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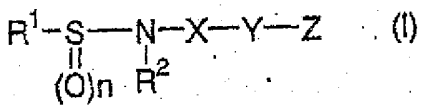
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(57) Resumo:

RESUMO

"ANTAGONISTAS DE Y5 DE NPY"

A invenção presente proporciona uma composição farmacêutica para utilização a título de antagonista dos receptores Y5 de NPY, que inclua um composto com a fórmula (I):



(I)

na qual

R^1 seja alquilo inferior, cicloalquilo, ou outro semelhante,

R^2 seja hidrogénio, alquilo inferior, ou outro semelhante,

n seja 0, 1 ou 2,

X seja alquileno inferior, alcenileno inferior, cicloalquileno, ou outro semelhante,

Y seja $CONR^7$, $CSNR^7$, NR^7CO, NR^7CS, ou outro semelhante,

Z seja alquilo inferior, carbociclico substituído opcionalmente, heterociclilo substituído opcionalmente, e R^7 seja hidrogénio ou alquilo inferior,

um seu precursor, sal aceitável do ponto de vista farmacêutico, ou solvato.

DESCRIÇÃO

"ANTAGONISTAS DE Y5 de NPY"

Domínio Técnico

A invenção presente diz respeito a uma composição farmacêutica para utilização a título de antagonista de receptores Y5 de NPY, especificamente a título de agente contra a obesidade e novos compostos com actividade anti-obesidade.

Estado da Técnica à Data da Invenção

O neuropéptido Y (doravante referido neste documento como NPY) é um péptido constituído por 36 resíduos de aminoácidos que foi isolado a partir do cérebro porcino em 1982. O NPY encontra-se largamente distribuído no sistema nervosa central e nos tecidos periféricos dos seres humanos e dos animais.

Foi descrito que o NPY possui uma actividade de estimulação do consumo de alimentos, uma actividade contra as convulsões, uma actividade de promoção da aprendizagem, uma actividade contra a ansiedade, uma actividade contra o stress, etc. no sistema nervoso central, e pode estar envolvido de forma fulcral nas doenças do sistema nervoso central tais como a depressão, a doença de Alzheimer e a doença de Parkinson. Pensa-se que o NPY se encontra

associado com as doenças cardiovasculares, uma vez que induz uma contracção dos músculos lisos tais como os dos vasos sanguíneos ou os músculos cardíacos nos tecidos periféricos. Para além disto, também se sabe que o NPY se encontra envolvido em doenças metabólicas tais como a obesidade, a diabetes, e as anormalidades hormonais (Trends in Pharmacological Sciences, Vol. **15**, 153 (1994)). Espera-se portanto que um antagonista de receptores de NPY seja um remédio para impedir ou para tratar diversas doenças envolvendo o receptor de NPY.

Os subtipos Y1, Y2, Y3, Y4, Y5, e Y6 já foram identificados a título de receptores de NPY (Trends in Pharmacological Sciences, Vol. **18**, e 372 (1997)). Foi sugerido que o receptor Y5 esteja pelo menos envolvido no comportamento de consumo alimentar e espera-se que o seu antagonista seja um agente contra a obesidade (Peptides, Vol. **18**, e 445 (1997)).

São descritos compostos de quinazolina com estruturas semelhantes às dos compostos da invenção presente e que exibem actividade antagonística em relação ao receptor de NPY nos WO 97/20.820, WO 97/20.821, WO 97/20.823 e outros semelhantes. Para além disto, está descrito que os derivados de ureia com um grupo sulfonamida e os derivados amida com um grupo sulfonilo no WO 99/64.349 bem como os derivados de benzilsulfonamida na EP 1010691-A, possuem uma actividade antagonista face ao NPY. No WO 99/32.466 são descritos derivados sulfonamida substituídos, composições farmacêuticas que os contêm e os seus cne? no

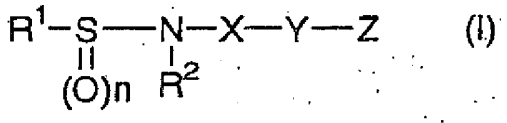
tratamento da obesidade e de patologias com ela relacionadas. São descritos compostos com estruturas semelhantes às dos compostos da invenção presente em JP 59-16871-A e no WO 97/15.567. As suas actividades são bastante diferentes das da invenção presente e estes documentos não sugerem a invenção presente.

Descrição da Invenção

O objecto da invenção presente é proporcionar uma composição farmacêutica melhor para utilização a título de antagonista dos receptores Y5 de NPY e novos compostos possuindo essa actividade.

A invenção presente proporciona

[1] A utilização de um composto com a fórmula (I):



(I)

na qual R^1 seja um alquilo inferior substituído opcionalmente, ou um cicloalquilo substituído

R^2 seja hidrogénio ou alquilo inferior, e R^1 e R^2 tomados em conjunto possam formar alquileno inferior, n seja 1 ou 2,

X seja alquileno inferior substituído opcionalmente, alcenileno inferior substituído opcionalmente, -CO-alquileno inferior substituído opcionalmente, -CO-alcenileno inferior substituído opcionalmente ou



em que R^3, R^4, R^5 e R^6 sejam cada um deles independentemente hidrogénio ou alquilo inferior,



seja cicloalquileno substituído opcionalmente, cicloalcenileno substituído opcionalmente, bicicloalquileno substituído opcionalmente, arileno substituído opcionalmente ou heterociclo-di-ilo substituído opcionalmente, e p e q seja cada um deles independentemente 0 ou 1,

$-NR^2-X-$ possa ser



em que



seja piperidinadi-ilo, piperazinadi-ilo, piridinadi-ilo, pirazinadi-ilo, pirrolidinadi-ilo ou pirroledi-ilo e U seja uma ligação simples, alquileno inferior ou alcenileno inferior,

Y seja $OCONR^7$, $CONR^7$, $CSNR^7$, NR^7CO ou NR^7CS,

R^7 seja hidrogénio ou alquilo inferior, e

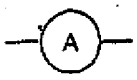
Z seja alquilo inferior substituído opcionalmente, alcenilo inferior substituído opcionalmente, amino substituído opcionalmente, alcoxilo inferior substituído opcionalmente, carbociclilo substituído opcionalmente ou heterociclilo substituído opcionalmente,

um seu sal ou um solvato aceitável do ponto de vista farmacêutico, para a preparação de uma composição farmacêutica tal como contendo um antagonista do receptor Y5 de NPY.

[2] A utilização tal como se descreveu em [1], na qual R^2 seja hidrogénio ou alquilo inferior e Z seja alquilo inferior

substituído opcionalmente, alcenilo inferior substituído opcionalmente, alcoxilo inferior substituído opcionalmente, carbociclilo substituído opcionalmente, heterociclilo substituído opcionalmente ou amino substituído opcionalmente, desde que R^1 seja um alquilo em C_3 a C_{10} substituído opcionalmente quando Z for amino substituído opcionalmente,

[3] A utilização tal como se descreveu em [1], na qual R^1 seja alquilo inferior substituído opcionalmente ou cicloalquilo substituído opcionalmente, X seja alquileno inferior substituído opcionalmente, alcenileno inferior substituído opcionalmente ou



em que



seja tal como se definiu em [1], e

Z seja alquilo inferior substituído opcionalmente, carbociclilo substituído

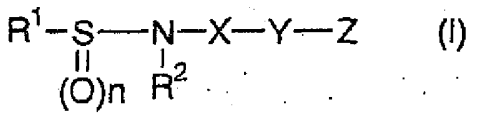
opcionalmente ou heterociclilo substituído opcionalmente,

[4] A utilização tal como se descreveu em qualquer uma de [1] a [3], na qual R^1 seja um alquilo C3 a C10 substituído opcionalmente,

[5] A utilização tal como se descreveu em qualquer uma de [1] a [4] a título de agente contra a obesidade,

[6] A utilização tal como descrita em qualquer uma de [1] a [4] a título de agente anoréctico,

[7] Um composto com a fórmula (I):



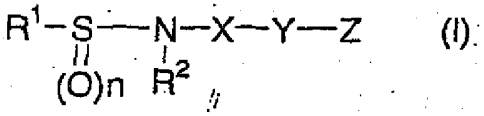
(I)

em que X seja alquileno C2 a C6 ou alcenileno C3 a C6, R^1 seja alquilo C3 a C10 substituído opcionalmente ou cicloalquilo C5 a C6 substituído opcionalmente e os outro símbolos sejam tal como foram definidos em [1], desde que Z não seja alquilfenilamino inferior, hidroxialquil(inferior)fenilamino e acilfenilamino quando Y for NR^7CO, os seus

sais e solvatos aceitáveis do ponto de vista farmacêutico,

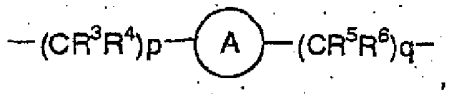
[8] O composto descrito em [7] no qual Z seja alquilo inferior substituído opcionalmente ou fenilo substituído opcionalmente, os seus sais e solvatos aceitáveis do ponto de vista farmacêutico,

[9] Um composto com a fórmula (I):



(I)

na qual X seja



e



seja *cicloalq*uileno substituído opcionalmente, cicloalcenileno substituído opcionalmente, bicicloalquileno substituído opcionalmente ou piperidinileno substituído opcionalmente, R^1 seja alquilo C3 a C10 substituído opcionalmente ou cicloalquilo C5

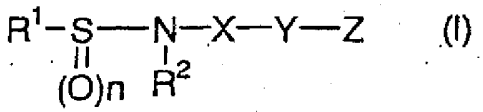
a C6 substituído opcionalmente, e os outros símbolos sejam tal como se definiram em [1], os precursores dos fármacos, os seus sais e solvatos aceitáveis do ponto de vista farmacêutico,

[10] O composto descrito em [9] o qual seja ciclohexileno substituído opcionalmente ou piperidinileno substituído opcionalmente e p e q sejam em simultâneo 0, precursores dos fármacos, os seus sais e solvatos aceitáveis do ponto de vista farmacêutico,

[11] O composto descrito em [9] ou em [10] no qual Y seja CONH, os precursores dos fármacos, os seus sais e solvatos aceitáveis do ponto de vista farmacêutico,

[12] O composto descrito em qualquer uma das [9] a [11] no qual Z seja um alquilo inferior substituído opcionalmente, um fenilo substituído opcionalmente, um piridilo substituído opcionalmente ou um benzopiranilo substituído opcionalmente, os precursores dos fármacos, os seus sais e solvatos aceitáveis do ponto de vista farmacêutico,

[13] Um composto com a fórmula (I):



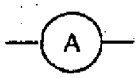
(I)

no qual X seja



,

e



seja heteroarileno, R^1 seja um alquilo C3 a C10 substituído opcionalmente ou um cicloalquilo C5 a C6 substituído opcionalmente e os outros símbolos tenham os significados que lhes foram atribuídos em [1], os seus sais e solvatos aceitáveis do ponto de vista farmacêutico,

[14] O composto descrito em [13], no qual



seja tiofenodi-ilo ou furanodi-ilo, os seus sais e solvatos aceitáveis do ponto de vista farmacêutico, e

[15] Uma composição farmacêutica que inclua um composto descrito em qualquer uma de [7] a [14], os seus sais e solvatos aceitáveis do ponto de vista farmacêutico.

Melhor Maneira de Levar a Cabo a Invenção

Na especificação presente, o termo "halogéneo" inclui flúor, cloro, bromo e iodo. É preferível flúor ou cloro.

A expressão "grupo protector" na expressão "hidroxilo protegido opcionalmente" e na expressão "hidroxialquilo(inferior) protegido opcionalmente" inclui todos os grupos protectores de hidroxilo que se utilizam habitualmente. Por exemplo, incluem-se acilos tais como acetilo, tricloroacetilo e benzoílo, alcoxicarbonilos inferiores tais como t-butoxicarbonilo, alquilsulfonilos inferiores tais como metanossulfonilo, alcoxil(inferior)alquilo(inferior) tal como metoximetilo, trialquilsililo tal como t-butildimetilsililo.

O termo "alquilo inferior" inclui alquilos com cadeia linear ou ramificada em C1 a C10. Os exemplos de "alquilo inferior" são metilo, etilo, n-propilo, isopropilo, n-butilo, isobutilo, sec-butilo, terc-butilo, n-pentilo, isopentilo, neopentilo, hexilo, isohexilo, n-heptilo, isoheptilo, n-octilo, iso-octilo, n-nonilo e n-decilo.

"Alquilo inferior" representado por R^1 é preferivelmente alquilo C3 a C10, mais preferivelmente alquilo C3 a C6, e de preferência isopropilo ou t-butilo.

"Alquilo inferior" nos outros casos é preferivelmente alquilo C1 a C6, e mais preferivelmente alquilo C1 a C4.

Os exemplos de substituintes em "alquilo inferior substituído opcionalmente" que são representados por Z são,

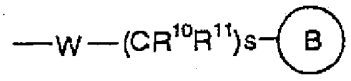
(1) halogéneo; (2) ciano;

(3) os grupos (i) a (xvi) que se seguem), que são substituídos opcionalmente com um ou mais substituintes seleccionados de entre "um conjunto de substituintes β" definido adiante,

(i) hidroxilo, (ii) alcoxilo inferior, (iii) mercapto, (iv) alquiltio inferior. (v) acilo, (vi) aciloxilo, (vii) carboxilo, (viii) alcoxicarbonilo inferior, (ix) imino, (x) carbamoílo, (xi) tiocarbamoílo, (xii) alquilcarbamoílo inferior, (xiii) alquiltiocarbamoílo inferior, (xiv) amino, (xv) alquilamino inferior ou (xvi) heterociclilcarbonilo;

ou

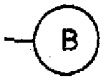
(4) um grupo com a fórmula:



em que R^{10} e R^{11} são cada um deles independentemente hidrogénio ou alquilo inferior e em que este grupo tenha dois ou mais R^{10} e/ou dois ou mais R^{11}, podendo cada um dos R^{10} e/ou cada um dos R^{11} ser diferente,

W seja uma ligação simples, O, S ou NR^{12},

R^{12} seja hidrogénio, alquilo inferior ou fenilo,



seja cicloalquilo, bicicloalquilo, cicloalcenilo, arilo ou heterociclilo, cada um dos quais seja substituído opcionalmente com um ou mais substituintes seleccionados de entre um "conjunto de substituintes α" definido adiante, e

s seja um inteiro de entre 0 e 4-

Na especificação presente, "um conjunto de substituintes α" é um conjunto constituído por (1) halogéneo; (2) oxo; (3) ciano; (4) nitro; (5) imino substituído opcionalmente com alquilo inferior ou com hidroxilo;

(6) os grupos (i) a (xxi) seguintes, que são substituídos opcionalmente com um ou mais grupos seleccionados de entre o conjunto de substituintes β,

(i) hidroxilo, (ii) alquilo inferior, (iii) alcenilo inferior, (iv) alcoxilo inferior, (v) carboxilo, (vi) alcoxicarbonilo inferior, (vii) acilo, (viii) aciloxilo, (ix) imino, (x) mercapto, (xi) alquiltio inferior, (xii) carbamoílo, (xiii) alquilcarbamoílo inferior, (xiv) cicloalquilcarbamoílo, (xv) tiocarbamoílo, (xvi) alquiltiocarbamoílo inferior, (xvii) alquilsulfinilo inferior, (xviii) alquilsulfonilo inferior, (xix) sulfamoílo, (xx) alquilsulfamoílo inferior e (xxi) cicloalquilsulfamoílo;

(7) os grupos (i) a (v) seguintes, que são substituídos opcionalmente com substituintes do conjunto β, alquilo inferior, alcoxil(inferior)alquilo inferior, hidroxialquilo(inferior) opcionalmente protegido, halogenoalquilo(inferior), alquilsulfonilo inferior e/ou arilsulfonilo,

(i) cicloalquilo, (ii) cicloalcenilo, (iii)cicloalquiloxilo, (iv) amino e (v) alquilenodioxilo;

e

(8) os grupos (i) a (xii) seguintes, que são substituídos opcionalmente com substituintes do conjunto β, alquilo inferior, halogenoalquilo(inferior) e/ou oxo,

(i) fenilo, (ii) naftilo, (iii) fenoxilo, (iv) fenilalcoxilo(inferior), (v) feniltio, (vi) fenilalquil(inferior)tio, (vii) fenilazo, (viii) heterociclilo, (ix) heterocicliloxilo, (x) heterocicliltio, (xi) heterociclilcarbonilo e (xii) heterociclilsulfonilo.

Os exemplos preferíveis do conjunto de substituintes α a título de substituintes do anel B são halogéneo; nitro; hidroxilo; alquilo inferior substituído opcionalmente em que os substituintes sejam halogéneo, ciano, fenilo, carboxilo e/ou alcoxicarbonilo inferior; alcenilo inferior; alcoxil(inferior)carbonilalcenilo(inferior); alcoxilo inferior substituído opcionalmente em que os substituintes sejam halogéneo, hidroxilo, alcoxilo inferior, carboxilo, alcoxicarbonilo inferior, alquilamino inferior e/ou ciano; acilo; hidroxi-imino; alquiltio inferior; alquilsulfinilo inferior; sulfamoílo; amino substituído opcionalmente em que os substituintes sejam alquilo inferior, hidroxialquilo(inferior) opcionalmente protegido, fenilo e/ou acilo; alquilenodioxilo; cianofenilo; heterociclilfenilo; bifenililo; fenoxilo; fenilazo substituído opcionalmente com alquilo inferior; ou heterociclilo substituído opcionalmente em que os substituintes sejam hidroxilo opcionalmente protegido, mercapto, halogéneo, alquilo inferior, cicloalquilo, alcoxicarbonio inferior, amino, alcoxil(inferior)carbonilamino, carbamoílo, oxo, fenilo, alcoxifenilo inferior ou heterociclilo.

São exemplos mais preferidos halogéneo; alquilo inferior substituído opcionalmente com halogéneo; ou alcoxilo inferior substituído opcionalmente com halogéneo.

O "conjunto de substituinte β" é um conjunto constituído por halogéneo, hidroxilo protegido

opcionalmente, mercapto, alcoxilo inferior, alcenilo inferior, amino, alquilamino inferior, alcoxicarbonilamino inferior, alquiltio inferior, acilo, carboxilo, alcoxicarbonilo inferior, carbamoílo, ciano, cicloalquilo, fenilo, fenoxilo, alquil(inferior)fenilo, alcoxil(inferior)fenilo, halogenofenilo, naftilo e heterociclilo.

São exemplos dos substituintes em "alquilo inferior substituído opcionalmente" representados por qualquer símbolo diferente de Z (por exemplo, R^1), um ou mais substituintes seleccionados de entre o conjunto de substituintes β. O alquilo inferior pode ser substituído com estes substituintes em qualquer das posições possíveis.

A parte de alquilo inferior em "alcoxilo inferior", "alcoxicarbonilo inferior", "alcoxicarbonil(inferior)alquilo inferior", "alquil(inferior)fenilo", "alcoxil(inferior)fenilo", "alquilcarbamoílo", "alquil(inferior)tiocarbamoílo", "alquilamino inferior", "halogenoalquilo inferior", "hidroxialquilo inferior", "fenilalcoxilo inferior", "alquiltio inferior", "fenilalquil(inferior)tio", "alcoxil(inferior)carbonilamino", "alcoxil(inferior)carbonilalcenilo (inferior)", "alquilsulfinilo inferior", "alquilsulfonilo inferior", "arilalcoxil(inferior)carbonilo", "alquil(inferior)benzoílo" e "alcoxil8inferior)benzoílo" é a mesma que se definiu acima para "alquilo inferior".

São exemplos de substituintes no "alcoxilo inferior substituído opcionalmente", um ou mais substituintes seleccionados de entre o conjunto de substituintes β. São exemplos preferidos fenilo, alquil(inferior)fenilo, alcoxil(inferior)fenilo, naftilo e heterociclilo.

O termo "cicloalquilo" inclui grupos alquilo cíclicos em C3 a C8, e preferivelmente em C5 a C6. São exemplos ciclopropilo, ciclobutilo, ciclopentilo, ciclohexilo, cicloheptilo e ciclo-octilo.

São exemplos de substituintes em "cicloalquilo substituído opcionalmente", um ou mais substituintes seleccionados de entre o conjunto de substituintes α, e o cicloalquilo pode ser substituído com estes substituintes em qualquer uma das posições possíveis.

O termo "bicicloalquilo" inclui um conjunto que é formado excluindo um hidrogénio de um alifático cíclico em C5 a C8, contendo dois anéis que possuam em comum dois ou mais átomos. São exemplos os grupos biciclo[2.1.0]pentilo, biciclo[2.2.1]heptilo, biciclo[2.2.2]octilo e biciclo[3.2.1]octilo.

O termo "acenilo inferior" inclui alcenilo em C2 a C10, preferivelmente em C2 a C8 e mais preferivelmente em C3 a C6, com cadeia linear ou ramificada, contendo uma ou mais ligações duplas em quaisquer posições em que sejam possíveis. São exemplos vinilo, propenilo, isopropenilo,

butenilo, isobutenilo, prenilo, butadienilo, pentenilo, isopentenilo, pentadienilo, hexenilo, isohexenilo, hexadienilo, heptenilo, octenilo, nonenilo e decenilo.

A parte "alcenilo inferior" em "alcoxil(inferior)carbonilalcenilo inferior" é a mesma que se definiu acima para "alcenilo inferior".

São exemplos dos substituintes de "alcenilo inferior substituído opcionalmente", halogéneo, alcoxilo inferior, alcenilo inferior, amino, alquilamino inferior, alcoxil8inferior)carbonilamino, alquiltio inferior, acilo, carboxilo alcoxicarbonilo, carbamoílo, ciano, cicloalquilo, fenilo, alquilfenilo inferior, alcoxifenilo inferior, naftilo e/ou heterociclilo.

O termo "acilo" inclui (1) alquilcarbonilo ou alcenilcarbonilo com cadeia linear ou ramificada, em C1 a C10, preferivelmente em C1 a C6 e mais preferivelmente em C1 a C4, (2) cicloalquilcarbonilo em C4 a C9 e preferivelmente em C4 a C7 e (3) arilcarbonilo em C7 a C11. São exemplos os grupos formilo, acetilo, propionilo, butirilo, isobutirilo, valerilo, pivaloílo, hexanoílo, acriloílo, propioloílo, metacriloílo, crotonoílo, ciclopropilcarbonilo, ciclohexilcarbonilo, ciclo-octilcarbonilo e benzoílo.

A parte "acilo" em "aciloxilo" é a mesma que se definiu acima.

O termo "cicloalcenilo" inclui um grupo contendo pelo menos uma ligação dupla em qualquer das posições em que ela é possível no cicloalquilo acima. São exemplos os grupos ciclopropenilo, ciclobutenilo, ciclopentenilo, ciclohexenilo e ciclohexadienilo.

São exemplos de substituintes em "cicloalcenilo substituído opcionalmente", um ou mais substituintes seleccionados de entre o conjunto de substituintes β.

São exemplos de substituintes em "amino substituído opcionalmente" os do conjunto de substituintes β, benzoílo substituído opcionalmente e/ou heterociclilcarbonilo substituído opcionalmente, em que os substituintes sejam hidroxilo, alquilo inferior, alcoxilo inferior e/ou alquiltio inferior.

O termo "arilo" inclui um grupo carbociclilo aromático monocíclico ou policíclico, de que são exemplos os grupos fenilo, naftilo, antrilo e fenantrilo. "Arilo" inclui arilo fundido com outro grupo carbociclilo não aromático, por exemplo, indanilo, indenilo, bifenililo, acenaftilo, tetrahidronaftilo e fluorenilo. É preferível fenilo.

A parte arilo em "arilalcoxil(inferior)carbonilo" é a mesma que se definiu acima.

O termo "arilo substituído opcionalmente" e o termo "fenilo substituído opcionalmente" representados por

Z, incluem respectivamente os grupos "arilo" e "fenilo", que podem ser substituídos com os substituintes do conjunto α ou com alquilo inferior que pode ser substituído com um ou mais grupos seleccionados de entre o conjunto de substituintes α.

São exemplos dos substituintes no "arilo substituído opcionalmente" e no "fenilo substituído opcionalmente" representados por qualquer símbolo diferente de Z, um ou mais grupos seleccionados de entre o conjunto de substituintes β.

O termo "carbociclilo" inclui os acima designados "cicloalquilo", "cicloalcenilo", "bicicloalquilo" e "arilo".

O termo "carbociclilo não aromático" inclui os acima designados "cicloalquilo", "cicloalcenilo" e "bicicloalquilo".

O termo "carbociclilo substituído opcionalmente" inclui os acima designados "cicloalquilo substituído opcionalmente", "cicloalcenilo substituído opcionalmente", "bicicloalquilo substituído opcionalmente" e "arilo substituído opcionalmente".

O termo "heterociclilo" inclui um grupo heterocíclico contendo pelo menos um heteroátomo seleccionado arbitrariamente de entre O, S e N. Por exemplo, heteroarilos com 5 ou com 6 membros tais como

pirrolilo, imidazolilo, pirazolilo, piridilo, piridazinilo, pirimidinilo, oxazolilo, oxadiazolilo, isotiazolilo, tiazolilo, tiadiazolilo, furilo e tienilo; heterociclilos fundidos constituídos por dois anéis tais como indolilo, isoindolilo, indazolilo, indolizinilo, indolinilo, isoindolinilo, quinolilo, isoquinolilo, cinolinilo, ftalazinilo, quinazolinilo, naftiridinilo, quinoxalinilo, purinilo, pteridinilo, benzopiranilo, benzimidazolilo, benzisoxazolilo, benzoxazolilo benzoxadiazolilo, benzisotiazolilo, benzotiazolilo, benzotiadiazolilo, benzofurilo, isobenzofurilo, benzotienilo, benzotriazolilo, imidazopiridilo, triazoropiridilo, imidazotiazolilo, pirazinopiridazinilo, quinazolinilo, quinolilo, isoquinolilo, naftiridinilo, dihidropiridilo, tetrahidroquinolilo e tetrahidrobenzotienilo; heterociclilos fundidos constituídos por três anéis tais como carbazolilo, acridinilo, xantenilo, fenotiazinilo, fenoxatiinilo, fenoxazinilo e dibenzofurilo; e heterociclilos não aromáticos tais como dioxanilo, tiiranilo, oxiranilo, oxatiolanilo, azetidinilo, tianilo, pirrolidinilo, pirrolinilo, imidazolidinilo, imidazolinilo, pirazolidinilo, pirazolinilo, piperidilo, piperazinilo, morfolinilo, morfolino, tiomorfolinilo, tiomorfolino, dihidropiridilo, tetrahidrofurilo, tetrahidropiranilo, tetrahidrotiazolilo e tetrahidroisotiazolilo.

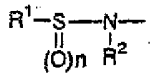
"Heterociclilo fundido" fundido com um anel que não seja um heterociclo (por exemplo, benzotiazolilo), podem ligar-se por qualquer uma das posições possíveis.

Os substituintes em "heterociclilo substituído opcionalmente" são os mesmos que nos acima designados "arilo substituído opcionalmente".

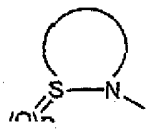
As partes heterociclilo em "heterociclilcarbonilo", "heterocicliloxilo", "heterocicliltio" e "fenilo substituído com heterociclilo" são os mesmos que para os acima designados "heterociclilo".

O termo "alquileno inferior" inclui um grupo bivalente contendo 1 a 6 metilenos, preferivelmente 2 a 6 metilenos e mais preferivelmente 3 a 6 metilenos. Por exemplo, estão incluídos os grupos metileno, etileno, trimetileno, tetrametileno, pentametileno e hexametileno. É preferível o tetrametileno.

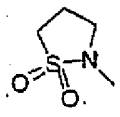
"R^1 e R^2 podem formar alquileno inferior quando tomados em conjunto" inclui o caso em que



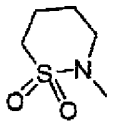
é



São exemplos preferíveis



e



A parte de alquileno inferior em "alquilenodioxilo inferior" é a mesma que a mencionada acima em "alquileno inferior". São preferíveis metilenodioxilo ou etilenodioxilo.

O termo "alcenileno inferior" inclui um grupo bivalente contendo 2 a 6 unidades de metileno, preferivelmente 3 a 6 unidades de metileno e mais preferivelmente 4 a 5 unidades de metileno, e incluindo pelo menos uma ligação dupla.

O termo "cicloalquileno" inclui um grupo bivalente que é formado excluindo um hidrogénio do grupo "cicloalquilo" acima. Um exemplo preferível de cicloalquileno representado por X é o 1, 4-ciclohexanodi-ilo.

O termo "cicloalcenileno" inclui um grupo que contenha pelo menos uma ligação dupla, no *cicloalq*uileno acima.

O termo "bicicloalquileno" inclui um grupo que é formado excluindo um hidrogénio do grupo "bicicloalquilo" acima. São exemplos o biciclo[2.1.0]pentileno, o

biciclo[2.2.1]heptileno, o biciclo[2.2.2]octileno, e o biciclo[3.2.1]octileno.

O termo "heterociclo-di-ilo" inclui um grupo bivalente que é formado excluindo um átomo de hidrogénio do grupo "heterociclilo" acima. São preferíveis piperidina-di-ilo, piperazina-di-ilo, piridina-di-ilo, pirimidina-di-ilo, pirazina-di-ilo, pirrolidina-di-ilo ou pirroledi-ilo e é mais preferível piperidina-di-ilo.

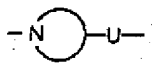
O termo "arileno" inclui um grupo bivalente formado excluindo um átomo de hidrogénio do grupo "arilo" acima. É preferível fenileno.

O termo "heteroarileno" inclui grupos aromáticos dos grupos "heterociclo-di-ilo". São exemplos pirrole-di-ilo, imidazole-di-ilo, pirazole-di-ilo, piridina-di-ilo, piridazina-di-ilo, pirimidina-di-ilo, pirazina-di-ilo, triazole-di-ilo, triazina-di-ilo, isoxazole-di-ilo, oxazole-di-ilo, oxadiazole-di-ilo, isotiazole-di-ilo, tiazole-di-ilo, tiadiazole-di-ilo, furan-di-ilo e tiofeno-di-ilo.

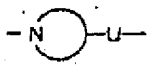
Um ou mais dos grupos seleccionados de entre o grupo de substituintes β são exemplos de substituintes para "alquileno inferior substituído opcionalmente", "alcenileno inferior substituído opcionalmente", "cicloalquileno substituído opcionalmente", "ciclohexileno substituído opcionalmente", "bicicloalquileno substituído opcionalmente", "cicloalcenileno substituído

opcionalmente", "fenileno substituído opcionalmente", "heterociclo-di-ilo substituído opcionalmente" e "piperidinileno substituído opcionalmente". São preferíveis halogéneo, hidroxilo, alquilo inferior, halogenoalquilo(inferior), alcoxilo inferior, amino, alquilamino inferior, acilo, carboxilo ou alcoxicarbonilo inferior. Estes substituintes podem ligar-se a qualquer uma das posições possíveis.

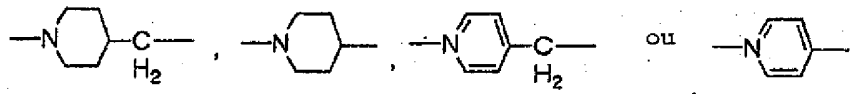
Quando $-NR^2-X-$ for



U é preferivelmente uma ligação simples ou metileno. Mais preferivelmente,



é



Os compostos da invenção presente incluem também quaisquer dos seus sais capazes de serem formado e aceitáveis do ponto de vista farmacêutico. São exemplos de um "sal aceitável do ponto de vista farmacêutico" os sais com ácidos inorgânicos tais como ácido clorídrico, ácido

sulfúrico, ácido azótico e ácido fosfórico; sais com ácidos orgânicos tais como ácido para-toluenossulfónico, ácido metanossulfónico, ácido oxálico e ácido cítrico; sais com bases orgânicas tais como os de amónio, trimetilamónio e trietilamónio; sais com metais alcalinos tais como sódio e potássio; e sais com metais alcalino-terrosos tais como o cálcio e o magnésio.

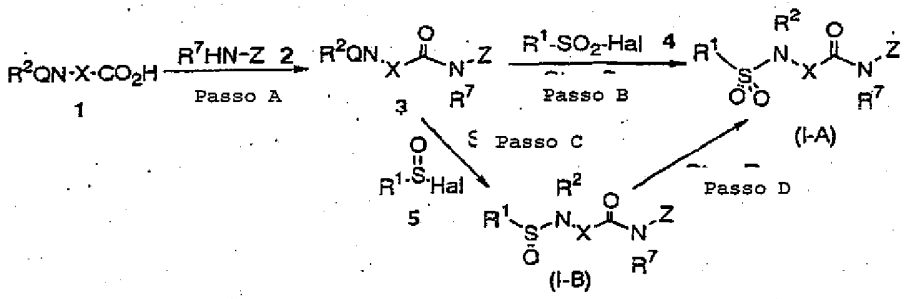
Os compostos da invenção presente incluem solvatos. Hidrato é preferível e pode coordenar-se com o composto da invenção presente um número arbitrário de moléculas de água.

Quando o composto (I) da invenção presente possui um átomo de carbono assimétrico, ele inclui os próprios racematos, todos os enantiómeros e todos os estereoisómeros, tais como os seus diastereómeros, epímeros e enantiómeros.

Quando o composto (I) da invenção presente contendo uma ou mais ligações duplas forma um isómero E ou um isómero Z, o composto (I) inclui ambos os isómeros. Quando X é cicloalquileno, o composto (I) inclui tanto o isómero cis como o isómero trans.

Por exemplo, o composto (I) da invenção presente pode ser sintetizado pelo método seguinte.

(Compostos nos quais Y=CONR^7)



em que Hal seja halogéneo, Q seja um grupo protector de amino e os outros símbolos são tais como acima.

Passo A

Faz-se reagir o composto 1 com o Composto Amino 2 possuindo os substituintes pretendidos Z e R^7 num solvente apropriado a entre 0°C e 50°C durante entre diversos minutos e diversas horas. A título de solvente, pode utilizar-se tetrahidrofurano, dimetilformamida, éter dietílico, diclorometano, tolueno, benzeno, xileno, ciclohexano, hexano, clorofórmio, acetato de etilo, acetato de butilo, pentano, heptano, dioxano, acetona, acetonitrilo, água, uma mistura de todos estes, etc.. Pode utilizar-se um activantes tal como cloreto de tionilo, um halogeneto de acilo, um anidrido de ácido e um éster activado, caso seja necessário.

Passo B

Desprotege-se o composto 3 pelo método habitual e faz-se reagir com o Halogeneto de Sulfonilo 4 que tinha o

substituinte R^1 pretendido num solvente adequado, a entre 0°C e 50°C durante entre diversos minutos e diversas horas para se obter o composto (I-A) no qual n é 2. Pode utilizar-se a título de solvente tetrahidrofurano, dimetilformamida, éter dietílico, diclorometano, tolueno, benzeno, xileno, ciclohexano, hexano, clorofórmio, acetato de etilo, acetato de butilo, pentano, heptano, dioxano, acetona, acetonitrilo, água e misturas de todos estes, etc..

Passo C

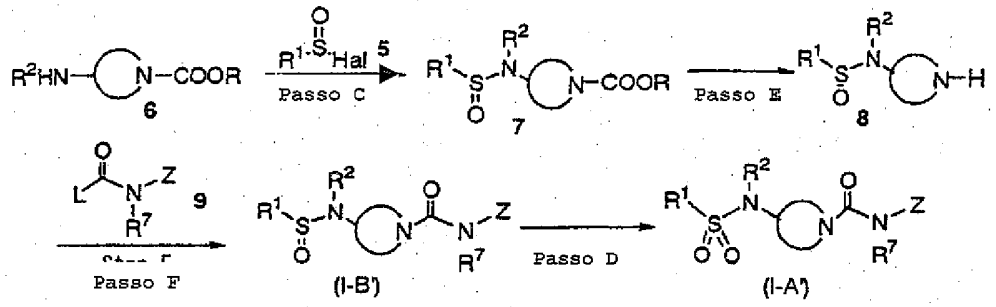
Pode sintetizar-se o Composto (I-B) no qual n é 1 fazendo reagir o Composto 3 com o Halogeneto de Sulfinilo 5 contendo o substituinte R^1. As condições reaccionais para a reacção são as mesmas que se utilizaram no Passo B.

Passo D

Oxida-se o Composto (I-B) obtido no Passo C pelo método habitual para se obter o Composto (I-A) no qual n é 2. Pode utilizar-se como oxidante ácido m-cloroperbenzóico, ácido peracético, peróxido de hidrogénio, ácido trifluoroperacético, periodato de sódio, hipoclorito de sódio, permanganato de potássio, etc., e pode levar-se a cabo a entre 0°C e 50°C. São exemplos de solventes, tetrahidrofurano, dimetilformamida, éter dietílico, diclorometano, tolueno, benzeno, xileno, ciclohexano, hexano, clorofórmio, acetato de etilo, acetato de butilo,

pentano, heptano, dioxano, acetona, acetonitrilo, água, metanol, etanol, isopropanol e uma mistura de todos estes.

Quando X é heterociclo-di-ilo contendo pelo menos um átomo de N e o átomo de N liga-se a $CONR^7$-Z no composto (I), pode empregar-se a reacção seguinte para se obter o Composto (I-A') ou (I-B'). Pode levar-se a cabo o Passo D logo após o Passo C ou o Passo E.



no qual R é alquilo inferior ou arilo e L é um grupo de saída.

Passo C

Faz-se reagir o Composto 5 com o Composto 6 de um modo semelhante ao Passo C acima, para se obter o Composto 7.

Passo E

O Composto 7 obtido desta forma é tratado com uma base num solvente adequado, para se obter o Composto 8. Por exemplo, o hidróxido de bário, hidróxido de sódio,

hidróxido de potássio, hidrazina ou propanotiolato de lítio como base. A título de solvente, pode aprovar-se o tetrahidrofurano, a dimetilformamida, o dioxano, a acetona, o acetonitrilo, o metanol, o etanol, o propanol, a água, qualquer mistura destes ou outros semelhantes. Pode levar-se a cabo a reacção a entre 0°C e 100°C durante entre diversos minutos e várias dezenas de horas.

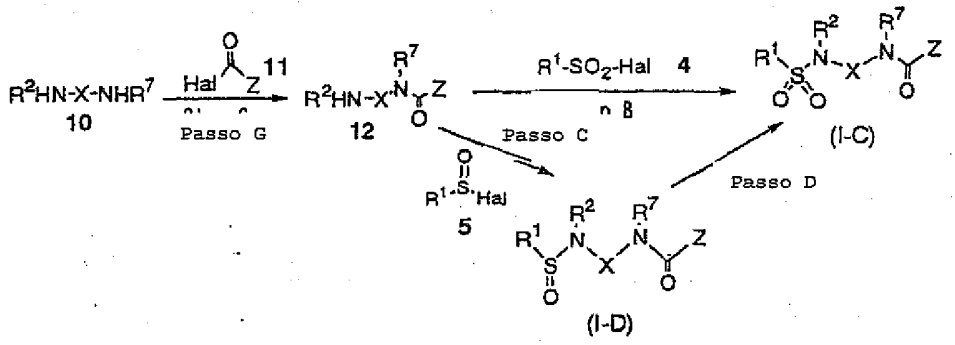
Passo F

Faz-se reagir o composto 8 com o Composto 9 contendo um grupo rejeitado e o substituinte pretendido, num solvente adequado, na presença ou na ausência de uma base, a entre 0°C e 100°C durante entre diversos minutos e diversos dias, para se obter o Composto (I-B'). São exemplos de grupo rejeitado fenoxilo, cloro e triclorometilo. São exemplos da base trietilamina, piridina, di-isopropiletilamina, hidróxido de sódio, carbonato de potássio e hidrogenocarbonato de sódio. São exemplos do solvente tetrahidrofurano, dimetilformamida, éter dietílico, diclorometano, tolueno, benzeno, xileno, ciclohexano, hexano, clorofórmio, acetato de etilo, acetato de butilo, pentano, heptano, dioxano, acetona, acetonitrilo, metanol, etanol e as misturas destes.

Passo D

Faz-se reagir o Composto (I-B') de uma maneira semelhante à do Passo D acima, para se obter o Composto (I-A').

(Composto no qual Y=NR^{7}CO)



em que todos os símbolos sejam tais como acima.

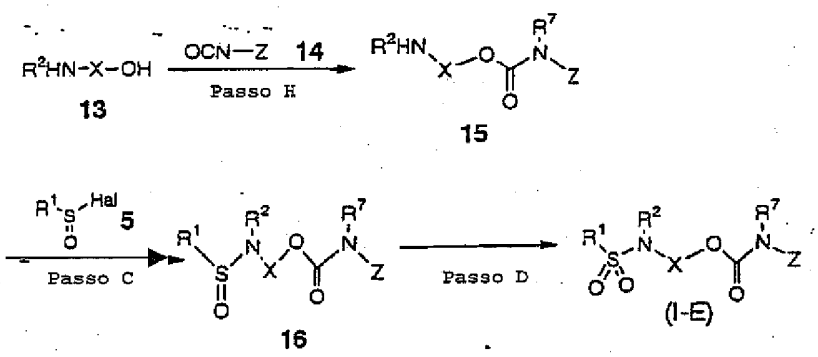
Passo G e Passo B

Faz-se reagir o Composto 10 com o Composto 11 nas mesmas condições reaccionais que no Passo B. Faz-se reagir o Composto 12 que desta forma se obtém de um modo semelhante ao do Passo B acima para se obter o Composto (I-C) no qual n=2.

Passo C e Passo D

Para se sintetizar o Composto (I-D), pode fazer-se reagir o Composto 12 obtido no Passo G de um modo semelhante aos do Passo C e do Passo D acima.

(Composto no qual Y=OCONR^7)



em que todos os símbolos são tal como acima.

Passo H

Faz-se reagir o Composto 13 com o Isocianato, Composto 14, contendo um substituinte Z, num solvente adequado e na presença de um catalisador apropriado, a entre 0°C e 100°C durante entre diversos minutos e diversos dias, para se obter o Composto 15. São exemplos do solvente, tetrahidrofurano, dimetilformamida, éter dietílico, diclorometano, tolueno, benzeno, xileno, ciclohexano, hexano, clorofórmio, acetato de etilo, acetato de butilo, pentano, heptano, dioxano, acetona, acetonitrilo e as misturas destes.

Passo C e Passo D

Faz-se reagir o Composto 15 que desta forma se obteve de modos semelhantes aos do Passo C e do Passo D para se obter o Composto (I-E) da invenção presente.

(Composto no qual Y=CSNR^7 ou NR^{7}CS)

Pode sintetizar-se o Composto (I) no qual Y seja $CSNR^7$ ou NR^7CS fazendo reagir o composto (I) no qual Y seja $CONR^7$ ou NR^7CO, sintetizado por qualquer um dos métodos acima, com o reagente de Lawesson ou com pentassulfureto de fósforo num solvente adequado a entre 30°C e 100°C durante entre diversos minutos e várias horas. São exemplos do solvente tetrahidrofurano, dimetilformamida, éter dietílico, diclorometano, tolueno, benzeno, xileno, ciclohexano, hexano, clorofórmio, acetato de etilo, acetato de butilo, pentano, heptano, dioxano, acetona, acetonitrilo e misturas de todos estes.

Podem proteger-se os grupos amino com um grupo protector adequado da forma habitual num passo apropriado. Por exemplo, pode utilizar-se como grupo protector a ftalimida, um alcoxicarbonilo inferior, um alceniloxicarbonilo inferior, um halogenoalcoxicarbonilo inferior, um aril-alcoxil(inferior)carbonilo, um trialquilsililo, um alquilsulfonilo inferior, um halogenoalquilsulfonilo inferior, um arilsulfonilo, um alquilcarbonilo inferior e um arilcarbonilo.

Depois da protecção do grupo amino, submete-se o composto às reacções mencionadas acima e desprotege-se o composto obtido por um tratamento com um ácido ou com uma base num solvente adequado, numa altura apropriada. São exemplos de um solvente, tetrahidrofurano, dimetilformamida, éter dietílico, diclorometano, tolueno, benzeno, xileno, ciclohexano, hexano, clorofórmio, acetato de etilo, acetato de butilo, pentano, heptano, dioxano,

acetona, acetonitrilo e as misturas destes. São exemplos de bases a hidrazina, a piridina, o hidróxido de sódio e o hidróxido de potássio e são exemplos de um ácido o ácido clorídrico, o ácido trifluoroacético e o ácido fluorídrico.

Todos os compostos da invenção presente têm uma actividade antagonista do Y5 de NPY e os compostos seguintes são especialmente preferidos.

Na fórmula (I),

um composto no qual R^1 seja alquilo inferior substituído opcionalmente ou cicloalquilo substituído opcionalmente (doravante referido neste documento como composto em que "R^1 seja R1-1"),

um composto no qual R^1 seja alquilo C3 a C10 ou cicloalquilo C5 ou C6, cada um dos quais seja substituído opcionalmente com halogéneo (doravante referido neste documento como "R^1 seja R1-2"),

um composto no qual R^1 seja alquilo C3 a C10 substituído opcionalmente com halogéneo (doravante referido neste documento como "R^1 seja R1-3"),

um composto no qual R^1 seja isopropilo ou t-butilo (doravante referido neste documento como "R^1 seja R1-4"),

um composto no qual R^2 seja hidrogénio ou alquilo C1 a C3 (doravante referido neste documento como "R^2 seja R2-1"),

um composto no qual R^2 seja hidrogénio (doravante referido neste documento como "R^2 seja R2-2"),

um composto no qual X seja alquileno inferior substituído opcionalmente, alcenileno inferior substituído opcionalmente ou



em que

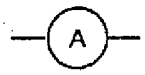


seja cicloalquileno substituído opcionalmente, cicloalcenileno substituído opcionalmente, bicicloalquileno substituído opcionalmente, fenileno substituído opcionalmente ou heterociclo-di-ilo substituído opcionalmente (doravante referido neste documento como "X seja X-1"),

um composto no qual X seja alquileno C2 a C6, alcenileno C3 a C6 ou

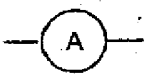


em que



seja cicloalquileno substituído opcionalmente, cicloalcenileno substituído opcionalmente, bicicloalquileno substituído opcionalmente, fenileno substituído opcionalmente, piperidinileno substituído opcionalmente, tiofeno-di-ilo substituído opcionalmente ou furano-di-ilo substituído opcionalmente (doravante referido neste documento como "X seja X-2"),

um composto no qual X seja alquileno C2 a C6 ou



que seja cicloalquileno substituído opcionalmente, fenileno substituído opcionalmente, piperidinileno substituído opcionalmente, tiofeno-di-ilo substituído opcionalmente ou furano-di-ilo substituído opcionalmente (doravante referido neste documento como "X seja X-3"),

um composto o qual X seja (i) alquileno C2 a C6 ou (ii) cicloalquileno ou fenileno, senso ambos substituídos opcionalmente com halogéneo, hidroxilo, alquilo inferior ou halogenoalquilo inferior (doravante referido neste documento como "X seja X-4"),

um composto no qual X seja alquileno C2 a C6 ou cicloalquileno C5 ou C6 (doravante referido neste documento como "X seja X-5"),

um composto no qual X seja alquileno C3 a C6 ou 1,4-ciclohexileno (doravante referido neste documento como "X seja X-6"),

um composto no qual Y seja $CONR^7$, $CSNR^7$, NR^7CO ou NR^7CS e R^7 seja hidrogénio ou alquilo C1 a C3 (doravante referido neste documento como "Y seja Y-1"),

um composto no qual Y seja CONH, CSNH ou NHCO (doravante referido neste documento como "Y seja Y-2"),

um composto no qual Y seja CONH (doravante referido neste documento como "Y seja Y-3"),

um composto no qual Z seja alquilo inferior substituído opcionalmente, carbociclilo substituído opcionalmente ou heterociclilo substituído opcionalmente (doravante referido neste documento como "Z seja Z-1"),

um composto no qual Z seja $-(CR^8\ R^9)_r-W-(CR^{10}R^{11})_s-V$, em que R^8, R^9, R^{10} e R^{11} sejam cada um deles independentemente hidrogénio ou alquilo inferior e quando Z tiver dois ou mais R^8, dois ou mais R^9, dois ou mais R^{10} e/ou dois ou mais R^{11}, todos os R^8, R^9, R^{10} e R^{11} possam ser diferentes, W seja uma ligação simples, O, S ou NR^{12}, R^{12} seja hidrogénio, alquilo inferior ou fenilo, V seja

hidrogénio, cicloalquilo substituído opcionalmente, bicicloalquilo substituído opcionalmente, arilo substituído opcionalmente ou heterociclilo substituído opcionalmente, r seja um inteiro de 1 a 4 e s seja um inteiro de 0 a 4 (doravante referido neste documento como "Z seja Z-2"),

uma composto no qual Z seja $-(CH_2)_r-W-(CH_2)_s-V$, em que W seja uma ligação simples, O, S ou NR^{12}, R^{12} seja hidrogénio ou alquilo inferior, V seja arilo substituído opcionalmente ou heterociclilo substituído opcionalmente em que os substituintes sejam halogéneo, hidroxilo, alquilo inferior, halogenoalquilo inferior, alcoxilo inferior, alcenilo inferior, amino, alquilamino inferior, acilo, carboxilo, alcoxicarbonilo inferior, fenilo ou heteroarilo monocíclico, r seja um inteiro de 1 a 4 e s seja um inteiro de 0 a 4 (doravante referido neste documento como "Z seja Z-3),

um composto no qual Z seja $-(CH_2)_r-W-(CH_2)_s-V$, em que W seja uma ligação simples, O, S, NH ou NMe, V seja fenilo substituído opcionalmente ou heteroarilo substituído opcionalmente em que os substituintes sejam halogéneo, alquilo inferior, halogenoalquilo inferior, alcoxilo inferior, amino ou alquilamino inferior, r seja um inteiro de 1 a 3 e s seja um inteiro de 0 ou 1 (doravante referido neste documento como "Z seja Z-4"),

um composto no qual Z seja carbociclilo substituído opcionalmente, em que o substituinte seja halogéneo; hidroxilo; alquilo inferior substituído

opcionalmente em que os substituintes sejam halogéneo, hidroxilo, carboxilo, alcoxicarbonilo inferior, ciano e/ou fenilo; alcenilo inferior substituído opcionalmente com alcoxicarbonilo inferior; alcoxilo inferior substituído opcionalmente em que os substituintes sejam halogéneo, hidroxilo, alcoxilo inferior, carboxilo, alcoxicarbonilo inferior, alquilamino inferior, cicloalquilo, ciano e/ou heterociclilo; cicloalquilo; cicloalquiloxilo; acilo; alquiltio inferior; carbamoílo; alquil(inferior)carbamoílo; cicloalquilcarbamoílo; hidroxi-imino; amino substituído opcionalmente amino em que os substituintes sejam alquilo inferior, hidroxialquilo inferior opcionalmente protegido, alcoxialquilo inferior, acilo, alquilsulfonilo inferior, arilsulfonilo e/ou fenilo; fenilo substituído opcionalmente com halogéneo, ciano, fenilo e/ou heterociclilo; alquilsulfinilo inferior; alquilsulfamoílo inferior; cicloalquilsulfamoílo; nitro; ciano; alquilenodioxilo; fenilazo substituído opcionalmente com alquilo inferior; fenoxilo; oxo; heterociclilo substituído opcionalmente em que os substituintes sejam hidroxilo opcionalmente protegido, mercapto, halogéneo, alquilo inferior, cicloalquilo, alcoxil(inferior)carbonilo, acilo, amino, alcoxil(inferior)carbonilamino, carbamoílo, oxo, fenilo, alcoxifenilo inferior, halogenofenilo, heterociclilo e/ou oxo; heterociclilsulfonilo substituído opcionalmente com alquilo inferior: heterocicliloxilo; heterociclilcarbonilo substituído opcionalmente com alquilo inferior (doravante referido neste documento como "Z seja Z-5"),

um composto no qual Z seja fenilo substituído opcionalmente no qual os substituintes sejam halogéneo; hidroxilo; alquilo inferior substituído opcionalmente com halogéneo, hidroxilo, alcoxicarbonilo inferior, ciano e/ou fenilo; alcoxil(inferior)carbonilalcenilo inferior; alcoxilo inferior substituído opcionalmente com halogéneo, alcoxilo inferior, alcoxicarbonilo inferior, cicloalquilo e/ou heterociclilo; cicloalquilo; cicloalquiloxilo; acilo; alquiltio inferior; carbamoílo; alquilcarbamoílo inferior; amino substituído opcionalmente com alquilo inferior, hidroxialquilo inferior, acilo, alquilsulfonilo inferior e/ou fenilo; fenilo substituído opcionalmente com halogéneo, ciano, fenilo e/ou heterociclilo; alquilsulfamoílo inferior; cicloalquilsulfamoílo; nitro; alquilenodioxilo; fenilazo substituído opcionalmente com alquilo inferior; fenoxilo; oxo; heterociclilo substituído opcionalmente com hidroxilo, halogéneo, alquilo inferior, alcoxicarbonilo inferior, amino, carbamoílo, fenilo, halogenofenilo, heterociclilo e/ou oxo; heterocicliloxilo; e/ou heterociclilsulfonilo substituído opcionalmente com alquilo inferior (doravante referido neste documento como "Z seja Z-6"),

um composto no qual Z seja fenilo substituído opcionalmente em que os substituintes sejam halogéneo; alquilo inferior substituído opcionalmente com halogéneo, hidroxilo, alcoxicarbonilo inferior e/ou fenilo; alcoxilo inferior substituído opcionalmente com halogéneo e/ou cicloalquilo; cicloalquilo; cicloalquiloxilo; acilo; alquiltio inferior; alquilcarbamoílo inferior; amino

substituído opcionalmente com alquilo inferior, hidroxialquilo inferior, acilo e/ou fenilo; fenilo substituído opcionalmente com piperidilo; cicloalquilsulfamoílo; alquilenodioxilo; fenoxilo; morfolinilo ou morfolino, sendo qualquer um destes substituído opcionalmente com alquilo inferior; piperidilo substituído opcionalmente com hidroxilo, alquilo inferior, alcoxicarbonilo inferior, fenilo, halogenofenilo e/ou oxo; pirrolidinilo substituído opcionalmente com hidroxilo, carbamoílo e/ou oxo; piperazinilo substituído opcionalmente com fenilo ou com pirimidinilo; dihidropiridilo; pirrolilo; pirrolinilo; imidazolilo substituído opcionalmente com halogéneo e/ou com alquilo inferior; pirazolilo; tienilo; tiadiazolilo; furilo; oxazolilo; isoxazolilo; tetrazolilo substituído opcionalmente com alquilo inferior e/ou com fenilo; indolinilo; indolilo; tetrahidroquinolilo; benzotiazolilo substituído opcionalmente com alquilo inferior; tetrahidroisotiazolilo substituído opcionalmente com oxo; benzopiranilo substituído opcionalmente com oxo; tetrahidropiraniloxilo; tetrahidrofuriloxilo; morfolinossulfonilo substituído opcionalmente com alquilo inferior; e/ou piperidilsulfonilo substituído opcionalmente com alquilo inferior (doravante referido neste documento como "Z seja Z-7"),

um composto no qual Z seja fenilo substituído opcionalmente em que os substituintes sejam halogéneo, alquilo inferior, halogenoalquilo inferior, alcoxilo inferior, cicloalquiloxilo, alquilcarbamoílo inferior, fenilo, alquilmorfolino inferior e/ou

tetrahidropiraniloxilo (doravante referido neste documento como "Z seja Z-8"),

um composto no qual Z seja heterociclilo substituído opcionalmente em que os substituintes sejam halogéneo, hidroxilo, alquilo inferior, halogenoalquilo inferior, alcoxilo inferior, mercapto, alquiltio inferior, acilo, carboxilo, alcoxicarbonilo inferior, alquilamino inferior, fenilo, naftilo, feniltio substituído opcionalmente com halogéneo, fenoxilo substituído opcionalmente com halogéneo, oxo, e/ou heterociclilo substituído opcionalmente com alquilo inferior (doravante referido neste documento como "Z seja Z-9"),

um composto no qual Z seja tienilo, pirazolilo, tiazolilo, tiadiazolilo, piridilo, pirimidinilo, pirazinilo, triazinilo, indolilo, isoindolilo, indolinilo, isoindolinilo, indazolilo, benzopiranilo, benzoxazolilo, benzotienilo, benzotiazolilo, benzotiazolinilo, benzotiadiazolilo, quinolilo, isoquinolilo, dihidrobenzofurilo, carbazolilo, acridinilo ou dibenzofurilo, todos os quais sejam substituídos opcionalmente com substituintes seleccionados de entre o conjunto constituído por alquilo inferior; halogenoalquilo inferior; alcoxilo inferior; alcoxicarbonilo inferior; acilo; alcoxil(inferior)carbonilalquilo inferior; mercapto; fenilo, naftilo, feniltio ou fenoxilo, todos os quais sejam substituídos opcionalmente com halogéneo; furilo; nitro; oxo; e morfolino substituído opcionalmente com alquilo

inferior) (doravante referido neste documento como "Z seja Z-10"),

um composto no qual Z seja tienilo, tiazolilo, tiadiazolilo, piridilo, pirazinilo, indolilo, isoindolinilo, benzopiranilo, quinolilo, carbazolilo, dibenzofurilo, benzopiranilo, benzotienilo ou benzotiazolilo, todos os quais sejam substituídos opcionalmente com um ou mais substituintes seleccionados de entre o conjunto constituído por alquilo inferior, halogenoalquilo inferior, alcoxilo inferior, alcoxicarbonilo inferior, acilo, fenilo, naftilo, feniltio, alquilmorfolino inferior e oxo, (doravante referido neste documento como "Z seja Z-11),

um composto no qual R^1 seja R1-2, R^2 seja R2-2, n seja 2 e uma combinação de X, Y e Z, isto é, (X, Y, Z), seja qualquer uma das seguintes.

(X, Y, Z) = (X-3, Y-2, Z-1), (X-3, Y-2, Z-2), (X-3, Y-2, Z-3), (X-3, Y-2, Z-4), (X-3, Y-2, Z-5), (X-3, Y-2, Z-6), (X-3, Y-2, Z-7), (X-3, Y-2, Z-8), (X-3, Y-2, Z-9), (X-3, Y-2, Z-10), (X-3, Y-2, Z-11), (X-3, Y-3, Z-1), (X-3, Y-3, Z-2), (X-3, Y-3, Z-3), (X-3, Y-3, Z-4), (X-3, Y-3, Z-5), (X-3, Y-3, Z-6), (X-3, Y-3, Z-7), (X-3, Y-3, Z-8), (X-3, Y-3, Z-9), (X-3, Y-3, Z-10), (X-3, Y-3, Z-11), (X-4, Y-2, Z-1), (X-4, Y-2, Z-2), (X-4, Y-2, Z-3), (X-4, Y-2, Z-4), (X-4, Y-2, Z-5), (X-4, Y-2, Z-6), (X-4, Y-2, Z-7), (X-4, Y-2, Z-8), (X-4, Y-2, Z-9), (X-4, Y-2, Z-10), (X-4, Y-2, Z-11), (X-4, Y-3, Z-1), (X-4, Y-3, Z-2), (X-4, Y-3, Z-3), (X-

4, Y-3, Z-4), (X-4, Y-3, Z-5), (X-4, Y-3, Z-6), (X-4, Y-3, Z-7), (X-4, Y-3, Z-8), (X-4, Y-3, Z-9), (X-4, Y-3, Z-10), (X-4, Y-3, Z-11), (X-5, Y-2, Z-1), (X-5, Y-2, Z-2), (X-5, Y-2, Z-3), (X-5, Y-2, Z-4), (X-5, Y-2, Z-5), (X-5, Y-2, Z-6), (X-5, Y-2, Z-7), (X-5, Y-2, Z-8), (X-5, Y-2, Z-9), (X-5, Y-2, Z-10), (X-5, Y-2, Z-11), (X-5, Y-3, Z-1), (X-5, Y-3, Z-2), (X-5, Y-3, Z-3), (X-5, Y-3, Z-4), (X-5, Y-3, Z-5), (X-5, Y-3, Z-6), (X-5, Y-3, Z-7), (X-5, Y-3, Z-8), (X-5, Y-3, Z-9), (X-5, Y-3, Z-10) ou (X-5, Y-3, Z-11), um seu sal, precursor ou solvato aceitável do ponto de vista farmacêutico.

O antagonista de receptores Y5 de NPY da invenção presente é eficaz para todas as doenças nas quais esteja envolvido o Y5 de NPY, e é especialmente útil para impedir e/ou tratar a obesidade e para suprimir o consumo de alimentos. Para além disto, o antagonista é eficaz para impedir e/ou tratar doenças nas quais a obesidade actua como factor de risco, por exemplo, a diabetes, a hipertensão, a hiperlipidémia, a aterosclerose e a síndrome aguda de coronárias.

Para além disto, o antagonista de receptor Y5 de NPY da invenção presente tem pequena afinidade para os receptores Y1 e Y2 de NPY Y1, e é altamente selectivo para o receptor Y5 de NPY. A NPY provoca uma acção vasoconstritora prolongada na periferia, e esta acção é sobretudo através do receptor Y1. Uma vez que o receptor Y5 não está de todo envolvido nesta acção, o antagonista do receptor Y5 de NPY apresenta um pequeno

risco de induzir efeitos colaterais baseados na vasoconstrição periférica, e espera-se que seja utilizado adequadamente como um medicamento seguro.

O antagonista de receptor Y5 de NPY evidencia um efeito contra a obesidade por suprimir o consumo de alimentos. Esta é uma das características deste antagonista para não apresentar efeitos colaterais, por exemplo uma indigestão provocada por um agente contra a obesidade que iniba a digestão e a absorção, e um efeito colateral central tal como efeito anti-depressivo provocado pela inibição de um transportador de serotonina que tenha um efeito contra a obesidade.

Um composto da invenção presente pode ser administrado por via oral ou parentérica como agente contra a obesidade ou anoréxico. No caso da administração por via oral, ele pode assumir qualquer uma das formas habituais tais como comprimidos, grânulos, pós, cápsulas, pílulas, soluções, xaropes, tabletes bucais e tabletes sublinguais. Quando o composto é administrado por via parentérica, qualquer uma das formas habituais é preferível, tais como, por exemplo, injecções (por exemplo, endovenosas, intramusculares), supositórios, agentes endérmicos e vapores. É especialmente preferida a administração por via oral porque os compostos da invenção presente apresentam uma elevada capacidade de sofrer absorção quando administrados pela via oral.

Uma composição farmacêutica pode ser fabricada misturando uma quantidade eficaz de um composto da invenção presente com diversos aditivos farmacêuticos adequados para a forma de administração, tais como excipientes, aglomerantes, agentes humidificantes, desintegrantes, lubrificantes e diluentes. Quando se tratar da composição para uma injecção, pode esterilizar-se um ingrediente activo em conjunto com um veículo adequado para se obter a composição farmacêutica.

Incluem-se nos exemplos dos excipientes a lactose, a sacarose, a glucose, o amido, o carbonato de cálcio e a celulose cristalina. Incluem-se nos exemplos dos aglomerantes a metilcelulose, a carboximetilcelulose, a hidroxipropilcelulose, a gelatina e a polivinilpirrolidona. Incluem-se nos exemplos de agentes desintegrantes a carboximetilcelulose, a carboximetilcelulose sódica, o amido, o alginato de sódio, o agar e o laurilsulfato de sódio. Incluem-se nos exemplos dos lubrificantes o talco, o estearato de magnésio e o macrogol. Podem utilizar-se a título de materiais de base para os supositórios a manteiga de cacau, o macrogol, a metilcelulose, etc.. Quando a composição for fabricada sob a forma de soluções, injecções emulsionadas ou injecções de suspensões, podem adicionar-se aceleradores da dissolução, agentes de suspensão, emulsionantes, estabilizadores, conservantes, agentes isotónicos e outros semelhantes. Para administração

por via oral, podem adicionar-se agentes edulcorantes, sabores e outros semelhantes.

Embora a dosagem de um composto da invenção presente a título de agente contra a obesidade ou de agente anoréxico deva ser determinada levando em consideração a idade e o peso do paciente, o tipo e o grau das suas doenças, a via de administração, etc., uma dosagem habitual por via oral para um adulto é de entre 0,05 e 100 mg/kg/dia, e é preferível uma dosagem de entre 0,1 e 10 mg/kg/dia. Para administração parentérica, embora a dosagem varie pronunciadamente com as vias de administração, uma dosagem habitual é de entre 0,005 e 10 mg/kg/dia, preferivelmente de entre 0,01 e 1 mg/kg/dia. Pode administrar-se a dosagem de uma vez, ou em diversas parte ao longo do dia.

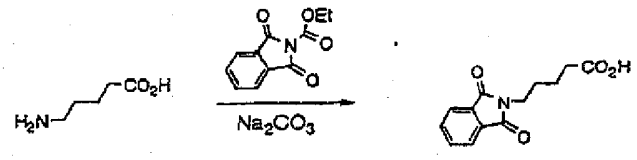
A invenção presente é explicada em mais pormenor pelos Exemplos e Experiências seguintes, que não se pretende seja limitativos do âmbito da invenção presente.

Nas figuras seguintes, Mol. Wt. significa Massa Molecular. (N do T)

Exemplos

Exemplo 1 Síntese do Composto (I-7)

Passo 1



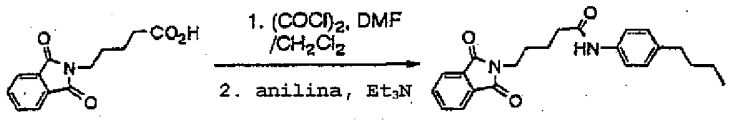
$C_5H_{11}NO2$
Mol. Wt.: 117.15

$C_{13}H_{13}NO4$
Mol. Wt.: 247.25

Dissolveu-se carbonato de sódio (995 mg, 9,38 mmol) em 30 mL de água e adicionaram-se à solução o aminoácido utilizado como matéria-prima (1,0 g, 8,53 mmol) e N-carbetoxiftalimida (2,49 g, 11,4 mmol). Agitou-se a mistura à temperatura ambiente de um dia para o outro. Ajustou-se o pH da mistura a 1 adicionando-lhe ácido clorídrico concentrado. Lavaram-se com água os cristais precipitados e secaram-se para se obter o composto pretendido (1,72 g, rendimento de 82 %).

RMN de ^1H (CD_3OD) δ ppm: 1,59-1,77 (m, 4H), 2,34 (t, 2H, J = 6,3 Hz), 3,69 (t, 2H, J = 6,6 Hz), 7,78-7,87 (m, 4H).

Passo 2



$C_{13}H_{13}NO4$
Mol. Wt.: 247.25

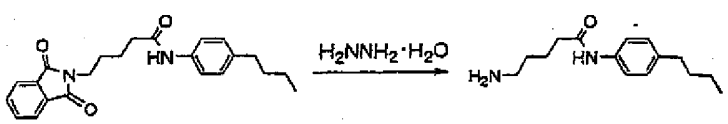
$C_{23}H_{26}N_2O3$
Mol. Wt.: 378.46

Dissolveu-se o composto obtido no Passo 1 (1,0 g, 4,0 mmol) em 5 mL de diclorometano, à temperatura ambiente.

Adicionaram-se à mistura cloreto de oxalilo (0,459 mL, 5,2 mmol) e uma quantidade vestigial de DMF, arrefecendo sobre gelo, e deixou-se reagir arrefecendo sobre gelo e à temperatura ambiente, 30 minutos para cada uma destas condições. Depois de se remover o solvente sob pressão reduzida, adicionou-se 5 mL de diclorometano. Arrefecendo sobre gelo, adicionaram-se á mistura 4-butilanilina (664 mg, 4,4 mmol) e trietilamina (0,564 mL, 4,4 mmol), e deixou-se a mistura reagir durante 30 minutos à temperatura ambiente. Verteu-se a mistura reaccional sobre água e extraiu-se com clorofórmio. Lavou-se a fase orgânica com água e secou-se sobre sulfato de magnésio anidro. Removeu-se o solvente sob pressão reduzida e purificou-se o resíduo por cromatografia sobre gel de sílica para se obter o composto pretendido (1,49 g, rendimento de 97 %).

RMN de ^1H ($CDCl_3$) δ ppm: 0,91 (t, 3H, J = 7,5 Hz), 1,27-1,39 (m, 2H), 1,51-1,62 (m, 2H), 1,72-1,84 (m, 4H), 2,40-2,46 (m, 2H), 2,56 (t, 2H, J = 7,5 Hz), 3,76 (t, 1H, J = 5,7 Hz), 7,12 (d, 2H, J = 7,8 Hz), 7,33 (s, 1H), 7,42 (d, 2H, J = 8,1 Hz), 7,71-7,73 (m, 2H), 7,83-7,86 (m,

Passo 3

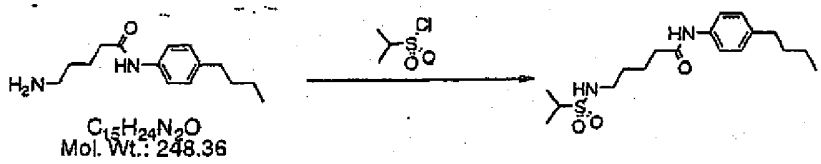


$C_{23}H_{26}N_2O3$
Mol. Wt.: 378.46

$C_{15}H_{24}N_2O$
Mol. Wt.: 248.36

Depois de se dissolver o composto obtido no Passo 2 (1,49 g, 3,9 mmol) em 30 mL de etanol, adicionou-se-lhe monohidrato de hidrazina (0,591 mg, 11,8 mmol) e deixou-se reagir a 50°C durante 3 horas. Removeu-se o solvente, adicionou-se uma solução aquosa de NaOH a 1 mol/L e extraiu-se a solução com acetato de etilo. Lavou-se a fase orgânica com água e secou-se sobre sulfato de magnésio anidro. Removeu-se o solvente sob pressão reduzida e purificou-se o resíduo por cromatografia sobre gel de sílica para se obter o composto pretendido (808 mg, rendimento de 83 %).

RMN de ^1H (CD_3OD) δ ppm: 0,93 (t, 3H, J = 7,2 Hz), 1,28-1,40 (m, 2H), 1,50-1,62 (m, 4H), 1,67-1,77 (m, 2H), 2,37 (t, 2H, J = 7,5 Hz), 2,56 (t, 2H, J = 7,8 Hz), 2,68 (t, 2H, J = 7,2 Hz), 7,11 (d, 2H, J = 8,1 Hz), 7,42 (d, 2H, J = 8,4 Hz).

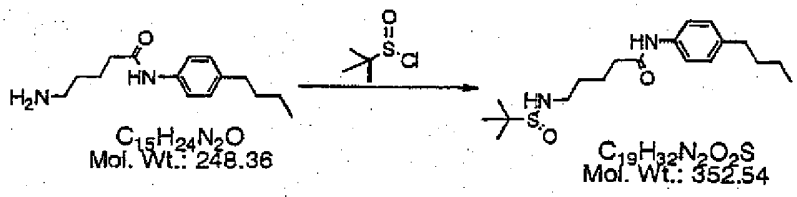


Suspendeu-se o composto obtido in Passo 3 (808 mg, 3,25 mmol) em 5 mL de diclorometano arrefecendo a mistura sobre gelo, e adicionaram-se-lhe cloreto de isopropilsulfonilo (696 mg, 4,9 mmol) e trietilamina (494 mg, 4,9 mmol). Depois de se deixar a mistura reagir arrefecendo-a sobre gelo durante uma hora, verteu-se a mistura reaccional sobre água e extraiu-se com clorofórmio.

Lavou-se a fase orgânica com água e secou-se sobre sulfato de magnésio anidro. Removeu-se o solvente sob pressão reduzida e purificou-se o resíduo por cromatografia sobre gel de sílica para se obter o composto pretendido quantitativamente.

RMN de ^1H ($CDCl_3$) δ ppm: 0,91 (t, 3H, J = 7,2 Hz), 1,27-1,40 (m, 2H), 1,36 (d, 6H, J = 6,6 Hz), 1,51-1,69 (m, 4H), 1,77-1,86 (m, 2H), 2,38 (t, 2H, J = 7,2 Hz), 2,56 (t, 2H, J = 7,5 Hz), 3,12-3,21 (m, 3H), 4,38 (t, 1H, J = 5,7 Hz), 7,11 (d, 2H, J = 8,4 Hz), 7,36-7,41 (m, 3H).

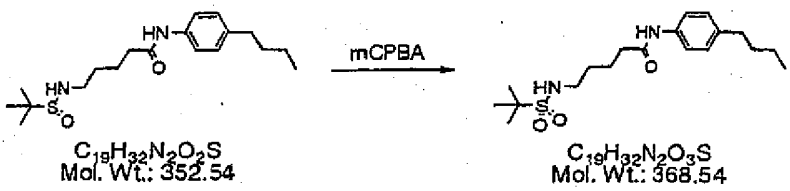
Exemplo 2 Síntese do Composto (I-10)



Sintetizou-se o composto pretendido de uma forma semelhante à do Passo 4 do Exemplo 1, excepto que se adicionaram cloreto de *terc*-butilsulfinilo (689 mg, 4,9 mmol) e trietilamina (494 mg, 4,9 mmol) ao composto obtido no Passo 3 do Exemplo 1.

RMN de ^1H ($CDCl_3$) δ ppm: 0,91 (t, 3H, J = 7,5 Hz), 1,22 (s, 9H), 1,30-1,37 (m, 2H), 1,51-1,68 (m, 4H), 1,76-1,86 (m, 2H), 2,31-2,40 (m, 2H), 2,56 (t, 2H, J = 7,5 Hz), 3,15-3,26 (m, 3H), 7,11 (t, 2H, J = 8,7 Hz), 7,42 (d, 2H, J = 8,1 Hz), 7,54 (s, 1H).

Exemplo 3 Síntese do Composto (I-11)



$C_{19}H_{32}N_2O_2S$
Mol. Wt.: 352.54

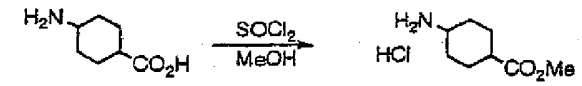
$C_{19}H_{32}N_2O_3S$
Mol. Wt.: 368.54

Dissolveu-se o composto obtido no Exemplo 2 (352 mg, 1,0 mmol) em 5 mL de diclorometano arrefecendo sobre gelo e adicionou-se mCPBA (259 mg, 1,5 mmol) à solução. Deixou-se a solução reagir à temperatura ambiente durante uma hora e separou-se o material insolúvel por filtração. Lavou-se o filtrado sucessivamente com uma solução de naOH a 1 mol/L, com solução de $Na_2S_2O_5$ e com água, e secou-se sobre sulfato de magnésio anidro. Removeu-se o solvente sob pressão reduzida e purificou-se o resíduo por cromatografia sobre gel de sílica para se obter o composto pretendido (338 mg, rendimento de 92 %).

RMN de ^1H ($CDCl_3$) δ ppm: 0,91 (t, 3H, J = 7,5 Hz), 1,29-1,39 (m, 2H), 1,39 (s, 9H), 1,51-1,68 (m, 4H), 1,76-1,84 (m, 2H), 2,37 (t, 2H, J = 7,5 Hz), 2,56 (t, 2H, J = 7,8 Hz), 3,19-3,26 (m, 2H), 4,20 (t, 1H, J = 5,7 Hz), 7,11 (t, 2H, J = 8,1 Hz), 7,42 (d, 2H, J = 8,7 Hz), 7,46 (s, 1H).

Exemplo 4. Síntese do Composto (I-72)

Passo 1



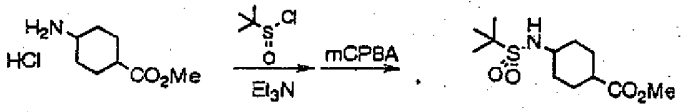
$C_7H_{13}NO2$
Mol. Wt.: 143.18

$C_8H_{16}ClNO2$
Mol. Wt.: 193.67

Dissolveu-se o aminoácido utilizado como matéria-prima (uma mistura dos isómeros cis e trans) (1,0 g, 8,53 mmol) em 7,5 mL de metanol. Adicionou-se à mistura cloreto de tionilo (1,0 mL, 13,7 mmol) arrefecendo sobre gelo e agitou-se a mistura à temperatura ambiente de um dia para o outro. Em seguida concentrou-se a mistura sob pressão reduzida, adicionou-se-lhe éter dietílico e separaram-se por filtração os cristais que haviam precipitado. Lavaram-se os cristais com éter dietílico e secaram-se para se obter o composto pretendido (1,25 g, rendimento de 93 %).

RMN de ^1H ($CDCl_3$) δ ppm: 1,50-2,60 (m, 9H), 3,08-3,36 (m, 1H), 3,67 (s, 3H, CO_2Me do isómero cis), 3,71 (s, 3H, CO_2Me do isómero trans), 8,15-8,55 (m, 3H).

Passo 2



$C_8H_{16}ClNO_2$
Mol. Wt.: 193.67

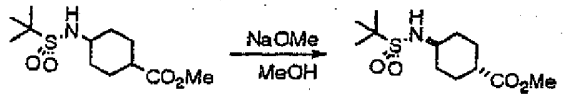
$C_{12}H_{23}NO_4S$
Mol. Wt.: 277.38

Sintetizou-se a sulfonamida pretendida (uma mistura do seu isómero cis com o seu isómero trans) a partir do éster metílico utilizado como matéria-prima de

modos semelhantes aos utilizados no Passo 3 do Exemplo 1 e do Exemplo 2.

isómero cis: RMN de ^1H ($CDCl_3$) δ ppm: 1,39 (s, 9H), 1,52-1,99 (m, 8H), 2,43-2,53 (m, 1H), 3,42-3,55 (m, 1H), 3,69 (s, 3H), 3,85 (d, 1H, J = 9,0 Hz).

Passo 3



$C_{12}H_{23}NO_4S$
Mol. Wt.: 277.38

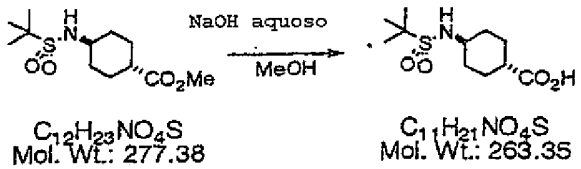
$C_{12}H_{23}NO_4S$
Mol. Wt.: 277.38

Dissolveu-se a sulfonamida utilizada como matéria-prima (19,4 g, 70,0 mmol, uma mistura do isómero cis com o isómero trans) em 30 mL de metanol. Adicionou-se à mistura metóxido de sódio a 28 % (284 mL, 140,0 mmol) e aqueceu-se ao refluxo sob agitação arrefecendo sobre gelo?. Depois de se remover o solvente, diluiu-se o resíduo com clorofórmio, e adicionou-se-lhe HCl a 1 mol/L sob arrefecimento até o pH da fase aquosa atingir 3. Extraiu-se a fase aquosa com clorofórmio, lavou-se a fase orgânica com água e secou-se sobre sulfato de magnésio anidro. Recristalizaram-se os cristais obtidos em bruto a partir de hexano-acetato de etilo para se obter a sulfonamida pretendida (isómero trans, 7,75 g, rendimento de 40 %).

isómero trans RMN de ^1H (CD_3OD) δ ppm: 1,16-1,32 (m, 2H), 1,39 (s, 9H), 1,44-1,52 (m, 2H), 1,98-2,09 (m,

2H), 2,14-2,29 (m, 3H), 3,18-3,37 (m, 1H), 3,63 (d, 1H, J = 9,0 Hz), 3,67 (s, 3H).

Passo 4



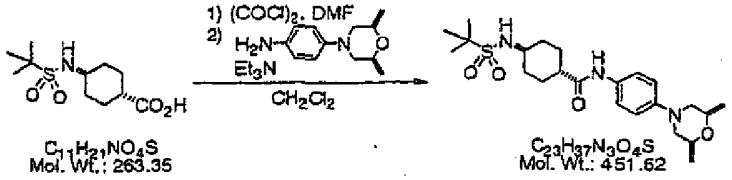
$C_{12}H_{23}NO_4S$
Mol. Wt.: 277.38

$C_{11}H_{21}NO_4S$
Mol. Wt.: 263.35

Dissolveu-se o éster metílico utilizado como matéria-prima (4,77 g, 17,2 mmol) em 95 mL de metanol e adicionou-se NaOH a 1 mol/L (43 mL, 43,0 mmol) sob agitação e arrefecendo sobre gelo. Agitou-se a mistura à temperatura ambiente de um dia para o outro e concentrou-se sob pressão reduzida. Em seguida adicionou-se HCl a 1 mol/L sob agitação até o pH da mistura atingir o valor de 3, sempre sobre arrefecimento com gelo, recolheram-se os cristais precipitados por filtração, lavaram-se com água e secaram-se. Recristalizaram-se os cristais obtidos em bruto a partir de hexano-acetato de etilo para se obter o ácido carboxílico pretendido (4,20 g, rendimento de 93 %).

RMN de ^1H ($CDCl_3$) δ ppm: 1,18-1,35 (m, 2H), 1,39 (s, 9H), 1,46-1,63 (m, 2H), 2,01-2,14 (m, 2H), 2,14-2,32 (m, 3H), 3,18-3,35 (m, 1H), 3,80 (d, 1H, J = 9,6 Hz).

Passo 5

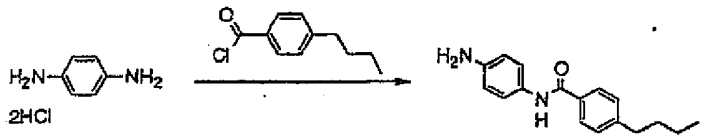


Dissolveu-se o ácido carboxílico utilizado como matéria-prima (5,86 g, 22,3 mmol) em 88 mL de diclorometano à temperatura ambiente. Adicionou-se à mistura cloreto de oxalilo (2,34 mL, 26,7 mmol) e uma quantidade catalítica de DMF enquanto se arrefecia sobre gelo e agitou-se à temperatura ambiente durante uma hora. Depois de se remover o solvente sob pressão reduzida, adicionaram-se diclorometano (115 mL), anilina substituída (5,05 g, 24,5 mmol) e trietilamina (4,65 mL, 33,4 mmol). Agitou-se a mistura à temperatura ambiente durante 2,5 horas, verteu-se sobre ela a água gelada de arrefecimento, e extraiu-se a mistura com clorofórmio. Lavou-se a fase orgânica com água e secou-se sobre sulfato de magnésio anidro. Removeu-se o solvente sob pressão reduzida e adicionaram-se ao resíduo acetato de etilo e hexano. Separaram-se os cristais precipitados por filtração para se obter a amida pretendida (7,00 g, rendimento de 70 %).

RMN de ^1H ($CDCl_3$) δ ppm: 1,25 (d, 6H, J = 6,3 Hz), 1,17-1,42 (m, 2H), 1,40 (s, 9H), 1,60-1,78 (m, 2H), 1,98-2,43 (m, 7H), 3,20-3,43 (m, 3H), 3,67 (d, 1H, J = 9,6 Hz), 3,74-3,86 (m, 2H), 6,86 (d, 2H, J = 9,0 Hz), 7,04 (s, 1H), 7,38 (d, 2H, J = 9,0 Hz).

Exemplo 5 Síntese do Composto (I-2)

Passo 1



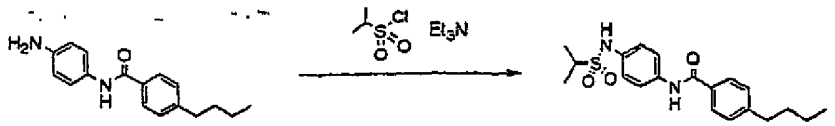
$C_6H_{10}Cl_2N2$
Mol. Wt.: 181.06

$C_{17}H_{20}N_2O$
Mol. Wt.: 268.35

Depois de se suspender a matéria-prima, uma diamina, (461 mg, 2,5 mmol) em diclorometano arrefecendo sobre gelo, adicionou-se-lhe um cloreto de acilo (500 mg, 2,5 mmol) e trietilamina (773 mg, 7,5 mmol) e deixou-se a mistura reagir durante 30 minutos. Adicionaram-se-lhe água e diclorometano e separaram-se materiais insolúveis por filtração. Lavou-se a fase orgânica com água e secou-se sobre sulfato de magnésio anidro. Removeu-se o solvente sob pressão reduzida para se obter o composto pretendido como resíduo (100 mg, rendimento de 15 %).

RMN de ^1H ($CDCl_3$) δ ppm: 0,93 (t, 3H, J = 7,2 Hz), 1,30-1,42 (m, 2H), 1,57-1,67 (m, 2H), 2,66 (t, 2H, J = 7,8 Hz), 3,50 (s lg, 1H), 6,57 (s, 1H), 6,68 (d, 2H, J = 8,7 Hz), 7,26 (d, 2H, J = 8,4 Hz), 7,39 (d, 2H, J = 8,7 Hz), 7,68 (s, 1H), 7,75 (d, 2H, J = 8,1 Hz).

Passo 2



$C_{17}H_{20}N_2O$
Mol. Wt.: 268.35

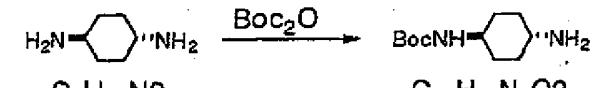
$C_{20}H_{26}N_2O_3S$
Mol. Wt.: 374.50

Sintetizou-se o composto pretendido de uma maneira semelhante à utilizada no Passo 4 do Exemplo 1.

RMN de ^{1}H-NMR ($CDCl_3$) δ ppm: 0,94 (t, 3H, J = 7,5 Hz), 1,34-1,44 (m, 2H), 1,40 (d, 6H, J = 6,6 Hz), 1,59-1,68 (m, 2H), 2,69 (t, 2H, J = 7,8 Hz), 3,24-3,35 (m, 1H), 6,49 (s, 1H), 7,23-7,32 (m, 4H), 7,6 (d, 2H, J = 8,7 Hz), 7,79 (d, 2H, J = 8,1 Hz), 7,85 (s, 1H).

Exemplo 6 Síntese do Composto (I-31)

Passo 1



$C_6H_{14}N2$
Mol. Wt.: 114.19

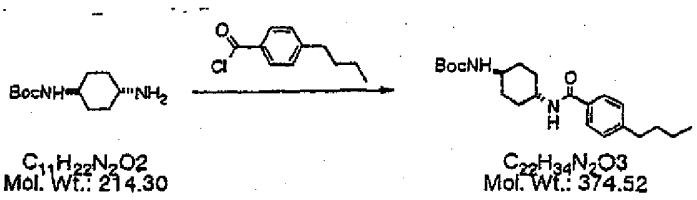
$C_{11}H_{22}N_2O2$
Mol. Wt.: 214.30

Dissolveu-se a diamina utilizada como matéria-prima (8,37 g, 73,3 mmol) em 30 mL de dioxano à temperatura ambiente e adicionou-se-lhe uma solução de Boc_2O (2 g, 9,2 mmol) em dioxano (30 mL). Fez-se reagir a mistura à temperatura ambiente durante 3 dias e removeu-se o solvente. Adicionou-se água ao resíduo e extraiu-se a mistura com clorofórmio. Lavou-se a fase orgânica com água e secou-se sobre sulfato de magnésio anidro. Removeu-se o

solvente sob pressão reduzida para se obter o composto sob a forma de um resíduo (1,8 g, rendimento de 92 % com base no Boc_2O).

RMN de ^1H-NMR ($CDCl_3$) δ ppm: 1,07-1,26 (m, 6H), 1,44 (s, 9H), 1,84-2,00 (m, 4H), 2,58-2,67 (m, 1H), 3,37 (s lg, 1H), 4,43 (s lg, 1H).

Passo 2



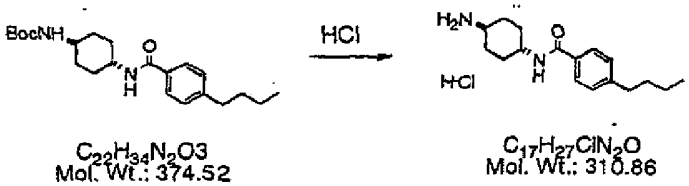
$C_{11}H_{22}N_2O2$
Mol. Wt.: 214.30

$C_{22}H_{34}N_2O3$
Mol. Wt.: 374.52

Sintetizou-se o composto pretendido de uma maneira semelhante à utilizada no Passo 1 do Exemplo 5.

RMN de ^1H ($CDCl_3$) δ ppm: 0,92 (t, 3H, J = 7,2 Hz), 1,26-1,42 (m, 6H), 1,45 (s, 9H), 1,54-1,68 (m, 2H), 1,99-2,12 (m, 4H), 2,64 (t, 2H, J = 7,8 Hz), 3,43 (s lg, 1H), 3,90-4,00 (m, 1H), 4,48 (d, 1H, J = 5,7 Hz), 5,95 (d, 1H, J = 8,4 Hz), 7,21 (d, 2H, J = 8,4 Hz), 7,65 (d, 2H, J = 8,4 Hz).

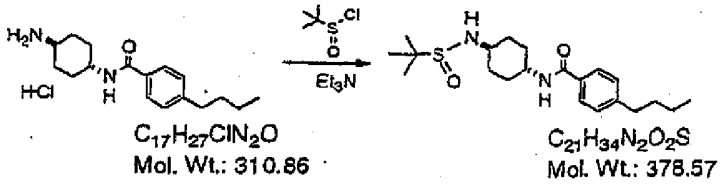
Passo 3



Dissolveu-se o composto de Boc utilizado como matéria-prima (2,08 g, 5,55 mmol) em 20 mL de acetato de etilo enquanto se arrefecia sobre gelo e adicionou-se 20 mL de HCl/AcOEt a 4 mol/L. Fez-se reagir a mistura à temperatura ambiente durante uma hora e removeu-se o solvente sob pressão reduzida para se obter o composto pretendido sob a forma de um resíduo (1,7 g, rendimento de 98 %).

RMN de ^1H (CD_3OD) δ ppm: 0,93 (t, 3H, J= 7,2 Hz), 1,29-1,41 (m, 2H), 1,50-1,66 (m, 6H), 2,02-2,18 (m, 4H), 2,66 (t, 2H, J = 7,8 Hz), 3,13 (s lg, 1H), 3,82-3,94 (m, 1H), 7,26 (d, 2H, J = 8,7 Hz), 7,72 (d, 2H, J = 8,4 Hz).

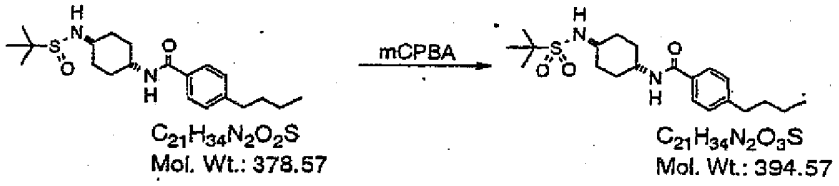
Passo 4



Sintetizou-se o composto pretendido de uma maneira semelhante à do Passo 4 no Exemplo 1.

RMN de ^1H ($CDCl_3$) δ ppm: 0,92 (t, 3H, J = 7,5 Hz), 1,21 (s, 9H), 1,28-1,62 (m, 8H), 2,07-2,14 (m, 4H), 2,64 (t, 2H, J = 7,8 Hz), 3,11 (d, 1H, J = 5,1 Hz), 3,20 (s lg, 1H), 3,90-4,04 (m, 1H), 6,06-6,14 (m, 1H), 7,21 (t, 2H, J = 8,1 Hz), 7,67 (t, 2H, J = 8,4 Hz).

Exemplo 7 Síntese do Composto (I-32)

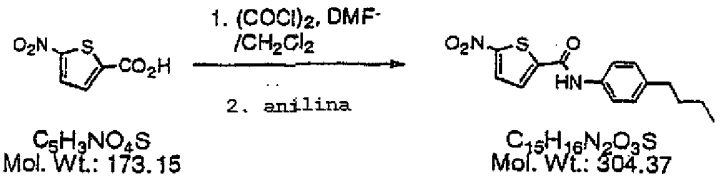


Sintetizou-se o composto pretendido a partir do composto obtido no Exemplo, de uma maneira semelhante à utilizada no Exemplo 3.

RMN de ^1H ($CDCl_3$) δ ppm: 0,92 (t, 3H, J = 7,2 Hz), 1,27-1,65 (m, 8H), 1,40 (s, 9H), 2,10-2,23 (m, 4H), 2,65 (t, 2H, J = 7,5 Hz), 3,23-3,35 (m, 1H), 3,49 (s, 1H), 3,88-4,02 (m, 1H), 5,84-5,92 (m, 1H), 7,13 (t, 2H, J = 8,4 Hz), 7,65 (d, 2H, J = 8,1 Hz).

Exemplo 8 Síntese do Composto (I-5)

Passo 1



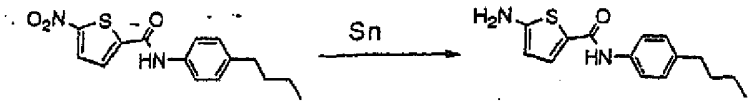
$C_5H_3NO_4S$
Mol. Wt.: 173.15

$C_{15}H_{16}N_2O_3S$
Mol. Wt.: 304.37

Sintetizou-se o composto pretendido de uma maneira semelhante à do Passo 2 do Exemplo 1.

RMN de ^1H ($CDCl_3$) δ ppm: 0,94 (t, 3H, J = 7,5 Hz), 1,30-1,42 (m, 2H), 1,50-1,65 (m, 2H), 2,61 (t, 2H, J = 7,8 Hz), 7,20 (d, 2H, J = 7,2 Hz), 7,48-7,51 (m, 3H), 7,72 (s, 1H), 7,88-7,90 (m, 1H).

Passo 2



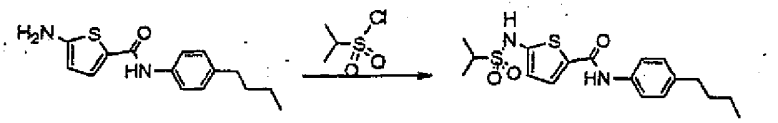
$C_{15}H_{16}N_2O_3S$
Mol. Wt.: 304.37

$C_{15}H_{18}N_2OS$
Mol. Wt.: 274.38

Adicionou-se a uma mistura do composto nitro utilizado como matéria-prima (593 mg, 1,95 mmol) com estanho (358 mg, 3,0 mmol), 30 mL de uma solução de HCl 6 mol/L e 6 mL de THF, e a reacção prosseguiu a 50°C durante 3 horas. Depois de arrefecer, removeu-se o solvente e neutralizou-se o resíduo com NaOH, extraindo-se com clorofórmio. Lavou-se a fase orgânica com água e secou-se sobre sulfato de magnésio anidro. Removeu-se o solvente sob pressão reduzida e purificou-se o resíduo por cromatografia sobre gel de sílica para se obter o composto pretendido (110 mg, rendimento de 21 %).

RMN de ^{1}H-NMR ($CDCl_3$) δ ppm: 0,91 (t, 3H, J = 7,2 Hz), 1,26-1,39 (m, 2H), 1,49-1,59 (m, 2H), 2,50 (t, 2H, J = 7,8 Hz), 4,37 (s, 1H), 6,65 (d, 2H, J = 8,4 Hz), 6,97 (d, 2H, J = 8,4 Hz), 7,14 (d, 1H, J = 8,4 Hz), 7,43 (d, 1H, J = 8,7 Hz).

Passo 3



$C_{15}H_{18}N_2OS$
Mol. Wt.: 274.38

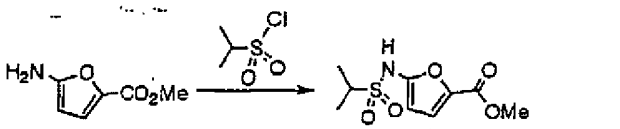
$C_{18}H_{24}N_2O_3S2$
Mol. Wt.: 380.53

Sintetizou-se o composto pretendido de uma maneira semelhante à do Passo 4 do Exemplo 1.

RMN de ^{1}H ($CDCl_3$) δ ppm: 0,92 (t, 3H, J = 7,2 Hz), 1,28-1,41 (m, 2H), 1,46 (d, 6H, J = 6,9 Hz), 1,53-1,63 (m, 2H), 2,59 (t, 2H, J = 7,8 Hz), 3,35-3,44 (m, 1H), 7,15 (d, 2H, J = 8,7 Hz), 7,38 (s, 1H), 7,45 (d, 2H, J = 8,7 Hz), 7,57 (s, 1H).

Exemplo 9 Síntese do Composto (I-4)

Passo 1



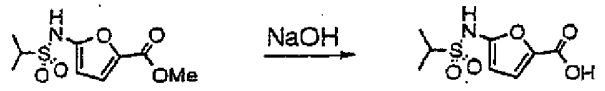
C_6H_7NO3
Mol. Wt.: 141.12

$C_9H_{13}NO_5S$
Mol. Wt.: 247.27

Sintetizou-se o composto pretendido de uma maneira semelhante à do Passo 4 do Exemplo 1.

RMN de ^1H ($CDCl_3$) δ ppm: 1,44 (d, 6H, J = 6,9 Hz), 3,33-3,43 (m, 1H), 3,88 (s, 9H), 6,24-6,26 (m, 1H), 7,11-7,14 (m, 2H).

Passo 2



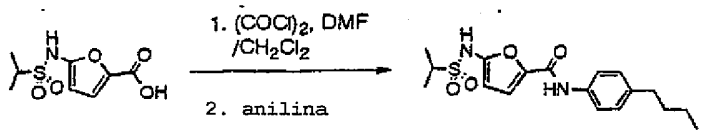
$C_9H_{13}NO_5S$
Mol. Wt.: 247.27

$C_8H_{11}NO_5S$
Mol. Wt.: 233.24

Sintetizou-se o composto pretendido de uma maneira semelhante à utilizada no Passo 4 do Exemplo 4.

RMN de ^1H ($CDCl_3$) δ ppm: 1,44 (d, 6H, J = 6,3 Hz), 3,33-3,45 (m, 1H), 6,25-6,28 (m, 1H), 7,27-7,28 (m, 1H), 7,51 (s, 1H).

Passo 3



$C_8H_{11}NO_5S$
Mol. Wt.: 233.24

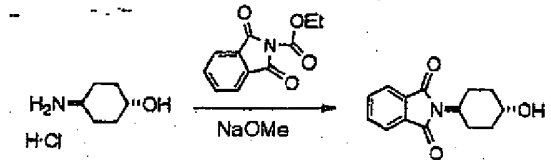
$C_{18}H_{24}N_2O_4S$
Mol. Wt.: 364.46

Sintetizou-se o composto pretendido de uma maneira semelhante à do Passo 2 no Exemplo 1.

RMN de ^1H (CD_3OD) δ ppm: 0,92 (t, 3H, J = 6,9 Hz), 1,28-1,41 (m, 2H), 1,46 (d, 6H, J = 6,3 Hz), 1,53-1,63 (m, 2H), 2,58 (t, 2H, J = 7,8 Hz), 3,33-3,43 (m, 1H), 6,27-6,29 (m, 1H), 7,14-7,16 (m, 3H), 7,50 (d, 2H, J = 8,4 Hz), 7,90 (s, 1H).

Exemplo 10 Síntese do Composto (I-28)

Passo 1



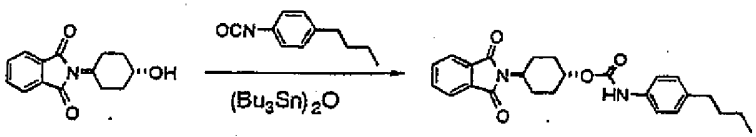
$C_8H_{14}ClNO$
Mol. Wt.: 151.63

$C_{14}H_{15}NO3$
Mol. Wt.: 245.27

Sintetizou-se o composto pretendido de uma maneira semelhante à utilizada no Passo 1 do Exemplo 1.

RMN de ^1H ($CDCl_3$) δ ppm: 1,37-1,52 (m, 3H), 1,74-1,79 (m, 2H), 2,07-2,13 (m, 2H), 2,28-2,42 (m, 2H), 3,72-3,81 (m, 1H), 4,09-4,20 (m, 1H), 7,68-7,73 (m, 2H), 7,81-7,85 (m, 2H).

Passo 2



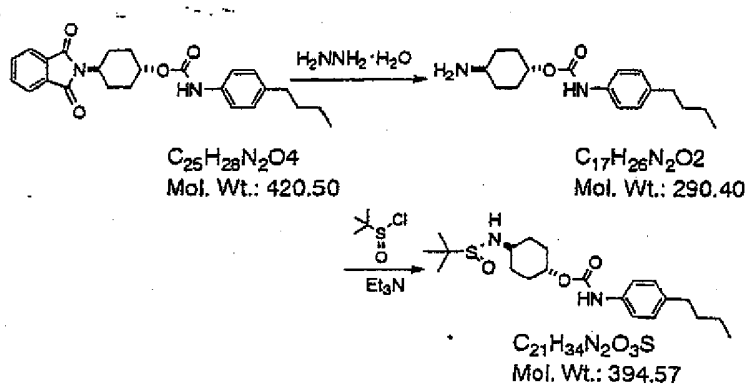
$C_{14}H_{15}NO3$
Mol. Wt.: 245.27

$C_{25}H_{28}N_2O4$
Mol. Wt.: 420.50

Dissolveu-se isocianato de 4-butilfenilo (2,85 g, 16,3 mmol) em 30 mL de THF, e adicionou-se o álcool utilizado como matéria-prima (1,0 g, 4,08 mmol) e óxido de bis(tributilestanho) (972 mg, 1,63 mmol). Em seguida agitou-se a mistura de um dia para o outro, removeu-se o solvente, adicionou-se água e extraiu-se a mistura com clorofórmio. Lavou-se a fase orgânica com água e secou-se sobre sulfato de magnésio anidro. Removeu-se o solvente sob pressão reduzida e purificou-se o resíduo por cromatografia sobre gel de sílica para se obter o composto pretendido (332 mg, rendimento de 19 %).

RMN de ^1H ($CDCl_3$) δ ppm: 0,92 (t, 3H, J = 6,9 Hz), 1,30-1,40 (m, 2H), 1,48-1,62 (m, 4H), 1,79-1,83 (m, 2H), 2,21-2,25 (m, 2H), 2,37-2,50 (m, 2H), 2,57 (t, 2H, J = 7,8 Hz), 4,11-4,22 (m, 1H), 4,77-4,87 (m, 1H), 6,49 (s, 1H), 7,11 (d, 2H, J = 8,7 Hz), 7,28 (d, 2H, J = 8,7 Hz), 7,69-7,73 (m, 2H), 7,80-7,84 (m, 2H).

Passo 3



Sintetizou-se o composto pretendido de maneira semelhante às utilizadas no Passo 3 do Exemplo 1 e no Exemplo 2.

RMN de ^1H ($CDCl_3$) δ ppm: 0,91 (t, 3H, J = 7,2 Hz), 1,21 (s, 9H), 1,30-1,62 (m, 8H), 2,08 (d, 4H, J = 11,1 Hz), 2,56 (t, 2H, J = 7,8 Hz), 3,04 (d, 1H, J = 4,8 Hz), 3,20-3,30 (m, 1H), 4,65-4,76 (m, 1H), 6,57 (s, 1H), 7,10 (d, 2H, J = 8,7 Hz), 7,26 (d, 2H, J = 8,1 Hz).

Exemplo 11 Síntese do Composto (I-29)



$C_{21}H_{34}N_2O_3S$
Mol. Wt.: 394.57

$C_{21}H_{34}N_2O_4S$
Mol. Wt.: 410.57

Sintetizou-se o composto pretendido de uma maneira semelhante à utilizada no Exemplo 3.

RMN de ^1H ($CDCl_3$) δ ppm: 0,91 (t, 3H, J = 7,2 Hz), 1,23-1,62 (m, 8H), 1,40 (s, 9H), 2,12 (d, 4H, J = 14,4 Hz), 2,56 (t, 2H, J = 7,8 Hz), 3,28-3,40 (m, 1H), 3,90 (s, 1H), 4,60-4,73 (m, 1H), 6,57 (s, 1H), 7,10 (d, 2H, J = 8,4 Hz), 7,25 (d, 2H, J = 8,4 Hz).

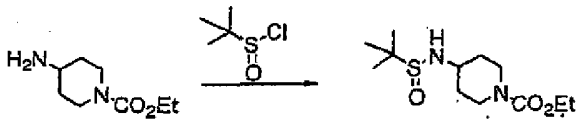
Exemplo 12 Síntese do Composto (I-114)



Adicionou-se reagente de Lawesson, 2,4-dissulfureto de [2,4-bis(4-metoxifenil)-1,3-ditia-2,4-difosfetano] (132 mg) a uma solução de 100 mg do Composto (I-110) sintetizado de uma maneira equivalente à utilizada no Exemplo 1, em tolueno (2,7 ml) e agitou-se a mistura a 80°C durante 3 horas. Concentrou-se a mistura reaccional sob pressão reduzida e purificou-se o resíduo por cromatografia sobre gel de sílica (acetato de etilo:n-hexano a 1:1) para se obterem cristais amarelo claros (82,3 mg, 79 %). Recristalizaram-se os cristais a partir de cloreto de metileno-éter di-isopropílico para se obter o composto pretendido sob a forma de agulhas incolores (50,5 mg, 48 %).

Exemplo 13 Síntese do Composto (I-120)

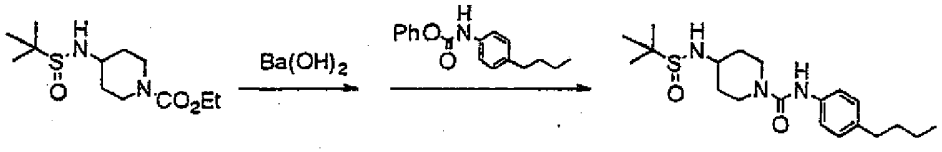
Passo 1



Dissolveram-se 4-amino-1-piperidinacarboxilato de etilo (300 mg) e trietilamina (258 mg) em 5 mL de diclorometano. Adicionou-se à mistura 2 mL de uma solução de cloreto de t-butilsulfinilo (222 mg) em diclorometano, e agitou-se a mistura à temperatura ambiente durante 4 horas. tratou-se esta mistura com uma solução aquosa de hidrogenossulfato de potássio e com acetato de etilo. Lavou-se a fase orgânica com salmoura e secou-se sobre

sulfato de magnésio anidro. Removeu-se o solvente sob pressão reduzida e purificou-se o resíduo por cromatografia sobre gel de sílica para se obterem 378 mg de 4-t-butylsulfinilamino-1-etoxicarbonilpiperidina.

Passo 2



Suspendeu-se numa mistura de 5 mL de 2-propanol e 5 mL de água, 378 mg de 4-t-butylsulfinilamino-1-etoxicarbonilpiperidina e adicionou-se-lhe 1,77 g de hidróxido de bário. Aqueceu-se a mistura ao refluxo com agitação e aquecimento durante 4 horas. Diluiu-se a mistura com metanol e separou-se por filtração o material insolúvel. Removeu-se o solvente sob pressão reduzida para se obter 4-t-butilsulfinilaminopiperidina. Sem purificação adicional dissolveu-se o material obtido em 5 mL de THF, e adicionou-se-lhe 984 mg de N-fenoxicarbonil-4-butil-anilina e 236 mg de di-isopropil-etilamina, agitando-se em seguida à temperatura ambiente de um dia para o outro. Adicionou-se à mistura uma solução aquosa de hidrogenossulfato de potássio e extraiu-se a mistura com acetato de etilo. Lavou-se a fase orgânica com salmoura e secou-se sobre sulfato de magnésio anidro. Removeu-se o solvente sob pressão reduzida e purificou-se o resíduo por cromatografia sobre gel de sílica para se obterem 291 mg de (4-t-

butilfenil)amida do ácido 4-t-butilsulfinilaminopiperidina-1-carboxílico.

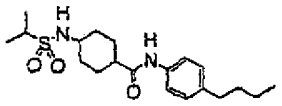
RMN de ^1H ($CDCl_3$) δ ppm: 0,89(t, 3H, J = 7,3 Hz), 1,19(s, 9H), 1,25-1,38(m, 4H), 1,40-1,60(m, 4H), 1,89-2,03(m, 3H), 2,52(t, 2H, J = 7,7 Hz), 2,89-3,04(m, 2H), 3,14(d, 1H, J = 5,2 Hz), 3,37(m, 1H), 3,96(m, 2H), 6,67(s, 1H), 7,05(d, 2H, J = 8,5 Hz), 7,22(d, 2H, J = 8,5 Hz).

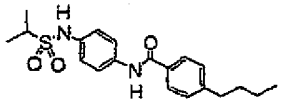
Passo 3

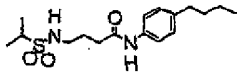


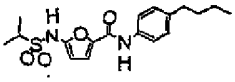
Numa mistura de 2 mL de metanol com 2 mL de cloreto de metileno, dissolveu-se 291 mg de (4-t-butilfenil)amida do ácido 4-t-butilsulfinilaminopiperidina-1-carboxílico. Adicionou-se à mistura 570 mg de MMPP (hexahidrato de monoperoxiftalato de magnésio) a 80 %, e agitou-se a mistura à temperatura ambiente durante 2 horas. Diluiu-se a solução com água e extraiu-se com acetato de etilo. Lavou-se a fase orgânica com salmoura e secou-se sobre sulfato de magnésio anidro. Removeu-se o solvente sob pressão reduzida e purificou-se o resíduo por cromatografia sobre gel de sílica para se obterem 130 mg de (4-butilfenil)amida do ácido 4-t-butilsulfonilaminopiperidina-1-carboxílico (I-120).

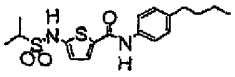
Sintetizam-se outros Compostos (I) por métodos semelhantes. Ilustram-se adiante as estruturas e as propriedades físicas deles.

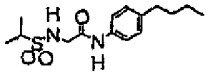
I-1 

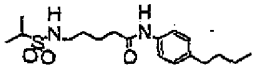
I-2 

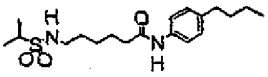
I-3 

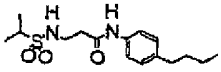
I-4 

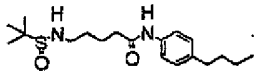
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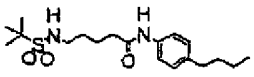
I-6 

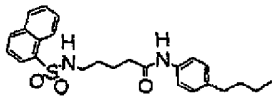
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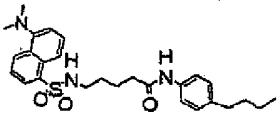
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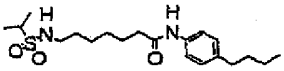
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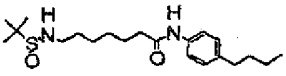
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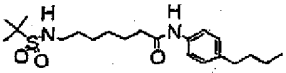
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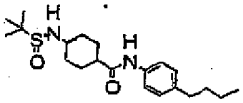
I-12 

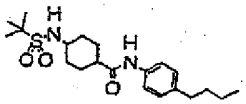
I-13 

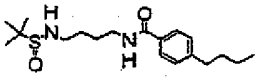
I-14 

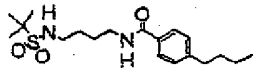
I-15 

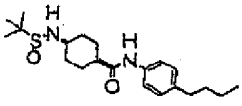
I-16 

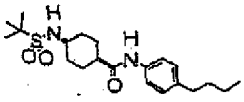
I-17 

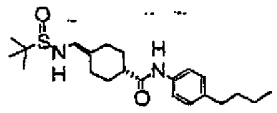
I-18 

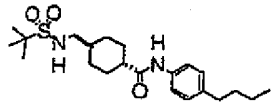
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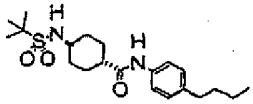
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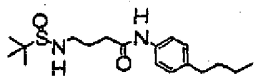
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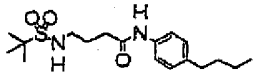
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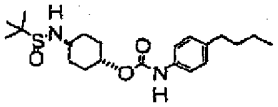
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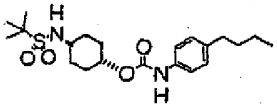
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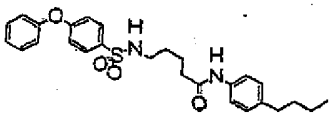
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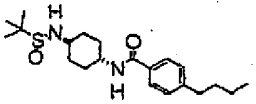
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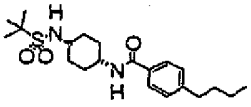
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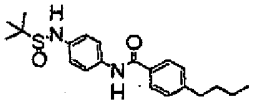
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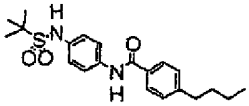
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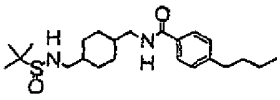
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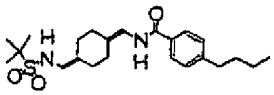
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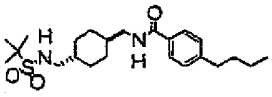
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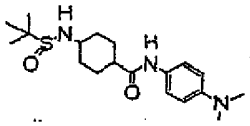
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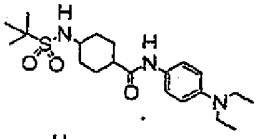
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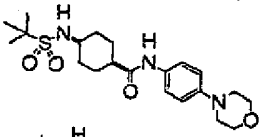
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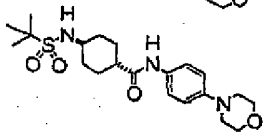
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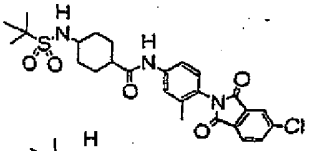
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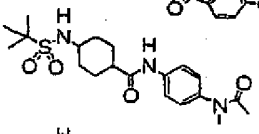
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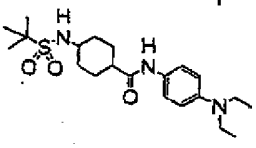
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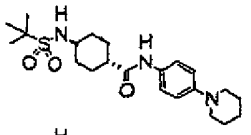
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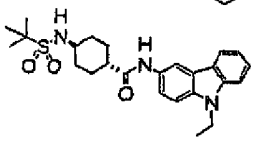
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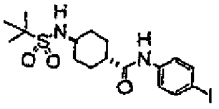
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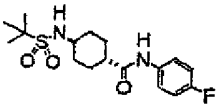
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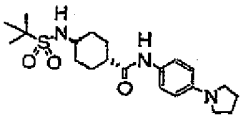
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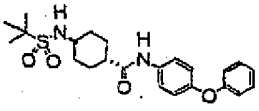
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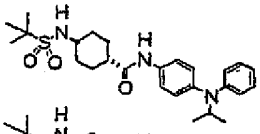
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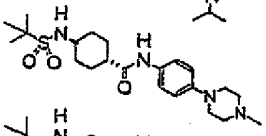
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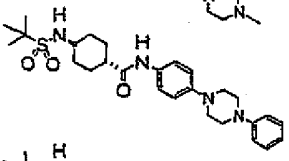
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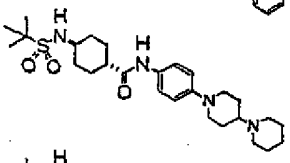
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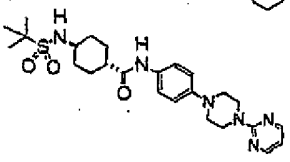
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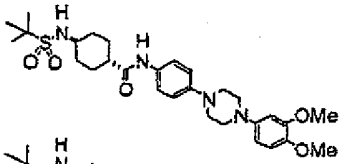
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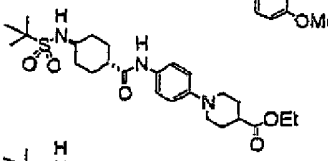
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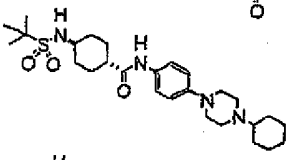
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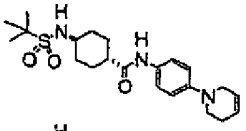
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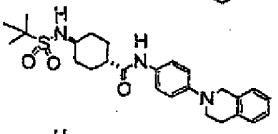
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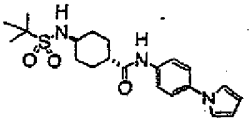
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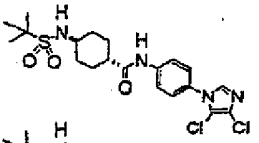
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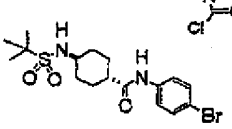
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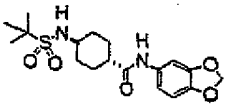
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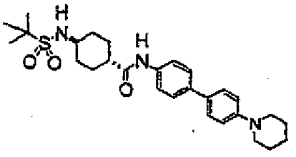
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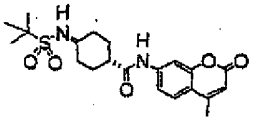
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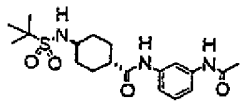
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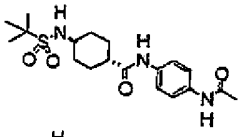
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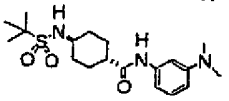
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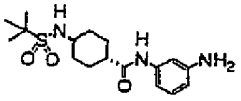
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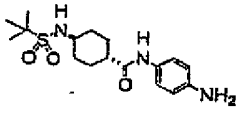
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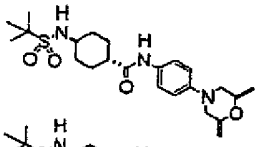
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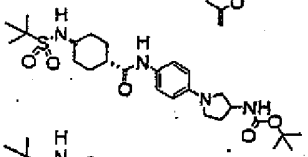
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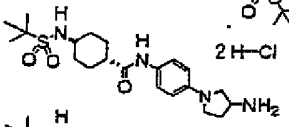
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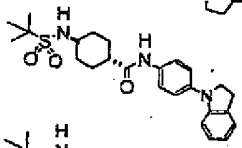
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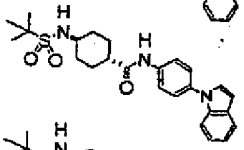
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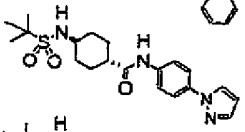
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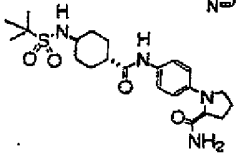
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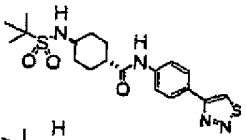
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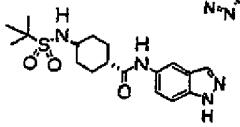
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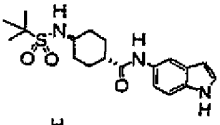
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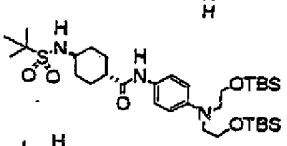
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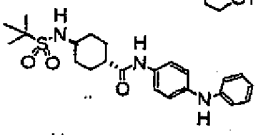
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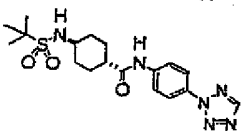
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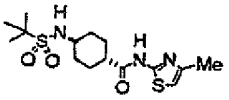
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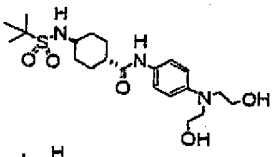
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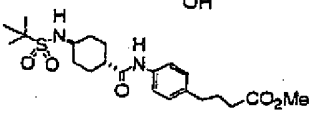
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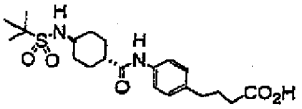
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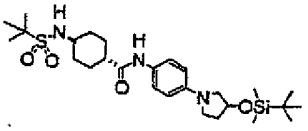
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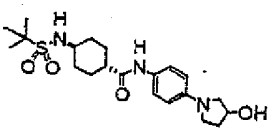
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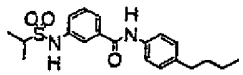
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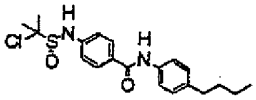
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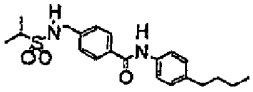
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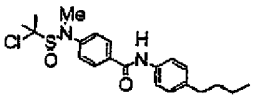
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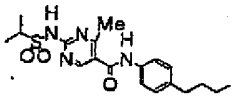
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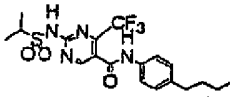
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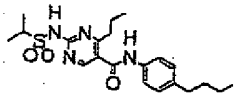
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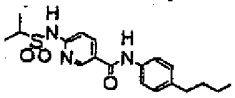
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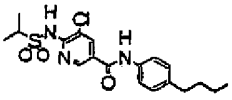
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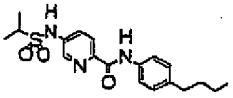
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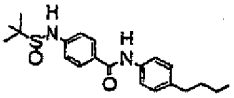
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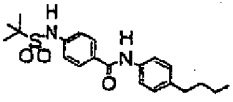
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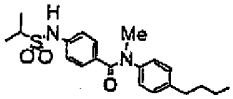
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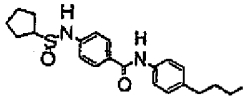
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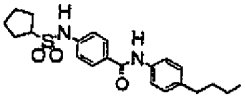
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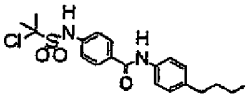
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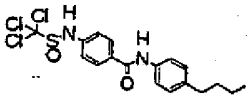
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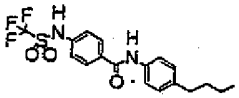
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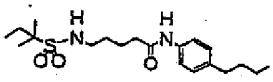
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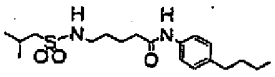
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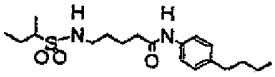
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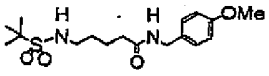
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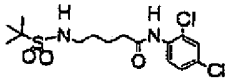
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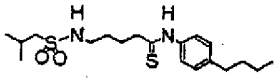
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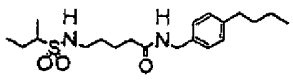
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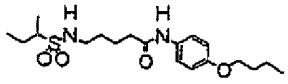
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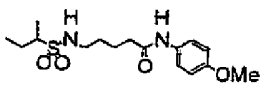
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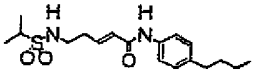
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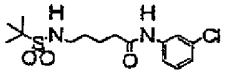
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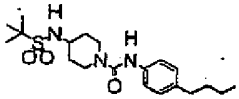
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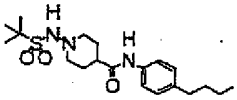
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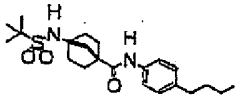
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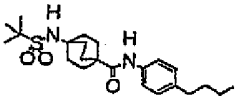
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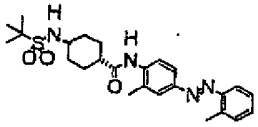
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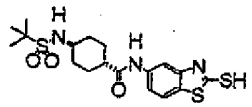
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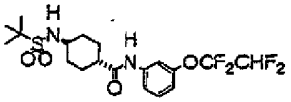
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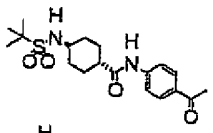
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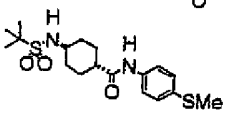
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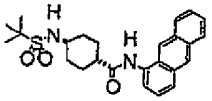
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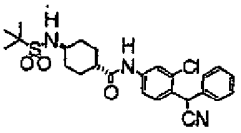
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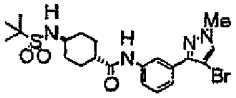
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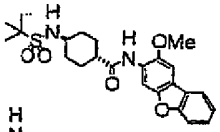
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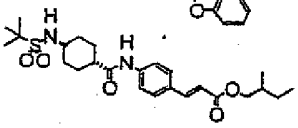
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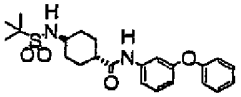
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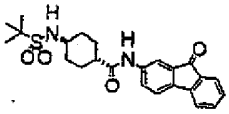
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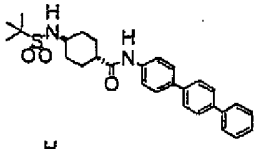
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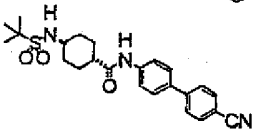
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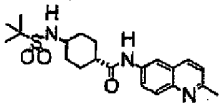
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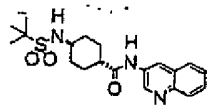
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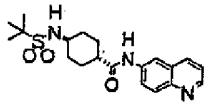
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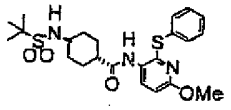
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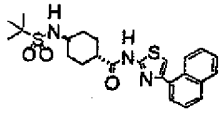
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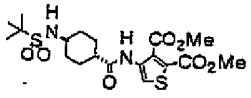
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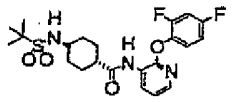
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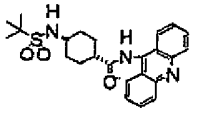
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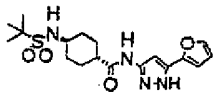
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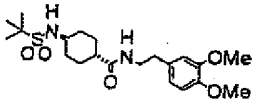
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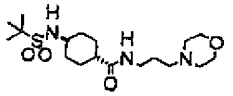
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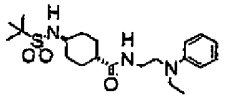
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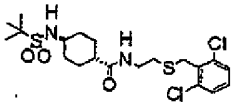
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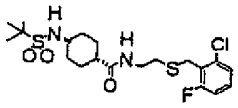
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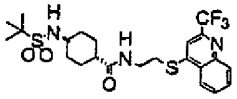
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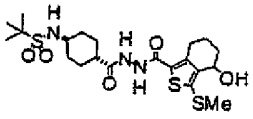
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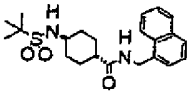
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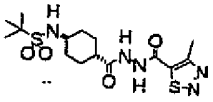
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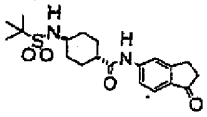
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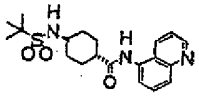
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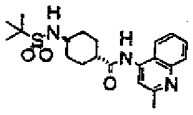
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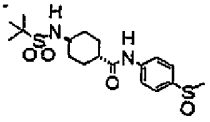
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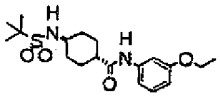
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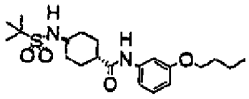
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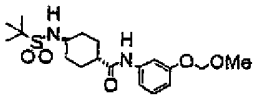
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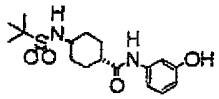
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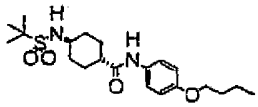
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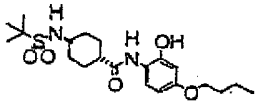
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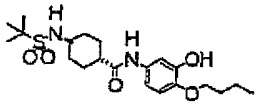
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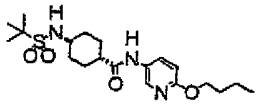
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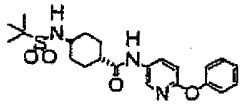
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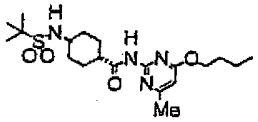
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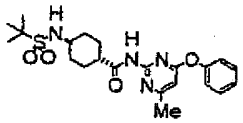
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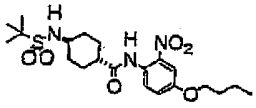
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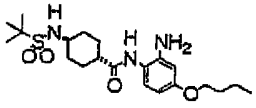
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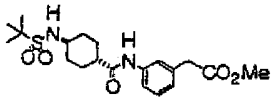
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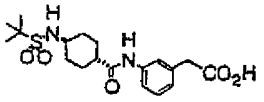
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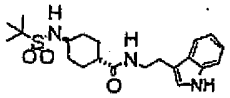
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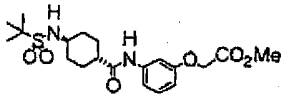
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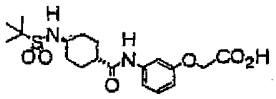
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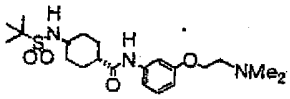
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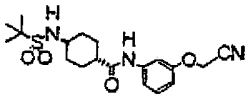
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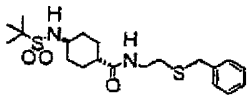
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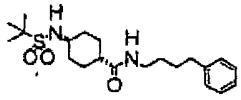
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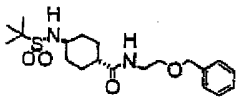
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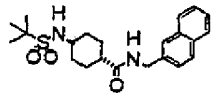
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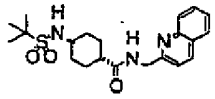
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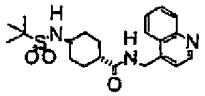
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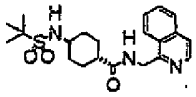
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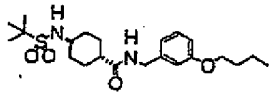
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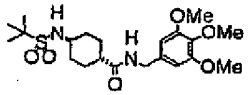
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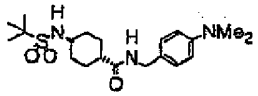
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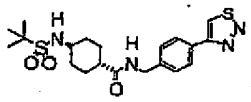
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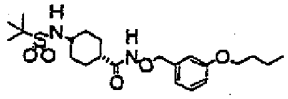
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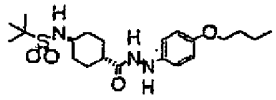
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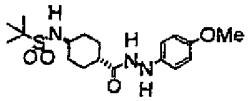
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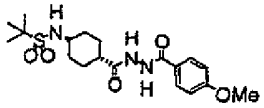
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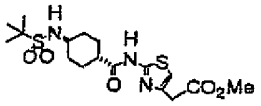
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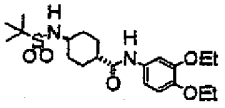
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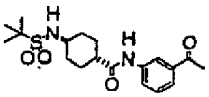
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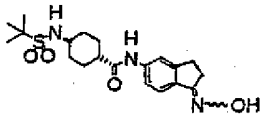
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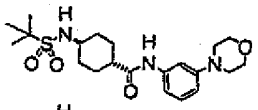
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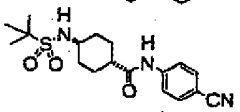
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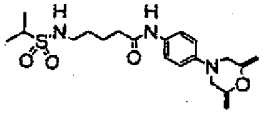
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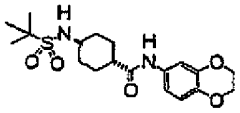
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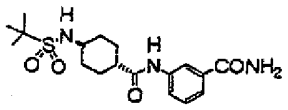
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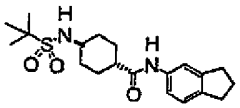
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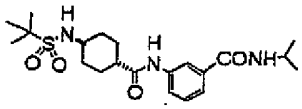
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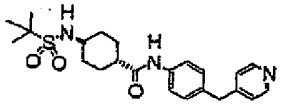
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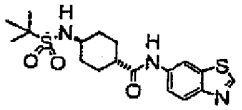
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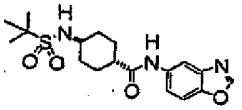
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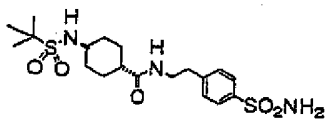
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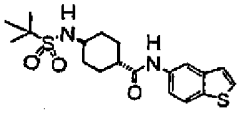
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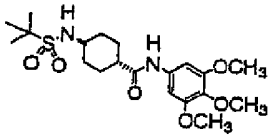
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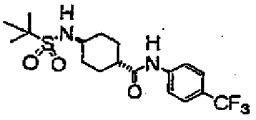
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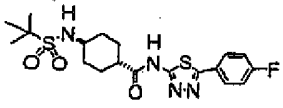
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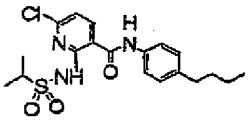
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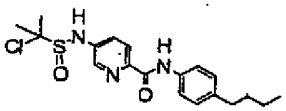
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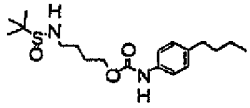
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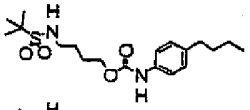
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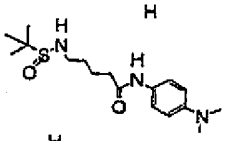
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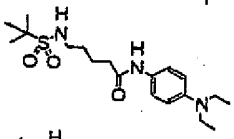
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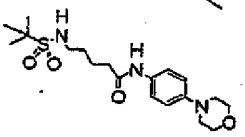
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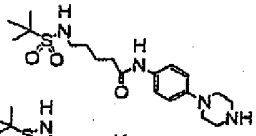
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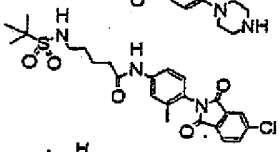
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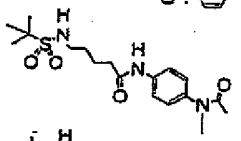
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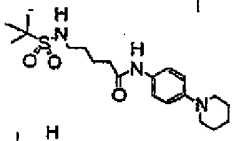
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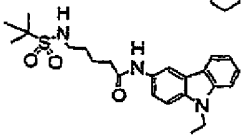
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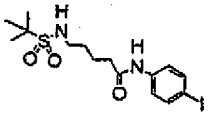
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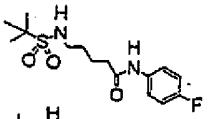
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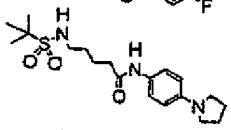
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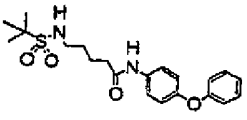
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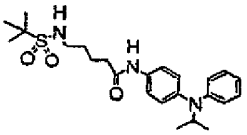
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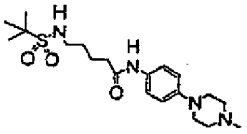
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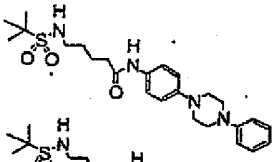
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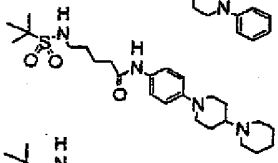
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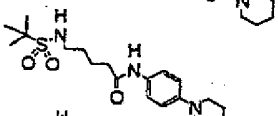
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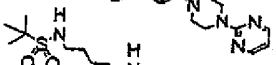
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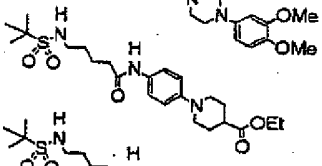
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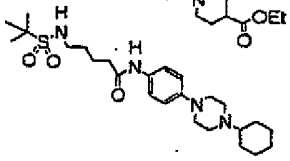
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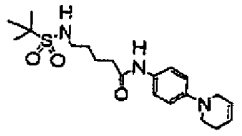
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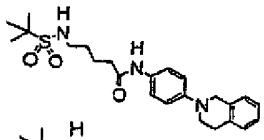
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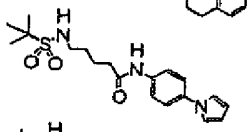
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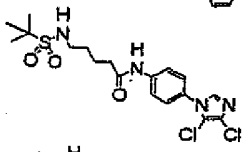
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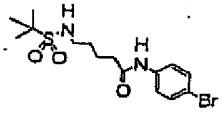
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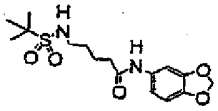
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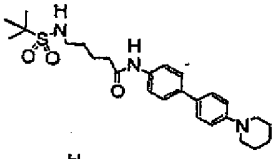
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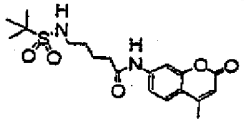
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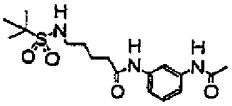
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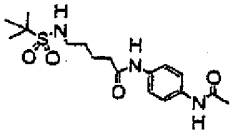
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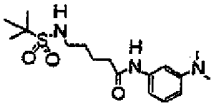
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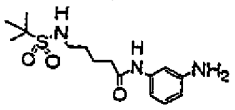
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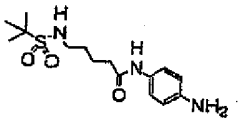
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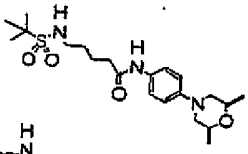
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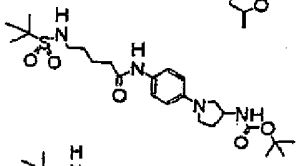
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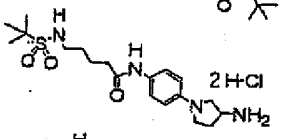
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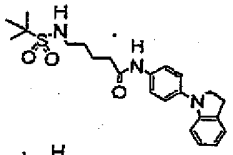
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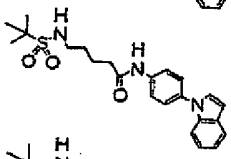
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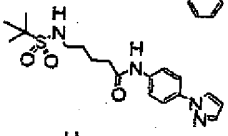
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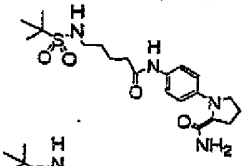
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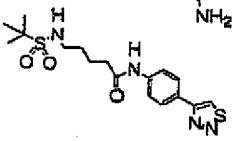
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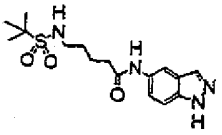
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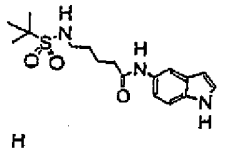
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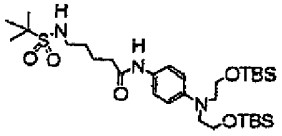
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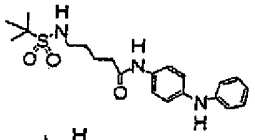
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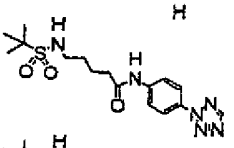
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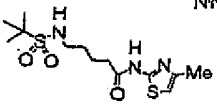
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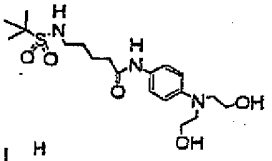
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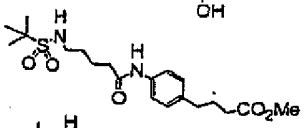
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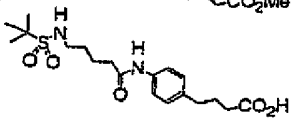
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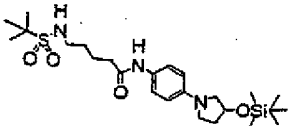
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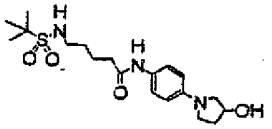
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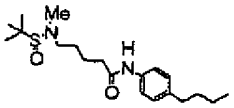
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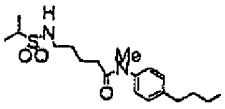
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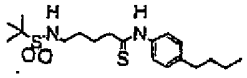
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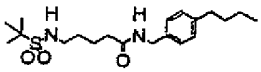
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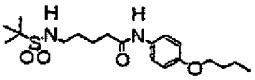
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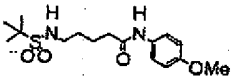
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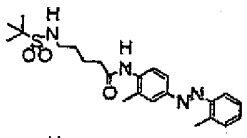
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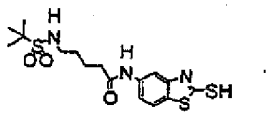
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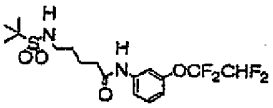
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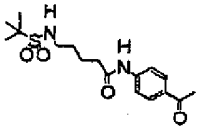
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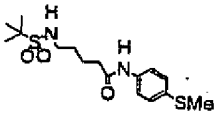
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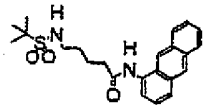
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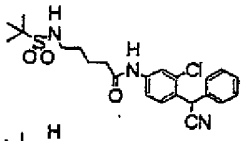
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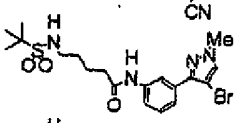
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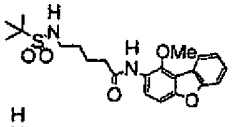
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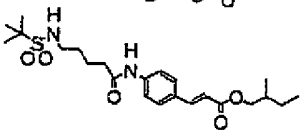
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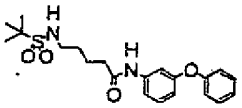
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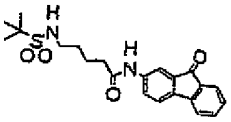
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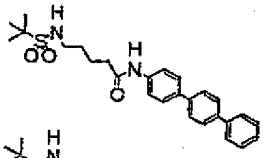
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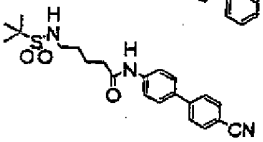
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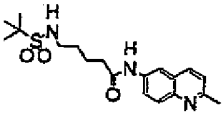
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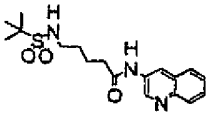
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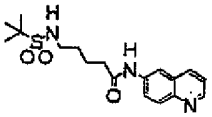
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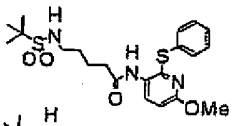
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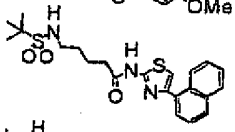
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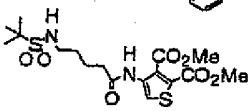
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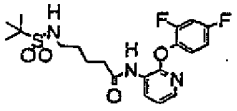
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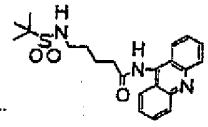
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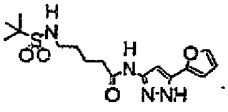
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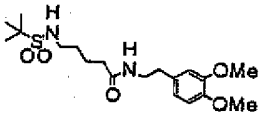
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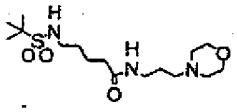
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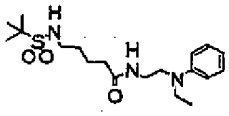
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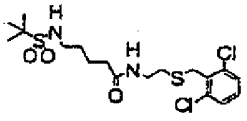
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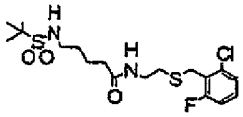
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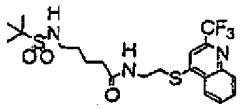
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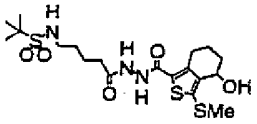
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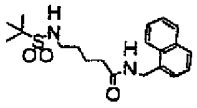
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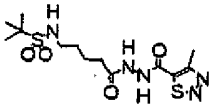
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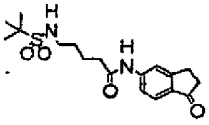
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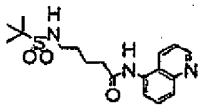
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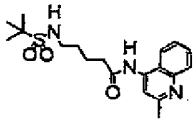
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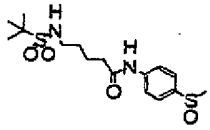
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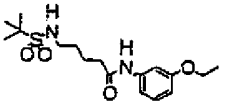
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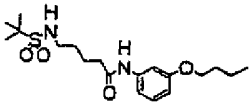
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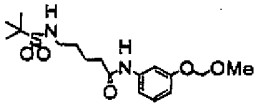
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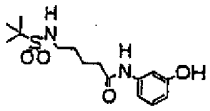
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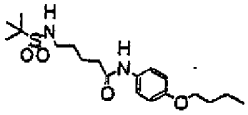
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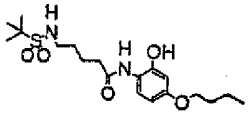
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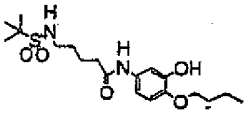
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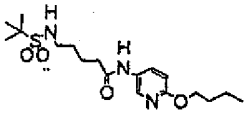
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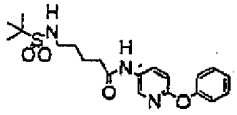
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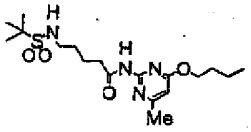
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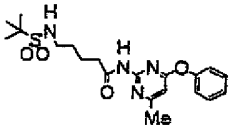
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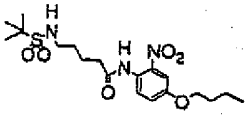
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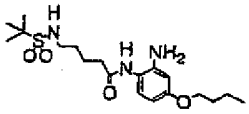
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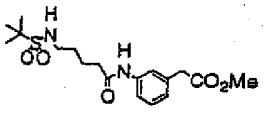
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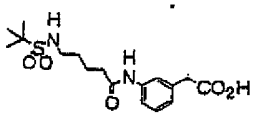
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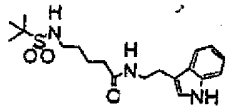
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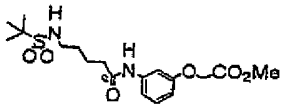
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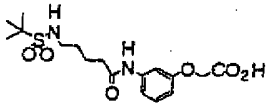
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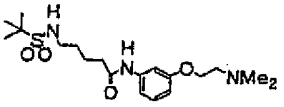
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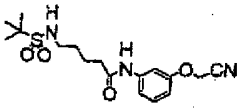
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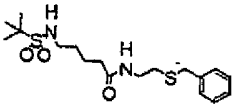
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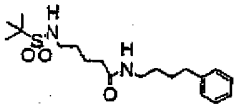
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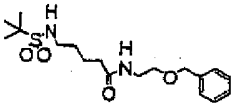
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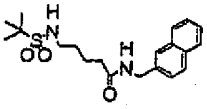
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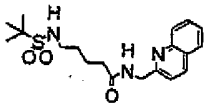
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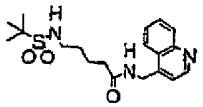
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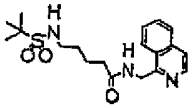
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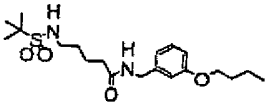
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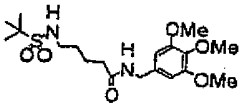
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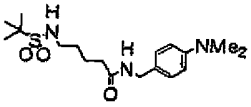
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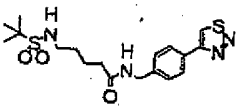
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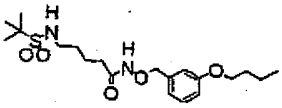
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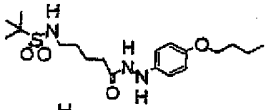
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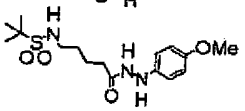
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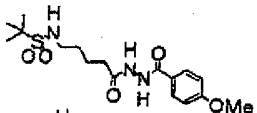
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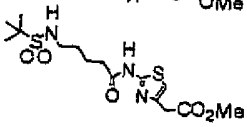
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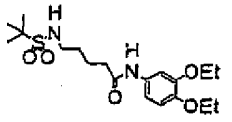
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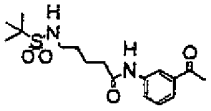
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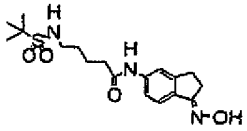
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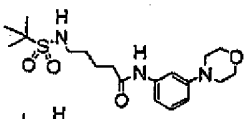
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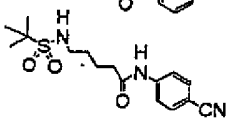
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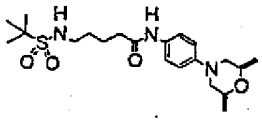
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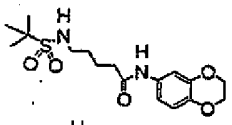
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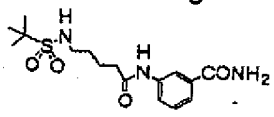
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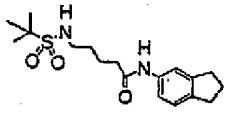
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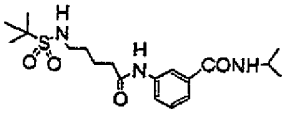
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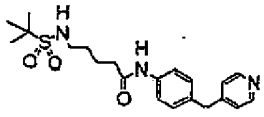
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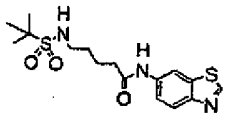
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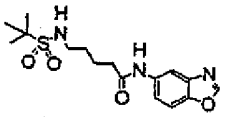
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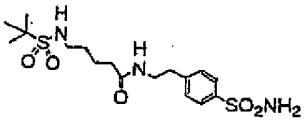
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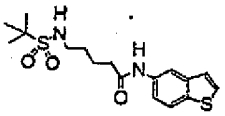
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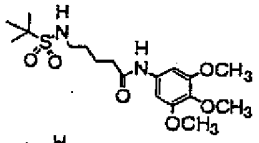
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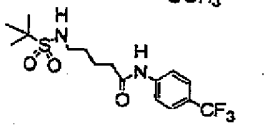
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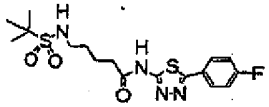
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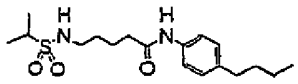
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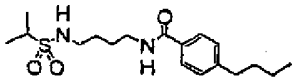
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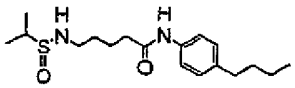
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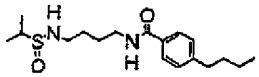
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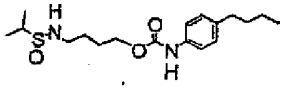
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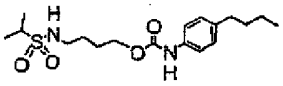
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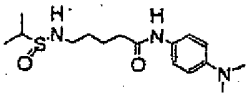
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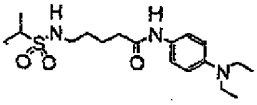
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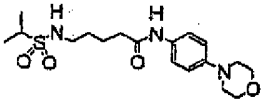
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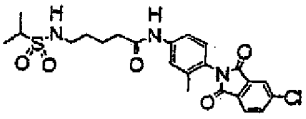
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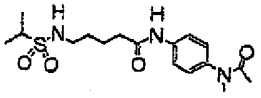
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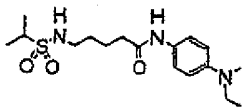
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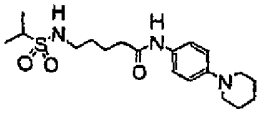
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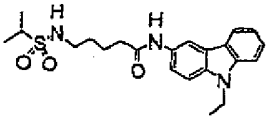
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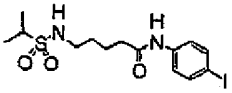
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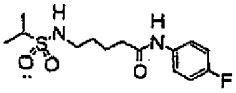
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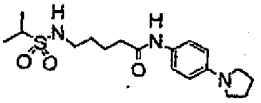
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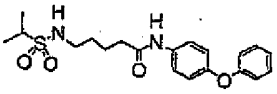
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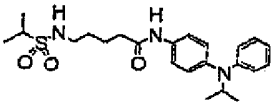
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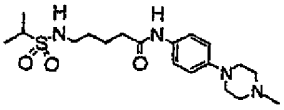
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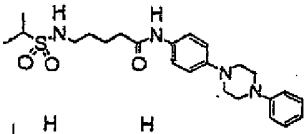
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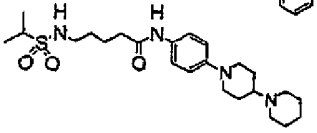
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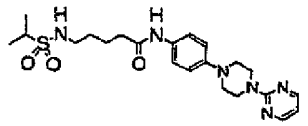
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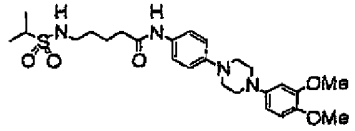
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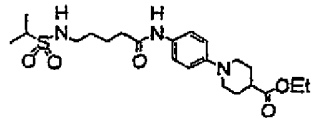
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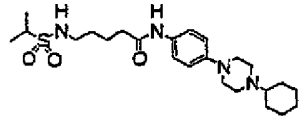
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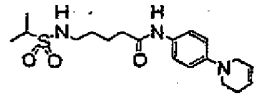
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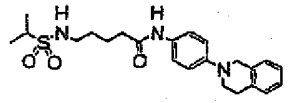
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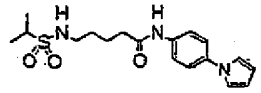
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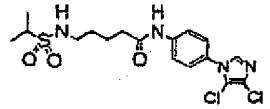
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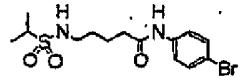
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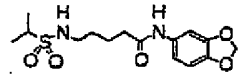
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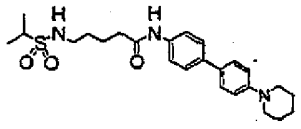
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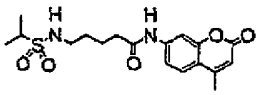
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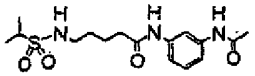
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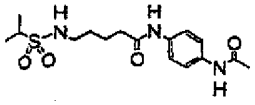
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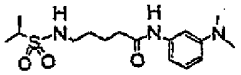
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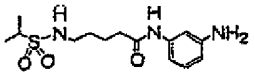
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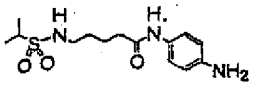
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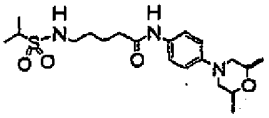
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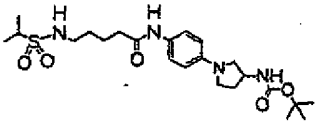
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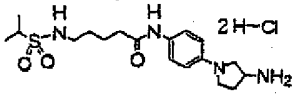
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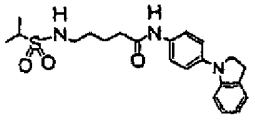
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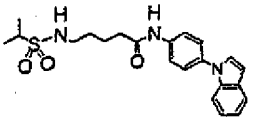
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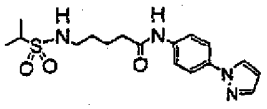
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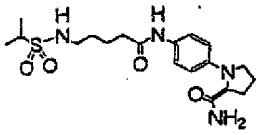
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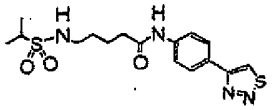
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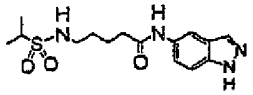
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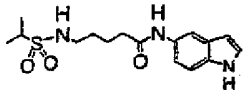
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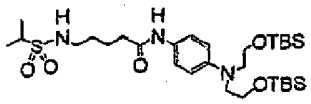
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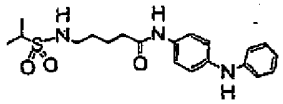
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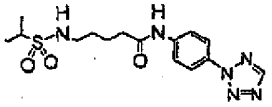
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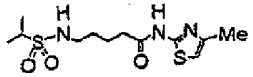
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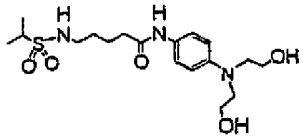
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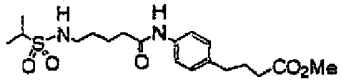
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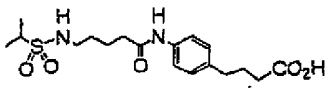
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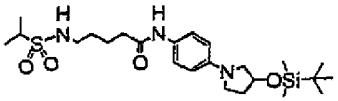
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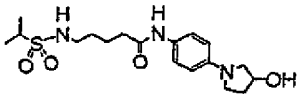
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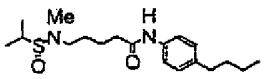
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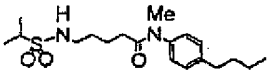
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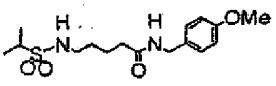
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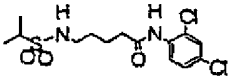
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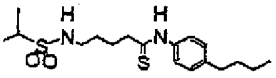
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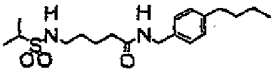
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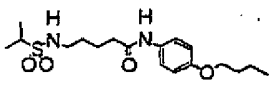
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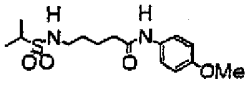
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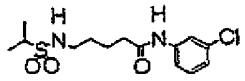
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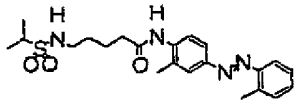
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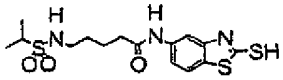
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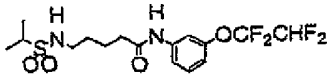
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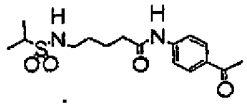
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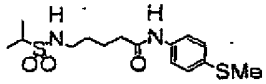
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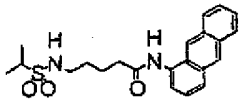
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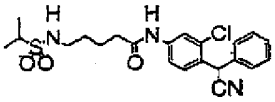
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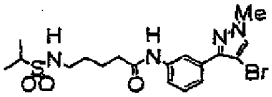
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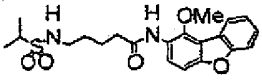
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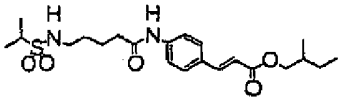
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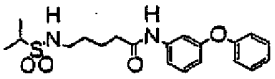
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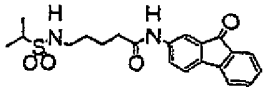
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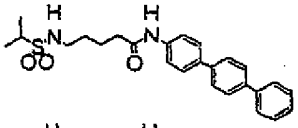
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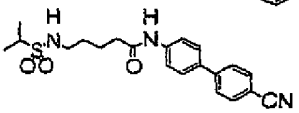
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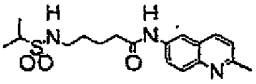
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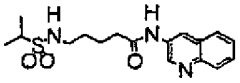
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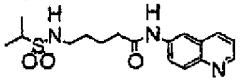
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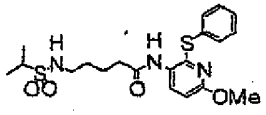
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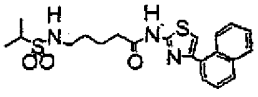
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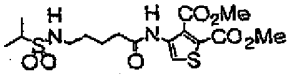
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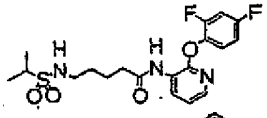
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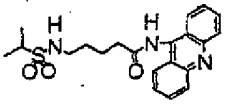
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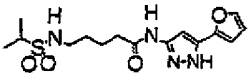
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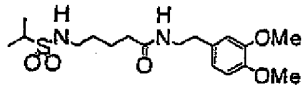
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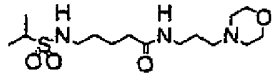
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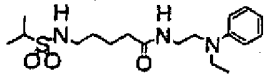
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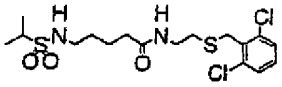
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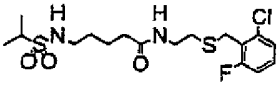
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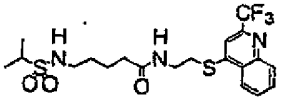
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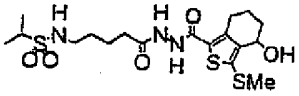
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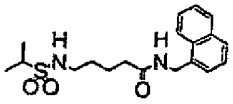
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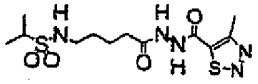
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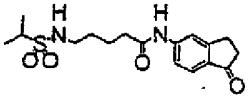
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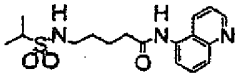
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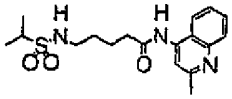
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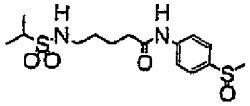
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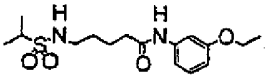
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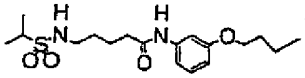
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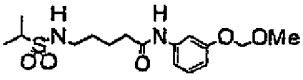
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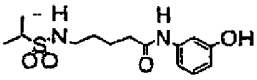
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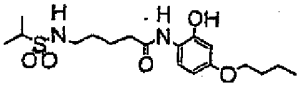
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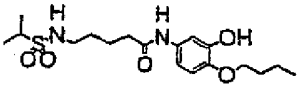
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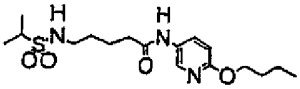
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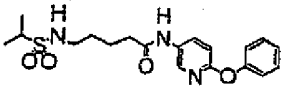
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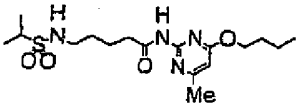
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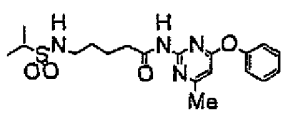
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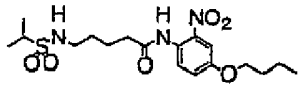
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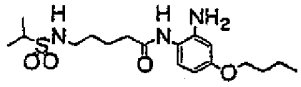
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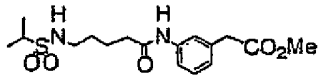
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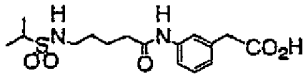
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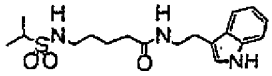
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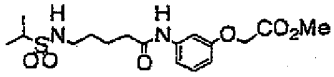
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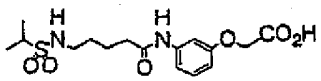
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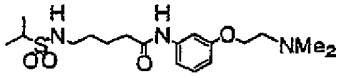
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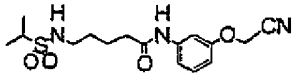
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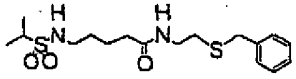
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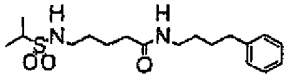
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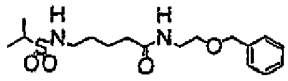
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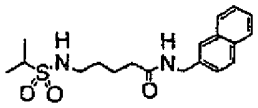
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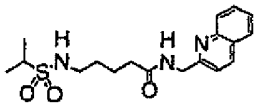
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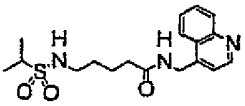
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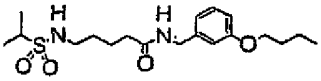
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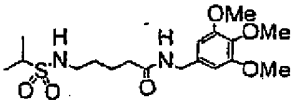
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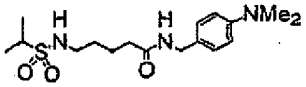
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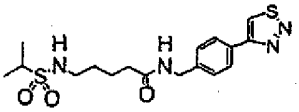
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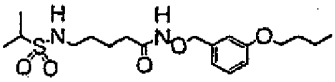
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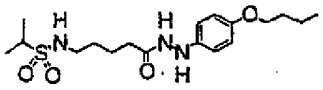
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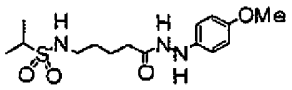
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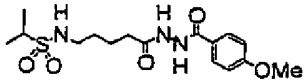
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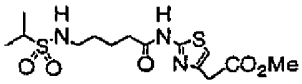
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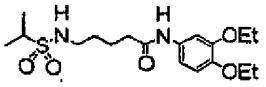
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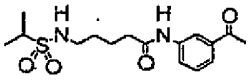
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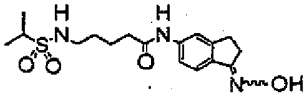
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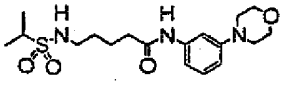
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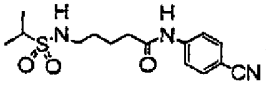
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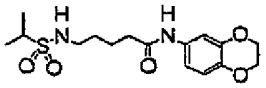
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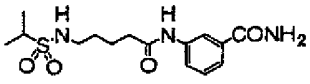
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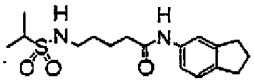
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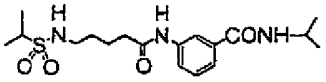
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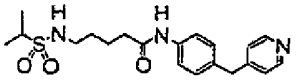
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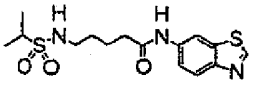
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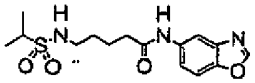
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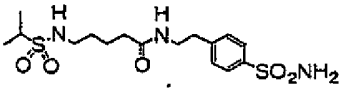
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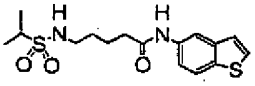
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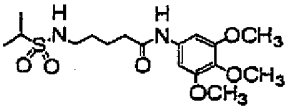
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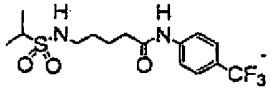
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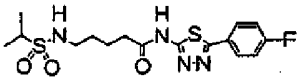
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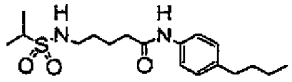
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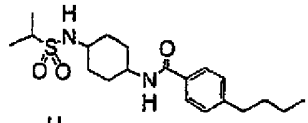
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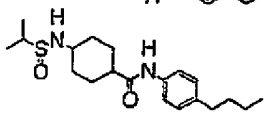
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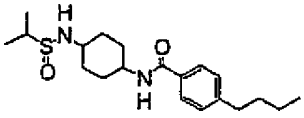
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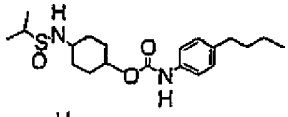
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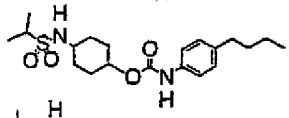
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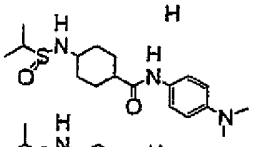
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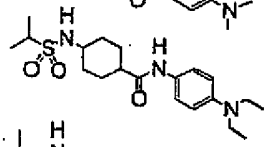
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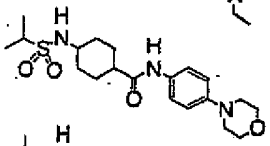
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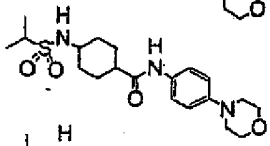
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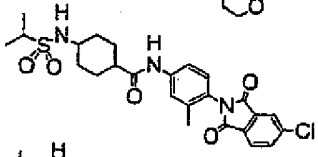
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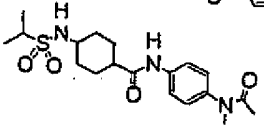
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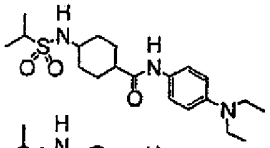
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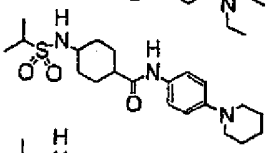
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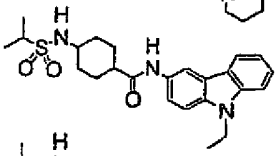
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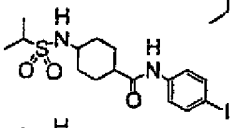
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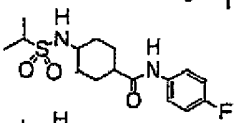
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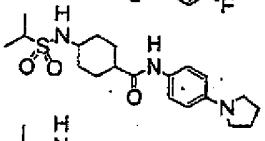
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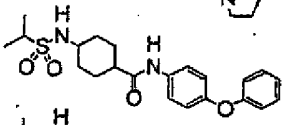
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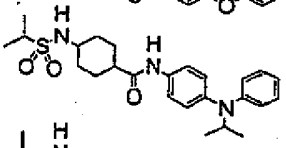
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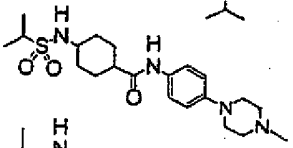
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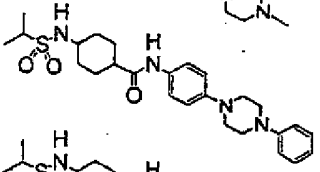
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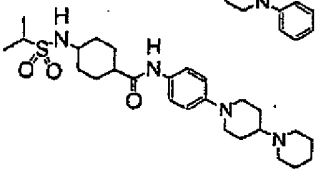
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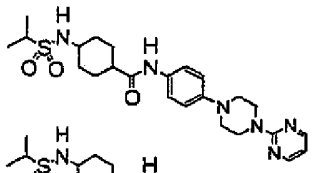
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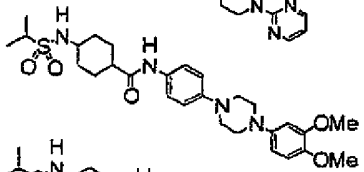
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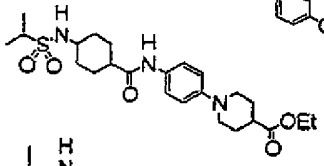
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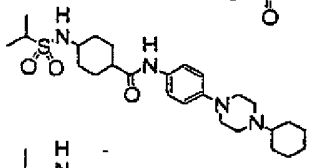
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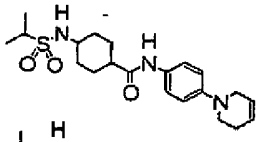
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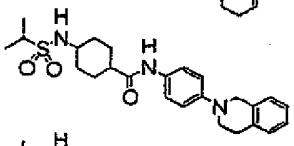
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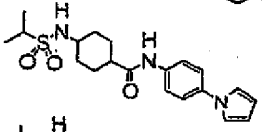
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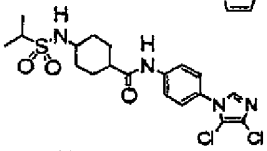
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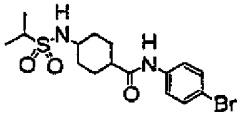
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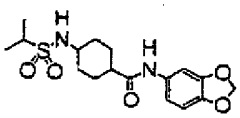
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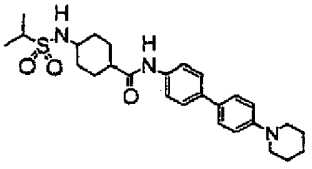
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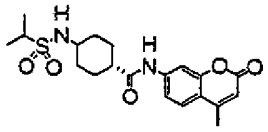
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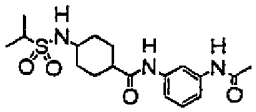
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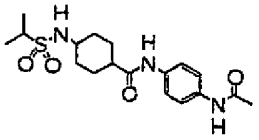
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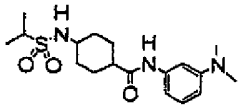
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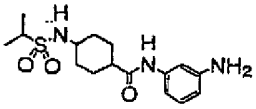
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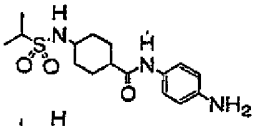
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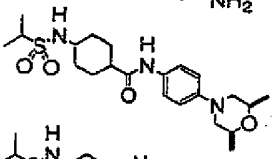
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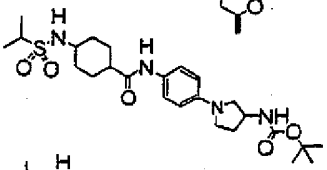
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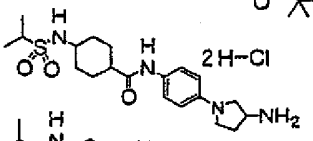
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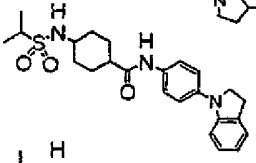
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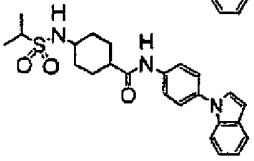
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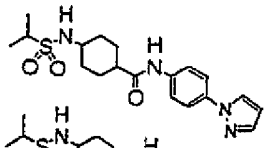
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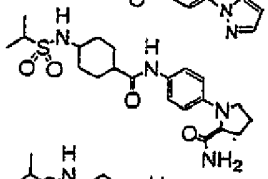
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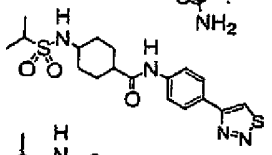
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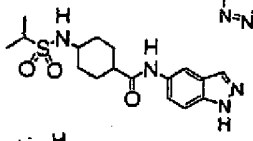
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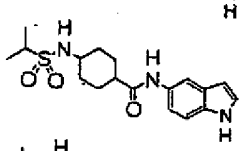
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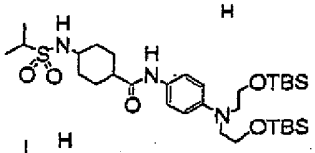
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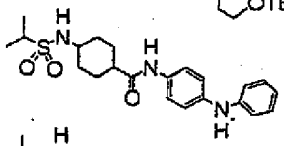
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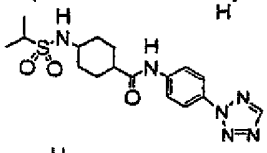
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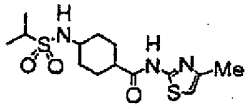
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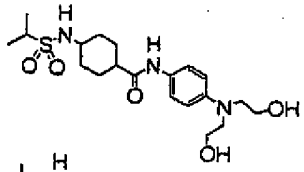
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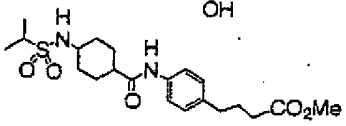
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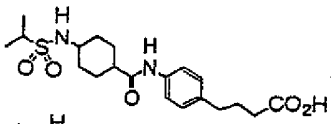
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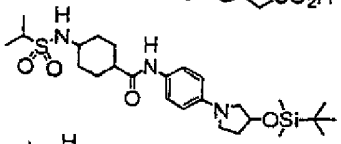
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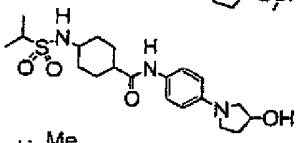
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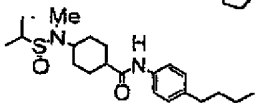
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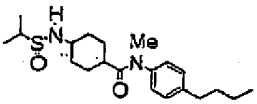
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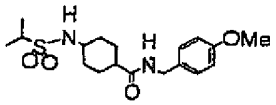
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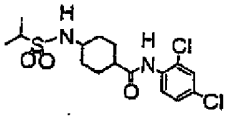
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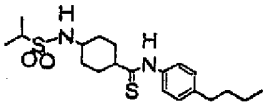
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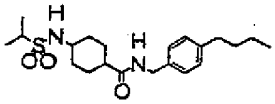
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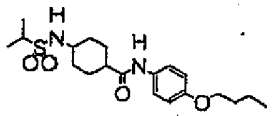
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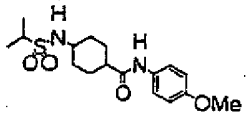
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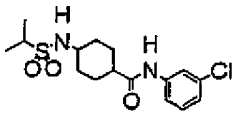
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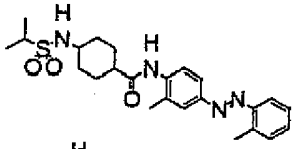
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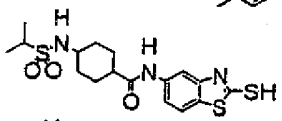
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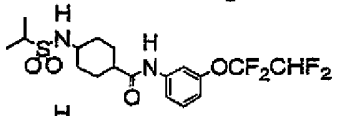
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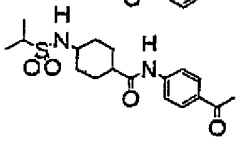
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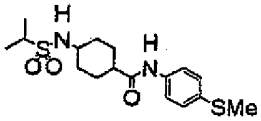
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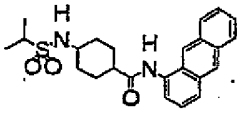
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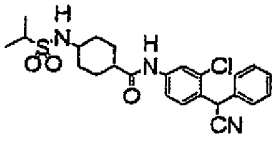
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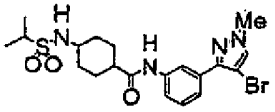
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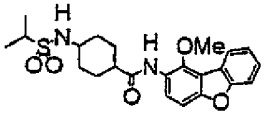
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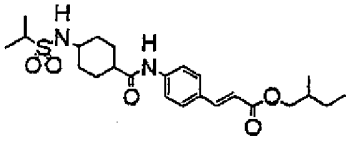
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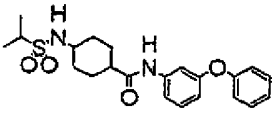
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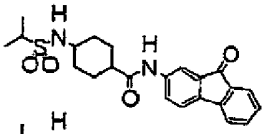
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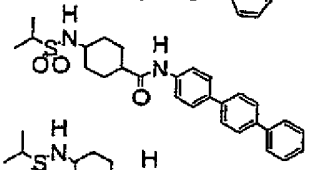
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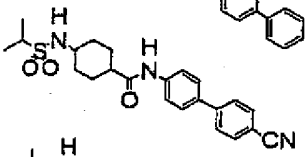
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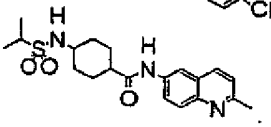
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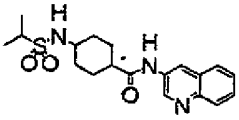
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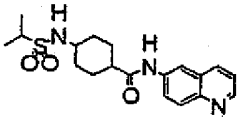
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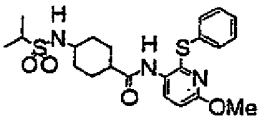
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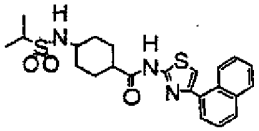
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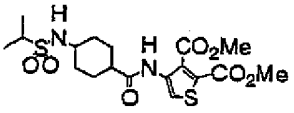
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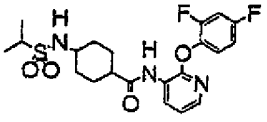
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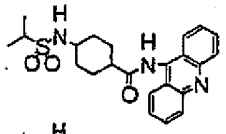
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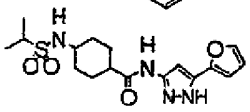
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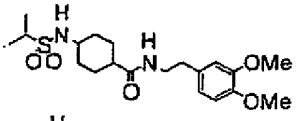
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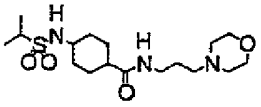
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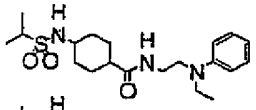
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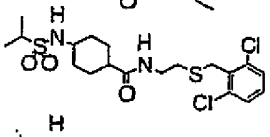
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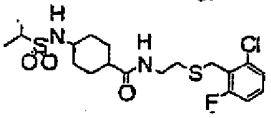
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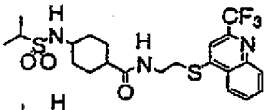
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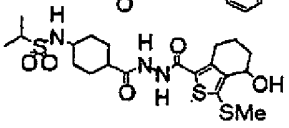
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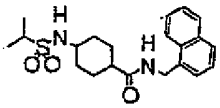
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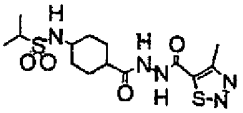
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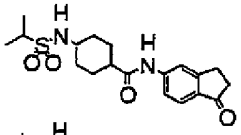
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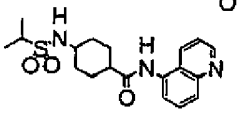
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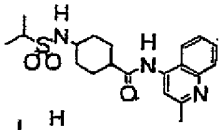
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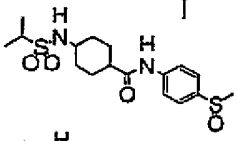
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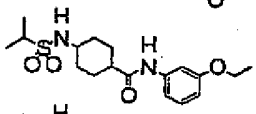
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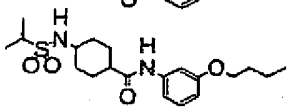
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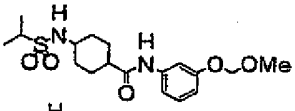
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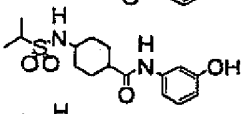
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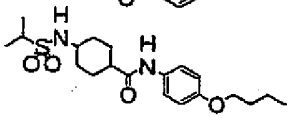
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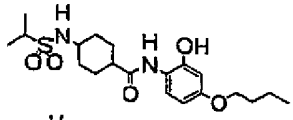
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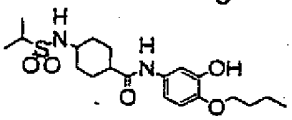
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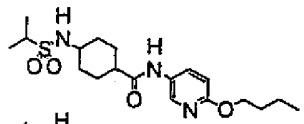
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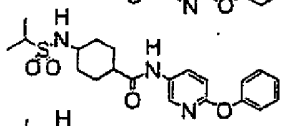
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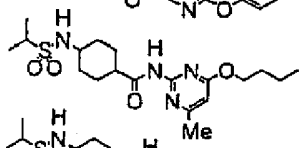
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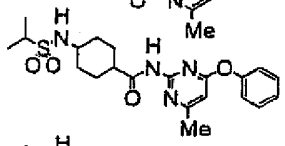
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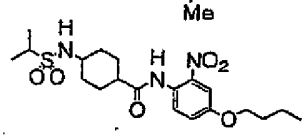
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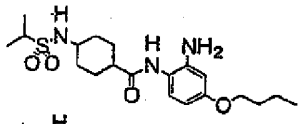
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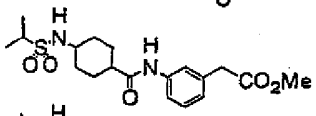
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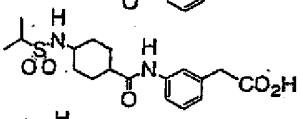
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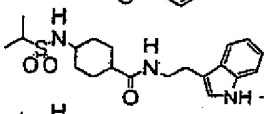
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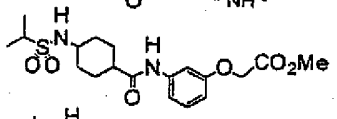
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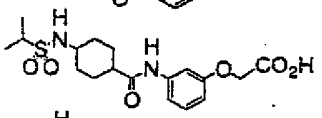
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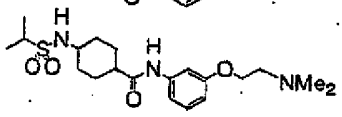
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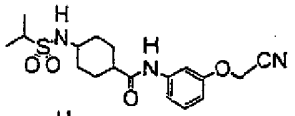
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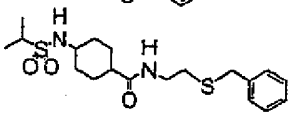
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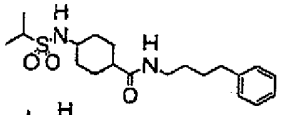
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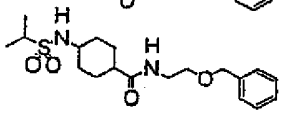
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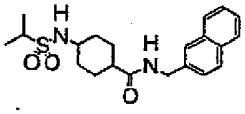
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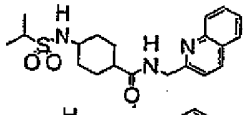
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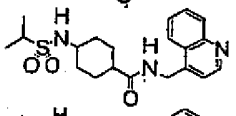
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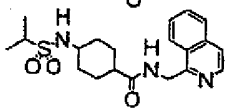
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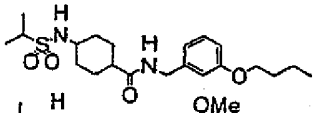
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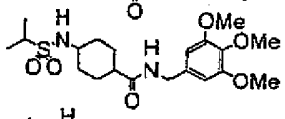
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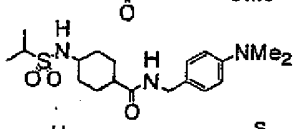
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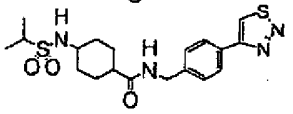
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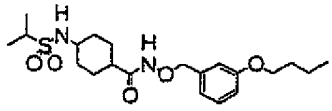
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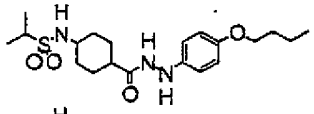
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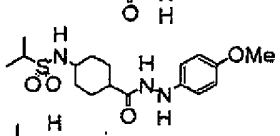
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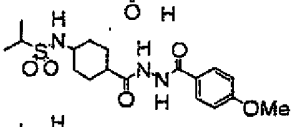
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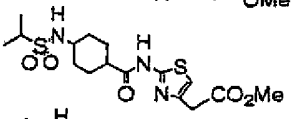
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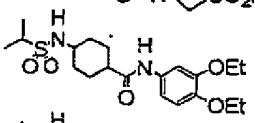
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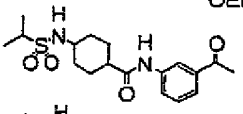
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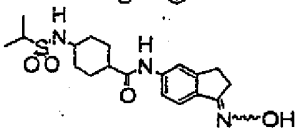
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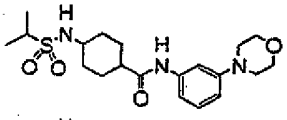
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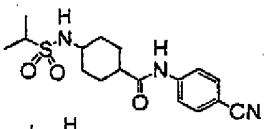
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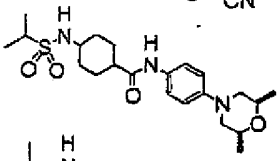
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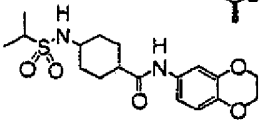
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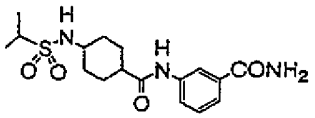
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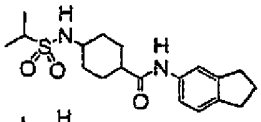
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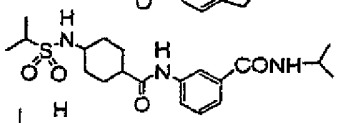
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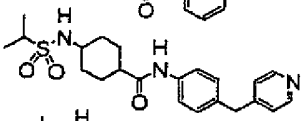
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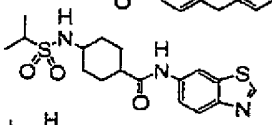
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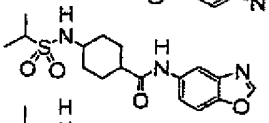
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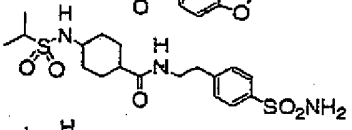
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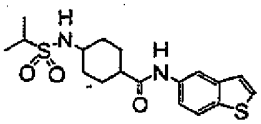
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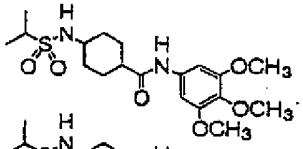
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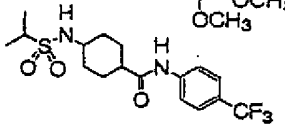
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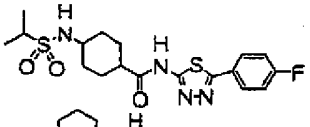
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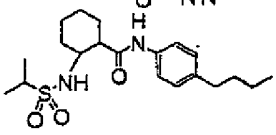
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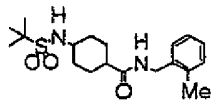
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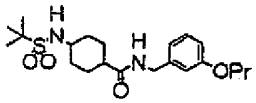
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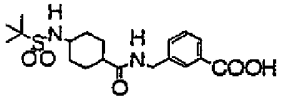
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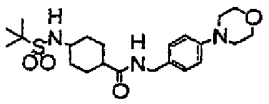
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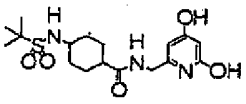
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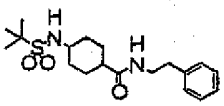
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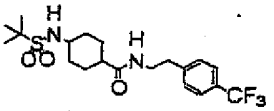
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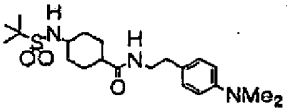
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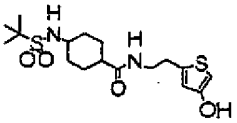
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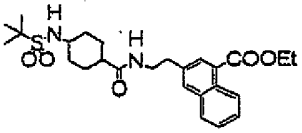
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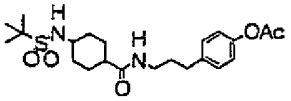
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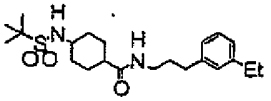
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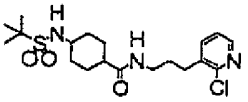
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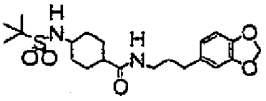
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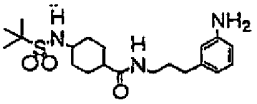
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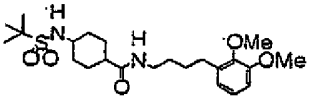
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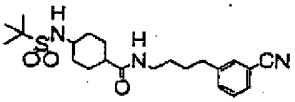
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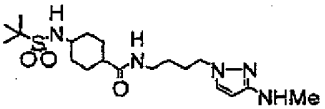
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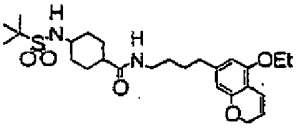
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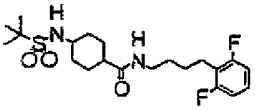
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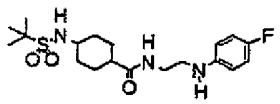
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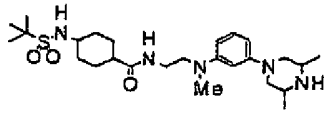
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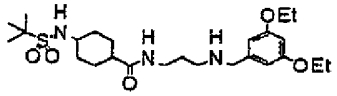
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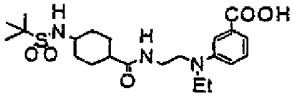
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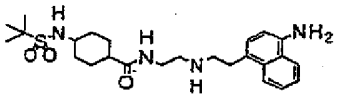
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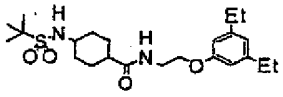
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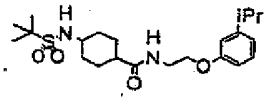
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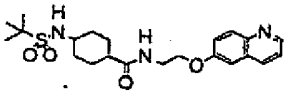
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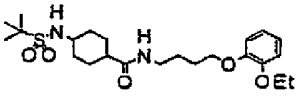
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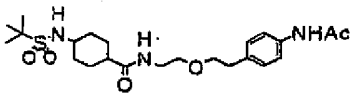
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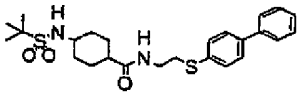
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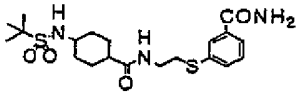
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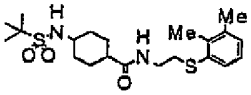
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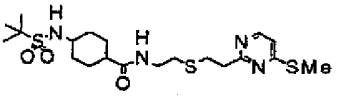
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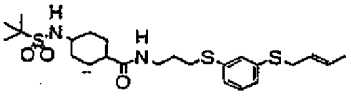
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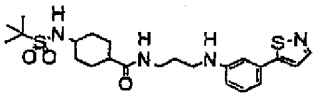
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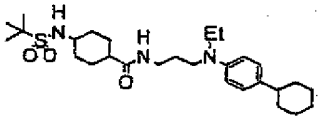
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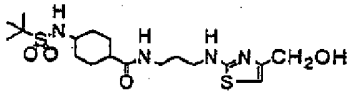
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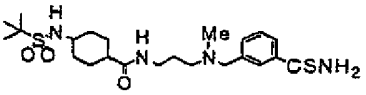
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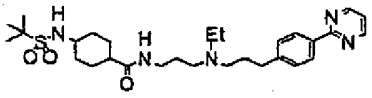
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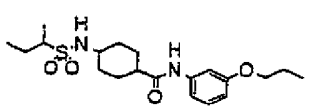
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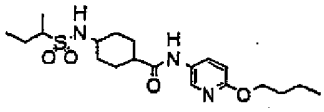
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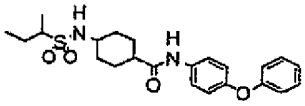
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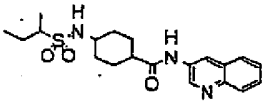
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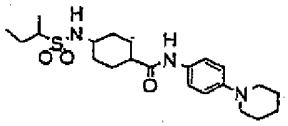
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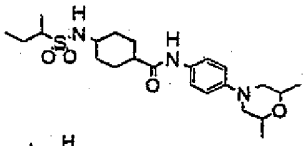
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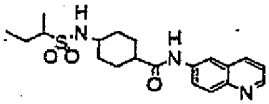
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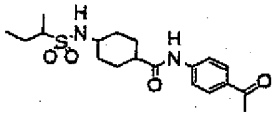
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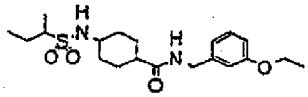
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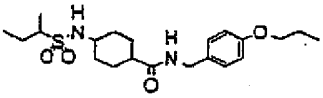
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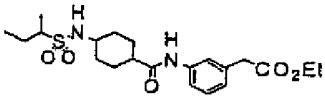
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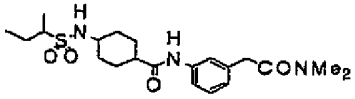
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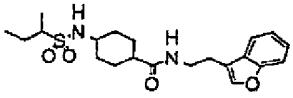
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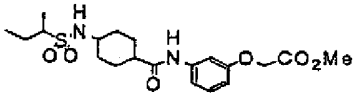
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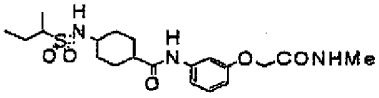
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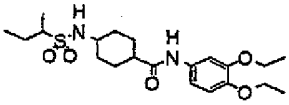
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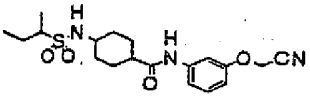
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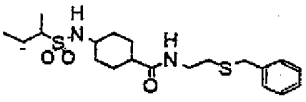
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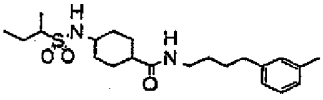
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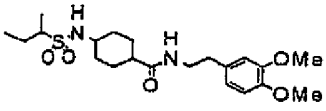
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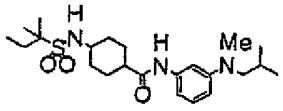
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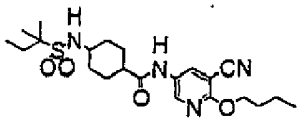
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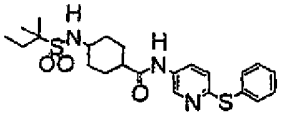
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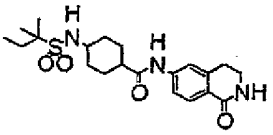
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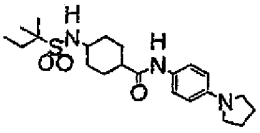
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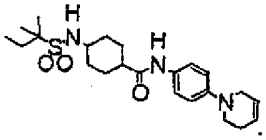
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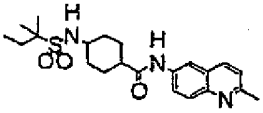
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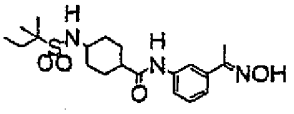
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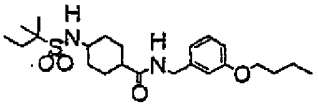
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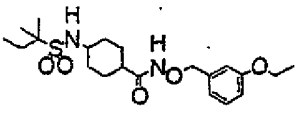
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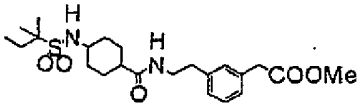
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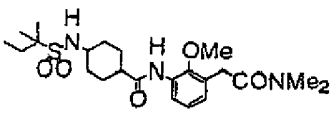
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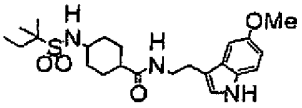
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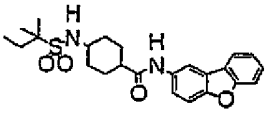
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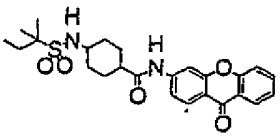
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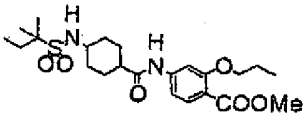
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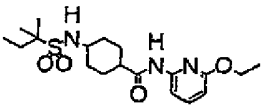
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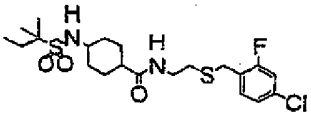
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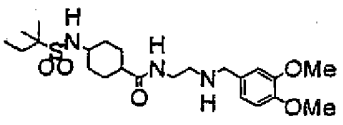
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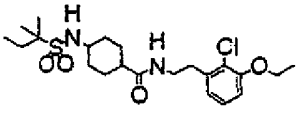
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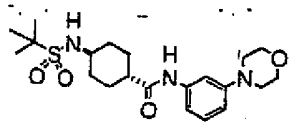
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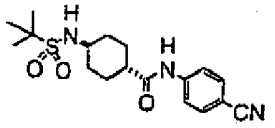
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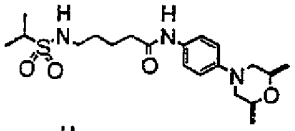
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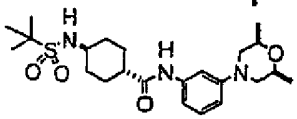
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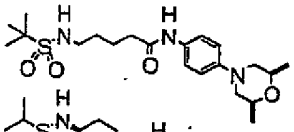
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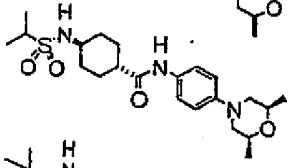
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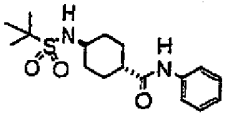
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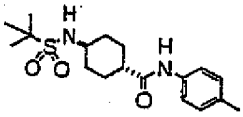
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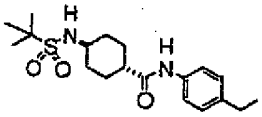
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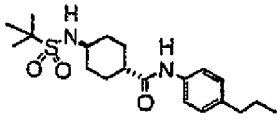
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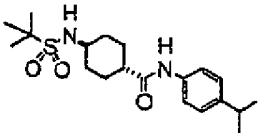
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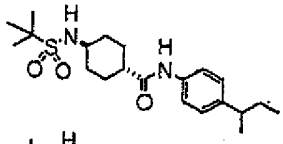
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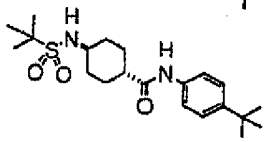
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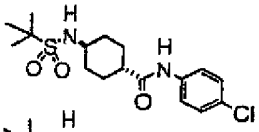
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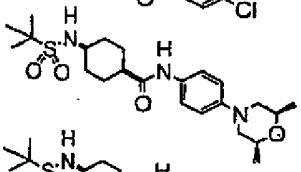
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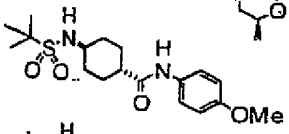
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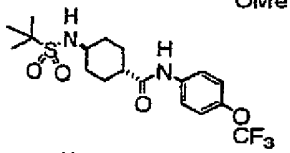
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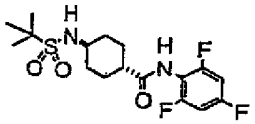
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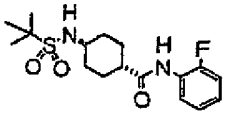
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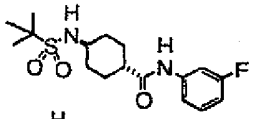
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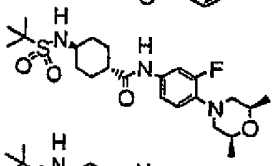
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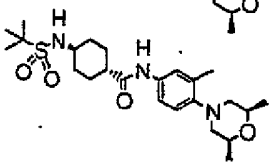
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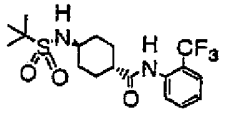
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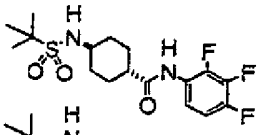
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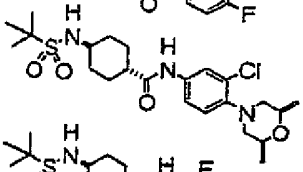
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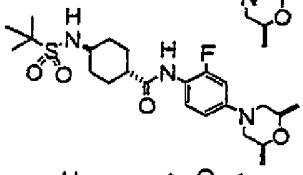
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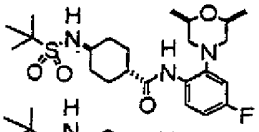
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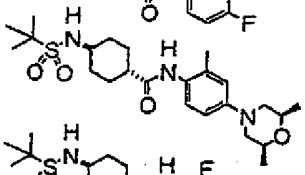
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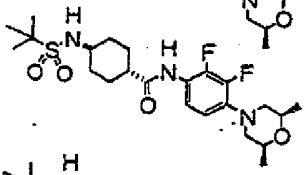
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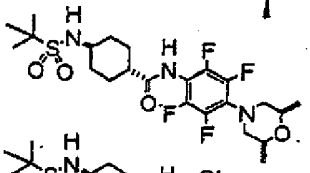
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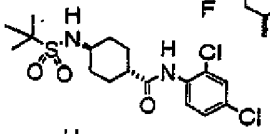
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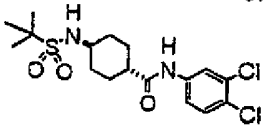
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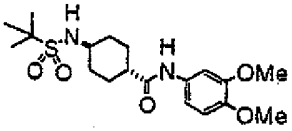
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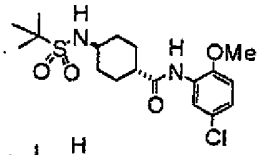
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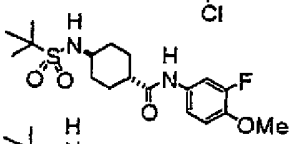
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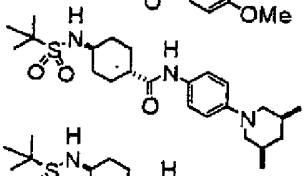
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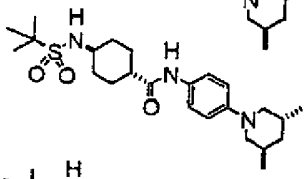
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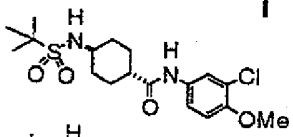
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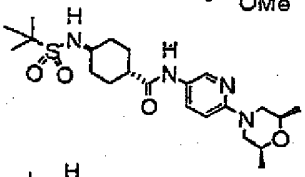
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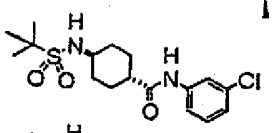
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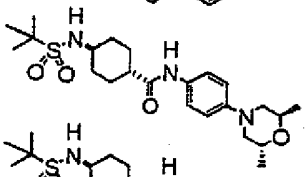
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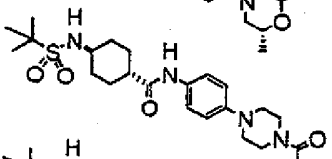
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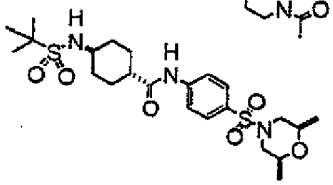
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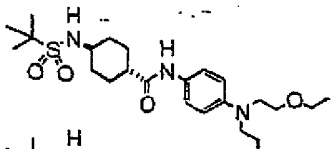
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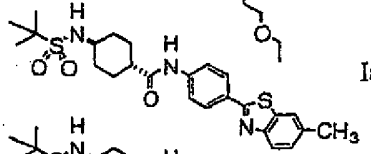
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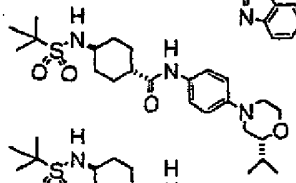
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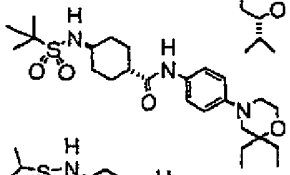
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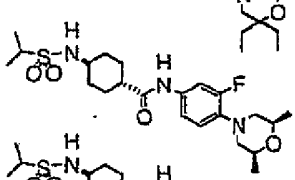
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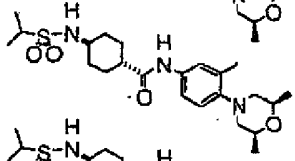
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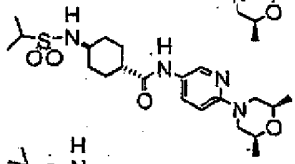
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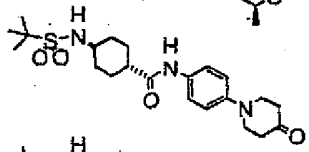
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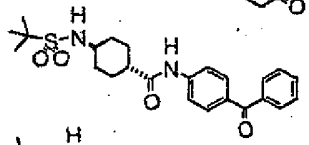
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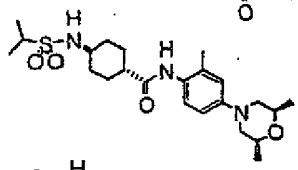
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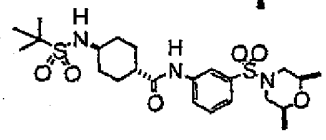
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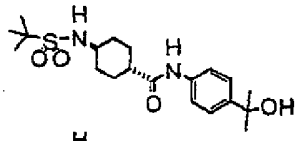
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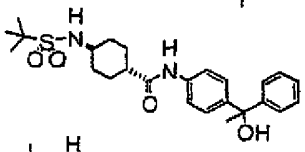
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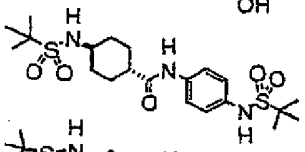
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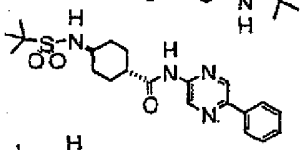
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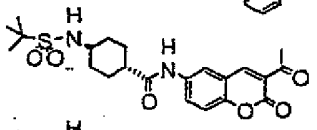
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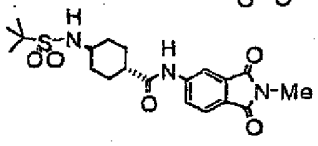
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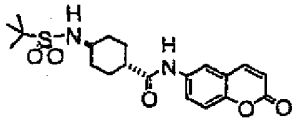
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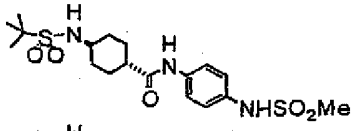
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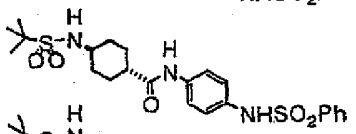
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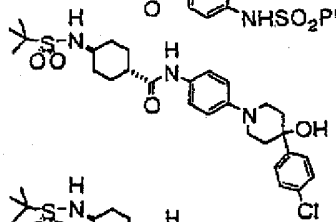
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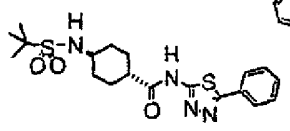
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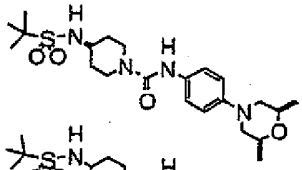
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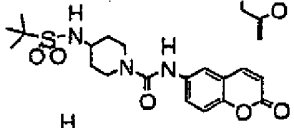
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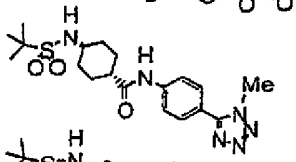
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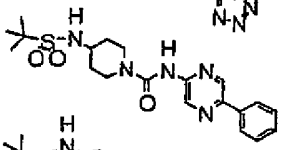
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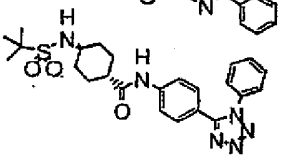
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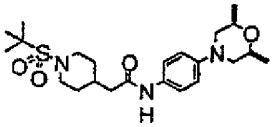
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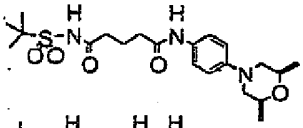
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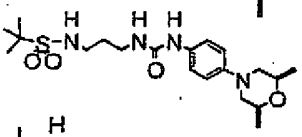
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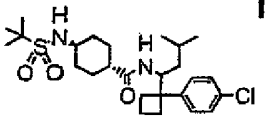
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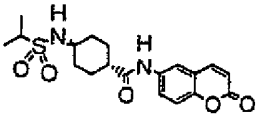
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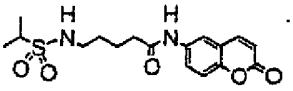
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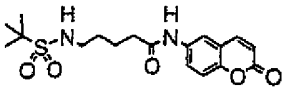
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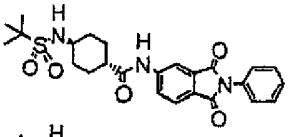
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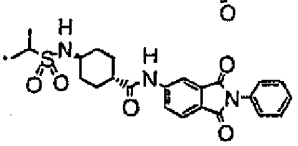
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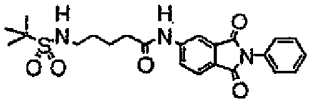
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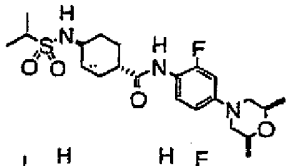
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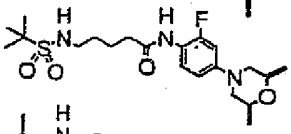
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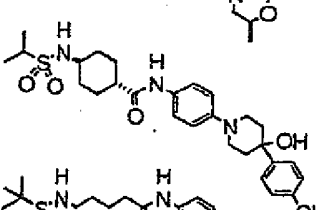
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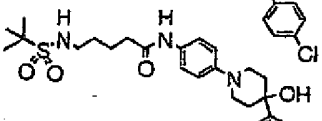
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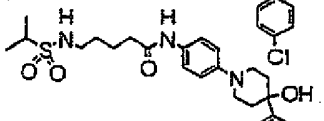
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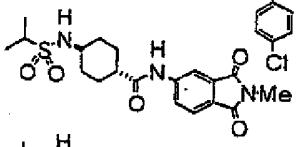
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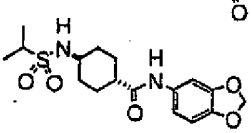
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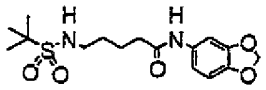
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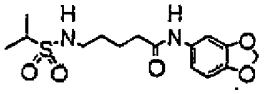
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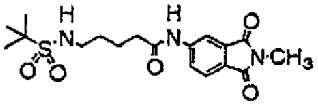
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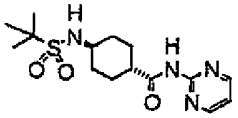
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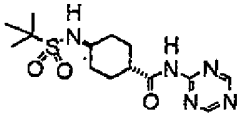
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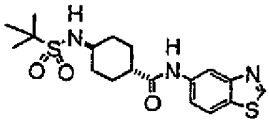
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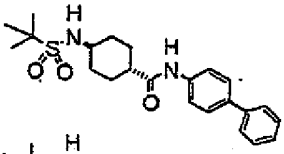
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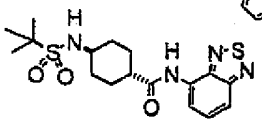
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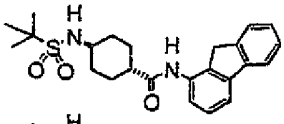
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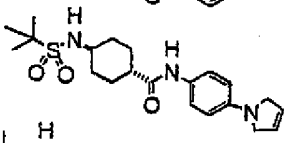
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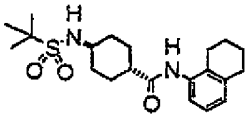
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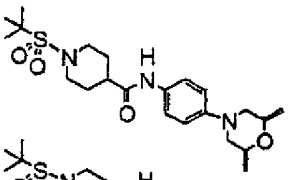
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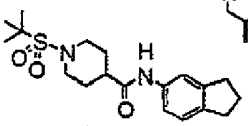
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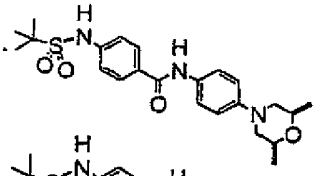
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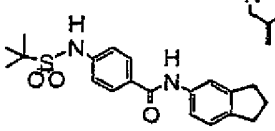
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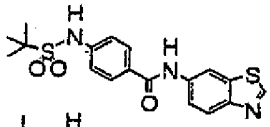
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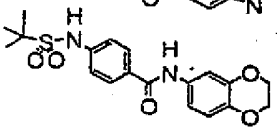
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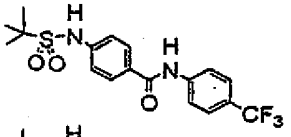
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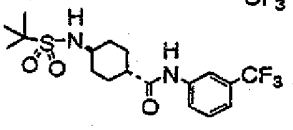
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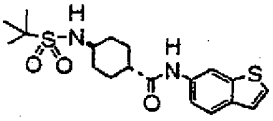
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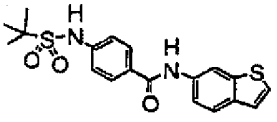
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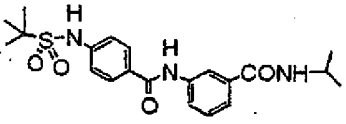
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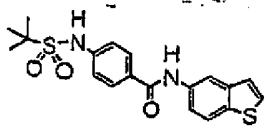
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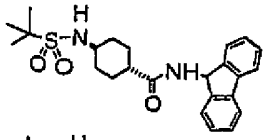
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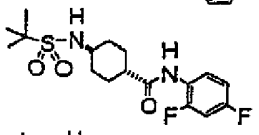
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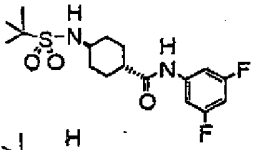
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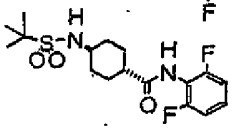
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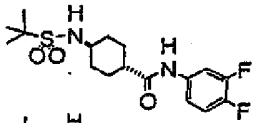
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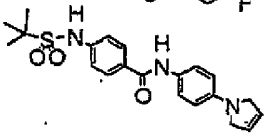
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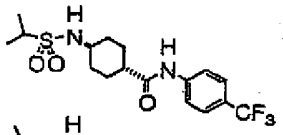
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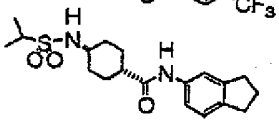
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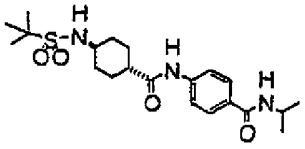
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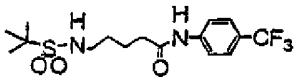
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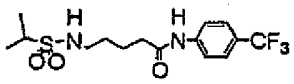
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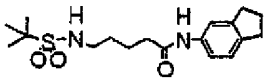
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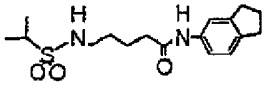
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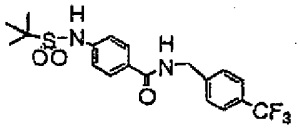
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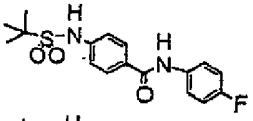
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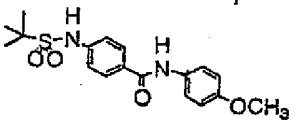
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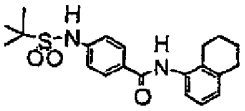
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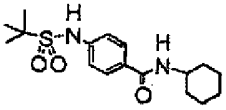
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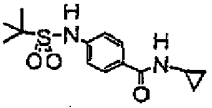
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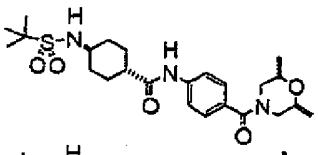
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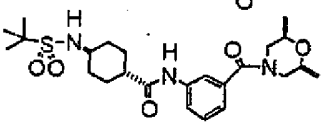
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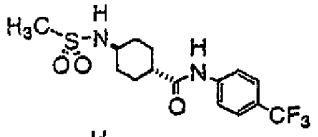
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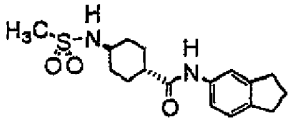
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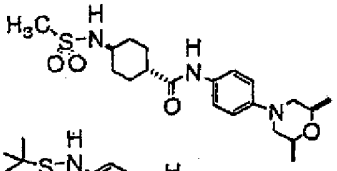
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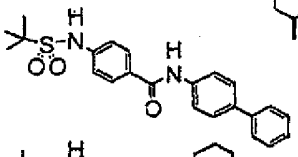
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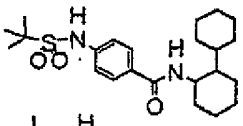
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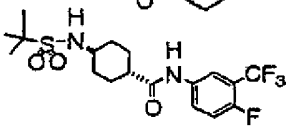
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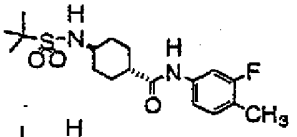
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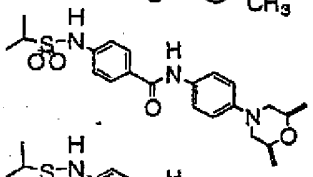
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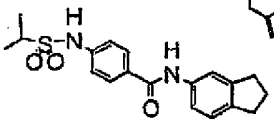
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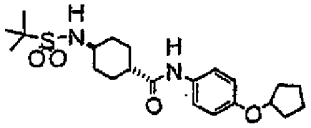
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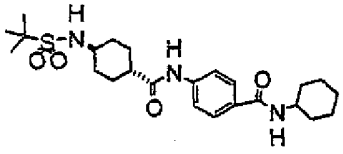
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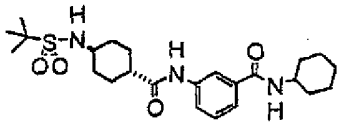
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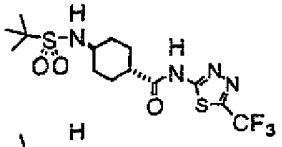
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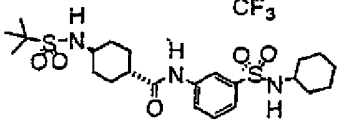
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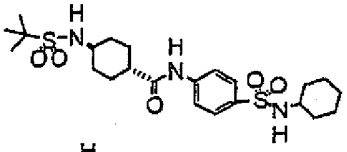
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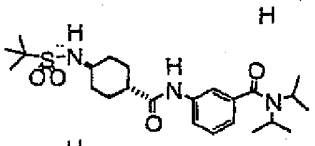
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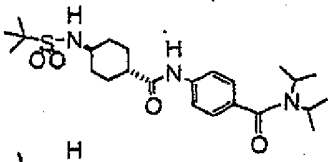
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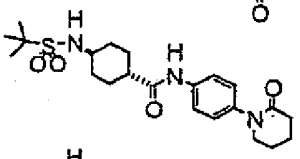
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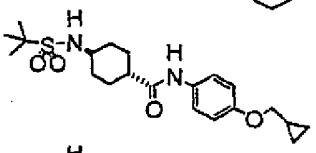
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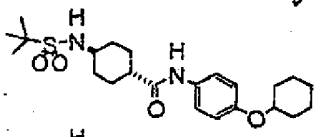
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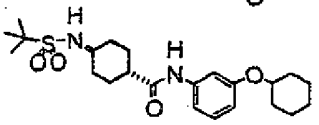
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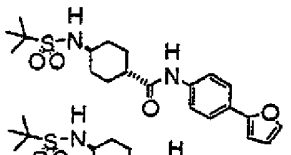
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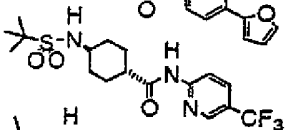
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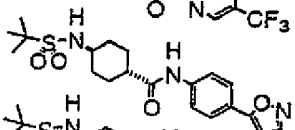
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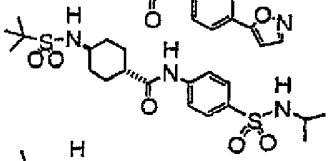
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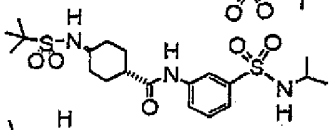
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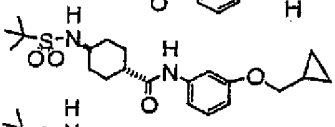
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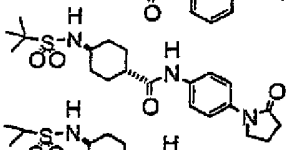
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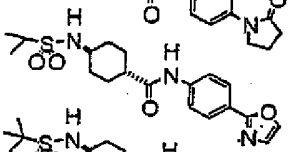
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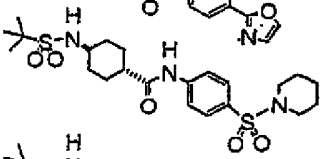
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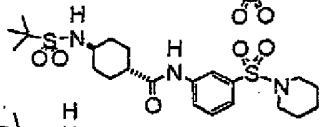
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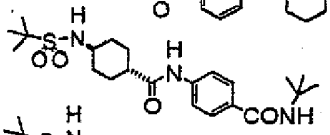
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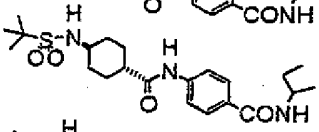
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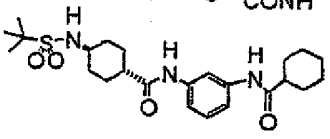
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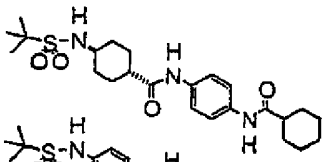
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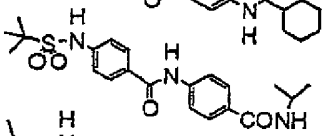
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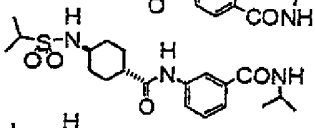
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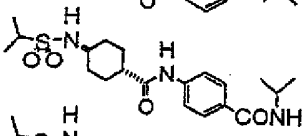
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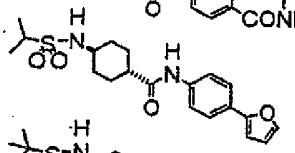
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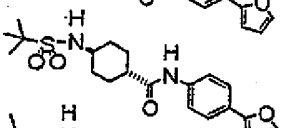
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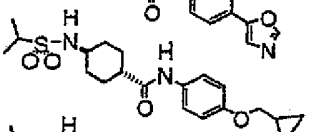
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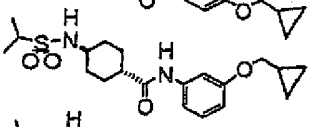
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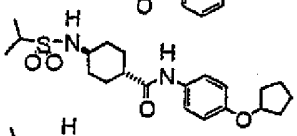
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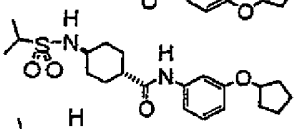
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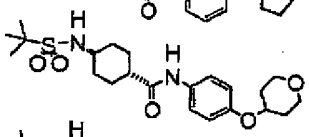
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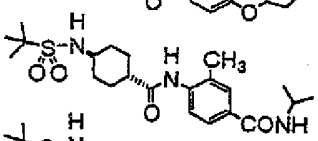
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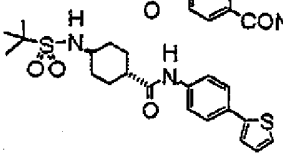
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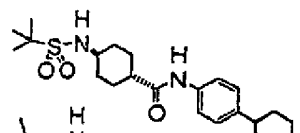
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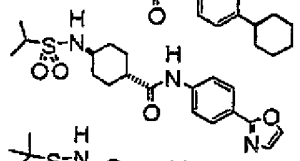
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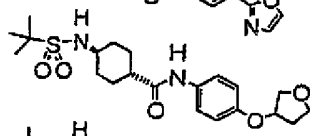
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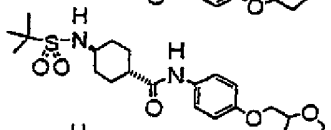
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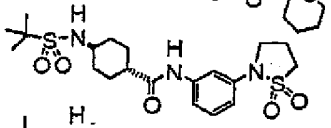
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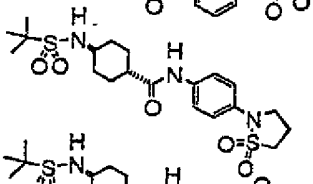
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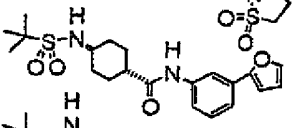
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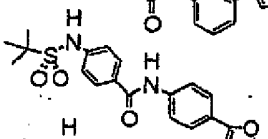
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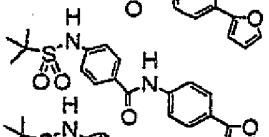
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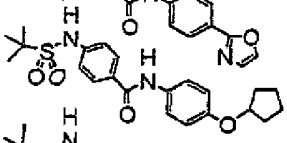
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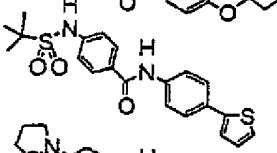
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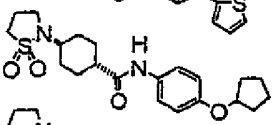
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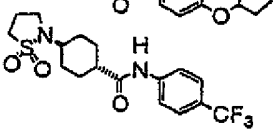
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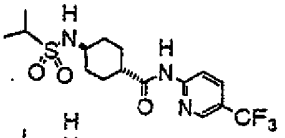
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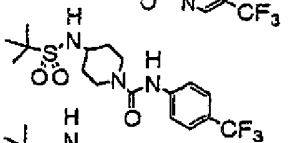
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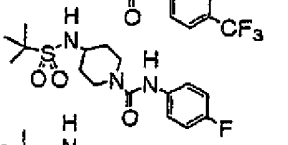
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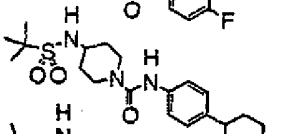
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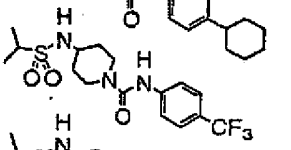
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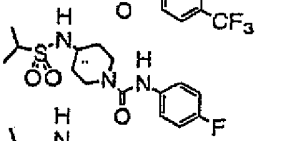
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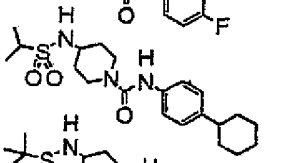
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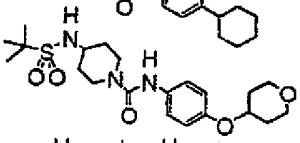
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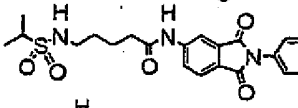
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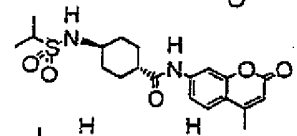
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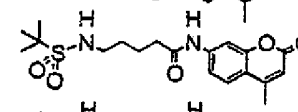
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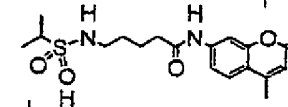
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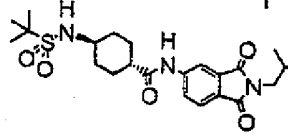
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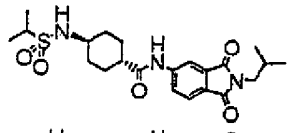
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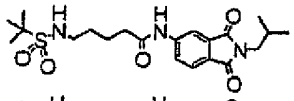
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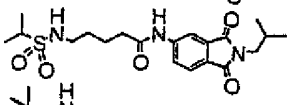
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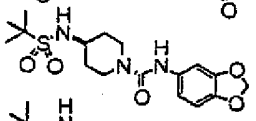
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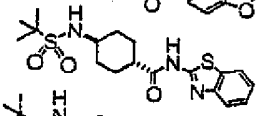
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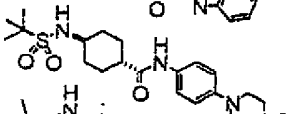
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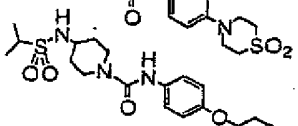
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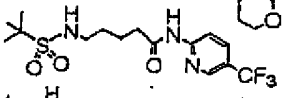
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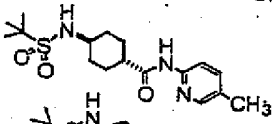
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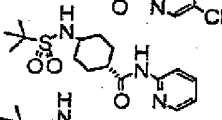
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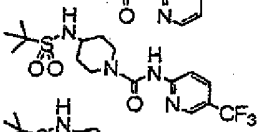
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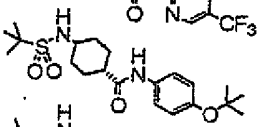
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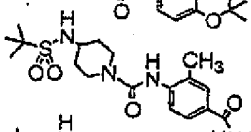
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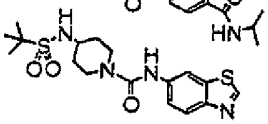
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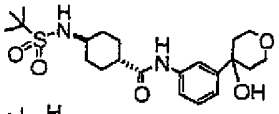
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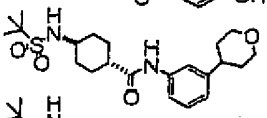
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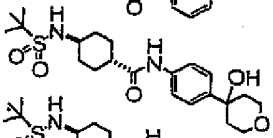
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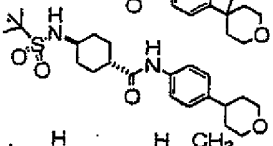
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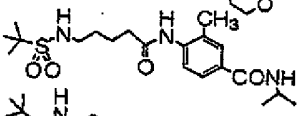
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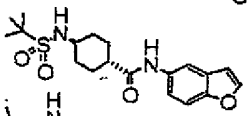
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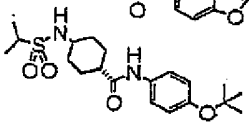
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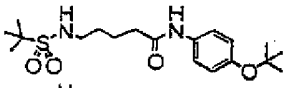
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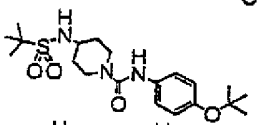
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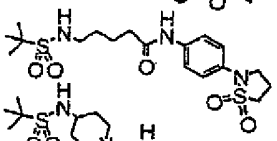
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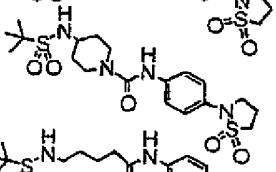
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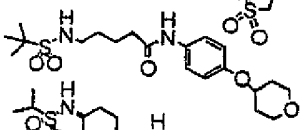
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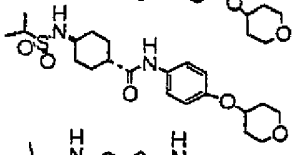
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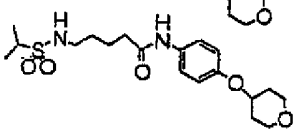
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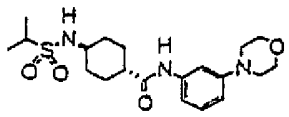
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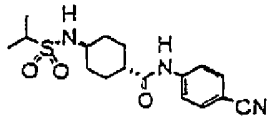
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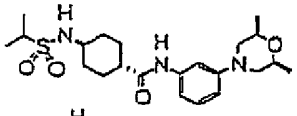
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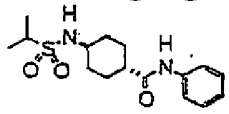
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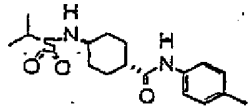
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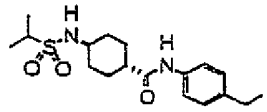
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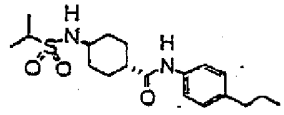
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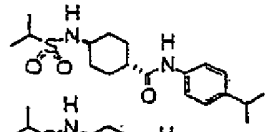
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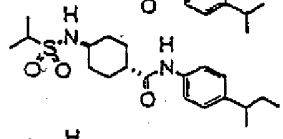
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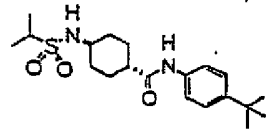
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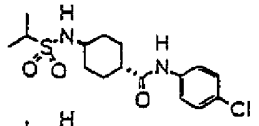
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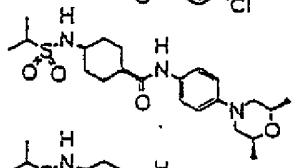
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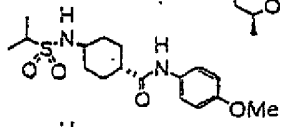
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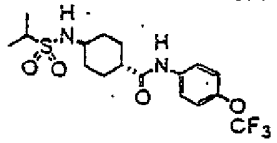
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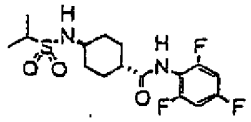
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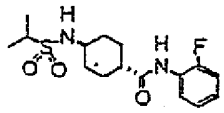
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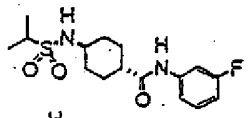
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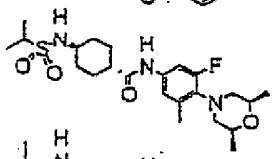
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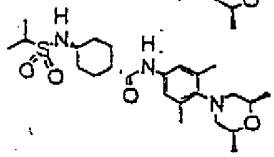
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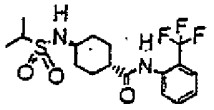
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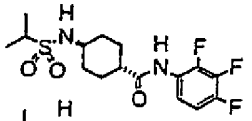
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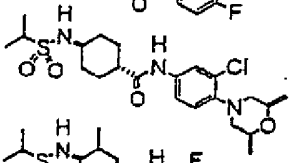
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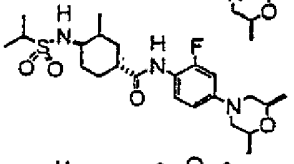
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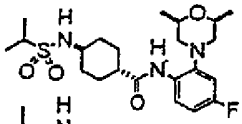
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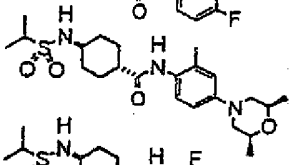
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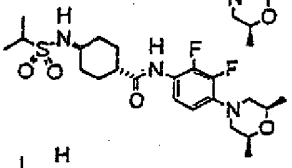
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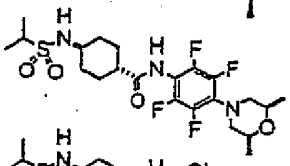
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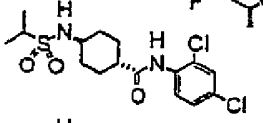
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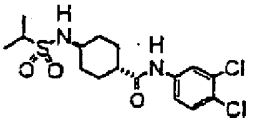
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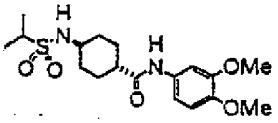
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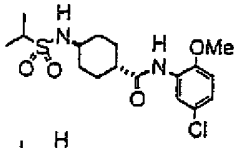
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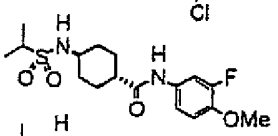
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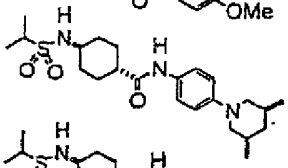
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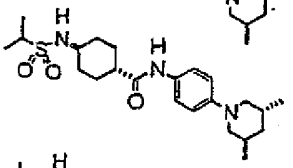
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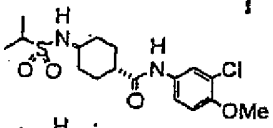
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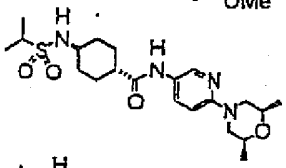
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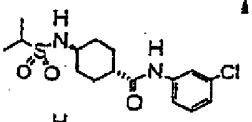
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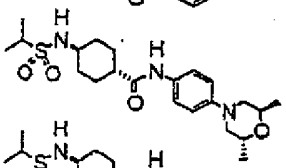
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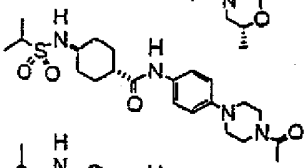
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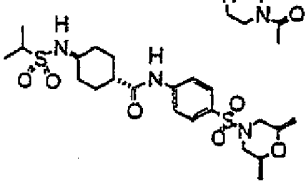
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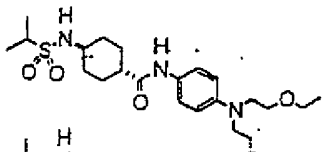
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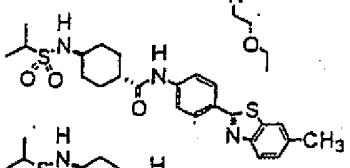
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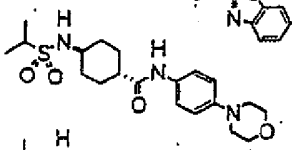
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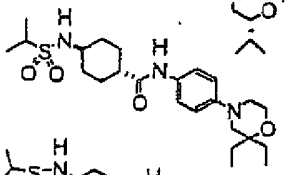
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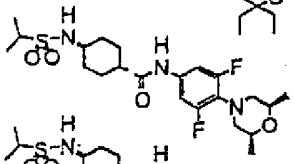
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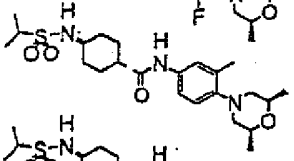
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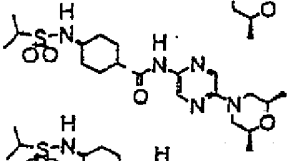
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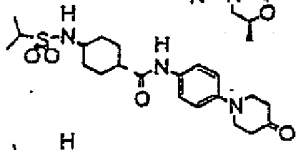
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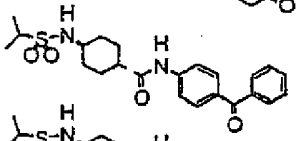
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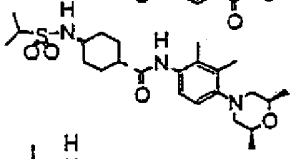
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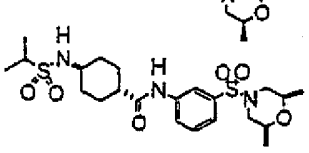
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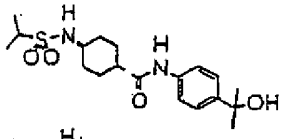
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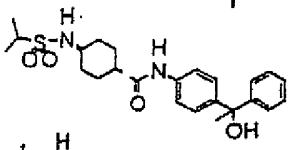
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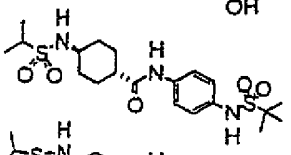
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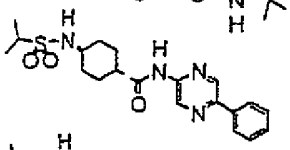
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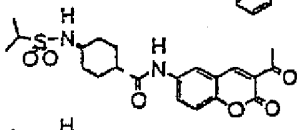
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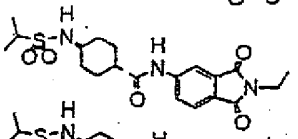
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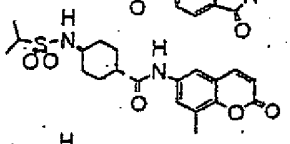
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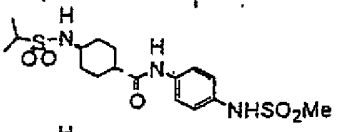
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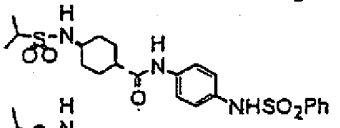
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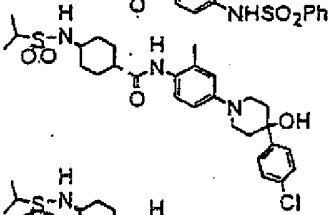
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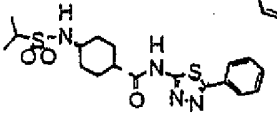
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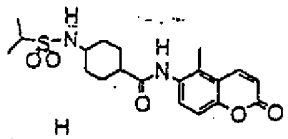
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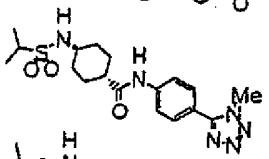
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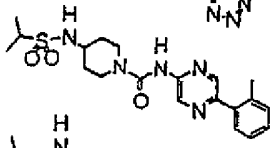
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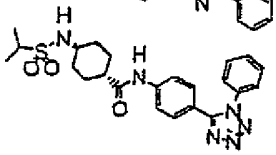
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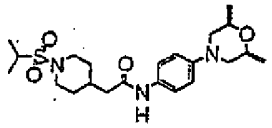
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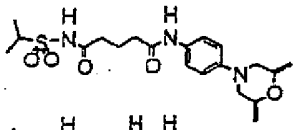
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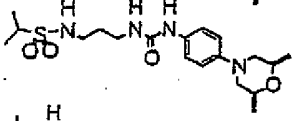
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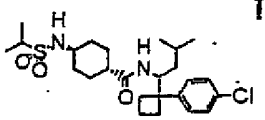
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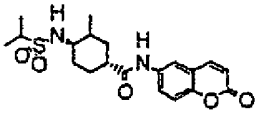
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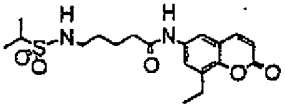
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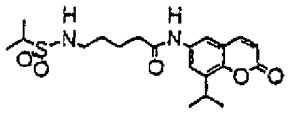
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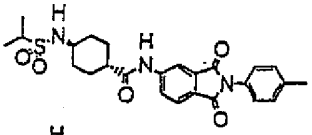
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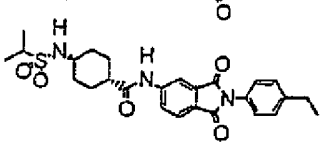
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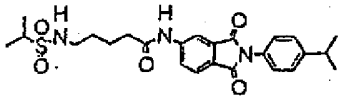
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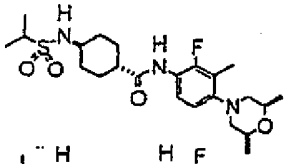
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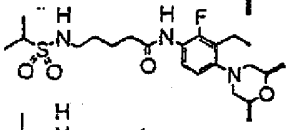
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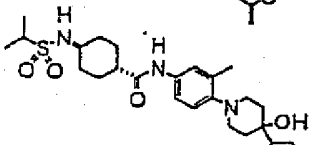
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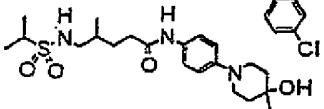
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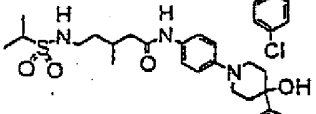
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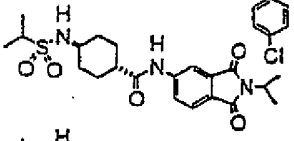
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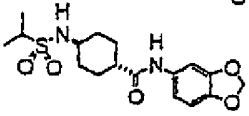
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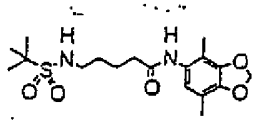
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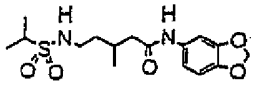
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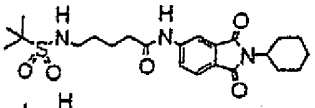
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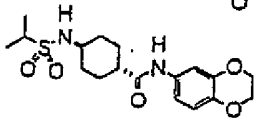
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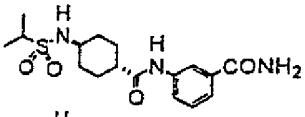
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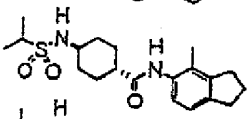
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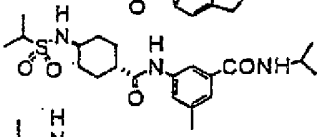
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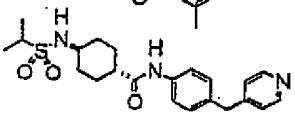
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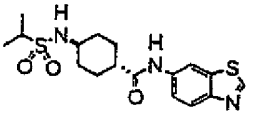
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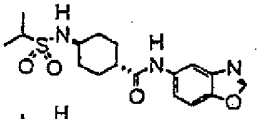
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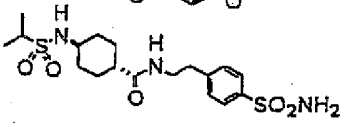
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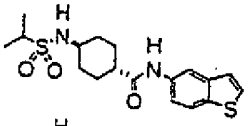
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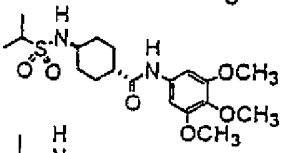
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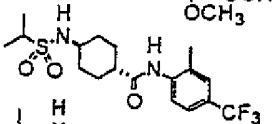
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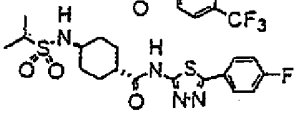
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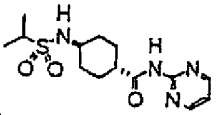
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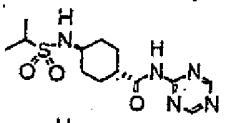
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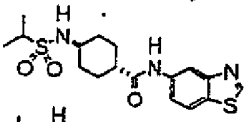
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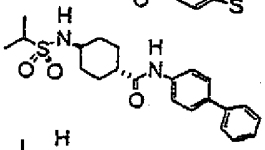
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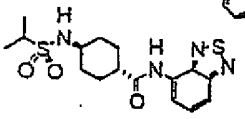
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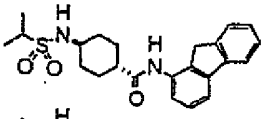
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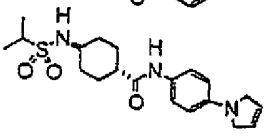
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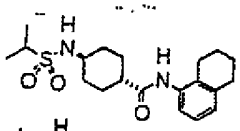
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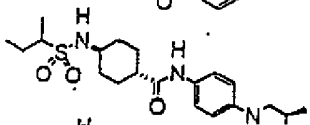
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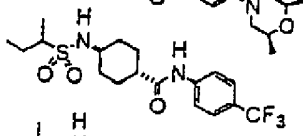
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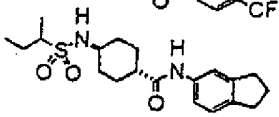
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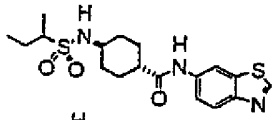
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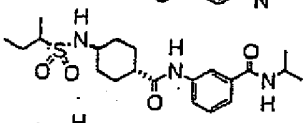
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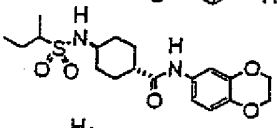
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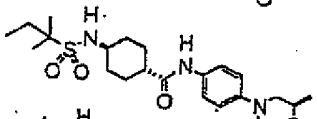
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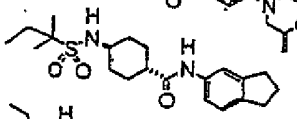
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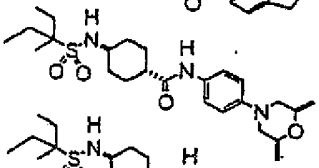
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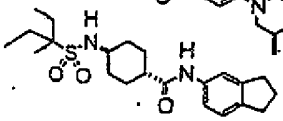
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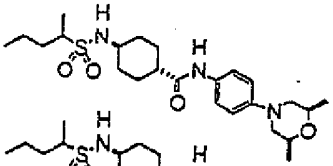
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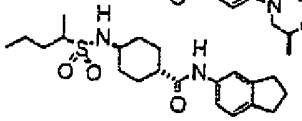
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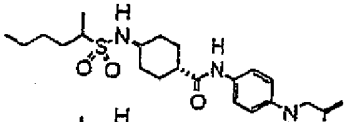
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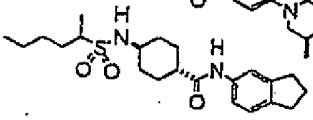
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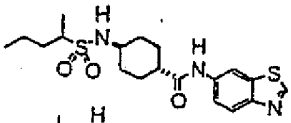
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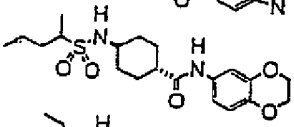
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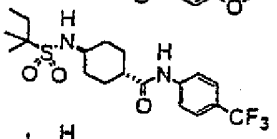
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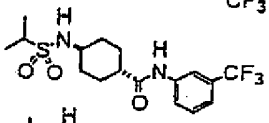
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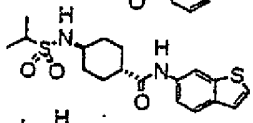
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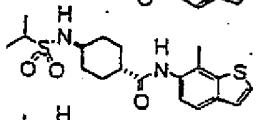
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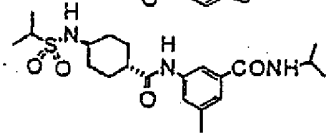
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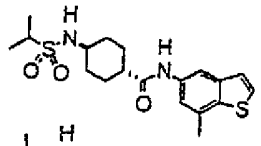
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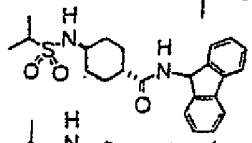
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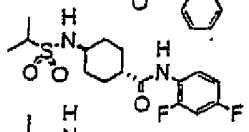
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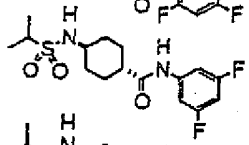
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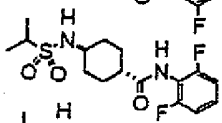
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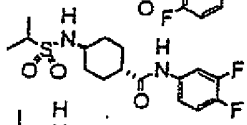
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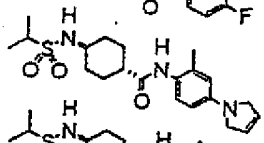
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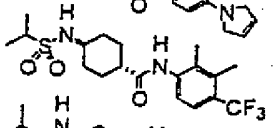
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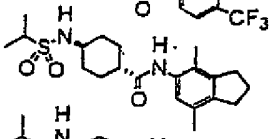
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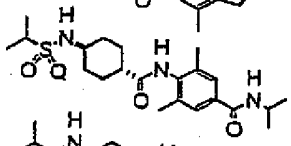
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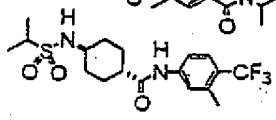
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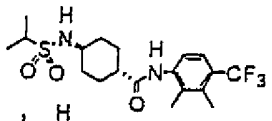
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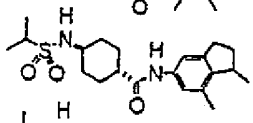
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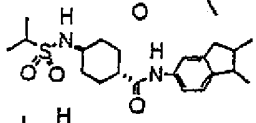
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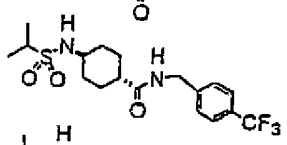
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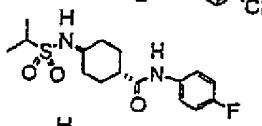
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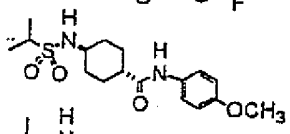
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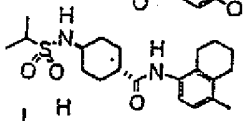
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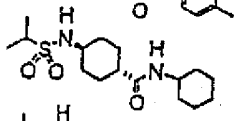
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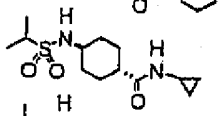
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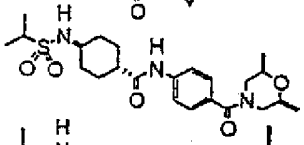
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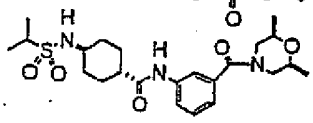
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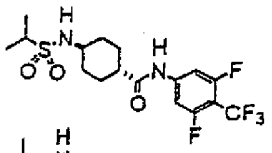
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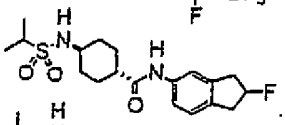
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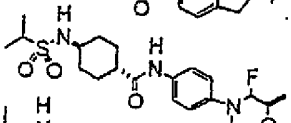
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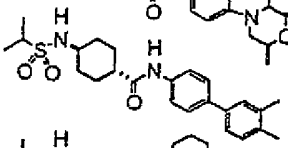
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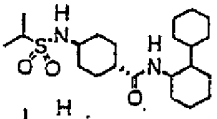
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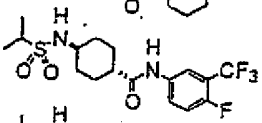
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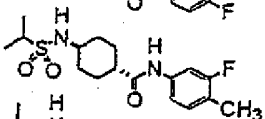
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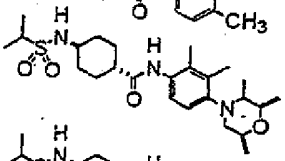
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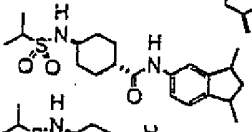
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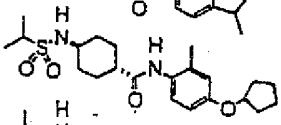
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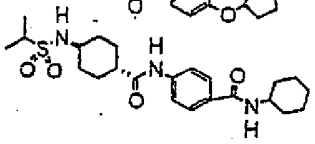
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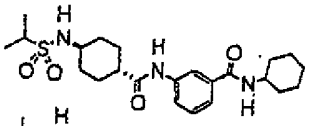
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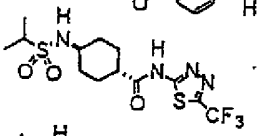
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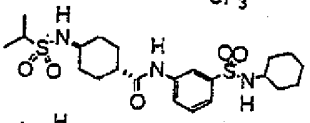
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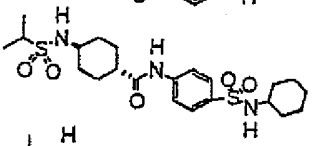
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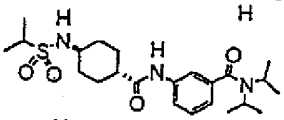
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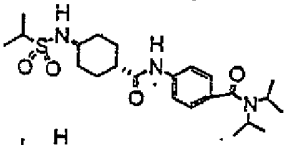
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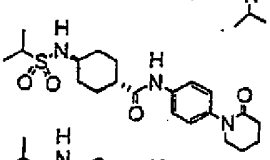
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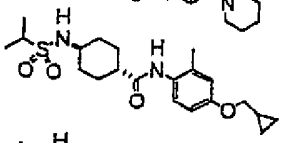
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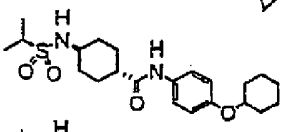
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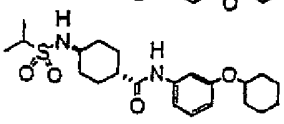
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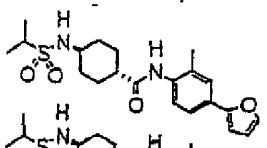
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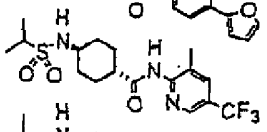
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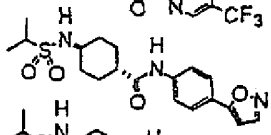
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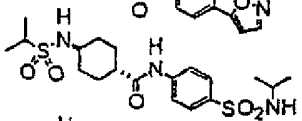
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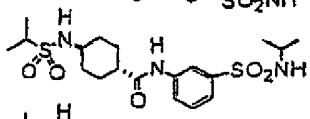
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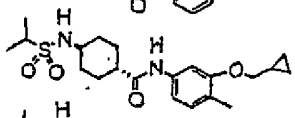
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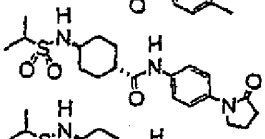
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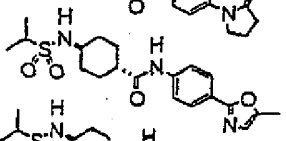
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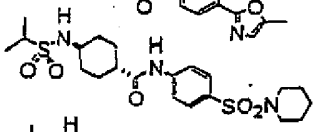
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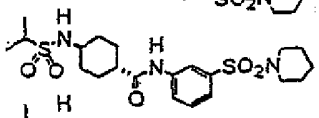
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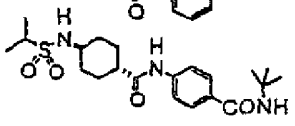
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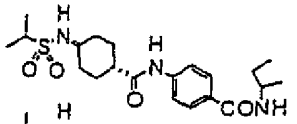
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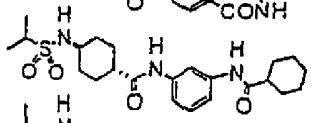
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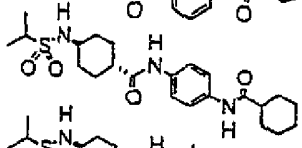
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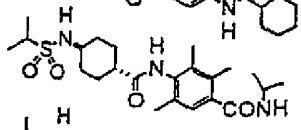
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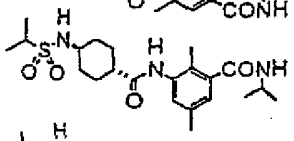
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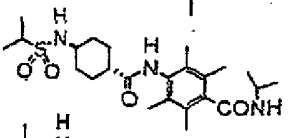
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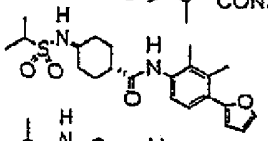
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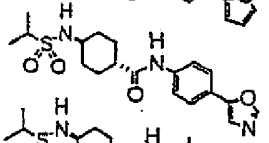
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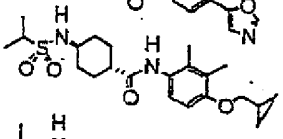
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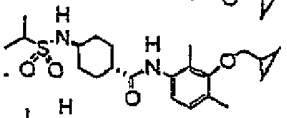
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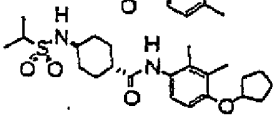
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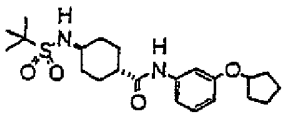
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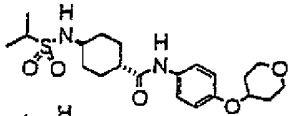
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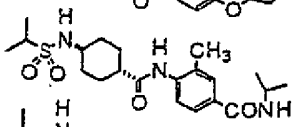
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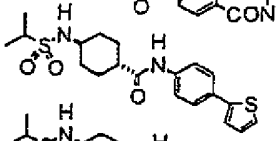
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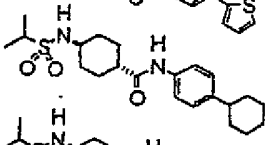
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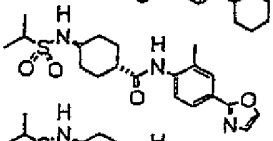
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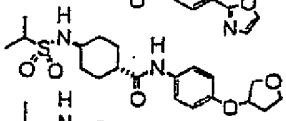
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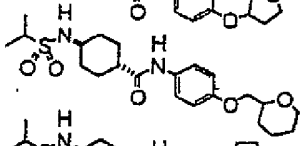
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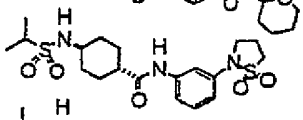
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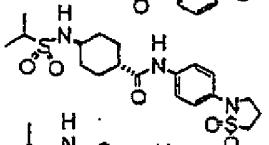
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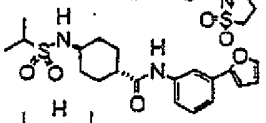
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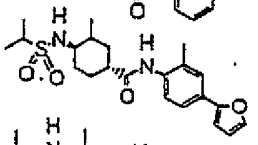
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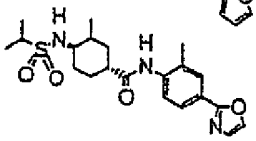
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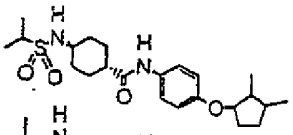
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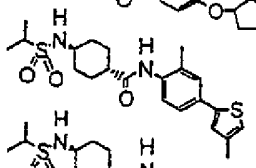
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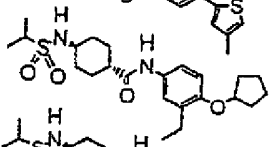
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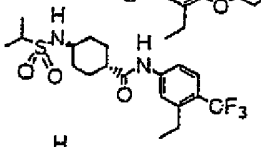
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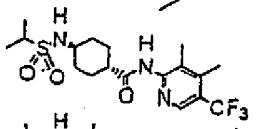
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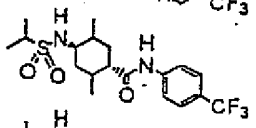
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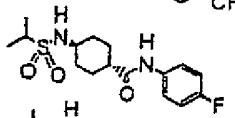
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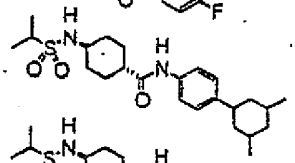
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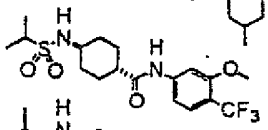
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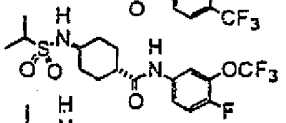
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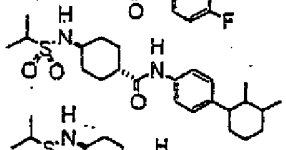
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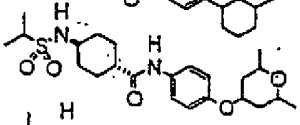
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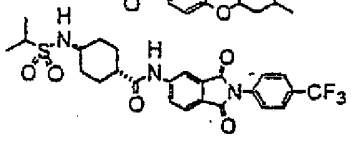
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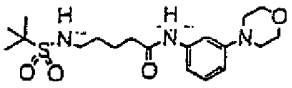
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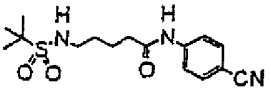
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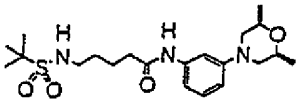
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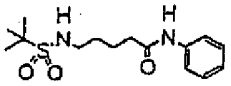
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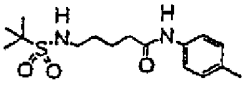
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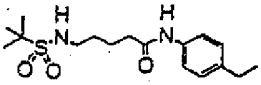
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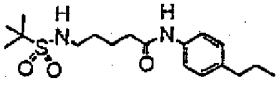
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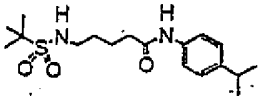
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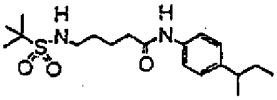
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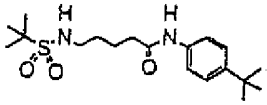
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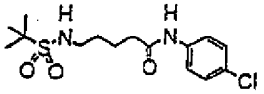
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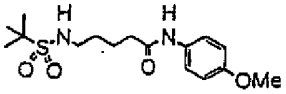
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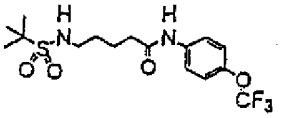
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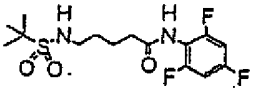
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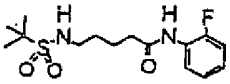
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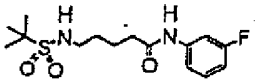
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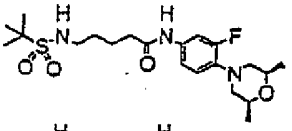
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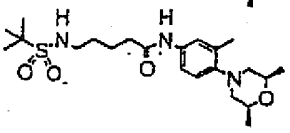
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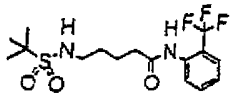
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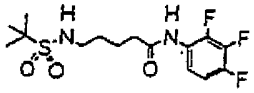
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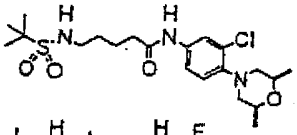
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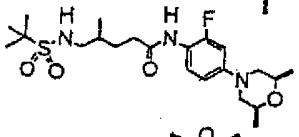
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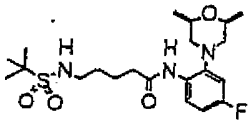
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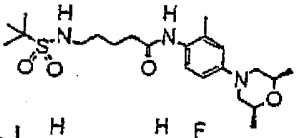
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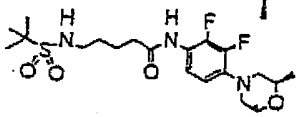
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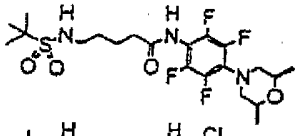
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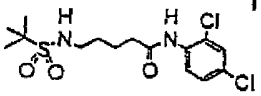
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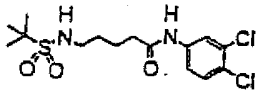
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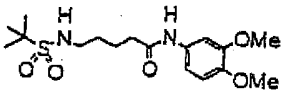
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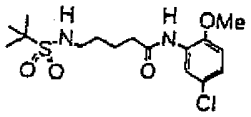
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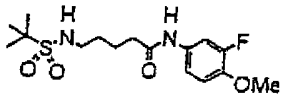
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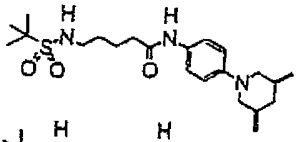
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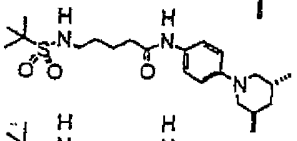
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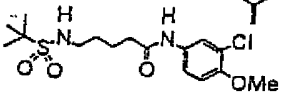
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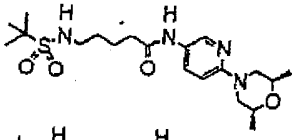
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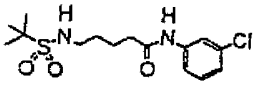
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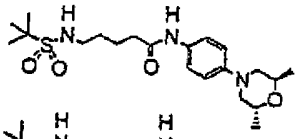
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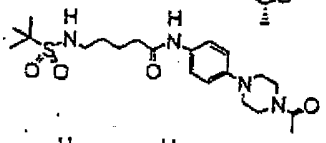
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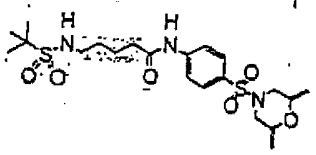
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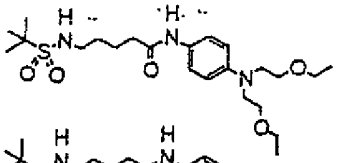
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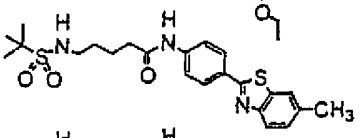
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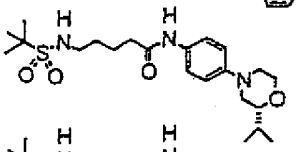
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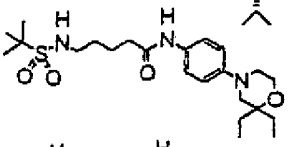
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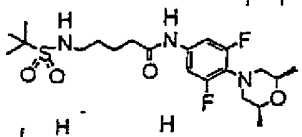
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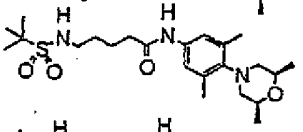
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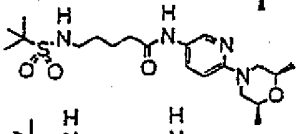
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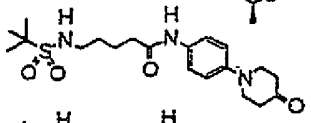
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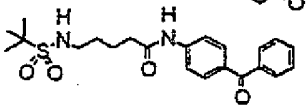
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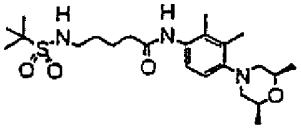
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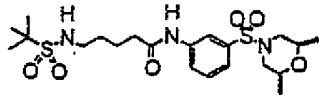
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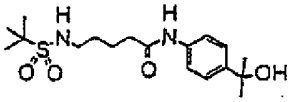
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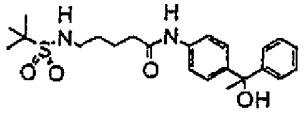
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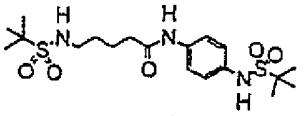
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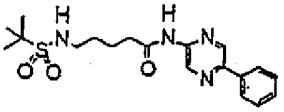
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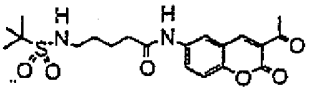
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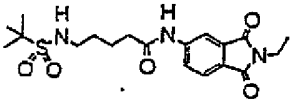
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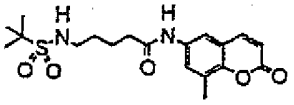
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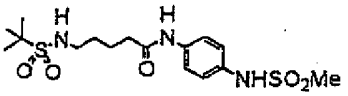
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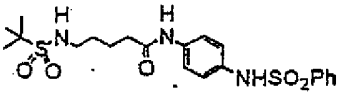
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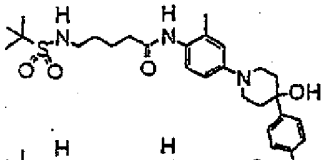
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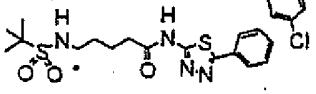
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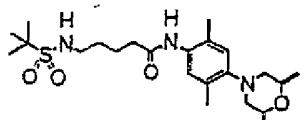
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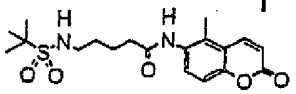
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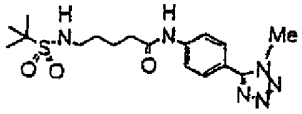
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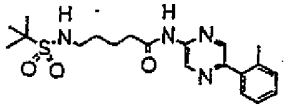
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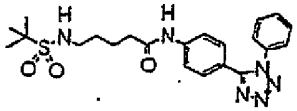
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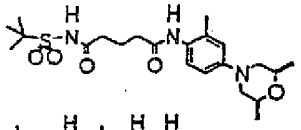
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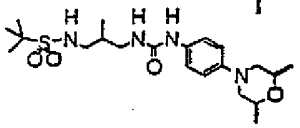
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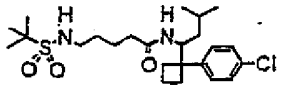
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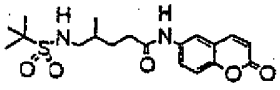
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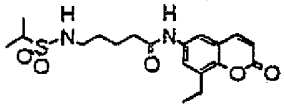
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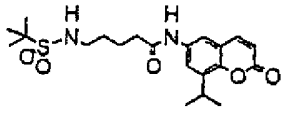
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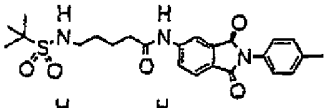
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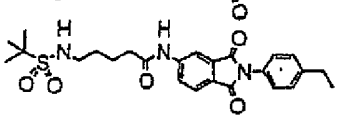
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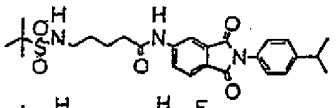
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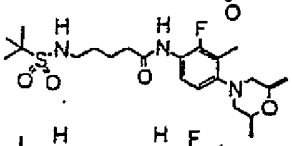
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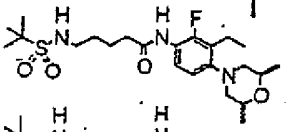
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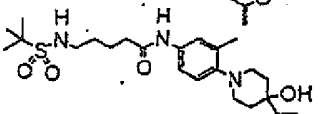
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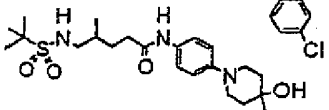
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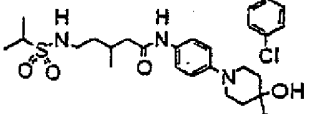
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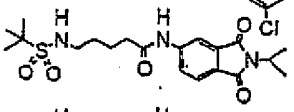
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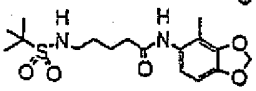
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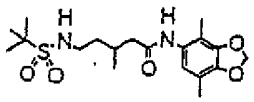
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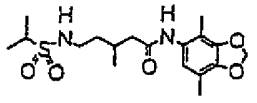
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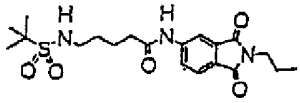
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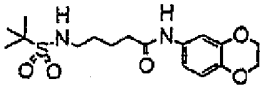
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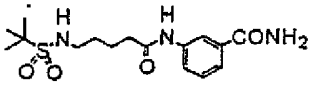
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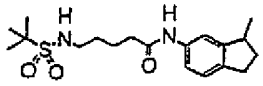
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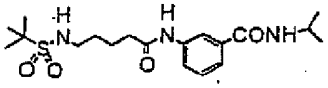
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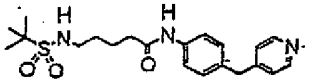
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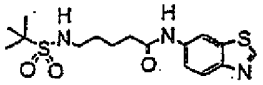
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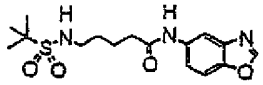
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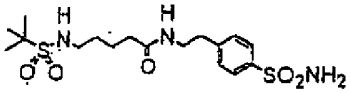
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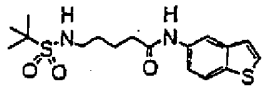
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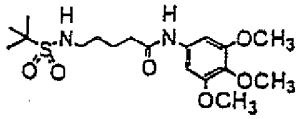
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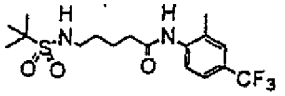
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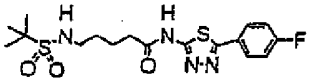
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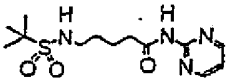
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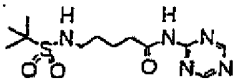
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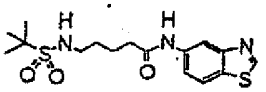
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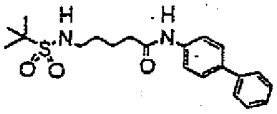
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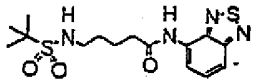
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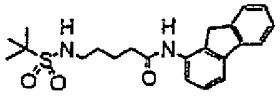
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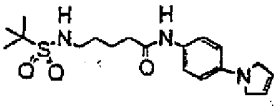
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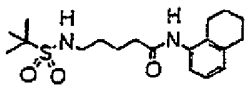
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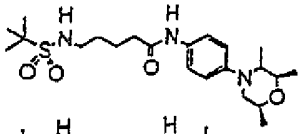
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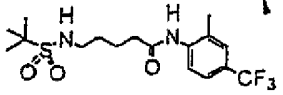
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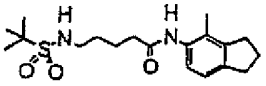
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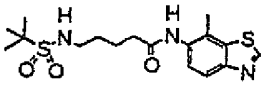
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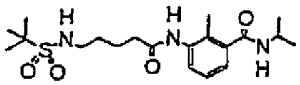
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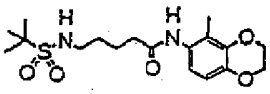
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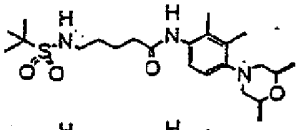
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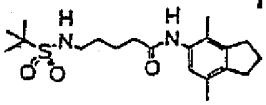
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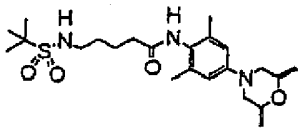
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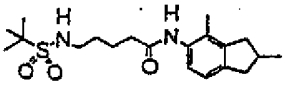
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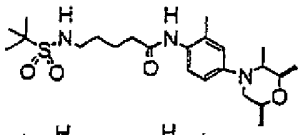
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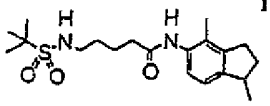
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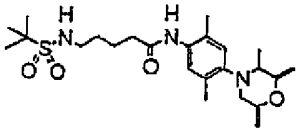
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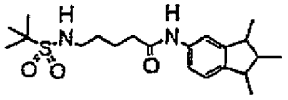
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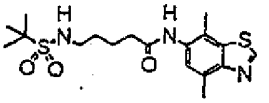
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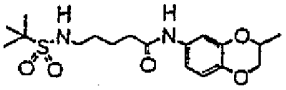
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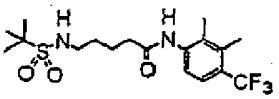
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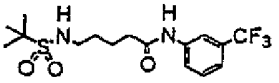
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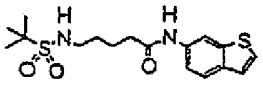
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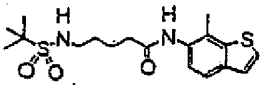
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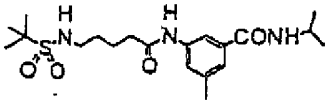
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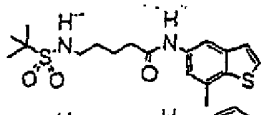
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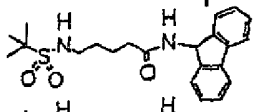
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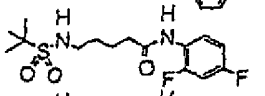
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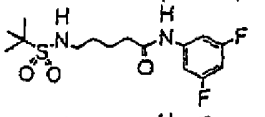
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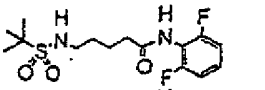
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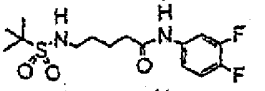
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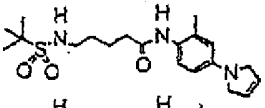
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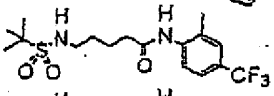
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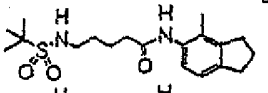
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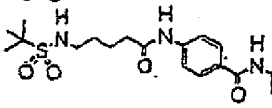
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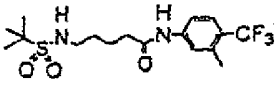
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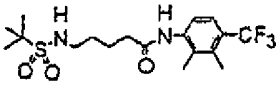
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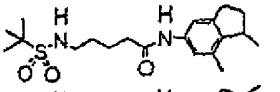
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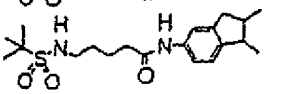
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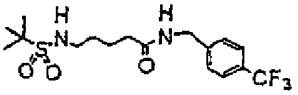
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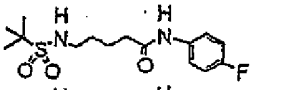
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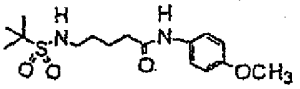
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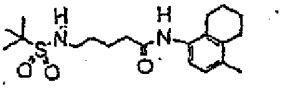
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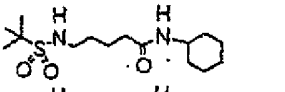
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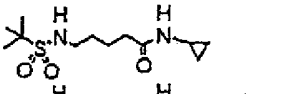
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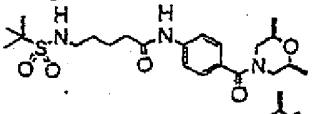
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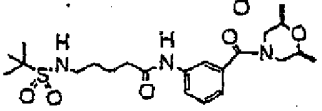
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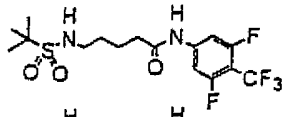
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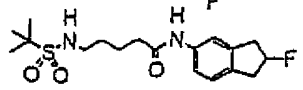
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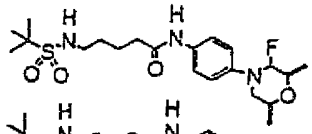
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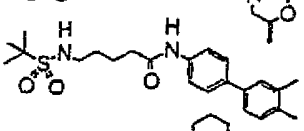
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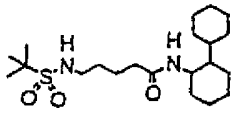
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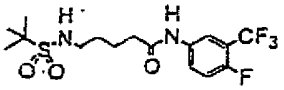
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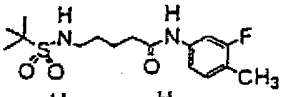
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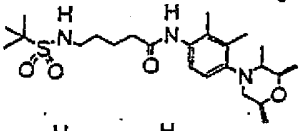
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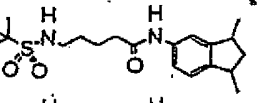
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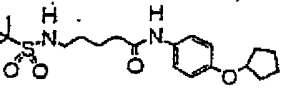
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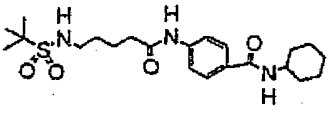
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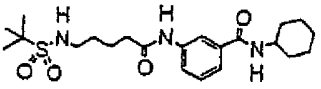
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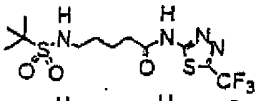
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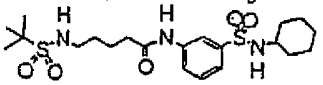
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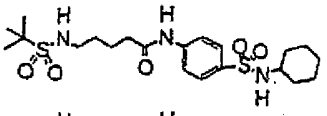
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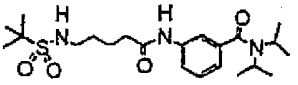
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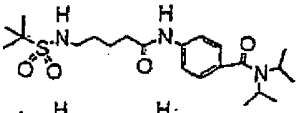
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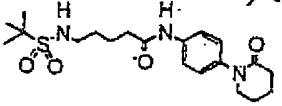
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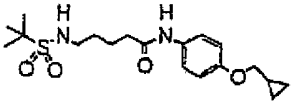
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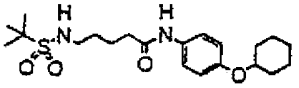
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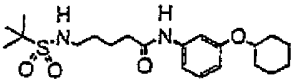
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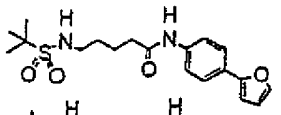
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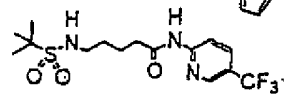
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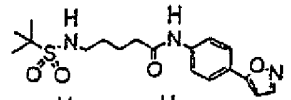
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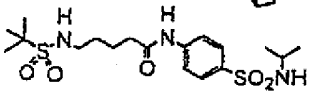
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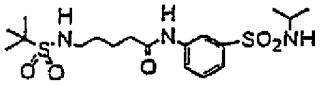
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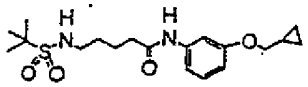
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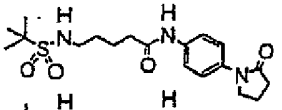
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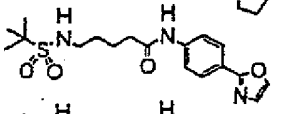
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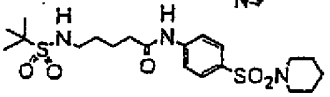
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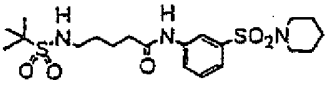
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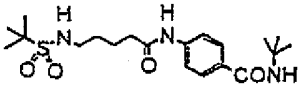
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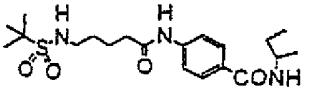
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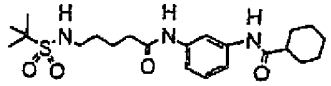
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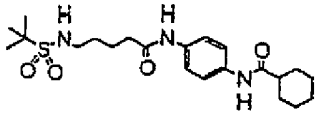
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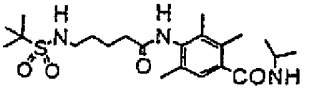
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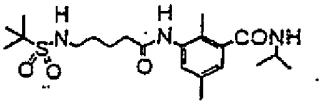
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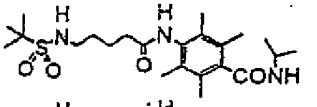
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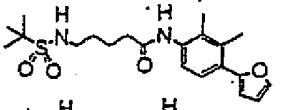
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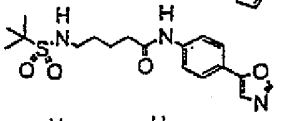
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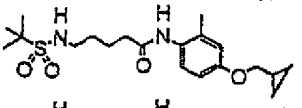
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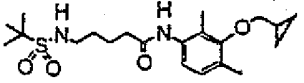
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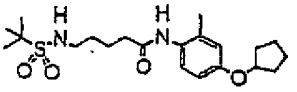
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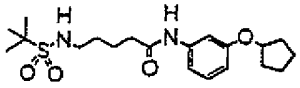
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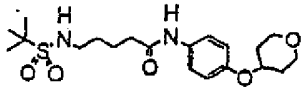
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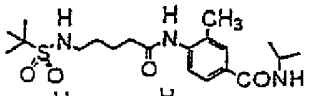
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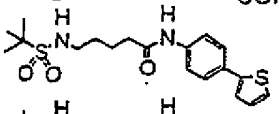
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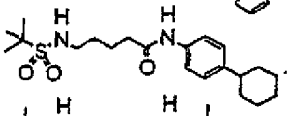
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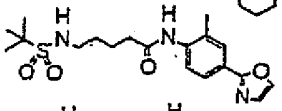
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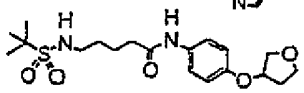
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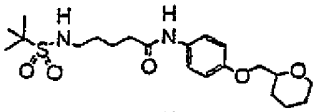
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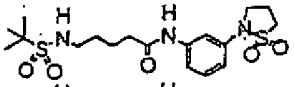
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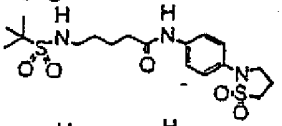
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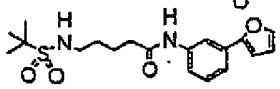
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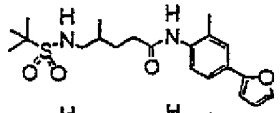
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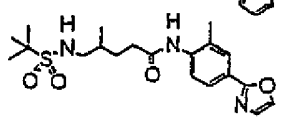
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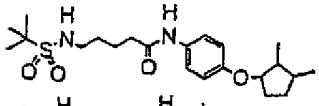
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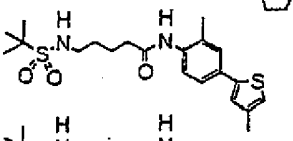
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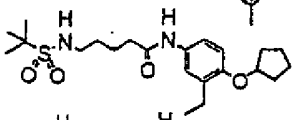
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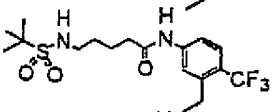
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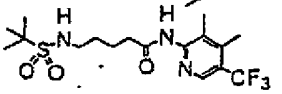
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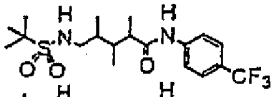
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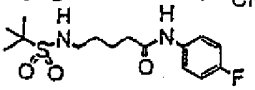
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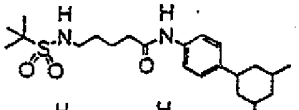
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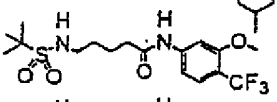
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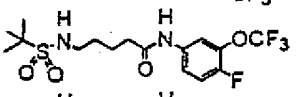
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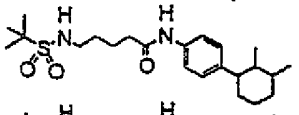
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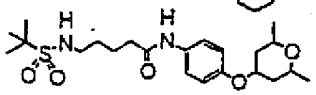
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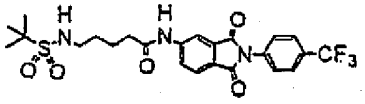
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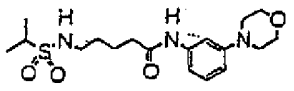
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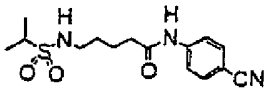
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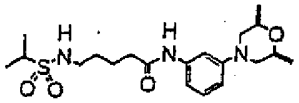
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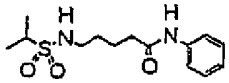
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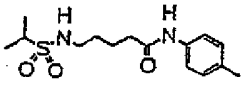
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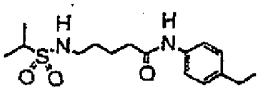
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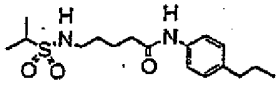
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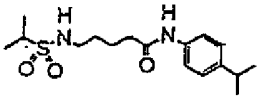
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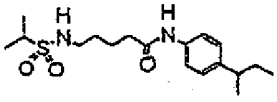
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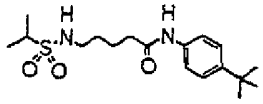
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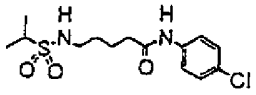
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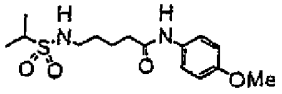
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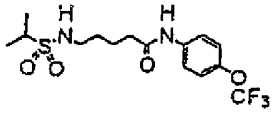
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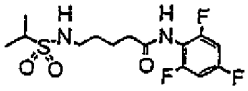
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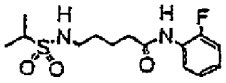
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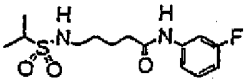
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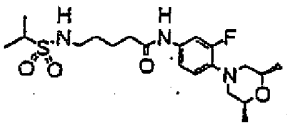
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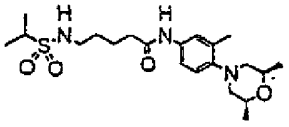
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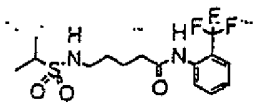
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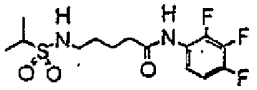
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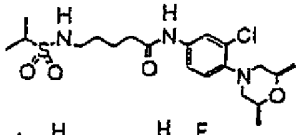
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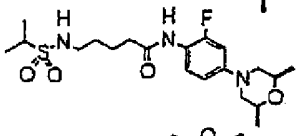
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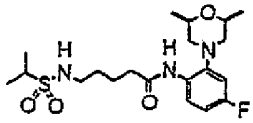
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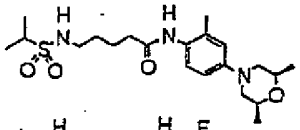
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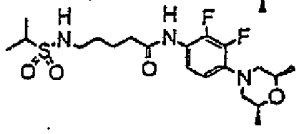
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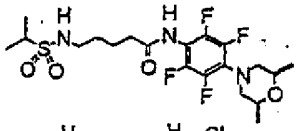
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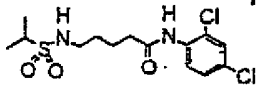
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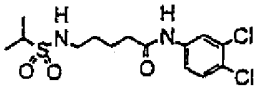
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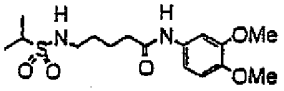
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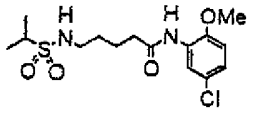
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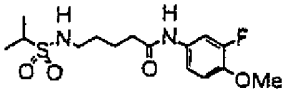
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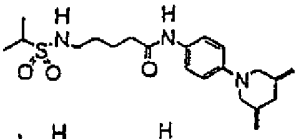
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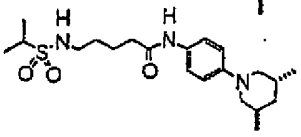
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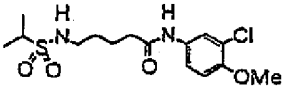
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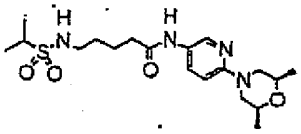
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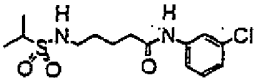
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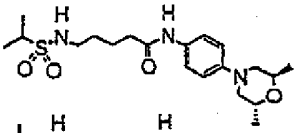
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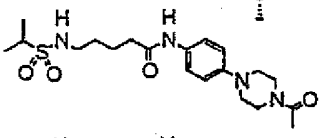
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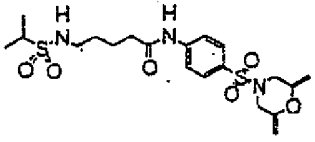
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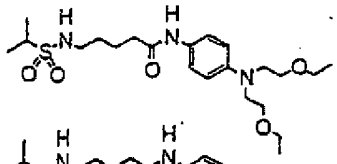
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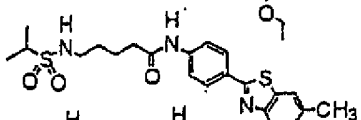
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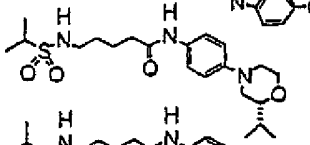
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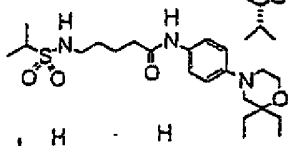
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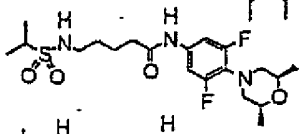
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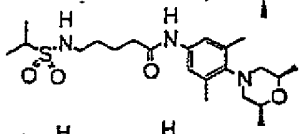
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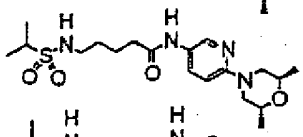
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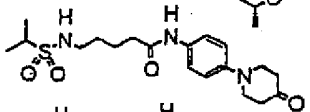
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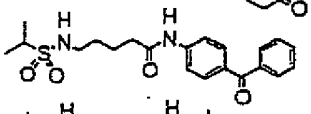
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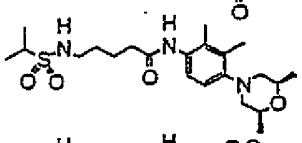
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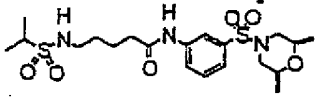
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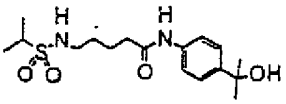
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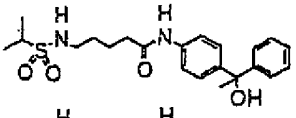
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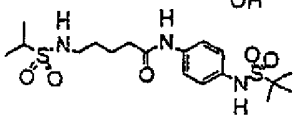
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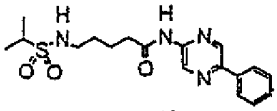
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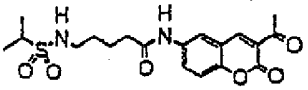
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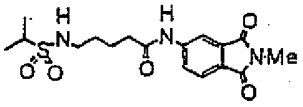
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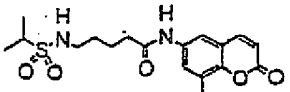
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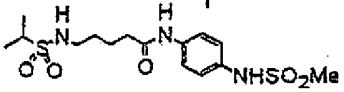
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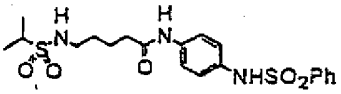
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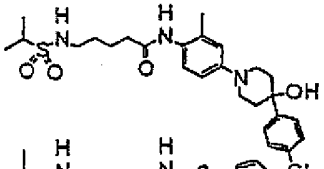
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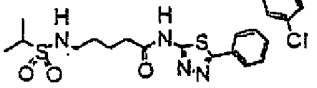
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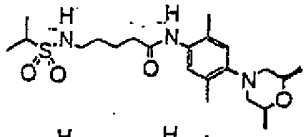
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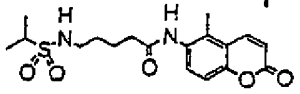
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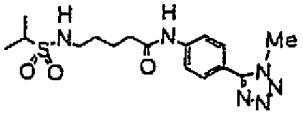
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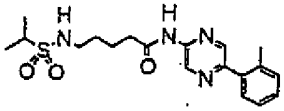
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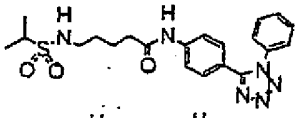
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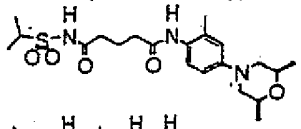
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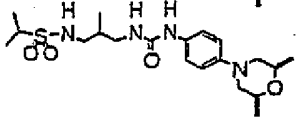
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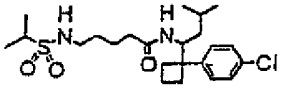
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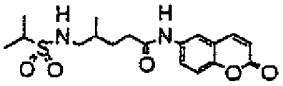
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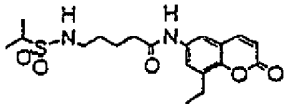
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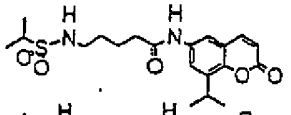
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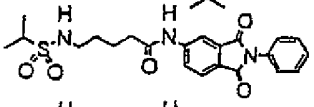
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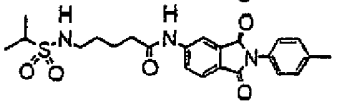
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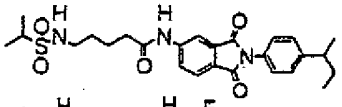
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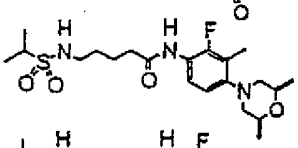
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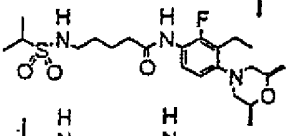
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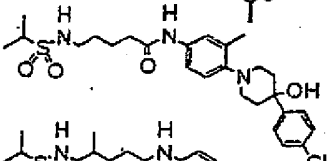
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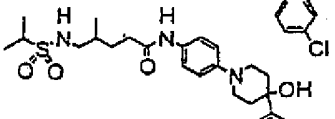
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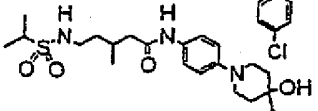
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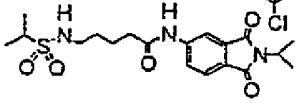
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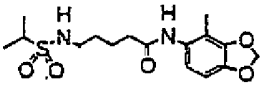
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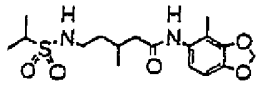
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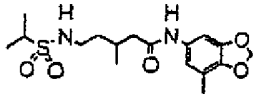
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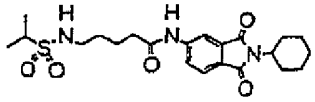
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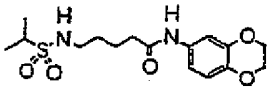
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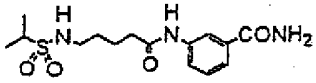
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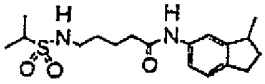
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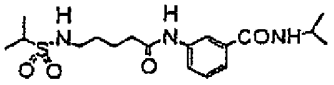
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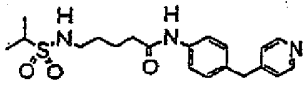
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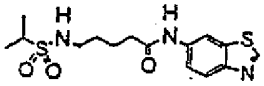
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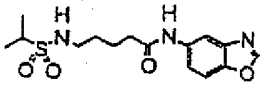
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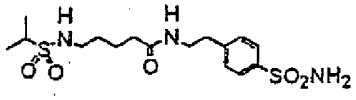
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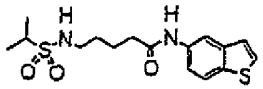
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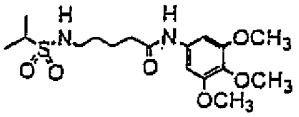
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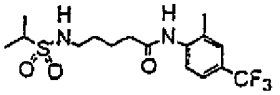
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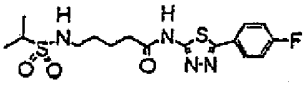
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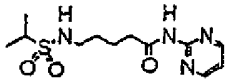
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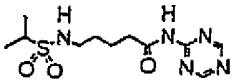
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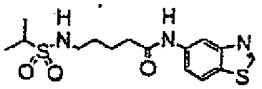
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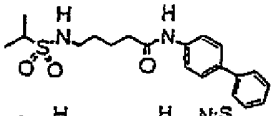
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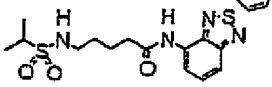
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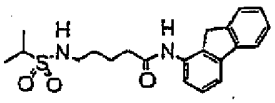
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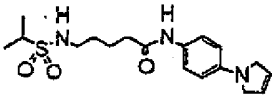
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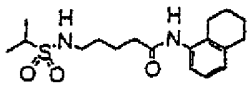
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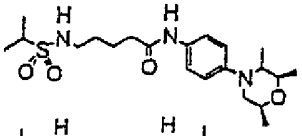
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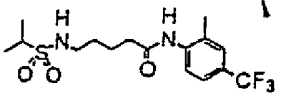
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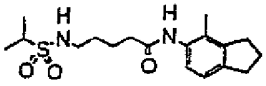
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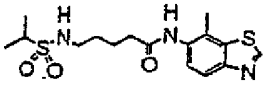
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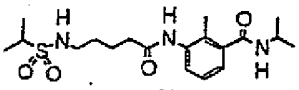
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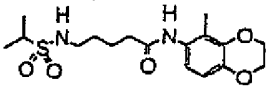
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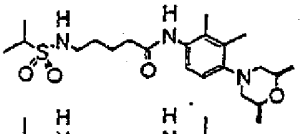
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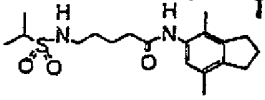
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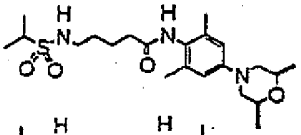
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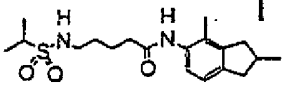
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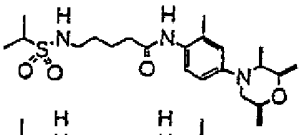
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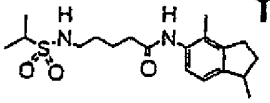
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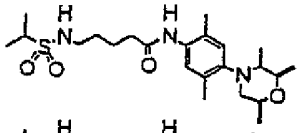
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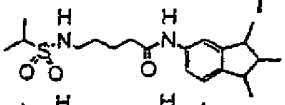
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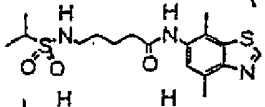
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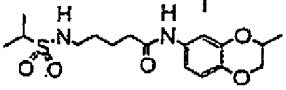
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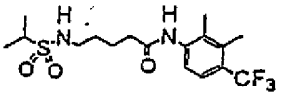
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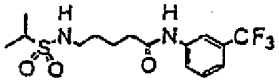
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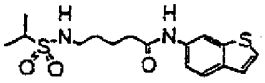
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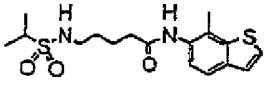
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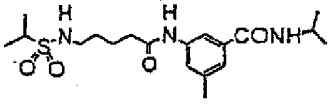
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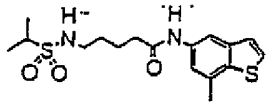
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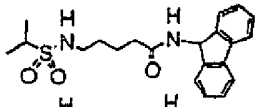
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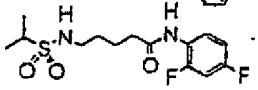
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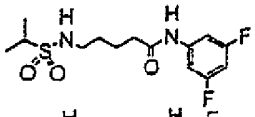
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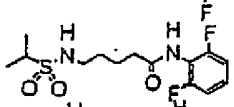
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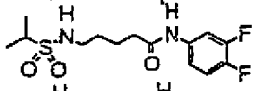
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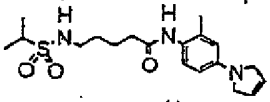
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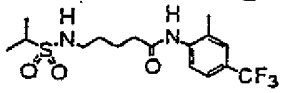
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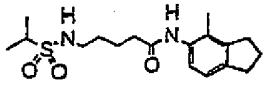
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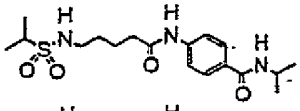
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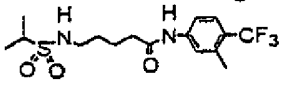
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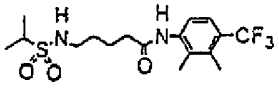
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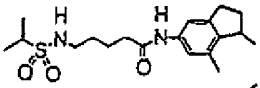
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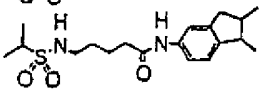
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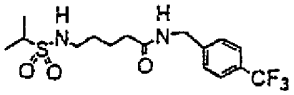
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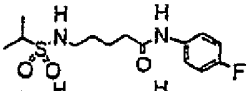
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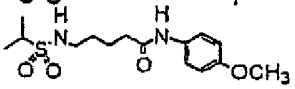
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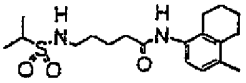
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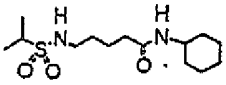
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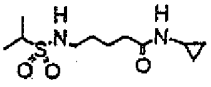
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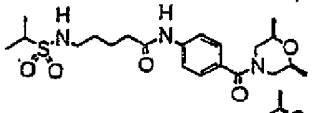
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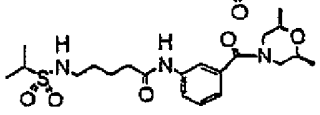
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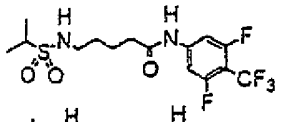
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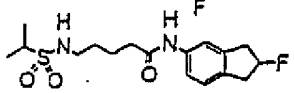
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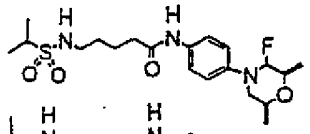
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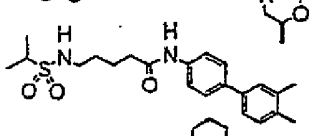
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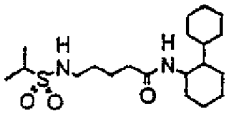
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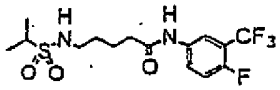
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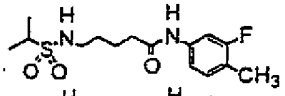
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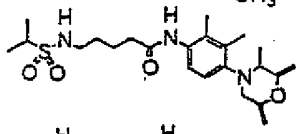
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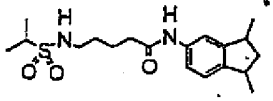
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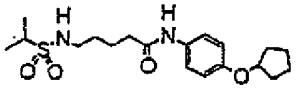
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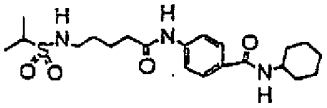
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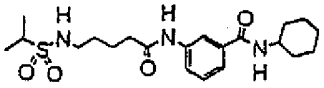
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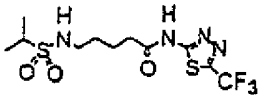
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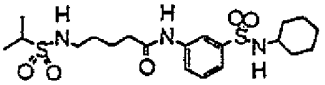
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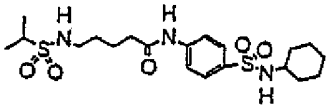
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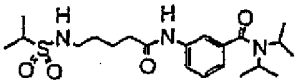
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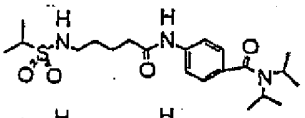
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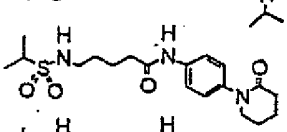
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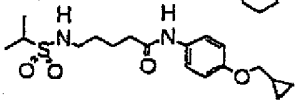
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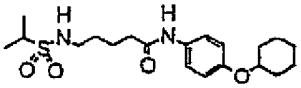
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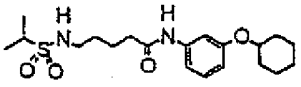
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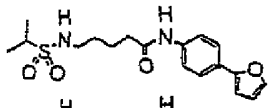
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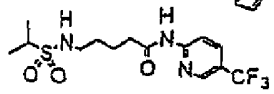
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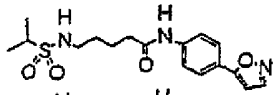
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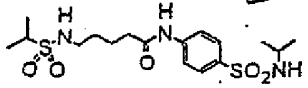
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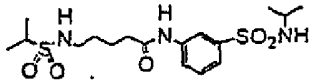
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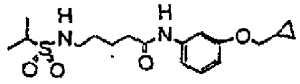
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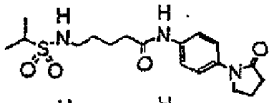
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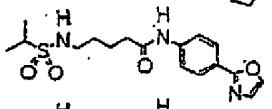
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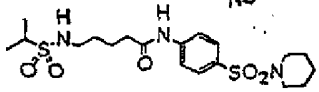
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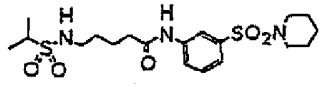
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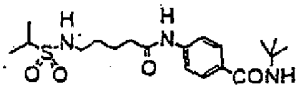
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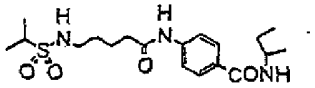
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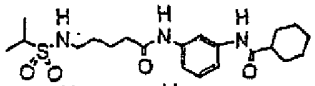
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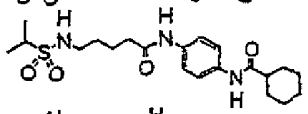
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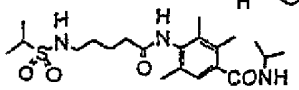
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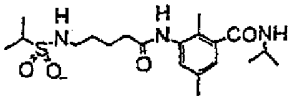
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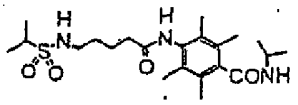
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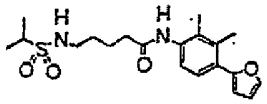
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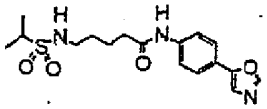
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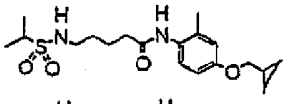
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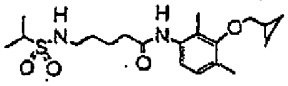
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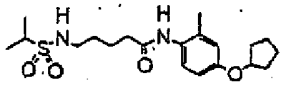
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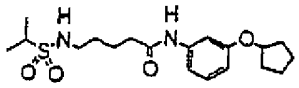
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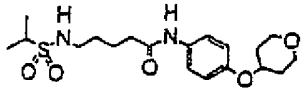
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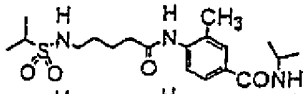
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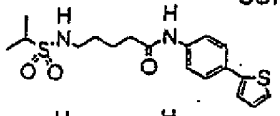
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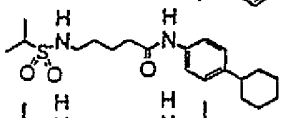
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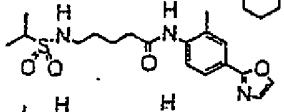
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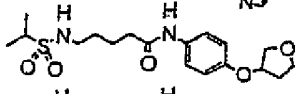
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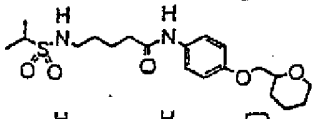
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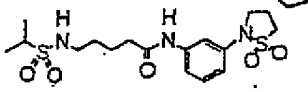
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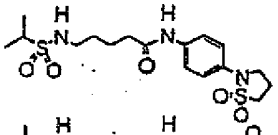
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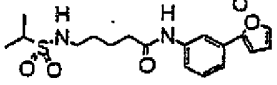
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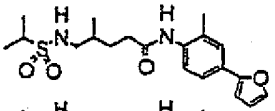
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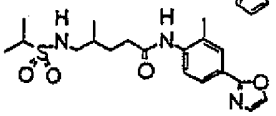
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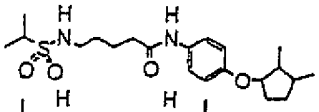
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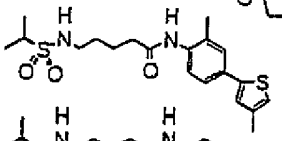
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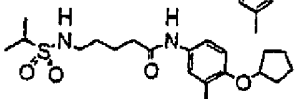
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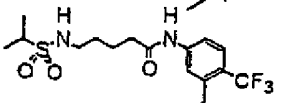
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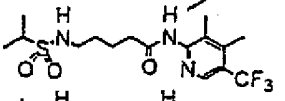
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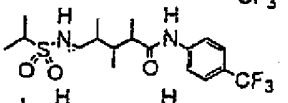
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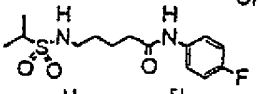
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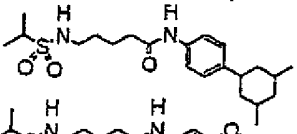
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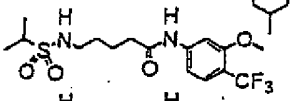
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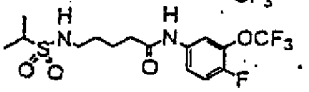
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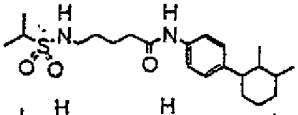
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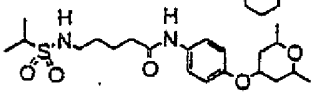
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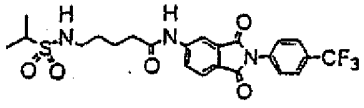
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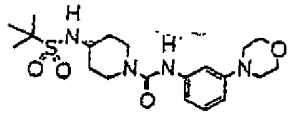
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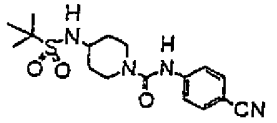
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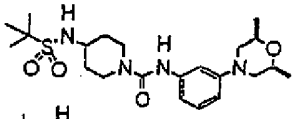
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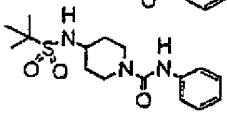
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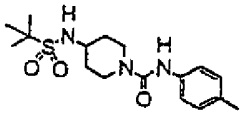
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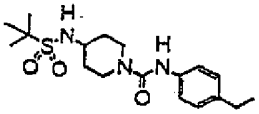
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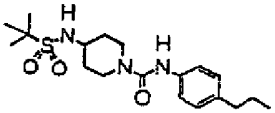
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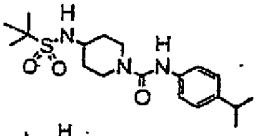
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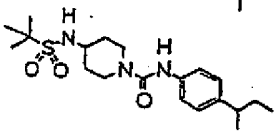
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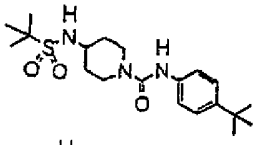
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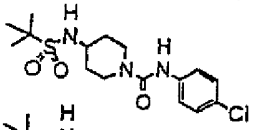
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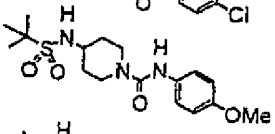
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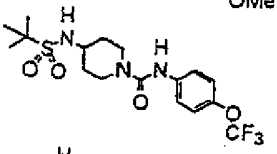
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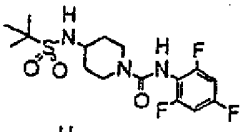
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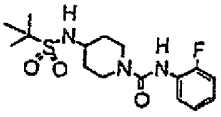
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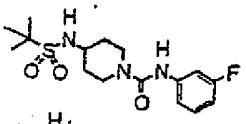
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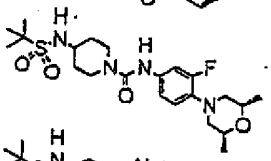
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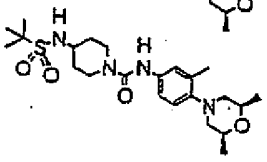
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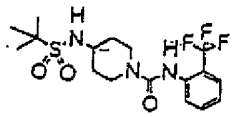
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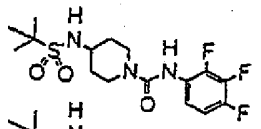
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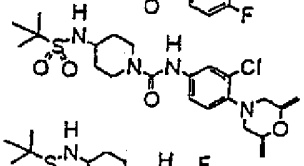
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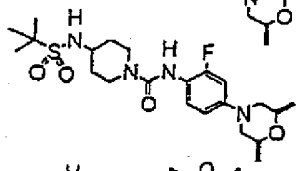
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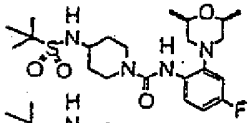
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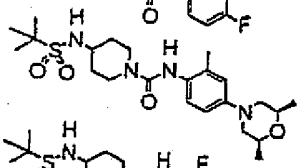
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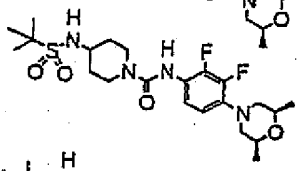
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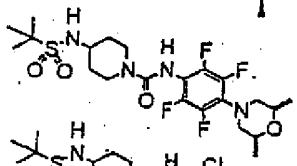
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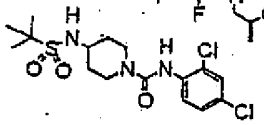
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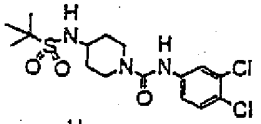
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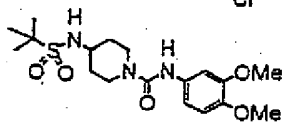
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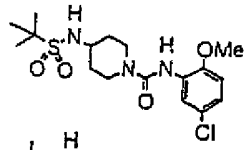
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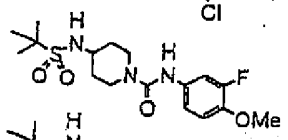
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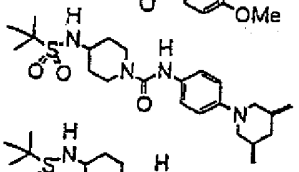
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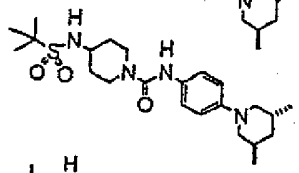
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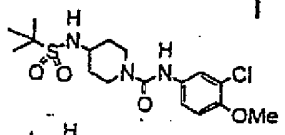
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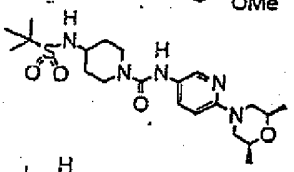
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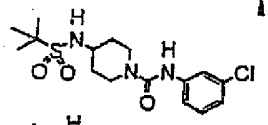
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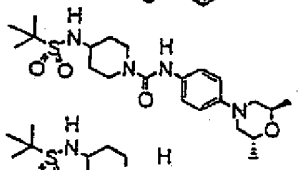
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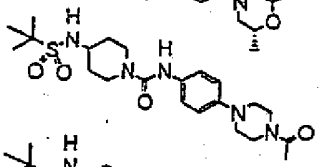
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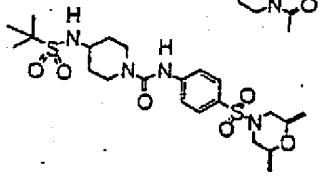
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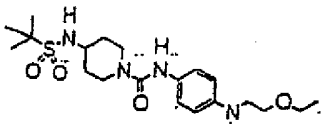
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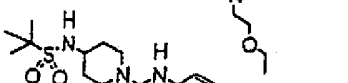
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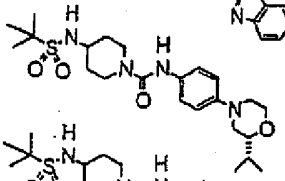
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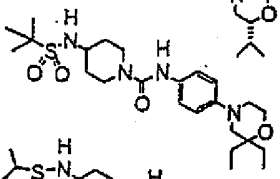
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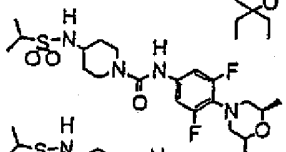
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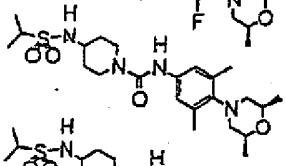
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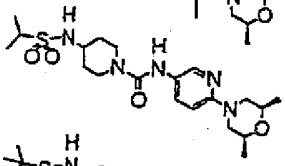
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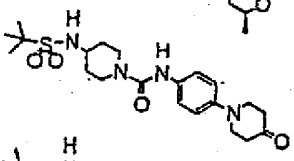
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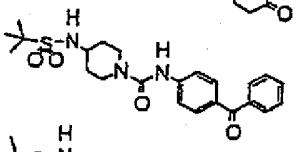
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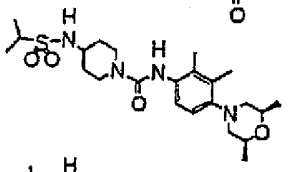
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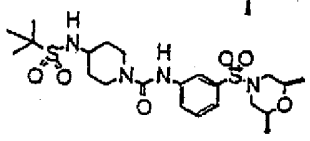
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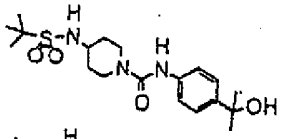
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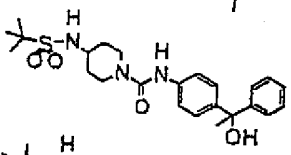
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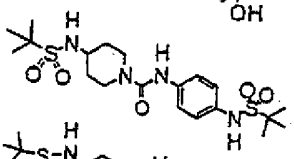
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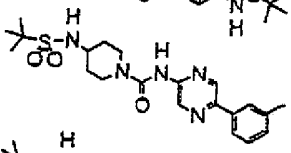
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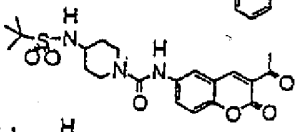
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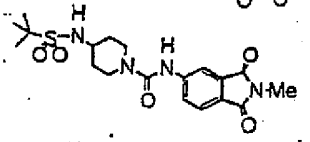
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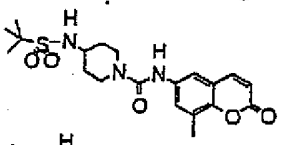
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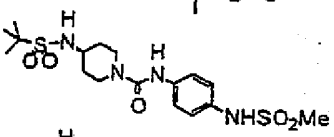
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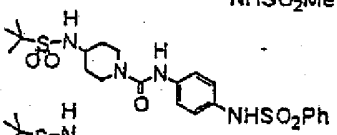
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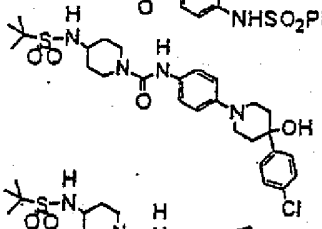
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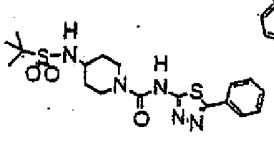
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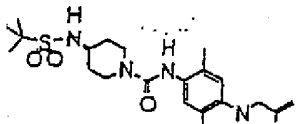
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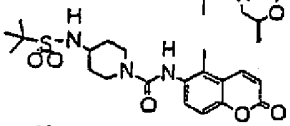
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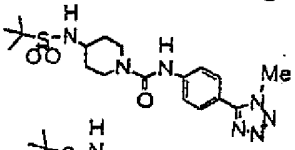
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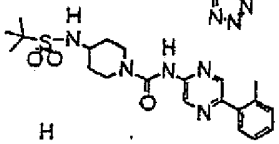
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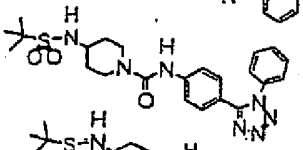
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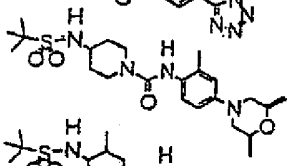
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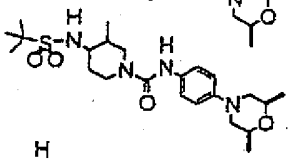
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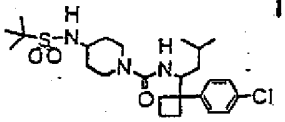
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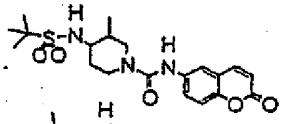
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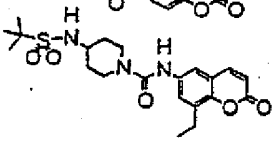
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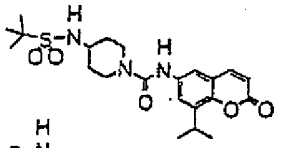
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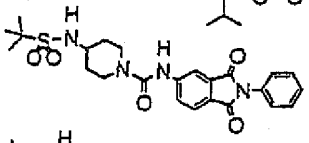
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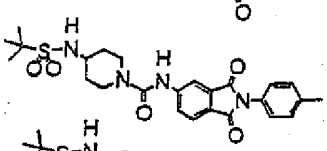
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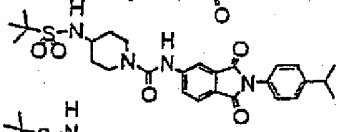
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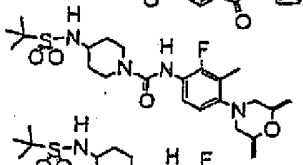
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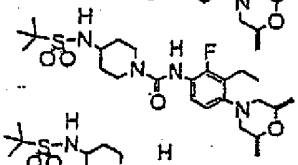
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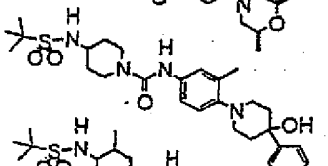
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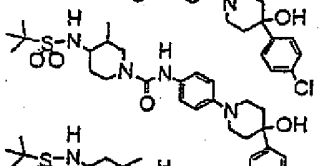
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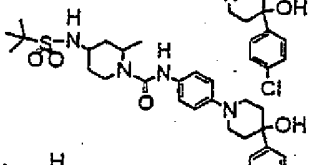
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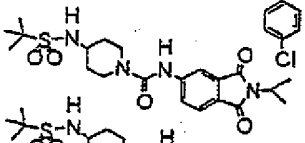
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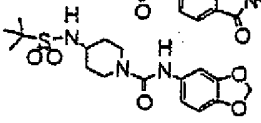
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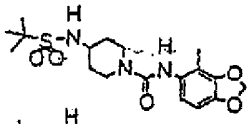
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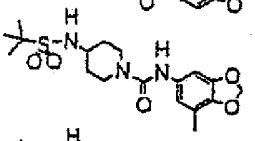
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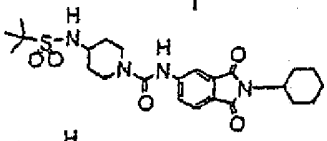
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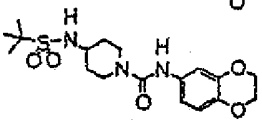
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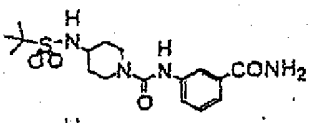
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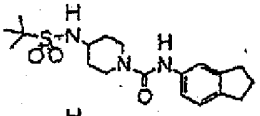
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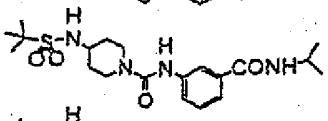
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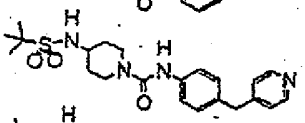
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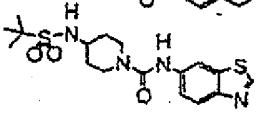
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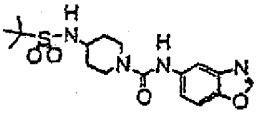
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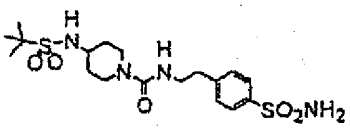
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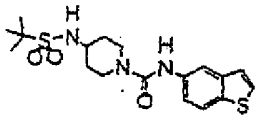
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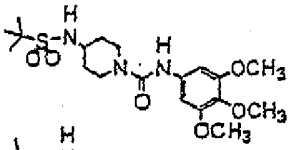
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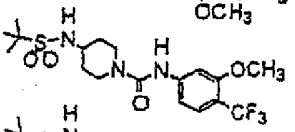
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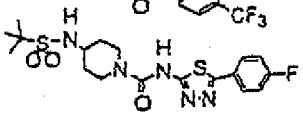
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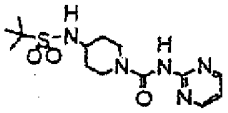
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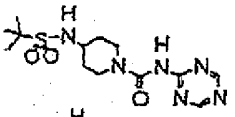
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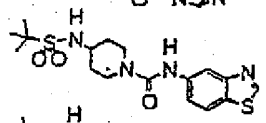
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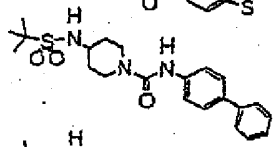
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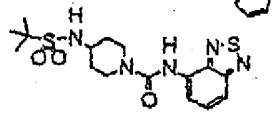
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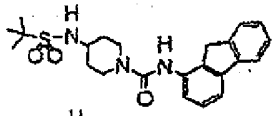
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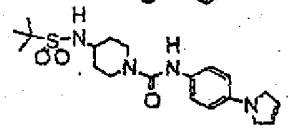
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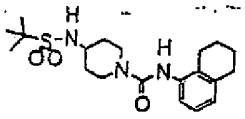
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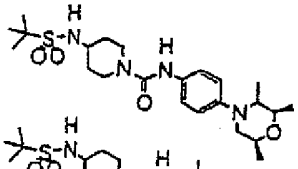
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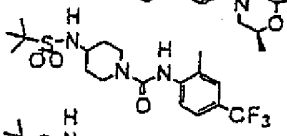
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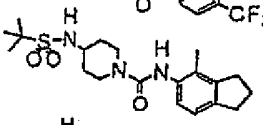
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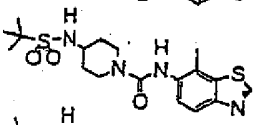
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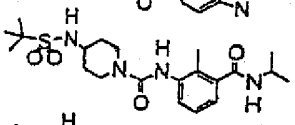
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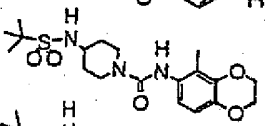
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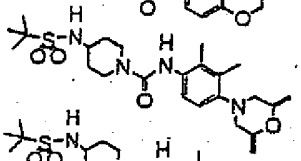
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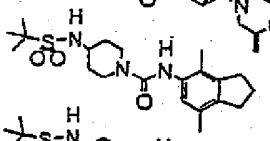
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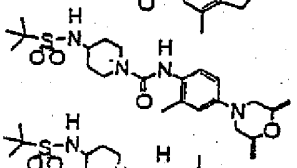
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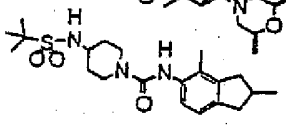
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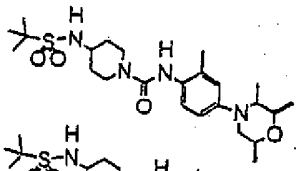
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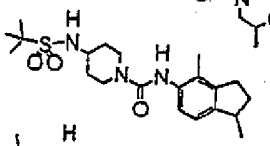
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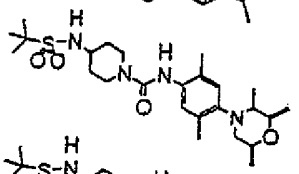
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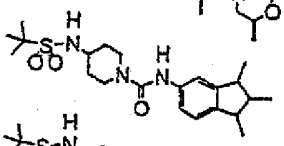
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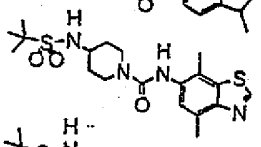
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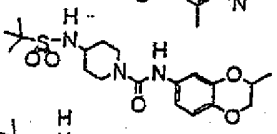
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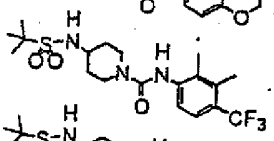
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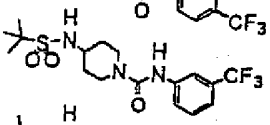
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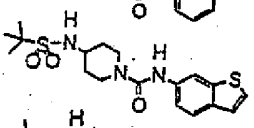
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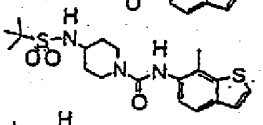
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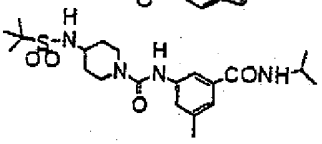
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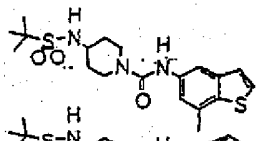
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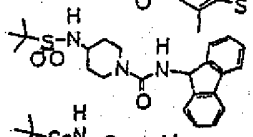
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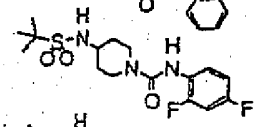
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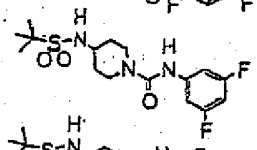
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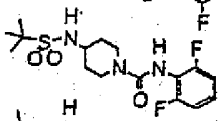
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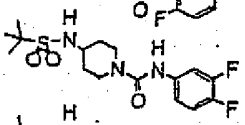
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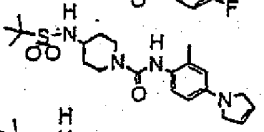
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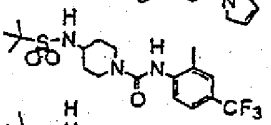
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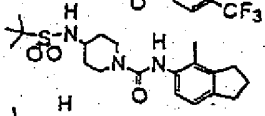
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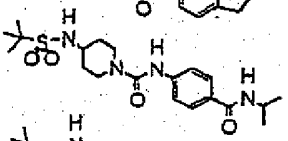
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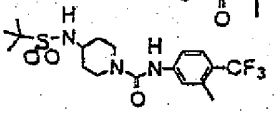
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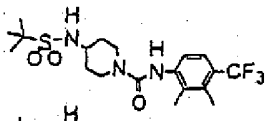
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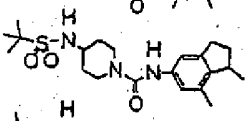
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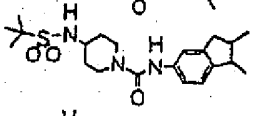
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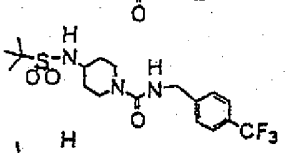
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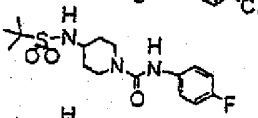
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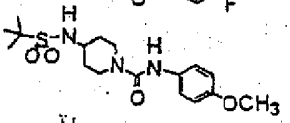
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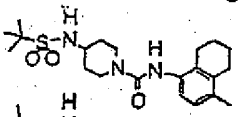
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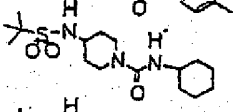
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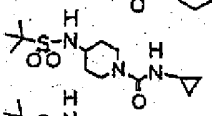
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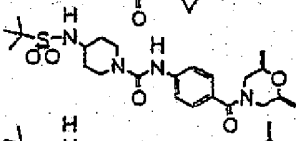
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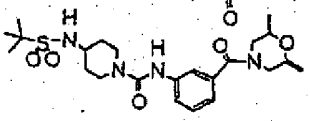
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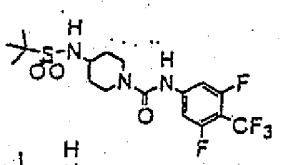
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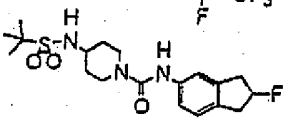
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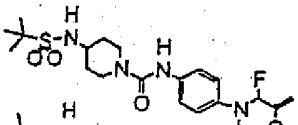
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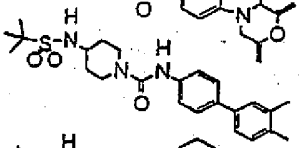
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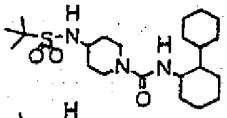
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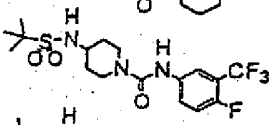
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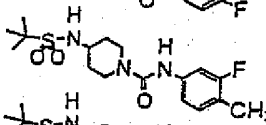
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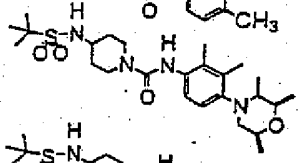
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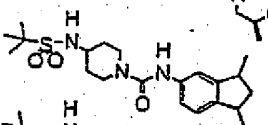
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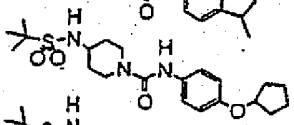
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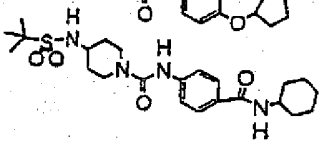
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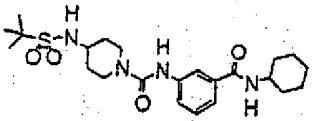
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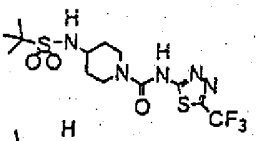
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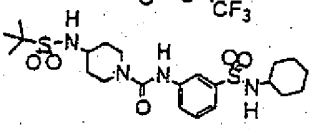
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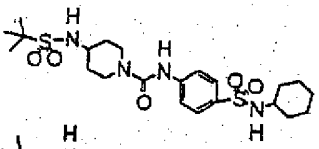
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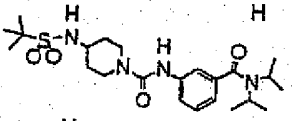
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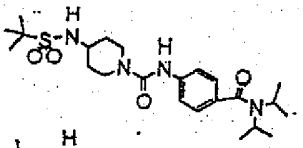
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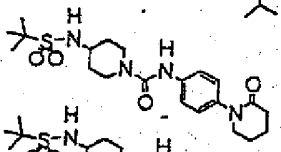
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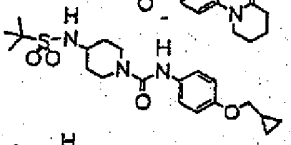
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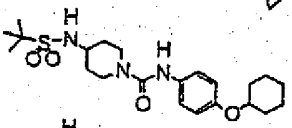
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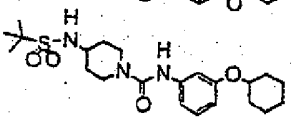
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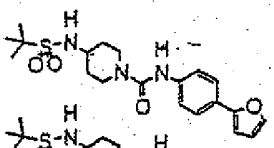
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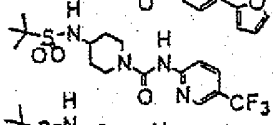
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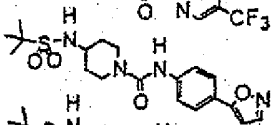
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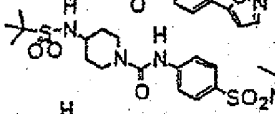
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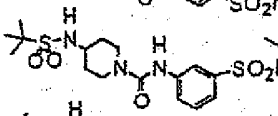
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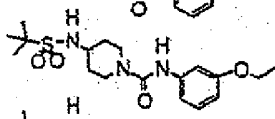
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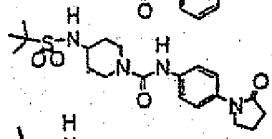
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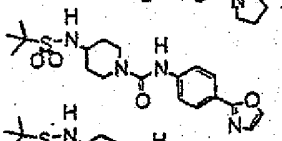
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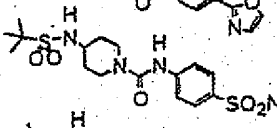
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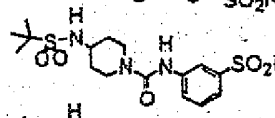
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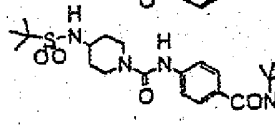
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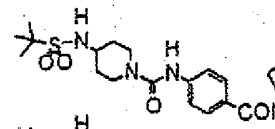
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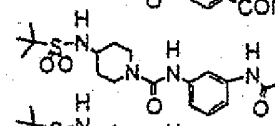
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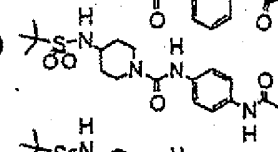
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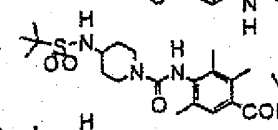
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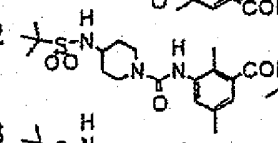
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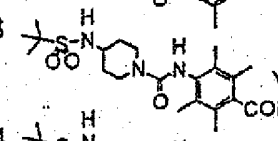
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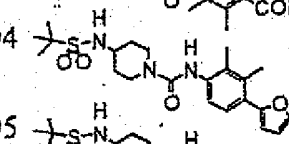
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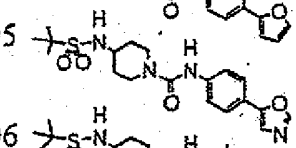
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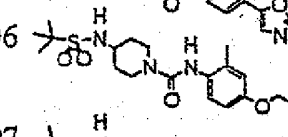
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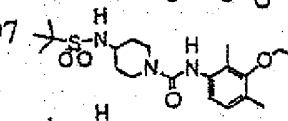
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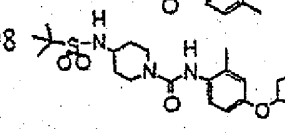
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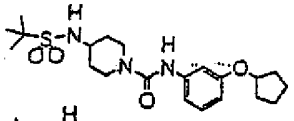
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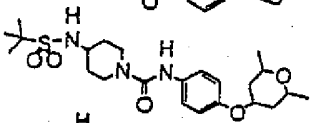
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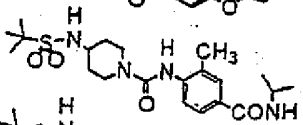
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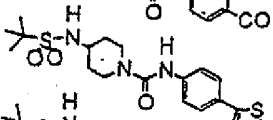
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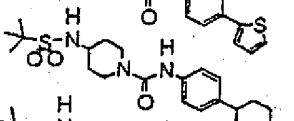
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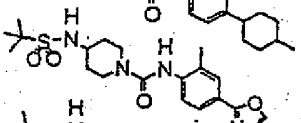
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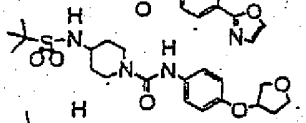
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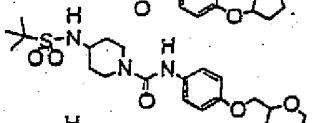
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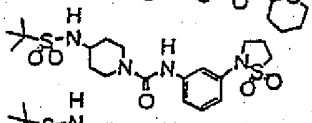
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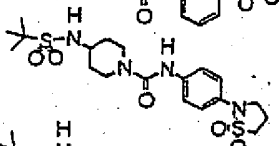
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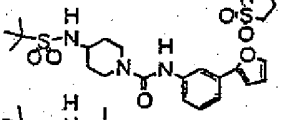
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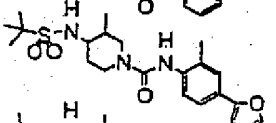
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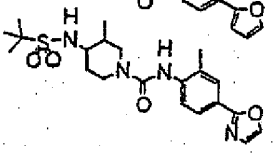
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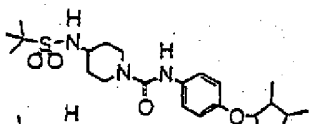
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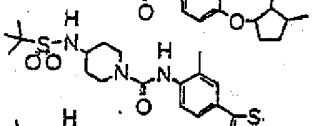
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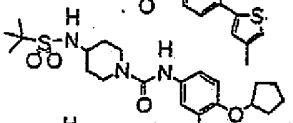
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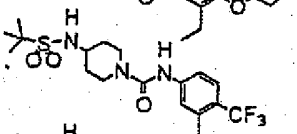
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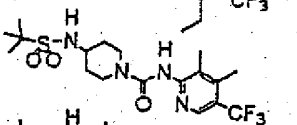
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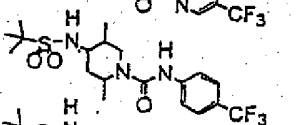
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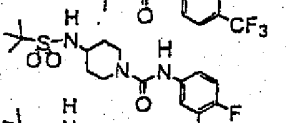
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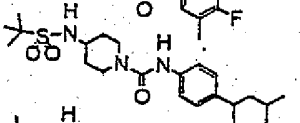
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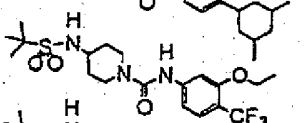
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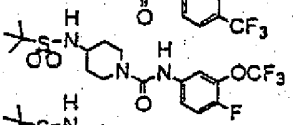
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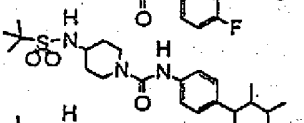
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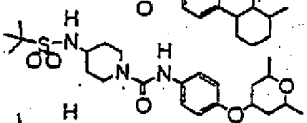
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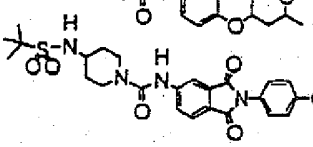
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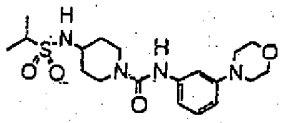
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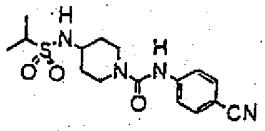
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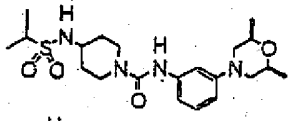
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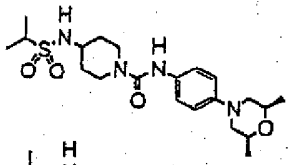
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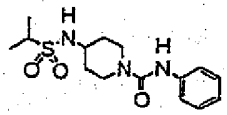
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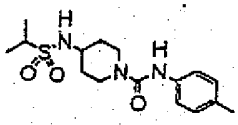
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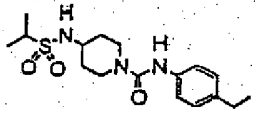
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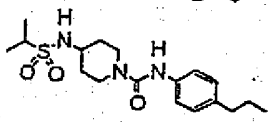
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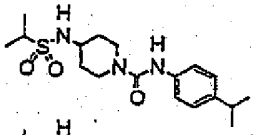
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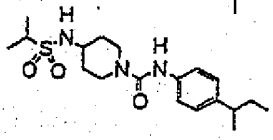
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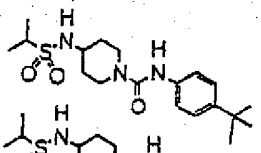
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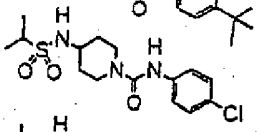
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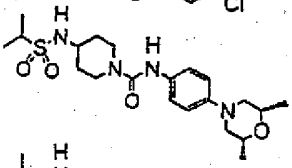
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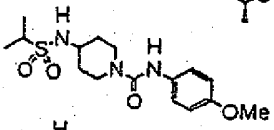
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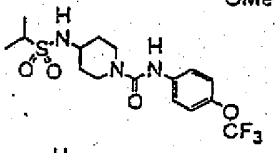
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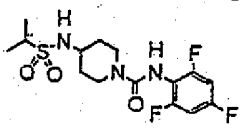
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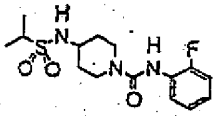
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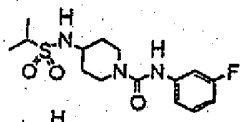
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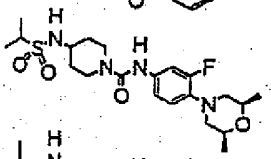
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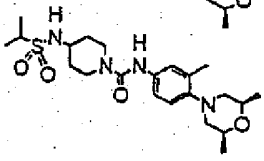
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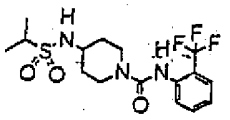
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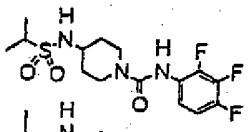
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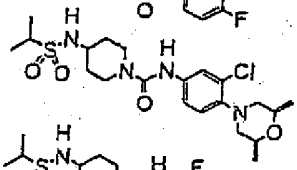
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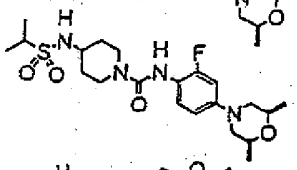
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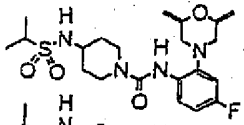
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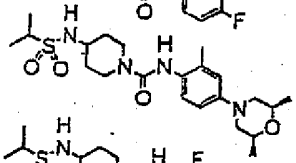
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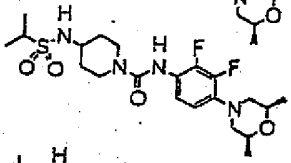
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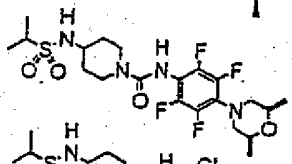
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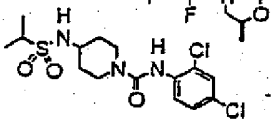
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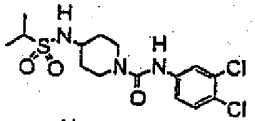
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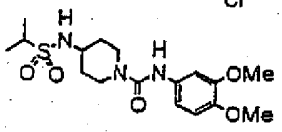
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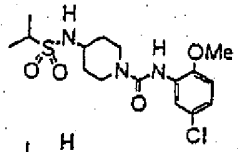
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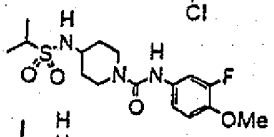
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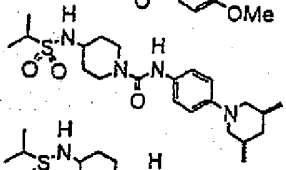
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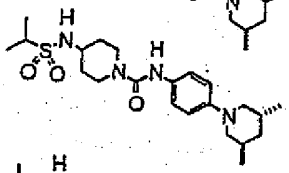
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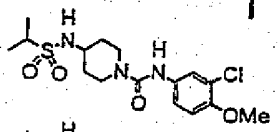
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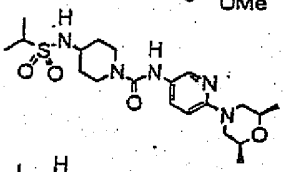
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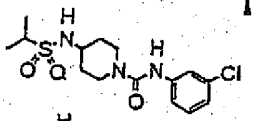
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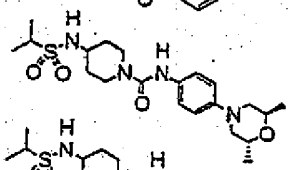
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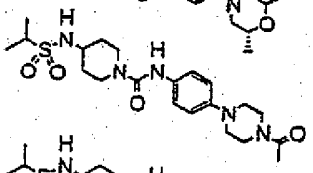
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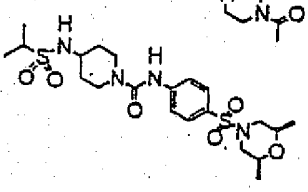
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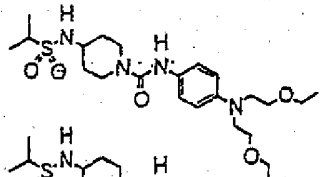
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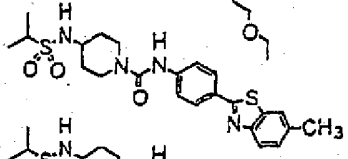
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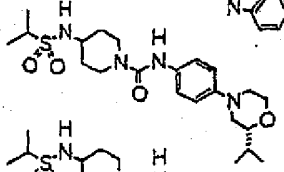
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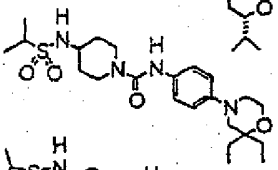
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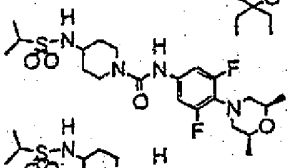
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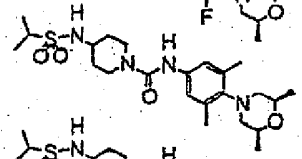
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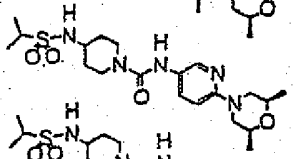
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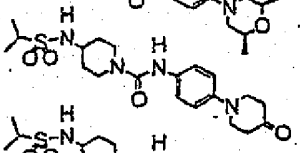
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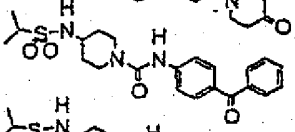
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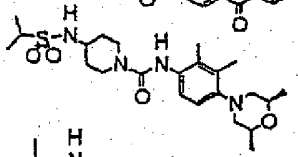
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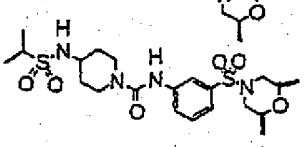
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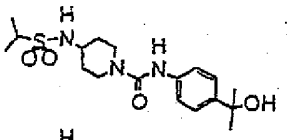
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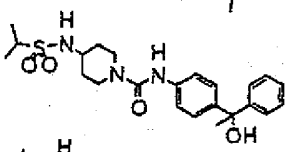
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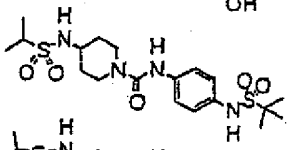
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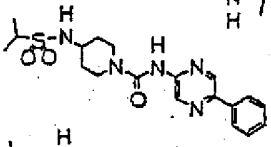
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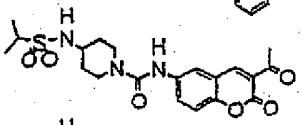
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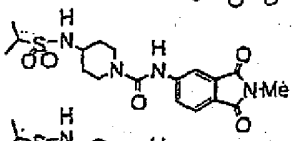
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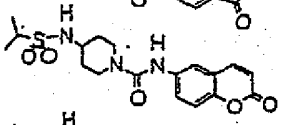
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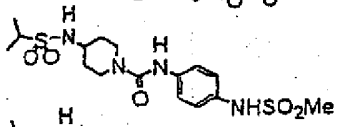
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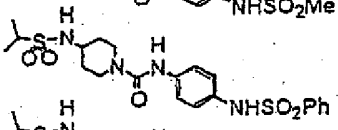
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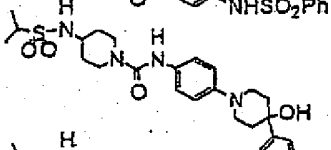
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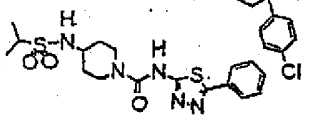
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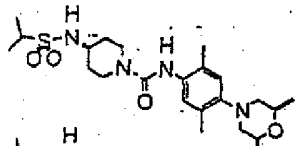
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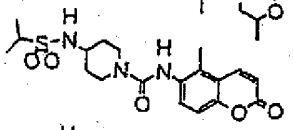
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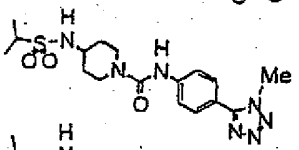
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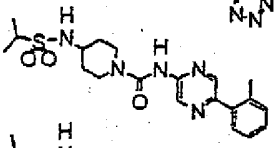
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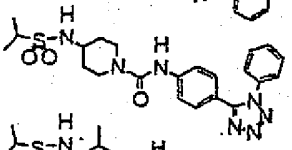
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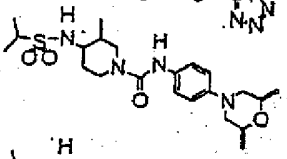
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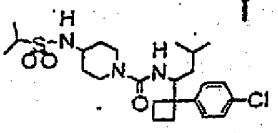
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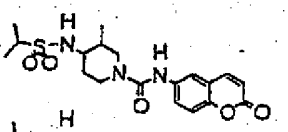
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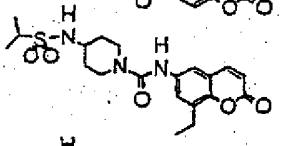
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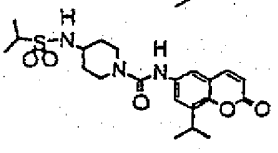
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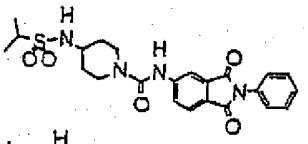
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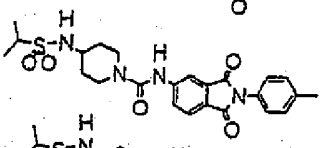
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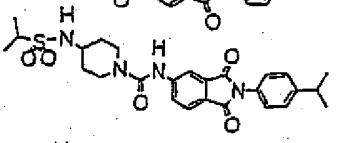
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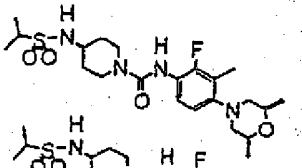
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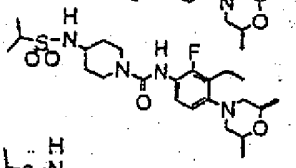
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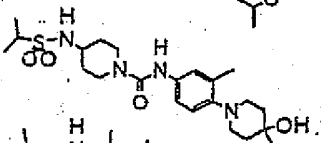
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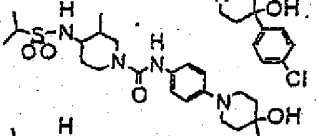
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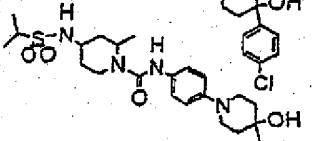
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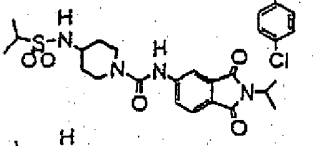
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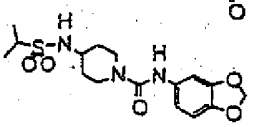
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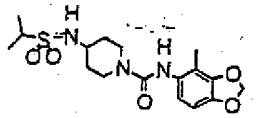
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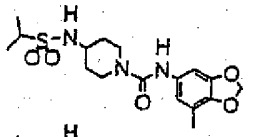
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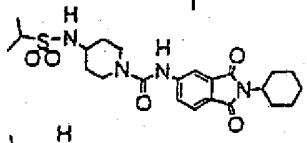
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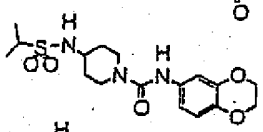
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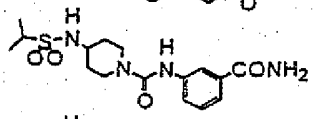
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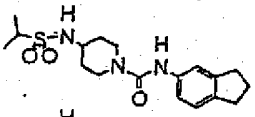
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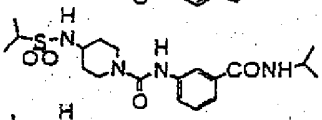
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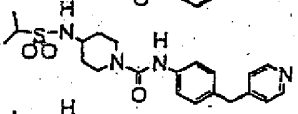
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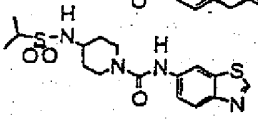
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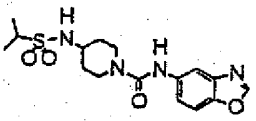
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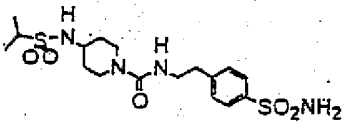
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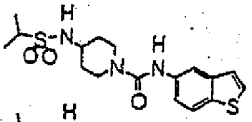
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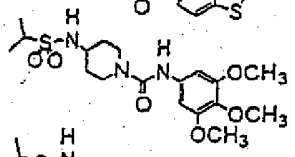
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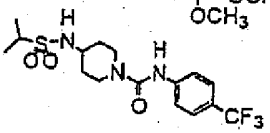
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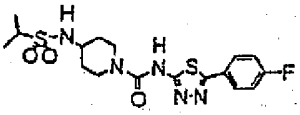
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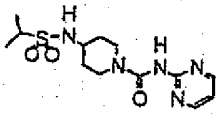
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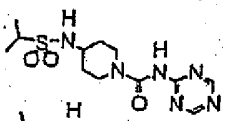
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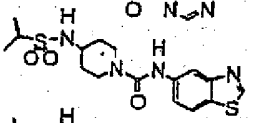
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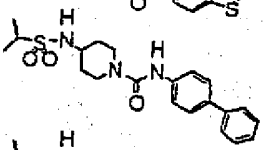
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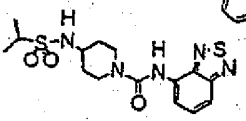
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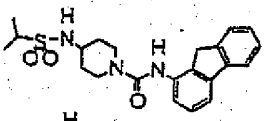
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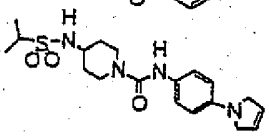
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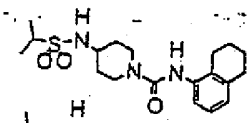
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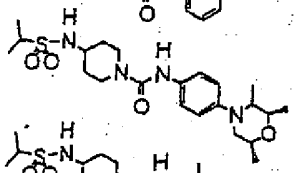
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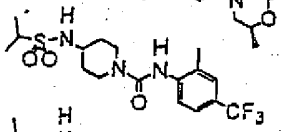
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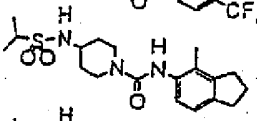
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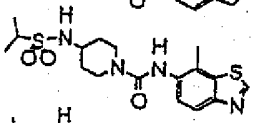
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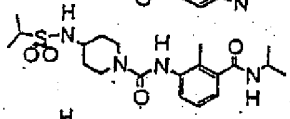
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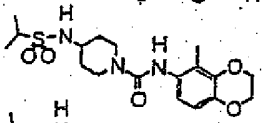
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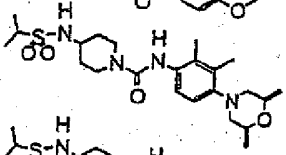
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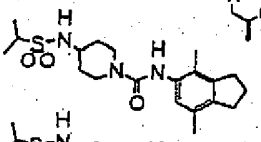
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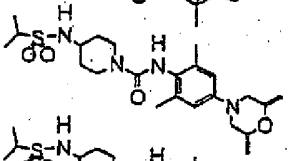
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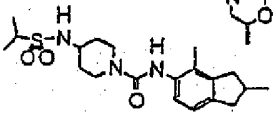
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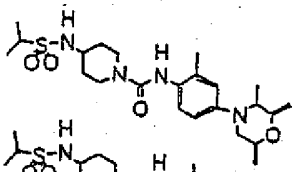
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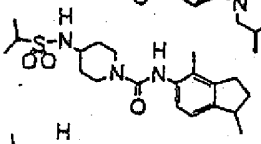
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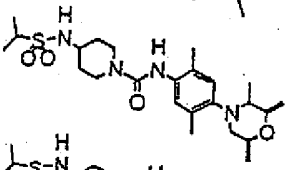
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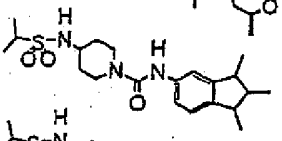
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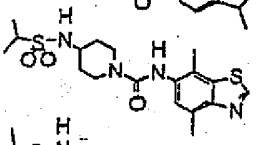
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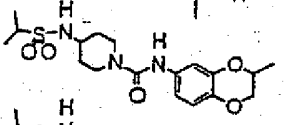
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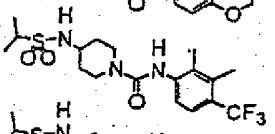
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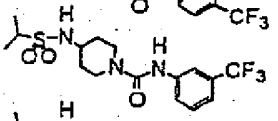
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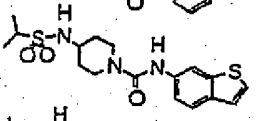
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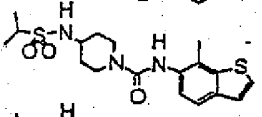
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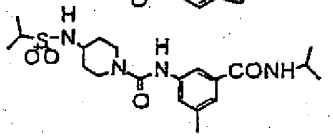
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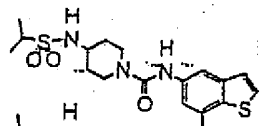
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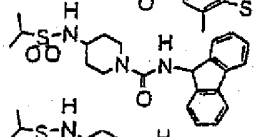
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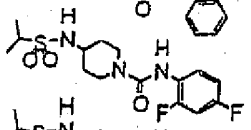
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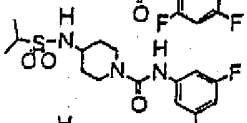
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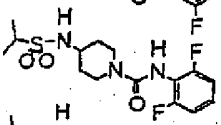
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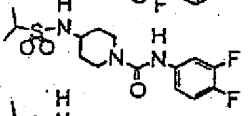
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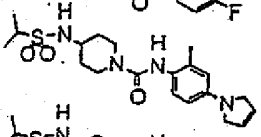
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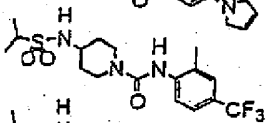
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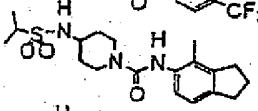
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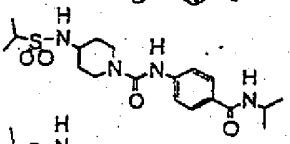
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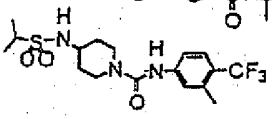
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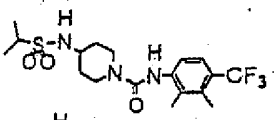
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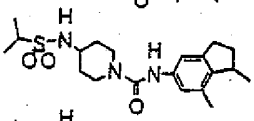
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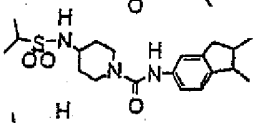
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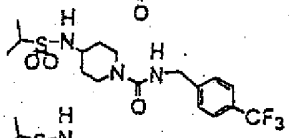
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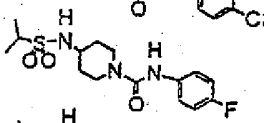
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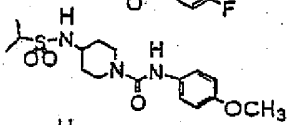
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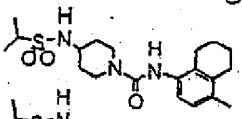
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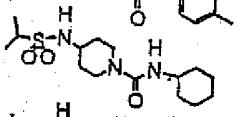
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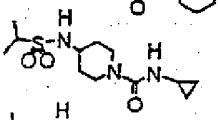
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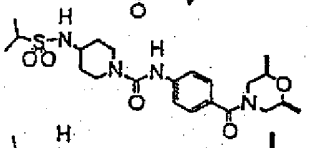
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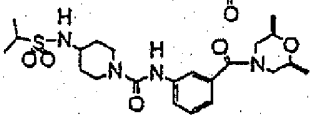
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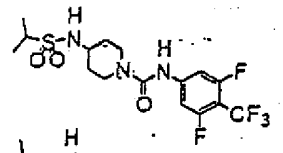
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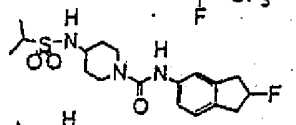
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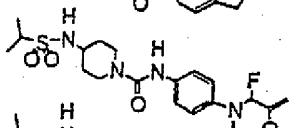
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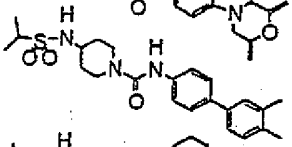
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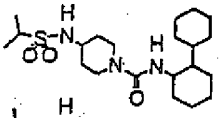
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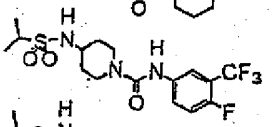
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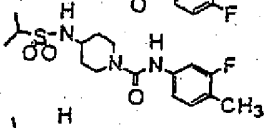
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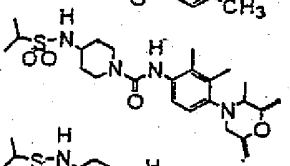
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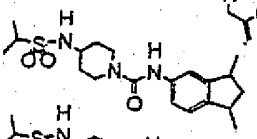
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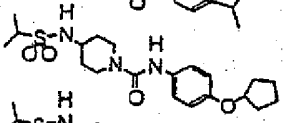
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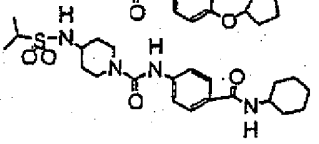
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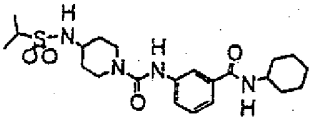
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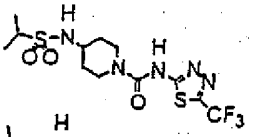
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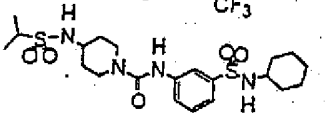
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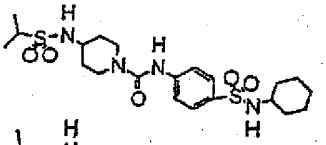
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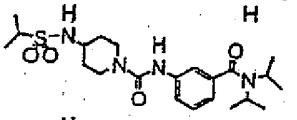
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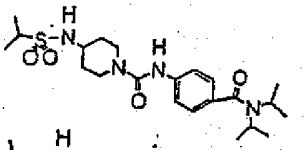
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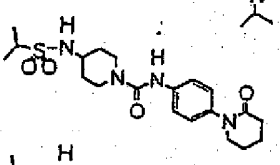
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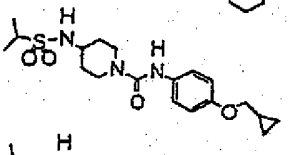
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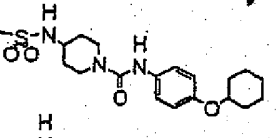
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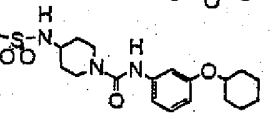
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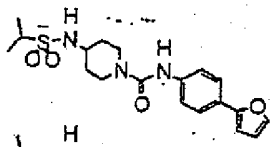
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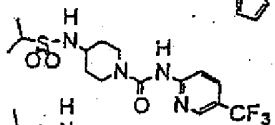
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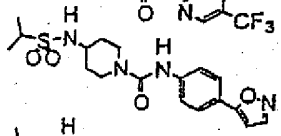
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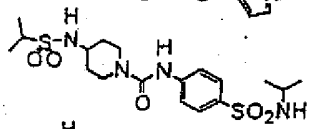
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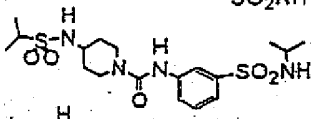
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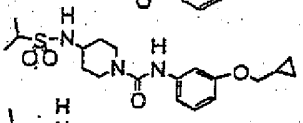
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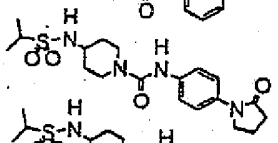
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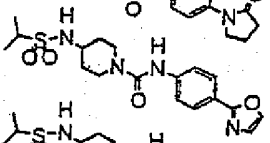
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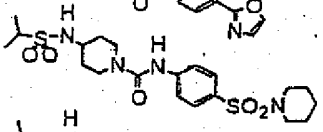
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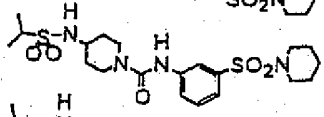
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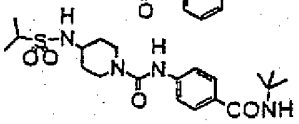
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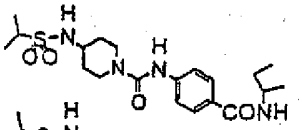
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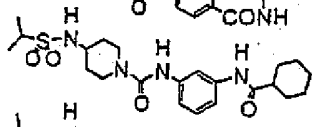
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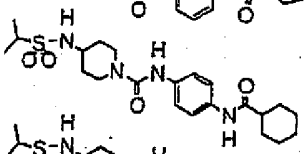
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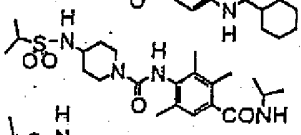
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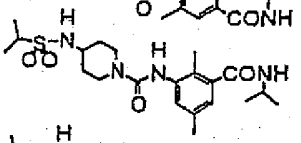
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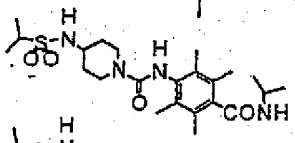
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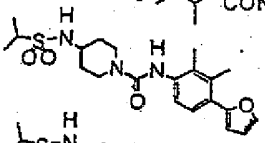
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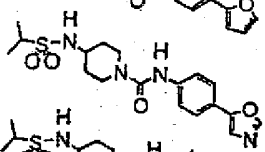
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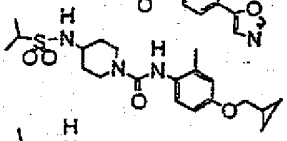
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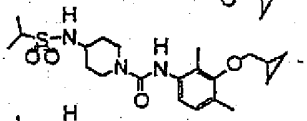
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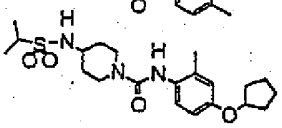
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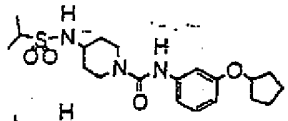
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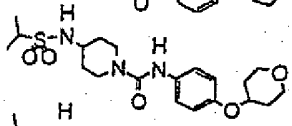
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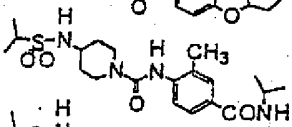
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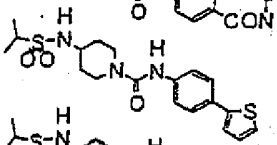
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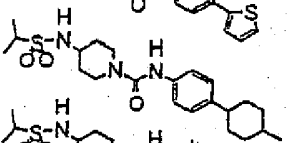
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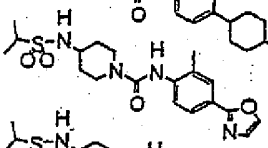
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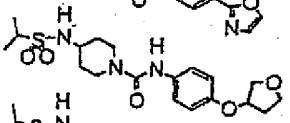
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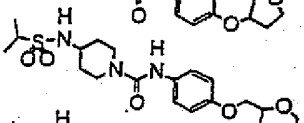
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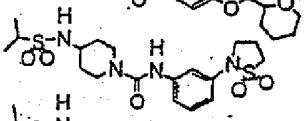
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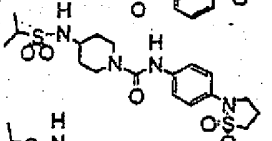
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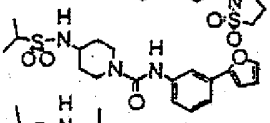
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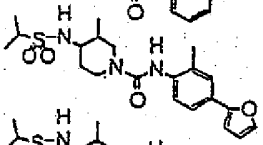
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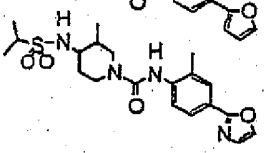
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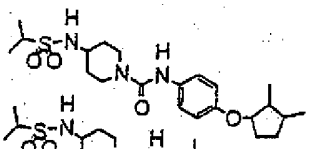
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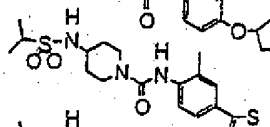
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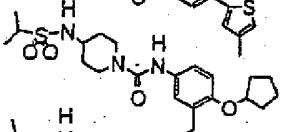
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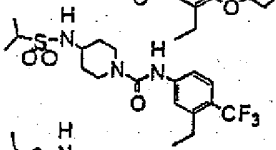
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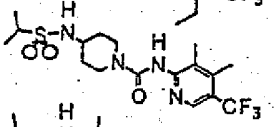
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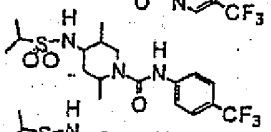
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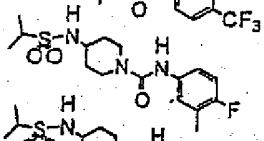
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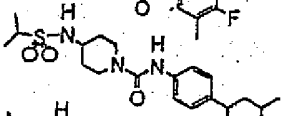
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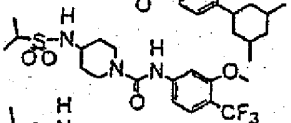
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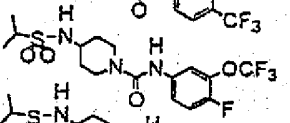
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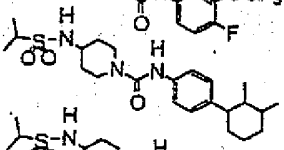
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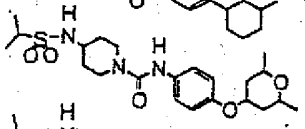
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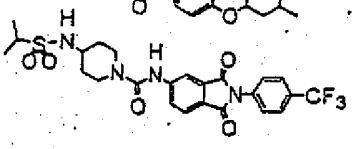
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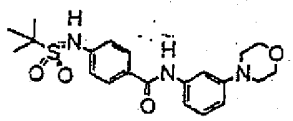
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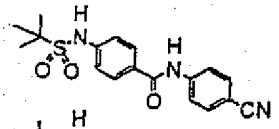
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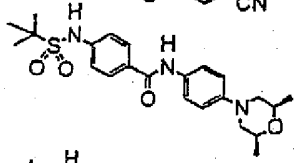
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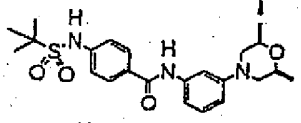
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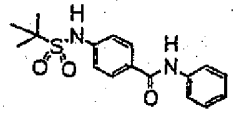
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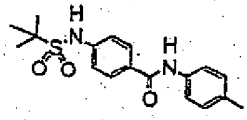
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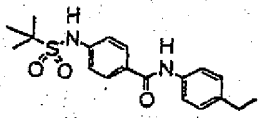
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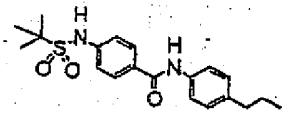
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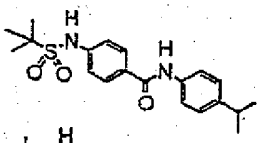
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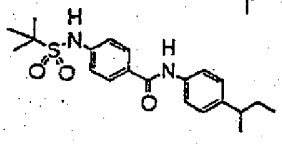
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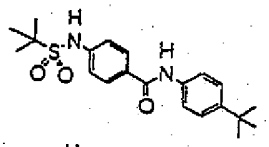
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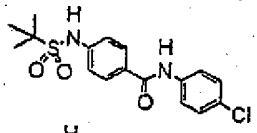
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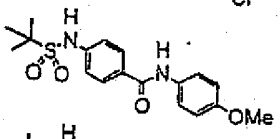
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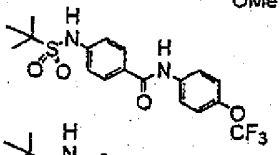
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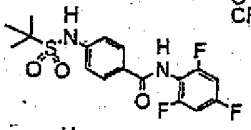
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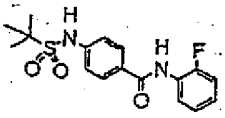
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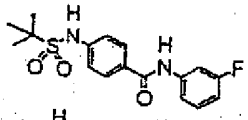
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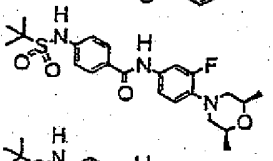
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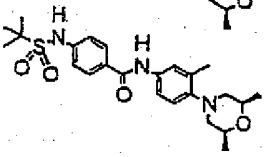
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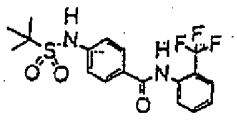
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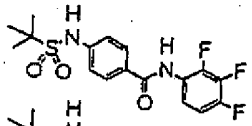
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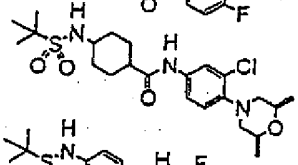
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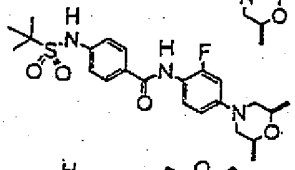
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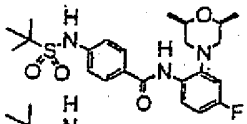
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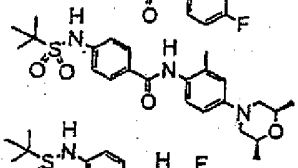
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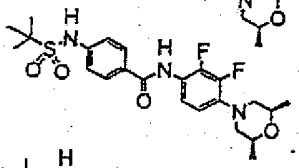
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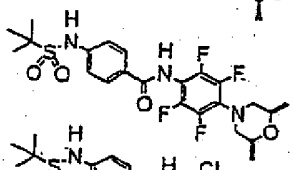
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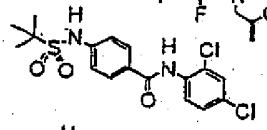
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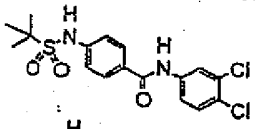
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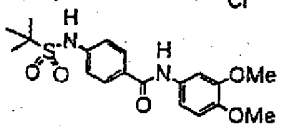
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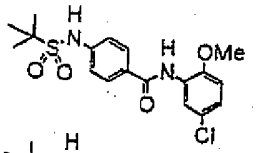
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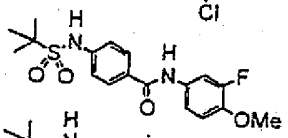
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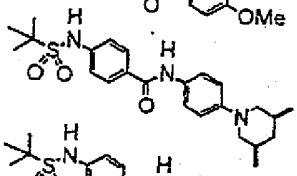
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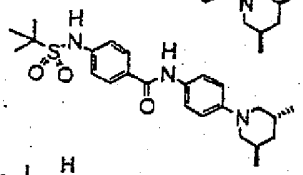
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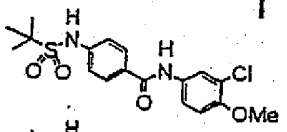
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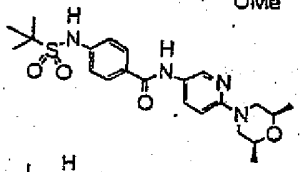
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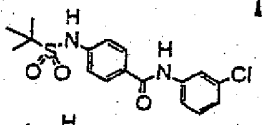
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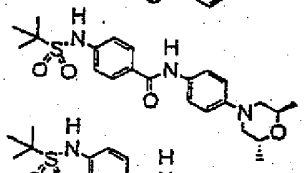
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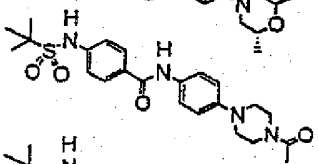
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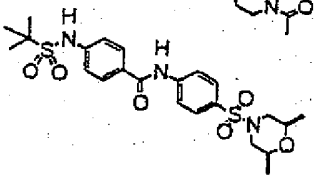
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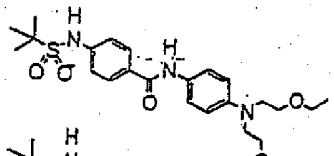
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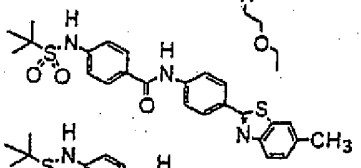
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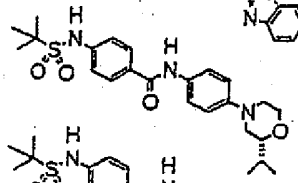
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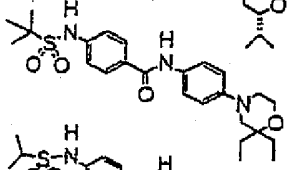
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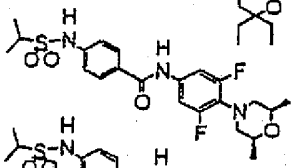
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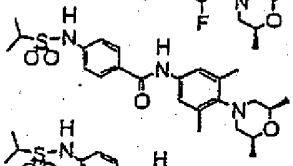
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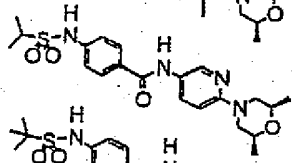
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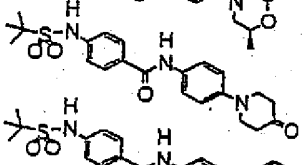
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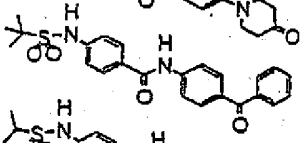
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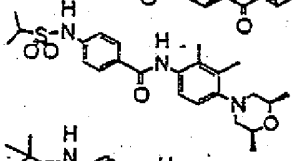
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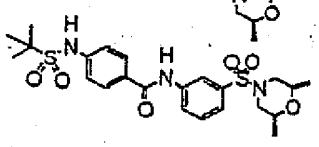
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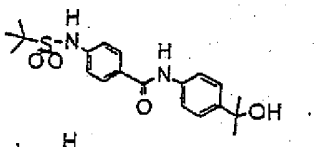
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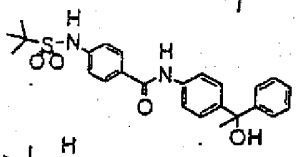
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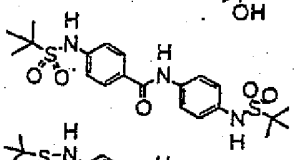
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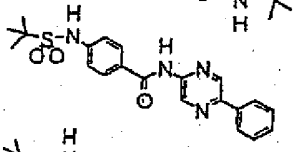
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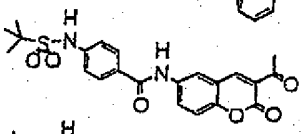
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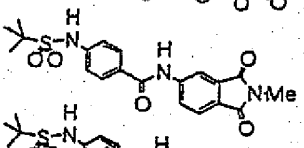
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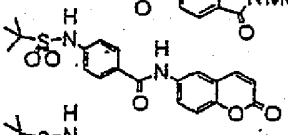
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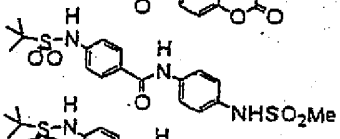
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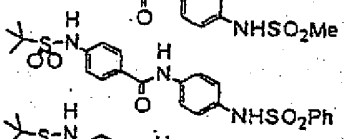
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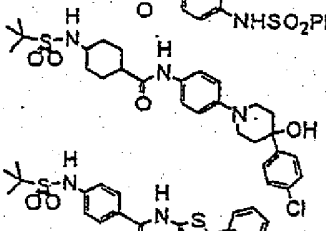
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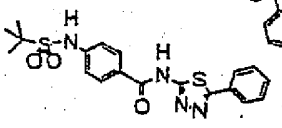
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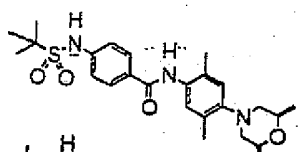
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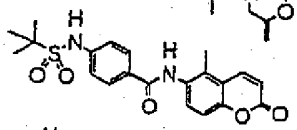
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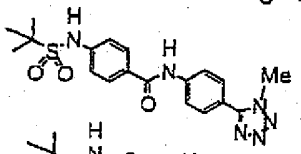
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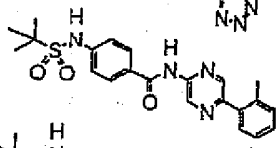
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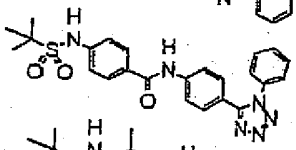
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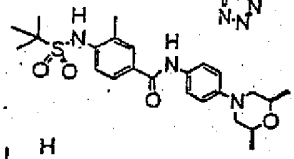
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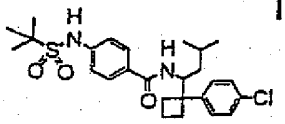
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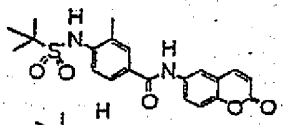
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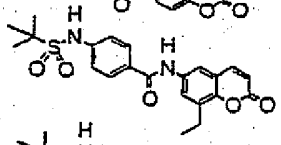
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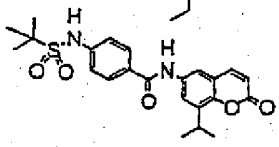
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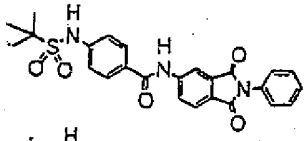
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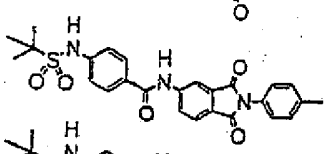
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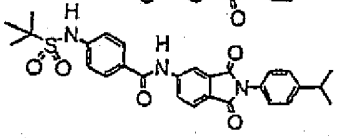
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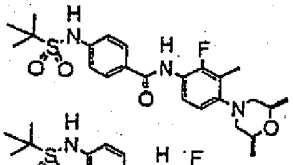
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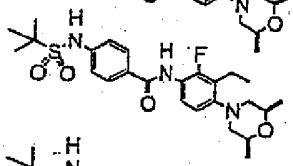
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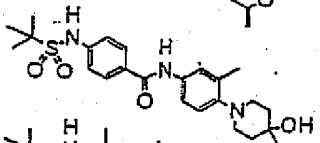
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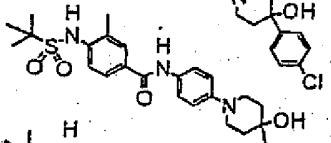
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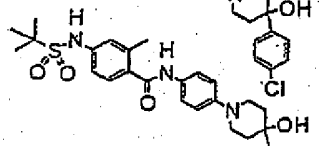
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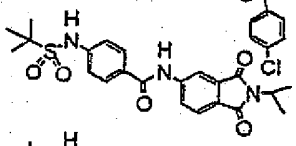
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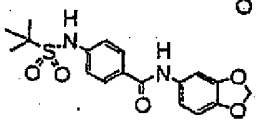
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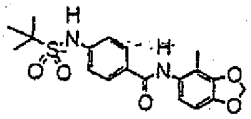
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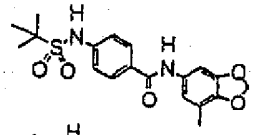
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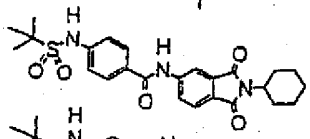
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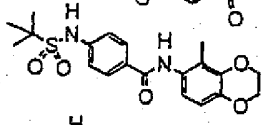
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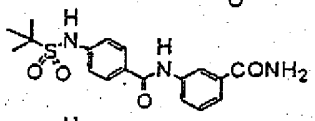
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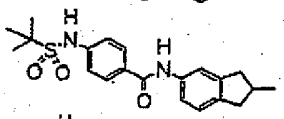
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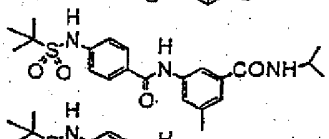
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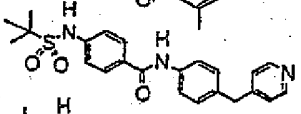
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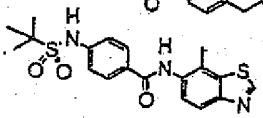
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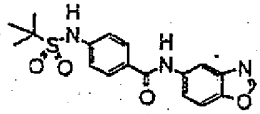
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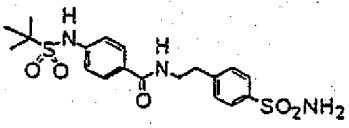
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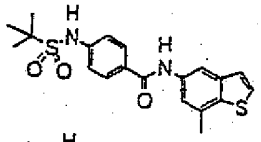
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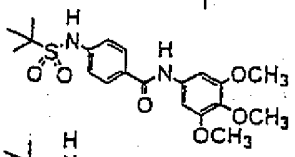
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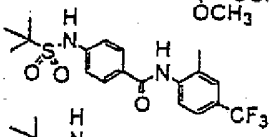
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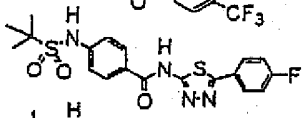
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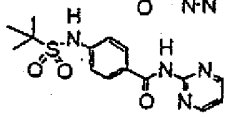
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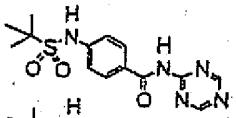
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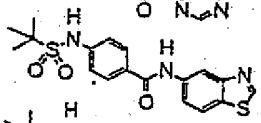
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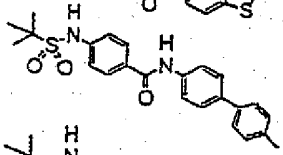
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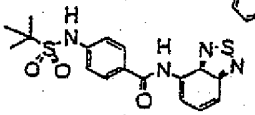
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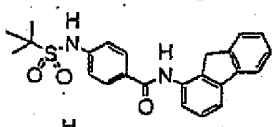
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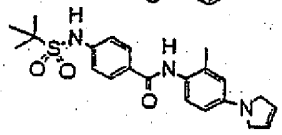
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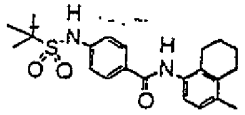
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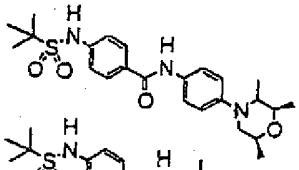
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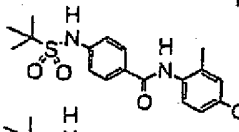
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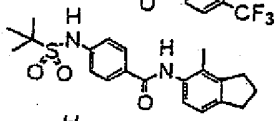
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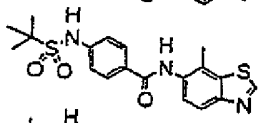
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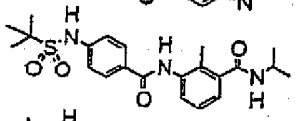
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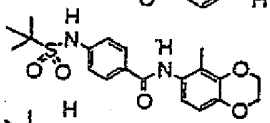
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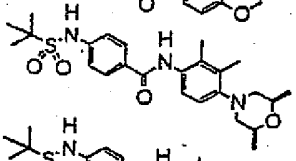
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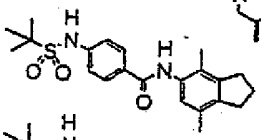
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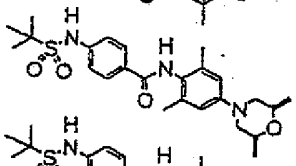
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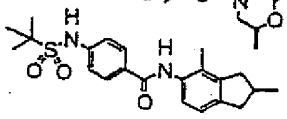
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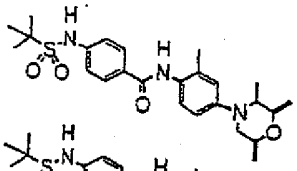
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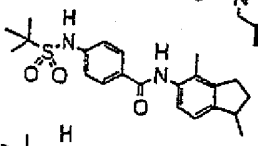
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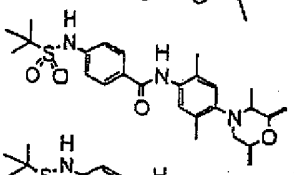
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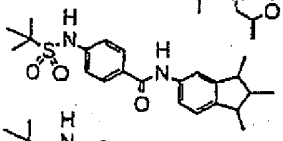
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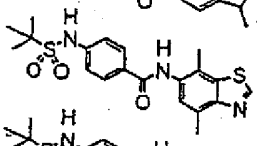
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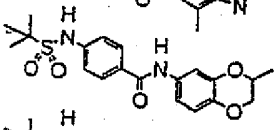
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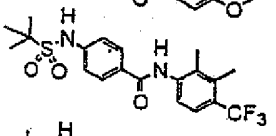
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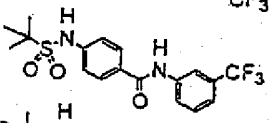
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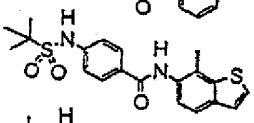
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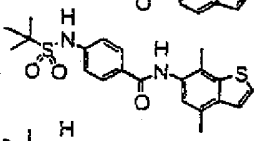
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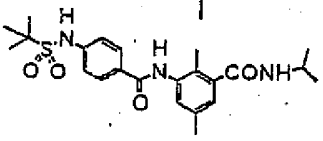
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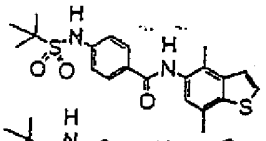
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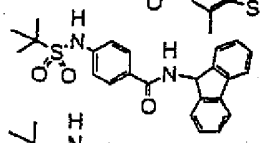
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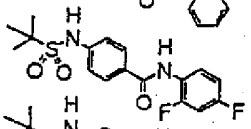
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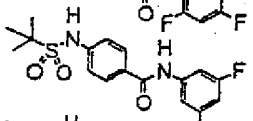
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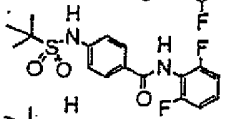
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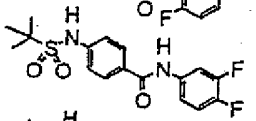
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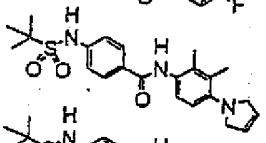
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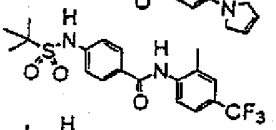
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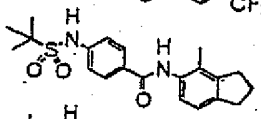
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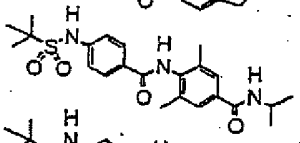
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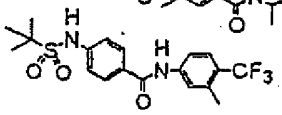
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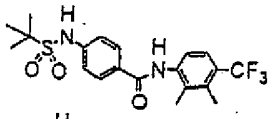
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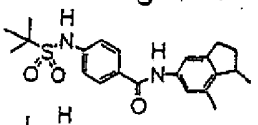
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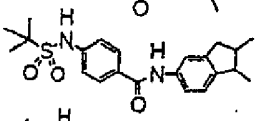
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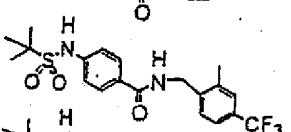
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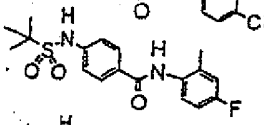
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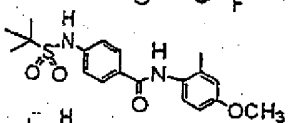
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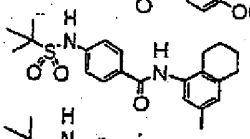
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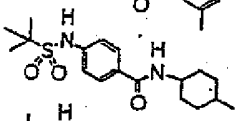
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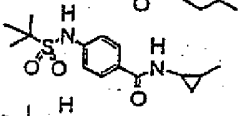
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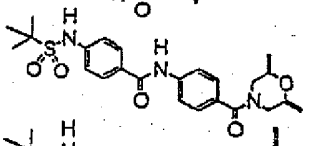
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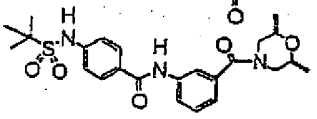
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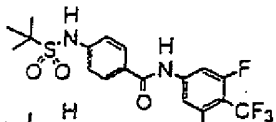
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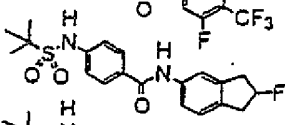
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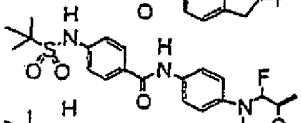
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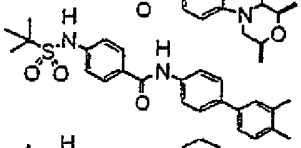
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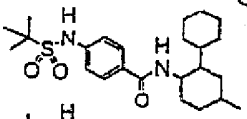
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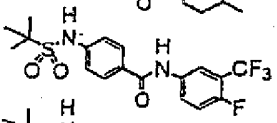
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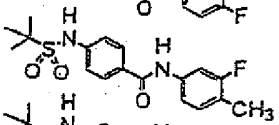
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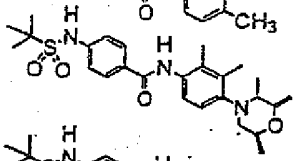
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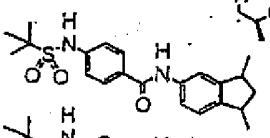
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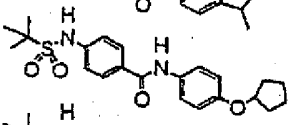
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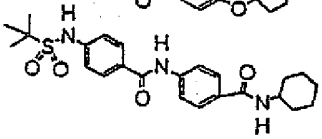
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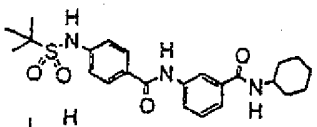
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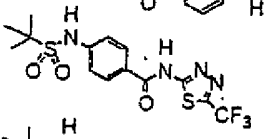
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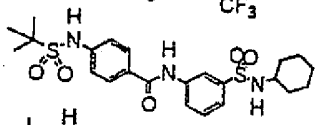
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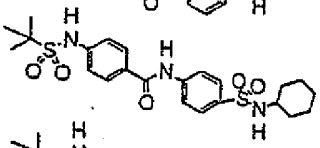
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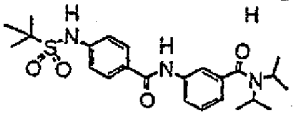
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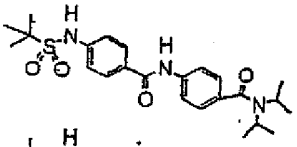
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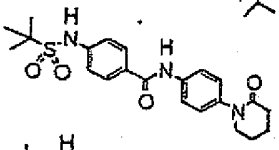
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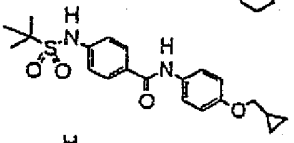
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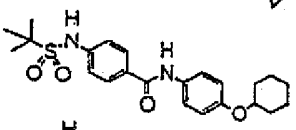
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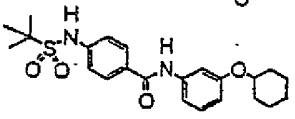
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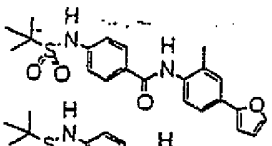
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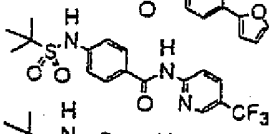
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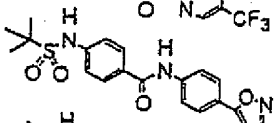
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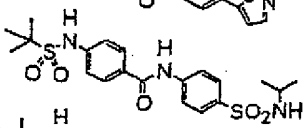
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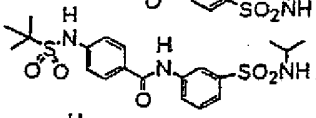
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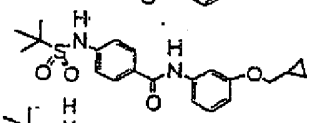
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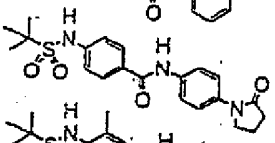
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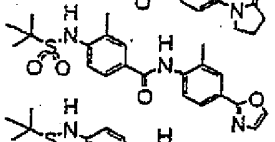
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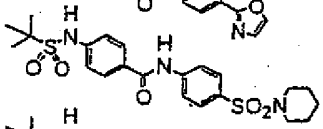
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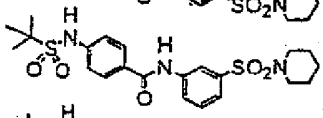
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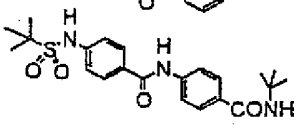
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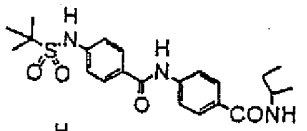
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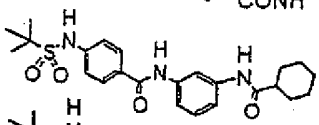
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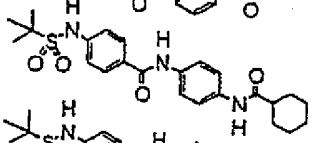
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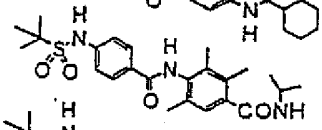
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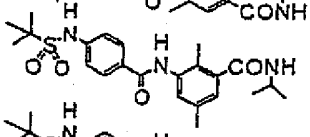
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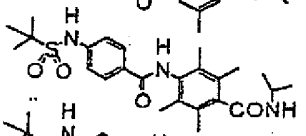
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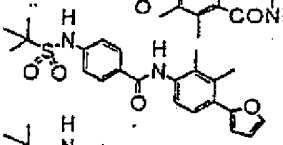
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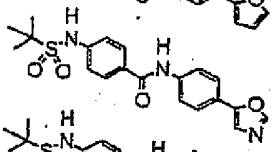
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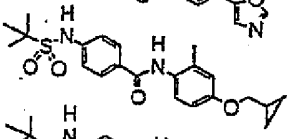
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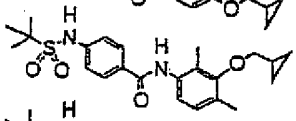
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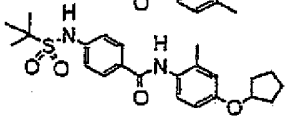
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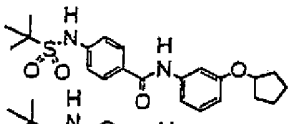
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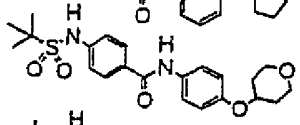
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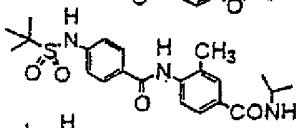
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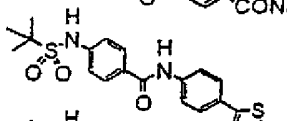
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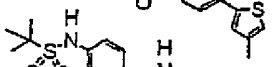
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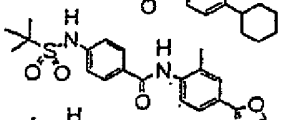
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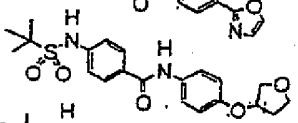
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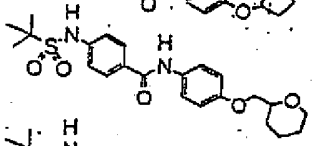
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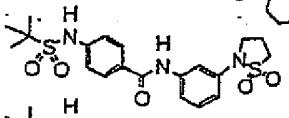
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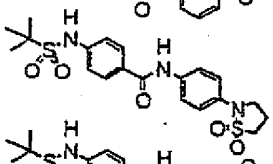
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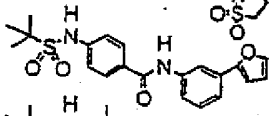
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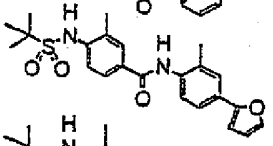
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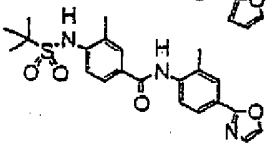
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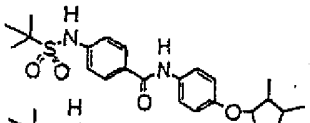
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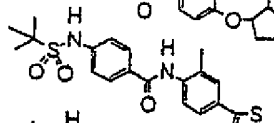
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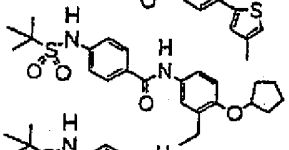
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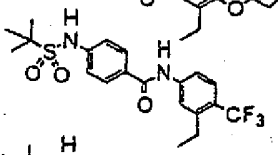
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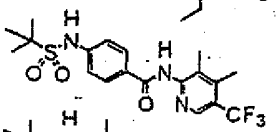
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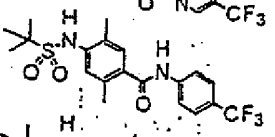
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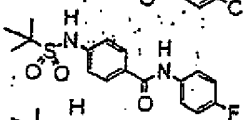
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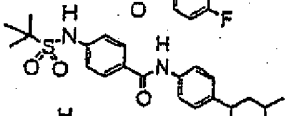
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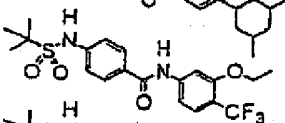
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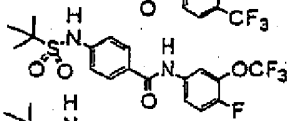
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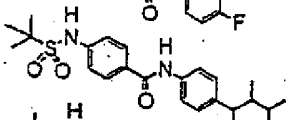
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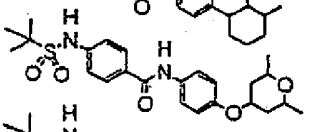
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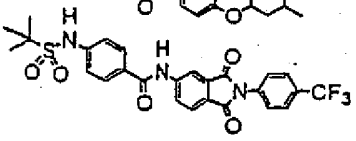
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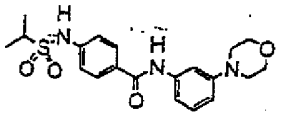
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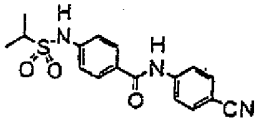
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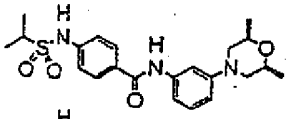
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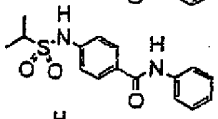
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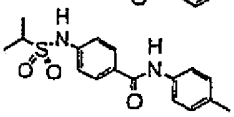
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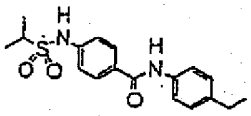
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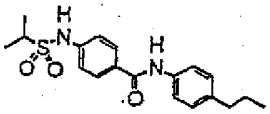
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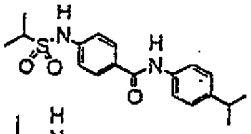
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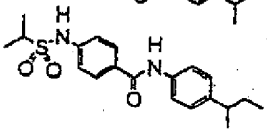
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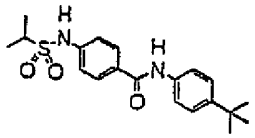
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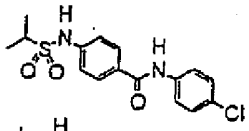
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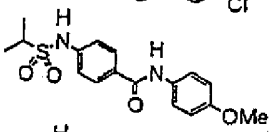
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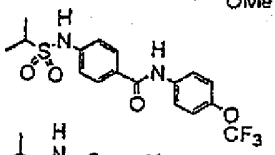
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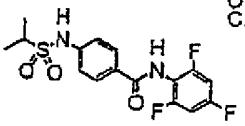
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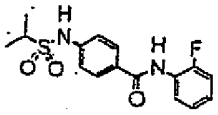
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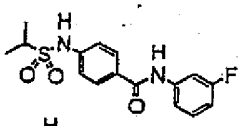
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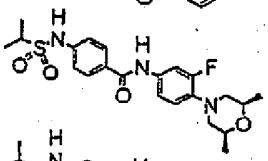
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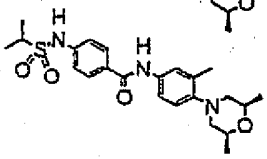
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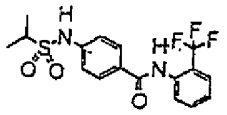
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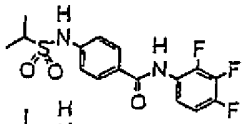
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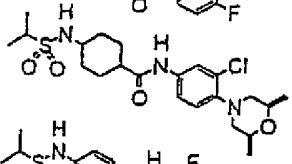
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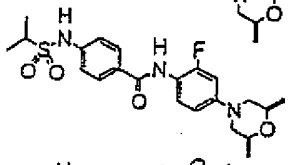
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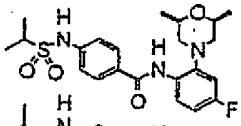
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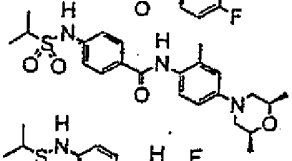
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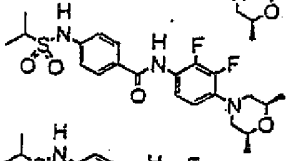
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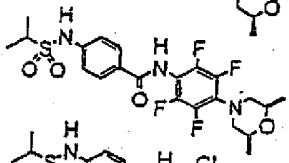
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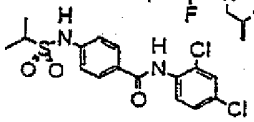
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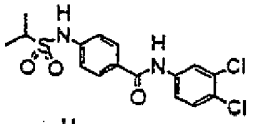
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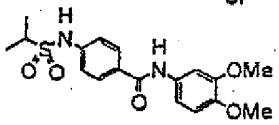
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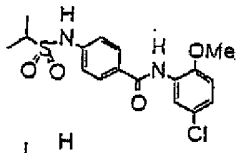
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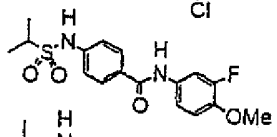
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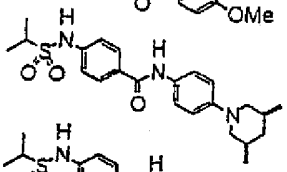
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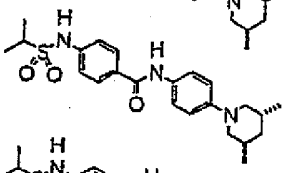
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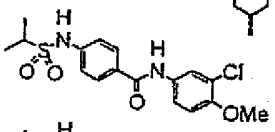
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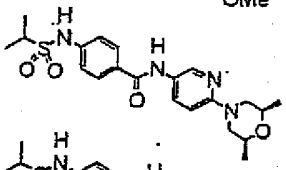
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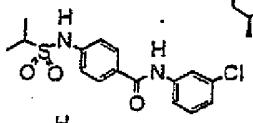
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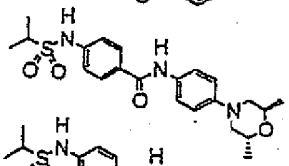
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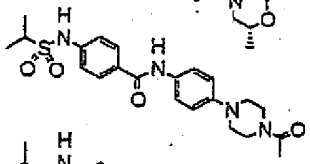
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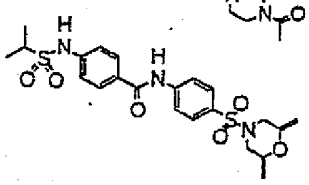
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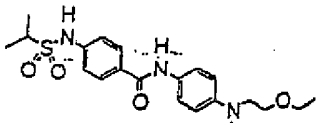
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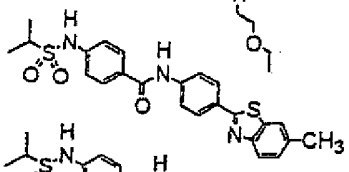
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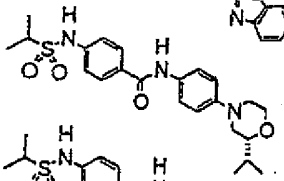
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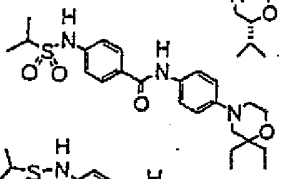
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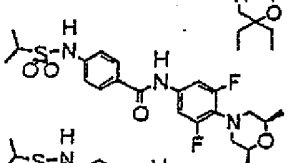
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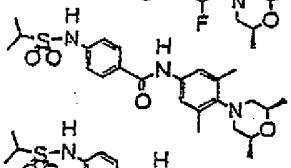
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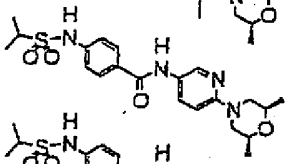
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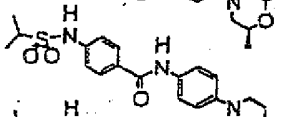
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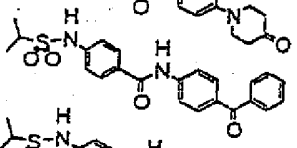
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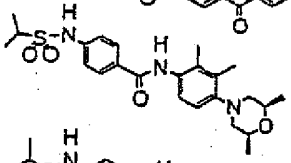
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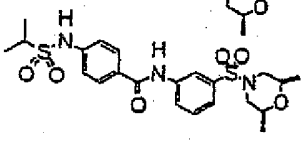
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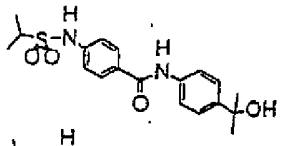
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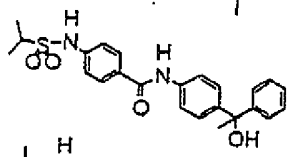
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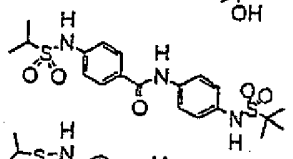
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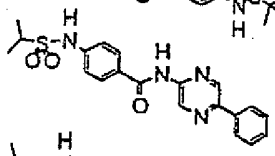
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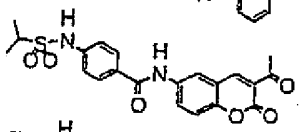
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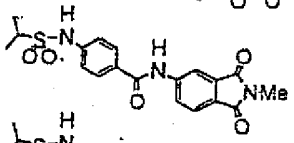
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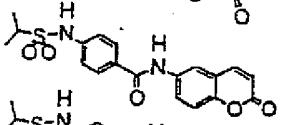
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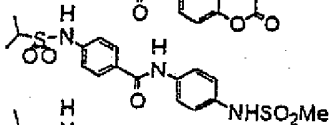
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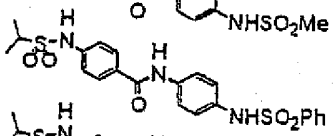
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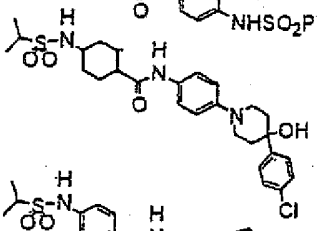
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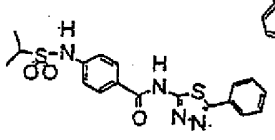
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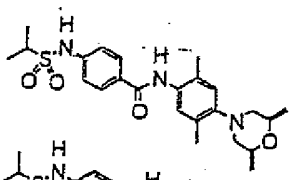
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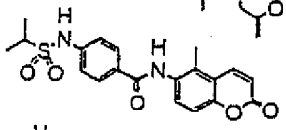
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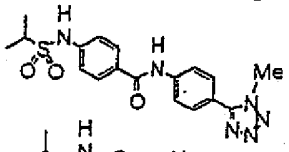
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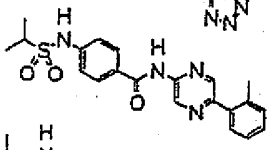
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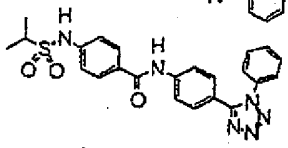
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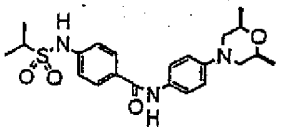
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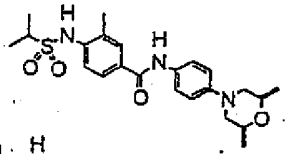
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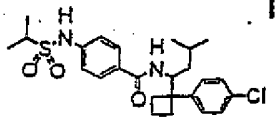
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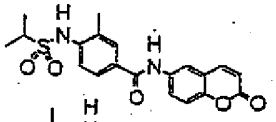
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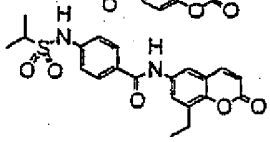
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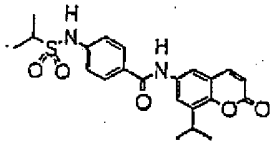
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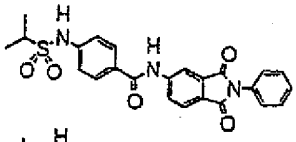
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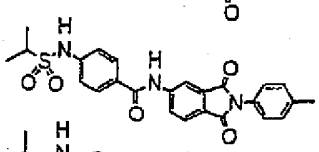
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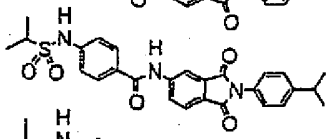
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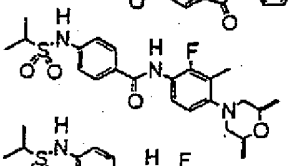
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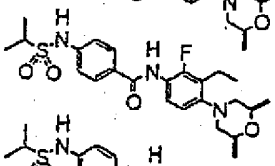
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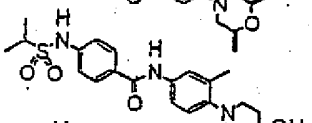
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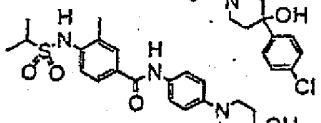
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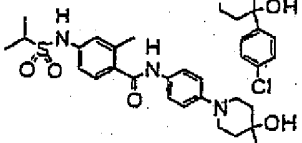
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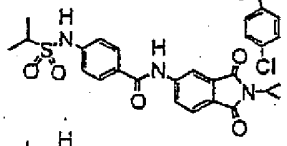
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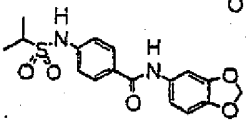
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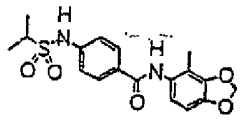
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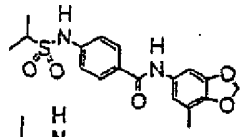
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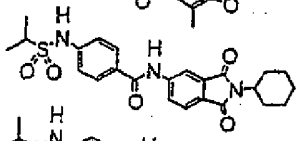
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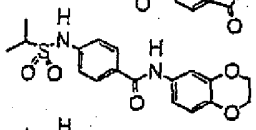
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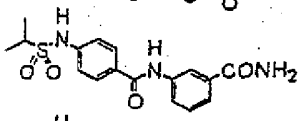
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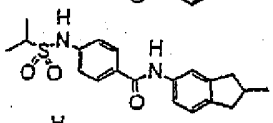
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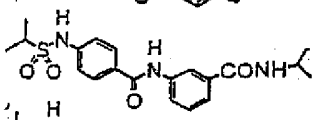
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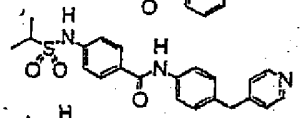
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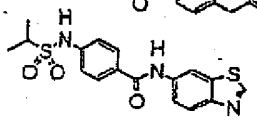
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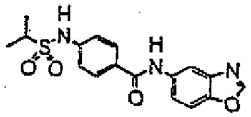
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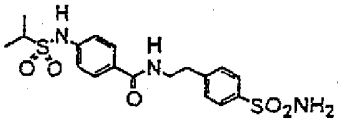
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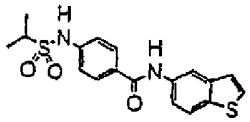
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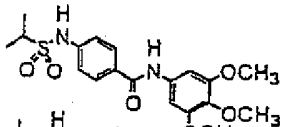
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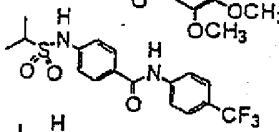
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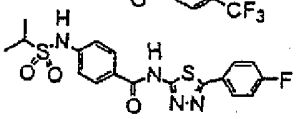
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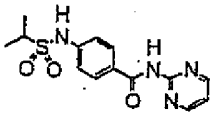
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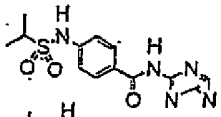
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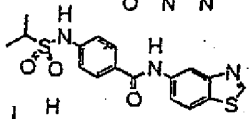
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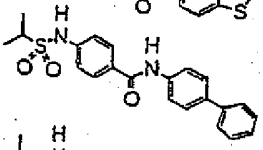
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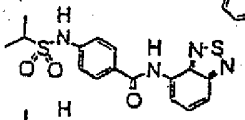
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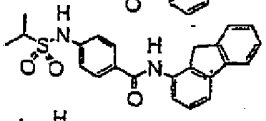
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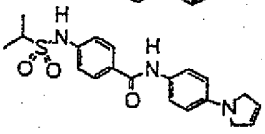
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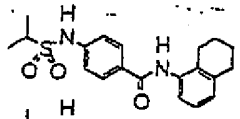
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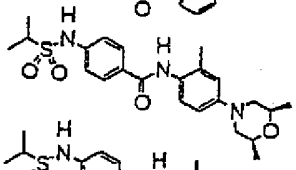
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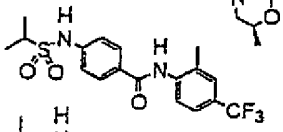
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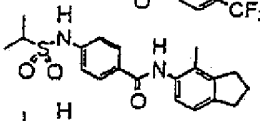
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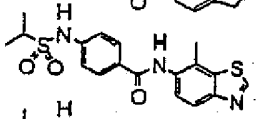
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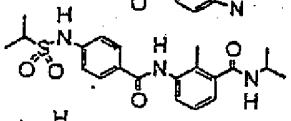
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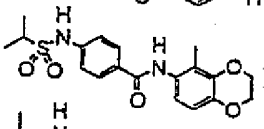
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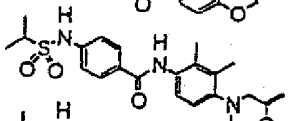
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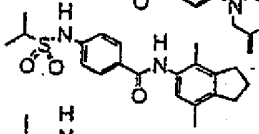
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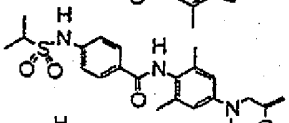
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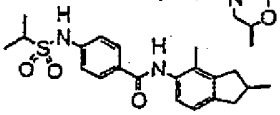
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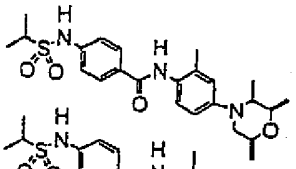
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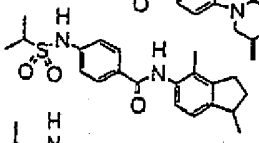
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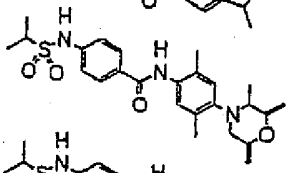
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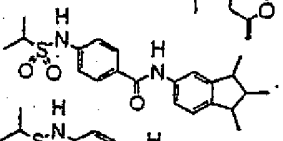
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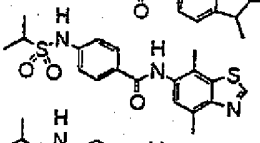
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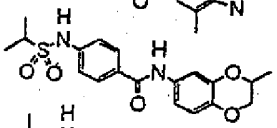
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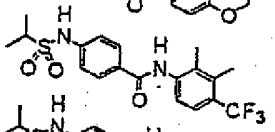
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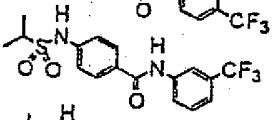
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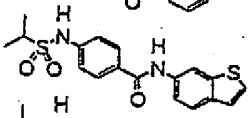
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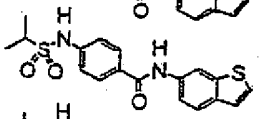
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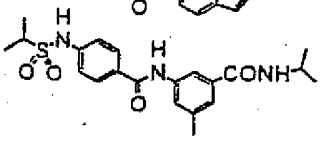
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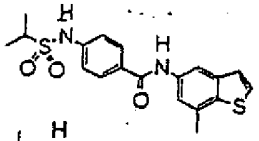
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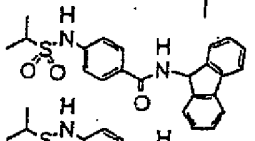
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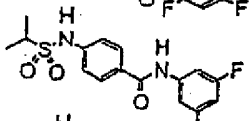
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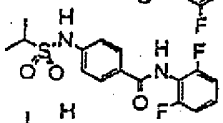
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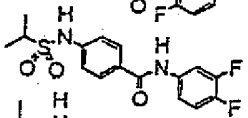
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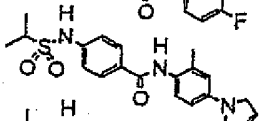
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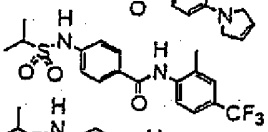
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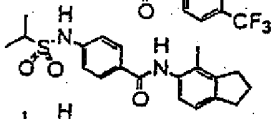
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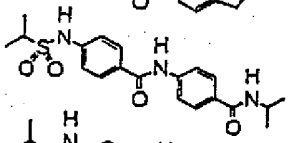
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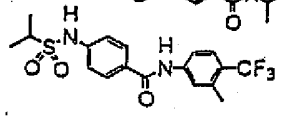
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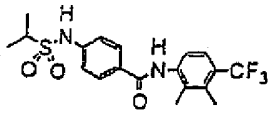
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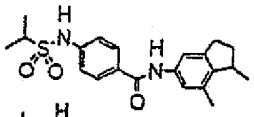
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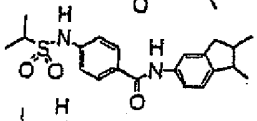
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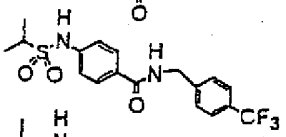
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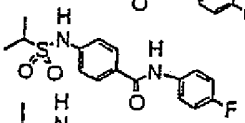
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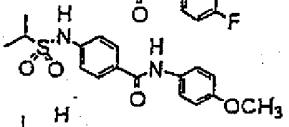
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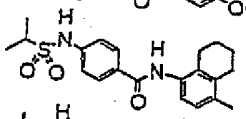
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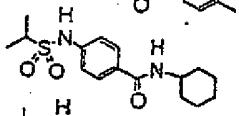
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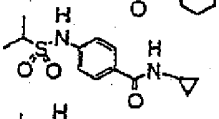
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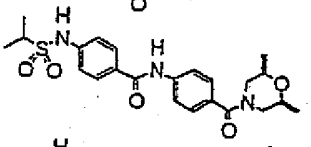
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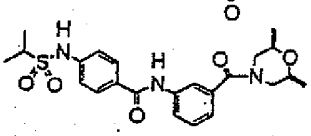
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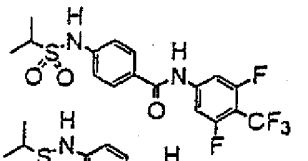
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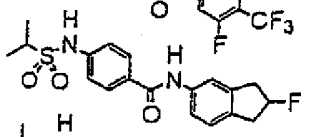
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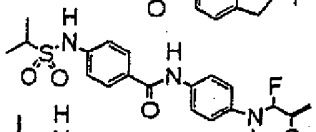
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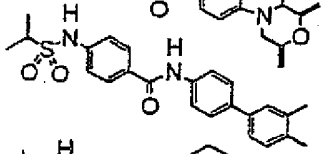
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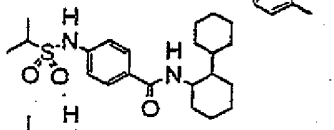
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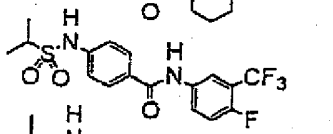
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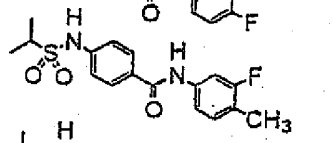
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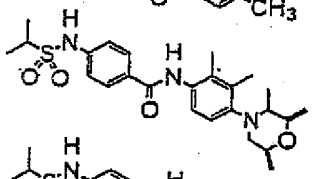
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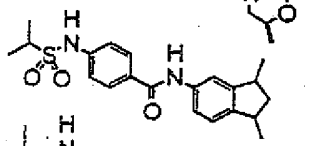
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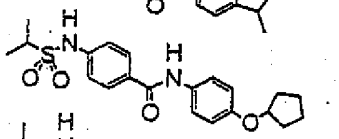
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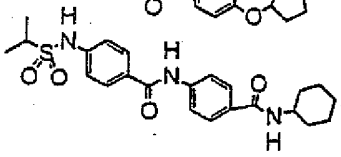
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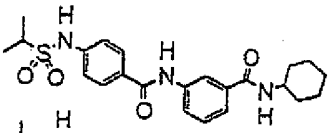
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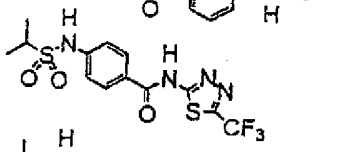
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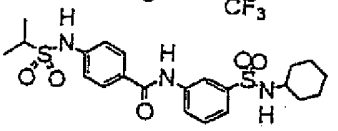
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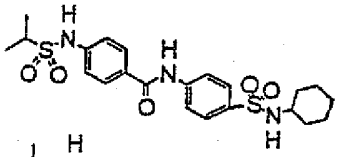
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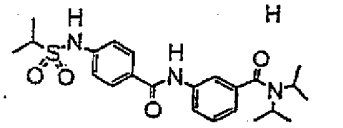
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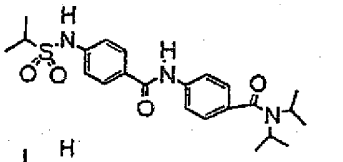
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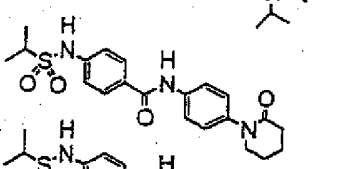
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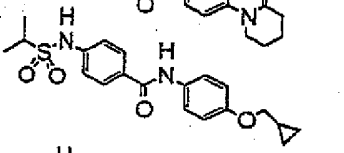
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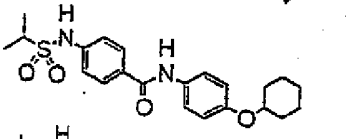
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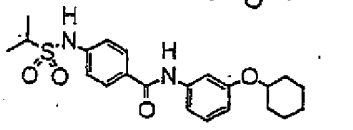
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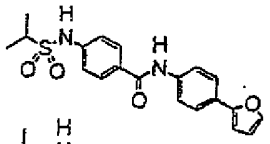
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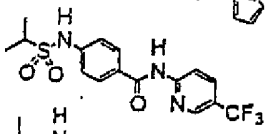
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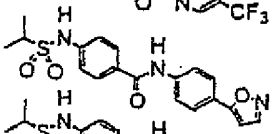
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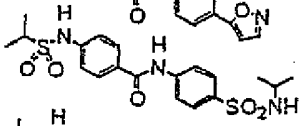
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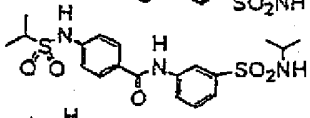
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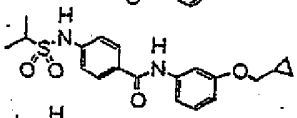
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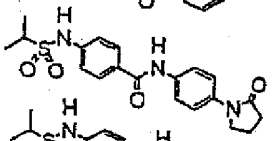
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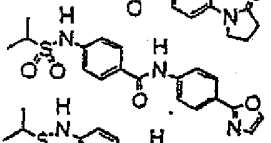
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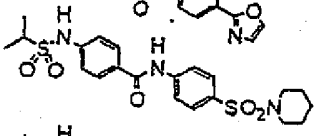
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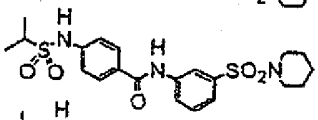
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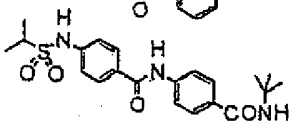
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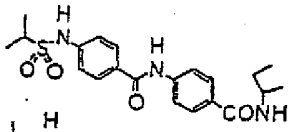
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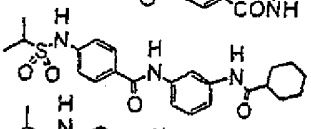
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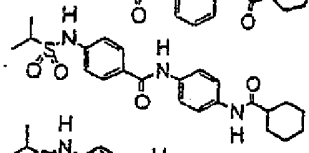
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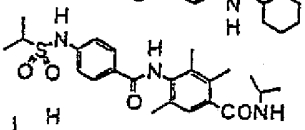
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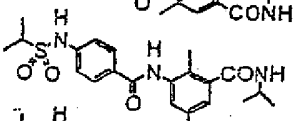
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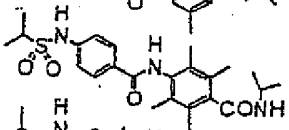
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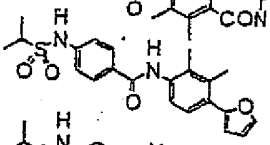
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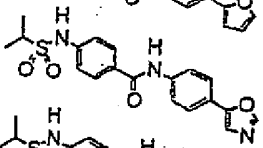
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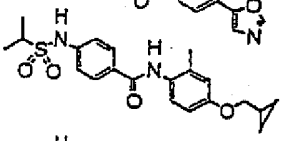
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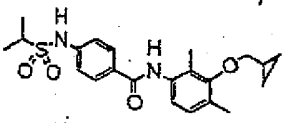
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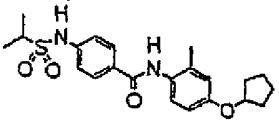
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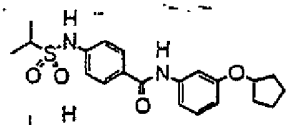
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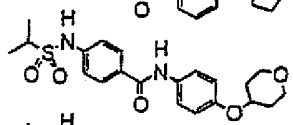
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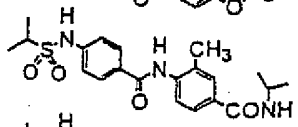
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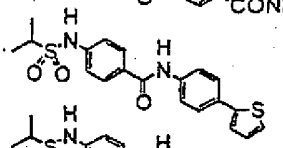
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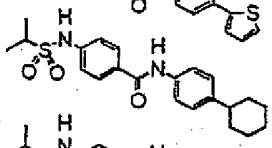
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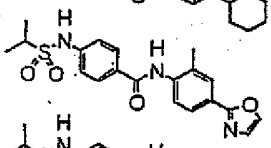
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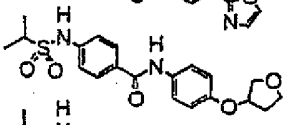
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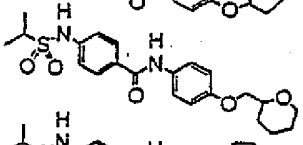
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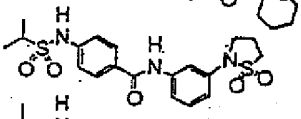
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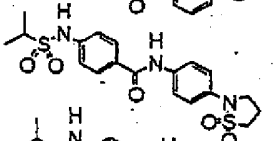
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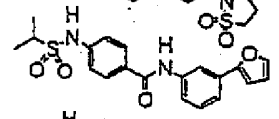
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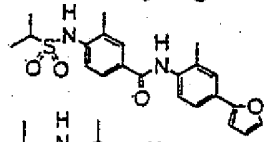
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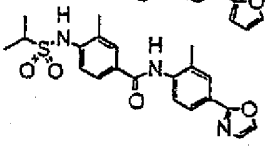
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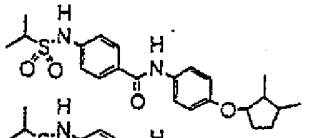
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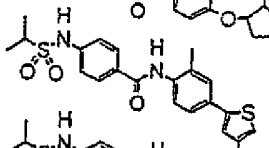
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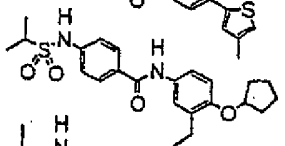
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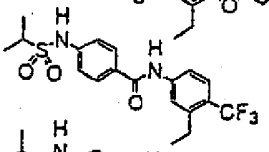
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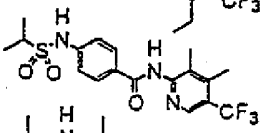
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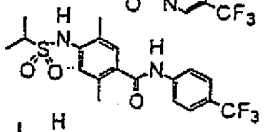
Ih-212 

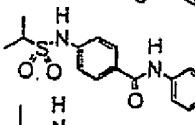
Ih-213 

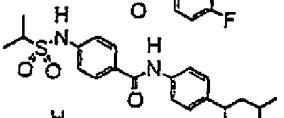
Ih-214 

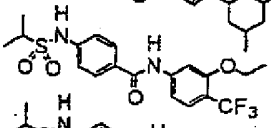
Ih-215 

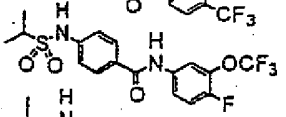
Ih-216 

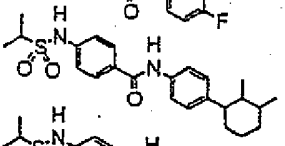
Ih-219 

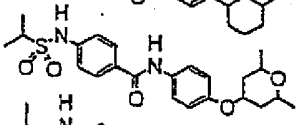
Ih-220 

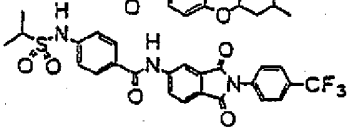
Ih-221 

Ih-222 

Ih-223 

Ih-224 

Ih-225 

Ih-226 

I-2

RMN de ^{1}H-NMR ($CDCl_3$) δ ppm: 0,94 (t, 3H, J = 7,5 Hz), 1,34-1,44 (m, 2H), 1,40 (d, 6H, J = 6,6 Hz), 1,59-1,68 (m, 2H), 2,69 (t, 2H, J = 7,8 Hz), 3,24-3,35 (m, 1H), 6,49

(s, 1H), 7,23-7,32 (m, 4H), 7,6 (d, 2H, J = 8,7 Hz), 7,79 (d, 2H, J = 8,1 Hz), 7,85 (s, 1H).

I-3

RMN de ^1H ($CDCl_3$) δ ppm: 0,92 (t, 3H, J = 7,2 Hz), 1,30-1,39 (m, 2H), 1,37 (d, 6H, J = 6,9 Hz), 1,57 (quinteto, 2H, J = 7,5 Hz), 1,96 (quinteto, 2H, J = 6,6 Hz), 2,49 (t, 2H, J = 6,6 Hz), 2,57 (t, 2H, J = 7,8 Hz), 3,16-3,26 (m, 3H), 4,62 (s lg, 1H), 7,12 (d, 2H, J = 8,1 Hz), 7,43 (d, 2H, J = 8,4 Hz), 7,64 (s, 1H).

I-4

RMN de ^1H (CD_3OD) δ ppm: 0,92 (t, 3H, J = 6,9 Hz), 1,28-1,41 (m, 2H), 1,46 (d, 6H, J = 6,3 Hz), 1,53-1,63 (m, 2H), 2,58 (t, 2H, J = 7,8 Hz), 3,33-3,43 (m, 1H), 6,27-6,29 (m, 1H), 7,14-7,16 (m, 3H), 7,50 (d, 2H, J = 8,4 Hz), 7,90 (s, 1H).

I-5

RMN de ^1H ($CDCl_3$) δ ppm: 0,92 (t, 3H, J = 7,2 Hz), 1,28-1,41 (m, 2H), 1,46 (d, 6H, J = 6,9 Hz), 1,53-1,63 (m, 2H), 2,59 (t, 2H, J = 7,8 Hz), 3,35-3,44 (m, 1H), 7,15 (d, 2H, J = 8,7 Hz), 7,38 (s, 1H), 7,45 (d, 2H, J = 8,7 Hz), 7,57 (s, 1H).

I-6

RMN de ^1H ($CDCl_3$) δ ppm: 0,91 (t, 3H, J = 7,5 Hz), 1,29-1,39 (m, 2H), 1,37 (d, 6H, J = 6,9 Hz), 1,55 (quinteto, 2H, J = 7,5 Hz), 2,55 (t, 2H, J = 5,1 Hz), 3,18-3,27 (m, 1H), 3,92 (d, 2H, J = 6,0 Hz), 5,51 (t, 1H, J = 5,7 Hz), 7,10 (d, 2H, J = 8,4 Hz), 7,39 (d, 2H, J = 8,4 Hz), 8,23 (s, 1H).

I-7

RMN de ^1H ($CDCl_3$) δ ppm: 0,91 (t, 3H, J = 7,2 Hz), 1,28-1,38 (m, 2H), 1,37 (d, 6H, J = 6,9 Hz), 1,51-1,67 (m, 4H), 1,78-1,88 (m, 2H), 2,39 (t, 2H, J = 7,2 Hz), 2,57 (t, 2H, J = 7,5 Hz), 3,12-3,22 (m, 3H), 4,30-4,37 (m, 1H), 7,12 (d, 2H, J = 8,4 Hz), 7,36-7,42 (m, 3H).

I-8

RMN de ^1R ($CDCl_3$) δ ppm: 0,91 (t, 3H, J = 7,5 Hz), 1,21-1,47 (m, 4H), 1,35 (d, 6H, J = 6,6 Hz), 1,51-1,63 (m, 4H), 1,67-1,77 (m, 2H), 2,34 (t, 2H, J = 7,5 Hz), 2,55 (t, 2H, J = 7,8 Hz), 3,08-3,17 (m, 3H), 4,71 (t, 1H, J = 6,0 Hz), 7,09 (d, 2H, J = 8,1 Hz), 7,43 (d, 2H, J = 8,4 Hz), 7,74 (s, 1H).

I-9

RMN de ^1H ($CDCl_3$) δ ppm: 0,91 (t, 3H, J = 7,2 Hz), 1,29-1,39 (m, 2H), 1,35 (d, 6H, J = 6,9 Hz), 1,50-1,60 (m, 2H), 2,54 (t, 2H, J = 7,8 Hz), 2,64 (t, 2H, J = 5,7 Hz), 3,14-3,23 (m, 1H), 3,41-3,47 (m, 2H), 5,29 (t, 1H, J =

6,3 Hz), 7,10 (d, 2H, J = 8,4 Hz), 7,39 (d, 2H, J = 8,4 Hz), 7,91 (s, 1H).

I-10

RMN de ^1H ($CDCl_3$) δ ppm: 0,91 (t, 3H, J = 7,5 Hz), 1,22 (s, 9H), 1,30-1,37 (m, 2H), 1,51-1,68 (m, 4H), 1,76-1,86 (m, 2H), 2,31-2,40 (m, 2H), 2,56 (t, 2H, J = 7,5 Hz), 3,15-3,26 (m, 3H), 7,11 (t, 2H, J = 8,7 Hz), 7,42 (d, 2H, J = 8,1 Hz), 7,54 (s, 1H).

I-11

pf: 128-129°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,91 (t; 3H, J = 7,5 Hz), 1,29-1,39 (m, 2H), 1,39 (s, 9H), 1,51-1,68 (m, 4H), 1,76-1,84 (m, 2H), 2,37 (t, 2H, J = 7,5 Hz), 2,56 (t, 2H, J = 7,8 Hz), 3,19-3,26 (m, 2H), 4,20 (t, 1H, J = 5,7 Hz), 7,11 (d, 2H, J = 8,1 Hz), 7,42 (d, 2H, J = 8,7 Hz), 7,46 (s, 1H).

I-12

RMN de ^1H ($CDCl_3$) δ ppm: 0,91 (t, 3H, J = 7,5 Hz), 1,28-1,37 (m, 2H), 1,47-1,68 (m, 6H), 2,23 (t, 2H, J = 7,2 Hz), 2,56 (t, 2H, J = 7,5 Hz), 2,90-2,97 (m, 2H), 5,10 (s lg, 1H), 7,11 (d, 2H, J = 8,4 Hz), 7,36 (d, 2H, J = 8,1 Hz), 7,50-7,68 (m, 3H), 7,93 (d, 1H, J = 8,1 Hz), 8,06 (d,

1H, J = 8,4 Hz), 8,24 (d, 1H, J = 7,5 Hz), 8,66 (d, 1H, J = 8,7 Hz).

I-13

RMN de ^1H ($CDCl_3$) δ ppm: 0,91 (t, 3H, J = 7,5 Hz), 1,28-1,40 (m, 2H), 1,45-1,73 (m, 6H), 2,23 (t, 2H, J = 7,5 Hz), 2,56 (t, 2H, J = 7,8 Hz), 2,88 (s, 6H), 2,88-2,95 (m, 2H), 5,04 (s lg, 1H), 7,10 (d, 2H, J = 8,1 Hz), 7,17 (d, 1H, J = 7,2 Hz), 7,37 (d, 2H, J = 8,4 Hz), 7,48-7,54 (m, 2H), 8,23 (d, 1H, J = 7,2 Hz), 8,30 (d, 1H, J = 8,7 Hz), 8,53 (d, 1H, J = 8,4 Hz).

I-14

RMN de ^1H ($CDCl_3$) δ ppm: 0,91 (t, 3H, J = 7,2 Hz), 1,30-1,43 (m, 6H), 1,36 (d, 6H, J = 6,6 Hz), 1,51-1,62 (m, 4H), 1,67-1,78 (m, 2H), 2,34 (t, 2H, J = 7,5 Hz), 2,56 (t, 2H, J = 7,8 Hz), 3,09-3,20 (m, 3H), 4,34 (s lg, 1H), 7,10 (d, 2H, J = 8,4 Hz), 7,41-7,44 (m, 3H).

I-15

RMN de ^1H ($CDCl_3$) δ ppm: 0,91 (t, 3H, J = 7,5 Hz), 1,23 (s, 9H), 1,27-1,80 (m, 12H), 2,30-2,38 (m, 2H), 2,56 (t, 2H, J = 7,5 Hz), 3,15 (s lg, 2H), 7,11 (d, 2H, J = 7,8 Hz), 7,43 (d, 2H, J = 7,8 Hz), 7,59 (s, 1H).

I-16

RMN de ^1H ($CDCl_3$) δ ppm: 0,91 (t, 3H, J = 7,5 Hz), 1,29-1,44 (m, 6H), 1,39 (s, 9H), 1,51-1,61 (m, 4H), 1,68-1,78 (m, 2H), 2,35 (t, 2H, J = 7,5 Hz), 2,56 (t, 2H, J = 8,1 Hz), 3,15-3,21 (m, 2H), 4,14-4,23 (m, 1H), 7,11 (d, 2H, J = 7,8 Hz), 7,36-7,44 (m, 3H).

I-19

RMN de ^1H ($CDCl_3$) δ ppm: 0,92 (t, 3H, J = 7,5 Hz), 1,21 (s, 9H), 1,30-1,40 (m, 2H), 1,55-1,72 (m, 6H), 2,64 (t, 2H, J = 7,8 Hz), 3,08-3,33 (m, 3H), 3,42-3,50 (m, 2H), 6,39 (s, 1H), 7,22 (d, 2H, J = 8,4 Hz), 7,69 (d, 2H, J = 8,1 Hz).

I-20

RMN de ^1H ($CDCl_3$) δ ppm: 0,92 (t, 3H, J = 7,2 Hz), 1,31-1,39 (m, 2H), 1,39 (s, 9H), 1,55-1,72 (m, 6H), 2,64 (t, 2H, J = 7,8 Hz), 3,24 (quarteto, 2H, J = 6,6 Hz), 3,48 (quarteto, 2H, J = 6,6 Hz), 4,21 (t, 1H, J = 6,3 Hz), 6,29 (s, 1H), 7,22 (d, 2H, J = 7,8 Hz), 7,67 (d, 2H, J = 8,1 Hz).

I-21

RMN de ^1H ($CDCl_3$) δ ppm: 0,91 (t, 3H, J = 7,2 Hz), 1,23 (s, 9H), 1,30-1,42 (m, 2H), 1,50-2,02 (m, 10H), 2,30-2,42 (m, 1H), 2,57 (t, 2H, J = 8,1 Hz), 3,10 (s lg, 1H), 3,57 (s lg, 1H), 7,12 (d, 2H, J = 8,4 Hz), 7,41 (d, 2H, J = 7,8 Hz).

I-22

pf: 78-79°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,91 (t, 3H, J = 7,2 Hz), 1,30-1,40 (m, 2H), 1,40 (s, 9H), 1,50-1,65 (m, 4H), 1,70-1,98 (m, 8H), 2,30-2,40 (m, 1H), 2,57 (t, 2H, J = 7,5 Hz), 3,58-3,70 (m, 1H), 4,16 (d, 1H, J = 9,3 Hz), 7,11-7,15 (m, 3H), 7,40 (d, 2H, J = 8,1 Hz).

I-23

RMN de ^1H ($CDCl_3$) δ ppm: 0,91 (t, 3H, J = 7,2 Hz), 1,21 (s, 9H), 1,21-1,41 (m, 4H), 1,51-1,64 (m, 4H), 1,86-2,01 (m, 4H), 2,12-2,25 (m, 1H), 2,56 (t, 2H, J = 7,5 Hz), 2,87-2,96 (m, 1H), 3,00-3,12 (m, 1H), 3,23-3,34 (m, 1H), 3,67-3,75 (m, 1H), 7,11 (d, 2H, J = 8,1 Hz), 7,40 (d, 2H, J = 8,4 Hz).

I-24

RMN de ^1H ($CDCl_3$) δ ppm: 0,91 (t, 3H, J = 7,2 Hz), 1,25-1,37 (m, 2H), 1,40 (s, 9H), 1,48-1,65 (m, 6H), 1,90 (d, 2H, J = 11,7 Hz), 2,02 (d, 2H, J = 11,7 Hz), 2,12-2,24 (m, 1H), 2,56 (t, 2H, J = 7,5 Hz), 3,04 (t, 2H, J = 6,3 Hz), 4,31 (t, 1H, J = 5,7 Hz), 7,11 (d, 2H, J = 8,1 Hz), 7,42 (d, 2H, J = 8,4 Hz).

I-25

pf: 232-233°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,91 (t, 3H, J = 7,5 Hz), 1,23-1,40 (m, 4H), 1,40 (s, 9H), 1,51-1,76 (m, 4H), 2,01-2,26 (m, 5H), 2,56 (t, 2H, J = 7,5 Hz), 3,22-3,38 (m, 1H), 3,79 (d, 1H, J = 9,3 Hz), 7,11 (d, 2H, J = 8,7 Hz), 7,17 (s, 1H), 7,40 (d, 2H, J = 8,4 Hz).

I-26

RMN de ^1H ($CDCl_3$) δ ppm: 0,91 (t, 3H, J = 7,2 Hz), 1,22 (s, 9H), 1,28-1,40 (m, 2H), 1,52-1,62 (m, 2H), 1,85-1,96 (m, 1H), 2,00-2,14 (m, 1H), 2,38-2,53 (m, 2H), 2,56 (t, 2H, J = 7,5 Hz), 3,22-3,37 (m, 3H), 7,11 (d, 2H, J = 8,4 Hz), 7,45 (d, 2H, J = 8,4 Hz), 8,19 (s, 1H).

I-27

RMN de ^1H ($CDCl_3$) δ ppm: 0,91 (t, 3H, J = 7,2 Hz), 1,30-1,40 (m, 2H), 1,40 (s, 9H), 1,52-1,61 (m, 2H), 1,95 (quinteto, 2H, J = 6,3 Hz), 2,50 (t, 2H, J = 6,9 Hz), 2,56 (t, 2H, J = 7,8 Hz), 3,31 (quarteto, 2H, J = 6,0 Hz), 4,30-4,36 (m, 1H), 7,12 (d, 2H, J = 8,4 Hz), 7,43 (d, 2H, J = 8,4 Hz), 7,65 (s, 1H).

I-28

RMN de ^1H ($CDCl_3$) δ ppm: 0,91 (t, 3H, J = 7,2 Hz), 1,21 (s, 9H), 1,30-1,62 (m, 8H), 2,08 (d, 4H, J = 11,1 Hz), 2,56 (t, 2H, J = 7,8 Hz), 3,04 (d, 1H, J = 4,8 Hz),

3,20-3,30 (m, 1H), 4,65-4,76 (m, 1H), 6,57 (s, 1H), 7,10 (d, 2H, J = 8,7 Hz), 7,26 (d, 2H, J = 8,1 Hz).

I-29

RMN de ^1H ($CDCl_3$) δ ppm: 0,91 (t, 3H, J = 7,2 Hz), 1,23-1,62 (m, 8H), 1,40 (s, 9H), 2,12 (d, 4H, J = 14,4 Hz), 2,56 (t, 2H, J = 7,8 Hz), 3,28-3,40 (m, 1H), 3,90 (s, 1H), 4,60-4,73 (m, 1H), 6,57 (s, 1H), 7,10 (d, 2H, J = 8,4 Hz), 7,25 (d, 2H, J = 8,4 Hz).

I-30

RMN de ^1H ($CDCl_3$) δ ppm: 0,91 (t, 3H, J = 7,5 Hz), 1,26-1,39 (m, 2H), 1,51-1,64 (m, 4H), 1,72-1,81 (m, 2H), 2,34 (t, 2H, J = 6,9 Hz), 2,56 (t, 2H, J = 7,8 Hz), 2,95-3,01 (m, 2H), 4,84 (t, 1H, J = 5,7 Hz), 6,99-7,12 (m, 6H), 7,19-7,24 (m, 1H), 7,30 (s, 1H), 7,38-7,43 (m, 4H), 7,79 (d, 2H, J = 8,7 Hz).

I-31

RMN de ^1H ($CDCl_3$) δ ppm: 0,92 (t, 3H, J = 7,5 Hz), 1,21 (s, 9H), 1,28-1,62 (m, 8H), 2,07-2,14 (m, 4H), 2,64 (t, 2H, J = 7,8 Hz), 3,11 (d, 1H, J = 5,1 Hz), 3,20 (s lg, 1H), 3,90-4,04 (m, 1H), 6,06-6,14 (m, 1H), 7,21 (t, 2H, J = 8,1 Hz), 7,67 (t, 2H, J = 8,4 Hz).

I-32

RMN de ^1H ($CDCl_3$) δ ppm: 0,92 (t, 3H, J = 7,2 Hz), 1,27-1,65 (m, 8H), 1,40 (s, 9H), 2,10-2,23 (m, 4H), 2,65 (t, 2H, J = 7,5 Hz), 3,23-3,35 (m, 1H), 3,49 (s, 1H), 3,88-4,02 (m, 1H), 5,84-5,92 (m, 1H), 7,13 (t, 2H, J = 8,4 Hz), 7,65 (d, 2H, J = 8,1 Hz).

I-33

RMN de ^1H ($CDCl_3$) δ ppm: 0,94 (t, 3H, J = 7,2 Hz), 1,30-1,42 (m, 2H), 1,32 (s, 9H), 1,57-1,66 (m, 2H), 2,67 (t, 2H, J = 7,8 Hz), 5,61 (s, 1H), 6,93 (d, 2H, J = 8,7 Hz), 7,25 (d, 2H, J = 8,4 Hz), 7,49 (d, 2H, J = 9,0 Hz), 7,80 (d, 2H, J = 8,1 Hz), 8,22 (s, 1H).

I-34

RMN de ^1H (CD_3OD) δ ppm: 0,95 (t, 3H, J = 7,5 Hz), 1,35 (s, 9H), 1,35-1,44 (m, 2H), 1,57-1,69 (m, 2H), 2,69 (t, 2H, J = 7,5 Hz), 7,28-7,33 (m, 4H), 7,56 (d, 2H, J = 9,0 Hz), 7,83 (d, 2H, J = 8,4 Hz).

I-36

RMN de ^1H ($CDCl_3$) δ ppm: 0,92 (t, 3H, J = 7,5 Hz), 1,31-1,70 (m, 11H), 1,39 (s, 9H), 1,75-1,85 (m, 1H), 2,65 (t, 2H, J = 8,1 Hz), 3,13 (t, 2H, J = 6,6 Hz), 3,40 (t, 2H, J = 7,2 Hz), 4,10 (t, 1H, J = 5,7 Hz), 6,21 (t, 1H, J = 5,7 Hz), 7,23 (d, 2H, J = 8,1 Hz), 7,67 (d, 2H, J = 8,4 Hz).

I-37

RMN de ^1H ($CDCl_3$) δ ppm: 0,92 (t, 3H, J = 7,5 Hz), 0,95-1,10 (m, 2H), 1,31-1,40 (m, 2H), 1,39 (s, 9H), 1,55-1,63 (m, 4H), 1,80-1,92 (m, 4H), 2,65 (t, 2H, J = 7,8 Hz), 3,03 (t, 2H, J = 6,6 Hz), 3,31 (t, 2H, J = 6,6 Hz), 4,06 (t, 1H, J = 6,0 Hz), 6,22 (t, 1H, J = 6,0 Hz), 7,23 (d, 2H, J = 8,4 Hz), 7,67 (d, 2H, J = 8,1 Hz).

I-39

RMN de ^1H ($CDCl_3$) δ ppm: 1,13 (t, 3H, J = 7,2 Hz), 1,39 (s, 9H), 1,69-1,97 (m, 8H), 2,27-2,38 (m, 1H), 3,29-3,35 (m, 4H), 3,60-3,70 (m, 1H), 4,52 (d, 1H, J = 9,3 Hz), 6,64 (d, 2H, J = 8,4 Hz), 7,22 (s, 1H), 7,31 (d, 2H, J = 9,0 Hz).

I-40

RMN de ^1H ($CDCl_3$) δ ppm: 1,38 (s, 9H), 1,68-1,96 (m, 8H), 2,30-2,40 (m, 1H), 3,11 (t, 4H, J = 4,8 Hz), 3,60-3,72 (m, 1H), 3,86 (t, 4H, J = 4,8 Hz), 4,51 (s lg, 1H), 6,89 (d, 2H, J = 9,0 Hz), 7,42 (d, 2H, J = 8,7 Hz).

I-41

pf: >278°C (dec.)

RMN de ^1H ($CDCl_3$) δ ppm: 1,18-1,40 (m, 2H), 1,40 (s, 9H), 1,62-1,75 (m, 2H), 2,01-2,27 (m, 5H), 3,10-3,13

(m, 4H), 3,22-3,38 (m, 1H), 3,72 (d, 1H, J = 9,3 Hz), 3,85-3,88 (m, 4H), 6,87 (d, 2H, J = 9,0 Hz), 7,10 (s, 1H), 7,40 (d, 2H, J = 9,0 Hz).

I-42

RMN de ^1H ($CDCl_3$) δ ppm: 1,40 (s, 9H), 1,61-1,97 (m, 8H), 2,16 (s, 3H), 2,33-2,43 (m, 1H), 3,60-3,70 (m, 1H), 4,66 (s lg, 1H), 7,12 (d, 1H, J = 8,7 Hz), 7,46-7,50 (m, 1H), 7,62 (s, H), 7,75-7,78 (m, 1H), 7,86-7,91 (m, 2H).

I-43

RMN de ^1H ($CDCl_3$) δ ppm: 1,40 (s, 9H), 1,62-2,00 (m, 8H), 1,87 (s, 3H), 2,36-2,47 (m, 1H), 3,24 (s, 3H), 3,64-3,74 (m, 1H), 4,87 (s lg, 1H), 7,13 (d, 2H, J = 9,0 Hz), 7,64 (d, 2H, J = 8,4 Hz), 7,81 (s, H).

I-44

pf: 235-236°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,13 (t, 6H, J = 6,9 Hz), 1,18-1,33 (m, 2H), 1,40 (s, 9H), 1,60-1,77 (m, 2H), 2,00-2,26 (m, 5H), 3,28-3,35 (m, 4H), 3,73 (d, 1H, J = 9,3 Hz), 6,60-6,70 (m, 2H), 7,03 (s lg, 1H), 7,31 (d, 2H, J = 7,8 Hz).

I-45

pf: >268 °C (dec.)

RMN de ^1H ($CDCl_3$) δ ppm: 1,20-1,34 (m, 2H), 1,40 (s, 9H), 1,56-1,76 (m, 8H), 2,00-2,26 (m, 5H), 3,06-3,14 (m, 4H), 3,24-3,36 (m, 1H), 3,72 (d, 1H, J = 9,3 Hz), 6,90 (d, 2H, J = 8,7 Hz), 7,09 (s, 1H), 7,36 (d, 2H, J = 8,7 Hz).

I-46

pf: > 272°C (dec.)

RMN de ^1H (DMSO-d_6) δ ppm: 1,28 (s, 9H), 1,31-1,59 (m, 7H), 1,87-2,00 (m, 4H), 2,23-2,34 (m, 1H), 3,00-3,16 (m, 1H), 4,35-4,45 (m, 2H), 6,81 (d, 1H, J = 9,0 Hz), 7,16 (t, 1H, J = 7,2 Hz), 7,43 (t, 1H, J = 8,4 Hz), 7,52-7,58 (m, 3H), 8,04 (d, 1H, J = 7,8 Hz), 8,43 (s, 1H).

I-47

RMN de ^1H ($CDCl_3$) δ ppm: 1,20-1,36 (m, 2H), 1,40 (s, 9H), 1,62-1,77 (m, 2H), 1,98-2,32 (m, 5H), 3,31-3,40 (m, 1H), 3,62 (d, 1H, J = 9,0 Hz), 7,08 (s, 1H), 7,29 (d, 2H, J = 9,0 Hz), 7,61 (d, 2H, J = 9,0 Hz).

I-48

RMN de ^1H ($CDCl_3$) δ ppm: 1,22-1,36 (m, 2H), 1,40 (s, 9H), 1,62-1,77 (m, 2H), 2,00-2,31 (m, 5H), 3,24-3,40

(m, 1H), 3,62 (d, 1H, J = 10,2 Hz), 7,01 (t, 2H, J = 8,7 Hz), 7,09 (s, 1H), 7,42-7,50 (m, 2H).

I-49

pf: 270°C (dec.)

RMN de ^1H ($CDCl_3$) δ ppm: 1,20-1,36 (m, 2H), 1,40 (s, 9H), 1,61-1,77 (m, 2H), 1,95-2,30 (m, 9H), 3,17-3,38 (m, 5H), 3,67 (d, 1H, J = 9,3 Hz), 6,50 (d, 2H, J = 9,0 Hz), 6,97 (s, 1H), 7,30 (d, 2H, J = 9,0 Hz).

I-50

pf: 252-253 C

RMN de ^1H ($CDCl_3$) δ ppm: 1,21-1,37 (m, 2H), 1,40 (s, 9H), 1,62-1,78 (m, 2H), 1,98-2,32 (m, 5H), 3,26-3,40 (m, 1H), 3,68 (d, 1H, J = 9,6 Hz), 6,94-7,02 (m, 4H), 7,08 (t, 1H, J = 7,5 Hz), 7,13 (s, 1H), 7,31 (t, 2H, J = 7,5 Hz), 7,46 (d, 2H, J = 9,0 Hz).

I-51

pf: 278-279°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,02 (d; 6H, J = 6,9 Hz), 1,35 (s, 9H), 1,39-1,71 (m, 6H), 1,90-2,09 (m, 2H), 3,16-3,30 (m, 1H), 3,46 (d, 1H, J = 9,0 Hz), 4,92-5,01 (m,

1H), 6,91-6,95 (m, 2H), 7,00-7,07 (m, 3H), 7,13-7,16 (m, 2H), 7,30-7,36 (m, 2H).

I-52

pf: 276-277°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,20-1,36 (m, 2H), 1,40 (s, 9H), 1,60-1,78 (m, 2H), 1,98-2,30 (m, 5H), 2,36 (s, 3H), 2,58 (t, 4H, J = 4,5 Hz), 3,17 (t, 4H, J = 4,5 Hz), 3,21-3,40 (m, 1H), 3,64 (d, 1H, J = 9,0 Hz), 6,88 (d, 2H, J = 9,0 Hz), 7,01 (s, 1H), 7,37 (d, 2H, J = 9,0 Hz).

I-53

pf: > 300°C

RMN de ^1H ($DMSO-d_6$) δ ppm: 1.20-1.54 (m, 4H), 1.27 (s, 9H), 1.73-1.88 (m, 2H), 1.89-2.01 (m, 2H), 2.13-2.25 (m, 1H), 2.98-3.12 (m, 1H), 3.15-3.31 (m, 8H), 6.76-6.84 (m, 2H), 6.93 (d, 2H, J = 9.0 Hz), 6.99 (d, 2H, J = 8.1 Hz), 7.24 (d, 2H, J = 8.1 Hz), 7.46 (d, 2H, J = 9.0 Hz), 9.60 (s, 1H).

I-54

pf: > 215°C (dec.)

RMN de ^1H ($DMSO-d_6$) δ ppm: 1.27 (s, 9H), 1.27-2.00 (m, 18H), 2.14-2.26 (m, 1H), 2.53-2.84 (m, 4H), 2.86-

3.30 (m, 2H), 3.46-3.54 (m, 1H), 3.62-3.74 (m, 2H), 6.78 (d, 1H, J = 8.7 Hz), 6.87 (d, 2H, J = 7.8 Hz), 7.42 (d, 2H, J = 8.7 Hz), 9.58 (s, 1H).

I-55

pf: > 290°C (dec.)

RMN de ^1H ($CDCl_3$) δ ppm: 1,23-1,40 (m, 2H), 1,40 (s, 9H), 1,60-1,76 (m, 2H), 2,02-2,27 (m, 5H), 3,20 (t, 4H, J = 5,4 Hz), 3,21-3,32 (m, 1H), 3,67 (d, 1H, J = 9,3 Hz), 3,98 (t, 4H, J = 4,8 Hz), 6,52 (t, 1H, J = 4,8 Hz), 6,93 (d, 2H, J = 8,4 Hz), 7,06 (s, 1H), 7,41 (d, 2H, J = 8,7 Hz), 8,33 (d, 2H, J = 4,8 Hz).

I-56

pf: > 232°C (dec.)

RMN de ^1H (DMSO-d_6) δ ppm: 1,27 (s, 9H), 1,27-1,48 (m, 4H), 1,80-1,99 (m, 4H), 2,14-2,25 (m, 1H), 3,04-3,24 (m, 8H), 3,68 (s, 3H), 3,76 (s, 3H), 6,44-6,47 (m, 1H), 6,66 (s, 1H), 6,76-6,84 (m, 2H), 6,92 (d, 2H, J = 8,4 Hz), 7,46 (d, 2H, J = 8,4 Hz), 9,61 (s, 1H).

I-57

pf: 284-285°C (dec.)

RMN de ^1H ($CDCl_3$) δ ppm: 1,27 (t, 3H, J = 7,2 Hz), 1,40 (s, 9H), 1,61-2,24 (m, 9H), 2,35-2,49 (m, 1H), 2,76 (t, 2H, J = 10,2 Hz), 3,04-3,15 (m, 2H), 3,20-3,36 (m, 1H), 3,55-3,59 (m, 2H), 3,87 (d, 1H, J = 9,6 Hz), 4,12-4,19 (m, 2H), 6,90 (d, 2H, J = 8,7 Hz), 2,79 (s, 1H), 7,40 (d, 2H, J = 8,7 Hz).

I-58

pf: > 299°C (dec.)

RMN de ^1H ($CDCl_3$) δ ppm: 1,26-1,33 (m, 2H), 1,40 (s, 9H), 1,56-2,42 (m, 19H), 2,73-2,81 (m, 4H), 3,16-3,26 (m, 4H), 3,64 (d, 1H, J = 9,6 Hz), 6,87 (d, 2H, J = 8,7 Hz), 7,04 (s, 1H), 7,37 (d, 2H, J = 9,0 Hz).

I-59

pf: > 270°C (dec.)

RMN de ^1H ($CDCl_3$) δ ppm: 1,26-1,47 (m, 2H), 1,47 (s, 9H), 1,60-1,80 (m, 4H), 2,01-2,32 (m, 5H), 3,28-3,40 (m, 3H), 3,62-3,74 (m, 3H), 5,74-5,96 (m, 2H), 6,92 (d, 2H, J = 8,7 Hz), 7,13 (s, 1H), 7,39 (d, 2H, J = 9,0 Hz).

I-60

pf: 247-250°C (dec.)

RMN de ^1H ($CDCl_3$) δ ppm: 1,20-1,37 (m, 2H), 1,40 (s, 9H), 1,60-1,78 (m, 2H), 1,98-2,33 (m, 5H), 2,93-3,03 (m, 2H), 3,22-3,40 (m, 1H), 3,52 (t, 2H, J = 6,0 Hz), 3,62 (d, 1H, J = 8,4 Hz), 4,36 (s, 2H), 6,93 (d, 2H, J = 8,7 Hz), 7,00 (s, 1H), 7,11-7,22 (m, 4H), 7,39 (d, 2H, J = 8,7 Hz).

I-61

pf: 280-281°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,21-1,38 (m, 2H), 1,41 (s, 9H), 1,64-1,80 (m, 2H), 2,02-2,33 (m, 5H), 3,24-3,40 (m, 1H), 3,61 (d, 1H, J = 9,0 Hz), 6,33 (t, 2H, J = 2,1 Hz), 7,04 (t, 2H, J = 2,1 Hz), 7,14 (s, 1H), 7,34 (d, 2H, J = 9,0 Hz), 7,56 (d, 2H, J = 9,0 Hz).

I-62

pf: 260-262°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,22-1,39 (m, 2H), 1,41 (s, 9H), 1,64-1,82 (m, 2H), 2,02-2,35 (m, 5H), 3,24-3,40 (m, 1H), 3,62 (d, 1H, J = 9,6 Hz), 7,31 (d, 2H, J = 9,0 Hz), 7,51 (s, 1H), 7,69 (d, 2H, J = 9,0 Hz).

I-63

pf: 248°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,20-1,38 (m, 2H), 1,40 (s, 9H), 1,61-1,78 (m, 2H), 1,98-2,32 (m, 5H), 3,22-3,45 (m, 1H), 3,64 (d, 1H, J = 9,3 Hz), 7,11 (s, 1H), 7,37-7,46 (m, 4H).

I-64

pf: 272-275°C (dec.)

RMN de ^1H (DMSO-d_6) δ ppm: 1,20-1,53 (m, 4H), 1,27 (s, 9H), 1,75-1,88 (m, 2H), 1,88-2,00 (m, 2H), 2,11-2,24 (m, 1H), 2,96-3,12 (m, 1H), 5,96 (s, 2H), 6,77 (d, 1H, J = 8,7 Hz), 6,82 (d, 1H, J = 8,4 Hz), 6,95 (dd, 1H, J = 1,8, 8,4 Hz), 7,29 (d, 1H, J = 1,8 Hz), 9,70 (s, 1H).

I-65

pf: 293-296°C (dec.)

RMN de ^1H (DMSO-d_6) δ ppm: 1,20-1,70 (m, 10H), 1,27 (s, 9H), 1,79-2,038 (m, 4H), 2,18-2,33 (m, 1H), 2,98-3,30 (m, 5H), 6,79 (d, 1H, J = 9,0 Hz), 6,97 (d, 2H, J = 8,1 Hz), 7,43-7,57 (m, 4H), 7,62 (d, 2H, J = 8,1 Hz), 9,82 (s, 1H).

I-66

pf: > 300°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,27 (s, 9H), 1,27-1,53 (m, 4H), 1,86-1,99 (m, 4H), 2,22-2,34 (m, 1H), 2,39 (s, 3H), 3,00-3,14 (m, 1H), 6,25 (s, 1H), 6,79 (d, 1H, J = 9,0 Hz), 7,47-7,50 (m, 1H), 7,69-7,76 (m, 1H), 10,27 (s, 1H).

I-67

pf: 248-249°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,20-1,54 (m, 4H), 1,27 (s, 9H), 1,77-1,90 (m, 2H), 1,90-2,02 (m, 2H), 2,02 (s, 3H), 2,17-2,32 (m, 1H), 2,96-3,13 (m, 1H), 6,78 (d, 1H, J = 8,7 Hz), 7,12-7,30 (m, 3H), 7,89 (s, 1H), 9,79 (s, 1H), 9,88 (s, 1H).

I-68

pf: > 300°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,20-1,54 (m, 4H), 1,27 (s, 9H), 1,77-1,89 (m, 2H), 1,89-2,03 (m, 2H), 2,00 (s, 3H), 2,14-2,28 (m, 1H), 2,95-3,13 (m, 1H), 6,78 (d, 1H, J = 8,7 Hz), 7,40-7,54 (m, 4H), 9,72 (s, 1H), 9,83 (s, 1H).

I-69

pf: 199-201°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,21-1,53 (m, 4H), 1,27 (s, 9H), 1,76-1,89 (m, 2H), 1,89-2,02 (m, 2H), 2,13-2,30 (m, 1H), 2,85 (s, 6H), 2,94-3,14 (m, 1H), 6,40 (dd, 1H, J = 2,4, 8,4 Hz), 6,78 (d, 1H, J = 8,7 Hz), 6,90 (d, 1H, J = 8,4 Hz), 7,05 (t, 2H, J = 8,4 Hz), 9,60 (s, 1H).

I-70

pf: 227-230°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,22-1,52 (m, 4H), 1,27 (s, 9H), 1,72-1,87 (m, 2H), 1,87-2,01 (m, 2H), 2,12-2,29 (m, 1H), 2,96-3,12 (m, 1H), 5,00 (s, 2H), 6,22 (d, 1H, J = 7,5 Hz), 6,66 (d, 1H, J = 7,5 Hz), 6,78 (d, 1H, J = 9,0 Hz), 6,86 (d, 1H, J = 7,5 Hz), 6,89-6,95 (m, 1H), 9,46 (s, 1H).

I-71

pf: 270-272°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,22-1,52 (m, 4H), 1,26 (s, 9H), 1,73-1,86 (m, 2H), 1,88-2,00 (m, 2H), 2,08-2,22 (m, 1H), 2,95-3,11 (m, 1H), 4,80 (s, 2H), 6,47 (d, 2H, J = 8,4 Hz), 6,77 (d, 1H, J = 8,4 Hz), 7,20 (d, 2H, J = 8,4 Hz), 9,35 (s, 1H).

I-72

pf: 262-263°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,25 (d, 6H, J = 6,3 Hz), 1,17-1,42 (m, 2H), 1,40 (s, 9H), 1,60-1,78 (m, 2H), 1,98-2,43 (m, 7H), 3,20-3,43 (m, 3H), 3,67 (d, 1H, J = 9,6 Hz), 3,74-3,86 (m, 2H), 6,86 (d, 2H, J = 9,0 Hz), 7,04 (s, 1H), 7,38 (d, 2H, J = 9,0 Hz).

I-73

pf: 218-219°C

RMN de ^1H (CD_3OD) δ ppm: 1,36 (s, 9H), 1,36-1,69 (m, 4H), 1,45 (s, 9H), 1,88-2,02 (m, 3H), 2,06-2,30 (m, 4H), 3,05-3,44 (m, 3H), 3,46-3,56 (m, 1H), 4,16-4,26 (m, 1H), 6,51 (d, 2H, J = 9,0 Hz), 7,30 (d, 2H, J = 8,7 Hz).

I-74

pf: 295-296°C (dec.)

RMN de ^1H (CD_3OD) δ ppm: 1,36 (s, 9H), 1,36-1,67 (m, 4H), 1,92-2,13 (m, 4H), 2,26-2,40 (m, 2H), 2,62-2,75 (m, 1H), 3,16-3,25 (m, 1H), 3,58-3,98 (m, 4H), 4,16-4,25 (m, 1H), 7,20-7,30 (m, 2H), 7,62 (d, 2H, J = 9,0 Hz).

I-75

pf: 250-251°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,23-1,55 (m, 4H), 1,27 (s, 9H), 1,78-1,90 (m, 2H), 1,90-2,02 (m, 2H), 2,15-

2,28 (m, 1H), 2,98-3,14 (m, 1H), 3,06 (t, 2H, J = 8,4 Hz), 3,87 (t, 2H, J = 8,4 Hz), 6,67 (dd, 1H, J = 1,5, 7,2 Hz), 6,80 (d, 1H, J = 8,4 Hz), 6,94-7,05 (m, 2H), 7,12-7,19 (m, 1H), 7,16 (d, 2H, J = 9,3 Hz), 7,57 (d, 2H, J = 9,3 Hz), 9,73 (s, 1H).

I-76

pf: 265-266°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,23-1,58 (m, 4H), 1,28 (s, 9H), 1,83-2,04 (m, 4H), 2,20-2,36 (m, 1H), 2,97-3,16 (m, 1H), 6,67 (d, 1H, J = 3,0 Hz), 6,82 (d, 1H, J = 8,4 Hz), 7,07-7,22 (m, 2H), 7,47-7,53 (m, 1H), 7,50 (d, 2H, J = 9,0 Hz), 7,58 (d, 1H, J = 3,0 Hz), 7,64 (d, 1H, J = 7,5 Hz), 7,79 (d, 2H, J = 9,0 Hz), 10,02 (s, 1H).

I-77

pf: 281°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,21-1,56 (m, 4H), 1,27 (s, 9H), 1,80-2,03 (m, 4H), 2,18-2,31 (m, 1H), 2,97-3,14 (m, 1H), 6,51 (dd, 1H, J = 2,1, 2,7 Hz), 6,81 (d, 1H, J = 9,0 Hz), 7,67-7,78 (m, 5H), 8,41 (d, 1H, J = 2,1 Hz), 9,96 (s, 1H).

I-78

pf: > 300°C (dec.)

RMN de ^1H (DMSO-d_6) δ ppm: 1,27 (s, 9H), 1,27-1,52 (m, 4H), 1,74-2,04 (m, 7H), 2,10-2,25 (m, 2H), 2,96-3,20 (m, 2H), 3,48-3,58 (m, 1H), 3,75-3,84 (m, 1H), 6,39 (d, 2H, J = 8,4 Hz), 6,79 (d, 1H, J = 8,4 Hz), 7,02 (s, 1H), 7,30 (s, 1H), 7,36 (d, 2H, J = 8,1 Hz), 9,48 (s, 1H).

I-79

pf: 248-250°C (dec.)

RMN de ^1H (DMSO-d_6) δ ppm: 1,27 (s, 9H), 1,27-1,54 (m, 4H), 1,85-1,99 (m, 4H), 2,24-2,33 (m, 1H),-3,00-3,14 (m, 1H), 6,82 (d, 1H, J = 8,7 Hz), 7,77 (d, 2H, J = 8,4 Hz), 8,07 (d, 2H, J = 8,4 Hz).

I-80

pf: > 300°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,22-1,58 (m, 4H), 1,27 (s, 9H), 1,80-2,03 (m, 4H), 2,18-2,32 (m, 1H), 2,98-3,14 (m, 1H), 6,80 (d, 1H, J = 8,7 Hz), 7,35-7,50 (m, 2H), 7,99 (s, 1H), 8,11 (s, 1H), 9,79 (s, 1H), 12,94 (s, 1H).

I-81

pf: 261-262°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,21-1,57 (m, 4H), 1,27 (s, 9H), 1,78-2,02 (m, 4H), 2,17-2,30 (m, 1H), 2,96-

3,16 (m, 1H), 6,34 (s, 1H), 6,80 (d, 1H, J = 8,7 Hz), 7,14-7,32 (m, 3H), 7,85 (s, 1H), 9,58 (s, 1H), 10,95 (s, 1H).

I-82

RMN de ^1H ($CDCl_3$) δ ppm: 0,86 (s, 18H), 1,24-1,37 (m, 2H), 1,37 (s, 9H), 1,56-1,74 (m, 2H), 1,95-2,19 (m, 5H), 3,18-3,32 (m, 1H), 3,44 (t, 4H, J = 6,3 Hz), 3,70 (t, 4H, J = 6,3 Hz), 4,39 (d, 1H, J = 9,0 Hz), 6,59 (d, 2H, J = 9,0 Hz), 7,31 (d, 2H, J = 8,7 Hz), 7,43 (s, 1H).

I-83

pf: 264-265°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,27 (s, 9H), 1,27-1,52 (m, 4H), 1,78-1,88 (m, 2H), 1,90-2,00 (m, 2H), 2,14-2,26 (m, 1H), 2,96-3,14 (m, 1H), 6,72-6,82 (m, 2H), 6,99 (t, 4H, J = 7,8 Hz), 7,18 (t, 2H, J = 7,5 Hz), 7,46 (d, 2H, J = 9,0 Hz), 8,00 (s, 1H), 9,65 (s, 1H).

I-84

pf: 257°C (dec.)

RMN de ^1H (DMSO-d_6) δ ppm: 1,23-1,57 (m, 4H), 1,27 (s, 9H), 1,83-2,03 (m, 4H), 2,23-2,35 (m, 1H), 2,98-3,15 (m, 1H), 6,80 (d, 1H, J = 8,1 Hz), 7,87 (d, 2H, J = 9,0 Hz), 8,34 (d, 2H, J = 9,0 Hz), 9,21 (s, 1H), 10,20 (s, 1H).

I-85

pf: 256-258°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,22-1,53 (m, 4H), 1,26 (s, 9H), 1,79-2,01 (m, 4H), 2,25 (s, 3H), 2,28-2,42 (m, 1H), 2,97-3,02 (m, 1H), 6,71 (d, 1H, J = 0,9 Hz), 6,80 (d, 1H, J = 8,1 Hz), 11,91 (s, 1H).

I-86

pf: 228-230°C

RMN de ^1H (CD_3OD) δ ppm: 1,36 (s, 9H), 1,36-1,48 (m, 2H), 1,55-1,70 (m, 2H), 1,87-1,98 (m, 2H), 2,08-2,17 (m, 2H), 2,20-2,32 (m, 1H), 3,15-3,27 (m, 1H), 3,50 (t, 4H, J = 5,7 Hz), 3,69 (t, 4H, J = 5,7 Hz), 6,72 (d, 2H, J = 9,0 Hz), 7,29-7,33 (m, 2H).

I-87

pf: 183-184°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,27 (s, 9H), 1,27-1,48 (m, 4H), 1,73-1,89 (m, 4H), 1,90-2,00 (m, 2H), 2,16-2,28 (m, 1H), 2,28 (t, 2H, J = 7,5 Hz), 2,51-2,54 (m, 2H), 2,97-3,13 (m, 1H), 3,58 (s, 3H), 6,79 (d, 1H, J = 8,7 Hz), 7,08 (d, 2H, J = 8,7 Hz), 7,49 (d, 2H, J = 8,4 Hz), 9,73 (s, 1H).

I-88

pf: 217-218°C

RMN de ^1H (CD_3OD) δ ppm: 1,36 (s, 9H), 1,36-1,46 (m, 2H), 1,55-1,69 (m, 2H), 1,83-2,00 (m, 4H), 2,07-2,18 (m, 2H), 2,26-2,36 (m, 3H), 2,61 (t, 2H, J = 7,5 Hz), 3,14-3,26 (m, 1H), 7,13 (d, 2H, J = 8,1 Hz), 7,44 (d, 2H, J = 8,1 Hz).

I-89

RMN de ^1H ($CDCl_3$) δ ppm: 0,08 (d, 6H, J = 3,3 Hz), 0,88(s, 9H), 1,21-1,36 (m, 2H), 1,39 (s, 9H), 1,61-1,74 (m, 2H), 1,88-2,23 (m, 6H), 3,06-3,11 (m, 1H), 3,24-3,74 (m, 4H), 3,92 (d, 1H, J = 9,6 Hz), 4,48-4,56 (m, 1H), 6,47 (d, 2H, J = 9,0 Hz), 7,17 (s, 1H), 7,32 (d, 2H, J = 9,0 Hz).

I-90

pf: amorfo

RMN de ^1H (CD_3OD) δ ppm: 1,36 (s, 9H), 1,36-1,47 (m, 2H), 1,56-1,70 (m, 3H), 1,88-2,30 (m, 6H), 3,05-3,49 (m, 5H), 4,50 (s lg, 1H), 6,50 (d, 2H, J = 9,0 Hz), 7,29 (d, 2H, J = 9,0 Hz).

I-91

pf: 105-106°C

RMN de ^1H ($CDCl_3$) δ ppm: 0.92 (t, 3H, J = 7.3 Hz), 1.25-1.27 (m, 2H), 1.36 (d, 6H, J = 6.9 Hz), 1.51-1.59 (m, 2H), 2.56 (t, 2H, J = 7.8 Hz), 3.27 (septeto, 1H, J = 6.9 Hz), 7.12 (d, 2H, J = 8.6 Hz), 7.32 (t, 1H, J = 7.8 Hz), 7.45 (d lg, 1H, J = 7.8 Hz), 7.53 (d, 2H, J = 8.6 Hz), 7.58 (d, 1H, J = 7.8 Hz), 7.71-7.72 (m, 2H), 8.27(s, 1H).

I-92

pf: 163-164°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,93 (t, 3H, J = 7,3 Hz), 1,32-1,39 (m, 2H), 1,55-1,65 (m, 2H), 1,87 (s, 3H), 1,95 (s, 3H), 2,60 (t, 2H, J = 7,6 Hz), 7,07 (d, 2H, J = 8,4 Hz), 7,18 (d, 2H, J = 8,5 Hz), 7,54 (d, 2H, J = 8,5 Hz), 7,91 (s lg, 1H), 8,18 (d, 2H, J = 8,4 Hz), 8,77 (s, 1H).

I-93

pf: 173°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,93 (t, 3H, J = 7,3 Hz), 1,32-1,40 (m, 2H), 1,39 (d, 6H, J = 6,9 Hz), 1,55-1,62 (m, 2H), 2,60 (t, 2H, J = 7,8 Hz), 3,13 (septeto, 1H, J = 6,9 Hz), 4,39 (d, 2H, J = 6,3 Hz), 4,45 (t, 1H, J = 6,3 Hz), 7,18 (d, 2H, J = 8,7 Hz), 7,46 (d, 2H, J = 8,7 Hz),

7,54 (d, 2H, J = 8,7 Hz), 7,80 (s, 1H), 7,85 (d, 2H, J = 8,7 Hz).

I-94

pf: 159-160°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,93 (t, 3H, J = 7,3 Hz), 1,32-1,39 (m, 2H), 1,54-1,80 (m, 2H), 1,79 (s, 3H), 1,80 (s, 3H), 2,60t, 2H, J = 7,7 Hz), 3,18 (s, 3H), 7,18 (d, 2H, J = 8,5 Hz), 7,30 (d, 2H, J = 8,8 Hz), 7,52 (d, 2H, J = 8,5 Hz), 7,70 (s lg, 1H), 7,84 (d, 2H, J = 8,8 Hz), 8,77 (s, 1H).

I-95

pf: 177-178°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,94 (t, 3H, J = 7,2 Hz), 1,31-1,48 (m, 8H), 1,54-1,66 (m, 2H), 2,55 (s, 3H), 2,62 (t, 2H, J = 7,6 Hz), 3,92 (septeto, 1H, J = 6,6 Hz), 7,20 (d, 2H, J = 8,45 Hz), 7,74 (d, 2H, J = 8,5 Hz), 9,01 (s lg, 1H), 9,17 (s, 1H).

I-96

pf: 220-223°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,93 (t, 3H, J = 7,3 Hz), 1,28-1,42 (m, 2H), 1,50 (d, 6H, J = 6,8 Hz), 1,54-1,65

(m, 2H), 2,62 (t, 2H, J = 7,6 Hz), 4,08 (septeto, 1H, J = 7,1 Hz), 7,20 (d, 2H, J = 8,5 Hz), 7,48 (d, 2H, J = 8,5 Hz), 7,71 (s lg, 1H), 8,51 (s lg, 1H), 8,95 (s, 1H).

I-97

pf: 195-197°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,91 (t, 3H, J = 7,6 Hz), 0,94 (t, 3H, J = 7,3 Hz), 1,32-1,44 (m, 6H), 1,54-1,64 (m, 2H), 1,66-1,78 (m, 2H), 2,62 (t, 2H, J = 7,7 Hz), 2,86 (s lg, 2H), 3,98 (septeto, 1H, J = 7,1 Hz), 7,19 (d, 2H, J = 8,5 Hz), 7,63 (d, 2H, J = 8,4 Hz), 8,72 (s lg, 1H), 8,81 (s lg, 1H).

I-98

pf: 216-218°C

RMN de ^1H ($CDCl_3$+CD_3OD) δ ppm: 0,93 (t, 3H, J = 7,4 Hz), 1,29-1,40 (m, 2H), 1,43 (d, 2H, J = 6,9 Hz), 1,51-1,63 (m, 2H), 2,60 (t, 2H, J = 7,8 Hz), 3,65 (septeto; 1H, J = 6,9 Hz), 7,18 (d, 2H, J = 8,5 Hz), 7,22 (d, 1H, J = 8,8 Hz), 7,55 (d, 2H, J = 8,5 Hz), 8,18 (dd, 1H, J = 8,8, 2,4 Hz), 8,63 (d, 1H, J = 2,4 Hz).

I-99

pf: 201-202°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,93 (t, 3H, J = 7,3 Hz), 1,22-1,40 (m, 2H), 1,49 (d, 2H, J = 7,1 Hz), 1,51-1,63 (m, 2H), 2,59 (t, 2H, J = 7,7 Hz), 4,22 (septeto, 1H, J = 7,1 Hz), 7,16 (d, 2H, J = 8,4 Hz), 7,41 (s lg, 1H), 7,52 (d, 2H, J = 8,4 Hz), 8,10 (s lg, 1H), 8,13 (d, 1H, J = 2,2 Hz), 8,61 (s lg, 1H).

I-100

pf: 160-162°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,93 (t, 3H, J = 7,3 Hz), 1,22-1,42 (m, 2H), 1,45 (d, 2H, J = 6,9 Hz), 1,51-1,63 (m, 2H), 2,61 (t, 2H, J = 7,8 Hz), 3,37 (septeto, 1H, J = 6,9 Hz), 6,89 (s lg, 1H), 7,19 (d, 2H, J = 8,4 Hz), 7,65 (d, 2H, J = 8,4 Hz), 7,80 (dd, 1H, J = 8,4, 2,4 Hz), 8,27 (d, 1H, J = 8,4 Hz), 8,45 (d, 1H, J = 2,4 Hz), 9,75 (s lg, 1H).

I-101, I-214

pf: 192-194°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,93 (t, 3H, J = 7,3 Hz), 1,27-1,41 (m, 2H), 1,35 (s, 9H), 1,50-1,66 (m, 2H), 2,60 (t, 2H, J = 7,6 Hz), 5,58 (s lg, 1H), 7,07 (d, 2H, J = 8,5 Hz), 7,17 (d, 2H, J = 8,5 Hz), 7,52 (d, 2H, J = 8,5 Hz), 7,71 (s lg, 1H), 7,79 (d, 2H, J = 8,5 Hz).

I-102

pf: 216-217°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,93 (t, 3H, J = 7,3 Hz), 1,26-1,42 (m, 2H), 1,45 (s, 9H), 1,70-1,83 (m, 2H), 2,60 (t, 2H, J = 7,7 Hz), 6,42 (s lg, 1H), 7,18 (d, 2H, J = 8,5 Hz), 7,35 (d, 2H, J = 8,5 Hz), 7,51 (d, 2H, J = 8,5 Hz), 7,68 (s lg, 1H), 7,82 (d, 2H, J = 8,5 Hz).

I-103

RMN de ^1H ($CDCl_3$) δ ppm: 0,91 (t, 3H, J = 7,3 Hz), 1,28-1,36 (m, 2H), 1,32 (d, 6H, J = 6,9 Hz), 1,49-1,59 (m, 2H), 2,54 (t, 2H, J = 7,7 Hz), 3,23 (septeto, 1H, J = 6,9 Hz), 3,46 (s, 3H), 6,76 (s lg, 1H), 6,91 (d, 2H, J = 8,2 Hz), 6,99 (d, 2H, J = 8,8 Hz), 7,03 (d, 2H, J = 8,2 Hz), 7,25 (d, 2H, J = 8,8 Hz).

I-104

pf: 182-183°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,93 (t, 3H, J = 7,3 Hz), 1,28-1,40 (m, 2H), 1,51-1,63 (m, 2H), 1,64-1,88 (m, 4H), 1,90-2,23 (m, 4H), 2,60 (t, 2H, J = 7,6 Hz), 3,39 (m, 1H), 6,16 (s lg, 1H), 7,07 (d, 2H, J = 8,5 Hz), 7,16 (d, 2H, J = 8,5 Hz), 7,52 (d, 2H, J = 8,5 Hz), 7,74 (s lg, 1H), 7,77 (d, 2H, J = 8,5 Hz).

I-105

pf: 190-191°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,93 (t, 3H, J = 7,3 Hz), 1,28-1,41 (m, 2H), 1,52-1,69 (m, 4H), 1,75-1,90 (m, 2H), 1,92-2,07 (m, 4H), 2,58 (t, 2H, J = 7,6 Hz), 3,59 (m, 1H), 6,53 (s lg, 1H), 7,18 (d, 2H, J = 8,5 Hz), 7,31 (d, 2H, J = 8,5 Hz), 7,52 (d, 2H, J = 8,5 Hz), 7,67 (s lg, 1H), 7,84 (d, 2H, J = 8,5 Hz).

I-106

pf: 194-197°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,93 (t, 3H, J = 7,3 Hz), 1,22-1,41 (m, 2H), 1,53-1,65 (m, 2H), 1,90 (s, 6H), 2,60 (t, 2H, J = 7,8 Hz), 6,86 (s lg, 1H), 7,18 (d, 2H, J = 8,5 Hz), 7,43 (d, 2H, J = 8,5 Hz), 7,51 (d, 2H, J = 8,5 Hz), 7,71 (s lg, 1H), 7,84 (d, 2H, J = 8,5 Hz).

I-107

pf: 211-212°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,93 (t, 3H, J = 7,3 Hz), 1,24-1,40 (m, 2H), 1,50-1,62 (m, 2H), 2,60 (t, 2H, J = 7,6 Hz), 6,19 (s lg, 1H), 7,17 (d, 2H, J = 8,5 Hz), 7,18 (d, 2H, J = 8,5 Hz), 7,51 (d, 2H, J = 8,5 Hz), 7,66 (s lg, 1H), 7,86 (d, 2H, J = 8,5 Hz).

I-108

pf: 298-300°C

RMN de ^1H (DMSO-d_6) δ ppm: 0,90 (t, 3H, J = 7,3 Hz), 1,22-1,39 (m, 2H), 1,48-1,60 (m, 2H), 2,54 (t, 2H, J = 7,3 Hz), 7,04 (d, 2H, J = 8,8 Hz), 7,12 (d, 2H, J = 8,5 Hz), 7,64 (d, 2H, J = 8,5 Hz), 7,69 (d, 2H, J = 8,8 Hz), 9,80 (s, 1H).

I-109

pf: 122-123°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,90 (t, 3H, J = 7,4 Hz), 0,97 (t, 3H, J = 7,7 Hz), 1,26-1,38 (m, 2H), 1,30 (s, 6H), 1,50-1,66 (m, 4H), 1,72-1,83 (m, 4H), 2,34 (t, 2H, J = 7,1 Hz), 2,55 (t, 2H, J = 7,6 Hz), 3,19 (q, 1H, J = 6,0 Hz), 4,60 (s lg, 1H), 7,08 (d, 2H, J = 8,5 Hz), 7,42 (d, 2H, J = 8,5 Hz), 7,85 (s, 1H).

I-110

pf: 109-110°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,91 (t, 3H, J = 7,4 Hz), 1,10 (d, 6H, J = 6,7 Hz), 1,29-1,38 (m, 2H), 1,55 (s, 9H), 1,60-1,70 (m, 2H), 1,78-1,89 (m, 2H), 2,26 (m, 1H), 2,39 (t, 2H, J = 7,0 Hz), 2,57 (t, 2H, J = 7,7 Hz), 2,90 (d, 2H, J = 6,6 Hz), 3,16 (s lg, 1H), 4,24 (s lg, 1H), 7,12 (d, 2H, J = 8,5 Hz), 7,40 (d, 2H, J = 8,5 Hz).

I-111

pf: 64-65°C

RMN de ^1H, ($CDCl_3$) δ ppm: 0,91 (t, 3H, J = 7,3 Hz), 1,02 (t, 3H, J = 7,5 Hz), 1,35 (d, 3H, J = 6,7 Hz), 1,26-1,38 (m, 2H), 1,48-1,69 (m, 5H), 1,76-1,87 (m, 2H), 2,04 (m, 1H), 2,38 (t, 2H, J= 7,3 Hz), 2,56 (t, 2H, J = 7,6 Hz), 2,91 (m, 1H), 3,16 (s lg, 2H), 4,42 (s lg, 1H), 7,11 (d, 2H, J = 8,5 Hz), 7,42 (d, 2H, J = 8,5 Hz), 7,47 (s lg, 1H).

I-112

pf: 79-80°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,36 (s, 9H), 1,52-1,62 (m, 2H), 1,67-1,76 (m, 2H), 2,22 (t, 2H, J = 7,4 Hz), 3,16 (q, 2H, J = 6,3 Hz), 3,78 (s, 3H), 4,33 (d, 2H, J = 5,4 Hz), 4,62 (s lg, 1H), 6,20 (s lg, 1H), 6,85 (d, 2H, J = 8,8 Hz), 7,19 (d, 2H, J = 8,8 Hz).

I-113

pf: 125-126°C

RMN de ^1H, ($CDCl_3$) δ ppm: 1,38 (s, 9H), 1,62-1,70 (m, 2H), 1,76-1,88 (m, 2H), 2,46 (t, 2H, J = 7,4 Hz), 3,22 (q, 2H, J = 6,1 Hz), 4,22 (t, 1H, J = 6,1 Hz), 7,24 (dd,

1H, J = 8,9, 2,3 Hz), 7,36 (d, 1H, J = 2,3 Hz), 7,65 (s lg, 1H), 8,29 (d, 1H, J = 8,9 Hz).

I-114

pf: 89-91°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,92 (t, 3H, J = 7,0 Hz), 1,06 (d, 6H, J = 7,0 Hz), 1,36 (m 1H), 1,50-1,72 (m ,5H), 1,94-2,06 (m, 2H), 2,26 (m, 1H), 2,60 (t, 2H, J = 7,7 Hz), 2,84 (t, 2H, J = 7,7 Hz), 2,93 (d, 2H, J = 6,3 Hz), 3,20 (t, 2H, J = 6,6 Hz), 4,30 (s lg, 1H), 7,19 (d, 2H, J = 8,5 Hz), 7,63 (d, 2H, J = 8,5 Hz), 9,15 (s lg, 1H).

I-115

pf: 94-95°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,92 (t, 3H, J = 7,5 Hz), 1,03 (t, 3H, J = 7,5 Hz), 1,23-1,40 (m ,5H), 1,42-1,65 (m, 6H), 1,75 (m, 1H), 2,02 (m, 1H), 2,24 (t, 2H, J = 7,0 Hz), 2,59 (t, 2H, J = 8,0 Hz), 2,90 (m, 1H), 3,14 (q, 2H, J = 6,6 Hz), 4,20 (m, 1H), 4,40 (d, 2H, J = 5,4 Hz), 5,70 (s lg, 1H), 7,14 (d, 2H, J = 8,1 Hz), 7,18 (d, 2H, J = 8.1 Hz).

I-116

pf: 89-91°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,97 (t, 3H, J = 7,3 Hz), 1,02 (t, 3H, J = 7,5 Hz), 1,35 (d, 3H, J = 7,0 Hz), 1,40-1,90 (m ,9H), 2,04 (m ,1H), 2,37 (t, 2H, J = 7,0 Hz), 2,90 (m, 1H), 3,17 (q, 2H, J = 6,6 Hz), 3,93 (t, 2H, J = 6,6 Hz), 4,32 (m, 1H), 6,84 (d, 2H, J = 9,0 Hz), 7,31 (s lg, 1H), 7,40 (d, 2H, J = 9,0 Hz).

I-117

pf: 110-111°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,02 (t, 3H, J = 7,5 Hz), 1,34 (d, 3H, J = 6,6 Hz), 1,45-1,70 (m ,3H), 1,75-1,85 (m, 2H), 2,05 (m ,1H), 2,36 (t, 2H, J = 7,5 Hz), 2,90 (m, 1H), 3,16 (q, 2H, J = 6,6 Hz), 3,78 (s, 3H), 4,50 (m, 1H), 6,84 (d, 2H, J = 6,8 Hz), 7,42 (d, 2H, J = 6,8 Hz), 7,48 (s lg, 1H).

I-118

pf: 113-115°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,92 (t, 3H, J = 7,0 Hz), 1,20-1,34 (m ,1H), 1,37 (d, 6H, J = 7,0 Hz), 1,48-1,70 (m, 3H), 2,43 (q, 2H, J = 6,6 Hz), 2,58 (t, 2H, J = 7,7 Hz), 3,10-3,31 (m, 3H), 4,75 (m, 1H), 6,04 (d, 1H, J = 15,0 Hz), 6,77 (dt, 1H, J = 7,7, 15,0 Hz), 7,14 (d, 2H, J = 8,4 Hz), 7,55 (d, 2H, J = 8,4 Hz), 7,85 (s lg, 1H).

I-119

pf: 139-140°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,19 (s, 9H), 1,47 (m, 2H), 1,61 (m, 2H), 2,18 (t, 2H, J = 7,6 Hz), 3,03 (q, 2H, J = 6,3 Hz), 4,09 (t, 1H, J = 5,9 Hz), 6,85 (d lg, 1H, J = 8,0 Hz), 7,00 (t, 1H, J = 8,0 Hz), 7,16 (d lg, 1H, J = 8,0), 7,48 (s lg, 1H), 7,57 (s lg, 1H).

I-120

pf: 183°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,91 (t, 3H, J = 7,3 Hz), 1,20-1,58 (m, 6H), 1,40 (s, 9H), 2,07 (dd, 1H, J = 12,9, 3,1 Hz), 2,52 (t, 2H, J = 7,7 Hz), 2,95 (dd, 2H, J = 11,5, 2,5 Hz), 3,46 (m, 1H), 3,88-4,07 (m, 3H), 6,47 (s, 1H), 7,08 (d, 2H, J = 8,5 Hz), 7,22 (d, 2H, J = 8,5 Hz).

I-121

pf: 163-166°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,91 (t, 3H, J = 7,3 Hz), 1,32-1,62 (m, 6H), 1,45 (s, 9H), 1,95-2,07 (m, 3H), 2,20 (m, 1H), 2,46 (td, 1H, J = 10,4, 3,7 Hz), 2,37 (t, 2H, J = 7,6 Hz), 3,43 (d lg, 2H, J = 10,4 Hz), 4,80 (s, 1H), 7,12 (d, 2H, J = 8,4 Hz), 7,14 (s, 1H), 7,39 (d, 2H, J = 8,4 Hz).

I-122

pf: 188-189°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,91 (t, 3H, J = 7,5 Hz), 1,25-1,41 (m ,2H), 1,42 (s, 9H), 1,50-1,62 (m ,2H), 1,78-1,95 (m ,4H), 2,00-2,20 (m ,6H), 2,57 (t, 2H, J = 7,5 Hz), 3,99 (s lg, 1H), 7,10 (s lg, 1H), 7,12 (d, 2H, J = 6,5 Hz), 7,41 (d, 2H, J = 6,5 Hz).

I-123

pf: 197-198°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,91 (t, 3H, J = 7,5 Hz), 1,24-1,40 (m ,2H), 1,39 (s, 9H), 1,50-1,70 (m ,2H), 1,99 (s lg , 12H), 2,56 (t, 2H, J = 7,5 Hz), 3,47 (s lg, 1H), 7,10 (s, 1H), 7,11 (d, 2H, J = 8,5 Hz), 7,38 (d, 2H, J = 8,5 Hz).

I-124

pf: 258-260°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,20-1,40 (m, 2H), 1,41 (s, 9H), 1,62-1,81 (m, 2H), 2,03-2,35 (m, 5H), 2,37 (s, 3H), 2,71 (s, 3H), 3,32 (m, 1H), 3,,64 (d, 1H, J = 8,4 Hz), 7,08 (s lg, 1H), 7,24 (m, 1H), 7,33 (m, 2H), 7,60 (d, 1H, J = 8,1 Hz), 7,77 (s, 1H), 7,80 (d, 1H, J = 8,4 Hz), 8,14 (m, 1H).

I-125

pf: 297-299°C

RMN de ^1H ($DMSO-d_6$) δ ppm: 1,27 (s, 9H), 1,28-1,56 (m, 4H), 1,80-2,01 (m, 4H), 2,47 (m, 1H), 2,76 (s lg, 1H), 3,05 (m, 2H), 6,78 (d, 1H, J = 9,0 Hz), 7,23 (d, 1H, J = 9,0 Hz), 7,46 (dd, 1H, J = 2,0, 9,0 Hz), 8,03 (d, 1H, J = 2,0 Hz).

I-126

pf: 198-199°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,18-1,39 (m, 2H), 1,40 (s, 9H), 1,60-1,79 (m, 2H), 1,98-2,35 (m, 5H), 3,30 (m, 1H), 3,67 (d, 1H, J = 9,6 Hz), 5,89 (tt, 1H, J = 3,0, 50,0 Hz), 6,97 (d, 1H, J = 7,8 Hz), 7,21 (s, 1H), 7,30,7,40 (m, 2H), 7,55 (s, 1H).

I-127

pf: 262-264°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,20-1,39 (m, 2H), 1,41 (s, 9H), 1,60-1,80 (m, 2H), 2,00-2,36 (m, 5H), 2,57 (s, 3H), 3,33 (m, 1H), 3,,62 (d, 1H, J = 8,7 Hz), 7,28 (s lg, 1H), 7,62 (d, 2H, J = 8,7 Hz), 7,94 (d, 2H, J = 8,7 Hz).

I-128

pf: 252-254°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,18-1,39 (m, 2H), 1,40 (s, 9H), 1,58-1,79 (m, 2H), 1,99-2,30 (m, 5H), 2,46 (s, 3H), 3,32 (m, 1H), 3,,64 (m, 1H), 7,11 (s lg, 1H), 7,23 (d, 2H, J = 9,0 Hz), 7,44 (d, 2H, J = 9,0 Hz).

I-129

pf: > 300°C

RMN de ^1H ($CDCl_3$+CD_3OD) δ ppm: 1,30-1,45 (m, 2H), 1,42 (s, 9H), 1,70-1,88 (m, 2H), 2,10-2,37 (m, 4H), 2,52 (m, 1H), 3,34 (m, 1H), 7,43-7,54 (m, 3H), 7,82 (d, 1H, J = 6,7 Hz), 7,88 (d, 1H, J = 8,5 Hz), 7,98-8,07 (m, 2H), 8,44 (s, 1H), 8,46 (s, 1H).

I-130

pf: 123-124°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,18-1,34 (m, 2H), 1,40 (s, 9H), 1,62-1,75 (m, 2H), 2,00-2,28 (m, 5H), 3,31 (m, 1H), 3,61 (d, 1H, J = 9,5 Hz), 5,59 (s, 1H), 7,17 (s, 1H), 7,30-7,37 (m, 6H), 7,41 (d, 1H, J = 8,5 Hz), 7,84 (d, 1H, J = 2,1 Hz).

1-131

pf: 202-204°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,27-1,38 (m, 2H), 1,38 (s, 9H), 1,62-1,75 (m, 2H), 1,97-2,04 (m, 2H), 2,18-2,27 (m, 3H), 3,26 (m, 1H), 3,81 (s, 3H), 4,62 (d, 1H, J = 7,9 Hz), 7,12 (d, 1H, J = 7,8 Hz), 7,40 (t, 1H, J = 7,8 Hz), 7,51 (s, 3H), 7,61 (d, 1H, J = 7,8 Hz), 7,71 (s, 1H), 8,21 (s lg, 1H).

I-132

pf: 236-237°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,23-1,43 (m, 2H), 1,41 (s, 9H), 1,66-1,80 (m, 2H), 2,08-2,12 (m, 2H), 2,23-2,31 (m, 3H), 3,34 (m, 1H), 3,87 (d, 1H, J = 9,5 Hz), 4,02 (s, 3H), 7,30 (td, 1H, J = 7,3, 1,1 Hz), 7,36 (s, 1H), 7,39 (td, 1H, J = 7,3, 1,5 Hz), 7,53 (d lg, 1H, J = 7,3 Hz), 7,84 (d lg, 1H, J = 7,3 Hz), 8,05 (s, 1H), 8,73 (s, 1H).

I-133

pf: 198-200°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,93 (t, 3H, J = 7,3 Hz), 0,97 (t, 3H, J = 6,7 Hz), 1,18-1,81 (m, 7H), 1,39 (s, 9H), 1,98-2,05 (m, 2H), 2,21-2,24 (m, 3H), 3,29 (m, 1H), 4,00 (dd, 1H, J = 10,7, 6,7 Hz), 4,09 (dd, 1H, J =10,7, 6,1 Hz), 4,27 (d, 1H, J = 9,8 Hz), 6,37 (d, 1H, J = 15,9 Hz), 7,47 (d, 2H, J = 8,5 Hz), 7,59 (d, 2H, J = 8,5 Hz), 7,62 (d, 1H, J = 15,9 Hz), 7,83 (s lg, 1H).

I-134

pf: 212-213°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,21-1,32 (m, 2H), 1,39 (s, 9H), 1,59-1,73 (m, 2H), 1,99-2,04 (m, 2H), 2,10-2,26 (m, 3H), 3,26 (m, 1H), 3,72 (d, 1H, J = 9,6 Hz), 6,74 (m, 1H), 7,02 (d, 2H, J = 7,4 Hz), 7,11 (t, 1H, J = 7,4 Hz), 7,13-7,19 (m, 2H), 7,22-7,26 (m, 2H), 7,34 (t, 2H, J = 7,4 Hz).

I-135

pf: 294-296°C

RMN de ^1H ($DMSO-d_6$) δ ppm: 1,27 (s, 9H), 1,28-1,55 (m, 4H), 1,81-2,05 (m, 4H), 2,26 (m, 1H), 2,98-3,20 (m, 2H), 6,78 (d; 1H, J = 9,0 Hz), 7,31 (t, 1H, J = 7,5 Hz), 7,54-7,72 (m, 5H), 7,94 (s lg, 1H).

I-136

pf: > 300°C

RMN de ^1H ($DMSO-d_6$) δ ppm: 1,28 (s, 9H), 1,29-1,59 (m, 4H), 1,81-2,02 (m, 4H), 2,27 (m, 1H), 3,06 (m, 1H), 6,81 (d, 1H, J = 8,7 Hz), 7,38 (t, 1H, J = 7,2 Hz), 7,48 (t, 2H, J = 7,2 Hz), 7,62-7,81 (m, 10H), 9,93 (s lg, 1H).

I-137

pf: 291-292°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,25-1,39 (m, 2H), 1,41 (s, 9H), 1,61-1,80 (m, 2H), 2,01-2,36 (m, 5H), 3,32 (m, 1H), 3,63 (d, 1H, J = 9,3 Hz), 7,20 (s lg, 1H), 7,53-7,74 (m, 8H).

I-138

pf: 259-262°C

RMN de ^1H (CD_3OD) δ ppm: 1,40 (s, 9H), 1,40-1,80 (m, 4H), 2,00-2,30 (m, 4H), 2,45 (m, 1H), 3,00 (s, 3H), 3,15-3,30 (m, 2H), 7,90 (d, 1H, J = 8,4 Hz), 8,12 (d, 1H, J = 9,0 Hz), 8,39 (d, 1H, J = 9,0 Hz), 8,72 (s, 1H), 8,92 (d, 1H, J = 8,4 Hz), 10,4 (s, 1H).

I-139

pf: 265-268°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,25-1,40 (m, 2H), 1,40 (s, 9H), 168-1,81 (m, 2H), 2,05-2,10 (m, 2H), 2,23-2,37 (m, 3H), 3,32 (m, 1H), 4,27 (d, 1H, J = 9,1 Hz), 7,53 (t, 1H, J = 7,9 Hz), 7,63 (td, 1H, J = 7,9, 1,4 Hz), 7,77 (d, 1H, J = 7,9 Hz), 8,03 (d, 1H, J = 7,9 Hz), 8,37 (s lg, 1H), 8,85-8,86 (m, 2H).

I-140

pf: 258-260°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,20-1,40 (m, 2H), 1,41 (s, 9H), 1,52-1,85 (m, 2H), 2,03-2,35 (m, 5H), 3,34 (m, 1H), 3,75 (m, 1H), 7,35-7,66 (m, 3H), 8,05 (d, 1H, J = 9,0 Hz), 8,11 (d, 1H, J = 9,0 Hz), 8,40 (s lg, 1H), 8,83 (s, 1H).

I-141

pf: 205-206°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,20-1,37 (m, 2H), 1,40 (s, 9H), 1,43-1,62 (m, 2H), 1,90-2,01 (m, 2H), 2,02-2,23 (m, 3H), 3,27 (m, 1H), 3,63 (d, 1H, J = 9,6 Hz), 3,70 (s, 3H), 6,64 (d, 1H, J = 8,8 Hz), 7,28-7,41 (m, 5H), 7,45 (s lg, 1H), 8,26 (d, 1H, J = 8,8 Hz).

I-142

pf: 277-280°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,23-0,34 (m, 2H), 1,34 (s, 9H), 1,34-1,55 (m, 5H), 1,76-1,80 (m, 2H), 2,97 (m, 1H), 3,31 (d, 1H, J = 9,6 Hz), 7,18 (s, 1H), 7,50-7,59 (m, 4H), 7,77 (dd, 1H, J = 7,4, 1,0 Hz), 7,91-7,98 (m, 2H), 8,39 (dd, 1H, J = 7,4, 1,9 Hz).

I-143

pf: 202-203°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,23-1,40 (m, 2H), 1,40 (s, 9H), 1,57-1,71 (m, 2H), 2,05-2,10 (m, 2H), 2,18-2,28 (m, 3H), 3,31 (m, 1H), 3,91 (s, 3H), 3,93 (s, 3H), 4,05 (d, 1H, J = 9,5 Hz), 8,15 (s, 1H), 9,56 (s, 1H).

I-144

pf: 177-178°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,27-1,39 (m, 2H), 1,40 (s, 9H), 1,65-1,79 (m, 2H), 2,04-2,07 (m, 2H), 2,12-2,34 (m, 3H), 3,22 (m, 1H), 3,93 (d, 1H, J = 9,1 Hz), 6,90-7,03 (m, 3H), 7,25 (m, 1H), 7,77 (dd, 1H, J = 4,9, 1,7 Hz), 7,81 (s lg, 1H), 8,72 (dd, 1H, J = 7,8, 1,5 Hz).

I-145

pf: > 300°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,30 (s, 9H), 1,44-1,70 (m, 4H), 2,05-2,19 (m, 4H), 2,73 (m, 1H), 3,18 (m, 1H), 6,86 (d, 1H, J = 8,8 Hz), 7,62 (t, 2H, J = 8,5 Hz), 7,86 (t, 2H, J = 8,5 Hz), 7,89 (d, 2H, J = 8,5 Hz), 8,16 (d, 2H, J = 8,5 Hz).

I-146

pf: 240-242°C

RMN de ^1H ($DMSO-d_6$) δ ppm: 1:26-1,53 (m, 4H), 1,27 (s, 9H), 1,74-1,83 (m, 2H), 1,90-1,97 (m, 2H), 2,26 (m, 1H), 3,04 (m, 1H), 6,59 (s lg, 1H), 6,74-6,79 (m, 3H), 7,74 (s, 1H), 10,32 (s, 1H), 12,80 (s, 1H).

I-147

pf: 167-169°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,05-1,28 (m, 2H), 1,38 (s, 9H), 1,47-1,70 (m, 2H), 1,80-2,00 (m, 3H), 2,13-2,25 (m, 2H), 2,75 (t, 2H, J = 6,9 Hz), 3,24 (m, 1H), 3,49 (dt, 2H, J = 6,3, 6,9 Hz), 3,58 (d, 1H, J = 8,7 Hz), 3,87 (s, 6H), 5,40 (s lg, 1H), 6,71 (m, 2H), 6,82 (d, 1H, J = 8,7 Hz).

I-148

pf: 171-172°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,16-1,38 (m, 2H), 1,39 (s, 9H), 1,50-1,79 (m, 4H), 1,85-2,02 (m, 3H), 2,15-2,30 (m, 2H), 2,35-2,56 (m, 6H), 3,25 (m, 1H), 3,33 (q, 2H, J = 6,0 Hz), 3,63 (d, 1H, J = 9,0 Hz), 3,72 (t, 4H, J = 4,6 Hz), 6,77 (s lg, 1H).

I-149

RMN de ^1H ($CDCl_3$) δ ppm: 1,20-1,36 (m, 2H), 1,28 (t, 3H, J = 7,2 Hz), 1,39 (s, 9H), 1,45-1,70 (m, 2H), 1,85-2,30 (m, 7H), 2,43 (s, 3H), 3,05-3,42 (m, 3H), 3,46-3,80 (m, 3H), 7,31 (d, 1H, J = 7,2 Hz), 7,40-7,52 (m, 3H), 8,18 (s lg, 1H).

I-150

pf: 203-204°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,15-1,37 (m, 2H), 1,39 (s, 9H), 1,42-1,70 (m, 2H), 1,85-2,29 (m, 5H), 2,76 (t, 2H, J = 6,0 Hz), 3,26 (m, 1H), 3,49 (q, 2H, J = 6,0 Hz), 3,61 (m, 1H), 4,03 (s, 2H), 5,88 (s lg, 1H), 7,15 (dd, 1H, J = 7,0, 8,8 Hz), 7,30-7,35 (m, 2H).

I-151

pf: 181-183°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,15-1,30 (m, 2H), 1,39 (s, 9H), 1,45-1,64 (m, 2H), 1,88-2,05 (m, 3H), 2,15-2,25 (m, 2H), 2,69 (t, 2H, J = 6,0 Hz), 3,28 (m, 1H), 3,47 (q, 2H, J = 6,0 Hz), 3,58 (d, 1H, J = 9,9 Hz), 3,87 (s, 2H), 5,83 (s lg, 1H), 7,00 (m, 1H), 7,20 (m, 2H).

I-152

pf: 222-224°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,16-1,37 (m, 2H), 1,39 (s, 9H), 1,49-1,70 (m, 2H), 1,90-2,25 (m, 5H), 3,26 (m, 1H), 3,36 (t, 2H, J = 6,4 Hz), 3,66 (dt, 3H, J = 6,0, 6,4 Hz), 5,87 (t, 1H, J = 6,0 Hz), 7,58 (s, 1H), 7,68 (dd, 1H, J = 7,0, 8,5 Hz), 7,83 (dd, 1H, J = 7,0, 8,5 Hz), 8,19 (t, 2H, J = 8,5 Hz).

I-153

pf: 207-209°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,05-1,25 (m, 2H), 1,38 (s, 9H), 1,40-2,03 (m, 10H), 2,05-2,25 (m, 2H), 2,58 (s, 3H), 2,76 (m, 1H), 3,05-3,35 (m, 2H), 3,97 (d, 1H, J = 9,5 Hz), 4,94 (t, 1H, J = 4,0 Hz), 8,42 (d, 1H, J = 5,5 Hz), 8,97 (d, 1H, J = 5,5 Hz).

I-154

pf: 184-185°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,05-1,25 (m, 2H), 1,37 (s, 9H), 1,50-1,69 (m, 2H), 1,85-2,05 (m, 3H), 2,10-2,21 (m, 2H), 3,24 (m, 1H), 3,64 (m, 1H), 4,87 (s, 1H), 4,88 (s, 1H), 5,67 (s lg, 1H), 7,42 (d, 2H, J = 5,5 Hz), 7,52 (m, 2H), 7,78 (m, 1H), 7,82 (m, 1H), 7,95 (d, 1H, J = 7,0 Hz).

I-155

pf: 208-210°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,26 (s, 9H), 1,27-1,50 (m, 4H), 1,75-2,00 (m, 4H), 2,16 (m, 1H), 2,81 (s, 3H), 3,02 (m, 1H), 6,79 (d, 1H, J = 8,5 Hz), 10,00 (s, 1H), 10,66 (s, 1H).

I-156

pf: 256-257°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,20-1,39 (m, 2H), 1,41 (s, 9H), 1,60-1,81 (m, 2H), 2,01-2,35 (m, 5H), 2,69 (t, 2H, J = 6,0 Hz), 3,11 (t, 2H, J = 6,0 Hz), 3,30 (m, 1H), 3,61 (d, 1H, J = 9,3 Hz), 7,21 (d, 1H, J = 8,0 Hz), 7,31 (s, 1H), 7,70 (d, 1H, J = 8,0 Hz), 7,99 (s, 1H).

I-157

pf: 269-271°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,20-1,45 (m, 2H), 1,41 (s, 9H), 1,70-1,90 (m, 2H), 2,10-2,45 (m, 5H), 3,37 (m, 1H), 3,68 (m, 1H), 7,45 (dd, 1H, J = 4,0, 8,0 Hz), 7,53 (s lg, 1H), 7,72 (t, 1H, J = 8,0 Hz), 7,83 (d, 1H, J = 8,0 Hz), 8,02 (d, 1H, J = 8,0 Hz), 8,18 (d, 1H, J = 8,0 Hz), 8,93 (d, 1H, J = 4,0 Hz).

I-158

pf: 253-255°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,20-1,40 (m, 2H), 1,42 (s, 9H), 1,60-1,90 (m, 2H), 2,06-2,50 (m, 5H), 2,72 (s, 3H), 3,33 (m, 1H), 3,78 (d, 1H, J = 9,2 Hz), 7,52 (t, 1H, J = 7,0 Hz), 7,62-7,80 (m, 2H), 7,94 (s lg, 1H), 8,05 (d, 1H, J = 8,5 Hz), 8,20 (s, 1H).

I-159

pf: 253-255°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,20-1,39 (m, 2H), 1,40 (s, 9H), 1,60-1,80 (m, 2H), 1,98-2,30 (m, 5H), 2,71 (s, 3H), 3,31 (m, 1H), 3,68 (d, 1H, J = 9,0 Hz), 7,41 (s lg, 1H), 7,61 (d, 2H, J = 9,0 Hz), 7,70 (d, 2H, J = 9,0 Hz).

I-160

pf: 211-212°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,20-1,32 (m, 2H), 1,39 (t, 3H, J = 7,0 Hz), 1,40 (s, 9H), 1,55-1,79 (m, 2H), 1,98-2,35 (m, 5H), 3,31 (m, 1H), 3,65 (d, 1H, J = 9,5 Hz), 4,03 (q, 2H, J = 7,0 Hz), 6,64 (d, 1H, J = 8,0 Hz), 6,92 (d, 1H, J = 8,0 Hz), 7,10 (s, 1H), 7,19 (t, 1H, J = 8,0 Hz), 7,30 (s lg, 1H).

I-161

pf: 202-203°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,96 (t, 1H, J = 7,3 Hz), 1,29-1,39 (m, 2H), 1,40 (s, 9H), 1,41-1,58 (m, 2H), 1,60-1,80 (m, 4H), 1,98-2,31 (m, 5H), 3,31 (m, 1H), 3,66 (d, 1H, J = 8,5 Hz), 3,96 (t, 2H, J = 6,4 Hz), 6,64 (d, 1H, J = 8,0 Hz), 6,90 (d, 1H, J = 8,0 Hz), 7,11 (s, 1H), 7,19 (t, 1H, J = 8,0 Hz), 7,31 (s lg, 1H).

I-162

pf: 177-180°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,18-1,38 (m, 2H), 1,39 (s, 9H), 1,59-1,78 (m, 2H), 1,95-2,05 (m, 2H), 2,07-2,25 (m, 3H), 3,26 (m, 1H), 3,46 (s, 3H), 4,17 (d, 1H, J = 9,5 Hz), 5,15 (s, 2H), 6,77 (d, 1H, J = 8,0 Hz), 7,10-7,23 (m, 2H), 7,34 (s, 1H), 7,58 (s, 1H).

I-163

pf: 175-178°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,27 (s, 9H), 1,28-1,50 (m, 4H), 1,78-2,00 (m, 4H), 2,22 (m, 1H), 2,96-3,15 (m, 2H), 6,67 (m, 1H), 6,79 (d, 1H, J = 8,5 Hz), 7,18 (m, 2H), 7,38 (s, 1H), 9,81 (s, 1H).

I-164

pf: 232-233°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,97 (t, 3H, J = 7,3 Hz), 1,22-1,30 (m, 2H), 1,40 (s, 9H), 1,44-1,51 (m, 2H), 1,67-1,77 (m, 4H), 2,02-2,24 (m, 5H), 3,22 (m, 1H), 3,62 (d, 1H, J = 9,6 Hz), 4,25 (t, 2H, J = 6,8 Hz), 6,71 (d, 1H, J = 8,4 Hz), 7,01 (s lg, 1H), 7,91 (dd, 1H, J = 8,4, 3,3 Hz), 8,08 (d, 1H, J = 3,3 Hz).

I-165

pf: 199-200°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,96 (t, 3H, J = 7,4 Hz), 1,24-1,50 (m, 4H), 1,40 (s, 9H), 1,67-1,76 (m, 3H), 2,03-2,08 (m, 2H), 2,24-2,35 (m, 3H), 3,29 (m, 1H), 3,76 (d, 1H, J = 9,1 Hz), 3,91 (t, 2H, J = 6,6 Hz), 6,41 (dd, 1H, J = 8,8, 2,5 Hz), 6,55 (d, 1H, J = 2,5 Hz), 6,82 (d, 1H, J = 8,8 Hz), 7,43 (s, 1H), 8,95 (s, 1H).

I-166

pf: 215-218°C

^1H ($CDCl_3$+CD_3OD) δ ppm: 0,97 (t, 3H, J = 7,4 Hz), 1,24-1,40 (m, 4H), 1,39 (s, 9H), 1,42-1,50 (m, 2H), 1,54-1,72 (m, 2H), 1,76-1,82 (m, 2H), 1,91-2,00 (m, 2H), 2,06-2,22 (m, 3H), 3,24 (m, 1H), 4,00 (t, 2H, J = 6,6 Hz), 6,78 (d, 1H, J = 8,8 Hz), 6,98 (dd, 1H, J = 8,8, 2,5 Hz), 7,09 (d, 1H, J = 8,8 Hz).

I-167

pf: 212-213°C

^{1}H ($CDCl_3$) δ ppm: 0,96 (t, 3H, J = 7,5 Hz), 1,26-1,34 (m, 2H), 1,40 (s, 9H), 1,45-1,50 (m, 2H), 1,68-1,77 (m, 4H), 2,03-2,08 (m, 2H), 2,17 (m, 1H), 2,26-2,29 (m, 2H), 3,29 (m, 1H), 3,60 (d, 1H, J = 9,0 Hz), 4,25 (t, 2H, J = 6,8 Hz), 6,71 (d, 1H, J = 8,4 Hz), 7,01 (s lg, 1H), 7,91 (dd, 1H, J = 8,4, 3,3 Hz), 8,08 (d, 1H, J = 3,3 Hz).

I-168

pf: 230-232°C

RMN de ^{1}H ($CDCl_3$) δ ppm: 1,22-1,35 (m, 2H), 1,40 (s, 9H), 1,63-1,77 (m, 2H), 2,03-2,08 (m, 2H), 2,15-2,29 (m, 3H), 3,31 (m, 1H), 3,63 (d, 1H, J = 9,3 Hz), 6,89 (d, 1H, J = 9,4 Hz), 7,10 (d lg, 2H, J = 7,4 Hz), 7,12 (s lg, 1H), 7,18 (t, 1H, J = 7,4 Hz), 7,36 (t lg, 2H, J = 7,4 Hz), 8,09-8,15 (m, 2H).

I-169

pf: 159-160°C

RMN de ^{1}H ($CDCl_3$) δ ppm: 0,97 (t, 3H, J = 7,3), 1,20-1,35 (m, 2H), 1,40 (s, 9H), 1,37-1,49 (m, 2H), 1,61-1,78 (m, 4H), 2,05-2,08 (m, 2H), 2,23-2,26 (m, 2H), 2,36 (s, 3H), 2,97 (s lg, 1H), 3,32 (m, 1H), 3,86 (s lg, 1H), 4,30 (t, 2H, J = 6,5 Hz), 6,25 (s, 1H), 7,92 (s lg, 1H).

I-170

pf: 180-181°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,88-0,89 (m, 2H), 1,39 (s, 9H), 1,42-1,60 (m, 2H), 1,86-1,90 (m, 2H), 2,04-2,09 (m, 2H), 2,42 (s, 3H), 2,91 (m, 1H), 3,20 (m, 1H), 3,63 (d, 1H, J = 9,2 Hz), 6,38 (s, 1H), 7,15 (m, 2H), 7,28 (m, 1H), 7,45 (m, 2H), 7,84 (s lg, 1H).

I-171

pf: 173-174°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,98 (t, 3H, J = 7,5 Hz), 1,29-1,40 (m, 2H), 1,40 (s, 9H), 1,55 (m, 2H), 1,62-1,83 (m, 4H), 2,09-2,12 (m, 2H), 2,24-2,32 (m, 3H), 3,32 (m, 1H), 3,63 (d, 1H, J = 9,5 Hz), 3,99 (t, 2H, J = 6,4 Hz), 7,22 (dd, 1H, J = 9,4, 2,7 Hz), 7,66 (d, 1H, J = 2,7 Hz), 8,63 (d, 1H, J = 9,4 Hz), 10,17 (s, 1H).

I-172

pf: 238-242°C

RMN de ^1H-NMF ($CDCl_3$) δ ppm: 0,96 (t, 3H, J = 7,3 Hz), 1,23-1,52 (m, 4H), 1,40 (s, 9H), 1,61-1,78 (m, 4H), 2,05-2,28 (m, 5H), 3,30 (m, 1H), 3,66 (d, 1H, J = 9,4 Hz), 3,84 (s lg, 2H), 3,90 (t, 2H, J = 6,4 Hz), 6,32-6,35 (m, 2H), 6,96 (s lg, 1H), 6,97 (d, 1H, J = 9,4 Hz).

I-173

pf: 165-166°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,23-1,26 (m, 2H), 1,40 (s, 9H), 1,67-1,72 (m, 2H), 2,01-2,06 (m, 2H), 2,11-2,28 (m, 3H), 3,31 (m, 1H), 3,60 (s, 2H), 3,69 (s, 3H), 4,02 (s lg, 1H), 7,01 (d, 1H, J = 8,0 Hz), 7,25 (t, 1H, J = 8,0 Hz), 7,43 (d, 1H, J = 8,0 Hz), 7,49 (s lg, 1H), 7,51 (s lg, 1H).

I-174

pf: 264-265°C

RMN de ^1H ($CDCl_3$+CD_3OD) δ ppm: 1,26-1,29 (m, 2H), 1,39 (s, 9H), 1,62-1,69 (m, 2H), 1,96-2,00 (m, 2H), 2,18-2,21 (m, 3H), 3,25 (m, 1H), 3,58 (s, 2H), 7,01 (d, 1H, J = 7,5 Hz), 7,26 (t, 1H, J = 7,5 Hz), 7,42 (s lg, 1H), 7,50 (d, 1H, J = 7,5 Hz).

I-175

pf: 90-94°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,16-1,23 (m, 2H), 1,37 (s, 9H), 1,44-1,56 (m, 2H), 1,73-1,85 (m, 3H), 2,11-2,15 (m, 2H), 3,57 (t, 2H, J = 6,4 Hz), 3,21 (m, 1H), 3,58 (m, 2H), 3,84 (d, 1H, J = 9,3 Hz), 5,56 (s lg, 1H), 7,01 (s, 1H), 7,11 (t, 1H, J = 7,5 Hz), 7,21 (t, 1H, J = 7,5 Hz),

7,38 (d, 1H, J = 7,5 Hz), 7,59 (d, 1H, J = 7,5 Hz), 8,24 (s lg, 1H).

I-176

pf: 116-118°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,18-1,38 (m, 2H), 1,40 (s, 9H), 1,60-1,79 (m, 2H), 1,95-2,30 (m, 5H), 3,30 (m, 1H), 3,69 (m, 1H), 3,80 (s, 3H), 4,64 (s, 2H), 6,67 (d, 1H, J = 8,0 Hz), 7,00 (d, 1H, J = 8,5 Hz), 7,15-7,24 (m, 2H), 7,32 (s lg, 1H).

I-177

pf: 219-220°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,27 (s, 9H), 1,28-1,50 (m, 4H), 1,75-2,01 (m, 4H), 2,18-2,30 (m, 1H), 2,95-3,15 (m, 2H), 4,61 (s, 2H), 6,56 (m, 1H), 6,80 (d, 1H, J = 8,5 Hz), 7,16 (m, 2H), 7,28 (s lg, 1H), 9,87 (s lg, 1H).

I-178

pf: 170-173°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,18-1,39 (m, 2H), 1,40 (s, 9H), 1,50-1,80 (m, 2H), 1,90-2,33 (m, 5H), 2,36 (s, 6H), 2,75 (t, 2H, J = 5,5 Hz), 3,30 (m, 1H), 3,70 (m, 1H),

4,08 (t, 2H, J = 5,5 Hz), 6,68 (d, 1H, J = 8,0 Hz), 6,94 (d, 1H, J = 7,5 Hz), 7,15-7,23 (m, 2H), 7,33 (s lg, 1H).

I-179

pf: 191-193°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,20-1,39 (m, 2H), 1,40 (s, 9H), 1,58-1,80 (m, 2H), 1,98-2,32 (m, 5H), 3,30 (m, 1H), 3,70 (d, 1H, J = 9,5 Hz), 4,77 (s, 2H), 6,73 (d, 1H, J = 8,0 Hz), 7,04 (d, 1H, J = 8,0 Hz), 7,20-7,31 (m, 2H), 7,48 (s lg, 1H).

I-180

pf: 174-176°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,10-1,30 (m, 2H), 1,40 (s, 9H), 1,45-1,65 (m, 2H), 1,81-2,02 (m, 3H), 2,15-2,30 (m, 2H), 2,58 (t, 2H, J = 6,5 Hz), 3,25 (m, 1H), 3,37 (dt, 2H, J = 5,5, 6,5 Hz), 3,60 (d, 1H, J = 9,5 Hz), 3,71 (s, 2H), 5,73 (s lg, 1H), 7,20-7,40 (m, 5H).

I-181

pf: 176-178°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,15-1,30 (m, 2H), 1,39 (s, 9H), 1,45-1,70 (m, 6H), 1,85-2,01 (m, 3H), 2,15-2,28 (m, 2H), 2,63 (t, 2H, J = 7,0 Hz), 3,25 (dt, 2H, J = 6,0,

7,0 Hz), 3,27 (m, 1H), 3,63 (m, 1H), 5,35 (s lg, 1H), 7,17 (m, 3H), 7,29 (m; 2H).

I-182

pf: 152-154°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,15-1,30 (m, 2H), 1,39 (s, 9H), 1,45-1,65 (m, 2H), 1,85-2,05 (m, 3H), 2,09-2,25 (m, 2H), 3,25 (m, 1H), 3,45 (dt, 2H, J = 5,0, 5,0 Hz), 3,55 (t, 2H, J = 5,0 Hz), 3,60 (m, 1H), 4,51 (s, 2H), 5,81 (s lg, 1H), 7,29-7,40 (m, 5H).

I-183

pf: 208-211°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,20-1,31 (m, 2H), 1,39 (s, 9H), 1,62-1,68 (m, 2H), 1,98-2,25 (m, 5H), 3,30 (m, 1H), 3,57 (d, 1H, J = 9,2 Hz), 4,59 (d, 2H, J = 5,8 Hz), 5,76 (s lg, 1H), 7,37 (dd, 1H, J = 8,4, 2,0 Hz), 7,46-7,52 (m, 2H), 7,69 (s lg, 1H), 7,78-7,83 (m, 3H).

I-184

pf: 180-182°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,22-1,37 (m, 2H), 1,40 (s, 9H), 1,60-1,69 (m, 2H), 2,05-2,09 (m, 2H), 2,21-2,27 (m, 3H), 3,45 (m, 1H), 3,64 (d, 1H, J = 9,6 Hz), 4,77 (d,

2H, J = 4,9 Hz), 7,43 (d, 1H, J = 8,6 Hz), 7,46 (s lg, 1H), 7,61 (t, 1H, J =7,7 Hz), 7,73 (t, 1H, J = 7,7 Hz), 7,87 (t, 1H, J = 7,7 Hz), 8,20 (t, 1H, J = 7,7 Hz), 8,24 (d, 1H, J = 8,6 Hz).

I-185

pf: 260-261°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,22-1,32 (m, 2H), 1,39 (s, 9H), 1,60-1,70 (m, 2H), 1,97-2,01 (m, 2H), 2,11 (m, 1H), 2,21-2,24 (m, 2H), 3,30 (m, 1H), 3,61 (d, 1H, J = 9,3 Hz),4,95 (d, 2H, J = 6,0 Hz), 5,85 (s lg, 1H), 7,33 (d, 1H, J = 4,8 Hz), 7,62 (dd, 1H, J = 8,4, 6,9 Hz), 7,75 (dd, 1H, J = 8,1, 6,9 Hz), 8,00 (d, 1H, J = 8,1 Hz), 8,20 (d, 1H, J = 8,4 Hz), 8,42 (d, 1H, J = 4,8 Hz).

I-186

pf: 231-233°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,23-1,40 (m, 2H), 1,40 (s, 9H), 1,62-1,76 (m, 2H), 2,04-2,10 (m, 2H), 2,22-2,32 (m, 3H), 3,30 (m, 1H), 3,95 (d, 1H, J = 9,3 Hz), 5,04 (d, 2H, J = 4,1 Hz), 7,61 (d, 1H, J = 5,8 Hz), 7,63 (s lg, 1H), 7,65 (dd, 1H, J = 8,2, 6,9 Hz), 7,73 (dd, 1H, J = 8,5, 6,9 Hz), 7,86 (d, 1H, J = 8,2 Hz), 8,10 (d, 1H, J = 8,5 Hz), 8,42 (d, 1H, J = 5,8 Hz).

I-187

pf: 184-187°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,97 (t, 3H, J = 7,3 Hz), 1,18-1,30 (m, 2H), 1,39 (s, 9H), 1,42-1,65 (m, 4H), 1,70-1,80 (m, 2H), 1,94-2,08 (m, 3H), 2,18-2,26 (m, 2H), 3,29 (m, 1H), 3,61 (d, 1H, J = 9,5 Hz), 3,93 (t, 2H, J = 6,4 Hz), 4,39 (d, 2H, J = 5,5 Hz), 5,67 (s lg, 1H), 6,79-6,83 (m, 3H), 7,23 (t, 1H, J = 7,6 Hz).

I-188

pf: 224-226°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,16-1,31 (m, 2H), 1,38 (s, 9H), 1,55-1,70 (m, 2H), 1,92-2,07 (m, 3H), 2,17-2,23 (m, 2H), 3,21 (m, 1H), 3,81 (s, 3H), 3,83 (s, 6H), 4,05 (d, 1H, J = 9,8 Hz), 4,34 (d, 2H, J = 5,8 Hz), 5,96 (s lg, 1H), 6,47 (s, 2H).

I-189

pf: 217-218°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,15-1,30 (m, 2H), 1,37 (s, 9H), 1,52-1,66 (m, 2H), 1,90-2,06 (m, 3H), 2,13-2,20 (m, 2H), 2,93 (s, 6H), 3,24 (m, 1H), 3,94 (d, 1H, J = 9,5 Hz), 4,30 (d, 2H, J = 5,5 Hz), 5,73 (s lg, 1H), 6,69 (d, 2H, J = 8,9 Hz), 7,12 (d, 2H, J = 8,9 Hz).

I-190

pf: sólido amorfo

RMN de ^1H ($CDCl_3$) δ ppm: 1,17-1,32 (m, 2H), 1,39 (s, 9H), 1,54-1,72 (m, 2H), 1,96-2,13 (m, 3H), 2,18-2,27 (m, 2H), 3,30 (m, 1H), 3,63 (d, 1H, J = 9,2 Hz), 4,51 (d, 2H, J = 5,8 Hz), 5,82 (s lg, 1H), 7,40 (d, 2H, J = 8,5 Hz), 8,02 (d, 2H, J = 8,5 Hz), 8,64 (s, 1H).

I-191

pf: 126-128°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,97 (t, 3H, J = 7,4 Hz), 1,10-1,28 (m, 2H), 1,36 (s, 9H), 1,42-1,86 (m, 9H), 2,06-2,18 (m, 2H), 3,22 (m, 1H), 3,95 (t, 2H, J = 4,5 Hz), 4,16 (s lg, 1H), 4,85 (s, 2H), 6,82-6,95 (m, 3H), 7,26 (t, 1H, J = 7,8 Hz), 8,54 (s lg, 1H).

I-192

pf: 178-181°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,96 (t, 3H, J = 7,3 Hz), 1,18-1,52 (m, 4H), 1,39 (s, 9H), 1,58-1,76 (m, 4H), 1,92-2,00 (m, 2H), 2,02-2,29 (m, 3H), 3,28 (m, 1H), 3,78 (d, 1H, J = 9,5 Hz), 3,89 (t, 2H, J = 6,6 Hz), 6,00 (s lg, 1H), 6,78 (s, 4H), 7,35 (s lg, 1H).

I-193

pf: 187-188°C

RMN de ^1H ($CDCl_3$+CD_3OD) δ ppm: 1,21-1,40 (m, 2H), 1,38 (s, 9H), 1,52-1,69 (m, 2H), 1,90-2,00 (m, 2H), 2,02-2,20 (m, 3H), 3,22 (m, 1H), 3,75 (s, 3H), 6,79 (s, 4H).

I-194

pf: 251-253°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,27 (s, 9H), 1,24-1,50 (m, 4H), 1,72-1,83 (m, 2H), 1,91-1,99 (m, 2H), 2,16 (m, 1H), 3,02 (m, 1H), 3,82 (s, 3H), 6,79 (d, 1H, J = 8,2 Hz), 7,01 (d, 2H, J = 8,8 Hz), 7,85 (d, 2H, J = 8,8 Hz), 9,72 (s lg, 1H), 8,64 (s lg, 1H).

I-195

pf: 183-185°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,22-1,37 (m, 2H), 1,40 (s, 9H), 1,58-1,75 (m, 2H), 2,05-2,10 (m, 2H), 2,20-2,30 (m, 3H), 3,32 (m, 1H), 3,70 (s, 2H), 3,73 (s, 3H), 6,79 (s, 1H), 8,83 (s lg, 1H).

I-196

pf: 185-187°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,20-1,39 (m, 2H), 1,40 (s, 9H), 1,44 (t, 6H, J = 7,0 Hz), 1,60-1,80 (m, 2H), 1,95-2,35 (m, 5H), 3,30 (m, 1H), 3,62 (d, 1H, J = 8,9 Hz), 4,06 (q, 2H, J = 7,0 Hz), 4,09 (q, 2H, J = 7,0 Hz), 6,08 (s, 1H), 7,02 (s, 1H), 7,36 (s, 1H).

I-197

pf: 211-213°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,20-1,40 (m, 2H), 1,41 (s, 9H), 1,60-1,80 (m, 2H), 2,00-2,36 (m, 5H), 2,61 (s, 3H), 3,32 (m, 1H), 3,64 (d, 1H, J = 9,2 Hz), 7,28 (s, 1H), 7,43 (t, 1H, J = 7,5 Hz), 7,69 (d, 1H, J = 7,5 Hz), 7,85 (d, 1H, J = 7,5 Hz), 8,02 (s, 1H).

I-198

pf: 268-269°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,20-1,39 (m, 2H), 1,40 (s, 9H), 1,42-2,32 (m, 7H), 2,90-3,10 (m, 4H), 3,30 (m, 1H), 3,68 (d, 1H, J = 8,8 Hz), 6,59 (s, 1H), 7,18 (d, 1H, J = 8,7 Hz), 7,59 (d, 1H, J = 8,7 Hz), 7,77 (s lg, 1H).

I-199 pf: 221-224°C

I-200 pf: 237-240°C

I-201 pf: 87-90°C

I-202 pf: 222-223°C

I-203 pf: 255-257°C

I-204 pf: 234-236°C

I-205 pf: 208-210°C

I-206 pf: 217-218°C

I-207 pf: 275-279°C

I-208 pf: 248-250°C

I-209 pf: 256-258°C

I-210 pf: 270-271°C

I-211 pf: 219-220°C

I-212 pf: 260-261°C

I-213 pf: >300 °C

I-214

pf: 206-207°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,93 (t, 3H, J = 7,4 Hz), 1,30-1,42 (m, 2H), 1,49 (d, 6H, J = 6,9 Hz), 1,53-1,65

(m, 2H), 2,61 (t, 2H, J = 7,7 Hz), 4,15 (septeto, 1H, J = 6,9 Hz), 7,04 (d, 1H, J = 8,2 Hz), 7,20 (d, 2H, J = 8,2 Hz), 7,51 (d, 2H, J = 8,2 Hz), 7,89 (d, 1H, J = 8,8 Hz), 8,18 (s, 1H), 10,55 (s, 1H).

I-215

RMN de ^1H ($CDCl_3$) δ ppm: 0,93 (t, 3H, J = 7,3 Hz), 1,30-1,41 (m, 2H), 1,52-1,63 (m, 2H), 1,95 (s, 6H), 2,61 (t, 2H, J = 7,8 Hz), 6,99 (s lg, 1H), 7,20 (d, 2H, J = 8,5 Hz), 7,65 (d, 2H, J = 8,5 Hz), 7,93 (dd, 1H, J = 8,5, 2,5 Hz), 8,28 (d, 1H, J = 8,5 Hz), 8,55 (d, 1H, J = 2,5 Hz), 9,76 (s lg, 1H).

Ia-1

pf: 221-224°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,19-1,38 (m, 2H), 1,40 (s, 9H), 1,62-1,77 (m, 2H), 2,00-2,31 (m, 5H), 3,18 (t, 4H, J = 4,8 Hz), 3,21-3,38 (m, 1H), 3,85 (t, 4H, J = 4,8 Hz), 6,64-6,32 (m, 2H), 7,11 (s, 1H), 7,20 (t, 1H, J = 7,8 Hz), 7,45 (s, 1H).

Ia-3

pf: 87-90°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,25 (d, 6H, J = 6,3 Hz), 1,37 (d, 6H, J = 6,9 Hz), 1,59-1,70 (m, 2H), 1,76-1,88

(m, 2H), 2,32-2,42 (m, 4H), 3,11-3,23 (m, 3H), 3,39 (d, 2H, J = 10,8 Hz), 3,74-3,86 (m, 2H), 4,34 (t, 1H, J = 9,0 Hz), 6,86 (d, 2H, J = 9,0 Hz), 7,30 (s, 1H), 7,40 (d, 2H, J = 9,0 Hz).

Ia-4

pf: 233-234°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,25 (d, 6H, J = 6,3 Hz), 1,40 (s, 9H), 1,26-1,37 (m, 2H), 1,62-1,78 (m, 2H), 2,00-2,22 (m, 5H), 2,42 (t, 2H, J = 11,7 Hz), 3,20-3,40 (m, 1H), 3,46 (d, 2H, J = 10,5 Hz), 3,67 (d, 1H, J = 9,3 Hz), 3,72-3,84 (m, 2H), 6,62-6,76 (m, 2H), 7,10 (s, 1H), 7,18 (t, 1H, J = 7,8 Hz), 7,42 (s, 1H).

Ia-5

pf: 125-126°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,25 (d, 6H, J = 6,3 Hz); 1,40 (s, 9H), 1,59-1,70 (m, 2H), 1,77-1,84 (m, 2H), 2,30-2,46 (m, 4H), 3,24 (q, 2H, J = 6,6 Hz), 3,38 (d, 2H, J = 11,7 Hz), 3,74-3,88 (m, 2H), 4,08 (t, 1H, J = 5,7 Hz), 6,87 (d, 2H, J = 8,7 Hz), 7,30 (s, 1H), 7,41 (d, 2H, J = 8,7 Hz).

Ia-6

pf: 229-230°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,25 (d, 6H, J = 6,3 Hz), 1,26-1,34 (m, 2H), 1,39 (d, 6H, J = 6,9 Hz), 1,61-1,77 (m, 2H), 1,98-1,26 (m, 5H), 2,32-2,46 (m, 2H), 3,15 (quinteto, 1H, J = 6,6 Hz), 3,22-3,35 (m, 1H), 3,39 (d, 2H, J = 11,4 Hz), 3,74-3,92 (m, 2H), 3,88 (d, 1H, J = 8,4 Hz), 6,96-6,71 (m, 2H), 7,05 (s lg, 1H), 7,39 (d, 2H, J = 9,3 Hz).

Ia-7

pf: 253-254°C

RMN de ^1H (DMSO) δ ppm: 1,24-1,60 (m, 4H), 1,27 (s, 9H), 1,77-2,07 (m, 4H), 2,16-2,34 (m, 1H), 2,97-3,15 (m, 1H), 6,78 (d, 1H, J = 7,2 Hz), 7,01 (t, 1H, J = 6,0 Hz), 7,27 (t, 2H, J = 6,6 Hz), 7,58 (d, 2H, J = 7,5 Hz), 9,78 (s, 1H).

Ia-8

pf: 257-258°C

RMN de ^1H (DMSO) δ ppm: 1,22-1,54 (m, 4H), 1,27 (s, 9H), 1,77-1,88 (m, 2H), 1,88-2,00 (m, 2H), 2,16-2,34 (m, 1H), 2,23 (s, 3H), 2,92-3,14 (m, 1H), 6,77 (d, 1H, J = 8,4 Hz), 7,07 (d, 2H, J = 8,4 Hz), 7,46 (d, 2H, J = 8,1 Hz), 9,68 (s, 1H).

Ia-9

pf: 231-232°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,21 (t, 3H, J = 7,5 Hz), 1,22-1,38 (m, 2H), 1,40 (s, 9H), 1,62-1,78 (m, 2H), 1,98-2,31 (m, 5H), 2,61 (q, 2H, J = 7,5 Hz), 3,24-3,38 (m, 1H), 3,70 (d, 1H, J = 9,9 Hz), 7,11 (s, 1H), 7,14 (d, 2H, J = 8,7 Hz), 7,40 (d, 2H, J = 8,7 Hz).

Ia-10

pf: 233-234°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,96 (t, 3H, J = 7,2 Hz), 1,20-1,37 (m, 2H), 1,40 (s, 9H), 1,56-1,78 (m, 4H), 1,98-2,32 (m, 5H), 2,54 (t, 2H, J = 7,2 Hz), 3,23-3,39 (m, 1H), 3,66 (d, 1H, J = 9,6 Hz), 7,08 (s, 1H), 7,12 (d, 2H, J = 8,4 Hz), 7,39 (d, 2H, J = 8,4 Hz).

Ia-11

pf: 243-244°C

RMN de ^1H (CDCl3) δ ppm: 1,22 (d, 6H, J = 6,9), 1,22-1,77 (m, 4H), 1,40 (s, 9H), 2,01-2,30 (m, 5H), 2,83-2,92 (m, 1H), 3,24-3,40 (m, 1H), 3,66-3,69 (m, 1H), 7,09 (s, 1H), 7,17 (d, 2H, J = 8,4 Hz), 7,41 (d, 2H, J = 8,1 Hz).

Ia-12

pf: 246-247°C

RMN de ^1H (CDCl3) δ ppm: 0,80 (t, 3H, J = 7,5), 1,20 (d, 3H, J = 7,2), 1,26-1,77 (m, 6H), 1,40 (s, 9H), 2,01-2,27 (m, 5H), 2,51-2,60 (m, 1H), 3,20-3,38 (m, 1H), 3,64-3,69 (m, 1H), 7,08 (s, 1H), 7,12 (d, 2H, J = 8,4 Hz), 7,41 (d, 2H, J = 8,4 Hz).

Ia-13

pf: 278-279°C

RMN de ^1H (CDCl3) δ ppm: 1,22-1,52 (m, 4H), 1,29 (s, 9H), 1,40 (s, 9H), 1,61-1,77 (m, 2H), 2,02-2,30 (m, 5H), 3,20-3,38 (m, 1H), 3,66-3,69 (m, 1H), 7,10 (s, 1H), 7,33 (d, 2H, J = 9,0 Hz), 7,42 (d, 2H, J = 8,7 Hz).

Ia-14

pf: 263-264°C

RMN de ^1H (DMSO) δ ppm: 1,24-1,51 (m, 4H), 1,27 (s, 9H), 1,82-1,99 (m, 4H), 2,19-2,28 (m, 1H), 2,98-3,12 (m, 1H), 6,78 (d, 1H, J = 8,7 Hz), 7,33 (d, 2H, J = 8,7 Hz), 7,61 (d, 2H, J = 9,0 Hz), 9,94 (s, 1H).

Ia-15

pf: 209-210°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,25 (d, 6H, J = 6,3 Hz), 1,40 (s, 9H), 1,70-1,98 (m, 8H), 2,19-2,38 (m, 3H), 3,39 (d, 2H, J = 11,7 Hz), 3,58-3,92 (m, 3H), 4,12-4,26 (m, 1H), 6,82-6,96 (m, 2H), 7,10 (lg, 1H), 7,41 (d, 2H, J = 8,1 Hz).

Ia-16

pf: 238-240°C

RMN de ^1H (DMSO) δ ppm: 1,22-1,52 (m, 4H), 1,27 (s, 9H), 1,81-1,84 (m, 2H), 1,93-1,97 (m, 2H), 2,16-2,23 (m, 1H), 2,95-3,12 (m, 1H), 3,70 (s, 3H), 6,77 (d, 1H, J = 8,4 Hz), 6,85 (d, 2H, J = 9,0 Hz), 7,48 (d, 2H, J = 9,3 Hz), 9,64 (s, 1H).

Ia-17

pf: 245-246°C

RMN de ^1H (DMSO) δ ppm: 1,22-1,52 (m, 4H), 1,27 (s, 9H), 1,83-1,87 (m, 2H), 1,94-1,99 (m, 2H), 2,20-2,28 (m, 1H), 2,98-3,12 (m, 1H), 6,78 (d, 1H, J = 8,7 Hz), 7,28 (d, 2H, J = 8,7 Hz), 7,69 (d, 2H, J = 9,0 Hz), 9,64 (s, 1H).

Ia-18

pf: 240-241°C

RMN de ^1H (CDCl3) δ ppm: 1,22-1,78 (m, 4H), 1,40 (s, 9H), 2,05-2,33 (m, 5H), 3,22-3,44 (m, 1H), 3,64-3,67 (m, 1H), 6,61 (s, 1H), 6,69-6,77 (m, 2H).

Ia-19

pf: 240-241 C

RMN de ^1H (CDCl3) δ ppm: 1,24-1,77 (m, 4H), 1,40 (s, 9H), 2,05-2,30 (m, 5H), 3,22-3,38 (m, 1H), 3,70-3,74 (m, 1H), 7,00-7,15 (m, 3H), 7,36 (s, 1H), 8,29-8,34 (m, 1H).

Ia-20

pf: 239-240°C

RMN de ^1H (CDCl3) δ ppm: 1,24-1,78 (m, 4H), 1,40 (s, 9H), 2,02-2,30 (m, 5H), 3,22-3,40 (m, 1H), 3,63-3,66 (m, 1H), 6,89-6,84 (m, 1H), 7,10-7,17 (m, 2H), 7,22-7,34 (m, 1H), 7,48-7,51 (m, 1H).

Ia-21

pf: 259-260°C

RMN de ^1H ($CDCl_3$/DMSO) δ ppm: 1,21 (d, 6H, J = 6,0 Hz), 1,22-1,44 (m, 2H), 1,40 (s, 9H), 1,60-1,78 (m, 2H), 1,87-2,03 (m, 2H), 2,08-2,29 (m, 3H), 2,39 (t, 2H, J = 10,2 Hz), 3,14-3,32 (m, 1H), 3,19 (d, 2H, J = 11,4 Hz),

3,77-3,93 (m, 2H), 5,33 (d, 1H, J = 9,0 Hz), 6,84 (dd, 1H, JFH, HH = 8,1, 8,1 Hz), 7,20 (d, 1H, J = 7,8 Hz), 7,49 (d, 1H, JFH = 14,7 Hz), 8,86 (s, 1H).

Ia-22

pf: 234-235°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,20 (d, 6H, J = 5,7 Hz), 1,22-1,44 (m, 2H), 1,38 (s, 9H), 1,54-1,76 (m, 2H), 1,94-2,32 (m, 5H), 2,27 (s, 3H), 2,39 (t, 2H, J = 10,8 Hz), 2,87 (d, 2H, J = 11,4 Hz), 3,20-3,40 (m, 1H), 3,76-3,92 (m, 2H), 3,91 (d, 1H, J = 9,3 Hz), 6,93 (d, 1H, J = 8,1 Hz), 7,21 (s lg, 1H), 7,27 (s lg, 1H), 7,36 (s lg, 1H).

Ia-23

pf: 195-196°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,20-1,44 (m, 4H), 1,41 (s, 9H), 1,59-1,76 (m, 2H), 2,03-2,14 (m, 2H), 2,15-2,33 (m, 3H), 3,20-3,40 (m, 1H), 3,64 (s, 1H, J = 9,0 Hz), 7,19-7,24 (m, 1H), 7,44 (s lg, 1H), 7,52-7,63 (m, 2H), 8,17 (d, 1H, J = 8,7 Hz).

Ia-24

pf: 209-210°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,22-1,39 (m, 2H), 1,56 (s, 9H), 1,61-1,78 (m, 2H), 2,00-2,12 (m, 2H), 2,17-2,33 (m, 3H), 3,24-3,39 (m, 1H), 3,67 (d, 1H, J = 9,6 Hz), 6,90-7,01 (m, 1H), 7,21 (s, 1H), 7,95-8,06 (m, 1H).

Ia-25

pf: 278-281°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,10 (d, 6H, J = 6,3 Hz), 1,27 (s, 9H), 1,28-1,55 (m, 4H), 1,78-2,00 (m, 4H), 2,11-2,26 (m, 1H), 2,31 (t, 2H, J = 11,1 Hz), 3,00-3,10 (m, 1H), 3,08 (d, 1H, J = 10,8 Hz), 3,67-3,80 (m, 2H), 6,78 (d, 1H, J = 8,7 Hz), 7,08 (d, 1H, J = 9,0 Hz), 7,41 (dd, 1H, J = 2,4, 8,7 Hz), 7,78 (d, 1H, J = 8,7 Hz), 9,85 (s, 1H).

Ia-26

pf: 253-255°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,13 (d, 6H, J = 6,0 Hz), 1,27 (s, 9H), 1,28-1,52 (m, 4H), 1,78-2,00 (m, 4H), 2,21 (t, 2H, J = 11,1 Hz), 2,26-2,36 (m, 1H), 2,96-3,10 (m, 1H), 3,56 (d, 1H, J = 12,3 Hz), 3,60-3,72 (m, 2H), 6,66-6,84 (m, 4H), 7,47 (t, 1H, J = 9,3 Hz), 9,28 (s, 1H).

Ia-27

pf: 223-226°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,09 (d, 6H, J = 6,3 Hz), 1,27 (s, 9H), 1,28-1,54 (m, 4H), 1,77-2,01 (m, 4H), 2,32 (t, 2H, J = 11,1 Hz), 2,32-2,42 (m, 1H), 2,90 (d, 1H, J = 11,4 Hz), 2,96-3,12 (m, 1H), 3,76-3,92 (m, 2H), 6,78-6,98 (m, 3H), 7,68 (dd, 1H, J = 3,3, 8,7 Hz), 8,84 (s, 1H).

Ia-28

pf: 237-238°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,22-1,44 (m, 2H), 1,25 (d, 6H, J = 6,3 Hz), 1,40 (s, 9H), 1,61-1,79 (m, 2H), 2,05-2,32 (m, 5H), 2,21 (s, 3H), 2,38 (t, 2H, J = 10,2 Hz), 3,22-3,42 (m, 1H), 3,40 (d, 2H, J = 11,1 Hz), 3,65 (d, 1H, J = 9,3 Hz), 3,72-3,90 (m, 2H), 6,70-6,78 (m, 2H), 6,81 (s lg, 1H), 7,50 (d, 1H, J = 9,6 Hz).

Ia-29

pf: 208-209°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,22 (d, 6H, J = 6,0 Hz), 1,23-1,40 (m, 2H), 1,40 (s, 9H), 1,60-1,78 (m, 2H), 2,00-2,16 (m, 2H), 2,14-2,33 (m, 3H), 2,45 (t, 2H, J = 11,1 Hz), 3,21 (d, 2H, J = 10,8 Hz), 3,24-3,38 (m, 1H), 3,63 (d, 1H, J = 9,3 Hz), 3,80-3,94 (m, 2H), 5,33 (d, 1H, J = 9,0 Hz), 6,66 (dd, 1H, JFH, HH = 6,6, 6,6 Hz), 7,16 (s lg, 1H), 7,89 (dd, 1H, JFH, HH = 9,0, 9,0 Hz).

Ia-30

pf: 284-287°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,08 (d, 6H, J = 6,0 Hz), 1,26 (s, 9H), 1,28-1,53 (m, 4H), 1,82-2,22 (m, 4H), 2,25-2,39 (m, 1H), 2,78 (t, 2H, J = 10,5 Hz), 2,97-3,14 (m, 1H), 3,18 (d, 2H, J = 11,4 Hz), 3,65-3,76 (m, 2H), 6,79 (d, 1H, J = 8,7 Hz), 9,75 (s, 1H).

Ia-31

pf: 200-201°C

RMN de ^1H (CDCl3) δ ppm: 1,22-1,40 (m, 2H), 1,40 (s, 9H), 1,62-1,76 (m, 2H), 2,04-2,32 (m, 5H), 3,22-3,40 (m, 1H), 3,62-3,66 (m, 1H), 7,22-7,24 (m, 1H), 7,38-7,38 (m, 1H), 7,60 (s, 1H), 8,33-8,36 (m, 1H).

Ia-32

pf: 260-261°C

RMN de ^1H ($CDCl_3$/DMSO) δ ppm: 1,25-1,42 (m, 2H), 1,38 (s, 9H), 1,64 (q, 2H, J = 13,5 Hz), 1,95 (d, 2H, J = 12,3 Hz), 2,16 (d, 2H, J = 10,5 Hz), 2,18-2,32 (m, 1H), 3,14-3,30 (m, 1H), 5,53 (d, 1H, J = 9,0 Hz), 7,31 (d, 1H, J = 8,7 Hz), 7,46 (dd, 1H, J = 2,4, 8,7 Hz), 7,90 (d, 1H, J = 2,1 Hz), 9,35 (s, 1H).

Ia-33

pf: 227°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,27 (s, 9H), 1,30-1,56 (m, 4H), 1,78-2,01 (m, 2H), 2,12-2,36 (m, 2H), 2,96-3,13 (m, 1H), 3,70 (s, 3H), 3,71 (s, 3H), 6,77 (d, 1H, J = 8,7 Hz), 6,85 (d, 1H, J = 8,7 Hz), 7,06 (dd, 1H, J = 2,4, 8,7 Hz), 7,33 (d, 1H, J = 2,4 Hz), 9,65 (s, 1H).

Ia-35

pf: 214-216°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,23-1,38 (m, 2H), 1,40 (s, 9H), 1,6a-1,76 (m, 2H), 2,00-2,12 (m, 2H), 2,20-2,32 (m, 3H), 3,24-3,39 (m, 1H), 3,68 (d, 1H, J = 9,0 Hz), 6,77 (d, 1H, J = 8,7 Hz), 7,00 (dd, 1H, J = 2,4, 8,7 Hz), 7,77 (s, 1H), 8,45 (d, 1H, J = 2,4 Hz).

Ia-36

pf: 241-242°C

RMN de ^1H ($CDCl_3$/DMSO) δ ppm: 1,25-1,42 (m, 2H), 1,37 (s, 9H), 1,62 (q, 2H, J = 11,7 Hz), 1,93 (d, 2H, J = 12,0 Hz), 2,12 (d, 2H, J = 10,8 Hz), 2,16-2,30 (m, 1H), 3,12-3,28 (m, 1H), 3,84 (s, 3H), 6,07 (d, 1H, J = 8,4 Hz), 6,89 (dd, 1H, JFH, HH = 9,3, 9,3 Hz), 7,24 (d, 1H, J = 8,7 Hz), 7,55 (d, 1H, JFH = 13,5 Hz), 9,32 (s, 1H).

Ia-37

pf: 248-249°C

RMN de ^1H (CDCl3) δ ppm: 0,60-0,73 (m, 1H), 0,91 (d, 6H, J = 6,6), 1,12-1,40 (m, 2H), 1,40 (s, 9H), 1,54-1,88 (m, 5H), 1,98-2,29 (m, 7H), 3,22-3,37 (m, 1H), 3,51-3,54 (m, 2H), 3,72 (d, 1H, J = 9,6), 6,88 (d, 1H, J = 8,7), 7,06 (s, 1H), 7,35 (d, 1H, J = 9,0).

Ia-38

pf: 237-238°C

RMN de ^1H (CDCl3) δ ppm: 1,01 (d, 6H, J = 6,6), 1,20-1,40 (m, 2H), 1,40 (s, 9H), 1,60-1,74 (m, 4H), 1,99-2,28 (m, 7H), 2,69-2,82 (m, 2H), 3,02-3,14 (m, 2H), 3,20-3,38 (m, 1H), 3,80-3,90 (m, 1H), 6,83-6,86 (m, 2H), 7,14 (s, 1H), 7,34 (d, 1H, J = 8,4).

Ia-39

pf: 234-235°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,20-1,36 (m, 2H), 1,40 (s, 9H), 1,60-1,77 (m, 2H), 1,90-2,32 (m, 5H), 3,21-3,39 (m, 1H), 3,65 (d, 1H, J = 9,6 Hz), 6,87 (d, 1H, J = 8,7 Hz), 7,04 (s, 1H), 7,37 (dd, 1H, J = 2,7, 8,7 Hz), 7,56 (d, 1H, J = 2,7 Hz).

Ia-40

pf: 257-258°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,14 (d, 6H, J = 6,0 Hz), 1,27 (s, 9H), 1,28-1,53 (m, 4H), 1,78-2,00 (m, 4H), 2,13-2,256 (m, 1H), 2,30 (t, 2H, J = 11,7 Hz), 2,97-3,12 (m, 1H), 3,53-3,67 (m, 2H), 4,01 (d, 1H, J = 12,3 Hz), 6,80 (dd, 1H, J = 3,0, 9,0 Hz), 7,79 (d, 1H, J = 9,0 Hz), 8,27 (s, 1H), 9,66 (s, 1H).

Ia-41

pf: 245-246°C

RMN de ^1H ($CDCl_3$/DMSO) δ ppm: 1,25-1,42 (m, 2H), 1,37 (s, 9H), 1,62 (q, 2H, J = 12,6 Hz), 1,94 (d, 2H, J = 11,1 Hz), 2,13 (d, 2H, J = 11,1 Hz), 2,18-2,35 (m, 1H), 3,11-3,29 (m, 1H), 6,07 (d, 1H, J = 8,1 Hz), 6,95-7,06 (m, 1H), 7,14-7,27 (m, 1H), 7,44 (d, 1H, J = 7,2 Hz), 7,79 (s, 1H), 9,48 (s, 1H).

Ia-43

pf: 294-295°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,26 (s, 9H), 1,28-1,53 (m, 4H), 1,76-1,87 (m, 2H), 1,89-2,00 (m, 2H), 2,13-2,25 (m, 1H), 2,96-3,10 (m, 5H), 3,52-3,60 (m, 4H), 6,78 (d, 1H, J = 9,0 Hz), 6,88 (d, 2H, J = 9,0 Hz), 7,44 (d, 2H, J = 9,0 Hz), 9,59 (s, 1H).

Ia-44

pf: 250-252°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,13 (d, 6H, J = 6,3 Hz), 1,21-1,38 (m, 2H), 1,41 (s, 9H), 1,63-1,80 (m, 2H), 1,93 (t, 2H, J = 10,8 Hz), 2,00-2,10 (m, 2H), 2,16-2,32 (m, 3H), 3,24-3,39 (m, 1H), 3,54 (d, 2H, J = 10,2 Hz), 3,64-3,78 (m, 3H), 7,47 (s, 1H), 7,69 (d, 2H, J = 9,0 Hz), 7,73 (d, 2H, J = 9,0 Hz).

Ia-45

pf: 193°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,10 (t, 6H, J = 7,2 Hz), 1,26 (s, 9H), 1,28-1,52 (m, 4H), 1,75-1,86 (m, 2H), 1,89-2,01 (m, 2H), 2,10-2,22 (m, 1H), 2,96-3,10 (m, 1H), 3,30-3,52 (m, 12H), 6,60 (d, 2H, J = 9,0 Hz), 6,80 (d, 1H, J = 9,0 Hz), 7,33 (d, 2H, J = 9,0 Hz), 9,46 (s, 1H).

Ia-46

pf > 300°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,28 (s, 9H), 1,28-1,58 (m, 4H), 1,83-2,04 (m, 4H), 2,23-2,36 (m, 1H), 2,46 (s, 3H), 3,00-3,14 (m, 1H), 6,79 (d, 1H, J = 8,7 Hz), 7,34 (d, 1H, J = 8,7 Hz), 7,78 (d, 2H, J = 8,7 Hz), 7,89 (d, 1H, J =

8,4 Hz), 7,91 (s, 1H), 8,00 (d, 2H, J = 8,7 Hz), 10,13 (s, 1H).

Ia-47

pf: 236-237°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,97 (d, 6H, J = 6,6 Hz), 1,01 (d, 6H, J = 6,6 Hz), 1,20-1,37 (m, 2H), 1,40 (s, 9H), 1,60-1,84 (m, 3H), 1,97-2,31 (m, 5H), 2,50 (t, 1H, J = 10,8 Hz), 2,78 (dt, 1H, J = 3,3, 11,4 Hz), 3,25-3,38 (m, 1H), 3,45 (d, 1H, J = 11,4 Hz), 3,75 (dt, 1H, J = 2,4, 11,4 Hz), 4,02 (dt, 1H, J = 2,4, 11,4 Hz), 6,88 (d, 2H, J = 9,0 Hz), 7,05 (s, 1H), 7,39 (d, 2H, J = 9,0 Hz).

Ia-48

pf: 228-229°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,88 (t, 6H, J = 7,2 Hz), 1,19-1,45 (m, 4H), 1,40 (s, 9H), 1,45-1,76 (m, 4H), 1,76-1,92 (m, 1H), 1,96-2,30 (m, 5H), 2,66-3,20 (m, 3H), 3,20-3,40 (m, 1H), 3,78 (d, 1H, J = 9,3 Hz), 3,82 (s, 1H), 6,62-6,98 (m, 2H), 7,09 (s lg, 1H), 7,37 (d, 2H, J = 7,8 Hz).

Ia-49

pf: 262-263°C

RMN de ^1H ($CDCl_3$/DMSO) δ ppm: 1,21 (d, 6H, J = 5,7 Hz), 1,26-1,34 (m, 2H), 1,37 (d, 6H, J = 5,4 Hz), 1,52-1,76 (m, 2H), 1,85-2,03 (m, 2H), 2,03-2,30 (m, 3H), 2,30-2,53 (m, 2H), 3,02-3,33 (m, 4H), 3,75-3,98 (m, 2H), 5,70 (s lg, 1H), 6,73-6,98 (m, 1H), 7,14-7,25 (m, 1H), 7,52 (d, 1H, JFH = 13,5 Hz), 8,86 (s lg, 1H).

Ia-50

pf: 232-233°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,21 (d, 6H, J = 6,3 Hz), 1,22-1,37 (m, 2H), 1,38 (d, 6H, J = 6,9 Hz), 1,68 (q, 2H, J = 12,6 Hz), 1,98-2,26 (m, 5H), 2,29 (s, 3H), 2,41 (t, 2H, J = 10,2 Hz), 2,88 (d, 2H, J = 11,1 Hz), 3,15 (septeto, 1H, J = 6,6 Hz), 3,21-3,37 (m, 1H), 3,77-3,92 (m, 2H), 3,87 (d, 1H, J = 7,8 Hz), 6,88-7,06 (m, 3H), 7,35 (s, 1H).

Ia-51

pf: 211-212°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,20-1,42 (m, 2H), 1,26 (d, 6H, J = 6,3 Hz), 1,38 (d, 6H, J = 6,9 Hz), 1,62-1,78 (m, 2H), 1,99-2,28 (m, 5H), 2,49 (dd, 2H, J = 10,5, 10,5 Hz), 3,17 (quinteto, 1H, J = 6,9 Hz), 3,20-3,38 (m, 1H), 3,66-3,99 (m, 2H), 3,90-4,01 (m, 3H), 6,62 (d, 1H, J = 9,0 Hz), 7,06 (s, 1H), 7,90 (dd, 1H, J = 2,4, 9,0 Hz), 8,09 (d, 1H, J = 2,4 Hz).

Ia-52

pf: 247-249°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,21-1,36 (m, 2H), 1,40 (s, 9H) 1,62-1,78 (m, 2H), 1,98-2,32 (m, 5H), 2,55 (t, 4H, J = 6,0 Hz), 3,23-3,38 (m, 1H), 3,55 (t, 4H, J = 6,0 Hz), 3,72 (d, 1H, J = 9,6 Hz), 6,94 (d, 2H, J = 9,0 Hz), 7,10 (s, 1H), 7,42 (d, 1H, J = 9,0 Hz).

Ia-53

pf: 234-235°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,22-1,38 (m, 2H), 1,41 (s, 9H) 1,64-1,80 (m, 2H), 2,00-2,32 (m, 5H), 3,25-3,40 (m, 1H), 3,73 (d, 1H, J = 9,3 Hz), 7,43 (s, 1H), 7,48 (t, 2H, J = 7,5 Hz), 7,55-7,66 (m, 3H), 7,68-7,89 (m, 4H).

Ia-54

pf: 235-236°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,24-1,39 (m, 2H), 1,25 (d, 6H, J = 6,3 Hz), 1,39 (d, 6H, J = 6,9 Hz), 1,60-1,80 (m, 2H), 2,00-2,28 (m, 5H), 2,21 (s, 3H), 2,38 (t, 2H, J = 10,8 Hz), 3,15 (septeto, 1H, J = 6,3 Hz), 3,23-3,38 (m, 1H), 3,40 (d, 2H, J = 11,7 Hz), 3,72-3,88 (m, 2H), 3,87 (d, 1H, J = 9,3 Hz), 6,78-6,86 (m, 3H), 7,50 (d, 1H, J = 9,6 Hz).

Ia-55

pf: 185-186°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,14 (d, 6H, J = 6,3 Hz), 1,22-1,38 (m, 2H), 1,41 (s, 9H), 1,62-1,78 (m, 2H), 2,02 (t, 2H, J = 10,5 Hz), 2,02-2,10 (m, 2H), 2,16-2,31 (m, 3H), 3,24-3,39 (m, 1H), 3,56 (d, 2H, J = 9,3 Hz), 3,63-3,80 (m, 3H), 7,46 (dd, 1H, J = 1,5, 8,1 Hz), 7,51 (t, 1H, J = 8,1 Hz), 7,63 (s, 1H), 7,81 (t, 1H, J = 1,8 Hz), 7,98 (dt, 1H, J = 1,8, 8,1 Hz).

Ia-56

pf: 229-230°C

RMN de ^1H (DMSO) δ ppm: 1,27 (s, 9H), 1,28-1,54 (m, 4H), 1,38 (s, 6H), 1,78-1,84 (m, 2H), 1,90-2,00 (m, 2H), 2,15-2,30 (m, 1H), 2,97-3,13 (m, 1H), 4,90 (s, 1H), 6,79 (d, 1H, J = 9,0 Hz), 7,34 (d, 2H, J = 8,7 Hz), 7,48 (d, 2H, J = 8,4 Hz), 9,72 (s, 1H).

Ia-57

pf: 211-212°C

RMN de ^1H ($CDCl_3$/DMSO) δ ppm: 1,24-1,40 (m, 2H), 1,38 (s, 9H), 1,57-1,74 (m, 2H), 1,91 (s, 3H), 1,92-2,01 (m, 2H), 2,12-2,24 (m, 2H), 2,51 (s lg, 1H), 3,18-3,33 (m,

1H), 4,96 (d, 1H, J = 9,3 Hz), 7,16-7,53 (m, 9H), 7,41 (s, 1H).

Ia-58

pf: 298-299°C

RMN de ^{1}H (DMSO-d_6) δ ppm: 1,24 (s, 9H), 1,27 (s, 9H), 1,28-1,54 (m, 4H), 1,75-2,02 (m, 4H), 2,14-2,28 (m, 1H), 2,97-3,11 (m, 1H), 6,78 (d, 1H, J = 8,4 Hz), 7,18 (d, 2H, J = 9,0 Hz), 7,48 (d, 2H, J = 9,0 Hz), 9,46 (s, 1H), 9,76 (s, 1H).

Ia-59

pf: 253-254°C

RMN de ^{1}H ($CDCl_3$) δ ppm: 1,22-1,40 (m, 2H), 1,41 (s, 9H), 1,65-1,81 (m, 2H), 2,04-2,16 (m, 2H), 2,22-2,36 (m, 2H), 3,24-3,41 (m, 1H), 3,74 (d, 1H, J = 9,6 Hz), 7,40-7,54 (m, 3H), 7,88-8,01 (m, 3H), 8,66 (d, 1H, J = 1,5 Hz), 9,57 (d, 1H, J = 1,2 Hz).

Ia-60

pf: 213-214°C

RMN de ^{1}H (DMSO) δ ppm: 1,32-1,50 (m, 2H), 1,35 (s, 9H), 1,52-1,70 (m, 2H), 1,88-2,00 (m, 2H), 2,04-2,16 (m, 2H), 2,22-2,38 (m, 1H), 2,65 (s, 3H), 2,99-3,15 (m,

1H), 6,46 (d, 1H, J = 9,3 Hz), 7,28 (d, 1H, J = 9,0 Hz), 7,81 (s, 1H), 8,20 (s, 1H), 8,47 (s, 1H), 9,89 (s, 1H).

Ia-61

pf: 274-275°C

RMN de ^1H (DMSO) δ ppm: 1,27 (s, 1H), 1,28-1,58 (m, 4H), 1,84-2,08 (m, 4H), 2,22-2,40 (m, 1H), 2,99-3,15 (m, 1H), 3,01 (s, 3H), 6,81 (d, 1H, J = 8,1 Hz), 7,78 (d, 2H, J = 7,8 Hz), 7,84 (d, 2H, J = 8,4 Hz), 8,18 (s, 1H), 10,43 (s, 1H).

Ia-62

pf: 235-236°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,22-1,39 (m, 2H), 1,41 (s, 3H), 1,66-1,80 (m, 2H), 2,01-2,12 (m, 2H), 2,14-2,22 (m, 1H), 2,23-2,34 (m, 2H), 3,24-3,42 (m, 1H), 3,69 (d, 1H, J = 9,5 Hz), 6,44 (d, 1H, J = 9,3 Hz), 7,27 (s lg, 1H), 7,28 (d, 1H, J = 9,3 Hz), 7,37 (dd, 1H, J = 2,4, 9,0 Hz), 7,68 (d, 1H, J = 9,6 Hz), 8,04 (d, 1H, J = 2,4 Hz).

Ia-63

pf: 277-279°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,27 (s, 9H), 1,28-1,54 (m, 4H), 1,77-2,02 (m, 4H), 2,15-2,29 (m, 1H), 2,90 (s,

3H), 2,96-3,13 (m, 1H), 6,79 (d, 1H, J = 8,7 Hz), 7,12 (d, 2H, J = 9,0 Hz), 7,54 (d, 2H, J = 9,0 Hz), 9,50 (s, 1H), 9,81 (s, 1H).

Ia-64

pf: 259-260°C

RMN de ^{1}H (DMSO-d_6) δ ppm: 1,26 (s, 9H), 1,26-1,50 (m, 4H), 1,74-1,99 (m, 4H), 2,10-2,25 (m, 1H), 2,95-3,10 (m, 1H), 6,78 (d, 1H, J = 8,7 Hz), 6,97 (d, 2H, J = 9,0 Hz), 7,42 (d, 2H, J = 9,0 Hz), 7,50-7,71 (m, 5H), 9,73 (s, 1H), 10,05 (s, 1H).

Ia-65

pf: 292-293°C

RMN de ^{1}H (DMSO-d_6) δ ppm: 1,27 (s, 9H), 1,28-1,54 (m, 4H), 1,62-1,72 (m, 2H), 1,77-1,87 (m, 2H), 1,91-2,10 (m, 4H), 2,13-2,25 (m, 1H), 2,98-3,12 (m, 1H), 3,41-3,52 (m, 2H), 5,09 (s, 1H), 6,79 (d, 1H, J = 9,0 Hz), 6,91 (d, 2H, J = 9,0 Hz), 7,37 (d, 2H, J = 9,0 Hz), 7,42 (d, 2H, J = 9,0 Hz), 7,51 (d, 2H, J = 9,0 Hz), 9,56 (s, 1H).

Ia-66

pf > 300°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,27 (s, 9H), 1,28-1,58 (m, 4H), 1,85-2,02 (m, 4H), 2,40-2,52 (m, 1H), 3,00-3,16 (m, 1H), 6,81 (d, 1H, J = 9,0 Hz), 7,50-7,58 (m, 3H), 7,90-7,97 (m, 2H), 12,58 (s, 1H).

Ia-67

pf: 199-200°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,14 (d, 6H, J = 6,3 Hz), 1,28 (s, 9H), 1,31-1,48 (m, 4H), 1,76-1,88 (m, 2H), 2,17 (t, 2H, J = 11,1 Hz), 2,82 (t, 2H, J = 11,7 Hz), 3,46 (d, 2H, J = 11,4 Hz), 3,20-3,36 (m, 1H), 3,62-3,74 (m, 2H), 4,02 (d, 2H, J = 12,9 Hz), 6,83 (d, 2H, J = 9,0 Hz), 6,89 (d, 1H, J = 8,7 Hz), 7,28 (d, 2H, J = 9,0 Hz), 8,27 (s, 1H).

Ia-68

pf: 237-239°C

RMN de ^1H ($CDCl_3$/DMSO) δ ppm: 1,40 (s, 9H), 1,49-1,65 (m, 2H), 1,99-2,10 (m, 2H), 2,95 (t, 2H, J = 11,1 Hz), 3,36-3,52 (m, 1H), 4,17 (d, 1H, J = 12,9 Hz), 5,84 (d, 1H, J = 8,7 Hz), 6,39 (d, 1H, J = 9,6 Hz), 7,21 (d, 1H, J = 9,3 Hz), 7,51 (dd, 1H, J = 2,4, 9,3 Hz), 7,72 (d, 1H, J = 9,9 Hz), 7,85 (d, 1H, J = 2,7 Hz), 8,04 (s, 1H).

Ia-69

pf: 259-260°C

RMN de ^1H (DMSO) δ ppm: 1,25-1,55 (m, 4H), 1,27 (s, 9H), 1,82-2,05 (m, 4H), 2,22-2,36 (m, 1H), 2,98-3,17 (m, 1H), 4,16 (s, 3H), 6,80 (d, 1H, J = 8,4 Hz), 7,77-7,87 (m, 4H), 10,16 (s, 1H).

Ia-70

pf: 259-260°C

RMN de ^1H (DMSO) δ ppm: 1,28 (s, 9H), 1,36-1,56 (m, 2H), 1,80-1,92 (m, 2H), 2,86-3,02 (m, 2H), 3,36-3,52 (m, 1H), 4,04-4,20 (m, 2H), 6,92 (d, 1H, J = 7,5 Hz), 7,38-7,58 (m, 3H), 8,00-8,14 (m, 2H), 8,90 (s, 1H), 9,08 (s, 1H), 9,63 (s, 1H).

Ia-71

pf: 228.229°C

RMN de ^1H ($CDCl_3$/DMSO) δ ppm: 1,27-1,42 (m, 2H), 1,38 (s, 9H), 1,57-1,75 (m, 2H), 1,90-2,02 (m, 2H), 2,12-2,34 (m, 3H), 3,14-3,32 (m, 1H), 5,37 (d, 1H, J = 9,3 Hz), 7,38-7,43 (m, 3H), 7,46 (d, 2H, J = 8,7 Hz), 7,51-7,60 (m, 2H), 7,68 (d, 2H, J = 9,0 Hz), 9,33 (s, 1H).

Ia-75

pf: 169-170°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,58-0,72 (m, 1H), 0,80 (d, 3H, J = 6,6 Hz), 0,94 (d, 3H, J = 6,0 Hz), 1,14-1,35 (m, 3H), 1,39 (s, 9H), 1,48-1,66 (m, 2H), 1,74-2,06 (m, 5H), 2,06-2,44 (m, 6H), 3,18-3,35 (m, 1H), 3,64-3,74 (m, 1H), 4,46-4,60 (m, 1H), 6,98-7,38 (m, 5H).

Ia-76

pf: 236-237°C

RMN de ^1H ($CDCl_3$/DMSO) δ ppm: 1,27-1,42 (m, 2H), 1,38 (d, 6H, J = 6,6 Hz), 1,60-1,78 (m, 2H), 1,94-2,06 (m, 2H), 2,12-2,30 (m, 3H), 3,06,3,34 (m, 2H), 5,10 (s lg, 1H), 6,41 (d, 1H, J = 9,9 Hz), 7,25 (d, 1H, J = 8,4 Hz), 7,48 (dd, 1H, J = 2,4, 8,7 Hz), 7,68 (d, 1H, J = 9,9 Hz), 8,12 (d, 1H, J = 2,4 Hz), 8,88 (s lg, 1H).

Ia-77

pf: 117-118°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,38 (d, 6H, J = 6,9 Hz), 1,65 (quintet0, 2H, J = 5,4 Hz), 1,75-1,91 (m, 2H), 2,42 (t, 2H, J = 7,4 Hz), 3,10-3,24 (m, 3H), 4,77 (s lg, 1H), 6,41 (d, 1H, J = 9,6 Hz), 7,18-7,26 (m, 1H), 7,48 (dd, 1H, J = 1,8, 8,7 Hz), 7,67 (d, 1H, J = 9,9 Hz), 8,01 (s, 1H), 8,23 (s lg, 1H).

Ia-78

pf: 138-139°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,41 (s, 9H), 1,64 (quinteto, 2H, J = 6,6 Hz), 1,84 (quinteto, 2H, J = 7,3 Hz), 2,42 (t, 2H, J = 7,5 Hz), 3,26 (q, 2H, J = 6,5 Hz), 4,59 (s lg, 1H), 6,41 (d, 1H, J = 9,3 Hz), 7,23 (d, 1H, J = 8,7 Hz), 7,49 (dd, 1H, J = 2,4, 9,0 Hz), 7,67 (d, 1H, J = 9,9 Hz), 8,03 (d, 1H, J = 2,4 Hz), 8,28 (s lg, 1H).

Ia-79

pf: 289-290°C

RMN de ^1H (DMSO) δ ppm: 1,24-1,63 (m, 4H), 1,28 (s, 9H), 1,84-2,08 (m, 4H), 2,24-2,41 (m, 1H), 3,00-3,16 (m, 1H), 6,82 (d, 1H, J = 8,1 Hz), 7,36-7,60 (m, 5H), 7,86-7,99 (m, 2H), 8,28 (s, 1H), 10,50 (s, 1H).

Ia-80

pf: 239-240°C

RMN de ^1H (DMSO) δ ppm: 1,22 (d, 1H, J = 6,6 Hz), 1,23-1,40 (m, 2H), 1,40-1,59 (m, 2H), 1,83-2,04 (m, 4H), 2,23-2,39 (m, 1H), 2,98-3,23 (m, 2H), 7,00 (d, 1H, J = 7,8 Hz), 7,36-7,59 (m, 5H), 7,85-7,97 (m, 2H), 8,29 (s, 1H), 10,50 (s, 1H).

Ia-81

pf: 205-206°C

RMN de ^1H ($CDCl_3$/DMSO) δ ppm: 1,40 (s, 9H), 1,66 (quinteto, 2H, J = 7,0 Hz), 1,85 (quinteto, 2H, J = 7,2 Hz), 2,45 (t, 2H, J = 7,5 Hz), 3,24 (t, 2H, J = 6,5 Hz), 5,17 (s lg, 1H), 7,36-7,54 (m, 5H), 7,85 (d, 1H, J = 8,4 Hz), 8,07 (dd, 1H, J =1,8, 8,1 Hz), 8,23 (d, 1H, J = 1,8 Hz), 9,61 (s, 1H).

Ia-82

pf: 216-217°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,14 (d, 6H, J = 6,3 Hz), 1,22 (d, 6H, J = 6,9 Hz), 1,22-1,53 (m, 4H), 1,76-1,98 (m, 2H), 2,21 (t, 2H, J = 10,8 Hz), 2,22-2,36 (m, 1H), 2,96-3,20 (m, 2H), 3,57 (d, 2H, J = 12,0 Hz), 3,60-3,74 (m, 1H), 6,66-6,85 (m, 2H), 6,98 (d, 1H, J = 7,8 Hz), 7,47 (d, 1H, J = 8,7 Hz), 9,30 (s, 1H).

Ia-83

pf: 118-119°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,41 (d, 6H, J = 6,3 Hz), 1,26 (s, 9H), 1,40-1,67 (m, 4H), 2,17-2,36 (m, 3H), 2,97-3,10 (m, 2H), 3,57 (d, 2H, J = 12,0 Hz), 3,61-3,74 (m, 1H), 6,67-6,92 (m, 3H), 7,48 (t, 1H, J = 9,0 Hz), 9,37 (s, 1H).

Ia-84

pf: 265-267°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,21 (d, 6H, J = 6,6 Hz), 1,20-1,57 (m, 4H), 1,60-2,30 (m, 9H), 2,99-3,20 (m, 4H), 3,40-3,52 (m, 2H), 5,09 (s, 1H), 6,91 (d, 2H, J = 8,7 Hz), 6,98 (d, 1H, J = 7,5 Hz), 7,37 (d, 2H, J = 8,7 Hz), 7,42 (d, 2H, J = 8,7 Hz), 7,51 (d, 2H, J = 8,7 Hz), 9,56 (s, 1H).

Ia-85

pf: 185-186°C

^1H (DMSO-d_6) δ ppm: 1,26 (s, 9H), 1,42-1,72 (m, 6H), 1,96-2,10 (m, 2H), 2,26 (t, 2H, J = 6,9 Hz), 2,96-3,12 (m, 4H), 3,41-3,52 (m, 2H), 5,09 (s, 1H), 6,88 (d, 1H, J = 8,7 Hz), 6,92 (d, 2H, J = 9,0 Hz), 7,37 (d, 2H, J = 8,7 Hz), 7,43 (d, 2H, J = 9,0 Hz), 7,52 (d, 2H, J = 8,7 Hz), 9,63 (s, 1H).

Ia-86

pf: 162-164°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,21 (d, 6H, J = 6,6 Hz), 1,41-1,73 (m, 6H), 1,96-2,10 (m, 2H), 2,26 (t, 2H, J = 7,2 Hz), 2,91-3,20 (m, 5H), 3,42-3,52 (m, 2H), 5,09 (s, 1H), 6,92 (d, 2H, J = 9,3 Hz), 6,99 (t, 1H, J = 6,0 Hz),

7,37 (d, 2H, J = 8,7 Hz), 7,43 (d, 2H, J = 9,3 Hz), 7,52 (d, 2H, J = 8,7 Hz), 9,64 (s, 1H).

Ia-87

pf: 245-247°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,22 (d, 6H, J = 6,6 Hz), 1,22-1,58 (m, 4H), 1,81-2,02 (m, 4H), 2,22,2,36 (m, 1H), 3,00-3,20 (m, 2H), 3,01 (s, 3H), 6,99 (d, 1H, J = 8,4 Hz), 7,75-7,88 (m, 2H), 8,19 (d, 1H, J = 1,2 Hz), 10,43 (s, 1H).

Ia-88

pf: 208-209°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,22 (d, 6H, J = 6,9 Hz), 1,22-1,55 (m, 4H), 1,75-1,98 (m, 4H), 2,11-2,24 (m, 1H), 2,98-3,20 (m, 2H), 5,96 (s, 2H), 6,82 (d, 1H, J = 8,4 Hz), 6,91-7,03 (m, 2H), 7,30 (d, 1H, J = 1,8 Hz), 9,72 (s, 1H).

Ia-89

pf: 142-143°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,27 (s, 9H), 1,40-1,66 (m, 4H), 2,26 (t, 2H, J = 7,5 Hz), 3,02 (q, 2H, J = 6,6 Hz), 5,96 (s, 2H), 6,82 (d, 1H, J = 8,4 Hz), 6,88 (t, 1H, J

= 8,4 Hz), 6,94 (dd, 1H, J = 1,8, 8,4 Hz), 7,30 (d, 1H, J = 1,8 Hz), 9,78 (s, 1H).

Ia-90

pf: 100°C

RMN de ^{1}H (DMSO-d_6) δ ppm: 1,20 (d, 6H, J = 6,9 Hz), 1,40-1,66 (m, 4H), 2,26 (t, 2H, J = 7,5 Hz), 2,89-2,99 (m, 2H), 3,13 (quinteto, 1H, J = 6,6 Hz), 5,96 (s, 2H), 6,83 (d, 1H, J = 8,1 Hz), 6,91-7,02 (m, 2H), 7,30 (d, 1H, J = 1,8 Hz), 9,78 (s, 1H).

Ia-91

pf: 189-190°C

RMN de ^{1}H (DMSO-d_6) δ ppm: 1,26 (s, 9H), 1,43-1,71 (m, 4H), 2,40 (t, 2H, J = 7,5 Hz), 2,97-3,09 (m, 2H), 3,01 (s, 3H), 6,85-6,93 (m, 1H), 7,76-7,88 (m, 2H), 8,20 (d, 1H, J = 1,2 Hz), 10,49 (s, 1H).

Ia-104

pf: 238-241°C

RMN de ^{1}H (DMSO) δ ppm: 1,27 (s, 9H), 1,3-1,5 (m, 4H), 1,8-2,0 (m, 4H), 2,50 (m, 1H), 3,05 (m, 1H), 6,55 (s lg, 1H), 6,79 (d, 1H, J= 8,2), 7,15 (t, 1H, J= 4,8), 8,64 (d, 2H, J= 4,8).

Ia-105

pf: 232-234°C

^{1}H (DMSO) δ ppm: 1,26 (s, 9H), 1,2-1,5, (m, 4H), 1,8-2,0 (m, 4H), 2,55 (m, 1H), 3,05 (m, 1H), 6,77 (d, 1H, J=8,7), 9,92 (s, 2H), 10,93 (s, 1H).

Ia-106

pf: 226-228°C

RMN de ^{1}H (DMSO) δ ppm: 1,28 (s, 9H), 1,22-1,58 (m, 4H), 1,82-2,04 (m, 4H), 2,29 (m, 1H), 3,07 (m, 1H), 6,79 (d, 1H, J = 8,7 Hz), 7,6 1 (dd, 1H, J = 1,8 Hz, 8,7 Hz), 8,04 (d, 1H, J,= 8,7 Hz), 8,48 (d, 1H, 2,1 Hz), 9,35 (s, 1H), 10,05 (s, 1H).

Ia-107

pf: 282-283°C

RMN de ^{1}H (DMSO) δ ppm: 1,22-1,57 (m, 4H), 1,27 (s, 9H), 1,80-2,04 (m, 4H), 2,27 (m, 1H), 3,06 (m, 1H), 6,81 (d, 1H, J = 8,7 Hz), 7,32 (m, 1H), 7,44 (t, 2H, J = 7,5 Hz), 7,57-7,72 (m, 6H), 9,91 (s, 1H).

Ia-108

pf: 191-192°C

RMN de ^1H (DMSO) δ ppm: 1,24-1,58 (m, 4H), 1,28 (s, 9H), 1,86-2,04 (m, 4H), 2,70 (m, 1H), 3,08 (m, 1H), 6,83 (d, 1H, J = 8,7 Hz), 7,63-7,79 (m, 2H), 8,31 (d, 1H, J = 7,2 Hz), 10,27 (s, 1H).

Ia-109

pf: 283-285°C

RMN de ^1H (DMSO) δ ppm: 1,24-1,60 (m, 4H), 1,28 (s, 9H), 1,87-2,04 (m, 4H), 2,42 (m, 1H), 3,09 (m, 1H), 3,87 (s, 2H), 6,82 (d, 1H, J = 8,7 Hz), 7,28-7,43 (m, 3H), 7,60 (d, 2H, J = 7,8 Hz), 7,68 (d, 1H, J = 7,2 Hz), 7,89 (d, 1H, J = 7,5 Hz), 9,48 (s, 1H).

Ia-110

pf: 263-265°C

RMN de ^1H (DMSO) δ ppm: 1,24-1,54 (m, 4H), 1,27 (s, 9H), 1,76-1,87 (m, 2H), 1,89-2,01 (m, 2H), 2,17 (m, 1H), 3,04 (m, 1H), 4,01 (s, 4H), 6,01 (s, 2H), 6,44 (d, 2H, J = 8,7 Hz), 6,77 (d, 1H, J = 8,7 Hz), 7,39 (d, 2H, J = 9,0 Hz), 9,44 (s, 1H).

Ia-111

pf: 239-241°C

RMN de ^1H (DMSO) δ ppm: 1,24-1,54 (m, 4H), 1,27 (s, 9H), 1,62-1,76 (m, 4H), 1,80-2,02 (m, 4H), 2,30 (m, 1H), 2,47-2,59 (m, 2H), 2,66-2,76 (m, 2H), 6,08 (m, 1H), 6,79 (d, 1H, J = 9,0 Hz), 6,88 (d, 1H, J = 6,9 Hz), 7,02 (t, 1H, J = 7,5 Hz), 7,13 (d, 1H, J = 7,5 Hz), 8,98 (s, 1H).

Ia-124

pf: 247-249°C

RMN de ^1H (DMSO) δ ppm: 1,15 (d, 6H, J = 6,3 Hz), 1,30 (s, 9H), 2,15-2,26 (m, 2H), 3,48-3,57 (m, 2H), 3,63-3,76 (m, 2H), 6,92 (d, 2H, J = 8,7 Hz), 7,59 (d, 2H, J = 9,0 Hz), 7,38 (d, 2H, J = 9,0 Hz), 7,87 (d, 2H, J = 8,7 Hz), 9,92 (s lg, 1H), 9,98 (s lg, 1H).

Ia-125

pf: 228-232°C

RMN de ^1H (DMSO) δ ppm: 1,30 (s, 9H), 1,95-2,08 (m, 2H), 2,77-2,89 (m, 4H), 7,17 (d, 1H, J = 8,4 Hz), 7,39 (d, 2H, J = 9,0 Hz), 7,42-7,48 (m, 1H), 7,64 (s lg, 1H), 7,87 (d, 2H, J = 9,0 Hz), 9,99 (s lg, 2H).

Ia-126

pf: 244-246°C

RMN de ^{1}H (DMSO) δ ppm: 1,31 (s, 9H), 7,42 (d, 2H, J = 8,4 Hz), 7,81 (dd, 1H, J = 2,1 Hz, 8,7 Hz), 7,93 (d, 2H, J = 9,0 Hz), 8,05 (d, 1H, J = 9,0 Hz), 8,66 (d, 1H, J = 2,1 Hz), 9,29 (s, 1H), 10,05 (s lg, 1H), 10,39 (s lg, 1H).

Ia-127

pf: 238-239°C

RMN de ^{1}H (DMSO) δ ppm: 1,30 (s, 9H), 4,18-4,27 (m, 4H), 6,81 (d, 1H, J = 8,4 Hz), 7,16 (dd, 1H, J = 2,7 Hz, 9,0 Hz), 7,34-7,42 (m, 3H), 7,85 (d, 2H, J = 8,4 Hz), 9,94 (s lg, 1H), 9,99 (s lg, 1H).

Ia-128

pf: 286-287°C

RMN de ^{1}H (DMSO) δ ppm: 1,31 (s, 9H), 7,41 (d, 2H, J = 8,7 Hz), 7,71 (d, 2H, J = 8,4 Hz), 7,91 (d, 2H, J = 8,7 Hz), 7,99 (d, 2H, J = 8,7 Hz), 10,05 (s lg, 1H), 10,44 (s lg, 1H).

Ia-129

pf: 232-234°C

RMN de ^{1}H (DMSO) δ ppm: 1,27 (s, 9H), 1,3-1,5 (m, 4H), 1,8-2,0 (m, 4H), 2,25 (1H, m), 3,07 (m, 1H), 6,80 (d,

1H, J=9,0), 7,37 (d, 1H, J= 8,1), 7,53 (t, 1H, J=8,1), 7,75 (t, 1H, J= 8,1), 8,12 s, 1H), 10,16 (s, 1H).

Ia-130

pf: 274-277°C

RMN de ^{1}H (DMSO) δ ppm: 1,27 (s, 9H), 1,23-1,58 (m, 4H), 1,81-2,03 (m, 4H), 2,28 (m, 1H), 3,07 (m, 1H), 6,80 (d, 1H, J = 8,4 Hz), 7,36 (dd, 1H, J = 0,9 Hz, 5,7 Hz), 7,43 (dd, 1H, J = 2,1 Hz, 8,7 Hz), 7,60 (d, 1H, J = 5,4 Hz), 7,78 (d, 1H, J = 8,7 Hz), 8,40 (d, 1H, 1,8 Hz), 9,97 (s lg, 1H).

Ia-131

pf: 259-260°C

RMN de ^{1}H (DMSO) δ ppm: 1,31 (s, 9H), 7,40 (d, 1H, J = 4,8 Hz), 7,41 (d, 2H, J = 8,7 Hz), 7,66 (d, 1H, J = 5,1 Hz), 7,67 (dd, 1H, J = 1,8 Hz, 8,7 Hz), 7,84 (d, 1H, J = 9,0 Hz), 7,92 (d, 2H, J = 8,7 Hz), 8,50 (s, 1H), 10,03 (s lg, 1H), 10,27 (s lg, 1H).

Ia-132

pf: 265-266°C

RMN de ^{1}H (DMSO) δ ppm: 1,17 (d, 6H, J = 6,6 Hz), 1,31 (s, 9H), 4,10 (m, 1H), 7,35-7,46 (m, 3H), 7,54 (d, 1H,

J = 7,5 Hz), 7,87-7,97 (m, 3H), 8,15 (s lg, 1H), 8,20 (d, 1H, J = 7,5 Hz), 10,03 (s lg, 1H), 10,25 (s lg, 1H).

Ia-133

pf: 249-250°C

RMN de ^{1}H (DMSO) δ ppm: 1,31 (s, 9H), 7,41 (d, 2H, J = 8,7 Hz), 7,45 (d, 1H, J = 5,4 Hz), 7,67 (dd, 1H, J = 1,8 Hz, 8,7 Hz), 7,76 (d, 1H, J = 5,4 Hz), 7,92 (d, 2H, J = 8,7 Hz), 7,95 (d, 1H, J = 8,1 Hz), 8,39 (d, 1H, J = 1,8 Hz), 10,02 (s lg, 1H), 10,23 (s lg, 1H).

Ia-134

pf: 305-306°C

RMN de ^{1}H (DMSO) δ ppm: 1,25 (m, 2H), 1,25 (s, 9H), 1,52 (m, 2H), 1,82 (m, 2H,), 1,94 (m, 2H), 2,13 (m, 1H), 3,04 (m, 1H), 6,00 (d, 1H, J= 8,1), 6,74 (d, 1H, J= 8,4), 7,3-7,5 (m, 6H), 7,85 (d, 2H, J=7,5), 8,31 (d, 1H, J=8,4).

Ia-135

pf: 220-222°C

RMN de ^{1}H (DMSO) δ ppm: 1,27 (s, 9H), 1,3-1,5 (m, 4H), 1,8-2,0 (m, 4H), 2,37 (m, 1H), 3,03 (m, 1H), 6,80

(d, 1H, J=8,7), 7,04 (m, 1H), 7,29 (m, 1H), 7,79 (m, 1H), 9,60 (s, 1H).

Ia-136

pf: 263-264°C

RMN de ^{1}H (DMSO) δ ppm: 1,27 (s, 9H), 1,3-1,5 (m, 4H), 1,8-2,0 (m, 4H), 2,20 (m, 1H), 3,03 (m, 1H), 6,80 (d, 1H, J= 8,4), 6,87 (m, 1H), 7,31 (m, 2H), 10,21 (s, 1H).

Ia-137

pf: 260-262°C

RMN de ^{1}H (DMSO) δ ppm: 1,27 (s, 9H), 1,3-1,5 (m, 4H), 1,8-2,0 (m, 4H), 2,30 (m, 1H), 3,05 (m, 1H), 6,80 (d, 1H, J= 8,4), 7,13 (t, 2H, J= 8,1), 7,31 (m, 1H), 9,52 (s, 1H).

Ia-138

pf: 270-273°C

RMN de ^{1}H (DMSO) δ ppm: 1,27 (s, 9H), 1,3-1,5 (m, 4H), 1,8-2,0 (m, 4H), 2,12 (m, 1H), 3,05 (m, 1H), 6,79 (d, 1H, J=9,0), 7,31 (m, 2H), 7,80 (m, 1H), 10,05 (s, 1H).

Ia-139

pf: 267-270°C

RMN de ^{1}H (DMSO) δ ppm: 1,30 (s, 9H), 4,05 (s, 4H), 6,04 (s, 2H), 6,51 (d, 2H, J = 8,7 Hz), 7,34 (d, 2H, J = 8,4 Hz), 7,54 (d, 2H, J = 8,4 Hz), 7,87 (d, 2H, J = 8,4 Hz), 9,82 (s lg, 1H), 9,97 (s lg, 1H).

Ia-140

pf: 227-229°C

RMN de ^{1}H (DMSO) δ ppm: 1,22 (d, 6H, J = 6,6 Hz), 1,20-1,57 (m 4H), 1,80-2,01 (m, 4H), 2,27 (m, 1H), 2,95-3,22 (m, 2H), 6,99 (d,1H, J = 7,8 Hz), 7,65 (d, 2H, J = 8,7 Hz), 7,80 (d, 2H, J = 8,4 Hz), 10,18 (s lg, 1H).

Ia-141

pf: 205-207°C

RMN de ^{1}H (DMSO) δ ppm: 1,22 (d, 6H, J = 6,9 Hz), 1,20-1,55 (m, 4H), 1,75-2,05 (m, 6H), 2,21 (m, 1H), 2,72-2,85 (m, 4H), 2,93-3,20 (m, 2H), 6,98 (d, 1H, J = 8,1 Hz), 7,10 (d, 1H, J = 8,1 Hz), 7,26 (dd, 1H, J = 2,1 Hz, 8,1 Hz), 7,51 (s, 1H), 9,67 (s lg, 1H).

Ia-142

pf: 295-296°C

RMN de ^{1}H (DMSO) δ ppm: 1,15 (d, 6H,J=6,6), 1,27 (s, 9H), 1,3-1,5 (m, 4H), 1,8-2,0 (m, 4H), 2,27 (m, 1H), 3,05 (m, 1H), 4,07 (m, 1H), 6,80 (d, 1H, J=8,7), 7,64 (d, 2H, J=8,7), 7,79 (d, 2H, J=8,7), 8,06 (d, 1H, J=7,5), 10,01 (s, 1H).

Ia-143

pf: 146-147°C

RMN de ^{1}H (DMSO) δ ppm: 1,26 (s, 9H), 1,5-1,7 (m, 4H), 2,36 (t, 2H, J=7,8), 3,03 (q, 2H, J=6,3), 6,89 (t, 1H, J=6,3), 7,66 (d, 2H, J=8,4), 7,80 (d, 2H, J=8,4), 10,25 (s, 1H).

Ia-144

pf: 138-140°C

RMN de ^{1}H (DMSO) δ ppm: 1,21 (d, 6H, J=6,0), 1,4-1,7 (m, 4H), 2,37 (t, 2H, J=7,5), 2,96 (q, 2H, J=6,3), 3,14 (m, 1H), 6,99 (t, 1H, J=5,4), 7,66 (d, 2H, J=7,8), 7,81 (d, 2H, J=7,8), 10,26 (s, 1H).

Ia-145

pf: 134-136°C

RMN de ^{1}H (DMSO) δ ppm: 1,26 (s, 9H), 1,39 (m, 2H), 1,4-1,7 (m, 4H), 2,28 (t, 2H, J=7,2), 2,79 (m, 4H),

3,02 (q, 2H, J=7,2), 6,88 (t, 1H, J=6,0), 7,10 (t, 1H, J=6,0), 7,51 (s, 1H), 9,73 (s, 1H).

Ia-146

pf: 135-137°C

RMN de ^{1}H (DMSO) δ ppm: 1,20 (d, 6H, J=6,6), 1,4-1,7 (m, 4H), 1,99 (m, 2H), 2,28 (t, 2H, J=7,2), 2,79 (m, 4H), 2,94 (q, 2H, J=6,3), 3,13 (m, 1H), 6,98 (t, 1H, J=6,9), 7,10 (d, 2H, J=8,1), 7,26 (d, 2H, J=8,1), 7,51 (s, 1H), 9,73 (s, 1H).

Ia-147

pf: 206-207 °C

RMN de ^{1}H (DMSO) δ ppm: 1,29 (s, 9H), 4,54 (d, 2H, J = 5,7 Hz), 7,35 (d, 2H, J = 9,0 Hz), 7,52 (d, 2H, J = 7,8 Hz), 7,69 (d, 2H, J = 8,1 Hz), 7,83 (d, 2H, J = 8,7 Hz), 9,02 (t, 1H, J = 5,7 Hz), 9,97 (s lg, 1H).

Ia-148

pf: 250-251°C

RMN de ^{1}H (DMSO) δ ppm: 1,30 (s, 9H), 7,18 (t, 2H, J = 9,3 Hz), 7,40 (d, 2H, J = 8,7 Hz), 7,76 (dd, 2H, J = 5,1 Hz, 9,3 Hz), 7,88 (d, 2H, J = 9,0 Hz), 10,02 (s lg, 1H), 10,17 (s lg, 1H).

Ia-149

pf: 220-222°C

RMN de ^{1}H (DMSO) δ ppm: 1,30 (s, 9H), 3,74 (s, 3H), 6,92 (d, 2H, J = 9,0 Hz), 7,38 (d, 2H, J = 9,0 Hz), 7,64 (d, 2H, J = 9,0 Hz), 7,87 (d, 2H, J = 9,0 Hz), 9,99 (s, 2H).

Ia-150

pf: 264-266°C

RMN de ^{1}H (DMSO) δ ppm: 1,31 (s, 9H), 1,66-1,76 (m, 4H), 2,57-2,66 (m, 2H), 2,71-2,80 (m, 2H), 6,98 (m, 1H), 7,06-7,16 (m, 2H), 7,38 (d, 2H, J = 9,0 Hz), 7,90 (d, 2H, J = 8,7 Hz), 9,60 (s, 1H), 9,99 (s, 1H).

Ia-151

pf: 235-236°C

RMN de ^{1}H (DMSO) δ ppm: 1,03-1,39 (m, 5H), 1,27 (s, 9H), 1,55-1,87 (m, 5H), 3,73 (m, 1H), 7,31 (d, 2H, J = 8,7 Hz), 7,76 (d, 2H, J = 8,4 Hz), 8,01 (d, 1H, J = 7,8 Hz), 9,90 (s, 1H).

Ia-152

pf: 244-246°C

RMN de ^1H (DMSO) δ ppm: 0,50-0,72 (m, 4H), 1,27 (s, 9H), 2,81 (m, 1H), 7,31 (d, 2H, J = 8,7 Hz), 7,73 (d, 2H, J = 8,7 Hz), 8,30 (d, 1H, J = 4,2 Hz), 9,91 (s lg, 1H).

Ia-153

pf > 300 °C

RMN de ^1H (DMSO) δ ppm: 1,06 (m, 6H), 1,27 (s, 9H), 1,2-1,5 (m, 4H), 1,8-2,0 (m, 4H), 2,25 (m, 1H), 2,7 (m, 1H), 3,05 (m, 1H), 3,51 (m, 4H), 4,30 (m, 1H), 6,80 (d, 1H, J=8,4), 7,34 (d, 2H, J=8,4), 7,65 (d; 2H, J=8,4), 10,01 (s, 1H).

Ia-154

pf: 247-249°C

RMN de ^1H (DMSO) δ ppm: 1,05 (m, 6H), 1,27 (s, 9H), 1,2-1,5 (m, 4H), 1,8-2,0 (m, 4H), 2,23 (m, 1H), 2,77 (m, 1H), 3,05 (m, 1H), 3,52 (m, 4H), 4,33 (m, 1H), 6,80 (d, 1H, J=9,0), 7,03 (d, 1H, J=7,8), 7,35 (t, 1H, J=7,8), 7,59 (d, 1H, J=7,8), 7,68 (s, 1H), 9,96 (s, 1H).

Ia-155

pf: 258-259°C

RMN de ^1H (DMSO) δ ppm: 1,25 (m, 2H), 1,50 (m,2H), 1,86 (m, 2H), 1,99 (m, 2H), 2,28 (m , 1H), 2,93 (s,

3H), 3,10 (m, 1H), 7,02 (d, 1H, J=7,5), 7,65 (d, 2H, J=8,4), 7,80 (d, 2H, J=8,4), 10,20 (s, 1H).

Ia-156

pf: 250-253°C

RMN de ^{1}H (DMSO) δ ppm: 1,28 (m, 2H), 1,50 (m, 2H), 1,82 (m, 2H), 2,00 (m, 4H), 2,22 (m, 1H), 2,79 (m, 4H), 2,92 (s, 3H), 3,11 (m, 1H), 7,01 (d, 1H, J= (,1), 7,26 (d, 1H, J=8,1), 7,51 (s, 1H), 9,68 (s, 1H).

Ia-157

pf: 259-262°C

RMN de ^{1}H (DMSO) δ ppm: 1,13 (d, 6H, J=6,0), 1,25 (m, 2H), 1,50 (m, 2H), 1,80 (m, 2H), 1,95 (m, 2H), 2,17 (m, 3H), 2,92 (s, 3H), 3,10 (m, 1H), 3,70 (m,2H), 3,68 (m, 2H), 6,86 (d, 2H J=9,3), 7,00 (d, 1H, J=7,2), 7,43 (d, 2H, J=9,3), 9,58 (s, 1H).

Ia-158

pf: 298-300°C

RMN de ^{1}H (DMSO) δ ppm: 1,31 (s, 9H), 7,30-7,50 (m, 5H), 7,63-7, 71 (m, 4H), 7,87 (d, 2H, J = 8,7 Hz), 7,91 (d, 2H, J = 9,0 Hz), 10,03 (s lg, 1H), 10,22 (s lg, 1H).

Ia-159

pf: 278-281°C

RMN de ^1H (DMSO) δ ppm: 0,74-1,87 (m, 20H), 1,29 (s, 9H), 3,76 (m, 1H), 7,32 (d, 2H, J = 8,4 Hz), 7,75 (d, 2H, J = 8,7 Hz), 7,75 (d, 1H, J = 8,7 Hz), 7,90 (s lg, 1H).

Ia-160

pf: 227-228°C

RMN de ^1H (DMSO) δ ppm: 1,22-1,55 (m, 4H), 1,27 (s, 9H), 1,80-2,02 (m, 4H), 2,23 (m, 1H), 3,06 (m, 1H), 6,78 (d, 1H, J = 8,7 Hz), 7,45 (t, 1H, J = 9,9 Hz), 7,82 (m, 1H), 8,12 (dd, 1H, J = 2,4 Hz, 6,3 Hz), 10,17 (s lg, 1H).

Ia-161

pf: 259-260°C

RMN de ^1H (DMSO) δ ppm: 1,22-1,54 (m, 4H), 1,27 (s, 9H), 1,78-2,01 (m, 4H), 2,16 (s, 3H), 2,21 (m, 1H), 3,05 (m, 1H), 6,77 (d, 1H, J = 8,4 Hz), 7,12-7,21 (m, 2H), 7,53 (m, 1H), 9,90 (s lg, 1H).

Ia-162

pf: 222-226°C

RMN de ^1H (DMSO) δ ppm: 1,15 (d,6H,J = 6,3 Hz), 1,26 (d, 6H, J = 6,9 Hz), 2,16-2,26 (m, 2H), 3,31 (m, 1H), 3,48-3,58 (m, 2H), 3,63-3,76 (m, 2H), 6,92 (d, 2H, J = 9,0 H), 7,32 (d, 2H, J = 8,7 Hz), 7,59 (d, 2H, 9,0 Hz), 7,89 (d, 2H, J = 9,0 Hz), 9,92 (s, 1H), 10,13 (s lg, 1H).

Ia-163

pf: 197-200°C

RMN de ^1H (DMSO) δ ppm: 1,26 (d, 6H, J = 6,3 Hz), 1,95-2,09 (m, 2H), 2,77-2,90 (m, 4H), 3,32 (m, 1H), 7,17 (d, 1H, J = 8,1 Hz), 7,32 (d, 2H, J = 8,7 Hz), 7,45 (dd, 1H, J = 1,8 Hz, 8,1 Hz), 7,64 (s lg, 1H), 7,90 (d, 2H, J = 8,7 Hz), 9,99 (s lg, 1H), 10,13 (s lg, 1H).

Ia-164

pf: 145-247°C

RMN de ^1H (DMSO) δ ppm: 1,27 (s, 9H), 1,3-2,0 (m, 16H), 2,19 (m, 1H), 3,05 (m, 1H), 4,74 (m, 1H), 6,79 (d, 1H, J=9,0), 6,80 (d, 2H, J=9,0), 7,47 (d, 2H, J=9,0), 9,63 (s, 1H).

Ia-165

pf > 300°C

RMN de ^1H (DMSO) δ ppm: 1,03-2,02 (m, 18H), 1,27 (s, 9H), 2,26 (m, 1H), 3,06 (m, 1H), 3,73 (m, 1H), 6,78 (d, 1H, J = 8,7 Hz), 7,63 (d, 2H, J = 9,0 Hz), 7,78 (d, 2H, J = 8,7 Hz), 8,02 (d, 1H, J = 8,1 Hz), 10,00 (s lg, 1H).

Ia-166

pf: 200-201°C

RMN de ^1H (DMSO) δ ppm: 1,03-2,02 (m, 18H), 1,27 (s, 9H), 2,25 (m, 1H), 3,06 (m, 1H), 3,73 (m, 1H), 6,78 (d, 1H, J = 8,7 Hz), 7,33 (t, 1H, J = 8,1 Hz), 7,46 (d, 1H, J = 8,1 Hz), 7,76 (m, 1H), 7,94 (m, 1H), 8,14 (d, 1H, J = 8,1 Hz), 9,92 (s lg, 1H).

Ia-167

pf: 282-285°C

RMN de ^1H (DMSO) δ ppm: 1,22-1,57 (m, 4H), 1,27 (s, 9H), 1,87-2,03 (m, 4H), 2,49 (m, 1H), 3,07 (m, 1H), 6,83 (d, 1H, J = 8,7 Hz), 13,20 (s lg, 1H).

Ia-168

pf: 120-124°C

RMN de ^1H (DMSO) δ ppm: 0,94-1,66 (m, 14H), 1,27 (s, 9H), 1,80-2,04 (m, 4H), 2,25 (m1H), 2,92 (m, 1H), 3,06 (m, 1H), 6,78 (d, 1H, J = 8,7 Hz), 7,42-7,53 (m, 2H), 7,63

(d, 1H, J = 7,2 Hz), 7,73 (m, 1H), 8,17 (m, 1H), 10,11 (s lg, 1H).

Ia-169

pf: 256-257°C

RMN de ^{1}H (DMSO) δ ppm: 0,93-1,20 (m, 5H), 1,24-1,64 (m, 9H), 1,27 (s, 9H), 1,80-2,02 (m, 4H), 2,27 (m, 1H), 2,87 (m, 1H), 3,06 (m, 1H), 6,79 (d, 1H, J = 9,0 Hz), 7,48 (d, 1H, J = 7,2 Hz), 7,68-7,79 (m, 4H), 10,17 (s lg, 1H).

Ia-171

pf: 242-244°C

RMN de ^{1}H (DMSO) δ ppm: 1,27 (m, 12H), 1,45 (m, 4H), 1,90 (m, 4H), 2,25 (m, 1H), 3,07 (m, 1H), 3,67 (m, 2H), 6,77 (d, 1H, J=8,7), 6,90 (d, 1H, J=7,8), 7,31 (t, 1H, J=7,5), 7,53 (d, 1H, J=7,8), 7,59 (s,1H), 9,89 (s, 1H).

Ia-172

pf > 310°C

RMN de ^{1}H (DMSO) δ ppm: 1,27 (m, 12H), 1,38 (m, 4H), 1,84 (m, 2H), 1,97 (m, 2H), 2,25 (m, 1H), 3,07 (m, 1H), 3,66 (m, 2H), 6,81 (d, 1H, J=8,7), 7,20 (d, 2H, J=6,7), 7,61 (d, 2H, J=8,7), 9,94 (s, 1H).

Ia-173

pf: 279-281°C

RMN de ^1H (DMSO) δ ppm: 1,27 (s, 9H), 1,3-1,5 (m, 4H), 1,83 (m, 6H), 1,93 (m, 2H), 2,21 (m, 1H), 2,36 (m, 2H), 3,05 (m, 1H), 3,54 (m, 2H), 6,79 (d, 1H, J=8,7), 7,16 (d, 2H, J=9,0), 7,56 (d, 2H, J=9,0), 9,83 (s, 1H).

Ia-174

pf: 258-262°C

RMN de ^1H (DMSO) δ ppm: 0,29 (m, 2H), 0,53 (m,2H), 1,20 (m, 1H), 1,27 (s, 9H), 1,3-1,5 (m, 4H), 1,7-2,0 (m, 4H), 2,20 (m, 1H), 3,05 (m, 1H), 3,75 (d, 2H, J=6,9), 6,79 (d, 1H, J=9,0), 6,83 (d, 2H, J=9,0), 7,46 (d, 2H, J=9,0), 9,64 (s, 1H).

Ia-175

pf: 246-248°C

RMN de ^1H (DMSO) δ ppm: 1,27 (s, 9H), 1,3-2,0 (m, 18H), 2,19 (m, 1H), 3,04 (m, 1H), 4,23 (m, 1H), 6,79 (d, 1H, J=8,7), 6,84 (d, 2H, J=9,0), 7,45 (d, 2H, J=9,0), 9,64 (s, 1H).

Ia-176

pf: 200-202°C

RMN de ^{1}H (DMSO) δ ppm: 1,27 (s, 9H), 1,3-2,0 (m, 18H), 2,21 (m, 1H), 3,05 (m, 1H), 4,23 (m, 1H), 6,57 (d, 1H, J=6,9), 6,80 (d, 1H, J=9,0), 7,0-7,2 (m, 2H), 7,28 (s, 1H), 9,74 (s, 1H).

Ia-177

pf: 266-268°C

RMN de ^{1}H (DMSO) δ ppm: 1,22-1,56 (m, 4H), 1,27 (s, 9H), 1,79-2,02 (m, 4H), 2,25 (m,1H), 3,05 (m, 1H), 6,56 (m, 1H), 6,77-6,84 (m, 2H), 7,58-7,71 (m, 5H), 9,92 (s lg, 1H).

Ia-178

pf: 223-224°C

RMN de ^{1}H (DMSO) δ ppm: 1,26-1,54 (m,4H), 1,27 (s, 9H), 1,81-2,02 (m,4H), 2,45 (m, 1H), 3,06 (m, 1H), 6,80 (d, 1H, J = 8,7 Hz), 8,15 (dd, 1H, J = 2,4 Hz, 9,0 Hz), 8,27 (d, 1H, J = 9,0 Hz), 8,70 (m, 1H), 10,85 (s lg, 1H).

Ia-179

pf: 224-227°C

RMN de ^1H (DMSO) δ ppm: 1,24-1,56 (m, 4H), 1,27 (s, 9H), 1,80-2,03 (m, 4H), 2,27 (m, 1H), 3,06 (m, 1H), 6,80 (d, 1H, J = 8,7 Hz), 6,90 (d, 1H, J = 1,8 Hz), 7,72-7,84 (m, 4H), 8,60 (d, 1H, J = 1,8 Hz), 10,09 (s lg, 1H).

Ia-180

pf: 226-227°C

RMN de ^1H (DMSO) δ ppm: 0,92 (d, 6H, J = 6,6 Hz), 1,26-1,55 (m, 4H), 1,27 (s, 9H), 1,80-2,03 (m, 4H), 2,27 (m, 1H), 3,05 (m, 1H), 3,20 (m, 1H), 6,80 (d, 1H, J = 8,7 Hz), 7,42 (d, 1H, J = 7,2 Hz), 7,67-7,79 (m, 4H), 10,19 (s lg, 1H).

Ia-181

pf: 191-192°C

RMN de ^1H (DMSO) δ ppm: 0,95 (d, 6H, J = 6,6 Hz), 1,26-1,55 (m, 4H), 1,27 (s, 9H), 1,80-2,03 (m, 4H), 2,25 (m, 1H), 3,06 (m, 1H), 3,23 (m, 1H), 6,80 (d, 1H, J = 8,4 Hz), 7,41-7,53 (m, 2H), 7,58 (d, 1H, J = 7,2 Hz), 7,73 (m, 1H), 8,18 (m, 1H), 10,13 (s lg, 1H).

Ia-182

pf: 192-193°C

RMN de ^1H (DMSO) δ ppm: 0,30 (m, 2H), 0,55 (m, 2H), 1,2-1,5 (m, 5H), 1,27 (s, 1H), 1,8-2,0 (m, 4H), 2,20 (m, 1H), 3,04 (m, 1H), 3,75 (d, 2H, J=6,9), 6,58 (m, 1H), 6,79 (d, 1H, J=8,7), 7,0-7,2 (m, 2H), 7,31 (s, 1H), 9,76 (s, 1H).

Ia-183

pf > 310°C

RMN de ^1H (DMSO) δ ppm: 1,27 (s, 9H), 1,3-1,5 (m,4H), 1,82 (m, 2H), 1,97 (m, 2H), 2,04 (m, 2H), 2,39 (m, 1H), 2,46 (t, 2H, J=7,8), 3,07 (m, 1H), 3,79 (t, 2H, J=7,5), 6,79 (d, 1H, J=8,7), 7,56 (m, 4H), 9,80 (s, 1H).

Ia-184

pf: 281-283°C

RMN de ^1H (DMSO) δ ppm: 1,24-1,57 (m, 4H), 1,27 (s, 9H), 1,80-2,04 (m, 4H), 2,27 (m, 1H), 3,06 (m, 1H), 6,80 (d, 1H, J = 9,0 Hz), 7,33 (s, 1H), 7,75 (d, 2H, J = 9,3 Hz), 7,91 (d, 2H, J = 8,7 Hz), 8,16 (s, 1H), 10,09 (s lg, 1H).

Ia-185

pf: 226-227°C

RMN de ^1H (DMSO) δ ppm: 1,24-1,58 (m, 10H), 1,27 (s, 9H), 1,81-2,02 (m, 4H), 2,28 (m, 1H), 2,78-2,88 (m, 4H), 3,06 (m, 1H), 6,80 (d, 1H, J = 8,7 Hz), 7,64 (d, 2H, J = 8,7 Hz), 7,82 (d, 2H, J = 8,7 Hz), 10,25 (s lg, 1H).

Ia-186

pf: 148-150°C

RMN de ^1H (DMSO) δ ppm: 1,25-1,60 (m, 10H), 1,27 (s, 9H), 1,82-2,03 (m, 4H), 2,24 (m, 1H), 2,82-2,92 (m, 4H), 3,06 (m, 1H), 6,79 (d, 1H, J = 8,4 Hz), 7,36 (m, 1H), 7,55 (t, 1H, J = 7,8 Hz), 7,84 (m, 1H), 8,06 (m, 1H), 10,18 (s lg, 1H).

Ia-187

pf > 310°C

RMN de ^1H (DMSO) δ ppm: 1,27 (s, 9H), 1,36 (s, 9H), 1,43 (m, 4H), 1,85 (m, 2H), 1,93 (m, 2H), 2,27 (m, 1H), 3,06 (m, 1H), 6,80 (d, 1H, J=8,7), 7,58 (s, 1H), 7,62 (d, 2H), 7,75 (d, 2H, J=9,0), 10,00 (s, 1H).

Ia-188

pf: 285-292°C

RMN de ^1H (DMSO) δ ppm: 0,85 (t, 3H, J=7,5), 1,11 (d, 3H, J=6,3), 1,26 (s, 9H), 1,3-1,6 (m, 6H), 1,85 (m,

2H), 1,95 (m, 2H), 2,27 (m, 1H), 3,06 (m, 1H), 3,90 (m, 1H), 6,80 (d, 1H, J=8,4), 7,64 (d, 2H, J=8,7), 7,79 (d, 2H, J=8,7), 7,99 (d, 1H, J=8,1), 10,02 (s, 1H).

Ia-189

pf: 278-281°C

RMN de ^{1}H (DMSO) δ ppm: 1,27 (s, 9H), 1,2-2,0 (m, 17H), 2,03 (m, 2H), 3,03 (m, 1H), 6,79 (d, 1H, J=8,4), 7,1-7,3 (m, 3H), 7,94 (s, 1H), 9,78 (m, 2H).

Ia-190

pf > 310°C

RMN de ^{1}H (DMSO) δ ppm: 1,1-2,0 (m, 17H), 1,27 (s, 9H), 2,25 (m, 2H), 3,03 (m, 1H), 6,79 (d, 1H, J=8,7), 7,48 (m, 4H), 9,71 (m, 2H).

Ia-191

pf: 275-277°C

RMN de ^{1}H (DMSO) δ ppm: 1,16 (d, 6H, J = 6,6 Hz), 1,31 (s, 9H), 4,09 (m, 1H), 7,41 (d, 2H, J = 8,7 Hz), 7,84 (s, 4H), 7,90 (d, 2H, J = 9,0 Hz), 8,11 (d, 1H, J = 7,5 Hz), 10,04 (s lg, 1H), 10,30 (s lg, 1H).

Ia-192

pf: 204-205°C

RMN de ^{1}H (DMSO) δ ppm: 1,15 (d, 6H, J = 6,6 Hz), 1,20-1,56 (m, 4H), 1,22 (d, 6H, J = 6,6 Hz), 1,78-2,00 (m, 4H), 2,25 (m, 1H), 2,98-3,22 (m, 2H), 4,06 (m, 1H), 6,99 (d, 1H, J = 8,1 Hz), 7,34 (t, 1H, J = 8,1 Hz), 7,46 (d, 1H, J = 7,8 Hz), 7,75 (m 1H), 7,96 (m, 1H), 8,17 (d, 1H, J = 8,7 Hz), 9,94 (s lg, 1H).

Ia-193

pf: 285-286°C

RMN de ^{1}H (DMSO) δ ppm: 1,15 (d, 6H, J = 6,6 Hz), 1,20-1,56 (m, 4H), 1,22 (d, 6H, J = 6,9 Hz), 1,79-2,00 (m, 4H), 2,26 (m, 1H), 2,97-3,20 (m, 2H), 4,07 (m, 1H), 6,99 (d, 1H, J = 7,8 Hz), 7,64 (d, 2H, J = 8,7 Hz), 7,79 (d, 2H, J = 8,7 Hz), 8,06 (d, 1H, J = 7,5 Hz), 10,02 (s lg, 1H).

Ia-194

pf: 248-250°C

RMN de ^{1}H (DMSO) δ ppm: 1,22-1,57 (m, 4H), 1,22 (d, 6H, J = 6,6 Hz), 1,78-2,00 (m, 4H), 2,25 (m, 1H), 2,98-3,22 (m, 2H), 6,56 (m, 1H), 6,82 (d, 1H, J = 3,3 Hz), 6,99 (d, 1H, J = 7,8 Hz), 7,58-7,71 (m, 5H), 9,92 (s lg, 1H).

Ia-195

pf: 271-275°C

RMN de ^1H (DMSO) δ ppm: 1,27 (s, 9H), 1,28-1,56 (m, 4H), 1,80-2,02 (m, 4H), 2,25 (m, 1H), 3,06 (m, 1H), 6,80 (d, 1H, J = 9,0 Hz), 7,57 (s, 1H), 7,62-7,74 (m, 4H), 8,39 (s, 1H), 9,99 (s lg, 1H).

Ia-196

pf: 226-228°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,30 (m, 2H), 1,23 (d, 6H, J=6,9), 1,2-2,0 (m, 4H), 2,20 (m, 1H), 3,10 (m, 2H), 3,76 (d, 2H, J=6,9), 6,83 (d, 2H, J=8,7), 6,99 (d, 1H, J=8,1), 7,46 (d, 2H, J=8,7), 9,65 (s, 1H).

Ia-197

pf: 173-175°C

RMN de ^1H (DMSO) δ ppm:0,31 (m, 2H), 0,56 (m, 2H), 1,22 (d, 6H, J=6,6), 1,2-1,5 (m, 4H), 1,8-2,0 (m, 4H), 2,22 (m, 1H), 3,10 (m, 1H), 3,76 (d, 1H, J=7,2), 6,58 (d, 1H, J=8,1), 7,0-7,2 (m, 2H), 7,32 (s, 1H), 9,78 (s, 1H).

Ia-198

pf: 233-235°C

RMN de ^1H (DMSO) δ ppm: 1,25 (d, 6H, J=6,9), 1,2-2,0 (m, 16H), 2,19 (m, 1H), 3,10 (m, 2H), 4,73 (m, 1H), 6,80 (d, 2H, J=8,7), 6,98 (d, 1H, J=7,8), 7,45 (d, 2H, J=8,7), 9,63 (s, 1H).

Ia-199

pf: 185-186°C

RMN de ^1H (DMSO) δ ppm: 1,22 (d, 6H, J=6,9), 1,2-2,0 (m, 16H), 2,22 (m, 1H), 3,10 (m, 2H), 4,73 (m, 1H), 6,54 (m, 1H), 7,0-7,2 (m, 2H), 7,3 (s, 1H), 9,75 (s, 1H).

Ia-200

pf: 235-237°C

RMN de ^1H (DMSO) δ ppm: 1,27 (s, 9H), 1,3-1,6 (m, 6H), 1,8-2,0 (m, 6H), 2,20 (m, 1H), 3,05 (m, 1H), 3,45 (m, 2H), 3,82 (m, 2H), 4,47 (m, 1H), 6,79 (d, 1H, J=9,0), 6,89 (d, 2H, J=9,0), 7,47 (d, 2H,J=9,0), 9,66 (s, 1H).

Ia-201

pf: 300-301°C

RMN de ^1H (DMSO) δ ppm: 1,15 (d, 6H, J = 6,6 Hz), 1,26-1,56 (m, 4H), 1,27 (s, 9H), 1,82-2,03 (m, 4H), 2,23 (s, 3H), 2,37 (m, 1H), 3,06 (m, 1H), 4,07 (m, 1H), 6,81 (d, 1H, J = 8,7 Hz), 7,52 (d, 1H, J = 8,4 Hz), 7,62 (d, 1H, J =

8,4 Hz), 7,68 (s, 1H), 8,09 (d, 1H, J = 7,5 Hz), 9,22 (s lg, 1H).

Ia-202

pf: 269-270°C

RMN de ^{1}H (DMSO) δ ppm: 1,25-1,26 (m, 4H), 1,27 (s, 9H), 1,80-2,03 (m, 4H), 2,25 (m, 1H), 3,07 (m, 1H), 6,80 (d, 1H, J = 8,4 Hz), 7,11 (m, 1H), 7,42 (d, 1H, J = 3,6 Hz), 7,48 (m, 1H), 7,58 (d, 2H, J = 8,7 Hz), 7,64 (d, 2H, J = 8,4 Hz), 9,92 (s lg, 1H).

Ia-203

pf: 271-273°C

RMN de ^{1}H (DMSO) δ ppm: 1,14-1,54 (m, 9H), 1,26 (s, 9H), 1,63-1,88 (m, 7H), 1,89-2,01 (m, 2H), 2,21 (m, 1H), 2,42 (m, 1H), 3,04 (m, 1H), 6,79 (d, 1H, J = 9,0 Hz), 7,11 (d, 2H, J = 8,4 Hz), 7,47 (d, 2H, J = 8,1 Hz), 9,70 (s lg, 1H).

Ia-204

pf: 250-251°C

RMN de ^{1}H (DMSO) δ ppm: 1,22-1,39 (m, 2H), 1,22 (d, 6H, J = 6,6 Hz), 1,40-1,57 (m 2H), 1,80-2,01 (m, 4H), 2,28 (m, 1H), 2,98-3,21 (m, 2H), 7,00 (d, 1H, J = 7,8 Hz),

7,34 (s, 1H), 7,75 (d, 2H, J = 9,0 Hz), 7,91 (d, 2H, J = 8,7 Hz), 8,17 (s, 1H), 10,10 (s lg, 1H).

Ia-205

pf: 239-240°C

RMN de ^{1}H (DMSO) δ ppm: 1,27 (s, 9H), 1,2-1,5 (m, 4H), 1,8-2,0 (m, 5H), 2,08 (m, 2H), 3,05 (m, 1H), 3,80 (m, 4H), 4,95 (m, 1H), 6,79 (d, 1H, J=8,7), 6,83 (d, 2H, J=8,7), 7,48 (d, 2H, J=8,7), 9,66 (s, 1H).

Ia-206

pf: 236-238°C

RMN de ^{1}H (DMSO) δ ppm:1,27 (s, 9H), 1,2-1,7 (m, 8H), 1,8-2,0 (m, 6H), 2,18 (m, 1H), 3,04 (m, 1H), 3,3-3,6 (m, 2H), 3,85 (m, 3H), 6,80 (d, 1H, J=9,0), 6,84 (d, 2H, J=9,0), 7,47 (d, 2H, J=9,0), 9,65 (s, 1H).

Ia-207

pf: 224-226°C

RMN de ^{1}H (DMSO) δ ppm: 1,27 (s, 9H), 1,2-1,5 (m, 4H), 1,8-2,0 (m, 4H), 2,24 (m, 1H), 2,39 (m, 2H), 3,06 (m, 1H), 3,50 (t, 2H, J=7,5), 3,70 (t, 2H, J=6,3), 6,78 (d, 1H, J=6,6), 6,83 (m, 1H), 7,25 (m, 1H), 7,27 (m, 1H), 7,54 (s,1H), 9,61 (s, 1H).

Ia-208

pf: 275-277°C

RMN de ^{1}H (DMSO) δ ppm: 1,27 (s, 9H), 1,3-1,5 (m, 4H), 1,8-2,0 (m, 4H), 2,22 (m, 1H), 2,38 (m, 2H), 3,07 (m, 1H), 3,47 (t, 2H, J=6,9), 3,69 (t, 2H, J=6,6), 6,80 (d, 1H, J=8,7), 7,14 (d, 2H, J=8,4), 7,58 (d, 2H, J=8,4), 9,83 (s, 1H).

Ia-209

pf: 214-215°C

RMN de ^{1}H (DMSO) δ ppm: 1,26-1,56 (m, 4H), 1,27 (s, 9H), 1,80-2,03 (m, 4H), 2,25 (m, 1H), 3,06 (m, 1H), 6,59 (m, 1H), 6,81 (d, 1H, J = 8,4 Hz), 6,86 (d, 1H, J = 2,7 Hz), 7,28-7,40 (m, 2H), 7,47 (m, 1H), 7,75 (s, 1H), 8,01 (s, 1H), 9,91 (s lg, 1H).

Ia-210

pf: 272-275°C

RMN de ^{1}H (DMSO) δ ppm: 1,31 (s, 9H), 6,59 (m, 1H), 6,87 (d, 1H, J = 3,3 Hz), 7,41 (d, 2H, J = 8,7 Hz), 7,68 (d, 2H, J = 8,7 Hz), 7,72 (m, 1H), 7,83 (d, 2H, J = 8,7 Hz), 7,90 (d, 2H, J = 8,7 Hz), 10,03 (s lg, 1H), 10,22 (s lg, 1H).

Ia-211

pf: 251-255°C

RMN de ^{1}H (DMSO) δ ppm: 1,31 (s, 9H), 7,36 (s, 1H), 7,41 (d, 2H, J = 8,4 Hz), 7,91 (d, 2H, J = 8,4 Hz), 7,92-8,00 (m, 4H), 8,19 (s, 1H), 10,06 (s lg, 1H), 10,38 (s lg, 1H).

Ia-212

pf: 241-244°C

RMN de ^{1}H (DMSO) δ ppm: 1,30 (s, 9H), 1,50-1,78 (m, 6H), 1,81-1,97 (m, 2H), 4,78 (m, 1H), 6,87 (d, 2H, J = 9,0 Hz), 7,38 (d, 2H, J = 8,7 Hz), 7,61 (d, 2H, J = 9,0 Hz), 7,87 (d, 2H, J = 8,7 Hz), 9,97 (s lg, 1H), 9,99 (s lg, 1H).

Ia-213

pf: 283-286°C

RMN de ^{1}H (DMSO) δ ppm: 1,31 (s, 9H), 7,12 (dd, 1H, J = 3,6 Hz, 5,1 Hz), 7,41 (d, 2H, J = 9,0 Hz), 7,46 (m, 1H), 7,50 (dd, 1H, J = 1,2 Hz, 5,1 Hz), 7,64 (d, 2H, J = 8,7 Hz), 7,82 (d, 2H, J = 8,7 Hz), 7,90 (d, 2H, J = 9,3 Hz), 10,03 (s lg, 1H), 10,22 (s lg, 1H).

Ia-216

pf: 224-225°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,22 (d, 6H, J=6,9), 1,2-1,5 (m, 4H), 1,8-2,0 (m, 4H), 2,45 (m, 1H), 3,12 (m, 2H), 6,99 (d, 1H, J=8,1), 8,15 (m, 1H), 8,27 (d, 1H, J=9,0), 8,69 (s, 1H), 10,86 (s, 1H).

Ia-219

pf: 270-272°C

RMN de ^1H (DMSO) δ ppm: 1,28 (s, 9H), 1,34-1,51 (m, 2H), 1,80-1,92 (m, 2H), 2,83- 2,97 (m, 2H), 3,32 (m, 1H), 3,99-4,12 (m 2H), 6,92 (d, 1H, J = 8,7 Hz), 7,57 (d, 2H, J = 8,7 Hz), 7,68 (d, 2H, J = 9,0 Hz), 8,90 (s lg, 1H).

Ia-220

pf: 187-189 °C

RMN de ^1H (DMSO) δ ppm: 1,28 (s, 9H), 1,31-1,51 (m, 2H), 1,78-1,90 (m, 2H), 2,78-2,93 (m, 2H), 3,30 (m, 1H), 3,97-4,09 (m, 2H), 6,90 (d, 1H, J = 8,7 Hz), 7,06 (t, 2H, J = 9,0 Hz), 7,44 (dd, 2H, J = 4,8 Hz, 9,0 Hz), 8,53 (s lg, 1H).

Ia-221

pf: 260-262°C

RMN de ^1H (DMSO) δ ppm: 1,12-1,50 (m, 7H), 1,28 (s, 9H), 1,63-1,90 (m, 7H), 2,40 (m, 1H), 2,76-2,91 (m, 2H), 3,28 (m, 1H), 3,96-4,09 (m, 2H), 6,90 (d, 1H, J = 8,7 Hz), 7,06 (d, 2H, J = 8,4 Hz), 7,32 (d, 2H, J = 8,4 Hz), 8,40 (s lg, 1H).

Ia-222

pf: 265-267°C

RMN de ^1H (DMSO) δ ppm: 1,23 (d, 6H, J = 6,6 Hz), 1,31-1,48 (m, 2H), 1,77-1,90 (m, 2H), 2,84-2,98 (m, 2H), 3,16 (m, 1H), 3,33 (m, 1H), 3,96-4,10 (m, 2H), 7,11 (d, 1H, J = 7,8 Hz), 7,57 (d, 2H, J = 8,7 Hz), 7,67 (d, 2H, J = 8,4 Hz), 8,90 (s lg, 1H).

Ia-223

pf: 183-186°C

RMN de ^1H (DMSO) δ ppm: 1,23 (d, 6H, J = 6,9 Hz), 1,28-1,47 (m, 2H), 1,76-1,88 (m, 2H), 2,80-3,16 (m, 2H), 3,16 (m, 1H), 3,32 (m, 1H), 3,94-4,07 (m, 2H), 7,00-7,14 (m, 3H), 7,44 (dd, 2H, J = 4,8 Hz, 9,0 Hz), 8,53 (s lg, 1H).

Ia-224

pf: 232-234°C

RMN de ^1H (DMSO) δ ppm: 1,12-1,46 (m, 7H), 1,23 (d, 6H, J = 6,6 Hz), 1,63-1,87 (m, 7H), 2,40 (m, 1H), 2,78-2,93 (m, 2H), 3,15 (m,1H), 3,31 (m,1H), 3,94-4,07 (m, 2H), 7,06 (d, 2H, J = 8,4 Hz), 7,09 (d, 1H, J = 8,1 Hz), 7,32 (d, 2H, J = 8,4 Hz), 8,39 (s lg, 1H).

Ia-225

pf: 222-224°C

RMN de ^1H (DMSO) δ ppm: 1,28 (s, 9H), 1,30-1,61 (m, 4H), 1,77-1,98 (m, 4H), 2,66-2,90 (m, 2H), 3,28 (m, 1H), 3,40-3,50 (m, 2H), 3,79-3,88 (m, 2H), 3,96-4,08 (m, 2H), 4,44 (m, 1H), 6,85 (d, 2H, J = 9,0 Hz), 6,91 (d, 1H, J = 9,0 Hz), 7,31 (d, 2H, J = 9,3 Hz), 8,34 (s lg, 1H).

Ia-226

pf: 194-195°C

RMN de ^1H ($CDCl_3$/DMSO) δ ppm: 1,39 (d, 6H, J = 7,2 Hz), 1,66 (quinteto, 2H, J = 6,8 Hz), 1,87 (quinteto, 2H, J = 7,7 Hz), 2,47 (t, 2H, J = 7,5 Hz), 3,11-3,22 (m, 1H), 3,21 (t, 2H, J = 6,2 Hz), 5,00 (s lg, 1H), 7,35-7,56 (m, 5H), 7,86 (d, 1H, J = 8,4 Hz), 8,05 (dd, 1H, J = 1,8, 8,1 Hz), 8,20 (d, 1H, J = 1,8 Hz), 9,24 (s, 1H).

Ia-227

pf > 300°C

RMN de ^1H (DMSO) δ ppm: 1,22 (d, 6H, J = 6,3 Hz), 1,20-1,40 (m, 4H), 1,74-2,10 (m, 4H), 2,20-2,40 (m, 1H), 2,39 (s, 3H), 3,00-3,30 (m, 2H), 6,25 (s, 1H), 6,99 (s lg, 1H), 7,43-7,57 (m, 1H), 7,71 (d, 1H, J = 8,1 Hz), 7,76 (s, 1H), 10,27 (s, 1H).

Ia-228

pf: 168-169°C

RMN de ^1H (DMSO) δ ppm: 1,26 (s, 9H), 1,49 (quinteto, 2H, J = 7,5 Hz), 1,64 (quinteto, 2H, J = 7,4 Hz), 2,38 (t, 2H, J = 7,2 Hz), 2,40 (s, 3H), 3,04 (q, 2H, J = 6,5 Hz), 6,25 (s, 1H), 6,89 (t, 1H, J = 6,0 Hz), 7,48 (dd, 1H, J = 1,8, 8,4 Hz), 7,71 (d, 1H, J = 8,4 Hz), 7,77 (d, 1H, J = 1,8 Hz), 10,33 (s, 1H).

Ia-229

pf: 174-175°C

RMN de ^1H (DMSO) δ ppm: 1,21 (d, 6H, J = 6,6 Hz), 1,42-1,56 (m, 2H), 1,56-1,70 (m, 2H), 2,33-2,42 (m, 2H), 2,40 (s, 3H), 2,90-3,02 (m, 2H), 3,14 (septeto, 1H, J= 6,5 Hz), 6,26 (s, 1H), 6,99 (s lg, 1H), 7,48 (d, 1H, J = 8,4 Hz), 7,71 (d, 1H, J = 8,7 Hz), 7,77 (s, 1H), 10,33 (s, 1H).

Ia-230

pf: 194-195°C

RMN de ^1H (DMSO) δ ppm: 0,86 (d, 6H, J = 6,9 Hz), 1,25-1,65 (m, 4H), 1,27 (s, 9H), 1,81-2,05 (m, 5H), 2,23-2,35 (m, 1H), 2,99-3,15 (m, 1H), 3,36 (d, 2H, J = 7,2 Hz), 6,80 (d, 1H, J = 8,4 Hz), 7,80 (d, 1H, J = 8,4 Hz), 7,87 (d, 1H, J = 8,4 Hz), 8,19 (s, 1H), 10,44 (s, 1H).

Ia-231

pf: 221-222°C

RMN de ^1H (DMSO) δ ppm: 0,86 (d, 6H, J = 6,9 Hz), 1,22-1,40 (m, 2H), 1,23 (d, 6H, J = 6,9 Hz), 1,40-1,58 (m, 2H), 1,82-2,04 (m, 5H), 2,22-2,37 (m, 1H), 3,00-3,16 (m, 1H), 3,15 (septeto, 1H, J = 6,6 Hz), 3,36 (d, 2H, J = 7,5 Hz), 6,99 (d, 1H, J = 7,5 Hz), 7,80 (d, 1H, J = 8,4 Hz), 7,86 (d, 1H, J = 8,4 Hz), 8,19 (s, 1H), 10,45 (s, 1H).

Ia-232

pf: 196-197°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,93 (d, 6H, J = 6,6 Hz), 1,42 (s, 1H), 1,60-1,70 (m, 2H), 1,88 (quintet0o 2H, J = 7,4 Hz), 2,02-2,20 (m, 1H), 2,46 (t, 2H, J = 7,7 Hz), 3,29 (q, 2H, J = 6,1 Hz), 3,48 (d, 2H, J = 7,8 Hz), 4,26 (t, 1H, J = 6,0 Hz), 7,76 (d, 1H, J = 8,1 Hz), 7,90 (dd, 1H, J = 1,8, 8,1 Hz), 8,07 (d, 1H, J = 1,5 Hz), 8,39 (s, 1H).

Ia-233

pf: 151-152°C

RMN de ^1H ($CDCl_3$) δ ppm: 0,93 (d, 6H, J = 6,6 Hz), 1,40 (d, 6H, J = 6,6 Hz), 1,62-1,69 (m, 2H), 1,88 (quinteto, 2H, J = 7,3 Hz), 2,03-2,16 (m, 1H), 2,47 (t, 2H, J = 7,5 Hz), 3,21 (septeto, 1H, J = 6,8 Hz), 3,23 (q, 2H, J = 6,3 Hz), 3,48 (d, 2H, J = 7,5 Hz), 4,43 (t, 1H, J = 6,0 Hz), 7,76 (d, 1H, J = 8,4 Hz), 7,91 (dd, 1H, J = 1,8, 8,4 Hz), 8,06 (d, 1H, J =1,8 Hz), 8,36 (s, 1H).

Ia-234

pf: 219-220°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,28 (s, 9H), 1,30-1,50 (m, 2H), 1,74-1,88 (m, 2H), 2,83 (t, 2H, J = 11,1 Hz), 3,20-3,32 (m, 1H), 3,94-4,07 (m, 2H), 5,94 (s, 2H), 6,77 (d, 1H, J= 8,8 Hz), 6,82 (dd, 1H, J = 1,8, 8,7 Hz), 6,89 (d, 1H, J = 8,7 Hz), 7,11 (d, 1H, J =1,8 Hz), 8,38 (s, 1H).

Ia-235

pf: 280-282°C

RMN de ^1H (DMSO-d_6) δ ppm: 1,27 (s, 9H), 1,26-1,57 (m, 4H), 1,86-2,03 (m, 4H), 2,38-2,50 (m, 1H), 3,00-3,14 (m, 1H), 6,81 (d, 1H, J = 8,4 Hz), 7,29 (t, 1H, J = 8,4 Hz), 7,43 (t, 1H, J = 7,5 Hz), 7,73 (d, 1H, J = 8,4 Hz), 7,96 (d, 1H, J = 7,5 Hz), 12,27 (s, 1H).

Ia-237

pf: 204-205°C

RMN de ^{1}H (DMSO) δ ppm: 1,23 (d, 6H, J = 6,6 Hz), 1,29-1,61 (m, 4H), 1,75-1,98 (m, 4H), 2,78-2,92 (m, 2H), 3,15 (m, 1H), 3,29 (m, 1H), 3,38-3,51 (m, 2H), 3,78-3,89 (m, 2H), 3,94-4,06 (m, 2H), 4,44 (m, 1H), 6,85 (d, 2H, J = 9,0 Hz), 7,10 (d, 1H, J = 7,8 Hz), 7,31 (d, 2H, J = 9,3 Hz), 8,34 (s lg, 1H).

Ia-238

pf: 128-130°C

RMN de ^{1}H (DMSO) δ ppm: 1,26 (s, 9H), 1,41-1,53 (m, 2H), 1,55-1,68 (m, 2H), 2,44 (t, 2H, J = 7,2 Hz), 2,98-3,07 (m, 2H), 6,90 (t, 1H, J = 6,0 Hz), 8,16 (dd, 1H, J = 2,1 Hz, 8,7 Hz), 8,29 (d, 1H, J = 8,7 Hz), 8,70 (m, 1H), 10,91 (s lg, 1H).

Ia-239

pf: 256-258°C

RMN de ^{1}H (DMSO) δ ppm: 1,26-1,53 (m, 4H), 1,26 (s, 9H), 1,76-2,00 (m, 4H), 2,23 (s, 3H), 2,39 (m, 1H), 3,04 (m, 1H), 6,80 (d, 1H, J = 8,7 Hz), 7,57 (dd, 1H, J = 2,4 Hz, 8,4 Hz), 7,97 (d, 1H, J = 8,4 Hz), 8,12 (m, 1H), 10,26 (s lg, 1H).

Ia-240

pf: 288-290°C

RMN de ^1H (DMSO) δ ppm: 1,26-1,53 (m, 4H), 1,27 (s, 9H), 1,78-1,90 (m, 4H), 2,40 (m, 1H), 3,04 (m, 1H), 6,81 (d, 1H, J = 8,7 Hz), 7,07 (m, 1H), 7,75 (m, 1H), 8,07 (d, 1H, J = 8,4 Hz), 8,29 (m, 1H), 10,36 (s lg, 1H).

Ia-241

pf: 249-250°C

RMN de ^1H (DMSO) δ ppm: 1,28 (s, 9H), 1,34-1,50 (m, 2H), 1,79-1,90 (m, 2H), 2,74-2,98 (m, 2H), 3,32 (m, 1H), 4,02-4,14 (m, 2H), 6,91 (d, 1H, J = 8,4 Hz), 7,94 (d, 1H, J = 9,0 Hz), 8,04 (dd, 1H, J = 2,1 Hz, 9,0 Hz), 8,60 (s, 1H), 9,76 (s lg, 1H).

Ia-242

pf: 250-252°C

RMN de ^1H (DMSO) δ ppm: 1,24 (s, 9H), 1,27 (s, 9H), 1,24-1,54 (m, 4H), 1,76-1,88 (m, 2H), 1,90-2,01 (m, 2H), 2,21 (m, 1H), 3,05 (m, 1H), 6,79 (d, 1H, J = 8,7 Hz), 6,88 (d, 2H, J = 9,0 Hz), 7,48 (d, 2H, J = 9,0 Hz), 9,72 (s lg, 1H).

136-0290

pf: 250-252°C

RMN de ^{1}H (DMSO) δ ppm: 1,15 (d, 6H, J = 6,6 Hz), 1,28 (s, 9H), 1,35-1,52 (m, 2H), 1,78-1,92 (m, 2H), 2,20 (s, 3H), 2,81-2,96 (m, 2H), 3,33 (m, 1H), 3,96-4,16 (m, 3H), 6,92 (d, 1H, J = 8,7 Hz), 7,27 (d, 1H, J = 8,1 Hz), 7,60 (m, 1H), 7,66 (m, 1H), 8,06 (d, 1H, J = 7,8 Hz), 8,14 (s lg, 1H).

Ia-244

pf: 211-213°C

RMN de ^{1}H (DMSO) δ ppm: 1,29 (s, 9H), 1,35-1,52 (m, 2H), 1,81-1,93 (m, 2H), 2,83-2,97 (m, 2H), 3,32 (m, 1H), 4,03-4,14 (m, 2H), 6,93 (d, 1H, J = 8,7 Hz), 7,55 (dd, 1H, J = 2,1 Hz, 9,0 Hz), 7,94 (d, III, J = 9,0 Hz), 8,29 (d, 1H, J =1,8 Hz), 8,78 (s lg, 1H), 9,19 (s, 1H).

Ia-245

pf: 196-197 °C

RMN de ^{1}H (DMSO) δ ppm: 1,27 (s, 9H), 1,2-1,6 (m, 6H), 1,8-2,0 (m, 6H), 2,23 (m, 1H), 3,05 (m, 1H), 3,73 (m, 4h), 4,99 (s, 1H), 6,79 (d, 1H, J=8,7), 7,13 (d, 1H, J=6,8), 7,22 (t, 1H, J=6,8), 7,49 (d, 1H, J=6,8), 7,72 (s, 1H), 9,78 (s, 1H).

Ia-246

pf: 242-244°C

RMN de ^1H (DMSO) δ ppm: 1,27 (s, 9H), 1,2-1,5 (m, 4H), 1,65 (m, 4H), 1,8-2,0 (m, 4H), 2,23 (m, 1H), 2,71 (m, 1H), 3,06 (m, 1H), 3,43 (m, 2H), 3,93 (m, 2H), 6,79 (d, 1H, J=8,7), 6,91 (d, 1H, J=8,7), 7,20 (t, 1H, J=7,5), 7,40 (d, 1H, J=7,5), 7,53 (s, 1H), 9,76 (s, 1H).

Ia-247

pf: 242-245°C

RMN de ^1H (DMSO) δ ppm: 1,27 (s, 9H), 1,2-1,6 (m, 6H), 1,8-2,0 (m, 6H), 2,23 (m, 1H), 3,05 (m, 1H), 3,74 (m, 4H), 4,94 (s lg, 1H), 6,79 (d, 1h, J=8,7), 7,38 (d, 1H, J=8,7), 7,52 (d, 1H, J=8,7), 9,76 (s, 1H).

Ia-248

pf: 272-274°C

RMN de ^1H ($CDCl_3$) δ ppm: 1,27 (s, 9H), 1,2-1,5 (m, 4H), 1,62 (m, 4H), 1,8-2,0 (m, 4H), 2,22 (m, 1H), 2,68 (m, 1H), 3,05 (m, 1H), 3,41 (m, 2H), 3,92 (m, 2H), 6,79 (d, 1H, J=9,0), 7,15 (d, 2H, J=8,7), 7,50 (d, 2H, J=8,7), 9,73 (s, 1H).

Ia-249 pf: 174-176 °C

Ia-250 pf: 255-257 °C

Ia-252 pf: 249-251 °C

Ia-253 pf: 120-121 °C

Ia-254 pf: 236-237 °C

Ia-255 pf: 172-174 °C

Ia-256 pf: 257-259 °C

Ia-257 pf: 179-180 °C

Ia-258 pf: 227-229 °C

Ia-259 pf: 135-136 °C

Experiência 1 Afinidade para o receptor Y5 de NPY

Clonou-se a sequência de cADN que codifica para um receptor humano Y5 de NPY (WO 96/16.542) no vector de expressão pME18S (Takebe *et al.*, Mol. Cell. Biol. **8**, 8957). Transfectou-se o vector de expressão obtido em células hospedeiras CHO utilizando um reagente Lipofect AMINE (Marca Registada, Gico BRL Co., Lda.), de acordo com um protocolo que integra instruções para se obterem as células que expressam o receptor Y5 de NPY de um modo estável.

Incubaram-se as membranas preparadas a partir das células CHO expressando o receptor Y5 de NPY, o composto da invenção presente e 30.000 cpm de péptido YY-[^{125}I] (60 pM de concentração final: Amersham), no tampão da experiência (tampão de HEPES-Hanks 20 mM contendo 0,1 % de albumina de soro de bovino, pH 7,4), a 25°C durante 2 horas, e depois filtrou-se a mistura através de um filtro em vidro GF/C tratado com polietilenoimina. Depois de se lavar o filtro em vidro com tampão Tris-HCl 50 mM (pH 7,4), mediu-se a radioactividade no filtro com um contador gama. Detectou-se a ligação não específica na presença de 200 nM de péptido YY. Calculou-se a concentração do composto em teste que

inibia especificamente em 50 % a ligação do péptido YY (valor de IC_{50}), (Inui, A. *et al.* Endocrinology **131**, 2090 - 2096 (1992)). Os resultados estão listados nas Tabelas 1 e 2.

Os compostos da invenção presente inibiam a ligação do péptido YY (homólogo da NPY) aos receptores Y5 de NPY. Por outras palavras, os compostos da invenção presente evidenciaram afinidade para o receptor Y5 de NPY.

Experiência 2 Actividade de produção de cAMP em células CHO

Depois de se incubarem células CHO que expressavam o receptor Y5 de NPY humano na presença de isobutilmetilxantina 2,5 mM (SIGMA) a 37°C durante 20 minutos, adicionou-se o composto da invenção presente e incubou-se durante 5 minutos. Em seguida adicionaram-se 50 nM de NPY e 10 µM de forscolina (SIGMA) às células e incubou-se durante mais 30 minutos. Terminada a reacção por adição de HCl 1 N, mediu-se a quantidade de cAMP no sobrenadante com o estojo EIA (Amersham LIFE SCIENCE). Considerou-se que a actividade inibitória da NPY contra o CAMP estimulado pela forscolina era 100 % e calcularam-se os valores das concentrações correspondentes a 50 % de inibição (valor de IC_{50}) dos compostos da invenção presente contra a actividade de NPY. Os resultados estão listados nas Tabelas 1 a 4.

Tabela 1

Compound	binding IC_{50}(nM)	cAMP IC_{50}(nM)
I-2	7.5	72
I-7	3	<10
I-11	1.3	5
I-18	4.4	29
I-20	7	21
I-22	8.6	51
I-24	9.6	71
I-25	0.6	2.6
I-41	5.3	38.2
I-44	1.0	13.4
I-45	1.2	27.9
I-46	0.8	10.5
I-47	0.6	14.9
I-49	0.4	8.1
I-50	0.3	8.4
I-53	4.1	21
I-55	9.0	40
I-57	4.8	47
I-59	0.8	35
I-60	0.69	18
I-61	0.26	5.3
I-62	0.58	16
I-63	1.3	50
I-64	2.2	80
I-65	1.8	72
I-66	1.5	30
I-67	2	17
I-69	3.8	13
I-72	2.3	2.1
I-75	0.55	3.4
I-76	0.61	5.5
I-77	1.8	28
I-79	0.59	25
I-83	0.61	29
I-84	1.3	25
I-86	3.4	100
I-87	0.66	21
I-90	2.8	50
I-92	7	61
I-101	3.9	38
I-102	1.7	14
I-106	6.4	29

. Tabela 2

I-109	1.2	3.2
I-110	4.3	13.6
I-111	1.8	6.1
I-114	7	30
I-116	1.2	11
I-120	1.4	4.8
I-123	1.8	168
I-126	0.6	13.2
I-127	1.4	30.4
I-128	1.8	10.2
I-129	2.1	174
I-130	1.1	42.5
I-131	1.1	34.8
I-132	2.2	30.4
I-133	0.9	21.1
I-134	0.5	10.0
I-135	0.7	22.0
I-136	2.8	-
I-137	1.4	68.2
I-138	1.0	18.6
I-139	0.41	7.6
I-140	0.48	8.9
I-141	0.42	7.4
I-142	0.49	28
I-143	3.5	44
I-144	3.4	52
I-146	2.3	20
I-147	7.1	63
I-149	0.83	15
I-150	0.17	5.2
I-151	0.17	2.6
I-152	0.88	46
I-153	1.7	29
I-154	1.1	11
I-156	0.81	17
I-160	0.61	8.8
I-161	0.49	3.1
I-162	1.7	32

I-163	2.3	83
I-164	0.71	5.9
I-165	0.44	47
I-166	0.37	9.7
I-167	0.72	39
I-168	2.1	32
I-171	2.4	71
I-172	0.91	36
I-187	0.58	13
I-191	1.1	11
I-196	1.4	6.8
I-197	6.7	38
I-198	7.2	33
I-199	4.8	31
I-202	6.7	67
I-204	1.0	6.3
I-205	2.9	17
I-206	5.9	54
I-207	4.6	23
I-210	1.1	13
I-212	0.67	7.5
I-213	0.44	4.0
Ia-1	4.8	31
Ia-3	9.2	150
Ia-4	1.4	15
Ia-5	1.6	43
Ia-6	2.4	23
Ia-8	2.9	34
Ia-9	0.94	11
Ia-10	0.47	2.7
Ia-11	0.64	7.2
Ia-12	0.94	5.5
Ia-13	1.5	3.3
Ia-14	4.8	28
Ia-16	0.1	-
Ia-17	0.1	1.9
Ia-20	4.9	100

Tabela 3

Ia-21	3.4	35
Ia-22	3.1	38
Ia-24	5.2	74
Ia-25	1.1	18
Ia-26	1.9	27
Ia-28	5.2	130
Ia-29	1	7.3
Ia-30	2.6	25
Ia-31	3.8	11
Ia-32	0.52	6.7
Ia-33	1.8	64
Ia-35	1.8	-
Ia-36	1.6	86
Ia-37	0.73	3.8
Ia-38	1	2.2
Ia-39	1.5	3.5
Ia-40	2.2	9.3
Ia-41	2.5	9
Ia-42	3.6	20
Ia-44	4.8	27
Ia-45	4.8	42
Ia-46	0.87	8.3
Ia-47	0.82	3.8
Ia-48	1.2	6.1
Ia-49	2.6	83
Ia-50	1.7	24
Ia-51	1.3	3.4
Ia-52	1.9	22
Ia-53	0.22	8.1
Ia-54	0.44	9
Ia-55	1.1	27
Ia-56	2.3	96
Ia-57	0.93	31
Ia-58	2.5	110
Ia-59	0.71	16
Ia-60	0.95	10
Ia-61	0.68	19
Ia-62	1.1	29
Ia-63	3.9	370
Ia-64	7.1	96
Ia-65	1.1	11

Ia-66	0.59	3.2
Ia-67	6.3	75
Ia-68	9.5	180
Ia-69	2.7	33
Ia-70	1.5	31
Ia-71	1.3	12
Ia-76	2.2	-
Ia-78	2	150
Ia-79	0.82	-
Ia-80	0.44	3.0
Ia-81	2.7	4.5
Ia-83	1.2	53
Ia-84	0.25	13
Ia-85	0.22	14
Ia-86	0.73	11
Ia-87	0.49	61
Ia-88	0.62	48
Ia-91	4	150
Ia-106	1.9	24
Ia-107	0.14	1.3
Ia-109	0.6	3.9
Ia-110	0.3	1.1
Ia-111	5.1	28
Ia-124	1.1	22
Ia-125	4.1	46
Ia-126	2.3	58
Ia-127	6.1	160
Ia-129	1.3	26
Ia-130	0.21	3
Ia-131	1.3	17
Ia-132	2.8	76
Ia-133	1.7	8.8
Ia-135	8.2	49
Ia-136	1.6	13
Ia-138	2.2	28
Ia-139	1.9	25
Ia-140	1	24
Ia-141	1	5.7
Ia-142	0.67	5.5

Tabela 4

Ia-143	7.8	39
Ia-144	6.1	57
Ia-145	7	86
Ia-146	9.9	79
Ia-158	0.71	1.7
Ia-160	0.76	140
Ia-161	1.9	18
Ia-163	7	400
Ia-164	0.38	4.7
Ia-168	0.95	13
Ia-169	1.9	88
Ia-173	6.9	140
Ia-174	0.35	5.4
Ia-175	0.49	9.2
Ia-176	0.63	5.1
Ia-177	0.49	7.5
Ia-178	4.6	16
Ia-179	0.89	19
Ia-180	1.9	11
Ia-181	7.7	25
Ia-182	0.24	2.1
Ia-183	1.9	7.8
Ia-184	0.38	-
Ia-185	0.94	4.4
Ia-186	0.93	12
Ia-187	1.9	60
Ia-188	0.75	28
Ia-189	3.5	95
Ia-190	0.34	1000
Ia-191	0.49	220
Ia-192	5.9	200
Ia-193	1.4	43
Ia-194	0.22	8.1
Ia-195	1.4	31
Ia-196	0.39	1.3
Ia-197	0.44	2.5
Ia-198	0.23	2.6
Ia-199	0.11	1.6
Ia-200	1.4	18
Ia-201	3.1	74
Ia-202	0.37	3.4

Ia-203	0.2	2.6
Ia-204	1	6.3
Ia-205	2.4	99
Ia-206	1.9	460
Ia-207	0.55	5.9
Ia-208	1.2	9.7
Ia-209	0.55	-
Ia-210	2.8	99
Ia-211	4.8	240
Ia-212	0.52	2.6
Ia-213	0.91	28
Ia-219	2.5	28
Ia-221	0.47	1.5
Ia-222	3.7	18
Ia-224	0.1	1.2
Ia-225	3.4	20
Ia-226	0.37	21
Ia-227	0.59	-
Ia-228	0.96	-
Ia-229	1.9	-
Ia-230	0.32	-
Ia-231	0.29	-
Ia-232	0.7	-
Ia-233	0.63	-
Ia-235	5.5	-
Ia-237	1.1	15
Ia-241	1.9	-
Ia-243	1.3	-
Ia-246	0.26	20
Ia-247	0.79	31
Ia-248	0.27	17
Ia-250	1.9	-
Ia-252	1.2	-
Ia-253	0.53	-
Ia-254	2.0	-
Ia-255	3.2	-
Ia-256	5.7	-
Ia-257	8.6	-
Ia-258	1.8	-

Tal como se evidencia nas Tabelas 1 a 4, os compostos da invenção presente apresentam actividade antagonista em relação ao receptor Y5 de NPY.

Experiência 3

Utilizando as membranas preparadas a partir de células humanas que expressavam Y1 (de neuroblastoma humano, SK-N-MC) e as membranas preparadas a partir de células de expressão de Y2 (neuroblastoma humano, SMS-KAN), levou-se a cabo a experiência de um modo semelhante ao utilizado na Experiência 1, para se determinar a afinidade em relação ao receptor Y1 de NPY e em relação ao receptor Y2 de NPY.

Os valores de IC_{50} para a ligação ao receptor Y1 de NPY e ao receptor Y2, dos compostos I-27, I-32, I-41, I-45, I-46, I-47, I-48, I-49, I-59, I-61, I-63, I-64, I-66, I-69, I-72, I-152, I-154, I-204, I-205, I-212, Ia-3, Ia-5, Ia-6, Ia-12, Ia-16, Ia-17, Ia-20, Ia-21, Ia-22, Ia-26, Ia-28, Ia-29, Ia-30, Ia-31, Ia-32, Ia-33, Ia-37, Ia-39, Ia-40, Ia-50, Ia-51, Ia-54, Ia-62, Ia-67, Ia-124, Ia-126, Ia-139, Ia-140, Ia-142, Ia-178, Ia-199 e Ia-200, foram de 100.000 nM ou maiores, e todos estes compostos eram selectivos em relação ao receptor Y5 de NPY.

Exemplo de Formulação 1 Comprimidos

Composto (I-1)	15 mg
Amido	15 mg
Lactose	15 mg
Celulose Cristalina	19 mg
Poli(álcool vinílico)	3 mg
Água destilada	30 mL
Estearato de Cálcio	3 mg

Depois de se misturarem até à uniformidade todos os ingredientes acima excepto o estearato de cálcio, mói-se a mistura e granula-se, e seca-se para se obterem grânulos com dimensões adequadas. Depois de se adicionar estearato de cálcio aos grânulos, formam-se comprimidos por moldagem e compressão.

Exemplo de Formulação 2 Cápsulas

Composto (I-2)	10 mg
Estearato de magnésio	10 mg
Lactose	80 mg

Depois de se misturarem os ingredientes acima para se obterem pós ou grânulos, estes são utilizados como enchimento das cápsulas.

Exemplo de Formulação 3 Grânulos

Composto (I-3)	30 g
Lactose	265 g
Estearato de magnésio	5 g

Depois de se misturarem os ingredientes acima uniformemente, e de os enformar por moldagem sob compressão, mói-se o produto obtido, granula-se e peneira-se para se preparar um volume adequado de grânulos.

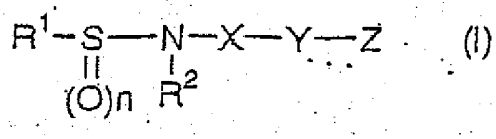
Aplicabilidade Industrial

Tal como se mostrou nas Experiências acima, os compostos da invenção presente apresentam uma actividade antagonista em relação ao receptor Y5 de NPY. Os compostos da invenção presente são portanto úteis como agentes contra a obesidade, e anoréxicos.

Lisboa, 9 de Outubro de 2008

REIVINDICAÇÕES

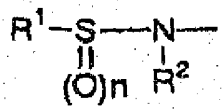
1. Utilização de um composto com a fórmula (I):



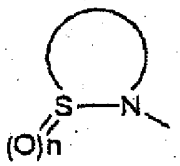
(I)

na qual R^1 seja um alquilo C_1-C_{10} substituído opcionalmente, ou um cicloalquilo C_3-C_8 substituído opcionalmente

R^2 seja hidrogénio ou alquilo C_1-C_{10}, e R^1 e R^2 tomados em conjunto possam formar alquileno C_1-C_{10}, incluindo o caso em que



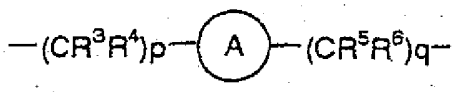
seja



n seja 1 ou 2,

X seja alquileno C_1-C_6 substituído opcionalmente, alcenileno C_2-C_6 substituído opcionalmente, -CO-alquileno

C_1-C_6 substituído opcionalmente, -CO-alcenileno C_2-C_6 substituído opcionalmente ou

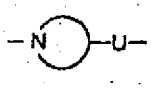


em que R^3, R^4, R^5 e R^6 sejam cada um deles independentemente hidrogénio ou alquilo C_1-C_{10},



seja cicloalquileno C_3-C_8 substituído opcionalmente, cicloalcenileno C_3-C_8 substituído opcionalmente, bicicloalquileno C_3-C_8 substituído opcionalmente, um grupo bivalente substituído opcionalmente e formado excluindo um átomo de hidrogénio de fenilo, naftilo, antrilo, indenilo, acenaftilo, tetrahidronaftilo e fluorenilo, arileno substituído opcionalmente ou heterociclo-di-ilo substituído opcionalmente, e p e q sejam cada um deles independentemente 0 ou 1,

$-NR^2-X-$ possa ser



em que



seja piperidinadi-ilo, piperazinadi-ilo, piridinadi-ilo, pirazinadi-ilo, pirrolidinadi-ilo ou pirroledi-ilo e U seja uma ligação simples, alquileno C_1-C_6 ou alcenileno C_1-C_6,

Y seja $OCONR^7$, $CONR^7$, $CSNR^7$, NR^7CO ou NR^7CS,

R^7 seja hidrogénio ou alquilo C_1-C_{10}, e

Z seja alquilo C_1-C_{10} substituído opcionalmente, alcenilo C_2-C_{10} substituído opcionalmente, amino substituído opcionalmente, alcoxilo C_1-C_{10} substituído opcionalmente, carbociclilo substituído opcionalmente ou heterociclilo substituído opcionalmente, em que o heterociclilo seja seleccionado de entre heteroarilos com 5 ou com 6 membros tais como pirrolilo, imidazolilo, pirazolilo, piridilo, piridazinilo, pirimidinilo, oxazolilo, oxadiazolilo, isotiazolilo, tiazolilo, tiadiazolilo, furilo e tienilo; heterociclilos fundidos constituídos por dois anéis tais como indolilo, isoindolilo, indazolilo, indolizinilo, indolinilo, isoindolinilo, quinolilo, isoquinolilo, cinolinilo, ftalazinilo, quinazolinilo, naftiridinilo, quinoxalinilo, purinilo, pteridinilo, benzopiranilo, benzimidazolilo, benzisoxazolilo, benzoxazolilo benzoxadiazolilo, benzisotiazolilo, benzotiazolilo, benzotiadiazolilo, benzofurilo, isobenzofurilo, benzotienilo, benzotriazolilo, imidazopiridilo, triazoropiridilo, imidazotiazolilo, pirazinopiridazinilo, quinazolinilo, quinolilo, isoquinolilo, naftiridinilo,

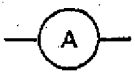
dihidropiridilo; e o heterociclo-di-ilo seja um grupo bivalente formado excluindo um hidrogénio dos heterociclilos acima, carbociclilo seja seleccionado de entre cicloalquilo C_3-C_8 cicloalcenilo C_3-C_8, bicicloalquilo C_3-C_8, e arilo, tal como definidos acima, de um seu sal ou solvato aceitável do ponto de vista farmacêutico, para a preparação de uma composição farmacêutica a título de antagonista de receptor Y5 de NPY.

2. A utilização de acordo com a Reivindicação 1, na qual R^2 seja hidrogénio ou alquilo C_1-C_{10}, e Z seja alquilo C_1-C_{10} substituído opcionalmente, alcenilo C_2-C_{10} substituído opcionalmente, alcoxilo C_1-C_{10} substituído opcionalmente, carbociclilo substituído opcionalmente, heterociclilo substituído opcionalmente ou amino substituído opcionalmente, desde que R^1 seja um alquilo em C_3 a C_{10} substituído opcionalmente quando Z for amino substituído opcionalmente, em que o carbociclilo e o heterociclilo sejam tal como se definiram acima, e os substituintes opcionais sejam tal como se definiram acima.

3. A utilização de acordo com a Reivindicação 1, na qual R^1 seja alquilo C_1-C_{10} substituído opcionalmente ou cicloalquilo C_3-C_8 substituído opcionalmente, X seja alquileno C_2-C_6 substituído opcionalmente, alcenileno C_2-C_6 substituído opcionalmente ou



em que p e q sejam 0,



seja um cicloalquileno C_3-C_8 substituído opcionalmente, um cicloalcenileno C_3-C_8 substituído opcionalmente, um bicicloalquileno C_5-C_8 substituído opcionalmente, um arileno substituído opcionalmente ou um heterociclo-di-ilo substituído opcionalmente, e

Z seja alquilo C_1-C_{10} substituído opcionalmente, carbociclilo substituído opcionalmente ou heterociclilo substituído opcionalmente, em que o arileno, o heterociclo-di-ilo e o heterociclilo sejam tal como definidos acima.

4. A utilização de acordo com qualquer uma das reivindicações 1 a 3, na qual R^1 seja um alquilo C3 a C10 substituído opcionalmente, em que os substituintes opcionais sejam tais como se definiram acima.

5. A utilização de acordo com qualquer uma das reivindicações 1 a 4, a título de agente contra a obesidade.

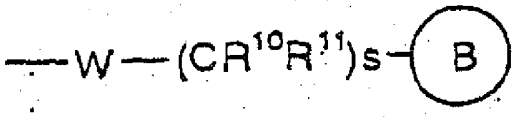
6. A utilização de acordo com qualquer uma das reivindicações 1 a 4, a título de agente anoréctico, em que os substituintes de "alquilo C_1-C_{10} substituído opcionalmente" representado por Z sejam (1) halogéneo; (2) ciano;

(3) um dos grupos (i) a (xiv) seguintes que sejam substituídos opcionalmente com um ou mais substituintes seleccionados de entre um "grupo de substituintes β" definido adiante,

(i) hidroxilo, (ii) alcoxilo C_1-C_{10}, (iii) mercapto, (iv) alquiltio C_1-C_{10}, (v) acilo, (vi) aciloxilo, (vii) carboxilo, (viii) alcoxicarbonilo C_1-C_{10}, (ix) imino, (x) carbamoílo, (xi) tiocarbamoílo, (xii) alquilcarbamoílo C_1-C_{10}, (xiii) alquiltiocarbamoílo inferior, (xiv) amino, (xv) alquilamino C_1-C_{10} ou heterociclilcarbonilo;

ou,

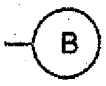
(4) um grupo com a fórmula:



na qual R^{10} e R^{11} sejam cada um deles independentemente hidrogénio ou alquilo C_1-C_{10} e em que quando este grupo tiver dois ou mais R^{10} e/ou dois ou mais R^{11}, possam cada um dos R^{10} e/ou cada um dos R^{11} ser diferentes,

W seja uma ligação simples, O, S ou NR^{12},

R^{12} seja hidrogénio, alquilo inferior ou fenilo,



seja cicloalquilo, bicicloalquilo, cicloalcenilo, arilo ou heterociclilo, cada um dos quais seja substituído opcionalmente com um ou mais substituintes seleccionados de entre um "conjunto de substituintes α" definido adiante, e

s seja um inteiro de entre 0 e 4-

O "grupo de substituintes α" seja um grupo constituído por (1) halogéneo; (2) oxo; (3) ciano; (4) nitro; (5)imino substituído opcionalmente com alquilo C_1-C_{10} ou com hidroxilo;

(6) os grupos (i) a (xxi) seguintes, que sejam substituídos opcionalmente comum ou mais grupos seleccionados de entre o grupo de substituintes β,

(i) hidroxilo; (ii) alquilo C_1-C_{10}, (iii) alcenilo C_2-C_{10}, (iv) alcoxilo C_1-C_{10}, (v) carboxilo; (vi) alcoxicarbonilo C_1-C_{10}, (vii) acilo; (viii) aciloxilo, (ix) imino; (x) mercapto; (xi) alquiltio C_1-C_{10},

(xii)carbamoílo, (xiii) alquilcarbamoílo C_1-C_{10}, (xiv) cicloalquilcarbamoílo, (xv) tiocarbamoílo; (xvi) alquiltiocarbamoílo C_1-C_{10}, (xvii) alquilsulfinilo C_1-C_{10}, (xviii) alquilsulfonilo C_1-C_{10}, (xix) sulfamoílo, (xx) alquilsulfamoílo C_1-C_{10} e (xxi) cicloalquilsulfamoílo,

(7) os grupos (i) a (v) seguintes, que sejam substituídos opcionalmente com substituintes do grupo de substituintes β, com alquilo C_1-C_{10}, alcoxil C_1-C_{10}-alquilo C_1-C_{10}, hidroxialquilo C_1-C_{10} protegido opcionalmente, halogenoalquilo C_1-C_{10}, alquilsulfonilo inferior e/ou arilsulfonilo,

(1) cicloalquilo, (ii) cicloalcenilo, (iii) cicloalcoxilo, (iv) amino e (v) alquilenodioxilo;

e

(8) os grupos (i) a (xii) seguintes, que sejam substituídos opcionalmente com substituintes do grupo de substituintes β, com alquilo C_1-C_{10}, halogenoalquilo C_1-C_{10} e/ou oxo,

(i) fenilo, (ii) naftilo, (iii) fenoxilo, (iv) fenilalcoxilo C_1-C_{10}, (v) feniltio, (vi) fenilalquiltio C_1-C_{10}, (vii) fenilazo, (viii)

heterociclilo, (ix) heterocicliloxilo, (x) heterocicliltio, (xi)heterociclilcarbonilo e (xii) heterociclilsulfonilo;

"o grupo de substituintes β" é um conjunto constituído por hidroxilo, mercapto, alcoxilo C_1-C_{10}, alcenilo C_2-C_{10}, amino, alquilamino C_1-C_{10}, alcoxicarbonilo C_1-C_{10}, alquiltio C_1-C_{10}, acilo, carboxilo, alcoxicarbonilo C_1-C_{10}, carbamoílo, ciano, cicloalquilo, fenilo, fenoxilo, alquilfenilo C_1-C_{10}, alcoxifenilo C_1-C_{10}, halogenofenilo, naftilo e heterociclilo;

os substituintes de "alquilo C_1-C_{10} substituído opcionalmente" não representado por Z são um ou mais substituintes seleccionados de entre o grupo de substituintes β;

os substituintes de "alcoxilo C_1-C_{10} substituído opcionalmente" são um ou mais substituintes seleccionados de entre o grupo de substituintes β;

os substituintes de "cicloalquilo substituído opcionalmente" são um ou mais substituintes seleccionados de entre o grupo de substituintes β;

os substituintes de "alcenilo inferior substituído opcionalmente" são halogéneo, alcoxilo inferior, amino, alquilamino inferior, alcoxicarbonilamino inferior, alquiltio inferior, acilo, carboxilo,

alcoxicarbonilo inferior, carbamoílo, ciano, cicloalquilo, fenilo, alquilfenilo inferior, alcoxifenilo inferior, naftilo e/ou heterociclilo;

os substituintes de "cicloalcenilo substituído opcionalmente" são um ou mais substituintes seleccionados de entre o grupo de substituintes β;

os substituintes de "amino substituído opcionalmente" são os substituintes do grupo de substituintes β, benzoílo substituído opcionalmente e/ou heterociclocarbonilo substituído opcionalmente, que podem ser substituídos com os substituintes do grupo de substituintes α ou com alquilo C_1-C_{10} que pode ser substituído com um ou mais grupos seleccionados de entre o grupo de substituintes β;

os termos "arilo substituído opcionalmente" e "fenilo substituído opcionalmente" representados por Z incluem respectivamente os grupos "arilo" e "fenilo", que podem ser substituídos com os substituintes do grupo de substituintes α ou com alquilo C_1-C_{10} que pode ser substituído com um ou mais grupos seleccionados de entre o grupo de substituintes α;

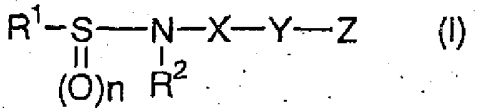
os substituintes de "arilo substituído opcionalmente" e de "fenilo substituído opcionalmente" não representados por Z são um ou mais grupos seleccionados de entre o grupo de substituintes β;

a expressão "carbociclilo substituído opcionalmente" inclui as expressões acima "cicloalquilo substituído opcionalmente", "cicloalcenilo substituído opcionalmente", "bicicloalquilo substituído opcionalmente" e "arilo substituído opcionalmente";

os substituintes de "heteroarilo substituído opcionalmente" são os mesmos que para os "arilo substituído opcionalmente" acima.

e um ou mais substituintes de entre os elementos do grupo de substituintes β são os substituintes de "alquileno C_1-C_6 substituído opcionalmente", de "alcenileno C_2-C_6 substituído opcionalmente", de "cicloalquileno substituído opcionalmente", de "ciclohexileno substituído opcionalmente", de "bicicloalquileno substituído opcionalmente", de "cicloalcenileno substituído opcionalmente", de "fenileno substituído opcionalmente", de "heterociclo-di-ilo substituído opcionalmente" e de "piperidinileno substituído opcionalmente".

7. Um composto com a fórmula (I):

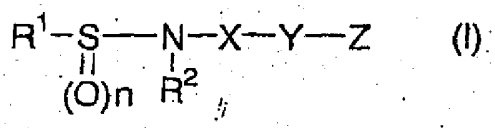


em que X seja alquileno C2 a C6 ou alcenileno C3 a C6, R^1 seja alquilo C3 a C10 substituído opcionalmente ou cicloalquilo C5 a C6 substituído opcionalmente e os outro

símbolos sejam tal como foram definidos na Reivindicação 1, desde que Z não seja alquilfenilamino C_1-C_{10}, hidroxialquil(C_1-C_{10})fenilamino e acilfenilamino quando Y for NR^7CO, os seus sais e solvatos aceitáveis do ponto de vista farmacêutico, em que os substituintes opcionais sejam definidos tal como acima.

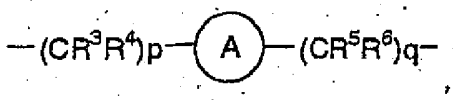
8. O composto descrito na Reivindicação 7, no qual Z seja alquilo C_1-C_{10} substituído opcionalmente ou fenilo substituído opcionalmente, os seus sais e solvatos aceitáveis do ponto de vista farmacêutico, em que os substituintes opcionais sejam definidos tal como acima.

9. Um composto com a fórmula (I):



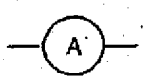
(I)

na qual X seja



,

e



seja cicloalquileno C_3-C_6 substituído opcionalmente, cicloalcenileno C_3-C_6 substituído

opcionalmente, bicicloalquileno C_5-C_8 substituído opcionalmente ou piperidinileno substituído opcionalmente, R^1 seja alquilo C3 a C10 substituído opcionalmente ou cicloalquilo C5 a C6 substituído opcionalmente, e os outros símbolos sejam tal como se definiram na Reivindicação 1, os precursores dos fármacos, os seus sais e solvatos aceitáveis do ponto de vista farmacêutico, em que os substituintes opcionais sejam definidos tal como acima.

10. O composto descrito na Reivindicação 9 em que o



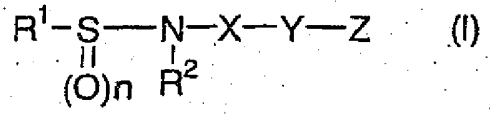
seja ciclohexileno substituído opcionalmente ou piperidinileno substituído opcionalmente e p e q sejam em simultâneo 0, os seus sais e solvatos aceitáveis do ponto de vista farmacêutico, em que os substituintes opcionais sejam definidos tal como acima.

11. O composto descrito nas Reivindicações 9 ou 10, no qual Y seja CONH, os precursores dos fármacos, os seus sais e solvatos aceitáveis do ponto de vista farmacêutico.

12. O composto descrito em qualquer uma das Reivindicações 9 a 11, no qual Z seja um alquilo C_1-C_{10} substituído opcionalmente, um fenilo substituído opcionalmente, um piridilo substituído opcionalmente ou um benzopiranilo substituído opcionalmente, os precursores dos

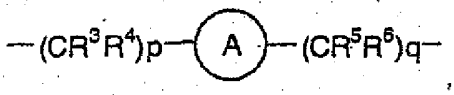
fármacos, os seus sais e solvatos aceitáveis do ponto de vista farmacêutico, em que os substituintes opcionais sejam definidos tal como acima.

13. Um composto com a fórmula (I):



(I)

no qual X seja

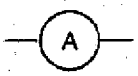


e



seja heteroarileno, R^1 seja um alquilo C3 a C10 substituído opcionalmente ou um cicloalquilo C5 a C6 substituído opcionalmente e os outros símbolos tenham os significados que lhes foram atribuídos na Reivindicação 1, os seus sais e solvatos aceitáveis do ponto de vista farmacêutico, em que os substituintes opcionais sejam definidos tal como acima.

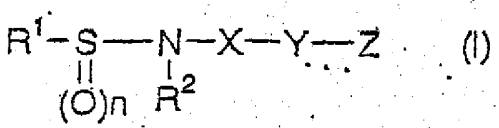
14. O composto descrito na Reivindicação 13, no qual



seja tiofenodi-ilo ou furanodi-ilo, os seus sais e solvatos aceitáveis do ponto de vista farmacêutico.

15. Uma composição farmacêutica que inclua um composto descrito em qualquer uma das Reivindicações 7 a 14, os seus sais e solvatos aceitáveis do ponto de vista farmacêutico.

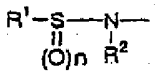
16. Um composto com a fórmula (I):



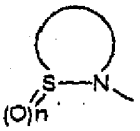
(I)

no qual R^1 seja alquilo C_1-C_{10} substituído opcionalmente, ou cicloalquilo C_3-C_8 substituído opcionalmente,

R^2 seja hidrogénio ou alquilo C_1-C_{10}, e R^1 e R^2 tomados em conjunto possam formar alquileno C_1-C_6, incluindo o caso em que

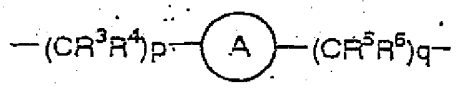


seja



n seja 1 ou 2,

X seja alquileno C_1-C_6 substituído opcionalmente, alcenileno C_2-C_6 substituído opcionalmente, alquileno -CO-C_1-C_6 substituído opcionalmente, alcenileno -CO-C_2-C_6 substituído opcionalmente ou

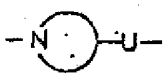


em que R^3, R^4, R^5e R^6 sejam cada um deles independentemente hidrogénio ou alquilo C_1-C_{10},

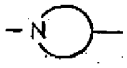


seja cicloalquileno C_3-C_8 substituído opcionalmente, cicloalcenileno C_3-C_8 substituído opcionalmente, bicicloalquileno C_5-C_8 substituído opcionalmente seleccionado de entre grupos bivalentes formados excluindo um hidrogénio de fenilo, naftilo, antrilo, fenantrilo, indanilo, indenilo, bifenililo, acenaftilo, tetrahidronaftilo e fluorenilo, arileno ou heterociclo-di-ilo substituído opcionalmente, e p e q sejam ambos independentemente 0 ou 1,

-NR^2-X- possa ser



em que



seja piperidina-di-ilo, piperazina-di-ilo, piridina-di-ilo, pirimidina-di-ilo, pirazina-di-ilo, pirrolidina-di-ilo ou pirroledi-ilo e U seja uma ligação simples, alquileno C_1-C_6 ou alcenileno C_2-C_6,

Y seja $OCONR^7$, $CONR^7$, $CSNR^7$, NR^7CO ou NR^7CS,

R^7 seja hidrogénio ou alquilo C_1-C_{10}, e

Z seja alquilo C_1-C_{10} substituído opcionalmente, alcenilo C_2-C_{10} substituído opcionalmente, amino substituído opcionalmente, alcoxilo C_1-C_{10} substituído opcionalmente, carbociclilo substituído opcionalmente ou heterociclilo substituído opcionalmente, em que o heterociclilo seja seleccionado de entre heteroarilos com 5 ou com 6 membros tais como pirrolilo, imidazolilo, pirazolilo, piridilo, piridazinilo, pirimidinilo, oxazolilo, oxadiazolilo, isotiazolilo, tiazolilo, tiadiazolilo, furilo e tienilo; heterociclilos fundidos constituídos por dois anéis tais como indolilo, isoindolilo, indazolilo, indolizinilo, indolinilo, isoindolinilo, quinolilo, isoquinolilo, cinolinilo, ftalazinilo, quinazolinilo, naftiridinilo,

quinoxalinilo, purinilo, pteridinilo, benzopiranilo, benzimidazolilo, benzisoxazolilo, benzoxazolilo benzoxadiazolilo, benzisotiazolilo, benzotiazolilo, benzotiadiazolilo, benzofurilo, isobenzofurilo, benzotienilo, benzotriazolilo, imidazopiridilo, triazoropiridilo, imidazotiazolilo, pirazinopiridazinilo, quinazolinilo, quinolilo, isoquinolilo, naftiridinilo, dihidropiridilo; e o heterociclo-di-ilo seja um grupo bivalente formado excluindo um hidrogénio dos heterociclilos acima, carbociclilo seja seleccionado de entre cicloalquilo C_3-C_8 cicloalcenilo C_3-C_8, bicicloalquilo C_3-C_8, e arilo, tal como definidos acima, de um seu sal ou solvato aceitável do ponto de vista farmacêutico, para a preparação de uma composição farmacêutica a título de antagonista de receptor Y5 de NPY, em que os substituintes do "alquilo inferior substituído opcionalmente" representado por Z sejam (1) halogéneo; (2) ciano;

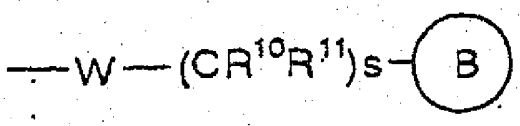
(3) um dos grupos (i) a (xiv) seguintes que sejam substituídos opcionalmente com um ou mais substituintes seleccionados de entre um "grupo de substituintes β" definido adiante,

(i) hidroxilo, (ii) alcoxilo C_1-C_{10}, (iii) mercapto, (iv) alquiltio C_1-C_{10}, (v) acilo, (vi) aciloxilo, (vii) carboxilo, (viii) alcoxicarbonilo C_1-C_{10}, (ix) imino, (x) carbamoílo, (xi) tiocarbamoílo, (xii) alquilcarbamoílo C_1-C_{10}, (xiii)

alquiltiocarbamoílo inferior, (xiv) amino, (xv) alquilamino C_1-C_{10} ou heterociclilcarbonilo;

ou,

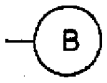
(4) um grupo com a fórmula:



na qual R^{10} e R^{11} sejam cada um deles independentemente hidrogénio ou alquilo C_1-C_{10} e em que quando este grupo tiver dois ou mais R^{10} e/ou dois ou mais R^{11}, possam cada um dos R^{10} e/ou cada um dos R^{11} ser diferentes,

W seja uma ligação simples, O, S ou NR^{12},

R^{12} seja hidrogénio, alquilo inferior ou fenilo,



seja cicloalquilo, bicicloalquilo, cicloalcenilo, arilo ou heterociclilo, cada um dos quais seja substituído opcionalmente com um ou mais substituintes seleccionados de entre um

"conjunto de substituintes α" definido adiante, e

s seja um inteiro de entre 0 e 4-

O "grupo de substituintes α" seja um grupo constituído por (1) halogéneo; (2) oxo; (3) ciano; (4) nitro; (5) imino substituído opcionalmente com alquilo C_1-C_{10} ou com hidroxilo;

(6) os grupos (i) a (xxi) seguintes, que sejam substituídos opcionalmente comum ou mais grupos seleccionados de entre o grupo de substituintes β,

(i) hidroxilo; (ii) alquilo C_1-C_{10}, (iii) alcenilo C_2-C_{10}, (iv) alcoxilo C_1-C_{10}, (v) carboxilo; (vi) alcoxicarbonilo C_1-C_{10}, (vii) acilo; (viii) aciloxilo, (ix) imino; (x) mercapto; (xi) alquiltio C_1-C_{10}, (xii) carbamoílo, (xiii) alquilcarbamoílo C_1-C_{10}, (xiv) cicloalquilcarbamoílo, (xv) tiocarbamoílo; (xvi) alquiltiocarbamoílo C_1-C_{10}, (xvii) alquilsulfinilo C_1-C_{10}, (xviii) alquilsulfonilo C_1-C_{10}, (xix) sulfamoílo, (xx) alquilsulfamoílo C_1-C_{10} e (xxi) cicloalquilsulfamoílo,

(7) os grupos (i) a (v) seguintes, que sejam substituídos opcionalmente com substituintes do grupo de substituintes β, com alquilo C_1-C_{10}, alcoxil C_1-C_{10}-alquilo C_1-C_{10}, hidroxialquilo C_1-C_{10} protegido opcionalmente, halogenoalquilo C_1-C_{10}, alquilsulfonilo inferior e/ou arilsulfonilo,

(1) cicloalquilo, (ii) cicloalcenilo, (iii) cicloalcoxilo, (iv) amino e (v) alquilenodioxilo;

e

(8) os grupos (i) a (xii) seguintes, que sejam substituídos opcionalmente com substituintes do grupo de substituintes β, com alquilo C_1-C_{10}, halogenoalquilo C_1-C_{10} e/ou oxo,

(i) fenilo, (ii) naftilo, (iii) fenoxilo, (iv) fenilalcoxilo C_1-C_{10}, (v) feniltio, (vi) fenilalquiltio C_1-C_{10}, (vii) fenilazo, (viii) heterociclilo, (ix) heterocicliloxilo, (x) heterociciltio, (xi)heterocililcarbonilo e (xii) heterociclilsulfonilo;

"o grupo de substituintes β" é um conjunto constituído por hidroxilo, mercapto, alcoxilo C_1-C_{10}, alcenilo C_2-C_{10}, amino, alquilamino C_1-C_{10}, alcoxicarbonilo C_1-C_{10}, alquiltio C_1-C_{10}, acilo, carboxilo, alcoxicarbonilo

C_1-C_{10}, carbamoílo, ciano, cicloalquilo, fenilo, fenoxilo, alquilfenilo C_1-C_{10}, alcoxifenilo C_1-C_{10}, halogenofenilo, naftilo e heterociclilo;

os substituintes de "alquilo C_1-C_{10} substituído opcionalmente" não representado por Z são um ou mais substituintes seleccionados de entre o grupo de substituintes β;

os substituintes de "alcoxilo C_1-C_{10} substituído opcionalmente" são um ou mais substituintes seleccionados de entre o grupo de substituintes β;

os substituintes de "cicloalquilo substituído opcionalmente" são um ou mais substituintes seleccionados de entre o grupo de substituintes β;

os substituintes de "alcenilo inferior substituído opcionalmente" são halogéneo, alcoxilo inferior, amino, alquilamino inferior, alcoxicarbonilamino inferior, alquiltio inferior, acilo, carboxilo, alcoxicarbonilo inferior, carbamoílo, ciano, cicloalquilo, fenilo, alquilfenilo inferior, alcoxifenilo inferior, naftilo e/ou heterociclilo;

os substituintes de "cicloalcenilo substituído opcionalmente" são um ou mais substituintes seleccionados de entre o grupo de substituintes β;

os substituintes de "amino substituído opcionalmente" são os substituintes do grupo de substituintes β, benzoílo substituído opcionalmente e/ou heterociclocarbonilo substituído opcionalmente, que podem ser substituídos com os substituintes do grupo de substituintes α ou com alquilo C_1-C_{10} que pode ser substituído com um ou mais grupos seleccionados de entre o grupo de substituintes β;

os termos "arilo substituído opcionalmente" e "fenilo substituído opcionalmente" representados por Z incluem respectivamente os grupos "arilo" e "fenilo", que podem ser substituídos com os substituintes do grupo de substituintes α ou com alquilo C_1-C_{10} que pode ser substituído com um ou mais grupos seleccionados de entre o grupo de substituintes α;

os substituintes de "arilo substituído opcionalmente" e de "fenilo substituído opcionalmente" não representados por Z são um ou mais grupos seleccionados de entre o grupo de substituintes β;

a expressão "carbociclilo substituído opcionalmente" inclui as expressões acima "cicloalquilo substituído opcionalmente", "cicloalcenilo substituído opcionalmente", "bicicloalquilo substituído opcionalmente" e "arilo substituído opcionalmente";

os substituintes de "heteroarilo substituído opcionalmente" são os mesmos que para os "arilo substituído opcionalmente" acima.

e um ou mais substituintes de entre os elementos do grupo de substituintes β são os substituintes de "alquileno C_1-C_6 substituído opcionalmente", de "alcenileno C_2-C_6 substituído opcionalmente", de "cicloalquileno substituído opcionalmente", de "ciclohexileno substituído opcionalmente", de "bicicloalquileno substituído opcionalmente", de "cicloalcenileno substituído opcionalmente", de "fenileno substituído opcionalmente", de "heterociclo-di-ilo substituído opcionalmente" e de "piperidinileno substituído opcionalmente".

17. Composto de acordo com a Reivindicação 16 no qual R^2 seja hidrogénio ou alquilo C_1-C_{10} e Z seja alquilo C_1-C_{10} substituído opcionalmente, alcenilo C_2-C_{10} substituído opcionalmente, alcoxilo C_1-C_{10} substituído opcionalmente, carbociclilo substituído opcionalmente, heterociclilo substituído opcionalmente ou amino substituído opcionalmente, desde que R^1 seja alquilo C3 a C10 substituído opcionalmente quando Z for amino substituído opcionalmente, e em que o carbociclilo e o heterociclilo sejam tal como se definiram acima e os substituintes opcionais sejam tal como se definiram acima.

18. Composto de acordo com a Reivindicação 16 no qual R^1 seja alquilo C_1-C_{10} substituído opcionalmente ou

cicloalquilo C_3-C_8 substituído opcionalmente, X seja alquileno C_2-C_6 substituído opcionalmente, alcenileno C_2-C_6 substituído opcionalmente ou



em que p e q sejam 0,



seja substituído opcionalmente cicloalquileno C_3-C_8 substituído opcionalmente, cicloalcenileno C_3-C_8 substituído opcionalmente, bicicloalquileno C_5-C_8 substituído opcionalmente, arileno substituído opcionalmente ou heterociclo-di-ilo substituído opcionalmente, e Z seja alquilo C_1-C_{10} substituído opcionalmente, carbociclilo substituído opcionalmente ou heterociclilo substituído opcionalmente, em que o arileno, o heterociclo-di-ilo e o heterociclilo sejam tal como se definiram acima e os substituintes opcionais sejam tal como se definiram acima.

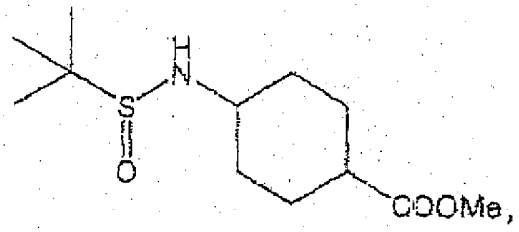
19. Composto de acordo com qualquer uma das Revindicações 16 a 18 no qual R^1 seja alquilo C3 a C10 substituído opcionalmente, em que os substituintes opcionais sejam tal como se definiram acima.

20. Composto de acordo com qualquer uma das

Revindicações 16 a 19 como agente contra a obesidade.

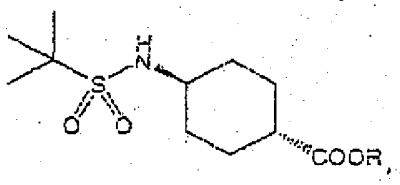
21. Composto de acordo com qualquer uma das Revindicações 16 a 19 como agente anoréxico.

22. Um composto com a fórmula:



no qual n seja 2.

23. Um composto com a fórmula:



no qual R seja hidrogénio ou metilo.

Lisboa, 9 de Outubro de 2008