264

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ABOGADOS

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EDIFICIO SI
CARRERA 4 No
BOGOTA 8, CO

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

No. 07-002730- -00001-0000

Dep 2020 NUEVA CREACIONI
ve 378 FASE NACIONAL
Folios 3

Señora Jefe de la
DIVISION DE NUEVAS CREACIONES
Superintendencia de Industria y Comercio
E. S. D.

Trámite : 011
Evento : 378
Actuación : 538

Referencia	:	Expediente No. 07.002.730
Asunto	:	SOLICITUD DE PATENTE PARA **INHIBIDORES DE POLIMERASA VIRAL**
Solicitante	:	**BOEHRINGER INGELHEIM INTERNATIONAL GMBH**
Publicada en	:	La Gaceta No. **578** del 31 de Julio de 2007
Fecha de solicitud	:	12 de Enero de 2007

1. Yo, Emilio FERRERO, identificado como aparece al pie de mi firma, actuando como apoderado en el asunto de la referencia, atentamente, solicito se efectúe el examen de patentabilidad de la solicitud en referencia presentada de acuerdo con el Capítulo I del PCT y según lo establecido en el artículo 44 de la Decisión 486 de la Comisión de la Comunidad Andina. Para tal efecto presento junto con este escrito el recibo por valor de $420.000.00, que corresponde a la tasa fijada según lo dispuesto en la resolución No. 44372 de 26 de diciembre de 2007.

2. Ruego atentamente a la Señora Jefe se sirva ordenar que se anexe este recibo para que se efectúe dicho examen y se continúe con el trámite de la solicitud.

Señora Jefe,

EMILIO FERRERO
T.P.A. No. 31.929

COLO-09255-841-059-0
AHP\MVN\ID-108543\WPCL9255
No. M-2007-108543\AHP

265

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

No. 07-002730- -00001-0000
Fecha: 2007-08-[illegible] 16:38:09 Dep: 2020 NUECREACIONE
Rad: 11 PATENTEYII Lve: 378 FASENACIONALI
Act: 535 PETICION Folios: 3

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

NIT : 800176089-2

RECIBO OFICIAL DE CAJA : 07 - 67,407
FECHA : AGOSTO 22 DE 2007

***** C O N S I G N A C I O N *****

DEPOSITANTE	TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PGO	Vr. PAGO
CAVELIER ABOGADOS	CONSIGNACION	BANCO POPULAR	050-00110-6	63769918	22/08/2007	35,155,000.00

***** C O N C E P T O *****

CANT.	RENTISTICO	CONCEPTO		TOTAL CONCEPTO
1	50005-01-01 SOLICITUDES	85	EXAMEN DE PATENTABILIDAD DE INVEN	404,000.00
			TOTAL : $	404,000.00

SON: CUATROCIENTOS CUATRO MIL PESOS

RESPONSABLE : _____

RECIBO DE CAJA APLICADO AL EXPEDIENTE No._____

C.C. 09255-841-059-0

266

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

NIT : 800176089-2

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

CERTIFICACION DE EXCEDENTE : 08 - 1,735
FECHA : ENERO 8 DE 2008

***** C O N S I G N A C I O N *****

DEPOSITANTE	TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PGO	Vr. PAGO
LIER ABOGADOS	CONSIGNACION	BANCO DE BOGOTA	062754387	2808481	08/01/2008	56,858,000.00

***** C O N C E P T O *****

CANT.	RENTISTICO	CONCEPTO	TOTAL CONCEPTO
1	50005-01-09 OTROS SERVICIOS DE PROPIEDAD I	99 OTROS SERVCIOS ADMINISTRATIVOS	16,000.00
		TOTAL : $	16,000.00

SON: DIEZ Y SEIS MIL PESOS

RESPONSABLE : _____

RECIBO DE CAJA APLICADO AL EXPEDIENTE No. _____

ESTA CERTIFICACION DE EXCEDENTE DE PAGO SOLO PODRA SER UTILIZADA COMO PARTE DE LA CANCELACION DE UNA TARIFA VIGENTE Y NO PODRA SER SUSTITUIDA POR NINGUN RECIBO.

Rdo 09255-841-059-0

267

Industria y Comercio
SUPERINTENDENCIA

DIVISIÓN DE NUEVAS CREACIONES

RADICACIÓN EXPEDIENTE No. 07-02730

EL EXTRACTO DE LA PRESENTE SOLICITUD DE **PATENTE DE INVENCIÓN**

FUE PUBLICADO EN LA GACETA DE PROPIEDAD INDUSTRIAL No **578** DE

FECHA **31 DE JULIO DE 2007** EL TÉRMINO HÁBIL SEÑALADO POR LA LEY

EXPIRA EL **26 DE OCTUBRE DE 2007**

NOTA: Dentro del plazo de los seis (6) meses siguientes a partir de la fecha de publicación en la gaceta de Propiedad Industrial, deberá solicitar y cancelar el examen de patentabilidad so pena de que la solicitud caiga en abandono, de acuerdo con lo establecido en el Artículo 44 de la Decisión 486/2000.

SE PRESENTARON OPOSICIONES POR PARTE DE TERCEROS.

SI _____ NO ____X____

(19) Canadian Intellectual Property Office
An Agency of Industry Canada

Office de la Propriété Intellectuelle du Canada
Un organisme d'Industrie Canada

(11) CA 2 449 180 (13) A1

(40) 06.02.2003
(43) 06.02.2003

(12)

(21) 2 449 180

(22) 18.07.2002

(51) Int. Cl.[7]: C07D 513/04, C07D 401/04, C07D 405/04, C07D 409/04, C07D 413/04, C07D 417/04, C07D 487/04, C07D 498/04, C07D 209/08, C07D 403/12, C07D 405/12, A61P 31/12, C07D 401/14, C07D 405/14, C07D 409/14, C07D 413/14, C07D 417/14, A61K 31/34, A61K 31/381, A61K 31/395, A61K 31/404, A61K 31/4353, A61K 31/44, A61K 31/495

(85) 01.12.2003

(86) PCT/CA02/01128

(87) WO03/010141

(30) 60/307,674 US 25.07.2001
60/338,061 US 07.12.2001

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JOLICOEUR, ERIC (CA).
BEAULIEU, PIERRE LOUIS (CA).
POIRIER, MARTIN (CA).
POUPART, MARC-ANDRE (CA).
GILLARD, JAMES (CA).
KUKOLJ, GEORGE (CA).

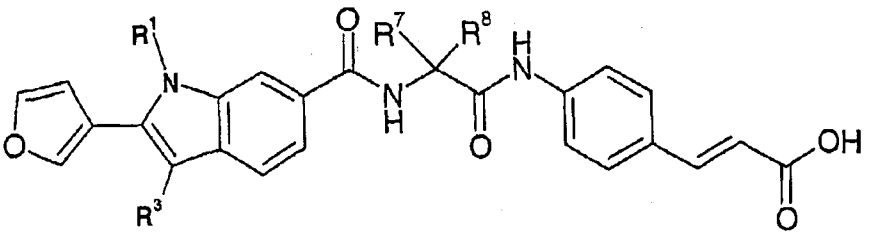
(74) BERNIER, LOUISE G.

(54) INHIBITEURS DE POLYMERASE VIRALE
(54) HEPATITIS C VIRUS POLYMERASE INHIBITORS WITH A HETEROBICYCLIC STRUCTURE

(57)

An isomer, enantiomer, diastereoisomer or tautomer of a compound, represented by formula I: wherein: A is O, S, NR1, or CR1, wherein R1 is defined herein; represents either a single or a double bond;R2 is selected from: H, halogen, R21, OR21, SR21, COOR21, SO2N(R22)2, N(R22)2, , CON(R22)2,NR22C(O)R22 or NR22C(O);NR22 wherein R21 and each R22 is defined herein, B is NR3 or CR3, with the proviso that one of A or B is either CR1 or CR3, wherein R3 is defined herein, K is N or CR4, wherein R4 is defined herein, L is N or CR5 wherein R5 has the same definition as R4; M is N or CR7 wherein R7 has the same definition as R4, Y1 is O or S, Z is N(R6a)R6 or OR6, wherein R6a is H or alkyl or NR61R62 wherein R61 and R62 are defined herein, and R6 is H, alkyl, cycloalkyl, alkenyl, Het, alkyl-aryl, alkyl-Het;or R6 is wherein R7 and R8 and Q are as defined herein; Y2 is O or S; R9 is H, (C1-6 alkyl), (C3-7)cycloalkyl or (C1-6)alkyl-(C3-7)cycloalkyl, aryl, Het, (C1-6)alkyl-aryl or (C1-6) alkyl-Het, all of which optionally substituted with R90 or R9 is covalently bonded to either of R7 or R8 to form a 5- or 6-membered heterocycle; a salt or a

TABLE 3



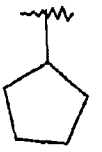
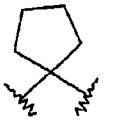
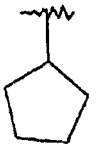
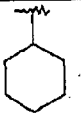
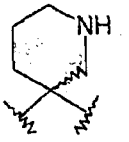
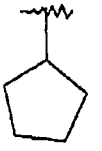
cpd. #	R^1	R^3	R^7 R^8	IC_{50}	EC_{50}	m/z $(M+H)^+$
3001	H			C	B	567.3
3002	H			C	B	552.2
3003	Me			C	B	526.2
3004	Me			C	C	538.3

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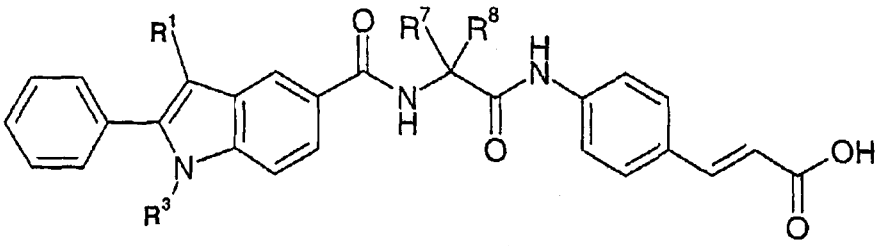
TABLE 4



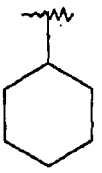
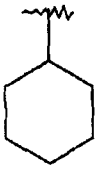
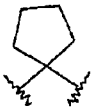
cpd. #	R^1	R^3	R^7 R^8	IC_{50}	EC_{50}	m/z $(M+H)^+$
4001	Me			B	B	590.3
4002	H			B	B	576.3

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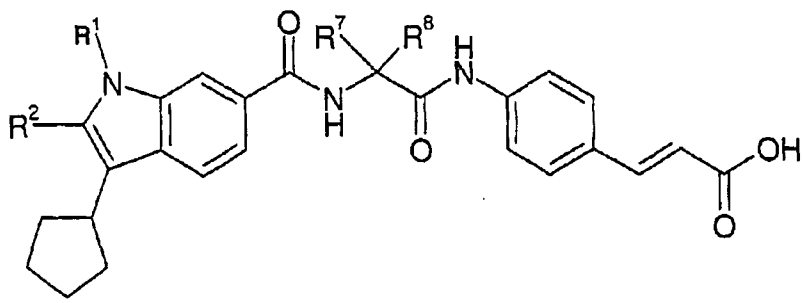
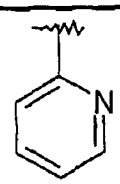
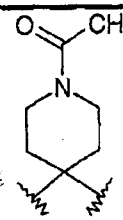
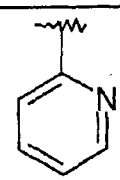
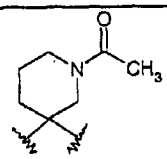
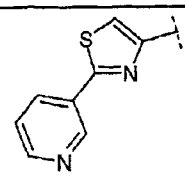
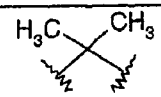
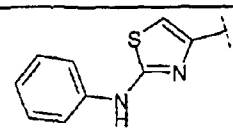
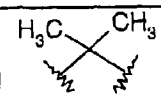
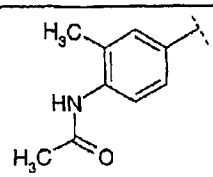
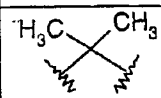
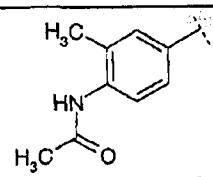
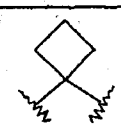
TABLE 6



cpd. #	R^1	R^2	R^7 R^8	IC_{50}	EC_{50}	m/z $(M+H)^+$
6001	CH_3			C	B	634.3
6002	CH_3			C	B	634.3
6003	CH_3			C	B	634.2
6004	CH_3			B	--	648.2
6005	CH_3			C	B	621.3
6006	CH_3			C	B	633.3

being optionally substituted with R^{160};

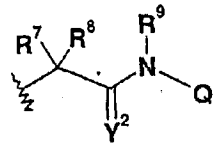
j) tetrazole, $COOR^{128}$ wherein R^{128} is H, (C_{1-6})alkyl, (C_{3-7})cycloalkyl, or(C_{1-6})alkyl-(C_{3-7})cycloalkyl, aryl, **Het**, $(C_{1-6}$alkyl)aryl or $(C_{1-6}$alkyl)**Het**, said (C_{1-6})alkyl, (C_{3-7})cycloalkyl, or(C_{1-6})alkyl-(C_{3-7})cycloalkyl, aryl, **Het**, $(C_{1-6}$alkyl)aryl and $(C_{1-6}$alkyl)**Het** being optionally substituted with R^{160}; and

k) $CONR^{129}R^{130}$ wherein R^{129} and R^{130} are independently H, (C_{1-6})alkyl, (C_{3-7})cycloalkyl, (C_{1-6})alkyl-(C_{3-7})cycloalkyl, aryl, **Het**, $(C_{1-6}$alkyl)aryl or $(C_{1-6}$alkyl)**Het**, or both R^{129} and R^{130} are covalently bonded together and to the nitrogen to which they are attached to form a 5, 6 or 7-membered saturated heterocycle, said alkyl, cycloalkyl, alkyl-cycloalkyl, aryl, **Het**, $(C_{1-6}$alkyl)aryl, $(C_{1-6}$alkyl)**Het** and heterocycle being optionally substituted with R^{160};

wherein R^{160} is defined as 1 or 2 substituents selected from: tetrazole, halogen, CN, C_{1-6}alkyl, haloalkyl, $COOR^{161}$, SO_3H, SO_2R^{161}, OR^{161}, $N(R^{162})_2$, $SO_2N(R^{162})_2$, $NR^{162}COR^{162}$ or $CON(R^{162})_2$, wherein R^{161} and R^{162} are as defined above;

or **Z** is $N(R^{6a})R^6$ wherein R^{6a} is as defined above and R^6 is (C_{3-6})cycloalkyl, (C_{2-6})alkenyl, 6- or 10-membered aryl, **Het**, (C_{1-6})alkyl-aryl, (C_{1-6})alkyl-**Het**, wherein said alkyl, cycloalkyl, alkenyl, aryl, **Het**, alkyl-aryl, or alkyl-**Het**, are all optionally substituted with R^{60};

or **Z** is OR^6 or $N(R^{6a})R^6$ wherein R^{6a} is as defined above and R^6 is:

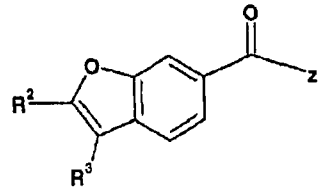


wherein R^7 and R^8 are each independently H, (C_{1-6})alkyl, haloalkyl, (C_{3-7})cycloalkyl, 6- or 10-membered aryl, **Het**, (C_{1-6})alkyl-aryl, (C_{1-6})alkyl-**Het**, wherein said alkyl, cycloalkyl, aryl, **Het**, (C_{1-6})alkyl-aryl, (C_{1-6})alkyl-**Het** are optionally substituted with R^{70}; or

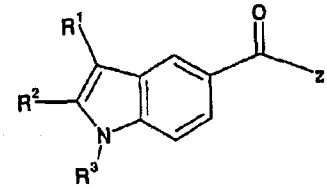
R^7 and R^8 are covalently bonded together to form second (C_{3-7})cycloalkyl or a 4, 5- or 6-membered heterocycle having from 1 to 3 heteroatom selected from O, N, and S; or when **Z** is $N(R^{6a})R^6$, either of R^7 or R^8 is covalently bonded to R^{6a} to form a

N. More preferably, **M**, **K** and **L** is CH.

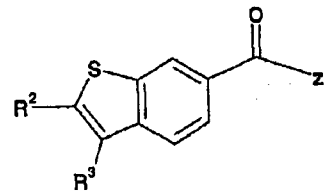
More preferably, compounds of the present invention have the following formulae:



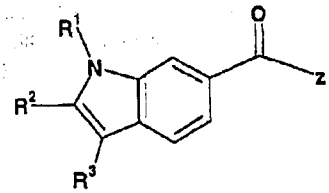
IIa



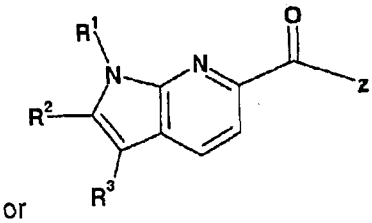
IIIa



IIb



IIc



or

IId

R^1:

Preferably R^1 is selected from the group consisting of: H or (C_{1-6})alkyl. More preferably, R^1 is H, CH_3, isopropyl, or isobutyl. Even more preferably, R^1 is H or CH_3. Most preferably, R^1 is CH_3.

R^2:

Preferably, R^2 is $CON(R^{22})_2$, wherein each R^{22} is independently H, (C_{1-6})alkyl, (C_{3-7})cycloalkyl, (C_{5-7})cycloalkenyl, 6 or 10-membered aryl or **Het**, or both R^{22} are bonded together to form a 5, 6 or 7-membered saturated heterocycle with the nitrogen to which they are attached;

or R^2 is selected from: H, halogen, (C_{1-6})alkyl, haloalkyl, (C_{2-6})alkenyl, (C_{5-7})cycloalkenyl, 6 or 10-membered aryl or **Het**; wherein each of said alkyl, haloalkyl, (C_{2-6})alkenyl, (C_{5-7})cycloalkenyl, aryl or **Het** is optionally substituted with R^{20}, wherein

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(12)

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(22) 18.07.2002

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(87) WO03/007945

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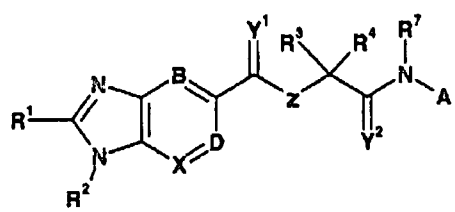
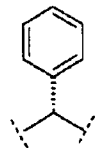
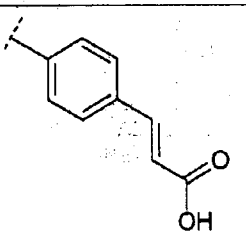
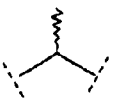
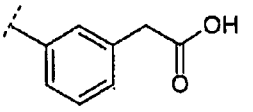
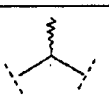
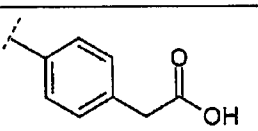
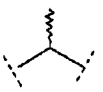
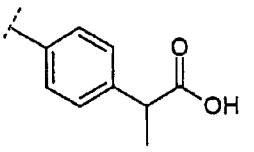
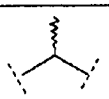
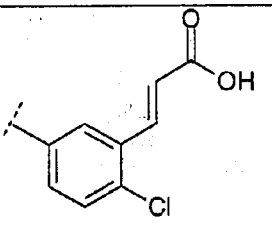
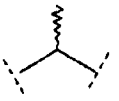
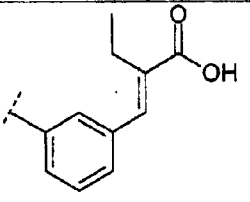
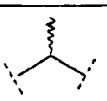
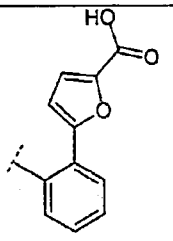
(57)

An isomer, enantiomer, diastereoisomer, or tautomer of a compound, represented by formula (I): wherein R1 is selected from: H, haloalkyl, (C1-6)alkyl, (C2-6)alkenyl, (C3-7)cycloalkyl, (C2-6)alkynyl, (C5-7) cycloalkenyl, 6 or 10- membered aryl, Het all optionally substituted; R2 is selected from (C1-6) alkyl, (C3-7)cycloalkyl, (C6-10)bicycloalkyl, 6- or 10-membered aryl, or Het all optionally substituted; B is N or CR5, wherein R5 is H, halogen, haloalkyl, (C1-6) alkyl, (C3-7)cycloalkyl or (C1-6)alkyl-(C3-7)cycloalkyl; X is N or CR5; D is N or CR5; each of Y1 and Y2 is independently O or S; Z is O, N, or NRz wherein Rz is H, (C1-6)alkyl, (C3-7)cycloalkyl or (C1-6)alkyl-(C3-7) cycloalkyl; R3 and R4 are each independently H, (C1-6) alkyl, first (C3-7)cycloalkyl, 6- or 10-membered aryl, Het (C1-6)alkyl-6- or 10-membered aryl, (C1-6)alkyl-Het, or each R3 and R4 are independently covalently bonded together to form second (C3-7)cycloalkyl, or heterocycle all optionally substituted; or when Z is N, either R3 or R4 are independently covalently bonded thereto to form a nitrogen-containing heterocycle; R7 is H, (C1-6 alkyl), (C3-7)cycloalkyl or (C1-6)alkyl-(C3-7)cycloalkyl or R7 is covalently bonded to either of R3 or R4 to form a heterocycle; A is (C1-6) alkyl-CONHR8 wherein R8 is 6- or 10-membered aryl, or Het; or A is a 6- or 10-membered aryl, or Het said aryl or Het being optionally substituted; or a salt or a derivative thereof; such compounds being potent inhibitors of HCV NS5B polymerase.



(I)

Cpd. #	R^3 R^4	A	IC_{50}	EC_{50}	m/z $(M+H)^+$
1006			B	--	589.3
1007			B	--	515.3
1008			B	--	515.3
1009			B	--	529.3
1010			B	--	562.1
1011			B	--	555.2
1012			B	--	567.2

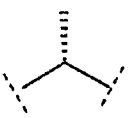
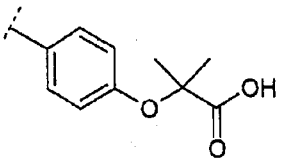
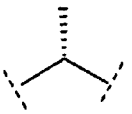
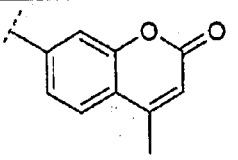
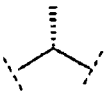
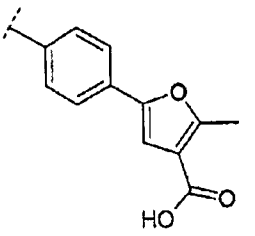
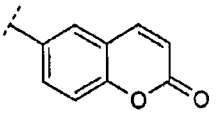
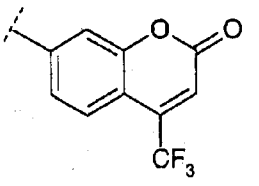
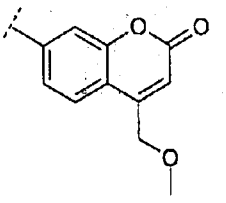
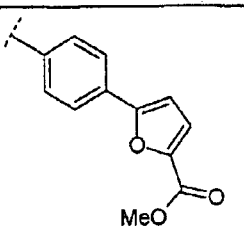
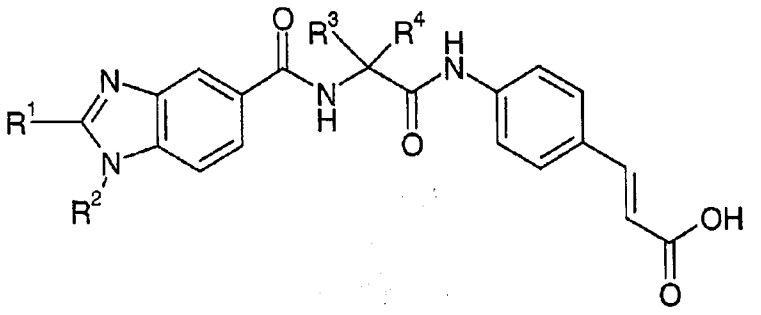
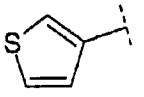
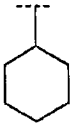
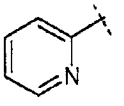
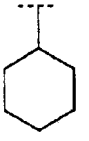
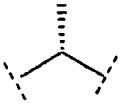
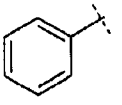
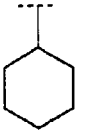
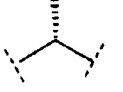
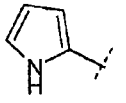
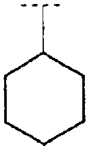
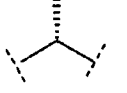
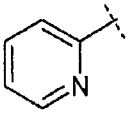
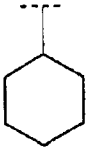
Cpd. #	R^3 R^4	A	IC_{50}	EC_{50}	m/z $(M+H)^+$
1025			B	--	559.2
1026			B	B	539.2
1027			B	--	581.2
1028			B	--	565.2
1029			A	--	633.2
1030			B	--	609.2
1031			B	--	621.2

TABLE 2



Cpd. #	R^1	R^2	R^3 R^4	IC_{50}	EC_{50}	m/z $(M+H)^+$
2001				C	B	583.2
2002				C	B	538.3
2003				B	A	537.2
2004				C	A	526.2
2005				C	B	578.3