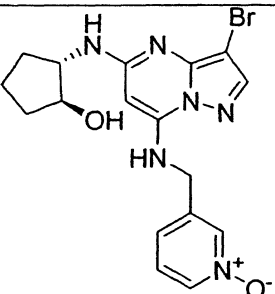
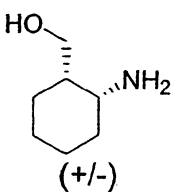
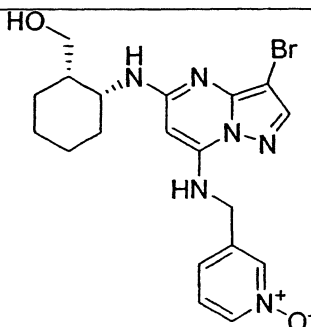
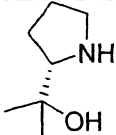
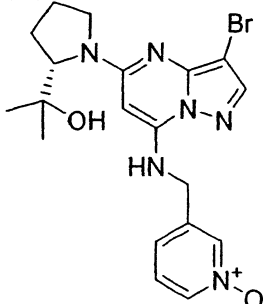
實例 398-416：

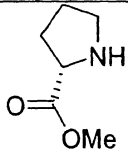
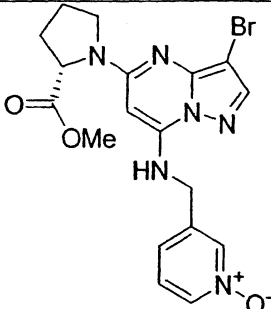
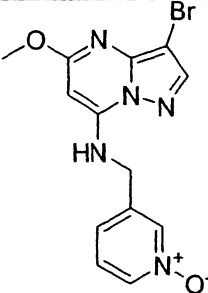
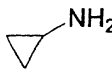
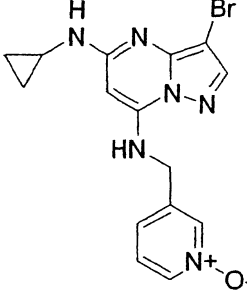
與實例 341 步驟 A 及 B 相同之程序，僅替代製備例 193.10 中製備之化合物，製備表 32 欄 4 之化合物。

表 32

實例	欄2	欄3	欄4	數據
398				MS: MH ⁺ = 419 m.p. 102 – 105 °C
399				MS: MH ⁺ = 421 m.p. 79 – 81 °C
400				MS: MH ⁺ = 421 m.p. 78 – 79 °C
401				MS: MH ⁺ = 433 m.p. 228-231 °C

402				MS: $MH^+ = 447$ m.p. 97-102 °C
403				MS: $MH^+ = 421$ m.p. °C
404				MS: $MH^+ = 421$ m.p. °C
405				MS: $MH^+ = 386$ m.p. °C

407		KOH		1. mp = 98-100 2. M+H = 390
408		TFA		1. mp = 170-173 2. M+H = 404
409		KOH		1. mp = 219-221 2. M+H = 420
410		KOH		1. mp = 110-112 2. M+H = 448
411		TFA		1. mp = 81-83 2. M+H = 448

412		TFA		1. mp = 136-138 2. M+H = 448
413	NaOMe	KOH		1. mp = 107-110 2. M+H = 351
414				LCMS: MH ⁺ = 375;

選用實例之額外數據列於下列：

實例 414: ¹H NMR (DMSO-d₆)δ 8.26 (s, 1H), 8.23 (m, 1H), 8.13 (m, 1H), 7.90 (s, 1H), 7.40-7.27 (m, 3H), 5.34 (s, 1H), 4.49 (d, J=6.3 Hz, 2H), 2.56 (m, 1H), 0.67 (m, 2H), 0.35 (m, 2H)。

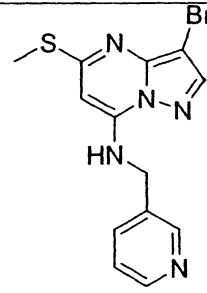
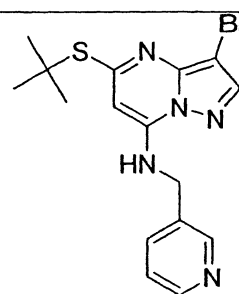
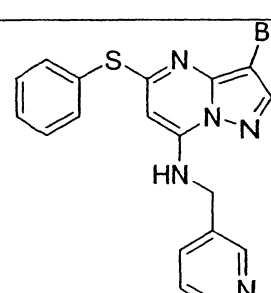
實例 403: ¹H NMR (DMSO-d₆+CDCl₃)δ 8.08 (s, 1H), 7.90 (d, J=6.3 Hz, 1H), 7.49 (s, 1H), 7.34 (t, J=6.3 Hz, 1H), 7.16-7.09 (m, 2H), 5.65 (d, J=6.6 Hz, 1H), 4.97 (s, 1H), 4.90 (s, 1H), 4.29 (d, J=6.3 Hz, 2H), 3.70 (m, 1H), 3.46 (m, 1H), 3.34 (m, 1H), 1.35-1.17 (m, 4H), 0.71 (t, J=7.2 Hz, 3H)。

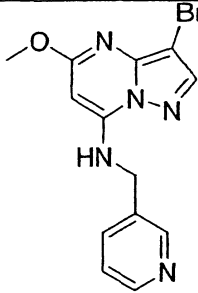
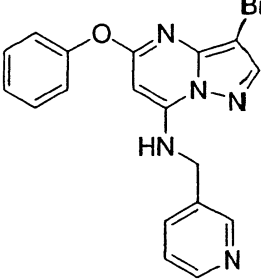
實例 404: ^1H NMR (DMSO- d_6) δ 8.21 (s, 1H), 8.12 (d, $J=6.6$ Hz, 1H), 8.06 (m, 1H), 7.86 (s, 1H), 7.38 (t, $J=7.8$ Hz, 1H), 7.30 (d, $J=7.5$ Hz, 1H), 6.73 (d, $J=8.7$ Hz, 1H), 5.28 (s, 1H), 4.70 (t, $J=5.1$ Hz, 1H), 4.41 (d, $J=6.6$ Hz, 2H), 4.00 (s, 1H), 3.39 (m, 1H), 1.53 (m, 1H), 1.36-1.25 (m, 3H), 0.86 (t, $J=7.0$ Hz, 3H)。

實例 417-421：

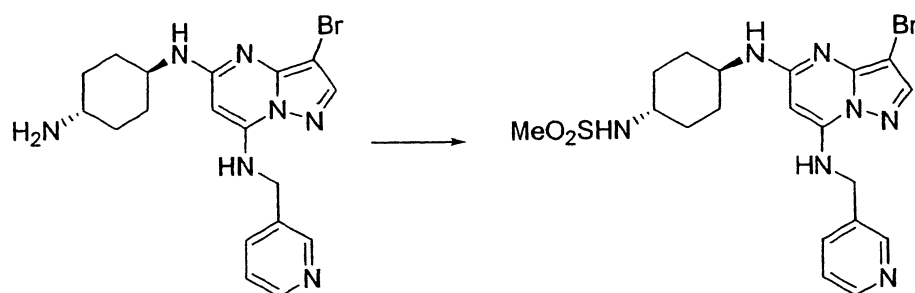
藉由 Chem. Pharm. Bull. 1999, 47, 928-938 中所列之程序，使用如表 33 所述欄 2 所示之氧或硫親核基，且使用表 33 欄 3 所用之斷鏈方法，製備表 33 欄 4 之化合物。

表 33

實例	欄2 (親核基)	欄3 (斷鏈方法)	欄4 (最終結構)	數據 1. mp. 2. M+H
417	NaSMe	TFA		1. mp = 172-175 2. M+H = 351
418	NaSt-Bu	TFA		1. mp = 165-168 2. M+H = 392
419	NaSPh	TFA		1. mp = 154-156 2. M+H = 412
420	NaOMe	TFA		1. mp = 161-163 2. M+H = 335

				
421	NaOPh	TFA		1. mp = 64-66 2. M+H = 397

實例 422：



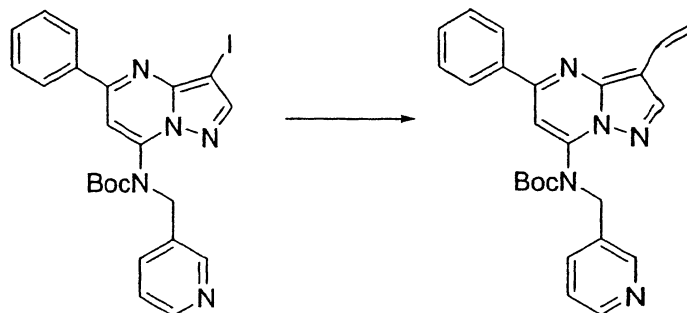
在室溫下，於含實例 373 之胺基化合物 (18 毫克，0.043 毫莫耳) 之 CH_2Cl_2 (1 毫升) 溶液中添加 DIPEA (10 微升，0.056 毫莫耳)，接著添加 MeSO_2Cl (4 毫升，0.052 毫莫耳)。混合物於室溫攪拌 12 小時且以 CH_2Cl_2 (2 毫升) 及飽和 NaHCO_3 水溶液 (2 毫升) 稀釋。使層分離且以食鹽水 (1x2 毫升) 萃取有機層。有機層經脫水 (Na_2SO_4)、過濾且減壓濃縮。粗物質以製備性薄層層析 (4x1000 μM) 經 $\text{CH}_2\text{Cl}_2/\text{MeOH}$ (20:1) 溶離純化，獲得 16 毫克 (75%) 白色固體。mp 152-154°C；M+H = 495。

實例 423-424：

利用實例 422 中所列之程序，使表 34 之胺基化合物 (欄 2) 轉化成對應之甲烷磺醯胺 (欄 3)。

表 34

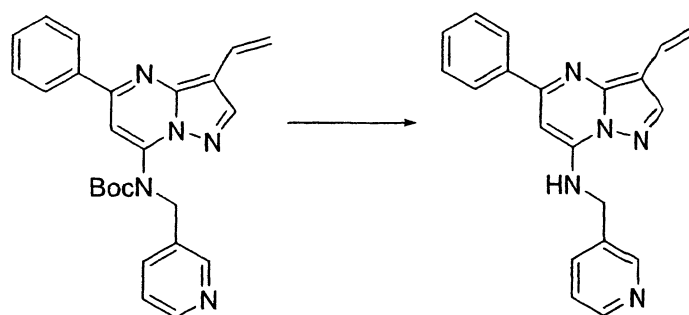
實例	欄2 (胺)	欄3 (最終結構)	數據 1. mp. 2. M+H
423			1. mp = 166-168 2. M+H = 467
424			1. mp = 165-168 2. M+H = 467

實例 425：步驟 A：

使製備例 194 之化合物 (132 毫克，0.25 毫莫耳)、三丁基乙

烯基錫(95毫克, 0.30毫莫耳)及肆(三苯膦)鈀(29毫克, 0.025毫莫耳)之無水二噁烷(5毫升)混合物在 N_2 下回流24小時。蒸發溶劑並藉快速層析使用2:1 CH_2Cl_2 :EtOAc作為溶離液純化, 獲得黃色蠟狀固體(53毫克, 50%)。LCMS: $MH^+=428$ 。

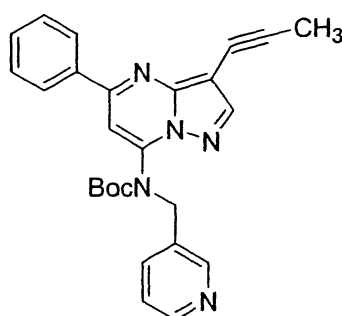
步驟 B:



使含實例425步驟A中製備之化合物(50毫克, 0.12毫莫耳)及KOH(100毫克, 1.80毫莫耳)之乙醇(3毫升)及 H_2O (0.6毫升)混合物在 N_2 中及 $70^\circ C$ 攪拌24小時。添加 $NaHCO_3$ (1.0克)、 Na_2SO_4 (2.0克)及 CH_2Cl_2 (20毫升), 搖晃混合物再過濾。蒸發溶劑, 殘留物以快速層析使用20:1:0.1之 CH_2Cl_2 :甲醇:濃 NH_4OH 作為溶離液純化, 獲得黃色蠟狀固體(17毫克, 45%)。LCMS: $MH^+=328$ 。Mp= $48-51^\circ C$ 。

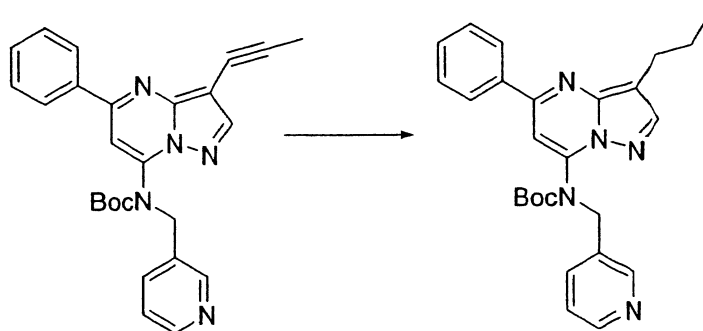
實例 426:

步驟 A:



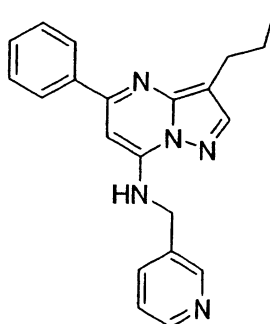
以基本上與實例425步驟A中所示相同之程序，但使用三丁基甲基乙炔基錫，製備上述化合物。

步驟 B：



在1大氣壓之 H_2 中使含實例426步驟A中製備之化合物(150毫克，0.34毫莫耳)及 PtO_2 (30毫克，0.13毫莫耳)之冰醋酸(5毫升)混合物攪拌20小時。混合物經過濾，添加新鮮 PtO_2 (30毫克，0.13毫莫耳)，且使混合物在1大氣壓 H_2 下攪拌2.5小時。將混合物倒入 Na_2CO_3 (20克)及 H_2O (200毫升)中，且以 CH_2Cl_2 (4x20毫升)萃取。合併之萃取液以 Na_2SO_4 脫水且過濾。蒸發溶劑，殘留物以快速層析使用1:1 CH_2Cl_2 :EtOAc作為溶離液純化，獲得黃色蠟狀固體(68毫克，45%)。

步驟 C：

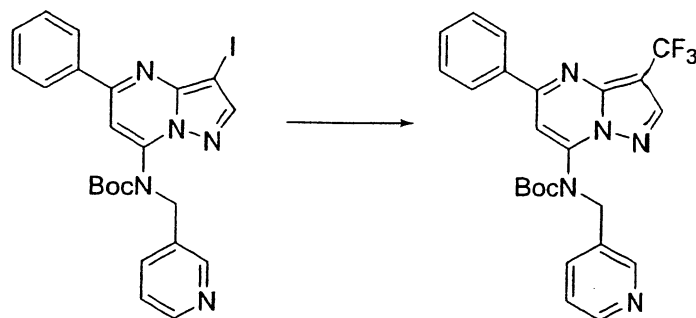


以基本上與實例425步驟B中所示相同程序，但以實例426步驟B中製備之化合物取代，製備上述化合物。MS: MH^+ =

344。 Mp=110-112℃。

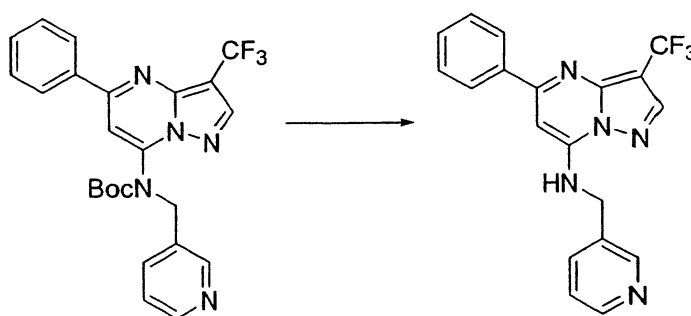
實例 427：

步驟 A：



在 80℃ 下於密封壓力容器中攪拌含製備例 194 製備之化合物 (527 毫克，1.00 毫莫耳)、三乙基(三氟甲基)矽烷 (666 毫克，3.60 毫莫耳)、氟化鉀 (210 毫克，3.60 毫莫耳) 及 CuI (850 毫克，4.46 毫莫耳) 之無水 DMF (4 毫升) 混合物 72 小時。添加 CH₂Cl₂ (80 毫升) 且使混合物經矽藻土過濾。蒸發溶劑，殘留物以快速層析使用 2:1 CH₂Cl₂ : EtOAc 作為溶離液純化，獲得淡橘色蠟狀固體 (70 毫克，15%)。LCMS: M⁺=470。

步驟 B：

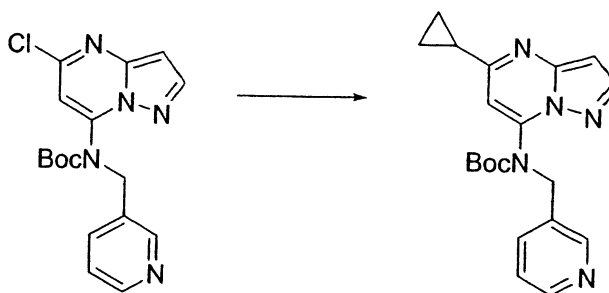


在 0℃ 及氮氣下，將 TFA (0.70 毫升) 添加於含實例 427 步驟 A 製備之化合物 (70 毫克，0.15 毫莫耳) 之無水 CH₂Cl₂ (3 毫升) 攪拌溶液中。使混合物在 0℃ 攪拌 10 分鐘，接著在 25℃ 攪拌

2 小時。將其倒入 10% Na_2CO_3 水溶液 (50 毫升) 中，以 CH_2Cl_2 (3x15 毫升) 萃取，以 Na_2SO_4 脫水且過濾。蒸發溶劑，殘留物以快速層析使用 EtOAc 作為溶離液純化，獲得灰白色固體 (40 毫克，73%)。LCMS: $M^+ = 370$ 。Mp = 156-158°C。

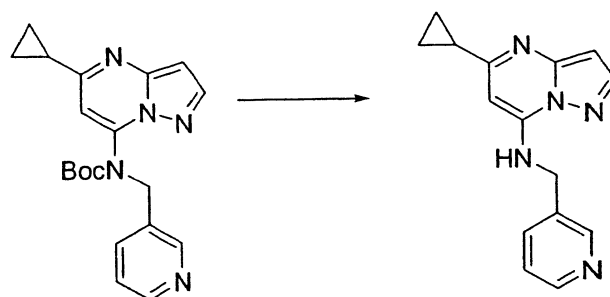
實例 428：

步驟 A：



在 N_2 中使含製備例 193 製備之化合物 (100 毫克，0.28 毫莫耳)、四環丙基錫 (91 毫克，0.32 毫莫耳)、 Pd_2dba_3 (8.0 毫克，0.009 毫莫耳) 及 $\text{Pd}(\text{Pt-Bu}_3)_2$ (9.0 毫克，0.017 毫莫耳) 之無水二噁烷 (3 毫升) 混合物回流 27 小時。蒸發溶劑，殘留物以快速層析使用 1:1 CH_2Cl_2 : EtOAc 作為溶離液純化，獲得無色蠟狀固體 (38 毫克，38%)。LCMS: $\text{MH}^+ = 366$ 。

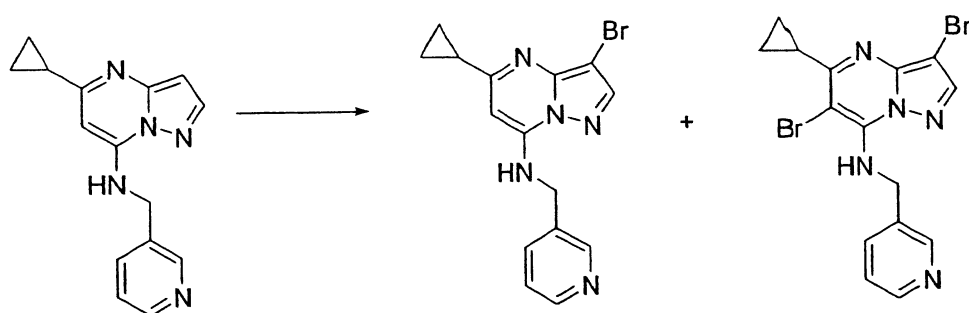
步驟 B：



使含實例 428 步驟 A 製備之化合物 (36 毫克，0.10 毫莫耳) 及 KOH (300 毫克，5.40 毫莫耳) 之乙醇 (3 毫升)、1,2-二甲氧

基乙烷(3.0毫升)及H₂O(0.8毫升)之混合物在N₂下回流4小時。將其倒入飽和NaHCO₃水溶液(100毫升)中，以CH₂Cl₂(5x10毫升)萃取，以Na₂SO₄脫水且過濾。蒸發溶劑，殘留物以快速層析使用30:1 EtOAc:MeOH作為溶離液純化，獲得無色蠟狀物(18毫克，69%)。LCMS: MH⁺=266。

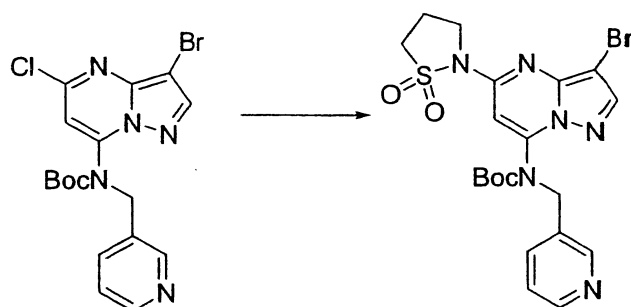
步驟 C：



在N₂中將含N-溴丁二醯亞胺(12毫克，0.068毫莫耳)之無水CH₃CN(2毫升)添加於含實例428步驟B製備之化合物(18毫克，0.068毫莫耳)之無水CH₃CN(2毫升)攪拌溶液中。混合物在25℃攪拌2小時。蒸發溶劑，殘留物以快速層析使用EtOAc作為溶離液純化，獲得5毫克(17%)二溴化合物(白色固體，LCMS: MH⁺=370, mp= 150-152°C)及8毫克(34%)單溴化合物(無色固體，LCMS: M⁺=344, mp=196-198°C)。

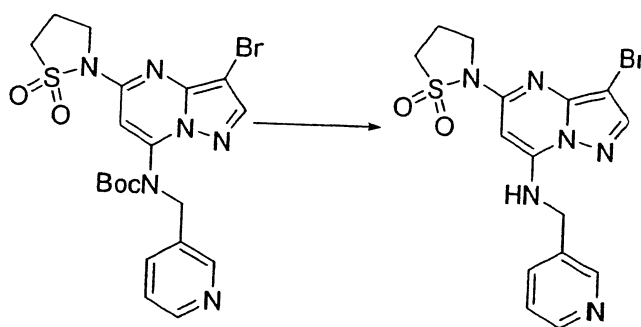
實例 429：

步驟 A：



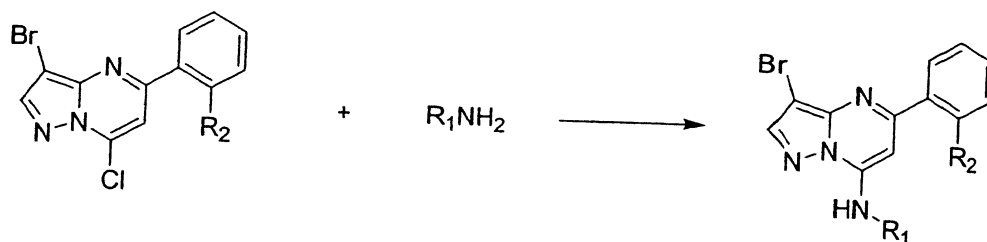
在 N_2 下將含1,3-丙烷萘迫磺內鹽胺(72毫克, 0.60毫莫耳)之無水DMF(3毫升)添加於60%NaH之礦物油(36毫克, 0.90毫莫耳)中。混合物攪拌20分鐘, 接著添加製備例196製備之化合物(200毫克, 0.46毫莫耳)。使混合物在 100°C 攪拌30分鐘, 蒸發溶劑, 殘留物以快速層析使用EtOAc作為溶離液純化, 獲得無色固體(150毫克, 63%)。LCMS: $M^+=523$ 。

步驟B:



在 0°C 及 N_2 中, 將TFA(1.5毫升)添加於含製備例196製備之化合物(140毫克, 0.27毫莫耳)之無水 CH_2Cl_2 (5毫升)攪拌溶液中。混合物在 0°C 攪拌10分鐘, 接著在 25°C 攪拌2小時。將其倒入 Na_2CO_3 (10克)中, 以 CH_2Cl_2 (3x50毫升)萃取且過濾。蒸發溶劑, 殘留物以快速層析使用40:1 EtOAc:MeOH作為溶離液純化, 獲得白色固體(32毫克, 28%)。LCMS: $M^+=423$ 。Mp= $218-220^\circ\text{C}$ 。

實例430:

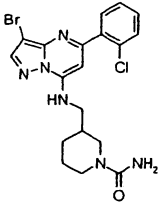
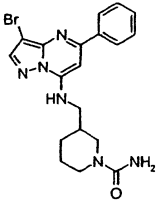
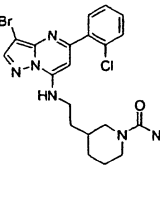
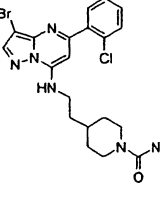
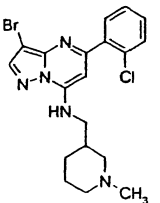


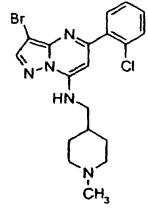
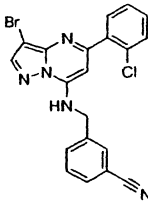
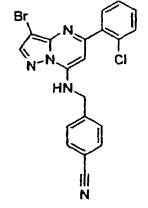
其中: $R_2 = \text{H}$ 或 Cl

將 3-溴-7-氯-5-(2-氯苯基)吡唑并[1,5-a]嘧啶(1當量)(如製備例129所述般製備)或 3-溴-7-氯-5-苯基吡唑并[1,5-a]嘧啶(1當量)(如製備例127所述般製備)、 R_1NH_2 (1.2當量)及二異丙基乙胺(2當量)溶於無水1,4-二噁烷中，且使混合物在75°C加熱表97中所列之時間。蒸發溶液至乾，殘留物在如表97所述之矽膠管柱上層析，獲得標題化合物。

使用適當之反應物且基本上如上述相同之程序，製備實例431至438之產物。反應條件之改變列於表35。

表 35

實例	結構	MW	FABMS MH ⁺	反應條件	產率	層析數據
431		463.8	463.0	75°C / 26h	52%	15x2.5cm 0.5-2% (10% 濃氫氧化 銨之甲醇) -二氯甲烷
432		429.3	429.2	75°C / 26h 25°C / 39h	53%	15x5cm 二氯甲烷; 1.5% (10% 濃氫氧化 銨之甲醇) -二氯甲烷
433		477.8	477.1	75°C / 26h	48%	15x5cm 二氯甲烷; 3.5-15% (10% 濃氫氧化 銨之甲醇) -二氯甲烷
434		477.8	477.0	75°C / 26h	50%	15x5cm 二氯甲烷; 3.5-15% (10% 濃氫氧化 銨之甲醇) -二氯甲烷
435		434.8	434.1	75°C / 24h 25°C / 65h	53%	15x2.5cm 3% (10% 濃氫氧化 銨之甲醇) -二氯甲烷
436		434.8	434.2	75°C / 27h	31%	15x2.5cm 3% (10% 濃氫氧化 銨之甲醇) -二氯甲烷

						
437		438.7	438.1	75°C / 21h 25°C / 46h	97%	15x2.5cm 0.25% (10% 濃氫氧化 銨之甲醇) -二氯甲烷
438		438.7	438.1	75°C / 28h -20°C / 72h	95%	60x2.5cm 20%乙酸乙 酯之己烷

化合物之額外物理數據列於下：

實例 431：反應物：3-溴-7-氯-5-(2-氯苯基)吡唑并[1,5-a]嘧啶(110毫克，0.318毫莫耳)(如製備例129所述般製備)；3-(胺基甲基)哌啶-1-羧醯胺(60毫克，0.382毫莫耳)(如上述製備例241所述般製備)；二異丙基乙胺(0.111毫升，0.636毫莫耳)；無水1,4-二噁烷(2.5毫升)。物理性質：HRFABMS: m/z 463.0628(MH⁺)。對C₁₉H₂₁N₆OBrCl之計算值：m/z 463.0649: δ_H (CDCl₃) 1.38 (1H, m, CH₂), 1.52 (1H, m, CH₂), 1.73 (1H, m, CH), 1.93 (1H, m, CH₂), 2.02 (1H, m, CH₂), 2.98 (1H, m, CH₂), 3.06 (1H, m, CH₂), 3.37 (2H, m, CH₂), 3.58 (1H, m, CH₂), 3.82 (1H, m, CH₂), 4.87 (2H, bm, CONH₂), 6.28 (1H, s, H₆), 7.02

(1H, m, NH), 7.36 (2H, m, Ar-H), 7.45 (1H, m, Ar-H), 7.68 (1H, m, Ar-H)及8.00 ppm (1H, s, H₂); δ_c (CDCl₃) CH₂: 23.7, 28.1 44.6, 45.5, 47.2; CH: 35.2, 87.4, 127.2, 130.1, 130.3, 131.6, 143.9; C: 83.1, 132.1, 138.6, 145.5, 146.5, 158.0, 158.4。

實例432：反應物：3-溴-7-氯-5-苯基吡啶并[1,5-a]嘧啶(500毫克，1.62毫莫耳)(如製備例127所述般製備)；3-(胺基甲基)哌啶-1-羧醯胺(306毫克，1.944毫莫耳)(如上述製備例241所述般製備)；二異丙基乙胺(0.566毫升，3.24毫莫耳)；無水1,4-二噁烷(13毫升)。物理性質：HRFABMS: m/z 429.1031 (MH⁺)。對C₁₉H₂₂N₆OBr之計算值：m/z 429.1038; δ_H (CDCl₃) 1.44 (1H, m, CH₂), 1.59 (1H, m, CH₂), 1.79 (1H, m, CH), 2.01 (1H, m, CH₂), 2.08 (1H, m, CH₂), 3.03 (1H, m, CH₂), 3.13 (1H, m, CH₂), 3.39 (1H, m, CH₂), 3.47 (1H, m, CH₂), 3.63 (1H, m, CH₂), 3.90 (1H, m, CH₂), 4.88 (2H, bm, CONH₂), 6.40 (1H, s, H₆), 6.90 (1H, m, NH), 7.53 (2H, m, Ar-H), 8.02 (1H, s, H₂)及8.12 (1H, m, Ar-H); δ_c (CDCl₃) CH₂: 23.7, 28.2, 44.7, 45.5, 47.3; CH: 35.2, 82.9, 127.5, 127.5, 128.7, 128.7, 130.0, 143.9; C: 83.0, 138.5, 145.8, 147.1, 158.3, 158.5。

實例433：反應物：3-溴-7-氯-5-(2-氯苯基)吡啶并[1,5-a]嘧啶(347毫克，1.01毫莫耳)(如製備例129所述般製備)；3-(胺基乙基)哌啶-1-羧醯胺(208毫克，1.21毫莫耳)(如上述製備例242所述般製備)；二異丙基乙胺(0.393毫升，2.02毫莫耳)；無水1,4-二噁烷(9毫升)。物理性質： δ_H (CDCl₃) 1.24 (1H,

m, CH₂), 1.55 (1H, m, CH), 1.72 (4H, m, CH₂), 1.93 (1H, m, CH₂), 2.69 (1H, m, CH₂), 2.94 (1H, m, CH₂), 3.55 (2H, m, CH₂), 3.73 (1H, m, CH₂), 3.98 (1H, m, CH₂), 4.83 (2H, bm, CONH₂), 6.55 (1H, s, H₆), 6.78 (1H, m, NH), 7.41 (2H, m, Ar-H), 7.50 (1H, m, Ar-H), 7.75 (1H, m, Ar-H)及8.04 ppm (1H, s, H₂); δ_c (CDCl₃) CH₂: 24.6, 30.7, 32.6, 39.9, 45.3, 49.3; CH: 33.3, 87.5, 127.4, 130.1, 130.2, 131.6, 143.8; C: 83.2, 132.1, 138.8, 145.7, 146.2, 158.1, 158.1。

實例434：反應物：3-溴-7-氯-5-(2-氯苯基)吡唑并[1,5-a]嘧啶(275毫克，0.803毫莫耳)(如製備例129所述般製備)；4-(胺基乙基)哌啶-1-羧醯胺(165毫克，0.963毫莫耳)(如上述製備例243所述般製備)；二異丙基乙胺(0.311毫升，0.963毫莫耳)；無水1,4-二噁烷(7.2毫升)。物理性質： δ_H (d₆-DMSO) 1.00 (2H, m, CH₂), 1.50 (1H, m, CH), 1.59 (2H, m, CH₂), 1.67 (2H, m, CH₂), 2.60 (2H, m, CH₂), 3.48 (2H, m, CH₂), 3.70 (2H, m, CH₂), 5.84 (2H, bs, CONH₂), 6.43 (1H, s, H₆), 7.50 (2H, m, Ar-H), 7.62 (2H, m, Ar-H), 8.30 (1H, s, H₂)及8.36 ppm (1H, m, NH); δ_c (d₆-DMSO) CH₂: 31.5, 31.5, 34.8, 43.5, 43.5, 43.5; CH: 32.8, 86.8, 127.1, 129.7, 130.3, 131.0, 143.3; C: 81.3, 131.0, 138.7, 145.1, 146.4, 157.3, 157.8。

實例435：反應物：3-溴-7-氯-5-苯基吡唑并[1,5-a]嘧啶(174毫克，0.507毫莫耳)(如製備例129所述般製備)及3-(胺基甲基)-1-甲基哌啶(65毫克，0.507毫莫耳)(如上述製備例244所述般製備)；二異丙基乙胺(0.178毫升，1.014毫莫耳)；無水

1,4-二噁烷(2.5毫升)。物理性質：HRFABMS: m/z 434.0742 (MH^+)。對 $C_{19}H_{22}N_5BrCl$ 之計算值： m/z 434.0747; δ_H ($CDCl_3$) 1.18 (1H, m, CH_2), 1.68 (1H, m, CH_2), 1.80 (1H, m, CH_2), 1.87 (1H, m, CH_2), 1.96 (1H, m, CH), 2.14 (2H, m, CH_2), 2.32 (3H, s, NCH_3), 2.75 (1H, m, CH_2), 2.29 (1H, m, CH_2), 3.42 (2H, m, $-NHCH_2CH$), 6.36 (1H, s, H_6), 6.64 (1H, bm, NH), 7.41 (2H, m, Ar-H), 7.51 (1H, m, Ar-H), 7.74 (1H, m, Ar-H) 及 8.06 ppm (1H, s, H_2); δ_C ($CDCl_3$) CH_3 : 46.6; CH_2 : 24.4, 27.9, 46.1, 56.1, 59.6; CH: 36.0, 87.4, 127.1, 130.1, 130.2, 131.6, 143.8; C: 83.2, 132.1, 138.9, 145.6, 146.4, 158.2。

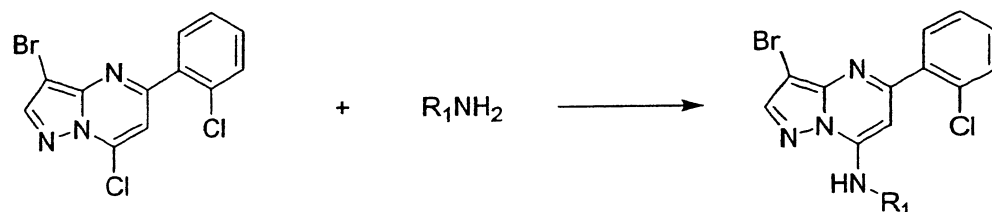
實例 436: 反應物: 3-溴-7-氯-5-苯基吡唑并[1,5-a]嘧啶(111.4 毫克, 0.325 毫莫耳)(如製備例 129 所述般製備); 4-(胺基甲基)-1-甲基哌啶(50 毫克, 0.39 毫莫耳)(如上述製備例 245 所述般製備); 二異丙基乙胺(0.1135 毫升, 0.65 毫莫耳); 無水 1,4-二噁烷(1.5 毫升)。物理數據: HRFABMS: m/z 434.0735 (MH^+)。對 $C_{19}H_{22}N_5BrCl$ 之計算值： m/z 434.0747; δ_H ($CDCl_3$) 1.42 (2H, m, CH_2), 1.72 (1H, m, CH), 1.82 (2H, m, CH_2), 1.93 (2H, m, CH_2), 2.20 (3H, s, NCH_3), 2.89 (2H, m, CH_2), 3.34 (2H, m, $-NHCH_2CH$), 6.31 (1H, s, H_6), 6.46 (1H, m, NH), 7.36 (2H, m, Ar-H), 7.46 (1H, m, Ar-H), 7.70 (1H, m, Ar-H) 及 8.00 ppm (1H, s, H_2); δ_C ($CDCl_3$) CH_3 : 46.4; CH_2 : 30.2, 30.2, 48.0, 55.3, 55.3; CH: 35.4, 87.5, 127.2, 130.2, 130.2, 131.6, 143.8; C: 83.3, 132.2, 138.9, 145.7, 146.4, 158.1。

實例 437: 反應物: 3-溴-7-氯-5-苯基吡唑并[1,5-a]嘧啶(191

毫克，0.557毫莫耳)(如製備例129所述般製備)；3-(胺基甲基)苄腈(88.3毫克，0.668毫莫耳)(如上述製備例246所述般製備)；二異丙基乙胺(0.192毫升，1.114毫莫耳)；無水1,4-二噁烷(4.5毫升)。物理數據：HRFABMS: m/z 438.0125 (MH^+)。對 $C_{19}H_{12}N_5BrCl$ 之計算值： m/z 438.0121； δ_H ($CDCl_3$) 4.76 (2H, d, $-CH_2NH-$), 6.32 (1H, s, H_6), 7.00 (1H, m, $-CH_2NH-$), 7.40 (2H, m, Ar-H), 7.46 (1H, m, Ar-H), 7.55 (1H, m, Ar-H), 7.67 (2H, m, Ar-H), 7.71 (1H, m, Ar-H), 7.75 (1H, m, Ar-H) 及 8.10 ppm (1H, s, H_2)； δ_C ($CDCl_3$) CH_2 : 45.5；CH: 88.2, 127.2, 130.0, 130.2, 130.4, 130.6, 131.4, 131.6, 131.9, 144.1；C: 83.8, 113.4, 118.3, 132.0, 137.8, 138.3, 145.6, 145.9, 158.0。

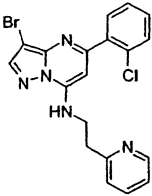
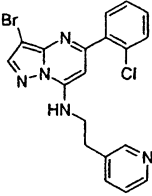
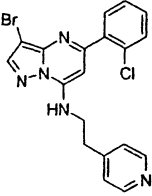
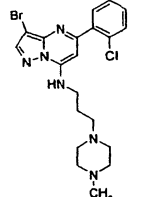
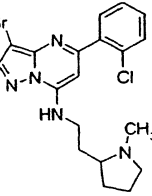
實例438：反應物：3-溴-7-氯-5-苯基吡啶并[1,5-a]嘧啶(233.5毫克，0.681毫莫耳)(如製備例129所述般製備)；4-(胺基甲基)苄腈(108毫克，0.817毫莫耳)(如上述製備例247所述般製備)；二異丙基乙胺(0.235毫升，1.362毫莫耳)；無水1,4-二噁烷(5.3毫升)。物理數據：HRFABMS: m/z 438.0117 (MH^+)。對 $C_{20}H_{14}N_5BrCl$ 之計算值： m/z 438.0121； δ_H ($CDCl_3$) 4.80 (2H, d, CH_2), 6.30 (1H, s, H_6), 7.01 (1H, m, NH), 7.40 (2H, m, Ar-H), 7.47 (1H, m, Ar-H), 7.70 (2H, m, Ar-H), 7.72 (2H, m, Ar-H), 7.80 (1H, m, Ar-H) 及 8.10 ppm (1H, s, H_2)； δ_C ($CDCl_3$) CH_2 : 45.8；CH: 88.2, 127.2, 127.7, 127.7, 130.2, 130.4, 131.6, 132.9, 132.9, 144.1；C: 83.8, 112.2, 118.4, 132.0, 138.2, 141.5, 145.5, 146.0, 158.0。

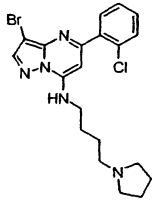
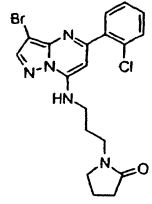
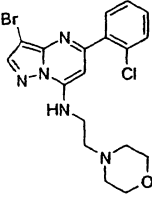
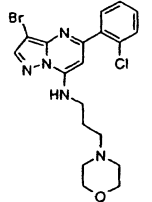
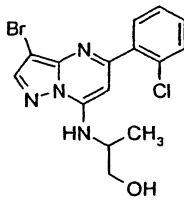
實例 439：



在 GeneVac 技術公司之旋轉反應管中，將 3-溴-7-氯-5-(2-氯苯基)吡唑并[1,5-a]嘧啶(50 毫克，0.146 毫莫耳)(如製備例 129 所述般製備)溶於無水 1,4-二噁烷(5 毫升)中。各管中添加 PS-二異丙基乙胺樹脂(161 毫克，0.5828 毫莫耳)。將新製備之含 1 M 適當胺 R_1NH_2 之無水 1,4-二噁烷溶液(0.2185 毫升，0.2185 毫莫耳)添加於各管中，將管密封，且於反應中之磁石攪拌下，在 70°C 加熱 78 小時。各管經過濾且以無水 1,4-二噁烷洗滌樹脂，再以二氯甲烷洗滌。合併各管之個別濾液蒸發至乾，且將殘留物分別再溶於無水 1,4-二噁烷(5 毫升)中，且置於 GeneVac 反應管中。各管中添加 PS-異氰酸酯樹脂(594 毫克，0.8742 毫莫耳)及 PS-參胺樹脂(129 毫克，0.4371 毫莫耳)，且使管於反應段上於 25°C 攪拌 20 小時。過濾樹脂且以無水 1,4-二噁烷及二氯甲烷洗滌。各管之濾液蒸發至乾，且將各殘留物在矽膠上使用表 36 所示之管柱尺寸及溶離液分別層析，獲得標題化合物。

表 36

實例	結構	MW	FABMS MH ⁺	產率	層析數據
440		428.7	428.0	81%	15x2.5cm 二氯甲烷; 0.5% 甲醇之 二氯甲烷
441		428.7	428.0	48%	20x2cm 二氯甲烷; 1.5% 甲醇之 二氯甲烷
442		428.7	428.0	24%	15x2.5cm 二氯甲烷; 1.5% 甲醇之 二氯甲烷
443		463.8	463.0	44%	15x2.2cm 二氯甲烷; 5% 甲醇之 二氯甲烷
444		434.8	434.1	63%	15x2.5cm 5% 甲醇之 二氯甲烷

445		448.8	448.2	65%	15x2.5cm 5% 甲醇之 二氯甲烷
446		448.8	448.1	40%	15x2.5cm 二氯甲烷; 0.5% 甲醇之 二氯甲烷
447		436.7	436.1	72%	15x2.5cm 0.5% 甲醇之 二氯甲烷
448		450.8	450.0	53%	20x2cm 二氯甲烷; 0.5% 甲醇之 二氯甲烷
449		381.7	381.0	44%	20x2cm 1.5% 甲醇之 二氯甲烷

化合物之額外物理數據列於下：

實例 440：物理性質：HRFABMS: m/z 428.0272(MH^+)。對 $C_{19}H_{16}N_5BrCl$ 之計算值： m/z 428.0278; δ_H ($CDCl_3$) 3.28 (2H, dd, $C_5H_4NCH_2CH_2NH-$), 3.94 (2H, ddd, $C_5H_4NCH_2CH_2NH-$), 6.40 (1H, s, H_6), 7.22-7.29 (3H, m, Ar-H), 7.38-7.44 (2H, m, Ar-H), 7.51 (1H, m, Ar-H), 7.68 (1H, ddd, Ar-H), 7.73 (1H, Ar-H), 8.18 (1H, s, H_2) 及 8.68 ppm (1H, NH); δ_C ($CDCl_3$) CH_2 : 36.4, 41.5; CH: 87.3, 122.1, 123.6, 127.1, 130.1, 130.1, 131.6, 137.0, 143.8, 149.5; C: 83.1, 132.1, 138.9, 145.7, 146.3, 158.0, 158.1。

實例 441：物理性質：HRFABMS: m/z 428.0272(MH^+)。對 $C_{19}H_{16}N_5BrCl$ 之計算值： m/z 428.0278; δ_H ($CDCl_3$) 3.12 (2H, dd, $C_5H_4NCH_2CH_2NH-$), 3.77 (2H, ddd, $C_5H_4NCH_2CH_2NH-$), 6.40 (1H, s, H_6), 6.59 (1H, m, Ar-H), 7.34 (1H, bm, Ar-H), 7.39-7.45 (2H, m, Ar-H), 7.52 (1H, m, Ar-H), 7.62 (1H, m, Ar-H), 7.75 (1H, m, Ar-H), 8.05 (1H, s, H_2) 及 8.63 ppm (1H, m, NH); δ_C ($CDCl_3$) CH_2 : 32.7, 43.1; CH: 87.5, 127.2, 130.2, 130.3, 131.6, 136.4, 142.9, 148.3, 149.8; C: 83.5, 132.0, 138.6, 145.6, 145.9, 158.1。

實例 442：物理性質：HRFABMS: m/z 428.0275(MH^+)。對 $C_{19}H_{16}N_5BrCl$ 之計算值： m/z 428.0278; δ_H ($CDCl_3$) 3.13 (2H, dd, $C_5H_4NCH_2CH_2NH-$), 3.80 (2H, ddd, $C_5H_4NCH_2CH_2NH-$), 6.42 (1H, s, H_6), 6.53 (1H, m, Ar-H), 7.23 (2H, m, Ar-H), 7.40-7.46 (2H, m, Ar-H), 7.62 (1H, m, Ar-H), 7.76 (1H, m,

Ar-H), 8.07 (1H, s, H₂)及8.63 ppm (1H, m, NH); δ_c (CDCl₃) CH₂: 34.7, 42.5; CH: 87.4, 124.5, 124.5, 127.2, 130.2, 130.3, 131.6, 144.0, 150.2, 150.2; C: 83.5, 132.0, 138.6, 145.6, 145.9, 146.6, 158.1。

實例443：物理性質：HRFABMS: m/z 463.1003(MH⁺)。對 C₂₀H₂₅N₆BrCl之計算值：m/z 463.1013; δ_H (CDCl₃) 1.98 (2H, m, =NCH₂CH₂NH-), 2.43 (3H, s, NCH₃), 2.67 (2H, m, =NCH₂CH₂NH-), 2.70 (8H, 哌啶CH₂), 3.58 (2H, m, =NCH₂CH₂NH-), 6.32 (1H, s, H₆), 7.37-7.43 (2H, m, Ar-H), 7.50 (1H, m, Ar-H), 7.73 (1H, m, Ar-H), 8.06 (1H, s, H₂)及8.60 ppm (1H, m, NH); δ_c (CDCl₃) CH₃: 46.1; CH₂: 24.1, 42.8, 53.3, 54.6, 54.6, 57.5, 57.5; CH: 87.1, 127.0, 130.0, 130.1, 131.5, 143.4; C: 82.7, 132.1, 139.2, 145.7, 146.7, 158.0。

實例444：物理性質：HRFABMS: m/z 434.0742(MH⁺)。對 C₁₉H₂₂N₅BrCl之計算值：m/z 434.0747; δ_H (CDCl₃) 1.72 (1H, m, CH/CH₂), 1.78-1.90 (2H, m, CH/CH₂), 2.02 (3H, m, CH/CH₂), 2.50 (1H, m, CH/CH₂), 2.45 (3H, s, NCH₃), 2.51 (1H, m, CH/CH₂), 3.23 (1H, m, CH/CH₂), 3.54 (1H, m, CH/CH₂), 3.60 (1H, m, CH/CH₂), 6.32 (1H, s, H₆), 7.38-7.44 (2H, m, Ar-H), 7.51 (1H, m, Ar-H), 7.75 (1H, m, Ar-H), 7.96 (1H, bm, NH)及8.05 ppm (1H, s, H₂); δ_c (CDCl₃) CH₃: 40.7; CH₂: 22.7, 29.3, 30.1, 39.4, 57.0; CH: 64.2, 87.1, 127.1, 130.0, 130.1, 131.6, 143.8; C: 82.8, 132.1, 139.1, 145.7, 146.4, 158.0。

實例445：物理性質：HRFABMS: m/z 448.0910(MH⁺)。對

$C_{20}H_{24}N_5BrCl$ 之計算值： m/z 448.0904; $\delta_H(CDCl_3)$ 1.90 (4H, m, CH_2), 2.00 (4H, m, CH_2), 2.84 (2H, m, CH_2), 2.95 (4H, m, CH_2), 3.51 (2H, m, CH_2), 6.32 (1H, s, H_6), 7.05 (1H, bm, NH), 7.37-7.43 (2H, m, Ar-H), 7.50 (1H, m, Ar-H), 7.73 (1H, m, Ar-H)及8.04 ppm (1H, s, H_2); $\delta_C(CDCl_3)$ CH_2 : 23.4, 23.4, 24.8, 26.4, 41.8, 53.9, 53.9, 55.2; CH: 87.3, 127.1, 130.1, 130.2, 131.6, 143.7; C: 83.0, 132.0, 138.9, 145.7, 146.3, 158.1。

實例446：物理性質：HRFABMS: m/z 448.0548(MH^+)。對 $C_{19}H_{20}N_5OBrCl$ 之計算值： m/z 448.0540; $\delta_H(CDCl_3)$ 1.94 (2H, m, CH_2), 2.09 (2H, m, CH_2), 2.49 (2H, m, CH_2), 3.45 (2H, m, CH_2), 3.51 (4H, m, CH_2), 6.32 (1H, s, H_6), 7.37-7.44 (3H, m, Ar-H/NH), 7.51 (1H, m, Ar-H), 7.75 (1H, m, Ar-H)及8.10 ppm (1H, s, H_2); $\delta_C(CDCl_3)$ CH_2 : 18.0, 26.3, 30.8, 39.2, 39.9, 47.5; CH: 87.0, 127.1, 130.1, 130.1, 131.6, 144.1; C: 82.9, 132.1, 138.9, 145.6, 146.2, 157.9, 176.2。

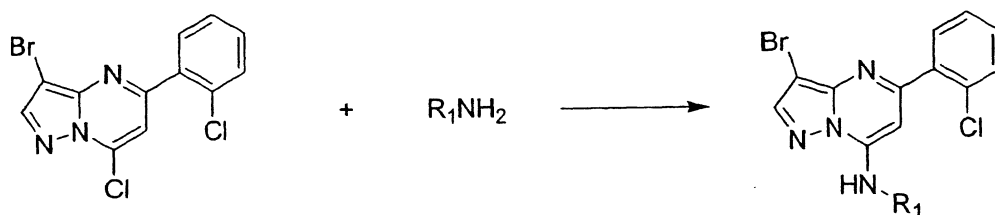
實例447：物理性質：HRFABMS: m/z 436.0532(MH^+)。對 $C_{18}H_{20}N_5OBrCl$ 之計算值： m/z 436.0540; $\delta_H(CDCl_3)$ 2.60 (4H, bm, $-N(\underline{CH_2CH_2})_2O$), 2.83 (2H, m, $=N\underline{CH_2CH_2}NH-$), 3.57 (2H, m, $=NCH_2\underline{CH_2}NH-$), 3.83 (4H, m, $-N(\underline{CH_2CH_2})_2O$), 6.37 (1H, s, H_6), 6.99 (1H, bm, NH), 7.38-7.45 (2H, m, Ar-H), 7.51 (1H, m, Ar-H), 7.75 (1H, m, Ar-H)及8.09 ppm (1H, s, H_2); $\delta_C(CDCl_3)$ CH_2 : 38.2, 53.3, 53.3, 56.2, 66.9, 66.9; CH: 87.6, 127.1, 130.1, 130.2, 131.6, 143.9; C: 83.1, 132.1, 138.9, 145.7, 146.2,

158.1。

實例 448：物理性質：HRFABMS: m/z 450.0688(MH^+)。對 $C_{19}H_{22}N_5OBrCl$ 之計算值： m/z 450.0696; δ_H ($CDCl_3$) 1.98 (2H, m, $=NCH_2CH_2CH_2NH-$), 2.58 (4H, m, $-N(CH_2CH_2)_2O$), 2.67 (2H, m, $=NCH_2CH_2CH_2NH-$), 3.59 (2H, m, $=NCH_2CH_2CH_2NH-$), 3.94 (4H, m, $-N(CH_2CH_2)_2O$), 6.31 (1H, s, H_6), 7.37-7.44 (2H, Ar-H), 7.51 (1H, m, Ar-H), 7.78 (1H, m, Ar-H), 8.08 (1H, s, H_2) 及 8.60 ppm (1H, bm, NH); δ_C ($CDCl_3$) CH_2 : 23.7, 42.7, 52.9, 52.9, 58.0, 66.6, 66.6; CH: 87.0, 127.1, 130.0, 130.1, 131.5, 143.6; C: 82.8, 132.1, 139.1, 145.7, 146.7, 158.0。

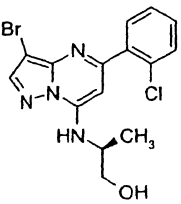
實例 449：物理性質：HRFABMS: m/z 381.0114(MH^+)。對 $C_{15}H_{15}N_4OBrCl$ 之計算值： m/z 381.0118; δ_H ($CDCl_3$) 1.39 (3H, d, $CHCH_3$), 2.76 (1H, bm, $-OH$), 3.71 (1H, m, $=CHCH_2OH$), 3.81 (1H, m, $=CHCH_2OH$), 3.88 (1H, m, $=CHCH_2OH$), 6.38 (1H, s, H_6), 7.38 (2H, m, Ar-H), 7.48 (1H, m, Ar-H), 7.68 (1H, m, Ar-H) 及 8.02 ppm (1H, s, H_2); δ_C ($CDCl_3$) CH_3 : 16.9; CH_2 : 65.0; CH: 50.0, 88.0, 127.1, 130.1, 130.3, 131.4, 143.8; C: 83.0, 132.0, 138.5, 145.6, 146.0, 158.2。

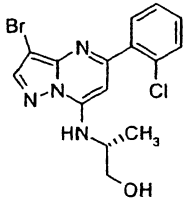
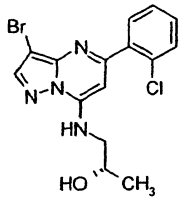
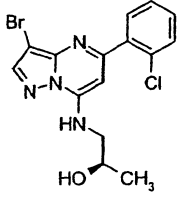
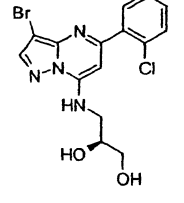
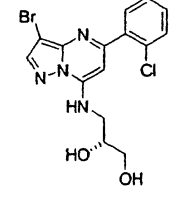
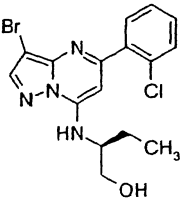
實例 450：

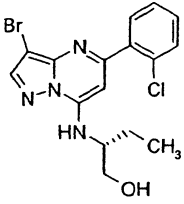
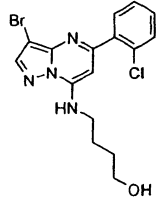


在 GeneVac 技術公司之旋轉反應管中，將 3-溴-7-氯-5-(2-氯苯基)吡唑并[1,5-a]嘓啶(50 毫克，0.146 毫莫耳)(如製備例 129 所述般製備)溶於無水 1,4-二噁烷(5 毫升)中。各管中添加 PS-二異丙基乙胺樹脂(161 毫克，0.5828 毫莫耳)。將新製備之含適當胺 R_1NH_2 (0.219 毫莫耳)之無水 1,4-二噁烷(0.3 毫升)溶液添加於各管中，但實例 99-5 中之胺係溶於 10% MeOH/1,4-二噁烷(0.3 毫升)中，將管密封，且於反應段中之磁石攪拌下，在 70°C 加熱 74 小時。各管經過濾且以無水 1,4-二噁烷洗滌樹脂，再以二氯甲烷洗滌。合併各管之個別濾液並蒸發至乾，且將殘留物分別再溶於無水 1,4-二噁烷(5 毫升)中，且置於 GeneVac 反應管中。各管中添加 PS-異氰酸酯樹脂(594 毫克，0.8742 毫莫耳)及 PS-參胺樹脂(129 毫克，0.4371 毫莫耳)，且使管於反應段上於 25°C 攪拌 20 小時。過濾樹脂且以無水 1,4-二噁烷及二氯甲烷洗滌。各管之濾液蒸發至乾，且將各殘留物在矽膠上使用表 37 所示之管柱尺寸及溶離液分別層析，獲得標題化合物。

表 37

實例	結構	MW	FABMS MH ⁺	產率	層析數據
451		381.7	380.9	66%	15x2.5cm; 0.5% 甲醇之 二氯甲烷

452		381.7	380.9	60%	20x2cm; 0.5% 甲醇之 二氯甲烷
453		381.7	380.9	69%	15x2.5cm; 0.35% 甲醇之 二氯甲烷
454		381.7	380.9	75%	15x2.5cm; 0.35% 甲醇之 二氯甲烷
455		397.7	397.2	84%	15x2.5cm; 1.5% 甲醇之 二氯甲烷
456		397.7			
457		395.7	395.0	60%	15x2.5cm; 0.35% 甲醇之 二氯甲烷

458		395.7	396.3	50%	15x2.5cm; 0.35% 甲醇之 二氯甲烷
459		395.7	396.0	76%	15x2.5cm; 0.35% 甲醇之 二氯甲烷

化合物之額外物理數據列於下：

實例 451：物理性質：HRFABMS: m/z 381.0115(MH^+)。對 $C_{15}H_{15}N_4OBrCl$ 之計算值： m/z 381.0118; $[\alpha]_D^{25^\circ} +1.4^\circ$ ($c=0.25$, MeOH); δ_H ($CDCl_3$) 1.44 (3H, d, $-CHCH_3$), 3.77 3.89 (1H, dd, $CHCH_2OH$), (1H, dd, $CHCH_2OH$), 3.94 (1H, m, $CHCH_2OH$), 6.41 (1H, s, H_6), 6.58 (1H, d, NH), 7.41 (2H, m, Ar-H), 7.51 (1H, m, Ar-H), 7.74 (1H, m, Ar-H) 及 8.04 ppm (1H, s, H_2); δ_C ($CDCl_3$) CH_3 : 17.1; CH_2 : 65.5; CH: 49.9, 88.0, 127.1, 130.1, 130.2, 131.6, 143.8; C: 83.2, 132.1, 138.7, 145.6, 145.8, 158.1。

實例 452：物理性質：HRFABMS: m/z 381.0115(MH^+)。對 $C_{15}H_{15}N_4OBrCl$ 之計算值： m/z 381.0118; $[\alpha]_D^{25^\circ} +6.5^\circ$ ($c=0.32$, MeOH); δ_H ($CDCl_3$) 1.44 (3H, d, $-CHCH_3$), 3.78 (1H, dd, $CHCH_2OH$), 3.89 (1H, dd, $CHCH_2OH$), 3.96 (1H, m, $CHCH_2OH$), 6.41 (1H, s, H_6), 6.58 (1H, d, NH), 7.41 (2H, m, Ar-H), 7.51

(1H, m, Ar-H), 7.75 (1H, m, Ar-H)及8.04 ppm (1H, s, H₂); δ_C (CDCl₃) CH₃: 17.1; CH₂: 65.5; CH: 49.9, 88.0, 127.1, 130.1, 130.3, 131.6, 143.8; C: 83.2, 132.1, 138.6, 145.6, 145.8, 158.1。

實例453：物理性質：HRFABMS: m/z 381.0115(MH⁺)。對 C₁₅H₁₅N₄OBrCl之計算值：m/z 381.0118; $[\alpha]_D^{25^\circ} +9.4^\circ$ (c= 0.27, MeOH); δ_H (CDCl₃) 1.33 (3H, d, CH₃), 2.25 (1H, bs, OH), 3.37 (1H, dd, CH₂), 3.51 (1H, m, CH₂), 4.16 (1H, m, CH₂OH), 6.35 (1H, s, H₆), 6.93 (1H, m, NH), 7.40 (2H, m, Ar-H), 7.50 (1H, m, Ar-H), 7.70 (1H, m, Ar-H)及8.04 ppm (1H, s, H₂); δ_C (CDCl₃) CH₃: 20.8; CH₂: 49.2; CH: 65.7, 87.8, 127.1, 130.1, 130.2, 131.2, 143.9; C: 83.1, 132.1, 138.5, 145.6, 146.6, 158.3。

實例454：物理性質：HRFABMS: m/z 381.0112(MH⁺)。對 C₁₅H₁₅N₄OBrCl之計算值：m/z 381.0118; $[\alpha]_D^{25^\circ} -3.2^\circ$ (c= 0.29, MeOH); δ_H (CDCl₃) 1.32 (3H, d, CH₃), 2.48 (1H, bs, OH), 3.35 (1H, dd, CH₂), 3.49 (1H, m, CH₂), 4.15 1H, m, CH₂OH), 6.34 (1H, s, H₆), 6.93 (1H, m, NH), 7.39 (2H, m, Ar-H), 7.49 (1H, m, Ar-H), 7.68 (1H, m, Ar-H)及8.03 ppm (1H, s, H₂); δ_C (CDCl₃) CH₃: 20.8; CH₂: 49.2; CH: 65.7, 87.7, 127.1, 130.1, 130.3, 131.4, 143.9; C: 83.0, 132.0, 138.6, 145.6, 146.6, 158.3。

實例455：物理性質：HRFABMS: m/z 397.0054(MH⁺)。對 C₁₅H₁₅N₄O₂BrCl之計算值：m/z 397.0067; $[\alpha]_D^{25^\circ} -9.5^\circ$ (c=

0.28, MeOH); δ_{H} (CDCl_3) 3.18 (2H, bs, OH), 3.47 (1H, dd, CH_2), 3.58 (1H, dd, CH_2), 3.63 (1H, dd, CH_2OH), 3.70 (1H, dd, CH_2OH), 3.98 (1H, m, CH), 6.35 (1H, s, H_6), 7.10 (1H, m, NH), 7.37 (2H, m, Ar-H), 7.46 (1H, m, Ar-H), 7.64 (1H, m, Ar-H) 及 8.01 ppm (1H, s, H_2); δ_{C} (CDCl_3) CH_2 : 44.7, 64.0; CH: 69.7, 87.7, 127.0, 130.1, 130.3, 131.3, 143.9; C: 82.9, 132.0, 138.4, 145.4, 146.7, 158.3。

實例 456：此對映異構物可藉基本上如上述之相同方式製備。

實例 457：物理性質：HRFABMS: m/z 395.0260(MH^+)。對 $\text{C}_{16}\text{H}_{17}\text{N}_4\text{OBrCl}$ 之計算值： m/z 395.0274; $[\alpha]_{\text{D}}^{25^\circ} -34.3^\circ$ ($c=0.28$, MeOH); δ_{H} (CDCl_3) 1.08 (3H, dd, CH_3), 1.78 (1H, m, CH_2), 1.86 (1H, m, CH_2), 2.35 (1H, bs, CH_2OH), 3.71 (1H, m, CHNH), 3.81 (1H, dd, CH_2OH), 3.90 (1H, dd, CH_2OH), 6.42 (1H, s, H_6), 6.53 (1H, m, NH), 7.41 (2H, m, Ar-H), 7.51 (1H, Ar-H), 7.75 (1H, m, Ar-H) 及 8.04 ppm (1H, s, H_2); δ_{C} (CDCl_3) CH_3 : 10.5; CH_2 : 24.5, 63.7; CH: 55.9, 88.0, 127.1, 130.1, 130.2, 131.6, 143.8; C: 83.2, 132.1, 138.6, 145.6, 146.3, 158.1。

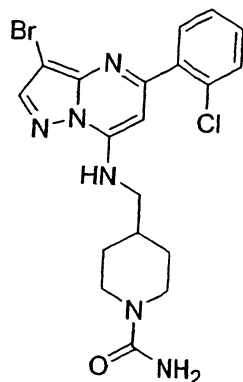
實例 458：物理性質：HRFABMS: m/z 395.0274(MH^+)。對 $\text{C}_{16}\text{H}_{17}\text{N}_4\text{OBrCl}$ 之計算值： m/z 395.0274; $[\alpha]_{\text{D}}^{25^\circ} +27.5^\circ$ ($c=0.25$, MeOH); δ_{H} (CDCl_3) 1.05 (3H, dd, CH_3), 1.76 (1H, m, CH_2), 1.85 (1H, m, CH_2), 2.28 (1H, bs, CH_2OH), 3.67 (1H, m, CHNH), 3.77 (1H, dd, CH_2OH), 3.84 (1H, dd, CH_2OH), 6.49

(1H, s, H₆), 6.66 (1H, m, NH), 7.39 (2H, m, Ar-H), 7.49 (1H, Ar-H), 7.71 (1H, m, Ar-H)及 8.04 ppm (1H, s, H₂); δ_c (CDCl₃) CH₃: 10.5; CH₂: 24.3, 63.3; CH: 56.1, 88.0, 127.1, 130.1, 130.3, 131.5, 143.8; C: 83.0, 132.1, 138.6, 145.6, 146.3, 158.2。

實例 459：物理性質：HRFABMS: m/z 395.0264(MH⁺)。對 C₁₆H₁₇N₄OBrCl 之計算值：m/z 395.0274; δ_H (CDCl₃) 1.77 (2H, m, -NHCH₂CH₂CH₂CH₂OH), 1.90 (1H, bm, -NHCH₂CH₂CH₂CH₂OH), 1.93 (2H, m, -NHCH₂CH₂CH₂CH₂OH), 3.54 (2H, m, -NHCH₂CH₂CH₂CH₂OH), 3.77 (2H, m, -NHCH₂CH₂CH₂CH₂OH), 6.37 (1H, s, H₆), 6.72 (1H, m, -NHCH₂CH₂CH₂CH₂OH), 7.41 (2H, m, Ar-H), 7.51 (1H, m, Ar-H), 7.75 (1H, m, Ar-H) 及 8.06 ppm (1H, s, H₂); δ_c (CDCl₃) CH₂: 25.7, 29.7, 42.2, 62.2; CH: 87.4, 127.1, 130.1, 130.2, 131.6, 143.8; C: 83.1, 132.1, 138.8, 145.6, 146.3, 158.1。

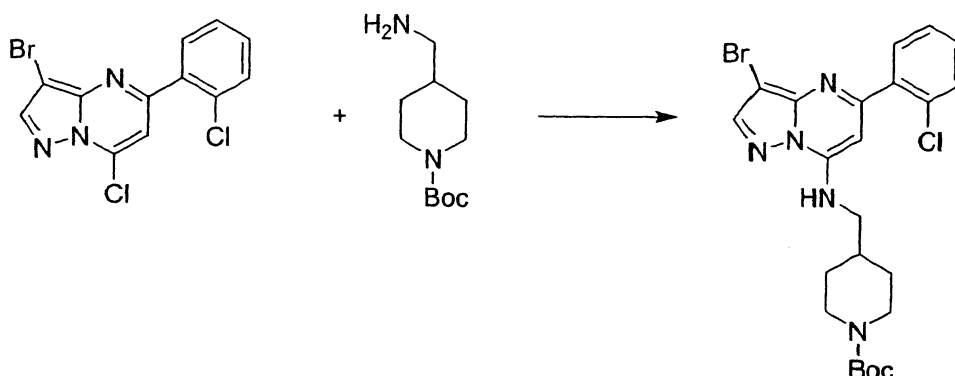
實例 460：

4-{[3-溴-5-(2-氯苯基)吡唑并[1,5-a]嘧啶-7-基胺基]甲基}哌啶-1-羧酸鹽胺：



A. 4-{[3-溴-5-(2-氯苯基)吡唑并[1,5-a]嘧啶-7-基胺基]甲基}

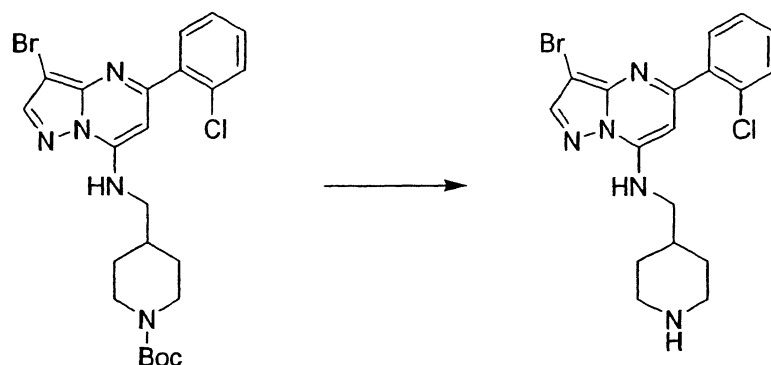
哌啶-1-羧酸第三丁酯：



將3-溴-7-氯-5-(2-氯苯基)吡唑并[1,5-a]嘧啶(300毫克，0.875毫莫耳)(如製備例129所述般製備)溶於無水1,4-二噁烷(6.8毫升)中。添加4-(胺基甲基)哌啶-1-羧酸第三丁酯(225毫克，1.05毫莫耳)及二異丙基乙胺(0.3055毫升，1.75毫莫耳)，使混合物在75℃加熱24小時。蒸發溶液至乾，殘留物在矽膠管柱(15x5公分)上，使用二氯甲烷作為溶離液層析，獲得4-{[3-溴-5-(2-氯苯基)吡唑并[1,5-a]嘧啶-7-基胺基]甲基}哌啶-1-羧酸第三丁酯(461.2毫克，100%)。FABMS: m/z 520.1 (MH^+); HRFABMS: m/z 520.1111 (MH^+)。對 $C_{23}H_{28}N_5O_2BrCl$ 之計算值: m/z 520.1115; δ_H ($CDCl_3$) 1.30 (2H, m, CH_2), 1.51 (9H, s, $-COOC(CH_3)_3$), 1.85 (2H, d, CH_2), 1.95 (1H, m, CH), 2.76 (2H, m, CH_2), 3.40 (2H, m, CH_2), 6.37 (1H, s, H_6), 6.55 (1H, m, NH), 7.42 (2H, m, Ar-H), 7.52 (1H, m, Ar-H), 7.76 (1H, m, Ar-H)及8.07 ppm (1H, s, H_2); δ_C ($CDCl_3$) CH_3 : 28.5, 28.5, 28.5; CH_2 : 29.1, 29.1, 43.5, 43.5, 47.9; CH: 36.3, 87.5, 127.2, 130.2, 130.3, 131.6, 143.9; C: 79.7, 83.3,

132.1, 138.6, 145.4, 146.3, 154.7, 158.1。

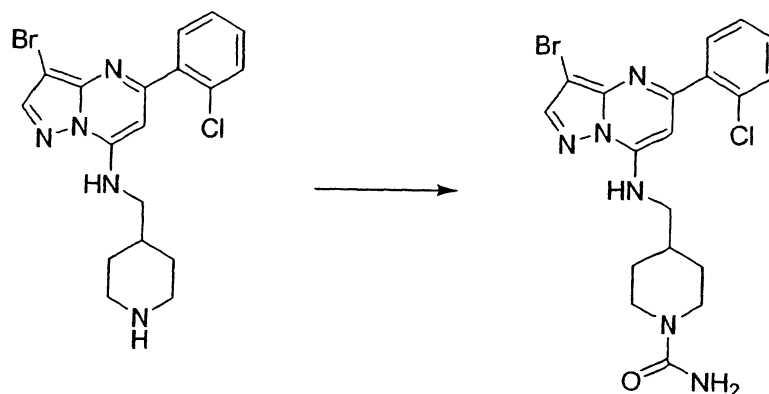
B. [3-溴-5-(2-氯苯基)吡唑并[1,5-a]嘧啶-7-基]哌啶-4-基甲基胺



將4-{[3-溴-5-(2-氯苯基)吡唑并[1,5-a]嘧啶-7-基胺基]甲基}哌啶-1-羧酸第三丁酯(441毫克, 0.847毫莫耳)(如實例460步驟A所述般製備)溶於甲醇(4.5毫升)中, 且添加10%(v/v)濃硫酸/1,4-二噁烷(11.46毫升)中。混合物在25℃攪拌0.5小時。產物如製備例241步驟B所述般驟冷, 且在矽膠管柱(15x5公分)上使用8%(10%濃氫氧化銨/甲醇)-二氯甲烷作為溶離液層析, 獲得[3-溴-5-(2-氯苯基)吡唑并[1,5-a]嘧啶-7-基]哌啶-4-基甲基胺(314.4毫克, 88%)。FABMS: m/z 420.0 (MH^+); HRFABMS: m/z 420.0585 (MH^+)。對 $C_{18}H_{20}N_5BrCl$ 計算值: m/z 420.0591; δ_H ($CDCl_3$) 1.34 (2H, m, CH_2), 1.86 (2H, m, CH_2), 1.91 (1H, m, CH), 2.10 (1H, bm, 哌啶-NH), 2.67 (2H, m, CH_2), 3.18 (2H, m, CH_2), 3.38 (2H, m, CH_2), 6.37 (1H, s, H_6), 6.53 (1H, m, NH), 7.42 (2H, m, Ar-H), 7.52 (1H, m, Ar-H), 7.76 (1H, m, Ar-H)及8.06 ppm (1H, s, Ar-H); δ_C ($CDCl_3$) CH_2 : 31.2, 31.2, 46.2, 46.2, 48.4; CH: 36.4,

89.5, 127.1, 130.1, 130.5, 131.6, 143.8; C: 83.2, 132.1, 138.9, 145.6, 146.4, 158.1。

C. 4-{[3-溴-5-(2-氯苯基)吡唑并[1,5-a]嘧啶-7-基氨基]甲基}哌啶-1-羧酸鹽胺

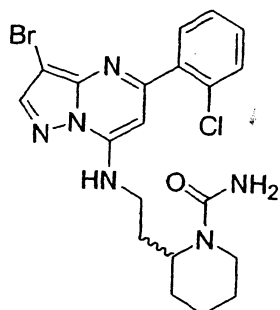


將[3-溴-5-(2-氯苯基)吡唑并[1,5-a]嘧啶-7-基]哌啶-4-基氨基胺(57毫克, 0.136毫莫耳)(如實例460步驟B所述般製備)溶於無水二氯甲烷(1.2毫升)中, 且添加三甲基矽烷基異氰酸酯(0.091毫升, 0.679毫莫耳)。混合物在25℃攪拌2.5小時。混合物以二氯甲烷稀釋, 且以飽和碳酸氫鈉水溶液洗滌。有機層經脫水(MgSO₄)、過濾且蒸發製乾。殘留物在矽膠管柱(30×2.5公分)上使用3%(10%濃氫氧化胺/甲醇)-二氯甲烷作為溶離液層析, 獲得4-{[3-溴-5-(2-氯苯基)吡唑并[1,5-a]嘧啶-7-基氨基]甲基}哌啶-1-羧酸鹽胺(53.7毫克, 86%)。FABMS: m/z 463.1 (MH⁺); HRFABMS: m/z 463.0647 (MH⁺)。對C₁₉H₂₁N₆OBrCl計算值: m/z 463.0649; δ_H (d₆-DMSO) 1.09 (2H, m, CH₂), 1.63 (2H, m, CH₂), 1.87 (1H, m, CH), 2.60 (2H, m, CH₂), 3.53 (2H, bm, CONH₂), 3.91 (2H, d, CH₂), 6.52 (1H, s, H₆), 7.50 (2H, m, Ar-H), 7.62 (2H, m,

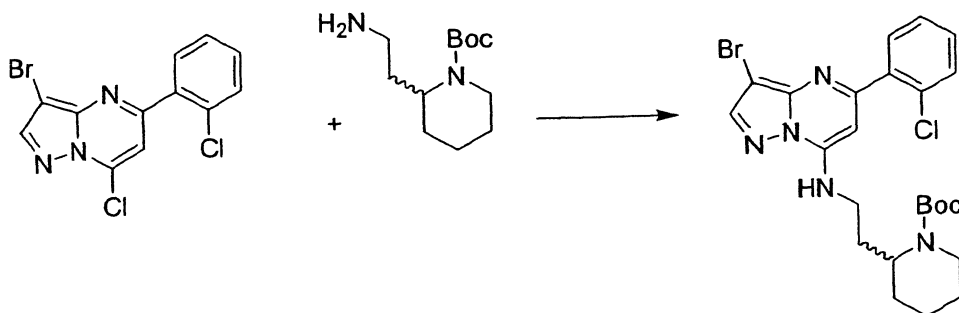
Ar-H), 8.33(1H, s, H₂)及 8.52 ppm (1H, m, NH); δ_c (d₆-DMSO) CH₂: 30.1, 30.1, 44.2, 44.2, 47.7; CH: 36.4, 88.2, 128.1, 130.7, 131.4, 132.1, 147.9; C: 82.1, 132.1, 139.4, 145.7, 147.9, 158.1, 158.8。

實例 461：

2-{2-[3-溴-5-(2-氯苯基)吡唑并[1,5-a]嘧啶-7-基胺基]乙基}哌啶-1-羧酸鹽胺：



A. 2-{2-[3-溴-5-(2-氯苯基)吡唑并[1,5-a]嘧啶-7-基胺基]乙基}哌啶-1-羧酸第三丁酯：

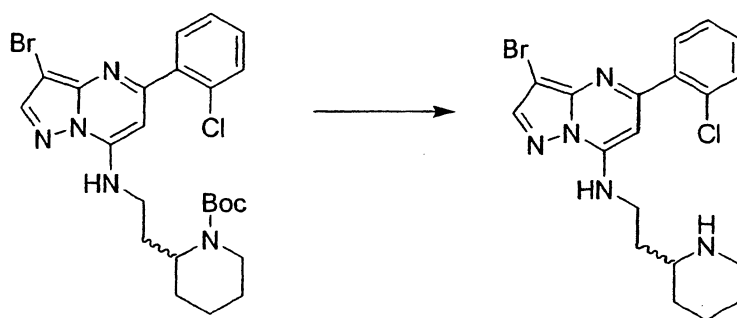


將 3-溴-7-氯-5-(2-氯苯基)吡唑并[1,5-a]嘧啶(400 毫克，1.166 毫莫耳)(如製備例 129 所述般製備)溶於無水 1,4-二噁烷(5.7 毫升)中。添加 2-胺基乙基哌啶-1-羧酸第三丁酯(266 毫克，1.166 毫莫耳)及二異丙基乙胺(0.409 毫升，2.33 毫莫耳)，使混合物在 75°C 加熱 48 小時。添加額外之二異丙基乙

胺(0.204毫升, 1.166毫莫耳), 且持續加熱至總計58小時。
蒸發溶液至乾, 殘留物在矽膠管柱(15x5公分)上, 使用二氯
甲烷, 接著使用0.3%(10%濃氫氧化銨/甲醇)-二氯甲烷作為
溶離液層析, 獲得2-{[3-溴-5-(2-氯苯基)吡唑并[1,5-a]嘧啶
-7-基胺基]乙基}哌啶-1-羧酸第三丁酯(491.1毫克, 79%)。

FABMS: m/z 534.1 (MH^+); HRESIMS: m/z 534.12797
(MH^+)。對 $C_{24}H_{30}N_5O_2BrCl$ 計算值: m/z 534.12714; δ_H ($CDCl_3$)
1.50 (2H, m, CH_2), 1.51 (9H, s, $COOC(CH_3)_3$), 1.57 (2H, m,
 CH_2), 1.68 (2H, m, CH_2), 1.76 (2H, m, CH_2), 2.24 (1H, bm,
 CH_2), 2.82/3.40/3.54/4.08/4.51 (5H, m, CH/CH_2), 6.34 (1H, s,
 H_6), 7.41 (2H, m, Ar-H), 7.51 (1H, m, Ar-H), 7.76 (1H, m,
Ar-H)及8.08 ppm (1H, s, H_2); δ_C ($CDCl_3$) CH_3 : 28.5, 28.5,
28.5; CH_2 : 19.2, 25.5, 29.2, 29.2, 39.2, 67.1; CH : ~47.4, 87.1,
127.1, 130.1, 130.1, 131.6, 143.9; C: 80.0, 83.0, 132.1, 138.9,
145.7, 146.2, 158.0。

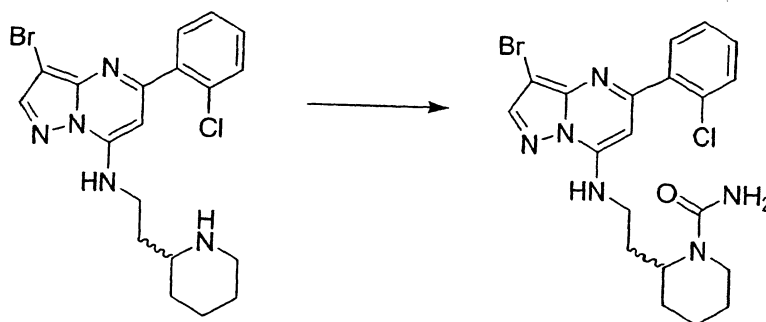
B. [3-溴-5-(2-氯苯基)吡唑并[1,5-a]嘧啶-7-基]-(2-哌啶-2-
基乙基)胺



將2-{[3-溴-5-(2-氯苯基)吡唑并[1,5-a]嘧啶-7-基胺基]乙
基}哌啶-1-羧酸第三丁酯(465毫克, 0.869毫莫耳)(如實例

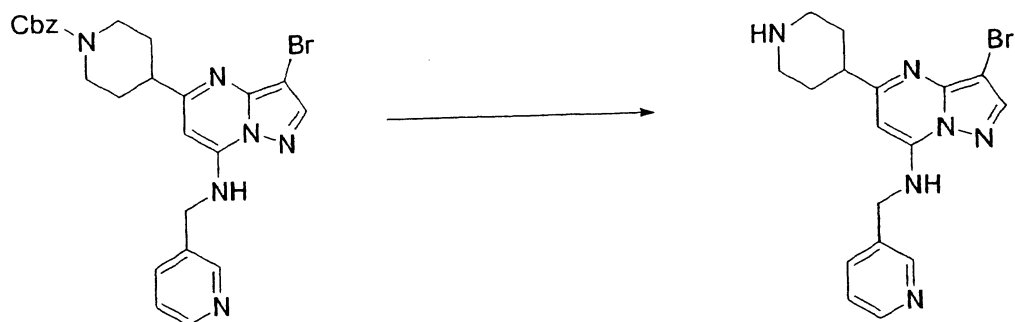
461步驟A所述般製備)溶於甲醇(4.5毫升)中，且添加10% (v/v)濃硫酸/1,4-二噁烷(11.76毫升)中。混合物在25℃攪拌1.5小時。產物如製備例241步驟B所述般驟冷，且在矽膠管柱(15x5公分)上使用3.5%(10%濃氫氧化銨/甲醇)-二氯甲烷作為溶離液層析，獲得[3-溴-5-(2-氯苯基)吡唑并[1,5-a]嘧啶-7-基](哌啶-2-基乙基)胺(365.6毫克，97%)。FABMS: m/z 434.1 (MH^+); HRFABMS: m/z 434.0726 (MH^+)。對 $C_{19}H_{22}N_5BrCl$ 之計算值: m/z 434.0747; δ_H ($CDCl_3$) 1.24 (1H, m, CH_2), 1.41 (1H, m, CH_2), 1.49 (1H, m, CH_2), 1.66 (1H, m, CH_2), 1.73 (1H, m, CH_2), 1.81 (1H, m, CH_2), 1.88 (2H, m, CH_2), 2.68 (1H, m, CH_2), 2.78 (1H, m, CH_2), 3.20 (1H, m, CH), 3.55 (1H, m, CH_2), 3.60 (1H, m, CH_2), 6.32 (1H, s, H_6), 7.41 (2H, m, Ar-H), 7.51 (1H, m, Ar-H), 7.74 (1H, m, Ar-H), 7.78 (1H, m, NH)及8.05 ppm (1H, s, H_2); δ_C ($CDCl_3$) CH_2 : 24.7, 26.8, 33.1, 35.2, 40.3, 47.0; CH: 55.7, 87.2, 127.1, 130.0, 130.1, 131.5, 143.8; C: 82.9, 132.1, 139.0, 145.7, 146.5, 158.1。

C. 2-{2-[3-溴-5-(2-氯苯基)吡唑并[1,5-a]嘧啶-7-基胺基]乙基}哌啶-1-羧酸醯胺



將[3-溴-5-(2-氯苯基)吡啶并[1,5-a]嘧啶-7-基](哌啶-2-基乙基)胺(200毫克, 0.46毫莫耳)(如實例461步驟B所述般製備)溶於無水二氯甲烷(2毫升)中, 且添加三甲基矽烷基異氰酸酯(0.31毫升, 2.3毫莫耳)。混合物在25°C攪拌1.25小時。添加額外之三甲基矽烷基異氰酸酯(0.155毫升, 1.15毫莫耳), 且持續攪拌總計3小時。混合物以二氯甲烷稀釋, 且以飽和碳酸氫鈉水溶液洗滌。有機層經脫水(MgSO₄)、過濾且蒸發製乾。殘留物在矽膠管柱(30x2.5公分)上使用2%(10%濃氫氧化胺/甲醇)-二氯甲烷作為溶離液層析, 獲得2-{2-[3-溴-5-(2-氯苯基)吡啶并[1,5-a]嘧啶-7-基胺基]乙基}哌啶-1-羧酸鹽胺(106.3毫克, 48%)。FABMS: m/z 477.0 (MH⁺); HRFABMS: m/z 477.0804 (MH⁺)。對C₂₀H₂₃N₆OBrCl之計算值: m/z 477.0805; δ_H (d₆-DMSO) 1.29 (1H, m, CH₂), 1.52 (5H, m, CH₂), 1.72 (1H, m, CH₂), 2.05 (1H, m, CH₂), 2.51 (2H, s, CONH₂), 2.79 (1H, dd, CH), 3.31 (1H, m, CH₂), 3.34 (1H, m, CH₂), 3.76 (1H, m, CH₂), 4.30 (1H, bm, CH₂), 6.42 (1H, s, H₆), 7.50 (2H, m, Ar-H), 7.60 (1H, m, Ar-H), 7.63 (1H, m, Ar-H), 8.29 (1H, s, H₂)及8.38 ppm (1H, dd, NH); δ_C (d₆-DMSO) CH₂: 18.6, 25.2, 28.2, 38.4, 38.6, 54.8; CH: 46.7, 86.6, 127.1, 129.7, 130.3, 131.0, 143.4; C: 81.2, 131.0, 138.7, 145.1, 146.4, 158.2。

實例462:



在周圍溫度下，於含實例204製備之化合物(1.11克，2.12毫莫耳)之無水乙腈(20毫升)溶液中滴加TMSI(1.70克，8.52毫莫耳)。10分鐘後，真空移除乙腈。所得黃色發泡體以2 N HCl溶液(7毫升)處理，且立即以Et₂O(5x)洗滌。水溶液之pH以50%NaOH(水溶液)調整至10，產物藉由以NaCl(s)使溶液飽和分離，接著以CH₂Cl₂(5x)萃取，獲得結晶產物(733毫克，產率89%)。MH⁺=387；m.p.=207.5℃。

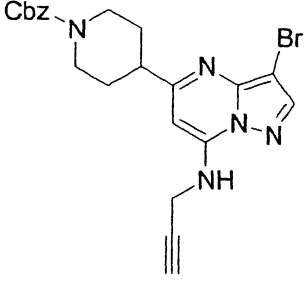
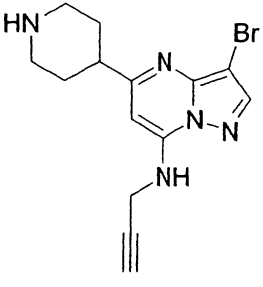
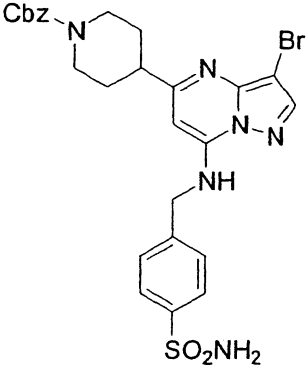
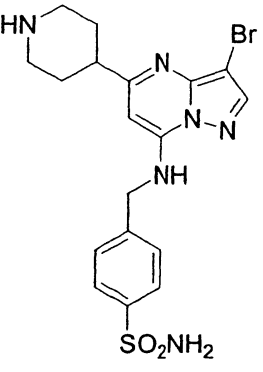
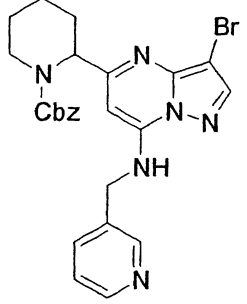
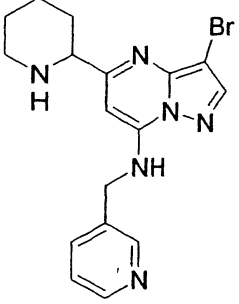
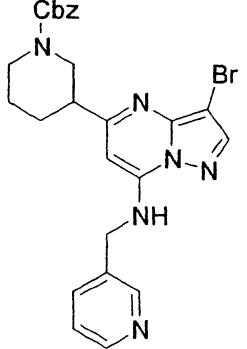
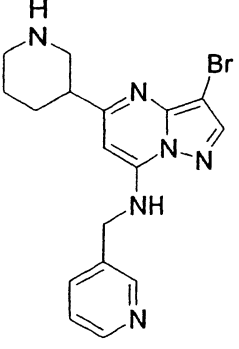
實例463-472：

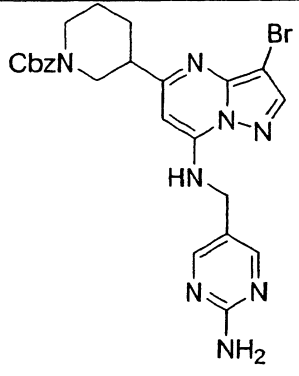
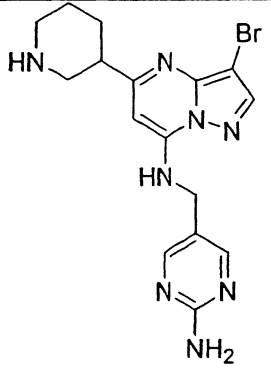
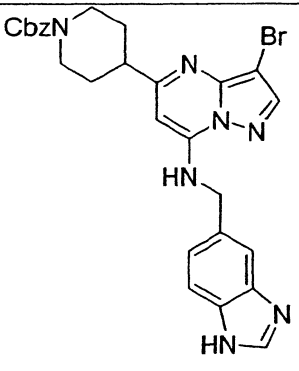
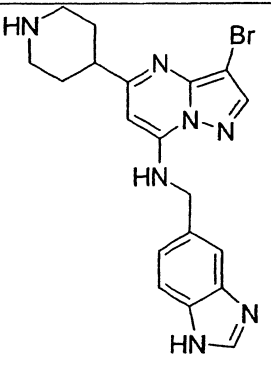
以基本上與實例462中所示相同之程序，僅替代表38欄2之化合物，製備表38欄3之化合物。

表 38

實例	欄2	欄3	數據
463			MH ⁺ = 403 ¹ H NMR (300MHz, CDCl ₃) δ 8.52 (s, 1H), 8.38 (d, 1H), 8.04 (s, 1H), 7.78 (d, 1H), 7.65 (t, 1H), 6.18 (s, 1H), 4.89 (s, 2H), 3.26–3.21 (d, 2H), 2.96–2.70 (m, 3H), 2.05–1.78 (m, 4H).

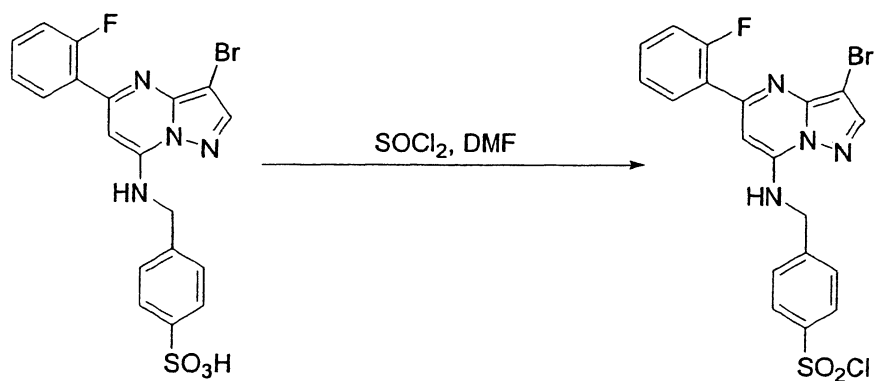


468			$MH^+ = 334$ m. p. = 176.2 °C
469			$MH^+ = 465$ m. p. = 250.4 °C
470			$MH^+ = 387$ m. p. = 68.5 °C
471			$MH^+ = 387$ m. p. = 59.4 °C

472			1. mp = 230-232 2. M+H = 396
472 .10			1. mp = 157-160 2. M+H = 427

實例 473：

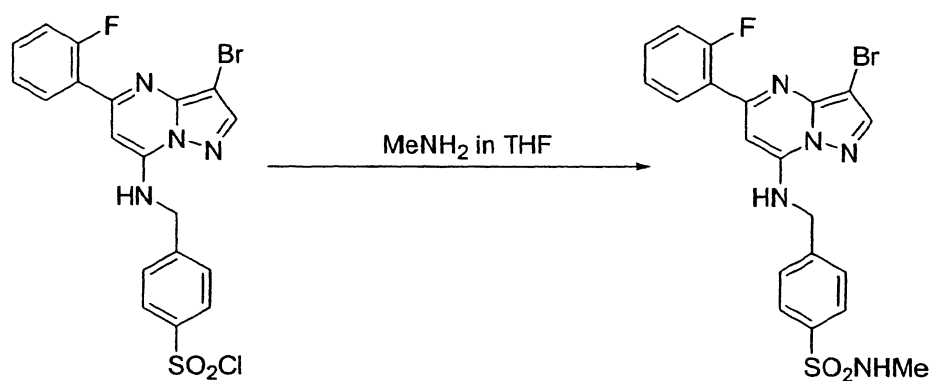
步驟 A：



將含磺酸(560毫克，1.17毫莫耳)之5毫升無水DMF溶液冷卻至0℃，且添加SOCl₂(278毫克，2.34毫莫耳)。使反應混合物達到室溫且攪拌隔夜。次日將內容物倒入冰中，將pH

小心調整至8。產物以EtOAc萃取，且脫水(Na_2SO_4)後移除溶劑，獲得240毫克(41%)粗磺醯氯，其未進一步純化用於下一步驟中。 ^1H NMR (CDCl_3) δ 8.20-8.10 (m, 1H), 8.10-7.95 (m, 3H), 7.65 (d, 2H), 7.45-7.35 (m, 1H), 7.35-7.20 (m, 1H), 7.15-7.05 (m, 1H), 6.95 (t, 1H), 4.85 (d, 2H)。

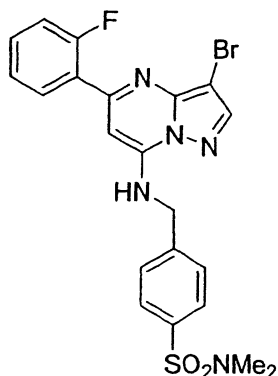
步驟B：



含實例473步驟A製備之化合物(120毫克，0.24毫莫耳)之10毫升THF溶液在室溫以2毫升1 M MeNH_2 (2.00毫莫耳)之THF處理隔夜。移除溶劑，殘留物以層析(矽膠，己烷： EtOAc (4：1 $\rightarrow$ 1：1))純化，或得56毫克(48%)磺醯胺。 ^1H NMR ($\text{DMSO}-d_6$) δ 9.05 (t, $J=9$ Hz, 1H), 8.35 (s, 1H), 7.90 (t, $J=7.5$ Hz, 1H), 7.75 (d, $J=9$ Hz, 2H), 7.62 (d, $J=9$ Hz, 2H), 7.55-7.46 (m, 1H), 7.45-7.38 (m, 1H), 7.38-7.25 (m, 1H), 6.50 (s, 1H), 4.80 (d, 2H), 3.30 (s, 3H)

LCMS: $\text{MH}^+ = 492.1$

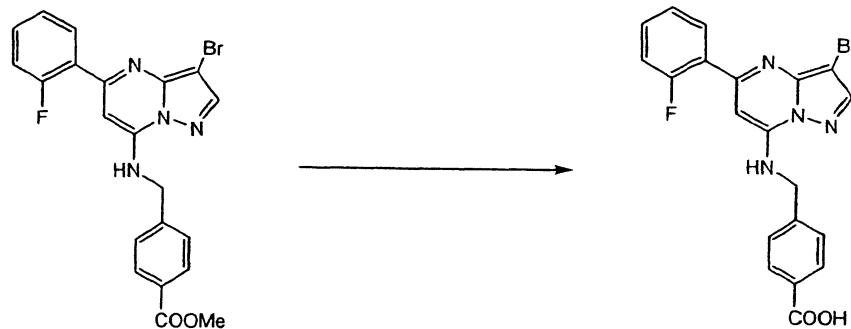
實例474：



以基本上與實例473相同之程序，僅替代二甲基胺，製備上述化合物。 ^1H NMR (CDCl_3) δ 8.14 (t, $J=9$ Hz, 1H), 8.00 (s, 1H), 7.76 (d, $J=9$ Hz, 2H), 7.54 (d, $J=9$ Hz, 2H), 7.34-7.44 (m, 1H), 7.26 (t, $J=9$ Hz, 1H), 7.14-7.04 (m, 1H), 6.93 (t, $J=6$ Hz, 1H), 6.45 (s, 1H), 4.75 (d, 2H), 2.70 (s, 6H)

LCMS: $\text{MH}^+ = 504.2$

實例 475：



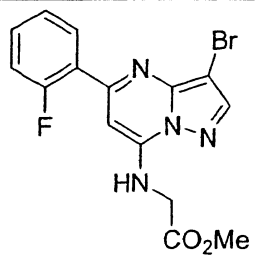
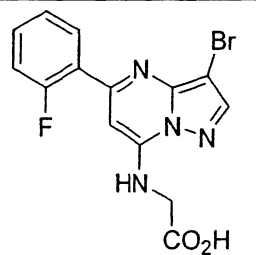
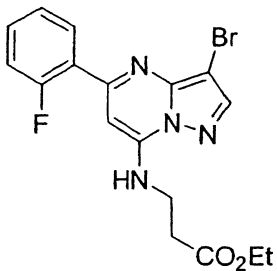
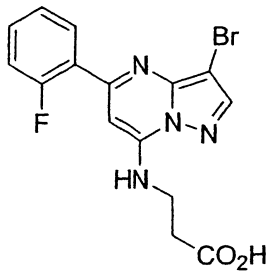
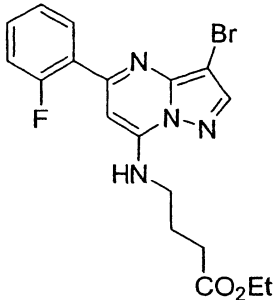
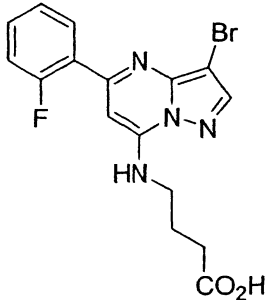
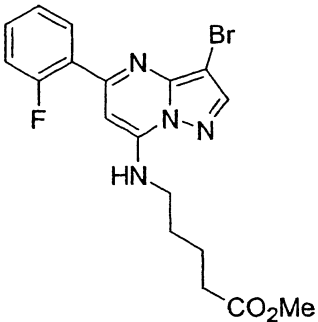
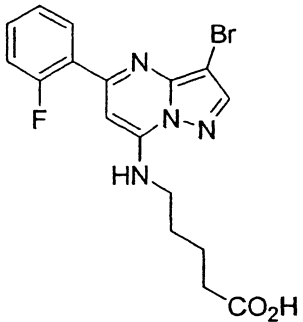
使實例129製備之化合物(300毫克，0.66毫莫耳)、NaOH(5克)、 $\text{CH}_3\text{OH}-\text{H}_2\text{O}$ (100毫升，90：10)之混合物在 25°C 攪拌約15小時。以TLC檢測水解之進行。濃縮反應混合物移除甲醇。濃縮液以50毫升水稀釋，且以乙醚萃取，移除任何未反應之酯。因此獲得之水溶液以3 N HCl中和至pH為4，獲得游離酸，經過濾且以水重複洗滌。該酸經真空乾燥(270

毫克，93%)，且未進一步純化使用。

實例 476-479：

以基本上與實例 475 相同之程序，僅替代表 39 欄 2 之化合物，製備表 39 欄 3 之化合物。

表 39

實例	欄2	欄3	數據
476			產率= 82% LCMS: MH ⁺ = 365
477			產率= 82% LCMS: MH ⁺ = 379
478			產率= 72% LCMS: MH ⁺ = 393
479			產率= 70% LCMS: MH ⁺ = 407

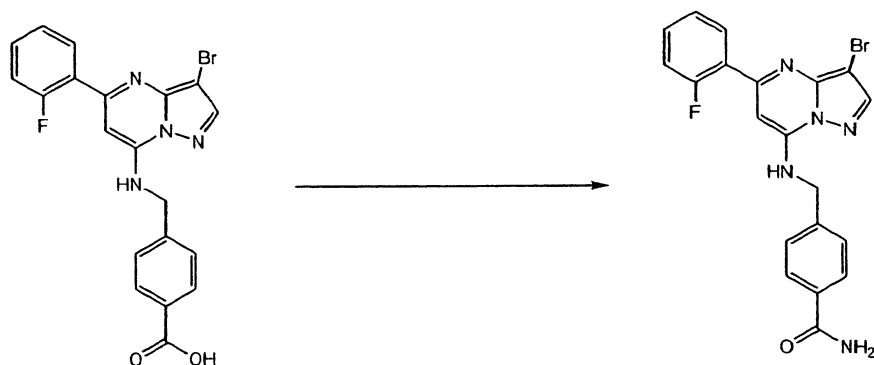
選用實例之額外數據列於下：

實例 476: ^1H NMR (CDCl_3) δ 8.15 (m, 2H), 8.0 (m, 1H), 7.6 (m, 1H), 7.3 (m, 2H), 6.6 (s, 1H), 4.2 (d, 2H)。

實例 477: ^1H NMR (CDCl_3) δ 8.15 (dt, 1H), 8.0 (s, 1H), 7.4 (m, 1H), 7.25 (dd, 1H), 7.15 (dd, 1H), 7.0 (t, 1H), 6.5 (s, 1H), 3.8 (dt, 2H), 2.6 (t, 2H)。

實例 479: ^1H NMR (CDCl_3) δ 8.15 (dt, 1H), 8.0 (s, 1H), 7.4 (m, 1H), 7.25 (dd, 1H), 7.15 (dd, 1H), 6.8 (t, 1H), 3.5 (dt, 2H), 2.4 (t, 2H), 1.8 (m, 4H)。

實例 480：



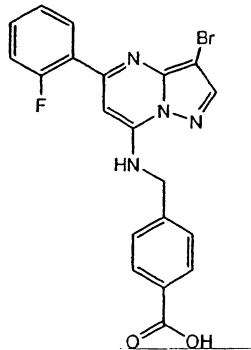
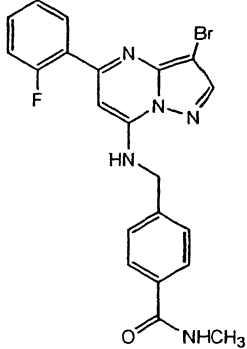
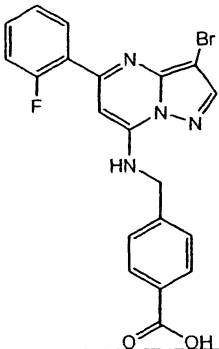
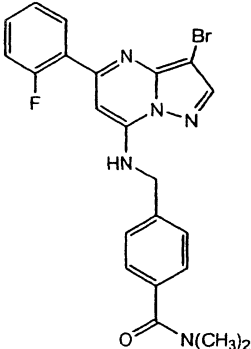
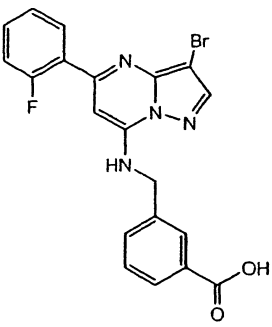
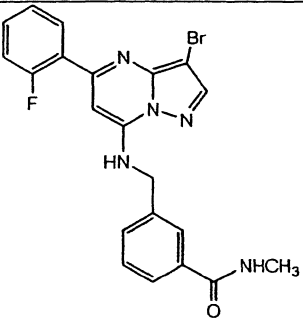
使含實例 475 之酸 (85 毫克，0.193 毫莫耳) 及 Et_3N (20 毫克，0.193 毫莫耳) 之 THF (20 毫升) 混合物在 25°C 攪拌 15 分鐘。將氯甲酸異丁酯 (28 毫克，0.205 毫莫耳) 添加於反應混合物中，且攪拌 10 分鐘，接著添加 NH_4OH 溶液 (0.5 毫升)。使反應混合物攪拌 1 小時，且濃縮至乾。經乾燥之物質以管柱層析純化。

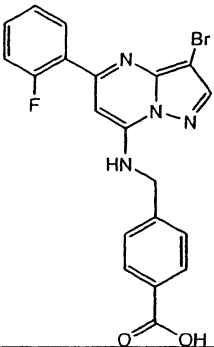
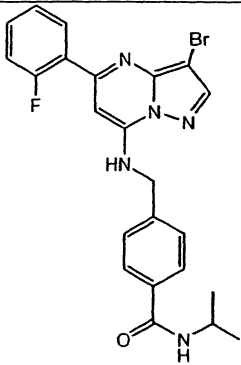
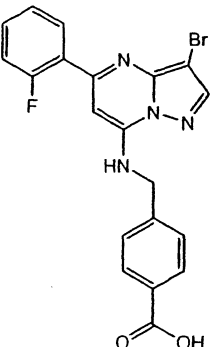
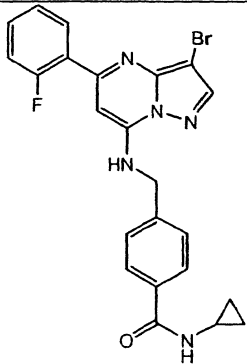
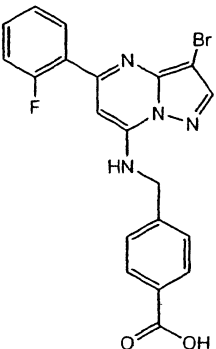
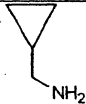
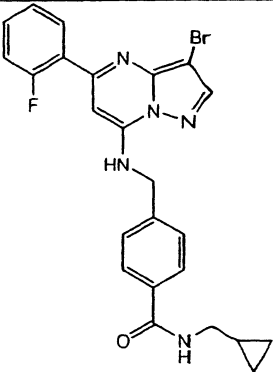
實例 481-509：

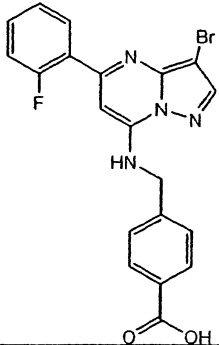
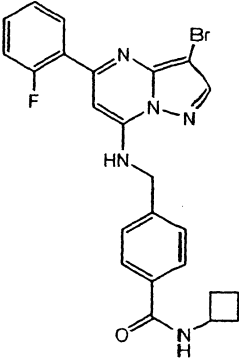
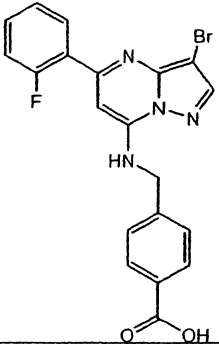
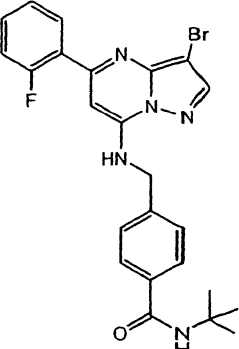
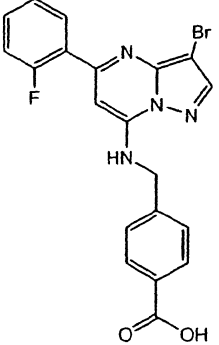
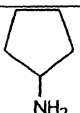
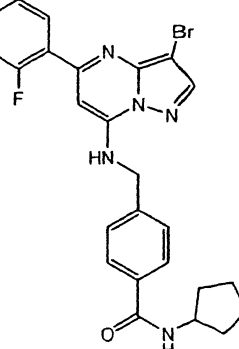
以實質上與實例 480 相同之程序，僅替代表 40 欄 2 之羧酸

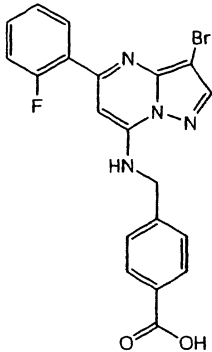
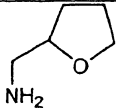
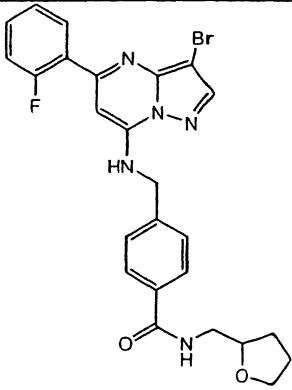
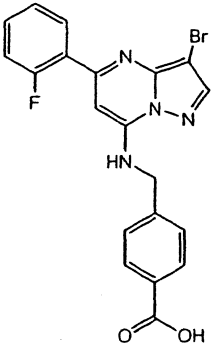
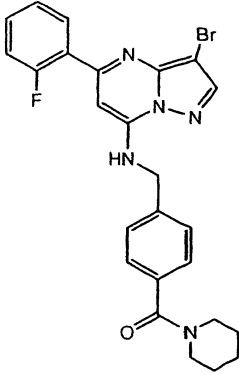
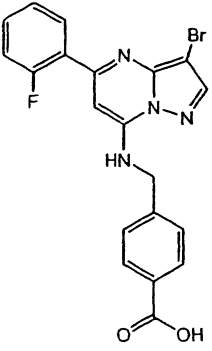
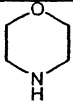
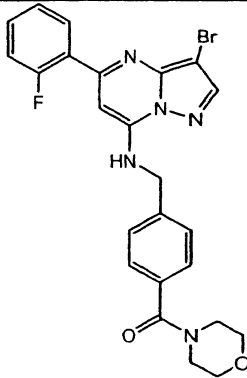
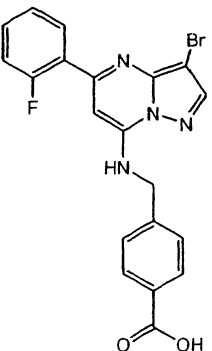
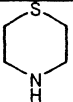
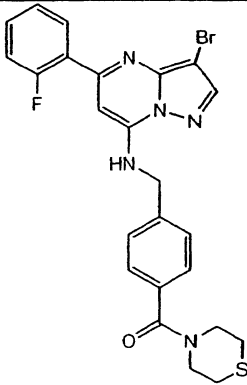
及表 40 欄 3 之胺，製備表 40 欄 4 之化合物。

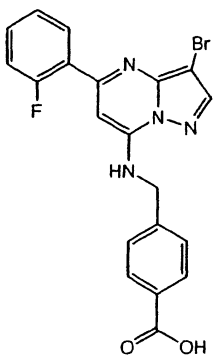
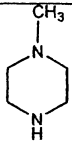
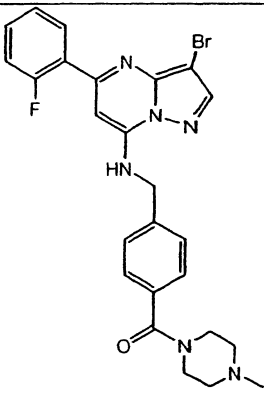
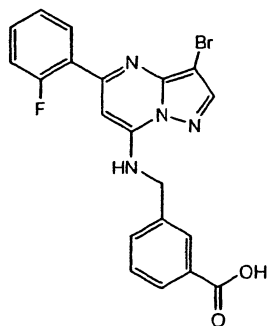
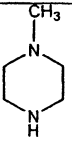
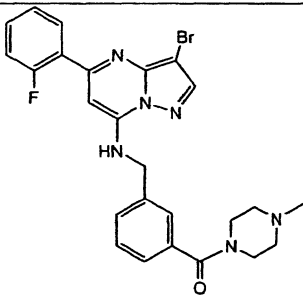
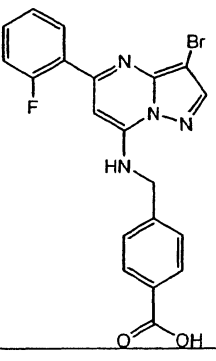
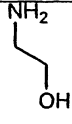
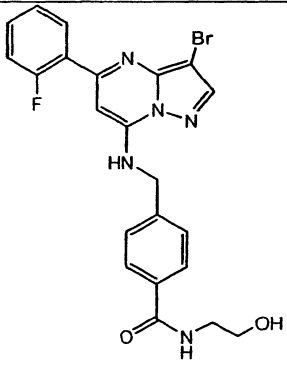
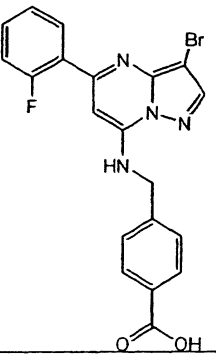
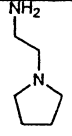
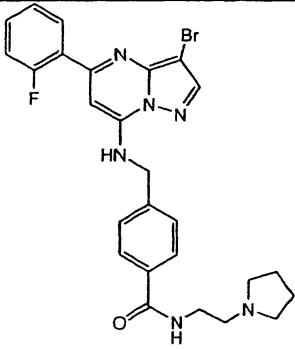
表 40

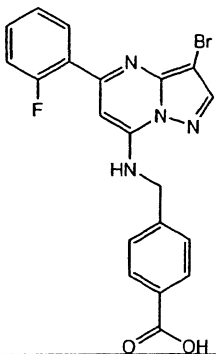
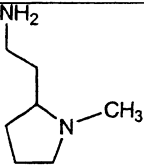
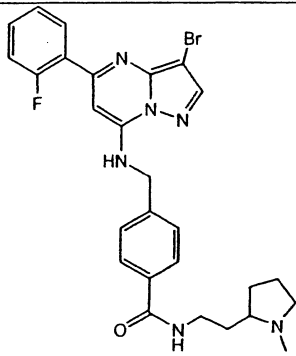
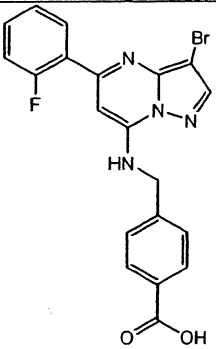
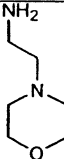
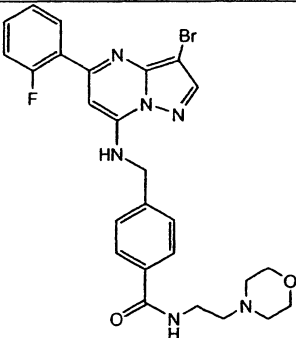
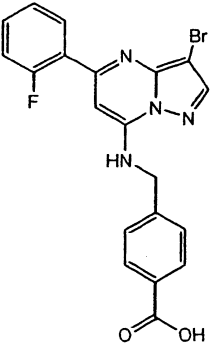
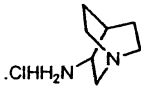
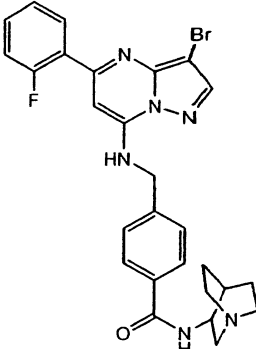
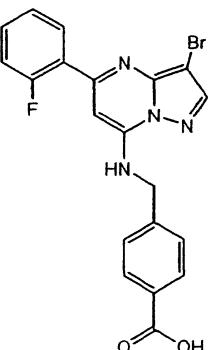
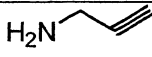
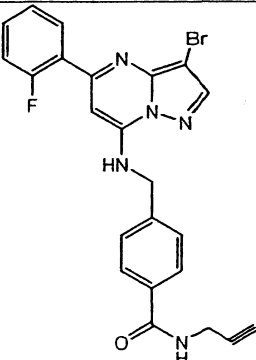
實例	欄2	欄3	欄4	數據
481		CH ₃ NH ₂		產率= 88% LCMS: MH ⁺ = 454
482		(CH ₃) ₂ NH		產率= 80 % LCMS MH ⁺ = 468
483		CH ₃ NH ₂		產率= 70 % LCMS MH ⁺ = 454.

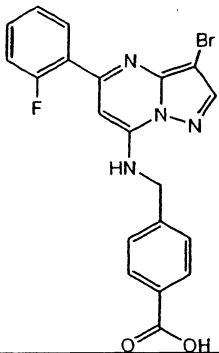
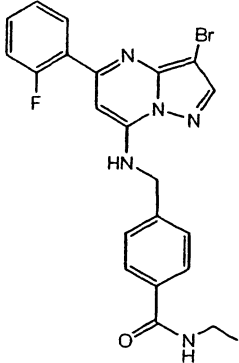
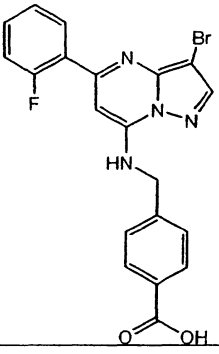
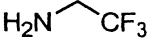
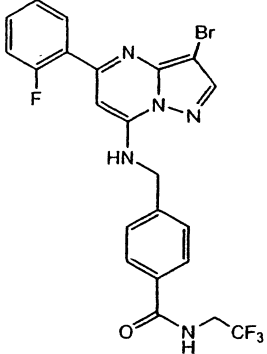
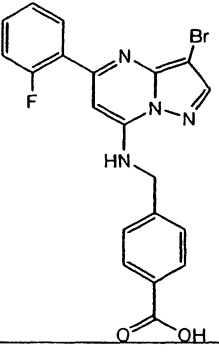
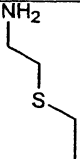
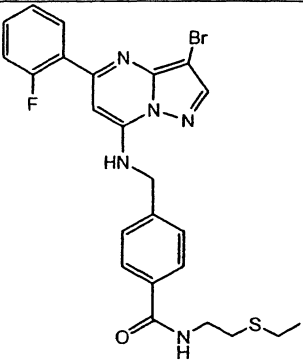
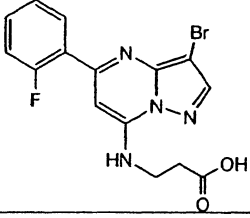
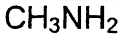
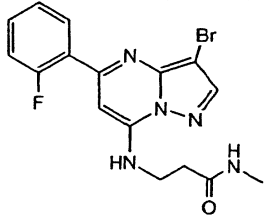
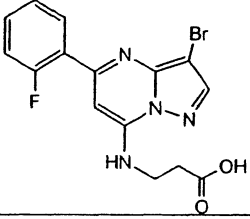
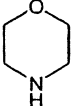
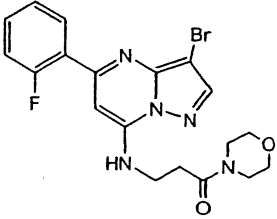
484				產率=75 % LCMS MH ⁺ = 482.1
485				產率=71 % LCMS MH ⁺ = 480.1
486				產率=75 % LCMS MH ⁺ = 494.1

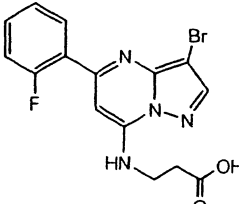
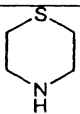
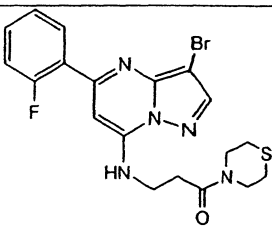
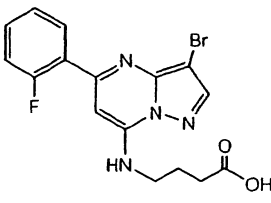
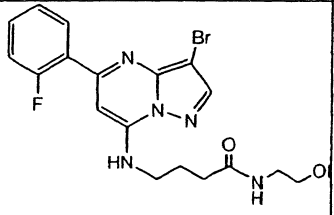
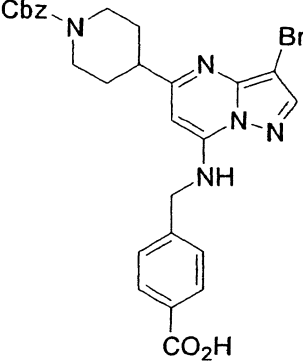
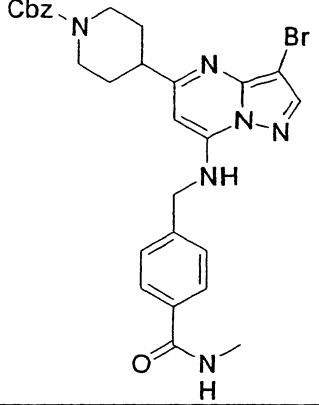
487				產率= 75 % MH ⁺ = 494.1
488				產率= 75 % MH ⁺ = 496.1
489				產率= 75 % LCMS MH ⁺ = 508.1

490				產率=78 % LCMS MH ⁺ = 524.1
491				產率=73 % LCMS MH ⁺ = 508.1
492				產率=73 % LCMS MH ⁺ = 510.1
493				產率=76 % LCMS MH ⁺ = 526.1

494				產率=76 % MH ⁺ = 523.1
495				產率=76 % MH ⁺ = 523.1
496				產率=:51 % LCMS MH ⁺ = 484.1
497				產率=66 % MH ⁺ = 537.1

498				產率=76 % LCMS MH ⁺ = 551.2
499				產率=79 % LCMS MH ⁺ = 552.1
500				產率=80 % MH ⁺ = 549.1
501				產率=80 % LCMS MH ⁺ = 478.1

502				產率=80 % LCMH ⁺ = 468.1
503				產率=80 % MH ⁺ = 522.1
504				產率=82 % LCMS MH ⁺ = 528.1
505				產率=60 % MH ⁺ = 392
506				產率=60 % LCMH ⁺ = 448.1

507				產率=70 % MH ⁺ = 464.1
508				產率=50 % LCMS MH ⁺ = 436.1
508 .10		CH ₃ NH ₂		產率= 92 MH ⁺ = 577

選用實例之額外數據列於下：

實例 481: ¹H NMR (CDCl₃)δ 8.15 (dt, 1H), 8.0 (s, 1H), 7.7 (d, 2H), 7.4 (s, 1H), 7.35 (d, 2H), 7.25 (dd, 1H), 7.1 (dd, 1H), 6.95 (t, 1H), 6.5 (s, 1H), 6.25 (bs, 1H), 4.7 (d, 2H), 3.0 (d, 3H),

實例 482: ¹H NMR (CDCl₃)δ 8.15 (dt, 1H), 8.0 (s, 1H), 7.45-7.35 (m, 4H), 7.25 (d, 2H), 7.15 (dd, 1H), 6.7 (t, 1H), 6.5 (s, 1H), 4.7 (d, 2H), 3.1 (s, 3H), 3.0 (s, 3H)。

實例 483: ¹H NMR (CDCl₃)δ 8.15 (dt, 1H), 8.0 (s, 1H), 7.8 (bs, 1H), 7.7 (d, 1H), 7.5-7.3 (m, 3H), 7.25 (d, 1H), 7.15 (dd, 1H),

6.75 (t, 1H), 6.5 (s, 1H), 6.2 (bs, 1H), 4.7 (d, 2H), 3.0 (d, 3H)。

實例 484: ^1H NMR (CDCl_3) δ 8.15 (dt, 1H), 8.0 (s, 1H), 7.7 (d, 2H), 7.4 (d, 2H), 7.35 (m, 1H), 7.25 (dd, 1H), 7.15 (dd, 1H), 6.8 (t, 1H), 6.5 (s, 1H), 6.0 (bs, 1H), 4.7 (d, 2H), 4.25 (m, 1H), 1.2 (d, 6H)。

實例 485: ^1H NMR (CDCl_3) δ 8.15 (dt, 1H), 8.0 (s, 1H), 7.7 (d, 2H), 7.4 (d, 2H), 7.35 (s, 1H), 7.25 (dd, 1H), 7.1 (dd, 1H), 6.9 (t, 1H), 6.5 (s, 1H), 6.3 (t, 1H), 4.7 (d, 2H), 2.9 (m, 1H), 0.8 (bt, 2H), 0.6 (bt, 2H)。

實例 486: ^1H NMR (CDCl_3) δ 8.15 (dt, 1H), 8.0 (s, 1H), 7.8 (d, 2H), 7.4 (d, 2H), 7.35 (d, 1H), 7.25 (dd, 1H), 7.1 (dd, 1H), 6.9 (t, 1H), 6.5 (s, 1H), 6.2 (t, 1H), 4.7 (d, 2H), 3.3 (dd, 2H), 1.05 (m, 1H), 0.5 (m, 2H), 0.25 (m, 2H)。

實例 487: ^1H NMR (CDCl_3) δ 8.15 (dt, 1H), 8.0 (s, 1H), 7.7 (d, 2H), 7.4 (d, 2H), 7.35 (m, 1H), 7.25 (dd, 1H), 7.15 (dd, 1H), 6.85 (t, 1H), 6.5 (s, 1H), 6.2 (bs, 1H), 4.7 (d, 2H), 4.6 (m, 1H), 2.4 (m, 2H), 1.95 (m, 1H), 1.75 (m, 2H)。

實例 488: ^1H NMR (CDCl_3) δ 8.5 (t, 1H), 8.15 (dt, 1H), 8.0 (s, 1H), 7.7 (d, 2H), 7.4 (d, 2H), 7.35 (m, 1H), 7.25 (dd, 1H), 7.15 (dd, 1H), 6.8 (t, 1H), 6.5 (s, 1H), 5.9 (bs, 1H), 4.7 (d, 2H), 1.4 (s, 9H)。

實例 489: ^1H NMR (CDCl_3) δ 8.15 (dt, 1H), 8.0 (s, 1H), 7.7 (d, 2H), 7.4 (d, 2H), 7.35 (m, 1H), 7.25 (dd, 1H), 7.15 (dd, 1H),

6.8 (t, 1H), 6.5 (s, 1H), 6.0 (bs, 1H), 4.7 (d, 2H), 4.4 (m, 1H), 2.05 (m, 2H), 1.7 (m, 4H), 1.4 (m, 2H)。

實例 490: ^1H NMR (CDCl_3) δ 8.15 (dt, 1H), 8.0 (s, 1H), 7.7 (d, 2H), 7.4 (d, 2H), 7.35 (m, 1H), 7.25 (dd, 1H), 7.15 (dd, 1H), 6.8 (t, 1H), 6.5 (s, 1H), 6.5 (bs, 2H), 4.7 (d, 2H), 4.1 (m, 1H), 3.9-3.7 (m, 3H), 3.3 (m, 1H), 2.0-1.9 (m, 4H)。

實例 491: ^1H NMR (CDCl_3) δ 8.15 (dt, 1H), 8.0 (s, 1H), 7.45-7.35 (m, 5H), 7.25 (dd, 1H), 7.1 (dd, 1H), 6.8 (t, 1H), 6.5 (s, 1H), 4.7 (d, 2H), 3.7 (bs, 2H), 3.3 (bs, 2H), 1.7 (bs, 4H), 1.5 (bs, 2H)。

實例 492: ^1H NMR (CDCl_3) δ 8.15 (dt, 1H), 8.0 (s, 1H), 7.45-7.35 (m, 5H), 7.25 (dd, 1H), 7.1 (dd, 1H), 6.85 (t, 1H), 6.5 (s, 1H), 4.7 (d, 2H), 3.8-3.4 (bm, 8H)。

實例 493: ^1H NMR (CDCl_3) δ 8.15 (dt, 1H), 8.0 (s, 1H), 7.45-7.35 (m, 5H), 7.25 (dd, 1H), 7.1 (dd, 1H), 6.80 (t, 1H), 6.5 (s, 1H), 4.7 (d, 2H), 4.0 (m, 2H), 3.6 (m, 2H), 2.8-2.45 (m, 4H)。

實例 494: ^1H NMR (CH_3OD) δ 8.15 (s, 1H), 8.0 (dt, 1H), 7.45-7.35 (m, 5H), 7.25 (dd, 1H), 7.1 (dd, 1H), 6.80 (t, 1H), 6.5 (s, 1H), 4.7 (d, 2H), 3.7 (bs, 2H), 3.4 (bs, 2H), 2.5-2.4 (m, 4H), 2.2 (s, 3H)。

實例 495: ^1H NMR (CDCl_3) δ 8.15 (dt, 1H), 8.0 (s, 1H), 7.45-7.35 (m, 5H), 7.25 (dd, 1H), 7.1 (dd, 1H), 6.80 (t, 1H), 6.5 (s, 1H), 4.7 (d, 2H), 3.75 (bs, 2H), 3.35 (bs, 2H), 2.4 (bs, 2H), 2.3 (s, 3H), 2.2 (bs, 2H)。

實例 496: ^1H NMR (CDCl_3) δ 7.95 (s, 1H), 7.9 (dt, 1H), 7.8 (t, 1H), 7.7 (d, 2H), 7.15 (m, 4H), 7.05 (dd, 1H), 6.9 (dd, 1H), 6.2 (s, 1H), 4.5 (d, 2H), 3.6 (t, 2H), 3.3 (dt, 2H)。

實例 497: ^1H NMR (CH_3OD) δ 8.1 (s, 1H), 7.9 (dt, 1H), 7.8 (d, 2H), 7.5 (d, 2H), 7.4 (m, 1H), 7.3 (dd, 1H), 7.2 (dd, 1H), 6.4 (s, 1H), 4.7 (d, 2H), 3.5 (t, 2H), 2.7 (m, 2H), 2.6 (bs, 4H), 1.8 (bs, 4H)。

實例 498: ^1H NMR (CDCl_3) δ 8.5 (t, 1H), 8.15 (dt, 1H), 8.0 (s, 1H), 7.8 (d, 2H), 7.4 (d, 2H), 7.35 (m, 1H), 7.25 (dd, 1H), 7.15 (dd, 1H), 6.8 (t, 1H), 6.5 (s, 1H), 4.7 (d, 2H), 3.7-2.5 (m, 4H), 2.35 (s, 3H), 2.2 (m, 1H), 1.9-1.6 (m, 6H)。

實例 499: ^1H NMR (CDCl_3) δ 8.15 (dt, 1H), 8.0 (s, 1H), 7.8 (d, 2H), 7.4 (d, 2H), 7.35 (m, 1H), 7.25 (dd, 1H), 7.15 (dd, 1H), 6.8 (t, 1H), 6.5 (s, 1H), 4.7 (d, 2H), 3.7 (m, 4H), 3.5 (dt, 2H), 2.6 (t, 2H), 2.5 (m, 4H)。

實例 500: ^1H NMR (CH_3OD) δ 8.15 (s, 1H), 7.9 (dt, 1H), 7.8 (d, 2H), 7.45 (d, 2H), 7.4 (m, 1H), 7.25 (dd, 1H), 7.15 (dd, 1H), 6.4 (s, 1H), 4.75 (d, 2H), 4.2 (m, 1H), 3.4-2.8 (m, 7H), 1.9-1.6 (m, 4H)。

實例 501: ^1H NMR (CDCl_3) δ 8.05 (dt, 1H), 8.0 (s, 1H), 7.6 (d, 2H), 7.4 (s, 1H), 7.35 (d, 2H), 7.25 (dd, 1H), 7.1 (dd, 1H), 6.9 (t, 1H), 6.5 (s, 1H), 6.4 (t, 1H), 4.7 (d, 2H), 4.2 (d, 2H), 2.3 (bs, 1H)。

實例 502: ^1H NMR (CDCl_3) δ 8.15 (dt, 1H), 8.0 (s, 1H), 7.75 (d,

2H), 7.45 (s, 1H), 7.4 (d, 2H), 7.3 (dd, 1H), 7.1 (dd, 1H), 6.8 (t, 1H), 6.5 (s, 1H), 6.1 (bs, 1H), 4.7 (d, 2H), 3.5 (dq, 2H), 1.2 (t, 3H)。

實例 503: ^1H NMR (CDCl_3) δ 8.15 (dt, 1H), 8.0 (s, 1H), 7.8 (d, 2H), 7.4 (d, 2H), 7.35 (m, 1H), 7.25 (dd, 1H), 7.15 (dd, 1H), 6.9 (t, 1H), 6.5 (s, 1H), 6.4 (t, 1H), 4.75 (d, 2H), 4.1 (m, 2H)。

實例 504: ^1H NMR (CDCl_3) δ 8.15 (dt, 1H), 8.0 (s, 1H), 7.8 (d, 2H), 7.45 (d, 2H), 7.4 (m, 1H), 7.25 (dd, 1H), 7.1 (dd, 1H), 6.8 (t, 1H), 6.6 (t, 1H), 6.5 (s, 1H), 4.7 (d, 1H), 3.6 (m, 2H), 2.8 (t, 2H), 2.6 (q, 2H), 1.3 (t, 3H)。

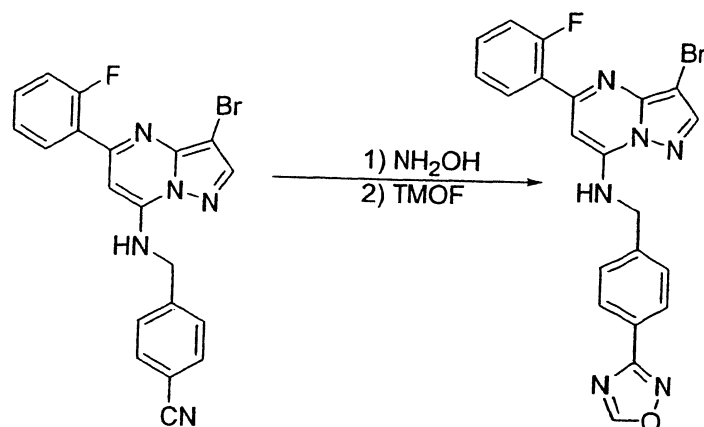
實例 505: ^1H NMR (CDCl_3) δ 8.15 (dt, 1H), 8.0 (s, 1H), 7.4 (m, 1H), 7.25 (dd, 1H), 7.15 (dd, 1H), 7.0 (t, 1H), 6.5 (s, 1H), 3.8 (m, 2H), 2.7 (t, 2H), 3.0 (d, 3H)。

實例 506: ^1H NMR (CDCl_3) δ 8.15 (dt, 1H), 8.0 (s, 1H), 7.4 (m, 1H), 7.25 (dd, 1H), 7.15 (dd, 1H), 7.0 (t, 1H), 6.5 (s, 1H), 3.8 (m, 2H), 3.6 (m, 6H), 3.4 (m, 2H), 2.7 (t, 2H)。

實例 507: ^1H NMR (CDCl_3) δ 8.15 (dt, 1H), 8.0 (s, 1H), 7.4 (m, 1H), 7.25 (dd, 1H), 7.15 (dd, 1H), 7.0 (t, 1H), 6.5 (s, 1H), 3.9 (t, 2H), 3.8 (dt, 2H), 3.7 (t, 2H), 2.7 (t, 2H), 2.6 (m, 4H)。

實例 508: ^1H NMR (CH_3OD) δ 8.1 (s, 1H), 7.95 (dt, 1H), 7.5 (m, 1H), 7.35-7.2 (m, 2H), 6.5 (s, 1H), 3.6 (m, 4H), 3.25 (m, 4H), 2.4 (t, 2H), 2.05 (dt, 2H)。

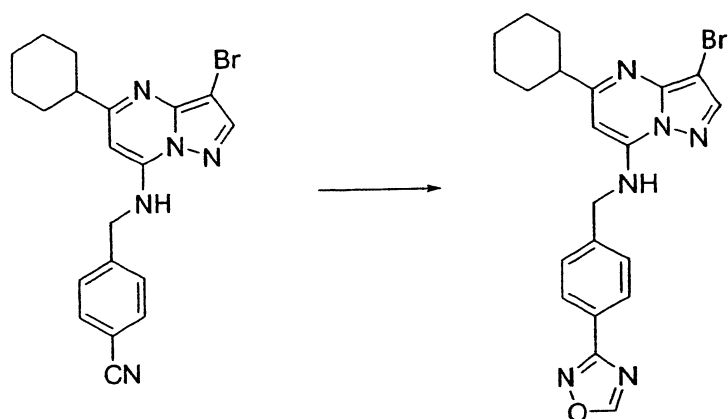
實例 509 :



在 0°C 下將含 NaOH (59 毫克, 1.47 毫莫耳) 之 1 毫升水溶液添加於含 $\text{NH}_2\text{OH} \cdot \text{HCl}$ (102 毫克, 1.47 毫莫耳) 之 10 毫升甲醇懸浮液中。5 分鐘後, 添加實例 210.10 製備之化合物 (208 毫克, 0.49 毫莫耳), 且使反應混合物回流隔夜。真空移除溶劑, 且將殘留物分配在水及 EtOAc 中。 EtOAc 曾經脫水 (Na_2SO_4) 且蒸發溶劑。將所得粗鹽胺基肪懸浮於含催化量 PTS 酸之原甲酸三甲酯中, 且回流隔夜。移除溶劑且將殘留物置於 EtOAc 中。 EtOAc 層以 NaHCO_3 水溶液洗滌, 接著以水及食鹽水洗滌。蒸發溶劑, 殘留物以層析 (矽膠, 己烷: EtOAc (1:1)) 純化, 獲得 80 毫克 (35%) 嘮二唑。 ^1H NMR (CDCl_3) δ 8.75 (s, 1H), 8.20-8.10 (m, 3H), 8.03 (s, 1H), 7.53 (d, $J=9$ Hz, 2H), 7.45-7.36 (m, 1H), 7.30-7.22 (m, 2H), 7.16-7.08 (m, 1H), 6.80 (t, $J=5$ Hz, 1H), 6.56 (s, 1H)。

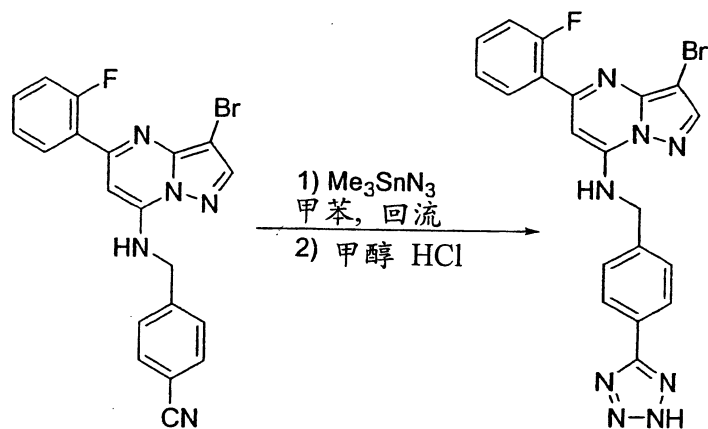
LCMS: $\text{MH}^+ = 465.2$

實例 510:



以基本上與實例 509 所示相同之程序，僅取代製備例 192 製備之化合物，製備上述化合物。產率=75%； $MH^+=453$ ； $m.p.=79.3^\circ C$ 。

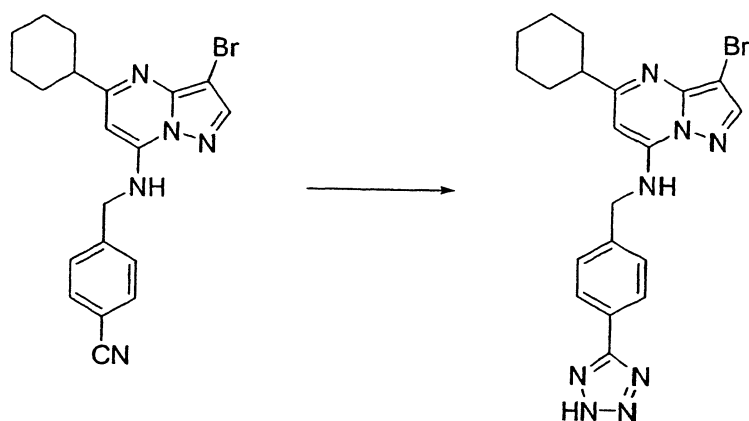
實例 511：



在 Ar 中使含腈 (235 毫克，0.56 毫莫耳) 及 Me_3SnN_3 (343 毫克，1.67 毫莫耳) 之 20 毫升無水甲苯混合物回流 2 天。真空移除溶劑，且將殘留物溶於無水甲醇中。使 HCl 氣泡通入溶液 15 分鐘，且使反應混合物在室溫攪拌隔夜。次日，移除溶劑；將殘留物置於水中，且將 pH 調整至 5。沉澱之產物以 EtOAc 萃取。經脫水 (Na_2SO_4) 後蒸發 EtOAc 層，獲得殘留物，

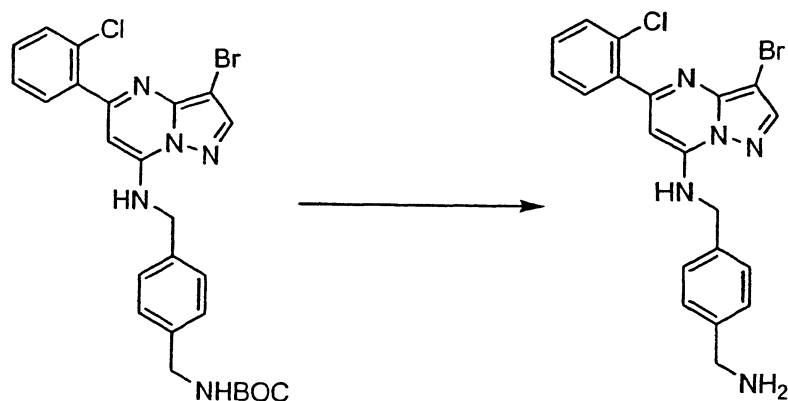
其以層析(矽膠，DCM：MeOH(98：2→95：5))純化，獲得50毫克(19%)純四唑。¹H NMR (CD₃OD)δ 8.10 (s, 1H), 8.00 (d, J=9 Hz, 2H), 7.90 (t, J=7 Hz, 1H), 7.65 (d, J=9 Hz, 2H), 7.50-7.40 (m, 1H), 7.30-7.10 (m, 2H), 6.45 (s, 1H), 4.80 (s, 2H); LCMS:MH⁺= 465.0

實例 512：



以基本上與實例511相同之程序，僅替代實例192之化合物，製備上述化合物。產率=64%；MH⁺=453；m.p.=238.9℃。

實例 513：



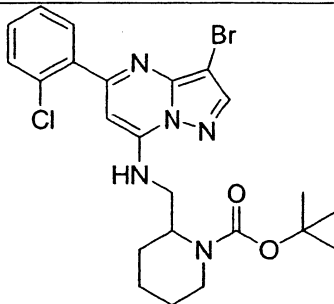
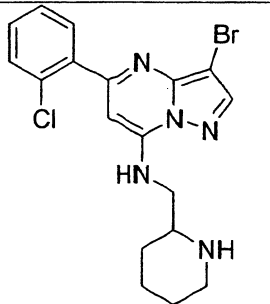
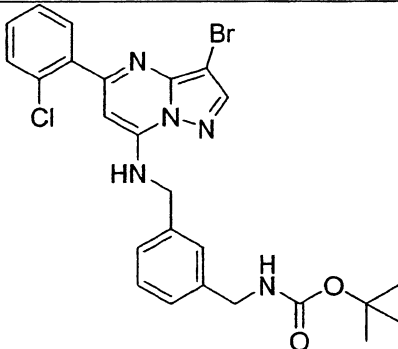
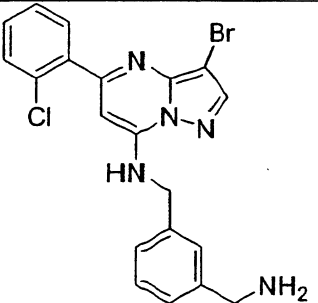
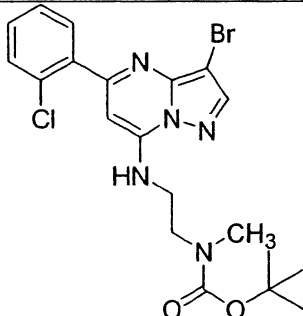
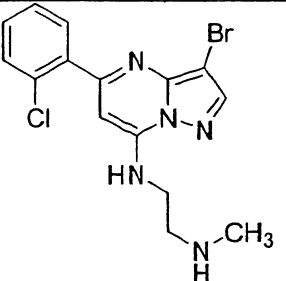
將實例157中製備之化合物溶於二噁烷(30毫升)中，且添加HCl-二噁烷溶液(4 M，30毫升)。反應混合物在室溫攪拌4

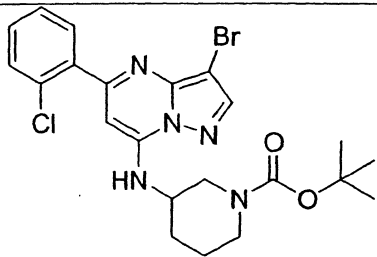
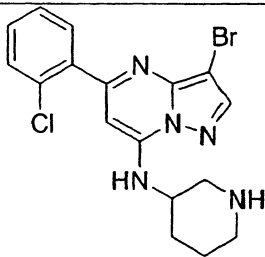
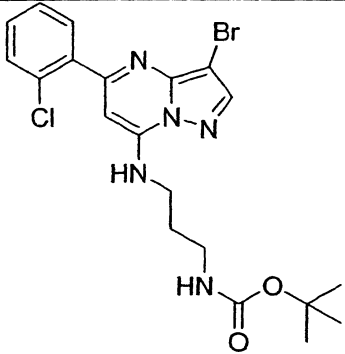
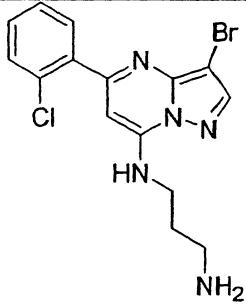
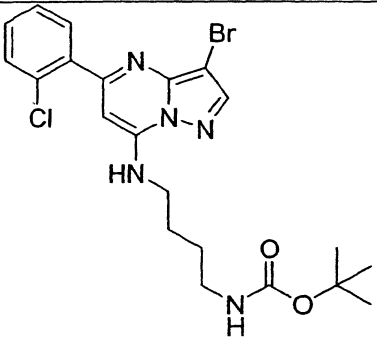
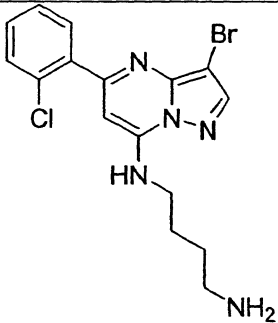
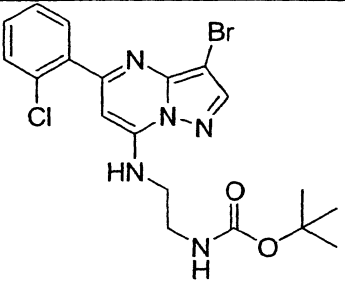
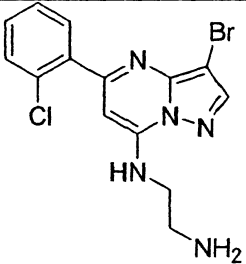
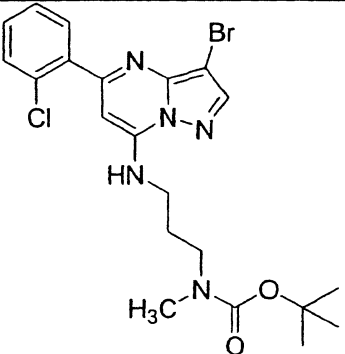
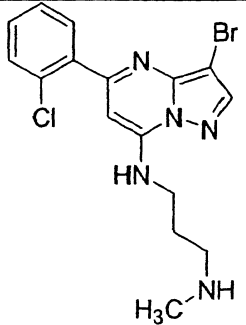
小時。減壓蒸發反應混合物，且添加乙酸乙酯(200毫升)。有機溶液以1 N氫氧化鈉洗滌，接著以飽和食鹽水洗滌。有機層以無水硫酸鈉脫水且減壓蒸發。 $MH^+ = 442.1$ 。

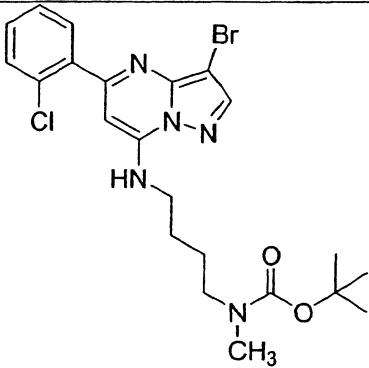
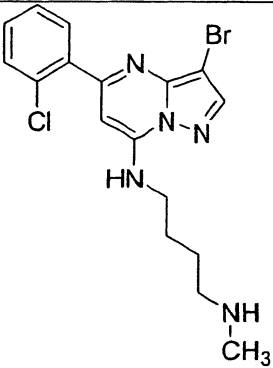
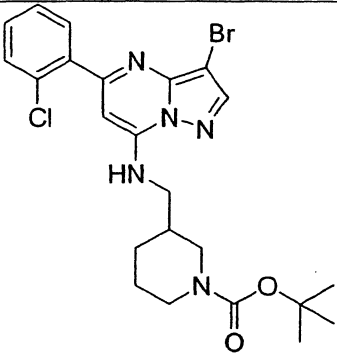
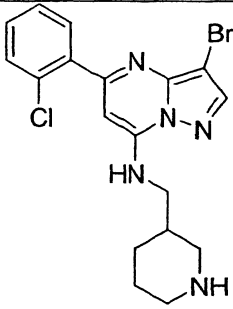
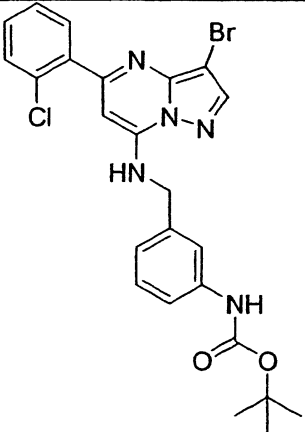
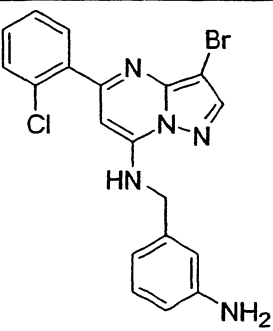
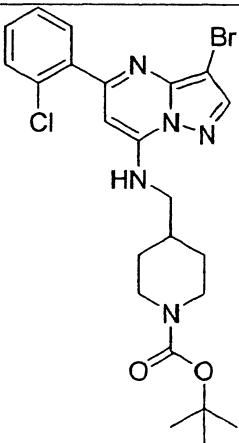
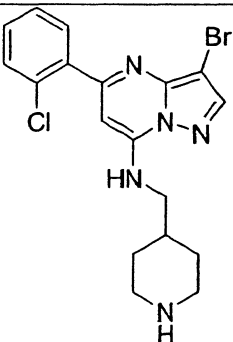
實例 514-526：

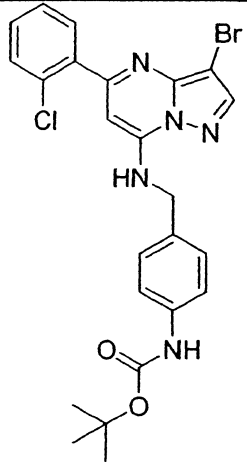
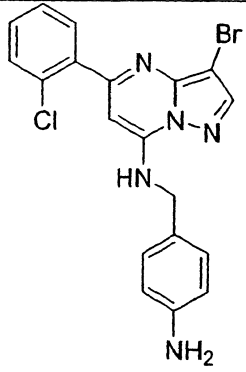
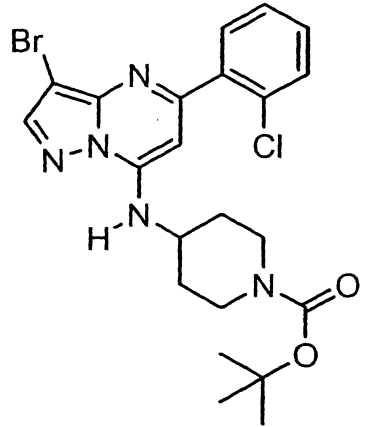
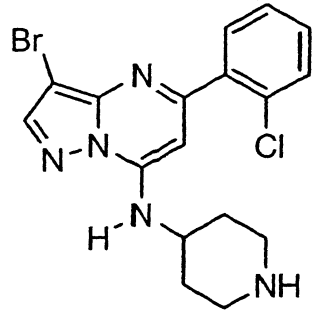
以基本上與實例 513 相同之程序，僅替代表 41 欄 2 所列之化合物，製備表 41 欄 3 所示之化合物。

表 41

實例	欄2	欄3	數據
514			$MH^+ = 420.1$
515			$MH^+ = 442.1$
516			$MH^+ = 380.1$

517			MH ⁺ = 406.1
518			MH ⁺ = 380.1
519			MH ⁺ = 394.1
520			MH ⁺ = 366
521			MH ⁺ = 394

522			MH ⁺ = 408.1
523			MH ⁺ = 420.1
524			
525			MH ⁺ = 420.1

526			MH ⁺ = 428.1
526.10			

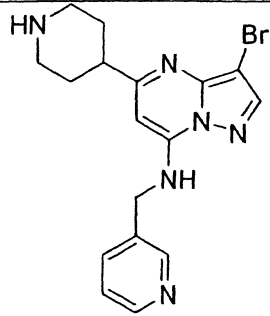
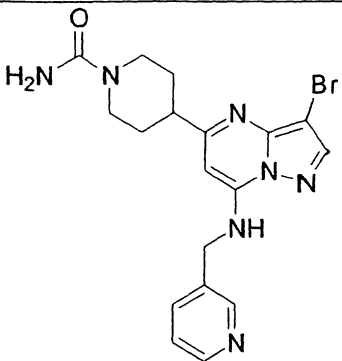
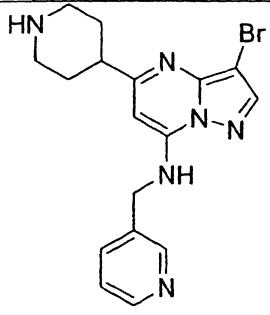
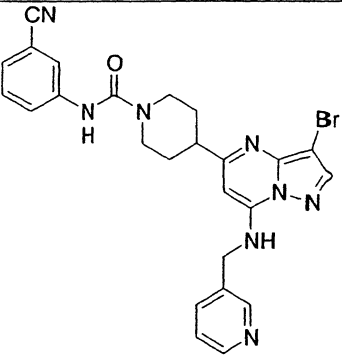
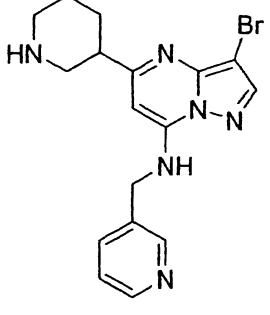
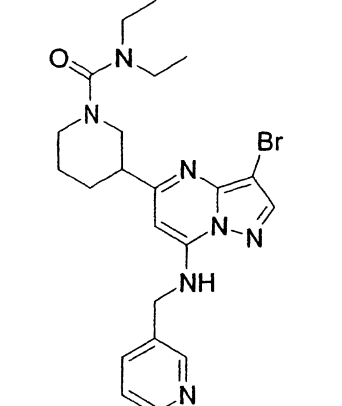
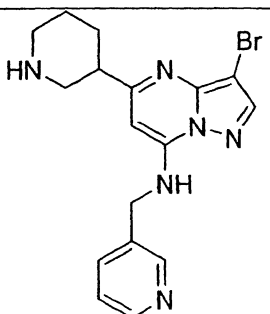
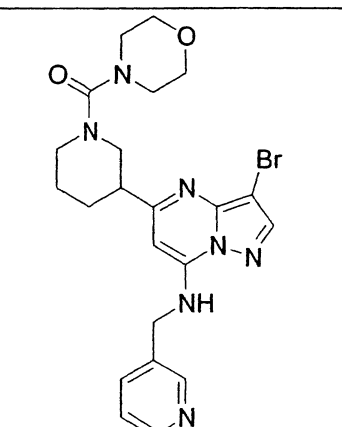
實例 528-564：

5-哌啶基平行形成之一般程序：

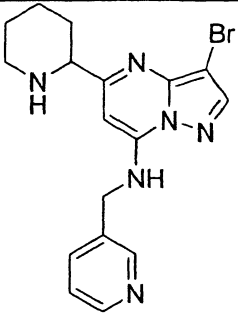
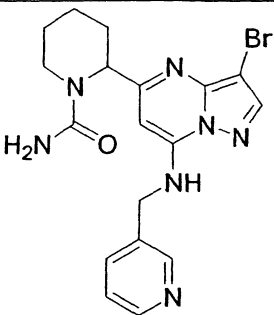
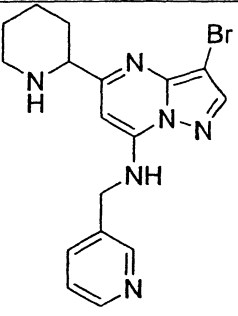
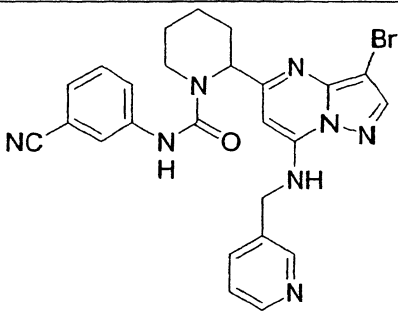
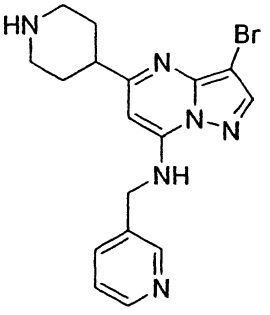
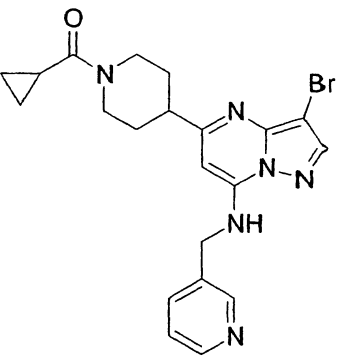
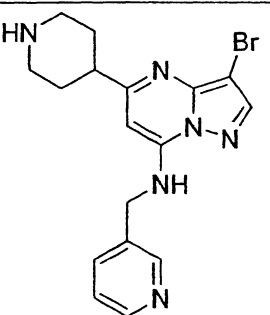
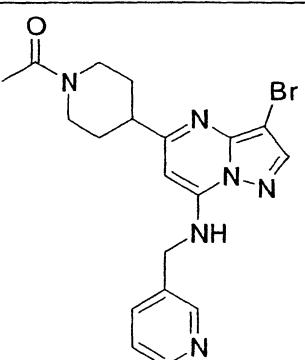
於含表 42 欄 2 所示起始物質 (80 毫克，0.21 毫莫耳) 之無水 CH₂Cl₂ (1.5 毫升) 混合物中添加 DIPEA (75 微升，0.42 毫莫耳) 及適當之遮蓋劑 (1.1 當量，0.23 毫莫耳)。1 至 2 小時後，將反應混合物加於 1000 微製備用 TLC 板上，接著使用 8-10% EtOH-CH₂Cl₂ 作為溶離液進行，獲得表 42 欄 3 所示之化合物。

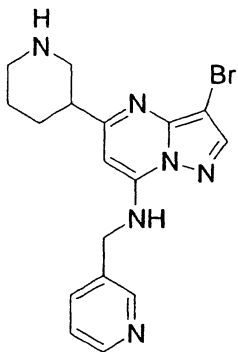
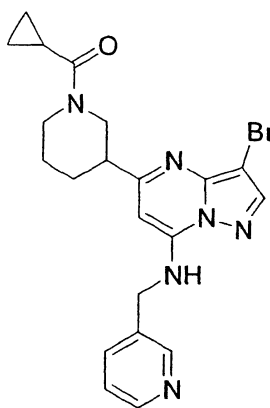
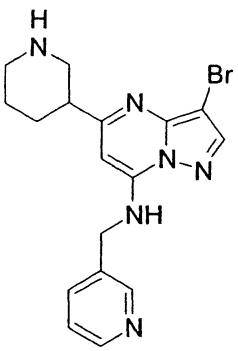
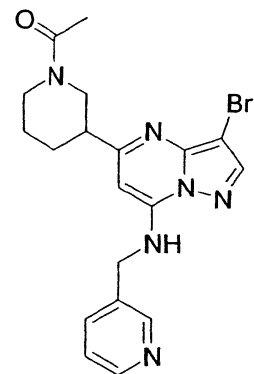
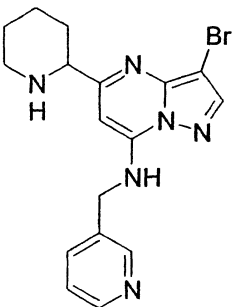
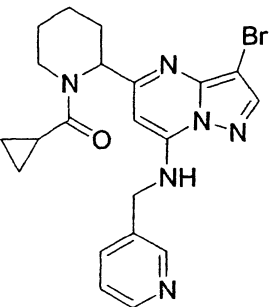
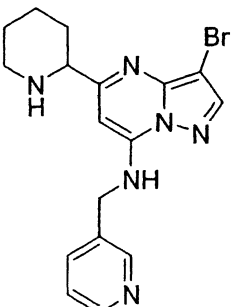
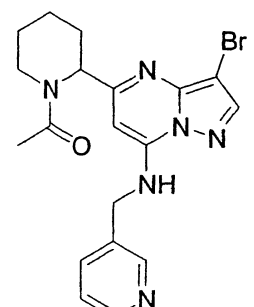
表 42

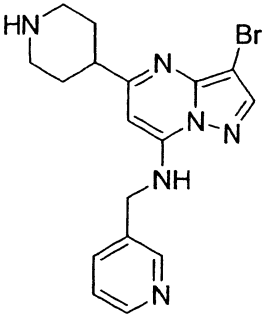
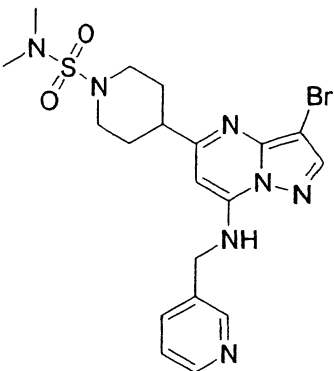
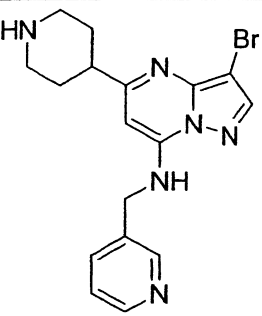
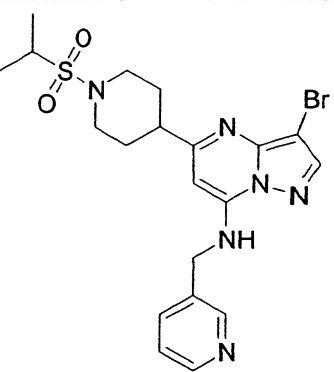
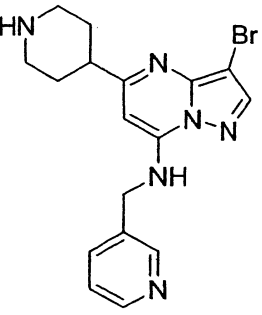
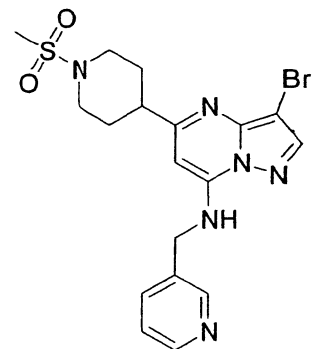
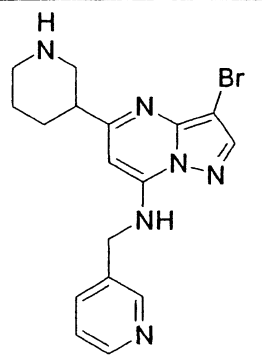
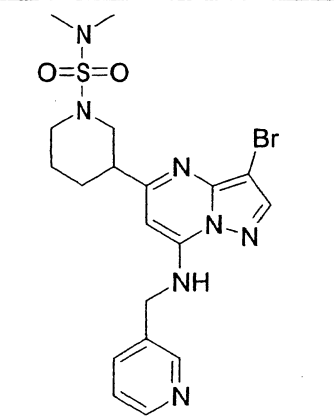
實例	欄2	欄3	數據
528			MH ⁺ = 608 m. p. = 230.1 °C
529			Yield = 82 MH ⁺ = 614 m. p. = 235.4 °C
530			MH ⁺ = 486 m. p. = 60.5 °C
531			MH ⁺ = 500 m. p. = 113.6 °C

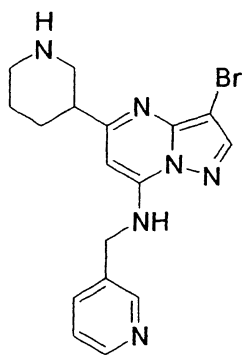
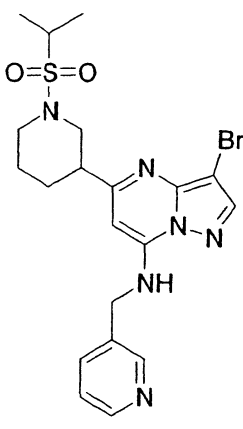
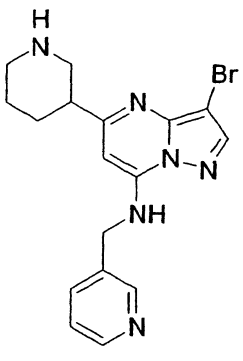
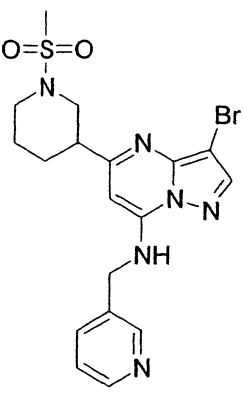
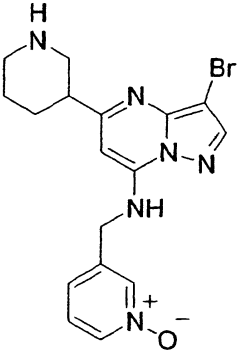
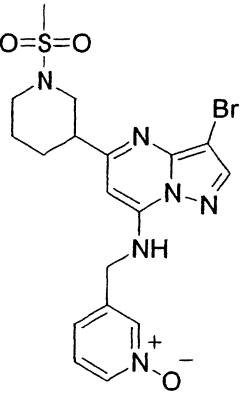
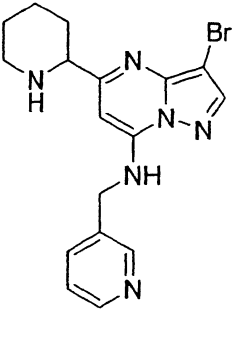
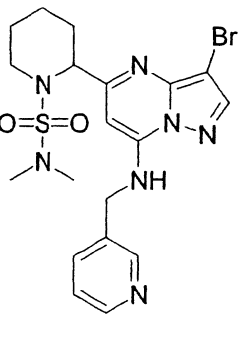
532			$MH^+ = 430$ m. p. = 158.3 – 159.2 °C
533			$MH^+ = 531$ m. p. = 105.9 °C
534			$MH^+ = 486$
535			$MH^+ = 500$

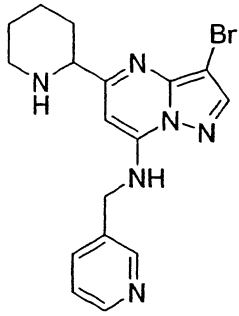
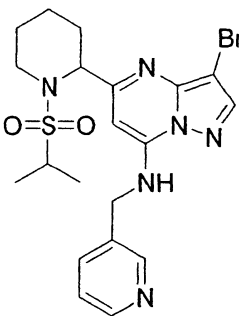
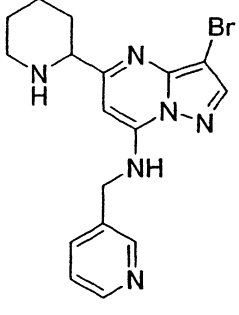
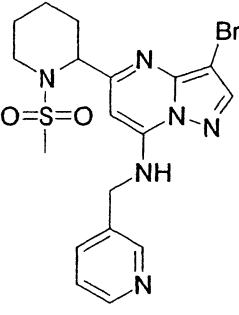
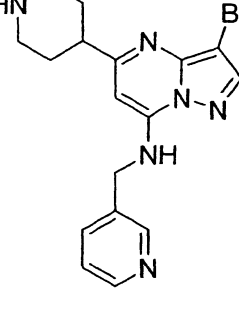
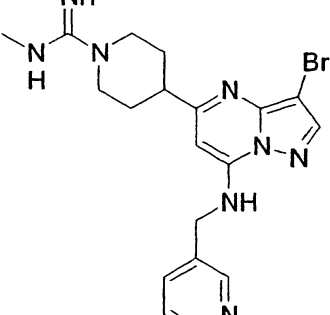
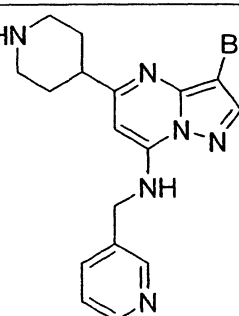
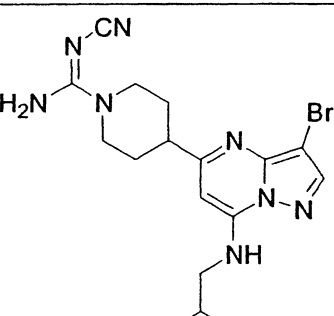
536			MH ⁺ = 430
537			MH ⁺ = 531
538			MH ⁺ = 486 m. p. = 69.6 °C
539			MH ⁺ = 500 m. p. = 82.3 °C

540			$MH^+ = 430$ m. p. = 223.6 °C
541			$MH^+ = 531$ m. p. = 118.1 °C
542			$MH^+ = 455$ m. p. = 109 – 110 °C
543			$MH^+ = 429$ m. p. = 111.5 °C

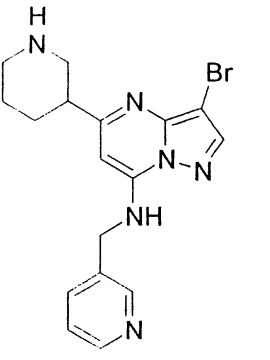
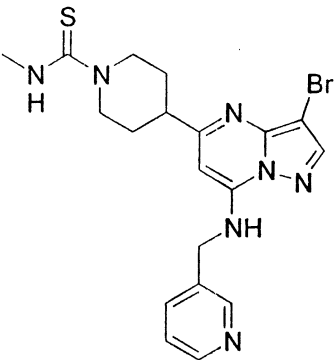
544			$MH^+ = 455$
545			$MH^+ = 429$
546			$MH^+ = 455$ m. p. = 80.1 °C
547			$MH^+ = 429$ m. p. = 64.7 °C

548			$MH^+ = 494$ m. p. = 76.5 °C
549			$MH^+ = 493$ m. p. = 83.6 °C
550			$MH^+ = 465$ m. p. = 207.5 °C
551			$MH^+ = 494$

552			MH ⁺ = 493
553			MH ⁺ = 465
554			MH ⁺ = 481 m. p. = 102.7 °C
555			MH ⁺ = 494 m. p. = 85.3 °C

556			MH ⁺ = 493 m. p. = 89.1 °C
557			MH ⁺ = 465 m. p. = 83.8 °C
558			Yield = quant. MH ⁺ = 443 m. p. = 98.3 °C (HCl salt)
559			MH ⁺ = 454

560		Yield = quant. MH ⁺ = 429 m. p. = 111.5 – 112.6 °C
561		MH ⁺ = 460 m. p. = 122.7 °C
562		MH ⁺ = 460 m. p. = 95.4 °C
563		MH ⁺ = 460

564			$MH^+ = 460$ m. p. = 95.4 °C
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選用實例之額外數據列於下：

實例 534: 1H NMR (300 MHz, $CDCl_3$) δ 8.66-8.62 (s, 1H), 8.62-8.58 (d, 1H), 7.95 (s, 1H), 7.72-7.68 (d, 1H), 7.36-7.31 (dd, 1H), 6.66-6.62 (t, 1H), 5.93 (s, 1H), 4.65-4.62 (d, 2H), 3.86-3.82 (d, 1H), 3.65-3.58 (m, 1H), 3.26-3.12 (dd, 4H), 3.02-2.80 (m, 3H), 2.10-2.00 (m, 1H), 1.67-1.57 (m, 3H)。

實例 535: 1H NMR (300 MHz, $CDCl_3$) δ 8.66-8.62 (s, 1H), 8.62-8.58 (d, 1H), 7.95 (s, 1H), 7.72-7.67 (d, 1H), 7.36-7.30 (dd, 1H), 6.70-6.64 (t, 1H), 5.90 (s, 1H), 4.63-4.61 (d, 2H), 3.93-3.86 (m, 1H), 3.69-3.61 (m, 4H), 3.27-3.23 (m, 4H), 3.10-3.01 (dd, 1H), 2.93-2.84 (m, 2H), 2.08-2.03 (m, 1H), 1.90-1.57 (m, 4H)。

實例 536: 1H NMR (300 MHz, $CDCl_3$) δ 8.67 (s, 1H), 8.62-8.58 (d, 1H), 7.96 (s, 1H), 7.72-7.68 (d, 1H), 7.36-7.30 (dd, 1H), 6.79-6.72 (t, 1H), 5.96 (s, 1H), 4.86 (br s, 2H), 4.66-4.63 (d, 2H), 3.89-3.73 (m, 2H), 3.55-3.32 (m, 2H), 3.00-2.89 (m, 1H), 2.10-1.97 (m, 2H), 1.70-1.53 (m, 2H)。

實例 537: ^1H NMR (300 MHz, CDCl_3) δ 8.66 (s, 1H), 8.62-8.58 (d, 1H), 7.98 (s, 1H), 7.77-7.76 (t, 1H), 7.72-7.69 (d, 1H), 7.63-7.59 (m, 1H), 7.56 (s, 1H), 7.36-7.29 (dd, 1H), 6.83-6.79 (t, 1H), 5.96 (s, 1H), 4.67-4.64 (d, 2H), 3.98-3.93 (dd, 1H), 3.79-3.68 (m, 2H), 3.37-3.28 (m, 1H), 3.03-2.94 (m, 1H), 2.12-1.99 (m, 1H), 1.76-1.56 (m, 3H)。

實例 544: ^1H NMR (300 MHz, CDCl_3) δ 8.66-8.62 (d, 1H), 8.61-8.58 (dd, 1H), 7.95 (s, 1H), 7.72-7.67 (d, 1H), 7.36-7.30 (dd, 1H), 6.80-6.62 (br s, 1H), 5.88 (s, 1H), 4.63 (s, 2H), 3.08-2.95 (m, 2H), 2.87-2.80 (m, 2H), 2.04 (m, 1H), 1.85-1.78 (m, 4H), 1.52-1.44 (m, 1H), 0.87-0.82 (m, 2H), 0.72-0.66 (m, 2H)。

實例 545: ^1H NMR (300 MHz, CDCl_3) δ 8.66 (s, 1H), 8.62-8.58 (br t, 1H), 7.97 (s, 1H), 7.73-7.68 (d, 1H), 7.36-7.30 (br t, 1H), 6.79-6.72 (br t, 1H), 5.96 (s, 1H), 4.64 (br s, 2H), 4.59-4.46 (br d, 1H), 3.95-3.74 (br m, 1H), 3.57-3.49 (dd, 1H), 3.10-3.01 (dd, 1H), 2.86-2.70 (m, 2H), 2.13 (s, 3H), 2.06-2.00 (m, 2H), 1.65-1.48 (m, 2H)。

實例 551: ^1H NMR (300 MHz, CDCl_3) δ 8.67 (s, 1H), 8.63-8.59 (d, 1H), 7.96 (s, 1H), 7.74-7.69 (d, 1H), 7.36-7.30 (dd, 1H), 6.69-6.64 (t, 1H), 5.95 (s, 1H), 4.67-4.63 (d, 2H), 3.85-3.65 (m, 1H), 3.75-3.65 (m, 1H), 3.25-3.18 (dd, 1H), 3.03-2.90 (m, 2H), 2.81 (s, 6H), 2.03-1.95 (m, 1H), 1.89-1.68 (m, 3H)。

實例 552: ^1H NMR (300 MHz, CDCl_3) δ 8.67 (s, 1H), 8.62-8.59

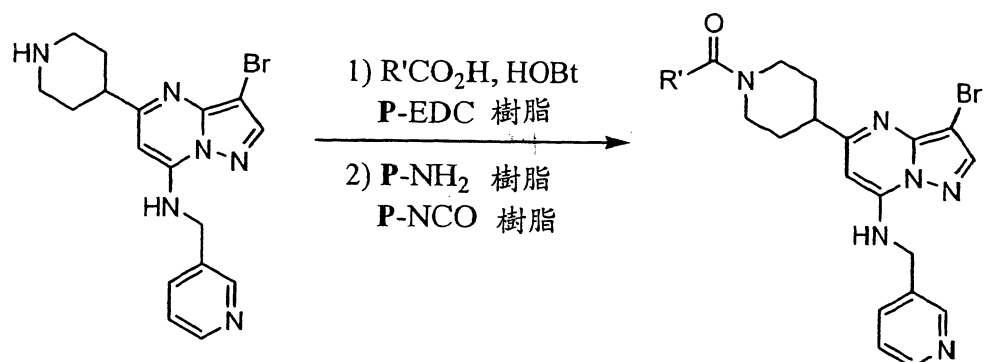
(d, 1H), 7.95 (s, 1H), 7.74-7.69 (d, 1H), 7.36-7.31 (dd, 1H), 6.67-6.60 (t, 1H), 5.98 (s, 1H), 4.67-4.63 (d, 2H), 3.92-3.86 (m, 1H), 3.85-3.75 (m, 1H), 3.40-3.30 (dd, 1H), 3.27-3.16 (m, 1H), 3.10-2.86 (m, 2H), 2.10-1.78 (m, 3H), 1.40-1.30 (d, 6H)。

實例 553: ^1H NMR (300 MHz, CDCl_3) δ 8.67 (s, 1H), 8.62 (br s, 1H), 7.96 (s, 1H), 7.74-7.69 (d, 1H), 7.36-7.31 (dd, 1H), 6.70-6.66 (t, 1H), 5.98 (s, 1H), 4.67-4.63 (d, 2H), 3.88-3.81 (m, 1H), 3.71-3.65 (m, 1H), 3.20-3.11 (dd, 1H), 3.02-2.91 (m, 1H), 2.90-2.80 (m, 4H), 2.01-1.80 (m, 3H)。

實例 559: ^1H NMR (300 MHz, CDCl_3) δ 8.66-8.60 (d, 1H), 8.50-8.44 (dd, 1H), 8.01 (s, 1H), 7.93 (m, 1H), 7.48-7.40 (dd, 1H), 6.08 (s, 1H), 4.80-4.74 (s, 2H), 4.32-4.19 (br d, 2H), 3.10-2.86 (m, 2H), 1.95-1.68 (m, 4H)。

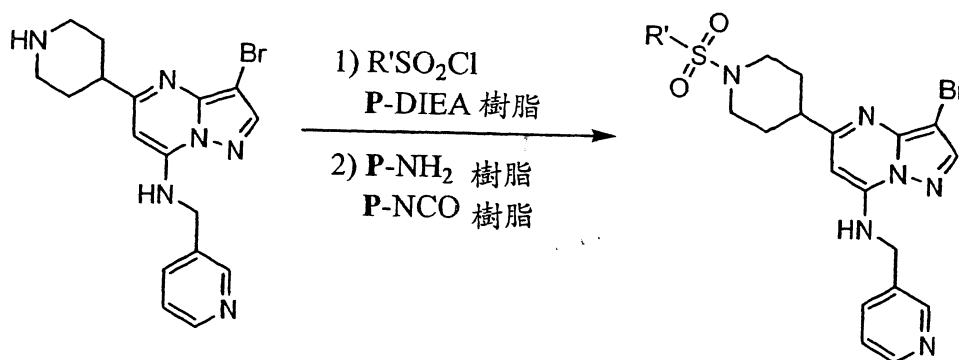
實例 563: ^1H NMR (300 MHz, CDCl_3) δ 8.66 (s, 1H), 8.62-8.58 (d, 1H), 7.96 (s, 1H), 7.73-7.68 (d, 1H), 7.36-7.30 (dd, 1H), 6.96-6.86 (br s, 1H), 6.79-6.74 (t, 1H), 6.00 (s, 1H), 4.67-4.64 (d, 2H), 4.37-4.30 (dd, 1H), 4.22-4.13 (m, 1H), 3.97-3.86 (dd, 1H), 3.73-3.64 (m, 1H), 3.17-3.14 (d, 3H), 3.07-2.99 (m, 1H), 2.20-1.97 (m, 2H), 1.68-1.48 (m, 2H)。

一般程序 1: 醯胺形成平行合成之程序:



在具有可移動上密封及固定下密封之聚丙烯96洞反應塊中進行平行合成。各反應洞均裝置20微米聚丙烯底部熔塊，且最大體積為3毫升。收集塊並未裝置底部熔塊。各反應洞均添加含胺(0.021毫莫耳)之DMF-THF-MeCN混合物(4:3:3 v/v, 0.95毫升)之溶液、EDC樹脂(P-EDC, 聚合物實驗室公司, 43毫克, 0.063毫莫耳)、1-羥基苯并三唑(HOBt, 5.67毫克, 0.042毫莫耳)及含羧酸之二甲基甲醯胺溶液(1 M, 0.0315毫升, 0.0315毫莫耳)。使反應混合物在室溫攪拌16小時。將粗產物溶液過濾於含參胺樹脂(P-NH₂, Argonaut技術公司, 30毫克, 0.126毫莫耳)及異氰酸酯樹脂(P-NCO, Argonaut技術公司, 35毫克, 0.063毫莫耳)之反應洞中。使反應混合物在室溫下攪拌16小時，且過濾於收集塊中。減壓蒸發產物溶液，獲得所需之醯胺產物。

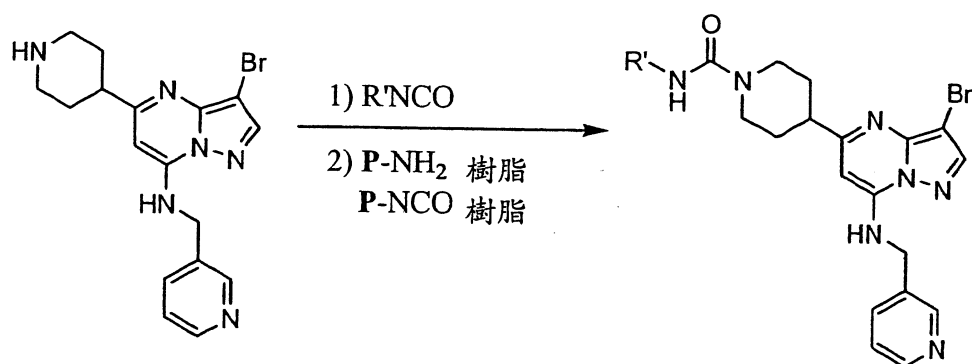
一般程序2：磺醯胺形成平行合成之程序



在具有可移動上密封及固定下密封之聚丙烯96洞反應塊中進行平行合成。各反應洞均裝置20微米聚丙烯底部熔塊，且最大體積為3毫升。收集塊並未裝置底部熔塊。各反應洞均添加含胺(0.021毫莫耳)之DMF-THF-MeCN混合物

(3:2:2 v/v, 0.95 毫升)之溶液、DIEA 樹脂 (P-DIEA, Argonaut 技術公司, 18 毫克, 0.063 毫莫耳) 及含磺醯氯之二甲基甲醯胺溶液 (1 M, 0.0315 毫升, 0.0315 毫莫耳)。使反應混合物在室溫攪拌 16 小時。將粗產物溶液過濾於含參胺樹脂 (P-NH₂, Argonaut 技術公司, 30 毫克, 0.126 毫莫耳) 及異氰酸酯樹脂 (P-NCO, Argonaut 技術公司, 35 毫克, 0.063 毫莫耳) 之反應洞中。使反應混合物在室溫攪拌 16 小時, 且過濾於收集塊中。減壓蒸發產物溶液, 獲得所需之磺醯胺產物。

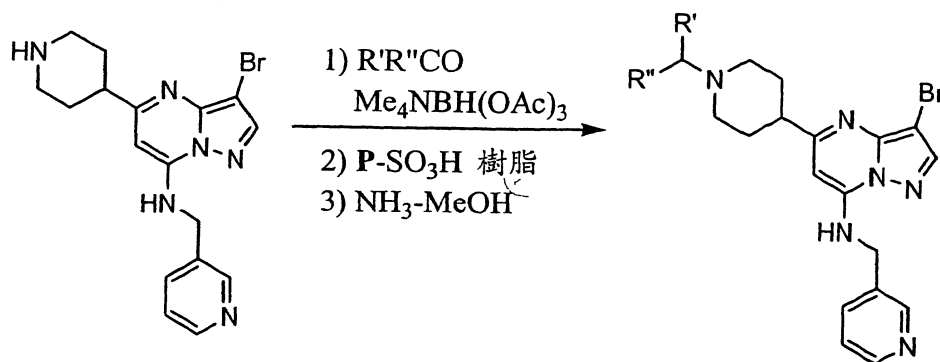
一般程序 3: 尿素形成平行合成之程序



在具有可移動上密封及固定下密封之聚丙烯 96 洞反應塊中進行平行合成。各反應洞均裝置 20 微米聚丙烯底部熔塊, 且最大體積為 3 毫升。收集塊並未裝置底部熔塊。各反應洞均添加含胺 (0.021 毫莫耳) 之 DMF-MeCN 混合物 (1:1 v/v, 0.95 毫升) 之溶液及含異氰酸酯之二氯甲烷溶液 (0.33 M, 0.126 毫升, 0.042 毫莫耳)。使反應混合物在室溫攪拌 16 小時。將粗產物溶液過濾於含參胺樹脂 (P-NH₂, Argonaut 技術公司, 30 毫克, 0.126 毫莫耳) 及異氰酸酯樹脂 (P-NCO, Argonaut 技術公司, 35 毫克, 0.063 毫莫耳) 之反應洞中。使

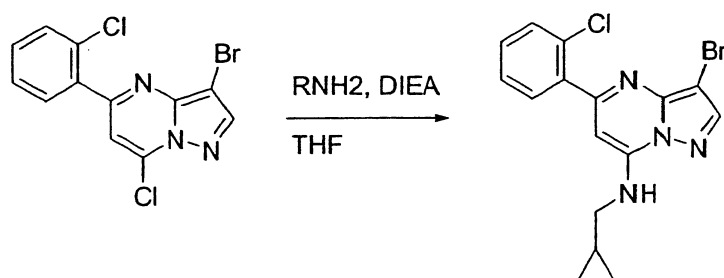
反應混合物在室溫下攪拌16小時，且過濾於收集塊中。減壓蒸發產物溶液，獲得所需之尿素產物。

一般程序4：還原性烷化平行合成之程序



在具有可移動上密封及固定下密封之聚丙烯96洞反應塊中進行平行合成。各反應洞均裝置20微米聚丙烯底部熔塊，且最大體積為3毫升。收集塊並未裝置底部熔塊。各反應洞均添加含胺(0.021毫莫耳)之AcOH-DCE混合物(1：99 v/v，0.5毫升)、含醛或酮之二氯甲烷溶液(1 M，0.147毫升，0.147毫莫耳)及含四甲基銨三乙醯氧基硼氫化物(11毫克，0.042毫莫耳)之AcOH-DCE混合物(1：99 v/v，0.5毫升)溶液。使反應混合物在室溫攪拌3天。將粗產物溶液過濾於含磺酸樹脂Lanterns(P-SO₃H，Mimotopes Pty Ltd.，0.3毫莫耳)之反應洞中。使反應混合物在室溫攪拌2小時且傾析。產物樹脂Lanterns以甲醇(1毫升)洗滌三次。添加含氫之甲醇溶液(2 M，1.2毫升)。在室溫下攪拌反應混合物30分鐘，且過濾於收集塊中。減壓蒸發產物溶液，獲得所需三級胺產物。

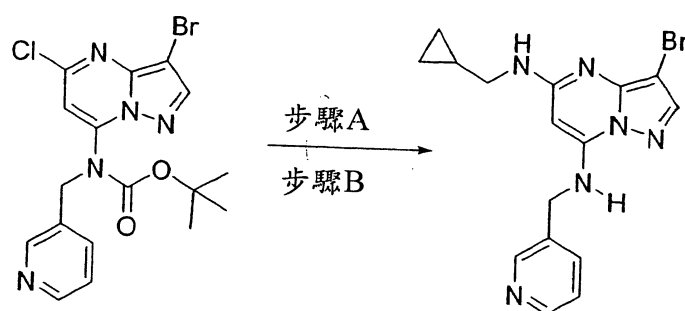
一般程序5：平行合成7,N-取代之吡唑并[1,5a]嘧啶之程序



於含 3-溴-7-氯-5-(2-氯-苯基)-吡唑并[1,5-a]嘧啶(9.0 毫克, 0.03 毫莫耳)之四氫呋喃中添加二異丙基乙胺(12 微升, 0.07 毫莫耳), 接著添加環丙基甲基胺(70 微升, 0.07 毫莫耳, DMF 之 1 M 溶液)。反應混合物加熱至 70°C 歷時 36 小時, 接著冷卻至室溫。混合物以 (P-NCO, Argonaut 技術公司, 70 毫克, 0.12 毫莫耳) 及 P-CO₃ (Argonaut 技術公司, 70 毫克, 0.24 毫莫耳) 處理, 且在室溫搖晃 12-18 小時。溶液經過濾且蒸發至乾, 獲得產物; 實測之 m/z 375.21。

一般程序 6: 5,N-取代之吡唑并[1,5a]嘧啶之平行合成程序
一般方法:

平行合成係在前述 96 洞聚丙烯塊中進行。該例中, 需要加熱, 反應係在分別以聚丙烯墊密封, 且以 96 洞熱傳塊達到加熱之 2.5 毫升玻璃管中進行。



步驟 A:

於含 3-溴-5-氯-7-N-Boc-烷基胺基-吡啶并[1,5-a]嘓啶(17毫克，0.04毫莫耳)之對-二噶烷中添加 DIEA(9微升，0.05毫莫耳)，接著添加環丙基甲基胺(80微升，0.08毫莫耳，異丙醇之 1 M 溶液)。反應混合物加熱至 90℃ 歷時 36 小時，再冷卻至室溫。混合物以 P-NCO(Argonaut 技術公司，70 毫克，0.12毫莫耳)及 P-CO₃(Argonaut 技術公司，70 毫克，0.24毫莫耳)處理，且搖晃 12-18 小時。溶液經過濾且蒸發至乾，獲得產物。

步驟 B(酸性)：

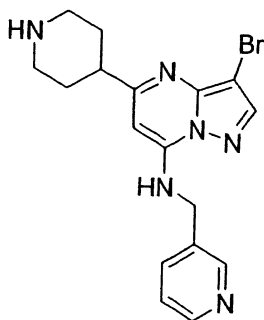
將步驟 A 之產物置於 35%TFA/DCM 中，且攪拌 4 小時，接著高度真空濃縮。殘留物以 10%HCl(水溶液)/MeOH 處理，攪拌 2 小時，再經濃縮，獲得所需產物。實測 m/z 375.21。

步驟 B(鹼性)：

將步驟 A 之產物置於 EtOH 中，且以 Ambersep®900-OH 離子交換樹脂(Across，100 毫克)處理，在溫和攪拌下回流加熱 48 小時。反應混合物冷卻至室溫，且濃縮獲得所需產物。

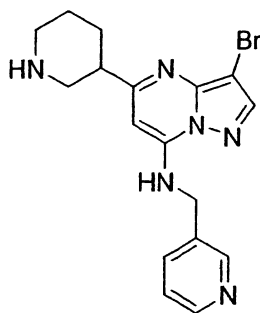
實例 565：

使用一般程序 1 所示之程序及下列實例 462 之化合物，製備表 43 中所示實測 m/z 之化合物。



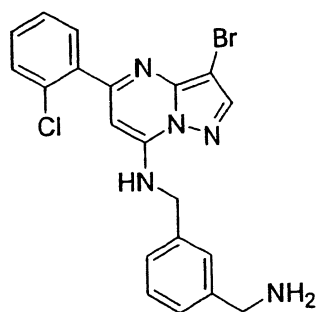
實例 566：

使用一般程序 1 所示之程序及下列實例 471 之化合物，製備具有實測 m/z 之表 44 所示之化合物。



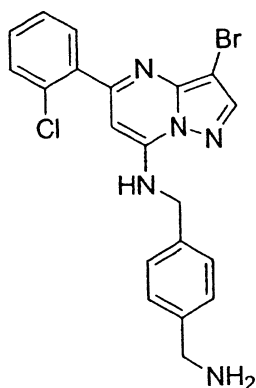
實例 567：

使用一般程序 1 所示之程序及下列實例 515 之化合物，製備具有實測 m/z 之表 45 所示之化合物。



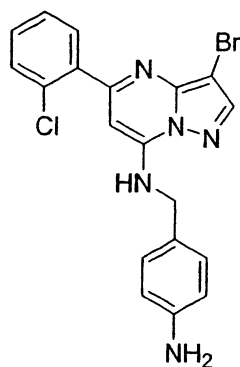
實例 568：

使用一般程序 1 所示之程序及下列實例 513 之化合物，製備具有實測 m/z 之表 46 所示之化合物。



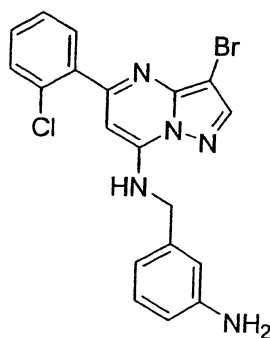
實例 569：

使用一般程序 1 所示之程序及下列實例 526 之化合物，製備具有實測 m/z 之表 47 所示之化合物。



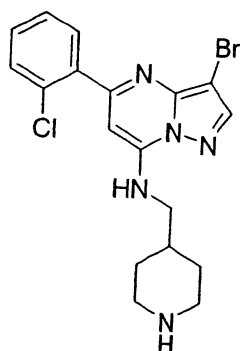
實例 570：

使用一般程序 1 所示之程序及下列實例 524 之化合物，製備具有實測 m/z 之表 48 所示之化合物。



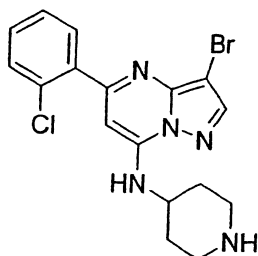
實例 571：

使用一般程序 1 所示之程序及下列實例 525 之化合物，製備具有實測 m/z 之表 49 所示之化合物。



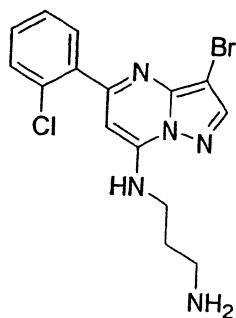
實例 572：

使用一般程序 1 所示之程序及下列實例 526.10 之化合物，
製備具有實測 m/z 之表 50 所示之化合物。



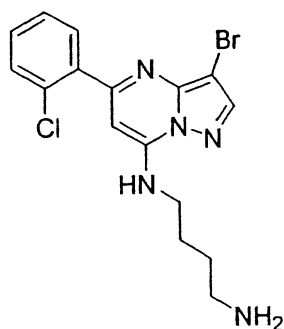
實例 573：

使用一般程序 1 所示之程序及下列實例 518 之化合物，製
備具有實測 m/z 之表 51 所示之化合物。



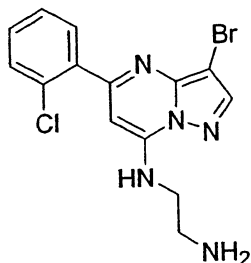
實例 574：

使用一般程序 1 所示之程序及下列實例 519 之化合物，製
備具有實測 m/z 之表 52 所示之化合物。



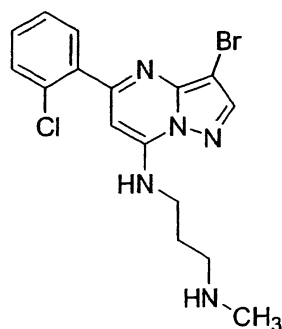
實例 575：

使用一般程序1所示之程序及下列實例520之化合物，製備具有實測 m/z 之表53所示之化合物。



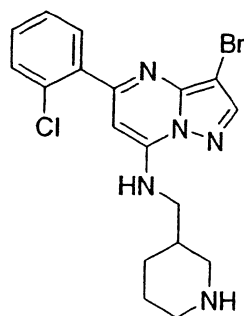
實例 576：

使用一般程序1所示之程序及下列實例522之化合物，製備具有實測 m/z 之表54所示之化合物。



實例 577：

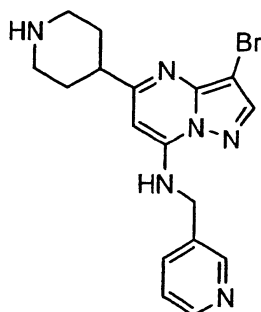
使用一般程序1所示之程序及下列實例523之化合物，製備具有實測 m/z 之表55所示之化合物。



實例 578：

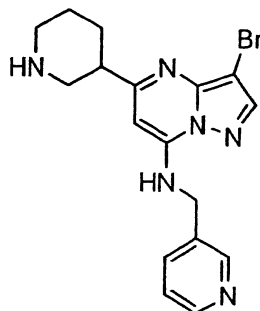
使用一般程序2所示之程序及下列實例462之化合物，製

備具有實測 m/z 之表 56 所示之化合物。



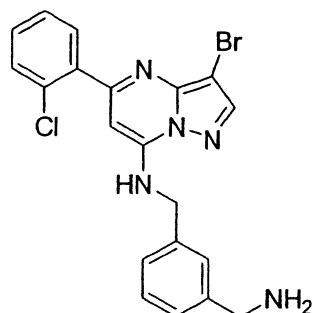
實例 579：

使用一般程序 2 所示之程序及下列實例 471 之化合物，製備具有實測 m/z 之表 57 所示之化合物。



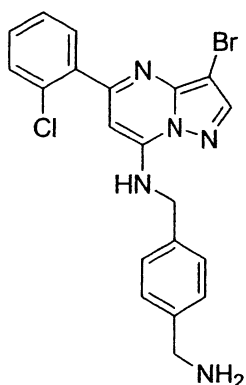
實例 580：

使用一般程序 2 所示之程序及下列實例 515 之化合物，製備具有實測 m/z 之表 58 所示之化合物。



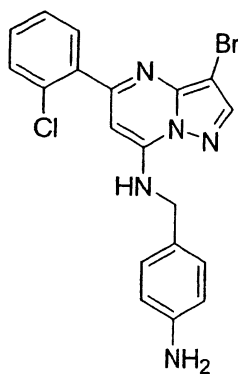
實例 581：

使用一般程序 2 所示之程序及下列實例 513 之化合物，製備具有實測 m/z 之表 59 所示之化合物。



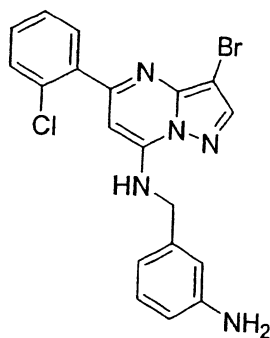
實例 582：

使用一般程序 2 所示之程序及下列實例 513 之化合物，製備具有實測 m/z 之表 60 所示之化合物。



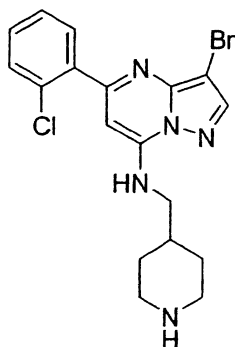
實例 583：

使用一般程序 2 所示之程序及下列實例 524 之化合物，製備具有實測 m/z 之表 61 所示之化合物。



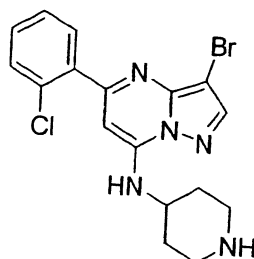
實例 584：

使用一般程序2所示之程序及下列實例525之化合物，製備具有實測 m/z 之表62所示之化合物。



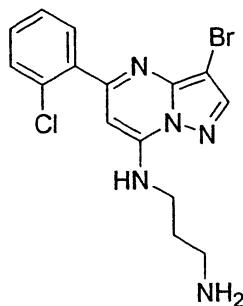
實例 585：

使用一般程序2所示之程序及下列實例526.10之化合物，製備具有實測 m/z 之表63所示之化合物。



實例 586：

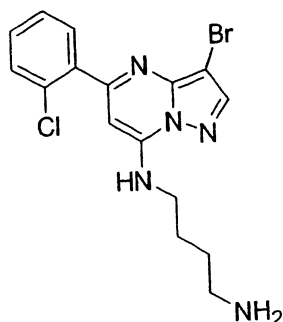
使用一般程序2所示之程序及下列實例518之化合物，製備具有實測 m/z 之表64所示之化合物。



實例 587：

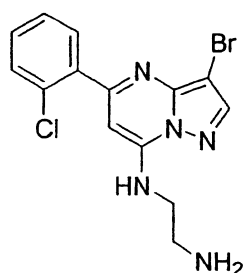
使用一般程序2所示之程序及下列實例519之化合物，製

備具有實測 m/z 之表 65 所示之化合物。



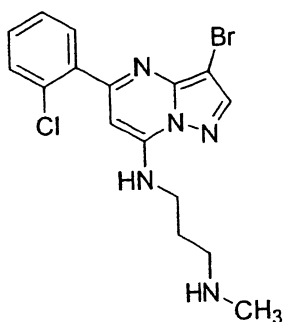
實例 588：

使用一般程序 2 所示之程序及下列實例 520 之化合物，製備具有實測 m/z 之表 67 所示之化合物。



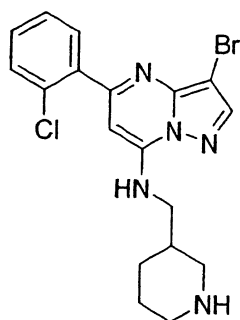
實例 589：

使用一般程序 2 所示之程序及下列實例 521 之化合物，製備具有實測 m/z 之表 68 所示之化合物。



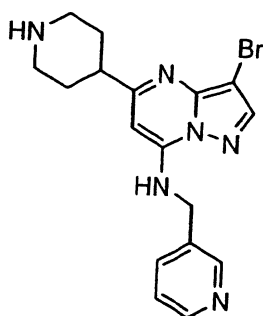
實例 590：

使用一般程序 2 所示之程序及下列實例 523 之化合物，製備具有實測 m/z 之表 69 所示之化合物。



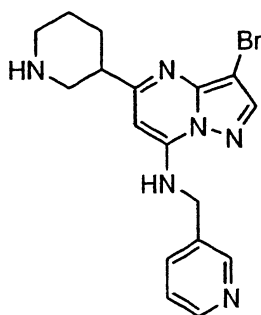
實例 591：

使用一般程序 3 所示之程序及下列實例 462 之化合物，製備具有實測 m/z 之表 70 所示之化合物。



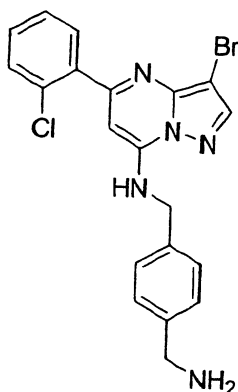
實例 592：

使用一般程序 3 所示之程序及下列實例 471 之化合物，製備具有實測 m/z 之表 71 所示之化合物。



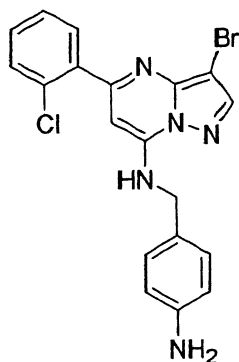
實例 593：

使用一般程序 3 所示之程序及下列實例 513 之化合物，製備具有實測 m/z 之表 72 所示之化合物。



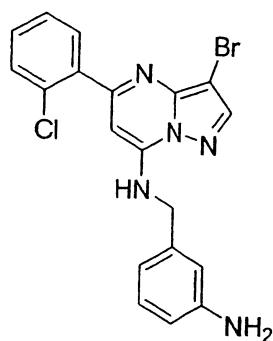
實例 594：

使用一般程序3所示之程序及下列實例524之化合物，製備具有實測 m/z 之表73所示之化合物。



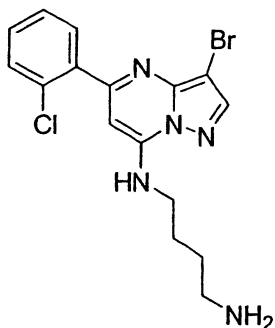
實例 595：

使用一般程序3所示之程序及下列實例524之化合物，製備具有實測 m/z 之表74所示之化合物。



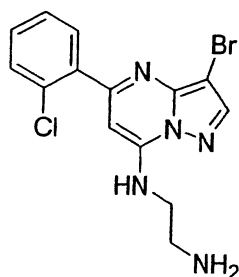
實例 596：

使用一般程序3所示之程序及下列實例519之化合物，製備具有實測 m/z 之表75所示之化合物。



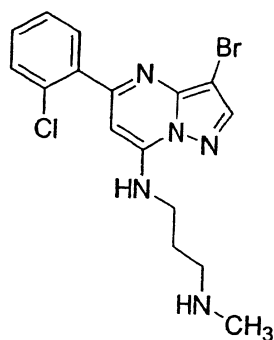
實例 597：

使用一般程序3所示之程序及下列實例520之化合物，製備具有實測 m/z 之表76所示之化合物。



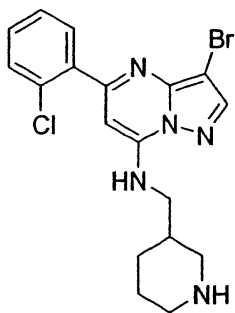
實例 598：

使用一般程序3所示之程序及下列實例521之化合物，製備具有實測 m/z 之表77所示之化合物。



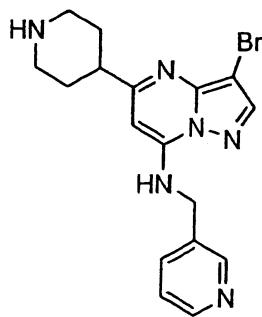
實例 599：

使用一般程序3所示之程序及下列實例523之化合物，製備具有實測 m/z 之表78所示之化合物。



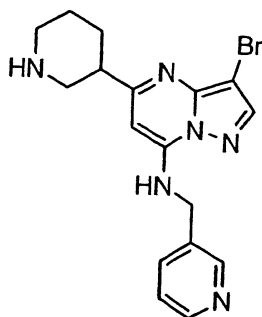
實例 600：

使用一般程序4所示之程序及下列實例462之化合物，製備具有實測 m/z 之表79所示之化合物。



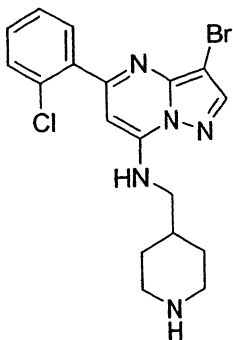
實例 601：

使用一般程序4所示之程序及下列實例471之化合物，製備具有實測 m/z 之表80所示之化合物。



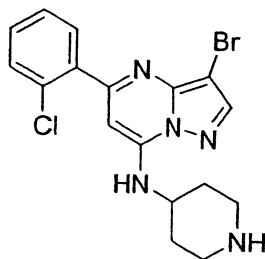
實例 602：

使用一般程序4所示之程序及下列實例525之化合物，製備具有實測 m/z 之表81所示之化合物。



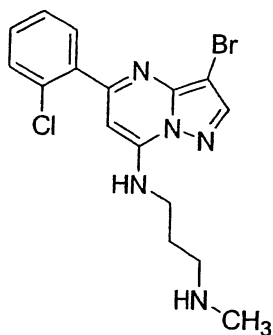
實例 603：

使用一般程序4所示之程序及下列實例526.10之化合物，製備具有實測 m/z 之表82所示之化合物。



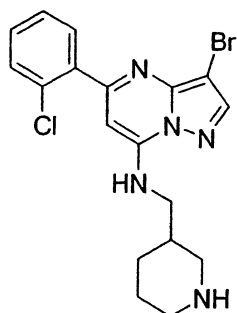
實例 604：

使用一般程序4所示之程序及下列實例521之化合物，製備具有實測 m/z 之表83所示之化合物。



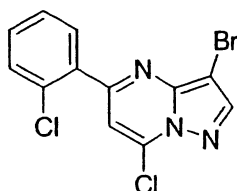
實例 605：

使用一般程序4所示之程序及下列實例523之化合物，製備具有實測 m/z 之表84所示之化合物。



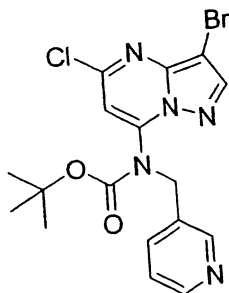
實例 606：

使用一般程序5所示之程序及下列製備例81之化合物，製備具有實測 m/z 之表85所示之化合物。



實例 607：

使用一般程序6所示之程序及下列製備例196之化合物，製備具有實測 m/z 之表86所示之化合物。



分析：

桿病毒架構：週期素 A 及 E 藉 PCR 選殖入 pFASTBAC (Invitrogen)，而在胺基端添加 GluTAG 序列(EYMPME)而在抗 -GluTAG 親合性管柱上純化。表現之蛋白質大小約為 46kDa(週期素 E)及 50kDa(週期素 A)。CDK2 藉 PCR 選殖入 pFASTBAC，而在羧基端添加凝血素抗原決定基 tag (YDVDPDYAS)。表現之蛋白質大小約為 34kDa。

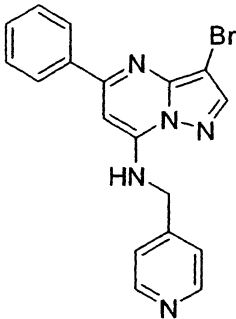
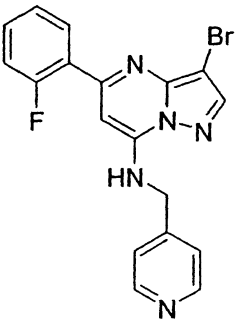
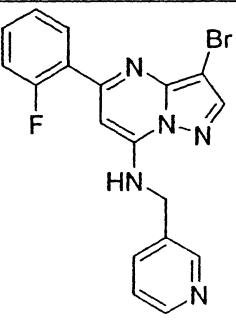
酵素製造：表現週期素 A、E 及 CDK2 之重組桿病毒以相等多價感染力 (MOI=5) 共同感染至 SF9 細胞中 48 小時。藉 1000 RPM 離心 10 小時收取細胞，接著含週期素之粒片與含 CDK2 之細胞粒片混合並在冰上於 5 倍粒片體積之含 50 mM Tris pH 8.0、0.5% NP40、1 mM DTT 及蛋白酶/磷脂酶抑制劑 (Roche 診斷 GmbH, Mannheim, 德國) 之溶胞緩衝液中溶胞 30 分鐘。混合物攪拌 30-60 分鐘以促進週期素-CDK2 錯合物形成。混合之溶胞物在 15000 RPM 旋轉 10 分鐘且保留上澄液。接著使用抗 -GluTAG 珠粒 (對一升 SF9 細胞而言) 以捕捉週期素-CDK2 錯合物。結合之珠粒於溶胞緩衝液中洗滌 3 次。蛋白質以含 100-200 微克/毫升之 GluTAG 肽之溶胞緩衝液競爭性溶離。溶離液於 2 升之含 50 mM Tris pH 8.0、1 mM DTT、10 mM MgCl₂、100 uM 原鈳酸鈉及 20% 甘油脂之激酶緩衝液中滲析隔夜。酵素整份在 -70°C 儲存。

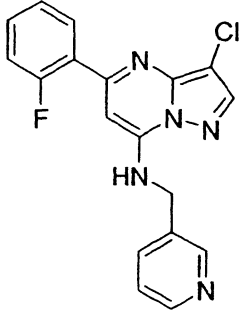
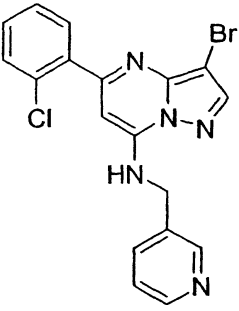
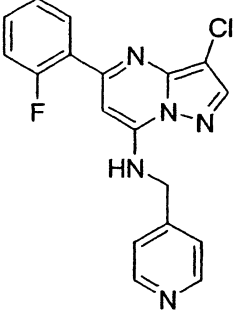
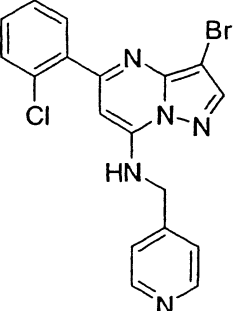
體外激酶分析：於低蛋白質結合之 96-洞盤 (Corning 公司, Corning, 紐約) 中進行 CDK2 激酶分析 (週期素 A 或 E-依賴性)。酵素於含 50 mM Tris pH 8.0、10 mM MgCl₂、1 mM DTT

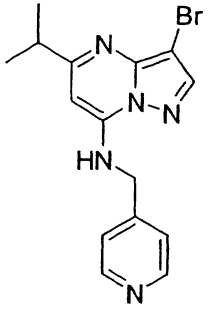
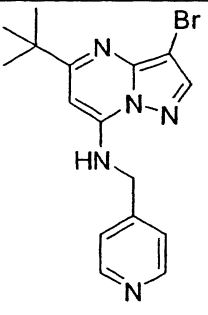
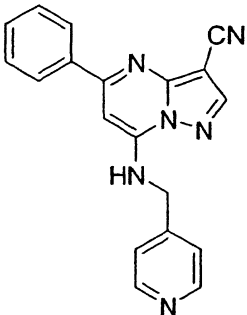
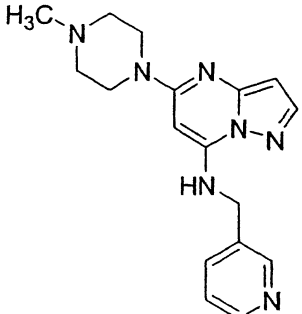
及 0.1 mM 原鈳酸鈉之激酶緩衝液中稀釋至終濃度 50 微克/毫升。該等反應中所用之受質為衍生自 Histone H1(購自 Amersham, 英國)之生物素化之肽。該受質在冰上解凍並於激酶緩衝液中稀釋至 2 μ M。化合物於 10% DMSO 中稀釋至所需濃度。對各激酶反應而言, 使 20 微升 50 微克/毫升之酵素溶液(1 微克酵素)及 20 微升 2 μ M 受質溶液混合, 接著於各洞中與 10 微升稀釋化合物混合供測試。激酶反應藉添加 50 微升 4 μ M ATP 及 1 μ Ci 之 33 P-ATP(購自 Amersham, 英國)起始。反應在室溫進行 1 小時。反應藉添加 200 微升含 0.1% Triton X-100、1 mM ATP、5 mM EDTA 及 5 毫克/毫升鏈黴肽塗佈之 SPA 珠粒(購自 Amersham, 英國)之終止緩衝液停止 15 分鐘。該 SPA 珠粒接著使用 Filtermate 環球收取機(Packard/Perkin Elmer 生命科學公司)捕捉至 96-洞 GF/B 過濾盤(Packard/Perkin Elmer 生命科學公司)上。藉 2 M NaCl 洗滌該珠粒 2 次接著以含 1% 磷酸之 2 M NaCl 洗滌 2 次而消除非專一訊號。接著使用 TopCount 96 洞液體閃爍計數器(購自 Packard/Perkin Elmer 生命科學公司)測量放射活性訊號。

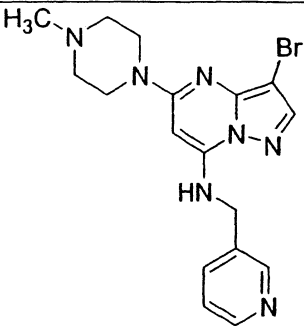
IC₅₀測定: 自所產生之抑制數據(各重複 2 次)自 8 個連續稀釋抑制化合物之點繪製劑量-相關曲線。化合物濃度相對%激酶活性(藉經處理樣品之 CPM 除以未經處理樣品之 CPM 所計算)作圖。為了產生 IC₅₀ 值, 接著將劑量相關曲線套入標準 S 型曲線並藉非線性回歸分析衍生 IC₅₀ 值。對本發明化合物所得之 IC₅₀ 值示於表 87。使用週期素 A 或週期素 E 使用上述分析產生該等激酶活性。

表 87

化合物	實例	IC ₅₀ (μM)
	1	0.020 0.029
	3	0.032 0.024
	4	0.011

	5	0.021
	8	0.003
	6	0.064 0.029
	7	0.01 0.006

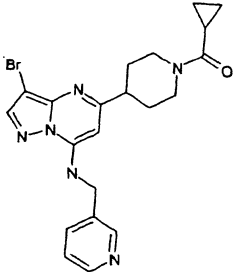
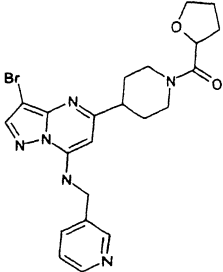
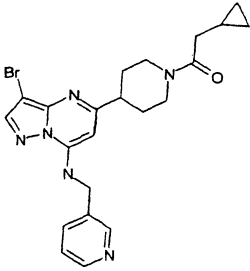
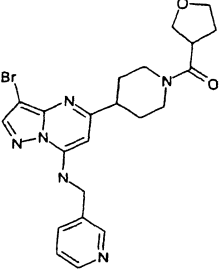
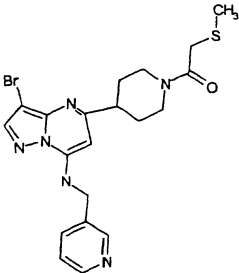
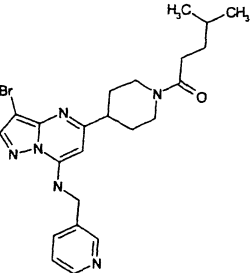
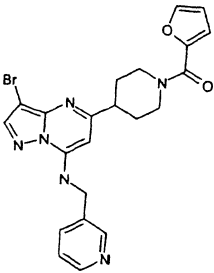
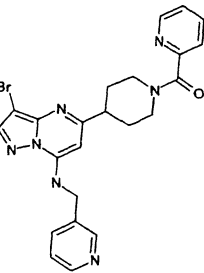
 <chem>CC(C)c1nc2c(ncn2Cn1Cc3cccnc3)Br</chem>	10	0.042
 <chem>CC(C)(C)c1nc2c(ncn2Cn1Cc3cccnc3)Br</chem>	12	0.17
 <chem>N#Cc1nc2c(ncn2Cn1Cc3cccnc3)c4ccccc4</chem>	16	0.62
 <chem>CN1CCN(CC1)c2nc3c(ncn3Cn2Cc4cccnc4)c5ccncc5</chem>	1	5.6

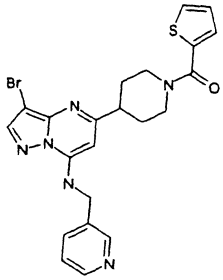
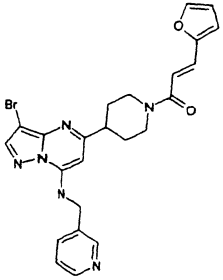
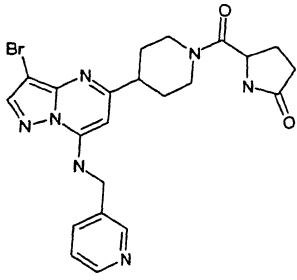
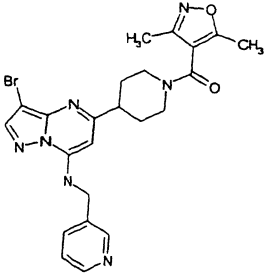
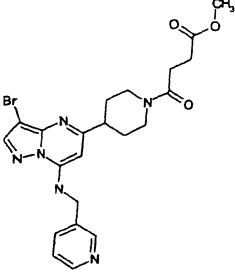
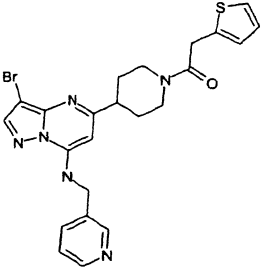
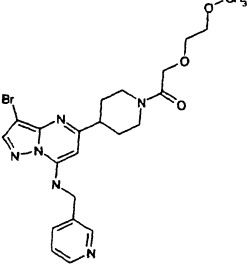
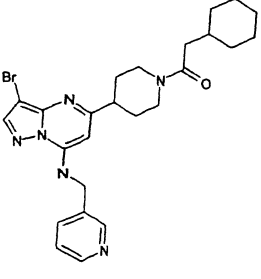
	3	0.14
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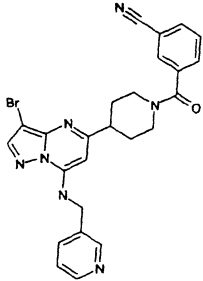
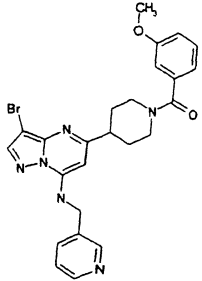
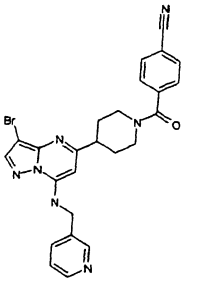
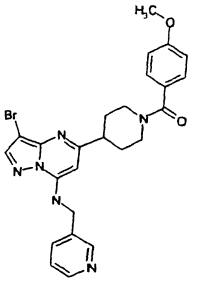
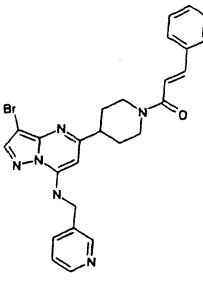
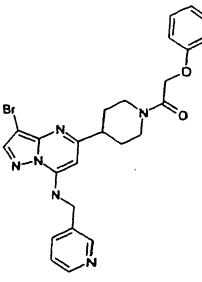
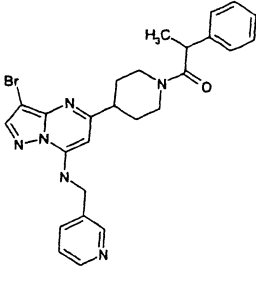
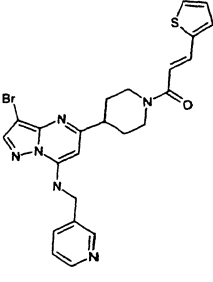
如上述分析值所證明，本發明化合物展現優異之CDK抑制性質。

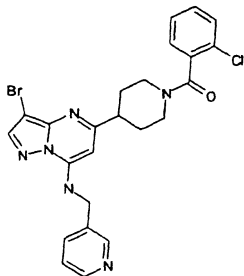
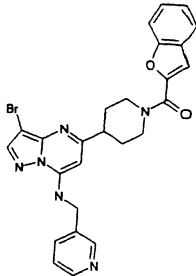
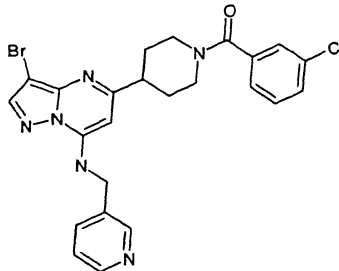
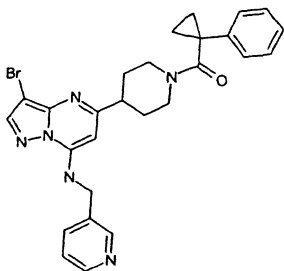
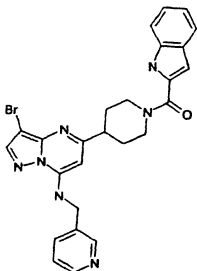
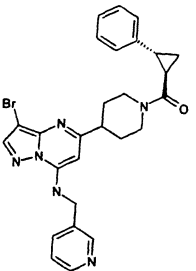
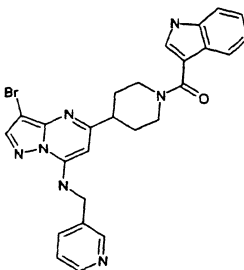
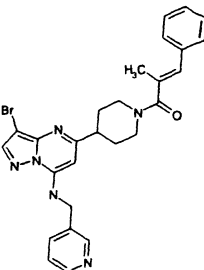
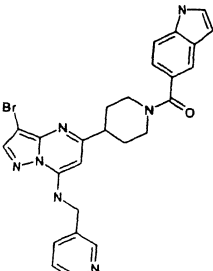
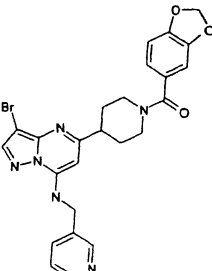
雖然本發明已藉上述特定具體例加以描述，但對熟知本技藝者而言之許多選擇、改質及其他變化將為易於推知者。所有該等選擇、改質及其他變化欲落入本發明之精神及範圍內。

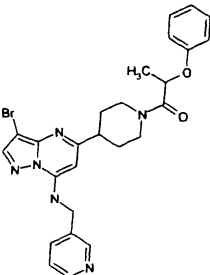
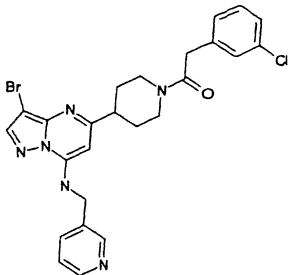
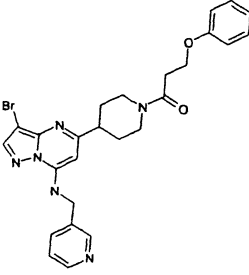
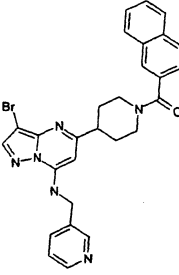
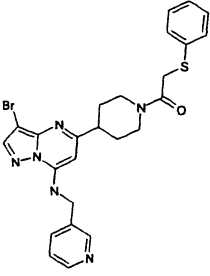
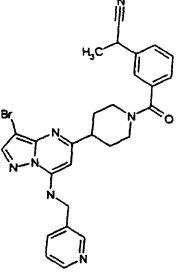
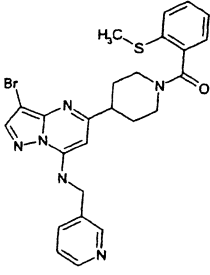
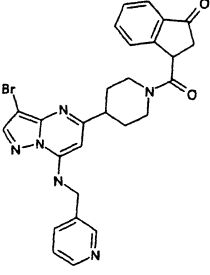
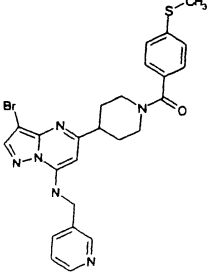
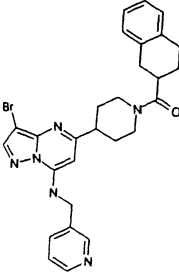
表43

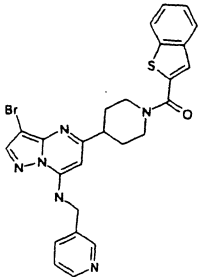
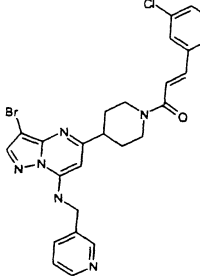
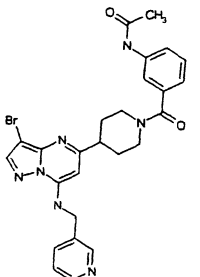
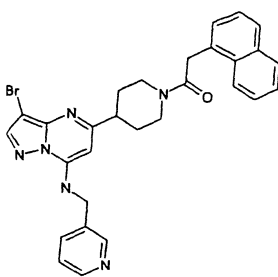
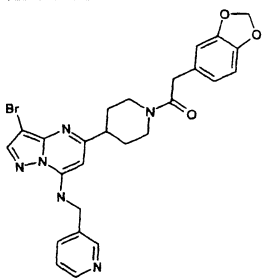
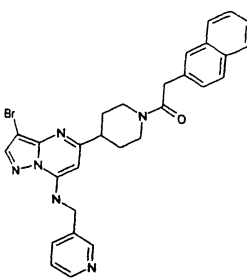
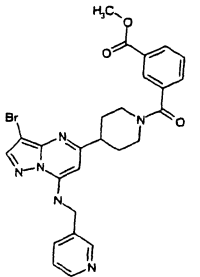
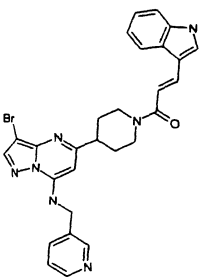
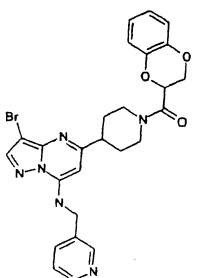
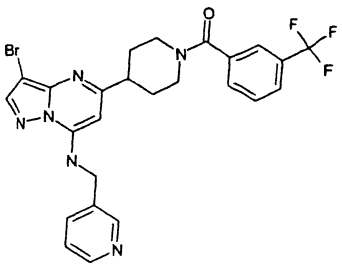
實例	化合物	m/z	實例	化合物	m/z
4301		457.25	4305		487.27
4302		471.26	4306		487.27
4303		477.26	4307		487.27
4304		483.27	4308		494.27

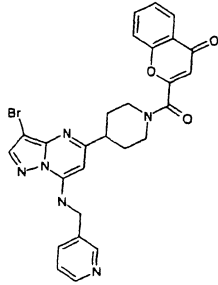
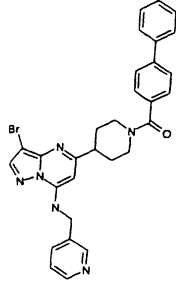
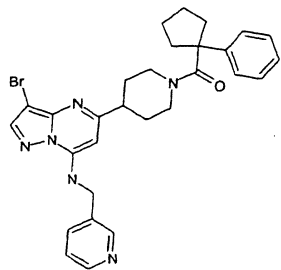
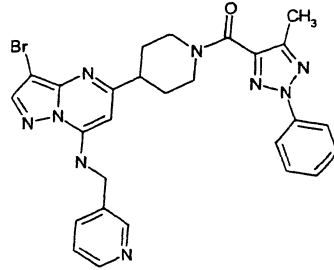
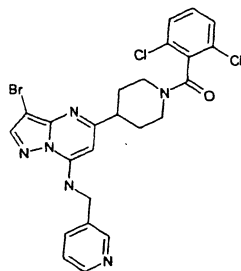
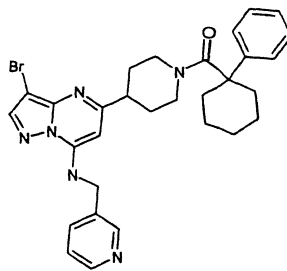
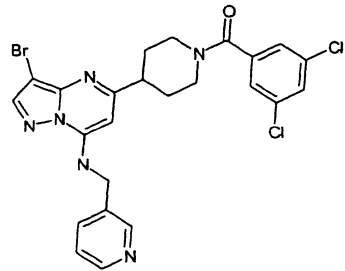
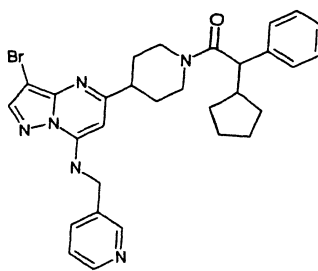
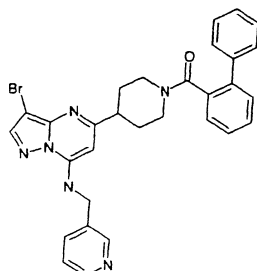
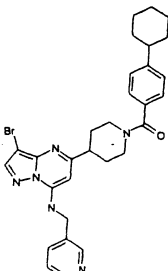
實例	產物	m/z	實例	產物	m/z
4309		499.27	4313		509.28
4310		500.27	4314		512.28
4311		503.28	4315		513.28
4312		505.28	4316		513.28

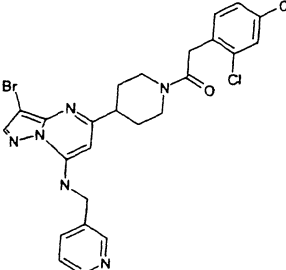
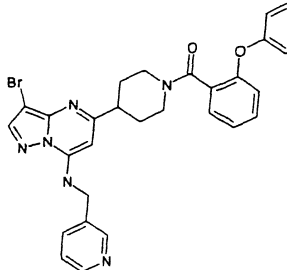
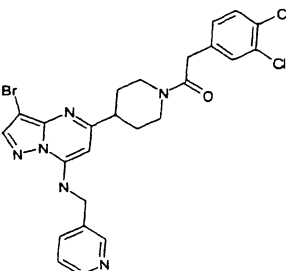
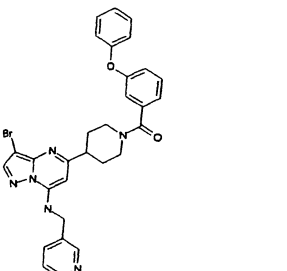
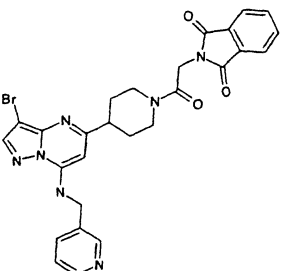
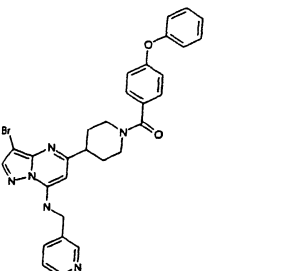
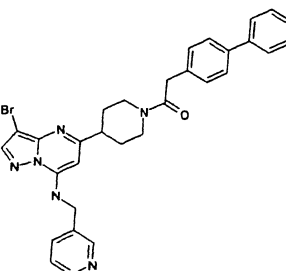
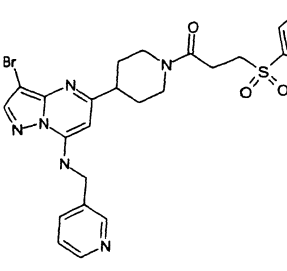
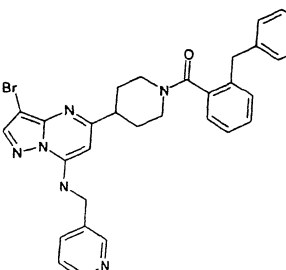
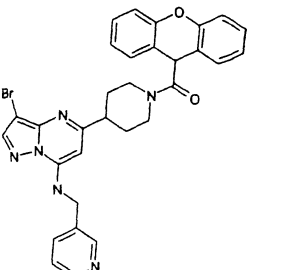
實例	產物	m/z	實例	產物	m/z
4317		518.28	4321		523.29
4318		518.28	4322		523.29
4319		519.29	4323		523.29
4320		521.29	4324		525.29

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4325 2. 527.29		1. 4330 2. 533.29
	1. 4326 2. 527.29		4331
	1. 4327 2. 532.29		1. 4332 2. 533.29
	1. 4328 2. 532.29		1. 4333 2. 533.29
	1. 4329 2. 532.29		1. 4334 2. 537.3

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4335 2. 537.3		1. 4340 2. 541.3
	1. 4336 2. 537.3		1. 4341 2. 543.3
	1. 4337 2. 539.3		1. 4342 2. 546.3
	1. 4338 2. 539.3		1. 4343 2. 547.3
	1. 4339 2. 539.3		1. 4344 2. 547.3

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4345 2. 549.3		1. 4350 2. 553.3
	1. 4346 2. 550.3		1. 4351 2. 557.31
	1. 4347 2. 551.3		1. 4352 2. 557.31
	1. 4348 2. 551.3		1. 4353 2. 558.31
	1. 4349 2. 551.3		1. 4354 2. 561.31

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4355 2. 561.31		1. 4360 2. 569.31
	1. 4356 2. 561.31		1. 4361 2. 574.32
	1. 4357 2. 561.31		1. 4362 2. 573.32
	1. 4358 2. 561.31		1. 4363 2. 573.32
	1. 4359 2. 569.31		1. 4364 2. 575.32

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4365 2. 575.32		1. 43700 2. 585.32
	1. 43666 2. 575.32		1. 4371 2. 583.32
	1. 4367 2. 574.32		1. 4372 2. 585.32
	1. 43688 2. 583.32		1. 4373 2. 585.32
	1. 4369 2. 583.32		1. 4374 2. 597.33

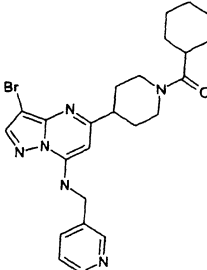
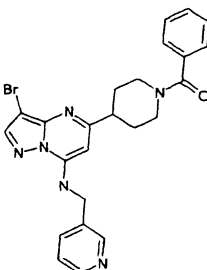
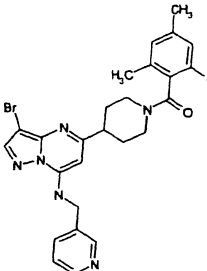
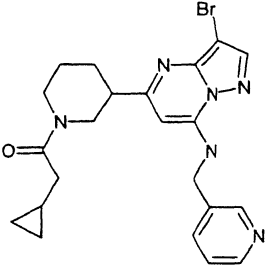
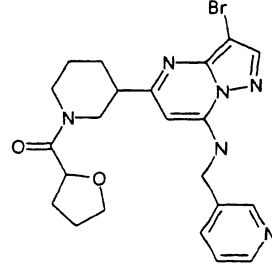
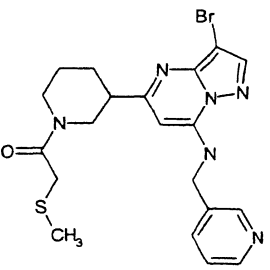
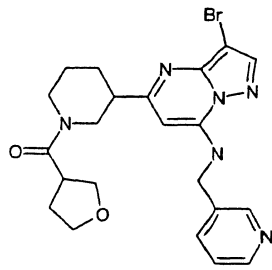
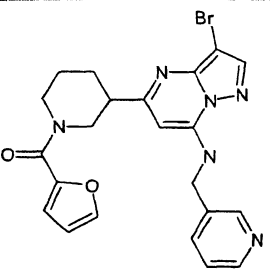
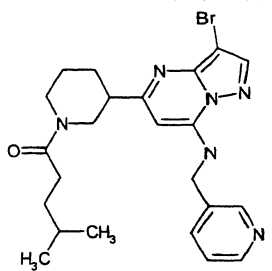
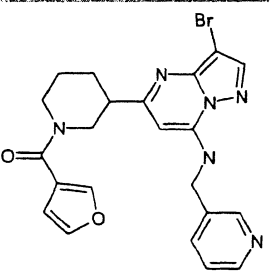
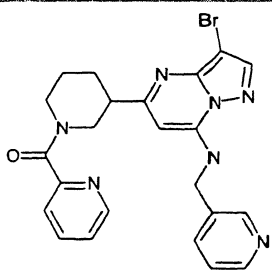
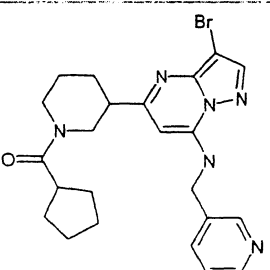
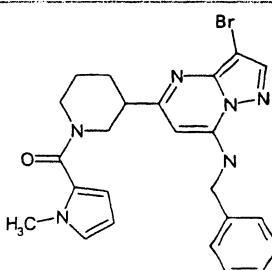
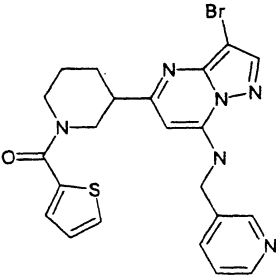
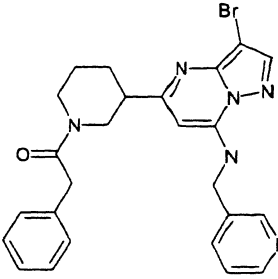
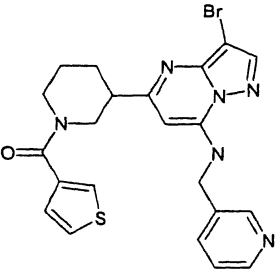
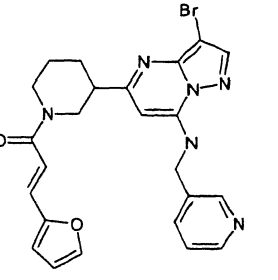
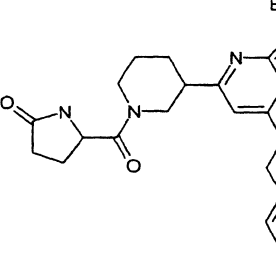
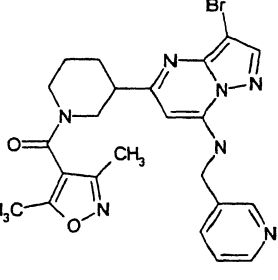
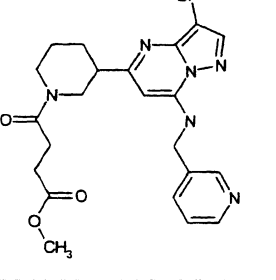
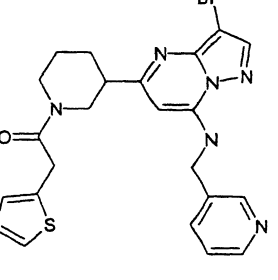
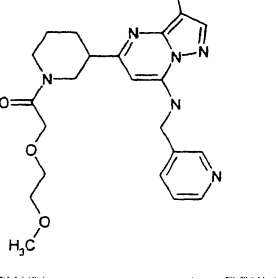
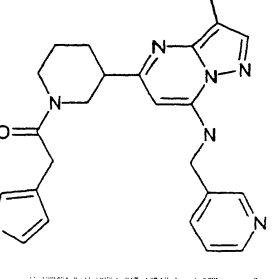
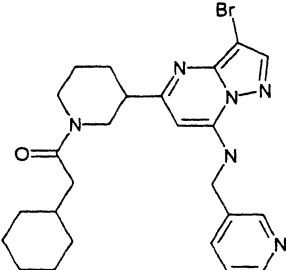
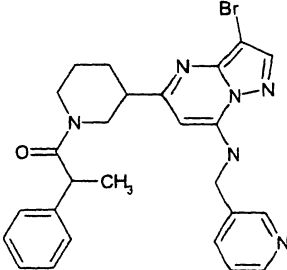
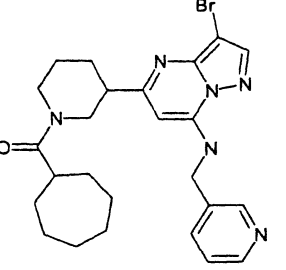
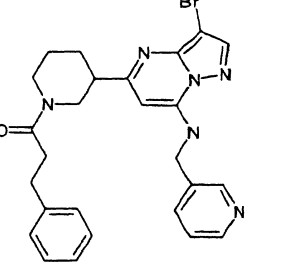
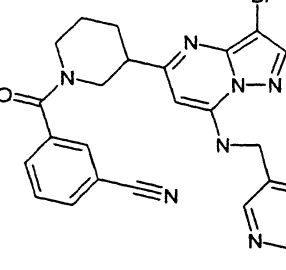
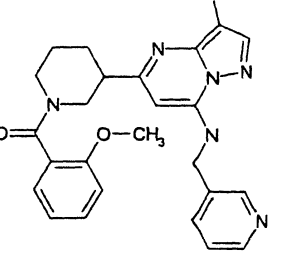
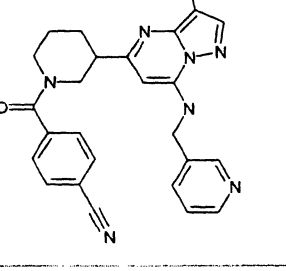
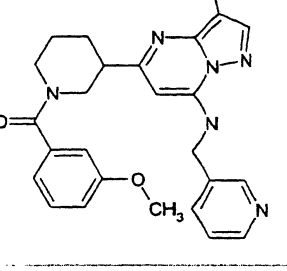
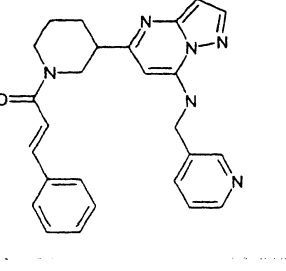
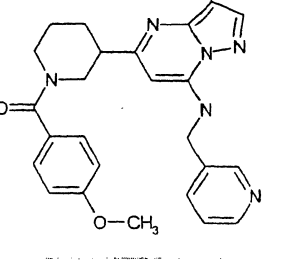
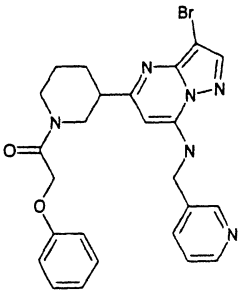
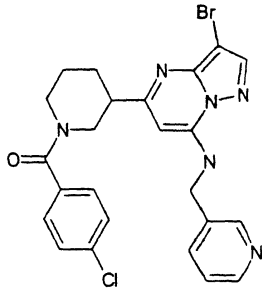
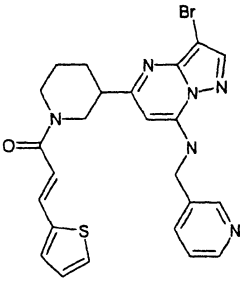
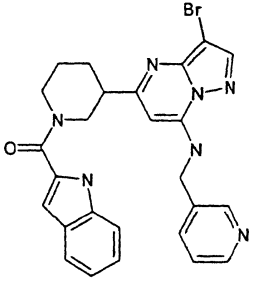
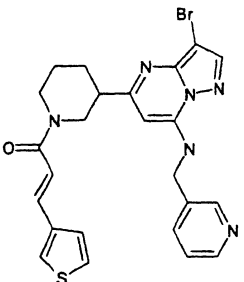
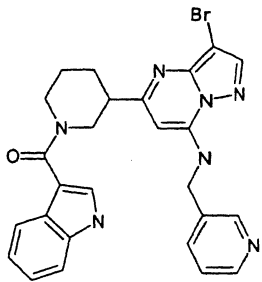
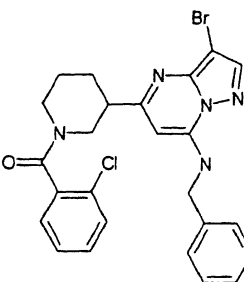
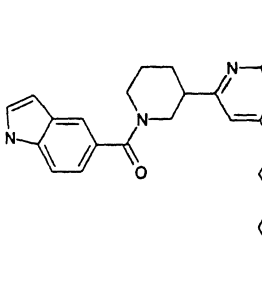
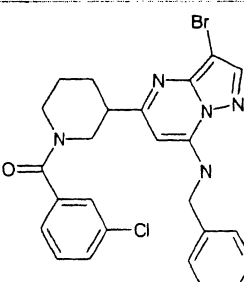
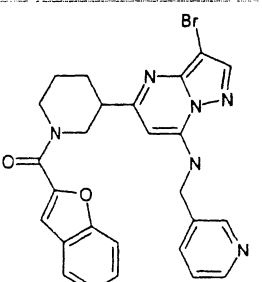
產物	1. 實例 2. m/z
	1. 4375 2. 499.27
	1. 4376 2. 493.27
	1. 4377 2. 535.29

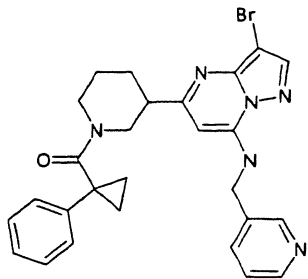
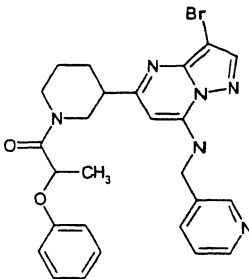
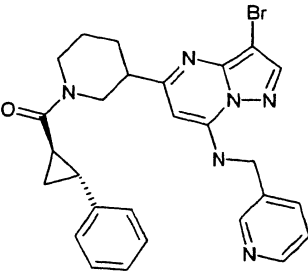
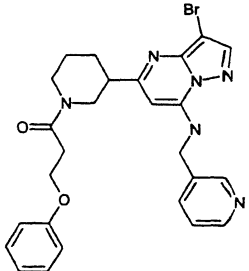
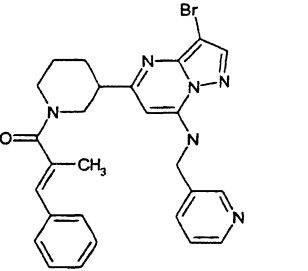
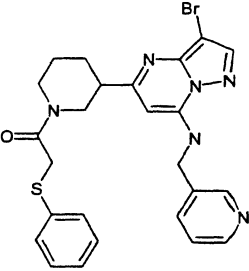
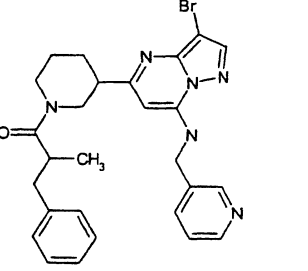
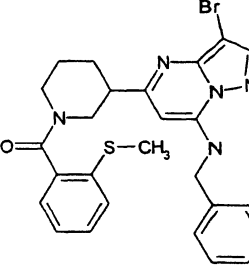
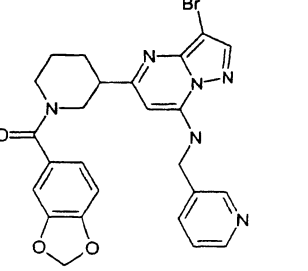
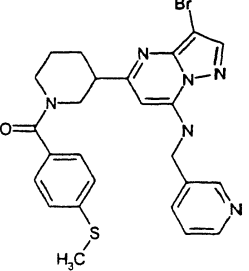
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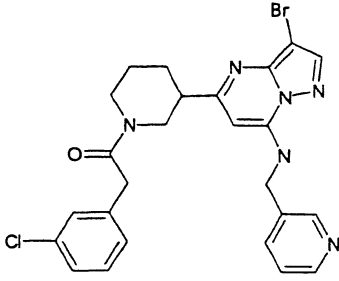
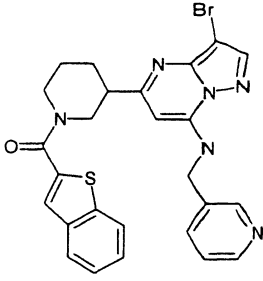
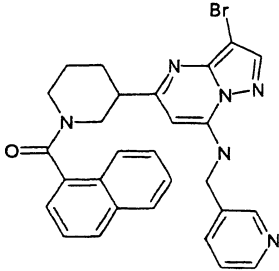
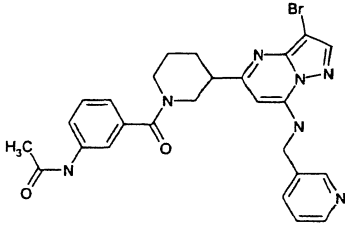
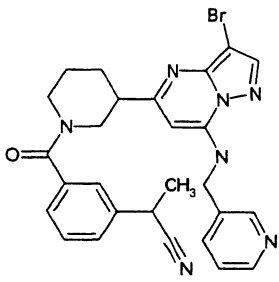
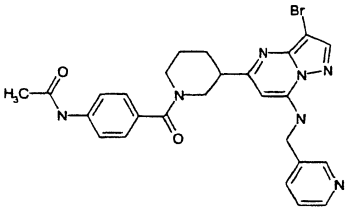
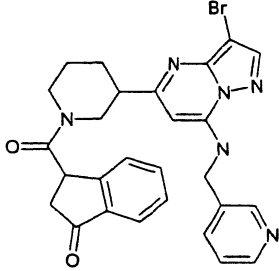
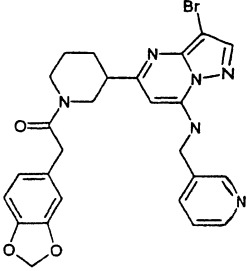
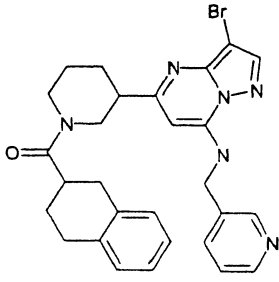
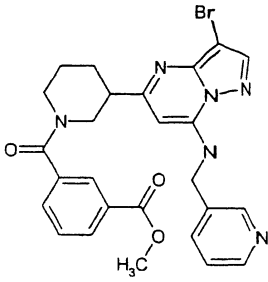
產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4401 2. 471.3		1. 4406 2. 487.27
	1. 4402 2. 475.26		1. 4407 2. 487.27
	1. 4403 2. 483.27		1. 4408 2. 487.27
	1. 4404 2. 481.26		1. 4409 2. 494.3
	1. 4405 2. 485.27		1. 4410 2. 496.27

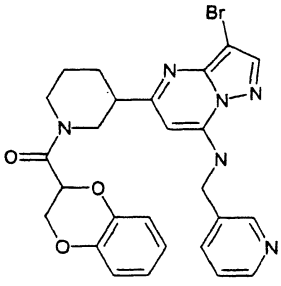
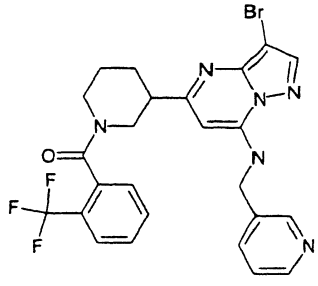
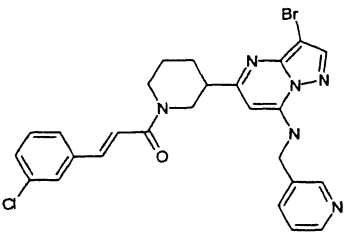
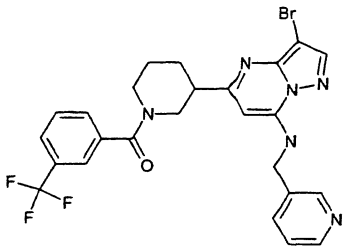
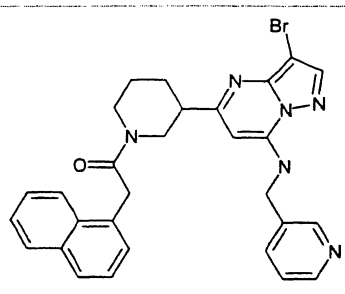
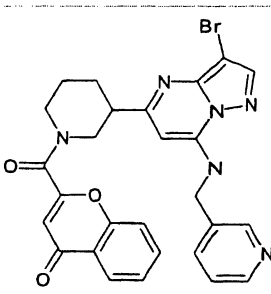
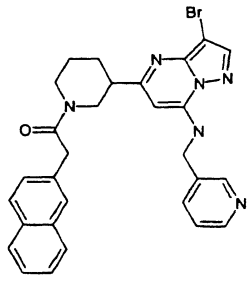
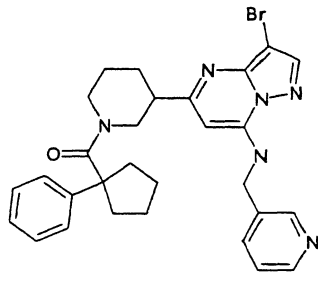
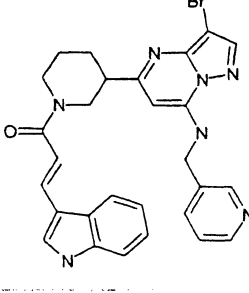
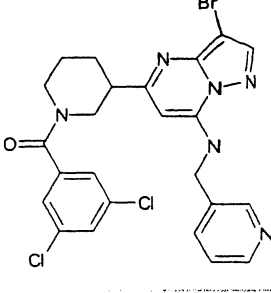
產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4411 2. 499.27		1. 4416 2. 507.28
	2. 4412 2. 499.27		1. 4417 2. 509.3
	1. 4413 2. 500.27		1. 4418 2. 512.28
	1. 4414 2. 503.28		1. 4419 2. 513.28
	1. 4415 2. 505.28		1. 4420 2. 513.28

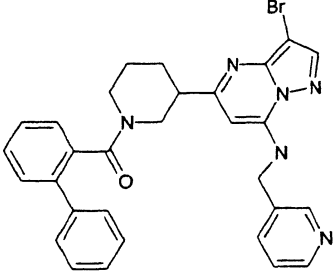
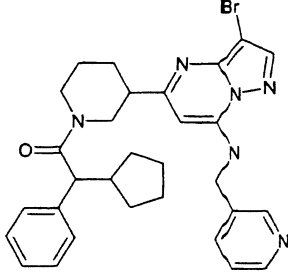
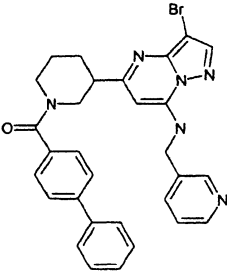
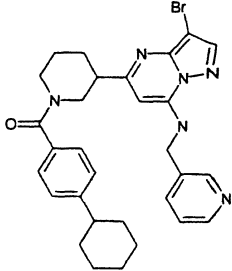
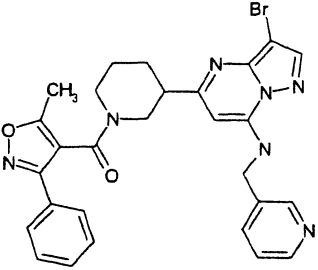
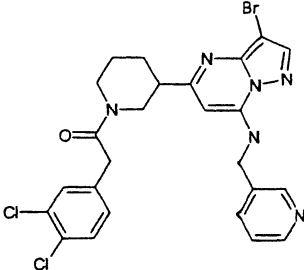
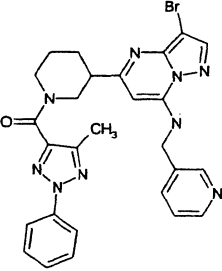
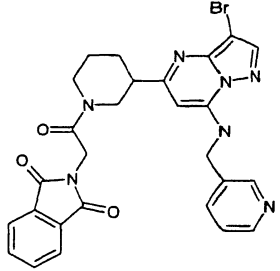
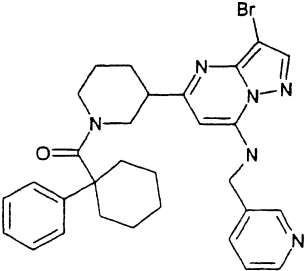
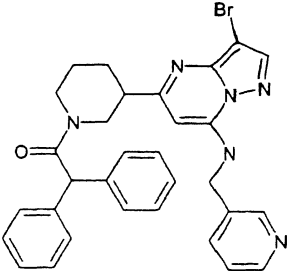
產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4421 2. 513.28		1. 4426 2. 521.29
	1. 4422 2. 513.28		1. 4428 2. 521.29
	1. 4423 2. 518.28		1. 4428 2. 523.29
	1. 4424 2. 518.28		1. 4429 2. 523.29
	1. 4425 2. 519.3		1. 4430 2. 523.29

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4431 2. 523.29		1. 4436 2. 527.29
	1. 4432 2. 525.29		1. 4437 2. 532.29
	1. 4433 2. 525.3		1. 4438 2. 532.29
	1. 4434 2. 527.29		1. 4439 2. 532.29
	1. 4435 2. 527.29		1. 4440 2. 531.29

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4441 2. 533.3		1. 4446 2. 537.3
	1. 4442 2. 531.29		1. 4447 2. 537.3
	1. 4443 2. 533.29		1. 4448 2. 539.3
	1. 4444 2. 535.29		1. 4449 2. 539.3
	1. 4445 2. 537.3		1. 4450 2. 539.3

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4451 2. 541.3		1. 4456 2. 549.3
	1. 4451 2. 543.3		1. 4457 2. 550.3
	1. 4453 2. 546.3		1. 4458 2. 550.3
	1. 4454 2. 547.3		1. 4459 2. 551.3
	1. 4455 2. 547.3		1. 4460 2. 551.3

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4461 2. 549.3		1. 4466 2. 561.31
	1. 4462 2. 553.3		1. 4467 2. 561.31
	1. 4463 2. 557.3		1. 4468 2. 561.31
	1. 4464 2. 557.31		1. 4469 2. 561.31
	1. 4465 2. 558.31		1. 4470 2. 562.3

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4471 2. 569.31		1. 4476 2. 572.31
	1. 4472 2. 569.31		1. 4477 2. 573.32
	1. 4473 2. 572.31		1. 4478 2. 574.32
	1. 4474 2. 572.31		1. 4479 2. 576.32
	1. 4475 2. 575.32		1. 4480 2. 583.32

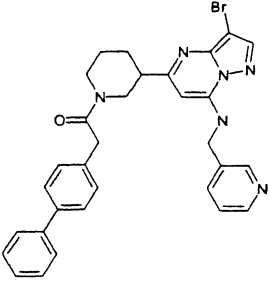
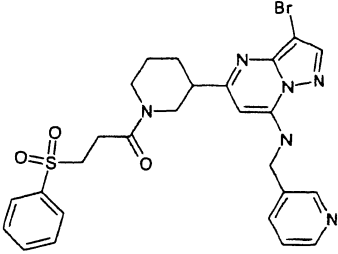
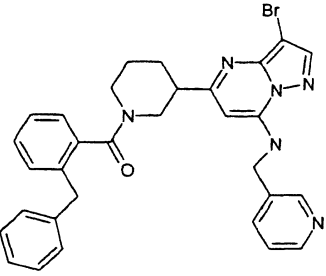
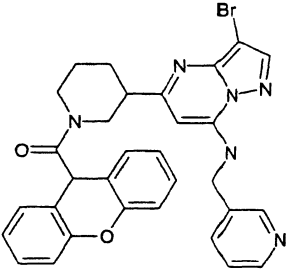
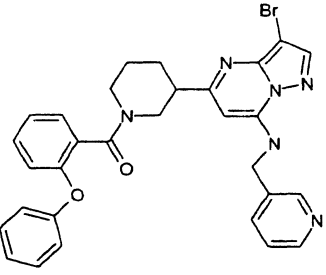
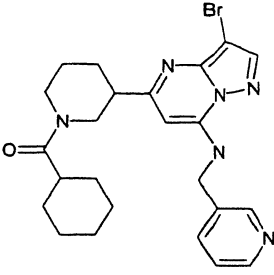
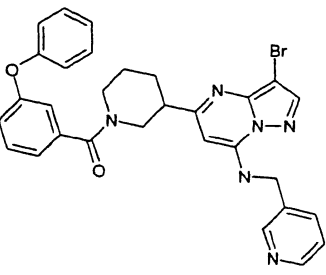
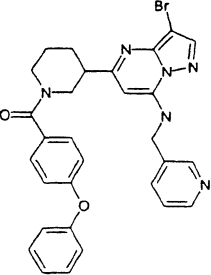
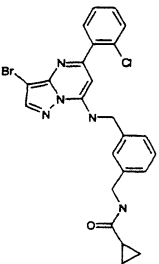
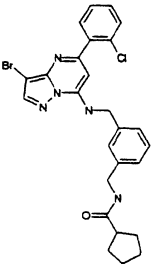
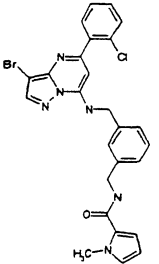
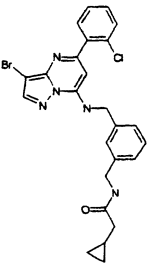
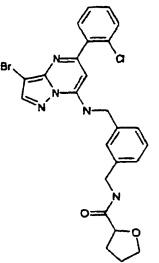
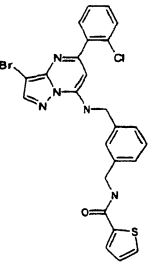
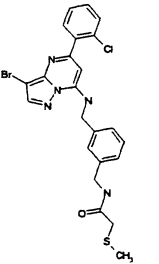
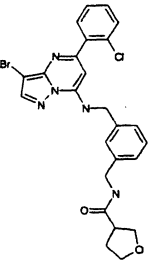
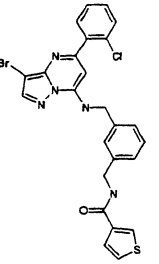
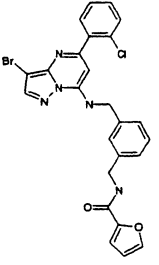
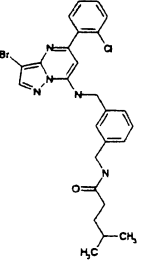
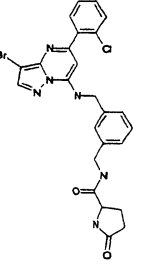
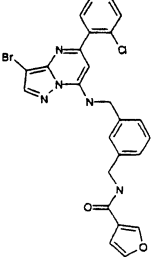
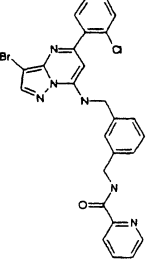
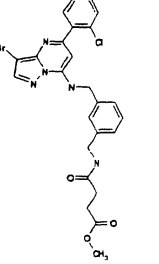
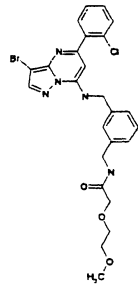
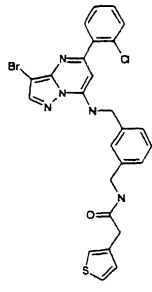
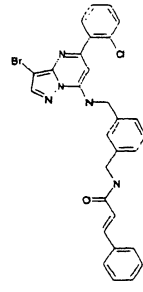
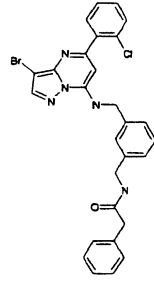
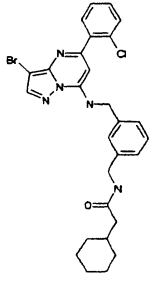
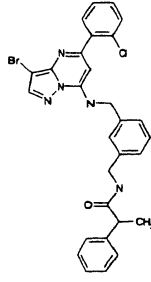
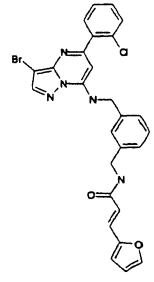
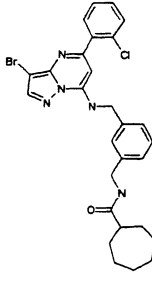
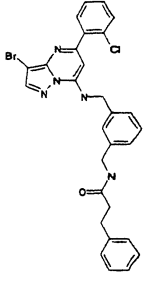
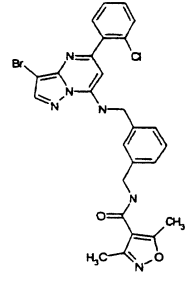
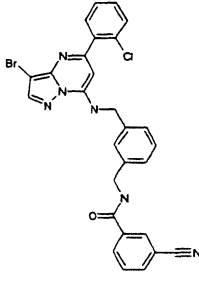
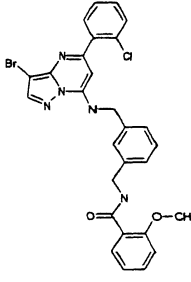
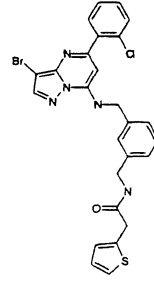
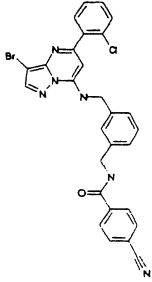
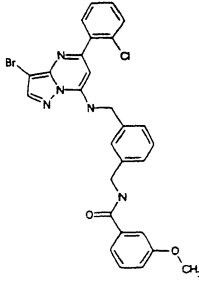
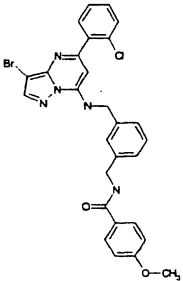
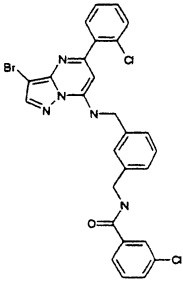
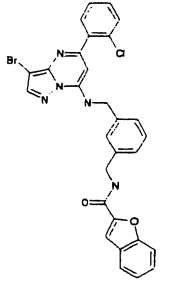
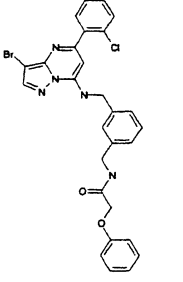
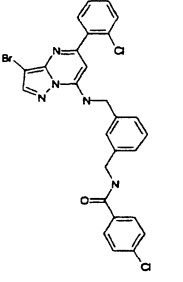
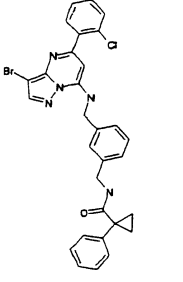
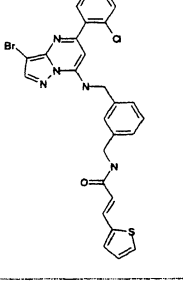
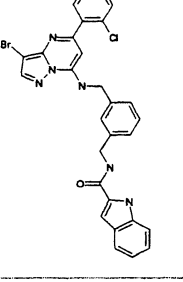
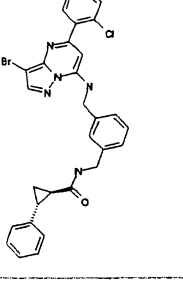
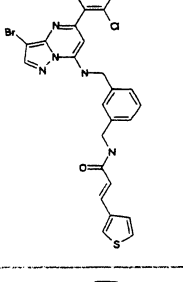
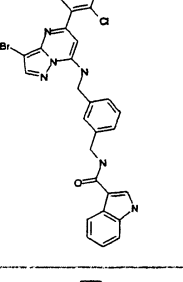
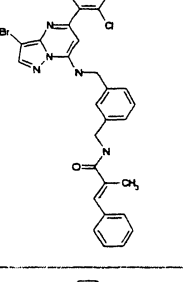
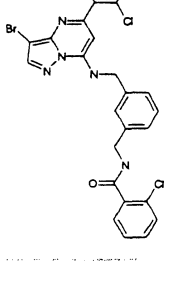
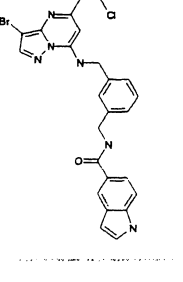
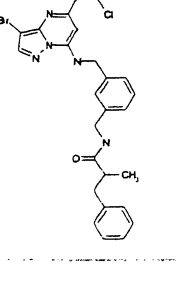
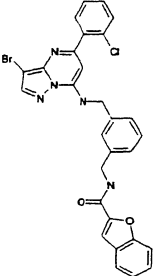
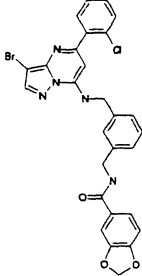
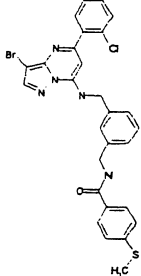
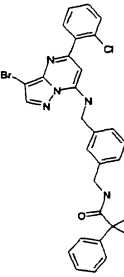
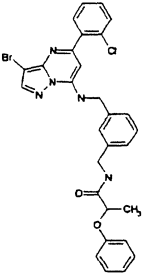
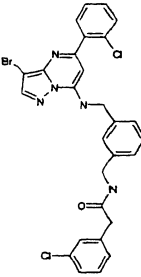
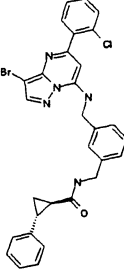
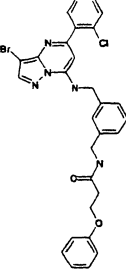
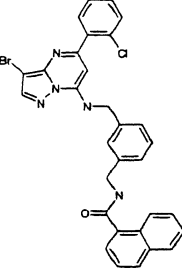
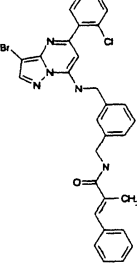
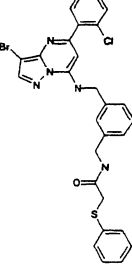
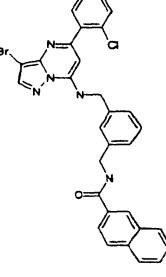
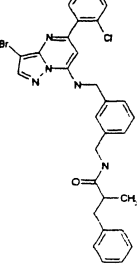
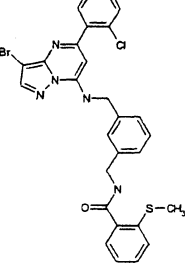
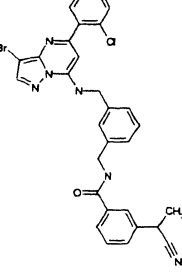
產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4481 2. 583.32		1. 4486 2. 585.32
	1. 4482 2. 583.32		1. 4487 2. 597.33
	1. 4483 2. 585.32		1. 4488 2. 499.27
	1. 4484 2. 585.32		
	1. 4485 2. 585.3		

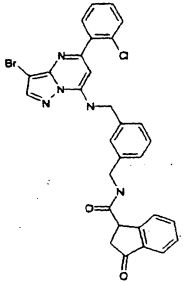
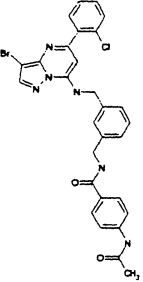
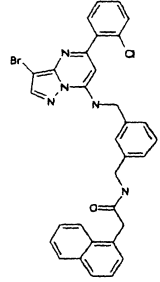
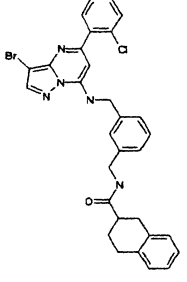
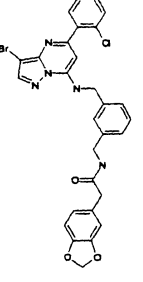
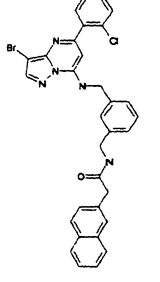
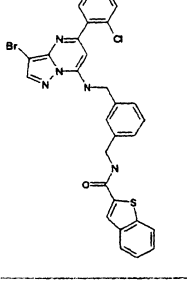
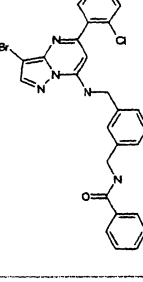
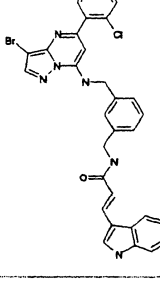
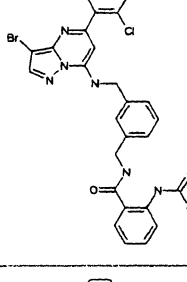
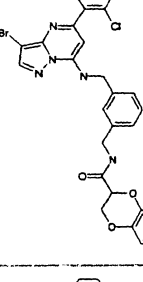
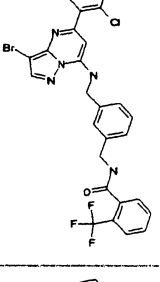
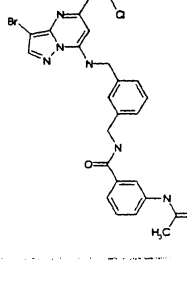
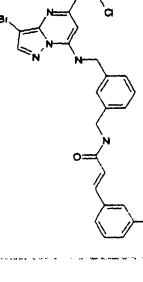
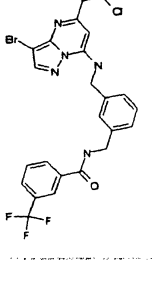
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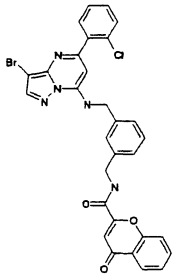
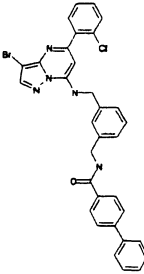
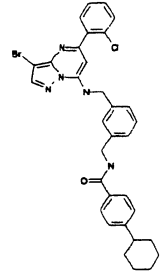
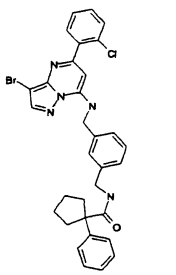
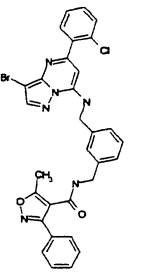
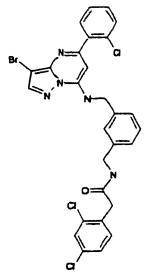
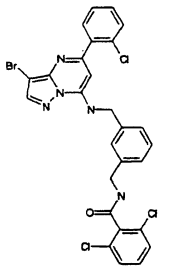
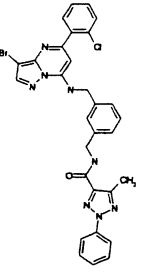
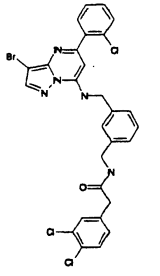
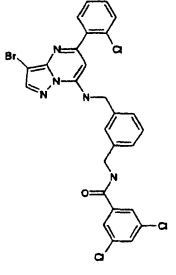
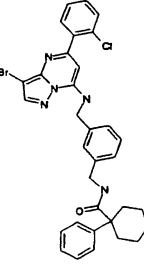
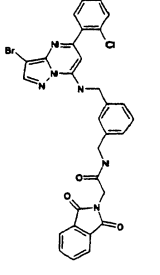
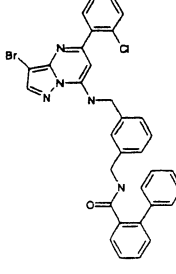
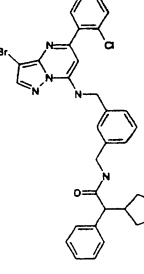
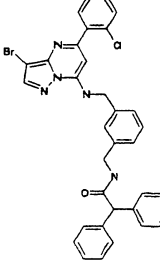
產物	1. 實例 2. m/z	產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4501 2. 512.28		1. 4506 2. 540.3		1. 4511 2. 551.3
	1. 4502 2. 526.29		1. 4507 2. 542.3		1. 4512 2. 554.3
	1. 4503 2. 532.29		1. 4508 2. 542.3		1. 4513 2. 554.3
	1. 4504 2. 538.3		1. 4509 2. 542.3		1. 4514 2. 555.31
	1. 4505 2. 538.3		1. 4510 2. 549.3		1. 4515 2. 558.31

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4516 2. 560.31		1. 4521 2. 568.31		1. 4526 2. 574.32
	1. 4517 2. 562.31		1. 4522 2. 568.31		1. 4527 2. 576.32
	1. 4518 2. 564.31		1. 4523 2. 568.31		1. 4528 2. 576.32
	1. 4519 2. 567.31		1. 4524 2. 573.32		1. 4529 2. 578.32
	1. 4520 2. 568.31		1. 4525 2. 573.32		1. 4530 2. 578.32

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4531 2. 578.32		1. 4536 2. 582.32		1. 4541 2. 588.32
	1. 4532 2. 578.32		1. 4537 2. 582.32		1. 4542 2. 588.32
	1. 4533 2. 580.32		1. 4538 2. 587.32		1. 4543 2. 588.32
	1. 4534 2. 580.32		1. 4539 2. 587.32		1. 4544 2. 588.32
	1. 4535 2. 582.32		1. 4540 2. 587.32		1. 4545 2. 590.32

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4546 2. 588.32		1. 4551 2. 592.33		1. 4556 2. 593.33
	1. 4547 2. 588.32		1. 4552 2. 592.33		1. 4557 2. 596.33
	1. 4548 2. 588.32		1. 4553 2. 592.33		1. 4558 2. 596.33
	1. 4549 2. 588.32		1. 4554 2. 594.33		1. 4559 2. 598.33
	1. 4550 2. 590.32		1. 4555 2. 594.33		1. 4560 2. 601.33

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4561 2. 602.33		1. 4665 2. 605.33		1. 4571 2. 612.34
	1. 4562 2. 602.33		1. 4567 2. 606.33		1. 4572 2. 612.34
	1. 4563 2. 604.33		1. 4568 2. 606.33		1. 4573 2. 613.34
	1. 4564 2. 603.3		1. 4569 2. 606.33		1. 4574 2. 616.34
	1. 4565 2. 605.33		1. 4570 2. 608.33		1. 4575 2. 616.34

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4576 2. 616.34		1. 4581 2. 624.34		1. 4586 2. 630.35
	1. 4577 2. 616.34		1. 4582 2. 629.35		1. 4587 2. 630.35
	1. 4578 2. 616.34		1. 4583 2. 629.35		1. 4588 2. 630.35
	1. 4579 2. 616.34		1. 4584 2. 630.35		1. 4589 2. 631.35
	1. 4580 2. 624.34		1. 4585 2. 630.35		1. 4590 2. 638.35

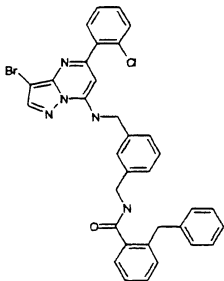
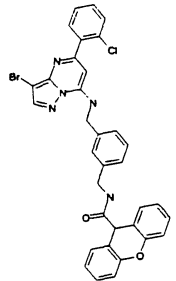
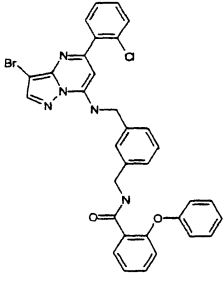
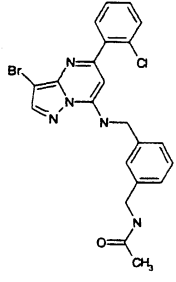
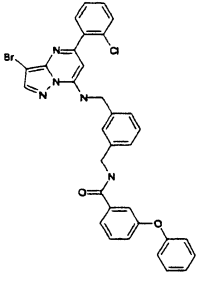
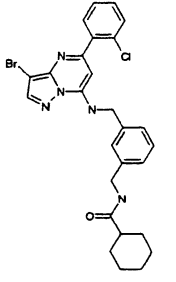
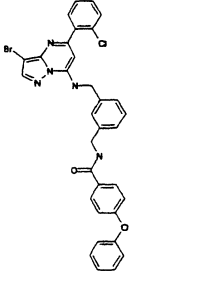
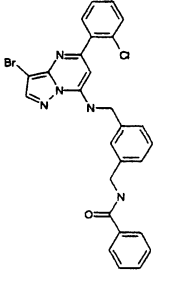
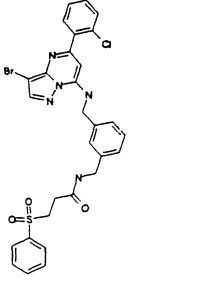
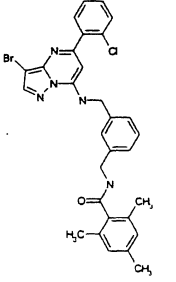
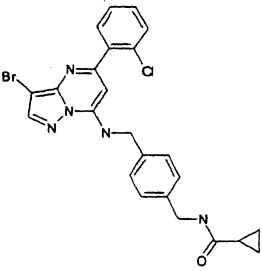
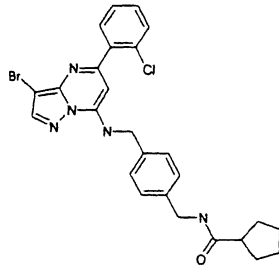
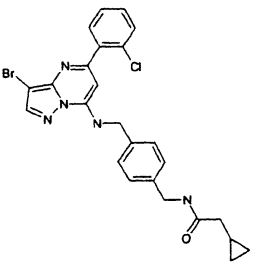
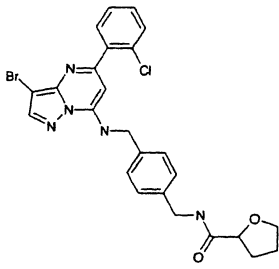
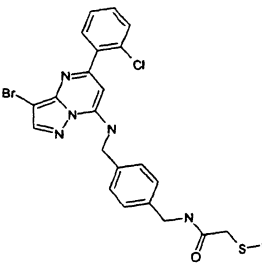
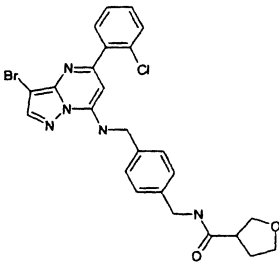
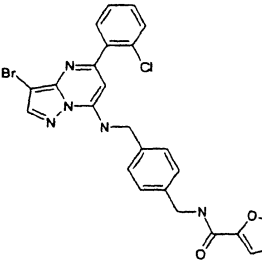
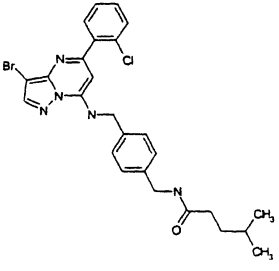
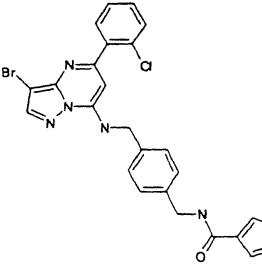
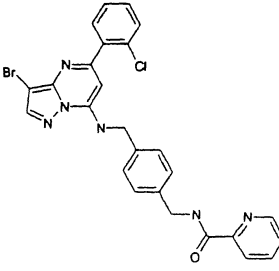
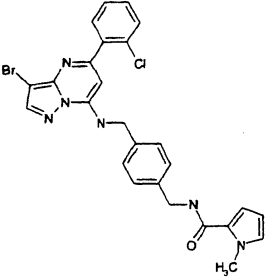
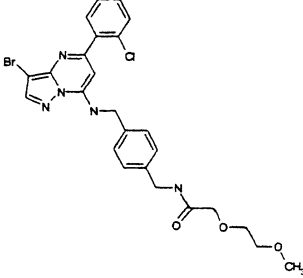
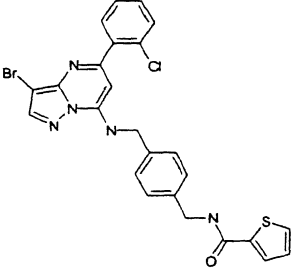
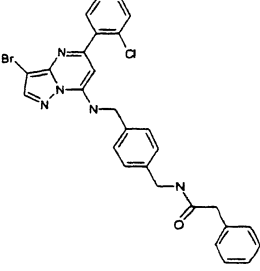
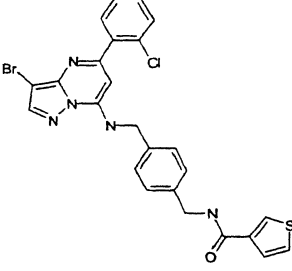
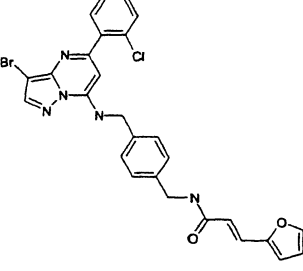
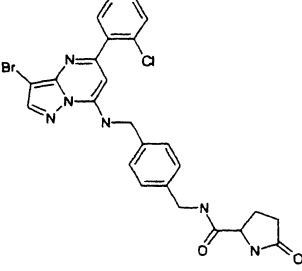
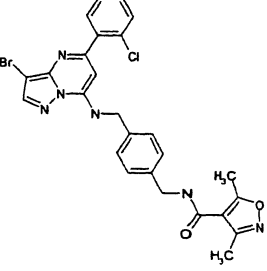
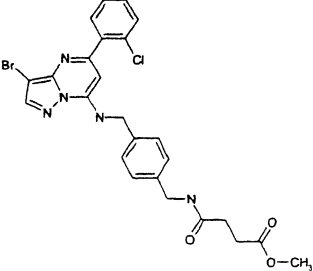
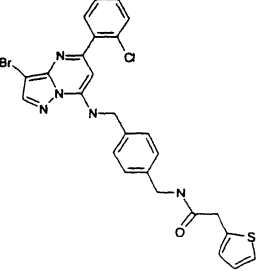
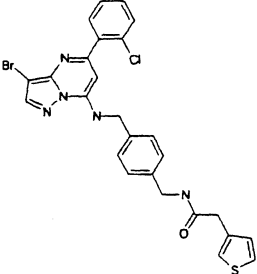
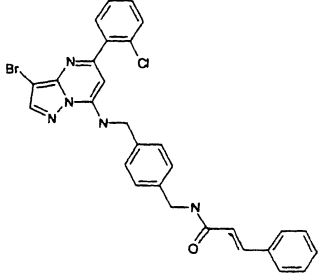
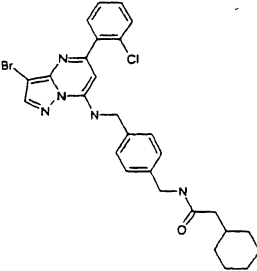
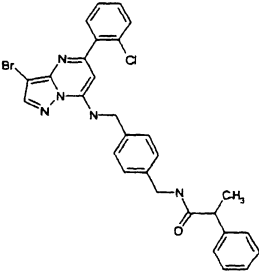
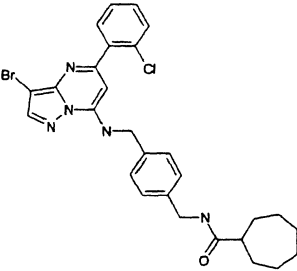
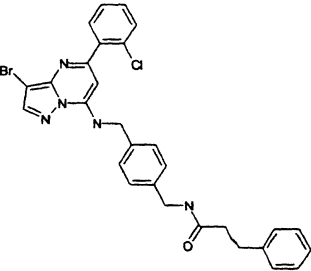
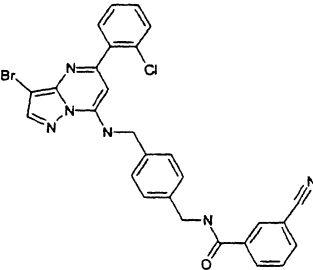
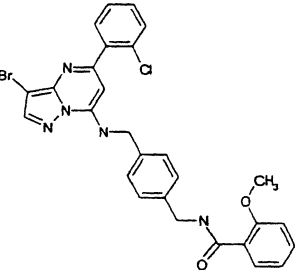
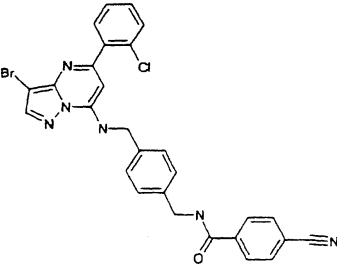
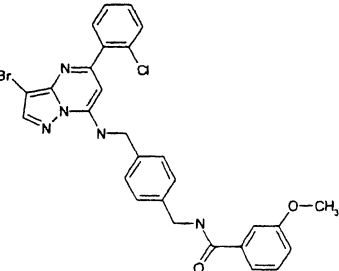
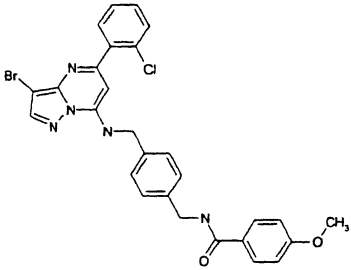
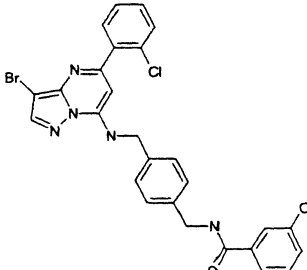
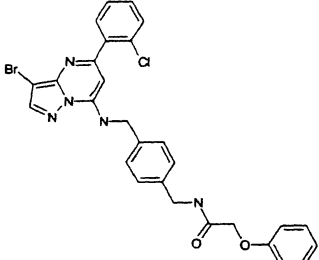
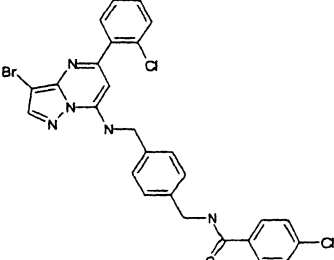
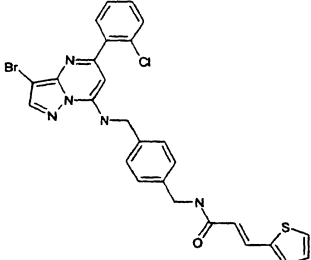
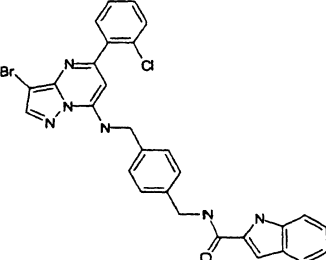
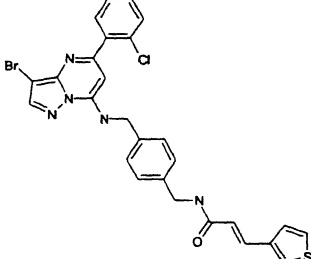
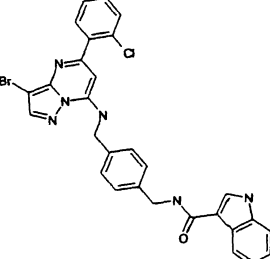
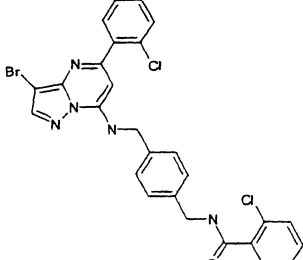
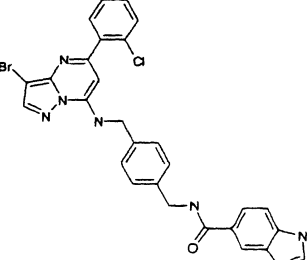
產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4591 2. 638.35		1. 4596 2. 652.36
	1. 4592 2. 640.35		1. 4597 2. 486.27
	1. 4593 2. 640.35		1. 4598 2. 554.3
	1. 4594 2. 640.35		1. 4599 2. 548.3
	1. 4595 2. 640.35		1. 45100 2.

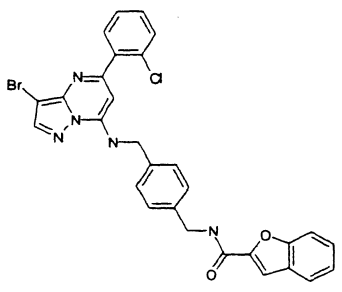
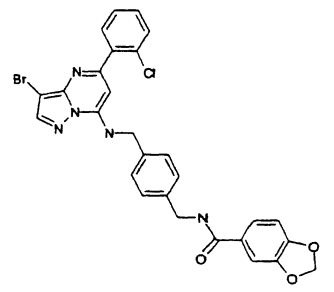
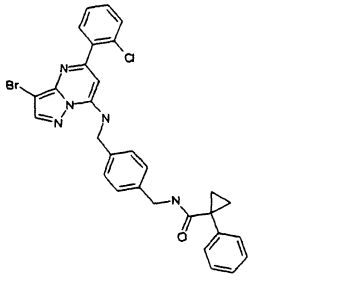
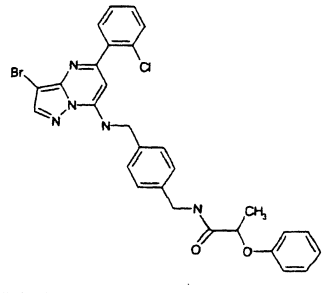
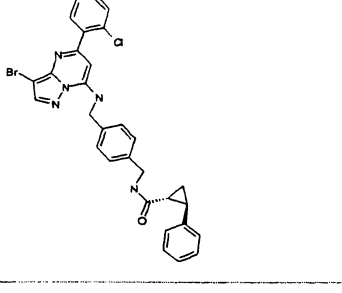
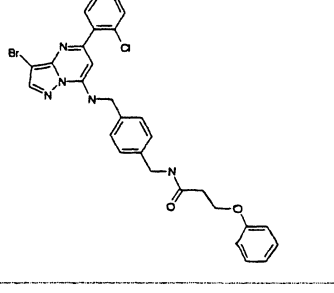
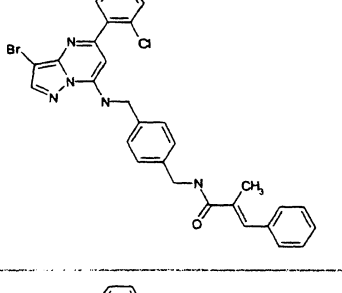
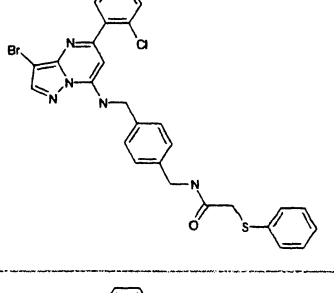
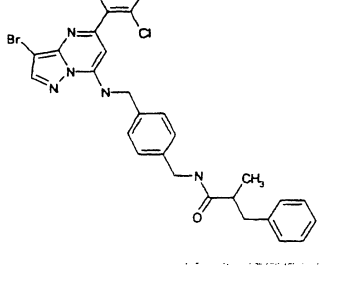
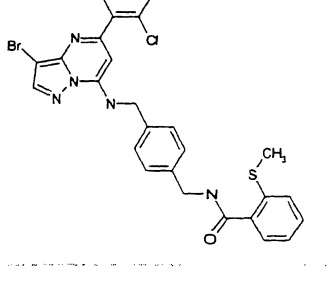
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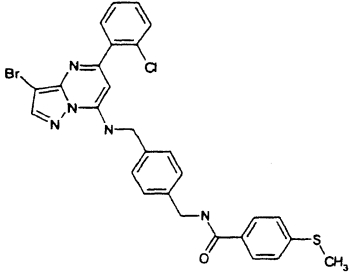
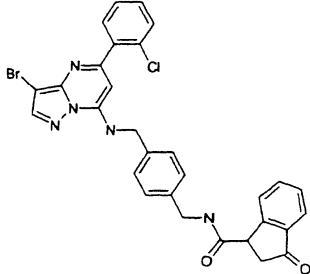
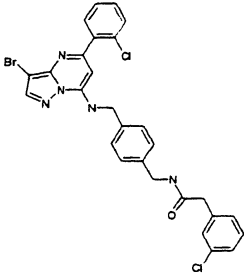
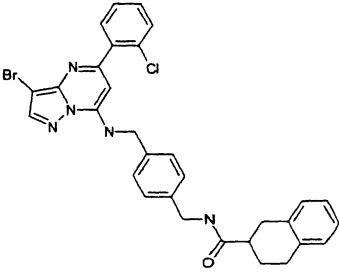
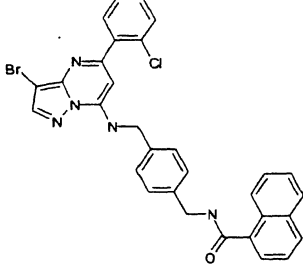
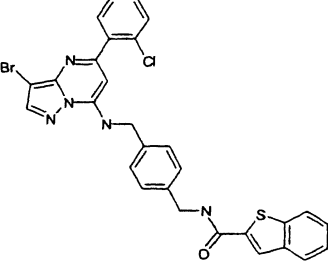
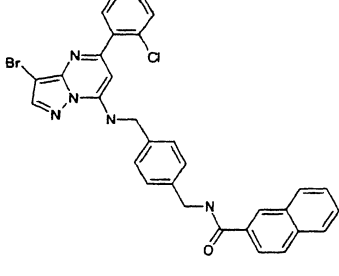
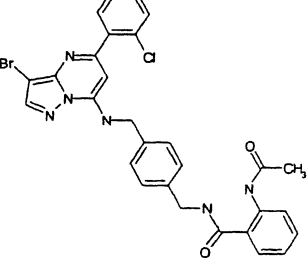
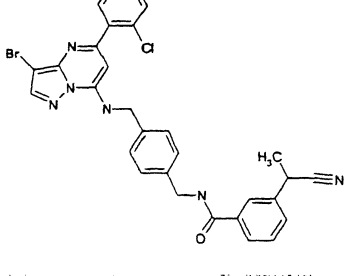
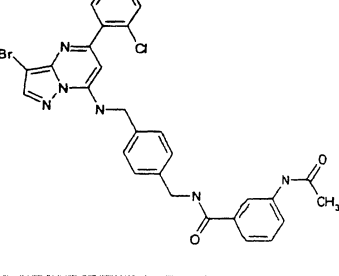
產物	1. 實例2. m/z	產物	1. 實例2. m/z
	1. 4601 2. 512.28		1. 4606 2. 540.3
	1. 4602 2. 526.29		1. 4607 2. 542.3
	1. 4603 2. 532.29		1. 4608 2. 542.3
	1. 4604 2. 538.3		1. 4609 2. 542.3
	1. 4605 2. 536.3		1. 4610 2. 547.3

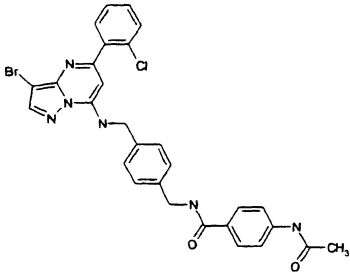
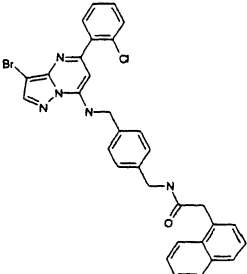
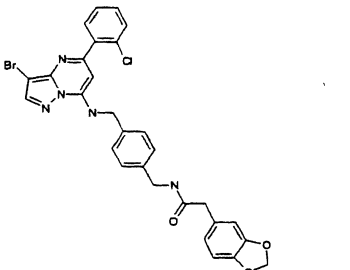
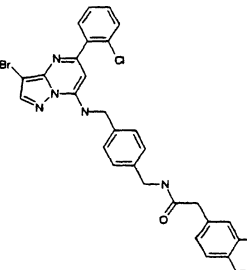
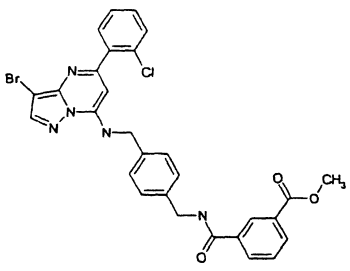
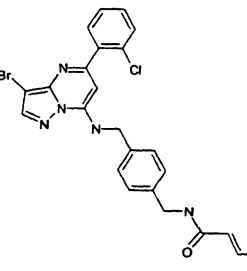
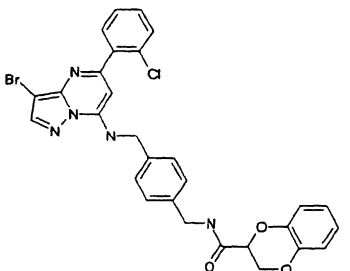
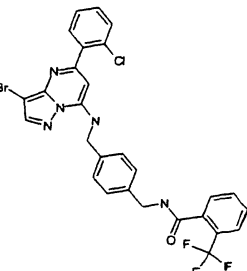
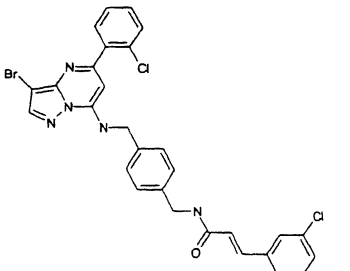
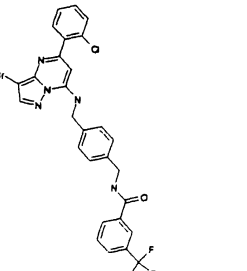
產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4611 2. 551.3		1. 4616 2. 560.31
	1. 4612 2. 552.3		1. 4617 2. 562.31
	1. 4613 2. 552.3		1. 4618 2. 562.3
	1. 4614 2. 555.31		1. 4619 2. 567.31
	1. 4615 2. 558.31		1. 4620 2. 568.31

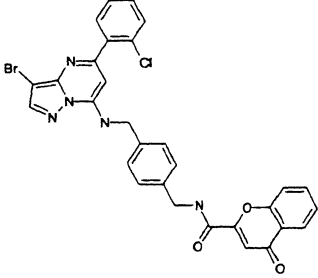
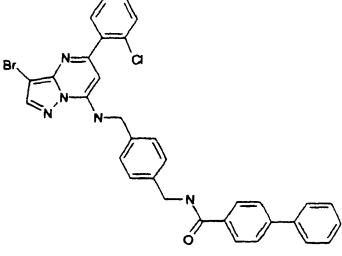
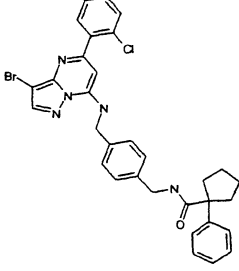
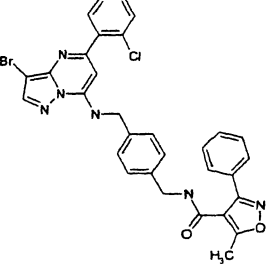
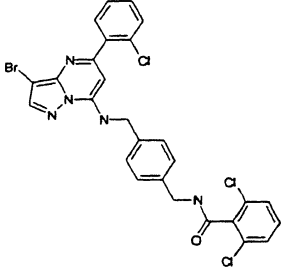
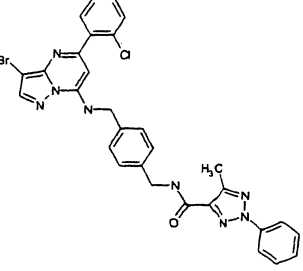
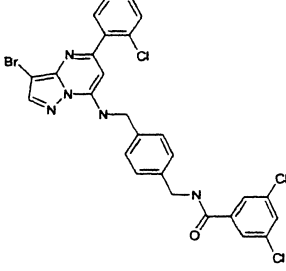
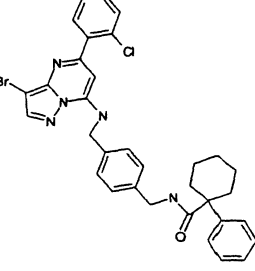
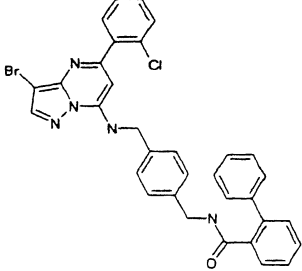
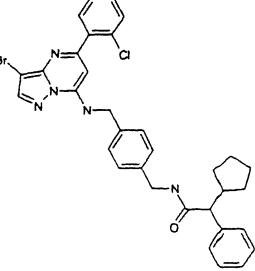
產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4621 2. 568.31		1. 4626 2. 574.32
	1. 4622 2. 568.31		1. 4627 2. 576.32
	1. 4623 2. 568.31		1. 4628 2. 576.32
	1. 4624 2. 573.32		1. 4629 2. 578.32
	1. 4625 2. 573.32		1. 4630 2. 578.32

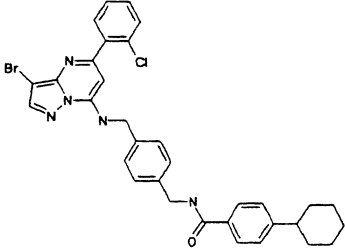
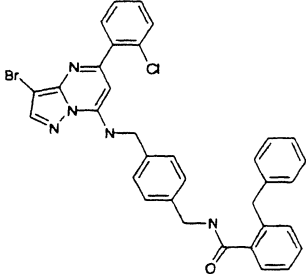
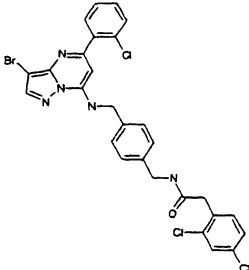
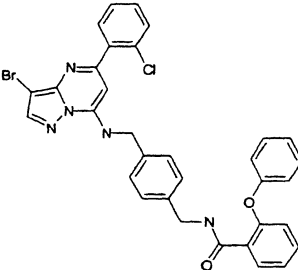
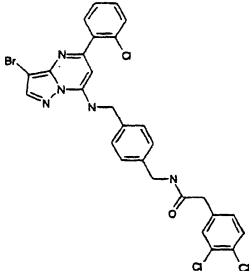
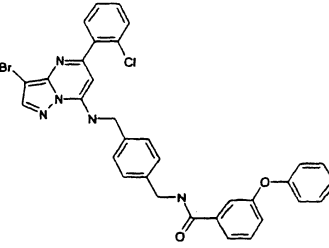
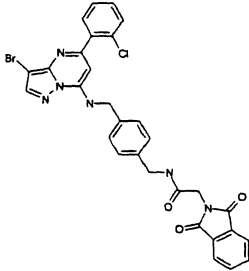
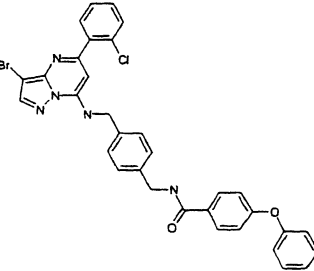
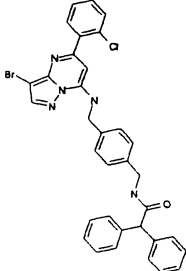
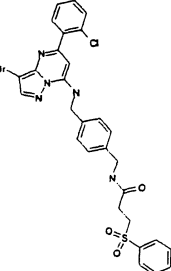
產物	1. 實例 2. m/x	產物	1. 實例 2. m/z
	1. 4631 2. 578.32		1. 4636 2. 582.32
	1. 4632 2. 578.32		1. 4637 2. 582.32
	1. 4633 2. 580.32		1. 4638 2. 587.32
	1. 4634 2. 580.32		1. 4639 2. 585.3
	1. 4635 2. 582.32		1. 4640 2. 585.3

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4641 2. 588.32		1. 4646 2. 592.33
	1. 4642 2. 588.32		1. 4647 2. 592.33
	1. 4643 2. 588.32		1. 4648 2. 592.33
	1. 4644 2. 588.32		1. 4649 2.
	1. 4645 2. 590.32		1. 4650 2. 594.33

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4651 2. 594.33		1. 4656 2. 602.33
	1. 4652 2. 596.33		1. 4657 2. 602.33
	1. 4653 2. 596.3		1. 4658 2. 604.33
	1. 4654 2. 598.33		1. 4659 2. 603.3
	1. 4655 2. 601.33		1. 4660 2. 605.33

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4661 2. 605.33		1. 4666 2. 612.34
	1. 4662 2. 606.33		1. 4667 2. 612.34
	1. 4663 2. 606.33		1. 4668 2. 613.34
	1. 4664 2. 606.33		1. 4669 2. 616.34
	1. 4665 2. 608.33		1. 4670 2. 616.34

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4671 2. 616.34		1. 4676 2. 624.34
	1. 4672 2. 616.34		1. 4677 2. 629.35
	1. 4673 2. 616.34		1. 4678 2. 629.35
	1. 4674 2. 616.34		1. 4679 2. 630.35
	1. 4675 2. 624.34		1. 4680 2. 630.35

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4681 2. 630.35		1. 4686 2. 638.35
	1. 4682 2. 630.35		1. 4687 2. 640.35
	1. 4683 2. 630.35		1. 4688 2. 640.35
	1. 4684 2. 631.35		4689 2.
	1. 4685 2. 638.35		1. 4690 2. 640.35

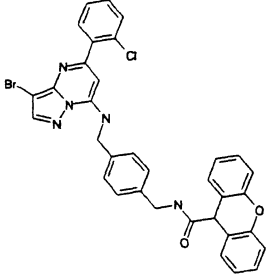
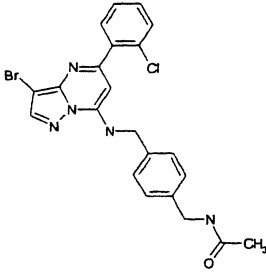
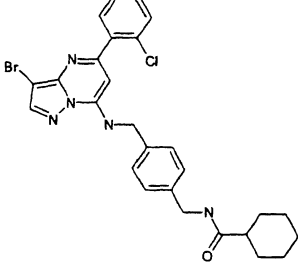
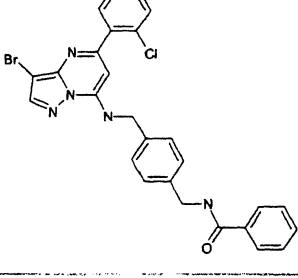
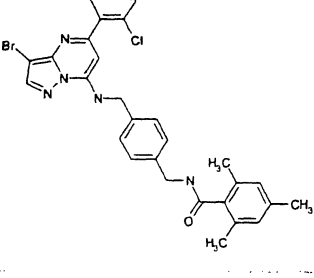
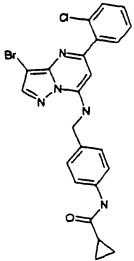
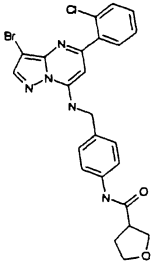
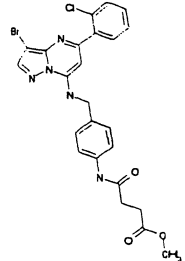
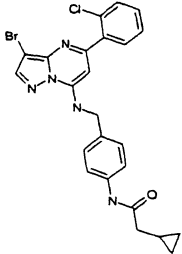
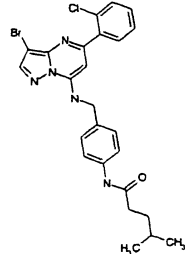
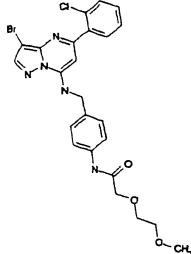
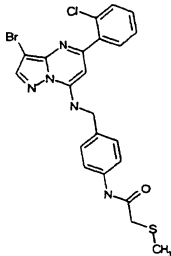
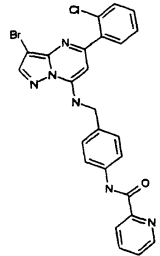
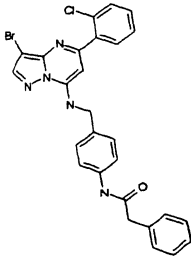
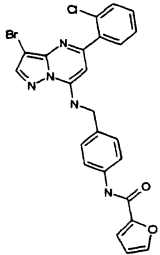
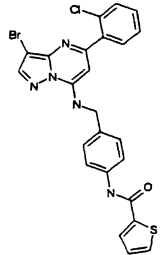
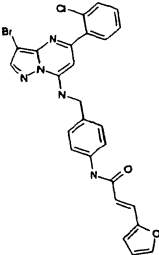
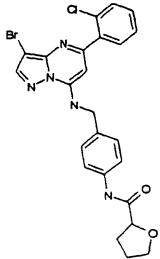
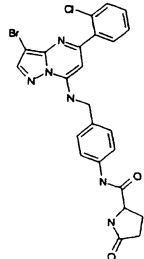
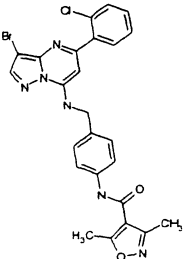
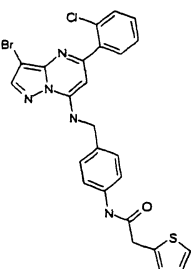
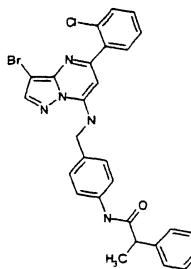
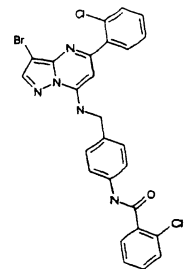
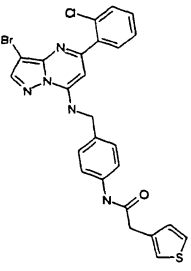
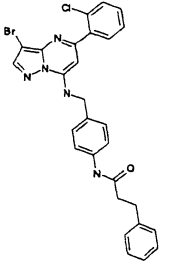
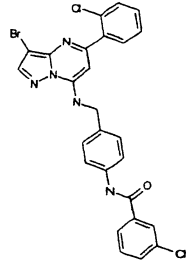
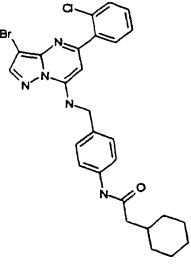
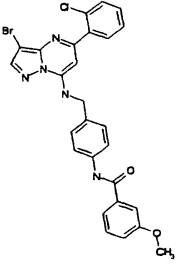
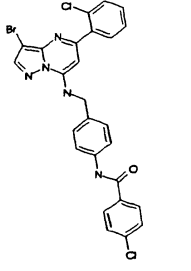
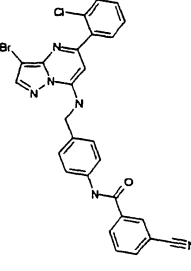
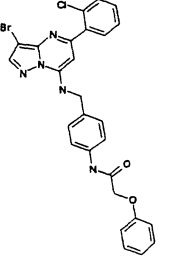
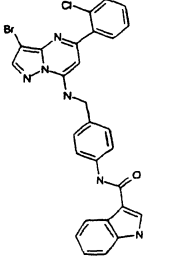
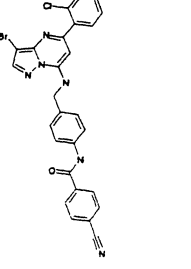
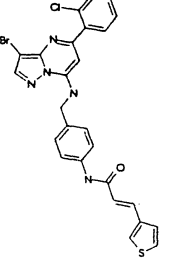
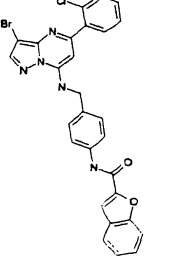
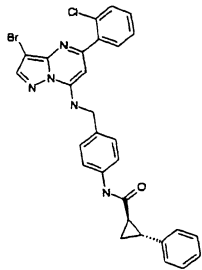
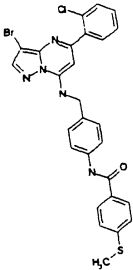
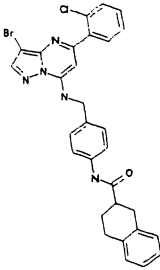
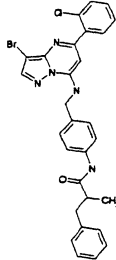
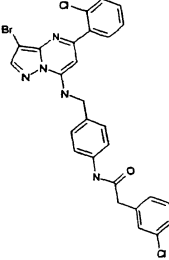
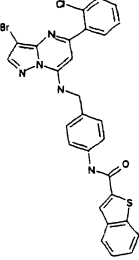
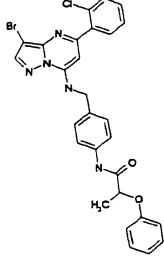
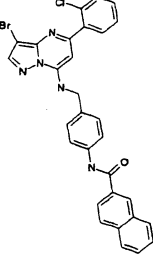
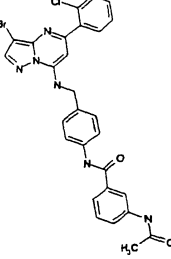
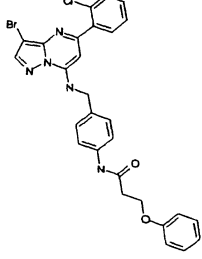
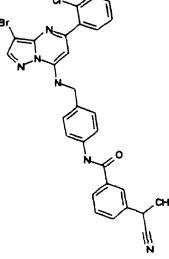
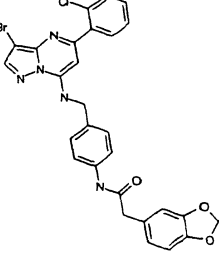
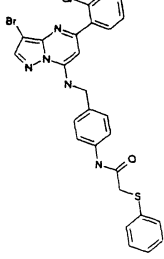
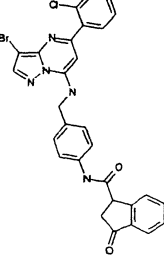
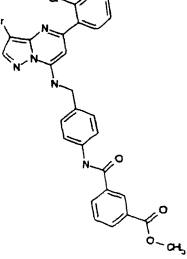
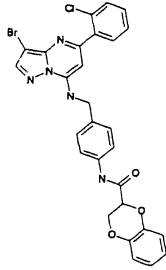
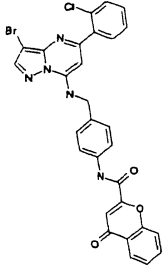
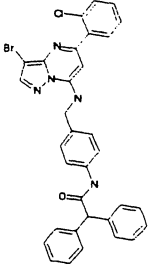
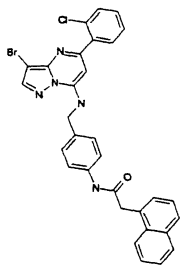
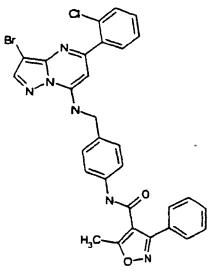
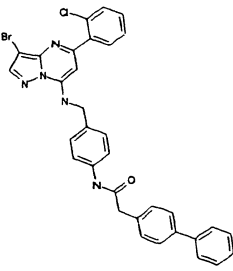
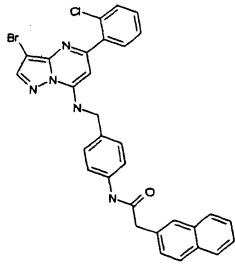
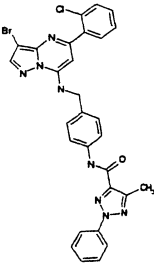
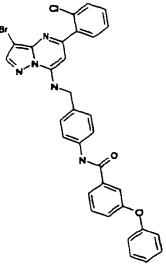
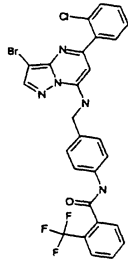
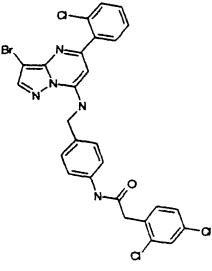
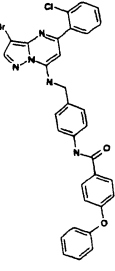
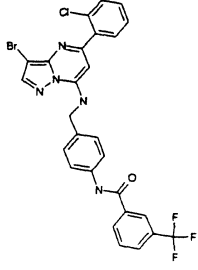
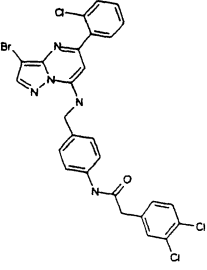
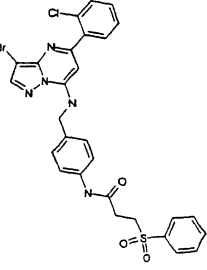
產物	1. 實例 2. m/z
	1. 4691 2. 652.36
	1. 4692 2. 484.3
	1. 4693 2. 554.3
	1. 4694 2. 548.3
	1. 4695 2. 590.32

表47

產物	1.實例2. m/z	產物	1.實例2. m/z	產物	1.實例2. m/z
	1. 4701 2. 498.27		1. 4706 2. 528.29		1. 4711 2. 544.3
	1. 4702 2. 512.28		1. 4707 2. 528.29		1. 4712 2. 546.3
	1. 4703 2. 518.28		1. 4708 2. 535.29		1. 4713 2. 548.3
	1. 4704 2. 524.29		1. 4709 2. 540.3		1. 4714 2. 550.3
	1. 4705 2. 528.29		1. 4710 2. 541.3		1. 4715 2. 553.3

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4716 2. 554.3		1. 4721 2. 562.31		1. 4726 2. 568.31
	1. 4717 2. 554.3		1. 4722 2. 562.31		1. 4727 2. 568.31
	1. 4718 2. 554.3		1. 4723 2. 564.31		1. 4728 2. 568.31
	1. 4719 2. 559.31		1. 4724 2. 564.31		1. 4729 2. 573.31
	1. 4720 2. 559.31		1. 4725 2. 566.31		1. 4730 2. 574.32

產物	1.實例2. m/z	產物	1.實例2. m/z	產物	1.實例2. m/z
	1. 4731 2. 574.32		1. 4736 2. 580.32		1. 4741 2. 588.32
	1. 4732 2. 576.32		1. 4737 2. 582.32		1. 4742 2. 590.32
	1. 4733 2. 578.32		1. 4738 2. 584.32		1. 4743 2. 591.33
	1. 4734 2. 578.32		1. 4739 2. 585.32		1. 4744 2. 592.33
	1. 4735 2. 580.32		1. 4740 2. 588.32		1. 4745 2. 592.33

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4746 2. 592.33		1. 4751 2. 602.33		1. 4756 2. 624.34
	1. 4747 2. 598.33		1. 4752 2. 615.34		1. 4757 2. 624.34
	1. 4748 2. 598.33		1. 4753 2. 615.34		1. 4758 2. 626.34
	1. 4749 2. 602.33		1. 4754 2. 616.34		1. 4759 2. 624.34
	1. 4750 2. 602.33		1. 4755 2. 616.34		1. 4760 2. 626.34

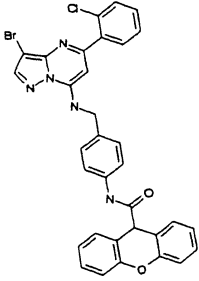
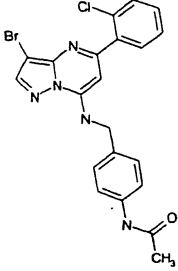
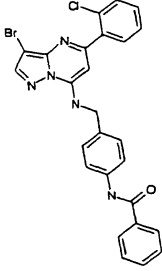
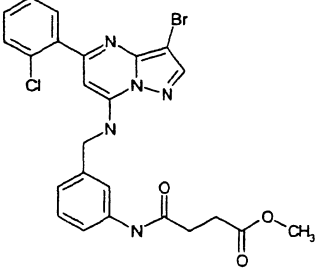
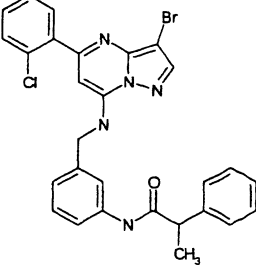
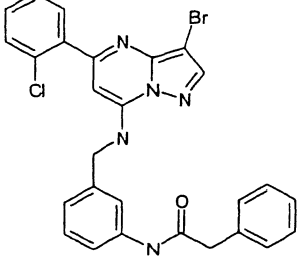
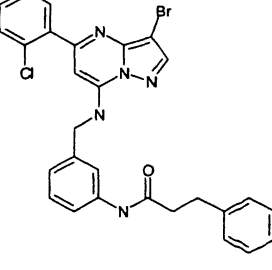
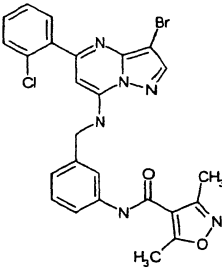
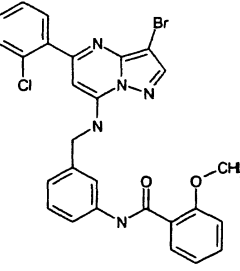
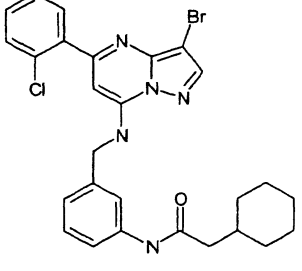
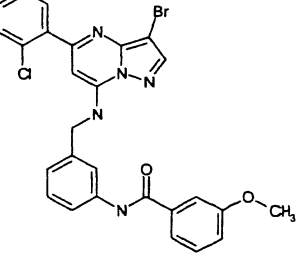
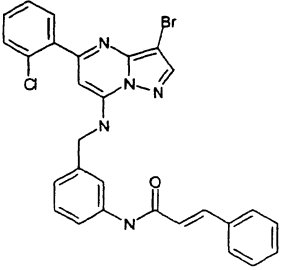
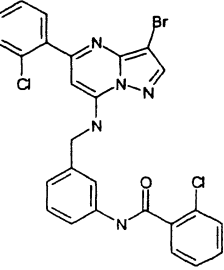
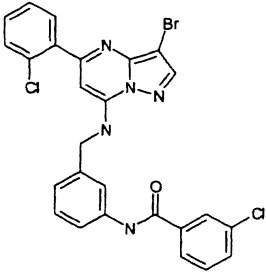
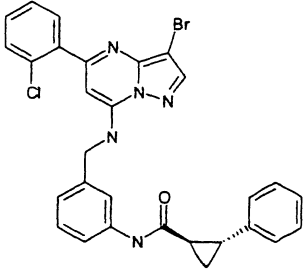
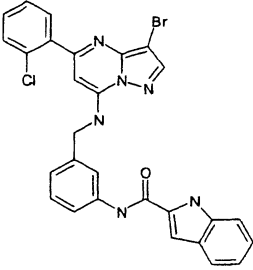
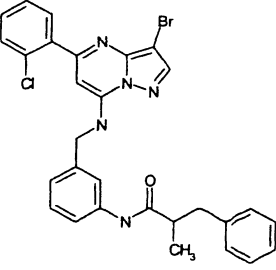
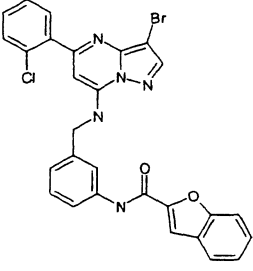
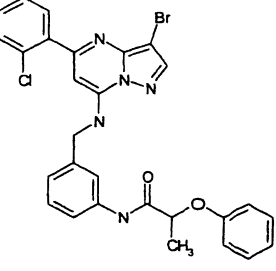
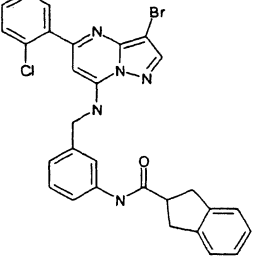
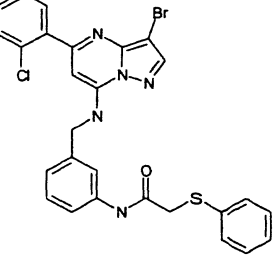
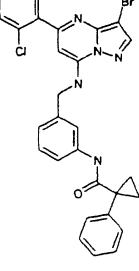
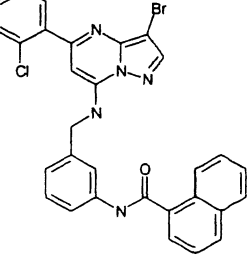
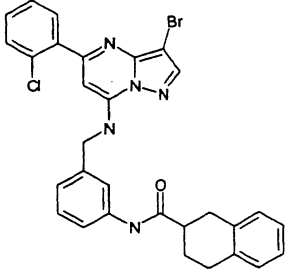
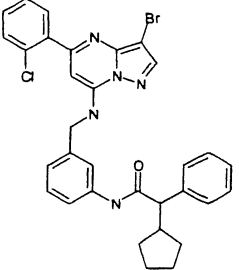
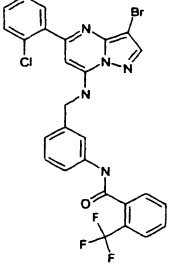
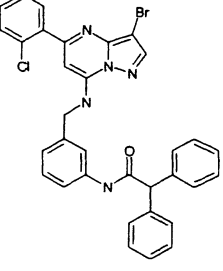
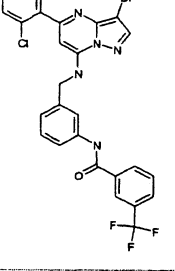
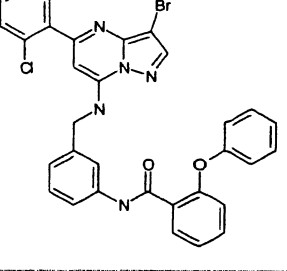
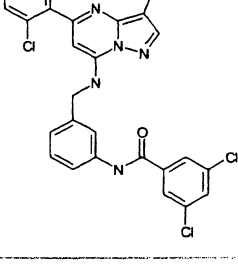
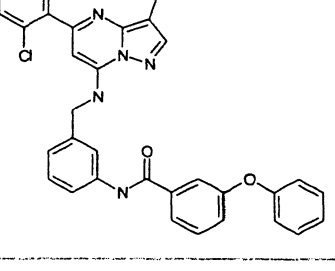
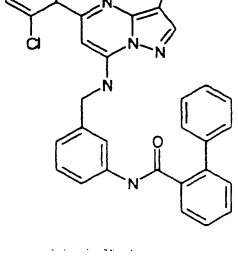
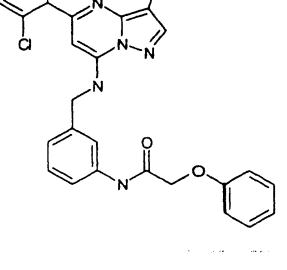
產物	1. 實例 m/z	2.
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	1. 4762 2. 472.26	
	1. 4763 2. 534.29	

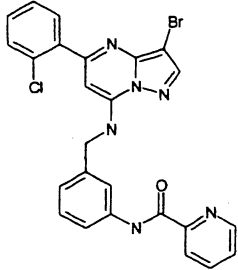
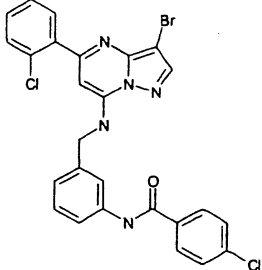
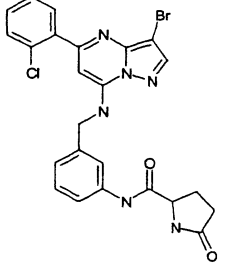
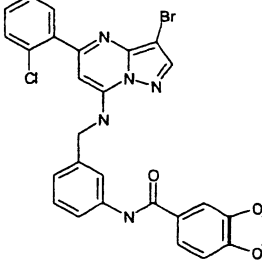
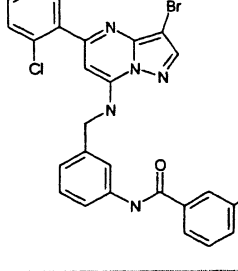
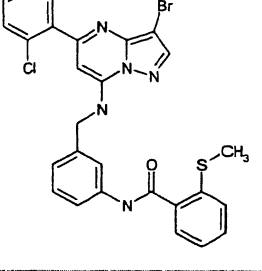
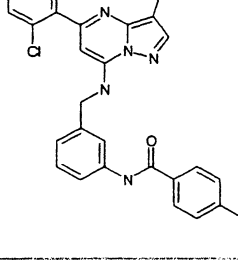
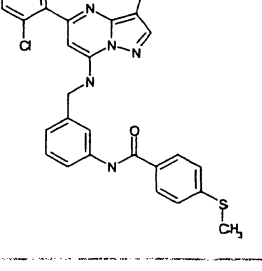
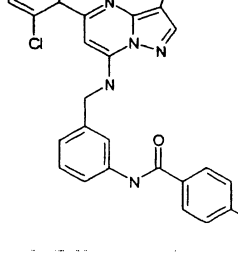
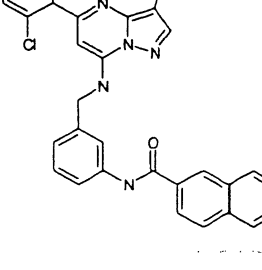
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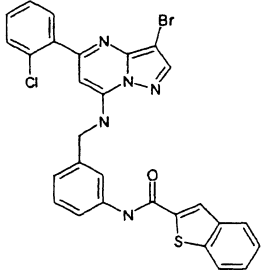
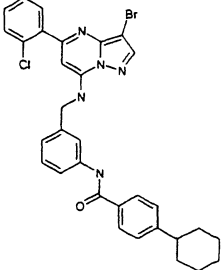
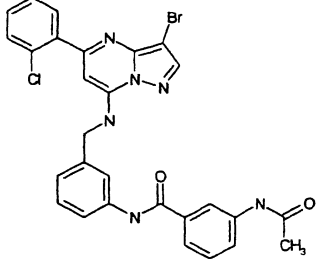
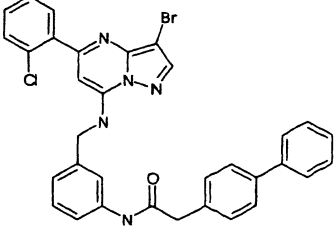
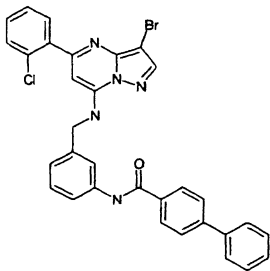
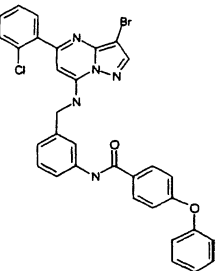
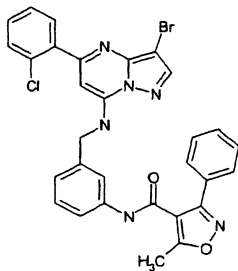
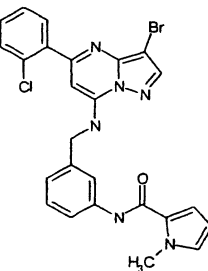
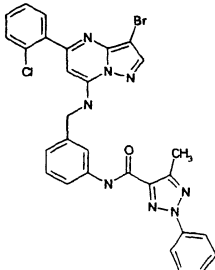
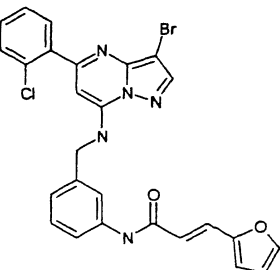
產物	1.實例 2. m/z	產物	1.實例 2. m/z
	1. 4801 2. 498.27		1.4806 2. 528.29
	1. 4802 2. 512.28		1.. 4807 2. 528.29
	1. 4803 2. 524.29		1. 4808 2. 528.29
	1. 4804 2. 524.29		1. 4809 2. 540.3
	1. 4805 2. 526.29		1. 4810 2. 540.3

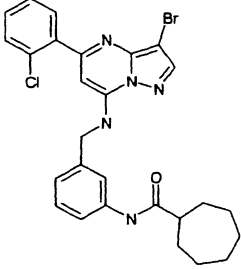
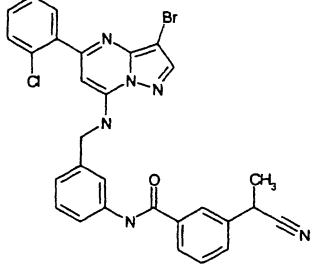
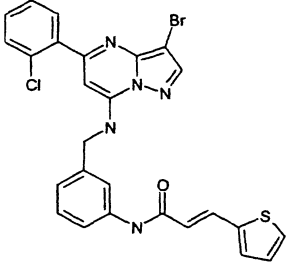
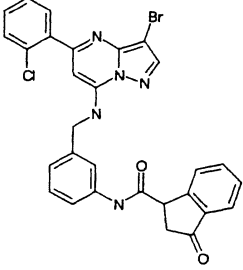
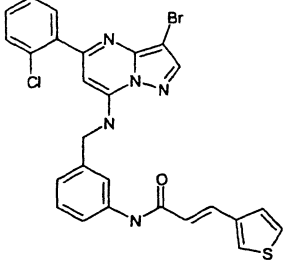
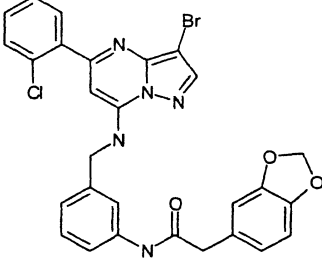
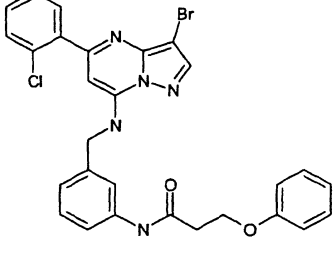
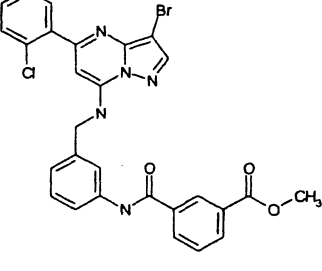
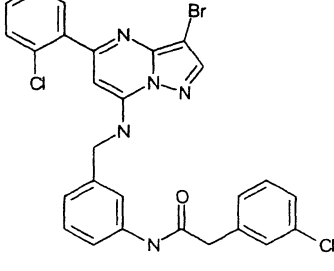
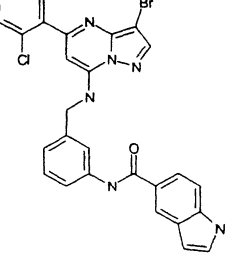
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	1. 4811 2. 544.3		1. 4816 2. 562.31
	1. 4812 2. 548.3		1. 4817 2. 562.31
	1. 4813 2. 553.3		1. 4818 2. 564.31
	1. 4814 2. 554.3		1. 4819 2. 564.31
	1. 4815 2. 560.31		1. 4820 2. 568.31

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4821 2. 568.31		1. 4826 2. 574.32
	1. 4822 2. 573.32		1. 4828 2. 576.32
	1. 4821 2. 574.32		1. 4829 2. 578.32
	1. 4824 2. 574.32		1. 4829 2. 580.32
	1. 4825 2. 574.32		1. 4830 2. 584.32

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4831 2. 588.32		1. 4836 2. 616.34
	1. 4832 2. 602.33		1. 4837 2. 624.34
	1. 4833 2. 602.33		1. 4838 2. 626.34
	1. 4834 2. 602.33		1. 4839 2. 626.34
	1. 4835 2. 610.34		1. 4840 2. 564.31

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4841 2. 535.29		1. 4846 2. 568.31
	1. 4842 2. 541.3		1. 4847 2. 578.32
	1. 4843 2. 559.31		1. 4848 2. 580.32
	1. 4844 2. 559.31		1. 4849 2. 580.32
	1. 4845 2. 564.31		1. 4850 2. 584.32

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4851 2. 590.32		1. 4856 2. 616.34
	1. 4852 2. 591.33		1. 4857 2. 624.34
	1. 4853 2. 610.34		1. 4858 2. 626.34
	1. 4854 2. 615.34		1. 4859 2. 537.3
	1. 4855 2. 615.34		1. 4860 2. 550.3

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4861 2. 554.3		1. 4866 2. 587.32
	1. 4862 2. 566.31		1. 4867 2. 588.32
	1. 4863 2. 566.31		1. 4868 2. 592.33
	1. 4864 2. 578.32		1. 4869 2. 592.33
	1. 4865 2. 582.32		1. 4870 2. 573.32

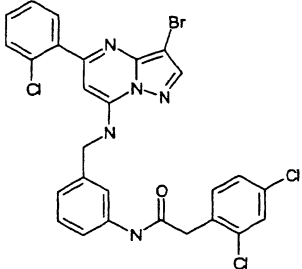
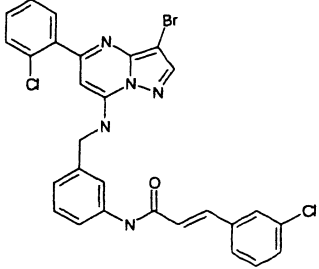
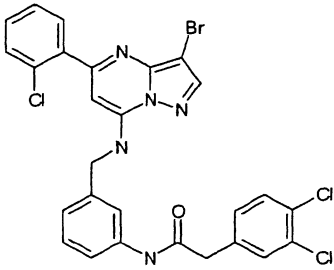
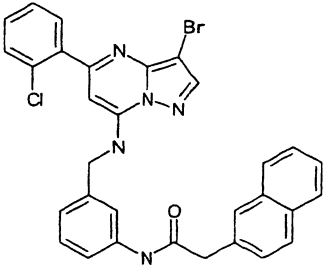
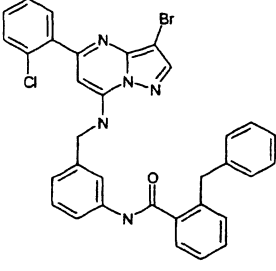
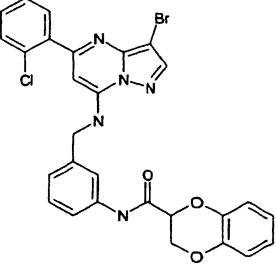
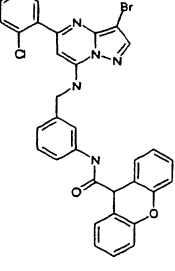
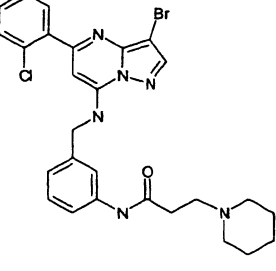
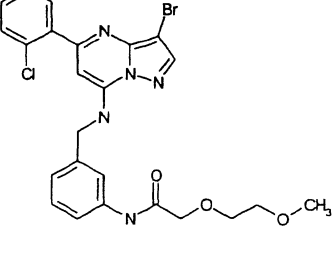
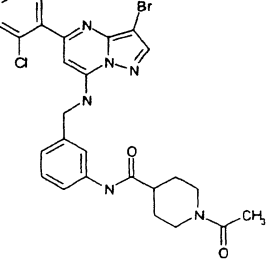
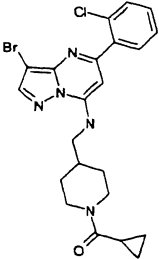
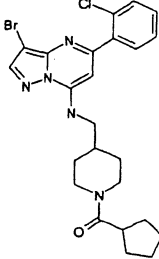
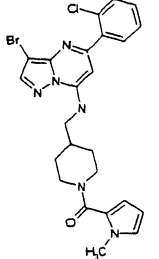
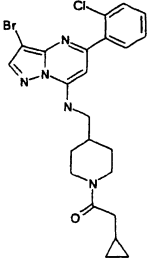
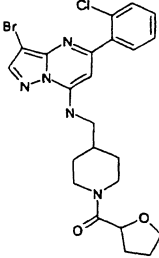
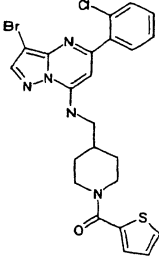
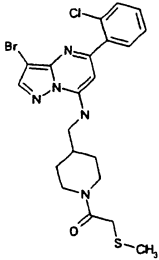
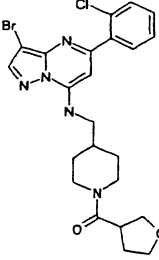
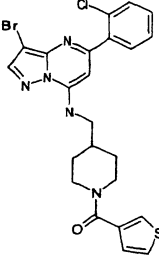
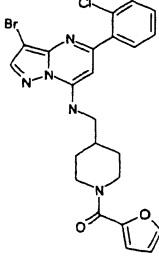
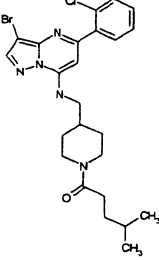
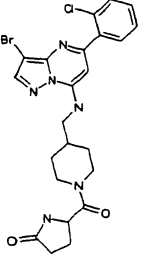
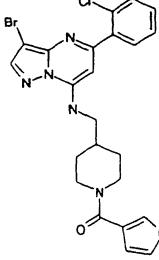
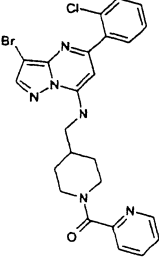
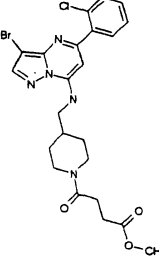
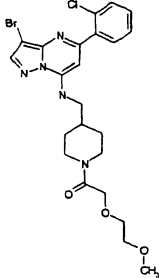
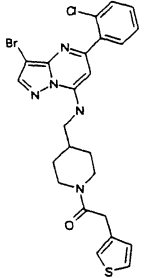
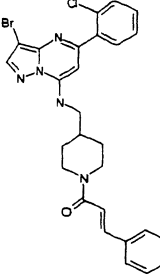
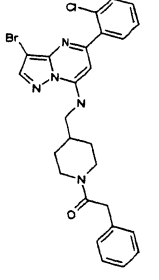
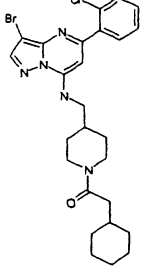
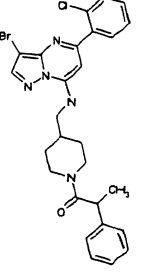
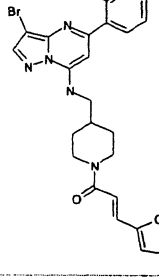
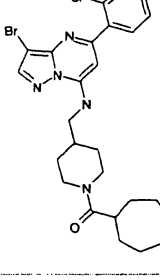
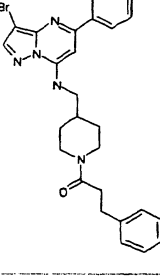
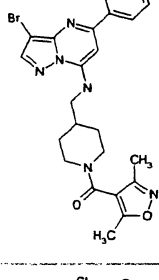
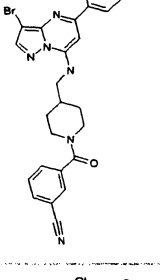
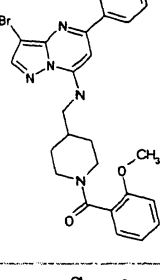
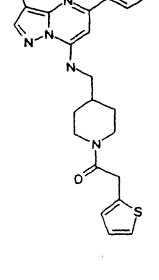
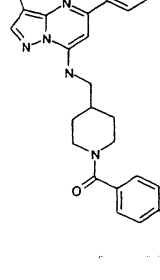
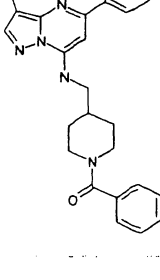
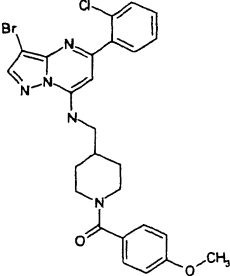
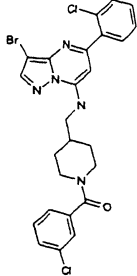
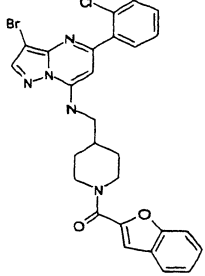
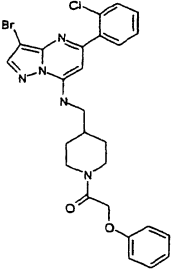
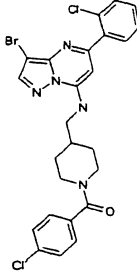
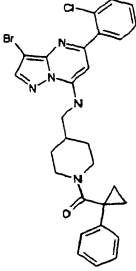
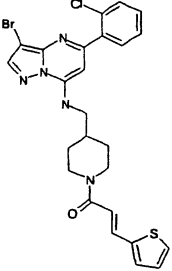
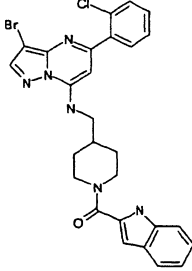
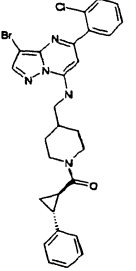
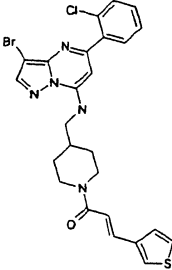
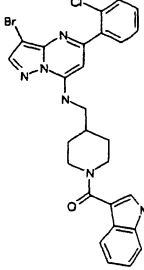
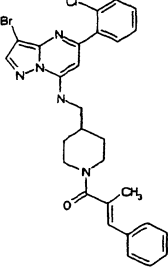
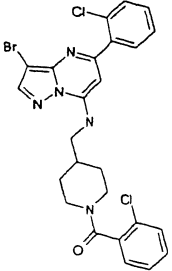
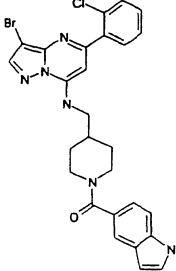
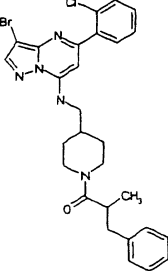
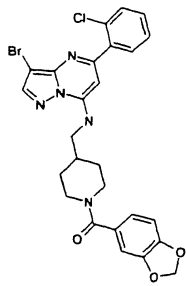
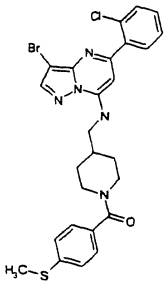
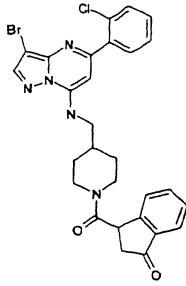
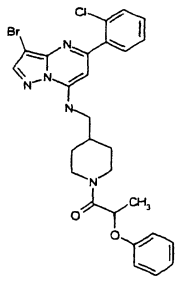
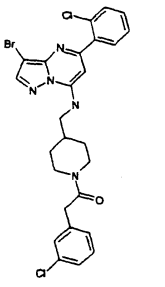
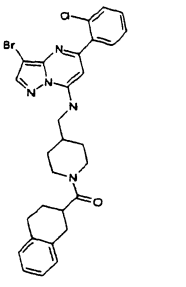
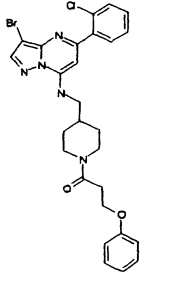
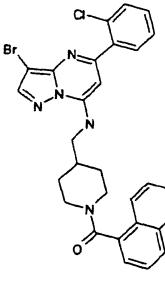
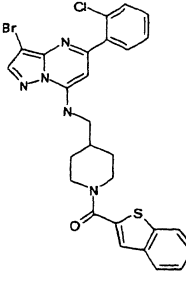
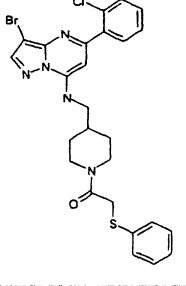
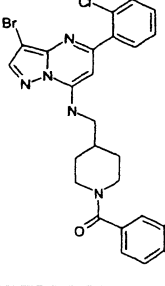
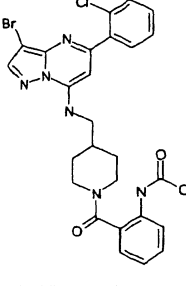
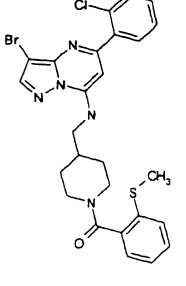
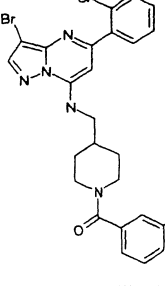
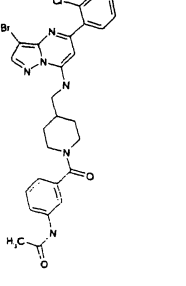
產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4871 2. 616.34		1. 4876 2. 594.33
	1. 4872 2. 616.34		1. 4877 2. 598.33
	1. 4873 2. 624.34		1. 4878 2. 592.33
	1. 4874 2. 638.35		1. 4879 2. 569.31
	1. 4875 2. 546.3		1. 4880 2. 583.32

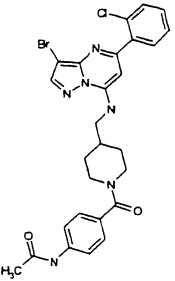
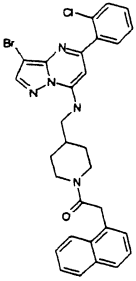
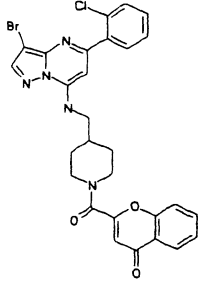
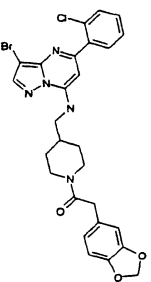
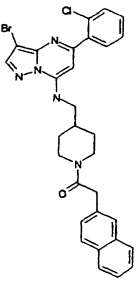
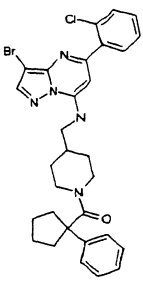
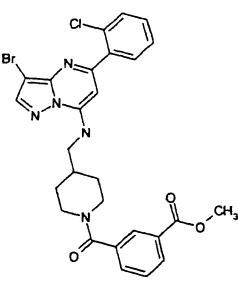
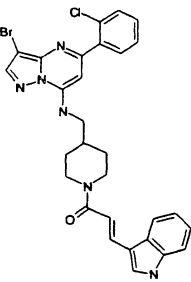
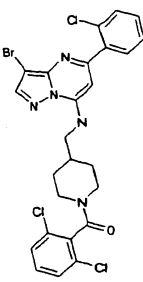
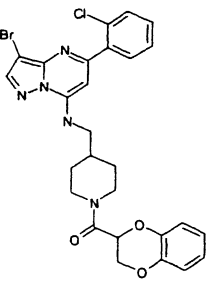
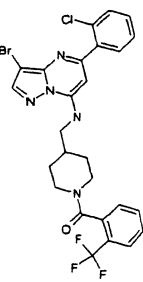
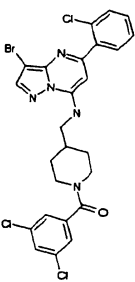
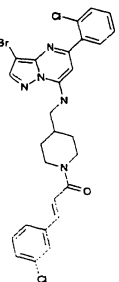
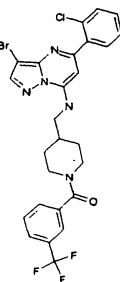
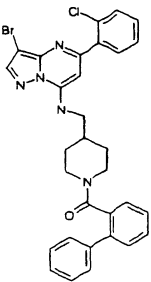
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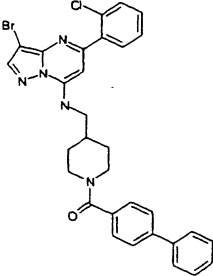
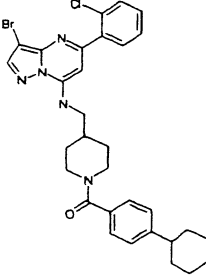
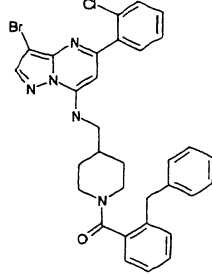
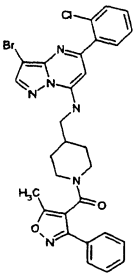
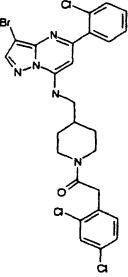
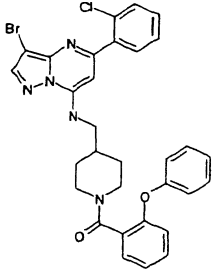
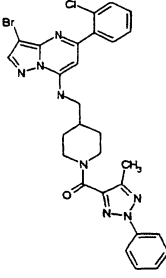
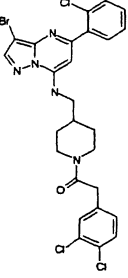
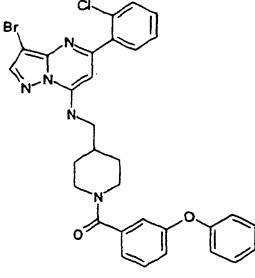
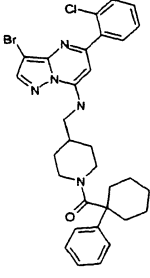
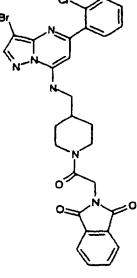
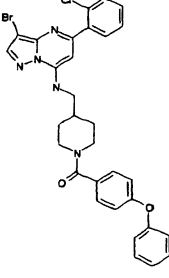
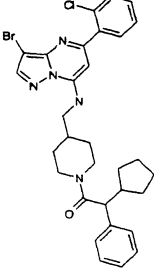
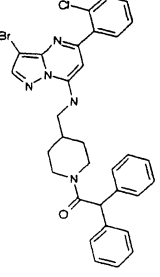
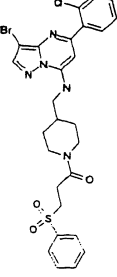
產物	1. 實例2. m/z	產物	1. 實例2. m/z	產物	1. 實例2. m/z
	1. 4901 2. 490.27		1. 4906 2. 518.28		1. 4911 2. 529.29
	1. 4902 2. 504.28		1. 4907 2. 520.29		1. 4912 2. 532.29
	1. 4903 2. 510.28		1. 4908 2. 520.29		1. 4913 2. 532.29
	1. 4904 2. 516.28		1. 4909 2. 520.29		1. 4914 2. 533.29
	1. 4905 2. 516.28		1. 4910 2. 527.29		1. 4915 2. 536.29

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4916 2. 538.3		1. 4921 2. 546.3		1. 4926 2. 552.3
	1. 4917 2. .540.3		1. 4922 2. 546.3		1. 4927 2. 554.3
	1. 4918 2. 542.3		1. 4923 2. 546.3		1. 4928 2. 554.3
	1. 4919 2. 545.3		1. 4924 2. 551.3		1. 4929 2. 556.31
	1. 4920 2. 546.3		1. 4925 2. 551.3		1. 4930 2. 556.31

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4931 2. 556.31		1. 4936 2. 560.31		1. 494 2. 566.3
	1. 4932 2. 556.31		1. 4937 2. 560.31		1. 4942 2. 566.3
	1. 4933 2. 558.31		1. 4938 2. 565.31		1. 4943 2. 566.31
	1. 4934 3. 558.31		1. 4939 2. 565.3		1. 4944 2. 566.31
	1. 4935 2. 560.31		1. 4940 2. 565.31		1. 4945 2. 568.31

產物	1.實例 2. m/z	產物	1.實例 2. m/z	產物	1.實例 2. m/z
	1. 4946 2. 570.31		1. 4951 2. 571.31		1. 4956 2. 580.32
	1. 4947 2. 570.31		1. 4952 2. 574.32		1. 4957 2. 580.32
	1. 4948 2. 570.31		1. 4953 2. 576.32		1. 4958 2. 582.32
	1. 4949 2. 572.31		1. 4954 2. 576.32		1. 4959 2. 583.32
	1. 4950 2. 572.31		1. 4955 2. 579.32		1. 4960 2. 583.32

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 4961 2. 583.32		1. 4966 2. 590.32		1. 4971 2. 594.33
	1. 4962 2. 584.32		1. 4967 2. 590.32		1. 4972 2. 594.33
	1. 4963 2. 584.32		1. 4968 2. 591.3		1. 4973 2. 594.33
	1. 4964 2. 584.32		1. 4969 2. 594.33		1. 4974 2. 594.33
	1. 4965 2. 586.32		1. 4970 2. 594.33		1. 4975 2. 602.33

產物	1. 實例2. m/z	產物	1. 實例2. m/z	產物	1. 實例2. m/z
	1. 4976 2. 602.33		1. 4981 2. 608.33		1. 4986 2. 616.34
	1. 4977 2. 607.33		1. 4982 2. 608.33		1. 4987 2. 618.34
	1. 4978 2. 607.33		1. 4983 2. 608.33		1. 4988 2. 618.34
	1. 4979 2. 605.33		1. 4984 2. 609.33		1. 4089 2. 618.34
	1. 4980 2. 608.33		1. 4985 2. 616.34		1. 4990 2. 618.34

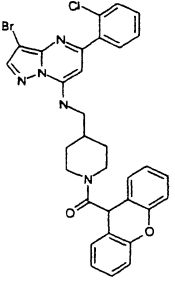
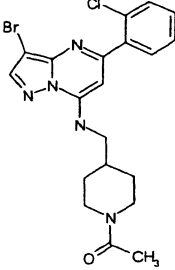
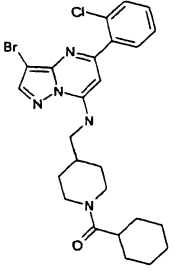
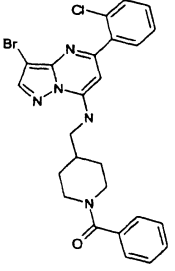
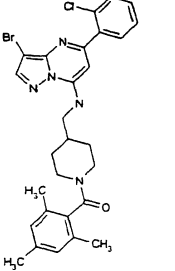
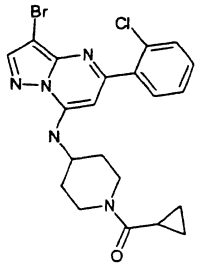
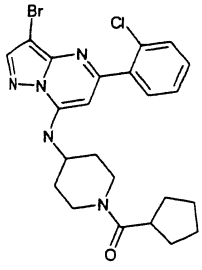
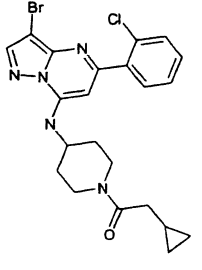
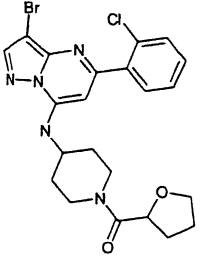
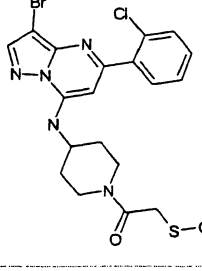
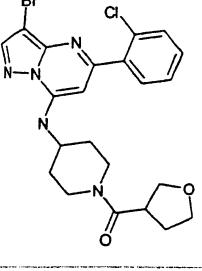
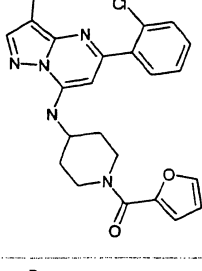
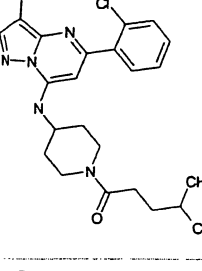
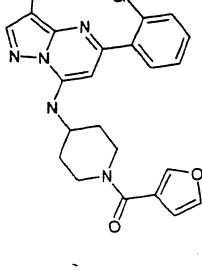
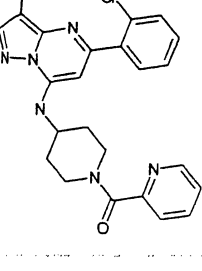
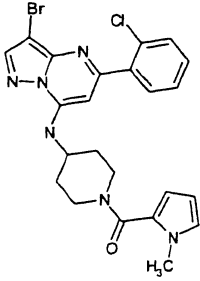
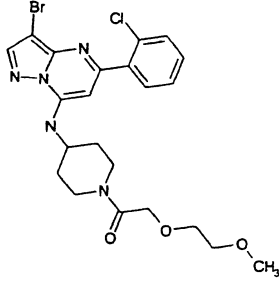
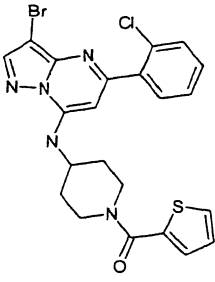
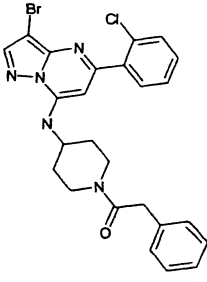
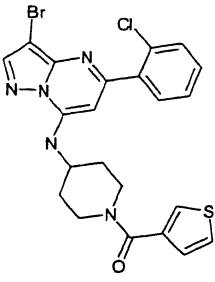
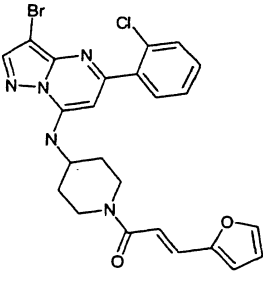
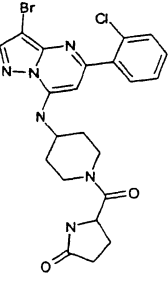
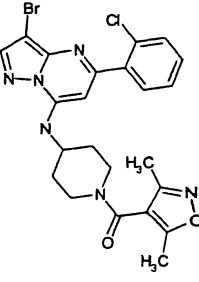
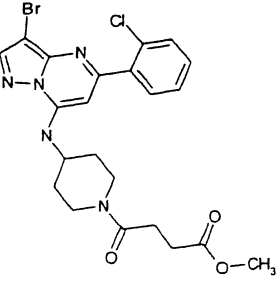
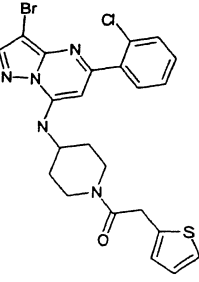
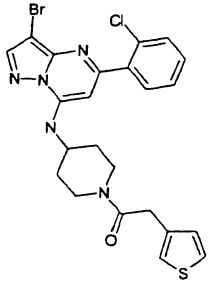
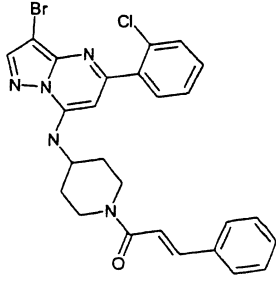
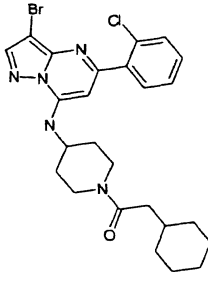
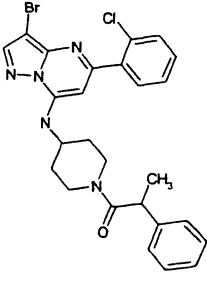
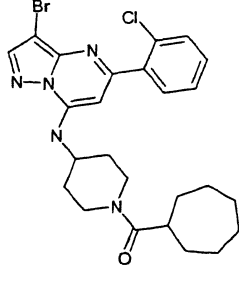
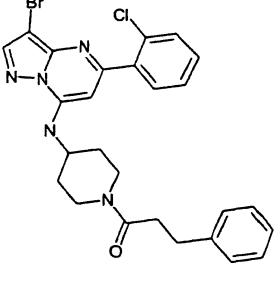
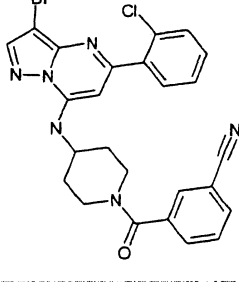
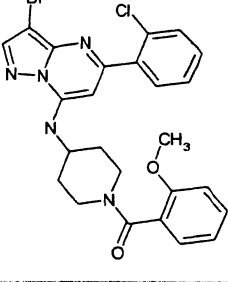
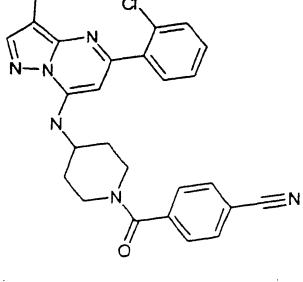
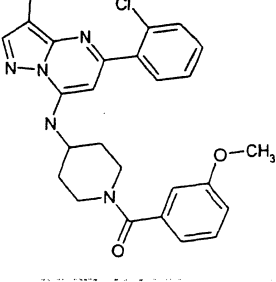
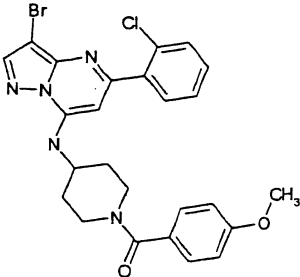
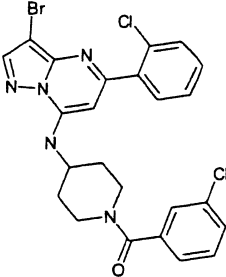
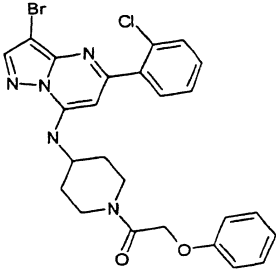
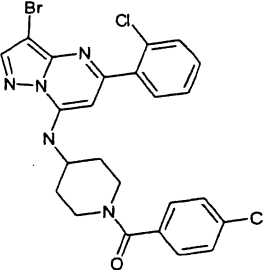
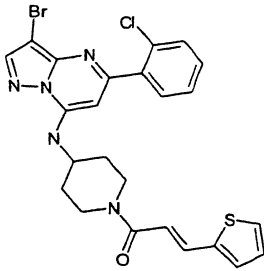
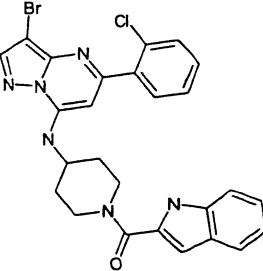
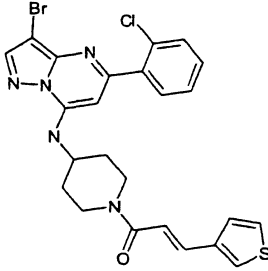
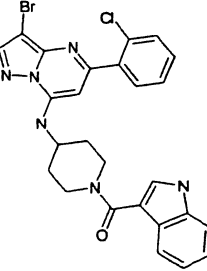
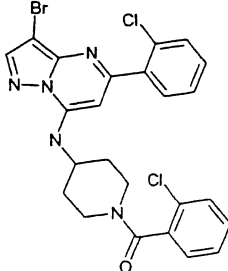
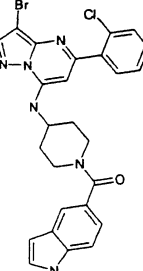
產物	1. 實例 2. m/z
	1. 4991 2. 630.35
	1. 4992 2. 464.26
	1. 4993 2. 532.29
	1. 4994 2. 526.29
	1. 4995 2. 568.31

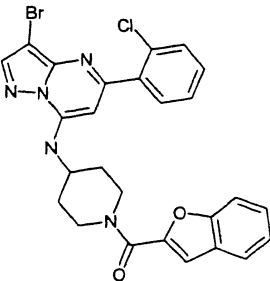
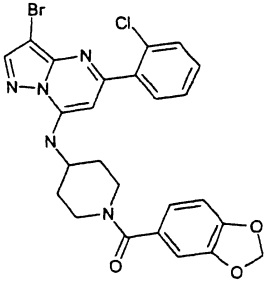
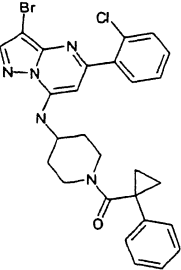
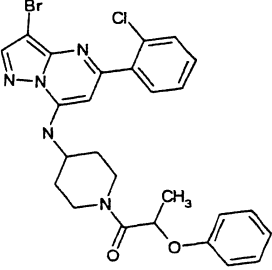
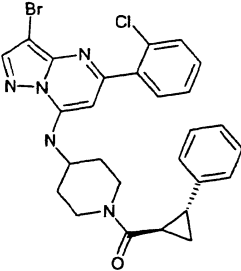
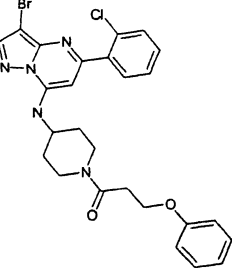
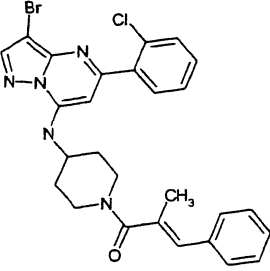
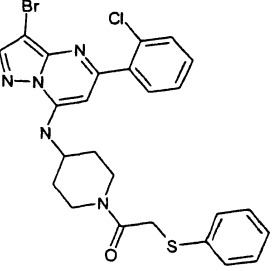
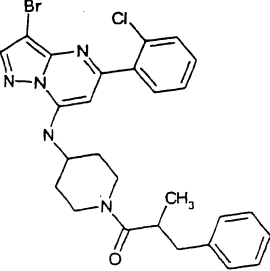
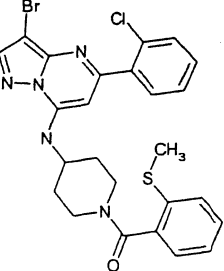
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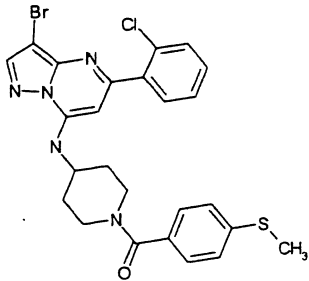
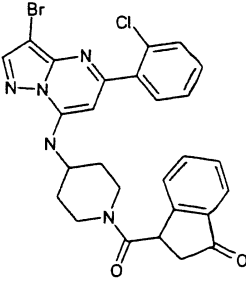
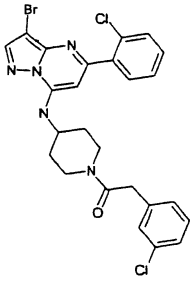
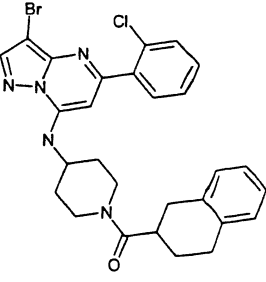
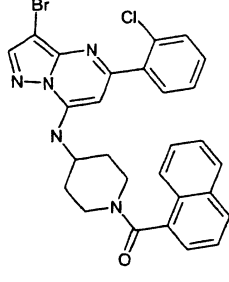
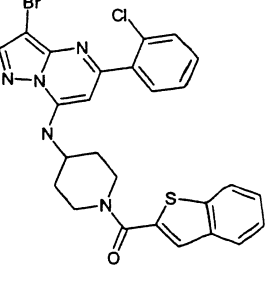
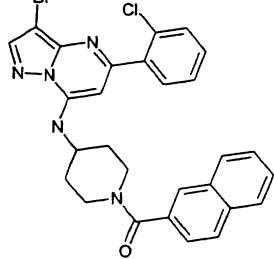
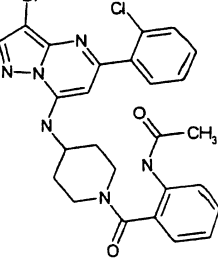
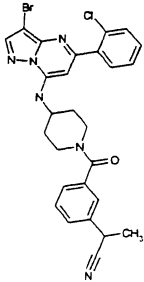
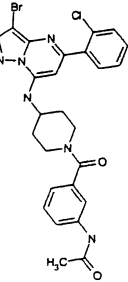
產物	1. 實例2. m/z	產物	1. 實例2. m/z
	1. 5001 2. 476.26		1. 5006 2. 504.28
	1. 5002 2. 490.27		1. 5007 2. 506.28
	1. 5003 2. 496.27		1. 5008 2. 506.28
	1. 5004 2. 502.28		1. 5009 2. 506.28
	1. 5005 2. 502.28		1. 5010 2. 513.28

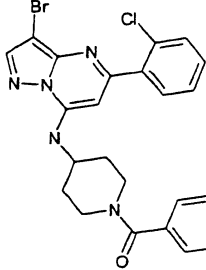
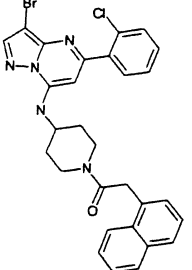
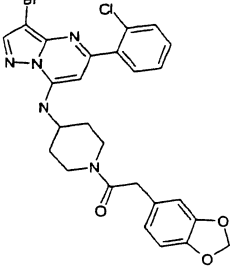
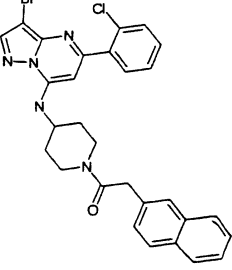
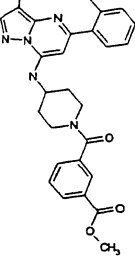
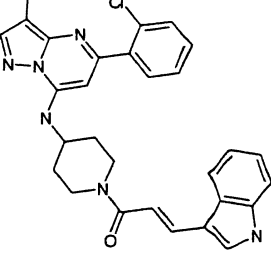
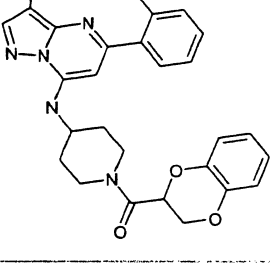
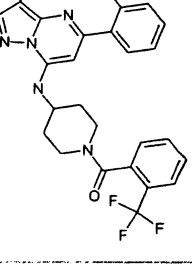
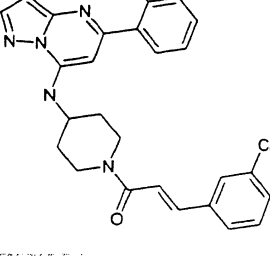
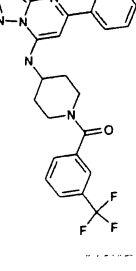
產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5011 2. 515.28		1. 5016 2. 524.29
	1. 5012 2. 518.28		1. 5017 2. 526.29
	1. 5013 2. 518.28		1. 5018 2. 528.29
	1. 5014 2. 519.29		1. 5019 2. 531.29
	1. 5015 2. 522.29		1. 5020 2. 532.29

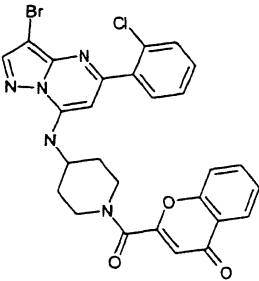
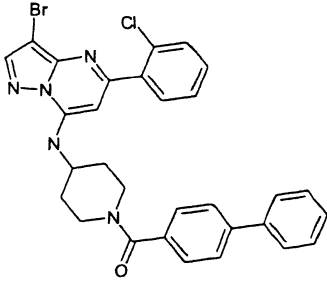
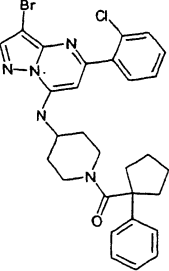
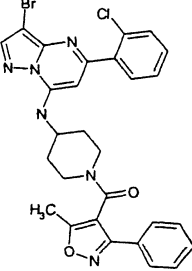
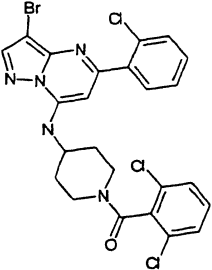
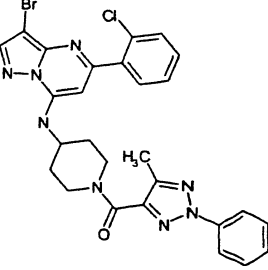
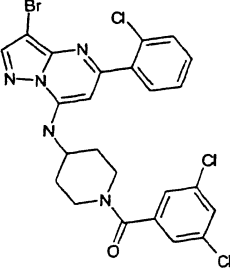
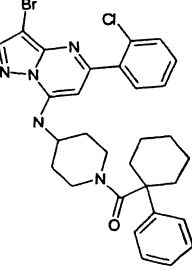
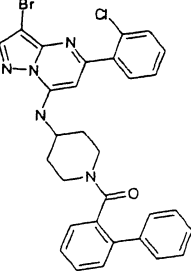
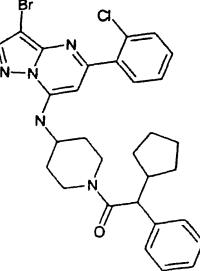
產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5021 2. 532.29		1. 5026 2. 538.3
	1. 5022 2. 532.29		1. 5027 2. 540.3
	1. 5023 2. 532.29		1. 5028 2. 540.3
	1. 5024 2. 537.3		1. 5029 2. 542.3
	1. 5025 2. 537.3		1. 5030 2. 542.3

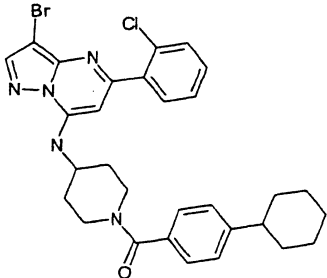
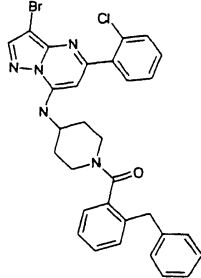
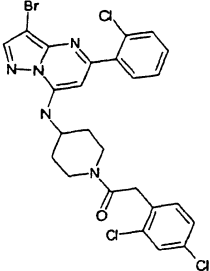
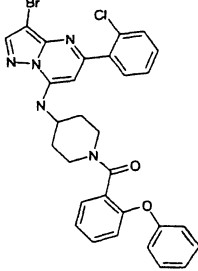
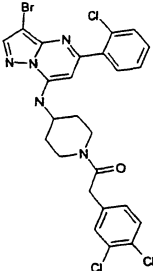
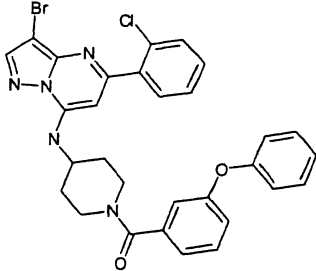
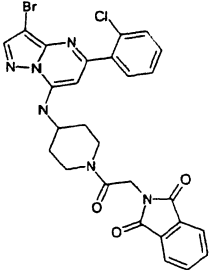
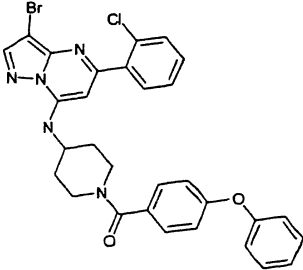
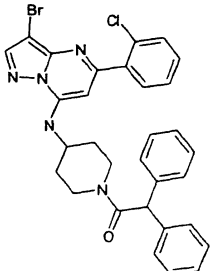
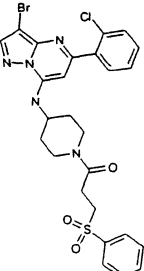
產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5031 2. 542.3		1. 5036 2. 546.3
	1. 5032 2. 542.3		1. 5037 2. .546.3
	1. 5033 2. 544.3		1. 5038 2. 551.3
	1. 5034 2. 544.3		1. 5039 2. 551.3
	1. 5035 2. .546.3		1. 5040

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5041 2. 552.3		1. 5046 2. 556.31
	1. 5042 2. 552.3		1. 5047 2. 556.31
	1. 5043 2. 552.3		1. 5048 2. 556.31
	1. 5044 2. 552.3		1. 5049 2. 558.31
	1. 5045 2. 554.3		1. 5050 2. 558.31

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5051 2. 558.31		1. 5056 2. 566.31
	1. 5052 2. 560.31		1. 5057 2. 566.31
	1. 5053 2. 562.31		1. 5058 2. 568.31
	1. 5054 2. 562.31		1. 5059 2. 569.31
	1. 5055 2. 565.31		1. 5060 2. 569.31

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5061		1. 5066 2. 576.32
	1. 5062 2. 570.31		1. 5067 2. 576.32
	1. 5063 2. 570.31		1. 5068 2. 577.32
	1. 5064 2. 570.31		1. 5069 2. 580.32
	1. 5065 572.31		1. 5070 2. 580.32

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5071 2. 580.32		1 5076 2. 588.32
	1. 5072 2. 580.32		1. 5077 2. 593.33
	1 5073 2. 580.32		1 5078 2. 593.33
	1 5074 2. 580.32		1. 5079 2. 594.33
	1 5075 2. 588.32		1. 5080 2. 594.33

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5081 2. 594.33		1. 5086 2. 602.33
	1. 5082 2. 594.33		1. 5087 2. 604.33
	1. 5083 2. 594.33		1. 5088 2. 604.33
	1. 5084 2. 595.33		1. 5089 2. 604.33
	1. 5085 2. 602.33		1. 5090 2. 604.33

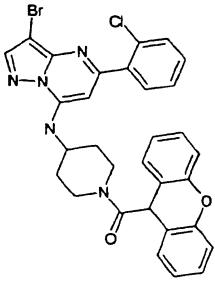
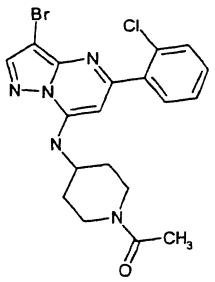
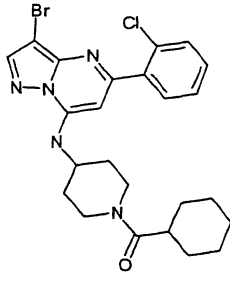
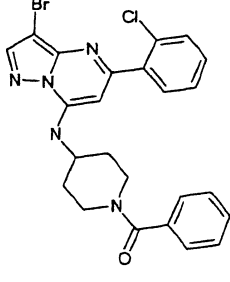
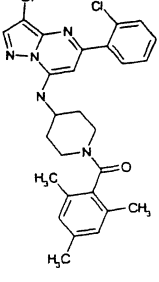
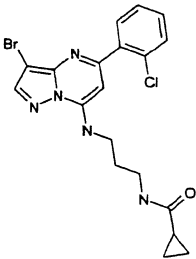
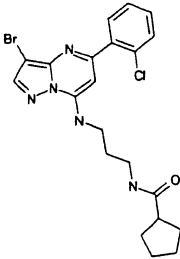
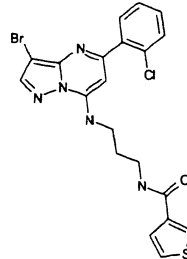
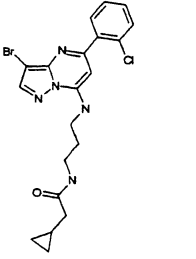
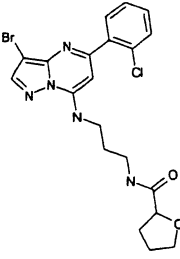
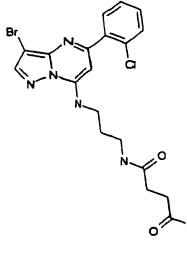
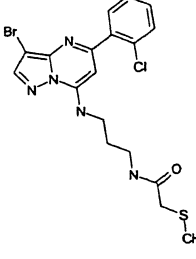
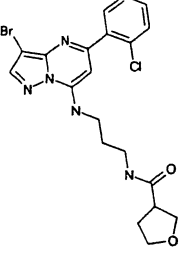
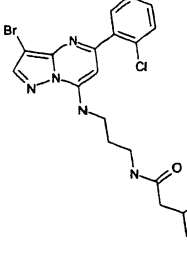
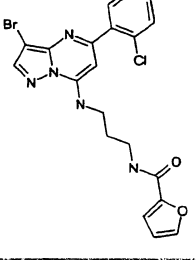
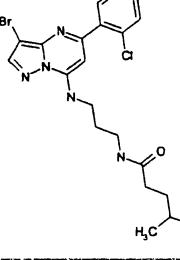
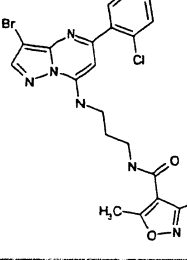
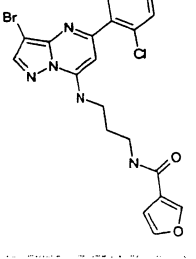
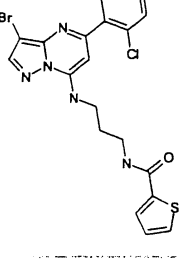
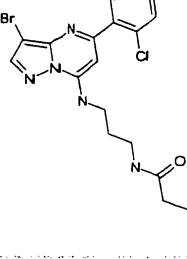
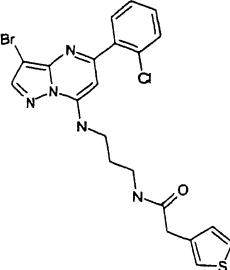
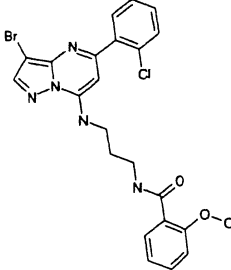
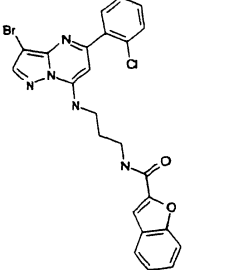
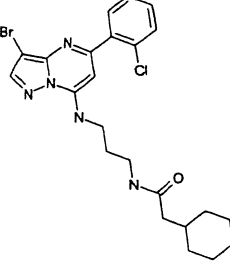
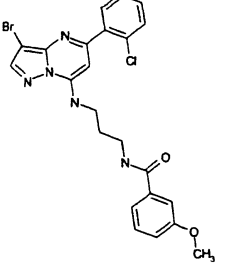
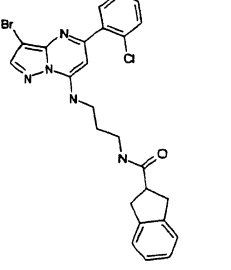
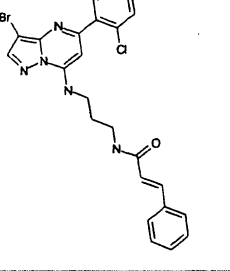
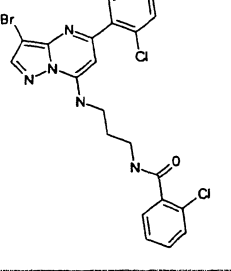
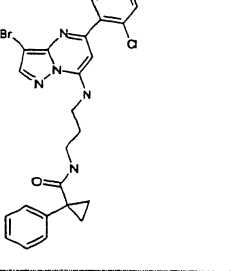
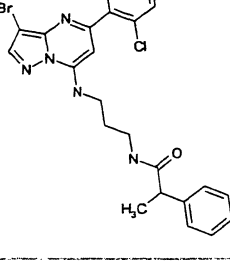
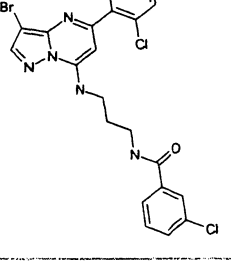
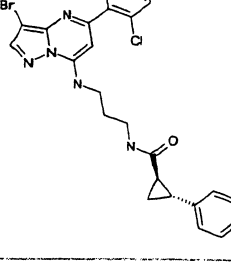
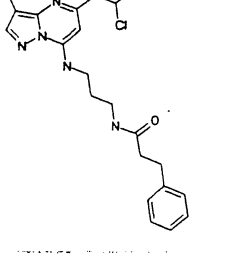
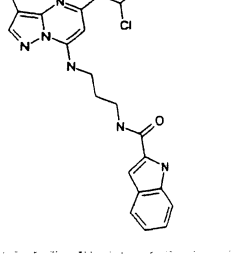
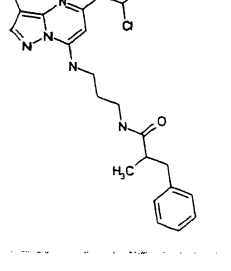
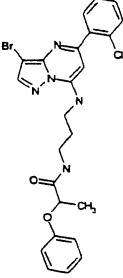
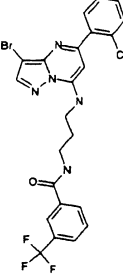
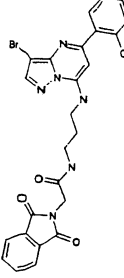
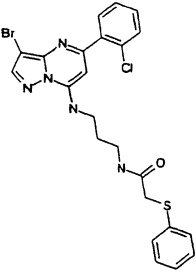
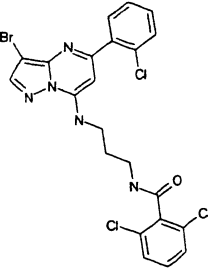
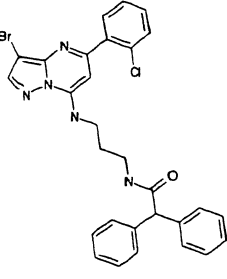
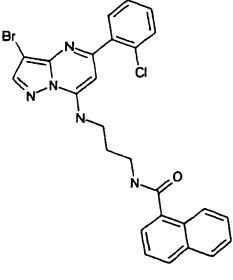
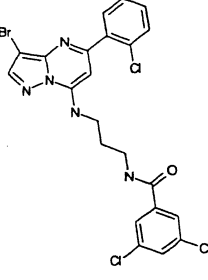
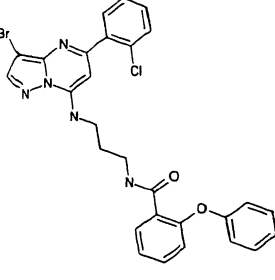
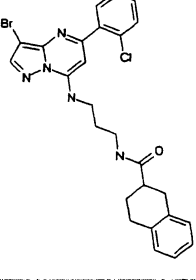
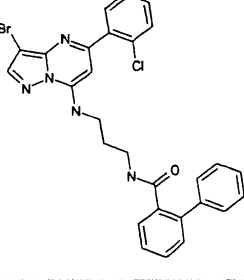
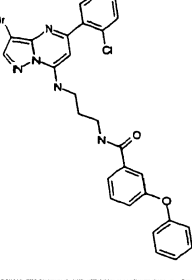
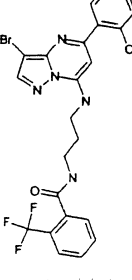
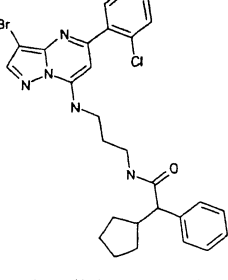
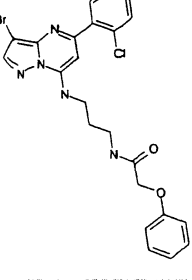
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	1. 5091 2. 616.34
	1. 5092 2. 450.25
	1. 5093 2. 518.28
	1. 5094 2. 512.28
	1. 5095 2. 554.3

表51

產物	1.實例2. m/z	產物	1.實例2. m/z	產物	1.實例2. m/z
	1. 5101 2. 448.8		1. 5106 2. 476.8		1. 5111 2. 490.8
	1. 5102 2. 462.8		1. 5107 2. 478.8		1. 5112 2. 494.8
	1. 5103 2. 468.8		1. 5108 2. 478.8		1. 5113 2. 498.8
	1. 5104 2. 474.7		1. 5109 2. 478.8		1. 5114 2. 503.8
	1. 5105 2. 474.7		1. 5110 2. 490.8		1. 5115 2. 504.8

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5116 2. 504.8		1. 5121 2. 514.8		1. 5126 2. 524.8
	1. 5117 2. 504.9		1. 5122 2. 514.8		1. 5127 2. 524.9
	1. 5118 2. 510.8		1. 5123 2. 519.2		1. 5128.2 2. 524.9
	1. 5119 2. 512.8		1. 5124 2. 519.2		1. 5129 2. 524.9
	1. 5120 2. 512.8		1. 5125 2. 523.8		1. 5130 2. 526.9

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5131 2. 528.8		1. 5136 2. 552.8		1. 5141 2. 567.8
	1. 5132 2. 530.9		1. 5137 2. 553.7		1. 5142 2. 574.9
	1. 5133 2. 534.8		1. 5138 2. 553.7		1. 5143 2. 576.9
	1. 5134 2. 538.9		1. 5139 2. 560.9		1. 5144 2. 576.9
	1. 5135 2. 552.8		1. 5140 2. 566.9		1. 5145 2. 514.8

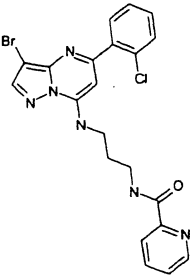
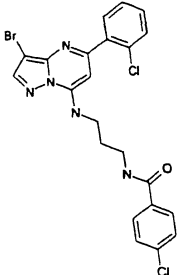
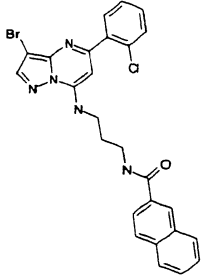
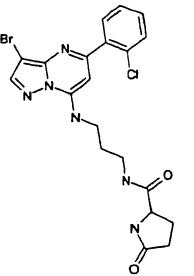
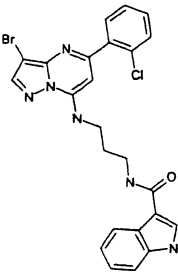
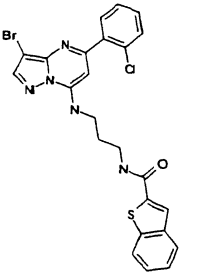
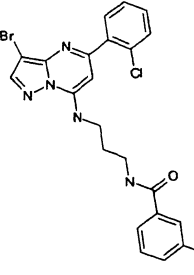
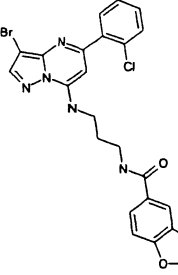
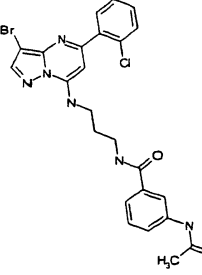
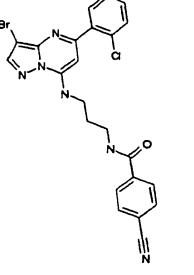
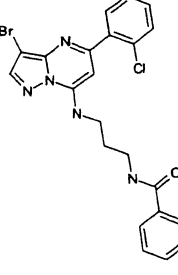
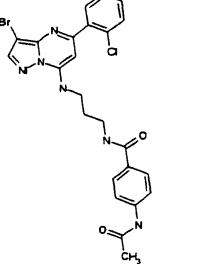
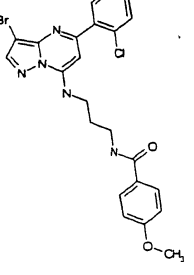
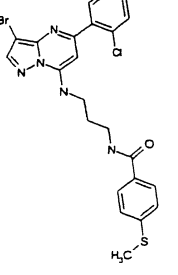
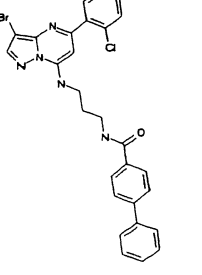
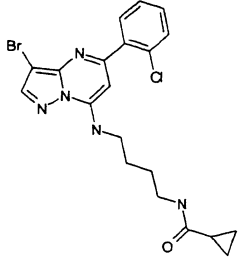
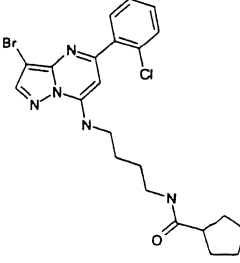
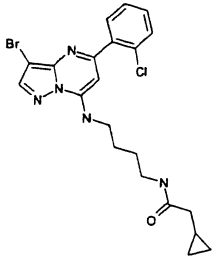
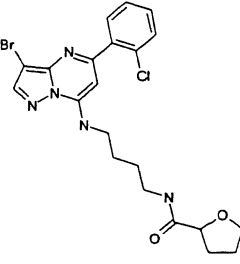
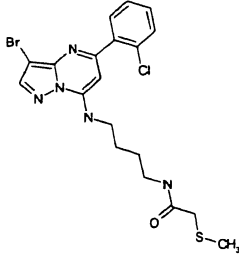
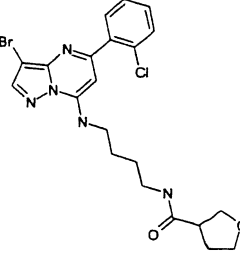
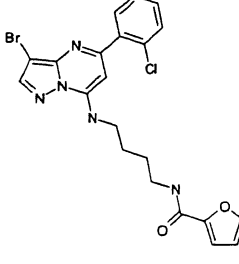
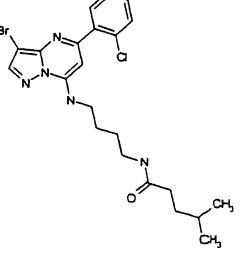
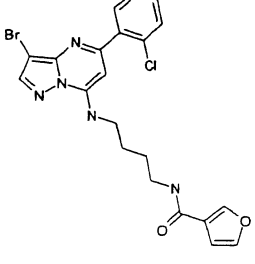
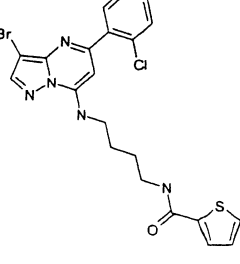
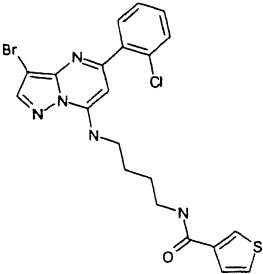
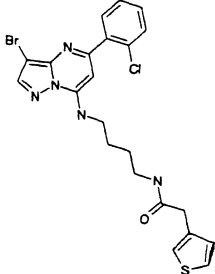
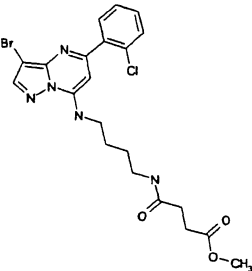
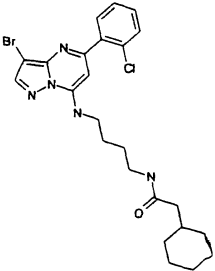
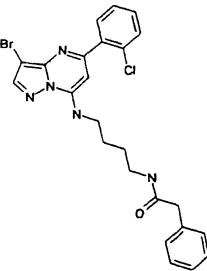
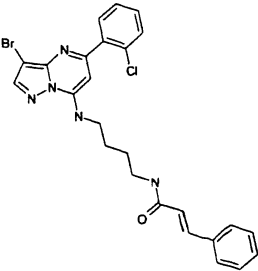
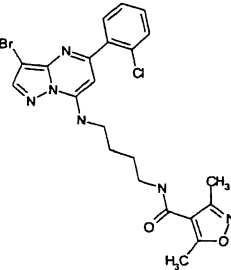
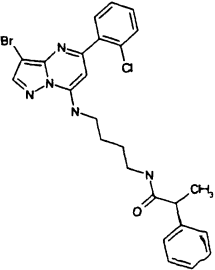
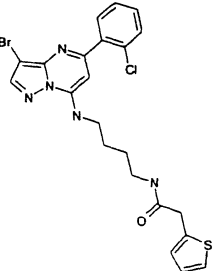
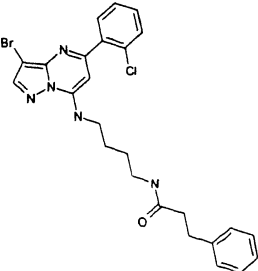
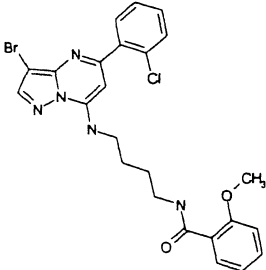
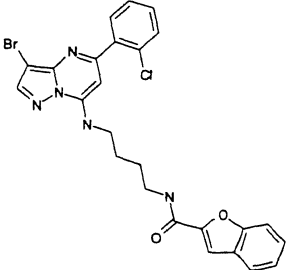
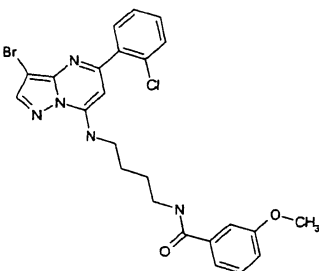
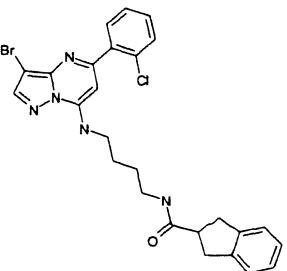
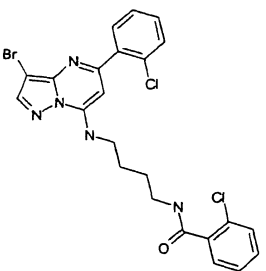
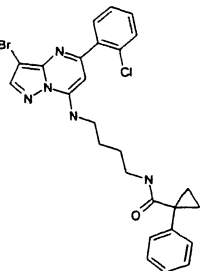
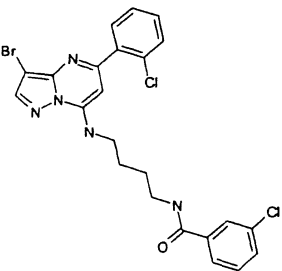
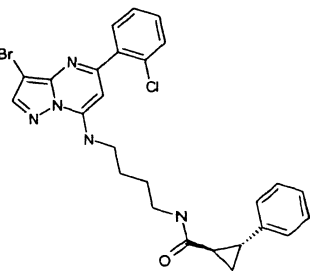
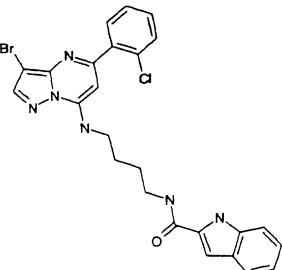
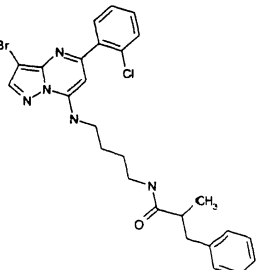
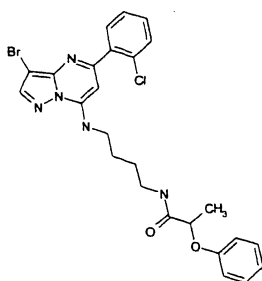
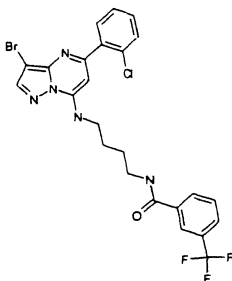
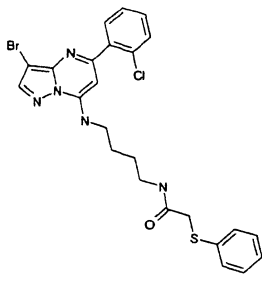
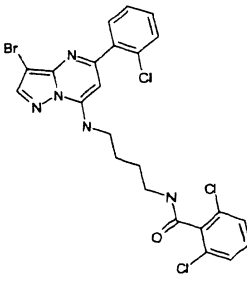
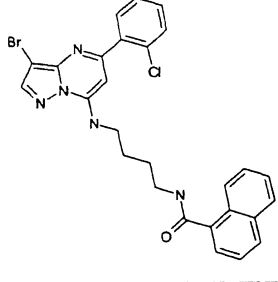
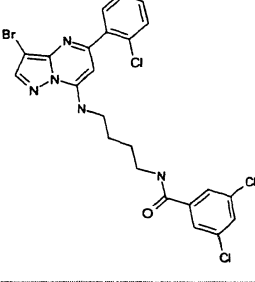
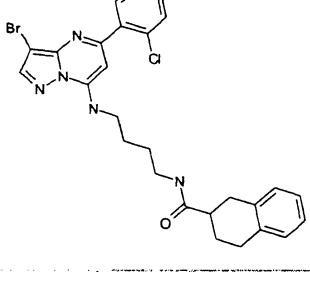
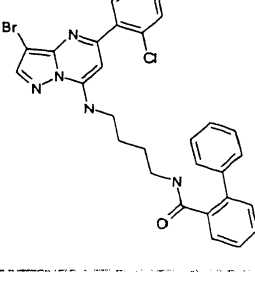
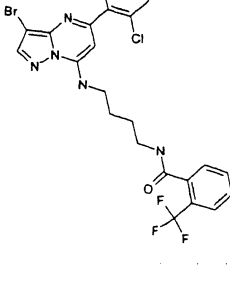
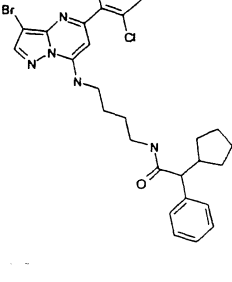
產物	1. 實例 2. m/z	產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
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	1. 5147 2. 491.8		1. 5152 2. 523.8		1. 5157 2. 540.9
	1. 5148 2. 509.8		1. 5153 2. 528.8		1. 5158 2. 541.8
	1. 5149 2. 509.8		1. 5154 2. 530.9		1. 5159 2. 541.8
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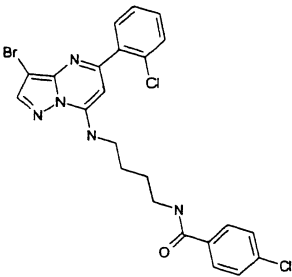
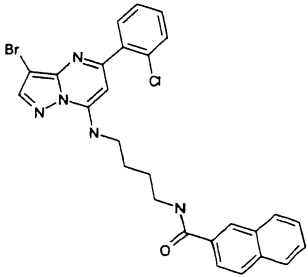
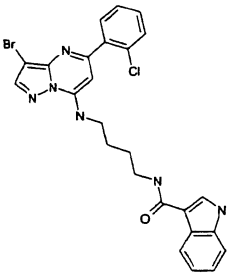
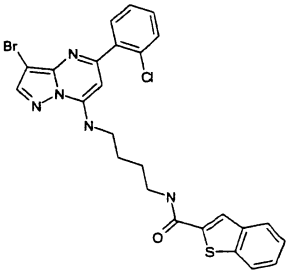
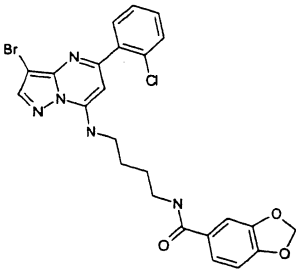
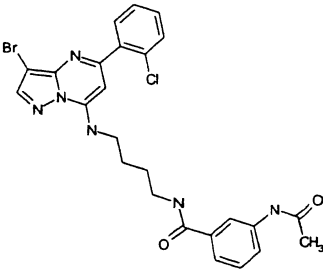
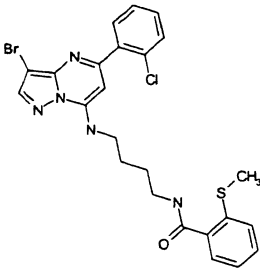
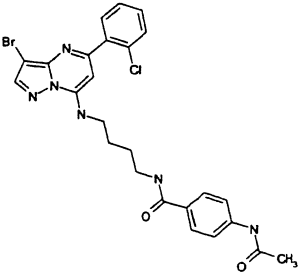
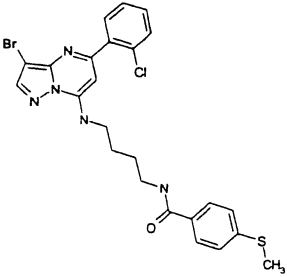
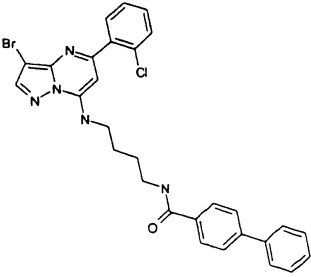
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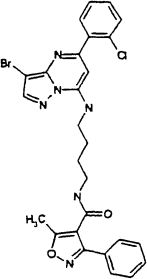
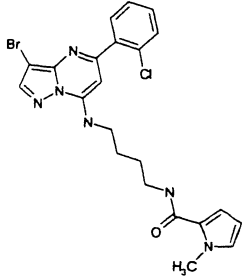
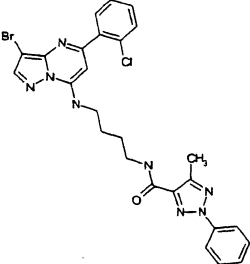
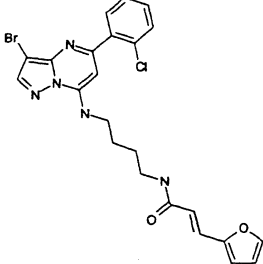
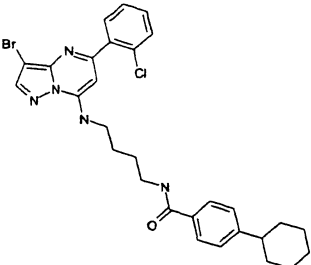
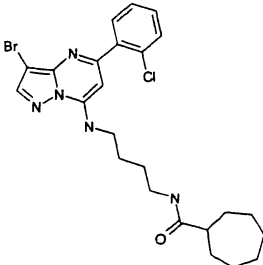
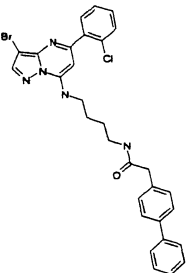
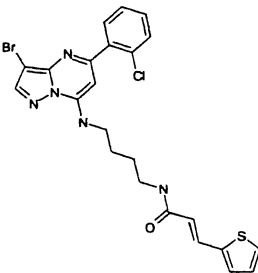
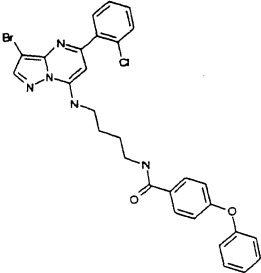
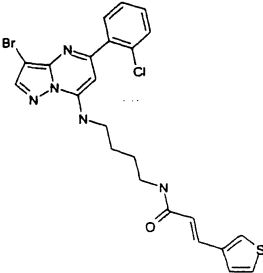
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	1. 5201 2. 462.8		1. 5206 2. 490.8
	1. 5202 2. 476.8		1. 5207 2. 492.8
	1. 5203 2. 482.8		1. 5208 2. 492.8
	1. 5204 2. 488.8		1. 52009 2. 492.9
	1. 5205 2. 488.8		1. 5210 2. 504.8

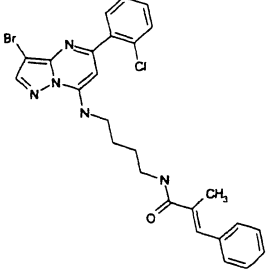
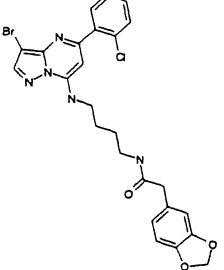
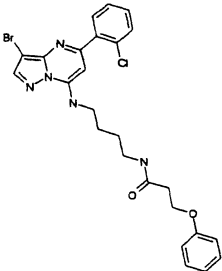
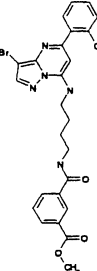
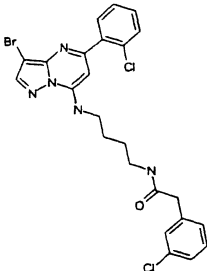
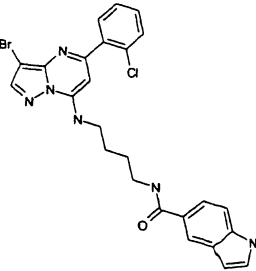
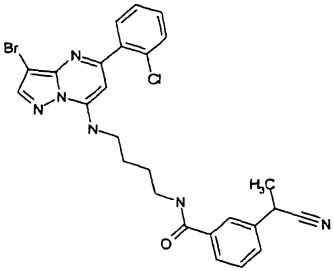
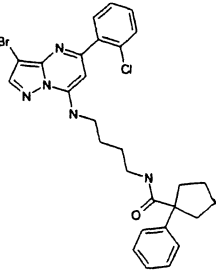
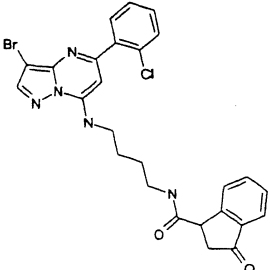
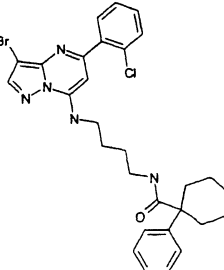
產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5211 2. 504.8		1. 5216 2. 518.9
	2. 5212 2. 508.8		1. 5217 2. 518.9
	1. 5213 2. 512.8		1. 5218 2. 524.9
	1. 5214 2. 517.8		1. 5219 2. 526.9
	1. 5215 2. 518.9		1. 5220 2. 526.9

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5221 2. 528.8		1. 5226 2. 538.8
	1. 5222 2. 528.8		1. 5227 2. 538.9
	1. 5223 2. 533.3		1. 5228 2. 538.9
	1. 5224 2. 533.3		1. 5229 2. 538.9
	1. 5225 2. 537.9		1. 5230 2. 540.9

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5231 2. 542.9		1. 5236 2. 566.8
	1. 5232 2. 544.9		1. 5237 2. 567.7
	1. 5233 2. 548.9		1. 5238 2. 567.7
	1. 5234 2. 552.9		1. 5239 2. 574.9
	1. 5235 2. 566.8		1. 5240 2. 581

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5241 2. 533.3		1. 5246 2. 548.9
	1. 5242 2. 537.9		1. 5247 2. 554.9
	1. 5243 2. 542.8		1. 5248 2. 555.9
	1. 5244 2. 544.9		1. 5249 2. 555.9
	1. 5245 2. 544.9		1. 5250 2. 574.9

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5251 2. 579.9		1. 5256 2. 501.8
	1. 5252 2. 579.9		1. 5257 2. 514.8
	1. 5253 2. 581		1. 5258 2. 518.9
	1. 5254 2. 588.9		1. 5259 2. 530.9
	1. 5255 2. 590.9		1. 5260 2. 530.9

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5261 2. 538.9		1. 5266 2. 556.9
	1. 5262 2. 542.9		1. 5267 2. 556.9
	1. 5263 2. 547.3		1. 5268 2. 537.9
	1. 5264 2. 551.9		1. 5269 2. 566.9
	1. 5265 2. 552.9		1. 5270 2. 581

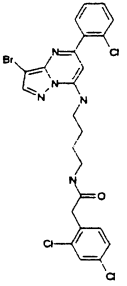
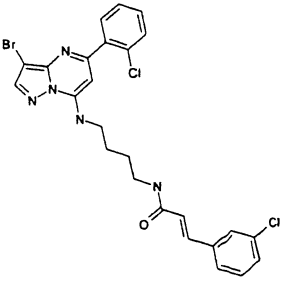
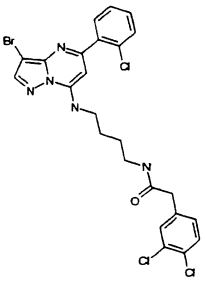
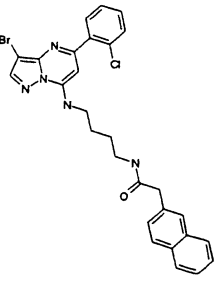
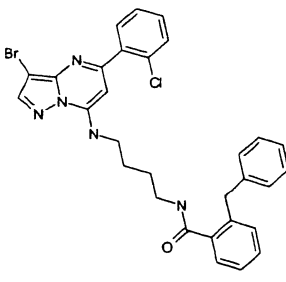
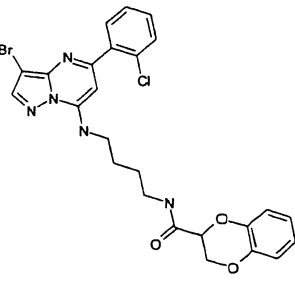
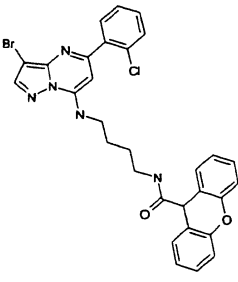
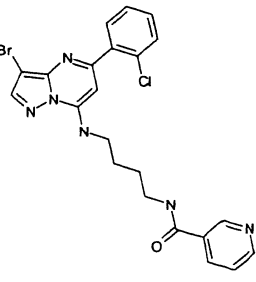
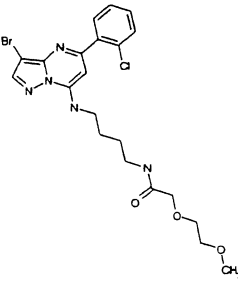
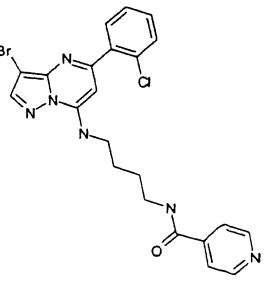
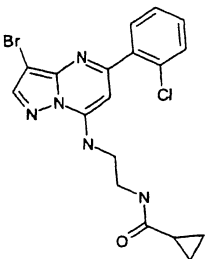
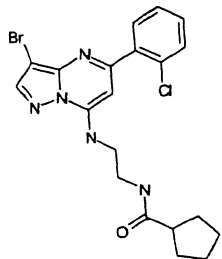
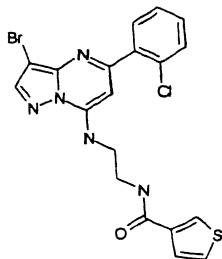
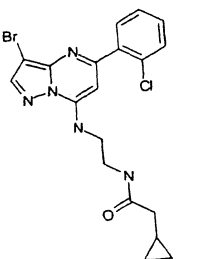
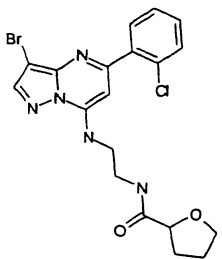
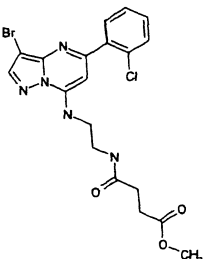
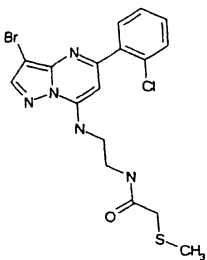
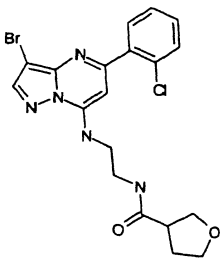
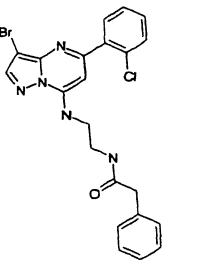
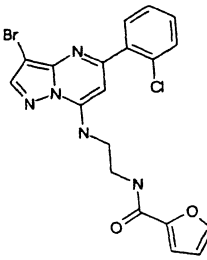
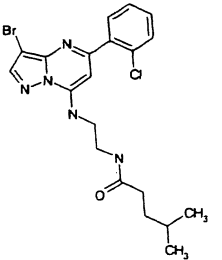
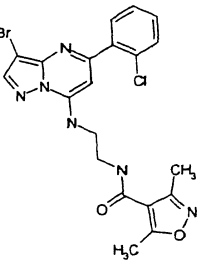
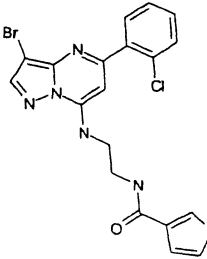
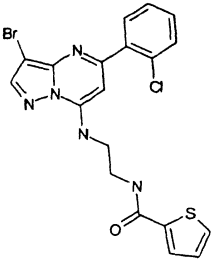
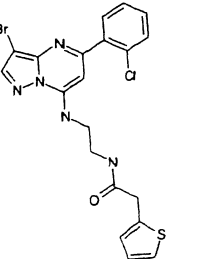
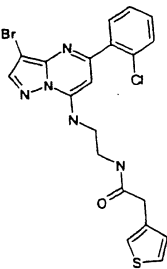
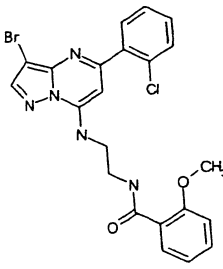
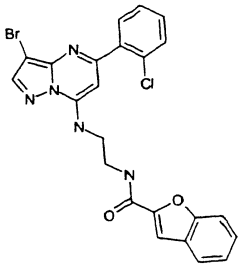
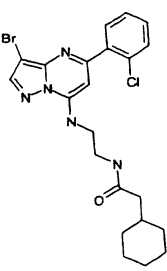
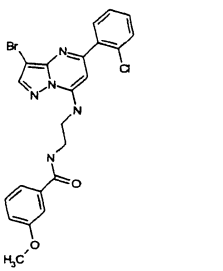
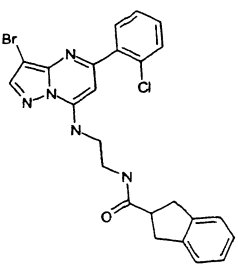
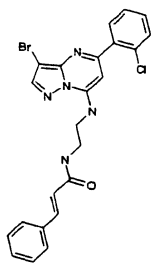
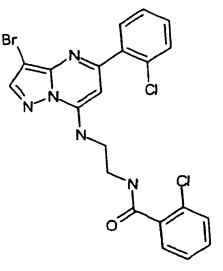
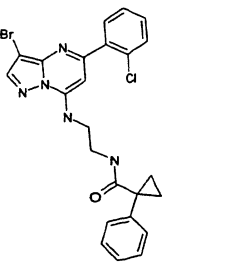
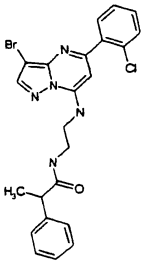
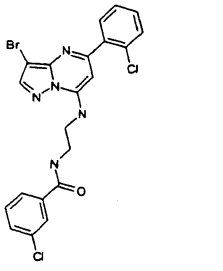
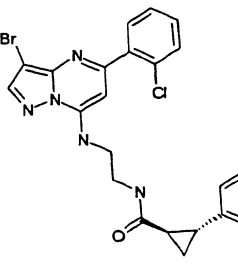
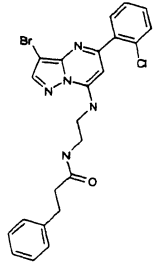
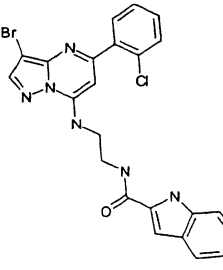
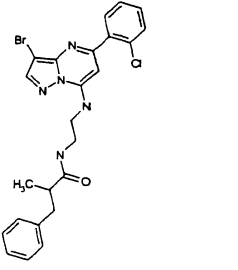
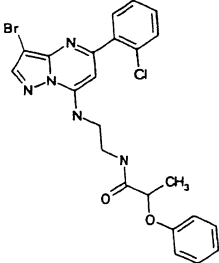
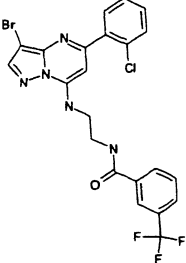
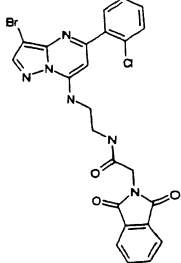
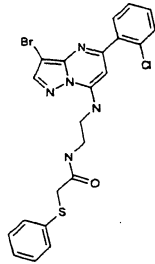
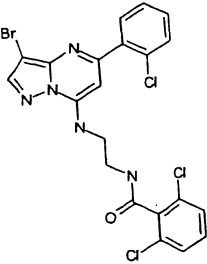
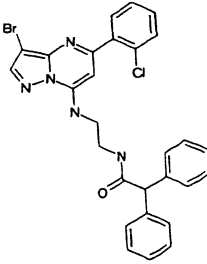
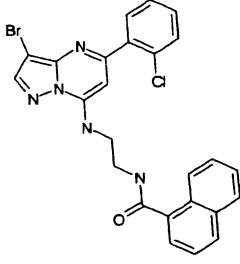
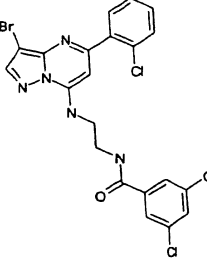
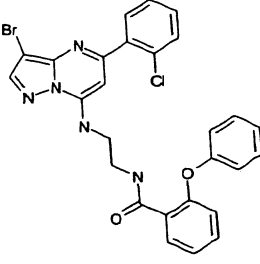
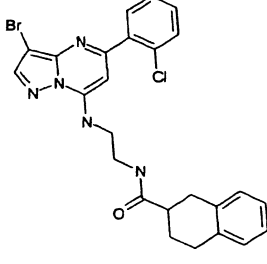
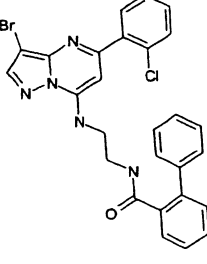
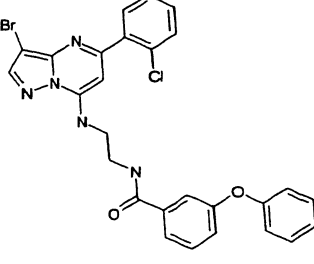
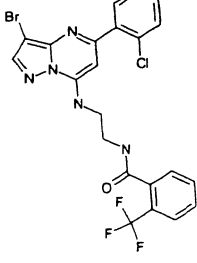
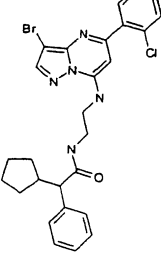
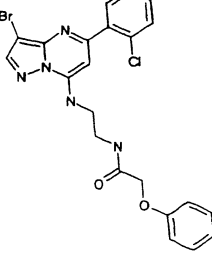
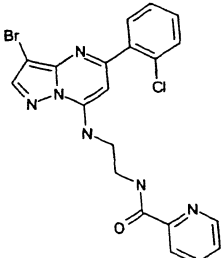
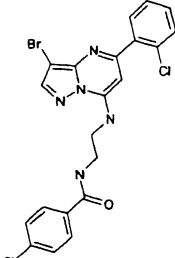
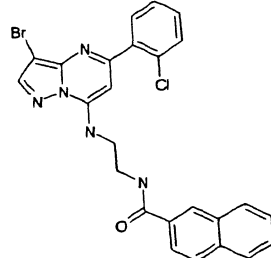
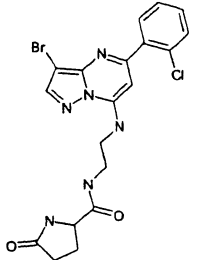
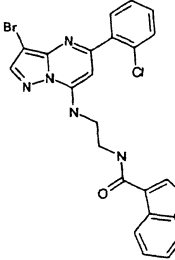
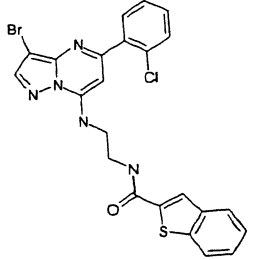
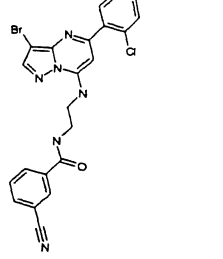
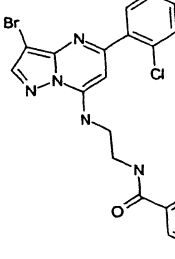
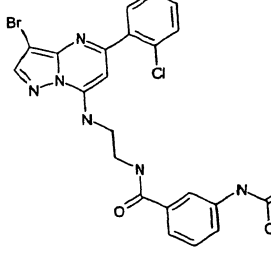
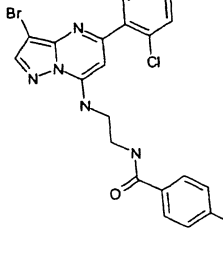
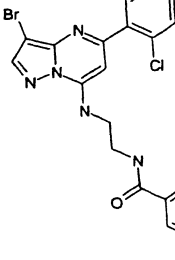
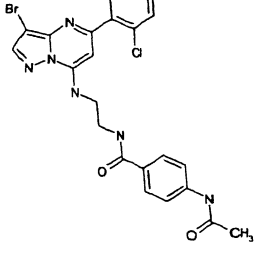
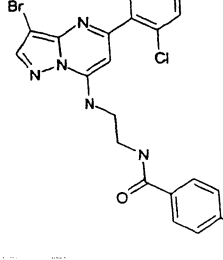
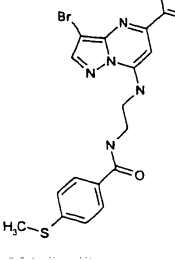
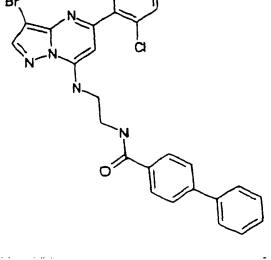
產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5271 2. 581.7		1. 5276 2. 559.3
	1. 5272 2. 581.7		1. 5277 2. 562.9
	1. 5273 2. 588.9		1. 5278 2. 556.9
	1. 5274 2. 602.9		1. 5279 2. 499.8
	1. 5275 2. 510.8		1. 5280 2. 499.8

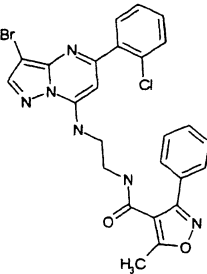
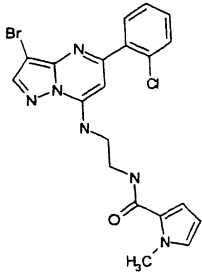
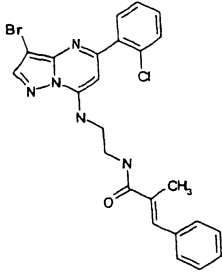
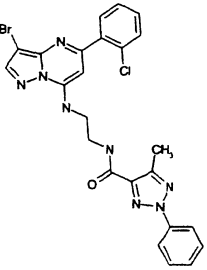
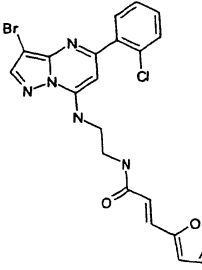
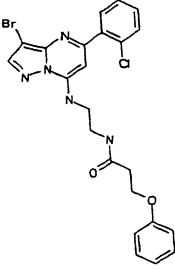
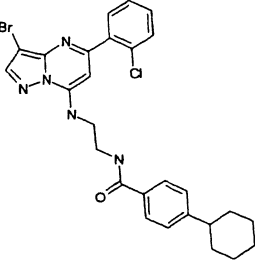
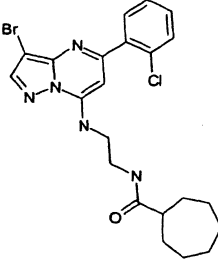
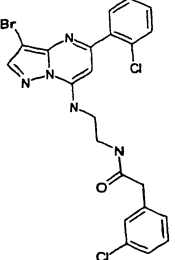
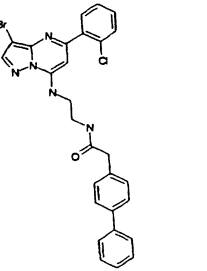
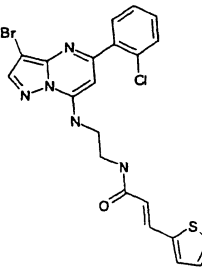
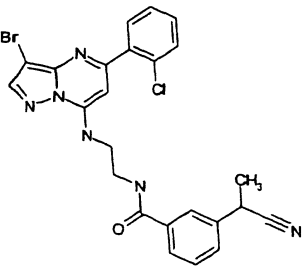
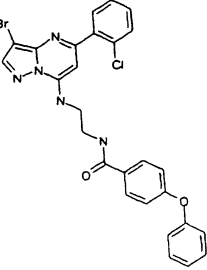
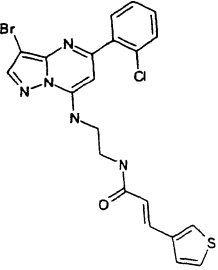
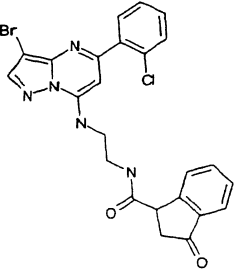
表53

產物	1.實例2. m/z	產物	1.實例2. m/z	產物	1.實例2. m/z
	1. 5301 2. 434.7		1. 5306 2. 462.8		1. 5311 2. 476.8
	1. 5302 2. 448.8		1. 5307 2. 464.8		1. 5312 2. 480.8
	1. 5303 2. 454.8		1. 5308 2. 464.8		1. 5313 2. 484.8
	1. 5304 2. 460.7		1. 5309 2. 464.8		1. 5314 2. 489.8
	1. 5305 2. 460.7		1. 5310 2. 476.8		1. 5315 2. 490.8

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5316 2. 490.8		1. 5321 2. 500.8		1. 5326 2. 510.8
	1. 5317 2. 490.8		1. 5322 2. 500.8		1. 5327 2. 510.8
	1. 5318 2. 496.8		1. 5323 2. 505.2		1. 5328 2. 510.8
	1. 5319 2. 498.8		1. 5324 2. 505.2		1. 5329 2. 510.8
	1. 5320 2. 498.8		1. 5325 2. 509.8		1. 5330 2. 512.8

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5331 2. 514.8		1. 5336 2. 538.8		1. 5341 2. 553.8
	1. 5332 2. 516.9		1. 5337 2. 539.6		1. 5342 2. 560.9
	1. 5333 2. 520.8		1. 5338 2. 539.6		1. 5343 2. 562.9
	1. 5334 2. 524.9		1. 5339 2. 546.9		1. 5344 2. 562.9
	1. 5335 2. 538.8		1. 5340 2. 552.9		1. 5345 2. 500.8

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5346 2. 471.7		1. 5351 2. 505.2		1. 5356 2. 520.8
	1. 5347 2. 477.8		1. 5352 2. 509.8		1. 5353 2. 526.8
	1. 5348 2. 495.8		1. 5353 2. 514.8		1. 5358 2. 527.8
	1. 5349 2. 495.8		1. 5355 2. 516.9		1. 5359 2. 527.8
	1. 5350 2. 500.8		1. 5356 2. 516.9		1. 5360 2. 546.9

產物	1. 實例2. m/z	產物	1. 實例2. m/z	產物	1. 實例2. m/z
	1. 5361 2. 551.8		1. 5366 2. 473.8		1. 5371 2. 510.8
	1. 5362 2. 551.8		1. 5367 2. 486.8		1. 5372 2. 514.8
	1. 5363 2. 552.9		1. 5368 2. 490.8		1. 5373 2. 519.2
	1. 5364 2. 560.9		1. 5369 2. 502.8		1. 5374 2. 523.8
	1. 5365 2. 562.9		1. 5370 2. 502.8		1. 5375 2. 524.8

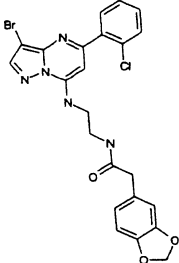
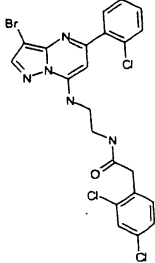
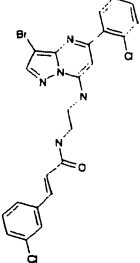
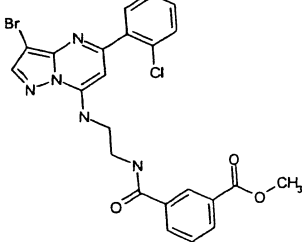
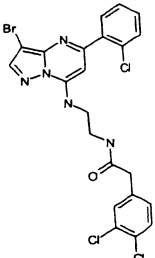
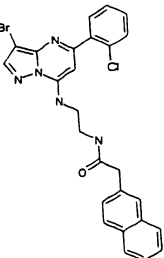
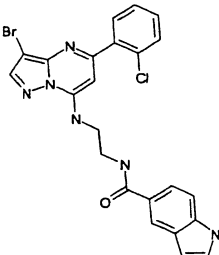
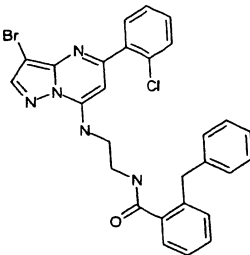
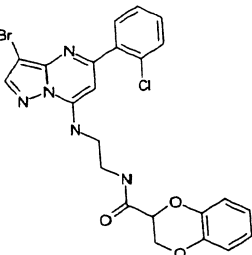
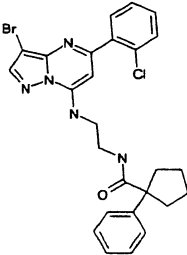
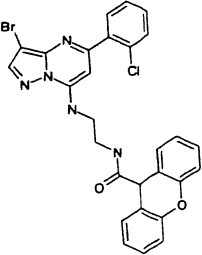
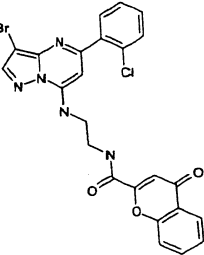
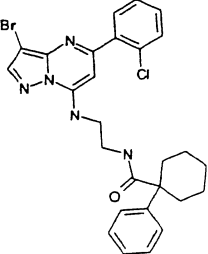
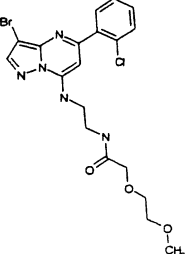
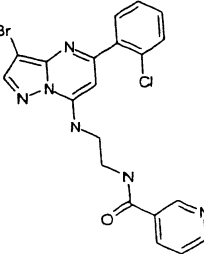
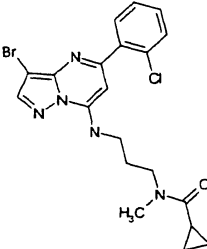
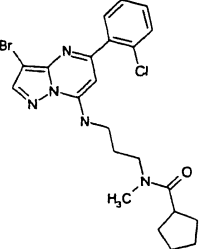
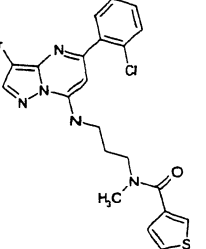
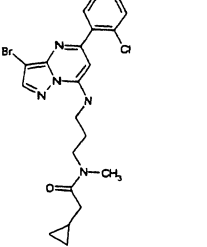
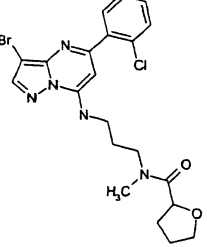
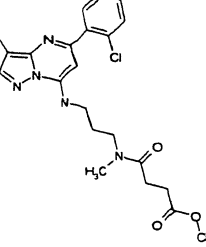
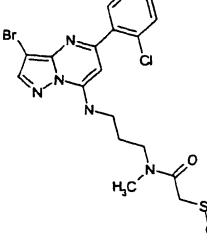
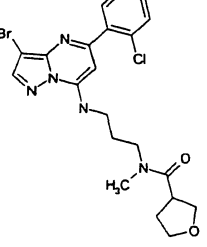
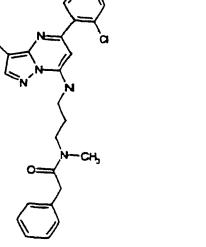
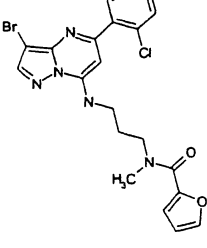
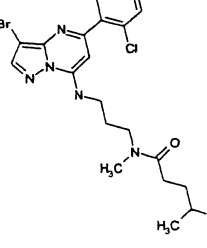
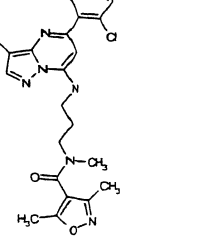
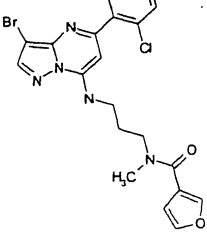
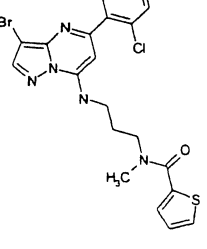
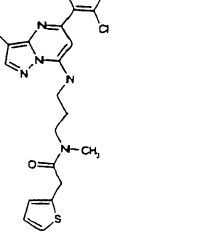
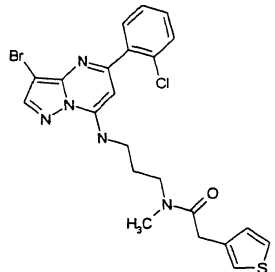
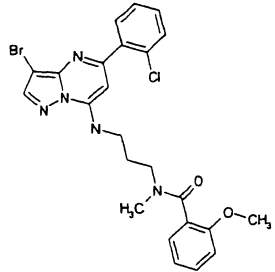
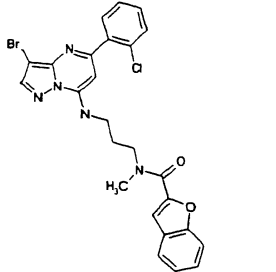
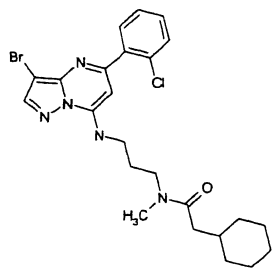
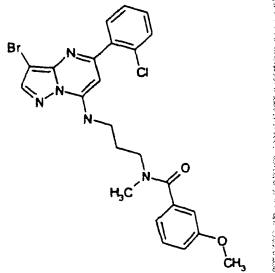
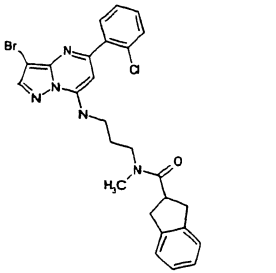
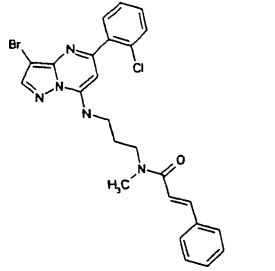
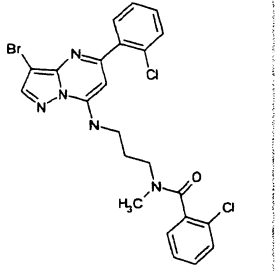
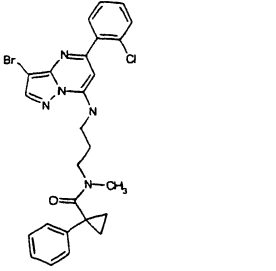
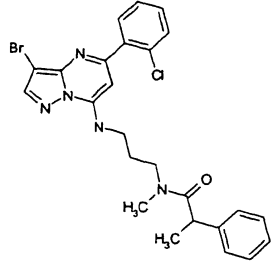
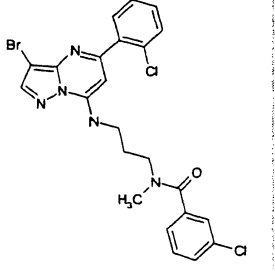
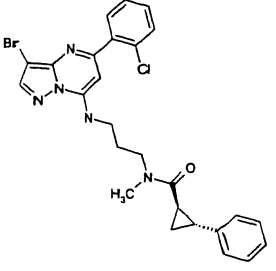
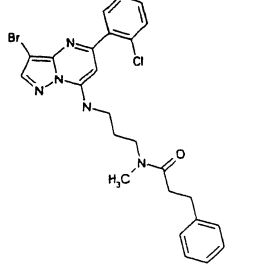
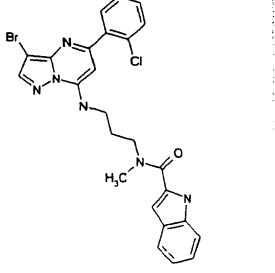
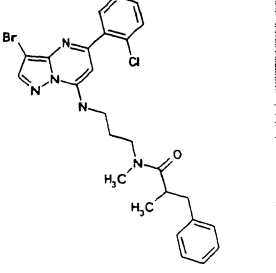
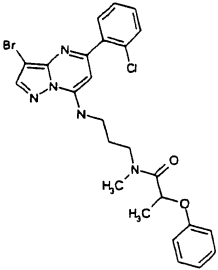
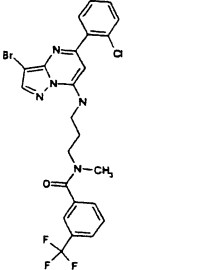
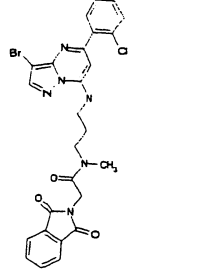
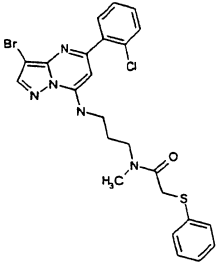
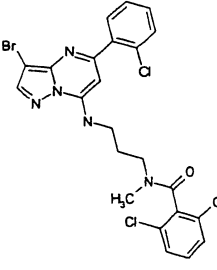
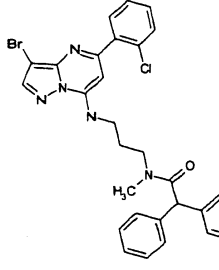
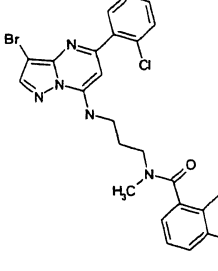
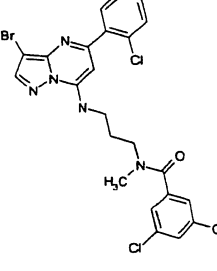
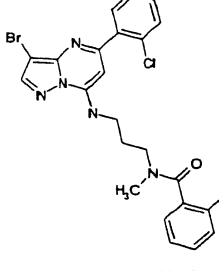
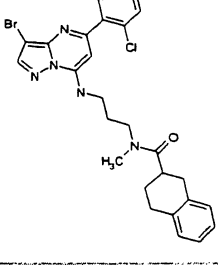
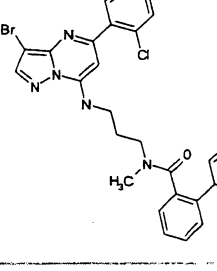
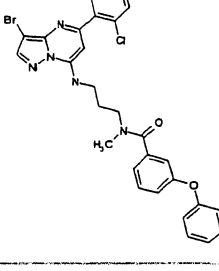
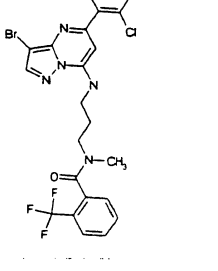
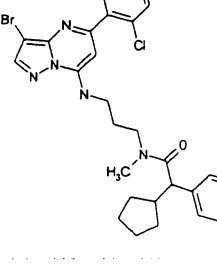
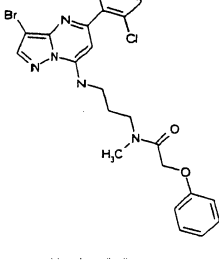
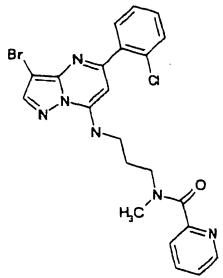
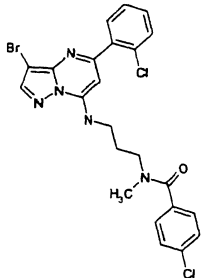
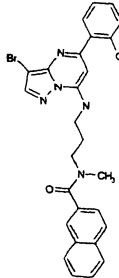
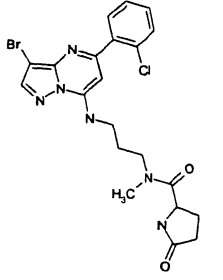
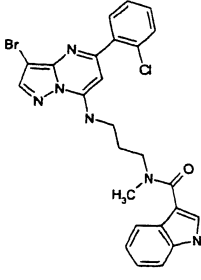
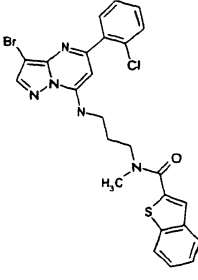
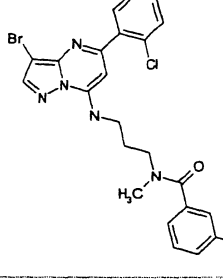
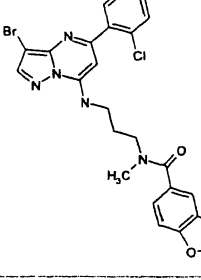
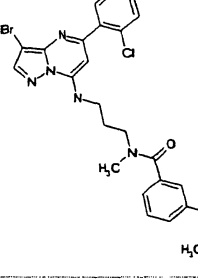
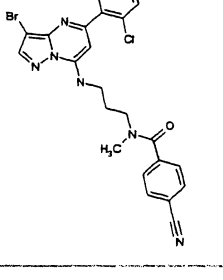
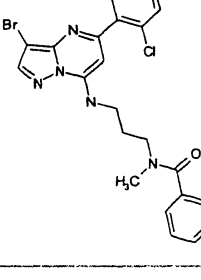
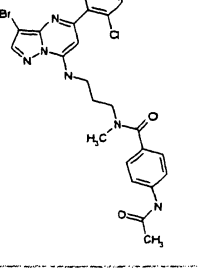
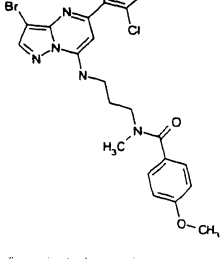
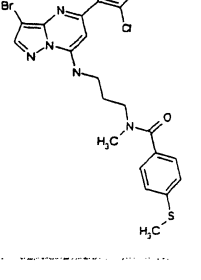
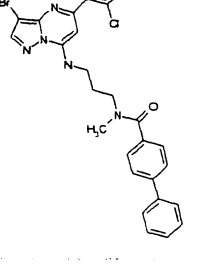
產物	1. 實例2. m/z	產物	1. 實例2. m/z	產物	1. 實例2. m/z
	1. 5376 2. 528.8		1. 5381 2. 553.7		1. 5386 2. 531.2
	1. 5377 2. 528.8		1. 5382 2. 553.7		1. 5387 2. 534.8
	1. 5378 2. 509.8		1. 5383 2. 560.9		1. 5388 2. 528.8
	1. 5379 2. 538.9		1. 5384 2. 574.9		1. 5389 2. 538.8
	1. 5380 2. 552.9		1. 5385 2. 482.8		1. 5390 2. 471.7

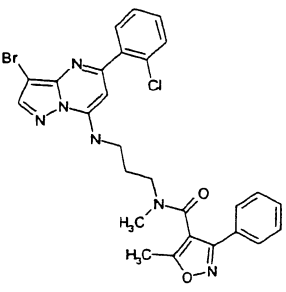
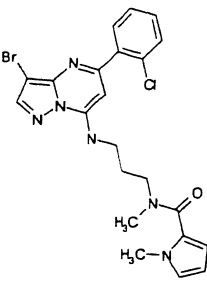
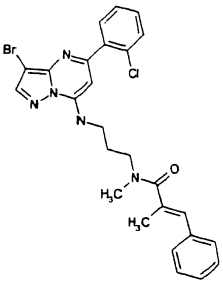
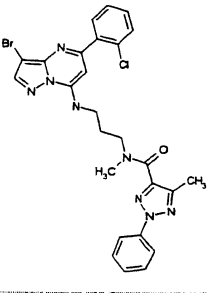
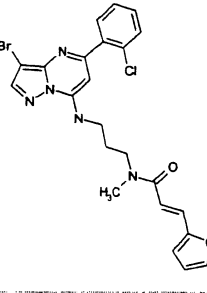
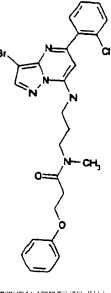
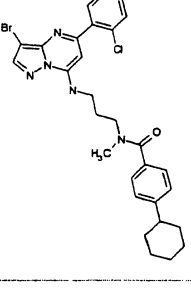
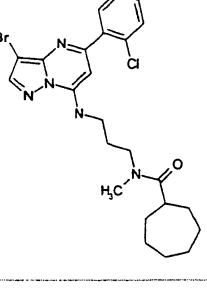
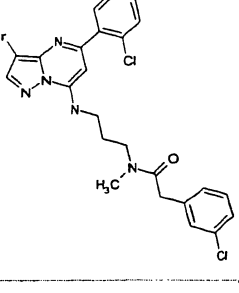
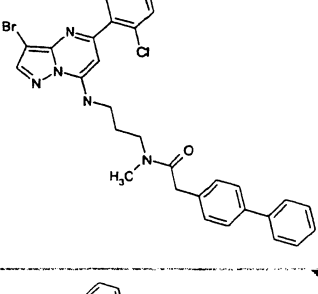
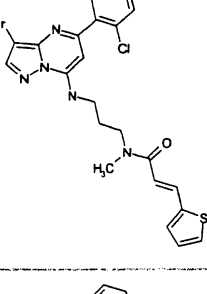
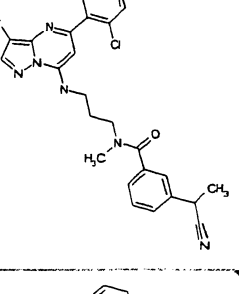
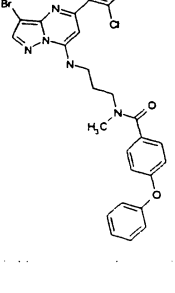
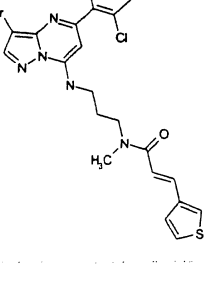
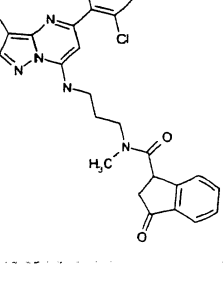
表54

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5401 2. 463.3		1. 5406 2. 491.3		1. 5411 2. 505.3
	1. 5402 2. 477.3		1. 5407 2. 493.3		1. 5412 2. 509.3
	1. 5403 2. 483.3		1. 5408 2. 493.3		1. 5413 2. 513.3
	1. 5404 2. 489.3		1. 5409 2. 493.3		1. 5414 2. 518.3
	1. 5405 2. 489.3		1. 5410 2. 505.3		1. 5415 2. 519.3

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5416 2. 519.3		1. 5121 2. 529.3		1. 5426 2. 539.3
	1. 5417 2. 519.3		1. 5422 2. 529.3		1. 5427 2. 539.3
	1. 5418 2. 525.3		1. 5423 2. 533.3		1. 5428 2. 539.3
	1. 5419 2. 527.3		1. 5424 2. 533.3		1. 5429 2. 539.3
	1. 5420 2. 527.3		1. 5425 2. 538.3		1. 5430 2. 541.3

產物	1.實例2. m/z	產物	1.實例2. m/z	產物	1.實例2. m/z
	1. 5431 2. 543.3		1. 5436 2. 567.3		1. 5441 2. 582.3
	1. 5432 2. 545.3		1. 5437 2. 567.3		1. 5447 2. 589.3
	1. 5433 2. 549.3		1. 5438 2. 567.3		1. 5443 2. 591.3
	1. 5434 2. 553.3		1. 5439 2. 575.3		1. 5444 2. 591.3
	1. 5435 2. 567.3		1. 5440 2. 581.3		1. 5445 2. 529.3

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5446 2. 500.3		1. 5451 2. 533.3		1. 5456 2. 549.3
	1. 5447 2. 830.5		1. 54525 2. 719.4		1. 5457 2. 555.3
	1. 5448 2. 524.3		1. 5453 2. 543.3		1. 5458 2. 556.3
	1. 5449 2. 524.3		1. 5454 2. 545.3		1. 5459 2. 556.3
	1. 5450 2. 529.3		1. 5455 2. 545.3		1. 5460 2. 575.3

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5461 2. 580.3		1. 5466 2. 502.3		1. 5471 2. 539.3
	1. 5462 2. 580.3		1. 5467 2. 515.3		1. 5472 2. 543.3
	1. 5463 2. 581.3		1. 5468 2. 519.3		1. 5473 2. 547.3
	1. 5464 2. 589.3		1. 5469 2. 531.3		1. 5474 2. 552.3
	1. 5465 2. 591.3		1. 5470 2. 531.3		1. 5475 2. 553.3

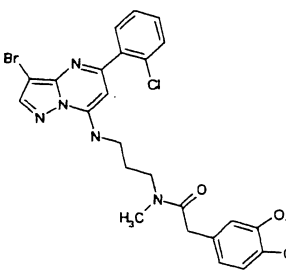
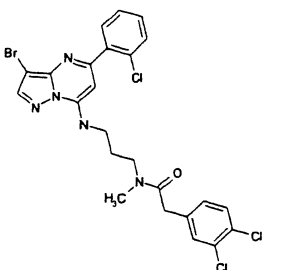
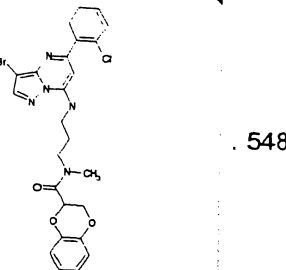
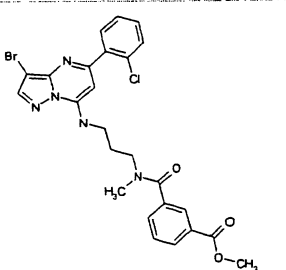
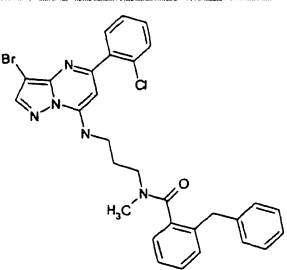
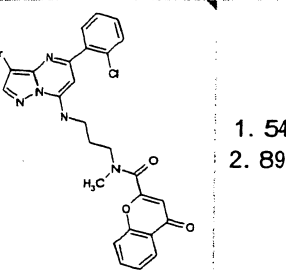
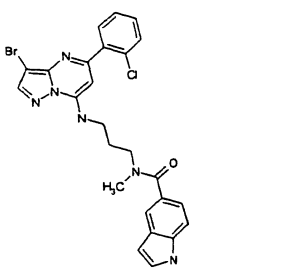
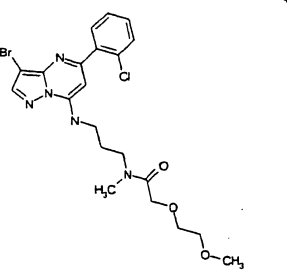
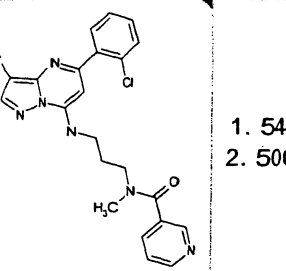
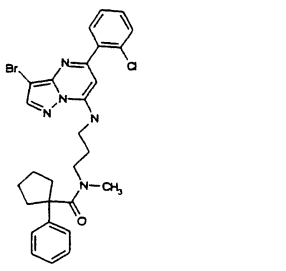
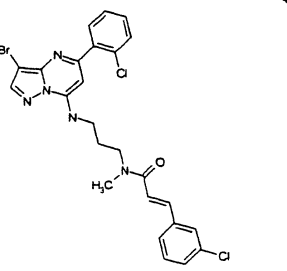
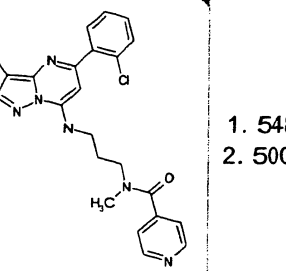
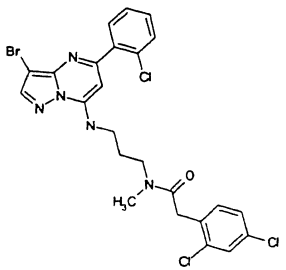
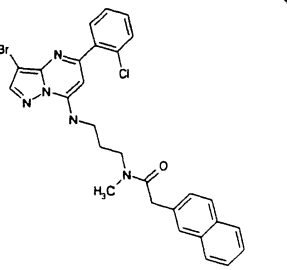
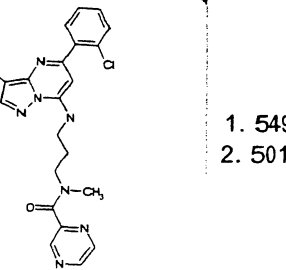
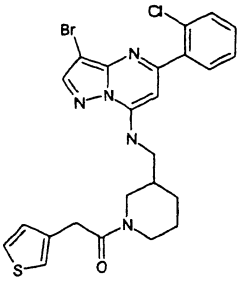
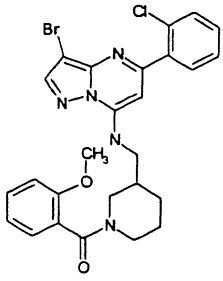
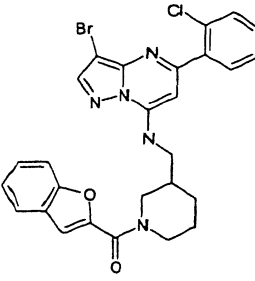
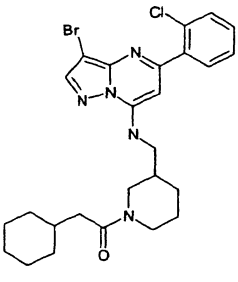
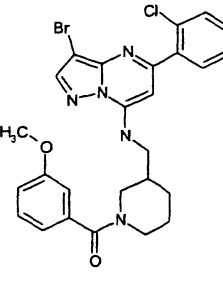
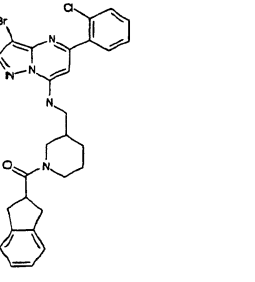
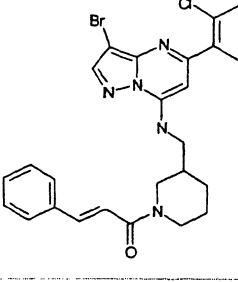
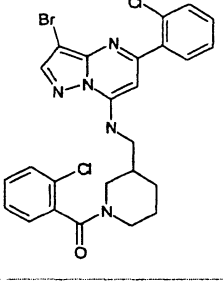
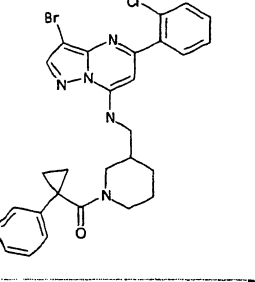
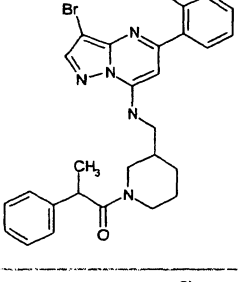
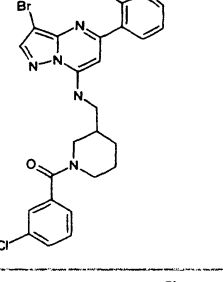
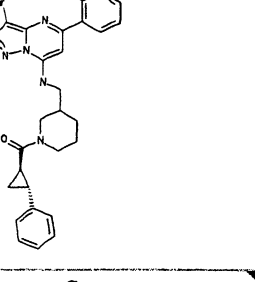
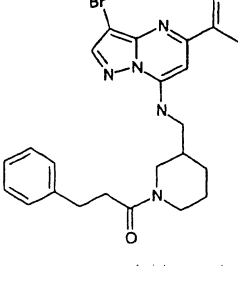
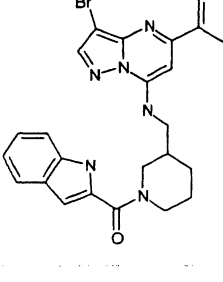
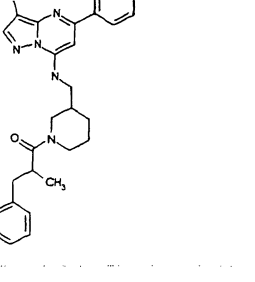
產物	1. 實例2. m/z	產物	1. 實例2. m/z	產物	1. 實例2. m/z
	1. 5476 2. 557.3		1. 5481 2. 581.3		1. 5486 2. 581.3
	1. 5477 2. 557.3		1. 5482 2. 589.3		1. 5487 2. 891.5
	1. 5478 2. 538.3		1. 5483 2. 511.3		1. 5488 2. 500.3
	1. 5479 2. 567.3		1. 5484 2. 559.3		1. 5489 2. 500.3
	1. 5480 2. 581.3		1. 5485 2. 563.3		1. 5490 2. 501.3

表55

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5501 2. 488.81		1. 5506 2. 516.87		1. 5511 2. 530.87
	1. 5502 2. 502.84		1. 5507 2. 518.84		1. 5512 2. 534.84
	1. 5503 2. 508.87		1. 5508 2. 518.84		1. 5513 2. 538.87
	1. 5504 2. 514.81		1. 5509 2. 518.88		1. 5514 2. 543.85
	1. 5505 2. 514.81		1. 5510 2. 530.87		1. 5515 2. 544.9

產物	1. 實例2. m/z	產物	1. 實例2. m/z	產物	1. 實例2. m/z
	1. 5516 2. 544.9		1. 5521 2. 554.87		1. 5526 2. 564.87
	1. 5517 2. 544.92		1. 5522 2. 554.87		1. 5527 2. 564.91
	1. 5518 2. 550.89		1. 5523 2. 559.29		1. 5528 2. 564.91
	1. 5519 2. 552.9		1. 5524 2. 559.29		1. 5529 2. 564.91
	1. 5520 2. 552.9		1. 5525 2. 563.88		1. 5530 2. 566.93

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5531 2. 568.9		1. 5536 2. 600.95		1. 5541
	1. 5532 2. 574.91		1. 5537 2. 606.99		1. 5542 2. 525.8
	1. 5533 2. 578.94		1. 5538 2. 614.97		1. 5543 2. 581.9
	1. 5534 2. 592.85		1. 5539 2. 616.95		1. 5544 2. 581.9
	1. 5535 2. 592.85		1. 5540 2. 616.95		1. 5545 2. 605.92

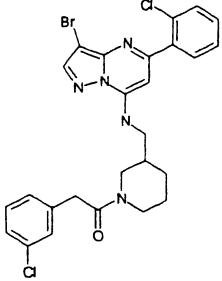
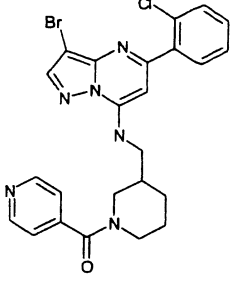
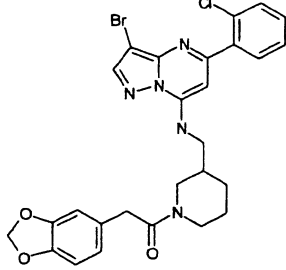
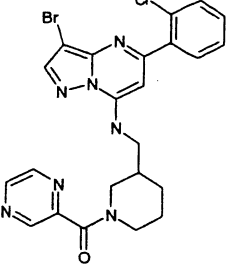
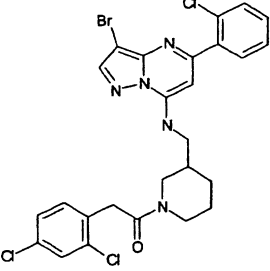
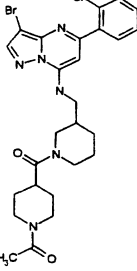
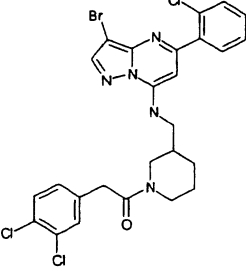
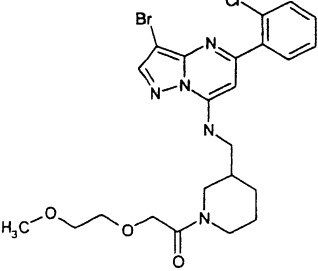
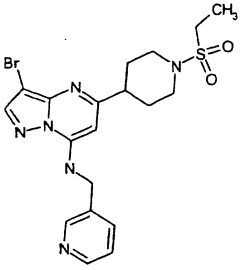
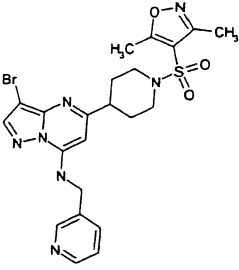
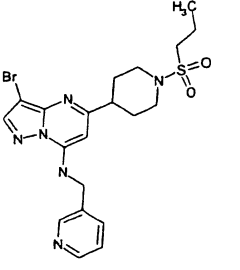
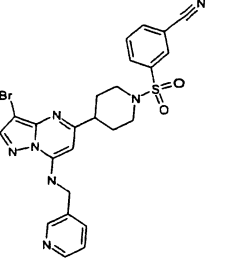
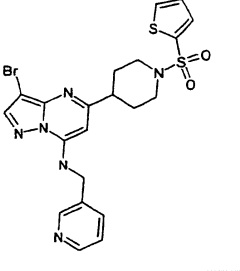
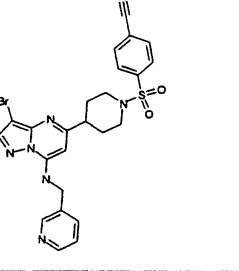
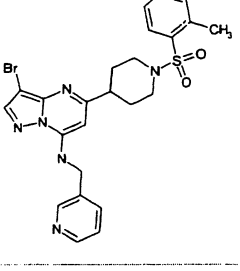
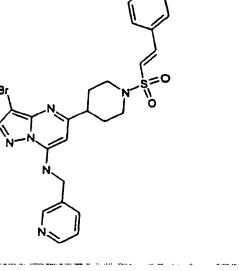
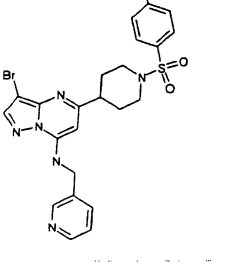
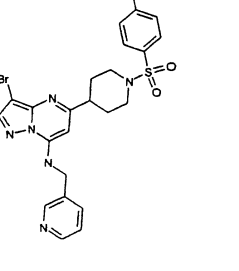
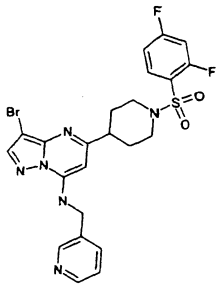
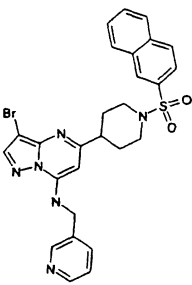
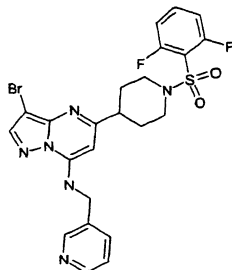
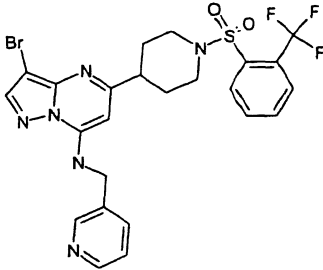
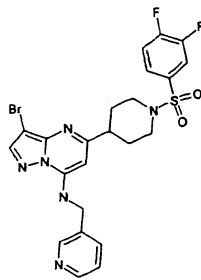
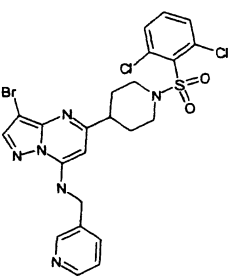
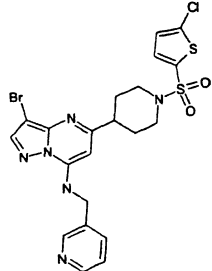
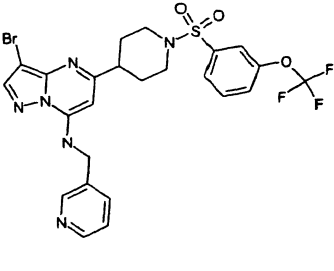
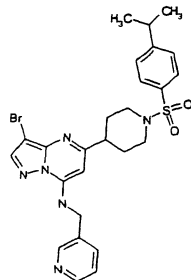
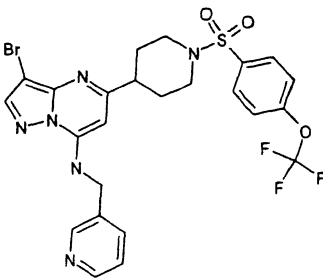
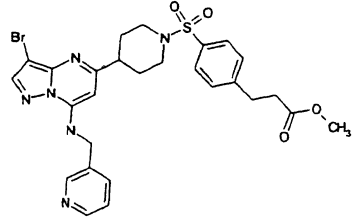
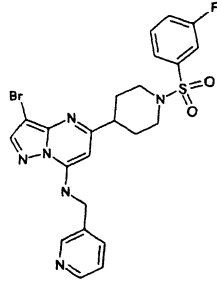
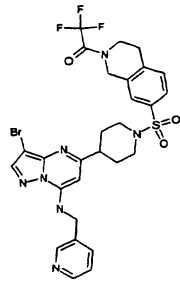
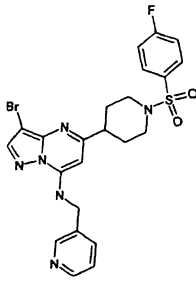
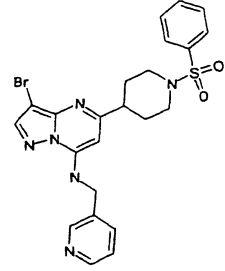
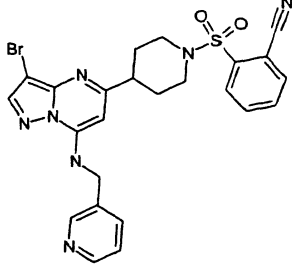
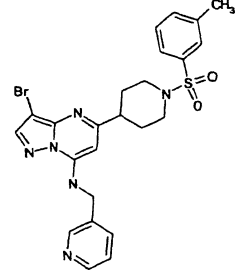
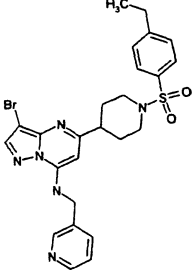
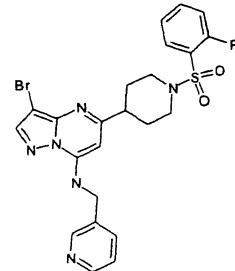
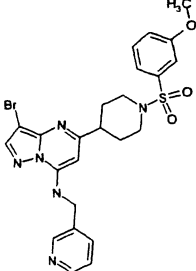
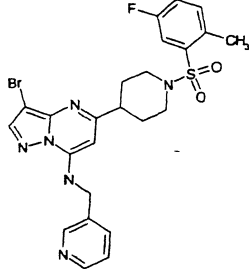
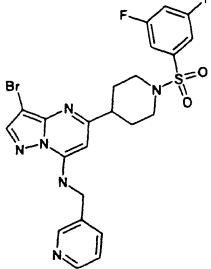
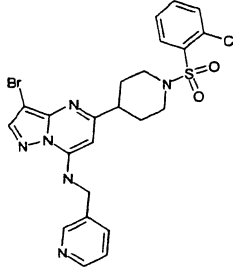
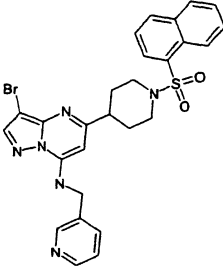
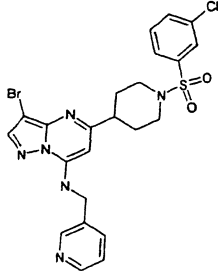
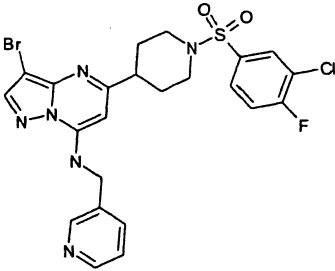
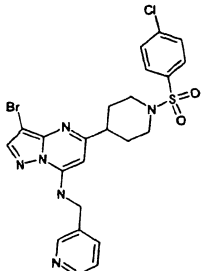
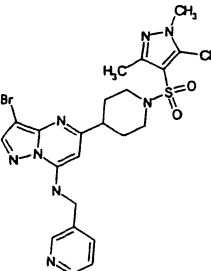
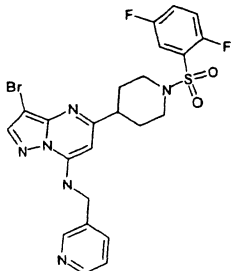
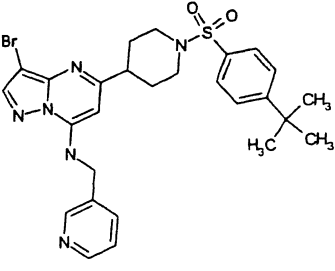
產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5546 2. 573.32		1. 5551 2. 525.83
	1. 5547 2. 582.88		1. 5552 2. 526.82
	1. 5548 2. 607.76		1. 5553 2. 573.92
	1. 5549 2. 607.76		
	1. 5550 2. 536.86		

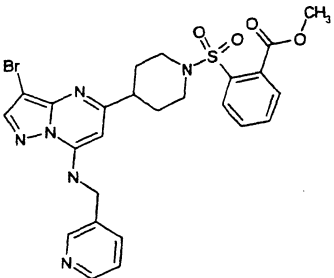
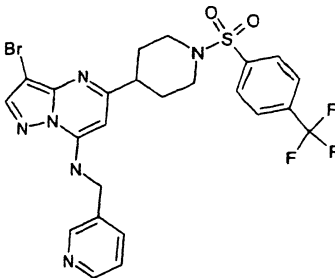
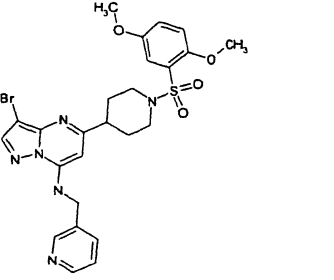
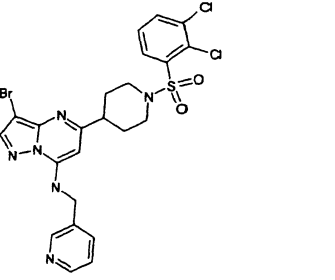
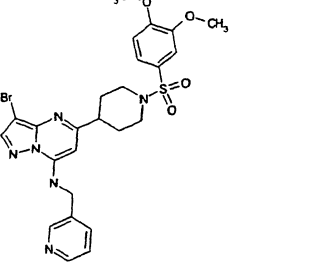
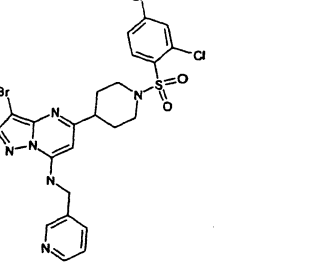
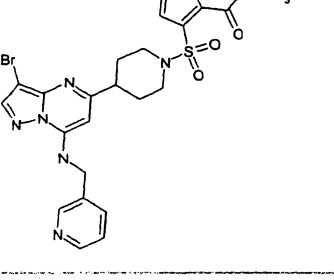
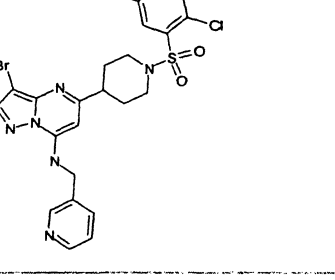
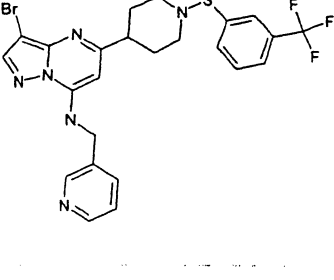
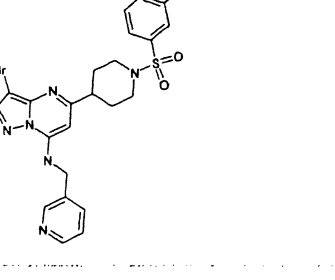
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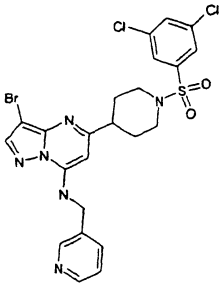
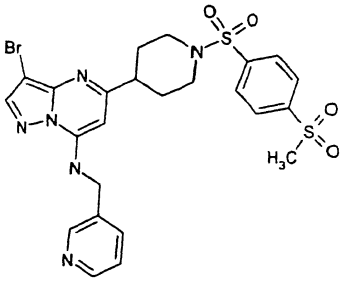
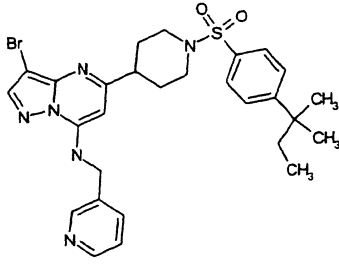
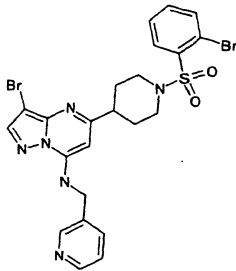
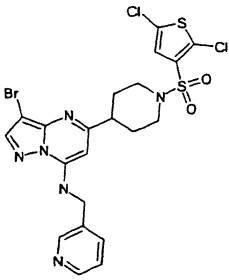
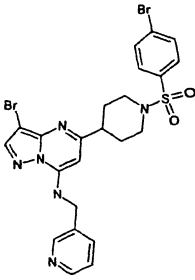
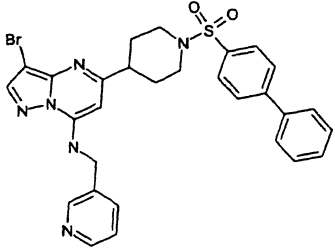
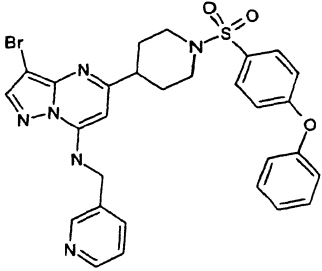
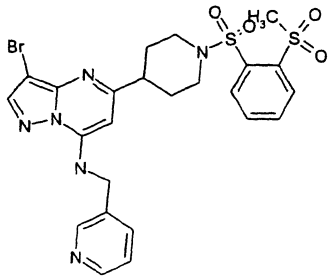
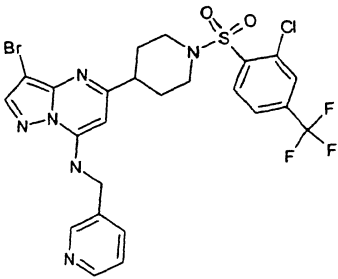
產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5601 2. 481.26		1. 5606 2. 548.3
	1. 5602 2. 495.27		1. 5607 2. 554.3
	1. 5603 2. 535.29		1. 5608 2. 554.3
	1. 5604 2. 543.3		1. 5609 2. 555.31
	1. 5605 2. 543.3		1. 5610 2. 559.31

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5611 2. 565.31		1. 5616 2. 579.32
	1. 5612 2. 565.31		1. 5617
	1. 5613 2. 565.31		1. 5618
	1. 5614 2. 569.31		1. 5619
	1. 5615 2. 571.31		1. 5620

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5621 2. 615.34		1. 5626 2. 547.3
	2. 5622 2. 680.37		1. 5627 2. 547.3
	1. 5623 2. 529.29		1. 5628 2. 554.3
	1. 5624 2. 543.3		1. 5629 2. 555.31
	1. 5625 2. 547.3		1. 5630 2. 559.31

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5631 2. 561.31		1. 5636 2. 565.31
	1. 5632 2. 563.31		1. 5637 2. 579.32
	1. 5633 2. 563.31		1. 5638 2. 581.32
	1. 5634 2. 563.31		1. 5639 2. 581.32
	1. 5635 2. 563.31		1. 5640 2. 585.32

產物	1. 實例2. m/z	產物	1. 實例2. m/z
	1. 5641 2. 587.32		1. 5646
	1. 5642 2. 589.32		1. 5647 2. 597.33
	1. 5643 2. 589.32		1. 5648 2. 597.33
	1. 5644 2. 593.33		1. 5649 2. 597.33
	1. 5645 2. 597.33		1. 5650 2. 597.33

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5651 2. 597.33		1. 5656 2. 607.33
	1. 5652 2. 599.33		1. 5657 2. 607.33
	1. 5653 2. 603.33		1. 5658 2. 607.33
	1. 5654 2. 605.33		1. 5659 2. 621.34
	1. 5655 2. 607.33		1. 5660 2. 631.35

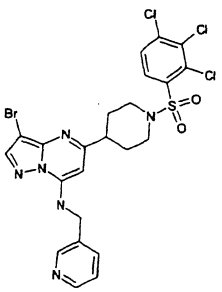
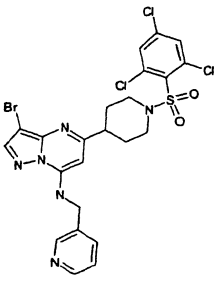
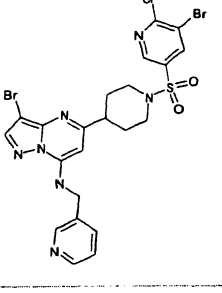
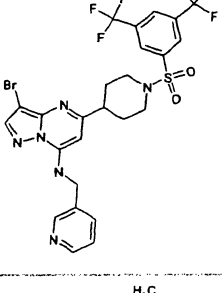
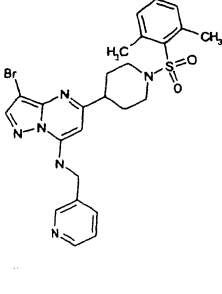
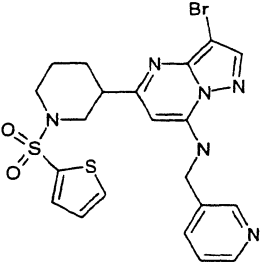
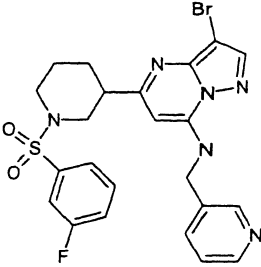
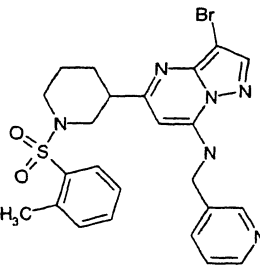
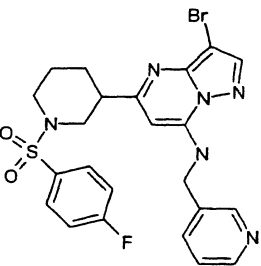
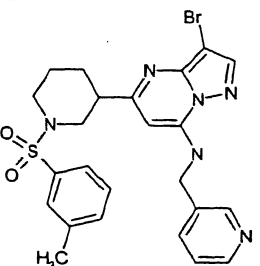
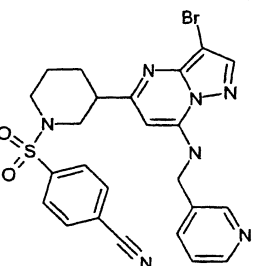
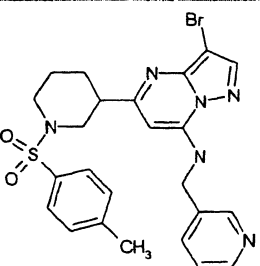
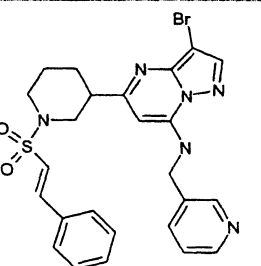
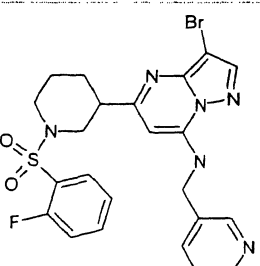
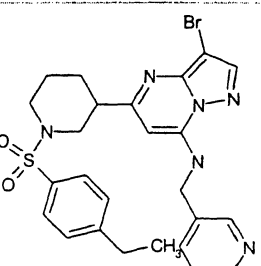
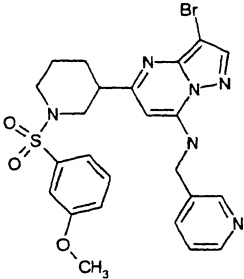
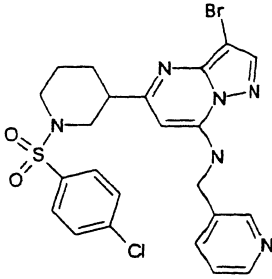
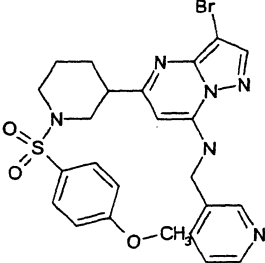
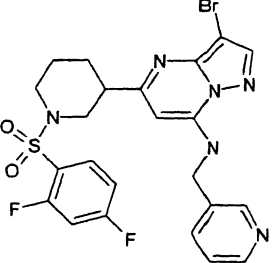
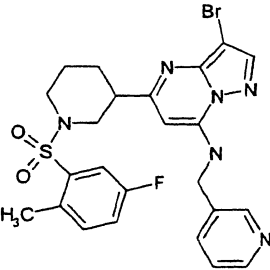
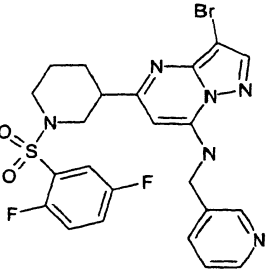
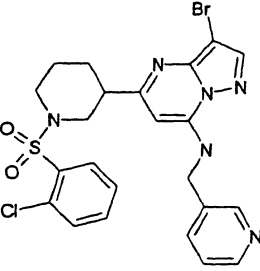
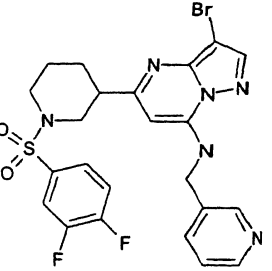
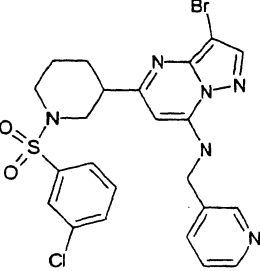
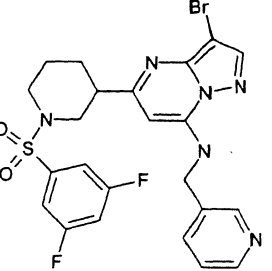
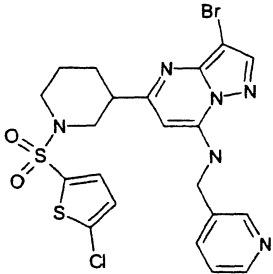
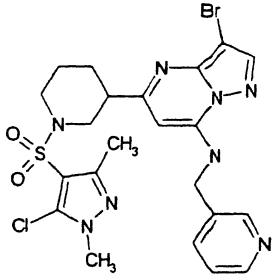
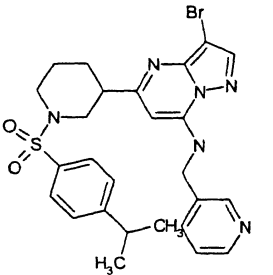
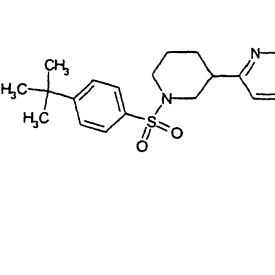
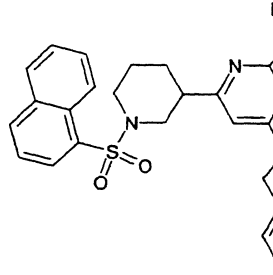
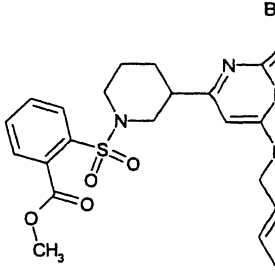
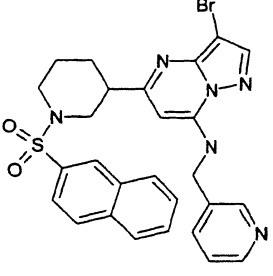
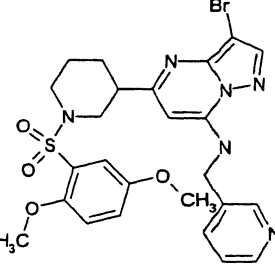
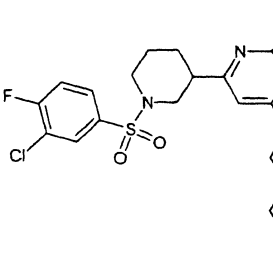
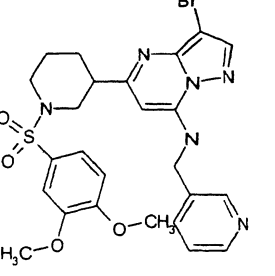
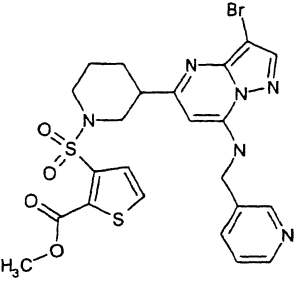
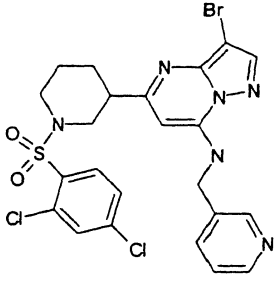
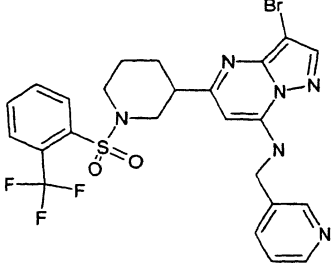
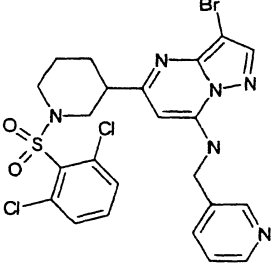
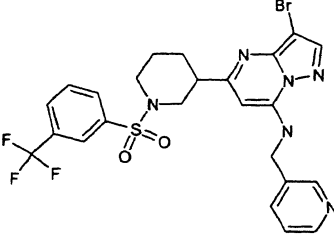
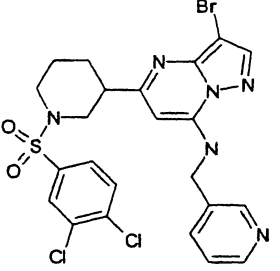
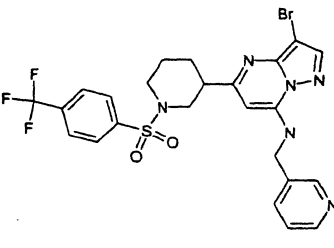
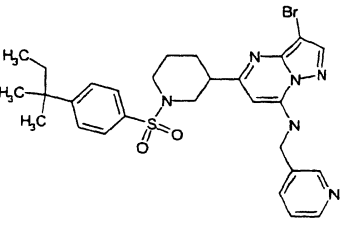
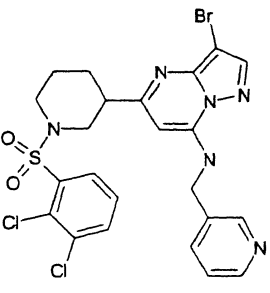
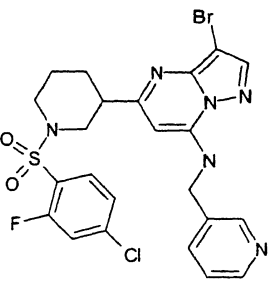
產物	1. 實例 2. m/z
	1. 5661 2. 631.35
	1. 5662 2. 631.35
	1. 5663 2. 642.35
	1. 5664 2. 665.37
	1. 5665 2. 571.31

表57

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5701 2. 535.29		1. 5706 2. 547.3
	1. 5702 2. 540.3		1. 5707 2. 547.3
	1. 5703 2. 543.3		1. 5708 2. 554.3
	1. 5704 2. 543.3		1. 5709 2. 555.31
	1. 5705 2. 547.3		1. 5710 2. 555.31

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5711 2. 559.31		1. 5716 2. 563.31
	1. 5712 2. 559.31		1. 5717 2. 565.31
	1. 5713 2. 561.31		1. 5718 2. 565.31
	1. 5714 2. 562.31		1. 5719 2. 565.31
	1. 5715 2. 563.31		1. 5720 2. 565.31

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5721 2. 569.31		1. 5726 2. 581.32
	1. 5722 2. 571.31		1. 5727 2. 585.32
	1. 5723 2. 579.32		1. 5728 2. 587.32
	1. 5724 2. 579.32		1. 5729 2. 589.32
	1. 5725 2. 581.32		1. 5730 2. 589.32

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5731 2. 591.33		1. 5736 2. 597.33
	1. 5732 2. 597.33		1. 5737 2. 597.33
	1. 5733 2. 595.33		1. 5738 2. 596.33
	1. 5734 2. 597.33		1. 5739 2. 597.33
	1. 5735 2. 597.33		1. 5740 2. 581.32

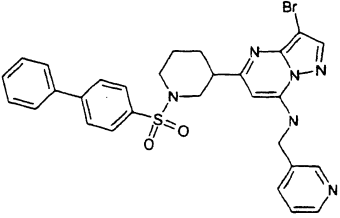
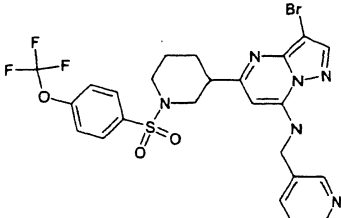
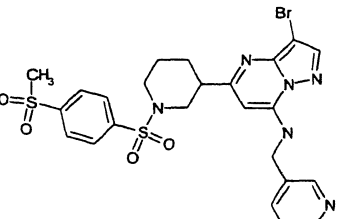
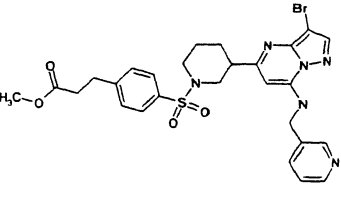
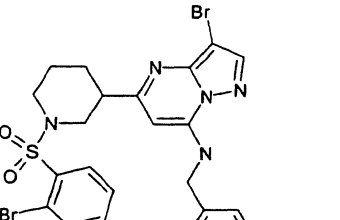
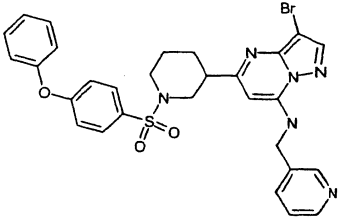
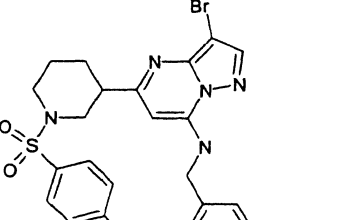
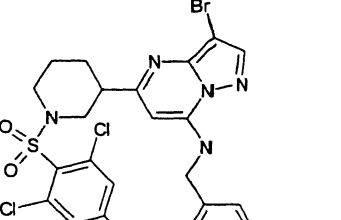
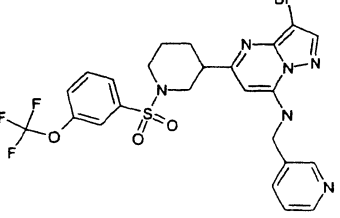
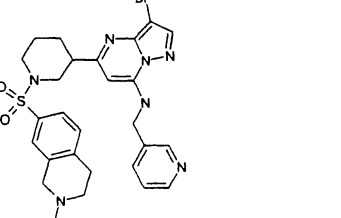
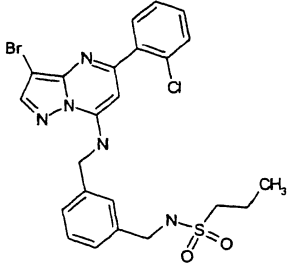
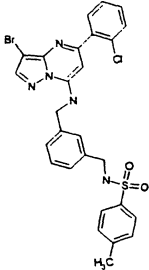
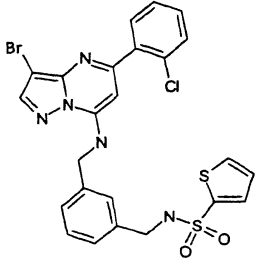
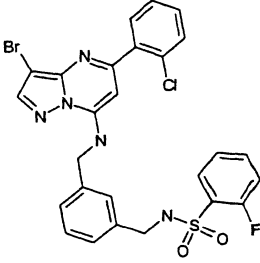
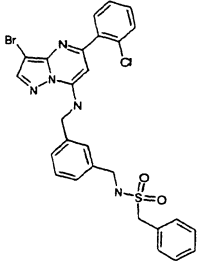
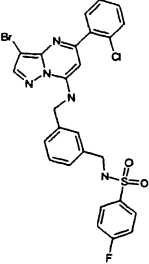
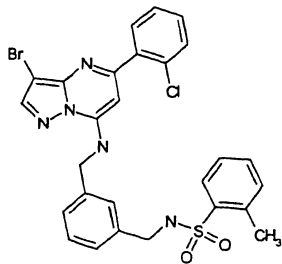
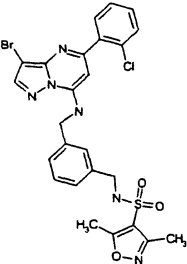
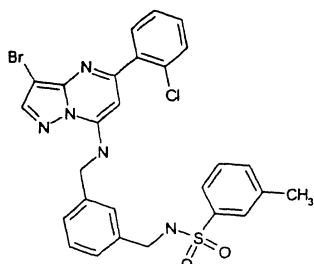
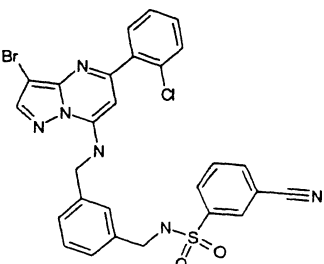
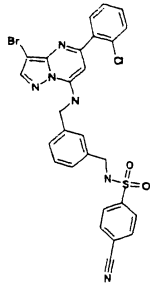
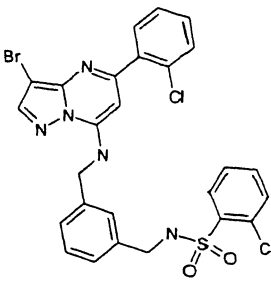
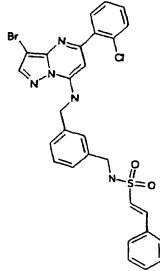
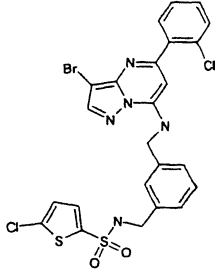
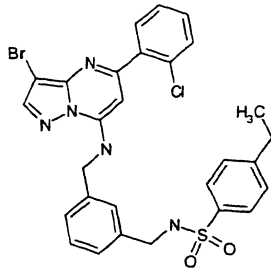
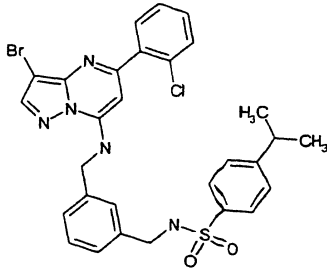
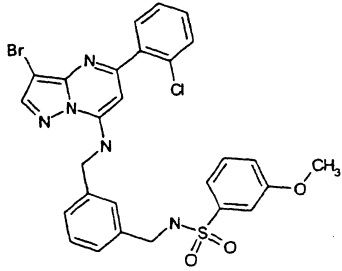
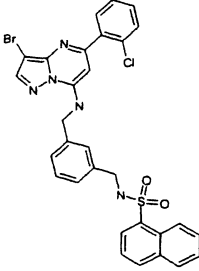
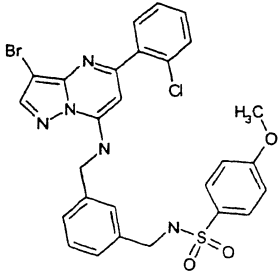
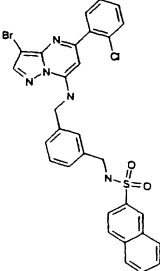
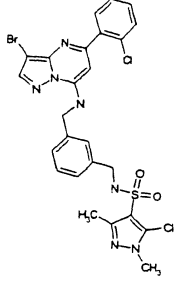
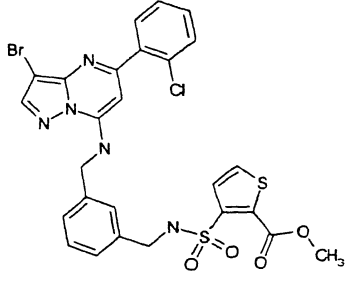
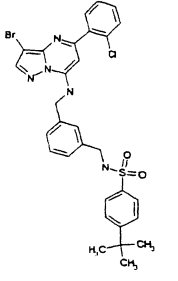
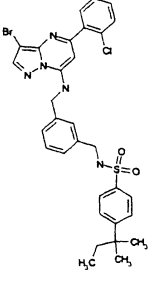
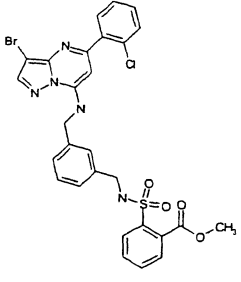
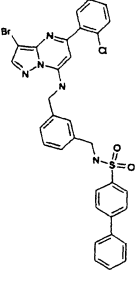
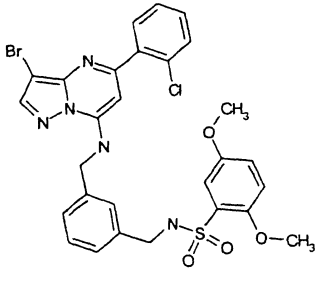
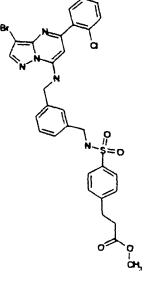
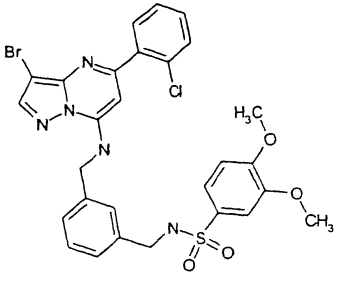
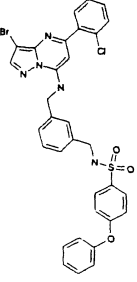
產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5741 2. 605.33		1. 5746 2. 613.34
	1. 5742 2. 607.33		1. 5747 2. 615.34
	1. 5743 2. 607.33		1. 5748 2. 621.34
	1. 5744 2. 607.33		1. 5749 2. 631.35
	1. 57454 2. 613.34		1. 5750 2. 680.37

表58

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5801 2. 550.3		1. 5806 2. 598.33
	1. 5802 2. 590.32		10 5807 2. 602.33
	1. 5803 2. 598.33		1. 5808 2. 602.33
	1. 5804 2. 598.33		1. 5809 2. 603.33
	1. 5805 2. 598.33		1. 5810 2. 609.33

產物	1. 實例2. m/z	產物	1. 實例2. m/z
	1. 5811 2. 609.33		1. 5816 2. 618.34
	1. 5812 2. 610.34		1. 5817 2. 624.34
	1. 5813 2. 612.34		1. 5818 2. 626.34
	1. 5814 2. 614.34		1. 5819 2. 634.35
	1. 5815 2. 614.34		1. 5820 2. 632.35

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 5821 2. 636.35		1. 5826 2. 648.36
	1. 5822 2. 640.35		1. 5827 2. 654.36
	1. 5823 2. 642.35		1. 5828 2. 660.36
	1. 5824 2. 644.35		1. 5829 2. 670.37
	1. 5825 2. 644.35		1. 5830 2. 676.37

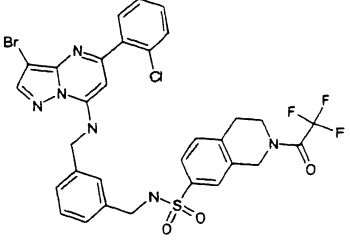
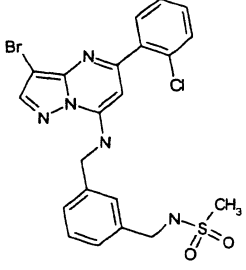
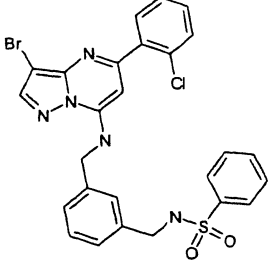
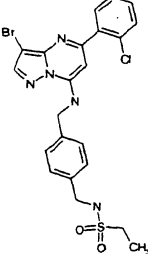
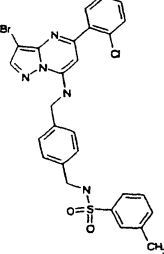
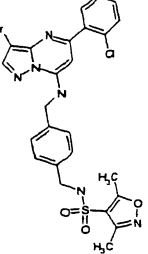
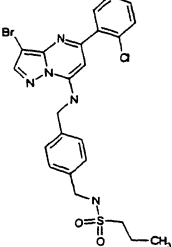
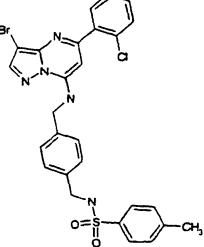
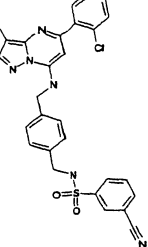
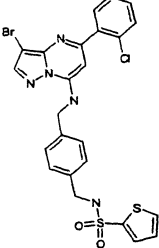
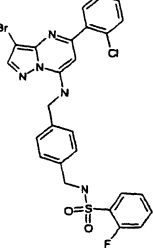
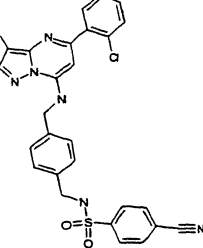
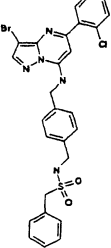
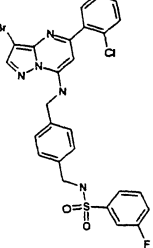
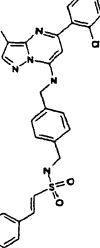
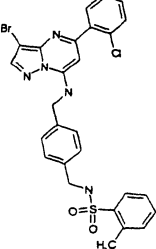
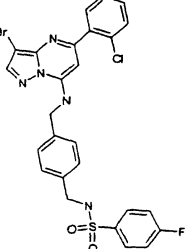
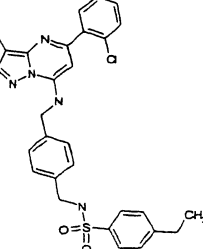
產物	1. 實例 2. m/z
	1. 5831 2. 735.4
	1. 5832 2. 522.29
	1. 5833 2. 584.32

表59

產物	1. 實例2. m/z	產物	1. 實例2. m/z	產物	1. 實例2. m/z
	1. 5901 2. 536.29		1. 5906 2. 598.33		1. 5911 2. 603.33
	1. 5902 2. 550.3		1. 5907 2. 598.33		1. 5912 2. 609.33
	1. 5903 2. 590.32		1. 5908 2. 602.33		1. 5913 2. 609.33
	1. 5904 2. 598.33		1. 5909 2. 602.33		1. 5914 2. 610.34
	1. 5905 2. 598.33		1. 5910 2. 602.33		1. 5915 2. 612.34

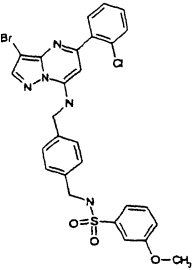
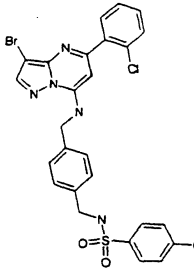
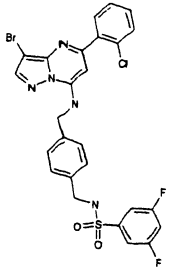
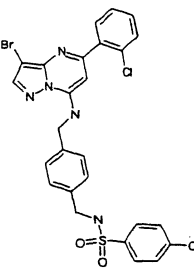
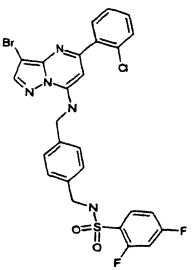
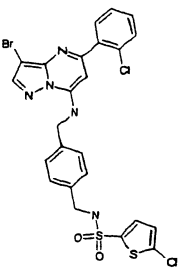
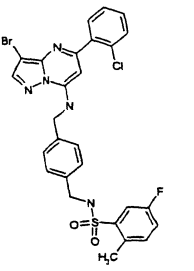
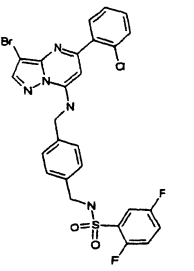
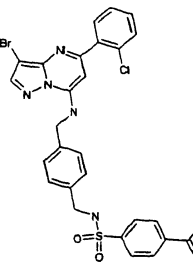
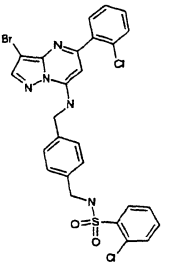
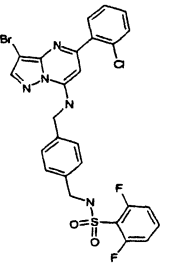
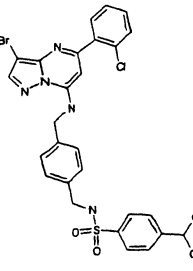
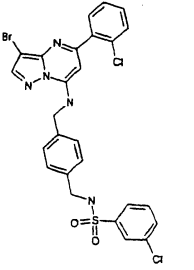
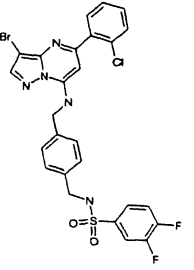
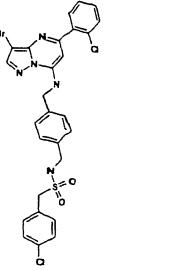
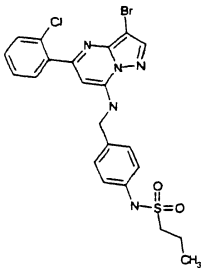
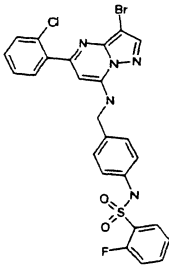
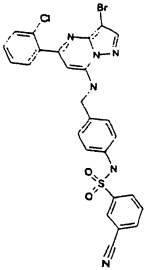
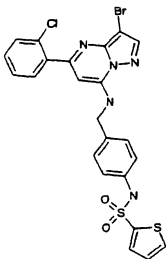
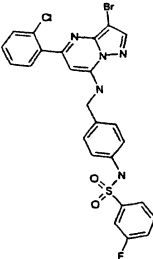
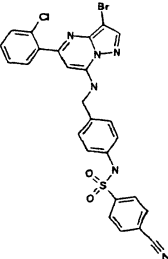
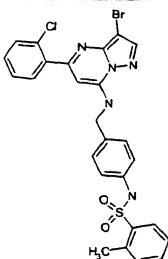
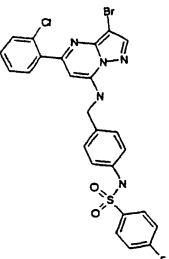
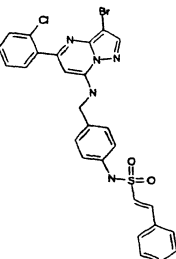
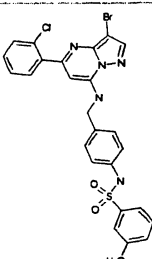
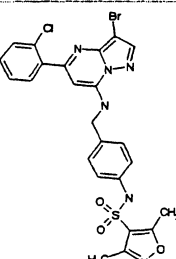
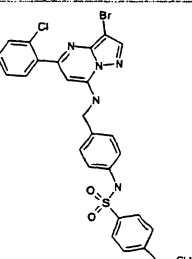
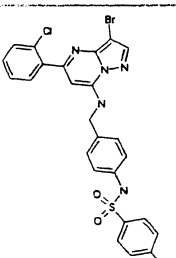
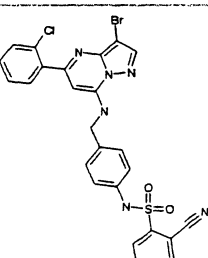
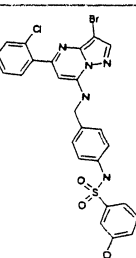
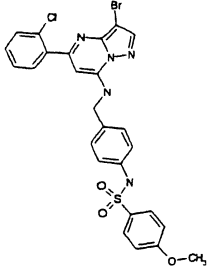
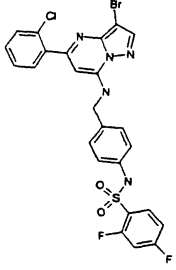
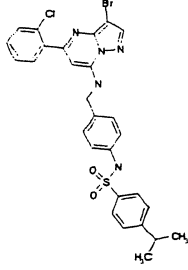
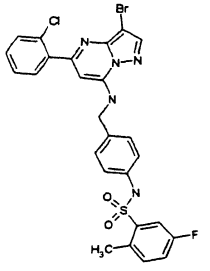
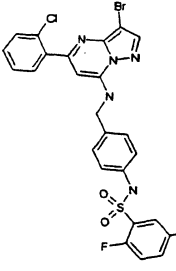
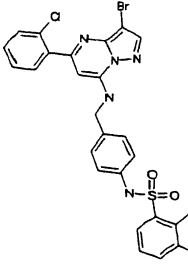
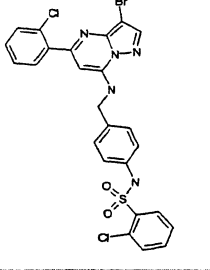
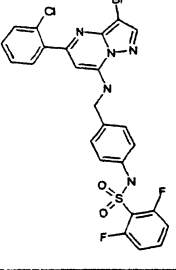
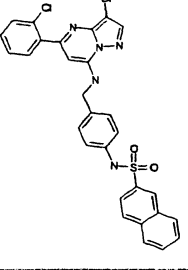
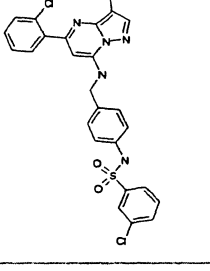
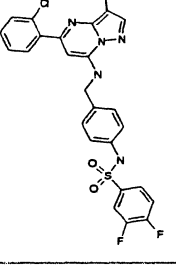
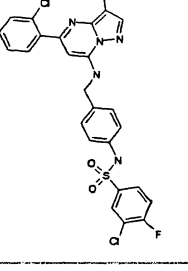
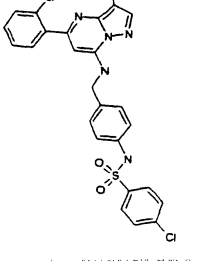
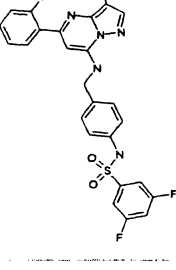
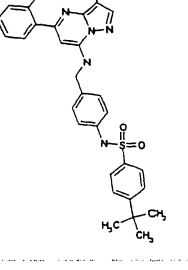
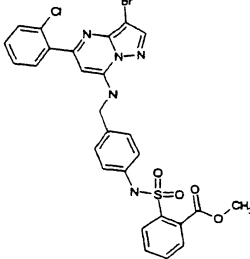
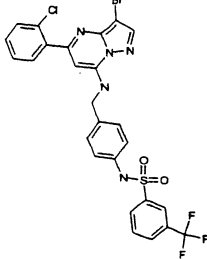
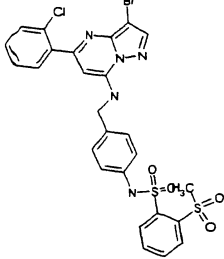
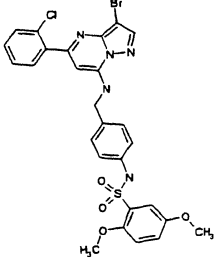
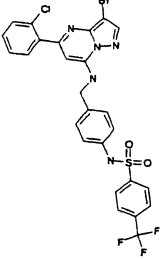
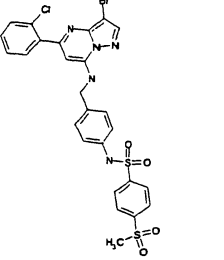
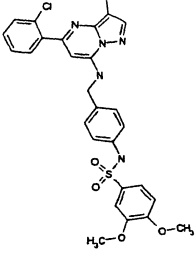
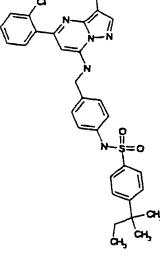
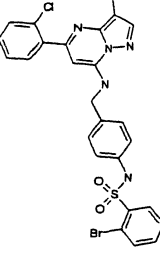
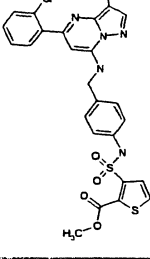
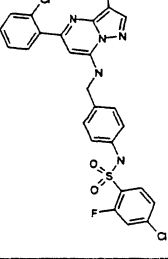
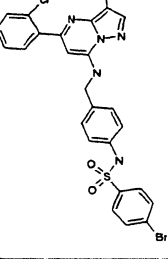
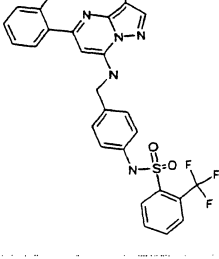
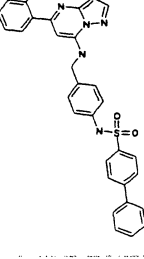
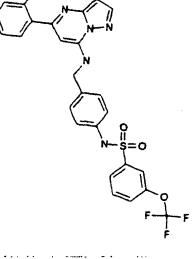
產物	1. 實例2. m/z	產物	1. 實例2. m/z	產物	1. 實例2. m/z
	1. 5916 2. 614.34		1. 5921 2. 618.34		1. 5926 2. 620.34
	1. 5917 2. 614.34		1. 5922 2. 620.34		1. 5927 2. 624.34
	1. 5918 2. 616.34		1. 5923 2. 620.34		1. 5928 2. 626.34
	1. 5919 2. 618.34		1. 5924 2. 620.34		1. 5929 2. 626.34
	1. 5920 2. 618.34		1. 5925 2. 620.34		1. 5930 2. 632.35

表60

產物	1. 實例2. m/z	產物	1. 實例2. m/z	產物	1. 實例2. m/z
	1. 6001 2. 536.29		1. 6006 2. 588.32		1. 6011 2. 595.33
	1. 6002 2. 576.32		1. 6007 2. 588.32		1. 6012 2. 595.33
	1. 6003 2. 584.32		1. 6008 2. 588.32		1. 6013 2. 596.33
	1. 6004 2. 584.32		1. 6009 2. 589.32		1. 6014 2. 598.33
	1. 6005 2. 584.32		1. 6010 2. 595.33		1. 6015 2. 600.33

產物	1.實例2. m/z	產物	1.實例2. m/z	產物	1.實例2. m/z
	1. 6016 2. 600.33		1. 6021 2. 606.33		1. 6026 2. 612.34
	1. 6017 2. 602.33		1. 6022 2. 606.33		1. 6027 2. 620.34
	1. 6018 2. 604.33		1. 6023 2. 606.33		1. 6028 2. 620.34
	1. 6019 2. 604.33		1. 6024 2. 606.33		1. 6029 2. 622.34
	1. 6020 2. 604.33		1. 6025 2. 606.33		1. 6030 2. 626.34

產物	1. 實例2. m/z	產物	1. 實例2. m/z	產物	1. 實例2. m/z
	1. 6031 2. 628.35		1. 6036 2. 638.35		1. 6041 2. 648.36
	1. 6032 2. 630.35		1. 6037 2. 638.35		1. 60425 2. 648.36
	1. 6033 2. 630.35		1. 6038 2. 638.35		1. 6043 2. 648.36
	1. 6034 2. 634.35		1. 6039 2. 622.34		1. 6044 2. 648.36
	1. 6035 2. 638.35		1. 6040 2. 646.36		1. 6045 2. 654.36

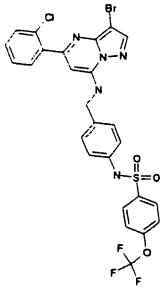
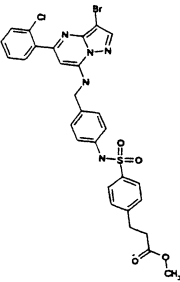
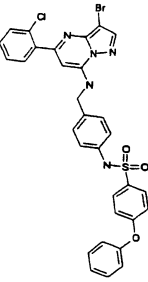
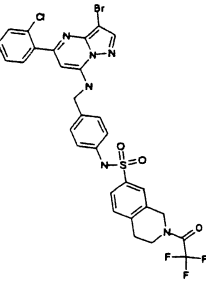
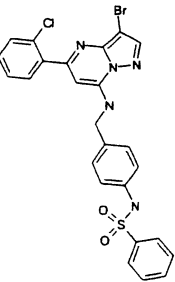
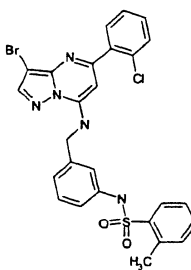
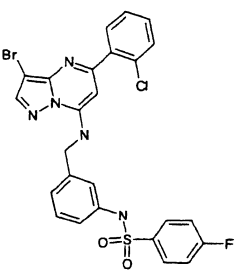
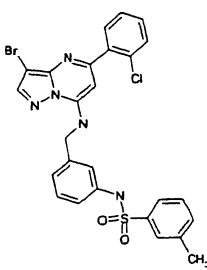
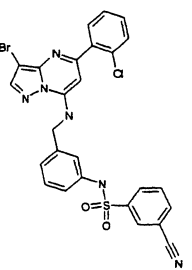
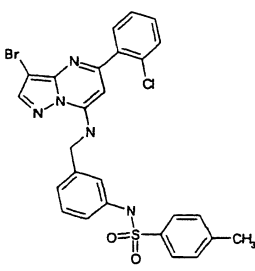
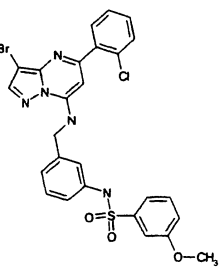
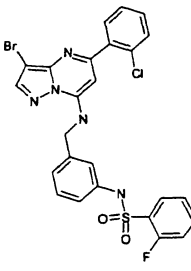
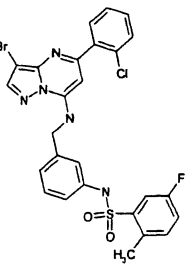
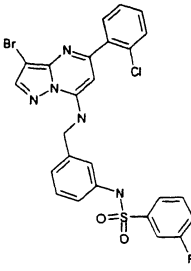
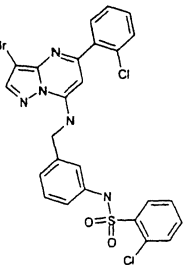
產物	1. 實例2. m/z
	1. 6046 2. 654.36
	1. 6047 2. 656.36
	1. 6048 2. 662.36
	1. 6049 2. 721.4
	1. 6050 2. 570.31

表61

產物	1. 實例2. m/z	產物	1. 實例2. m/z
	1. 6101 2. 584.32		1. 6106 2. 588.32
	1. 6102 2. 584.32		1. 6107 2. 595.33
	1. 6103 2. 584.32		1. 6108 2. 600.33
	1. 6104 2. 588.32		1. 6109 2. 602.33
	1. 6105 2. 588.32		1. 6110 2. 604.33

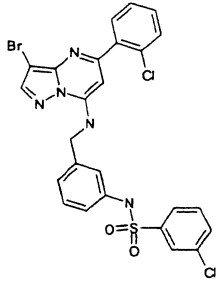
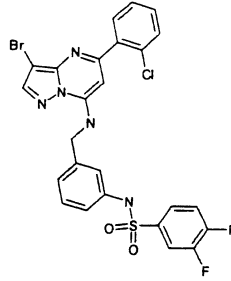
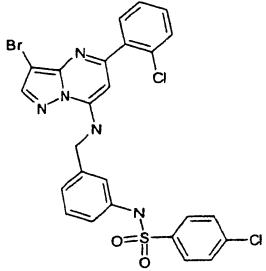
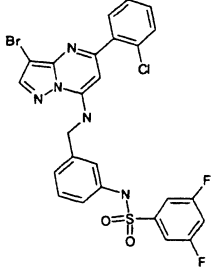
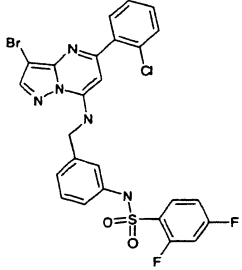
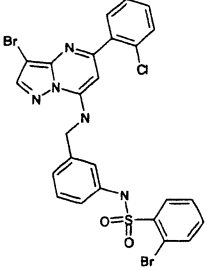
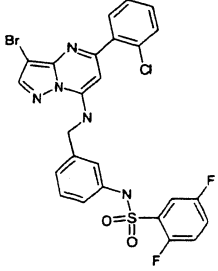
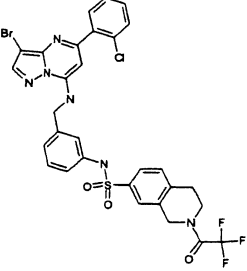
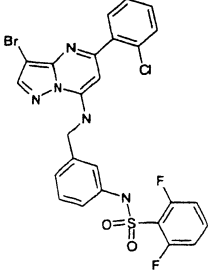
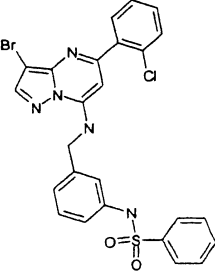
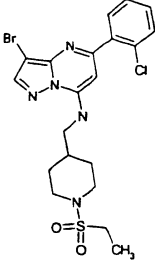
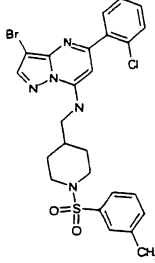
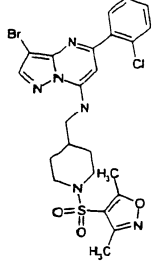
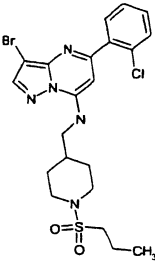
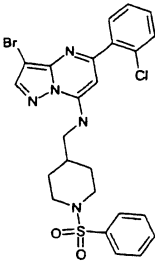
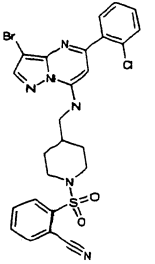
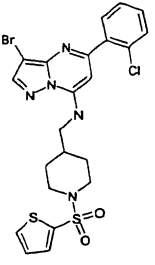
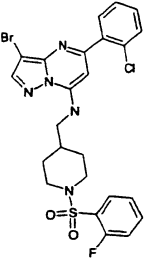
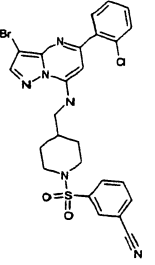
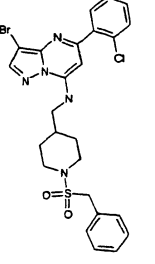
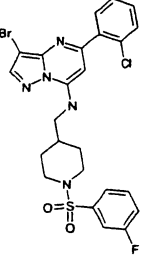
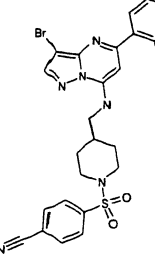
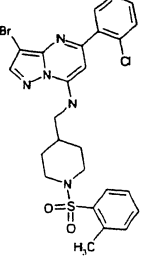
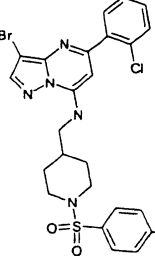
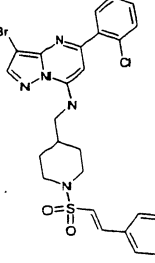
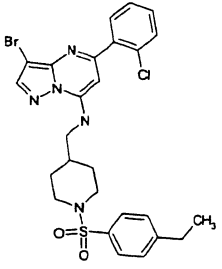
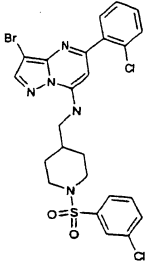
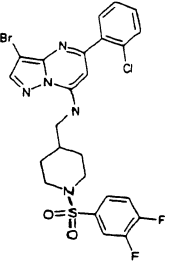
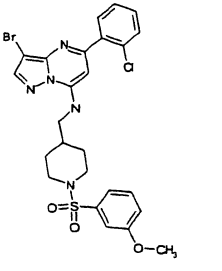
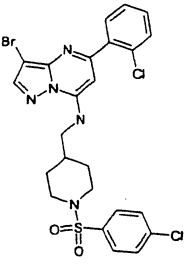
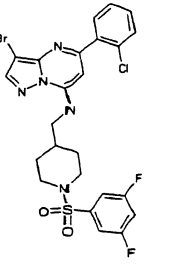
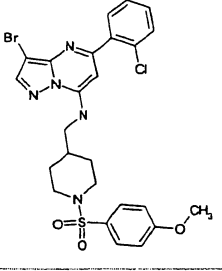
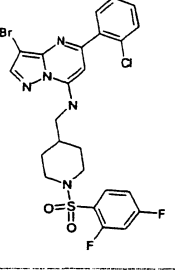
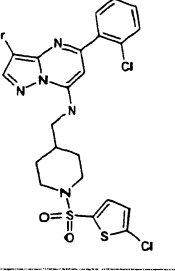
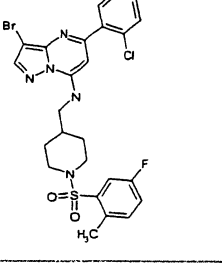
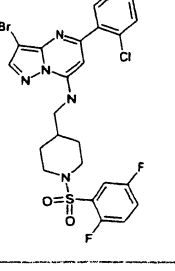
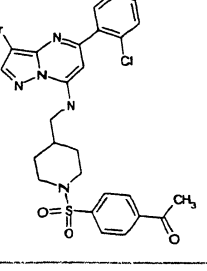
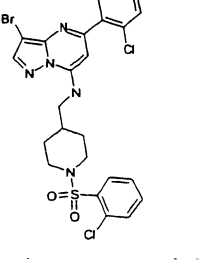
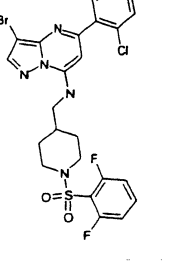
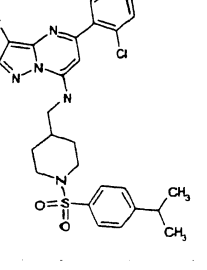
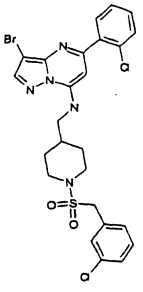
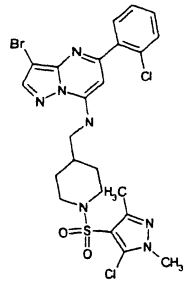
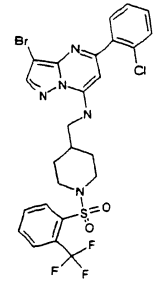
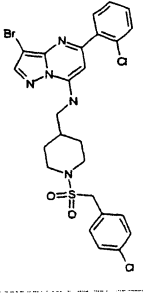
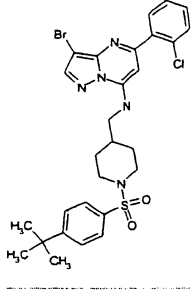
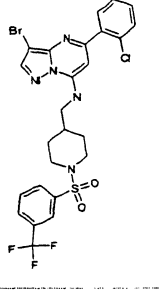
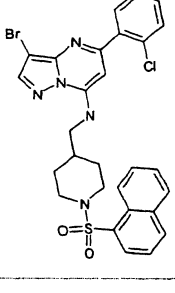
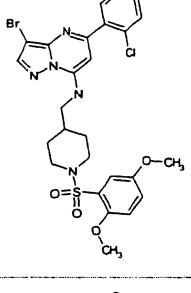
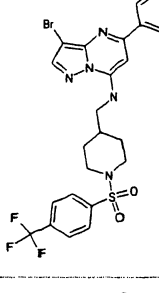
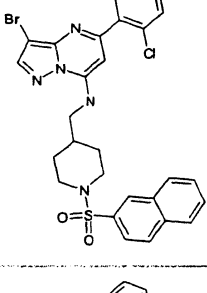
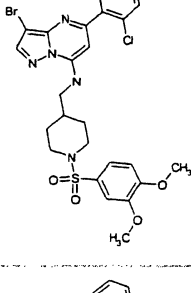
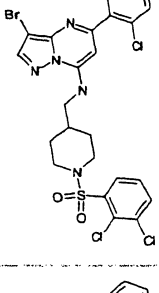
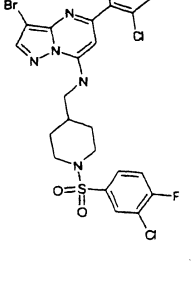
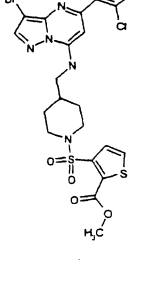
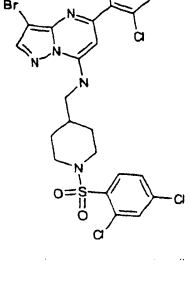
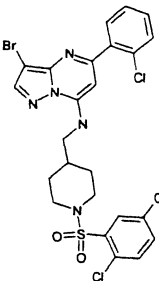
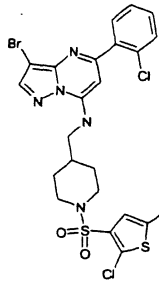
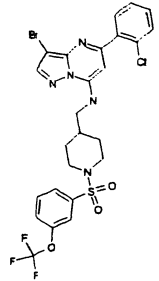
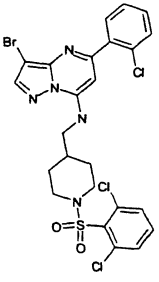
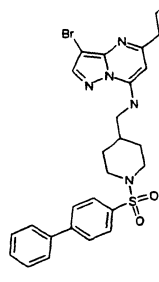
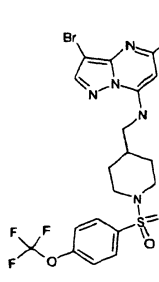
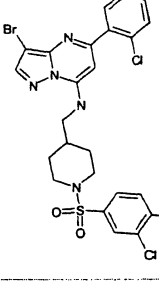
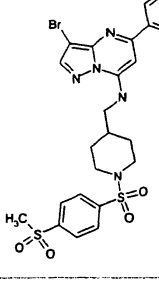
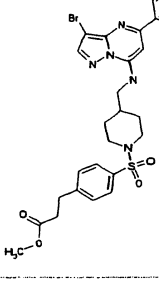
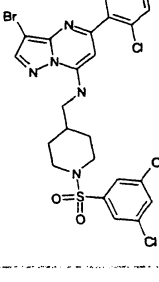
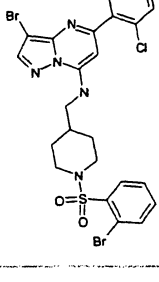
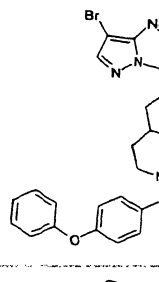
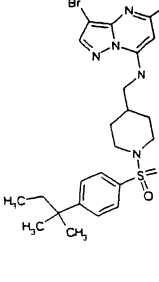
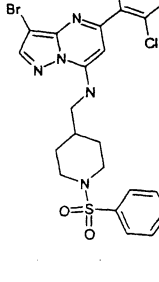
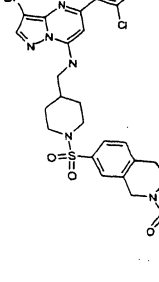
產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 6111 2. 604.33		1. 6116 2. 606.33
	1. 6112 2. 604.33		1. 6117 2. 606.33
	1. 6113 2. 606.33		1. 6118 2. 648.36
	1. 6114 2. 606.33		1. 6119 2. 721.4
	1. 6115 2. 606.33		1. 6120 2. 570.31

表62

產物	1. 實例2. m/z	產物	1. 實例2. m/z	產物	1. 實例2. m/z
	1. 6201 2. 514.28		1. 6206 2. 576.32		1. 6211 2. 581.32
	1. 6202 2. 528.29		1. 6207 2. 576.32		1. 6212 2. 587.32
	1. 6203 2. 568.31		1. 6208 2. 580.32		1. 6213 2. 587.32
	1. 6204 2. 576.32		1. 6209 2. 580.32		1. 6214 2. 587.32
	1. 6205 2. 576.32		1. 6210 2. 580.32		1. 6215 2. 588.32

產物	1.實例2. m/z	產物	1.實例2. m/z	產物	1.實例2. m/z
	1. 6216 2. 590.32		1. 6221 2. 596.33		1. 6226 2. 598.33
	1. 6217 2. 592.33		1. 6222 2. 596.33		1. 6227 2. 596.33
	1. 6218 2. 592.33		1. 6223 2. 598.33		1. 6228 2. 602.33
	1. 6219 2. 592.33		1. 6224 2. 596.33		1. 6229 2. 604.33
	1. 6220 2. 594.33		1. 6225 2. 598.33		1. 6230 2. 604.33

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 6231 2. 610.34		1. 6236 2. 614.34		1. 6241 2. 630.35
	1. 6232 2. 610.34		1. 6237 2. 618.34		1. 6242 2.
	1. 6233 2. 612.34		1. 6238 2. 622.34		1. 6243 2. 630.35
	1. 6234 2. 612.34		1. 6239 2. 622.34		1. 6244 2. 630.35
	1. 6235 2. 614.34		1. 6240 2. 626.34		1. 6245 2. 630.35

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 6246 2. 630.35		1. 6251 2. 636.35		1. 6256 2. 646.36
	1. 6247 2. 630.35		1. 6252 2. 638.35		1. 6257 2. 646.36
	1. 6248 2. 630.35		1. 6253 2. 640.35		1. 6258 2. 648.36
	1. 6249 2. 630.35		1. 6254 2. 640.35		1. 6259 2. 654.36
	1. 6250 2. 632.35		1. 6255 2. 638.35		1. 6260 2. 713.39

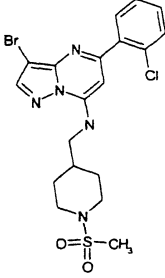
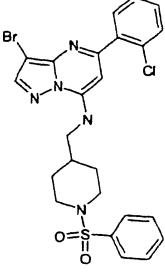
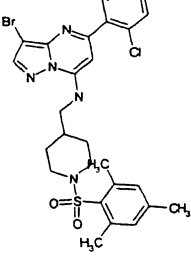
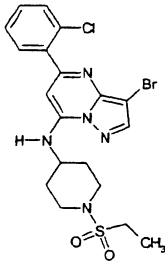
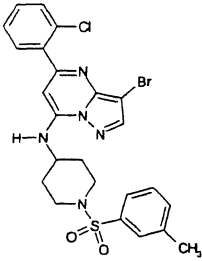
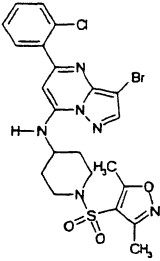
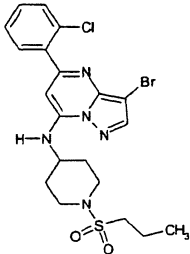
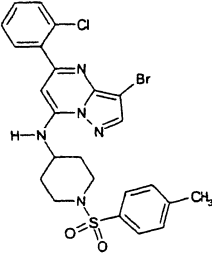
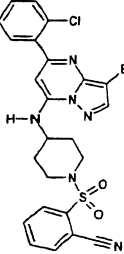
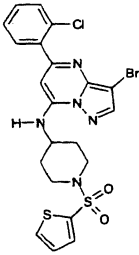
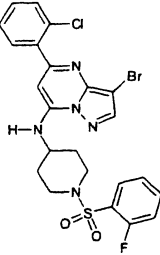
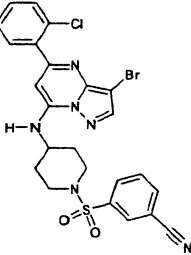
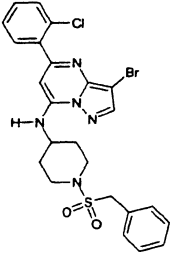
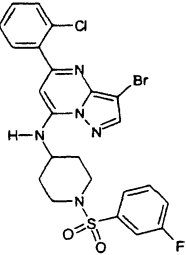
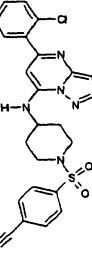
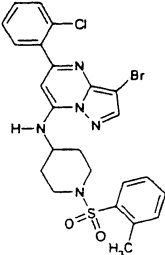
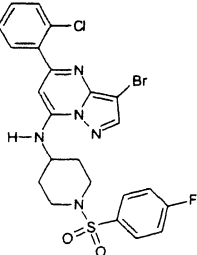
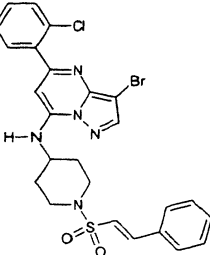
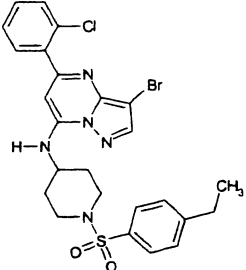
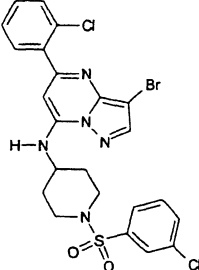
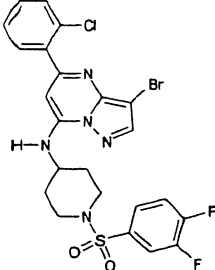
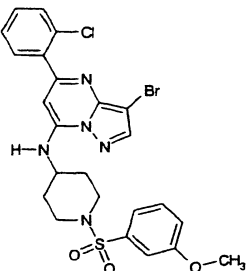
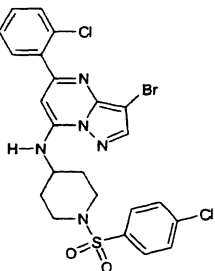
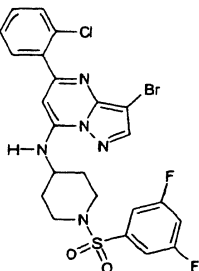
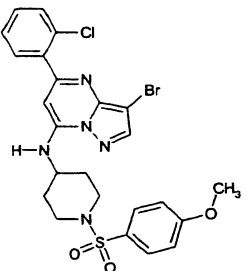
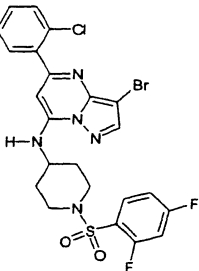
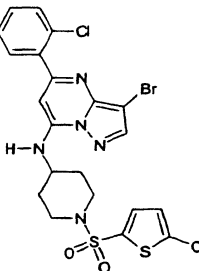
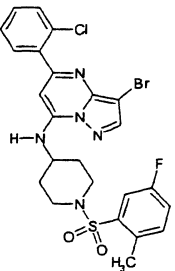
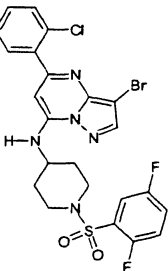
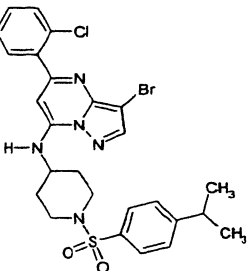
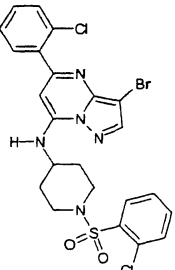
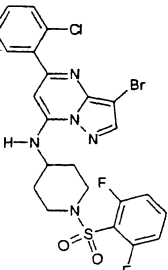
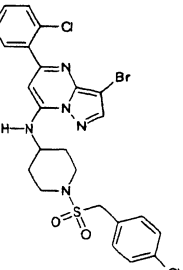
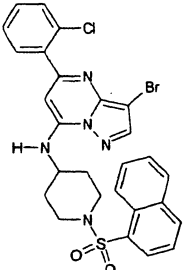
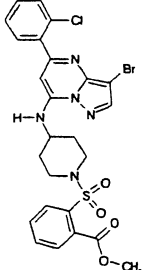
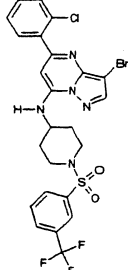
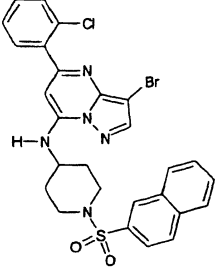
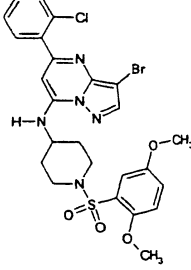
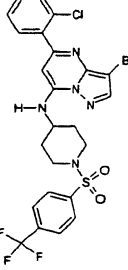
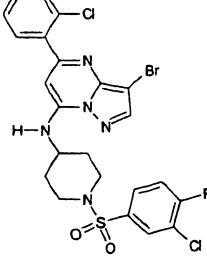
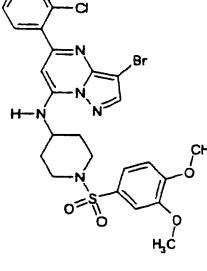
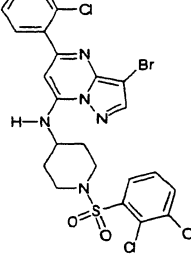
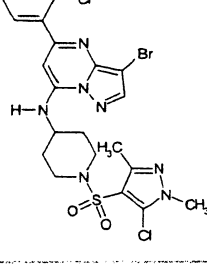
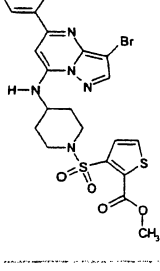
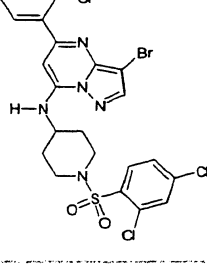
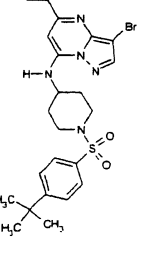
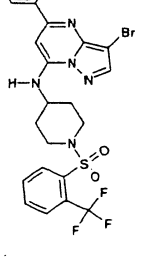
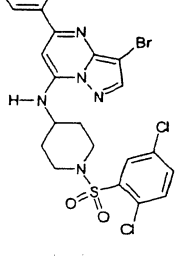
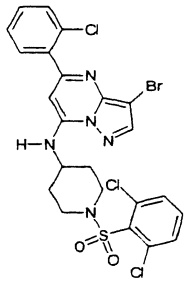
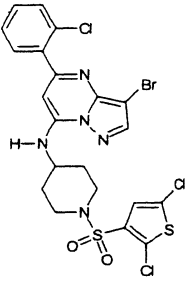
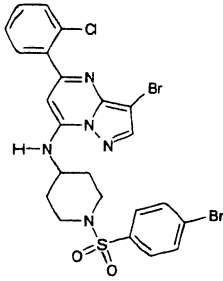
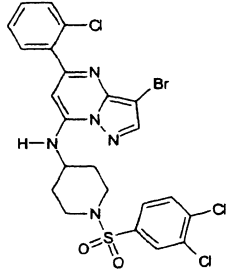
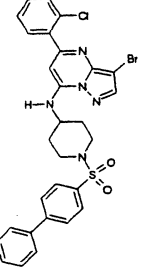
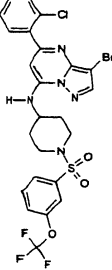
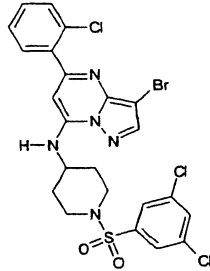
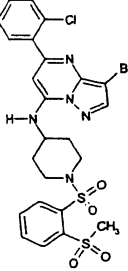
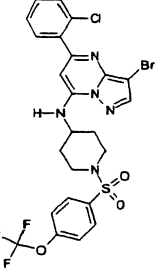
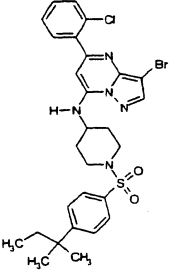
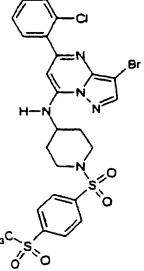
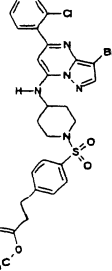
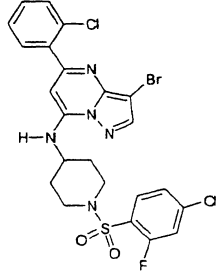
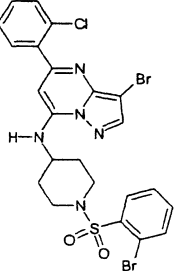
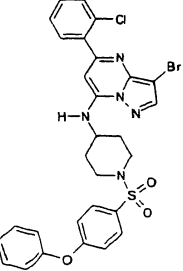
產物	1. 實例 2. m/z
	1. 6261 2. 500.27
	1. 6262 2. 562.31
	1. 6263 2. 604.33

表63

產物	1. 實例2. m/z	產物	1. 實例2. m/z	產物	1. 實例2. m/z
	1. 6301 2. 500.27		1. 6306 2. 562.31		1. 6311 2. 567.31
	1. 6302 2. 514.28		1. 6307 2. 562.31		1. 6312 2. 573.32
	1. 6303 2. 554.3		1. 6308 2. 566.31		1. 6313 2. 573.32
	1. 6304 2. 562.31		1. 6309 2. 566.31		1. 6314 2. 573.32
	1. 6305 2. 562.31		1. 6310 2. 566.31		1. 6315 2. 574.32

產物	1.實例 2. m/z	產物	1.實例 2. m/z	產物	1.實例 2. m/z
	1. 6316 2. 576.32		1. 6321 2. 582.32		1. 6326 2. 584.32
	1. 6317 2. 578.32		1. 6322 2. 582.32		1. 6327 2. 584.32
	1. 6318 2. 578.32		1. 6323 2. 584.32		1. 6328 2. 588.32
	1. 6319 2. 580.32		1. 6324 2. 582.32		1. 6329 2. 590.32
	1. 6320 2. 582.32		1. 6325 2. 584.32		1. 6330 2. 596.33

產物	1. 實例2. m/z	產物	1. 實例2. m/z	產物	1. 實例2. m/z
	1. 6331 2. 598.33		1. 6336 2. 606.33		1. 6341 2. 616.34
	1. 6332 2. 598.33		1. 6337 2. 608.33		1. 6342 2. 616.34
	1. 6333 2. 600.33		1. 6338 2. 608.33		1. 6343 2. 616.34
	1. 6334 2. 600.33		1. 6339 2. 612.34		1.6344 2. 616.34
	1. 6335 2. 604.33		1. 6340 2. 616.34		1. 6345 2. 616.34

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 6346 2. 616.34		1. 6351 2. 622.34		1. 6356 2. 626.34
	1. 6347 2. 616.34		1. 6352 2. 624.34		1. 6357 2. 632.35
	1. 6348 2. 616.34		1. 6353 2. 626.34		1. 6358 2. 632.35
	1. 6349 2. 618.34		1. 6354 2. 626.34		1. 6359 2. 634.35
	1. 6350 2. 600.33		1. 6355 2. 626.34		1. 6360 2. 640.35

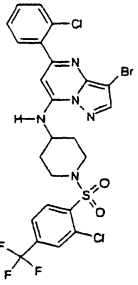
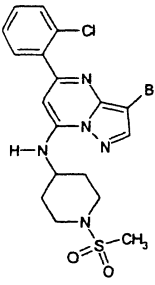
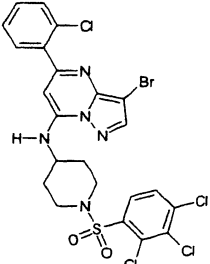
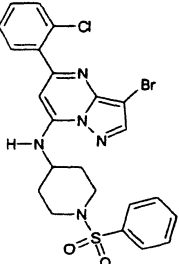
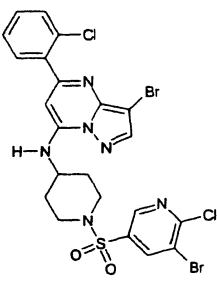
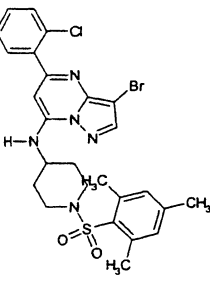
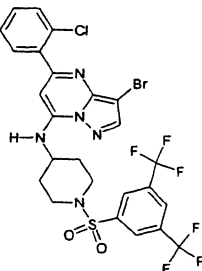
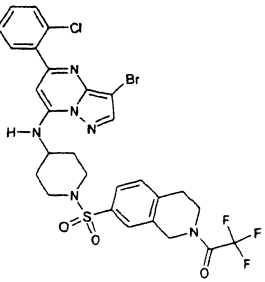
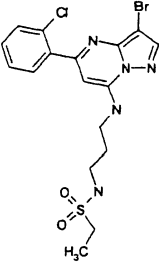
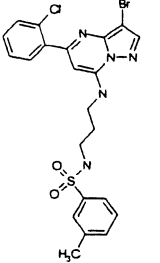
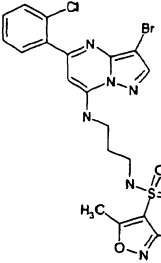
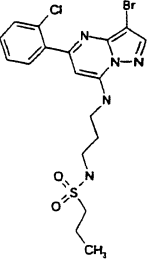
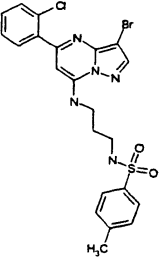
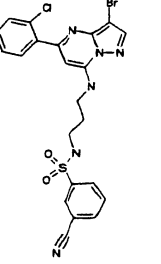
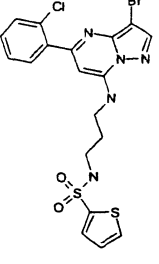
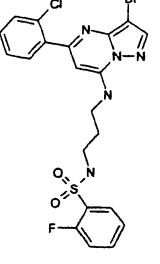
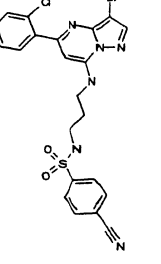
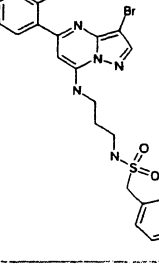
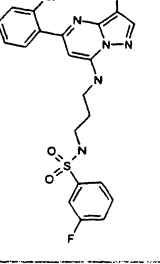
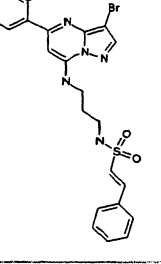
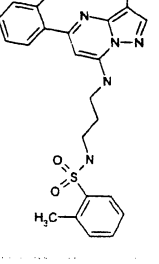
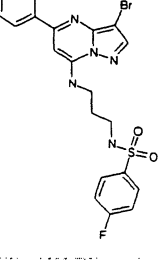
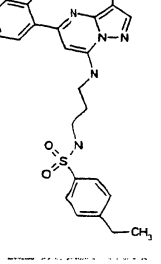
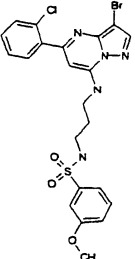
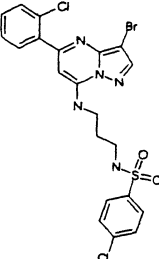
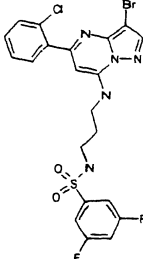
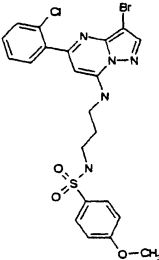
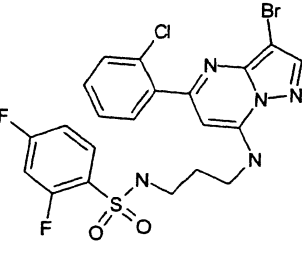
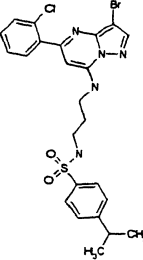
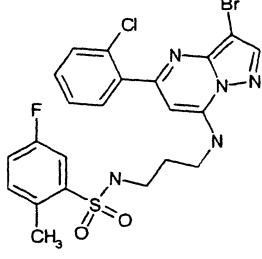
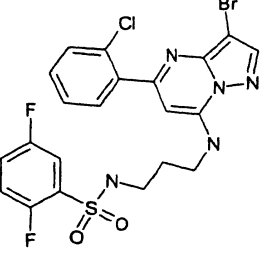
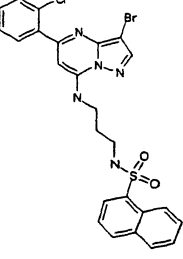
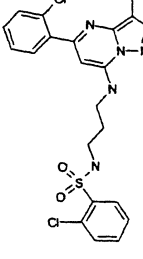
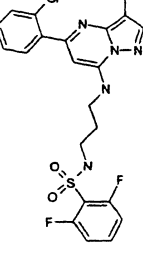
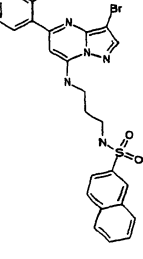
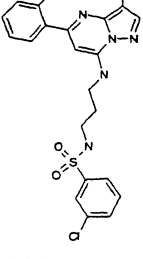
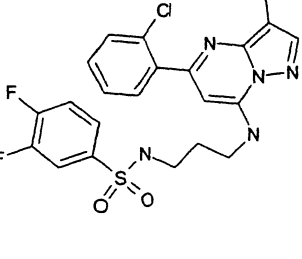
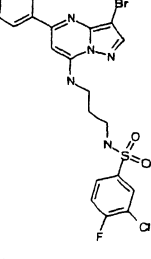
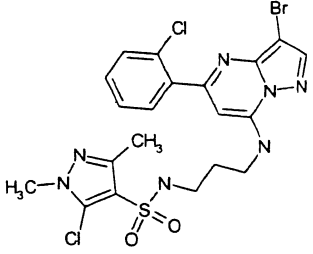
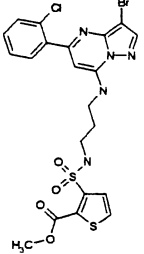
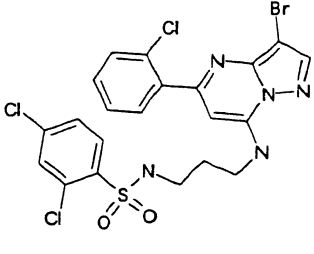
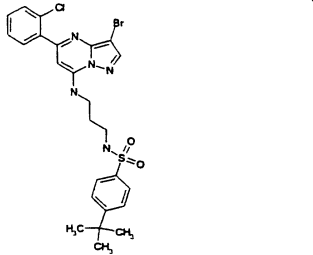
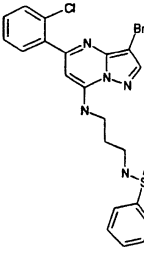
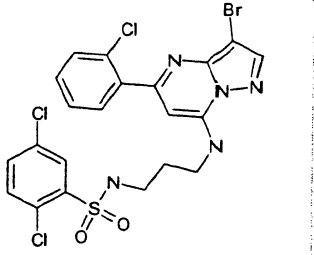
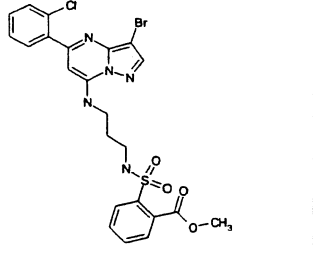
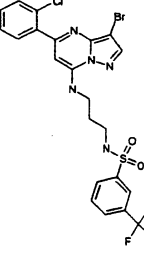
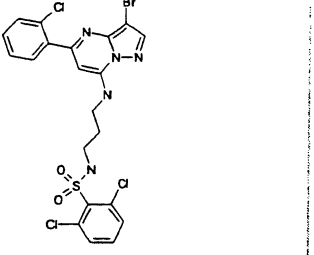
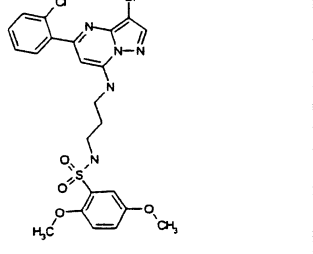
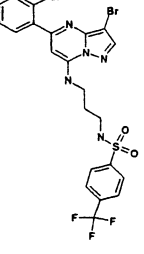
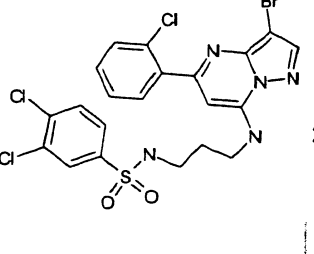
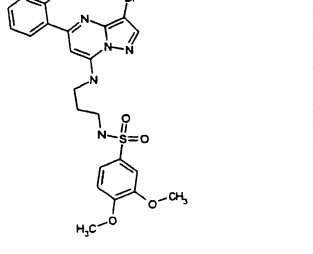
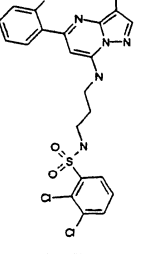
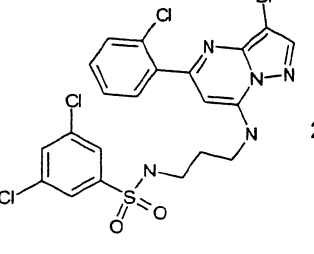
產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 6361 2. 650.36		1. 6366 2. 486.27
	1. 6362 2. 650.36		1. 6367 2. 548.3
	1. 6363 2. 661.36		1. 6368 2. 590.32
	1. 6364 2. 684.38		
	1. 6365 2. 699.38		

表64

產物	1.實例2. m/z	產物	1.實例2. m/z	產物	1.實例2. m/z
	1. 6401 2. 474.26		1. 6406 2. 536.29		1. 6411 2. 541.3
	1. 6402 2. 488.27		1. 6407 2. 536.29		1. 6412 2. 547.3
	1. 6403 2. 528.29		1. 6408 2. 540.3		1. 6413 2. 547.3
	1. 6404 2. 536.29		1. 6409 2. 540.3		1. 6414 2. 548.3
	1. 6405 2. 536.29		1. 6410 2. 540.3		1. 6415 2. 550.3

產物	1. 實例2. m/z	產物	1. 實例2. m/z	產物	1. 實例2. m/z
	1. 6416 2. 552.3		1. 6421 2. 556.31		1. 6426 2. 558.31
	1. 6417 2. 552.3		1. 6122 2. 558.31		1. 6427 2. 564.31
	1. 6418 2. 554.3		1. 6423 2. 558.31		1. 6428 2. 572.31
	1. 6419 2. 556.31		1. 6424 2. 558.31		1. 6429 2. 572.31
	1. 6420 2. 556.31		1. 6425 2. 558.31		1. 6430 2. 574.32

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 6431 2. 574.32		1. 6436 2. 586.32		1. 6441 2. 590.32
	1. 6432 2. 578.32		1. 6437 2. 590.32		1. 6442 2. 590.32
	1. 6433 2. 580.32		1. 6438 2. 590.32		1. 6443 2. 590.32
	1. 6434 2. 582.32		1. 6439 2. 590.32		1. 6444 2. 590.32
	1. 6435 2. 582.32		1. 6440 2. 589.32		1. 6445 2. 590.32

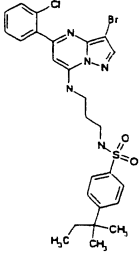
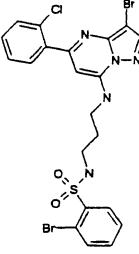
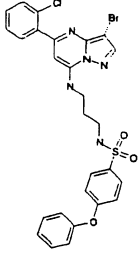
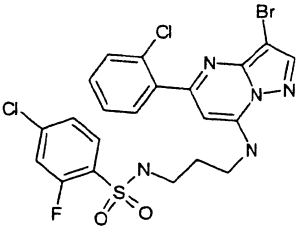
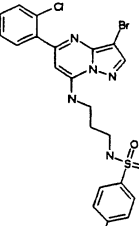
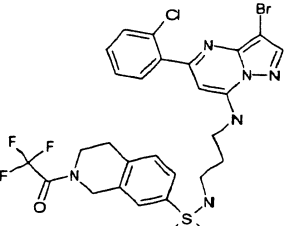
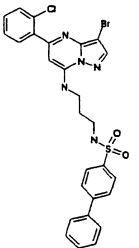
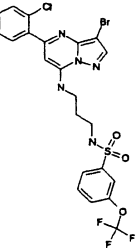
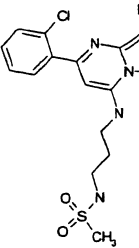
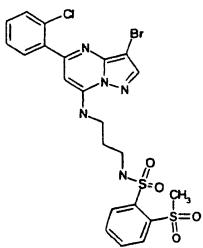
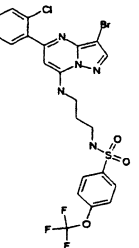
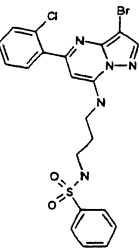
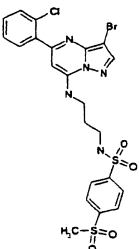
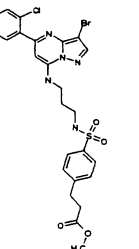
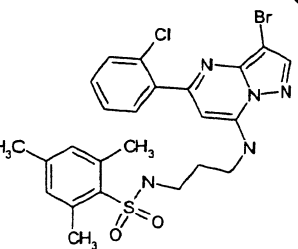
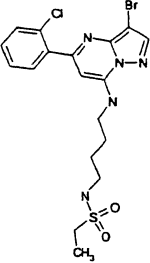
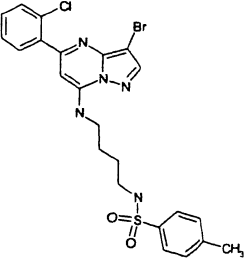
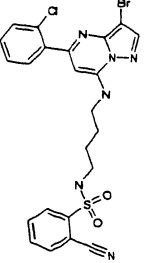
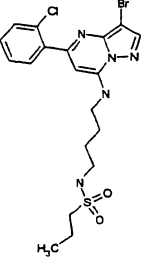
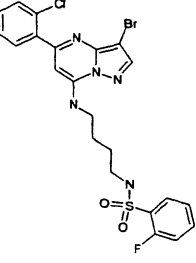
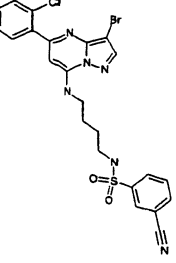
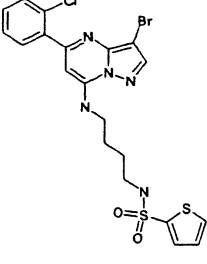
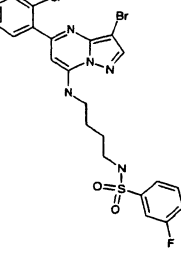
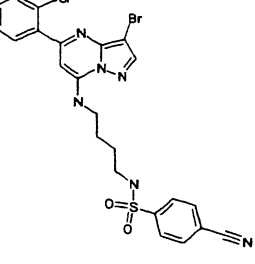
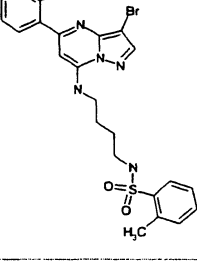
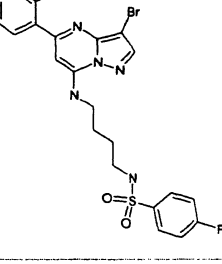
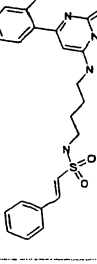
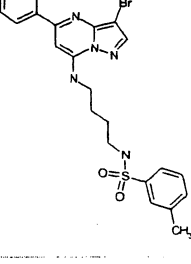
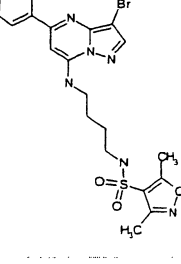
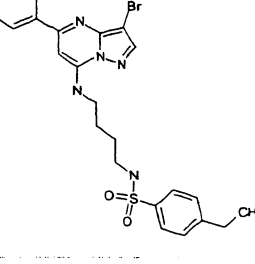
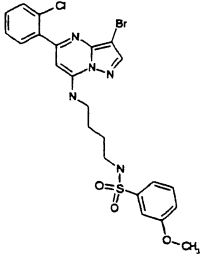
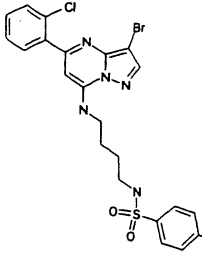
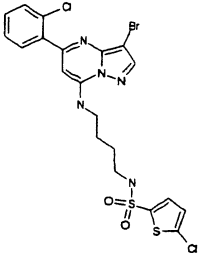
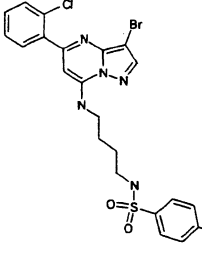
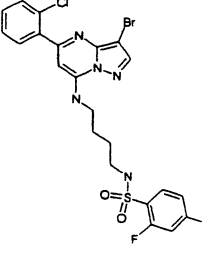
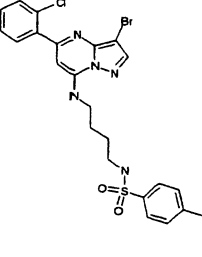
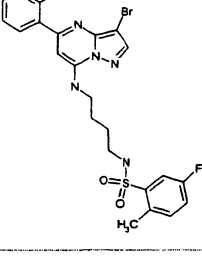
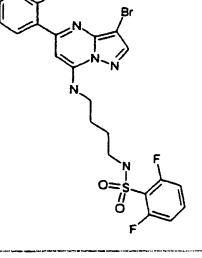
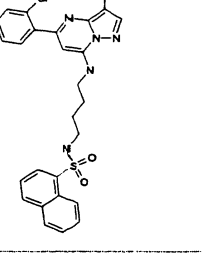
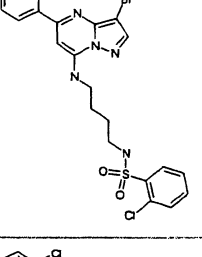
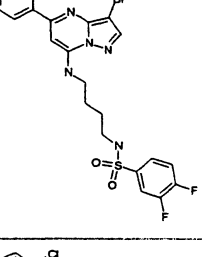
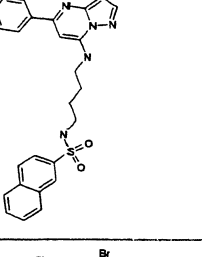
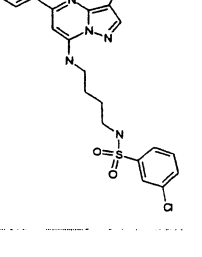
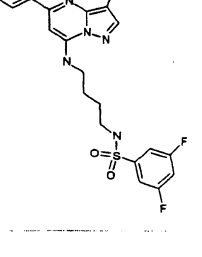
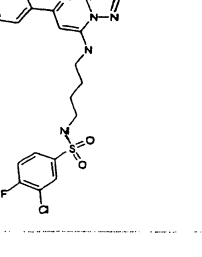
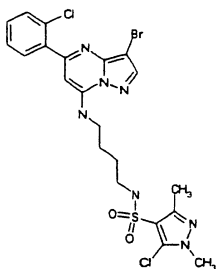
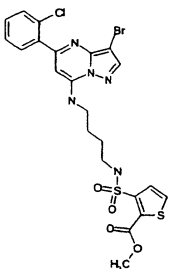
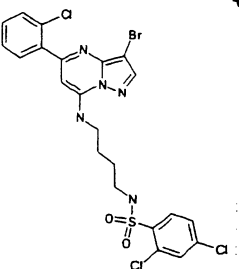
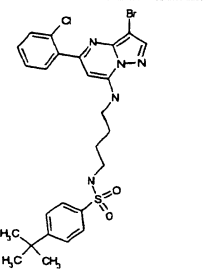
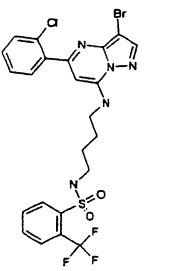
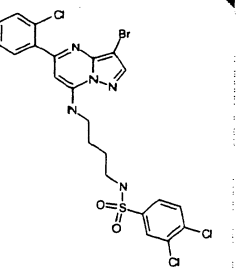
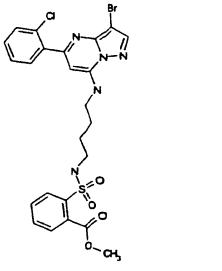
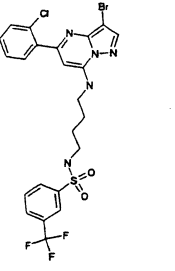
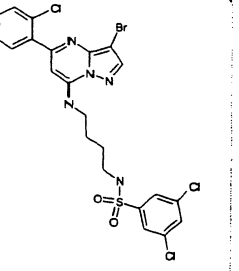
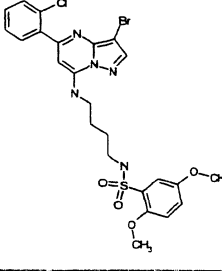
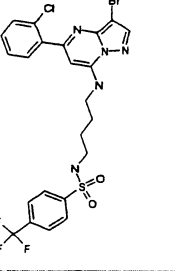
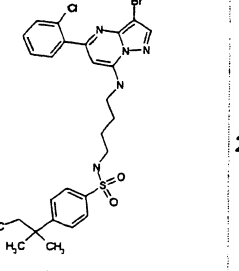
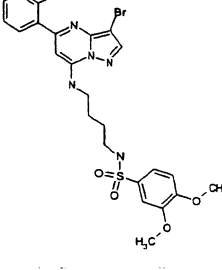
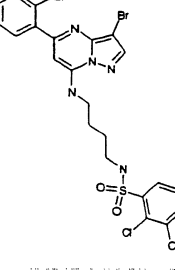
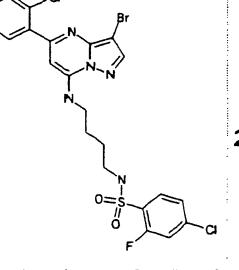
產物	1. 實例2. m/z	產物	1. 實例2. m/z	產物	1 實例2. m/z
	1. 6446 2. 592.33		1. 6451 2. 600.33		1. 6456 2. 614.34
	1. 6447 2. 574.32		1. 6452 2. 600.33		1. 6447 2. 673.34
	1. 6448 2. 598.33		1. 6453 2. 606.33		1. 6458 2. 460.25
	1. 6449 2. 600.33		1. 6454 2. 606.33		6459 2.
	1. 6450 2. 600.33		1. 6455 2. 608.33		1. 6460 2. 564.31

表65

產物	1. 實例2. m/z	產物	1. 實例2. m/z	產物	1. 實例2. m/z
	1. 6501 2. 488.27		1. 6506 2. 550.3		1. 6511 2. 561.31
	1. 6502 2. 502.28		1. 6507 2. 554.3		1. 6512 2. 561.31
	1. 6503 2. 542.3		1. 6508 2. 554.3		1. 6213 2. 561.31
	1. 6504 2. 550.3		1. 6509 2. 554.3		1. 6514 2. 562.31
	1. 6505 2. 550.3		1. 6510 2. 555.31		1. 6515 2. 564.31

產物	1. 實例2. m/z	產物	1. 實例2. m/z	產物	1. 實例2. m/z
	1. 6516 2. 566.31		1. 6521 2. 570.31		1. 6526 2. 576.32
	1. 6517 2. 566.31		1. 6522 2. 572.31		1. 6527 2. 578.32
	1. 6518 2. 568.31		1. 6523 2. 572.31		1. 6528 2. 586.32
	1. 6519 2. 570.31		1. 6524 2. 572.31		1. 6529 2. 586.32
	1. 6520 2. 570.31		1. 6525 2. 572.31		1. 6530 2. 588.32

產物	1. 實例2. m/z	產物	1. 實例2. m/z	產物	1. 實例2. m/z
	1. 6531 2. 588.33		1. 6536 2. 600.33		1. 6541 2. 604.33
	1. 6532 2. 592.33		1. 6537 2. 604.33		1. 6542 2. 604.33
	1. 6533 2. 594.33		1. 6538 2. 604.33		1. 6543 2. 604.33
	1. 6534 2. 596.33		1. 6539 2. 604.33		1. 6544 2. 606.33
	1. 6535 2. 596.33		1. 6540 2. 604.33		1. 6545 2. 588.32

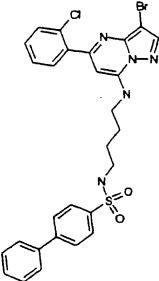
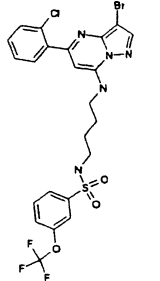
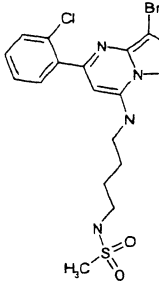
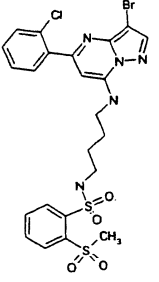
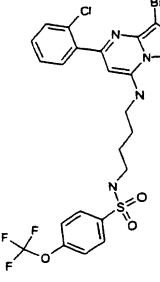
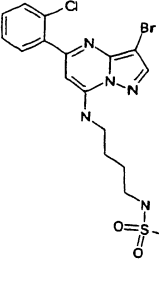
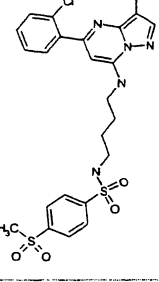
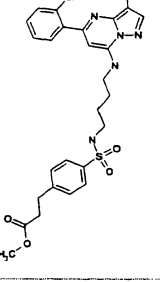
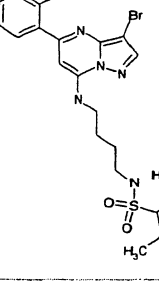
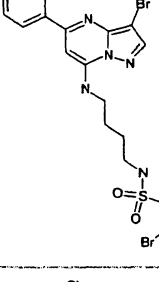
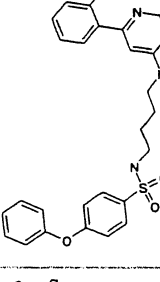
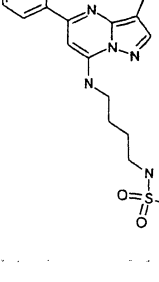
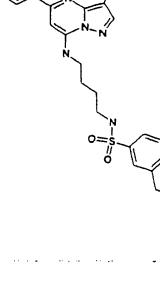
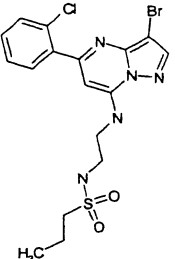
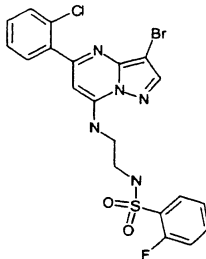
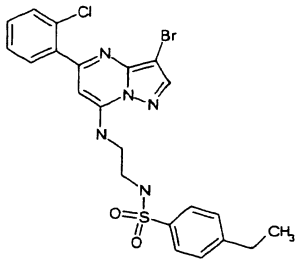
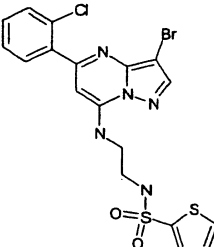
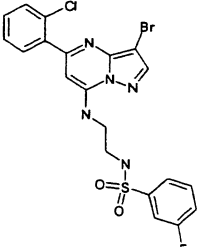
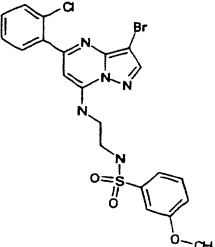
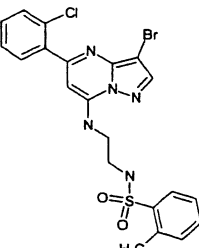
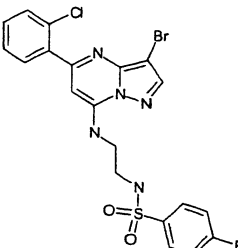
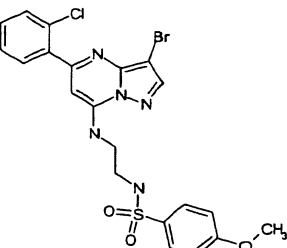
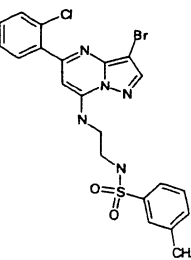
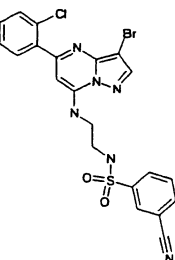
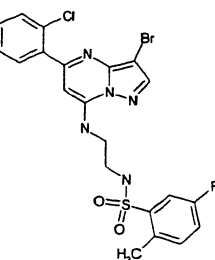
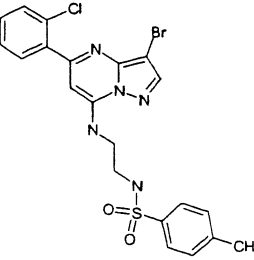
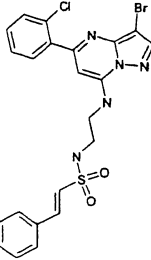
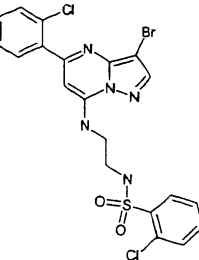
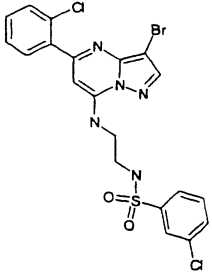
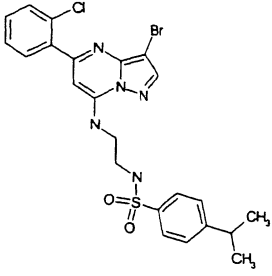
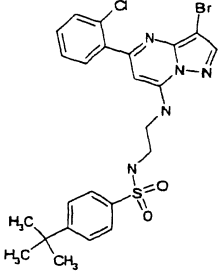
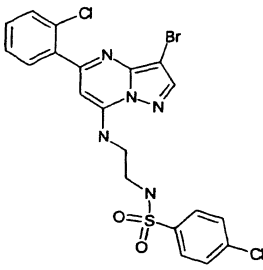
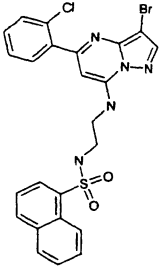
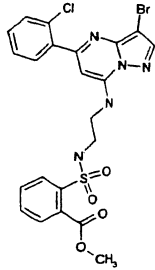
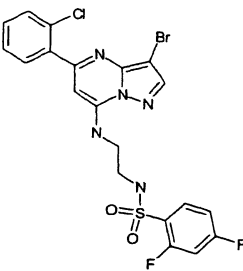
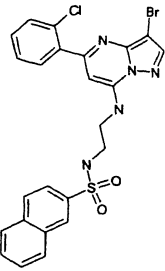
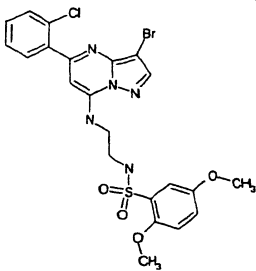
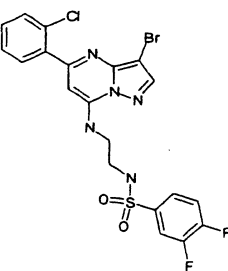
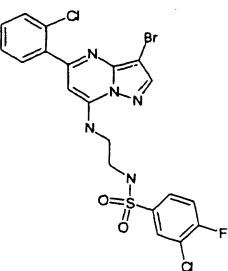
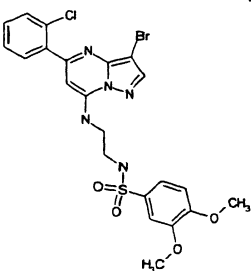
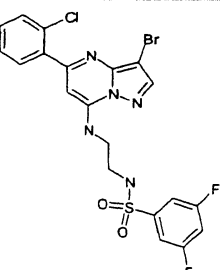
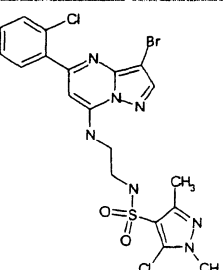
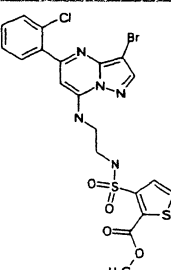
產物	1.實例 2. m/z	產物	1.實例 2. m/z	產物	1.實例 2. m/z
	1. 6546 2. 612.34		1. 6551 2. 620.34		1. 6556 2. 474.26
	1. 6547 2. 614.34		1. 6552 2. 620.34		1. 6557 2. 536.29
	1. 6548 2. 614.34		1. 6553 2. 622.34		1. 6558 2. 578.32
	1. 6549 2. 614.34		1. 6554 2. 628.35		
	1. 6550 2. 614.34		1. 6555 2. 687.38		

表67

產物	1.實例2. m/z	產物	1.實例2. m/z	產物	1.實例2. m/z
	1. 6701 2. 474.26		1. 6706 2. 526.29		1. 6711 2. 536.29
	1. 6702 2. 514.28		1. 6707 2. 526.29		1. 6712 2. 538.3
	1. 6703 2. 522.29		1. 6708 2. 526.29		1. 6713 2. 538.3
	1. 6704 2. 522.29		1. 6709 2. 533.29		1. 6714 2.
	. 6705 522.29		1. 6710 2. 534.29		1. 6715 2. 542.3

產物	1. 實例2. m/z	產物	1. 實例2. m/z	產物	1. 實例2. m/z
	1. 6716 2. 542.3		1. 6721 2. 550.3		1. 6726 2. 564.31
	1. 6717 2. 542.3		1. 6722 2. 558.31		1. 6727 2. 566.31
	1. 6718 2. 544.3		1. 6723 2. 558.31		1. 6728 2. 568.31
	1. 6719 2. 544.3		1. 6724 2. 560.31		1. 6729 2. 568.31
	1. 6720 2. 544.3		1. 6725 2. 560.31		1. 6730 2. 572.31

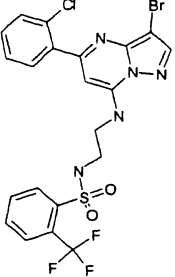
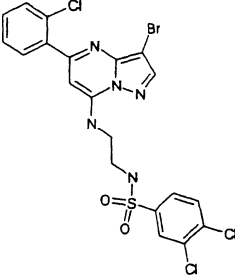
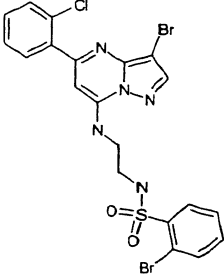
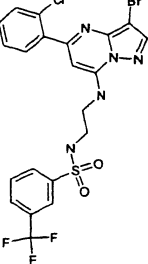
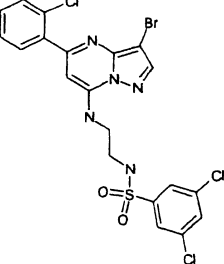
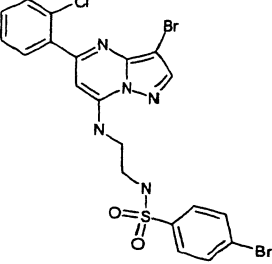
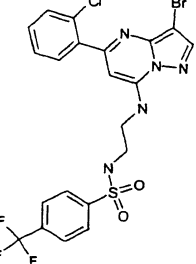
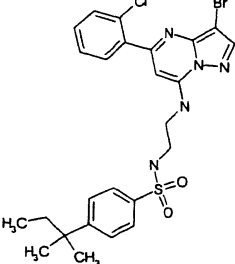
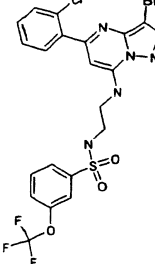
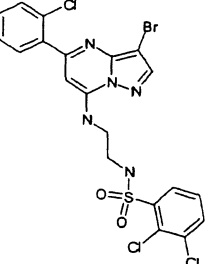
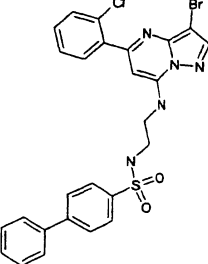
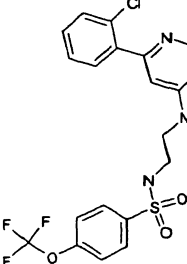
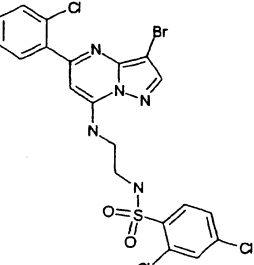
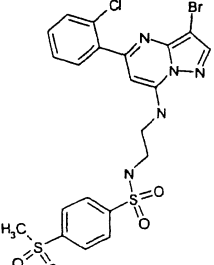
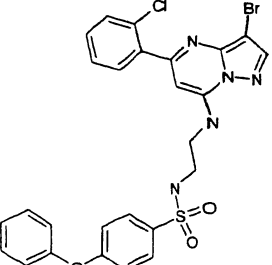
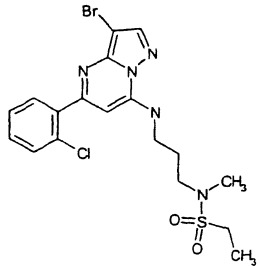
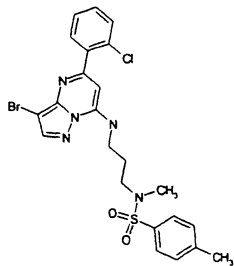
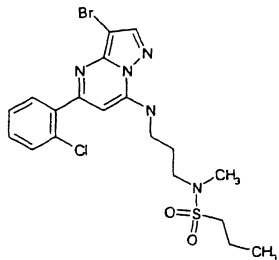
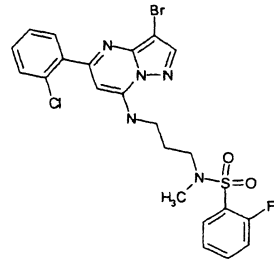
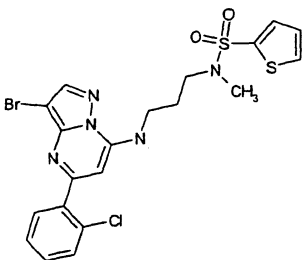
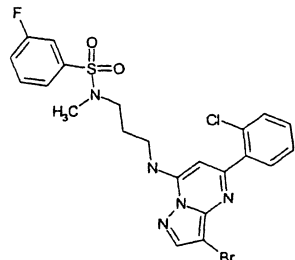
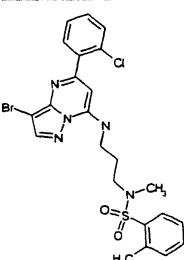
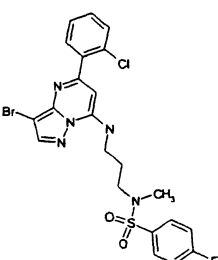
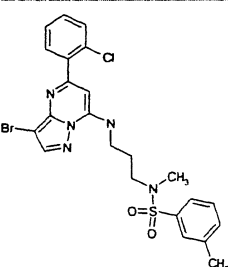
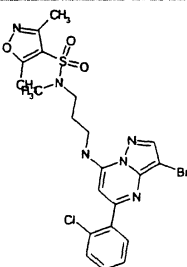
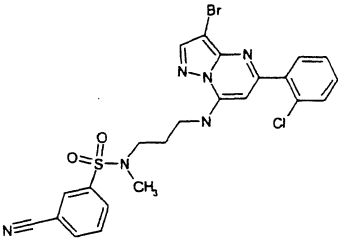
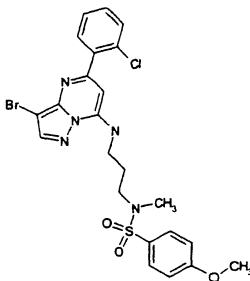
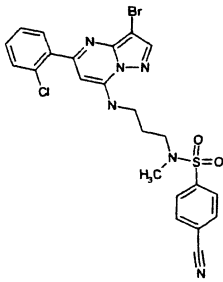
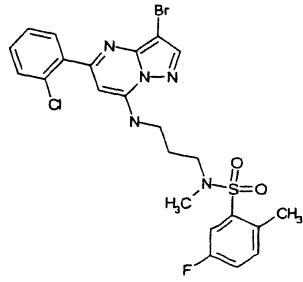
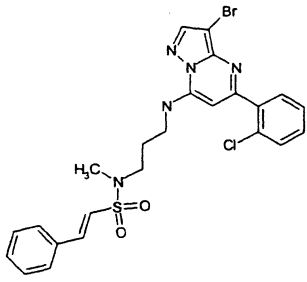
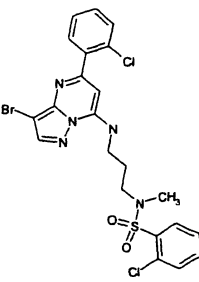
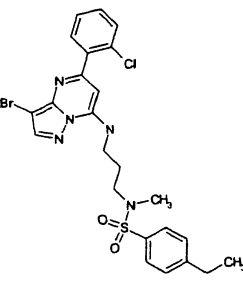
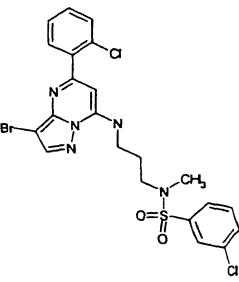
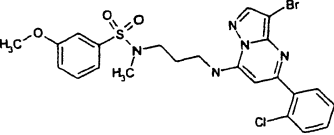
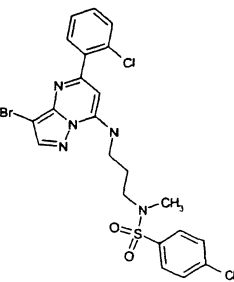
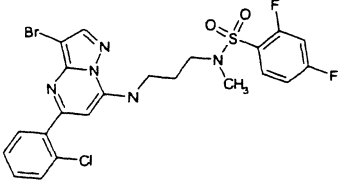
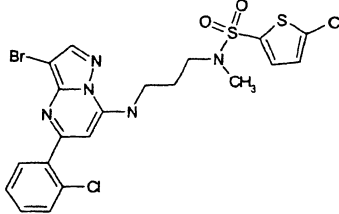
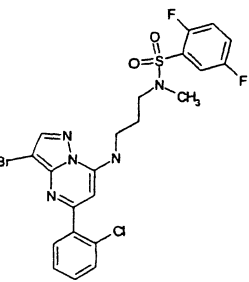
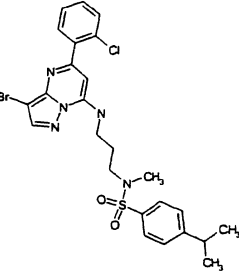
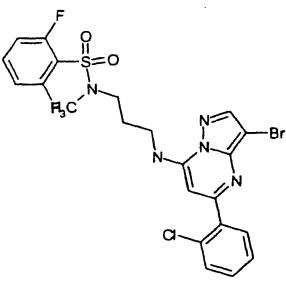
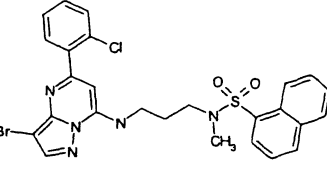
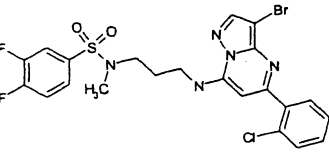
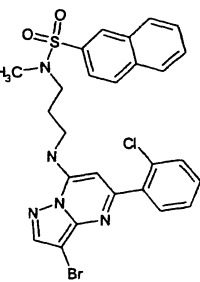
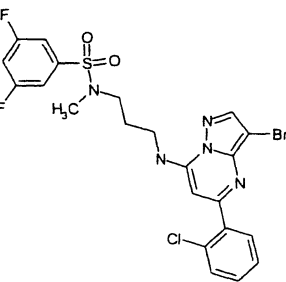
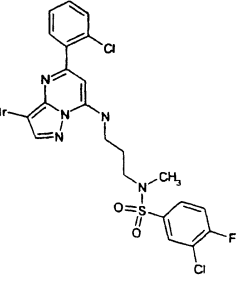
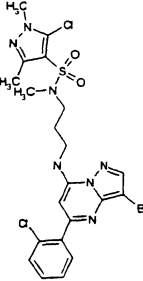
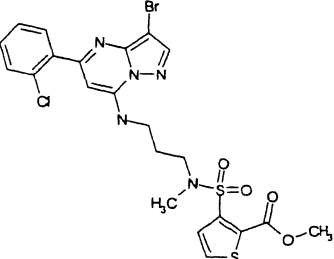
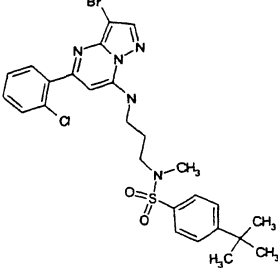
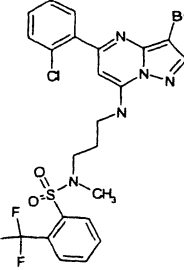
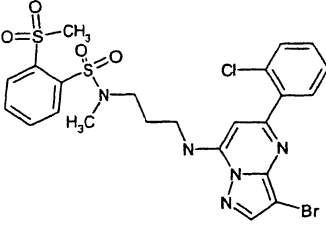
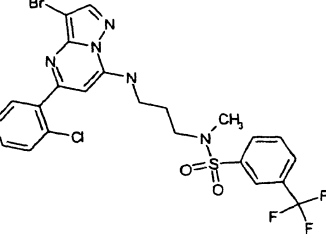
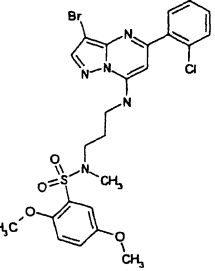
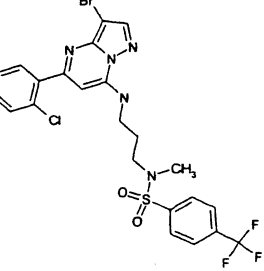
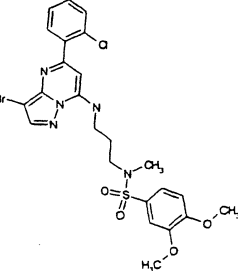
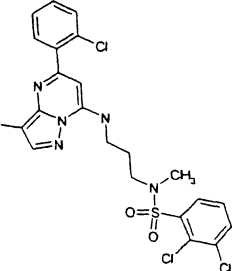
產物	1. 實例 2. m/z	產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
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	1. 6732 2. 576.32		1. 6737 2. 576.32		1. 6744 2. 586.32
	1. 6733 2. 576.32		1. 6738 2. 576.32		1. 6743 2. 592.33
	1. 6734 2. 576.32		1. 6739 2. 584.32		1. 6744 2. 592.33
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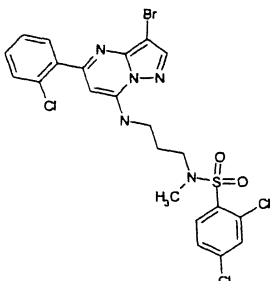
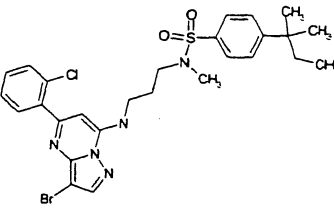
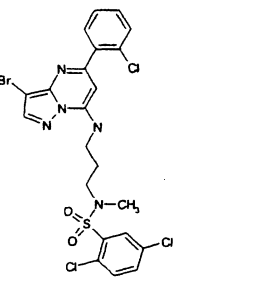
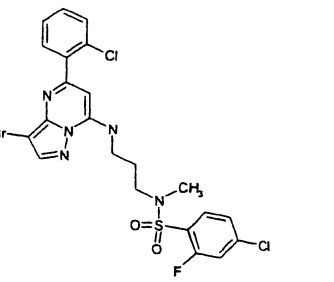
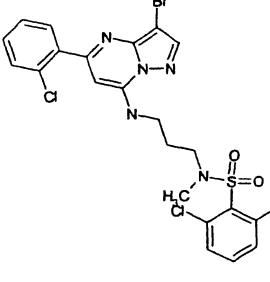
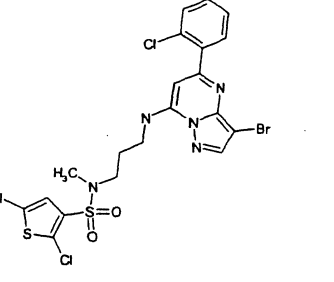
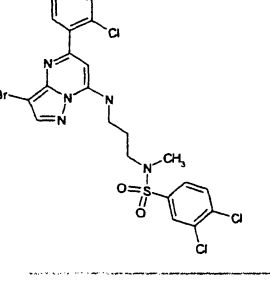
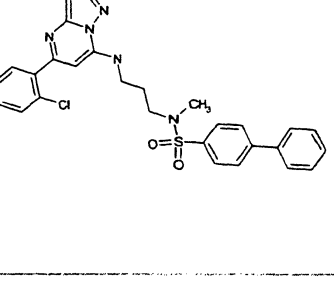
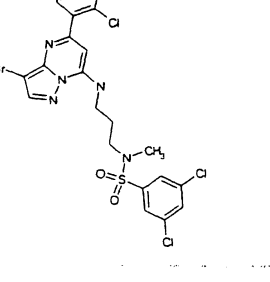
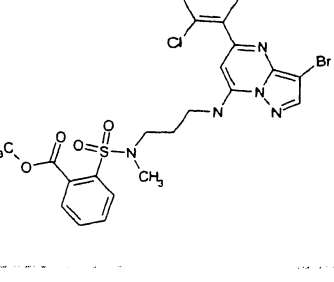
表68

產物	1. 實例2. m/z	產物	1. 實例2. m/z
	1. 6801 2. 488.27		1. 6806 2. 550.3
	1. 6802 2. 502.28		1. 6807 2. 554.3
	1. 6803 2. 542.3		1. 6808 2. 554.3
	1. 6804 2. 550.3		1. 6809 2. 554.3
	1. 68058 2. 550.3		1. 6810 2. 555.31

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 6811 2. 561.31		1. 6816 2. 566.31
	1. 6812 2. 561.31		1. 6817 2. 568.31
	1. 6813 2. 562.31		1. 6818 2. 570.31
	1. 6814 2. 564.31		1. 6819 2. 570.31
	1. 6815 2. 566.31		1. 6820 2. 570.31

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 6821 2. 571.31		1. 6826 2. 576.32
	1. 6822 2. 572.31		1. 6827 2. 578.32
	1. 6823 2. 572.31		1. 6828 2. 586.32
	1. 6824 2. 572.31		1. 6829 2. 586.32
	1. 6825 2. 572.31		1. 6830 2. 588.32

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 6831 2. 588.32		1. 6836 2. 600.33
	1. 6832 2. 592.33		1. 6837 2. 602.33
	1. 6833 2. 614.34		1. 6838 2. 604.33
	1. 6834 2. 596.33		1. 6839 2. 604.33
	1. 6835 2. 596.33		1. 6840 2. 604.33

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 6841 2. 604.33		1. 6846 2. 606.33
	1. 6842 2. 604.33		1. 6847 2. 588.32
	1. 6843 2. 605.33		1. 6848 2. 610.34
	1. 6844 2. 604.33		1. 6849 2. 612.34
	1. 6845 2. 604.33		1. 6850 2. 594.33

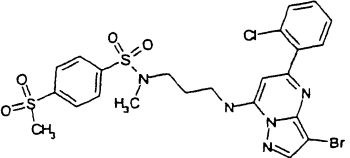
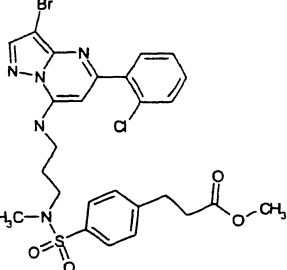
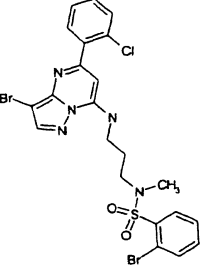
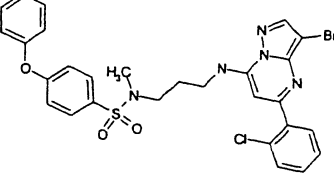
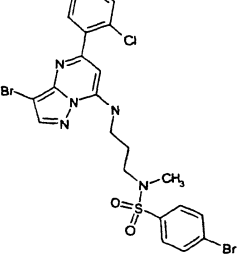
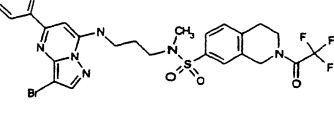
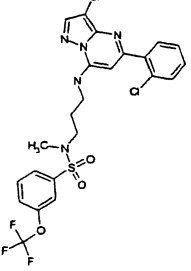
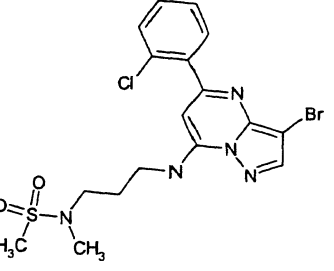
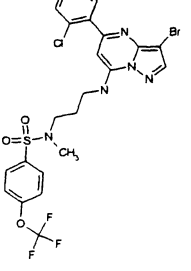
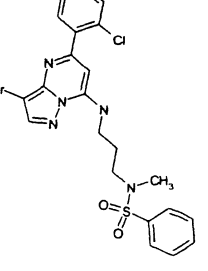
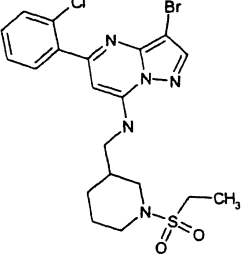
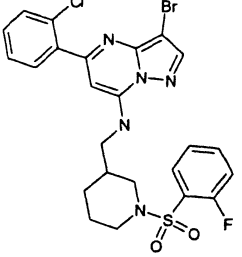
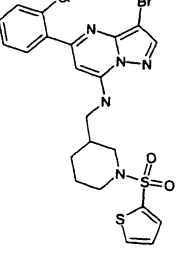
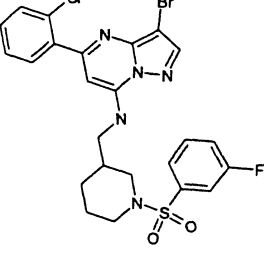
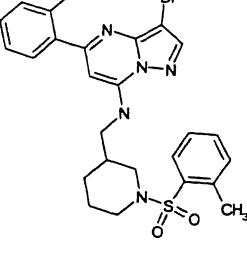
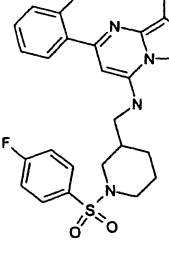
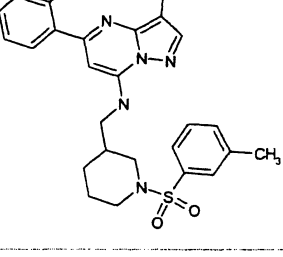
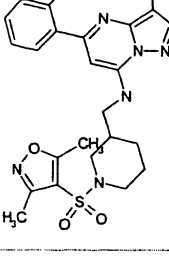
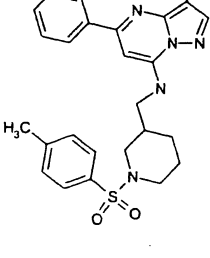
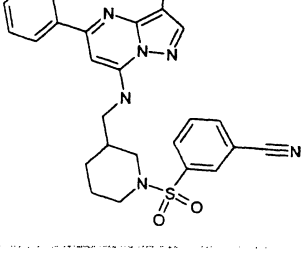
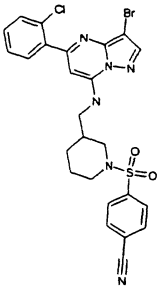
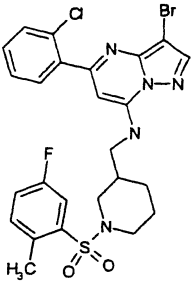
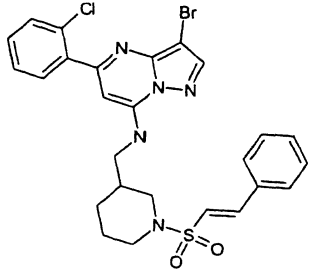
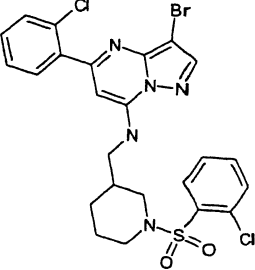
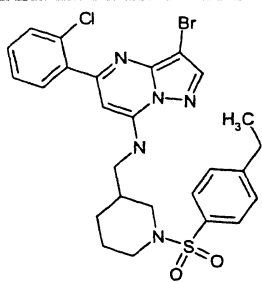
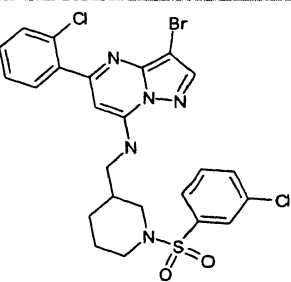
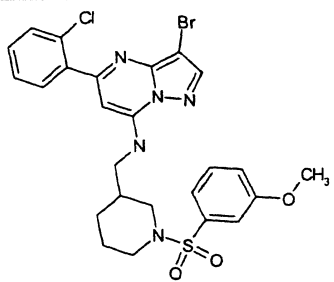
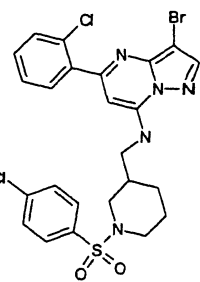
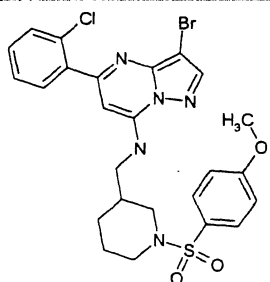
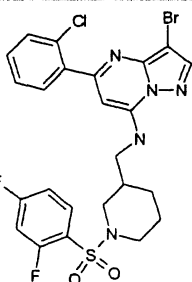
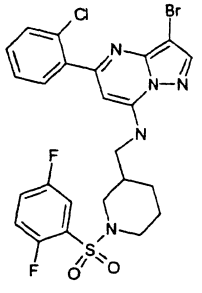
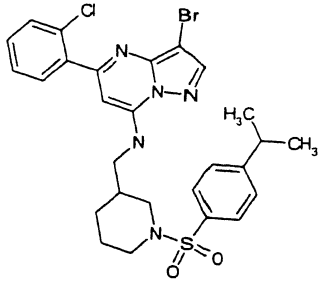
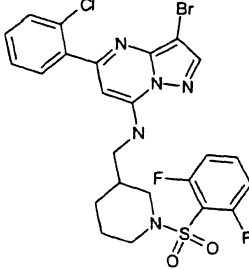
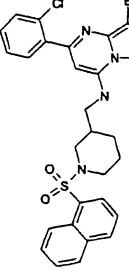
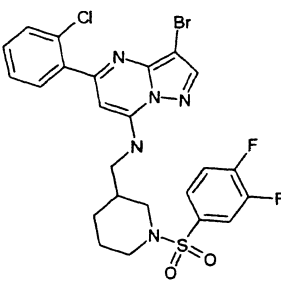
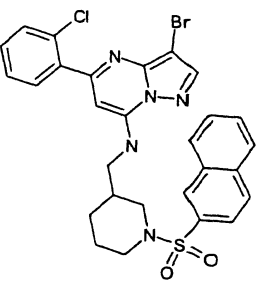
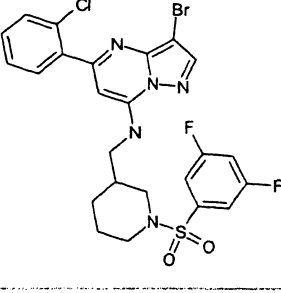
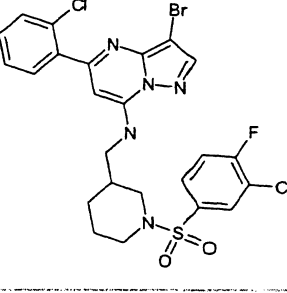
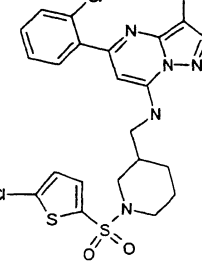
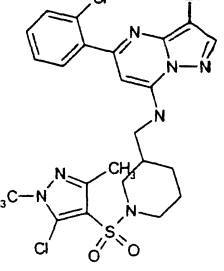
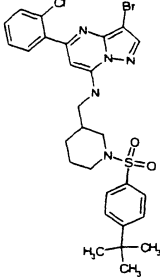
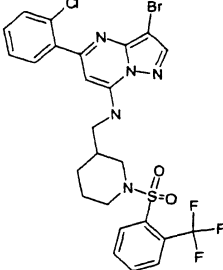
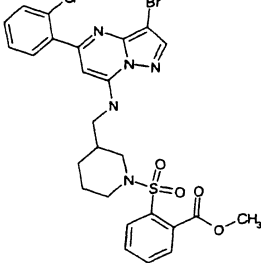
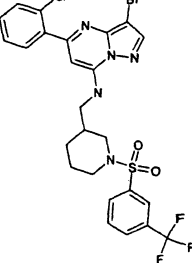
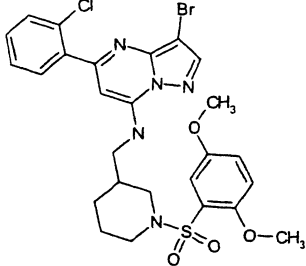
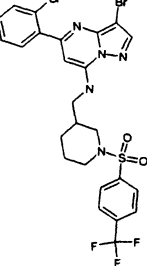
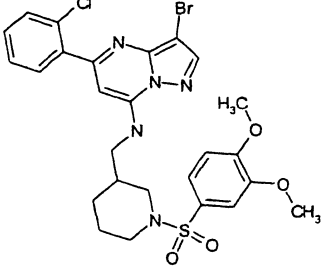
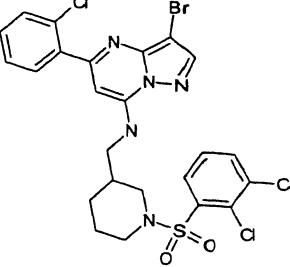
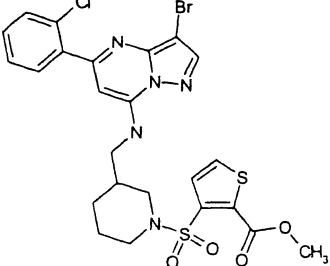
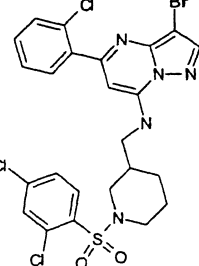
產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 6851 2. 614.34		1. 6856 2. 620.34
	1. 6852 2. 614.34		1. 6856 2. 628.35
	1. 6853 2. 614.34		1. 6857 2. 687.38
	1. 6854 2. 620.34		1. 6859 2. 474.26
	1. 6855 2. 620.34		1. 6860 2. 536.29

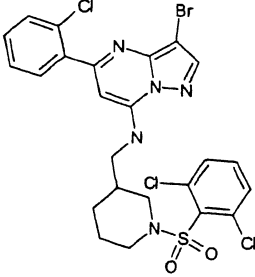
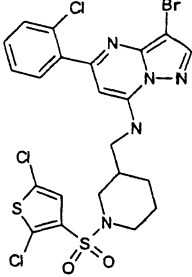
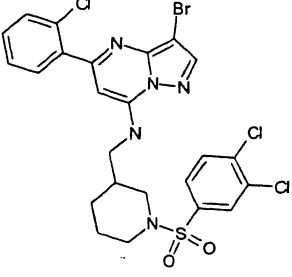
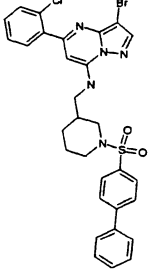
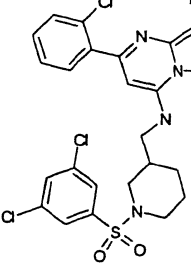
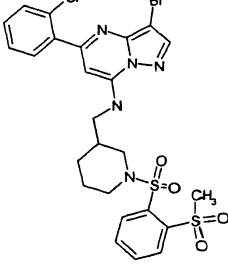
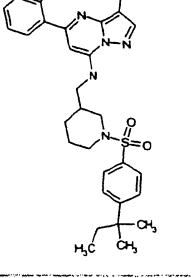
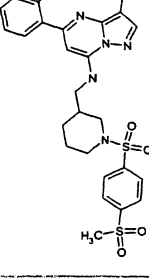
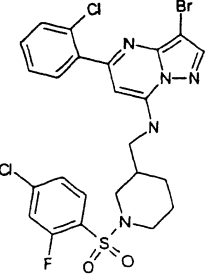
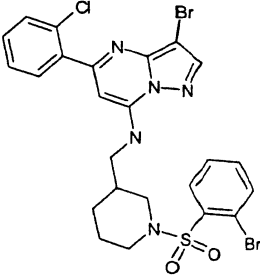
表69

產物	1.實例 2. m/z	產物	1.實例 2. m/z
	1. 6901 2. 514.28		1. 6906 2. 580.32
	1. 6902 2. 568.31		1. 6907 2. 580.32
	1. 6903 2. 576.32		1. 6908 2. 580.32
	1. 6904 2. 576.32		1. 6909 2. 581.32
	1. 6905 2. 576.32		1. 6910 2. 587.32

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 6911 2. 587.32		1. 6916 2. 594.33
	1. 6912 2. 588.32		1. 6917 2. 596.33
	1. 6913 2. 590.32		1. 6918 2. 596.33
	1. 6914 2. 592.33		1. 6919 2. 596.33
	1. 6915 2. 592.33		1. 6920 2. 598.33

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 6921 2. 598.33		1. 6926 2. 604.33
	1. 6922 2. 598.33		1. 6927 2. 612.34
	1. 6923 2. 598.33		1. 6928 2. 612.34
	1. 6924 2. 598.33		1. 6929 2. 614.34
	1. 6925 2. 602.33		1. 6930 2. 614.34

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 6931 2. 618.34		1. 6936 2. 630.35
	1. 6932 2. 620.34		1. 6937 2. 630.35
	1. 6933 2. 622.34		1. 6938 2. 630.35
	1. 6934 2. 622.34		1. 6939 2. 630.35
	1. 6935 2. 626.34		1. 6940 2. 630.35

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 6941 2. 630.35		1. 6946 2. 636.35
	1. 6942 2. 630.35		1. 6947 2. 638.35
	1. 6943 2. 630.35		1. 6948 2. 640.35
	1. 6944 2. 632.35		1. 6949 2. 640.35
	1. 6945 2. 614.34		1. 6950 2. 640.35

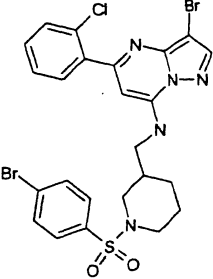
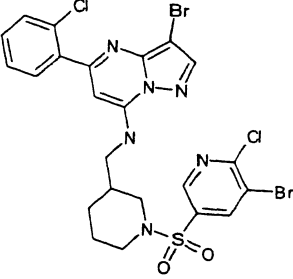
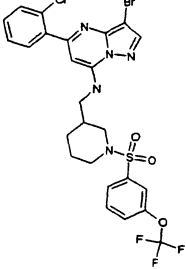
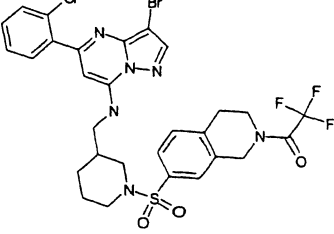
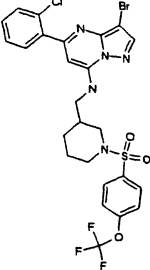
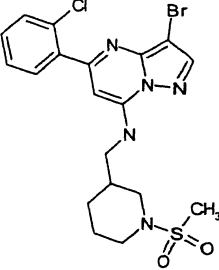
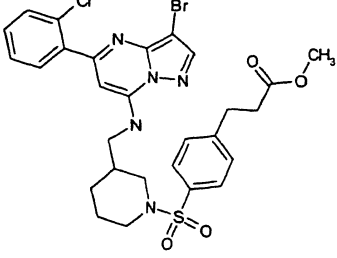
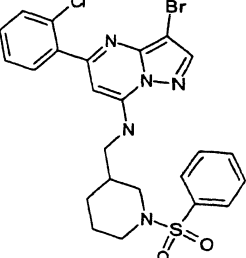
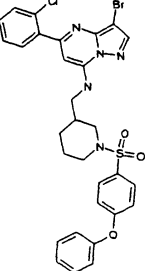
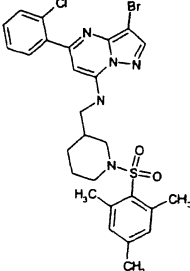
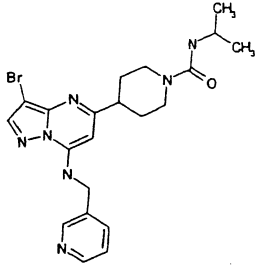
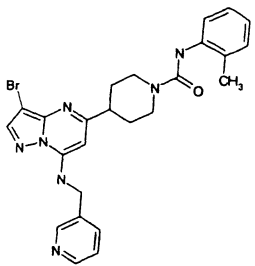
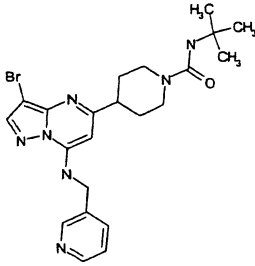
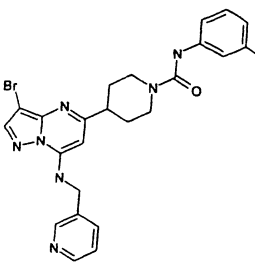
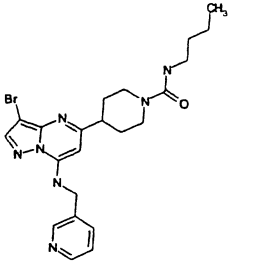
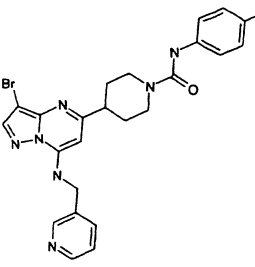
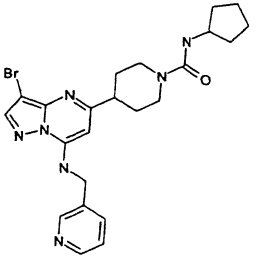
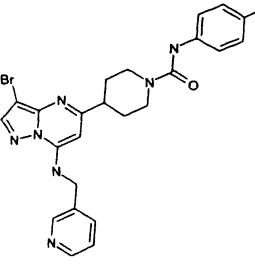
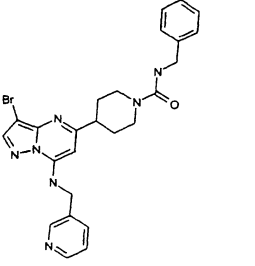
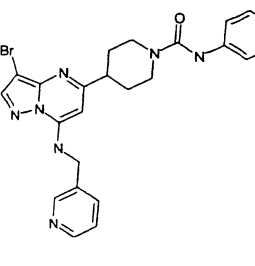
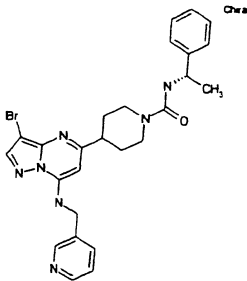
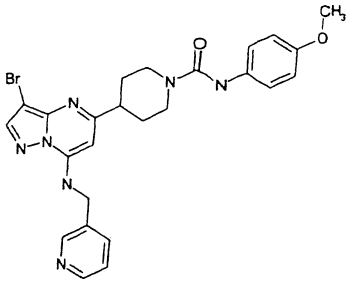
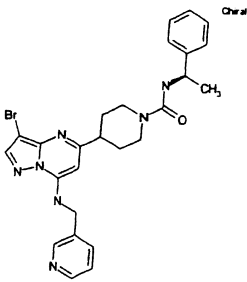
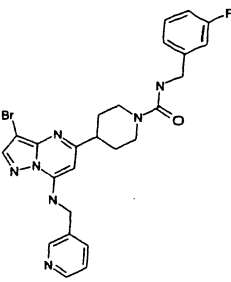
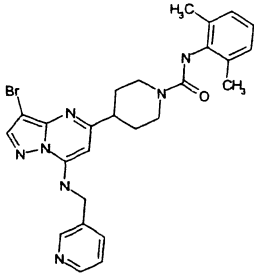
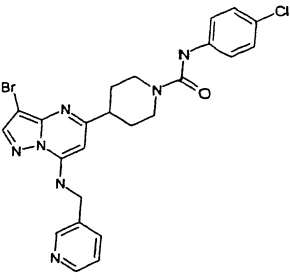
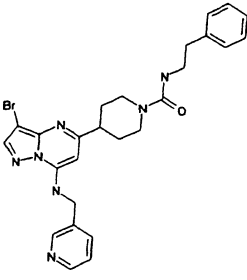
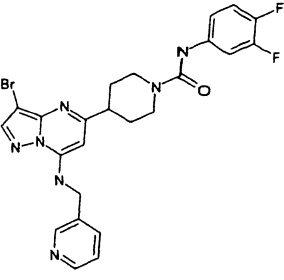
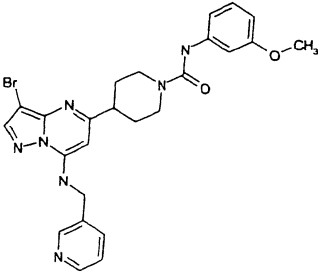
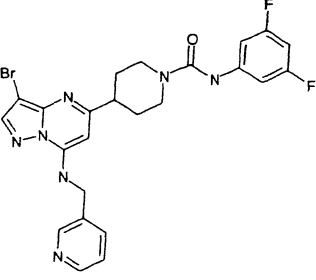
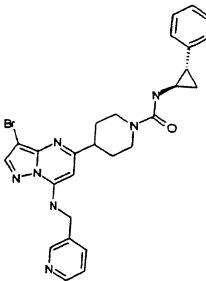
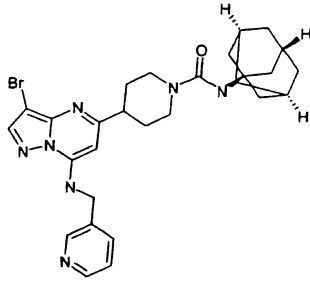
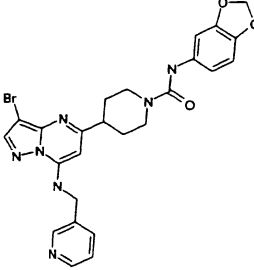
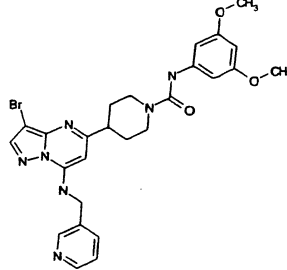
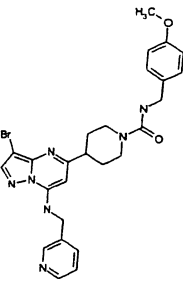
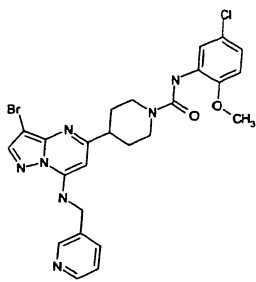
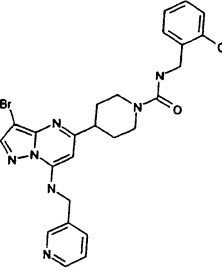
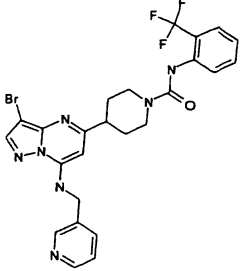
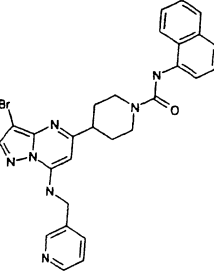
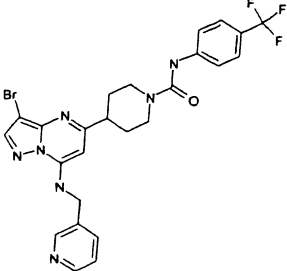
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	1. 6951 2. 640.35		1. 6956 2. 675.23
	1. 6952 2. 646.36		1. 6957 2. 713.39
	1. 6953 2. 646.36		1. 6958 2. 500.27
	1. 6954 2. 648.36		1. 6959 2. 562.31
	1. 6955 2. 654.36		1. 6960 2. 604.33

表70

產物	1.實例2. m/z	產物	1.實例2. m/z
	1. 7001 2. 472.26		1. 7006 2. 522.29
	1. 7002 2. 488.27		1. 7007 2. 520.29
	1. 7003 2. 488.27		1. 7008 2. 520.29
	1. 7004 2. 500.27		1. 7009 2. 526.29
	1. 7005 2. 520.29		1. 7010 2. 533.29

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 7011 2. 536.29		1. 7016 2. 538.3
	1. 7012 2. 536.29		1. 7017 2. 540.3
	1. 7013 2. 536.29		1. 7018 2. 542.3
	1. 7014 2. 536.29		1. 7019 2. 544.3
	1. 7015 2. 536.29		1. 7020 2. 544.3

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 7021 2. 548.3		1. 7026 2. 566.31
	1. 7022 2. 552.3		1. 7027 2. 568.31
	1. 7023 2. 552.3		1. 7028 2. 572.31
	1. 7024 2. 556.31		1. 7029 2. 576.32
	1. 7025 2. 558.31		1. 7030 2. 576.32

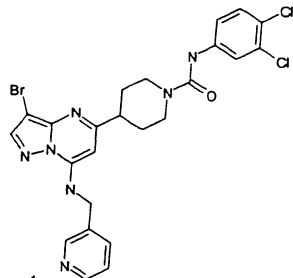
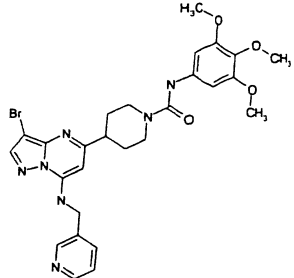
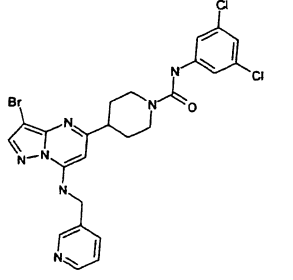
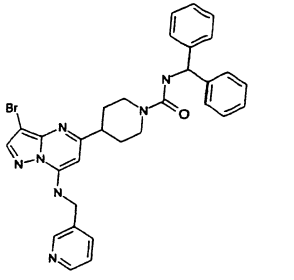
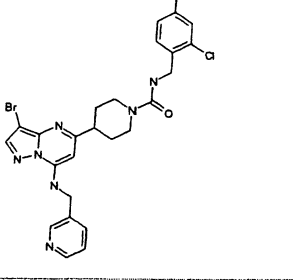
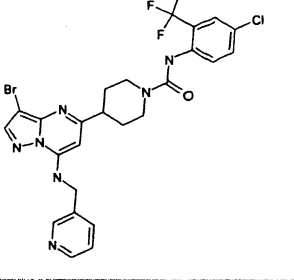
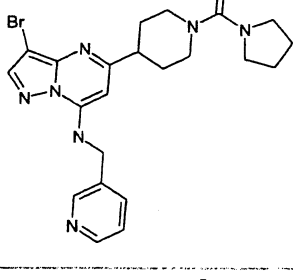
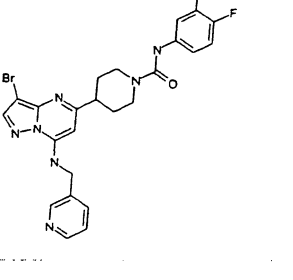
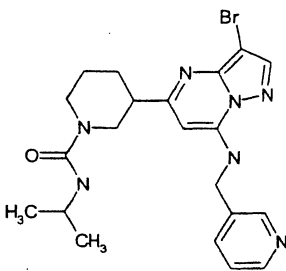
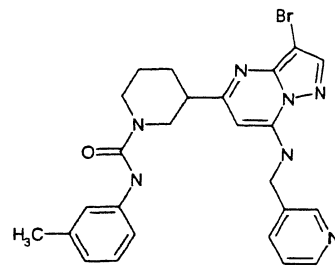
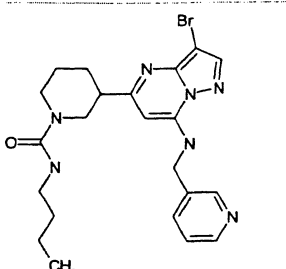
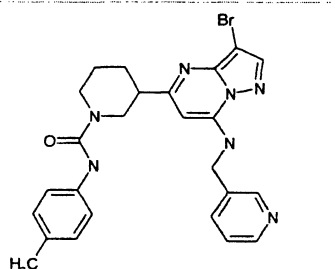
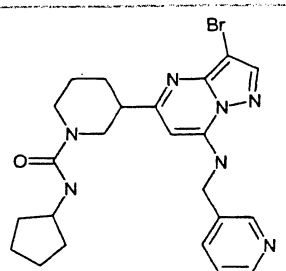
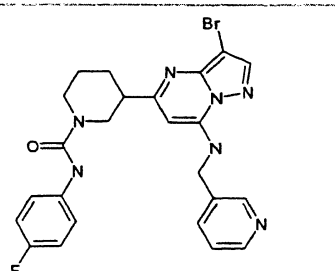
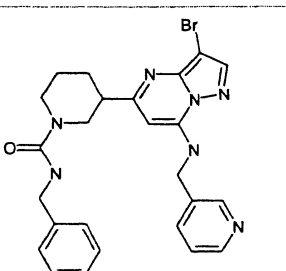
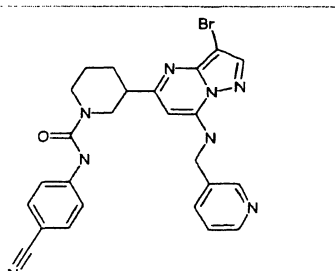
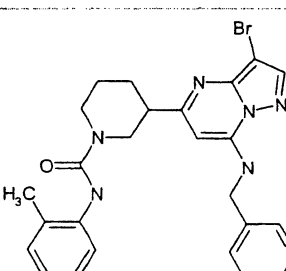
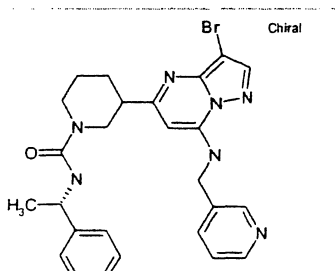
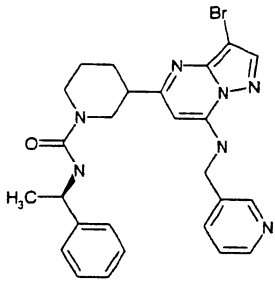
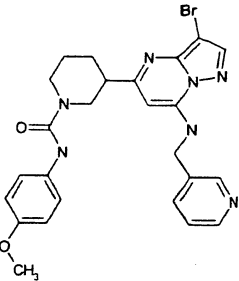
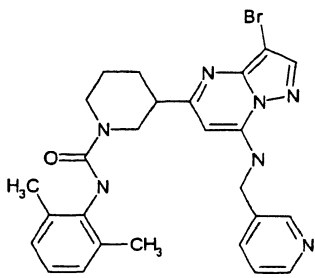
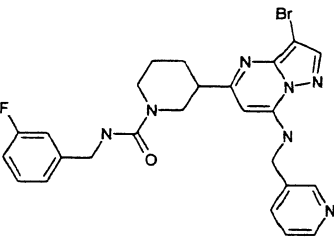
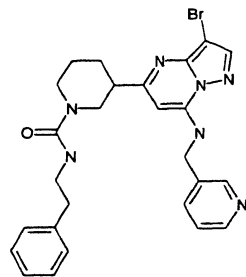
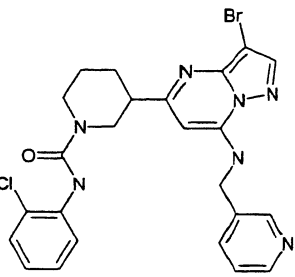
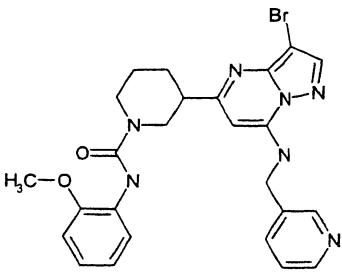
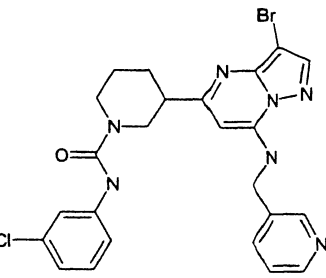
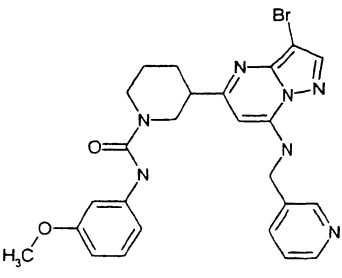
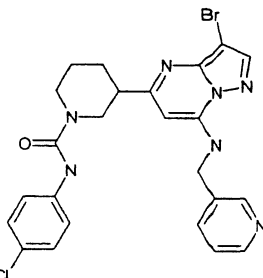
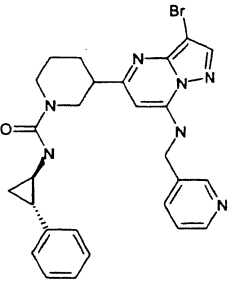
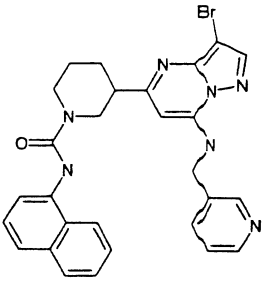
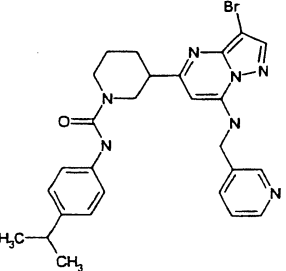
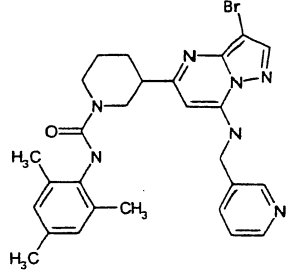
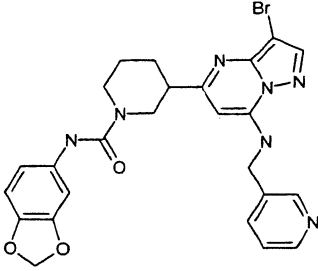
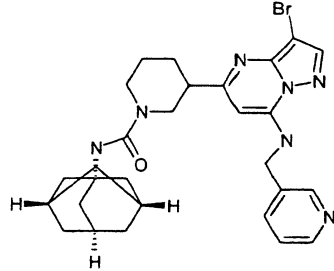
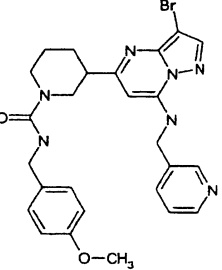
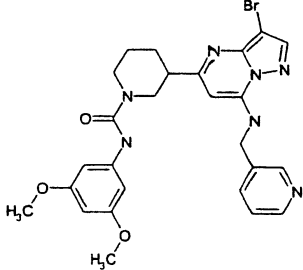
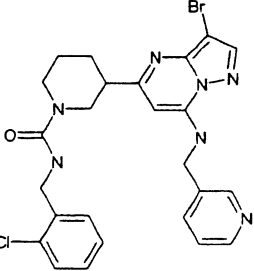
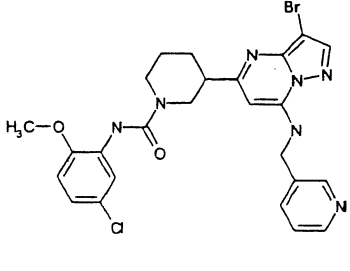
產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 7031 2. 576.32		1. 7036 2. 598.33
	1. 7032 2. 576.32		1. 7037 2. 598.33
	1. 7033 2. 590.32		1. 7038 2. 610.34
	1. 7034 2. 486.27		
	1. 7035 2. 594.33		

表71

產物	1.實例 2. m/z	產物	1.實例 2. m/z
	1. 7101 2. 474.26		1. 7106 2. 522.29
	1. 7102 2. 488.27		1. 7107 2. 522.29
	1. 7103 2. 500.27		1. 7108 2. 526.3
	1. 7104 2. 522.29		1. 7109 2. 533.29
	1. 7105 2. 522.29		1. 7110 2. 536.29

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
 Chiral	1. 7111 2. 536.29		1. 7116 2. 538.3
	1. 7112 2. 536.29		1. 7117 2. 540.3
	1. 7113 2. 536.29		1. 7118 2. 542.3
	1. 7114 2. 536.29		1. 7119 2. 542.3
	1. 7115 2. 536.3		1. 7120 2. 542.3

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 7121 2. 546.3		1. 7126 2. 558.31
	1. 7122 2. 550.3		1. 7127 2. 550.3
	1. 7123 2. 552.3		1. 7128 2. 566.31
	1. 7124 2. 552.3		1. 7129 2. 565.31
	1. 7125 2. 556.31		1. 7130 2. 572.31

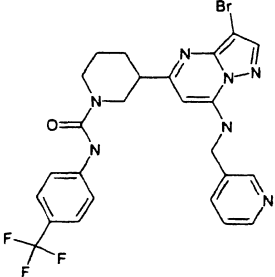
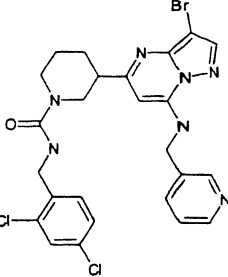
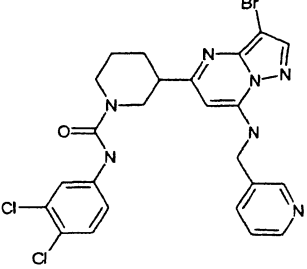
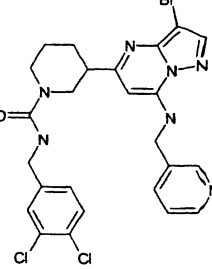
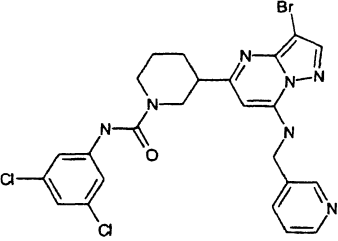
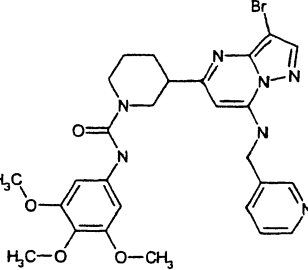
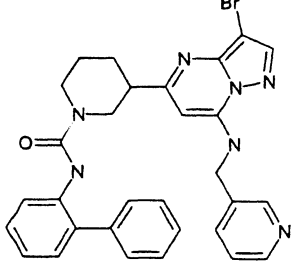
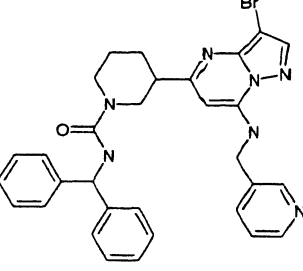
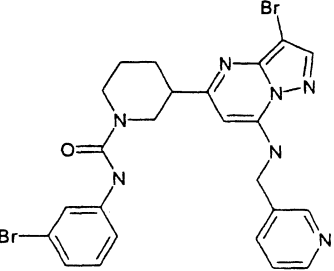
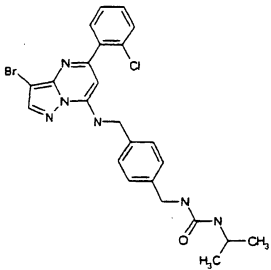
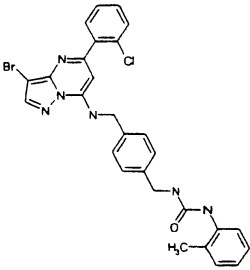
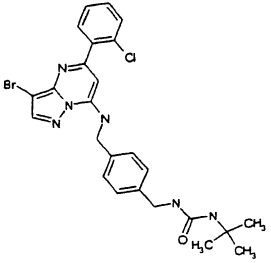
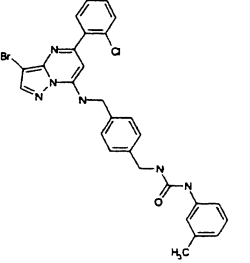
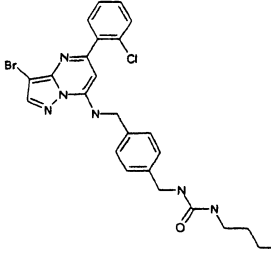
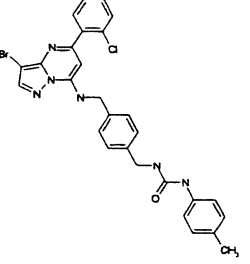
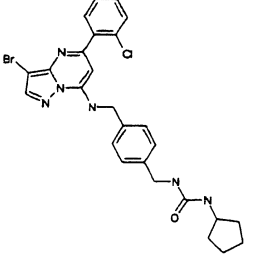
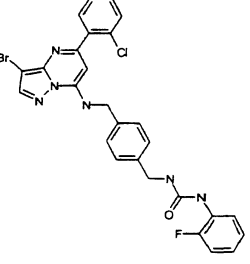
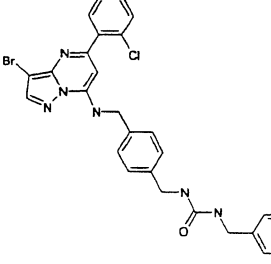
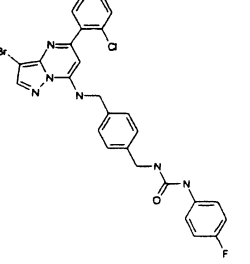
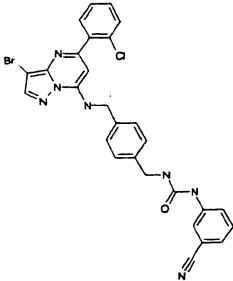
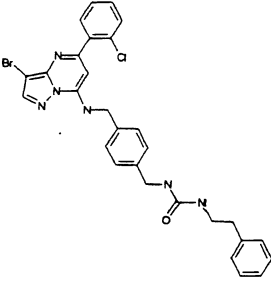
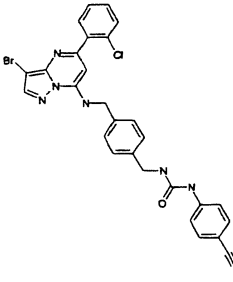
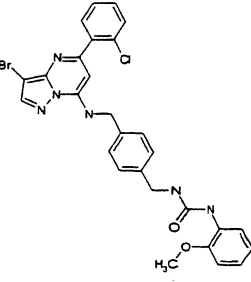
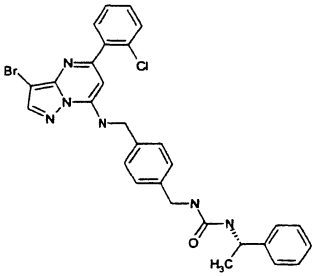
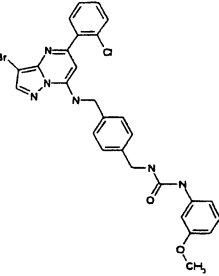
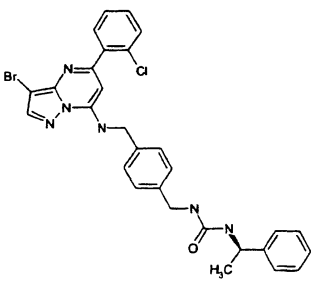
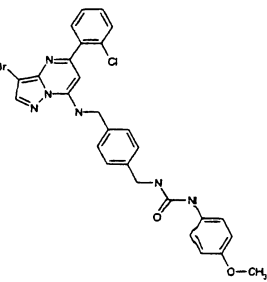
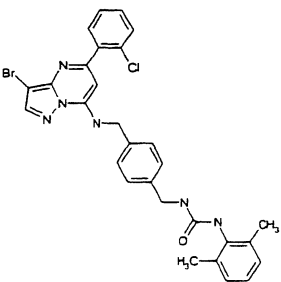
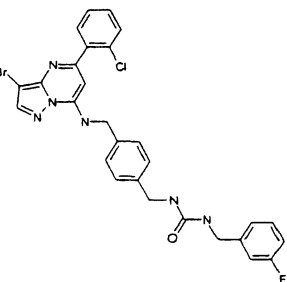
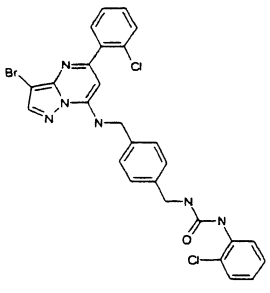
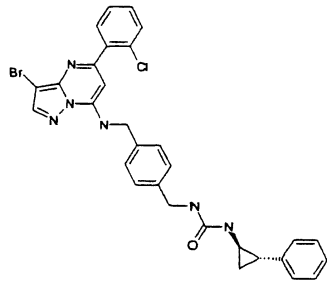
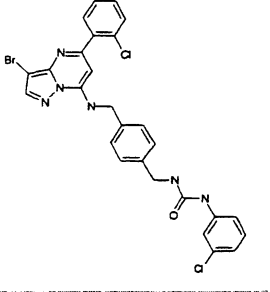
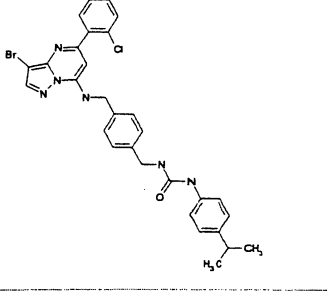
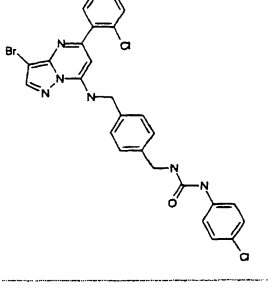
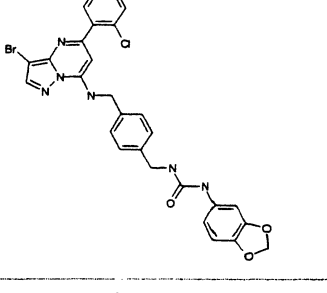
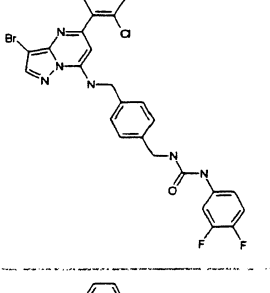
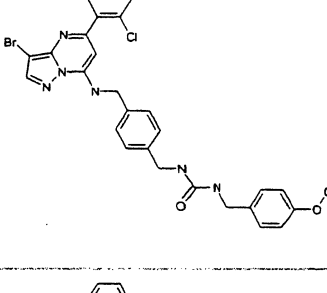
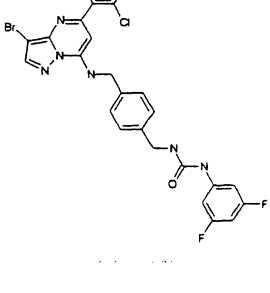
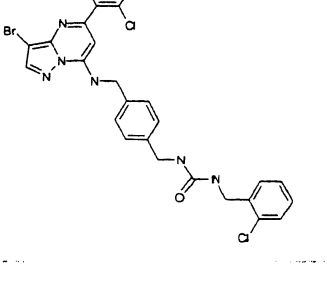
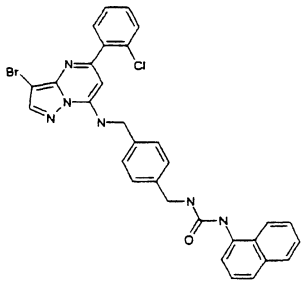
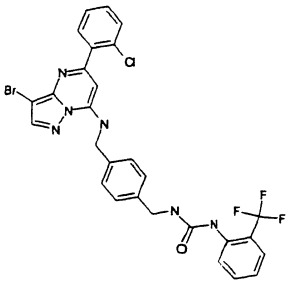
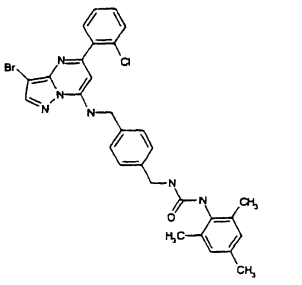
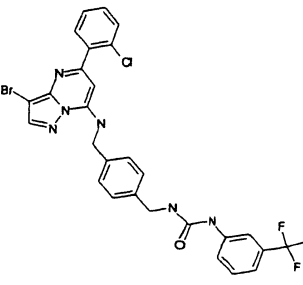
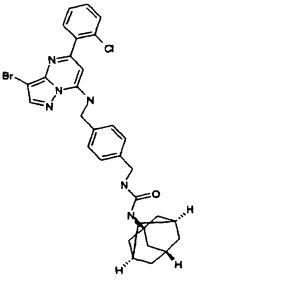
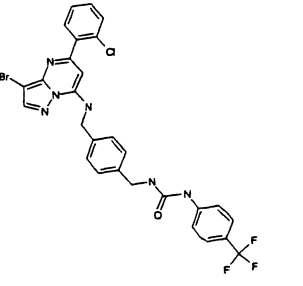
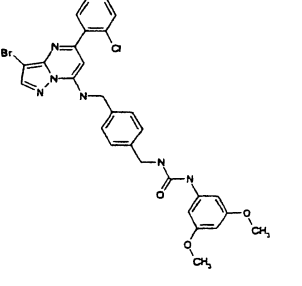
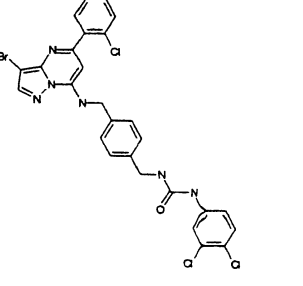
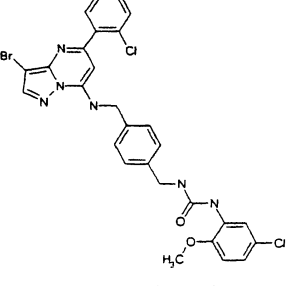
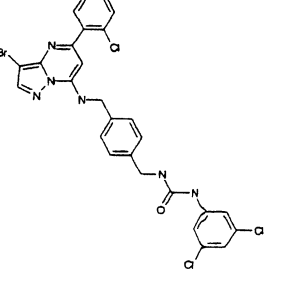
產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 7131 2. 576.32		1. 7136 2. 590.32
	1. 7132 2. 576.32		1. 7137 2. 590.32
	1. 7133 2. 576.32		1. 7138 2. 598.33
	1. 7134 2. 584.32		1. 7139 2. 598.33
	1. 7135 2. 585.3		

表72

產物	1. 實例2. m/z	產物	1. 實例2. m/z
	1. 7201 2. 529.29		1. 7206 2. 577.32
	1. 7202 2. 543.3		1. 7207 2. 577.32
	1. 7203 2. 543.3		1. 7208 2. 577.32
	1. 7204 2. 555.31		1. 7209 2. 581.32
	1. 7205 2. 577.32		1. 7210 2. 581.32

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 7211 2. 588.32		1. 7216 2. 591.33
	1. 7212 2. 588.32		1. 7217 2. 593.33
	1. 7213 2. 591.33		1. 7218 2. 593.33
	1. 7214 2. 591.33		1. 7219 2. 593.33
	1. 7215 2. 591.33		1. 7220 2. 595.33

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 7221 2. 597.33		1. 7226 2. 603.33
	1. 7222 2. 597.33		1. 7227 2. 603.33
	1. 7223 2. 597.33		1. 7228 2. 607.33
	1. 7224 2. 599.33		1. 7229 2. 607.14
	1. 7225 2. 599.33		1. 7230 2. 611.34

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 7231 2. 613.34		1. 7236 2. 631.35
	1. 7232 2. 605.33		1. 7237 2. 631.35
	1. 7233 2. 621.34		1. 7238 2. 631.35
	1. 7234 2. 623.34		1. 7239 2. 631.35
	1. 7235 2. 627.34		1. 7240 2. 631.35

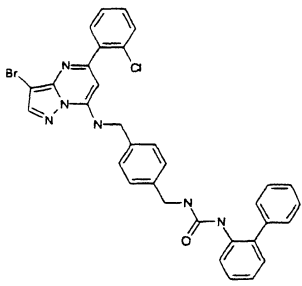
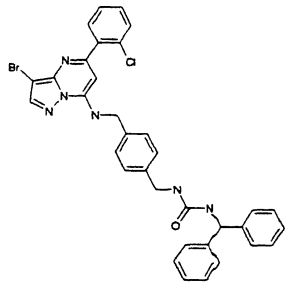
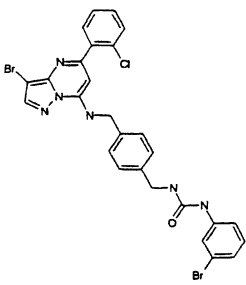
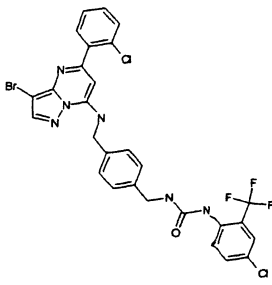
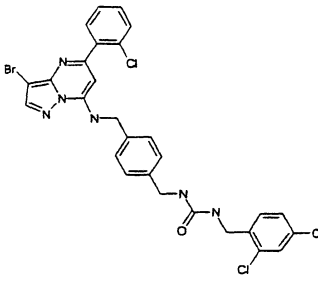
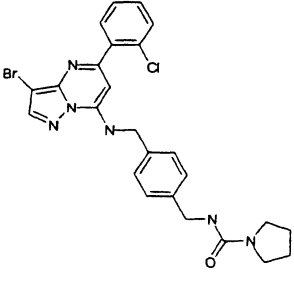
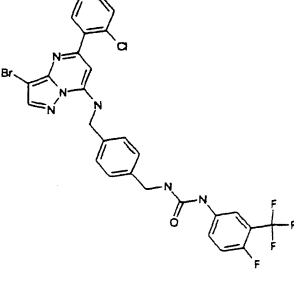
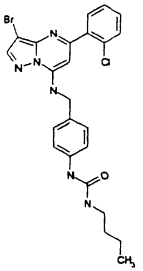
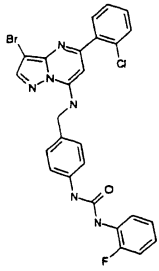
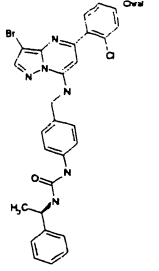
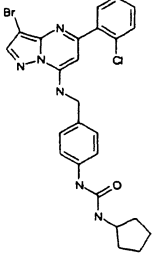
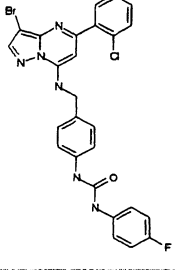
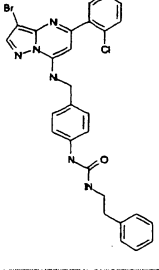
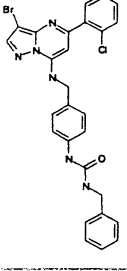
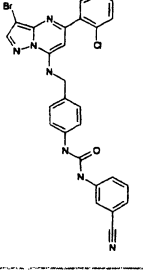
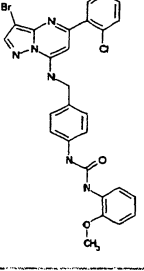
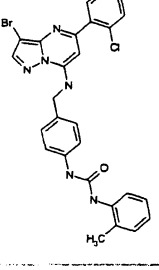
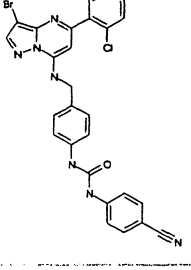
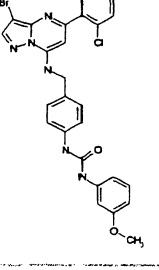
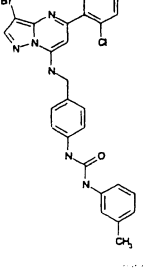
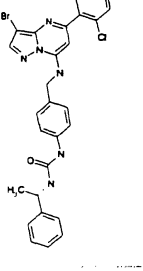
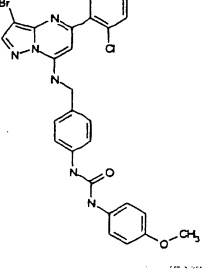
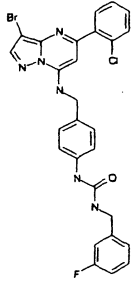
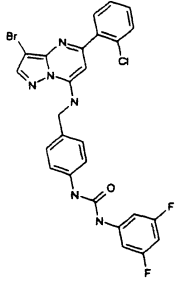
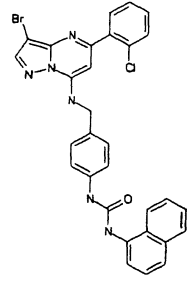
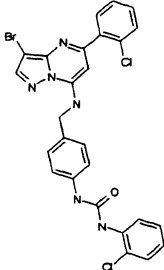
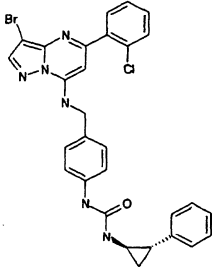
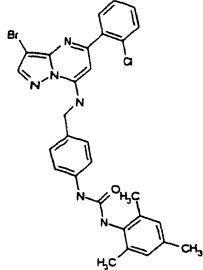
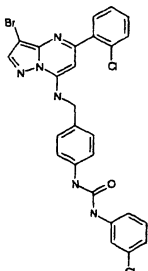
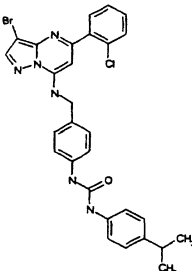
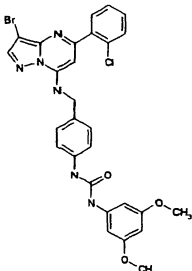
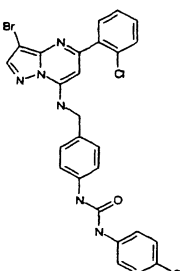
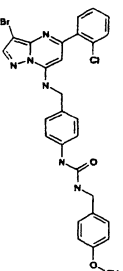
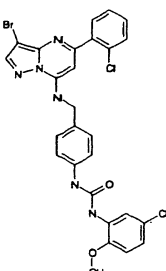
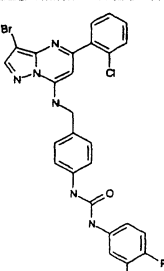
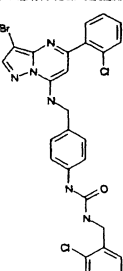
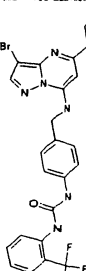
產物	1. 實例2. m/z	產物	1. 實例2. m/z
	1. 7241 2. 639.35		1. 7246 2. 653.36
	1. 7242 2. 641.35		1. 7247 2. 665.37
	1. 7243 2. 645.35		
	1. 7244 2. 541.3		
	1. 7245 2. 649.36		

表73

產物	1. 實例2. m/z	產物	1. 實例2. m/z	產物	1. 實例2. m/z
	1. 7301 2. 529.29		1. 7306 2. 567.31		1. 7311 2. 577.32
	1. 7302 2. 541.3		1. 7307 2. 567.31		1. 7312 2. 577.32
	1. 7303 2. 563.13		1. 7308 2. 574.32		1. 7313 2. 579.32
	1. 7304 2. 563.31		1. 7309 2. 574.32		1. 7314 2. 579.32
	1. 7305 2. 563.31		1. 7310 2. 577.32		1. 7315 2. 579.32

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 7316 2. 581.32		1. 7321 2. 585.32		1. 7326 2. 599.33
	1. 7317 2. 583.32		1. 7322 2. 589.32		1. 7327 2. 591.33
	1. 7318 2. 583.32		1. 7323 2. 591.33		1. 7328
	1. 7319 2. 583.32		1. 7324 2. 593.33		1. 7329 2. 613.34
	1. 7320 2. 585.32		1. 7325 2. 597.33		1. 7330 2. 617.34

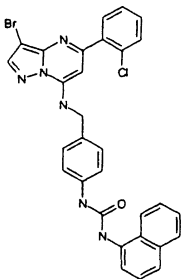
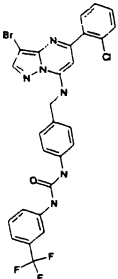
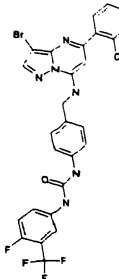
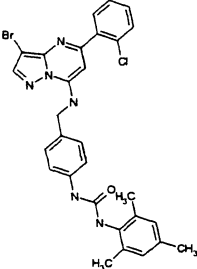
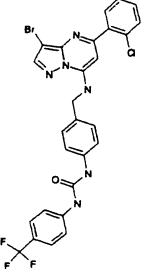
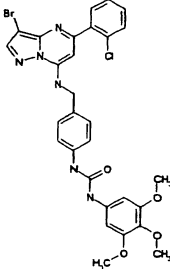
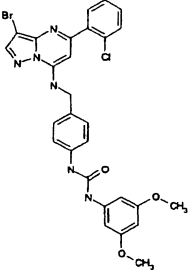
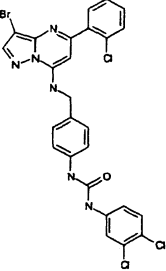
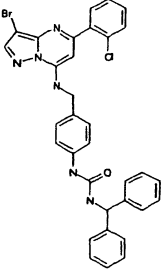
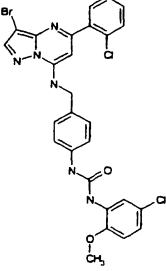
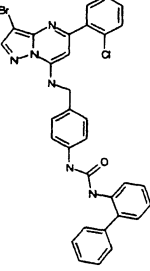
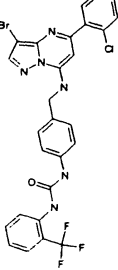
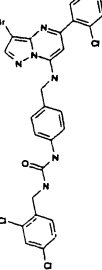
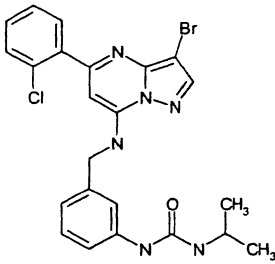
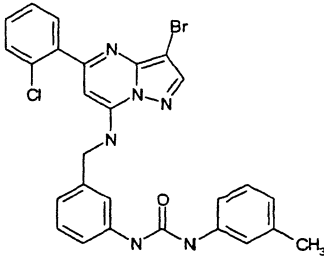
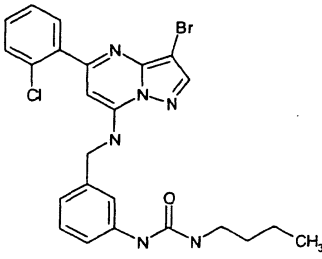
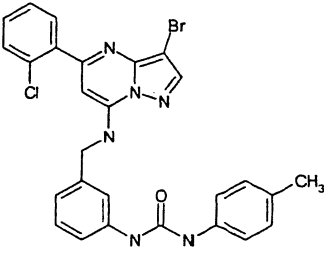
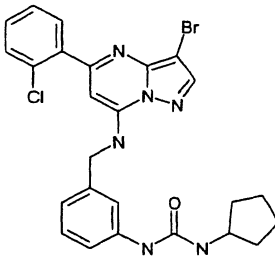
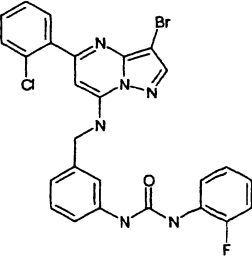
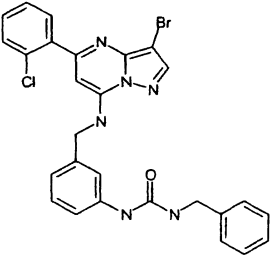
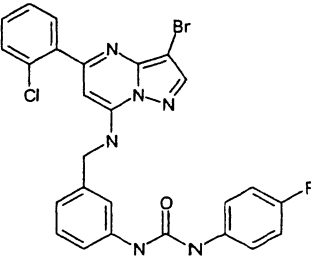
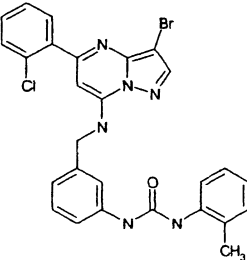
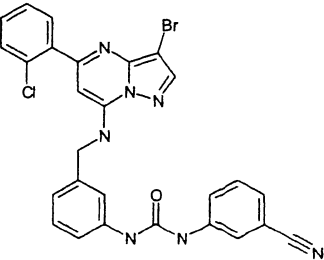
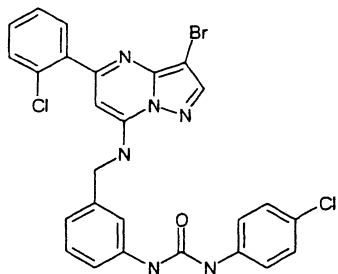
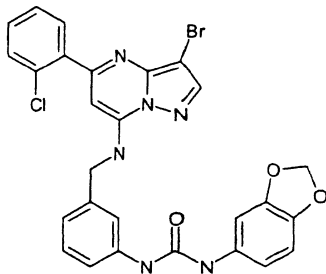
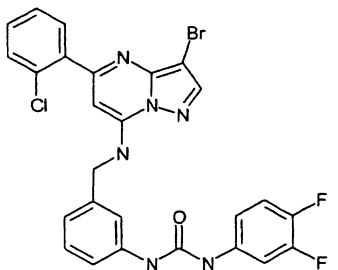
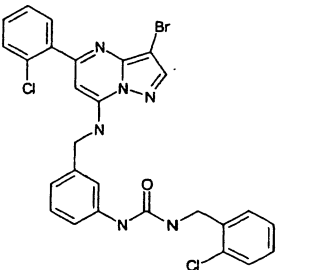
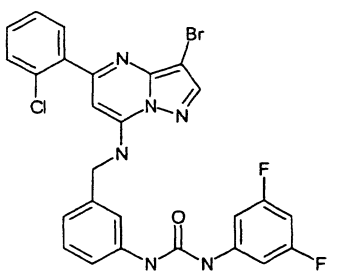
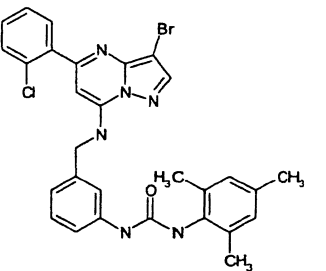
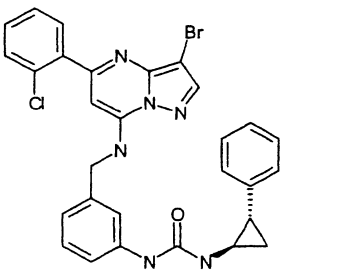
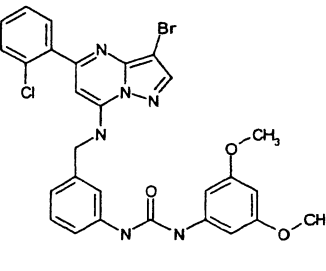
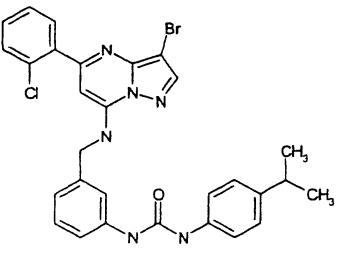
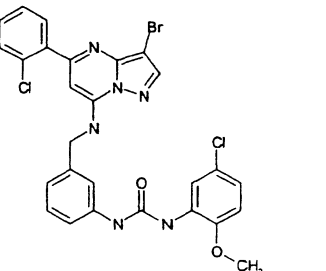
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	1. 7331 2. 599.33		1. 7336 2. 617.34		1. 73412. 2. 635.35
	1. 7332 2. 591.33		1. 7337 2. 617.34		1. 7342 2. 639.35
	1. 7333 2. 609.33		1. 7338 2. 617.34		1. 7343 2. 639.35
	1. 7334 2. 613.34		1. 7339 2. 625.34		
	1. 7335 2. 617.34		1. 7340 2. 631.35		

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產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 7401 2. 515.28		1. 7406 2. 563.31
	1. 7402 2. 529.29		1. 7407 2. 563.31
	1. 7403 2. 541.3		1. 7408 2. 567.31
	1. 7404 2. 563.13		1. 7409 2. 567.31
	1. 7405 2. 563.31		1. 7410 2. 574.32

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 7411 2. 574.32		1. 7416 2. 579.32
	1. 7412 2. 577.14		1. 7417 2. 579.32
	1. 7413 2. 577.32		1. 7418 2. 579.32
	1. 7414 2. 577.32		1. 7419 2. 581.32
	1. 7415 2. 577.32		1. 7420 2. 583.32

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 7421 2. 583.32		1. 7426 2. 593.33
	1. 7422 2. 585.32		1. 7427 2. 597.33
	1. 7423 2. 585.32		1. 7428 2. 591.33
	1. 7424 2. 589.32		1. 7429 2. 609.33
	1. 7425 2. 591.33		1. 7430 2. 613.34

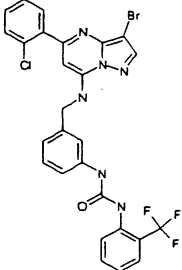
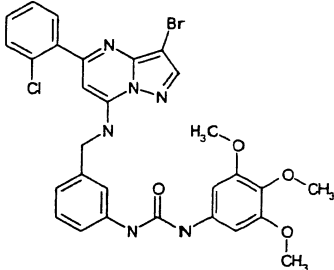
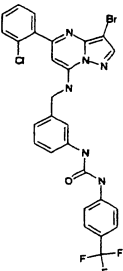
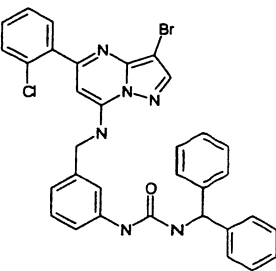
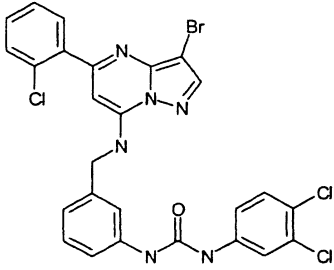
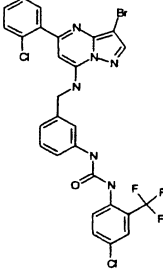
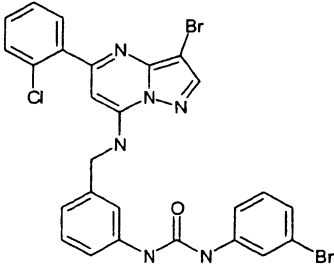
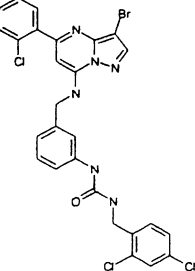
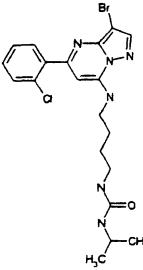
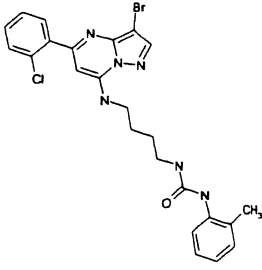
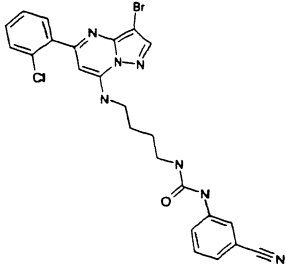
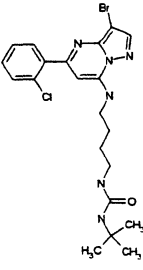
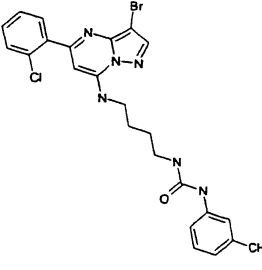
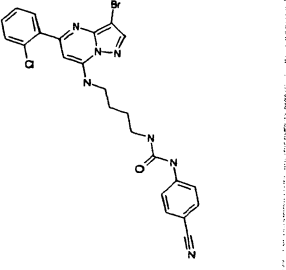
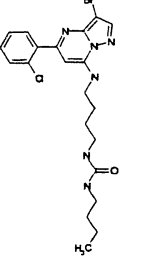
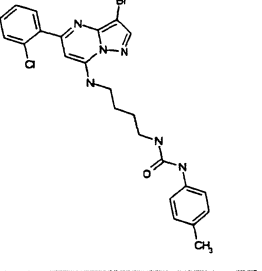
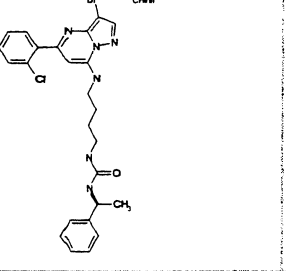
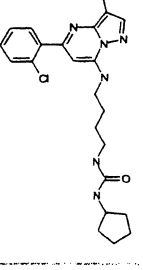
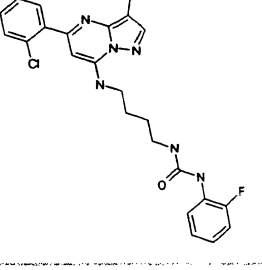
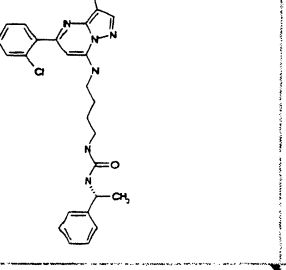
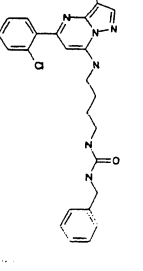
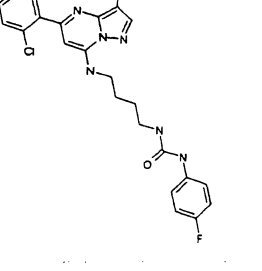
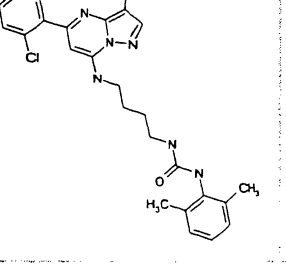
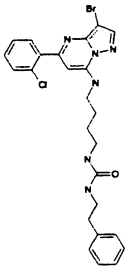
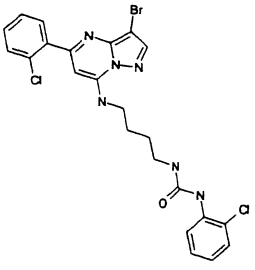
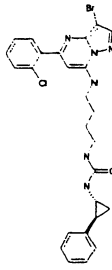
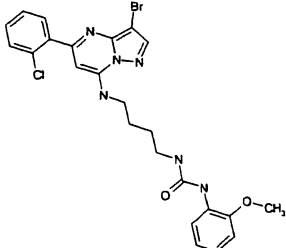
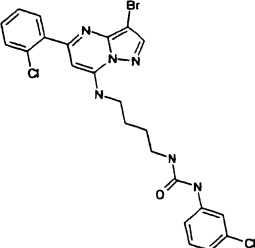
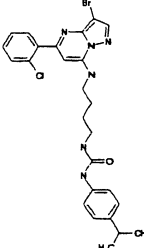
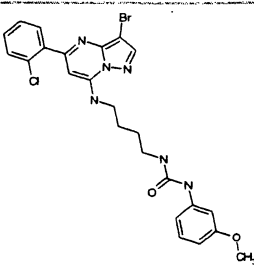
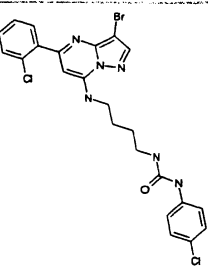
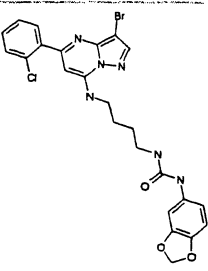
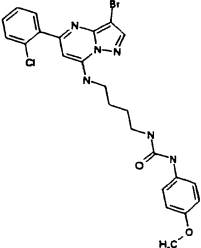
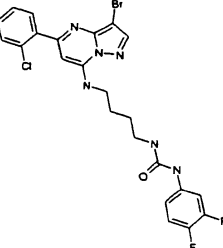
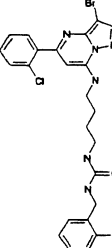
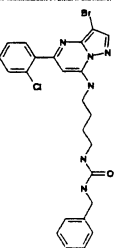
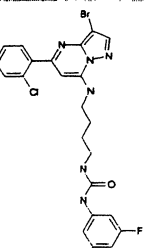
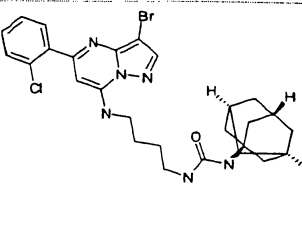
產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 7431 2. 617.34		1. 7436 2. 639.35
	1. 7432 2. 617.34		1. 7437 2. 639.35
	1. 7433 2. 617.34		1. 7438 2. 651.36
	1. 7434 2. 627.34		
	1. 7435 2. 631.35		

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產物	1.實例2. m/z	產物	1.實例2. m/z	產物	1.實例2. m/z
	1. 7501 2. 481.26		1. 7506 2. 529.29		1. 7511 2. 540.3
	1. 7502 2. 495.27		1. 7507 2. 529.29		1. 7512 2. 540.3
	1. 7503 2. 495.27		1. 7508 2. 529.29		1. 7513 2. 543.3
	1. 7504 2. 507.28		1. 7509 2. 533.29		1. 7514 2. 543.3
	1. 7505 2. 529.29		1. 7510 2. 533.29		1. 7515 2. 543.3

產物	1.實例2. m/z	產物	1.實例2. m/z	產物	1.實例2 m/z
	1. 7516 2. 543.3		1. 7521 2. 549.3		1. 7526 2. 555.3
	1. 7517 2. 545.3		1. 7522 2. 549.3		1. 7527 2. 557.3
	1. 7518 2. 545.3		1. 7523 2. 549.3		1. 7528 2. 559.31
	1. 7519 2. 545.3		1. 7524 2. 551.3		1. 7529 2. 560.31
	1. 7520 2. 547.3		1. 7525 2. 551.3		1. 7530 2. 573.32

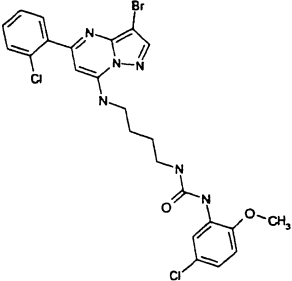
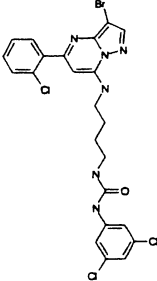
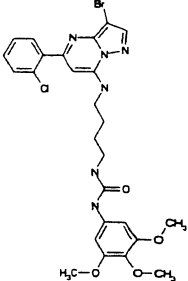
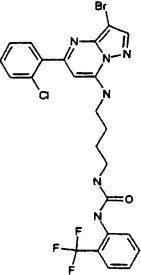
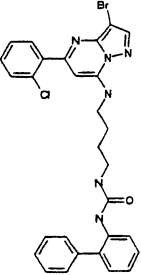
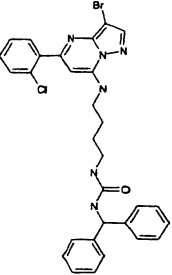
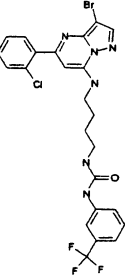
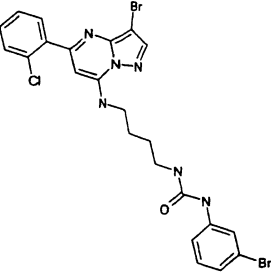
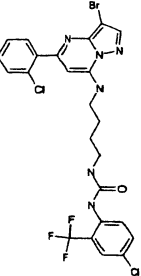
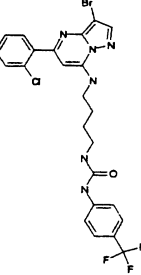
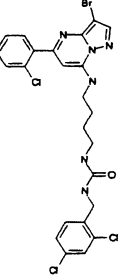
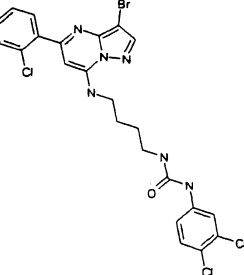
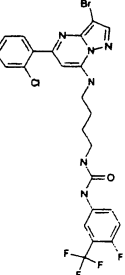
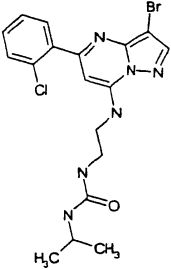
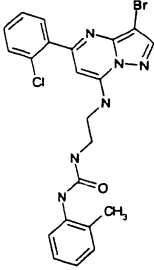
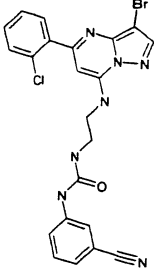
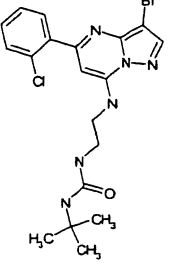
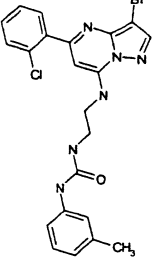
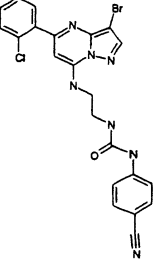
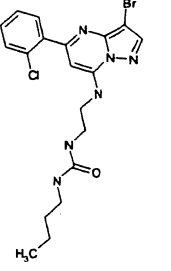
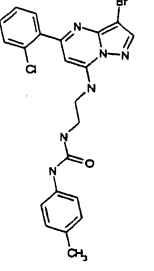
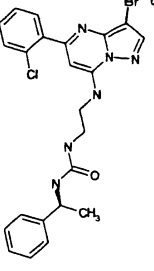
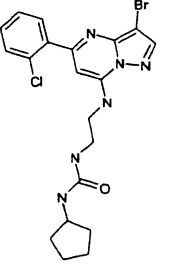
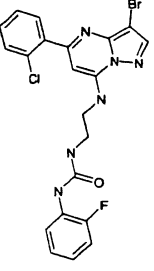
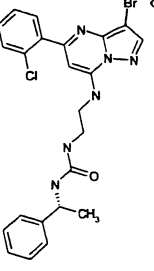
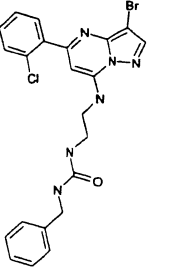
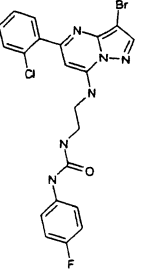
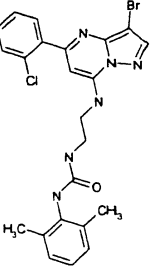
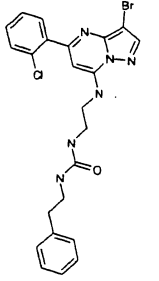
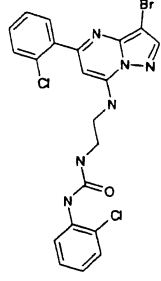
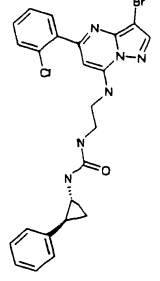
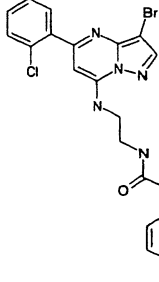
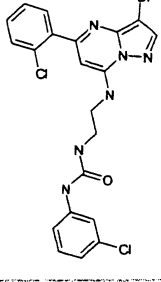
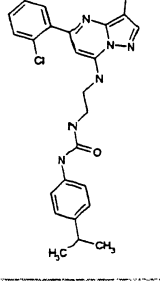
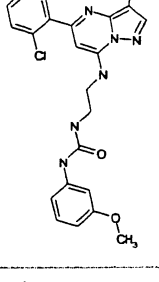
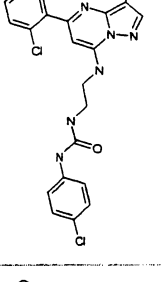
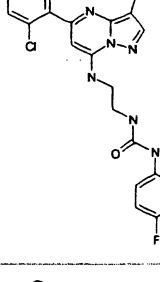
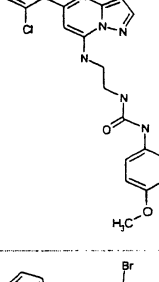
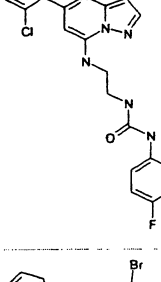
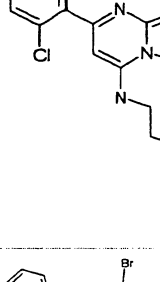
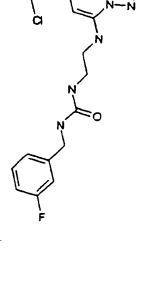
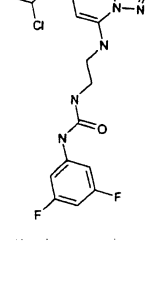
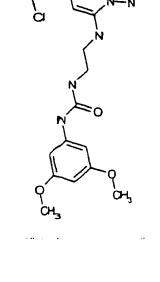
產物	1.實例 2. m/z	產物	1.實例 2. m/z	產物	1.實例 2. m/z
	1. 7531 2. 579.32		1. 7536 2. 583.32		1. 7541 2. 605.33
	1. 7532 2. 583.32		1. 7537 2. 591.33		1. 7542 2. 605.33
	1. 7533 2. 583.32		1. 7538 2. 593.33		1. 7543 2. 614.34
	1. 7534 2. 583.32		1. 7539 2. 597.33		
	1. 7535 2. 583.32		1. 7540 2. 601.33		

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產物	1.實例2. m/z	產物	1.實例2. m/z	產物	1.實例2. m/z
	1. 7601 2. 453.25		1. 7606 2. 501.28		1. 7611 2. 512.28
	1. 7602 2. 467.26		1. 7607 2. 501.28		1. 7612 2. 512.28
	1. 7603 2. 467.26		1. 7608 2. 501.28		1. 7613 2. 515.28
	1. 7604 2. 479.26		1. 7609 2. 505.28		1. 7614 2. 515.28
	1. 7605 2. 501.28		1. 7610 2. 505.28		1. 7615 2. 515.28

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 761 6 2. 515.28		1. 7621 2. 521.29		1. 7626 2. 527.29
	1. 7617 2. 517.28		1. 7622 2. 521.29		1. 7627 2. 529.29
	1. 7618 2. 517.28		1. 7623 2. 521.29		1. 7628 2. 541.3
	1. 7619 2. 517.28		1. 7624 2. 523.29		1. 7629 2. 545.3
	1. 7620 2. 519.29		1. 7625 2. 523.29		1. 7630 2. 547.3

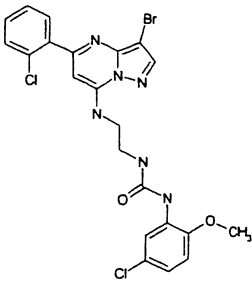
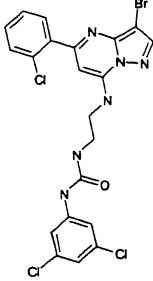
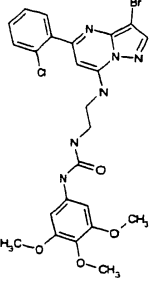
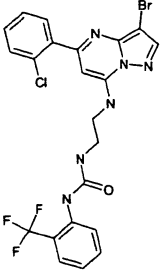
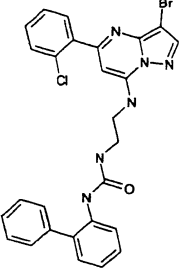
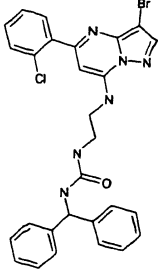
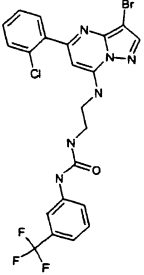
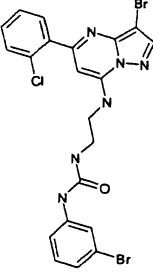
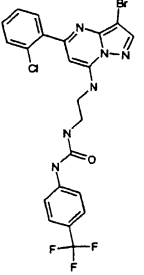
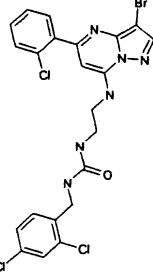
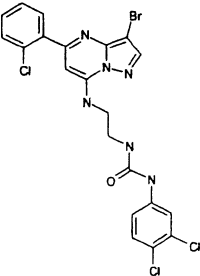
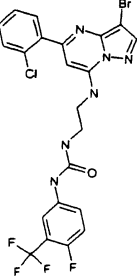
產物	1. 實例 2. m/z	產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 7631 2. 551.3		1. 7636 2. 555.31		1. 7641 2. 577.32
	1. 7632 2. 555.31		1. 7637 2. 563.31		1. 7642 2. 577.32
	1. 7633 2. 555.31		1. 7638 2. 565.31		
	1. 7634 2. 555.31		1. 7639 2. 569.31		
	1. 7635 2. 555.31		1. 7640 2. 573.32		

表77

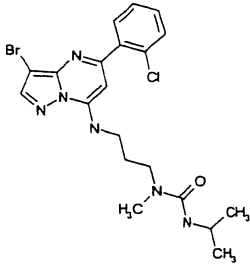
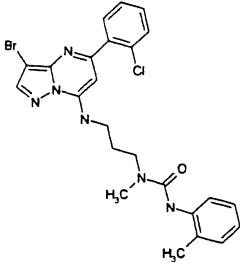
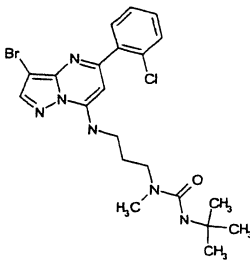
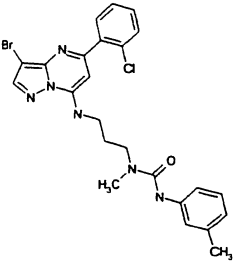
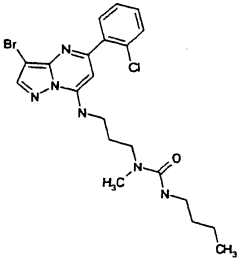
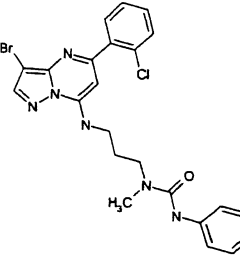
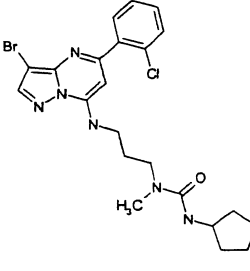
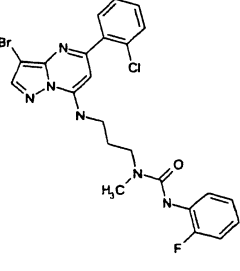
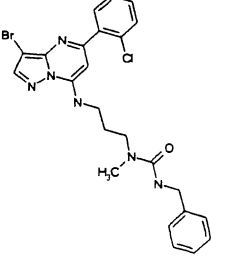
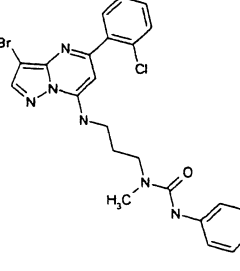
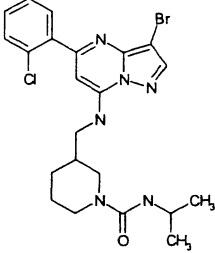
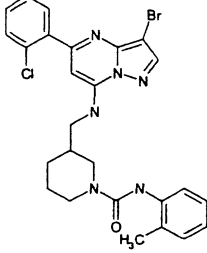
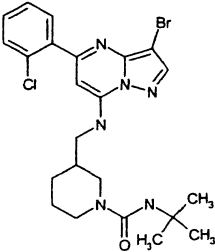
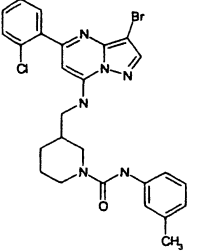
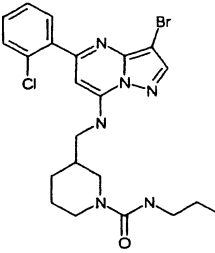
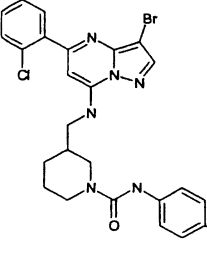
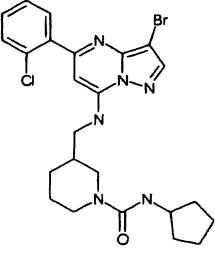
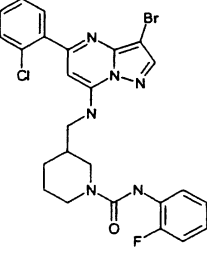
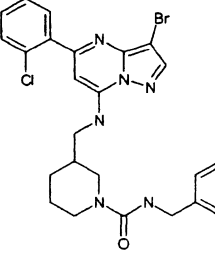
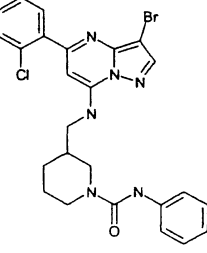
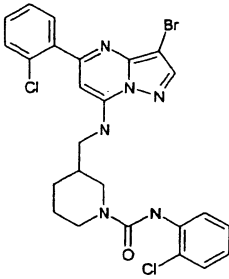
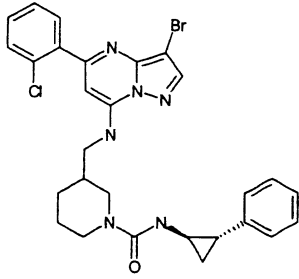
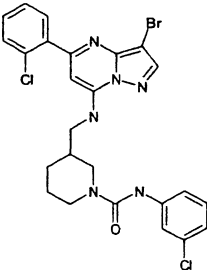
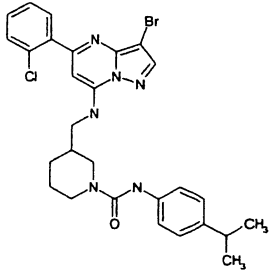
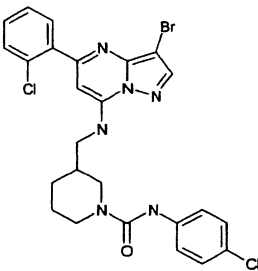
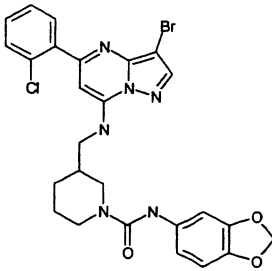
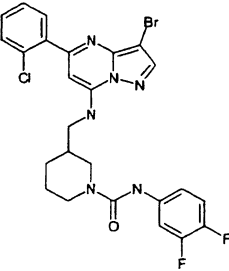
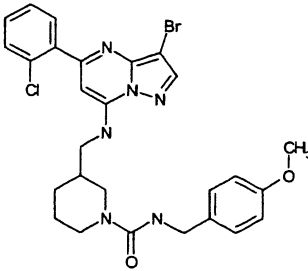
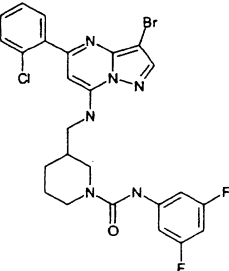
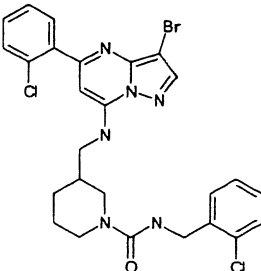
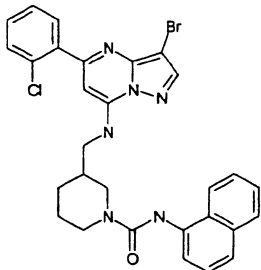
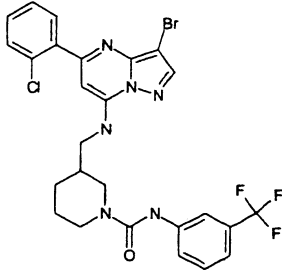
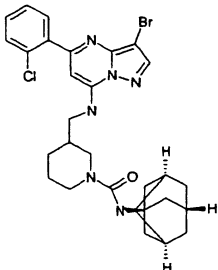
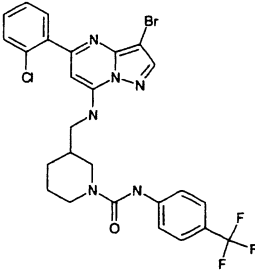
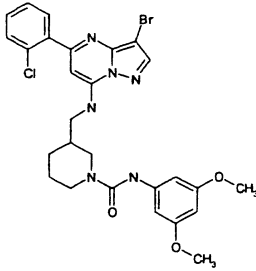
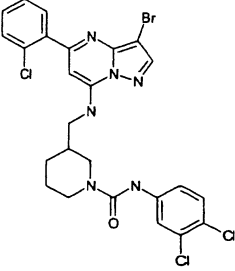
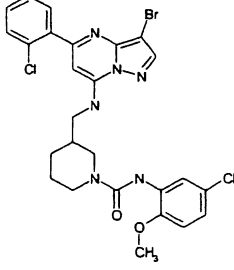
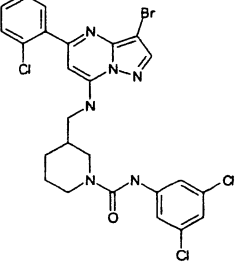
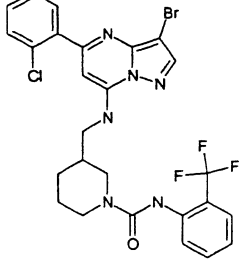
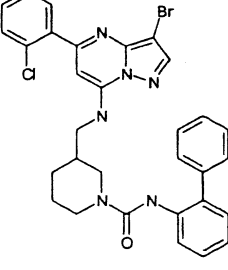
產物	1. 實例2. m/z	產物	1. 實例2. m/z
	1. 7701 2. 481.26		1. 7706 2. 529.29
	1. 7702 2. 495.27		1. 7707 2. 529.29
	1. 7703 2. 495.27		1. 7708 2. 529.29
	1. 7704 2. 507.28		1. 7709 2. 533.29
	1. 7705 2. 529.29		1. 7710 2. 533.29

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產物	1.實例2. m/z	產物	1.實例2. m/z
	1. 7801 2. 507.28		1. 7806 2. 555.31
	1. 7802 2. 521.29		1. 7807 2. 555.31
	1. 7803 2. 521.29		1. 7808 2. 555.31
	1. 7804 2. 533.29		1. 7809 2. 559.31
	1. 7805 2. 555.31		1. 7810 2. 559.31

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 7811 2. 566.31		1. 7816 2. 569.31
	1. 7812 2. 566.31		1. 7817 2. 571.31
 Chiral	1. 7813 2. 569.31		1. 7818 2. 571.31
 Chiral	1. 7814 2. 569.31		1. 7819 2. 571.31
	1. 7815 2. 569.31		1. 7820 2. 573.32

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 7821 2. 575.32		1. 7826 2. 581.32
	1. 7822 2. 575.32		1. 7827 2. 583.32
	1. 7823 2. 575.32		1. 7828 2. 585.32
	1. 7824 2. 577.32		1. 7829 2. 585.32
	1. 7825 2. 577.32		1. 7830 2. 589.32

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 7831 2. 591.33		1. 7836 2. 609.33
	1. 7832 2. 599.33		1. 7837 2. 609.33
	1. 7833 2. 601.33		1. 7838 2. 609.33
	1. 7834 2. 605.33		1. 7839 2. 609.33
	1. 7835 2. 609.33		1. 7840 2. 617.34

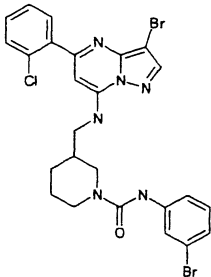
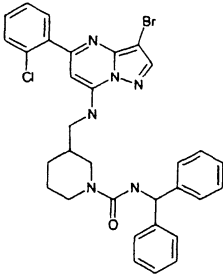
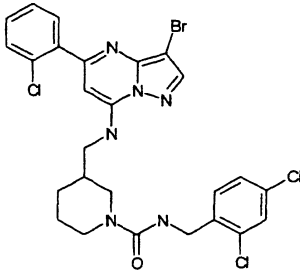
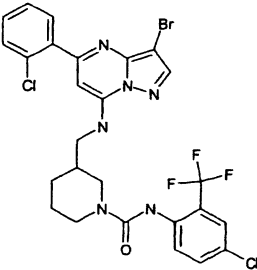
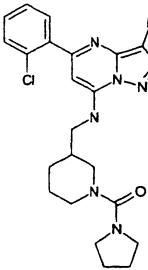
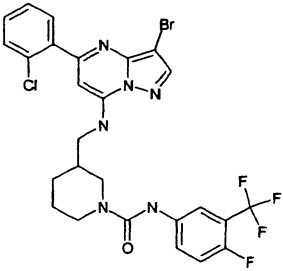
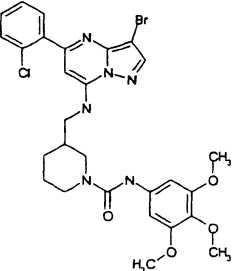
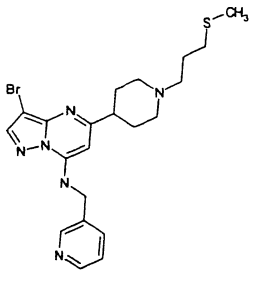
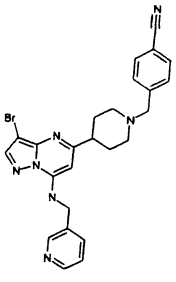
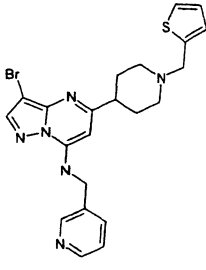
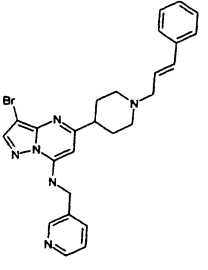
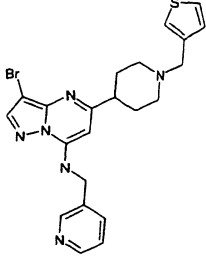
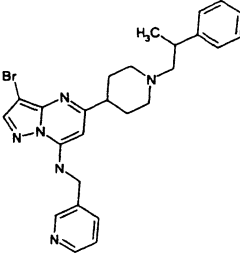
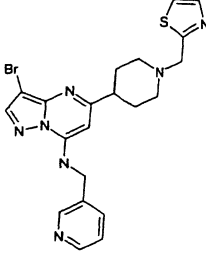
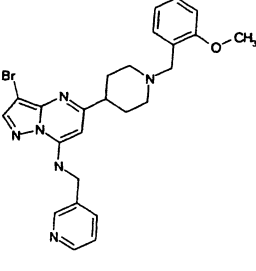
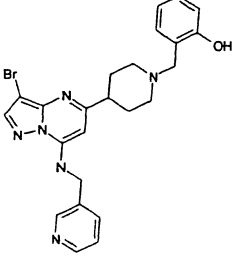
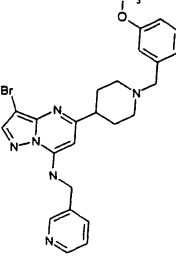
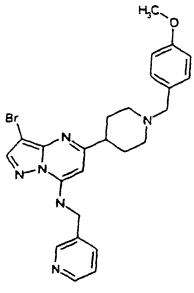
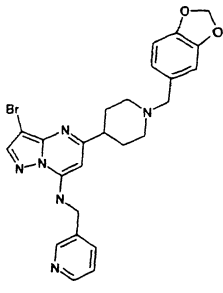
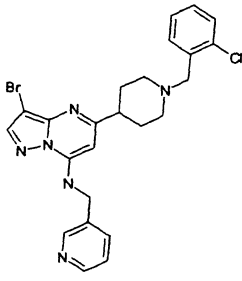
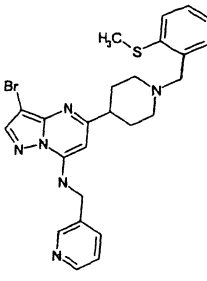
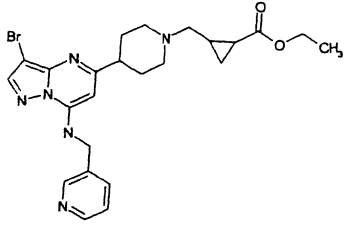
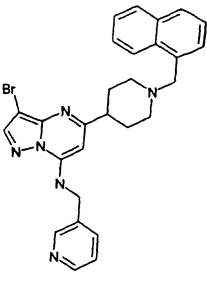
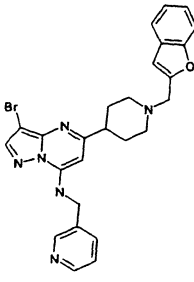
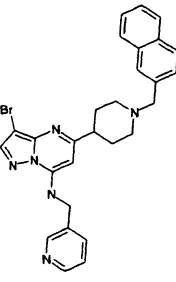
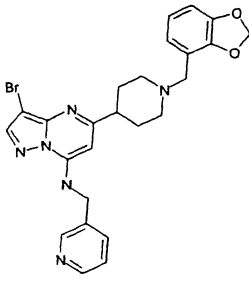
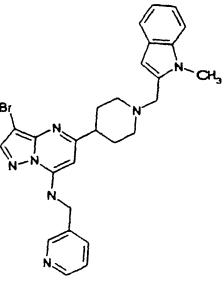
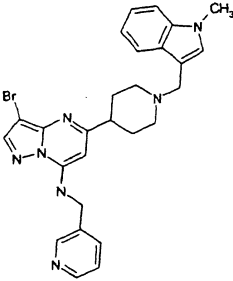
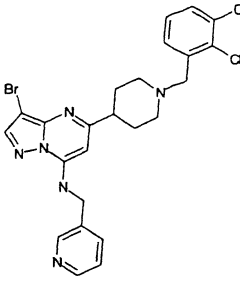
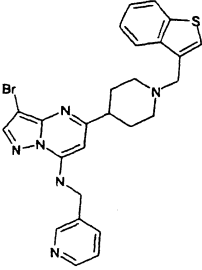
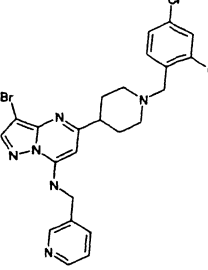
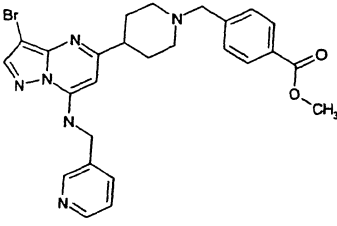
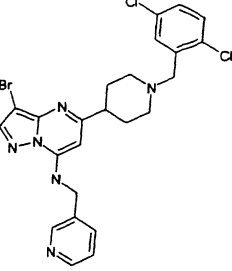
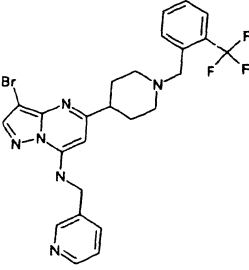
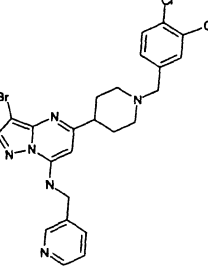
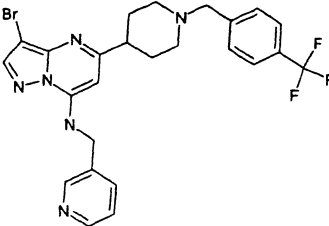
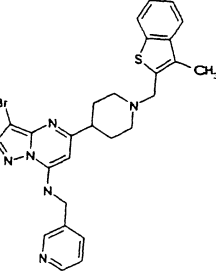
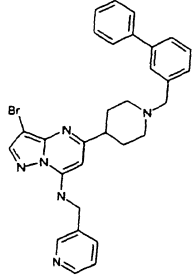
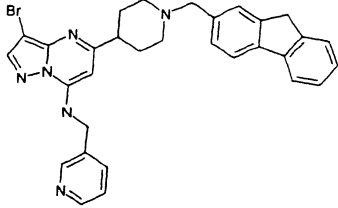
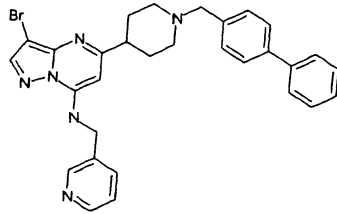
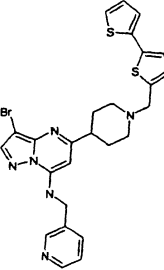
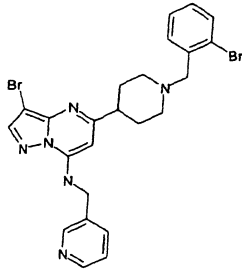
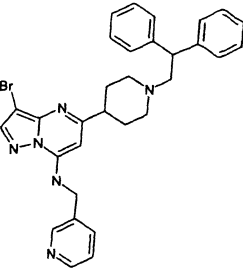
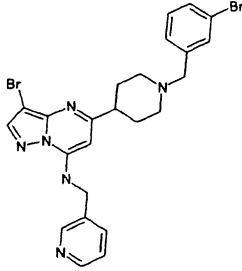
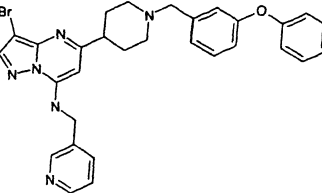
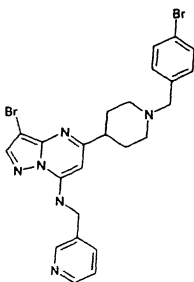
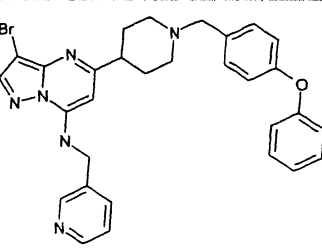
產物	1. 實例2. m/z	產物	1. 實例2. m/z
	1. 7841 2. 619.34		1. 7846 2. 631.35
	1. 7842 2. 623.34		1. 7847 2. 643.35
	1. 7843 2. 519.29		
	1. 7844 2. 627.34		
	1. 7845 2. 631.35		

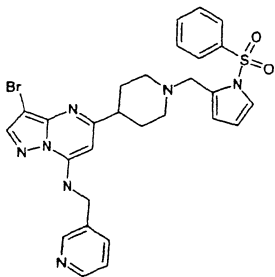
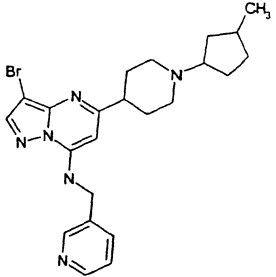
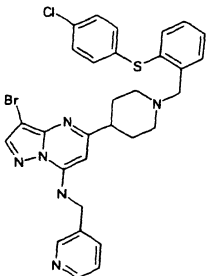
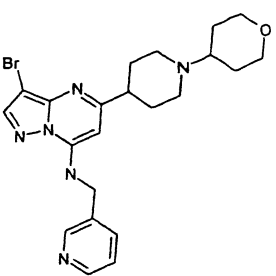
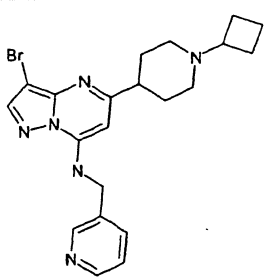
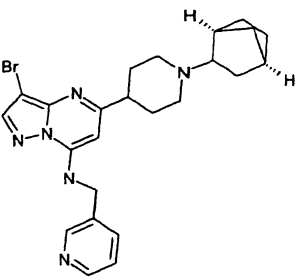
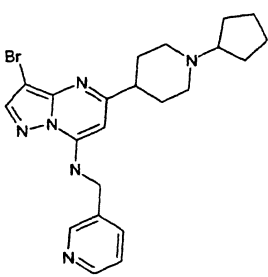
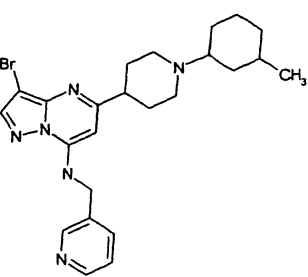
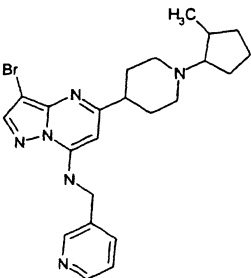
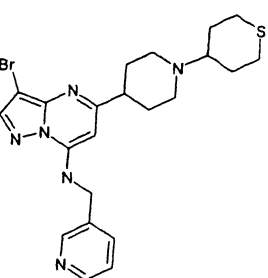
表79

產物	1. 實例2. m/z	產物	1. 實例2. m/z
	1. 7901 2. 477.26		1. 7906 2. 504.28
	1. 7902 2. 485.27		1. 7907 2. 505.28
	1. 7903 2. 485.27		1. 7908 2. 507.28
	1. 7904 2. 486.27		1. 7909 2. 509.28
	1. 7905 2. 495.27		1. 7910 2. 509.28

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 7911 2. 509.28		1. 7916 2. 523.29
	1. 7912 2. 513.28		1. 7917 2. 525.29
	1. 7913 2. 515.28		1. 7918 2. 529.29
	1. 7914 2. 519.29		1. 7919 2. 529.29
	1. 7915 2. 523.29		1. 7920 2. 530.29

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 7921 2. 530.29		1. 7926 2. 547.3
	1. 7922 2. 535.29		1. 7927 2. 547.3
	1. 7923 2. 537.3		1. 7928 2. 547.3
	1. 7924 2. 547.3		1. 7929 2. 547.3
	1. 7925 2. 547.3		1. 7930 2. 549.3

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 7931 2. 555.31		1. 7936 2. 567.31
	1. 7932 2. 555.31		1. 7937 2. 567.31
	1. 7933 2. 557.31		1. 7938 2. 569.31
	1. 7934 2. 557.31		1. 7939 2. 571.31
	1. 7935 2. 557.31		1. 7940 2. 571.31

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 7941 2. 608.33		1. 7946 2. 471.26
	1. 7942 2. 621.34		1. 7947 2. 473.26
	1. 7943 2. 443.24		1. 7948 2. 483.27
	1. 7944 2. 457.25		1. 7949 2. 485.27
	1. 7945 2. 471.26		1. 7950 2. 489.27

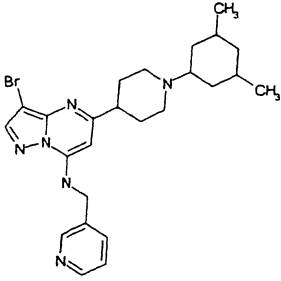
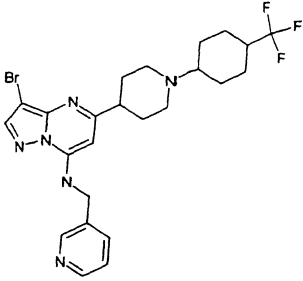
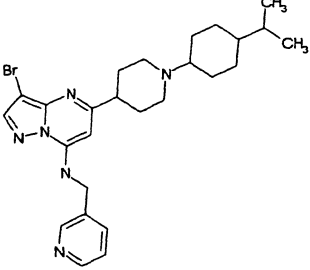
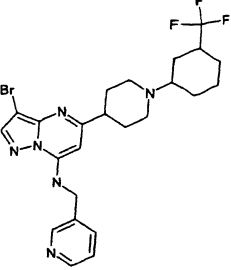
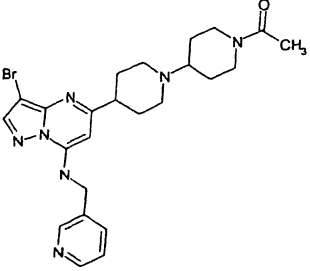
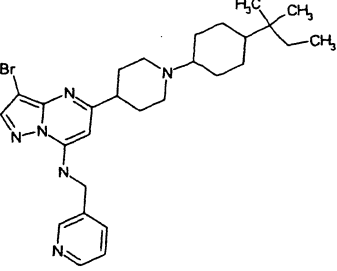
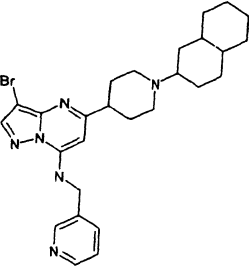
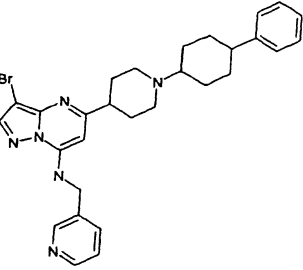
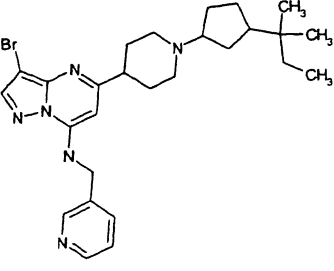
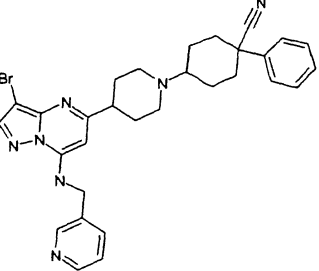
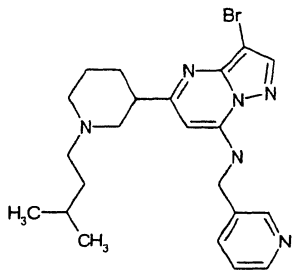
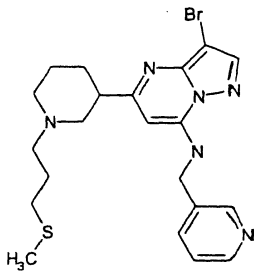
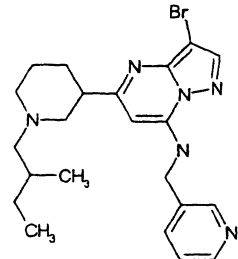
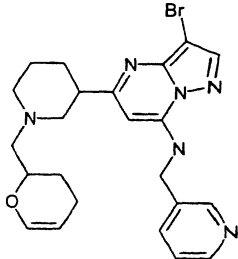
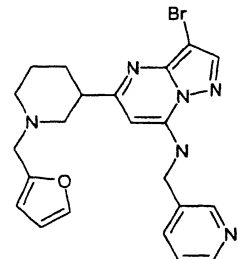
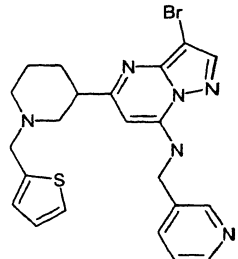
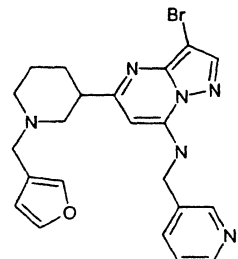
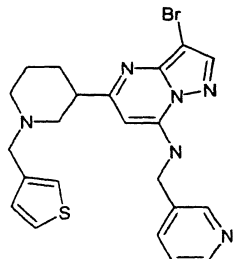
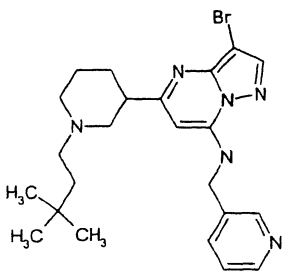
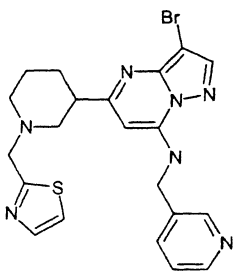
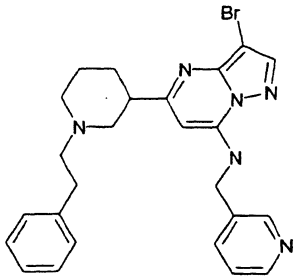
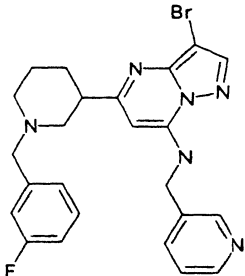
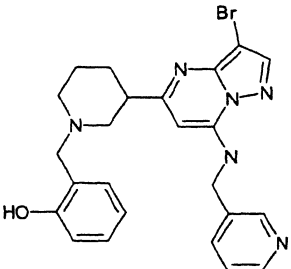
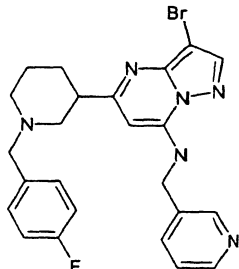
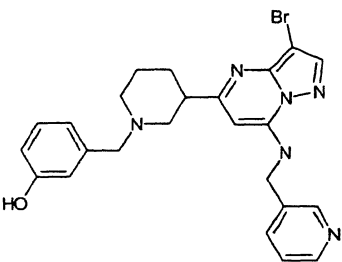
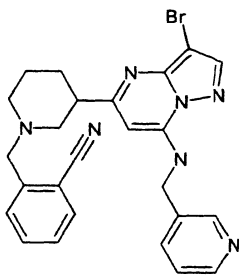
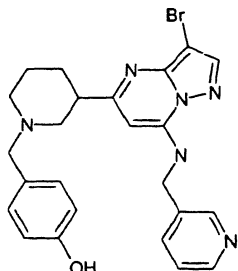
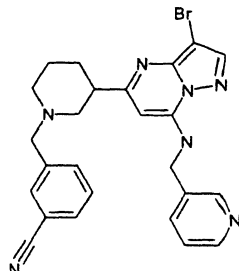
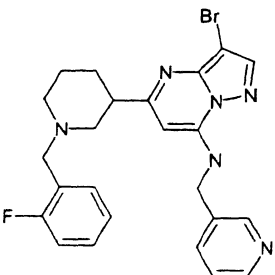
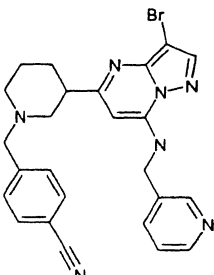
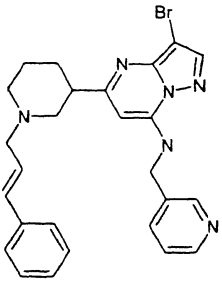
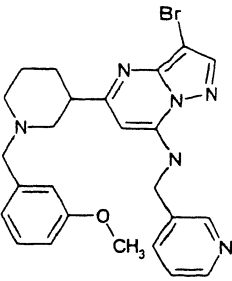
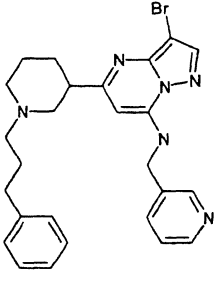
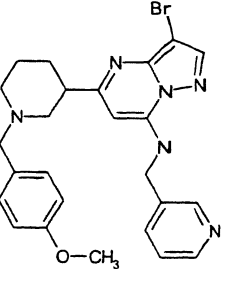
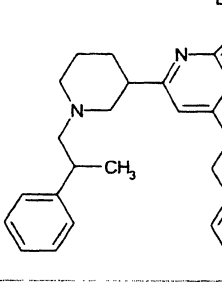
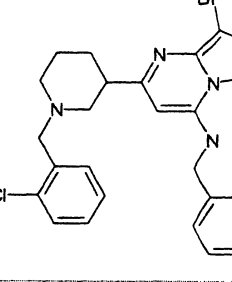
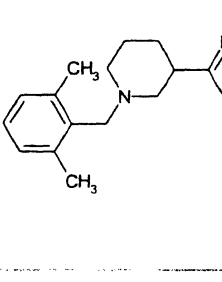
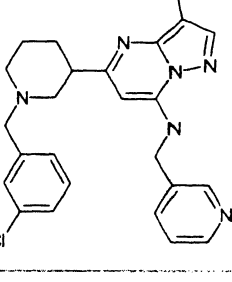
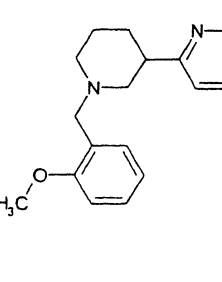
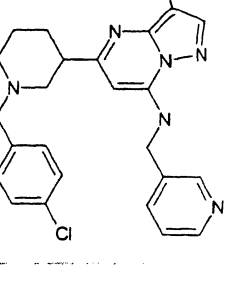
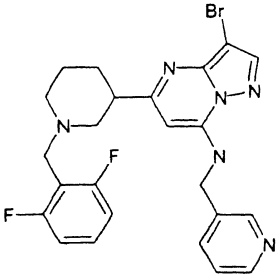
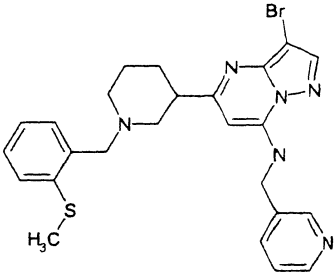
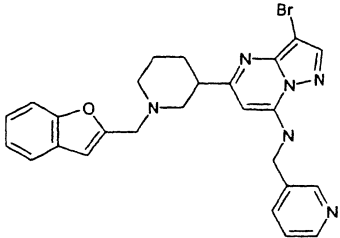
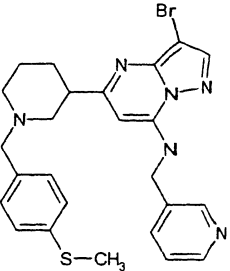
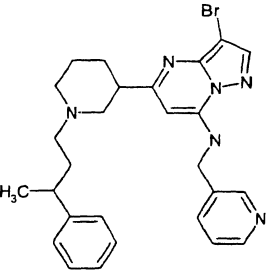
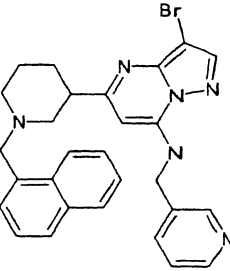
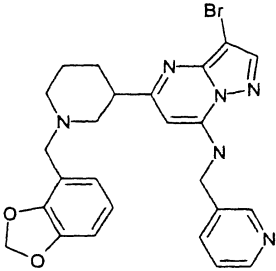
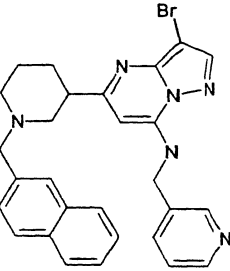
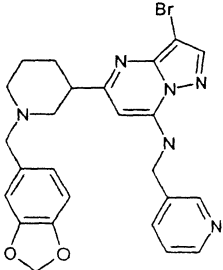
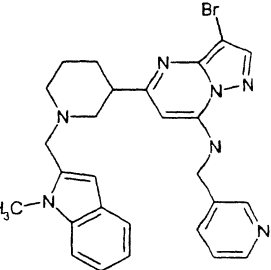
產物	1. 實例2. m/z	產物	1. 實例2. m/z
	1. 7951 2. 499.27		1. 7956 2. 536.29
	1. 7952 2. 513.28		1. 7957 2. 539.3
	1. 7953 2. 514.28		1. 7958 2. 541.3
	1. 7954 2. 525.29		1. 7959 2. 547.3
	1. 7955 2. 525.29		1. 7960 2. 572.31

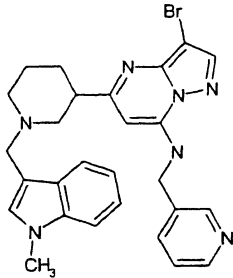
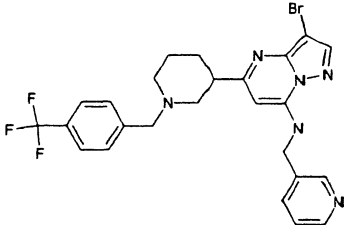
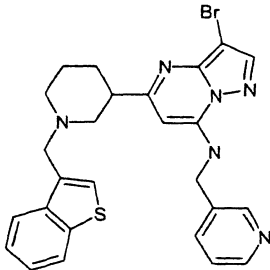
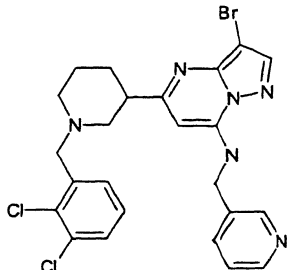
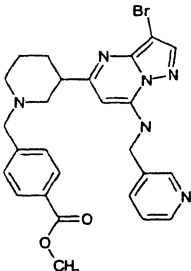
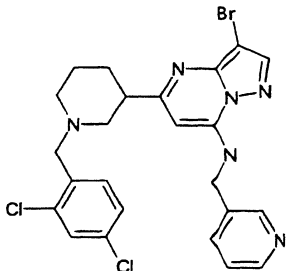
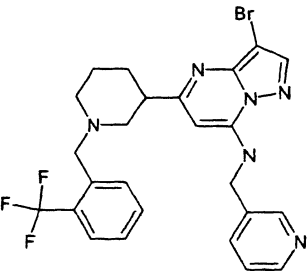
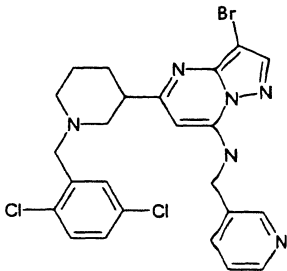
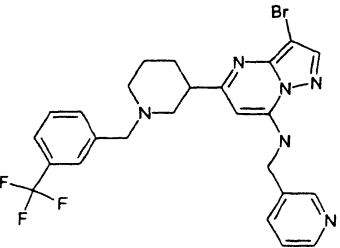
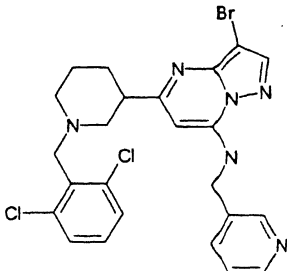
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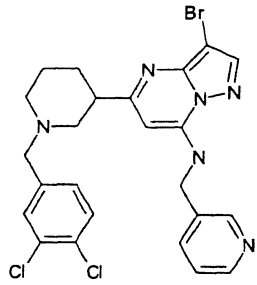
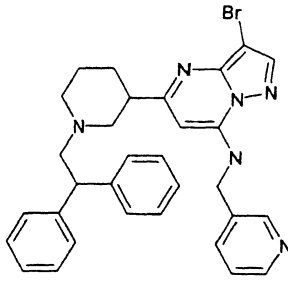
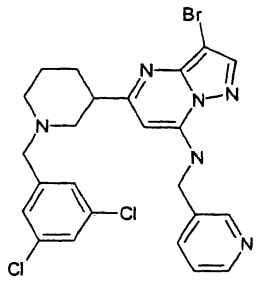
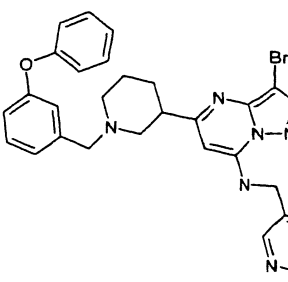
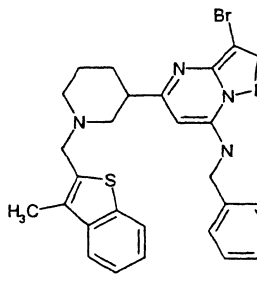
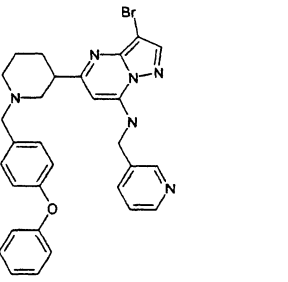
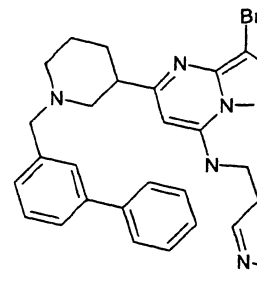
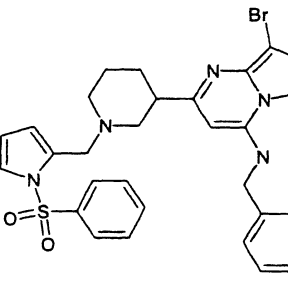
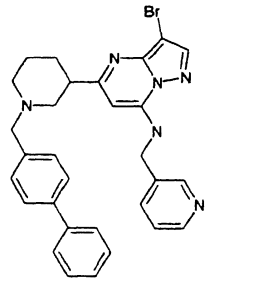
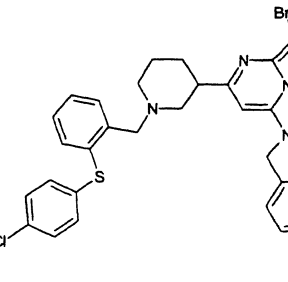
產物	1. 實例2. m/z	產物	1. 實例2. m/z
	1. 8001 2. 459.25		1. 8006 2. 477.26
	1. 8002 2. 459.25		1. 8007 2 485.27
	1. 8003 2. 469.26		1. 8008 2. 485.27
	1. 8004 2. 469.26		1. 8009 2. 485.27
	1. 8005 2. 473.26		1. 8010 2. 486.27

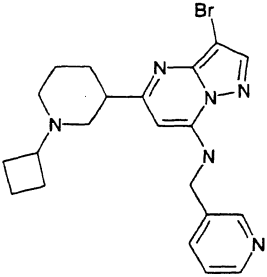
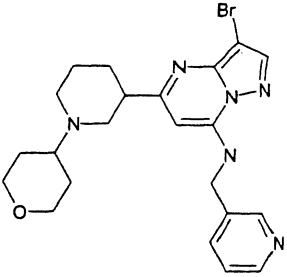
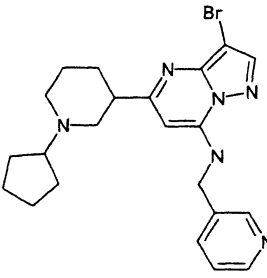
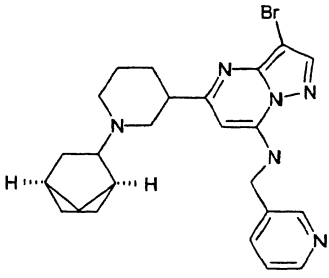
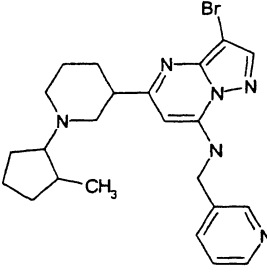
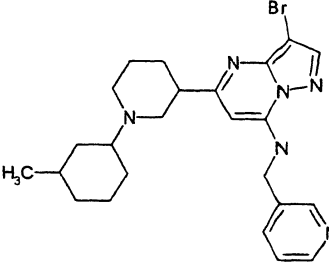
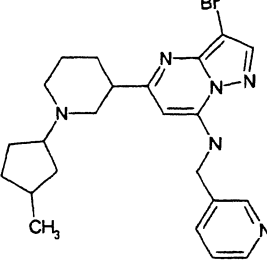
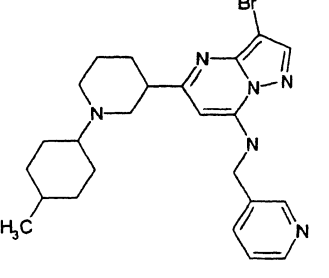
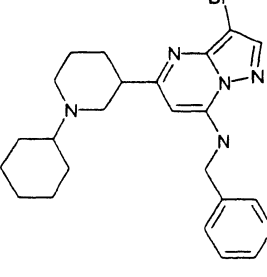
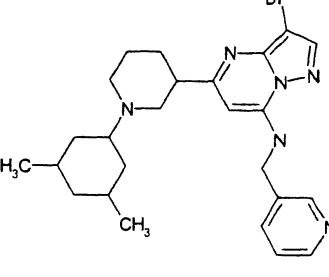
產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 8011 2. 493.27		1. 8016 2. 495.27
	1. 8012 2. 495.27		1. 8017 2. 495.27
	1. 8013 2. 495.27		1. 8018 2. 502.28
	1. 8014 2. 495.27		1. 8019 2. 502.28
	1. 8015 2. 495.27		1. 8020 2. 502.28

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 8021 2. 505.28		1. 8026 2. 509.28
	1. 8022 2. 505.28		1. 8027 2. 509.28
	1. 8023 2. 507.28		1. 8028 2. 513.28
	1. 8024 2. 507.28		1. 8029 2. 513.28
	1. 8025 2. 507.28		1. 8030 2. 513.28

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 8031 2. 515.28		1. 8036 2. 523.29
	1. 8032 2. 519.29		1. 8037 2. 525.29
	1. 8033 2. 521.29		1. 8038 2. 529.29
	1. 8034 2. 523.29		1. 8039 2. 529.29
	1. 8035 2. 523.29		1. 8040 2. 530.29

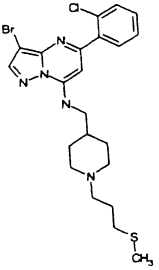
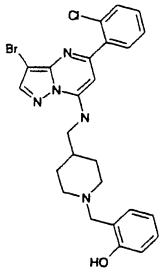
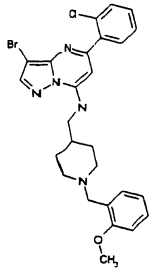
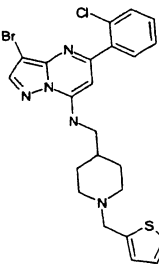
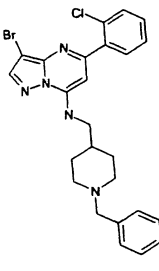
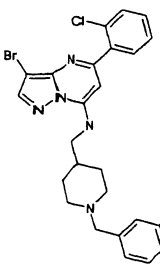
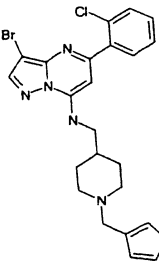
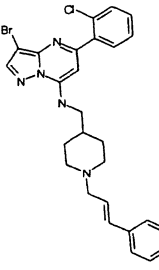
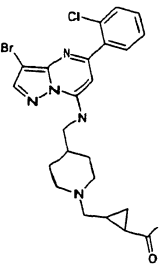
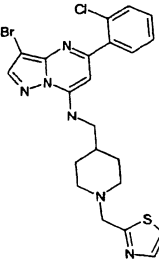
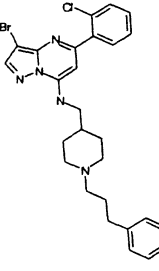
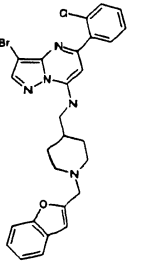
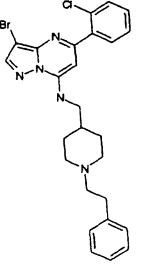
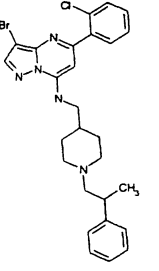
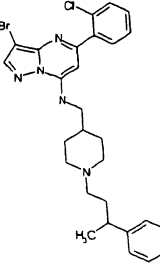
產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 8041 2. 530.29		1. 8046 2. 547.3
	1. 8042 2. 535.29		1. 8047 2. 544.3
	1. 8043 2. 537.3		1. 8048 2. 547.3
	1. 8044 2. 547.3		1. 8049 2. 547.3
	1. 8045 2. 547.3		1. 8050 2. 547.3

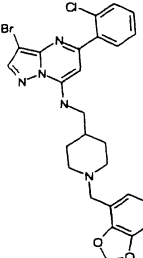
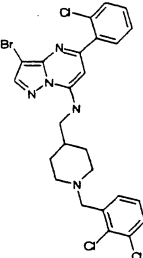
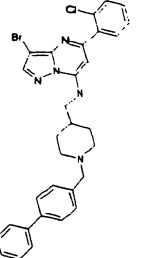
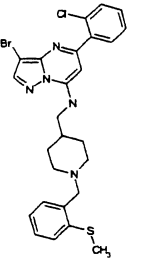
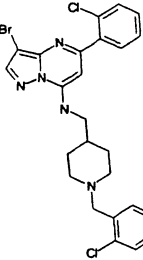
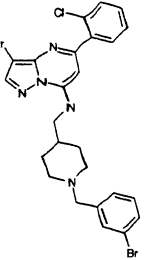
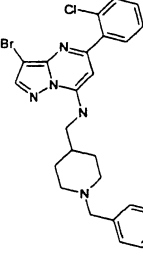
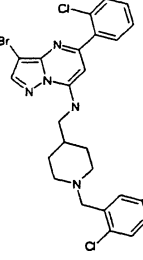
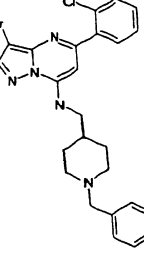
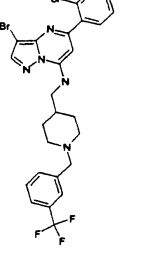
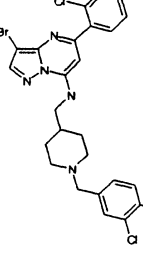
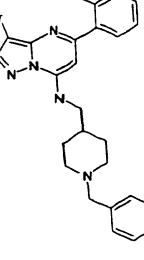
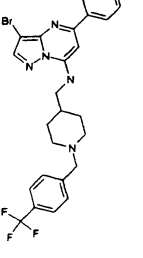
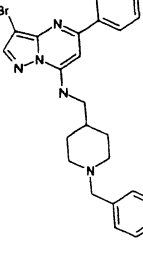
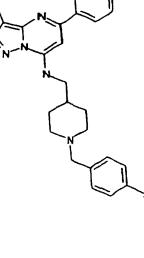
產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 8051 2. 548.3		1. 8056 2. 569.31
	1. 8052 2. 548.3		1. 8057 2. 569.31
	1. 8053 2. 547.3		1. 8058 2. 571.31
	1. 8054 2. 555.31		1. 8059 2. 608.33
	1. 8055 2. 553.3		1. 8060 2. 621.34

產物：	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 8061 2. 443.24		1. 8066 2. 473.26
	1. 8062 2. 457.25		1. 8067 2. 483.27
	1. 8063 2. 471.26		1. 8068 2. 485.27
	1. 8064 2. 471.26		1. 8069 2. 483.27
	1. 8065 2. 469.26		1. 8070 2. 499.27

	産物	1. 實例 2. m/z
		1. 8071 2. 505.2 8
		1. 8072 2. 537.3
		1. 8073 2. 537.3
		1. 8074 2. 547.3

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產物	1. 實例2. m/z	產物	1. 實例2. m/z	產物	1. 實例2. m/z
	1. 8101 2. 510.28		1. 8106 2. 528.29		1. 8111 2. 542.3
	1. 8102 2. 518.28		1. 8107 2. 537.3		1. 8112 2. 542.3
	1. 8103 2. 518.28		1. 8108 2. 538.3		1. 8113 2. 548.3
	1. 8104 2. 519.29		1. 8109 2. 540.3		1. 8114 2. 552.3
	1. 8105 2. 526.29		1. 8110 2. 540.3		1. 8115 2. 554.3

產物	1. 實例 m/z	2. 實例 m/z	產物	1. 實例 m/z	2. 實例 m/z	產物	1. 實例 m/z	2. 實例 m/z
	1. 8116 2. 556.31			1. 8121 2. 580.32			1. 8126 2. 588.32	
	1. 8117 2. 558.31			1. 8122 2. 580.32			1. 8127 2. 590.32	
	1. 8118 2. 562.31			1. 8123 2. 580.32			1. 8128 2. 590.32	
	1. 8119 2. 580.32			1. 8125 2. 580.32			1. 8129 2. 604.33	
	1. 8120 2. 580.32			1. 8126 2. 588.32			1. 8130 2. 612.34	

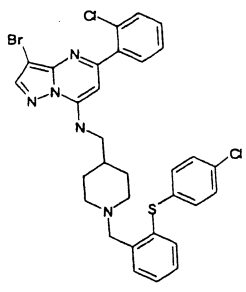
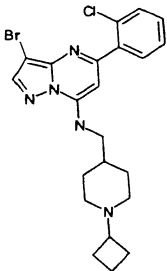
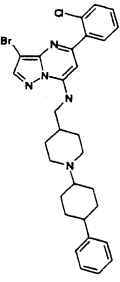
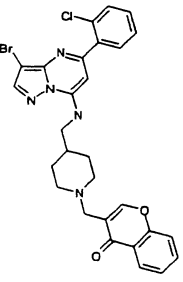
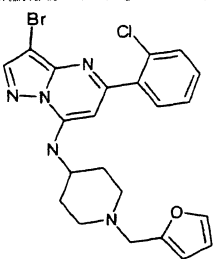
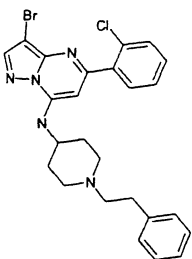
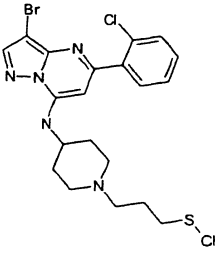
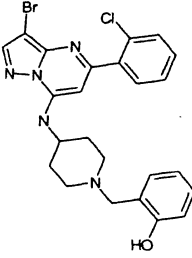
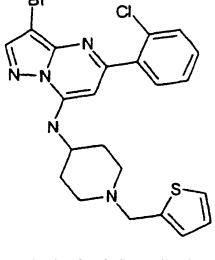
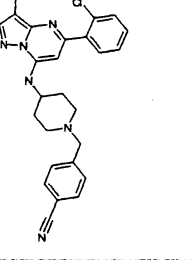
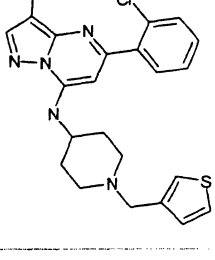
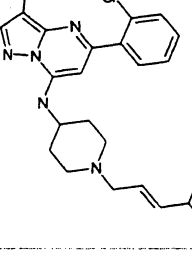
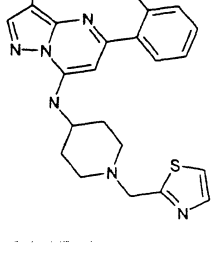
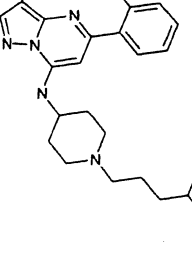
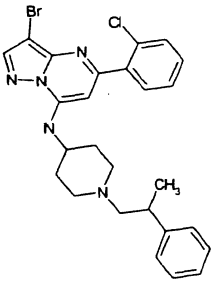
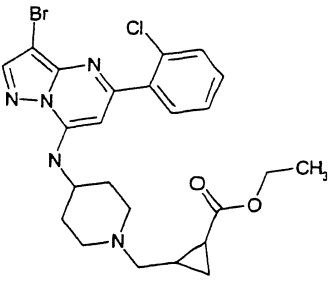
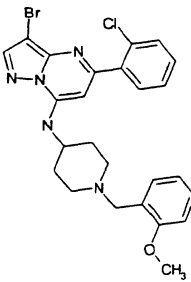
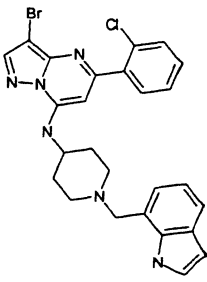
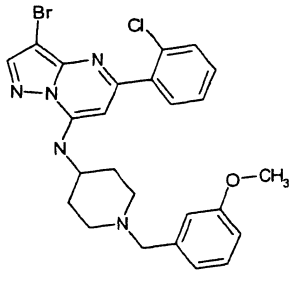
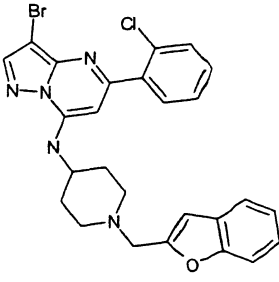
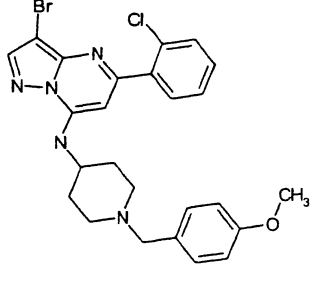
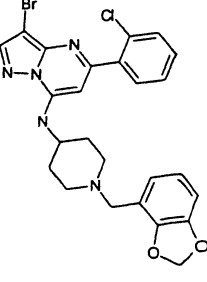
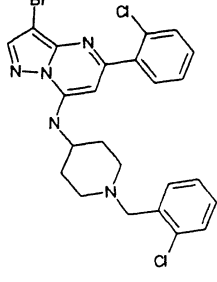
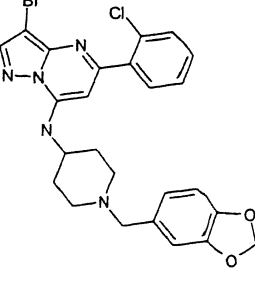
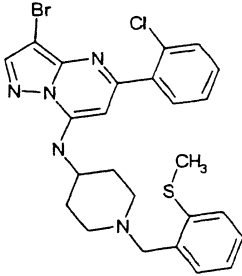
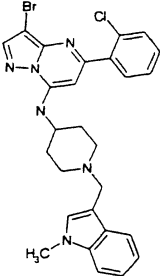
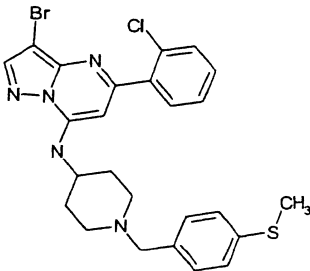
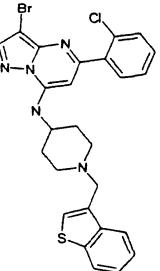
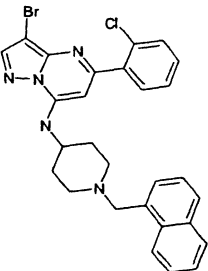
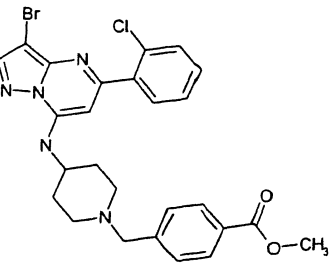
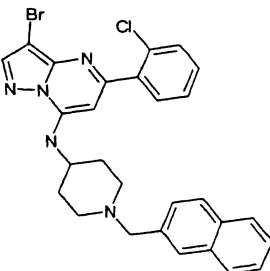
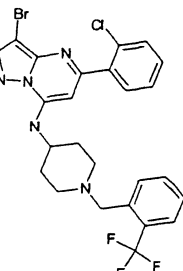
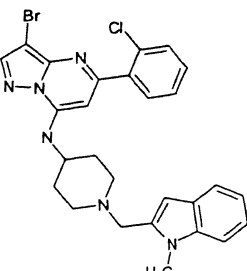
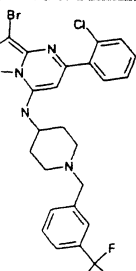
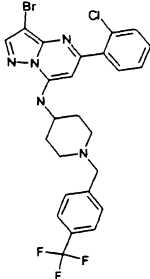
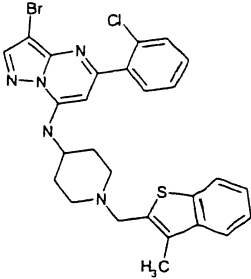
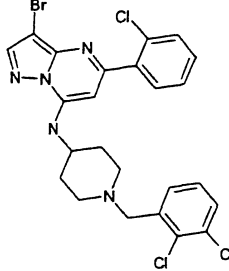
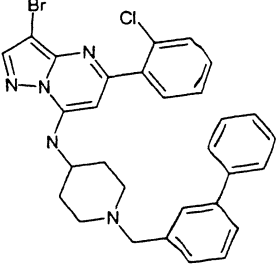
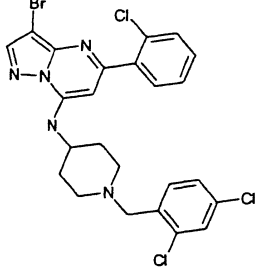
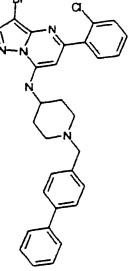
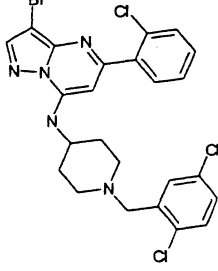
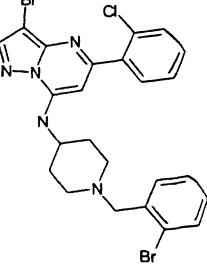
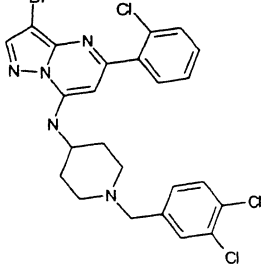
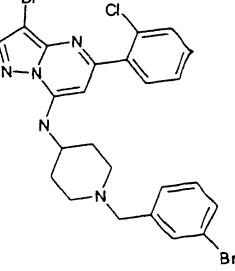
產物	1. 實例 2. m/z
	1. 8131 2. 654.36
	1. 8132 2. 476.26
	1. 8133 2. 580.32
	1. 8134 2. 580.32

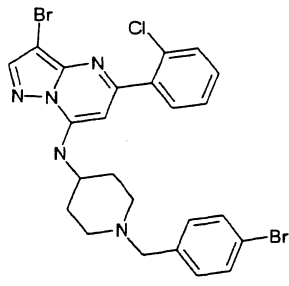
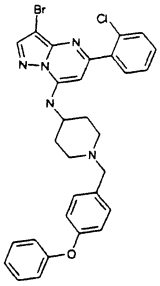
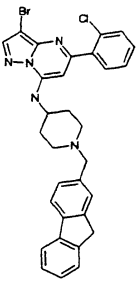
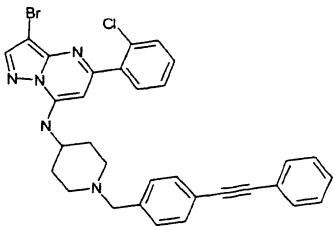
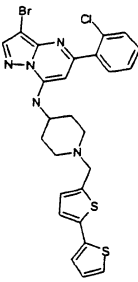
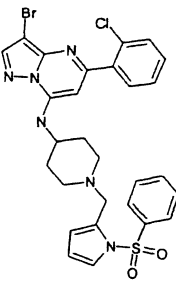
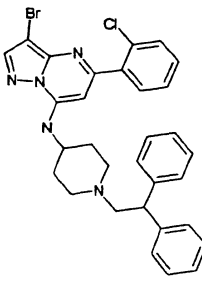
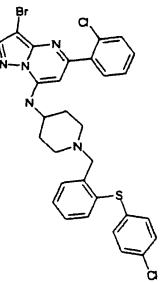
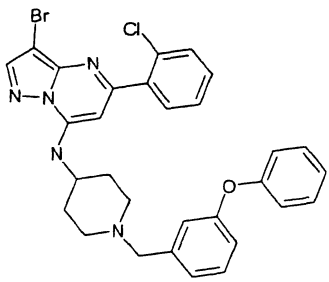
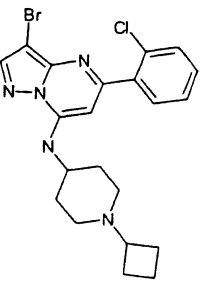
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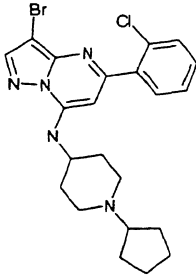
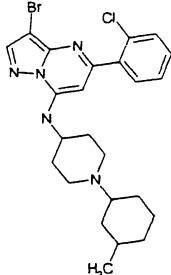
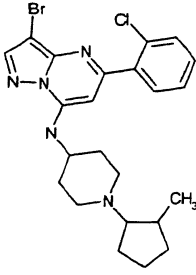
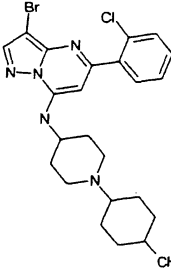
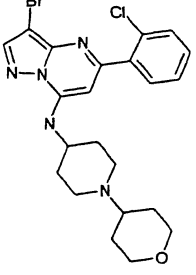
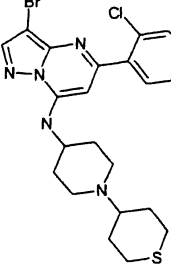
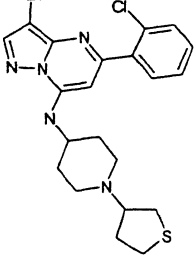
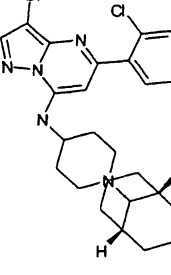
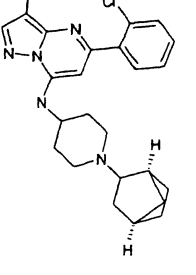
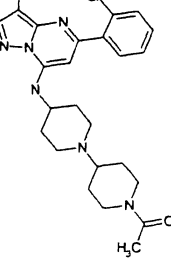
產物	1. 實例2. m/z	產物	1. 實例2. m/z
	1. 8201 2. 488.27		1. 8206 2. 512.28
	1. 8202 2. 496.27		1. 8207 2. 514.28
	1. 8203 2. 504.28		1. 8208 2. 523.29
	1. 8204 2. 504.28		1. 8209 2. 524.29
	1. 8205 2. 505.28		1. 8210 2. 526.29

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 8211 2. 526.29		1. 8216 2. 534.29
	1. 8212 2. 528.29		1. 8217 2. 537.3
	1. 8213 2. 528.29		1. 8218 2. 538.3
	1. 8214 2. 528.29		1. 8219 2. 542.3
	1. 8215 2. 532.29		1. 8220 2. 542.3

產物	1. 實例2. m/z	產物	1. 實例2. m/z
	1. 8221 2. 544.3		1. 8226 2. 551.3
	1. 8222 2. 544.3		1. 8227 2. 554.3
	1. 8223 2. 548.3		1. 8228 2. 556.31
	1. 8224 2. 548.3		1. 8229 2. 566.31
	1. 8225 2. 551.3		1. 8230 2. 566.31

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 8231 2. 566.31		1. 8236 2. 568.31
	1. 8232 2. 566.31		1. 8237 2. 574.32
	1. 8233 2. 566.31		1. 8238 2. 574.32
	1. 8243 2. 566.31		1. 8239 2. 576.32
	1. 8235 2. 566.31		1. 8240 2. 576.32

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 8241 2. 576.32		1. 8246 2. 590.32
	1. 8242 2. 586.32		1. 8247 2. 598.33
	1. 8243 2. 586.32		1. 8248 2. 627.34
	1. 8244 2. 588.32		1. 8249 2. 640.35
	1. 8245 2. 590.32		1. 8250 2. 462.25

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 8251 2. 476.26		1. 8256 2. 504.28
	1. 8252 2. 490.27		1. 8257 2. 504.28
	1. 8253 2. 492.27		1. 8258 2. 508.28
	1. 8254 2. 492.27		1. 8259 2. 530.29
	1. 8255 2. 502.28		1. 8260 2. 533.29

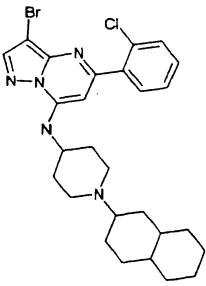
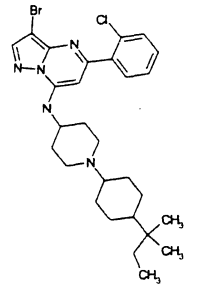
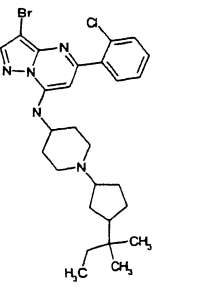
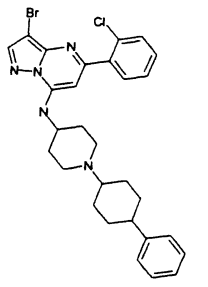
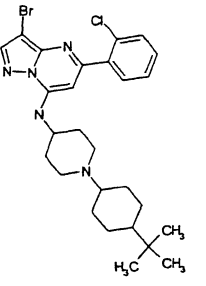
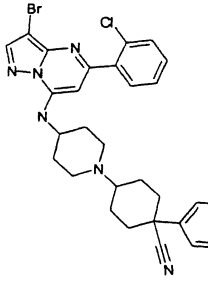
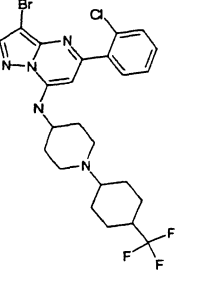
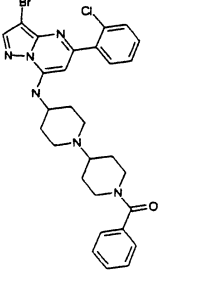
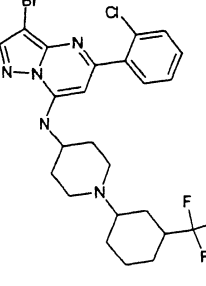
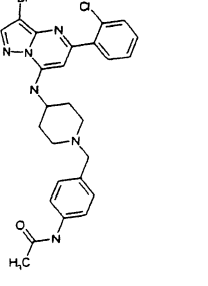
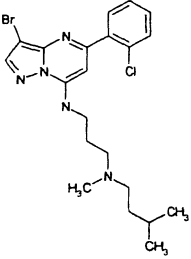
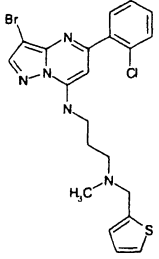
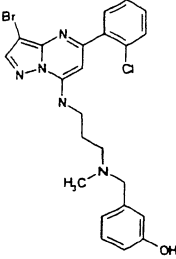
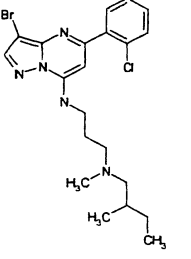
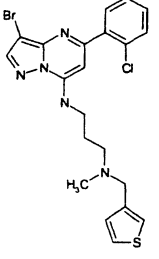
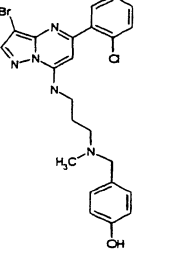
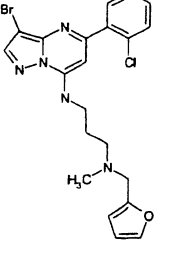
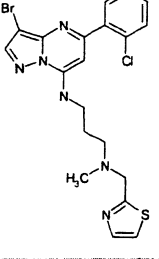
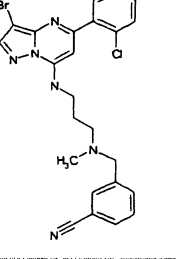
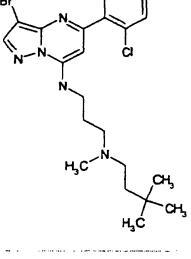
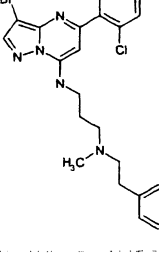
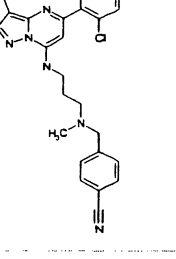
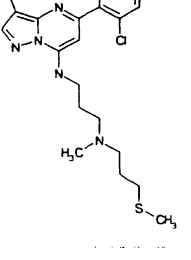
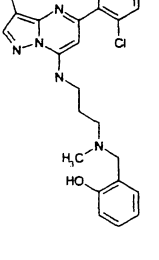
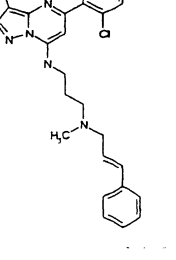
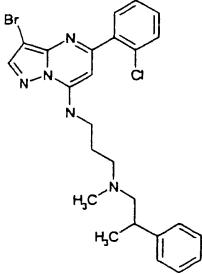
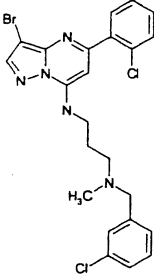
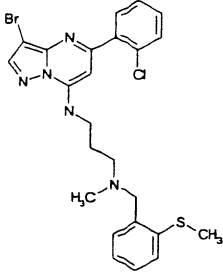
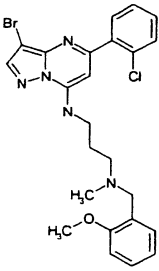
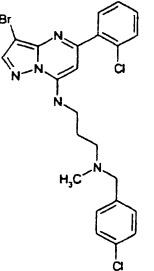
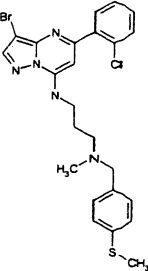
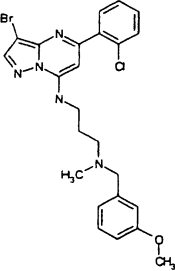
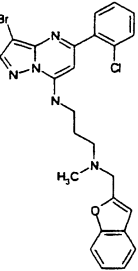
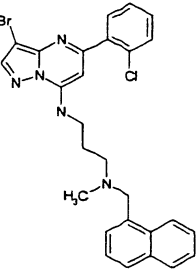
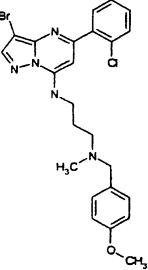
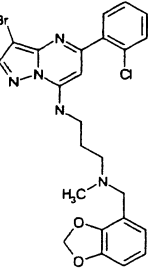
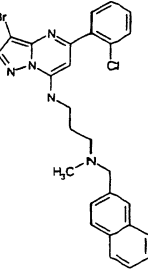
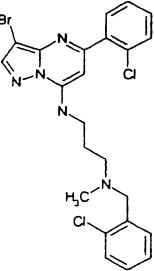
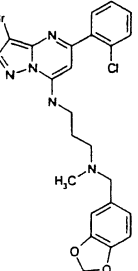
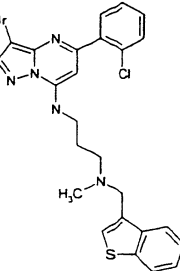
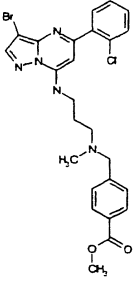
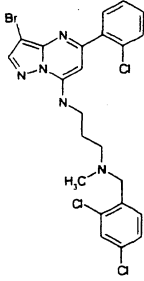
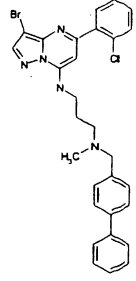
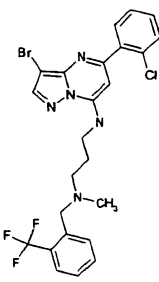
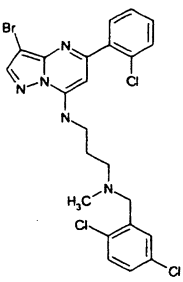
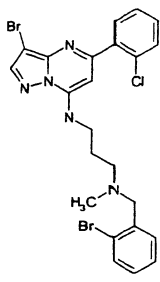
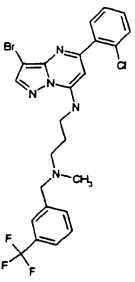
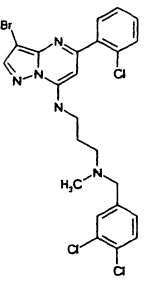
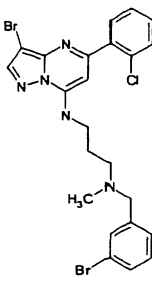
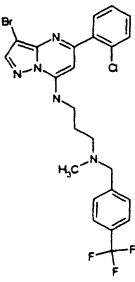
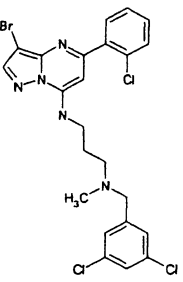
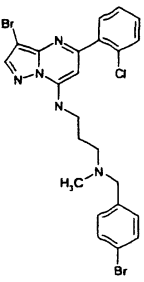
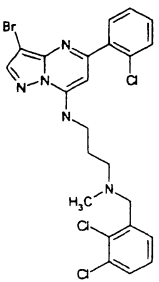
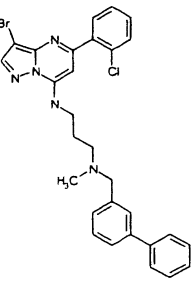
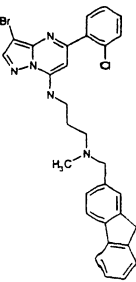
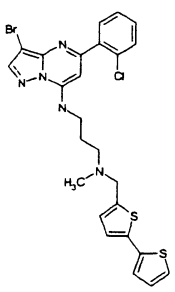
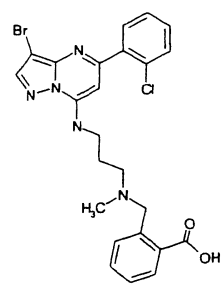
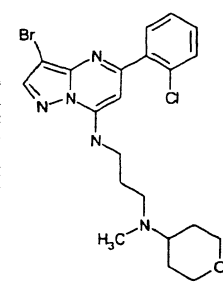
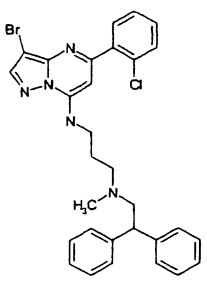
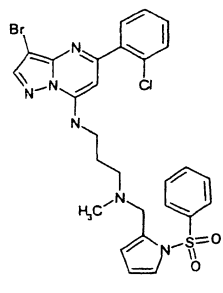
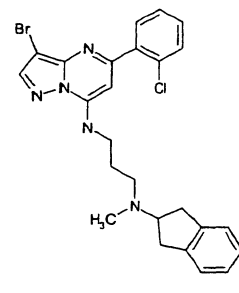
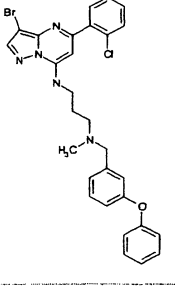
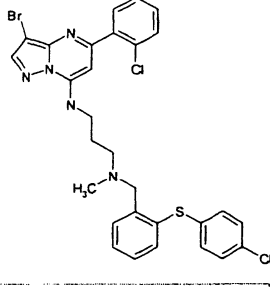
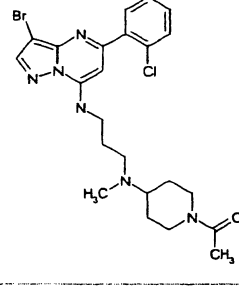
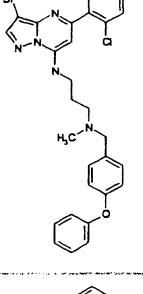
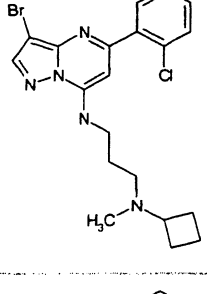
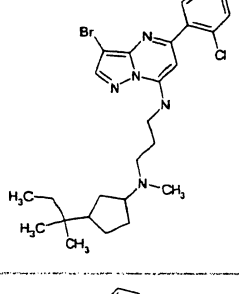
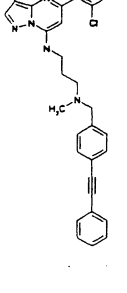
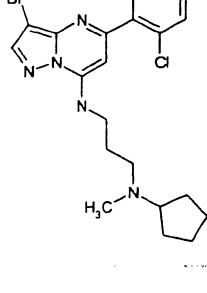
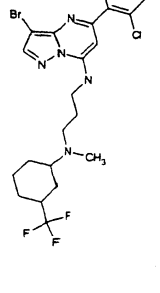
產物	1.實例 2. m/z	產物	1.實例 2. m/z
	1. 8261 2. 544.3		1. 8266 2. 560.31
	1. 8262 2. 546.3		1. 8267 2. 566.31
	1. 8263 2. 546.3		1. 8268 2. 591.33
	1. 8264 2. 558.31		1. 8269 2. 595.33
	1. 8265 2. 558.31		1. 8270 2. 555.31

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產物	1.實例2. m/z	產物	1.實例2. m/z	產物	1.實例2. m/z
	1. 8301 2. 465.882		1. 8306 2. 491.79		1. 8311 2. 501.825
	1. 8302 2. 465.885		1. 8307 2. 491.792		1. 8312 2. 501.833
	1. 8303 2. 475.827		1. 8308 2. 492.787		1. 8313 2. 510.822
	1. 8304 2. 479.89		1. 8309 2. 499.846		1. 8314 2. 510.821
	1. 8305 2. 483.829		1. 8310 2. 501.826		1. 8315 2. 511.841

產物	1.實例 2. m/z	產物	1.實例 2. m/z	產物	1.實例 2. m/z
	1. 8316 2. 513.855		1. 8321 2. 519.783		1. 8326 2. 531.804
	1. 8317 2. 515.832		1. 8322 2. 519.781		1. 8327 2. 531.812
	1. 8318 2. 515.832		1. 8323 2. 525.813		1. 8328 2. 535.83
	1. 8319 2. 515.837		1. 8324 2. 529.806		1. 8329 2. 535.831
	1. 8320 2. 519.782		1. 8325 2. 529.81		1. 8330 2. 541.788

產物	1.實例 2. m/z	產物	1.實例 2. m/z	產物	1.實例 2. m/z
	1. 8331 2. 543.821		1. 8336 2. 554.727		1. 8341 2. 561.838
	1. 8332 2. 553.797		1. 8337 2. 554.738		1. 8342 2. 564.714
	1. 8333 2. 553.796		1. 8338 2. 554.738		1. 8343 2. 564.704
	1. 8334 2. 553.795		1. 8339 2. 554.727		1. 8344 2. 564.72
	1. 8335 2. 554.73		1. 8340 2. 561.836		1. 8345 2. 573.823

產物	1.實例 2. m/z	產物	1.實例 2. m/z	產物	1.實例 2. m/z
	1. 8346 2. 573.735		1. 8351 2. 529.808		1. 8356 2. 479.856
	1. 8347 2. 575.839		1. 8352 2. 614.763		1. 8357 2. 511.842
	1. 8348 2. 577.818		1. 8353 2. 628.727		1. 8358 2. 520.859
	1. 8349 2. 577.814		1. 8354 2. 449.857		1. 8359 2. 533.903
	1. 9350 2. 585.818		1. 8355 2. 463.867		1. 8360 2. 545.823

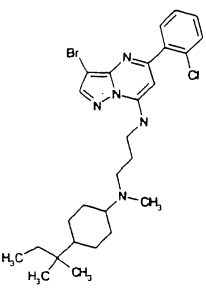
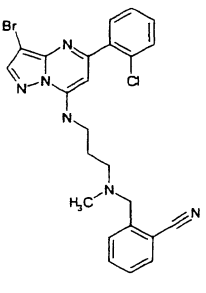
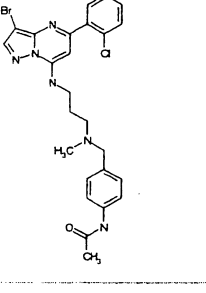
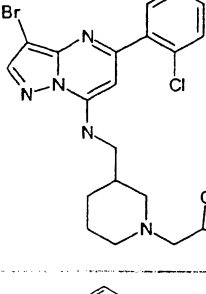
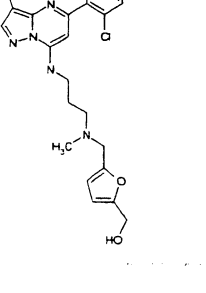
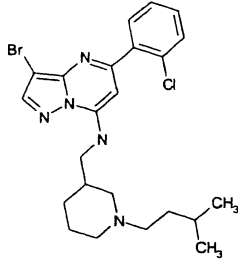
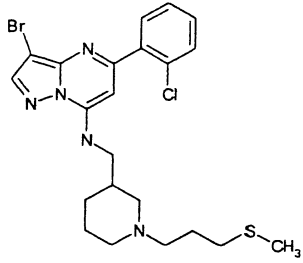
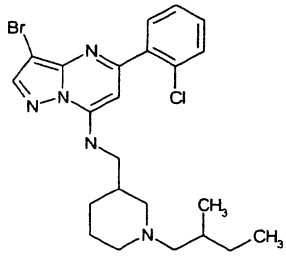
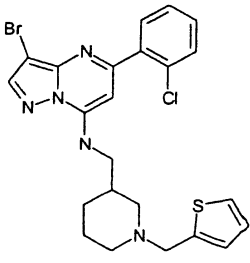
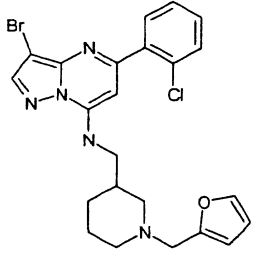
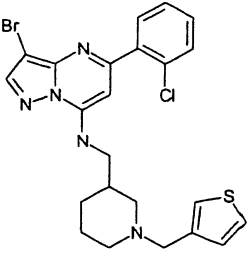
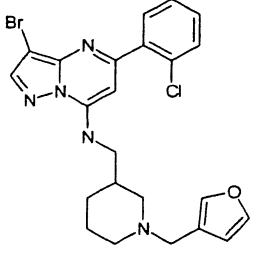
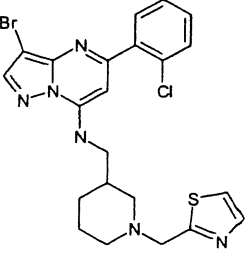
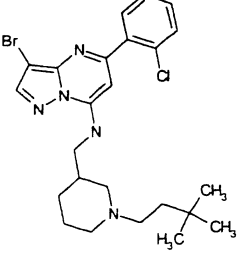
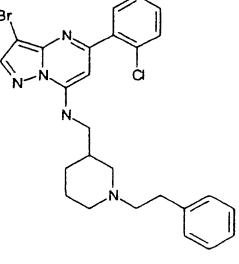
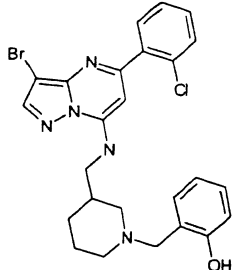
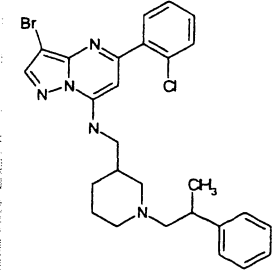
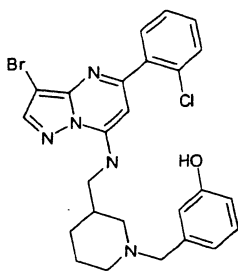
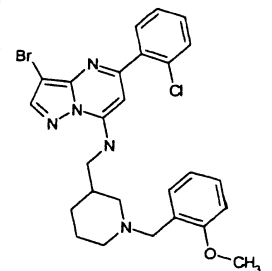
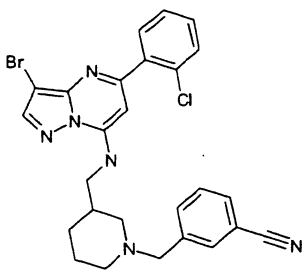
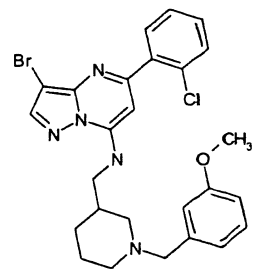
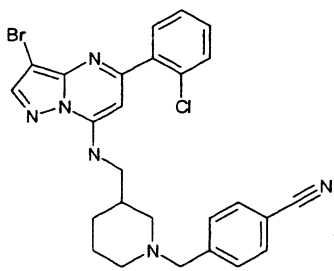
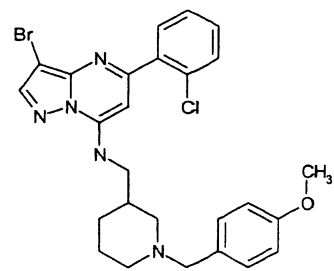
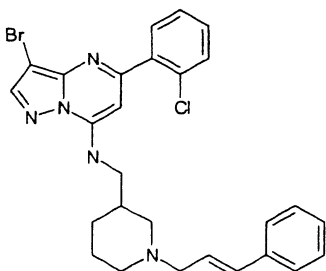
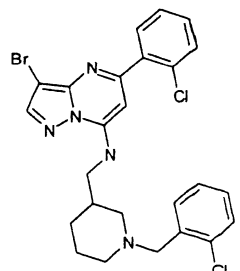
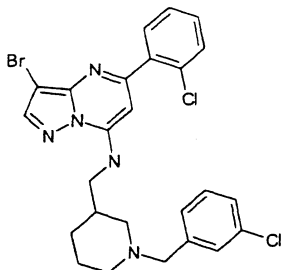
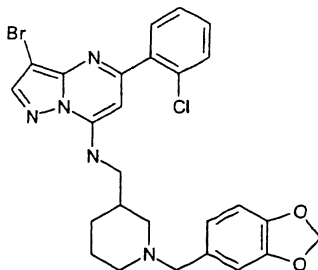
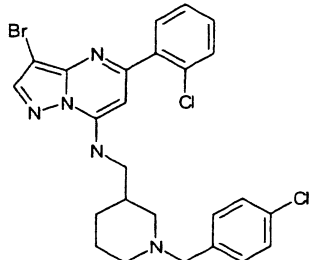
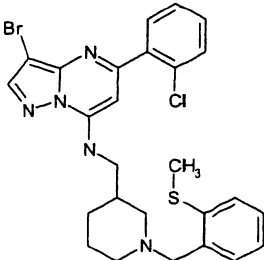
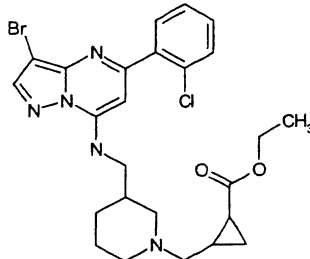
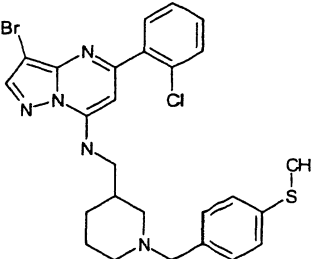
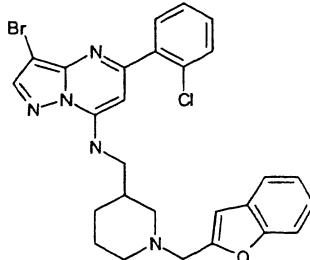
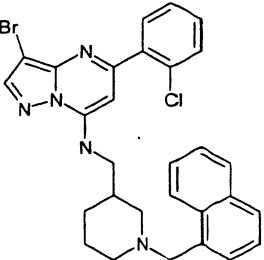
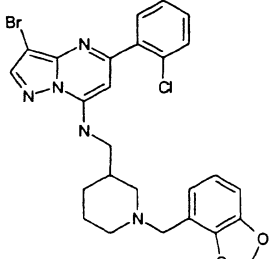
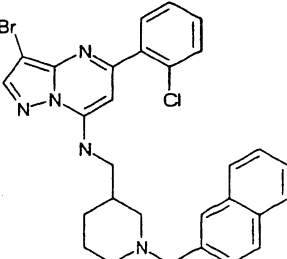
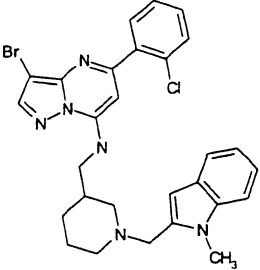
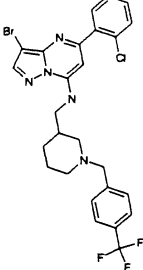
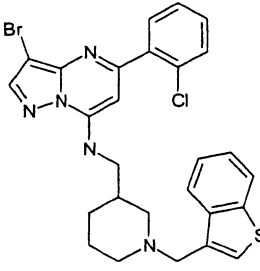
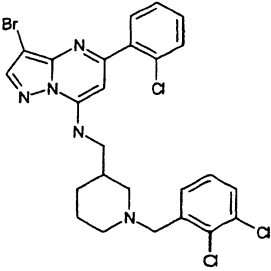
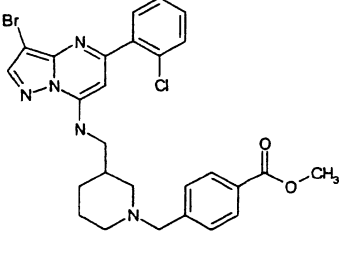
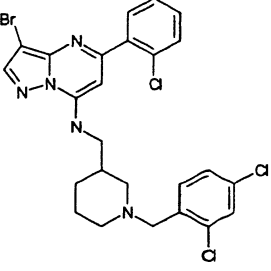
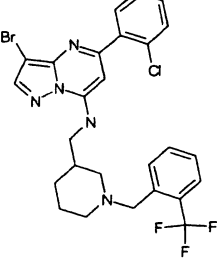
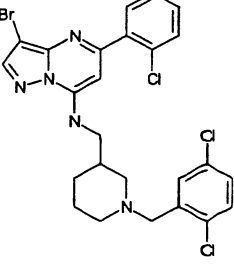
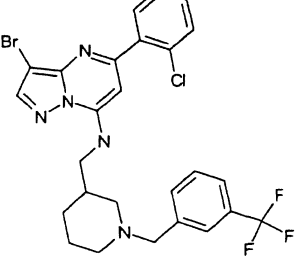
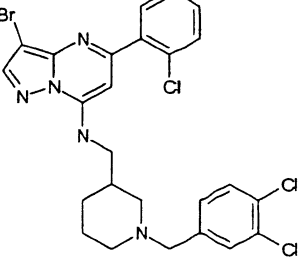
產物	1. 實例 2. m/z
	1. 8361 2. 547.909
	1. 8362 2. 510.817
	1. 8363 2. 542.833
	1. 8364 2. 573.815
	1. 8365 2. 547.798

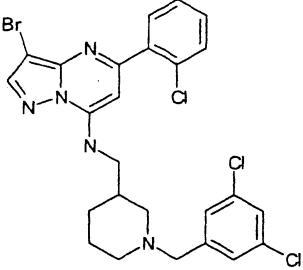
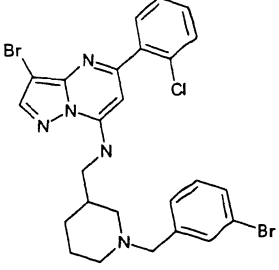
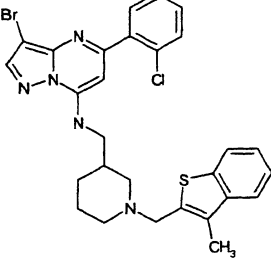
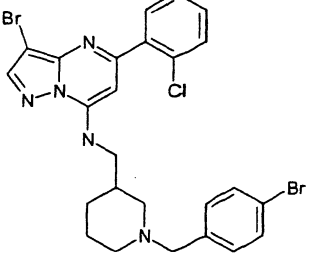
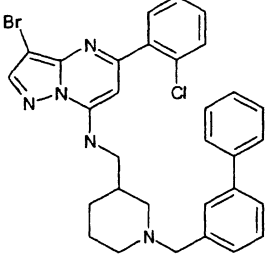
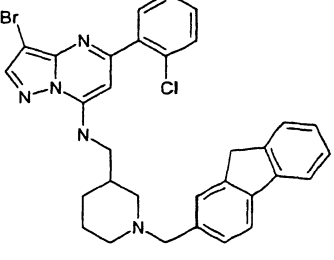
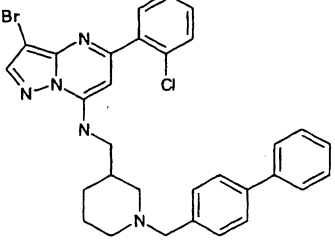
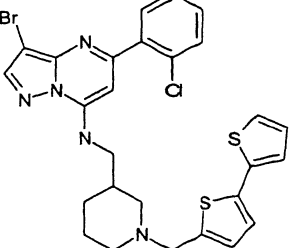
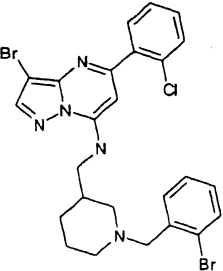
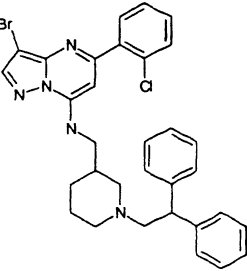
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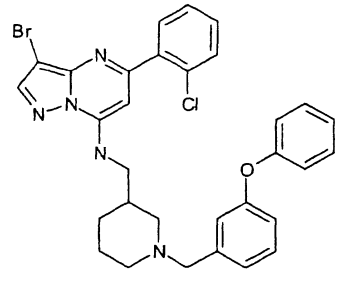
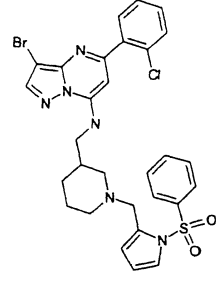
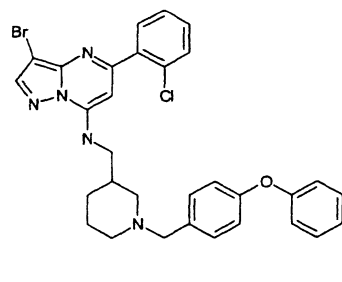
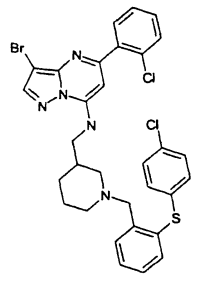
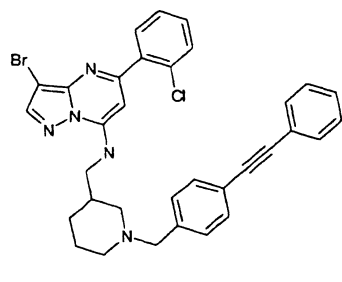
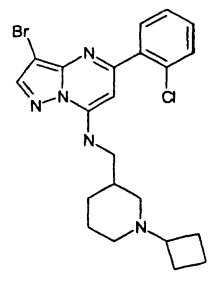
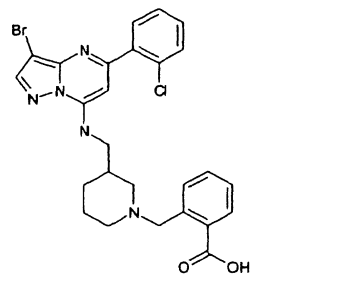
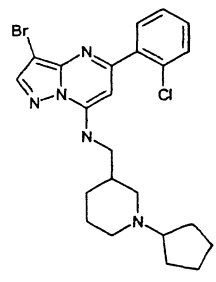
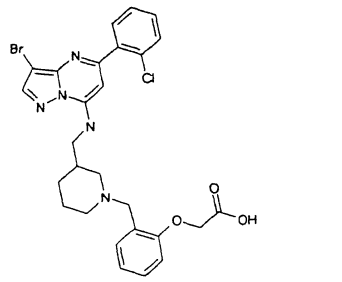
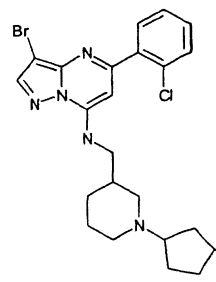
產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 8401 2. 491.883		1. 8406 2. 509.829
	1. 8402 2. 491.883		1. 8407 2. 517.795
	1. 8403 2. 501.823		1. 8408 2. 517.799
	1. 8404 2. 501.827		1. 8409 2. 518.796
	1. 8405 2. 505.89		1. 8410 2. 525.851

產物	1. 實例2. m/z	產物	1. 實例2. m/z
	1. 8411 2. 527.831		1. 8416 2. 539.859
	1. 8412 2. 527.833		1. 8417 2. 541.84
	1. 8413 2. 536.833		1. 8418 2. 541.843
	1. 8414 2. 536.829		1. 8419 2. 541.843
	1. 8415 2. 537.845		1. 8420 2. 546.786

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 8421 2. 546.792		1. 8426 2. 555.817
	1. 8422 2. 546.79		1. 8427 2. 557.81
	1. 8423 2. 547.854		1. 8428 2. 557.813
	1. 8424 2. 551.826		1. 8429 2. 561.839
	1. 8425 2. 555.819		1. 8430 2. 561.833

產物	1.實例 2. m/z	產物	1.實例 2. m/z
	1. 8431 2. 564.841		1. 8436 2. 579.794
	1. 8432 2. 567.795		1. 8437 2. 580.738
	1. 8433 2. 569.823		1. 8438 2. 580.732
	1. 8434 2. 579.797		1. 8439 2. 580.733
	1. 8435 2. 579.796		1. 8440 2. 580.734

產物	1.實例 2. m/z	產物	1.實例 2. m/z
	1. 8441 2. 580.726		1. 8446 2. 590.726
	1. 8442 2. 581.805		1. 8447 2. 590.724
	1. 8443 2. 587.844		1. 8448 2. 599.834
	1. 8444 2. 587.835		1. 8449 2. 599.749
	1. 8445 2. 590.723		1. 8450 2. 601.854

產物：	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 8451 2. 603.831		1. 8456 2. 640.779
	1. 8452 2. 603.83		1. 8457 2. 654.746
	1. 8453 2. 611.83		1. 8458 2. 475.871
	1. 8454 2. 555.824		1. 8459 2. 489.879
	1. 8455 2. 585.817		1. 8460 2. 503.885

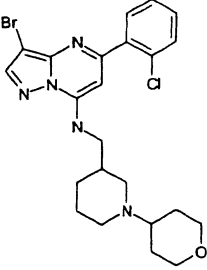
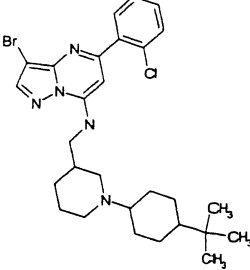
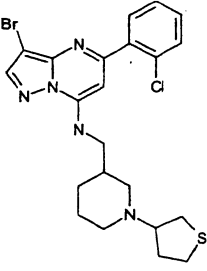
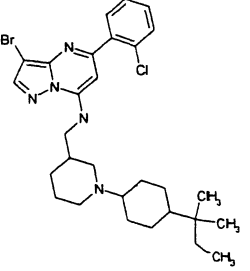
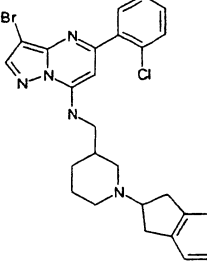
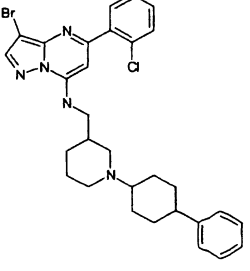
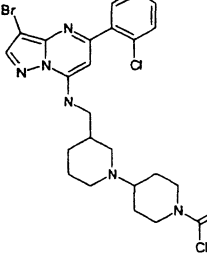
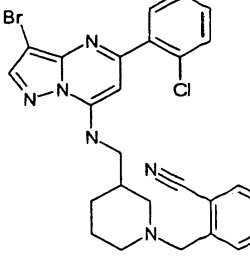
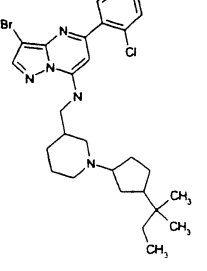
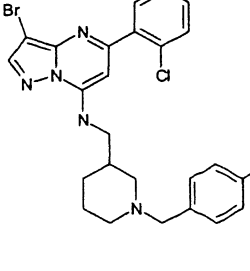
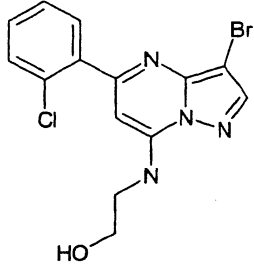
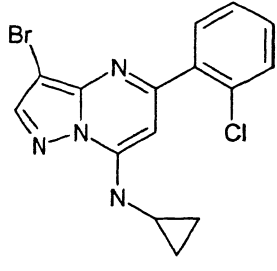
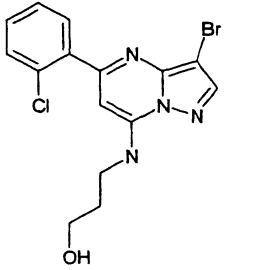
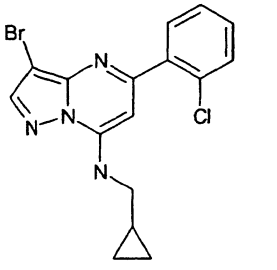
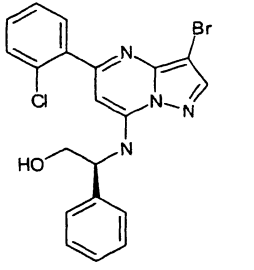
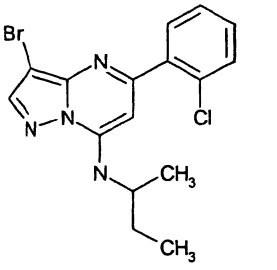
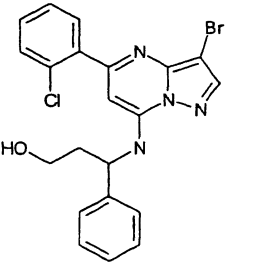
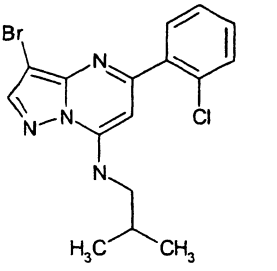
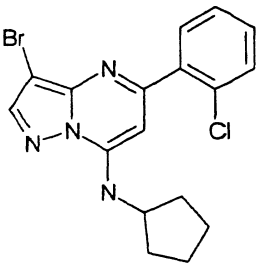
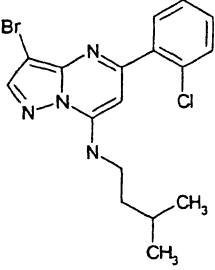
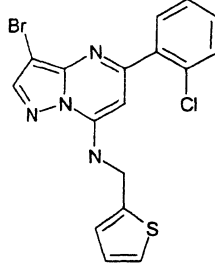
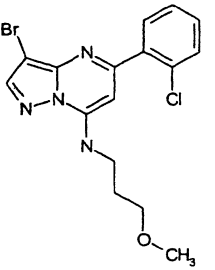
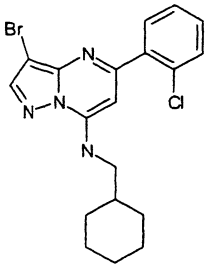
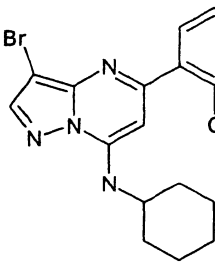
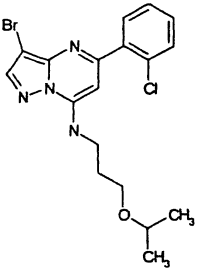
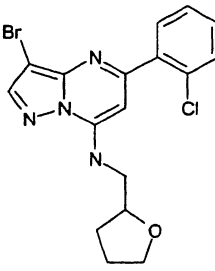
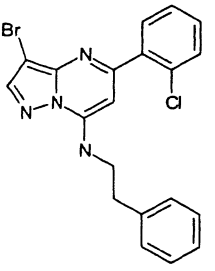
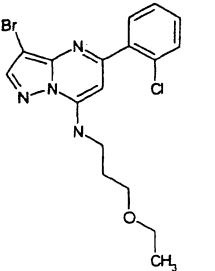
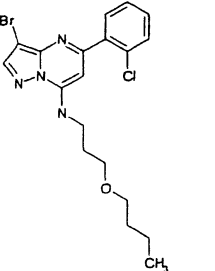
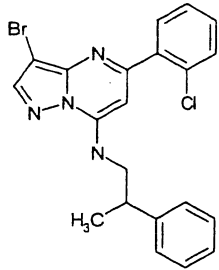
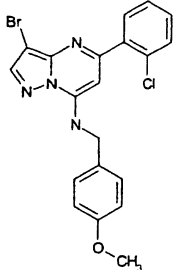
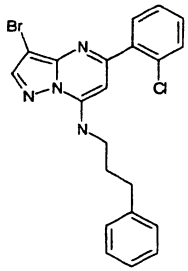
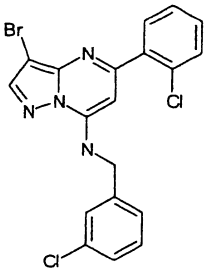
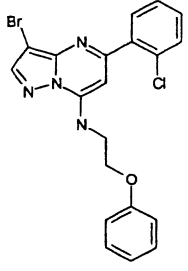
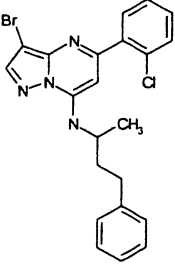
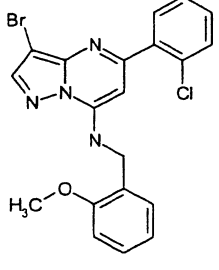
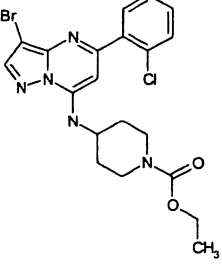
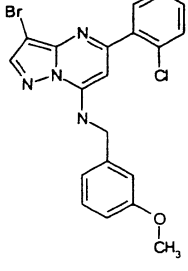
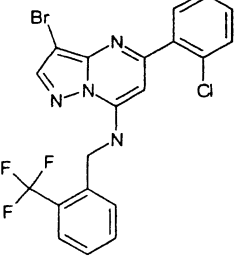
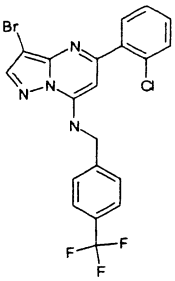
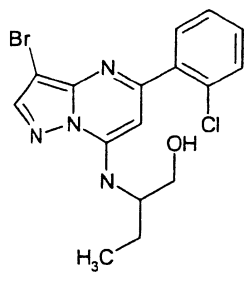
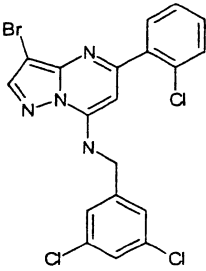
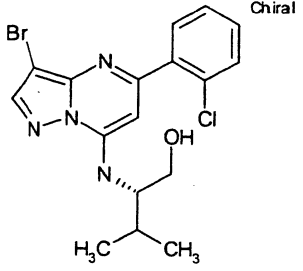
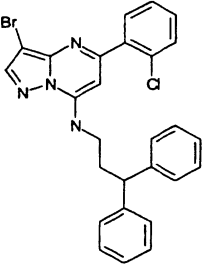
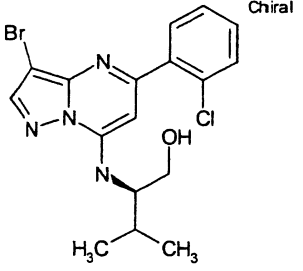
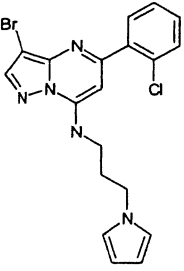
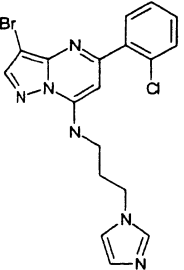
產物	1.實例 2. m/z	產物	1.實例 2. m/z
	1. 8461 2. 505.866		1. 8466 2. 559.919
	1. 8462 2. 507.828		1. 8467 2. 573.925
	1. 8463 2. 537.859		1. 8468 2. 579.876
	1. 8464 2. 546.877		1. 8469 2. 536.831
	1. 8465 2. 559.921		1. 8470 2. 568.843

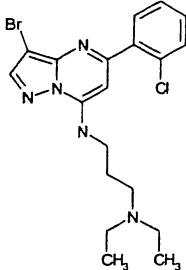
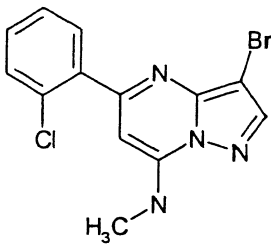
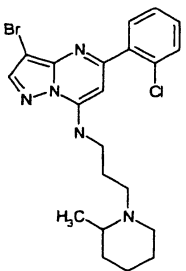
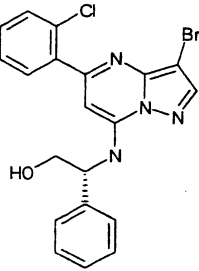
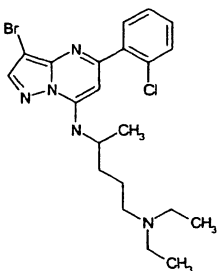
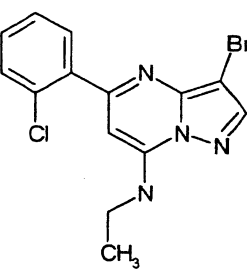
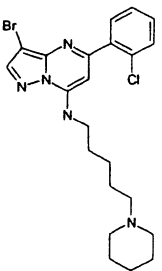
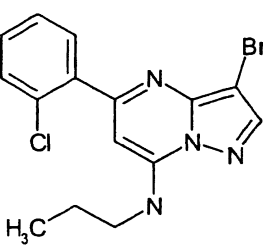
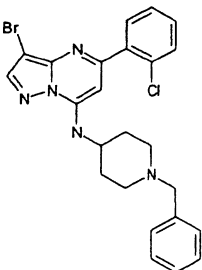
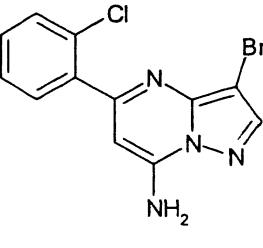
表85

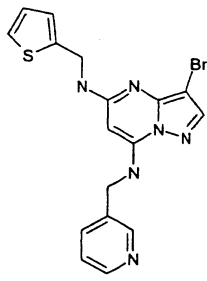
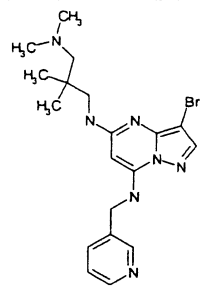
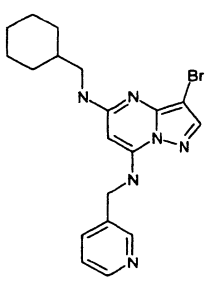
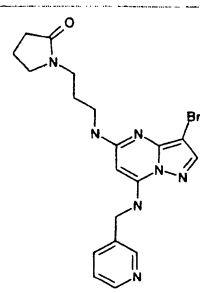
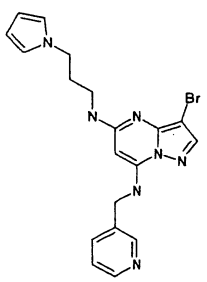
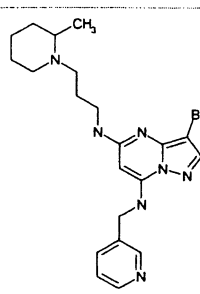
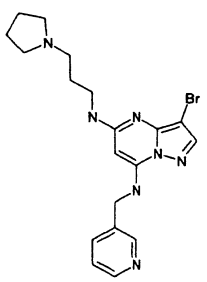
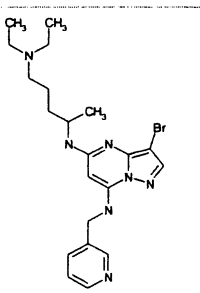
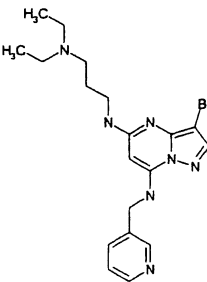
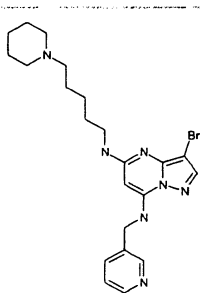
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	1. 8501 2. 367.2		1. 8506 2. 443.1
	1. 8502 2. 381.2		1. 8507 2. 323.1
	1. 8503 2. 443.2		1. 8508 2. 365.2
	1. 8504 2. 457.3		1. 8509 2. 379.21
			1. 8510 2. 381.21

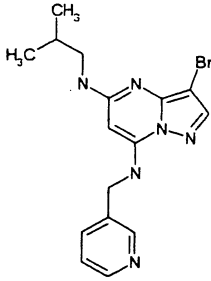
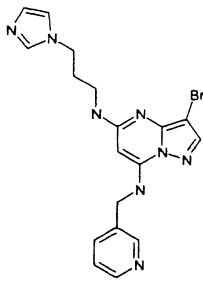
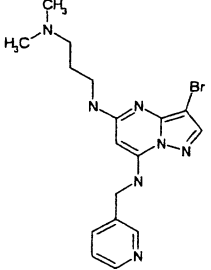
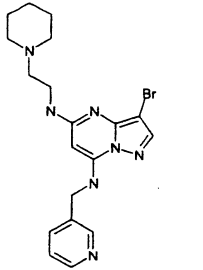
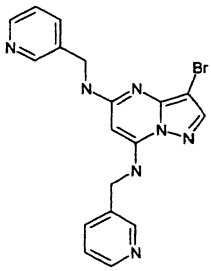
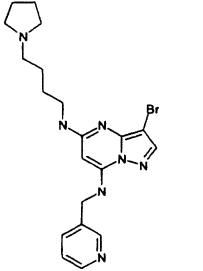
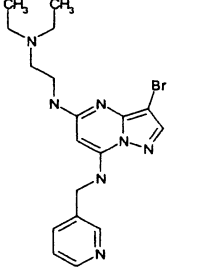
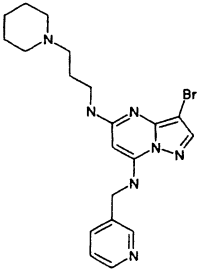
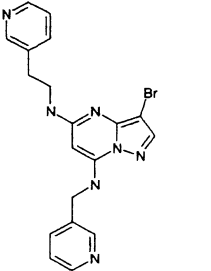
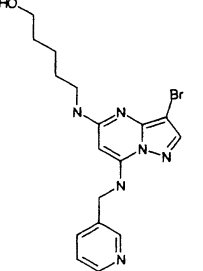
產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 8511 2. 381.21		1. 8516 2. 409.22
	1. 8512 2. 393.22		1. 8517 2. 411.23
	1. 8513 2. 395.22		1. 8518 2. 421.23
	1. 8514 2. 397.22		1. 8519 2. 421.23
	1. 8515 2. 407.22		1. 8520 2. 425.23

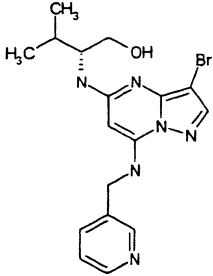
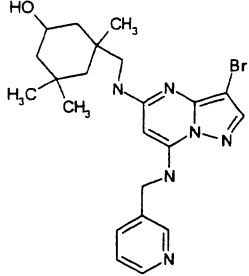
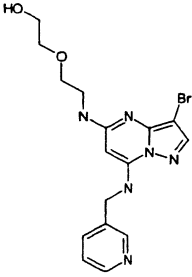
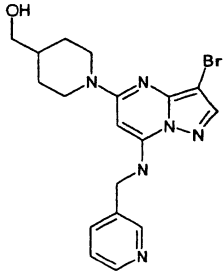
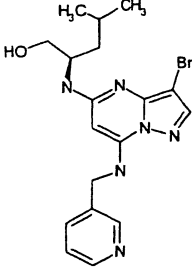
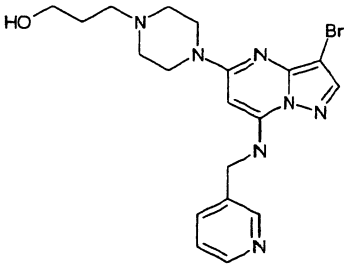
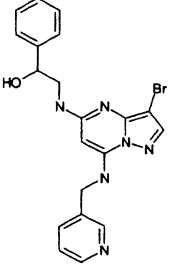
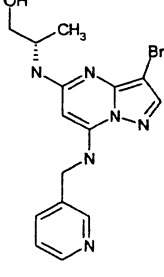
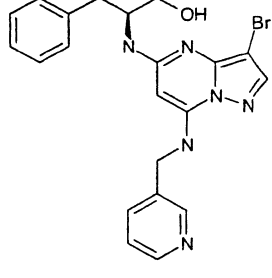
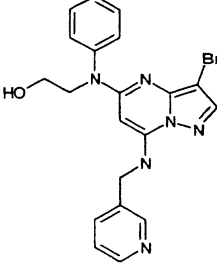
產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 8521 2. 429.24		1. 8526 2. 445.24
	1. 8522 2. 439.24		1. 8527 2. 444.24
	1. 8523 2. 443.24		1. 8528 2. 444.24
	1. 8524 2. 443.24		1. 8529 2. 446.25
	1. 8525 2. 445.24		1. 8530 2. 457.25

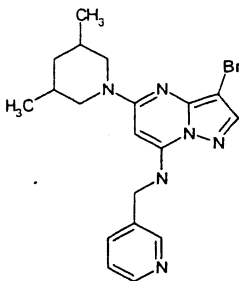
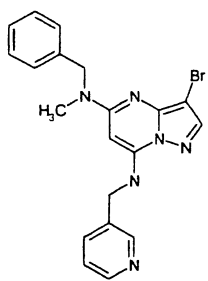
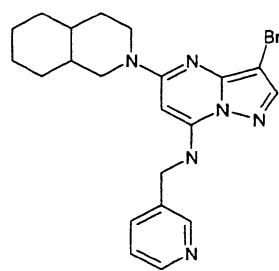
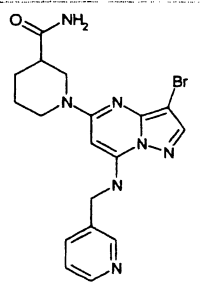
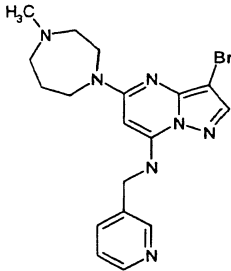
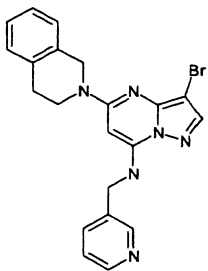
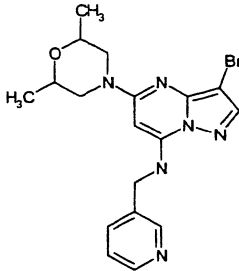
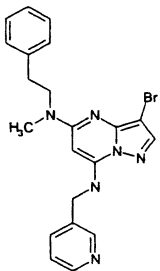
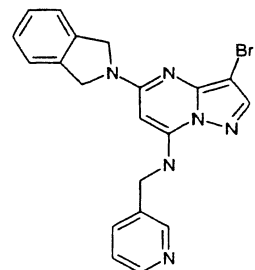
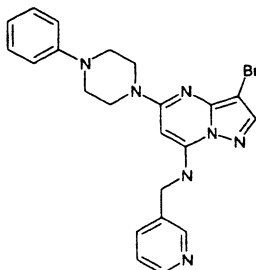
產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 8531 2. 480.26		1. 8536 2. 431.24
	1. 8532 2. 483.27		1. 8537 2. 429.24
	1. 8533 2. 483.27		1. 8538 2. 397.22
			1. 8539 2. 411.23
			1. 8540 2. 411.23

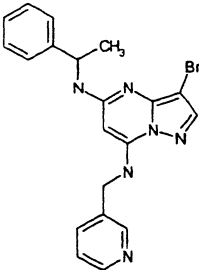
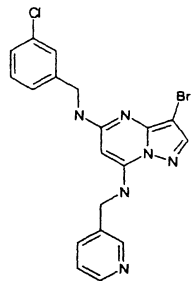
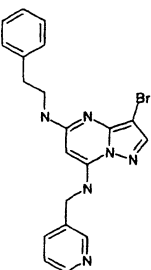
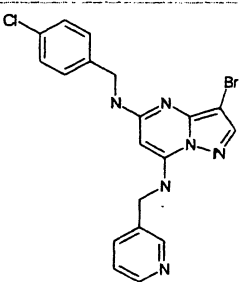
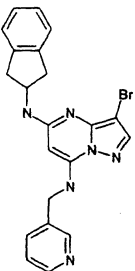
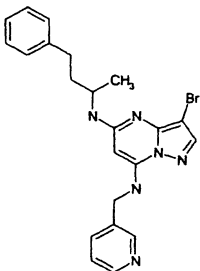
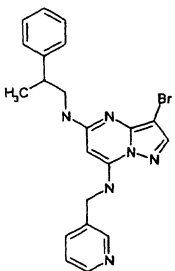
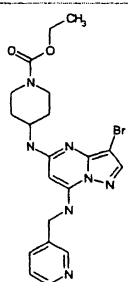
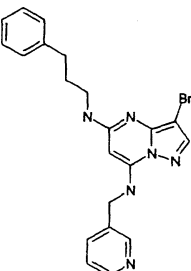
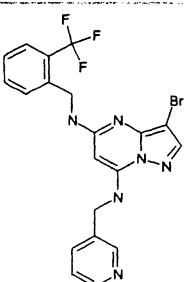
產物	1.實例 2. m/z	產物	1.實例 2. m/z
	1. 8541 2. 432.24		1. 8547 2. 478.26
	1. 8542 2. 433.24		1. 8548 2. 498.27
	1. 8543 2. 438.24		1. 8549 2. 365.1
	1. 8545 2. 464.26		1. 8549 2. 337.1
	1. 8546 2. 466.26		1. 8550 2. 351.1

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 8611 2. 417.23		1. 8616 2. 434.24
	1. 8612 2. 415.23		1. 8617 2. 446.25
	1. 8613 2. 428.24		1. 8618 2. 460.25
	1. 8614 2. 430.24		1. 8619 2. 459.25
	1. 8615 2. 434.24		1. 8620 2. 474.26

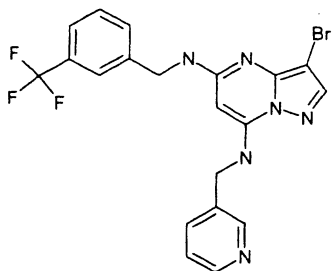
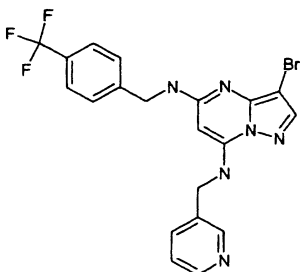
產物	1.實例 2. m/z	產物	1.實例 2. m/z
	1. 8621 2. 377.21		1. 8626 2. 427.23
	1. 8622 2. 406.22		1. 8627 2. 431.24
	1. 8623 2. 412.23		1. 8628 2. 446.25
	1. 8624 2. 420.23		1. 8629 2. 446.25
	1. 8625 2. 426.23		1. 8630 2. 407.2

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
 Chiral	1. 8631 2. 407.2		1. 8636 2. 475.3
	1. 8632 2. 409.2		1. 8637 2. 419.2
 Chiral	1. 8633 2. 421.2		1. 8638 2. 448.2
	1. 8634 2. 439.2	 Chiral	1. 8639 2. 379.2
	1. 8635 2. 455.3		1. 8640 2. 437.2

產物	1. 實例 2. m/z	產物	1. 實例 2. m/z
	1. 8641 2. 415.23		1. 8646 2. 423.23
	1. 8642 2. 443.24		1. 8647 2. 430.24
	1. 8643 2. 416.23		1. 8648 2. 437.24
	1. 8644 2. 417.23		1. 8649 2. 439.24
	1. 8645 2. 423.23		1. 8650 2. 466.26

產物	1.實例 2. m/z	產物	1.實例 2. m/z
	1. 8651 2. 423.23		1. 8656 2. 445.24
	1. 8652 2. 425.23		1. 8657 2. 445.24
	1. 8653 2. 437.24		1. 8658 2. 451.25
	1. 8654 2. 437.24		1. 8659 2. 476.26
	1. 8655 2. 437.24		1. 8660 2. 479.26

產物：

1. 實例 2.
m/z1. 8661
2. 477.261. 8662
2. 479.26

伍、中文發明摘要：

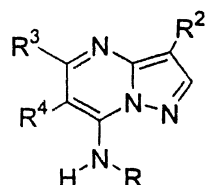
許多具體例中，本發明提供作為週期素依賴性激酶之抑制劑之新一類吡唑并[1,5-a]嘧啶化合物、製備此化合物之方法、含一或多種此化合物之醫藥組合物、製備包括一或多種此化合物之醫藥調配物之方法、及使用此化合物或醫藥組合物治療、預防、抑制或舒緩與CDKs有關之一或多種疾病之方法。

陸、英文發明摘要：

In its many embodiments, the present invention provides a novel class of pyrazolo[1,5-a]pyrimidine compounds as inhibitors of cyclin dependent kinases, methods of preparing such compounds, pharmaceutical compositions containing one or more such compounds, methods of preparing pharmaceutical formulations comprising one or more such compounds, and methods of treatment, prevention, inhibition, or amelioration of one or more diseases associated with the CDKs using such compounds or pharmaceutical compositions.

拾、申請專利範圍：

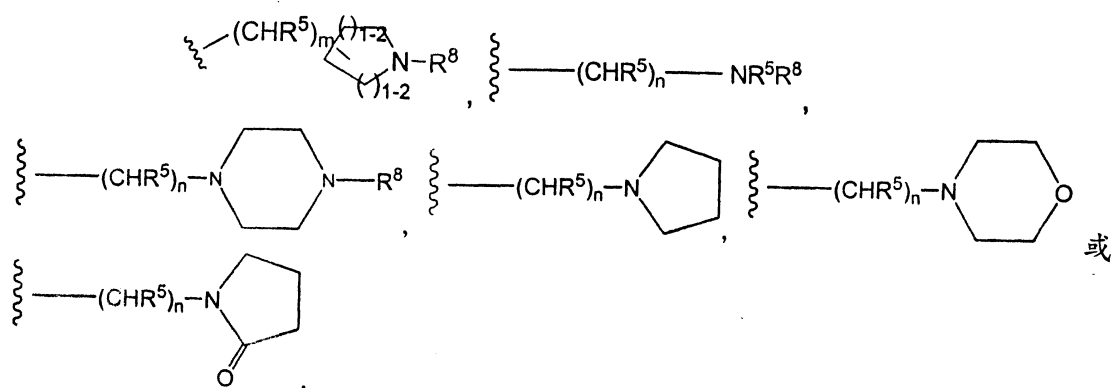
1. 一種下列結構式所示之化合物，



或該化合物之醫藥可接受性鹽或溶劑化物，

其中：

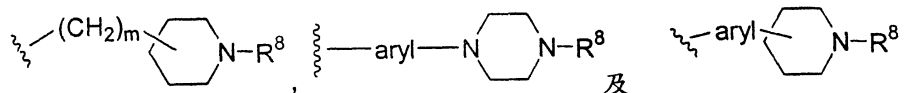
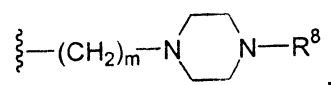
R為H、烷基、烯基、炔基、芳基烷基、芳基烯基、環烷基、環烷基烷基、烯基烷基、炔基烷基、雜環基、雜環基烷基、雜芳基烷基(包含該雜芳基之N-氧離子)、 $-(CHR^5)_n$ -芳基、 $-(CHR^5)_n$ -雜芳基、



其中該烷基、烯基、炔基、芳基、環烷基、雜環基及雜芳基各可為未經取代或視情況經一或多個可相同或不同之基團取代，各基團獨立選自下列所組成之組群：鹵素、烷基、芳基、環烷基、雜環基烷基、 CF_3 、 OCF_3 、 CN 、 $-OR^5$ 、 $-NR^5R^{10}$ 、 $-C(R^4R^5)_p-R^9$ 、 $-N(R^5)Boc$ 、 $-(CR^4R^5)_p$ 、 OR^5 、 $-C(O_2)R^5$ 、 $-C(O)R^5$ 、 $-C(O)NR^5R^{10}$ 、 $-SO_3H$ 、 $-SR^{10}$ 、

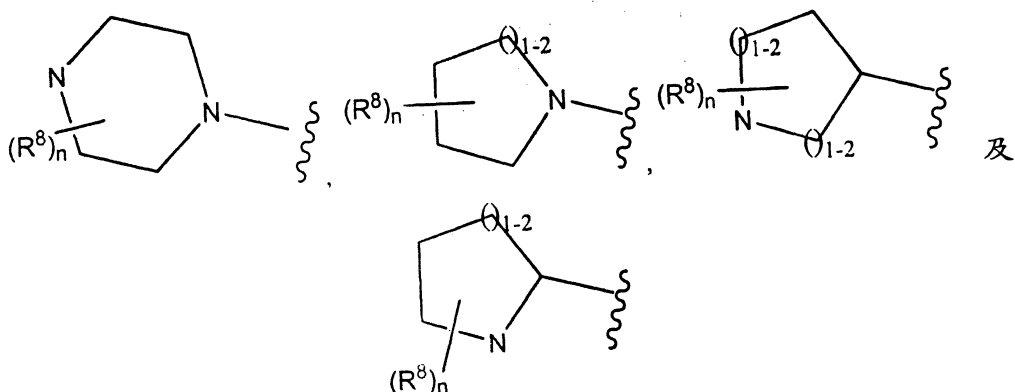
$-\text{S}(\text{O}_2)\text{R}^7$ 、 $-\text{S}(\text{O}_2)\text{NR}^5\text{R}^{10}$ 、 $-\text{N}(\text{R}^5)\text{S}(\text{O}_2)\text{R}^7$ 、 $-\text{N}(\text{R}^5)\text{C}(\text{O})\text{R}^7$ 及 $-\text{N}(\text{R}^5)\text{C}(\text{O})\text{NR}^5\text{R}^{10}$ ；

R^2 係選自由 R^9 、烷基、烯基、炔基、 CF_3 、雜環基、雜環基烷基、鹵素、鹵烷基、芳基、芳基烷基、雜芳基烷基、炔基烷基、環烷基、雜芳基、經1-6個 R^9 基取代之烷基(該 R^9 基可相同或不同且各 R^9 基係獨立選自後述所列之 R^9)、經1-3個可相同或不同之芳基或雜芳基(獨立選自苯基、吡啶基、噻吩基、呋喃基及噻唑基)取代之芳基、與芳基或雜芳基稠合之芳基、經1-3個可相同或不同之芳基或雜芳基(獨立選自苯基、吡啶基、噻吩基、呋喃基及噻唑基)取代之芳基、與芳基或雜芳基稠合之雜芳基、



其中 R^2 之上述定義中該一或多個芳基及/或一或多個雜芳基可為未經取代或視情況經一或多個基團取代，該基團可相同或不同且獨立選自由鹵素、 $-\text{CN}$ 、 $-\text{OR}^5$ 、 SR^5 、 $-\text{S}(\text{O}_2)\text{R}^6$ 、 $-\text{S}(\text{O}_2)\text{NR}^5\text{R}^6$ 、 $-\text{NR}^5\text{R}^6$ 、 $-\text{C}(\text{O})\text{NR}^5\text{R}^6$ 、 CF_3 、烷基、芳基及 OCF_3 所組成之組群；

R^3 係選自由下列所組成之組群： H 、鹵素、 $-\text{NR}^5\text{R}^6$ 、 $-\text{OR}^6$ 、 $-\text{SR}^6$ 、 $-\text{C}(\text{O})\text{N}(\text{R}^5\text{R}^6)$ 、烷基、炔基、環烷基、芳基、芳基烷基、雜環基、雜環基烷基、雜芳基及雜芳基烷基、



其中 R^3 之該烷基、環烷基、芳基、芳基烷基、雜環基、雜環基烷基、雜芳基及雜芳基烷基及對上述 R^3 剛顯示之結構之雜環基團各可經或視情況可獨立經一或多個可相同或不同之基團取代，各基團獨立選自下列所組成之組群：鹵素、烷基、芳基、環烷基、 CF_3 、 CN 、 $-OCF_3$ 、 $-(CR^4R^5)_pOR^5$ 、 $-OR^5$ 、 $-NR^5R^6$ 、 $-(CR^4R^5)_pNR^5R^6$ 、 $-C(O_2)R^5$ 、 $-C(O)R^5$ 、 $-C(O)NR^5R^6$ 、 $-SR^6$ 、 $-S(O_2)R^6$ 、 $-S(O_2)NR^5R^6$ 、 $-N(R^5)S(O_2)R^7$ 、 $-N(R^5)C(O)R^7$ 及 $-N(R^5)C(O)NR^5R^6$ ；但條件為與雜環基環上之氮原子相鄰之碳原子不帶有 $-OR^5$ 基；

R^4 為H、鹵基或烷基；

R^5 為H、烷基、芳基或環烷基；

R^6 係選自由H、烷基、烯基、芳基、芳基烷基、芳基烯基、環烷基、雜環基、雜環基烷基、雜芳基及雜芳基烷基所組成之組群，其中該烷基、芳基、芳基烷基、環烷基、雜環基、雜環基烷基、雜芳基及雜芳基烷基各可為未經取代或視情況經一或多個可相同或不同之基團

取代，各基團獨立選自下列所組成之組群：鹵素、烷基、芳基、環烷基、雜環基烷基、 CF_3 、 OCF_3 、 CN 、 $-\text{OR}^5$ 、 $-\text{NR}^5\text{R}^{10}$ 、 $-\text{C}(\text{R}^4\text{R}^5)_p-\text{R}^9$ 、 $-\text{N}(\text{R}^5)\text{Boc}$ 、 $-(\text{CR}^4\text{R}^5)_p\text{OR}^5$ 、 $-\text{C}(\text{O}_2)\text{R}^5$ 、 $-\text{C}(\text{O})\text{R}^5$ 、 $-\text{C}(\text{O})\text{NR}^5\text{R}^{10}$ 、 $-\text{SO}_3\text{H}$ 、 $-\text{SR}^{10}$ 、 $-\text{S}(\text{O}_2)\text{R}^7$ 、 $-\text{S}(\text{O}_2)\text{NR}^5\text{R}^{10}$ 、 $-\text{N}(\text{R}^5)\text{S}(\text{O}_2)\text{R}^7$ 、 $-\text{N}(\text{R}^5)\text{C}(\text{O})\text{R}^7$ 及 $-\text{N}(\text{R}^5)\text{C}(\text{O})\text{NR}^5\text{R}^{10}$ ；

R^{10} 係選自由H、烷基、芳基、芳基烷基、環烷基、雜環基、雜環基烷基、雜芳基及雜芳基烷基所組成之組群，其中該烷基、芳基、芳基烷基、環烷基、雜環基、雜環基烷基、雜芳基及雜芳基烷基各可為未經取代或視情況經一或多個可相同或不同之基團取代，各基團獨立選自下列所組成之組群：鹵素、烷基、芳基、環烷基、雜環基烷基、 CF_3 、 OCF_3 、 CN 、 $-\text{OR}^5$ 、 $-\text{NR}^4\text{R}^5$ 、 $-\text{C}(\text{R}^4\text{R}^5)_p-\text{R}^9$ 、 $-\text{N}(\text{R}^5)\text{Boc}$ 、 $-(\text{CR}^4\text{R}^5)_p\text{OR}^5$ 、 $-\text{C}(\text{O}_2)\text{R}^5$ 、 $-\text{C}(\text{O})\text{NR}^4\text{R}^5$ 、 $-\text{C}(\text{O})\text{R}^5$ 、 $-\text{SO}_3\text{H}$ 、 $-\text{SR}^5$ 、 $-\text{S}(\text{O}_2)\text{R}^7$ 、 $-\text{S}(\text{O}_2)\text{NR}^4\text{R}^5$ 、 $-\text{N}(\text{R}^5)\text{S}(\text{O}_2)\text{R}^7$ 、 $-\text{N}(\text{R}^5)\text{C}(\text{O})\text{R}^7$ 及 $-\text{N}(\text{R}^5)\text{C}(\text{O})\text{NR}^4\text{R}^5$ ；

或視情況(i)基團 $-\text{NR}^5\text{R}^{10}$ 中之 R^5 及 R^{10} 或(ii)基團 $-\text{NR}^5\text{R}^6$ 中之 R^5 及 R^6 可一起形成環烷基或雜環基基團，該環烷基或雜環基基團各為未經取代或視情況獨立經一或多個 R^9 基取代；

R^7 係選自由烷基、環烷基、芳基、芳基烯基、雜芳基、芳基烷基、雜芳基烷基、雜芳基烯基及雜環基所組成之組群，其中該烷基、環烷基、雜芳基烷基、芳基、

雜芳基及芳基烷基各可為未經取代或視情況獨立經一或多個可相同或不同之基團取代，各基團獨立選自下列所組成之組群：鹵素、烷基、芳基、環烷基、 CF_3 、 OCF_3 、 CN 、 $-\text{OR}^5$ 、 $-\text{NR}^5\text{R}^{10}$ 、 $-\text{CH}_2\text{OR}^5$ 、 $-\text{C}(\text{O}_2)\text{R}^5$ 、 $-\text{C}(\text{O})\text{NR}^5\text{R}^{10}$ 、 $-\text{C}(\text{O})\text{R}^5$ 、 $-\text{SR}^{10}$ 、 $-\text{S}(\text{O}_2)\text{R}^{10}$ 、 $-\text{S}(\text{O}_2)\text{NR}^5\text{R}^{10}$ 、 $-\text{N}(\text{R}^5)\text{S}(\text{O}_2)\text{R}^{10}$ 、 $-\text{N}(\text{R}^5)\text{C}(\text{O})\text{R}^{10}$ 及 $-\text{N}(\text{R}^5)\text{C}(\text{O})\text{NR}^5\text{R}^{10}$ ；

R^8 係選自由 R^6 、 $-\text{OR}^6$ 、 $-\text{C}(\text{O})\text{NR}^5\text{R}^{10}$ 、 $-\text{S}(\text{O}_2)\text{NR}^5\text{R}^{10}$ 、 $-\text{C}(\text{O})\text{R}^7$ 、 $-\text{C}(=\text{N}-\text{CN})-\text{NH}_2$ 、 $-\text{C}(=\text{NH})-\text{NHR}^5$ 、雜環基及 $-\text{S}(\text{O}_2)\text{R}^7$ 所組成之組群；

R^9 係選自由鹵素、 $-\text{CN}$ 、 $-\text{NR}^5\text{R}^{10}$ 、 $-\text{C}(\text{O}_2)\text{R}^6$ 、 $-\text{C}(\text{O})\text{NR}^5\text{R}^{10}$ 、 $-\text{OR}^6$ 、 $-\text{SR}^6$ 、 $-\text{S}(\text{O}_2)\text{R}^7$ 、 $-\text{S}(\text{O}_2)\text{NR}^5\text{R}^{10}$ 、 $-\text{N}(\text{R}^5)\text{S}(\text{O}_2)\text{R}^7$ 、 $-\text{N}(\text{R}^5)\text{C}(\text{O})\text{R}^7$ 及 $-\text{N}(\text{R}^5)\text{C}(\text{O})\text{NR}^5\text{R}^{10}$ 所組成之組群；

m 為0至4；

n 為1至4；及

p 為1至4；

但條件為當 R^2 為苯基，則 R^3 不為烷基、炔基或鹵素，且當 R^2 為芳基， R 不為 $\left\{ \text{---}(\text{CHR}^5)_n\text{---NR}^5\text{R}^8 \right\}$ ，

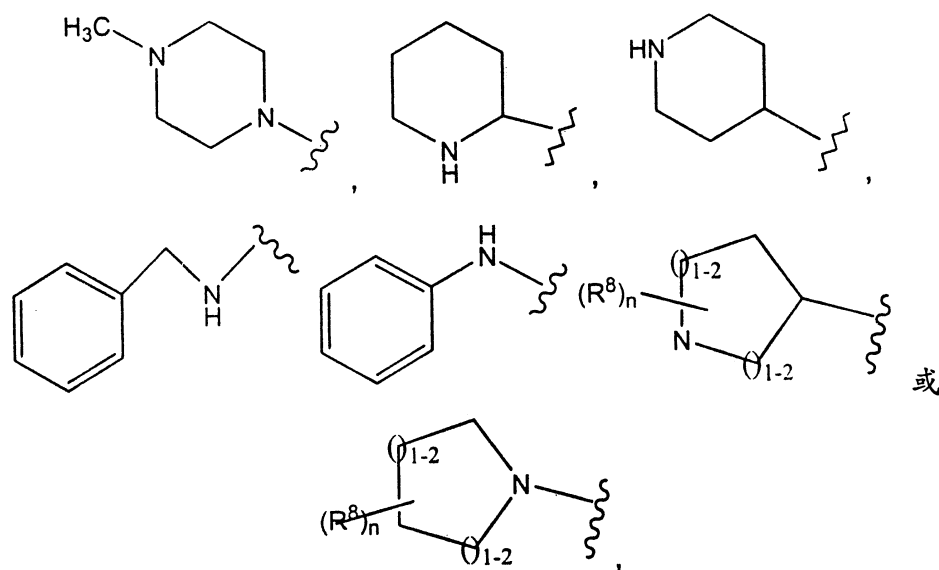
且又當 R 為芳基烷基時，該芳基烷基之芳基上任何雜芳基取代基含有至少三個雜原子。

2. 如申請專利範圍第1項之化合物，其中 R 為 $-(\text{CHR}^5)_n$ -芳基、 $-(\text{CHR}^5)_n$ -雜芳基、烷基、環烷基、雜環基或雜芳基烷基(包含該雜芳基之 N -氧離子)，其中該烷基、芳基、環烷基、雜環基及雜芳基各可為未經取代或視情況經一或

多個如申請專利範圍第1項所述之基團取代；

R^2 為鹵素、烷基、鹵烷基、CN、環烷基、雜環基或炔基；

R^3 為H、低碳烷基、芳基、雜芳基、環烷基、 $-NR^5R^6$ 、



其中上述 R^3 剛述及之該烷基、芳基、雜芳基、環烷基及雜環基結構視情況經一或多個可相同或不同之基團取代，各基團獨立選自下列所組成之組群：鹵素、 CF_3 、 OCF_3 、低碳烷基、CN、 $-C(O)R^5$ 、 $-S(O_2)R^5$ 、 $-C(=NH)-NH_2$ 、 $-C(=CN)-NH_2$ 、羥基烷基、烷氧基羰基、 $-SR^5$ 及 OR^5 ，但在與雜環基環之氮原子相鄰之碳原子上不帶有 $-OR^5$ 基團；

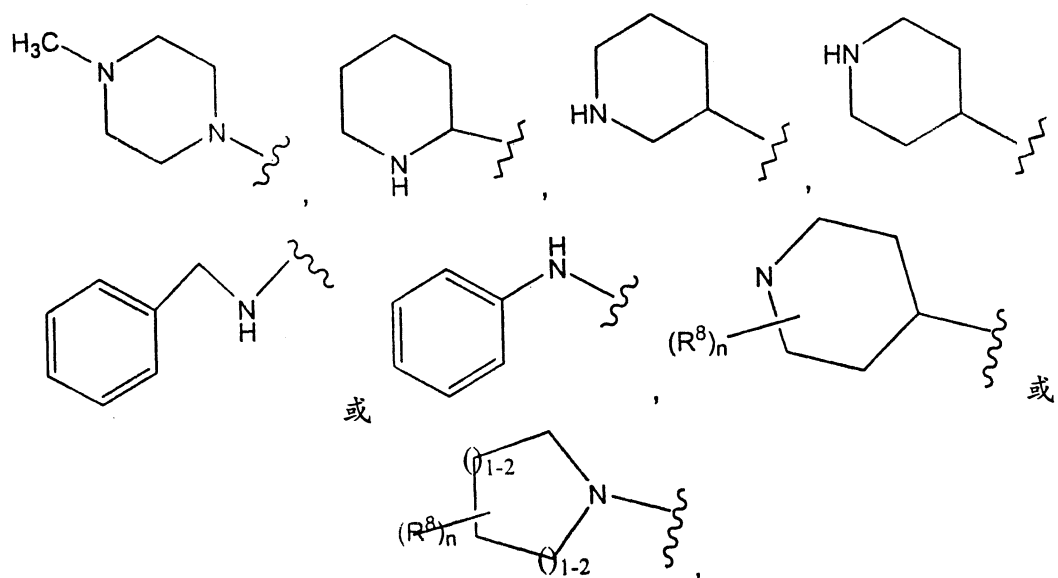
R^4 為H或低碳烷基；

R^5 為H、低碳烷基或環烷基；

n 為1至2；及

p 為1或2。

3. 如申請專利範圍第2項之化合物，其中R為羥基烷基、 $-(CHR^5)_n$ -芳基或 $-(CHR^5)_n$ -雜芳基，其中該芳基及雜芳基各為未經取代或經一或多個可相同或不同之基取代，各基獨立選自雜芳基、胺、雜環基、 $-C(O)N(R^5R^6)$ 、 $-S(O_2)R^5$ 、 $-S(O_2)N(R^5R^6)$ 、烷氧基及鹵基所組成之組群。
4. 如申請專利範圍第2項之化合物，其中 R^2 為Br、Cl、 CF_3 、CN、低碳烷基、環丙基、炔基、經 $-OR^6$ 取代之烷基或四氫呋喃基。
5. 如申請專利範圍第2項之化合物，其中 R^3 為H、低碳烷基、芳基、雜芳基、環烷基、



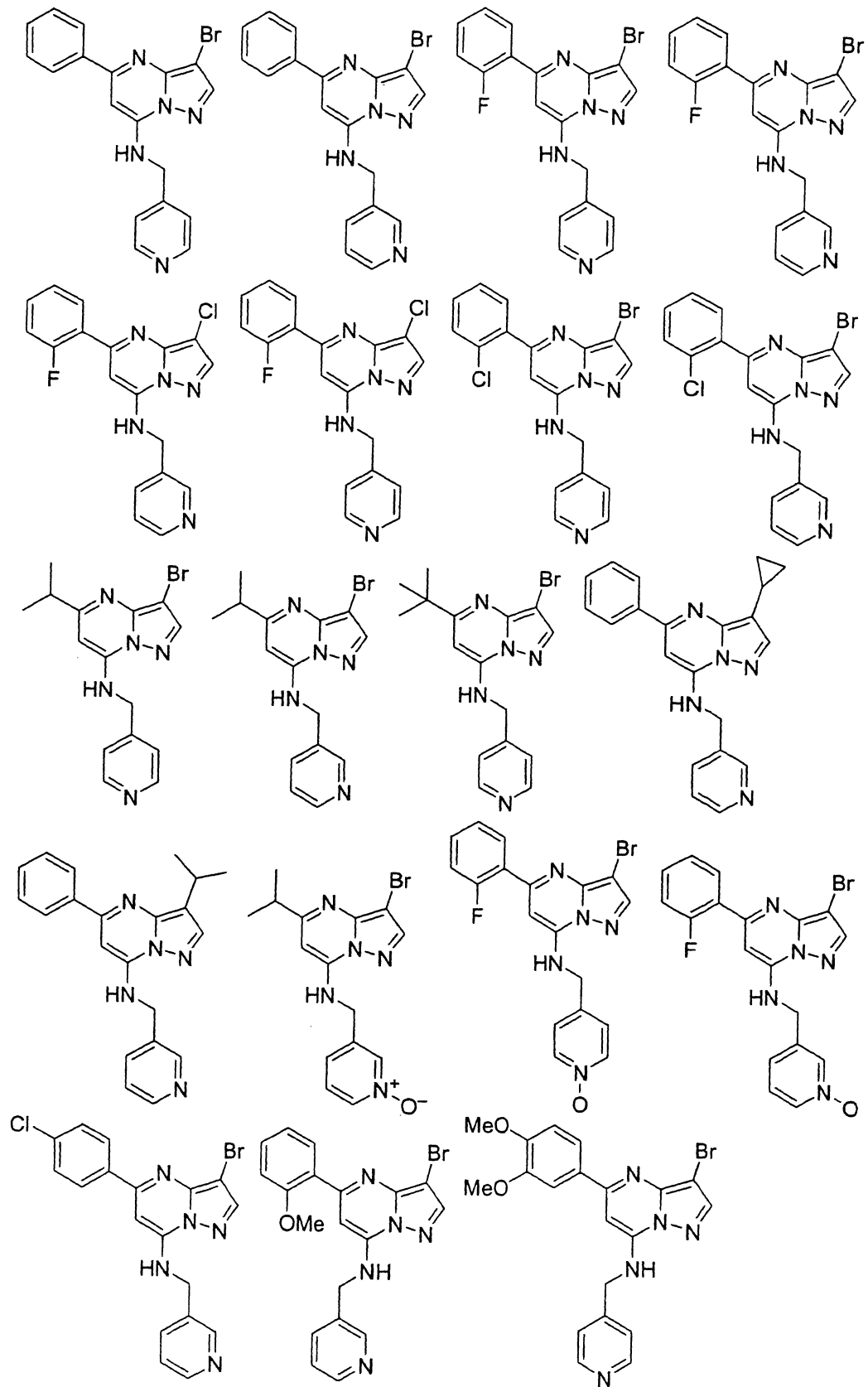
其中上述 R^3 剛述及之該烷基、芳基、雜芳基、環烷基及雜環基結構視情況經一或多個可相同或不同之基團取代，各基團獨立選自下列所組成之組群：鹵素、 CF_3 、 OCF_3 、低碳烷基、CN及 OR^5 ，但在與雜環基環之氮原子

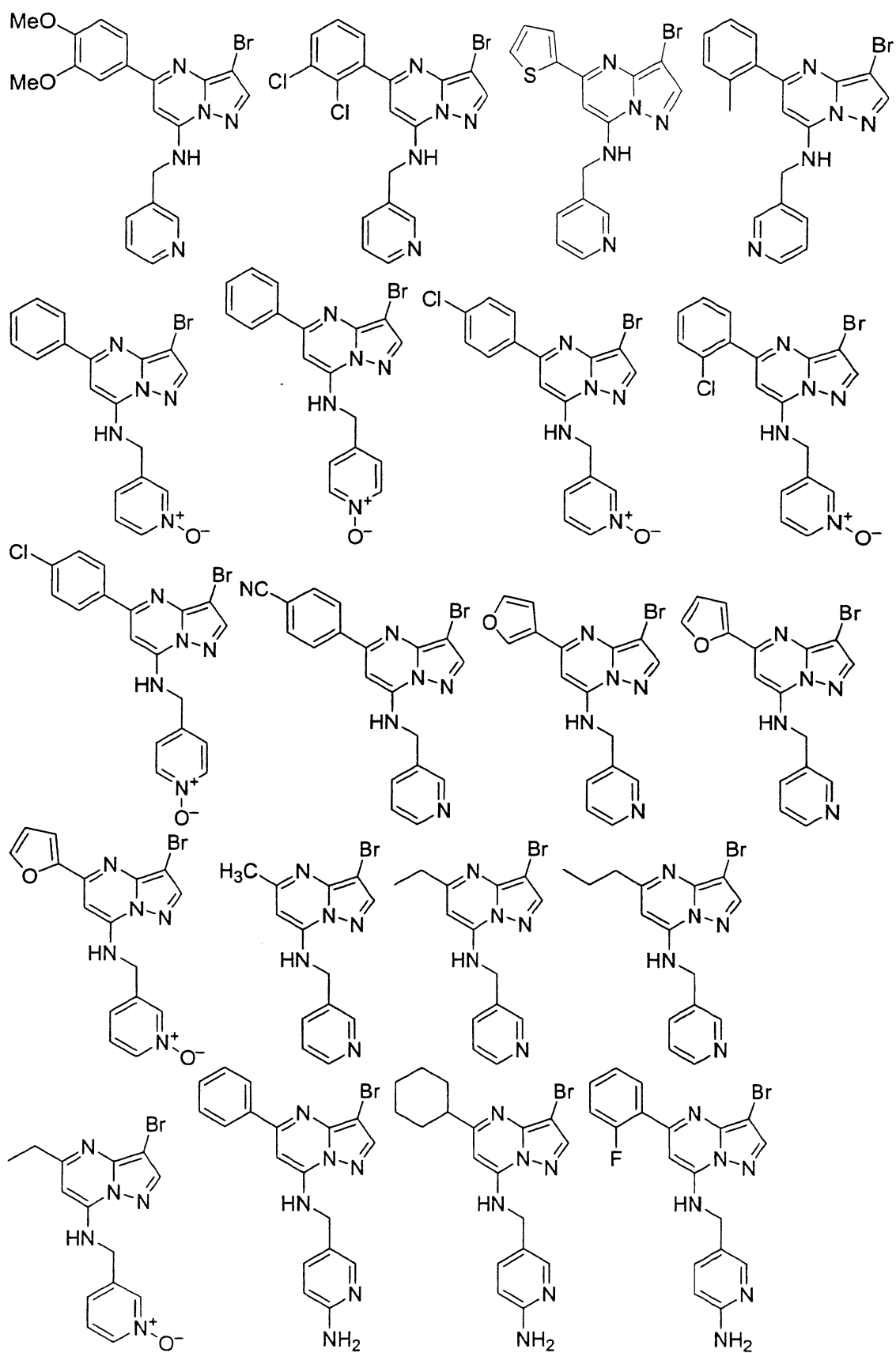
相鄰之碳原子上不帶有-OR⁵基團。

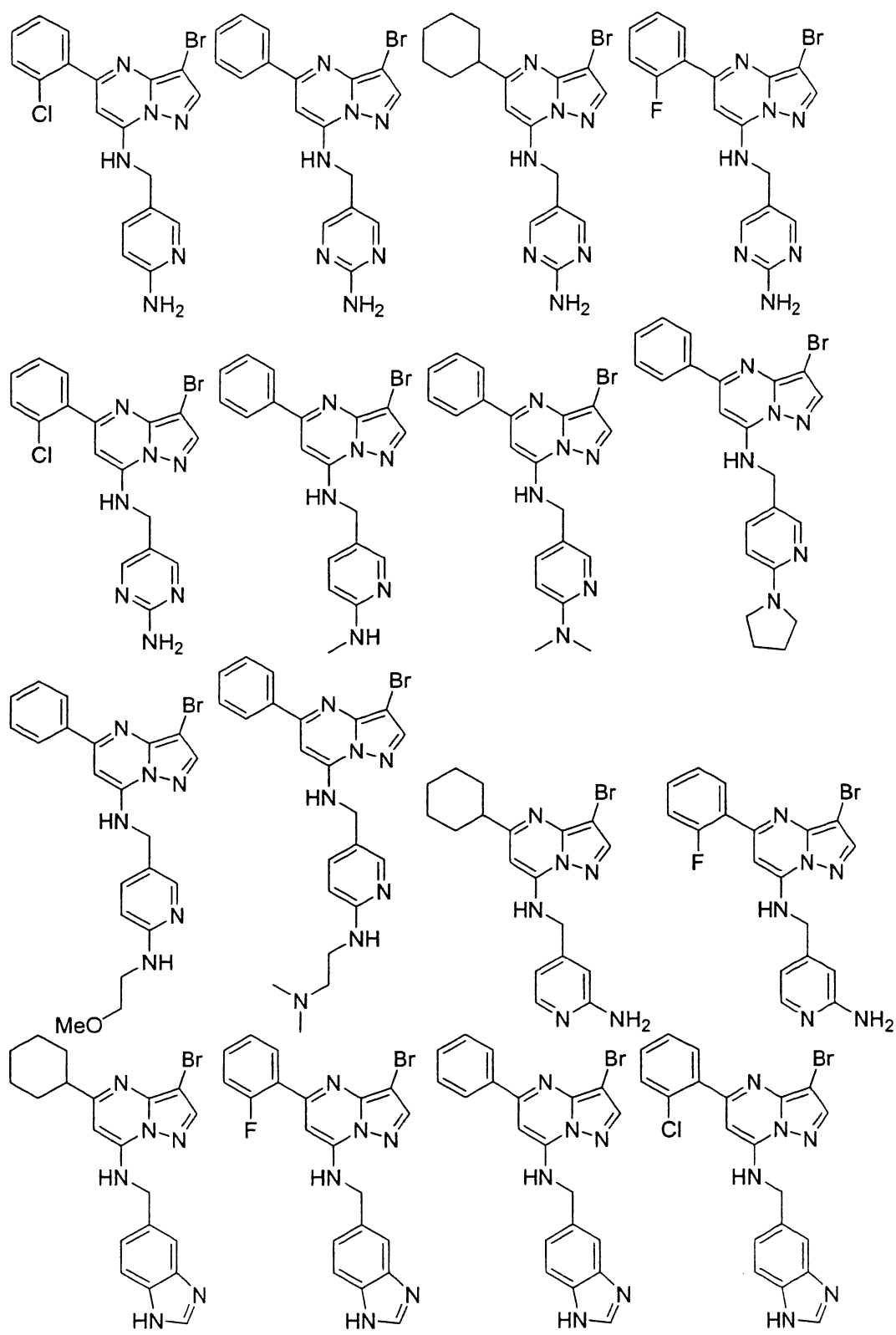
6. 如申請專利範圍第2項之化合物，其中R⁴為H或低碳烷基。
7. 如申請專利範圍第2項之化合物，其中R⁵為H。
8. 如申請專利範圍第2項之化合物，其中n為1。
9. 如申請專利範圍第1項之化合物，其中p為1。
10. 如申請專利範圍第2項之化合物，其中R為苄基或羥基烷基。
11. 如申請專利範圍第2項之化合物，其中R為吡啶-3-基甲基，其中該吡啶基可未經取代或視情況獨立經一或多個如申請專利範圍第1項所述基團取代。
12. 如申請專利範圍第2項之化合物，其中R為吡啶-4-基甲基，其中該吡啶基可未經取代或視情況獨立經一或多個如申請專利範圍第1項所述基團取代。
13. 如申請專利範圍第2項之化合物，其中R為吡啶-2-基甲基、吡啶-3-基甲基或吡啶-4-基甲基之N-氧離子，其中該吡啶基各可未經取代或視情況獨立經一或多個如申請專利範圍第1項所述基團取代。
14. 如申請專利範圍第4項之化合物，其中R²為Br。
15. 如申請專利範圍第4項之化合物，其中R²為Cl。
16. 如申請專利範圍第4項之化合物，其中R²為乙基。
17. 如申請專利範圍第4項之化合物，其中R²為環丙基。
18. 如申請專利範圍第4項之化合物，其中R²為乙炔基。
19. 如申請專利範圍第2項之化合物，其中R³為低碳烷基、環烷基、雜環基、芳基或-N(R⁵R⁶)。

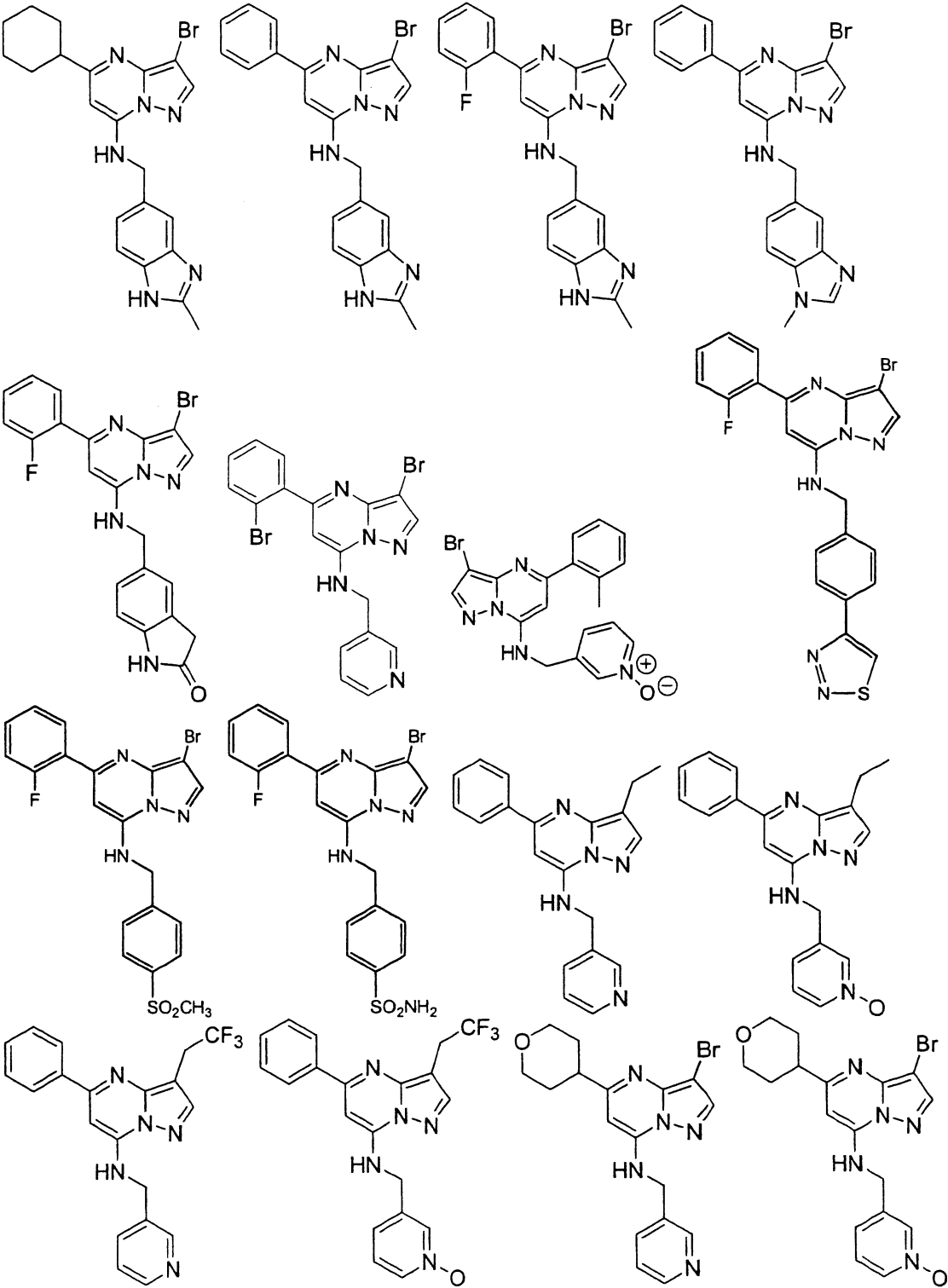
20. 如申請專利範圍第19項之化合物，其中 R^3 為異丙基。
21. 如申請專利範圍第19項之化合物，其中 R^3 為環己基或原冰片基，其中該環烷基或原冰片基各可為未經取代或視情況經一或多個相同或不同之基取代，各基獨立選自由烷基及羥基烷基所組成之組群。
22. 如申請專利範圍第19項之化合物，其中 R^3 為未經取代之苯基。
23. 如申請專利範圍第19項之化合物，其中 R^3 為經一或多個相同或不同之基取代之苯基，各基獨立選自由F、Br、Cl及 CF_3 所組成之組群。
24. 如申請專利範圍第19項之化合物，其中該 $-N(R^5R^6)$ 中之 R^5 為H或羥基烷基，且該 $-N(R^5R^6)$ 中之 R^6 係選自由烷基、羥基烷基、環烷基及亞甲二氧基所組成之組群，其中該烷基及環烷基各可為未經取代或經一或多個可相同或不同之基取代，各基獨立選自由胺、乙氧羰基、醯胺、羥基烷基、羥基所組成之組群。
25. 如申請專利範圍第19項之化合物，其中該 $-N(R^5R^6)$ 中之 R^5 及 R^6 一起形成雜環基，其中該雜環基可為未經取代或視情況獨立經一或多個可相同或不同之基取代，各基係選自由羥基烷基、醯胺、 $-C(O)R^5$ 、 $>C(CH_3)_2$ 、 $-S(O_2)R^5$ 、 $-S(O_2)N(R^5R^6)$ 、 $-C(=NH)N(R^5R^6)$ 及 $-C(=N-CN)N(R^5R^6)$ 所組成之組群。
26. 如申請專利範圍第25項之化合物，其中由 R^5 及 R^6 所形成之該雜環基為吡咯啉或哌啉環。

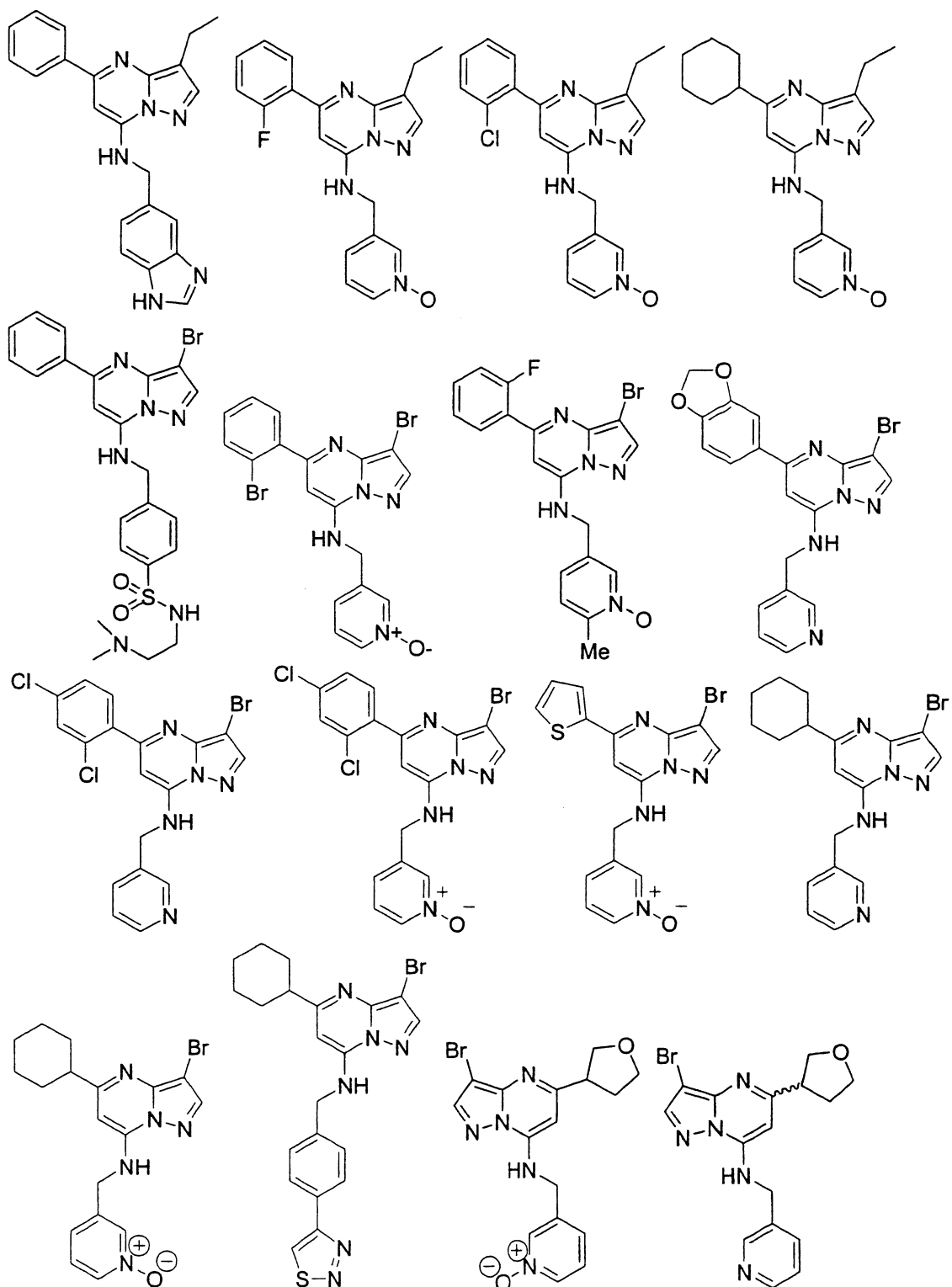
27. 一種下式之化合物，

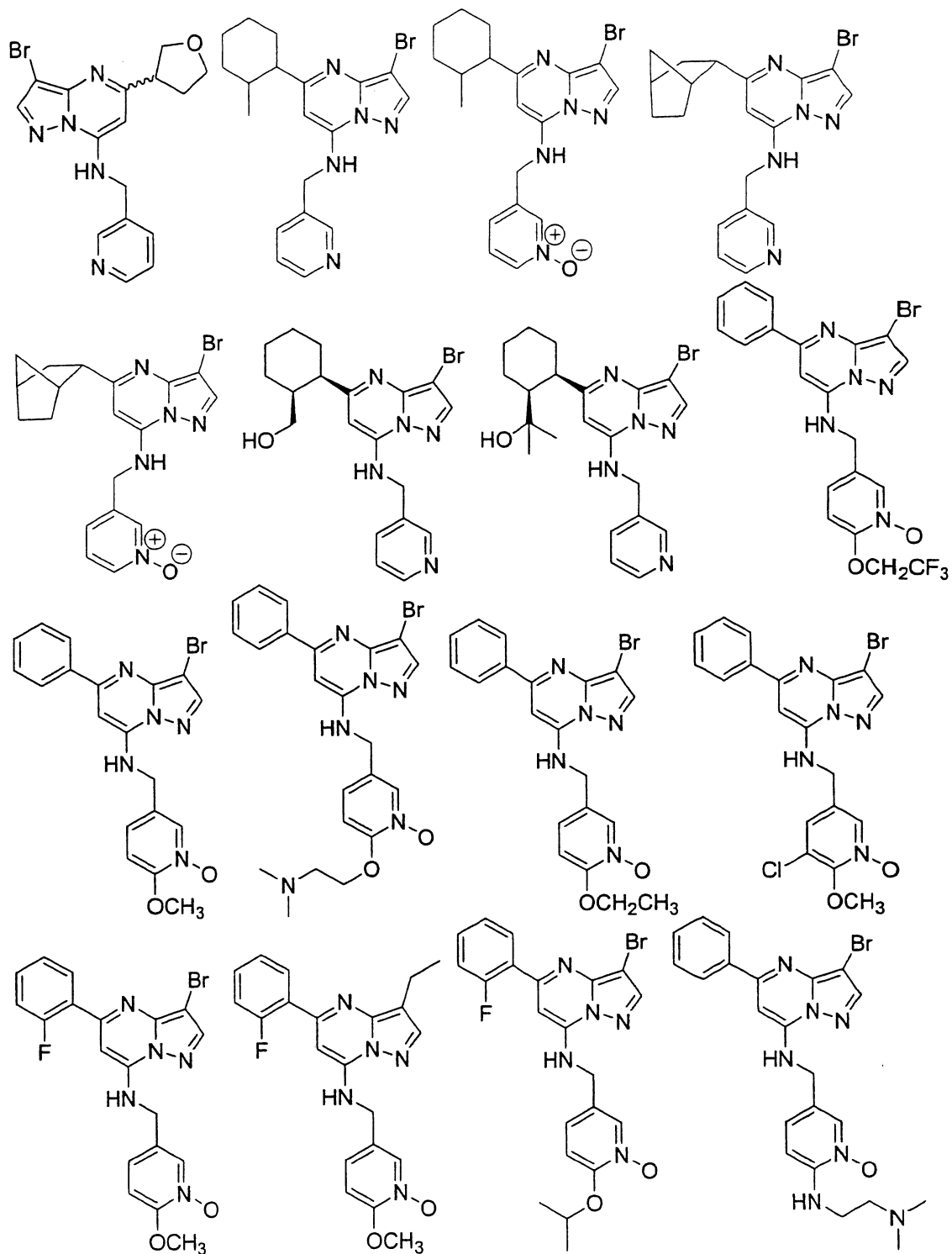


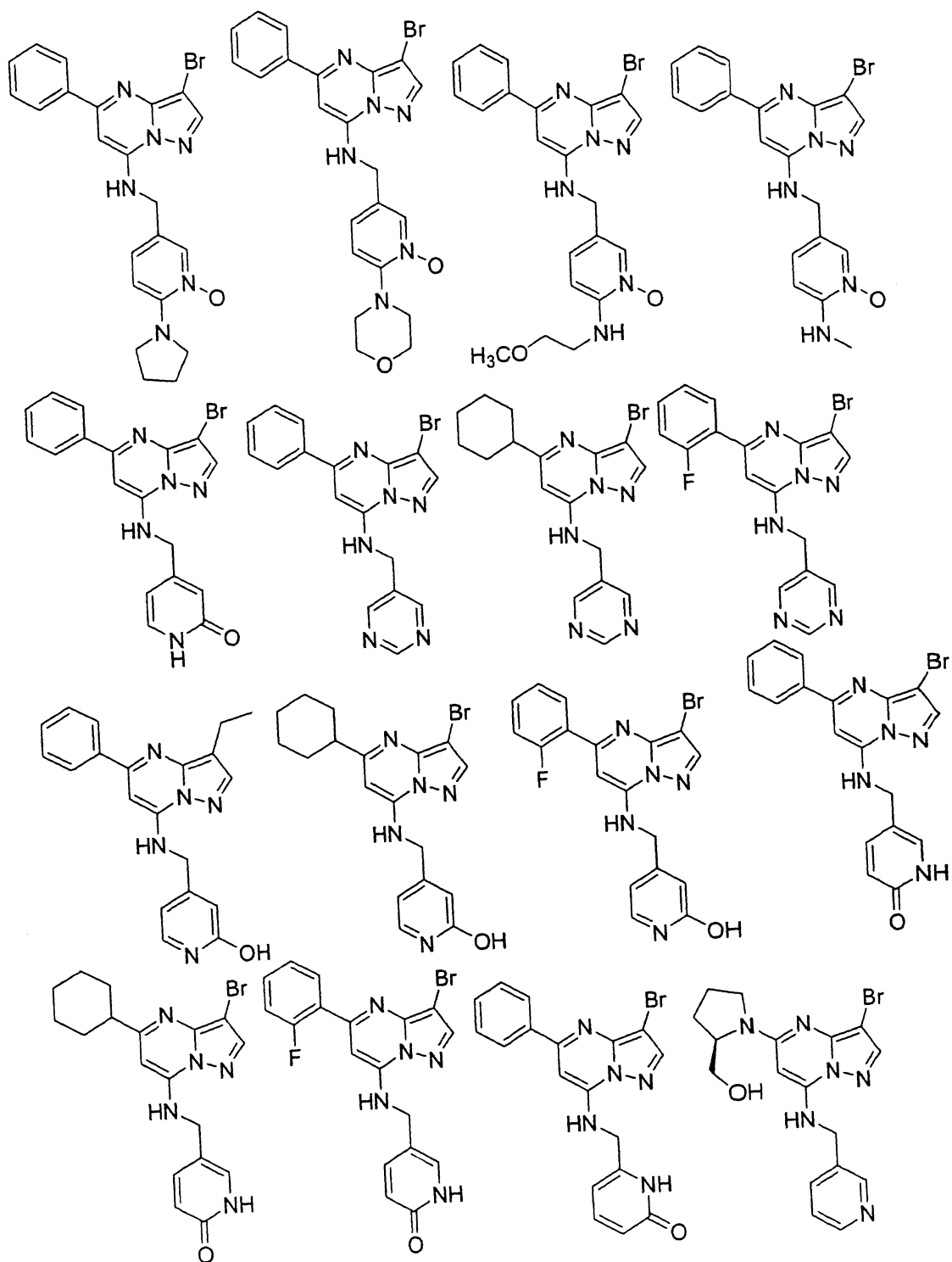


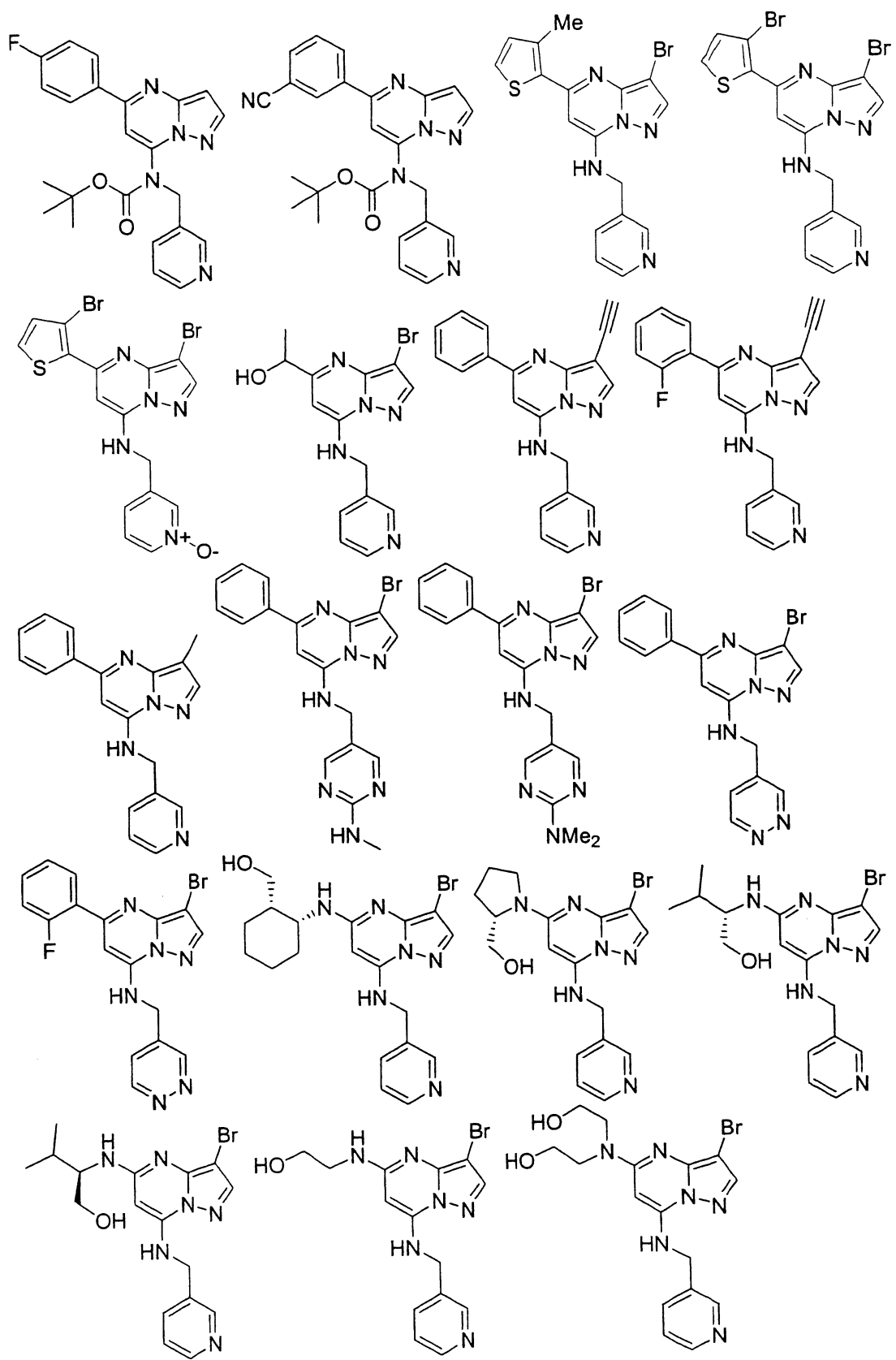


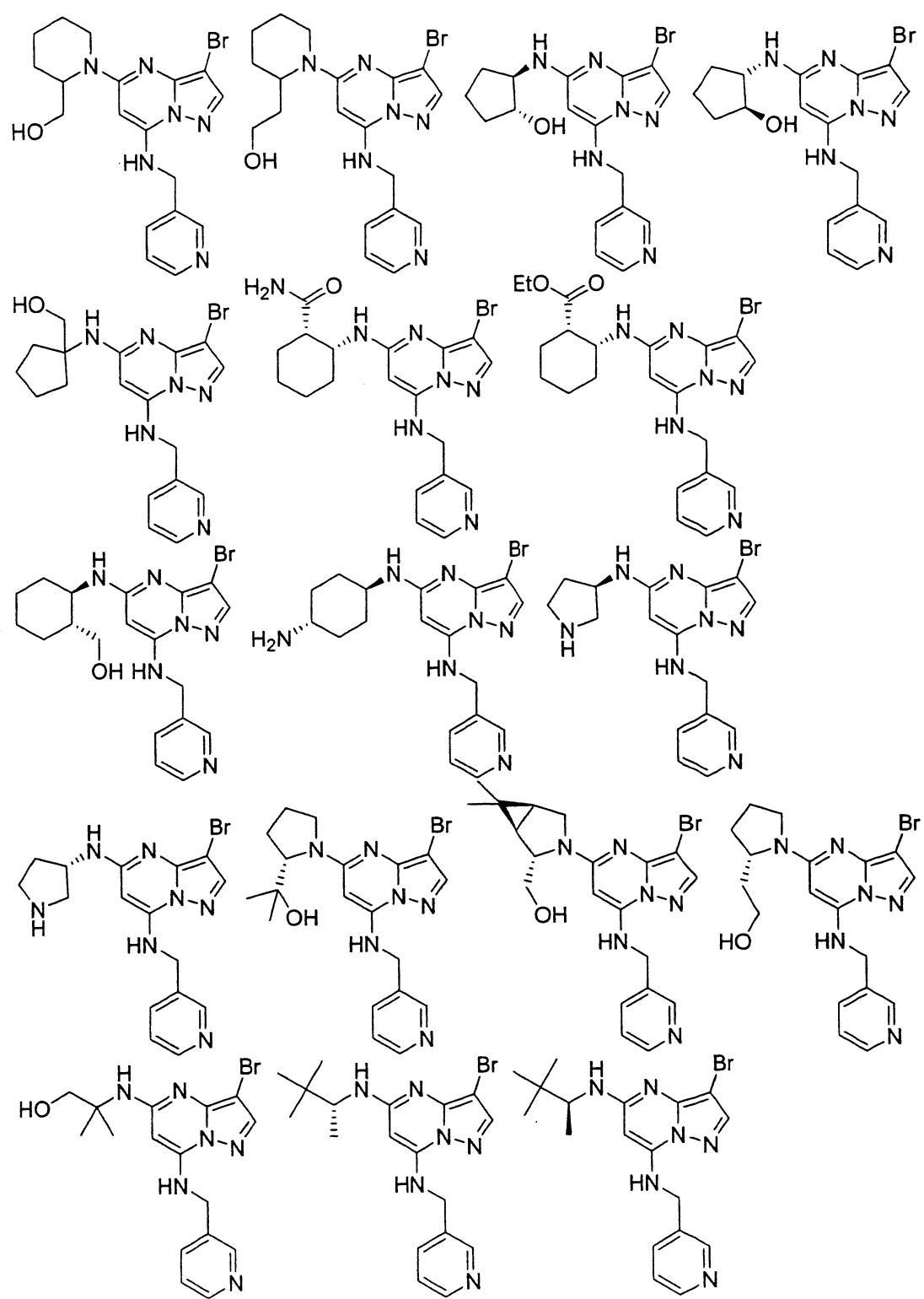


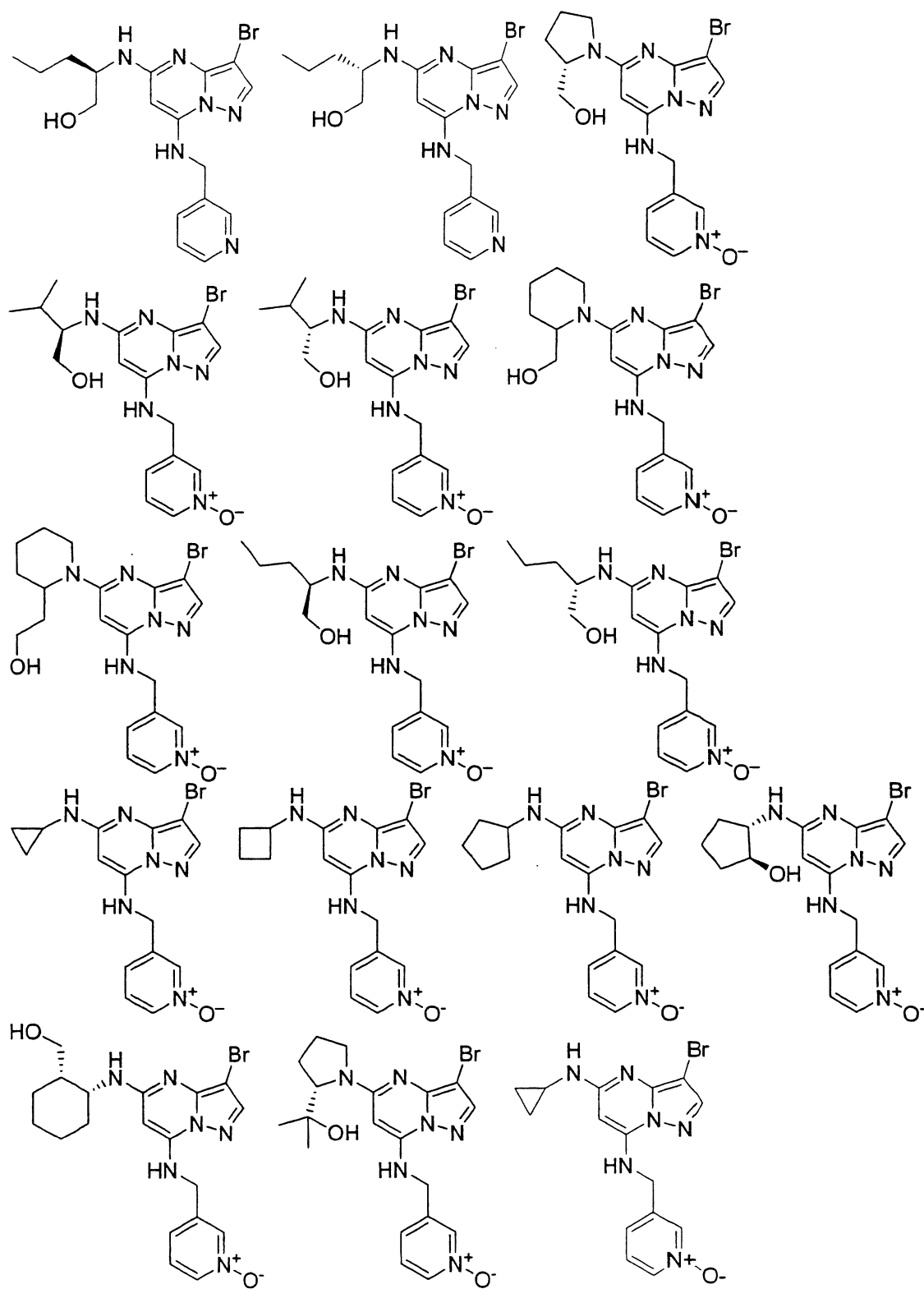


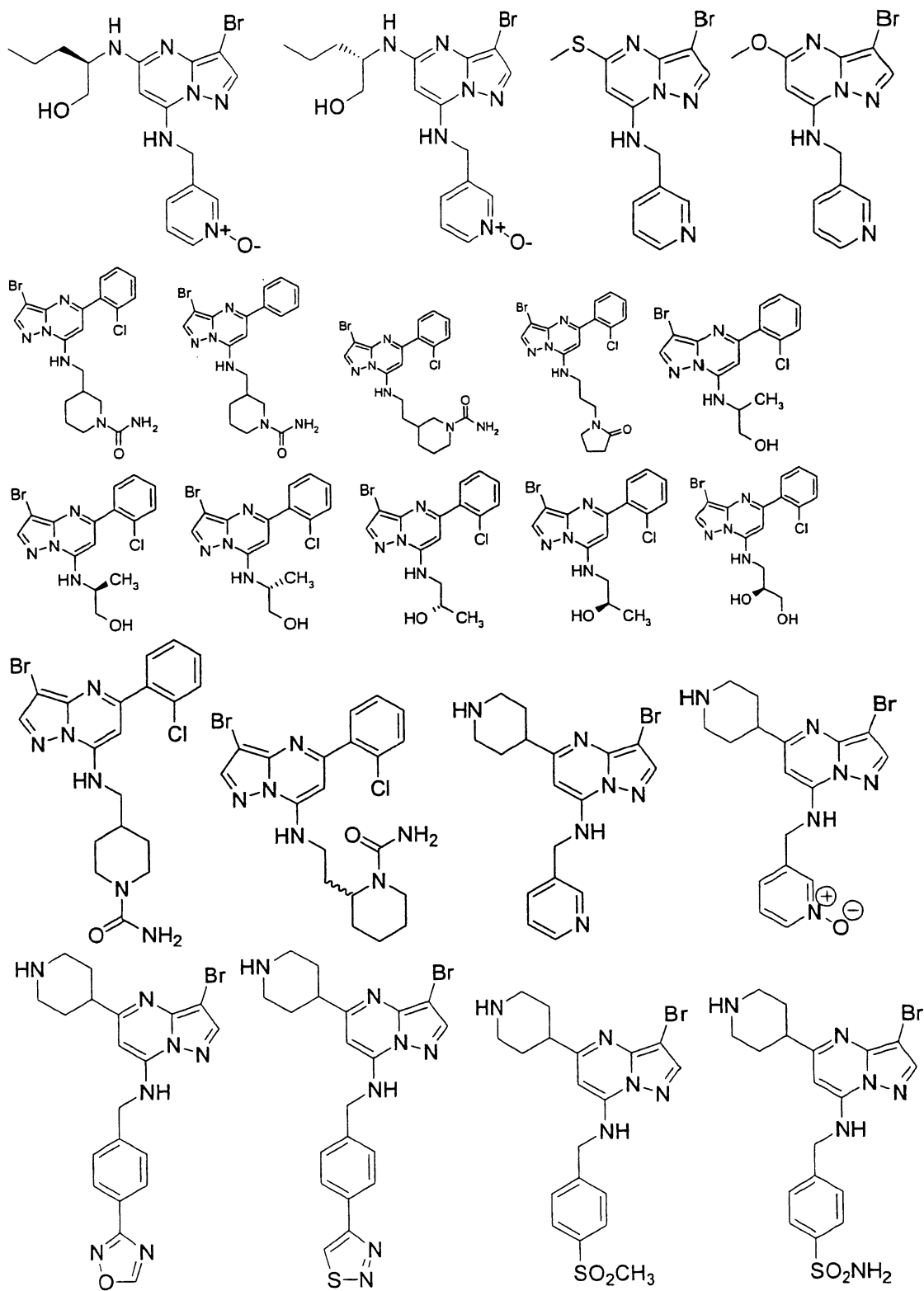


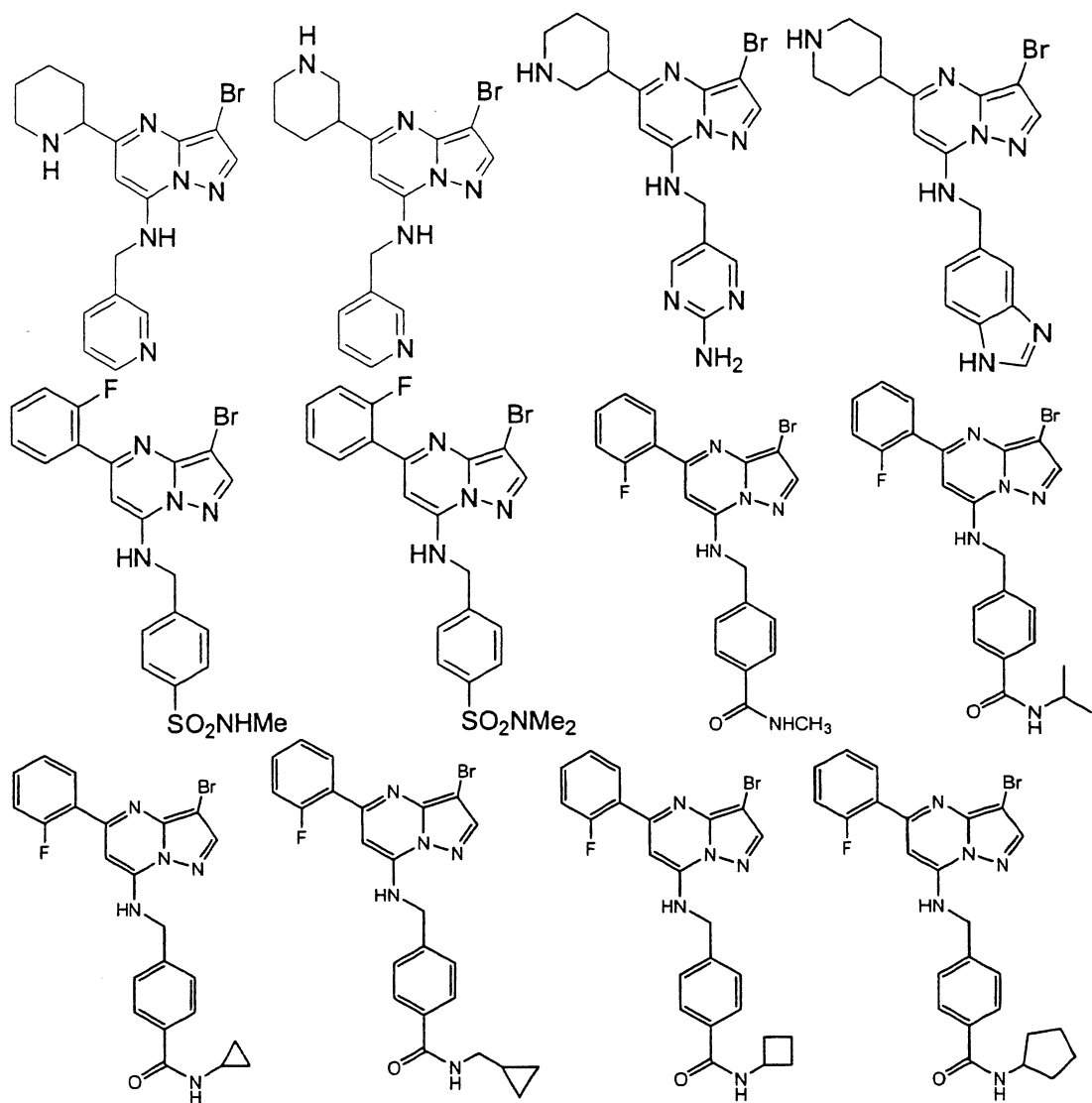


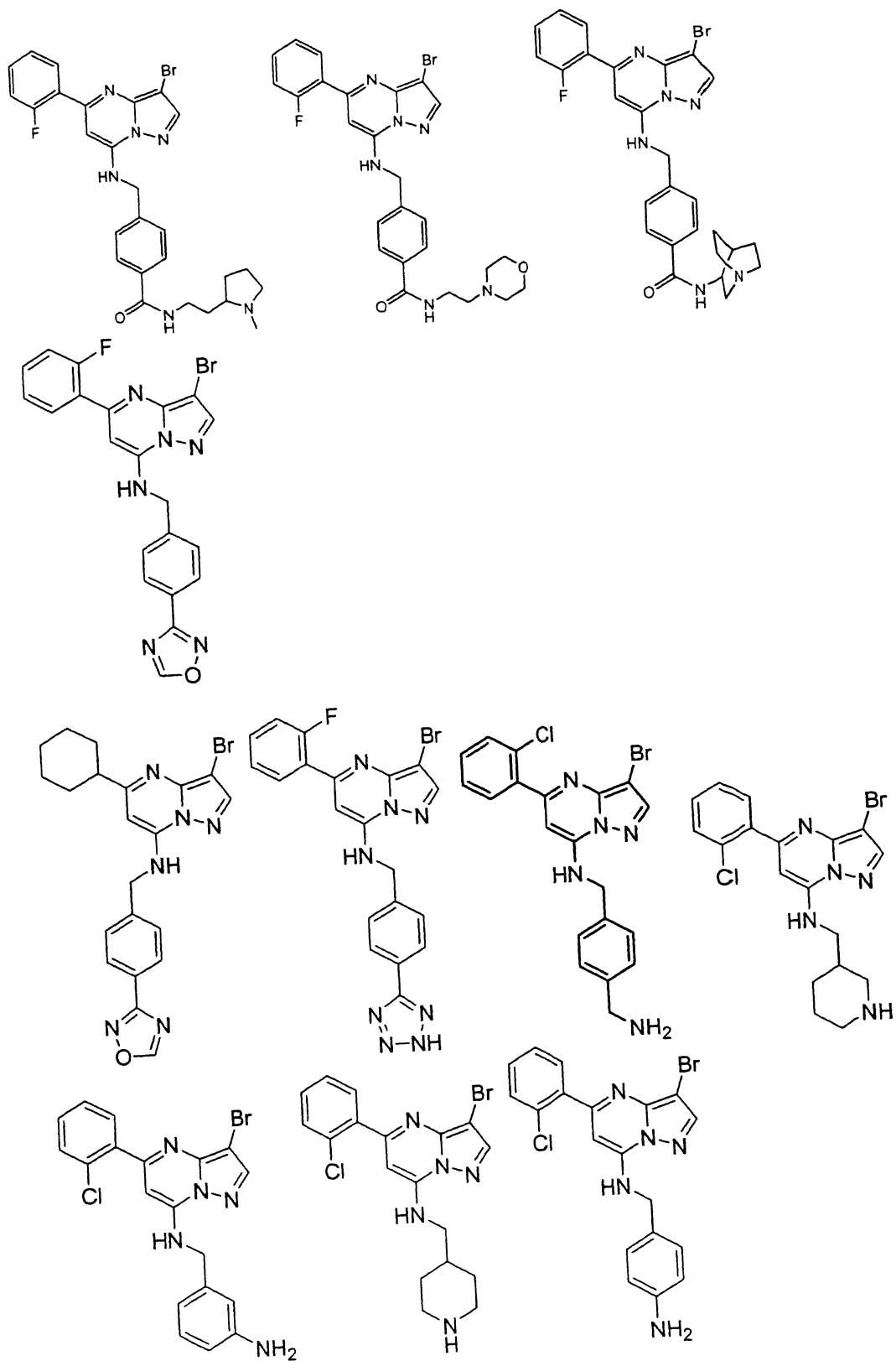


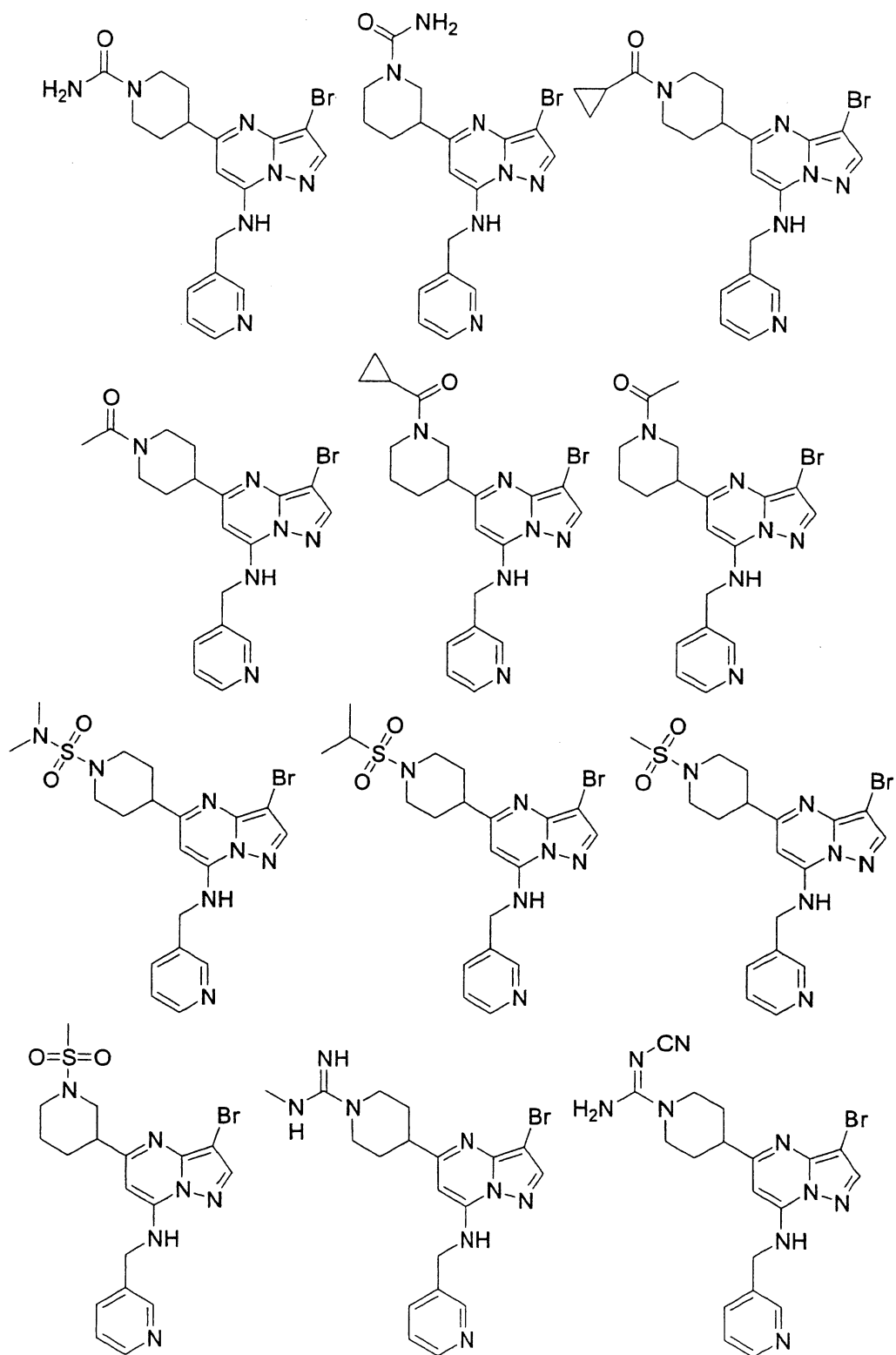


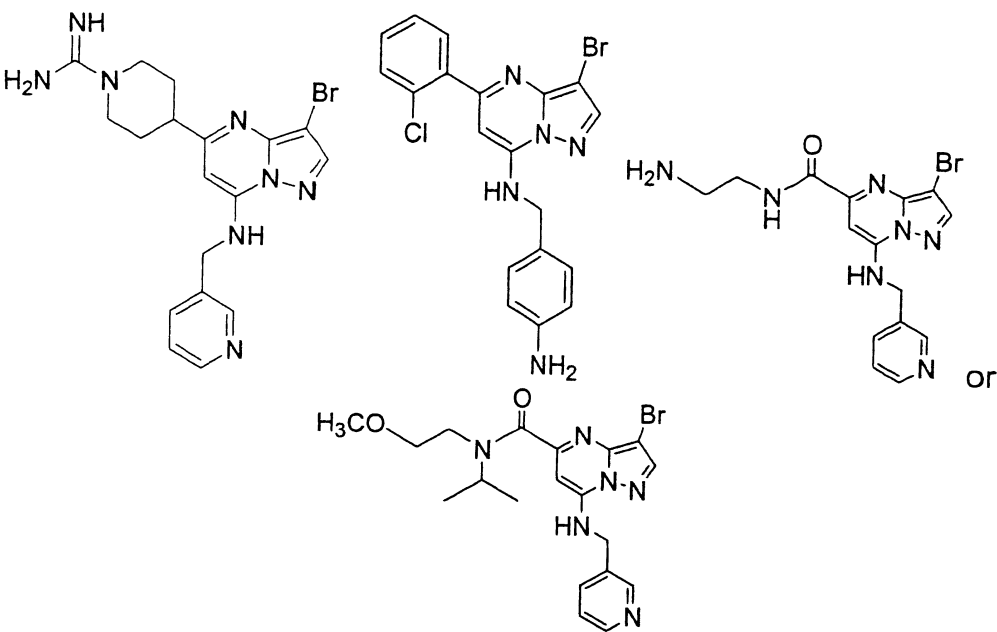






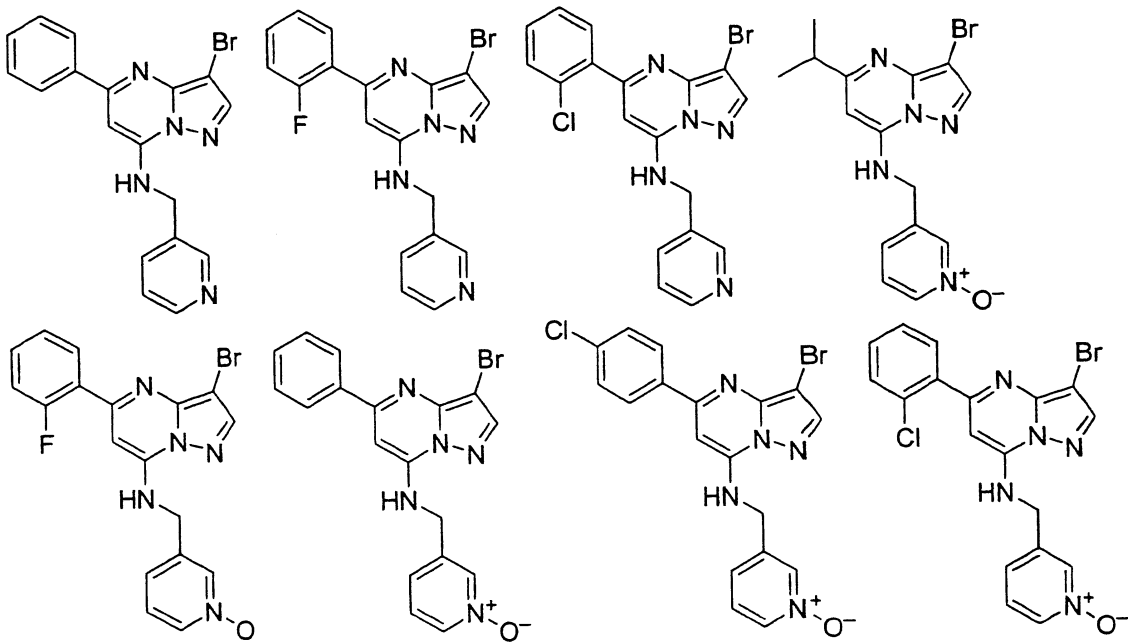


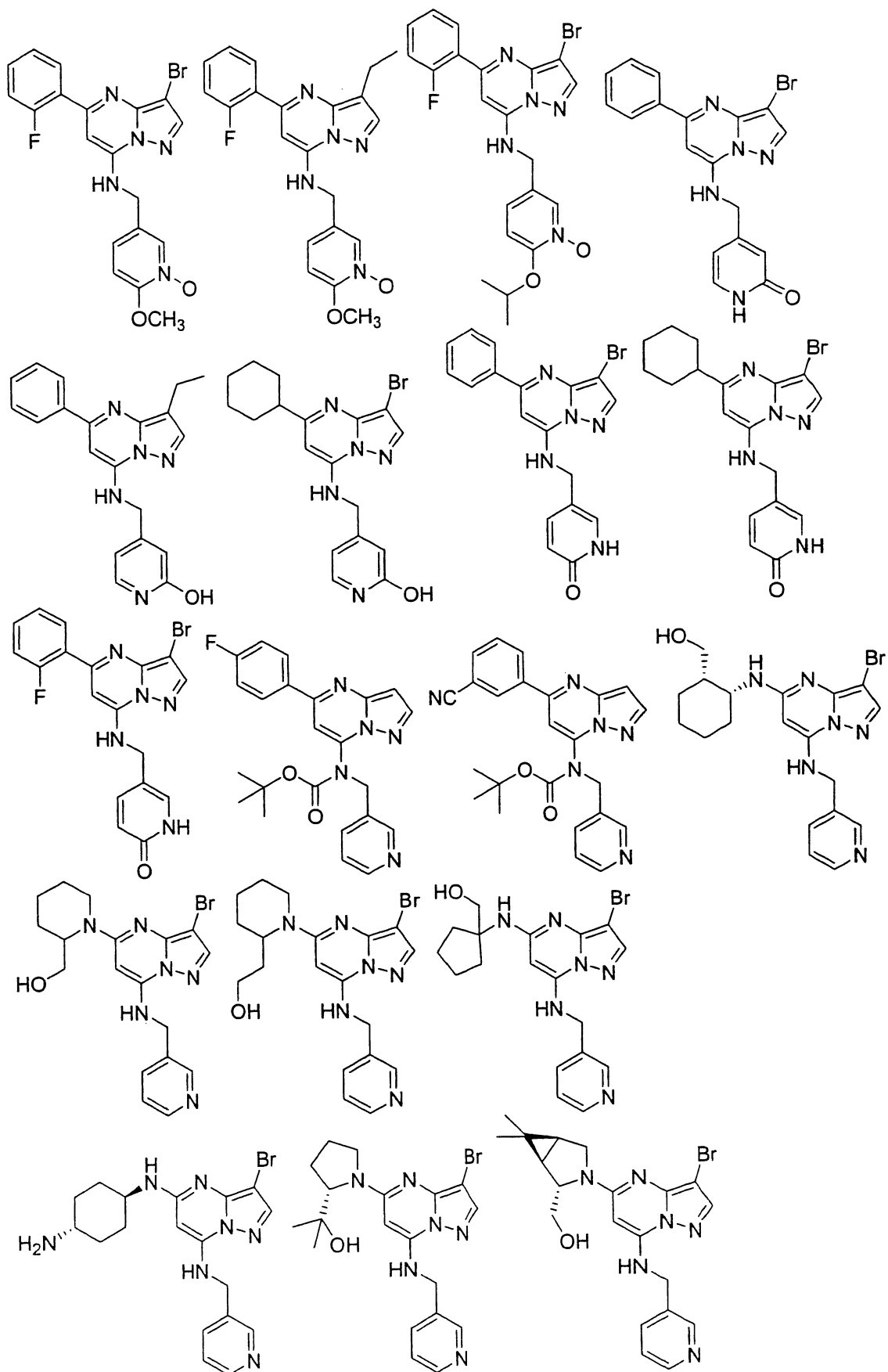


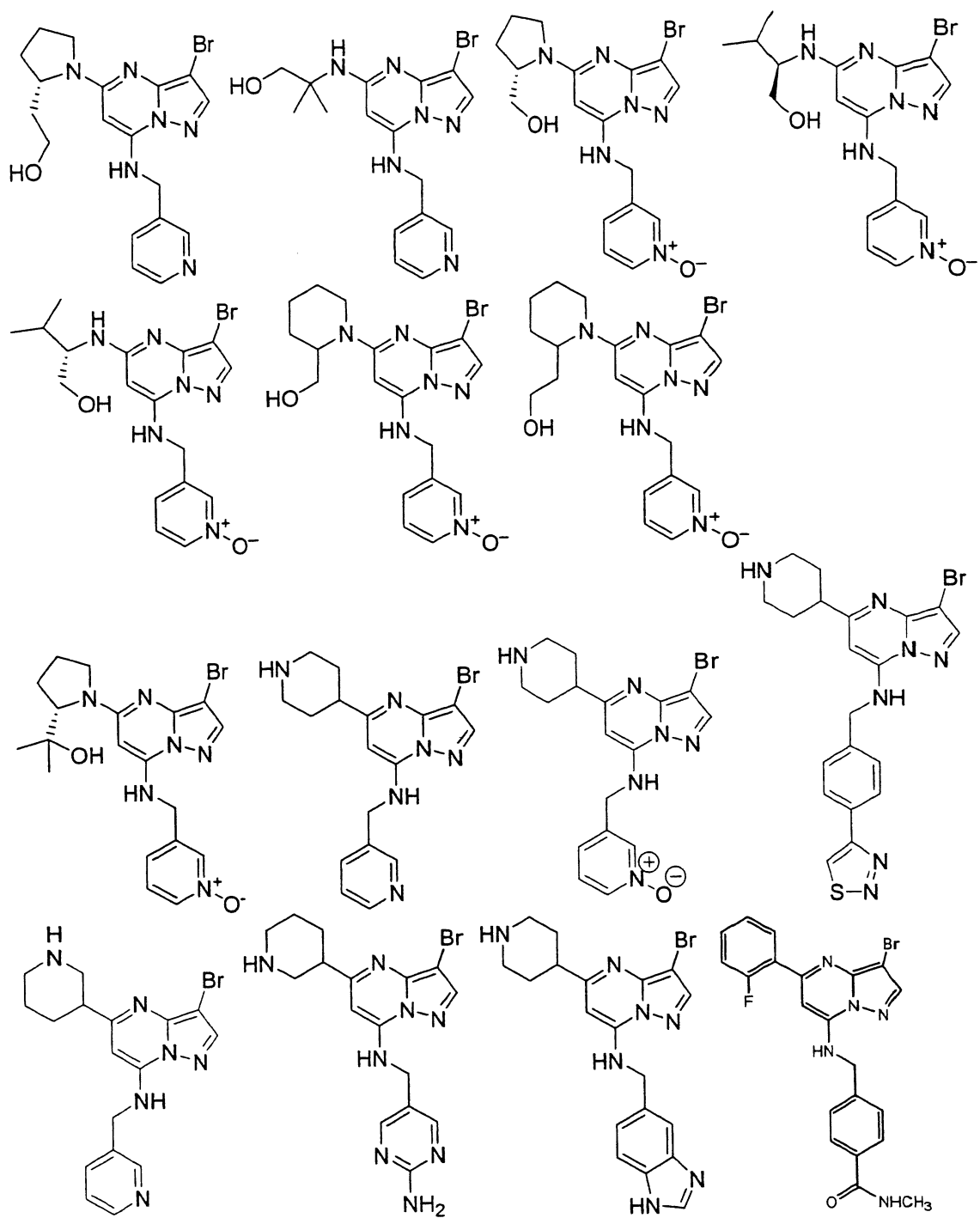


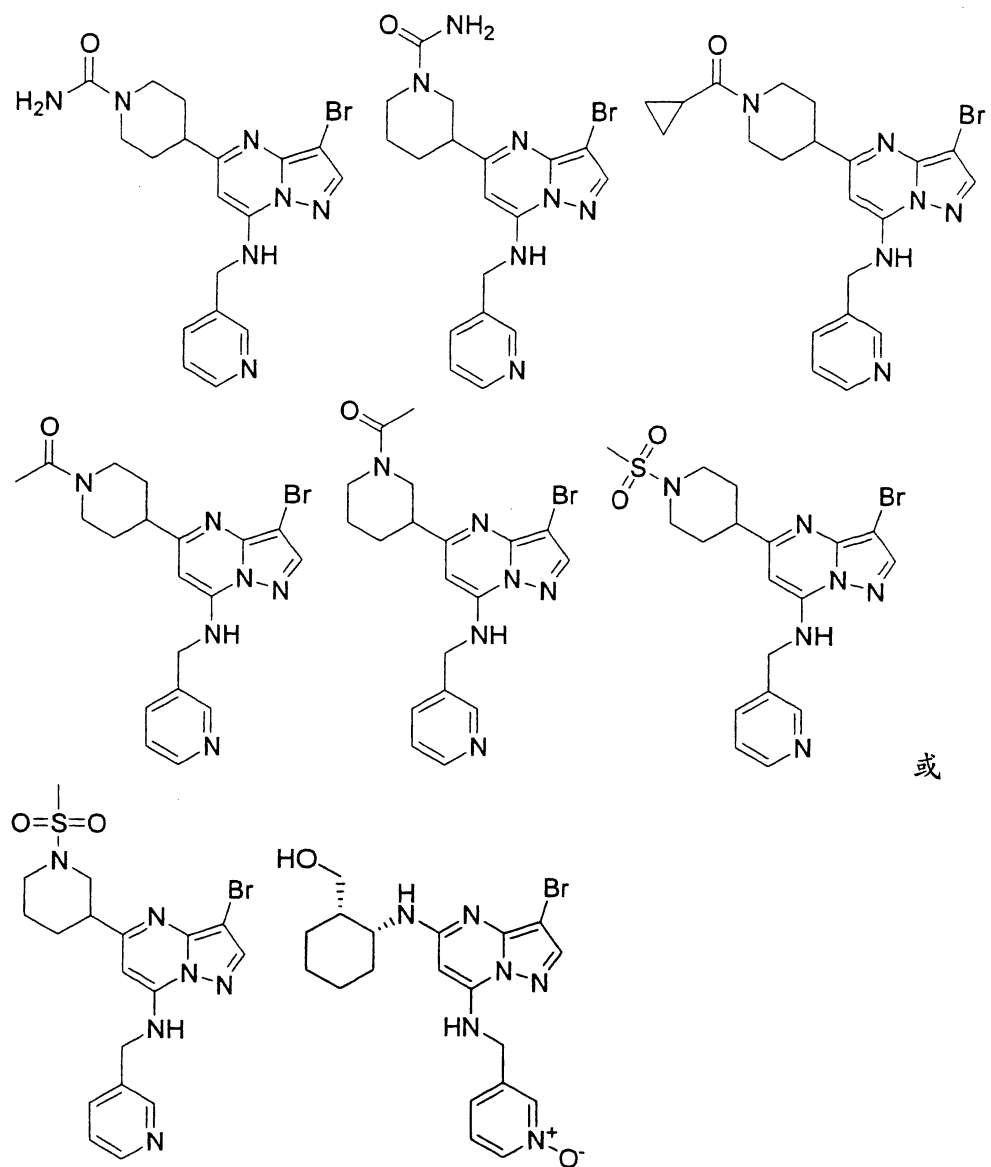
或其醫藥可接受性鹽或溶劑化物。

28. 一種下式之化合物，



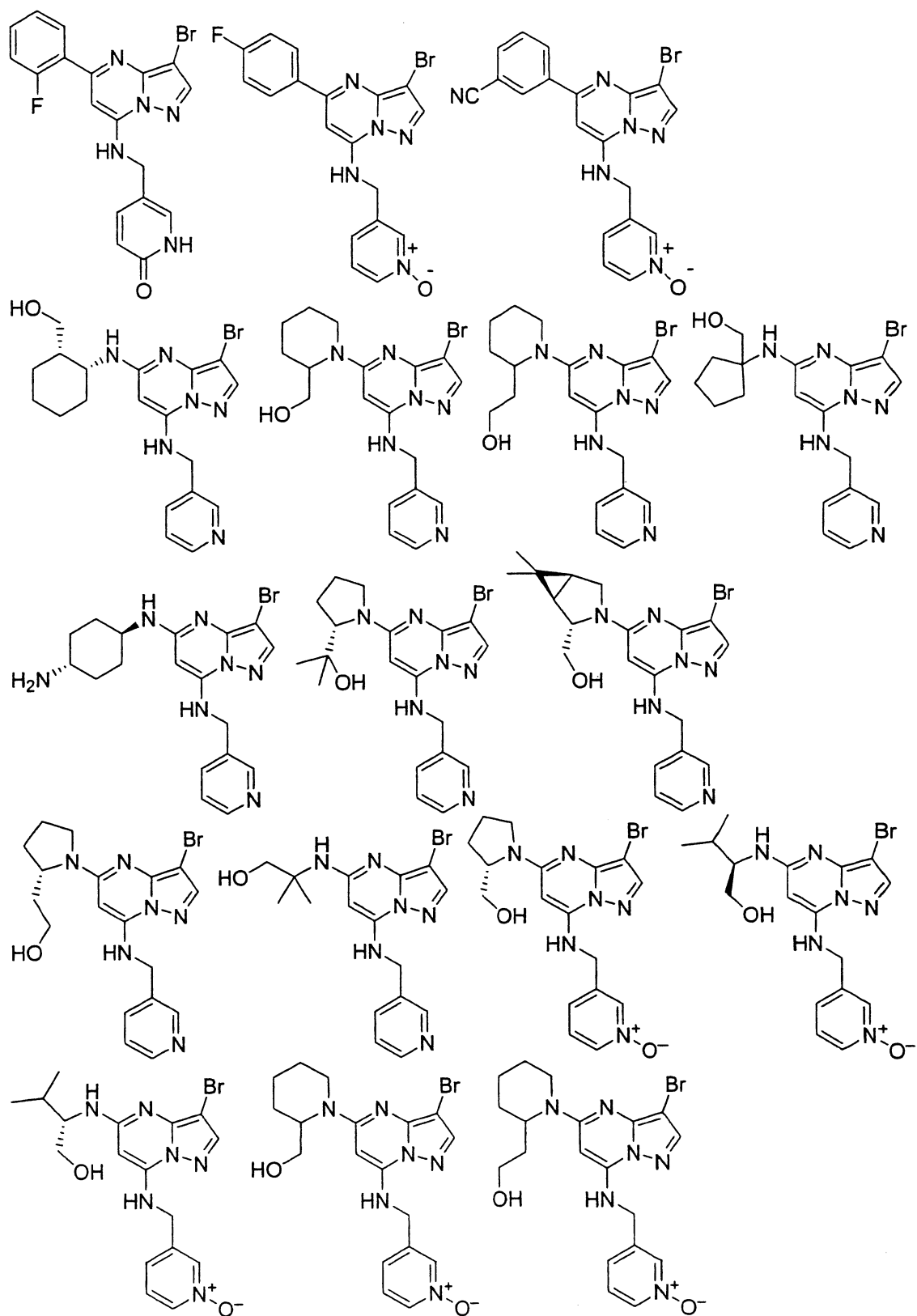


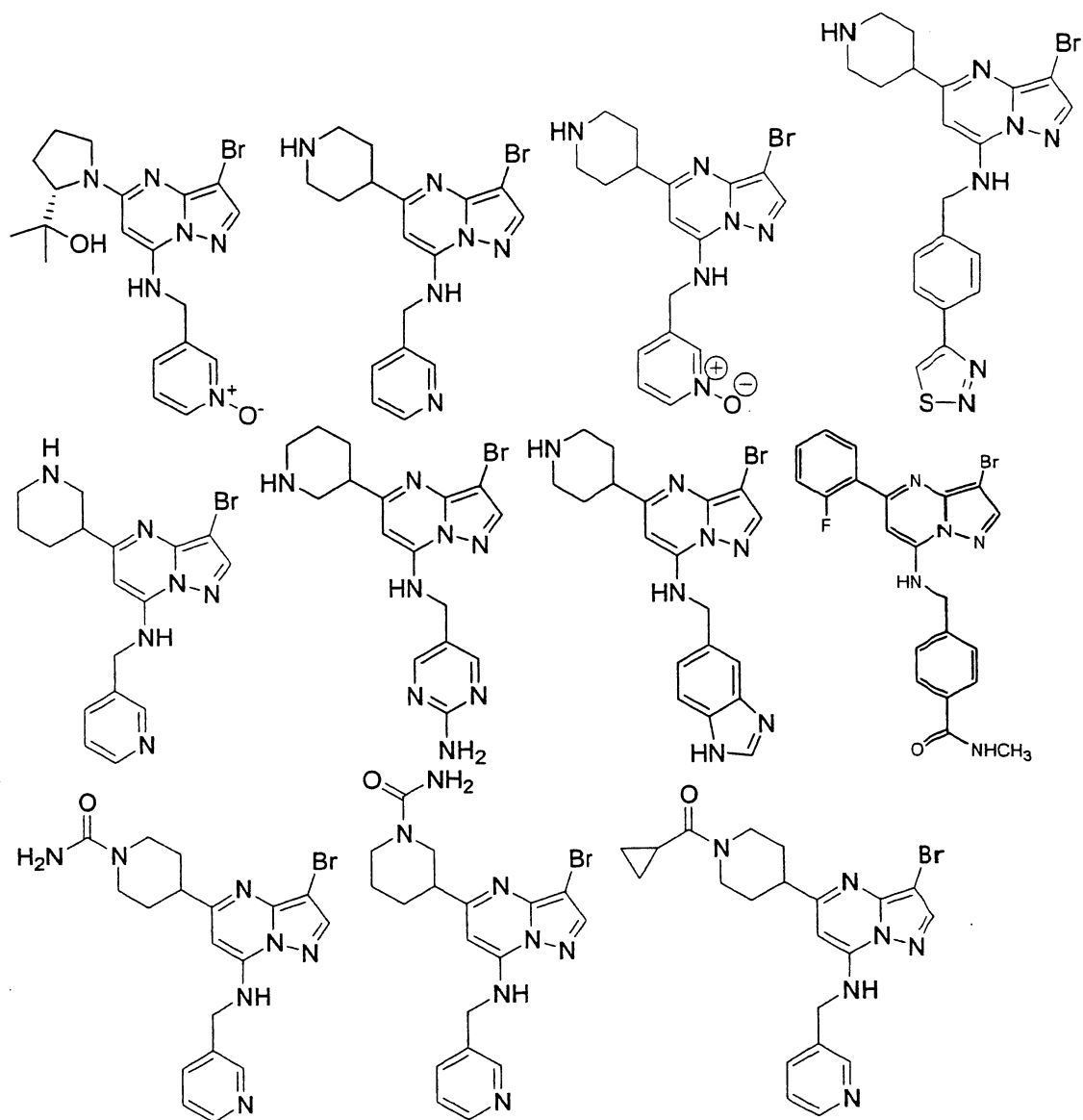


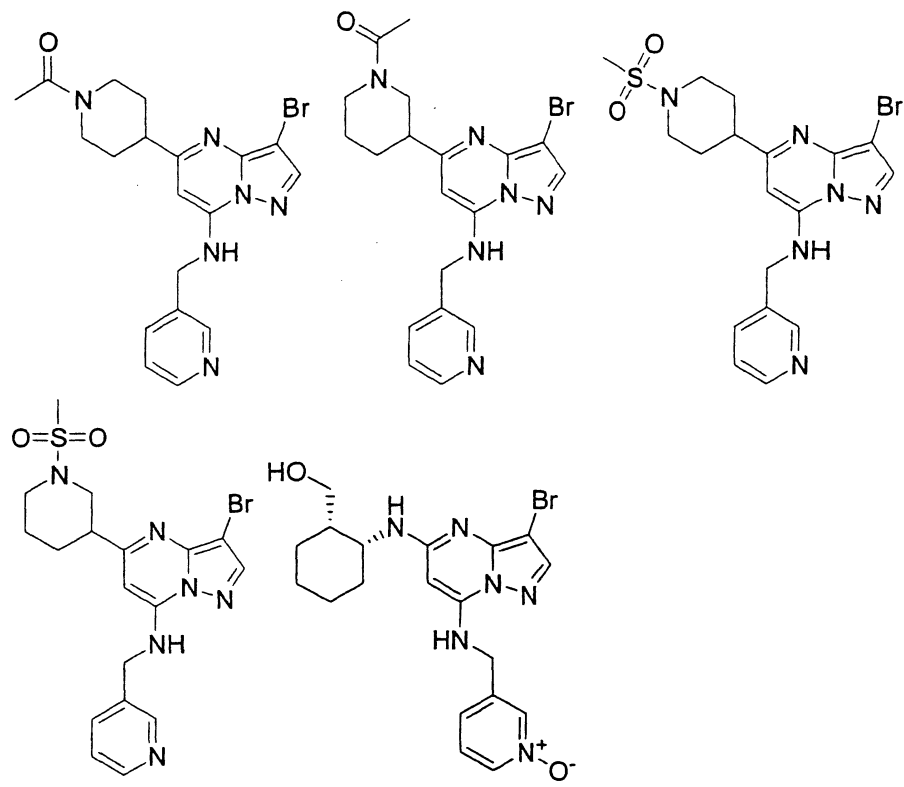


或其醫藥可接受性鹽或溶劑化物。

29. 一種下式之化合物，

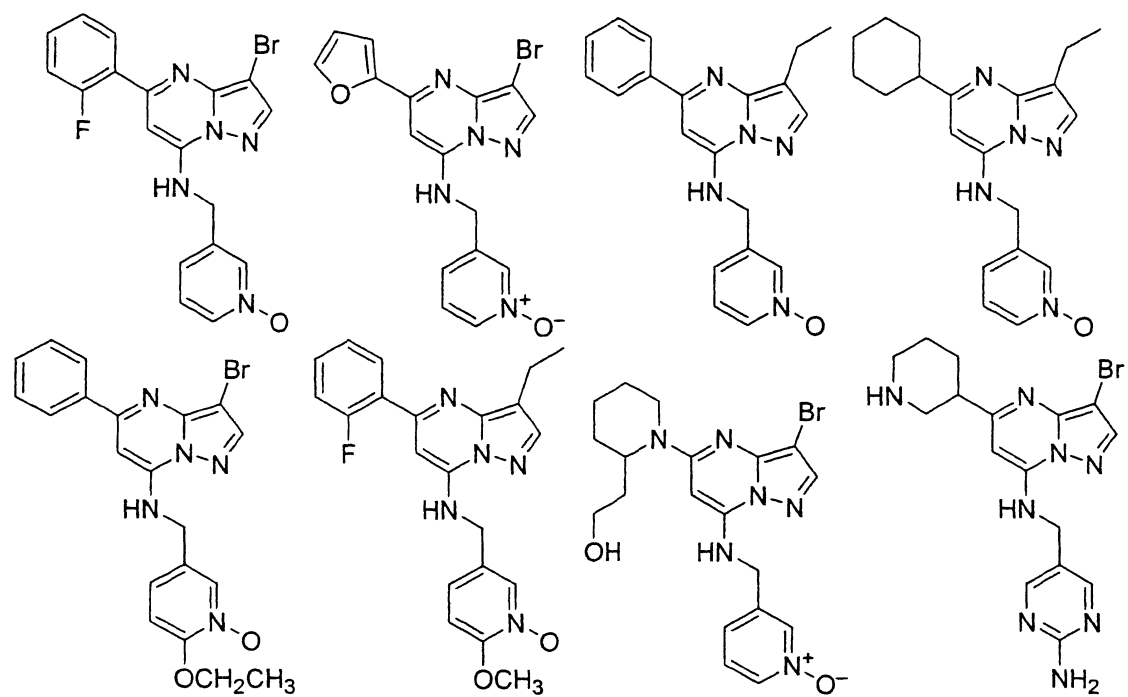


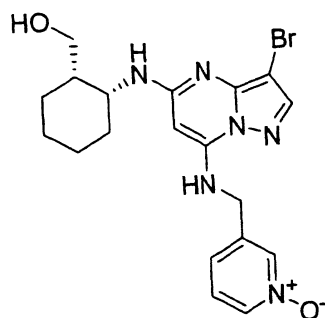




或其醫藥可接受性鹽或溶劑化物。

30. 一種下式之化合物，





或其醫藥可接受性鹽或溶劑化物。

31. 一種用以抑制一或多種週期素依賴性激酶之醫藥組合物，包括治療有效量之至少一種如申請專利範圍第1項之化合物以及至少一種醫藥可接受性載劑。
32. 一種用以治療一或多種與週期素依賴性激酶有關之疾病之醫藥組合物，包括治療有效量之至少一種如申請專利範圍第1項之化合物以及至少一種醫藥可接受性載劑。
33. 如申請專利範圍第32項之醫藥組合物，其中該週期素依賴性激酶為CDK2。
34. 如申請專利範圍第32項之醫藥組合物，其中該週期素依賴性激酶為有絲分裂原活化之蛋白質激酶(MAPK/ERK)。
35. 如申請專利範圍第32項之醫藥組合物，其中該週期素依賴性激酶為醣原合成酶激酶3(GSK3 β)。
36. 如申請專利範圍第32項之醫藥組合物，其中該疾病係選自下列所組成之組群：

膀胱癌、乳癌、結腸癌、腎癌、肝癌、肺癌、小細胞肺癌、食道癌、膽囊癌、卵巢癌、胰癌、胃癌、頸癌、甲狀腺癌、前列腺癌及皮膚癌、包括鱗狀細胞癌；

白血癌、急性淋巴白血癌、急性淋巴胚細胞白血癌、B-細胞淋巴瘤、T-細胞淋巴瘤、霍金氏(Hodgkins)淋巴瘤、非霍金氏淋巴瘤、髮細胞淋巴瘤及布克特氏(Burkett's)淋巴瘤；

急性及慢性骨髓性白血癌、脊髓發育不良徵候群及前骨髓細胞白血癌；

纖維肉瘤、橫紋肌肉瘤；

星細胞瘤、神經母細胞瘤、神經膠瘤及神經鞘瘤；

黑色瘤、精細胞瘤、畸胎瘤、骨肉瘤、外生性色素頸瘤、keratoctanthoma、甲狀腺卵胞癌及卡波西氏(Kaposi's)肉瘤。

37. 一種治療一或多種與週期素依賴性激酶有關之疾病之醫藥組合，包括：

某量之第一種化合物，其為如申請專利範圍第1項之化合物或其醫藥可接受鹽或其溶劑化物；及

某量之至少一種第二種化合物，該第二種化合物為抗癌劑；

其中該量之第一種化合物及該第二種化合物可產生治療效果；以及至少一種醫藥可接受性載劑。

38. 如申請專利範圍第37項之醫藥組合，又包括放射療法。

39. 如申請專利範圍第37項之醫藥組合，其中該抗癌劑係選自下列所組成之組群：制細胞劑、順氯胺鉑、多索鹵賓(doxorubicin)、坦羅特(taxotere)、坦醇(taxol)、依托塞(etoposide)、CPT-11、艾諾泰肯(irinotecan)、肯托斯塔

(camptostar)、托譜泰肯(topotecan)、帕克利坦(paclitaxel)、多塞坦(docetaxel)、艾譜塞酮(epothilones)、坦墨希分(tamoxifen)、5-氟尿嘧啶、胺甲喋呤(methoptrexate)、5FU、泰默鹽胺(temozolomide)、環磷鹽胺、SCH 66336、R115777、L778,123、BMS 214662、愛利沙(Iressa)、塔希瓦(Tarceva)、對EGFR之抗體、Gleevec、干擾酮(intron)、ara-C、阿霉素(adriamycin)、胞色烷(cytosan)、葛希塔賓(gemcitabine)、尿嘧啶氮芥、氮芥(Chlormethine)、艾法鹽胺(Ifosfamide)、美法倫(Melphalan)、苯丁酸氮芥(Chlorambucil)、柏溴烷(Pipobroman)、曲他胺(Triethylenemelamine)、三伸乙基硫代磷鹽胺(Triethylenethiophosphoramine)、馬利蘭(Busulfan)、卡默斯汀(Carmustine)、羅姆斯汀(Lomustine)、斯特唑辛(Streptozocin)、達卡貝吡(Dacarbazine)、氟索利啶(Floxuridine)、塞塔賓(Cytarabine)、6-氫硫基嘌呤、6-硫代胍、磷酸氟達賓(Fludarabine phosphate)、喏利鉑(oxaliplatin)、雷可瓦寧(leucovirin)、ELOXATINTM、分妥斯達汀(Pentostatine)、長春鹼、長春新鹼、長春地辛(Vindesine)、平陽黴素(Bleomycin)、更生黴素(Dactinomycin)、柔紅黴素(Daunorubicin)、多索鹵賓(Doxorubicin)、艾比鹵賓(Epirubicin)、艾達鹵賓(Idarubicin)、光輝黴素(Mithramycin)、去氧助間型黴素(Deoxycoformycin)、絲裂黴素-C(Mitomycin-C)、L-門冬鹽胺酶、替尼泊(Teniposide)

17 α - 乙炔基雌二醇、己烯雌酚、孕酮、潑尼松 (Prednisone)、氟甲孕酮 (Fluoxymesterone)、多莫斯坦酮丙酸鹽 (Dromostanolone propionate)、孕內酯 (Testolactone)、甲地孕酮乙酸鹽 (Megestrolacetate)、甲基潑尼松、甲基孕丸酮、強的松 (Prednisolone)、鼻浪花 (Triamcinolone)、氯烯雌醚 (Chlorotrianisene)、羥孕酮 (Hydroxyprogesterone)、胺鹵米特 (Aminoglutethimide)、雌莫斯汀 (Estramustine)、甲羥孕酮乙酸鹽 (Medroxyprogesteroneacetate)、利普胺 (Leuprolide)、福特胺 (Flutamide)、托瑞米分 (Toremifene)、高瑞林 (goserelin)、順氯胺鉑、碳胺鉑 (Carboplatin)、羥基尿素、胺沙林 (Amsacrine)、普卡貝吡 (Procarbazine)、米多坦 (Mitotane)、米托山酮 (Mitoxantrone)、左米梭 (Levamisole)、納瓦賓 (Navelbene)、CPT-11、胺斯塔唑 (Anastrozole)、雷塔唑 (Letrozole)、卡配烯塔賓 (Capecitabine)、雷羅色分 (Reloxafine)、多羅塞分 (Droloxafine) 或六甲蜜胺。

40. 一種醫藥組合物，包括至少一種治療有效量之如申請專利範圍第1項之化合物與至少一種醫藥可接受性載劑之組合。
41. 如申請專利範圍第38項之醫藥組合，其中該抗癌劑係選自下列所組成之組群：制細胞劑、順氯胺鉑、多索鹵賓 (doxorubicin)、坦羅特 (taxotere)、坦醇 (taxol)、依托塞 (etoposide)、CPT-11、艾諾泰肯 (irinotecan)、肯托斯塔 (camptostar)、托譜泰肯 (topotecan)、帕克利坦 (paclitaxel)

、多塞坦(docetaxel)、艾譜塞酮(epothilones)、坦墨希分(tamoxifen)、5-氟尿嘧啶、胺甲喋呤(methotrexate)、5FU、泰默鹽胺(temozolomide)、環磷鹽胺、SCH 66336、R115777、L778,123、BMS 214662、愛利沙(Iressa)、塔希瓦(Tarceva)、對EGFR之抗體、Gleevec、干擾酮(intron)、ara-C、阿霉素(adriamycin)、胞色烷(cytosan)、葛希塔賓(gemcitabine)、尿嘧啶氮芥、氮芥(Chlormethine)、艾法鹽胺(Ifosfamide)、美法倫(Melphalan)、苯丁酸氮芥(Chlorambucil)、柏溴烷(Pipobroman)、曲他胺(Triethylenemelamine)、三伸乙基硫代磷鹽胺(Triethylenethiophosphoramine)、馬利蘭(Busulfan)、卡默斯汀(Carmustine)、羅姆斯汀(Lomustine)、斯特唑辛(Streptozocin)、達卡貝咩(Dacarbazine)、氟索利啶(Floxuridine)、塞塔賓(Cytarabine)、6-氮硫基嘌呤、6-硫代胍、磷酸氟達賓(Fludarabine phosphate)、分妥斯達汀(Pentostatine)、長春鹼、長春新鹼、長春地辛(Vindesine)、平陽黴素(Bleomycin)、更生黴素(Dactinomycin)、柔紅黴素(Daunorubicin)、多索鹵賓(Doxorubicin)、艾比鹵賓(Epirubicin)、艾達鹵賓(Idarubicin)、光輝黴素(Mithramycin)、去氧助間型黴素(Deoxycoformycin)、絲裂黴素-C(Mitomycin-C)、L-門冬鹽胺酶、替尼泊(Teniposide)、 17α -乙炔基雌二醇、己烯雌酚、睪酮、潑尼松(Prednisone)、氟甲睪酮(Fluoxymesterone)、多莫斯坦酮丙酸鹽(Dromostanolone propionate)、睪內酯(Testolactone)、

甲地孕酮乙酸鹽(Megestrolacetate)、甲基潑尼松、甲基甞丸酮、強的松(Prednisolone)、鼻浪花(Triamcinolone)、氯烯雌醚(Chlorotrianisene)、羥孕酮(Hydroxyprogesterone)、胺鹵米特(Aminoglutethimide)、雌莫斯汀(Estramustine)、甲羥孕酮乙酸鹽(Medroxyprogesteroneacetate)、利普胺(Leuprolide)、福特胺(Flutamide)、托瑞米分(Toremifene)、高瑞林(goserelin)、順氯胺鉑、碳胺鉑(Carboplatin)、羥基尿素、胺沙林(Amsacrine)、普卡貝咩(Procarbazine)、米多坦(Mitotane)、米托山酮(Mitoxantrone)、左米梭(Levamisole)、納瓦賓(Navelbene)、CPT-11、胺斯塔唑(Anastrozole)、雷塔唑(Letrozole)、卡配烯塔賓(Capecitabine)、雷羅色分(Reloxafine)、多羅塞分(Droloxafine)或六甲蜜胺。

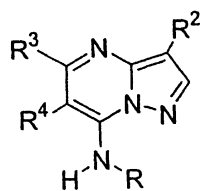
42. 如申請專利範圍第1項之化合物，係呈純化態。

柒、指定代表圖：

(一)本案指定代表圖為：第 () 圖。

(二)本代表圖之元件代表符號簡單說明：

捌、本案若有化學式時，請揭示最能顯示發明特徵的化學式：



Formula III