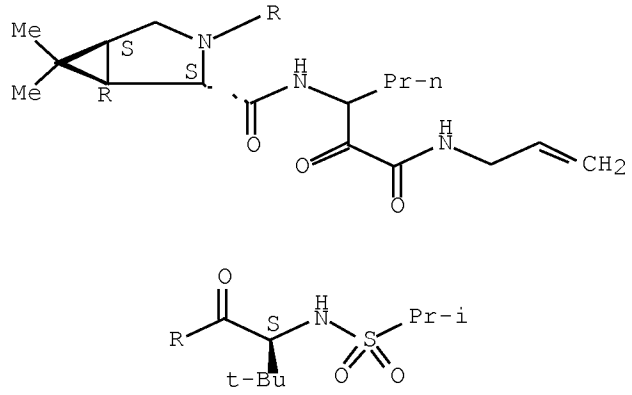
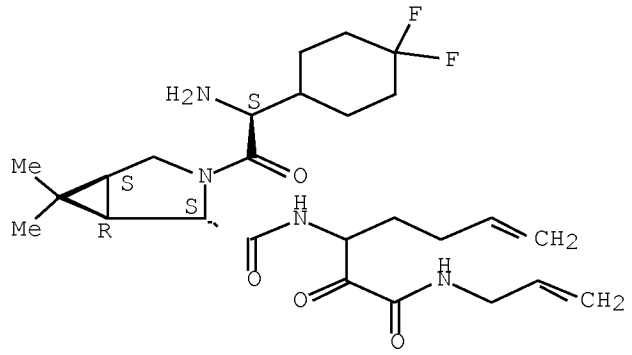


RN 394726-95-5 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carboxamide,

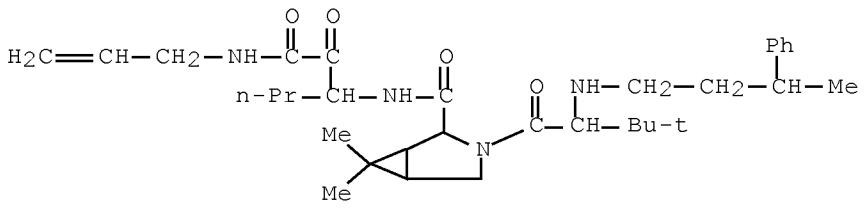
3-[(2S)-2-amino-2-(4,4-difluorocyclohexyl)acetyl]-6,6-dimethyl-N-[1-[2-oxo-2-(2-propen-1-ylamino)acetyl]-4-penten-1-yl]-, (1R,2S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



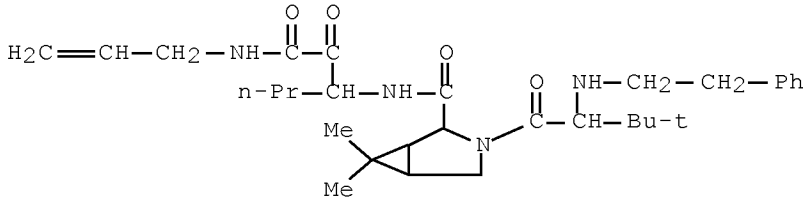
RN 394727-13-0 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carboxamide,

3-[3,3-dimethyl-1-oxo-2-[(3-phenylbutyl)amino]butyl]-6,6-dimethyl-N-[1-[2-oxo-2-(2-propen-1-ylamino)acetyl]butyl]- (CA INDEX NAME)



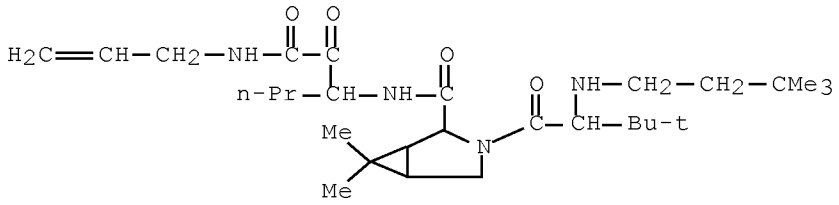
RN 394727-14-1 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carboxamide,

3-[3,3-dimethyl-1-oxo-2-[(2-phenylethyl)amino]butyl]-6,6-dimethyl-N-[1-[2-oxo-2-(2-propen-1-ylamino)acetyl]butyl]- (CA INDEX NAME)



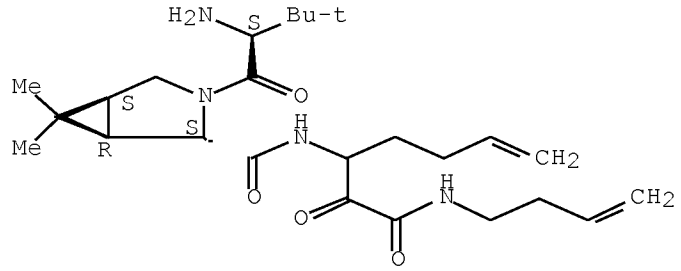
RN 394727-15-2 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carboxamide,

3-[2-[(3,3-dimethylbutyl)amino]-3,3-dimethyl-1-oxobutyl]-6,6-dimethyl-N-[1-[2-oxo-2-(2-propen-1-ylamino)acetyl]butyl]- (CA INDEX NAME)

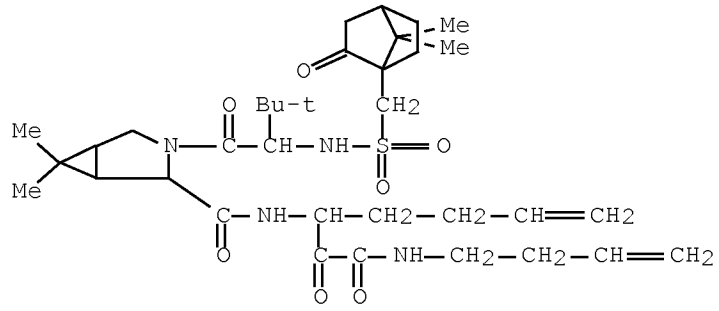


RN 394727-18-5 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carboxamide,
3-[(2S)-2-amino-3,3-dimethyl-1-oxobutyl]-N-[1-[2-(3-buten-1-ylamino)-2-oxoacetyl]-4-penten-1-yl]-6,6-dimethyl-, (1R,2S,5S)- (CA INDEX NAME)

Absolute stereochemistry.

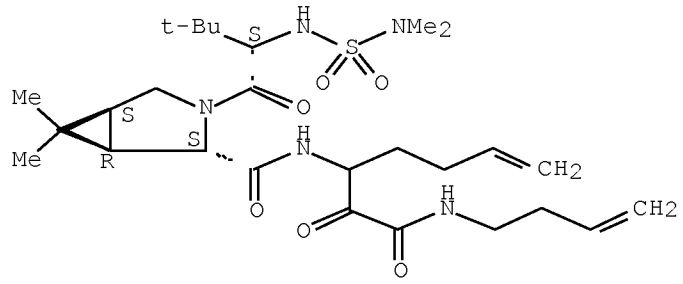


RN 394727-36-7 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carboxamide, N-[1-[2-(3-buten-1-ylamino)-2-oxoacetyl]-4-penten-1-yl]-3-[(2S)-2-[[[[(1R,4S)-7,7-dimethyl-2-oxobicyclo[2.2.1]hept-1-yl]methyl]sulfonyl]amino]-3,3-dimethyl-1-oxobutyl]-6,6-dimethyl-, (1R,2S,5S)- (CA INDEX NAME)



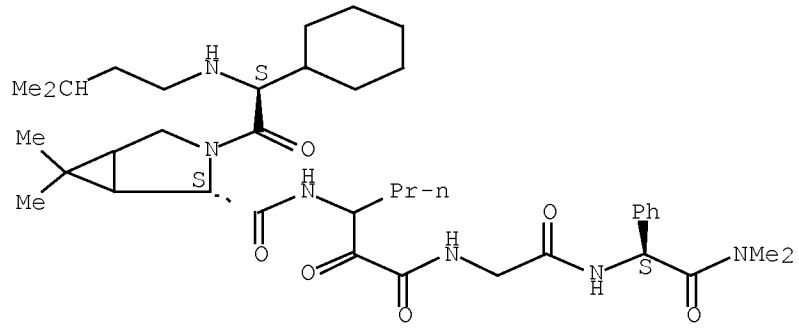
RN 394727-38-9 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carboxamide, N-[1-[2-(3-buten-1-ylamino)-2-oxoacetyl]-4-penten-1-yl]-3-[(2S)-2-[[(dimethylamino)sulfonyl]amino]-3,3-dimethyl-1-oxobutyl]-6,6-dimethyl-, (1R,2S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



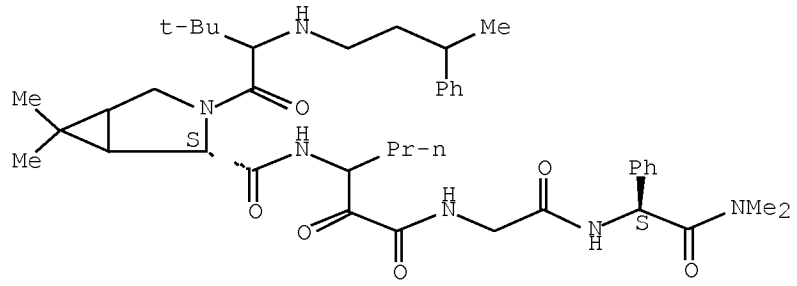
RN 395649-30-6 HCAPLUS
CN Glycinamide,
(2S)-2-cyclohexyl-N-(3-methylbutyl)glycyl-(2S)-6,6-dimethyl-3-azabicyclo[3.1.0]hexane-2-carbonyl-3-amino-2-oxohexanoylglycyl-N,N-dimethyl-2-phenyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



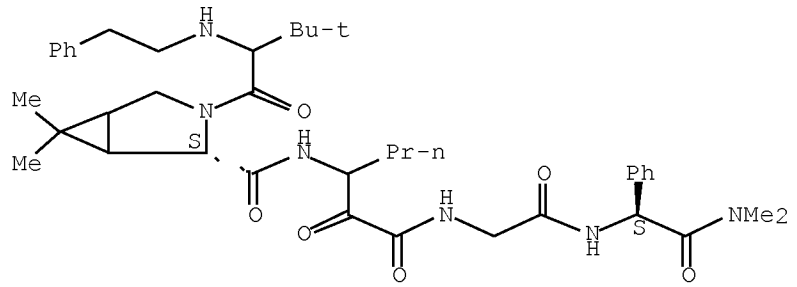
RN 395649-34-0 HCAPLUS
CN Glycinamide, 3-methyl-N-(3-phenylbutyl)valyl-(2S)-6,6-dimethyl-3-azabicyclo[3.1.0]hexane-2-carbonyl-3-amino-2-oxohexanoylglycyl-N,N-dimethyl-2-phenyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



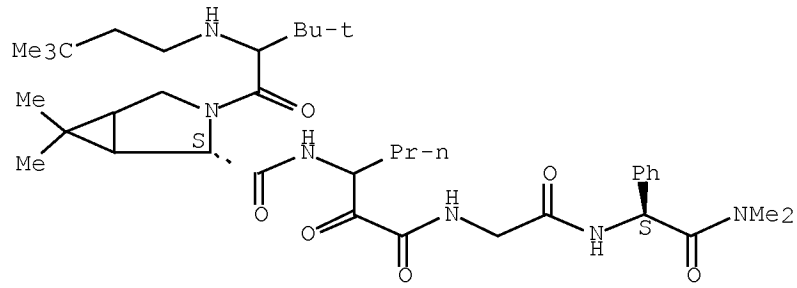
RN 395649-35-1 HCAPLUS
CN Glycinamide, 3-methyl-N-(2-phenylethyl)valyl-(2S)-6,6-dimethyl-3-azabicyclo[3.1.0]hexane-2-carbonyl-3-amino-2-oxohexanoylglycyl-N,N-dimethyl-2-phenyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 395649-36-2 HCAPLUS
CN Glycinamide, N-(3,3-dimethylbutyl)-3-methylvalyl-(2S)-6,6-dimethyl-3-azabicyclo[3.1.0]hexane-2-carbonyl-3-amino-2-oxohexanoylglycyl-N,N-dimethyl-2-phenyl-, (2S)- (9CI) (CA INDEX NAME)

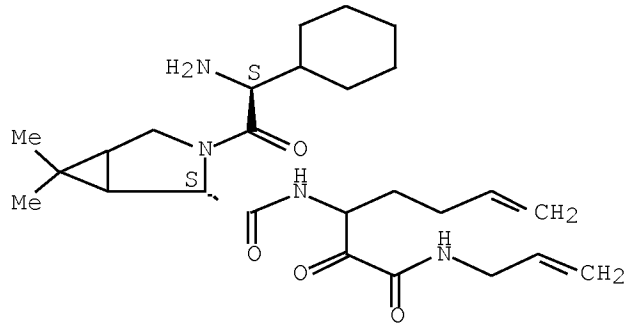
Absolute stereochemistry.



RN 395652-00-3 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carboxamide,

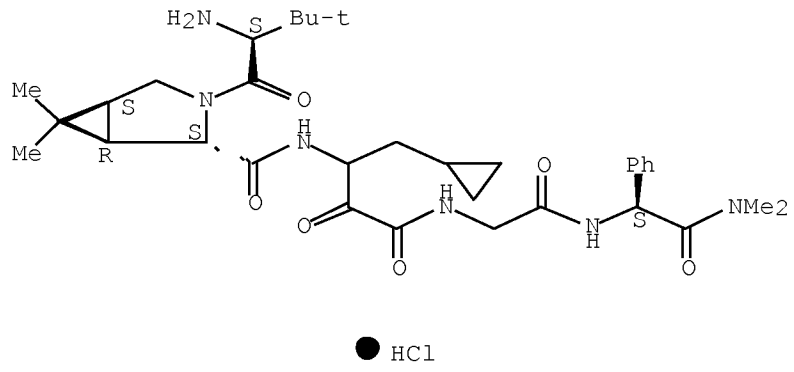
3-[(2S)-2-amino-2-cyclohexylacetyl]-6,6-dimethyl-N-[1-[2-oxo-2-(2-propen-1-ylamino)acetyl]-4-penten-1-yl]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



IT 394735-46-7P 394735-49-0P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of peptides as NS3-serine protease inhibitors of hepatitis C virus)
RN 394735-46-7 HCAPLUS
CN Glycinamide, 3-methyl-L-valyl-(1R,2S,5S)-6,6-dimethyl-3-azabicyclo[3.1.0]hexane-2-carbonyl-β-amino-α-oxocyclopropanebutanoylglycyl-N,N-dimethyl-2-phenyl-, monohydrochloride, (2S)- (CA INDEX NAME)

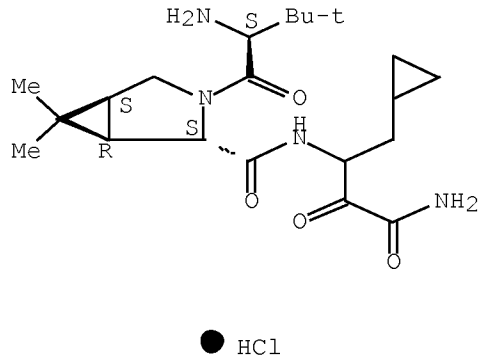
Absolute stereochemistry.



● HCl

RN 394735-49-0 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carboxamide, N-[3-amino-1-(cyclopropylmethyl)-2,3-dioxopropyl]-3-[(2S)-2-amino-3,3-dimethyl-1-oxobutyl]-6,6-dimethyl-, hydrochloride (1:1), (1R,2S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



● HCl

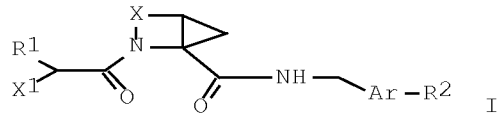
OS.CITING REF COUNT: 35 THERE ARE 35 CAPLUS RECORDS THAT CITE THIS RECORD (40 CITINGS)

L49 ANSWER 77 OF 87 HCAPLUS COPYRIGHT 2012 ACS on STN
ACCESSION NUMBER: 2000:790173 HCAPLUS Full-text
DOCUMENT NUMBER: 133:350506
TITLE: Preparation of 2,3-methano-amino acid derivatives as anticoagulant agents
INVENTOR(S): De Nanteuil, Guillaume; Gloanec, Philippe; Verbeuren, Tony; Rupin, Alain
PATENT ASSIGNEE(S): Adir et Compagnie, Fr.
SOURCE: Eur. Pat. Appl., 34 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1050534	A1	20001108	EP 2000-401197	20000502 <--
EP 1050534	B1	20011205		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
FR 2793248	A1	20001110	FR 1999-5601	19990503 <--
FR 2793248	B1	20010629		
PL 198571	B1	20080630	PL 2000-339967	20000428 <--
CN 1277961	A	20001227	CN 2000-119227	20000430 <--
CN 1130347	C	20031210		
NO 2000002314	A	20001106	NO 2000-2314	20000502 <--
NZ 504298	A	20010126	NZ 2000-504298	20000502 <--
HU 2000001712	A2	20010328	HU 2000-1712	20000502 <--
HU 2000001712	A3	20020228		
US 6288077	B1	20010911	US 2000-561618	20000502 <--
AT 210131	T	20011215	AT 2000-401197	20000502 <--
MX 2000004241	A	20020308	MX 2000-4241	20000502 <--
PT 1050534	E	20020531	PT 2000-401197	20000502 <--
ES 2169716	T3	20020716	ES 2000-401197	20000502 <--
CA 2308780	A1	20001103	CA 2000-2308780	20000503 <--
CA 2308780	C	20030422		
ZA 2000002152	A	20001107	ZA 2000-2152	20000503 <--
AU 2000031325	A	20001130	AU 2000-31325	20000503 <--
AU 763670	B2	20030731		
BR 2000002075	A	20010102	BR 2000-2075	20000503 <--
JP 2000344745	A	20001212	JP 2000-134144	20000508 <--
JP 3200053	B2	20010820		
HK 1032237	A1	20040514	HK 2001-102869	20010423 <--

PRIORITY APPLN. INFO.: FR 1999-5601 A 19990503 <--
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 133:350506
ED Entered STN: 10 Nov 2000
GI



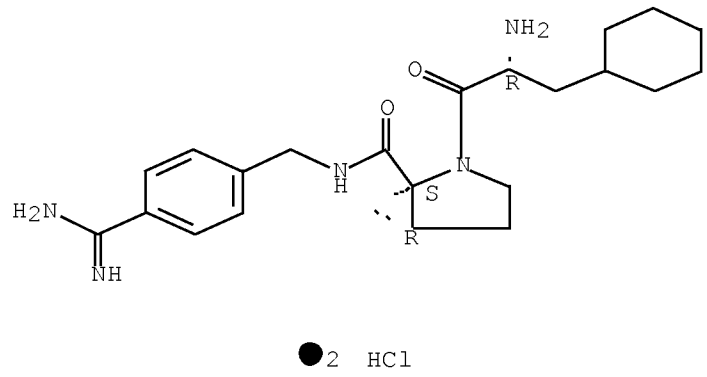
I

AB Amino acid derivs. I [X = (CH2)n; n = 2, 3; R1 = cycloalkyl; R2 = amino, alkyl, OH, guanidinoisothiourido; Ar = aryl, heteroaryl; X1 = OH, substituted amine] were prepared as anticoagulants. Thus, 1-(N-carboxymethyl-(2R)-3-cyclohexylalanyl)-N-(4-amidinobenzyl)-(2S,3R)-

2,3-methanoprolinamide hydrochloride was prepared and tested for its anticoagulant activity (IC50 = 5.3 μM).

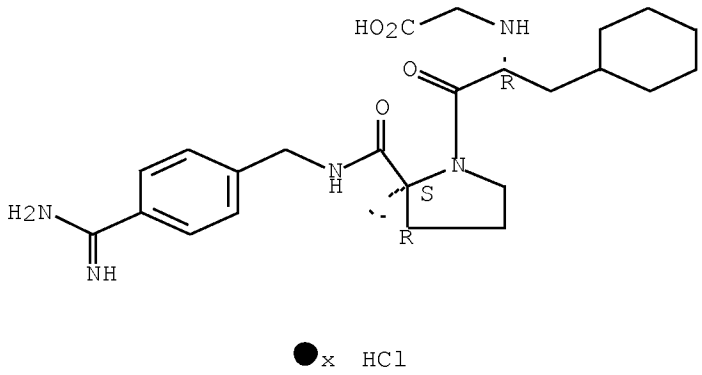
IT 304910-16-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 2,3-methano-amino acid derivs. as anticoagulant agents)
RN 304910-16-5 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-1-carboxamide, 2-[(2R)-2-amino-3-cyclohexyl-1-oxopropyl]-N-[[4-(aminoiminomethyl)phenyl]methyl]-, hydrochloride (1:2), (1S,5R)- (CA INDEX NAME)

Absolute stereochemistry.



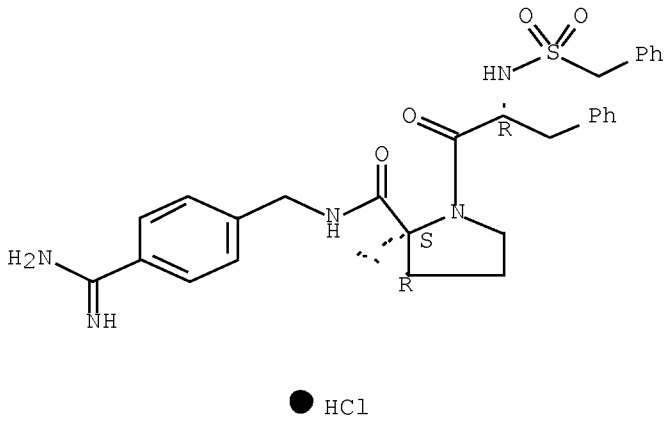
IT 304910-17-6P 304910-19-8P 304910-20-1P
304910-21-2P 304910-22-3P 304910-23-4P
304910-24-5P 304910-26-7P 304910-27-8P
304910-28-9P 304910-29-0P 304910-71-2P
304910-72-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2,3-methano-amino acid derivs. as anticoagulant agents)
RN 304910-17-6 HCAPLUS
CN Glycine, N-[(1R)-2-[(1S,5R)-1-[[[[4-(aminoiminomethyl)phenyl]methyl]amino]carbonyl]-2-azabicyclo[3.1.0]hex-2-yl]-1-(cyclohexylmethyl)-2-oxoethyl]-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



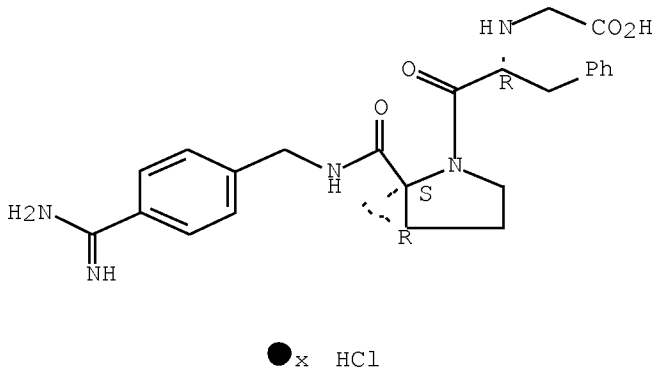
RN 304910-19-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-1-carboxamide, N-[[4-(aminoiminomethyl)phenyl]methyl]-2-[(2R)-1-oxo-3-phenyl-2-[[(phenylmethyl)sulfonyl]amino]propyl]-, hydrochloride (1:1), (1S,5R)-(CA INDEX NAME)

Absolute stereochemistry.



RN 304910-20-1 HCAPLUS
CN Glycine, N-[(1R)-2-[(1S,5R)-1-[[[[4-(aminoiminomethyl)phenyl]methyl]amino]carbonyl]-2-azabicyclo[3.1.0]hex-2-yl]-2-oxo-1-(phenylmethyl)ethyl]-, hydrochloride (9CI) (CA INDEX NAME)

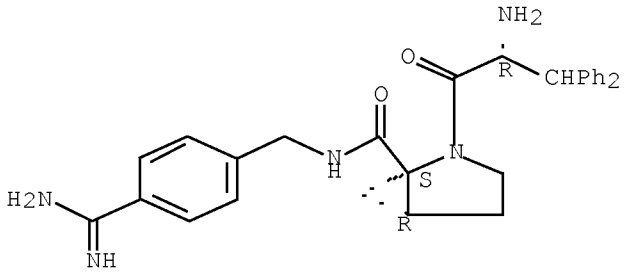
Absolute stereochemistry.



● x HCl

RN 304910-21-2 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-1-carboxamide,
N-[[4-(aminoiminomethyl)phenyl]methyl]-2-[(2R)-2-amino-1-oxo-3,3-diphenylpropyl]-, hydrochloride (1:2), (1S,5R)- (CA INDEX NAME)

Absolute stereochemistry.

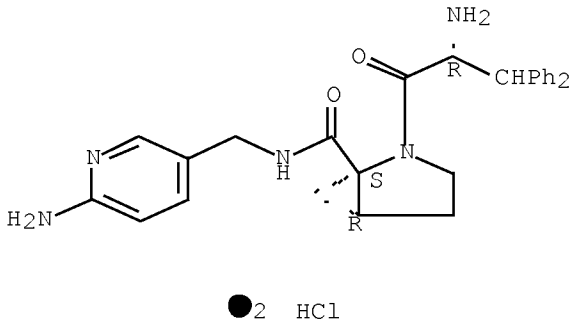


● 2 HCl

RN 304910-22-3 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-1-carboxamide,

2-[(2R)-2-amino-1-oxo-3,3-diphenylpropyl]-N-[(6-amino-3-pyridinyl)methyl]-, hydrochloride (1:2), (1S,5R)- (CA INDEX NAME)

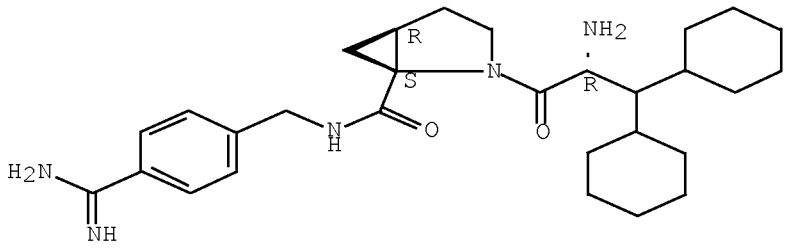
Absolute stereochemistry.



●2 HCl

RN 304910-23-4 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-1-carboxamide, 2-[(2R)-2-amino-3,3-dicyclohexyl-1-oxopropyl]-N-[[4-(aminoiminomethyl)phenyl]methyl]-, hydrochloride (1:2), (1S,5R)- (CA INDEX NAME)

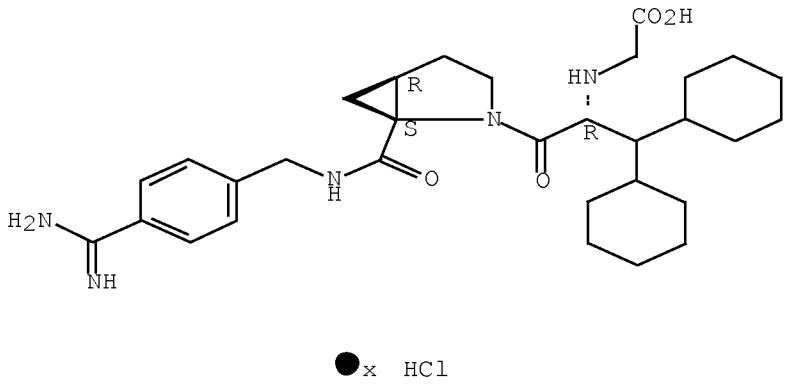
Absolute stereochemistry.



●2 HCl

RN 304910-24-5 HCAPLUS
CN Glycine, N-[(1R)-2-[(1S,5R)-1-[[[[4-(aminoiminomethyl)phenyl]methyl]amino]carbonyl]-2-azabicyclo[3.1.0]hex-2-yl]-1-(dicyclohexylmethyl)-2-oxoethyl]-, hydrochloride (9CI) (CA INDEX NAME)

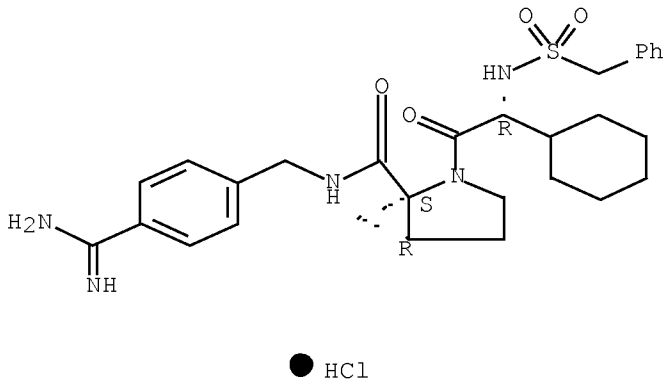
Absolute stereochemistry.



● x HCl

RN 304910-26-7 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-1-carboxamide, N-[[4-(aminoiminomethyl)phenyl]methyl]-2-[(2R)-2-cyclohexyl-2-[[(phenylmethyl)sulfonyl]amino]acetyl]-, hydrochloride (1:1), (1S,5R)-(CA INDEX NAME)

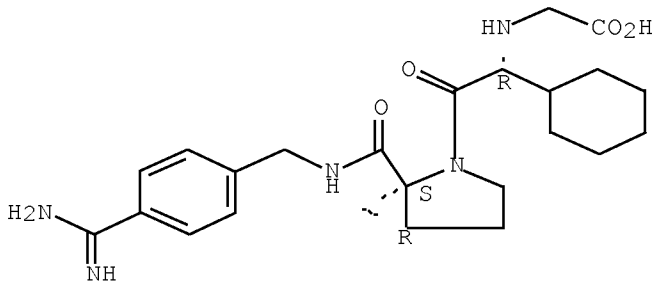
Absolute stereochemistry.



● HCl

RN 304910-27-8 HCAPLUS
CN Glycine, N-[(1R)-2-[(1S,5R)-1-[[[[4-(aminoiminomethyl)phenyl]methyl]amino]carbonyl]-2-azabicyclo[3.1.0]hex-2-yl]-1-cyclohexyl-2-oxoethyl]-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

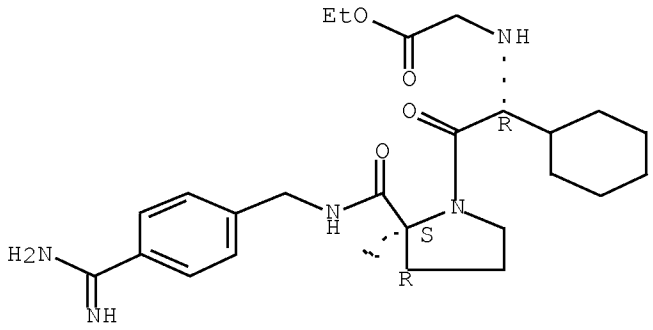


●x HCl

RN 304910-28-9 HCAPLUS
CN Glycine, N-[(1R)-2-[(1S,5R)-1-[[[[4-

(aminoiminomethyl)phenyl]methyl]amino]carbonyl]-2-azabicyclo[3.1.0]hex-2-yl]-1-cyclohexyl-2-oxoethyl]-, ethyl ester, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

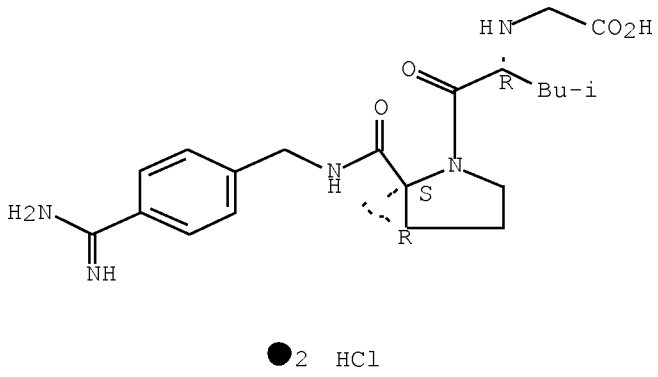


●2 HCl

RN 304910-29-0 HCAPLUS
CN Glycine, N-[(1R)-1-[[(1S,5R)-1-[[[[4-

(aminoiminomethyl)phenyl]methyl]amino]carbonyl]-2-azabicyclo[3.1.0]hex-2-yl]carbonyl]-3-methylbutyl]-, dihydrochloride (9CI) (CA INDEX NAME)

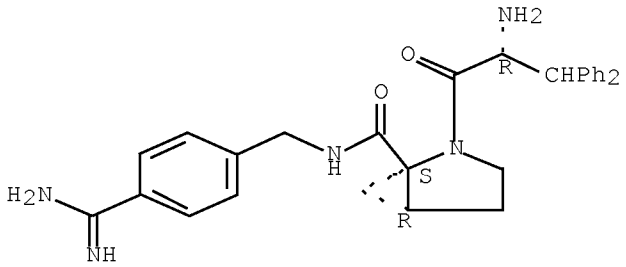
Absolute stereochemistry.



● 2 HCl

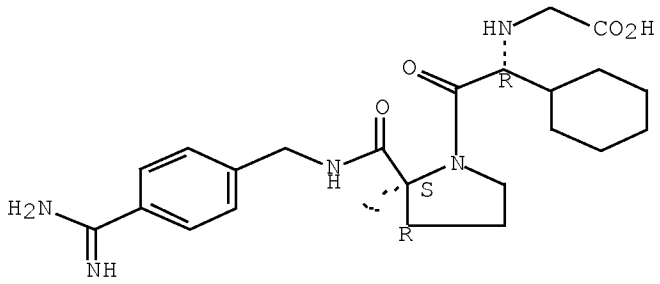
RN 304910-71-2 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-1-carboxamide, N-[[4-(aminoiminomethyl)phenyl]methyl]-2-[(2R)-2-amino-1-oxo-3,3-diphenylpropyl]-, (1S,5R)- (CA INDEX NAME)

Absolute stereochemistry.



RN 304910-72-3 HCAPLUS
CN Glycine, N-[(1R)-2-[(1S,5R)-1-[[[[4-(aminoiminomethyl)phenyl]methyl]amino]carbonyl]-2-azabicyclo[3.1.0]hex-2-yl]-1-cyclohexyl-2-oxoethyl]- (CA INDEX NAME)

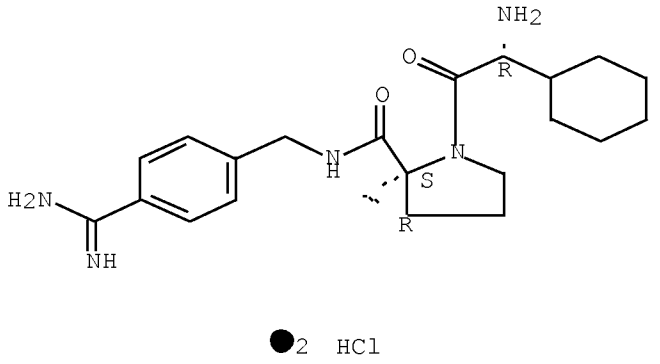
Absolute stereochemistry.



IT 304910-25-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 2,3-methano-amino acid derivs. as anticoagulant agents)
RN 304910-25-6 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-1-carboxamide,

2-[(2R)-2-amino-2-cyclohexylacetyl]-N-[[4-(aminoiminomethyl)phenyl]methyl]-
, hydrochloride (1:2), (1S,5R)- (CA INDEX NAME)

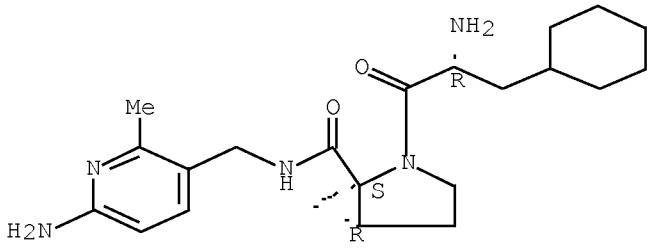
Absolute stereochemistry.



●2 HCl

IT 304910-15-4P 304910-18-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation of 2,3-methano-amino acid derivs. as anticoagulant agents)
RN 304910-15-4 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-1-carboxamide,
2-[(2R)-2-amino-3-cyclohexyl-1-oxopropyl]-N-[(6-amino-2-methyl-3-
pyridinyl)methyl]-, hydrochloride (1:2), (1S,5R)- (CA INDEX NAME)

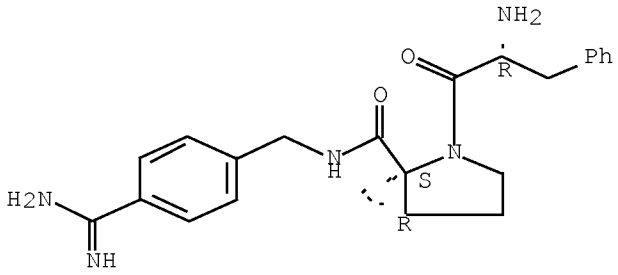
Absolute stereochemistry.



●2 HCl

RN 304910-18-7 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-1-carboxamide, N-[[4-(aminoiminomethyl)phenyl]methyl]-2-[(2R)-2-amino-1-oxo-3-phenylpropyl]-, hydrochloride (1:2), (1S,5R)- (CA INDEX NAME)

Absolute stereochemistry.



●2 HCl

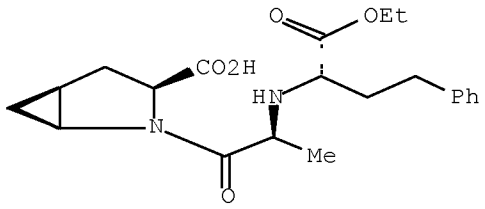
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L49 ANSWER 78 OF 87 HCAPLUS COPYRIGHT 2012 ACS on STN
ACCESSION NUMBER: 1991:506007 HCAPLUS Full-text
DOCUMENT NUMBER: 115:106007
ORIGINAL REFERENCE NO.: 115:17985a,17988a
TITLE: Treatment of cardiac and vascular hypertrophy and hyperplasia with angiotensin-converting enzyme inhibitors
INVENTOR(S): Linz, Wolfgang; Schoelkens, Bernward; Scholz, Wolfgang; Wiemer, Gabriele; Urbach, Hans Joerg; Henning, Rainer; Teetz, Volker
PATENT ASSIGNEE(S): Hoechst A.-G., Germany
SOURCE: Ger. Offen., 12 pp.

CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3926606	A1	19910214	DE 1989-3926606	19890811 <--
EP 417473	A1	19910320	EP 1990-115230	19900808 <--
EP 417473	B1	19930915		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 94409	T	19931015	AT 1990-115230	19900808 <--
ES 2059931	T3	19941116	ES 1990-115230	19900808 <--
DD 297063	A5	19920102	DD 1990-343366	19900809 <--
US 5231083	A	19930727	US 1990-564618	19900809 <--
IL 95327	A	19951031	IL 1990-95327	19900809 <--
CA 2023089	A1	19910212	CA 1990-2023089	19900810 <--
CA 2023089	C	20030114		
NO 9003532	A	19910212	NO 1990-3532	19900810 <--
NO 306979	B1	20000124		
AU 9060920	A	19910214	AU 1990-60920	19900810 <--
AU 631914	B2	19921210		
HU 54504	A2	19910328	HU 1990-4966	19900810 <--
HU 205008	B	19920330		
JP 03083957	A	19910409	JP 1990-210564	19900810 <--
JP 3452199	B2	20030929		
ZA 9006327	A	19910529	ZA 1990-6327	19900810 <--
CS 277644	B6	19930317	CS 1990-3958	19900810 <--
KR 185969	B1	19990501	KR 1990-12267	19900810 <--

PRIORITY APPLN. INFO.: DE 1989-3926606 A 19890811 <--
EP 1990-115230 A 19900808
<--
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 115:106007
ED Entered STN: 23 Sep 1991
GI

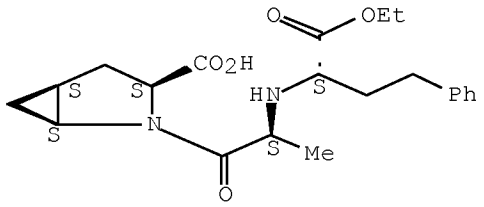


AB The angiotensin-converging enzyme inhibitors R(CH2)nCH(CO2R2)NHCHR1CONR5CHR4CO2R1 (R = H, aliphatic radical, aryl, etc.; R1 = H, aliphatic radical, aryl, heterocyclyl, etc.; R2, R3 = H, aliphatic

radical, alicyclic radical, aryl, etc.; R4, R5 together with the carrier atoms are heterocyclyl; n = 1, 2) are drugs for the treatment of cardiac and vascular hypertrophy and hyperplasia, in newborns. Oral administration of tablets containing N-(1-S-carbetoxy-3-phenylpropyl)-S-alanyl-cis-endo-2-azabicyclo[3.3.0]octane-3,S-carboxylic acid (1 or 10 μg/kg/day, for 3 wk) normalized the weight and wall thickness in the heart of rats with exptl. cardiac hypertrophy, induced by stricture of the abdominal aorta. Formulation examples are given.

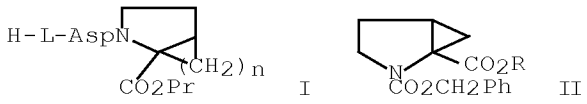
IT 99781-97-2
RL: BIOL (Biological study)
(cardiac and vascular hypertrophy and hyperplasia treatment by)
RN 99781-97-2 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carboxylic acid,
2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-,
[1S-[1α,2[R*(R*)],3β,5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L49 ANSWER 79 OF 87 HCAPLUS COPYRIGHT 2012 ACS on STN
ACCESSION NUMBER: 1991:450274 HCAPLUS Full-text
DOCUMENT NUMBER: 115:50274
ORIGINAL REFERENCE NO.: 115:8757a,8760a
TITLE: Synthesis and conformational analysis of L-aspartylproline and L-aspartyl-2,3-methanoproline propyl esters
AUTHOR(S): Matsui, S.; Srivastava, V. P.; Holt, E. M.; Taylor, E. W.; Stammer, C. H.
CORPORATE SOURCE: Sch. Chem. Sci., Univ. Georgia, Athens, GA, 30602, USA
SOURCE: International Journal of Peptide & Protein Research (1991), 37(4), 306-14
CODEN: IJPPC3; ISSN: 0367-8377
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 10 Aug 1991
GI

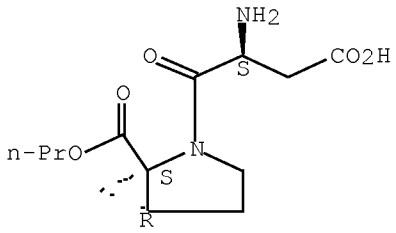


AB The (+)- and (-)-diastereomers of the title compds. I (n = 1, 0) were prepared and their conformations were studied via crystal structure, NMR, and mol. mechanics. The (+)- and (-)-isomers of 2,3-methanoproline II (R = H) were obtained from (±)-II (R = CMe3) via resolution of (±)-II (R = H). All solid dipeptides had a bitter taste with no indication of sweetness.

IT 134666-90-3P 134732-59-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation, conformation, and taste of)

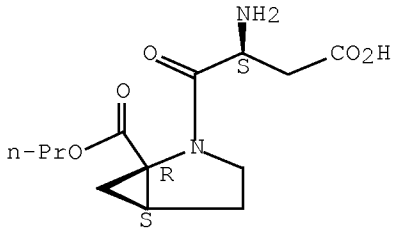
RN 134666-90-3 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-2-butanoic acid, β-amino-γ-oxo-1-(propoxycarbonyl)-, [1S-[1α,2(R*),5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 134732-59-5 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-2-butanoic acid, β-amino-γ-oxo-1-(propoxycarbonyl)-, [1R-[1α,2(S*),5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

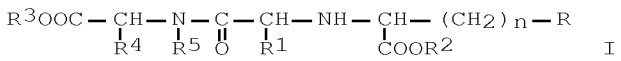


OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

L49 ANSWER 80 OF 87 HCAPLUS COPYRIGHT 2012 ACS on STN
ACCESSION NUMBER: 1988:516052 HCAPLUS Full-text
DOCUMENT NUMBER: 109:116052
ORIGINAL REFERENCE NO.: 109:19241a,19244a
TITLE: Nootropic pharmaceutical containing angiotensin-converting-enzyme inhibitors (ACE inhibitors) and their use for the treatment of cognitive dysfunction
INVENTOR(S): Hock, Franz; Scholtholt, Josef
PATENT ASSIGNEE(S): Hoechst A.-G., Fed. Rep. Ger.
SOURCE: Ger. Offen., 15 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3610391	A1	19871008	DE 1986-3610391	19860327 <--
EP 243645	A2	19871104	EP 1987-103938	19870318 <--
EP 243645	A3	19900124		
EP 243645	B1	19940316		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 102954	T	19940415	AT 1987-103938	19870318 <--
ES 2061447	T3	19941216	ES 1987-103938	19870318 <--
FI 8701304	A	19870928	FI 1987-1304	19870325 <--
FI 91876	B	19940513		
FI 91876	C	19940825		
HU 46046	A2	19880928	HU 1987-1308	19870325 <--
HU 203117	B	19910528		
DD 280765	A5	19900718	DD 1987-301118	19870325 <--
HU 202118	B	19910228	HU 1989-6609	19870325 <--
DK 8701535	A	19870928	DK 1987-1535	19870326 <--
DK 172221	B1	19980112		
NO 8701282	A	19870928	NO 1987-1282	19870326 <--
NO 178546	B	19960108		
NO 178546	C	19960417		
AU 8770649	A	19871001	AU 1987-70649	19870326 <--
AU 621278	B2	19920312		
JP 62240698	A	19871021	JP 1987-70541	19870326 <--
ZA 8702230	A	19871028	ZA 1987-2230	19870326 <--
SU 1836335	A3	19930823	SU 1987-4202302	19870326 <--
CA 1341064	C	20000801	CA 1987-533092	19870326 <--
CN 87102304	A	19871230	CN 1987-102304	19870327 <--
CN 1031267	C	19960313		
CS 276179	B6	19920415	CS 1987-2126	19870327 <--
CS 276385	B6	19920513	CS 1989-6519	19870327 <--

US 5231084 A 19930727 US 1991-711719 19910607 <--
PRIORITY APPLN. INFO.: DE 1986-3610391 A 19860327 <--
EP 1987-103938 A 19870318
<--
US 1987-29905 B1 19870325 <--
US 1988-226521 B1 19880801 <--
US 1989-362288 B3 19890606 <--
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 109:116052
ED Entered STN: 01 Oct 1988
GI



I

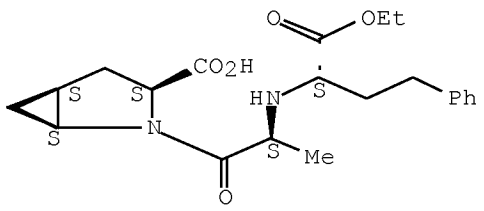
AB ACE inhibitors (I; R = H, optionally substituted C1-8 aliphatic, C3-9 alicyclic, C6-12 aromatic , C7-14 araliph., C7-14 aliphatic-alicyclic hydrocarbyl, SR6, OR6; R1 = H, optionally substituted C1-6 aliphatic, C3-9 alicyclic , C4-13 alicyclic-aliphatic , aryl, C7-16 araliph. hydrocarbyl, C5-12 heteroaryl or protected amino acid side chain; R2, R3 = C1-6 aliphatic , C3-9 alicyclic , C6-12 aromatic, C7-16 araliph. hydrocarbyl; CNR4R5 = C3-15 mono-, bi-, tricyclic heterocyclyl; R6 = C1-4 aliphatic , C5-12 aromatic hydrocarbyl , C5-12 heteroaryl; n = 1, 2) or their salts are nootropic pharmaceuticals. Gelatin capsules contained 1'-[N-(1-S-carbethoxy-3-phenylpropyl)-S-alanyl]-(3'S,5'S)-spirobicyclo[2.2.2]octane-2,3'-pyrrolidin-5'-ylcarboxylic acid 10, Mg stearate 1, and lactose 214 mg. The nootropic efficacy of I was tested by the inhibitory passive avoidance test in mice using the step-through model. Scopolamine-induced amnesia was reversed with a min. ED (MED) of 1.0-30 mg/kg orally in mice, whereas for Piracetam, MED was 500-1000 mg/kg.

IT 99781-97-2
RL: BIOL (Biological study)
(nootropic drug)

RN 99781-97-2 HCAPLUS

CN 2-Azabicyclo[3.1.0]hexane-3-carboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-, [1S-[1α,2[R*(R*)],3β,5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

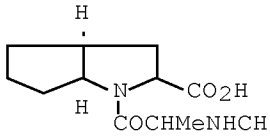


OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

L49 ANSWER 81 OF 87 HCAPLUS COPYRIGHT 2012 ACS on STN
ACCESSION NUMBER: 1987:591020 HCAPLUS Full-text
DOCUMENT NUMBER: 107:191020
ORIGINAL REFERENCE NO.: 107:30449a,30452a
TITLE: Method and pharmaceutical composition containing an angiotensin-converting enzyme inhibitor for treatment of atherosclerosis, thrombosis, and peripheral vascular disease.
INVENTOR(S): Schoelkens, Bernward
PATENT ASSIGNEE(S): Hoechst A.-G., Fed. Rep. Ger.
SOURCE: Ger. Offen., 10 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3536687	A1	19870416	DE 1985-3536687	19851015 <--
EP 219782	A2	19870429	EP 1986-114097	19861011 <--
EP 219782	A3	19900530		
EP 219782	B1	19930929		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 95064	T	19931015	AT 1986-114097	19861011 <--
ES 2059301	T3	19941116	ES 1986-114097	19861011 <--
AU 8663890	A	19870416	AU 1986-63890	19861014 <--
AU 594711	B2	19900315		
DK 8604904	A	19870416	DK 1986-4904	19861014 <--
JP 62087524	A	19870422	JP 1986-242206	19861014 <--
ZA 8607771	A	19870527	ZA 1986-7771	19861014 <--
CA 1320904	C	19930803	CA 1986-520434	19861014 <--
US 5231080	A	19930727	US 1991-678187	19910329 <--
PRIORITY APPLN. INFO.:			DE 1985-3536687 A	19851015 <--
			US 1986-917430 B1	19861010 <--
			EP 1986-114097 A	19861011 <--
			US 1989-393058 B1	19890811 <--

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 107:191020
ED Entered STN: 27 Nov 1987
GI



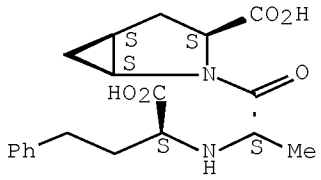
COCHMeNHCH(CO2Et)CH2CH2Ph II

AB Angiotensin-converting enzyme inhibitors R3O2CCHR4NR5COCHR1NHCH(CO2R2)(CH2)nR (I) [n = 1,2; R = H, (substituted) hydrocarbyl, alkoxy, alkylthio, etc.; R1 = H, (substituted) hydrocarbyl, (substituted) heteroaryl, (protected) amino acid side chain; R2, R3 = H, (substituted) hydrocarbyl; R4CHNR5 = C4-15 heterocyclic mono-, bi-, or tricyclic ring system] are inhibitors of blood platelet aggregation and are useful for treatment of atherosclerosis, thrombosis, and peripheral vascular disease. II, administered orally at 1.0-10.0 mg/kg to rabbits, inhibited platelet aggregation in vitro and potentiated the action of PGI2. Tablets were prepared by mixing II 10 and corn starch 140 with a solution of gelatin 7.5 g in water, drying, granulating, adding microcryst. cellulose 2.5 and Mg stearate 2.5 g, and pressing into tablets each containing 10 mg II.

IT 97251-00-8 99781-97-2
RL: BIOL (Biological study)
(blood platelet aggregation inhibition by)

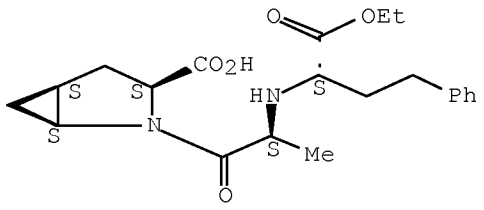
RN 97251-00-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carboxylic acid, 2-[2-[(1-carboxy-3-phenylpropyl)amino]-1-oxopropyl]-, [1S-[1α,2[R*(R*)],3β,5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 99781-97-2 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-, [1S-[1α,2[R*(R*)],3β,5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

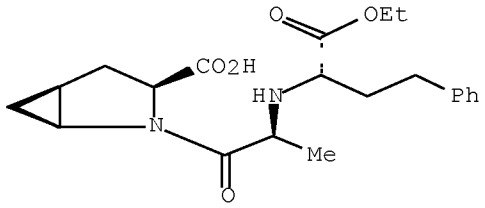


OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)

L49 ANSWER 82 OF 87 HCAPLUS COPYRIGHT 2012 ACS on STN
ACCESSION NUMBER: 1987:446283 HCAPLUS Full-text
DOCUMENT NUMBER: 107:46283
ORIGINAL REFERENCE NO.: 107:7613a,7616a
TITLE: Treatment of glaucoma using angiotensin-convertings-enzyme inhibitors
INVENTOR(S): Urbach, Hansjoerg; Henning, Rainer; Geiger, Rolf; Teetz, Volker
PATENT ASSIGNEE(S): Hoechst A.-G., Fed. Rep. Ger.
SOURCE: Ger. Offen., 31 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3410732	A1	19850926	DE 1984-3410732	19840323 <--
EP 158157	A1	19851016	EP 1985-103022	19850315 <--
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
DK 8501315	A	19850924	DK 1985-1315	19850322 <--
AU 8540288	A	19850926	AU 1985-40288	19850322 <--
AU 578079	B2	19881013		
JP 60209527	A	19851022	JP 1985-55779	19850322 <--
ZA 8502156	A	19851127	ZA 1985-2156	19850322 <--
PRIORITY APPLN. INFO.:			DE 1984-3410732 A	19840323 <--

OTHER SOURCE(S): MARPAT 107:46283
ED Entered STN: 08 Aug 1987
GI



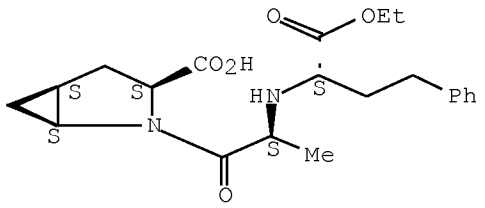
AB The title compds. R3O2CCHR4NR5COCHR1NHCH(CO2R2)(CH2)nR (R = H, alkyl, aryl, R6O, R6S, R6 = alkyl, aryl, etc.; R1 = H, alkyl, aryl, amino acyl, etc.; R2, R3 = H, alkyl, aryl, etc.; R4CHNR5 = heterocyclyl; n = 1, 2) are drugs for the treatment of glaucoma. Thus, tablets were made, containing N-(1-S-carbethoxy-3-phenylpropyl)-S-alanyl-1S,3S,5S-2-azabicyclo[3.3.0]octane-3-carboxylic acid 10, corn starch 140, gelatin 7.5, microcrystn. cellulose 2.5, and Mg stearate 2.5 g.

IT 99781-97-2
RL: BIOL (Biological study)
(angiotensin-converting-enzyme inhibitor, as drug for treatment of glaucoma)

RN 99781-97-2 HCAPLUS

CN 2-Azabicyclo[3.1.0]hexane-3-carboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-, [1S-[1α,2[R*(R*)],3β,5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L49 ANSWER 83 OF 87 HCAPLUS COPYRIGHT 2012 ACS on STN

ACCESSION NUMBER: 1986:207685 HCAPLUS Full-text

DOCUMENT NUMBER: 104:207685

ORIGINAL REFERENCE NO.: 104:32945a,32948a

TITLE: Amino acid derivatives as enzyme inhibitors

INVENTOR(S): Patchett, Arthur A.; Taub, David; Wyvratt, Matthew J. Jr.

PATENT ASSIGNEE(S): Merck and Co., Inc., USA

SOURCE: S. African, 81 pp.

CODEN: SFXXAB
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

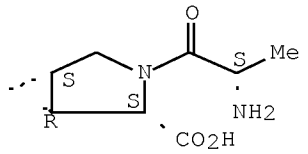
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ZA 8304454	A	19850227	ZA 1983-4454	19830617 <--
PRIORITY APPLN. INFO.:			US 1982-389735 A	19820618 <--

ED Entered STN: 14 Jun 1986
GI For diagram(s), see printed CA Issue.
AB Dipeptides I (R, R3 = H, alkyl, aryl; R1 = H, (un)substituted alkyl, aryl, or heteroaryl, aralkyl, heteroarylalkyl; R2 = H, alkyl, aminoalkyl; system A is a mono- or bicyclic heterocycle), useful as angiotensin-converting enzyme inhibitors, were prepared Thus, the reductive N-alkylation of an alanylproline derivative with PhCH2CH2COCO2H and NaBH3CN gave dipeptide derivative II.
IT 102044-77-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reductive alkylation of, by Et oxophenylbutyrate)
RN 102044-77-9 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carboxylic acid, 3-(2-amino-1-oxopropyl)-, [1R-[1α,2β,3(S*),5α]]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

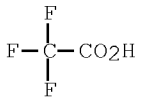
CRN 101952-31-2
CMF C9 H14 N2 O3

Absolute stereochemistry.



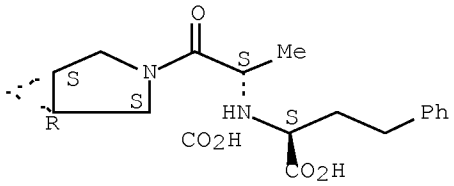
CM 2

CRN 76-05-1
CMF C2 H F3 O2



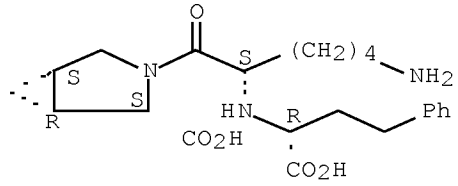
IT 101952-28-7P 101952-30-1P 102044-73-5P
102044-74-6P 102044-75-7P 102044-76-8P
102045-14-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as angiotensin converting enzyme inhibitor)
RN 101952-28-7 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carboxylic acid,
3-[2-[(1-carboxy-3-phenylpropyl)amino]-1-oxopropyl]-,
[1R-[1α,2β,3[S*(S*)],5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



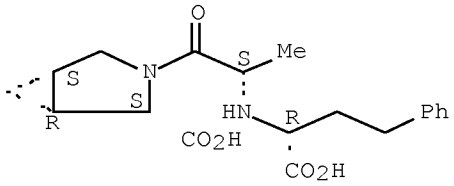
RN 101952-30-1 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carboxylic acid,
3-[6-amino-2-[(1-carboxy-3-phenylpropyl)amino]-1-oxohexyl]-,
[1R-[1α,2β,3[S*(R*)],5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



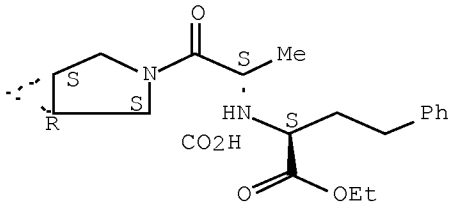
RN 102044-73-5 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carboxylic acid,
3-[2-[(1-carboxy-3-phenylpropyl)amino]-1-oxopropyl]-,
[1R-[1α,2β,3[S*(R*)],5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



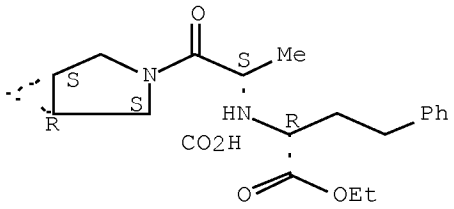
RN 102044-74-6 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carboxylic acid,
3-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-,
[1R-[1α,2β,3[S*(S*)],5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

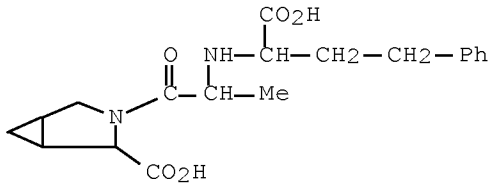


RN 102044-75-7 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carboxylic acid,
3-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-,
[1R-[1α,2β,3[S*(R*)],5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

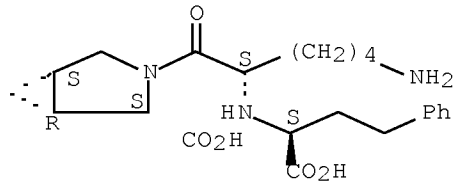


RN 102044-76-8 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carboxylic acid,
3-[2-[(1-carboxy-3-phenylpropyl)amino]-1-oxopropyl]- (CA INDEX NAME)



RN 102045-14-7 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carboxylic acid, 3-[6-amino-2-[(1-carboxy-3-phenylpropyl)amino]-1-oxohexyl]-, [1R-[1α,2β,3[S*(S*)],5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

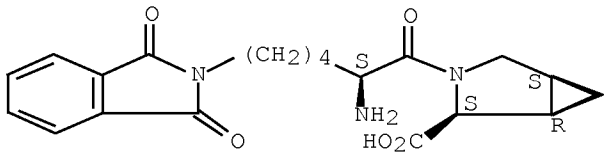


IT 101952-34-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(reductive alkylation of, by glyoxylic acid derivative)
RN 101952-34-5 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carboxylic acid, 3-[2-amino-6-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)-1-oxohexyl]-, [1R-[1α,2β,3(S*),5α]]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

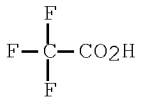
CRN 101952-33-4
CMF C20 H23 N3 O5

Absolute stereochemistry.



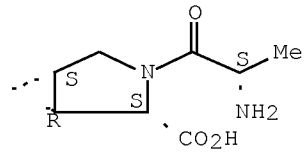
CM 2

CRN 76-05-1
CMF C2 H F3 O2

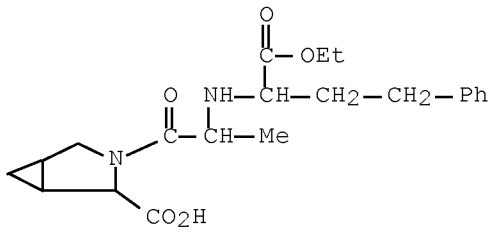


IT 101952-31-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(reductive amination by, of phenyloxobutyric acid)
RN 101952-31-2 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carboxylic acid, 3-(2-amino-1-oxopropyl)-, [1R-[1α,2β,3(S*),5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



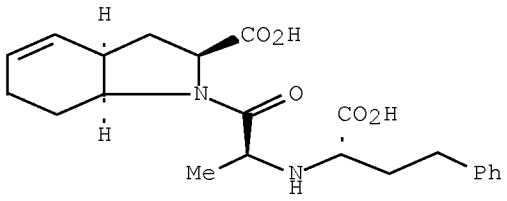
IT 101952-29-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(sapoification of)
RN 101952-29-8 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carboxylic acid, 3-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]- (CA INDEX NAME)



L49 ANSWER 84 OF 87 HCAPLUS COPYRIGHT 2012 ACS on STN
ACCESSION NUMBER: 1986:39761 HCAPLUS Full-text
DOCUMENT NUMBER: 104:39761
ORIGINAL REFERENCE NO.: 104:6423a,6426a
TITLE: Treatment of coronary insufficiency
INVENTOR(S): Henning, Rainer; Urbach, Hansjoerg; Teetz, Volker; Geiger, Rolf; Schoelkens, Bernward
PATENT ASSIGNEE(S): Hoechst A.-G., Fed. Rep. Ger.
SOURCE: Ger. Offen., 27 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3413710	A1	19851024	DE 1984-3413710	19840412 <--
EP 158927	A2	19851023	EP 1985-104028	19850403 <--
EP 158927	A3	19890322		
EP 158927	B1	19931208		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
EP 551927	A1	19930721	EP 1993-102949	19850403 <--
EP 551927	B1	19980923		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
AT 98128	T	19931215	AT 1985-104028	19850403 <--
AT 171376	T	19981015	AT 1993-102949	19850403 <--
CA 1246457	A1	19881213	CA 1985-478724	19850410 <--
AU 8541048	A	19851017	AU 1985-41048	19850411 <--
AU 585502	B2	19890622		
JP 60231696	A	19851118	JP 1985-75489	19850411 <--
JP 07045410	B	19950517		
ZA 8502685	A	19851127	ZA 1985-2685	19850411 <--
US 5403856	A	19950404	US 1994-188745	19940131 <--
US 5744496	A	19980428	US 1994-359860	19941220 <--
US 5684016	A	19971104	US 1995-445543	19950522 <--
US 5747504	A	19980505	US 1996-709286	19960906 <--
HK 1012008	A1	20000811	HK 1998-113025	19981209 <--

PRIORITY APPLN. INFO.: DE 1984-3413710 A 19840412 <--
EP 1985-104028 A 19850403 <--
US 1985-721705 B1 19850410 <--
US 1989-313491 B1 19890222 <--
US 1991-636001 B1 19910103 <--
US 1992-920173 B1 19920727 <--
US 1994-188745 A3 19940131 <--
US 1994-359860 A3 19941220 <--
US 1995-445543 A1 19950522 <--
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 104:39761
ED Entered STN: 08 Feb 1986
GI



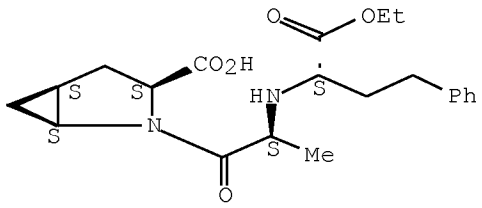
AB The angiotensin-converting enzyme inhibitors R(CH2)nCH(CO2R2)NHCHR1CONR5CHR4CO2R3 [R = H, (un)substituted alkyl, aryl, etc.; R1 = alkyl, cycloalkyl, heterocyclic radical; R2, R3 = H, alkyl, aryl, etc.; R4CHNR2 = heterocyclic radical; n = 1, 2] are drugs for the treatment of cardiac insufficiency. Thus, tablets are formulated, containing 1-N-(1-S-carbethoxy-3-phenylpropyl)-S-alanyl-1S,3S,5S-2-azabicyclo[3.3.0]octane-3-carboxylic acid.

IT 99781-97-2
RL: BIOL (Biological study)
(pharmaceutical, for treatment of cardiac insufficiency)

RN 99781-97-2 HCAPLUS

CN 2-Azabicyclo[3.1.0]hexane-3-carboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-, [1S-[1α,2[R*(R*)],3β,5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

L49 ANSWER 85 OF 87 HCAPLUS COPYRIGHT 2012 ACS on STN

ACCESSION NUMBER: 1985:560858 HCAPLUS Full-text

DOCUMENT NUMBER: 103:160858

ORIGINAL REFERENCE NO.: 103:25849a,25852a

TITLE: N-Alkylated dipeptides and their esters

INVENTOR(S): Urbach, Hansjoerg; Henning, Rainer; Wissmann, Hans; Teetz, Volker

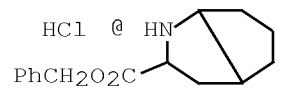
PATENT ASSIGNEE(S): Hoechst A.-G., Fed. Rep. Ger.

SOURCE: Eur. Pat. Appl., 32 pp.

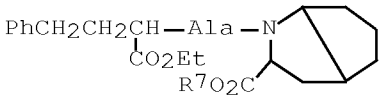
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 135181	A2	19850327	EP 1984-110677	19840907 <--
EP 135181	A3	19860402		
EP 135181	B1	19900131		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
DE 3333455	A1	19850411	DE 1983-3333455	19830916 <--
AT 49979	T	19900215	AT 1984-110677	19840907 <--
HU 36140	A2	19850828	HU 1984-3417	19840910 <--
HU 198303	B	19890928		
FI 8403591	A	19850317	FI 1984-3591	19840913 <--
FI 80275	B	19900131		
FI 80275	C	19900510		
CA 1338162	C	19960312	CA 1984-463071	19840913 <--
DK 8404404	A	19850317	DK 1984-4404	19840914 <--
DK 166027	B	19930301		
DK 166027	C	19930712		
NO 8403663	A	19850318	NO 1984-3663	19840914 <--
NO 167808	B	19910902		
NO 167808	C	19911218		
AU 8433071	A	19850321	AU 1984-33071	19840914 <--
AU 575585	B2	19880804		
JP 60089498	A	19850520	JP 1984-191869	19840914 <--
JP 07098836	B	19951025		
ZA 8407259	A	19850529	ZA 1984-7259	19840914 <--
ES 535918	A1	19851001	ES 1984-535918	19840914 <--
IL 72946	A	19900429	IL 1984-72946	19840914 <--
US 5055591	A	19911008	US 1988-173024	19880323 <--
PRIORITY APPLN. INFO.:			DE 1983-3333455 A	19830916 <--
			EP 1984-110677 A	19840907 <--
			US 1984-650714 B1	19840914 <--
			US 1986-943881 B1	19861219 <--

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
ED Entered STN: 16 Nov 1985
GI



II



III

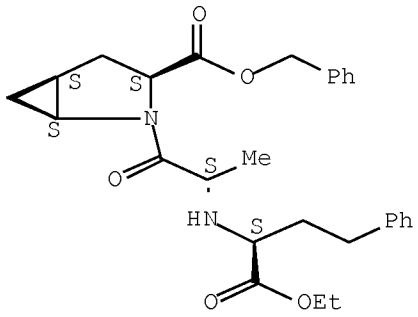
AB Title compds. R3O2CCHR4NR5COCHR1NHCH(CO2R2)(CH2)nR [I; n = 1, 2; R = H, (un)substituted C1-8 aliphatic, C3-9 alicyclic, C6-12 aromatic, C7-14 araliph., or C7-14 alicyclic aliphatic residue, OR6, SR6 [R6 = (un)substituted C1-4 aliphatic, C6-12 aromatic, or heteroarom. residue]; R1 = H, (un)substituted C3-9 alicyclic, C4-13 alicyclic aliphatic, C6-12 aromatic, C7-16 araliph., or heteroarom. residue, amino acid side chain; R2, R3 = H, (un)substituted C1-6 aliphatic, C3-9 alicyclic, C6-12 aromatic, or C7-16 araliph. residue; CHR4NR5 = C5-15 heterocyclic mono-, bi-, or tricyclic ring system] were prepared via the condensation of HO2CCHR1NHCH(CO2R2)(CH2)nR with R3O2CCHR4NHR5 in the presence of an alkanephosphoric acid anhydride. Thus, (S,S,S)-azabicyclo[3.3.0]octane II was condensed with (S)-PhCH2CH2CH(CO2Et)-(S)-Ala-OH by n-propanephosphonic acid anhydride in CH2Cl2 in the presence of N-ethylmorpholine to give peptide derivative III (R7 = CH2Ph), which was debenzylated to give III (R7 = H) (all-S isomer). I inhibit angiotensin-converting enzyme and can be used as antihypertensives (no data).

IT 97250-98-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 97250-98-1 HCAPLUS

CN 2-Azabicyclo[3.1.0]hexane-3-carboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-, phenylmethyl ester, [1S-[1α,2[R*(R*)],3β,5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



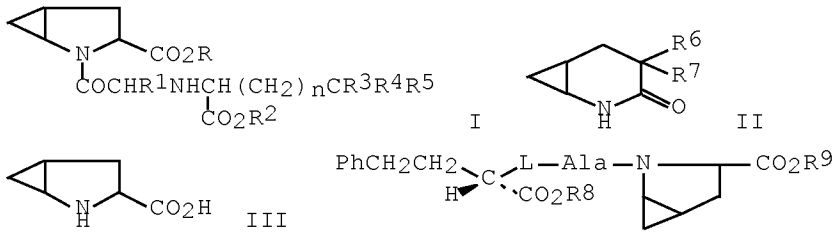
OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L49 ANSWER 86 OF 87 HCAPLUS COPYRIGHT 2012 ACS on STN
ACCESSION NUMBER: 1985:454461 HCAPLUS Full-text
DOCUMENT NUMBER: 103:54461
ORIGINAL REFERENCE NO.: 103:8792h,8793a
TITLE: 2-Azabicyclo[3.1.0]hexane-3-carboxylic acid derivatives, intermediates, and their use
INVENTOR(S): Urbach, Hansjoerg; Henning, Rainer; Becker, Reinhard
PATENT ASSIGNEE(S): Hoechst A.-G., Fed. Rep. Ger.
SOURCE: Ger. Offen., 30 pp.

CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3324263	A1	19850117	DE 1983-3324263	19830706 <--
EP 131226	A2	19850116	EP 1984-107607	19840630 <--
EP 131226	A3	19870826		
EP 131226	B1	19900530		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
AT 53203	T	19900615	AT 1984-107607	19840630 <--
HU 37803	A2	19860228	HU 1984-2563	19840702 <--
HU 209413	B	19940530		
HU 39160	A2	19860828	HU 1985-4538	19840702 <--
HU 194827	B	19880328		
US 4591598	A	19860527	US 1984-627639	19840703 <--
FI 8402691	A	19850107	FI 1984-2691	19840704 <--
ES 534001	A1	19850416	ES 1984-534001	19840704 <--
DK 8403302	A	19850107	DK 1984-3302	19840705 <--
AU 8430298	A	19850110	AU 1984-30298	19840705 <--
AU 573227	B2	19880602		
ZA 8405160	A	19850227	ZA 1984-5160	19840705 <--
JP 60051199	A	19850322	JP 1984-138111	19840705 <--
JP 07010879	B	19950208		
CA 1263000	A1	19891114	CA 1984-458205	19840705 <--
ES 535452	A1	19850516	ES 1984-535452	19840828 <--
ES 535453	A1	19850516	ES 1984-535453	19840828 <--
CA 1267902	A2	19900417	CA 1988-583193	19881104 <--

PRIORITY APPLN. INFO.: DE 1983-3324263 A 19830706 <--
EP 1984-107607 A 19840630 <--
CA 1984-458205 A3 19840705 <--
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 103:54461
ED Entered STN: 24 Aug 1985
GI

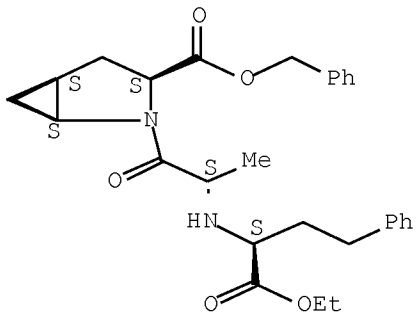


AB Title derivs. I [R = H, C1-6 alkyl, C2-6 alkenyl, (C6-12 aryl)-C1-4 alkyl; R1 = H, (un)substituted C1-6 alkyl, C2-6 alkenyl, C5-9 cycloalkyl, C5-9 cycloalkenyl, etc.; R2 = H, C1-6 alkyl, C2-6 alkenyl, (C6-12 aryl)-C1-4 alkyl; R3 = H, OH, R4 = H; R3R4 = O; R5 = C1-6 alkyl, C2-6 alkenyl, C2-6 alkenyl, C5-9 cycloalkyl, (un)substituted C6-12 aryl; n = 0, 1] were prepared as antihypertensives (no data) due to their ability to inhibit angiotensin-converting enzyme. Thus, cis-bicyclo[3.1.0]hexan-2-one was treated with H2NOSO3H and then subjected to the Beckman rearrangement to give cis-azabicyclo[4.1.0]heptane cis-II (R6 = R7 = H), which was chlorinated with PCl5 to give cis-II (R6 = R7 = Cl), which was dechlorinated by hydrogenation over Raney Ni to give cis-II (R6 = Cl, R7 = H). The latter was hydrolyzed in the presence of Ba(OH)2 to give cis-azabicyclo[3.1.0]hexane-3-carboxylate cis-III, which was separated into its exo and endo isomers. The latter were esterified with PhCH2OH via SOCl2 to give the corresponding benzyl esters, which were condensed with (S)-PhCH2CH2CH(CO2Et)-L-Ala-OH by DCC/1-hydroxybenzotriazole to give the exo and endo isomers of title compound cis-IV (R8 = Et, R9 = CH2Ph), which were separated into the 3S-endo, 3R-endo, 3S-exo, and 3R-exo isomers. The latter were debenzylated by hydrogenolysis over Pd/C and then treated with HCl/EtOH to give the corresponding cis-IV.HCl (R8 = Et, R9 = H). 3S-endo-cis-IV.HCl (R8 = Et, R9 = H) was saponified to give 3S-endo-cis-IV (R8 = R9 = H); 3S-exo-cis-IV (R8 = R9 = H) was also prepared

IT 97250-98-1P 97277-17-3P 97277-18-4P 97277-19-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenolysis of)

RN 97250-98-1 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-, phenylmethyl ester, [1S-[1α,2[R*(R*)],3β,5α]]- (9CI) (CA INDEX NAME)

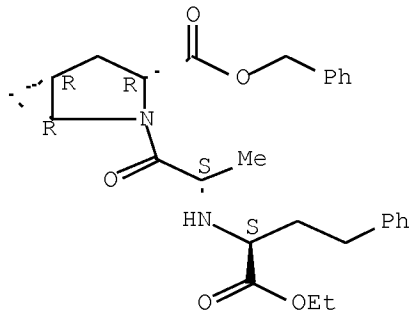
Absolute stereochemistry.



RN 97277-17-3 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-, phenylmethyl ester, [1R-[1α,2[S*(S*)],3β,5α]]- (9CI) (CA

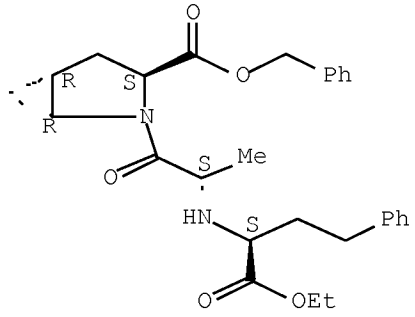
INDEX NAME)

Absolute stereochemistry.



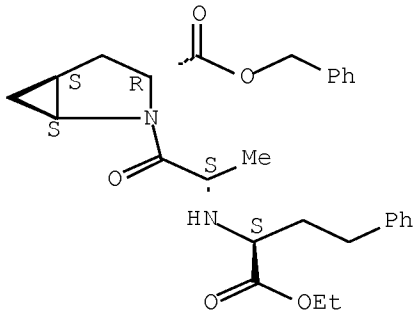
RN 97277-18-4 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-, phenylmethyl ester, [1R-[1α,2[S*(S*)],3α,5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



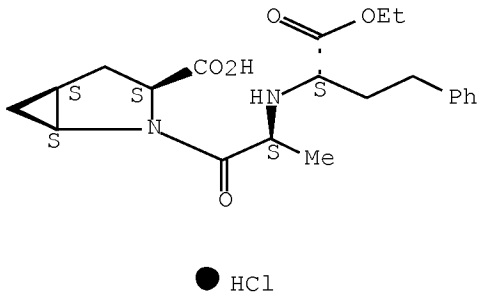
RN 97277-19-5 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-, phenylmethyl ester, [1S-[1α,2[R*(R*)],3α,5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



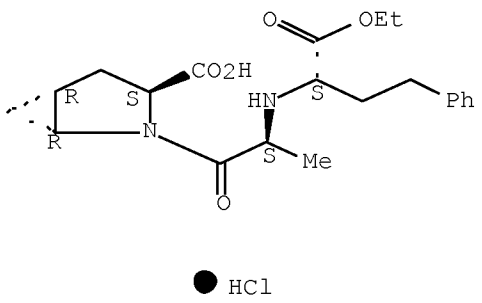
IT 97250-99-2P 97277-21-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and saponification of)
RN 97250-99-2 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-, monohydrochloride, [1S-[1α,2[R*(R*)],3β,5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



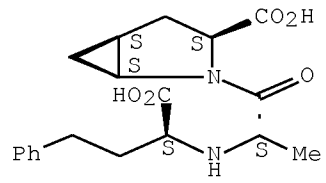
RN 97277-21-9 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-, monohydrochloride, [1R-[1α,2[S*(S*)],3α,5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



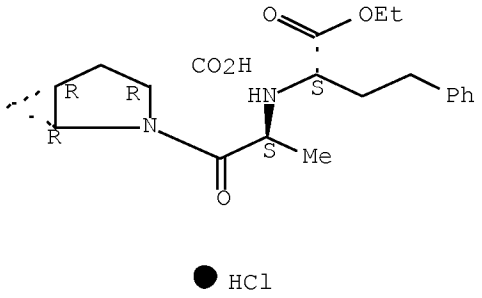
IT 97251-00-8P 97277-20-8P 97277-22-0P
97334-49-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 97251-00-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carboxylic acid,
2-[2-[(1-carboxy-3-phenylpropyl)amino]-1-oxopropyl]-,
[1S-[1α,2[R*(R*)],3β,5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 97277-20-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carboxylic acid,
2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-,
monohydrochloride, [1R-[1α,2[S*(S*)],3β,5α]]- (9CI) (CA
INDEX NAME)

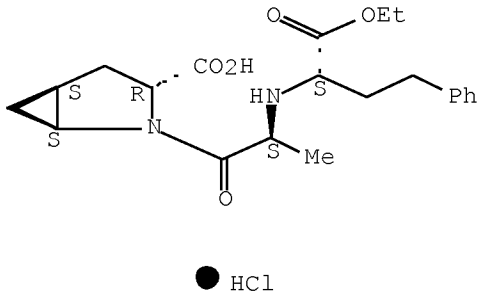
Absolute stereochemistry.



● HCl

RN 97277-22-0 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-, monohydrochloride, [1S-[1α,2[R*(R*)],3α,5α]]- (9CI) (CA INDEX NAME)

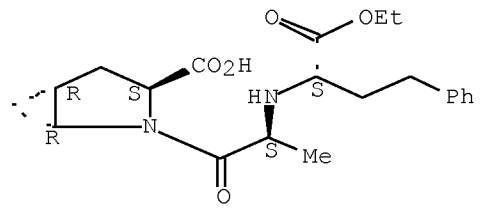
Absolute stereochemistry.



● HCl

RN 97334-49-1 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-, [1R-[1α,2[S*(S*)],3α,5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

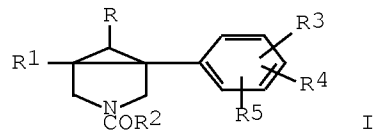


OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)

L49 ANSWER 87 OF 87 HCAPLUS COPYRIGHT 2012 ACS on STN
ACCESSION NUMBER: 1978:529383 HCAPLUS Full-text
DOCUMENT NUMBER: 89:129383
ORIGINAL REFERENCE NO.: 89:20017a,20020a
TITLE: Acylazabicyclohexanes
INVENTOR(S): Fanshawe, William Joseph; Epstein, Joseph William; Crawley, Lantz Stephen; Hofmann, Corris Mabelle; Safir, Sidney Robert
PATENT ASSIGNEE(S): American Cyanamid Co., USA
SOURCE: U.S., 5 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4088652	A	19780509	US 1976-749578	19761210 <--
GB 1590901	A	19810610	GB 1977-33818	19770811 <--
PRIORITY APPLN. INFO.:			US 1975-600559	A1 19750731 <--

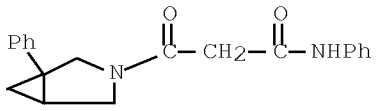
OTHER SOURCE(S): CASREACT 89:129383; MARPAT 89:129383
ED Entered STN: 12 May 1984
GI



I

AB The acylazabicyclohexanes I (R, R1 = H, C1-6 alkyl; R2 = H, C1-6 alkyl, C3-6 cycloalkyl, Ph, halophenyl, furyl, adamantyl, naphthyl, norbornyl; R3, R5 = H, halo, C1-6 alkoxy; R4 = H, halo, C1-6 alkyl, C1-6 alkoxy, F3C, NO2, NH2, AcNH, HO) were prepared Thus, 1-phenyl-1,2-cyclopropanedicarboximide was reduced with Na(MeOCH2CH2O)2AlH2 to give 1-phenyl-3-azabicyclo[3.1.1]hexane, which was acylated with cyclopropanecarbonyl chloride to give I (R, R1, R3, R4, R5 = H, R2 = cyclopropyl).
IT 67644-24-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 67644-24-0 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-3-propanamide, β-oxo-N,1-diphenyl- (CA

INDEX NAME)



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)

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L1             1 SEA FILE=HCAPLUS SPE=ON  ABB=ON  PLU=ON  US2001-788173/APPS
L12              STR
L14         8057 SEA FILE=REGISTRY SSS FUL L12
L17              STR
L19            4 SEA FILE=REGISTRY SUB=L14 SSS FUL L17
L20              STR
L22         8057 SEA FILE=REGISTRY SUB=L14 SSS FUL L20
L23         8053 SEA FILE=REGISTRY SPE=ON  ABB=ON  PLU=ON  L22 NOT L19
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L44          427 SEA FILE=HCAPLUS SPE=ON  ABB=ON  PLU=ON  L42
L45           15 SEA FILE=HCAPLUS SPE=ON  ABB=ON  PLU=ON  L44 AND (L24 OR L25
                 OR L26 OR L27 OR L28 OR L29 OR L30)
L46            0 SEA FILE=HCAPLUS SPE=ON  ABB=ON  PLU=ON  L1 NOT L45
L47           15 SEA FILE=HCAPLUS SPE=ON  ABB=ON  PLU=ON  (L45 OR L46)


=> d his l56

     (FILE 'MEDLINE, BIOSIS, EMBASE, CABA, BIOTECHNO, DRUGU, VETU, TOXCENTER,
     NAPRALERT' ENTERED AT 09:09:45 ON 01 MAY 2012)
CHARGED TO COST=TC1600
L56           10 S L55 AND L24-L30


=> d que nos l56
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L14         8057 SEA FILE=REGISTRY SSS FUL L12
L17              STR
L19            4 SEA FILE=REGISTRY SUB=L14 SSS FUL L17
L20              STR
L22         8057 SEA FILE=REGISTRY SUB=L14 SSS FUL L20
L23         8053 SEA FILE=REGISTRY SPE=ON  ABB=ON  PLU=ON  L22 NOT L19
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L28              QUE  SPE=ON  ABB=ON  PLU=ON  MAGNIN, D?/AU,AUTH,IN
L29              QUE  SPE=ON  ABB=ON  PLU=ON  HAMANN, L?/AU,AUTH,IN
L30              QUE  SPE=ON  ABB=ON  PLU=ON  BETEBENNER, D?/AU,AUTH,IN
L39              STR
L41         6632 SEA FILE=REGISTRY SUB=L14 SSS FUL L39
L42         1421 SEA FILE=REGISTRY SPE=ON  ABB=ON  PLU=ON  L23 NOT L41
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L54         961 SEA FILE=REGISTRY SPE=ON  ABB=ON  PLU=ON  L42 AND (MEDLINE OR
                BIOSIS OR EMBASE OR CABA OR BIOTECHNO OR DRUGU OR VETU OR
                TOXCENTER OR NAPRALERT)/LC
L55         859 SEA L54
L56          10 SEA L55 AND (L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR L30)


=> dup rem l47 l56
FILE 'HCAPLUS' ENTERED AT 09:18:09 ON 01 MAY 2012
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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CHARGED TO COST=TC1600
PROCESSING COMPLETED FOR L47
PROCESSING COMPLETED FOR L56
L57          16 DUP REM L47 L56 (9 DUPLICATES REMOVED)
                ANSWERS '1-15' FROM FILE HCAPLUS
                ANSWER '16' FROM FILE EMBASE

=> file stnguide
FILE 'STNGUIDE' ENTERED AT 09:18:22 ON 01 MAY 2012
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CHARGED TO COST=TC1600

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Apr 27, 2012 (20120427/UP).
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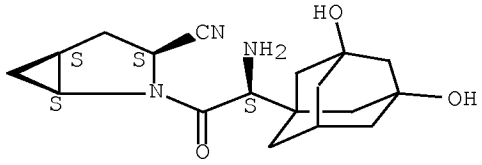
=> d ibib ed abs hitstr 1-15
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, EMBASE' - CONTINUE? (Y)/N:y

L57 ANSWER 1 OF 16 HCAPLUS COPYRIGHT 2012 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2009:672585 HCAPLUS Full-text
DOCUMENT NUMBER: 151:115551
TITLE: Pharmacokinetics of the dipeptidyl peptidase 4 inhibitor saxagliptin in rats, dogs, and monkeys and clinical projections
AUTHOR(S): Fura, Aberra; Khanna, Ashish; Vyas, Viral; Koplowitz, Barry; Chang, Shu-Ying; Caporuscio, Christian; Boulton, David W.; Christopher, Lisa J.; Chadwick, Kristina D.; Hamann, Lawrence G.; Humphreys, W. Griffith; Kirby, Mark
CORPORATE SOURCE: Pharmaceutical Candidate Optimization, Research and Development, Bristol-Myers Squibb, Princeton, NJ, USA
SOURCE: Drug Metabolism and Disposition (2009), 37(6), 1164-1171
CODEN: DMDSAI; ISSN: 0090-9556
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 04 Jun 2009
AB Saxagliptin is a potent, selective, reversible dipeptidyl peptidase 4 (DPP4) inhibitor specifically designed for extended inhibition of the DPP4 enzyme and is currently under development for the treatment of type-2 diabetes. The pharmacokinetics of saxagliptin were evaluated in rats, dogs, and monkeys and used to predict its human pharmacokinetics. Saxagliptin was rapidly absorbed and had good bioavailability (50-75%) in the species tested. The plasma clearance of saxagliptin was higher in rats (115 mL/min/kg) than in dogs (9.3 mL/min/kg) and monkeys (14.5 mL/min/kg) and was predicted to be low to moderate in humans. The plasma elimination half-life was between 2.1 and 4.4 h in rats, dogs, and monkeys, and both metabolism and renal excretion contributed to the overall elimination. The primary metabolic clearance pathway involved the formation of a significant circulating, pharmacol. active hydroxylated metabolite, M2. The volume of distribution values observed in rats, dogs, and monkeys (1.3-5.2 l/kg) and predicted for humans (2.7 l/kg) were greater than those for total body water, indicating extravascular distribution. The in vitro serum protein binding was low (≤30%) in rats, dogs, monkeys, and humans. After intra-arterial administration of saxagliptin to Sprague-Dawley and Zucker diabetic fatty rats, higher levels of saxagliptin and M2 were observed in the intestine (a proposed major site of drug action) relative to that in plasma. Saxagliptin has prolonged pharmacodynamic properties relative to its plasma pharmacokinetic profile, presumably due to addnl. contributions from M2, distribution of saxagliptin and M2 to the intestinal tissue, and prolonged dissociation of both saxagliptin and M2 from DPP4.
IT 841302-24-7
RL: PKT (Pharmacokinetics); BIOL (Biological study)

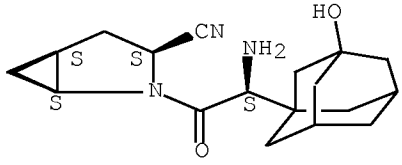
(pharmacokinetics of dipeptidyl peptidase 4 inhibitor saxagliptin in rats, dogs, and monkeys and clin. projections)
RN 841302-24-7 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(3,5-dihydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



IT 361442-04-8, Saxagliptin
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacokinetics of dipeptidyl peptidase 4 inhibitor saxagliptin in rats, dogs, and monkeys and clin. projections)
RN 361442-04-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.

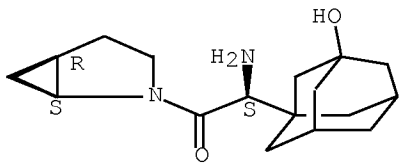


OS.CITING REF COUNT: 20 THERE ARE 20 CAPLUS RECORDS THAT CITE THIS RECORD (20 CITINGS)
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L57 ANSWER 2 OF 16 HCAPLUS COPYRIGHT 2012 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2008:187464 HCAPLUS Full-text
DOCUMENT NUMBER: 148:443309
TITLE: Involvement of DPP-IV catalytic residues in enzyme-saxagliptin complex formation
AUTHOR(S): Metzler, William J.; Yanchunas, Joseph; Weigelt, Carolyn; Kish, Kevin; Klei, Herbert E.; Xie, Dianlin;

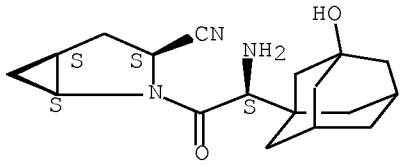
Zhang, Yaqun; Corbett, Martin; Tamura, James K.; He, Bin; Hamann, Lawrence G.; Kirby, Mark S.; Marcinkeviciene, Jovita
CORPORATE SOURCE: Department of Molecular Biosciences, Bristol-Myers Squibb Research and Development, Princeton, NJ, 08543-4000, USA
SOURCE: Protein Science (2008), 17(2), 240-250
CODEN: PRCIEI; ISSN: 0961-8368
PUBLISHER: Cold Spring Harbor Laboratory Press
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 14 Feb 2008
AB The inhibition of DPP-IV by saxagliptin has been proposed to occur through formation of a covalent but reversible complex. To evaluate further the mechanism of inhibition, we determined the x-ray crystal structure of the DPP-IV:saxagliptin complex. This structure reveals covalent attachment between S630 and the inhibitor nitrile carbon (C-O distance <1.3 Å). To investigate whether this serine addition is assisted by the catalytic His-Asp dyad, we generated two mutants of DPP-IV, S630A and H740Q, and assayed them for ability to bind inhibitor. DPP-IVH740Q bound saxagliptin with an .apprx.1000-fold reduction in affinity relative to DPP-IVWT, while DPP-IVS630A showed no evidence for binding inhibitor. An analog of saxagliptin lacking the nitrile group showed unchanged binding properties to the both mutant proteins, highlighting the essential role S630 and H740 play in covalent bond formation between S630 and saxagliptin. Further supporting mechanism-based inhibition by saxagliptin, NMR spectra of enzyme-saxagliptin complexes revealed the presence of three downfield resonances with low fractionation factors characteristic of short and strong hydrogen bonds (SSHB). Comparison of the NMR spectra of various wild-type and mutant DPP-IV:ligand complexes enabled assignment of a resonance at .apprx.14 ppm to H740. Two addnl. DPP-IV mutants, Y547F and Y547Q, generated to probe potential stabilization of the enzyme-inhibitor complex by this residue, did not show any differences in inhibitor binding either by ITC or NMR. Together with the previously published enzymic data, the structural and binding data presented here strongly support a histidine-assisted covalent bond formation between S630 hydroxyl oxygen and the nitrile group of saxagliptin.
IT 841302-20-3, BMS 538305
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(BMS 538305; involvement of dipeptidyl peptidase-IV catalytic residues in enzyme-saxagliptin complex formation)
RN 841302-20-3 HCAPLUS
CN Ethanone, 2-amino-1-(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl-2-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



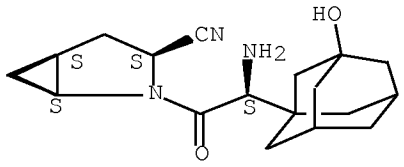
IT 361442-04-8DP, Saxagliptin, complex with dipeptidyl peptidase IV
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation)
(involvement of dipeptidyl peptidase-IV catalytic residues in enzyme-saxagliptin complex formation)
RN 361442-04-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



IT 361442-04-8, Saxagliptin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(involvement of dipeptidyl peptidase-IV catalytic residues in enzyme-saxagliptin complex formation)
RN 361442-04-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



OS.CITING REF COUNT: 19 THERE ARE 19 CAPLUS RECORDS THAT CITE THIS RECORD (19 CITINGS)
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L57 ANSWER 3 OF 16 HCAPLUS COPYRIGHT 2012 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2007:789960 HCAPLUS Full-text

DOCUMENT NUMBER: 147:189414
TITLE: Preparation of human glucagon-like peptide-1 receptor modulators and their use in the treatment of diabetes and related conditions
INVENTOR(S): Haque, Tasir Shamsul; Ewing, William R.; Mapelli, Claudio; Lee, Ving G.; Sulsky, Richard B.; Riexinger, Douglas James; Martinez, Rogelio L.; Zhu, Yeheng; Ruan, Zheming
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 193pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2007082264	A2	20070719	WO 2007-US60383		20070111
WO 2007082264	A3	20071221			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW					
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA					
US 20070238669	A1	20071011	US 2007-622142		20070111
EP 1976873	A2	20081008	EP 2007-717953		20070111
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, HR					
JP 2009523177	T	20090618	JP 2008-550516		20070111
NO 2008002958	A	20080826	NO 2008-2958		20080703
IN 2008DN06096	A	20080926	IN 2008-DN6096		20080711
CN 101400699	A	20090401	CN 2007-80008789		20080911
PRIORITY APPLN. INFO.:			US 2006-758096P	P	20060111
			US 2006-758107P	P	20060111
			US 2006-758164P	P	20060111
			US 2006-758165P	P	20060111
			WO 2007-US60383	W	20070111

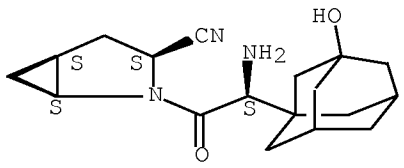
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 147:189414; MARPAT 147:189414
ED Entered STN: 20 Jul 2007
AB The invention provides novel human glucagon-like peptide-1 (GLP-1) receptor modulators Xaa1-Xaa2-Xaa3-Xaa4-Xaa5-Xaa6-Xaa7-Xaa8-Xaa9-Xaa10- Xaa11 [Xaa1-Xaa3, Xaa5-Xaa11 are (certain) naturally or non-naturally occurring amino acid residues; Xaa4 is glycine] that have biol. activity similar or superior to native GLP-1 peptide and thus are useful for the treatment or prevention of diseases or disorders associated with GLP activity. The

compds. include chemical-modified peptides that not only stimulate insulin secretion in type II diabetics, but also produce other beneficial insulinotropic responses. These synthetic peptide GLP-1 receptor modulators exhibit increased stability to proteolytic cleavage making them ideal therapeutic candidates for oral or parenteral administration. The disclosed and claimed peptides show desirable pharmacokinetic properties and desirable potency in efficacy models of diabetes. Thus, MeOCOHis-(S)-α-MePro-EGT-L-α-MePhe(2-fluoro)-TSD-Bip(2'-ethyl-4'-methoxy)-(S)-2-amino-4-(3-phenylphenoxy)butanamide (E, G, T, T, S and D are one-letter amino acid symbols, Bip = biphenylalanine residue) was prepared by the solid-phase method and shown to lower the plasma glucose in an IP glucose tolerance test after s.c. administration in ob/ob mice. NOTE:for 8016 keep the first index entry; for 7050, keep both entries; for 7054, keep first entry.

IT 361442-04-8, Saxagliptin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of human GLP-1 receptor modulators and their use in treatment of diabetes and related conditions)

RN 361442-04-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)

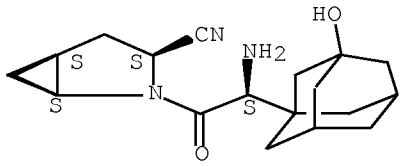
L57 ANSWER 4 OF 16 HCAPLUS COPYRIGHT 2012 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 2007:1279241 HCAPLUS Full-text
DOCUMENT NUMBER: 148:121939
TITLE: Potent non-nitrile dipeptidic dipeptidyl peptidase IV inhibitors
AUTHOR(S): Simpkins, Ligaya M.; Bolton, Scott; Pi, Zulan; Sutton, James C.; Kwon, Chet; Zhao, Guohua; Magnin, David R.; Augeri, David J.; Gungor, Timur; Rotella, David P.; Sun, Zhong; Liu, Yajun; Slusarchyk, William S.; Marcinkeviciene, Jovita; Robertson, James G.; Wang, Aiying; Robl, Jaffrey A.; Atwal, Karnail S.; Zahler, Robert L.; Parker, Rex A.; Kirby, Mark S.; Hamann, Lawrence G.
CORPORATE SOURCE: Bristol-Myers Squibb Research and Development, Princeton, NJ, 08543-5400, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2007), 17(23), 6476-6480
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 148:121939
ED Entered STN: 09 Nov 2007

AB The synthesis and structure-activity relationships of novel dipeptidyl peptidase IV (DDP-IV) inhibitors replacing the classical cyanopyrrolidine P1 group with other small nitrogen heterocycles are described. A unique potency enhancement was achieved with β-branched natural and unnatural amino acids, particularly adamantylglycines, linked to a (2S,3R)-2,3-methanopyrrolidine based scaffold.

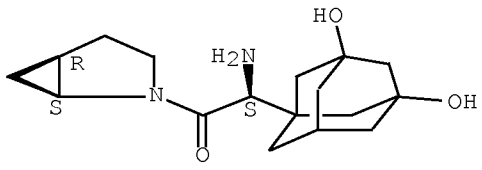
IT 361442-04-8, Saxagliptin
RL: PAC (Pharmacological activity); BIOL (Biological study)
(preparation and DDP-IV-inhibiting activity of non-nitrile dipeptides as potential antidiabetes agents)
RN 361442-04-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



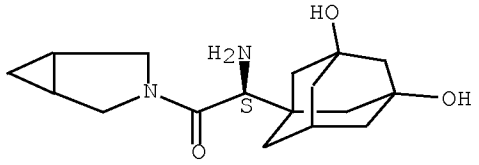
IT 841302-21-4P 841302-27-0P 841302-28-1P
841302-51-0P 1000689-35-9P 1000689-36-0P
1000689-37-1P 1000689-38-2P 1000689-39-3P
1000689-40-6P 1000689-41-7P 1000689-43-9P
1000689-44-0P 1000689-45-1P 1000689-46-2P
1000689-47-3P 1000689-48-4P 1000689-49-5P
1000689-50-8P 1000689-52-0P 1000689-53-1P
1000689-54-2P 1000689-55-3P 1000689-56-4P
1000689-57-5P 1000689-59-7P 1000689-60-0P
1000689-61-1P 1000689-66-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and DDP-IV-inhibiting activity of non-nitrile dipeptides as potential antidiabetes agents)
RN 841302-21-4 HCAPLUS
CN Ethanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-2-(3,5-dihydroxytricyclo[3.3.1.13,7]dec-1-yl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



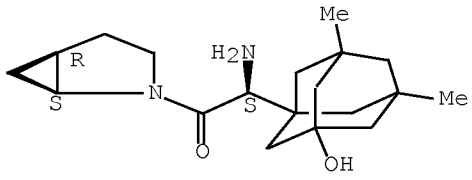
RN 841302-27-0 HCAPLUS
CN Ethanone, 2-amino-1-(3-azabicyclo[3.1.0]hex-3-yl)-2-(3,5-dihydroxytricyclo[3.3.1.13,7]dec-1-yl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



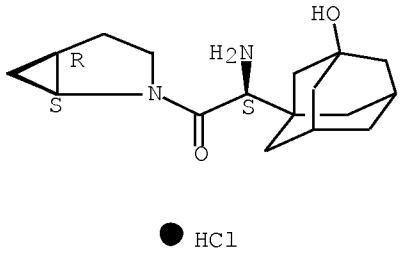
RN 841302-28-1 HCAPLUS
CN Ethanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-2-(3-hydroxy-5,7-dimethyltricyclo[3.3.1.13,7]dec-1-yl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



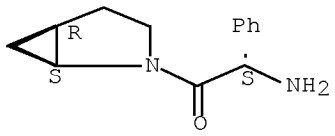
RN 841302-51-0 HCAPLUS
CN Ethanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-2-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)-, hydrochloride (1:1), (2S)- (CA INDEX NAME)

Absolute stereochemistry.



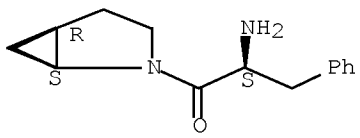
RN 1000689-35-9 HCAPLUS
CN Ethanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-2-phenyl-, (2S)-
(CA INDEX NAME)

Absolute stereochemistry.



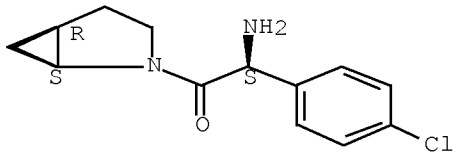
RN 1000689-36-0 HCAPLUS
CN 1-Propanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-3-phenyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



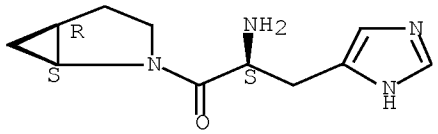
RN 1000689-37-1 HCAPLUS
CN Ethanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-2-(4-chlorophenyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



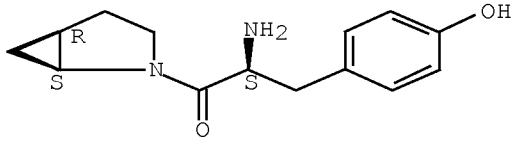
RN 1000689-38-2 HCAPLUS
CN 1-Propanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-3-(1H-imidazol-5-yl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



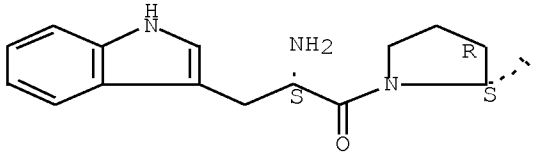
RN 1000689-39-3 HCAPLUS
CN 1-Propanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-3-(4-hydroxyphenyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



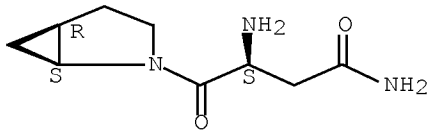
RN 1000689-40-6 HCAPLUS
CN 1-Propanone,
2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-3-(1H-indol-3-yl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



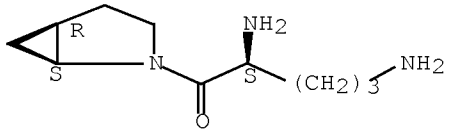
RN 1000689-41-7 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-2-butanamide, β-amino-γ-oxo-, (βS,1S,5R)- (CA INDEX NAME)

Absolute stereochemistry.



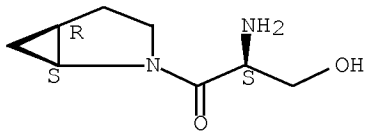
RN 1000689-43-9 HCAPLUS
CN 1-Pentanone, 2,5-diamino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



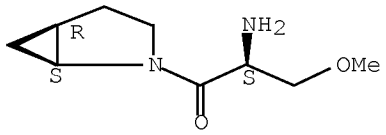
RN 1000689-44-0 HCAPLUS
CN 1-Propanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-3-hydroxy-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



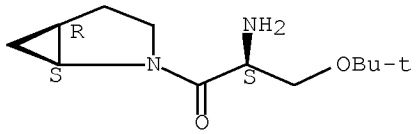
RN 1000689-45-1 HCAPLUS
CN 1-Propanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-3-methoxy-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



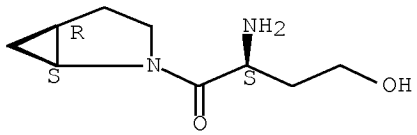
RN 1000689-46-2 HCAPLUS
CN 1-Propanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-3-(1,1-dimethylethoxy)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



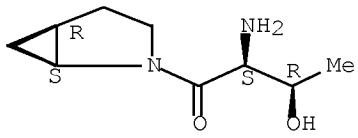
RN 1000689-47-3 HCAPLUS
CN 1-Butanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-4-hydroxy-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



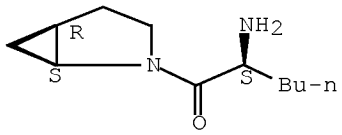
RN 1000689-48-4 HCAPLUS
CN 1-Butanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-3-hydroxy-, (2S,3R)- (CA INDEX NAME)

Absolute stereochemistry.



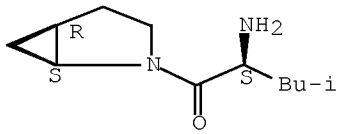
RN 1000689-49-5 HCAPLUS
CN 1-Hexanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



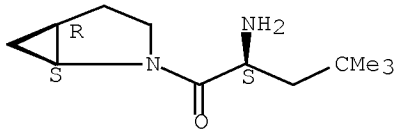
RN 1000689-50-8 HCAPLUS
CN 1-Pentanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



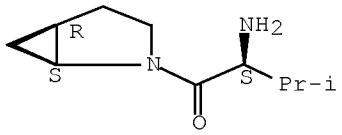
RN 1000689-52-0 HCAPLUS
CN 1-Pentanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-4,4-dimethyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



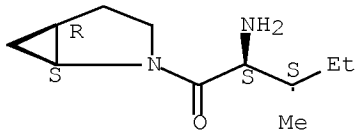
RN 1000689-53-1 HCAPLUS
CN 1-Butanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-3-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



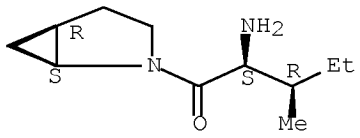
RN 1000689-54-2 HCAPLUS
CN 1-Pentanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-3-methyl-, (2S,3S)- (CA INDEX NAME)

Absolute stereochemistry.



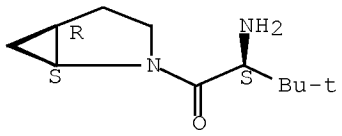
RN 1000689-55-3 HCAPLUS
CN 1-Pentanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-3-methyl-, (2S,3R)- (CA INDEX NAME)

Absolute stereochemistry.



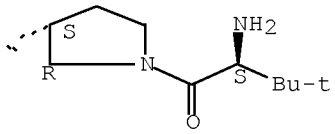
RN 1000689-56-4 HCAPLUS
CN 1-Butanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-3,3-dimethyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



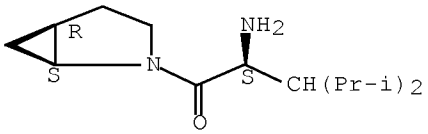
RN 1000689-57-5 HCAPLUS
CN 1-Butanone,
2-amino-1-[(1R,5S)-2-azabicyclo[3.1.0]hex-2-yl]-3,3-dimethyl-,
(2S)- (CA INDEX NAME)

Absolute stereochemistry.



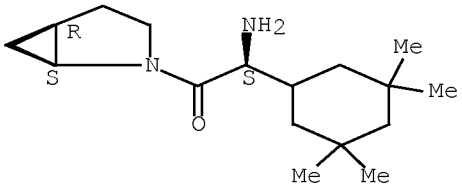
RN 1000689-59-7 HCAPLUS
CN 1-Pentanone,
2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-4-methyl-3-(1-
methylethyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 1000689-60-0 HCAPLUS
CN Ethanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-2-(3,3,5,5-
tetramethylcyclohexyl)-, (2S)- (CA INDEX NAME)

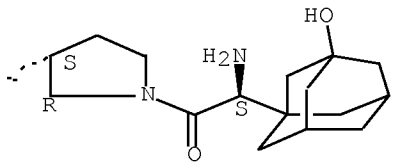
Absolute stereochemistry.



RN 1000689-61-1 HCAPLUS
CN Ethanone, 2-amino-1-[(1R,5S)-2-azabicyclo[3.1.0]hex-2-yl]-2-(3-

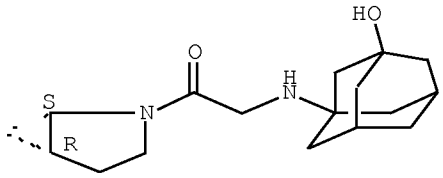
hydroxytricyclo[3.3.1.13,7]dec-1-yl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 1000689-66-6 HCAPLUS
CN Ethanone, 1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-2-[(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)amino]- (CA INDEX NAME)

Absolute stereochemistry.



OS.CITING REF COUNT: 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L57 ANSWER 5 OF 16 HCAPLUS COPYRIGHT 2012 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 2005:1351306 HCAPLUS Full-text
DOCUMENT NUMBER: 144:186959
TITLE: Mechanism of Gly-Pro-pNA cleavage catalyzed by dipeptidyl peptidase-IV and its inhibition by saxagliptin (BMS-477118)
AUTHOR(S): Kim, Young B.; Kopcho, Lisa M.; Kirby, Mark S.; Hamann, Lawrence G.; Weigelt, Carolyn A.; Metzler, William J.; Marcinkeviciene, Jovita
CORPORATE SOURCE: Department of Chemical Enzymology, Pharmaceutical Research Institute, Bristol Myers-Squibb Pharmaceutical Company, Princeton, NJ, 08543-5400, USA
SOURCE: Archives of Biochemistry and Biophysics (2006), 445(1), 9-18
CODEN: ABBIA4; ISSN: 0003-9861
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

ED Entered STN: 30 Dec 2005

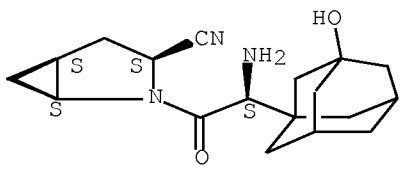
AB Dipeptidyl peptidase-IV (DPP-IV) is a serine protease with a signature Asp-His-Ser motif at the active site. Our pH data suggest that Gly-Pro-pNA cleavage catalyzed by DPP-IV is facilitated by an ionization of a residue with a pK of 7.2±0.1. By analogy to other serine proteases this pK is suggestive of His-Asp assisted Ser addition to the P1 carbonyl carbon of the substrate to form a tetrahedral intermediate. Solvent kinetic isotope effect studies yielded a D20kcat/Km = 2.9±0.2 and a D20kcat = 1.7±0.2 suggesting that kinetically significant proton transfers contribute to rate limitation during acyl intermediate formation (leaving group release) and hydrolysis. A "burst" of product release during pre steady-state Gly-Pro-pNA cleavage indicated rate limitation in the deacylation half-reaction. Nevertheless, the amplitude of the burst exceeded the enzyme concentration significantly (.apprx.15-fold), which is consistent with a branching deacylation step. All of these data allowed us to better understand DPP-IV inhibition by saxagliptin (BMS-477118). We propose a two-step inhibition mechanism wherein an initial encounter complex is followed by covalent intermediate formation. Final inhibitory complex assembly (kon) depends upon the ionization of an enzyme residue with a pK of 6.2±0.1, and we assigned it to the catalytic His-Asp pair which enhances Ser nucleophilicity for covalent addition An ionization with a pK of 7.9±0.2 likely reflects the P2 terminal amine of the inhibitor hydrogen bonding to Glu205/Glu206 in the enzyme active site. The formation of the covalent enzyme-inhibitor complex was reversible and dissociated with a koff of (5.5±0.4) × 10-5 s-1, thus yielding a K*i (as koff/kon) of 0.35 nM, which is in good agreement with the value of 0.6 nM obtained from steady-state inhibition studies. Proton NMR spectra of DPP-IV showed a downfield resonance at 16.1 ppm. Two addnl. peaks in the 1H NMR spectra at 17.4 and 14.1 ppm were observed upon mixing the enzyme with saxagliptin. Fractionation factors (.vphi.) of 0.6 and 0.5 for the 17.4 and 14.1 ppm peaks, resp., are suggestive of short strong hydrogen bonds in the enzyme-inhibitor complex.

IT 361442-04-8, Saxagliptin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Glu205/Glu206 residue of dipeptidyl peptidase-IV plays important role in saxagliptin binding through short strong hydrogen bonds)

RN 361442-04-8 HCAPLUS

CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



OS.CITING REF COUNT: 30 THERE ARE 30 CAPLUS RECORDS THAT CITE THIS

RECORD (31 CITINGS)
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L57 ANSWER 6 OF 16 HCAPLUS COPYRIGHT 2012 ACS on STN DUPLICATE 6
ACCESSION NUMBER: 2005:493507 HCAPLUS Full-text
DOCUMENT NUMBER: 143:43869
TITLE: Preparation of nitrogen containing bicyclic pyridine-based derivatives as inhibitors of HMG CoA reductase
INVENTOR(S): O'Connor, Stephen P.; Robl, Jeffrey; Ahmad, Saleem; Bisaha, Sharon; Murugesan, Natesan; Ngu, Khehyong; Shi, Yan; Stein, Philip D.; Soundararajan, Nachimuthu; Natalie, Kenneth J., Jr.; Kolla, Laxma R.; Sausker, Justin; Quinlan, Sandra L.; Fan, Junying; Petsch, Dejah; Guo, Zhenrong
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 193 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005051386	A1	20050609	WO 2004-US39051	20041119
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 20050171140	A1	20050804	US 2004-989138	20041115
US 7420059	B2	20080902		
EP 1684754	A1	20060802	EP 2004-811719	20041119
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR, IS, YU				

PRIORITY APPLN. INFO.:		
US 2003-523546P	P	20031120
US 2004-989138	A	20041115
WO 2004-US39051	W	20041119

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 143:43869
ED Entered STN: 10 Jun 2005
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

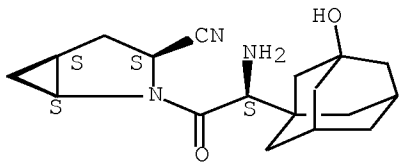
AB Title compds. I [Het = 5- to 8-membered ring including at least one nitrogen atom with provisions; n = 0-1; R1 and R2 independently = H, alkyl, alkenyl, etc.; R3 = H, aryl, cycloalkyl, etc.; R4 and R5 independently = H, alkyl; X = -CR6R7-CR6aR7a-, -CR6=CR7-; R6, R7, R6a and R7a independently = H, alkyl] and their pharmaceutically acceptable salts, are prepared and disclosed as inhibitors of HMG CoA reductase. Thus, e.g., II was prepared by cyclization of Et 2-amino-4-(4-fluorophenyl)-6-isopropyl-5-methoxycarbonyl-3-pyridinepropanoate (preparation given) followed by a reduction/sulfonylation/reduction sequence to give [4-(4-fluorophenyl)-2-isopropyl-8-methanesulfonyl-5,6,7,8-tetrahydro[1,8]naphthyridin-3-yl]-methanol (III). III was oxidized to the resp. aldehyde and coupled with 1,1-dimethylethyl(4R,6S)-2,2-dimethyl-6-(1-phenyl-1H-tetrazole-5-sulfonylmethyl)-[1,3]dioxan-4-yl-acetate followed by ring opening to give II. I should display activity as inhibitors of HMG CoA reductase (no data given). I as inhibitors of HMG CoA reductase inhibitors should prove useful in the treatment of, but not limited to, hyperlipidemia, dyslipidemia, and atherosclerosis. Pharmaceutical compns. comprising I are disclosed.

IT 361442-04-8, BMS 477118
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(claimed co-drug; preparation of nitrogen-containing bicyclic pyridine-based
derivs. as inhibitors of HMG CoA reductase)

RN 361442-04-8 HCAPLUS

CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L57 ANSWER 7 OF 16 HCAPLUS COPYRIGHT 2012 ACS on STN DUPLICATE 7

ACCESSION NUMBER: 2005:543673 HCAPLUS Full-text

DOCUMENT NUMBER: 143:221803

TITLE: Discovery and Preclinical Profile of Saxagliptin (BMS-477118): A Highly Potent, Long-Acting, Orally

Active Dipeptidyl Peptidase IV Inhibitor for the Treatment of Type 2 Diabetes

AUTHOR(S): Augeri, David J.; Robl, Jeffrey A.; Betebenner, David A.; Magnin, David R.; Khanna, Ashish; Robertson, James G.; Wang, Aiying; Simpkins, Ligaya M.; Taunk, Prakash; Huang, Qi; Han, Song-Ping; Abboa-Offei, Benoni; Cap, Michael; Xin, Li; Tao, Li; Tozzo, Effie; Welzel, Gustav E.; Egan, Donald M.; Marcinkeviciene, Jovita; Chang, Shu Y.; Biller, Scott A.; Kirby, Mark S.; Parker, Rex A.; Hamann, Lawrence G.

CORPORATE SOURCE: Department of Discovery Chemistry, Bristol-Myers Squibb, Princeton, NJ, 08543-5400, USA

SOURCE: Journal of Medicinal Chemistry (2005), 48(15), 5025-5037
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 143:221803

ED Entered STN: 24 Jun 2005

AB Efforts to further elucidate structure-activity relationships (SAR) within the authors previously disclosed series of β-quaternary amino acid linked L-cis-4,5-methanoprolinenitrile dipeptidyl peptidase IV (DPP-IV) inhibitors led to the investigation of vinyl substitution at the β-position of α-cycloalkyl-substituted glycines. Despite poor systemic exposure, vinyl-substituted compds. showed extended duration of action in acute rat ex vivo plasma DPP-IV inhibition models. Oxygenated putative metabolites were prepared and were shown to exhibit the potency and extended duration of action of their precursors in efficacy models measuring glucose clearance in Zuckerfa/fa rats. Extension of this approach to adamantylglycine-derived inhibitors led to the discovery of highly potent inhibitors, including hydroxyadamantyl compound BMS-477118 (saxagliptin), a highly efficacious, stable, and long-acting DPP-IV inhibitor, which is currently undergoing clin. trials for treatment of type 2 diabetes.

IT 361441-54-5P 361441-75-0P 361441-99-8P
361442-05-9P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(discovery and preclin. profile of saxagliptin (BMS-477118) as highly potent and long-acting and orally active dipeptidyl peptidase IV inhibitor for treatment of type 2 diabetes)

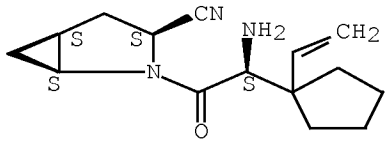
RN 361441-54-5 HCAPLUS

CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(1-ethenylcyclopentyl)acetyl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

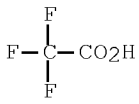
CRN 361441-53-4
CMF C15 H21 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

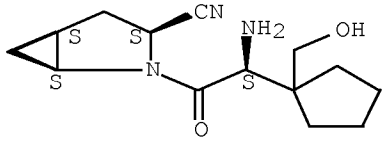


RN 361441-75-0 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-[1-(hydroxymethyl)cyclopentyl]acetyl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

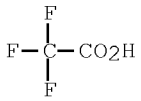
CRN 361441-74-9
CMF C14 H21 N3 O2

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

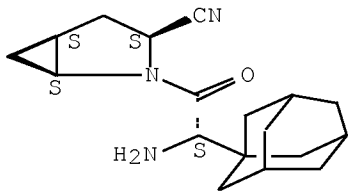


RN 361441-99-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-tricyclo[3.3.1.13,7]dec-1-ylacetyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

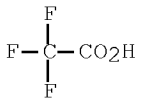
CRN 361441-98-7
CMF C18 H25 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

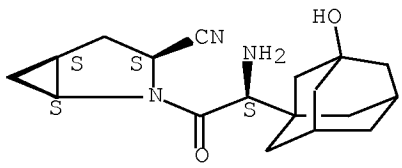


RN 361442-05-9 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-,
(1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

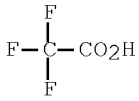
CRN 361442-04-8
CMF C18 H25 N3 O2

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

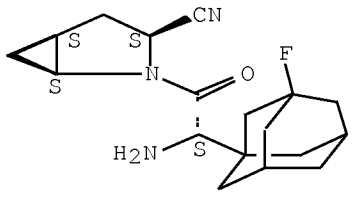


IT 361442-09-3P 361442-44-6P 841302-57-6P
862590-85-0P 862590-86-1P 862590-87-2P
862590-88-3P 862590-89-4P 862590-90-7P
862590-91-8P 862590-93-0P 862590-94-1P
862590-95-2P 862590-96-3P 862590-97-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(discovery and preclin. profile of saxagliptin (BMS-477118) as highly potent and long-acting and orally active dipeptidyl peptidase IV inhibitor for treatment of type 2 diabetes)
RN 361442-09-3 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(3-fluorotricyclo[3.3.1.13,7]dec-1-yl)acetyl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

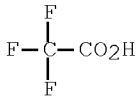
CRN 361442-08-2
CMF C18 H24 F N3 O

Absolute stereochemistry.



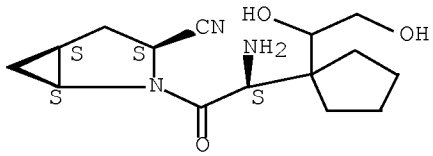
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 361442-44-6 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-[1-(1,2-dihydroxyethyl)cyclopentyl]acetyl]-,
(1S,3S,5S)-
(CA INDEX NAME)

Absolute stereochemistry.

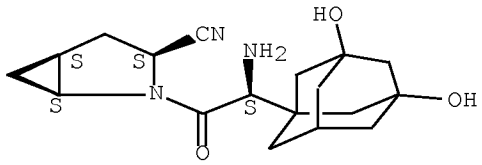


RN 841302-57-6 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(3,5-dihydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-,
(1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

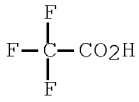
CRN 841302-24-7
CMF C18 H25 N3 O3

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

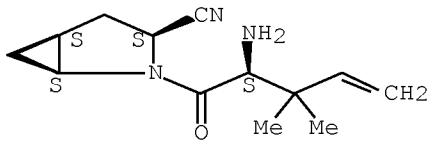


RN 862590-85-0 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-3,3-dimethyl-1-oxo-4-penten-1-yl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

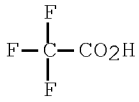
CRN 361441-62-5
CMF C13 H19 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

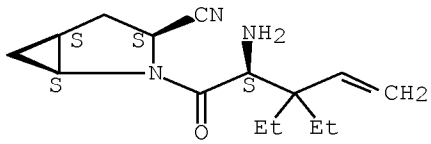


RN 862590-86-1 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-3,3-diethyl-4-methylene-1-oxobutyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

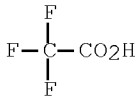
CRN 361441-63-6
CMF C15 H23 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

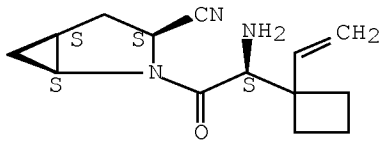


RN 862590-87-2 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(1-ethenylcyclobutyl)acetyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

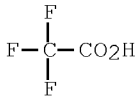
CRN 361441-55-6
CMF C14 H19 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

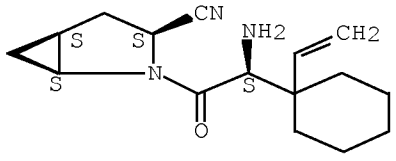


RN 862590-88-3 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(1-ethenylcyclohexyl)acetyl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

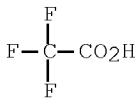
CRN 361441-56-7
CMF C16 H23 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

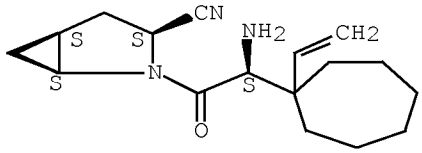


RN 862590-89-4 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(1-ethenylcycloheptyl)acetyl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

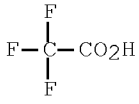
CRN 361441-57-8
CMF C17 H25 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

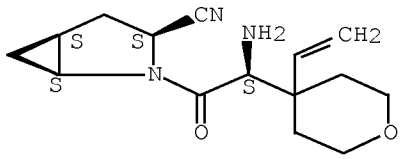


RN 862590-90-7 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(4-ethenyltetrahydro-2H-pyran-4-yl)acetyl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

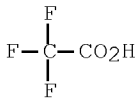
CRN 361441-60-3
CMF C15 H21 N3 O2

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

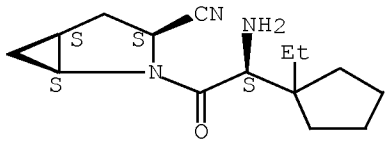


RN 862590-91-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(1-ethylcyclopentyl)acetyl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

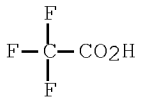
CRN 361441-85-2
CMF C15 H23 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

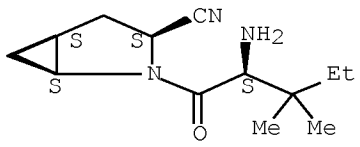


RN 862590-93-0 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-3,3-dimethyl-1-oxopentyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

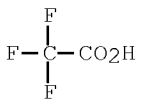
CRN 361441-90-9
CMF C13 H21 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



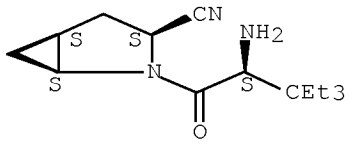
RN 862590-94-1 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-3,3-diethyl-1-oxopentyl]-, (1S,3S,5S)-,

2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

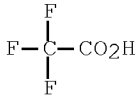
CRN 361441-91-0
CMF C15 H25 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

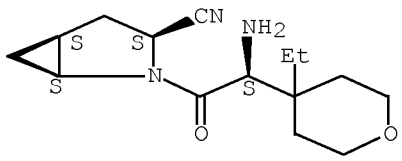


RN 862590-95-2 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(4-ethyltetrahydro-2H-pyran-4-yl)acetyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

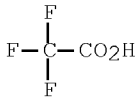
CRN 361441-89-6
CMF C15 H23 N3 O2

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

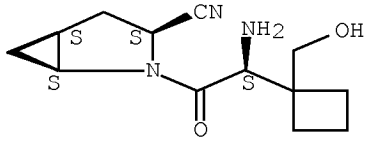


RN 862590-96-3 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-[1-(hydroxymethyl)cyclobutyl]acetyl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

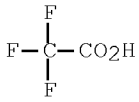
CRN 361441-77-2
CMF C13 H19 N3 O2

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



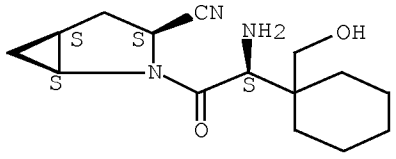
RN 862590-97-4 HCAPLUS

CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-[1-(hydroxymethyl)cyclohexyl]acetyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361441-78-3
CMF C15 H23 N3 O2

Absolute stereochemistry.



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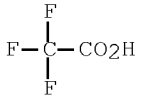
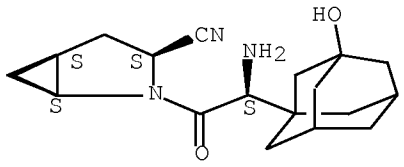
CRN 76-05-1
CMF C2 H F3 O2



IT 361442-04-8, Saxagliptin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(discovery and preclin. profile of saxagliptin (BMS-477118) as highly potent and long-acting and orally active dipeptidyl peptidase IV inhibitor for treatment of type 2 diabetes)
RN 361442-04-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-,
(1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



OS.CITING REF COUNT: 205 THERE ARE 205 CAPLUS RECORDS THAT CITE THIS RECORD (206 CITINGS)
REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L57 ANSWER 8 OF 16 HCAPLUS COPYRIGHT 2012 ACS on STN DUPLICATE 8
ACCESSION NUMBER: 2001:693281 HCAPLUS Full-text
DOCUMENT NUMBER: 135:257147
TITLE: Preparation of fused cyclopropylpyrrolidine-based inhibitors of dipeptidyl peptidase IV
INVENTOR(S): Robl, Jeffrey A.; Sulsky, Richard B.; Augeri, David J.; Magnin, David R.; Hamann, Lawrence G.; Betebenner, David A.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Co., USA
SOURCE: PCT Int. Appl., 135 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001068603	A2	20010920	WO 2001-US7151	20010305
WO 2001068603	A3	20020214		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 20020019411	A1	20020214	US 2001-788173	20010216
US 6395767	B2	20020528		
CA 2402894	A1	20010920	CA 2001-2402894	20010305
CA 2402894	C	20120417		
AU 2001045466	A	20010924	AU 2001-45466	20010305
EP 1261586	A2	20021204	EP 2001-918383	20010305
EP 1261586	B1	20080521		
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JP 4460205	B2	20100512		

HU 2003002792	A2	20031229	HU 2003-2792	20010305
HU 2003002792	A3	20070328		
BR 2001009115	A	20031230	BR 2001-9115	20010305
NZ 520821	A	20041126	NZ 2001-520821	20010305
AU 2001245466	B2	20050512	AU 2001-245466	20010305
CN 1213028	C	20050803	CN 2001-806315	20010305
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TW 258468	B	20060721	TW 2001-104965	20010305
RU 2286986	C2	20061110	RU 2002-125491	20010305
AT 396176	T	20080615	AT 2001-918383	20010305
PT 1261586	E	20080804	PT 2001-918383	20010305
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SG 152030	A1	20090529	SG 2004-5783	20010305
IL 151372	A	20091224	IL 2001-151372	20010305
IL 177018	A	20100328	IL 2001-177018	20010305
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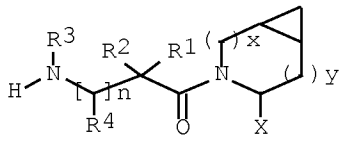
MX 2002008837	A	20030425	MX 2002-8837	20020910
HK 1049330	A1	20081114	HK 2003-101079	20030214
KR 758407	B1	20070914	KR 2006-7004515	20060303
IN 2007MN00184	A	20080215	IN 2007-MN184	20070205
JP 2010077163	A	20100408	JP 2010-6181	20100114

PRIORITY APPLN. INFO.:

US 2000-188555P	P	20000310
CN 2001-806315	A3	20010305
EP 2001-918383	A3	20010305
EP 2005-5368	A3	20010305
IL 2001-151372	A3	20010305
JP 2001-567699	A3	20010305
WO 2001-US7151	W	20010305
IN 2002-MN1154	A3	20020823
KR 2002-7011806	A3	20020909

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 135:257147
ED Entered STN: 21 Sep 2001
GI



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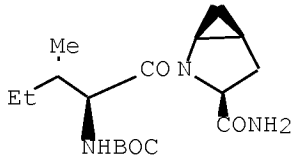

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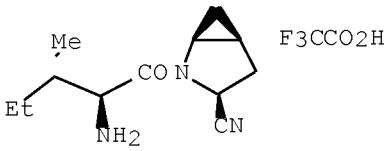


III

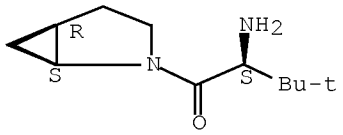
AB Dipeptidyl peptidase IV inhibiting compds. I (x = 0 or 1 and y = 0 or 1 provided that x = 1 when y = 0 and x = 0 when y = 1; n = 0, 1; X = H, CN; R1, R2, R3 and R4 = same or different and independently selected from H, (un)substituted chain or cyclic components) and the pharmaceutically acceptable salts or prodrugs (no data) were prepared Thus L-pyroglutamic acid Et ester was protected, cyclopropanated and reacted further with (S)-N-BOC-isoleucine providing an intermediate II which reacted further to yield the fused cyclopropylpyrrolidine III in 57% yield. A method is also provided for treating diabetes and related diseases, especially Type II diabetes, and other diseases by employing a title DP 4 inhibitor or a combination of DP 4 inhibitor and one or more of another antidiabetic agent such as metformin, glyburide, troglitazone, pioglitazone, rosiglitazone and/or insulin and/or one or more of a hypolipidemic agent and/or anti-obesity agent and/or other therapeutic agent.

IT 1000689-56-4 1098535-01-3 1098535-02-4
1098535-03-5 1098535-04-6 1098535-05-7
1098535-06-8 1098535-07-9 1098535-08-0
1098535-09-1 1098535-10-4 1098535-11-5
1098535-12-6 1098535-13-7 1098535-14-8
1098535-15-9 1098535-16-0 1098535-17-1
1098535-21-7 1098535-23-9
RL: PRPH (Prophetic)
(Preparation of fused cyclopropylpyrrolidine-based inhibitors of dipeptidyl peptidase IV)

RN 1000689-56-4 HCAPLUS

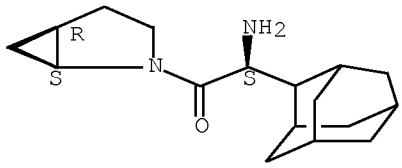
CN 1-Butanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-3,3-dimethyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



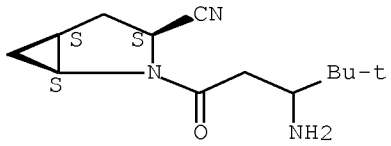
RN 1098535-01-3 HCAPLUS
CN Ethanone, 2-amino-1-(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl-2-tricyclo[3.3.1.13,7]dec-2-yl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



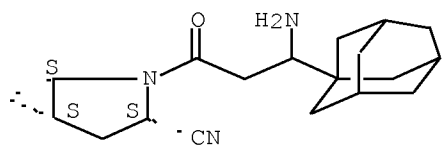
RN 1098535-02-4 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-(3-amino-4,4-dimethyl-1-oxopentyl)-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



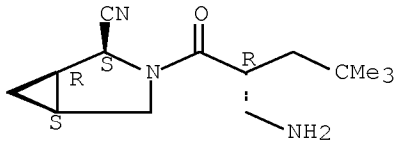
RN 1098535-03-5 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-(3-amino-1-oxo-3-tricyclo[3.3.1.13,7]dec-1-ylpropyl)-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



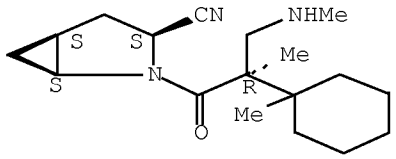
RN 1098535-04-6 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile,
3-[(2R)-2-(aminomethyl)-4,4-dimethyl-1-oxopentyl]-, (1R,2S,5S)- (CA INDEX
NAME)

Absolute stereochemistry.



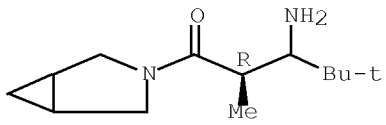
RN 1098535-05-7 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2R)-2-methyl-3-(methylamino)-2-(1-methylcyclohexyl)-1-oxopropyl]-,
(1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



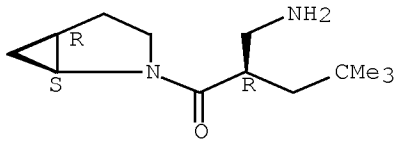
RN 1098535-06-8 HCAPLUS
CN 1-Pentanone, 3-amino-1-(3-azabicyclo[3.1.0]hex-3-yl)-2,4,4-trimethyl-,
(2R)- (CA INDEX NAME)

Absolute stereochemistry.



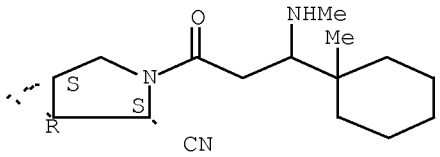
RN 1098535-07-9 HCAPLUS
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



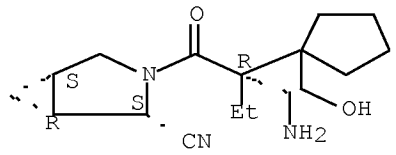
RN 1098535-08-0 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile, 3-[3-(methylamino)-3-(1-methylcyclohexyl)-1-oxopropyl]-, (1R,2S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



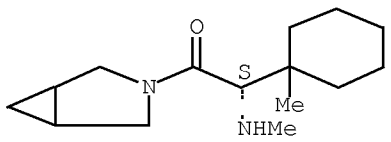
RN 1098535-09-1 HCAPLUS
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



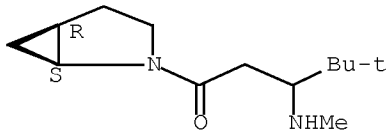
RN 1098535-10-4 HCAPLUS
CN Ethanone, 1-(3-azabicyclo[3.1.0]hex-3-yl)-2-(methylamino)-2-(1-methylcyclohexyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



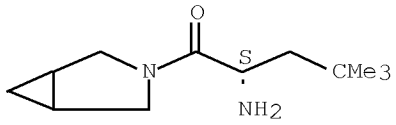
RN 1098535-11-5 HCAPLUS
CN 1-Pentanone, 1-(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl-4,4-dimethyl-3-(methylamino)- (CA INDEX NAME)

Absolute stereochemistry.



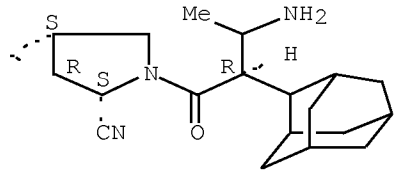
RN 1098535-12-6 HCAPLUS
CN 1-Pentanone, 2-amino-1-(3-azabicyclo[3.1.0]hex-3-yl)-4,4-dimethyl-, (2S)-(CA INDEX NAME)

Absolute stereochemistry.



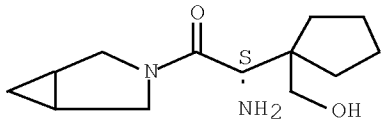
RN 1098535-13-7 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile, 3-[(2R)-3-amino-1-oxo-2-tricyclo[3.3.1.13,7]dec-2-ylbutyl]-, (1R,2S,5S)-(CA INDEX NAME)

Absolute stereochemistry.



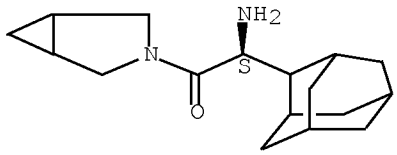
RN 1098535-14-8 HCAPLUS
CN Ethanone, 2-amino-1-(3-azabicyclo[3.1.0]hex-3-yl)-2-[1-(hydroxymethyl)cyclopentyl]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



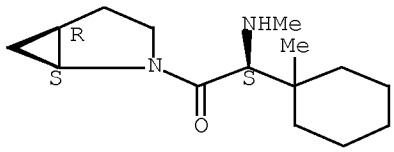
RN 1098535-15-9 HCAPLUS
CN Ethanone, 2-amino-1-(3-azabicyclo[3.1.0]hex-3-yl)-2-tricyclo[3.3.1.13,7]dec-2-yl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



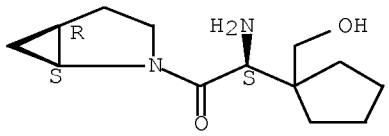
RN 1098535-16-0 HCAPLUS
CN Ethanone, 1-(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl-2-(methylamino)-2-(1-methylcyclohexyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



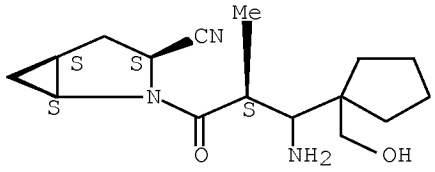
RN 1098535-17-1 HCAPLUS
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



RN 1098535-21-7 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-3-amino-3-[1-(hydroxymethyl)cyclopentyl]-2-methyl-1-oxopropyl]-,
(1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



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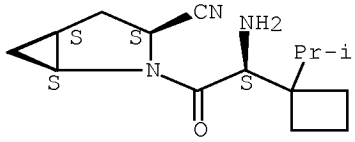
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-[1-(1-methylethyl)cyclobutyl]acetyl]-, (1S,3S,5S)- (CA
INDEX NAME)

Absolute stereochemistry.



IT 361440-65-5P 361440-66-6P 361440-73-5P
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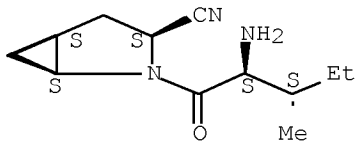
361442-52-6P 361442-53-7P 361442-54-8P
361442-55-9P 361442-56-0P 361442-58-2P
361485-95-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of fused cyclopropylpyrrolidine-based inhibitors of dipeptidyl
peptidase IV)

RN 361440-65-5 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.

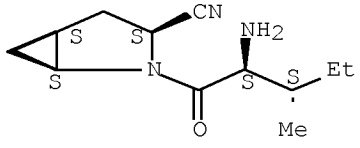


RN 361440-66-6 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

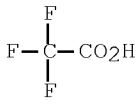
CRN 361440-65-5
CMF C12 H19 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

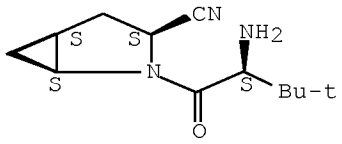


RN 361440-73-5 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-3,3-dimethyl-1-oxobutyl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

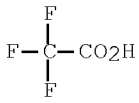
CRN 361440-72-4
CMF C12 H19 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



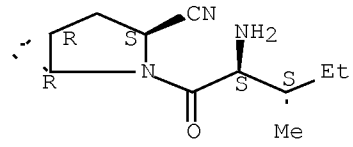
RN 361440-77-9 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,

2-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]-, (1R,3S,5R)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

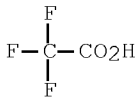
CRN 361440-76-8
CMF C12 H19 N3 O

Absolute stereochemistry.



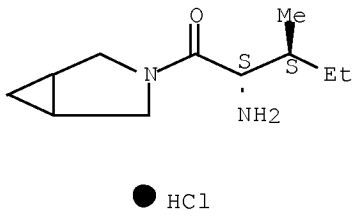
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 361440-79-1 HCAPLUS
CN 1-Pentanone, 2-amino-1-(3-azabicyclo[3.1.0]hex-3-yl)-3-methyl-,
hydrochloride (1:1), (2S,3S)- (CA INDEX NAME)

Absolute stereochemistry.



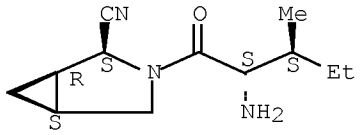
RN 361440-88-2 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile,

3-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]-, (1R,2S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

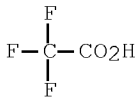
CRN 361440-87-1
CMF C12 H19 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

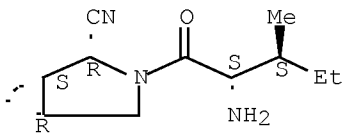


RN 361440-91-7 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile,
3-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]-, (1S,2R,5R)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

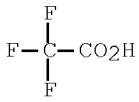
CRN 361440-90-6
CMF C12 H19 N3 O

Absolute stereochemistry.



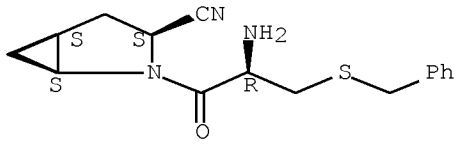
CM 2

CRN 76-05-1
CMF C2 H F3 O2



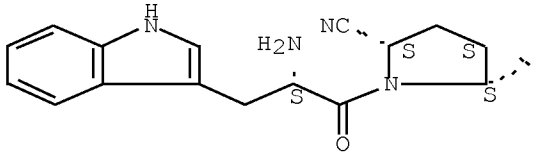
RN 361440-95-1 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2R)-2-amino-1-oxo-3-[(phenylmethyl)thio]propyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



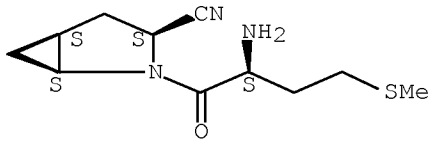
RN 361440-97-3 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-3-(1H-indol-3-yl)-1-oxopropyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



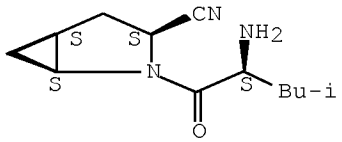
RN 361440-99-5 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-4-(methylthio)-1-oxobutyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



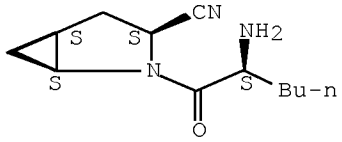
RN 361441-01-2 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-4-methyl-1-oxopentyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



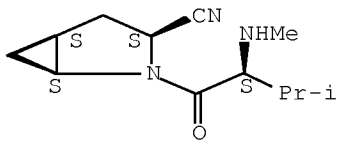
RN 361441-03-4 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-1-oxohexyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



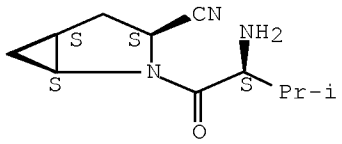
RN 361441-04-5 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-3-methyl-2-(methylamino)-1-oxobutyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



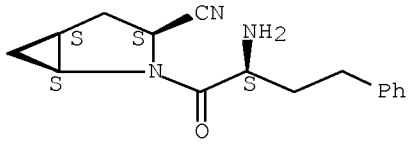
RN 361441-05-6 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-3-methyl-1-oxobutyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



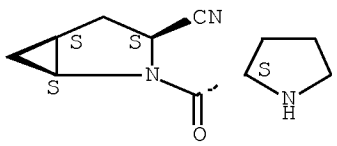
RN 361441-06-7 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-1-oxo-4-phenylbutyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



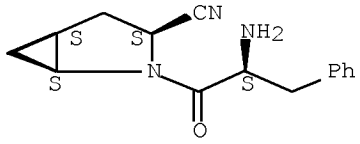
RN 361441-07-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-pyrrolidinylcarbonyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



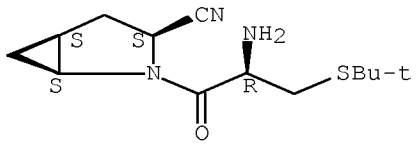
RN 361441-08-9 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-1-oxo-3-phenylpropyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



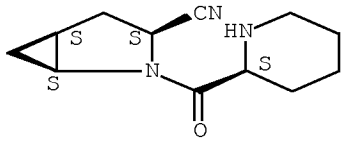
RN 361441-09-0 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2R)-2-amino-3-[(1,1-dimethylethyl)thio]-1-oxopropyl]-, (1S,3S,5S)-
(CA INDEX NAME)

Absolute stereochemistry.



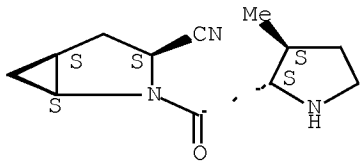
RN 361441-10-3 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-piperidinylcarbonyl]-,
(1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



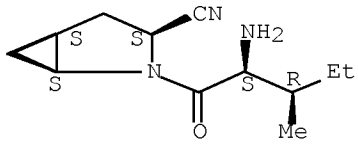
RN 361441-11-4 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[[(2S,3S)-3-methyl-2-pyrrolidinyl]carbonyl]-, (1S,3S,5S)- (CA INDEX
NAME)

Absolute stereochemistry.



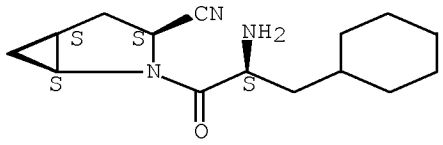
RN 361441-12-5 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S,3R)-2-amino-3-methyl-1-oxopentyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



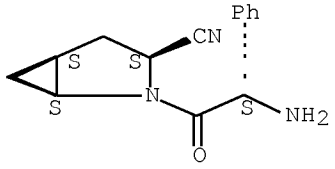
RN 361441-13-6 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-3-cyclohexyl-1-oxopropyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



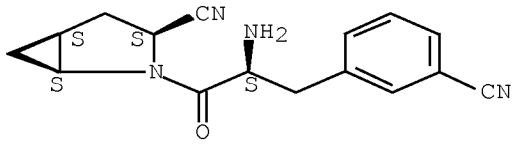
RN 361441-14-7 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-phenylacetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



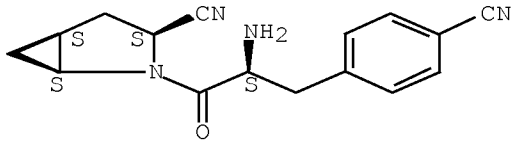
RN 361441-15-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-3-(3-cyanophenyl)-1-oxopropyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



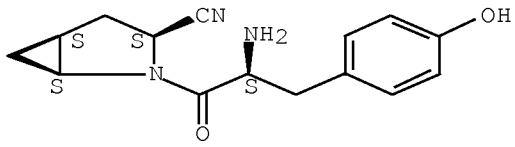
RN 361441-16-9 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-3-(4-cyanophenyl)-1-oxopropyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



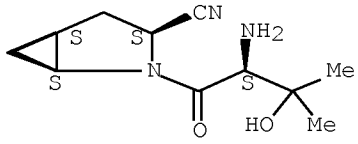
RN 361441-17-0 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-3-(4-hydroxyphenyl)-1-oxopropyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



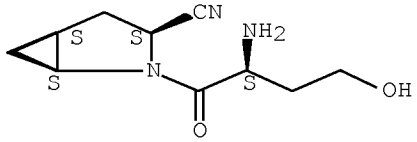
RN 361441-28-3 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-3-hydroxy-3-methyl-1-oxobutyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



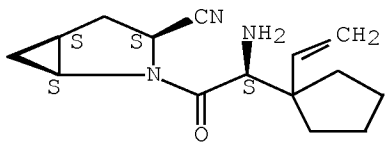
RN 361441-39-6 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-4-hydroxy-1-oxobutyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 361441-53-4 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(1-ethenylcyclopentyl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.

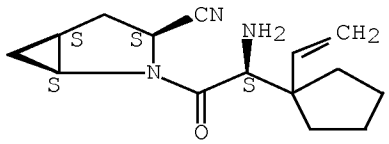


RN 361441-54-5 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(1-ethenylcyclopentyl)acetyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

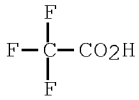
CRN 361441-53-4
CMF C15 H21 N3 O

Absolute stereochemistry.



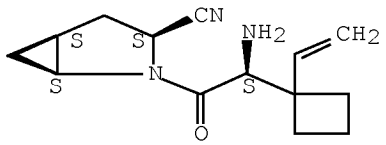
CM 2

CRN 76-05-1
CMF C2 H F3 O2



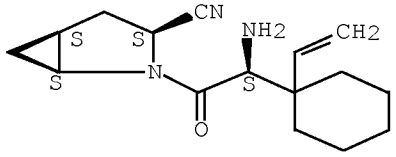
RN 361441-55-6 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(1-ethenylcyclobutyl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



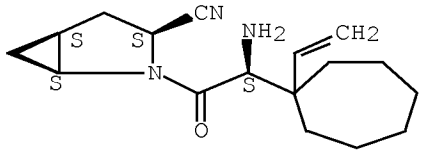
RN 361441-56-7 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(1-ethenylcyclohexyl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



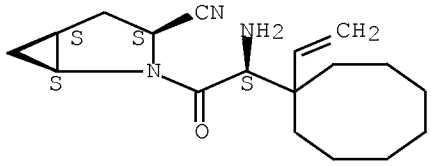
RN 361441-57-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(1-ethenylcycloheptyl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 361441-58-9 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(1-ethenylcyclooctyl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

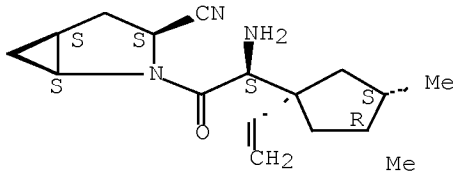
Absolute stereochemistry.



RN 361441-59-0 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,

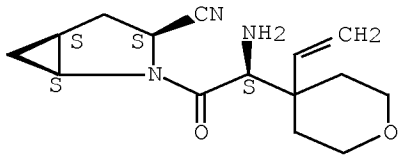
2-[(2S)-2-amino-2-[(3R,4S)-1-ethenyl-3,4-dimethylcyclopentyl]acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



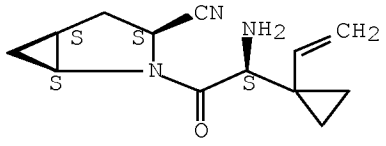
RN 361441-60-3 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(4-ethenyltetrahydro-2H-pyran-4-yl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



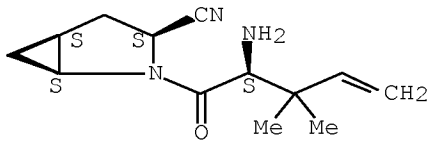
RN 361441-61-4 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(1-ethenylcyclopropyl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



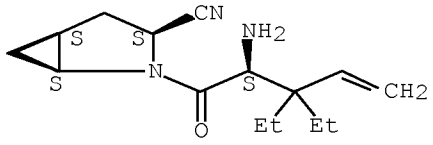
RN 361441-62-5 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-3,3-dimethyl-1-oxo-4-penten-1-yl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



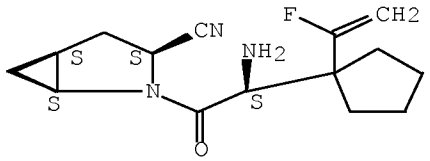
RN 361441-63-6 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-3,3-diethyl-1-oxo-4-pentenyl]-, (1S,3S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



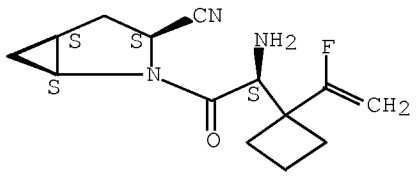
RN 361441-65-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-[1-(1-fluoroethenyl)cyclopentyl]acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



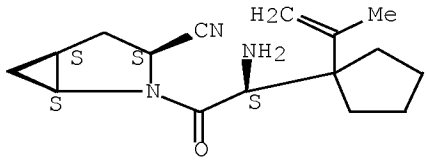
RN 361441-67-0 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-[1-(1-fluoroethenyl)cyclobutyl]acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



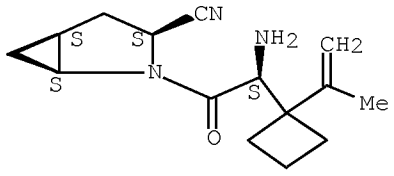
RN 361441-69-2 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-[1-(1-methylethenyl)cyclopentyl]acetyl]-, (1S,3S,5S)-
(CA INDEX NAME)

Absolute stereochemistry.



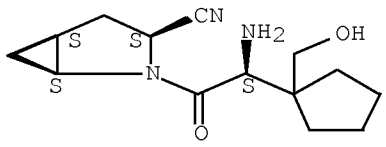
RN 361441-71-6 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-[1-(1-methylethenyl)cyclobutyl]acetyl]-, (1S,3S,5S)-
(CA INDEX NAME)

Absolute stereochemistry.



RN 361441-74-9 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-[1-(hydroxymethyl)cyclopentyl]acetyl]-, (1S,3S,5S)-
(CA
INDEX NAME)

Absolute stereochemistry.

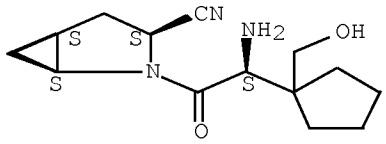


RN 361441-75-0 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-[1-(hydroxymethyl)cyclopentyl]acetyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

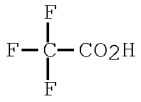
CRN 361441-74-9
CMF C14 H21 N3 O2

Absolute stereochemistry.



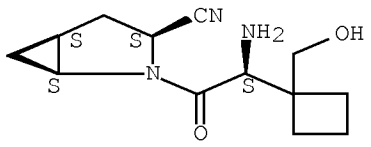
CM 2

CRN 76-05-1
CMF C2 H F3 O2



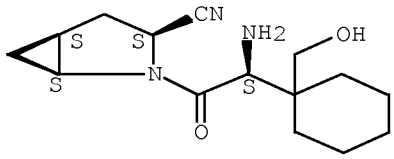
RN 361441-77-2 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-[1-(hydroxymethyl)cyclobutyl]acetyl]-, (1S,3S,5S)- (CA
INDEX NAME)

Absolute stereochemistry.



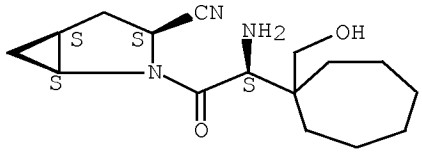
RN 361441-78-3 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-[1-(hydroxymethyl)cyclohexyl]acetyl]-, (1S,3S,5S)- (CA
INDEX NAME)

Absolute stereochemistry.



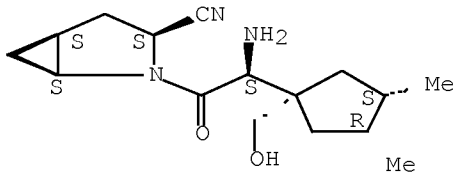
RN 361441-79-4 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-[1-(hydroxymethyl)cycloheptyl]acetyl]-, (1S,3S,5S)-
(CA
INDEX NAME)

Absolute stereochemistry.



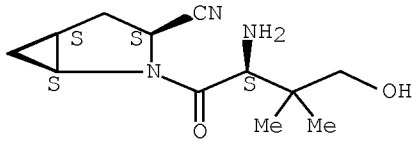
RN 361441-80-7 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-[(3R,4S)-1-(hydroxymethyl)-3,4-
dimethylcyclopentyl]acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



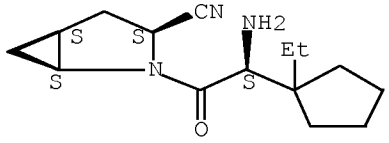
RN 361441-83-0 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-4-hydroxy-3,3-dimethyl-1-oxobutyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



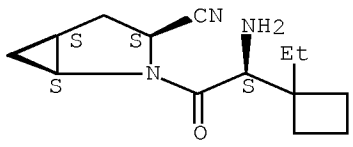
RN 361441-85-2 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(1-ethylcyclopentyl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



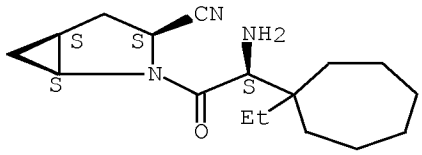
RN 361441-87-4 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(1-ethylcyclobutyl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



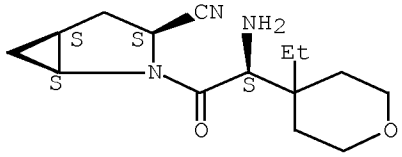
RN 361441-88-5 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(1-ethylcycloheptyl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



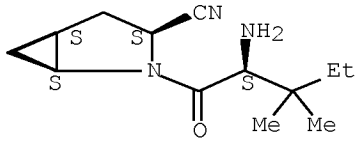
RN 361441-89-6 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(4-ethyltetrahydro-2H-pyran-4-yl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



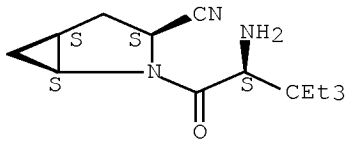
RN 361441-90-9 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-3,3-dimethyl-1-oxopentyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



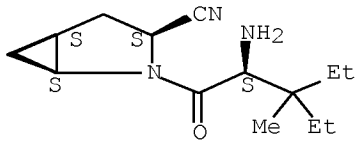
RN 361441-91-0 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-3,3-diethyl-1-oxopentyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



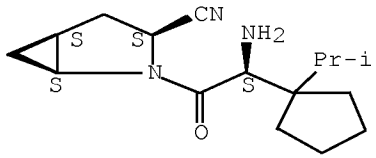
RN 361441-92-1 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-3-ethyl-3-methyl-1-oxopentyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 361441-93-2 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-[1-(1-methylethyl)cyclopentyl]acetyl]-, (1S,3S,5S)-
(CA
INDEX NAME)

Absolute stereochemistry.



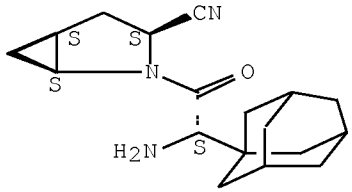
RN 361441-99-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,

2-[(2S)-2-amino-2-tricyclo[3.3.1.13,7]dec-1-ylacetyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

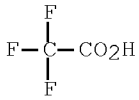
CRN 361441-98-7
CMF C18 H25 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

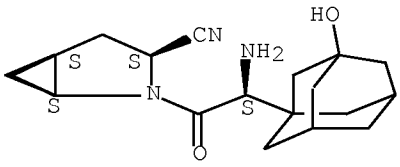


RN 361442-05-9 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-,
(1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

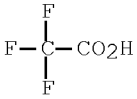
CRN 361442-04-8
CMF C18 H25 N3 O2

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

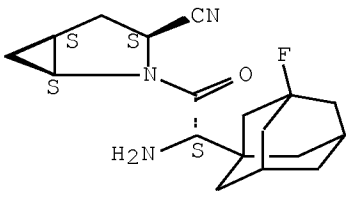


RN 361442-09-3 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(3-fluorotricyclo[3.3.1.13,7]dec-1-yl)acetyl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

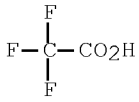
CRN 361442-08-2
CMF C18 H24 F N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

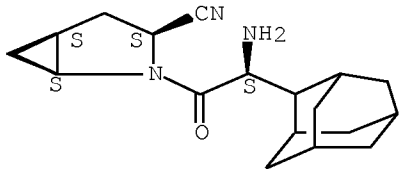


RN 361442-11-7 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-tricyclo[3.3.1.13,7]dec-2-ylacetyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

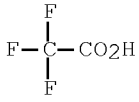
CRN 361442-10-6
CMF C18 H25 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

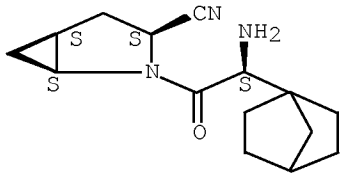


RN 361442-15-1 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-bicyclo[2.2.1]hept-1-ylacetyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

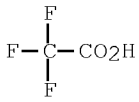
CRN 361442-14-0
CMF C15 H21 N3 O

Absolute stereochemistry.



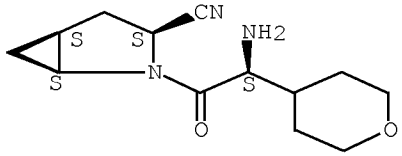
CM 2

CRN 76-05-1
CMF C2 H F3 O2



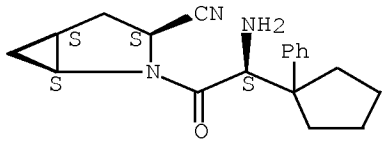
RN 361442-16-2 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(tetrahydro-2H-pyran-4-yl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



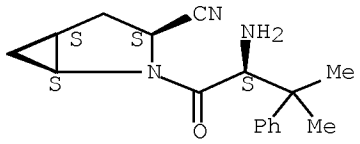
RN 361442-18-4 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(1-phenylcyclopentyl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



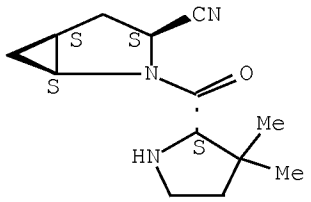
RN 361442-19-5 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-3-methyl-1-oxo-3-phenylbutyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



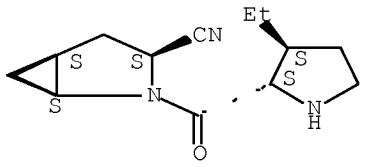
RN 361442-23-1 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[[(2S)-3,3-dimethyl-2-pyrrolidinyl]carbonyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



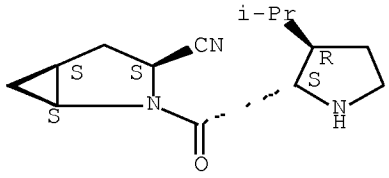
RN 361442-25-3 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[[(2S,3S)-3-ethyl-2-pyrrolidinyl]carbonyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



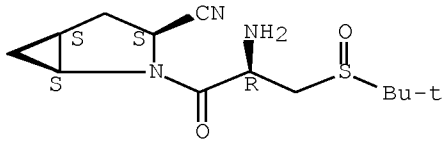
RN 361442-30-0 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[[(2S,3R)-3-(1-methylethyl)-2-pyrrolidinyl]carbonyl]-, (1S,3S,5S)- (CA
INDEX NAME)

Absolute stereochemistry.



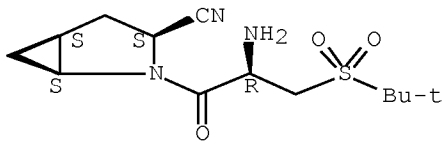
RN 361442-33-3 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2R)-2-amino-3-[(1,1-dimethylethyl)sulfinyl]-1-oxopropyl]-,
(1S,3S,5S)-
(CA INDEX NAME)

Absolute stereochemistry.



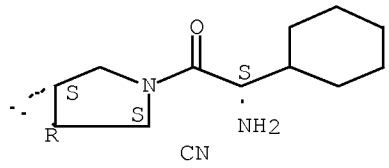
RN 361442-35-5 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2R)-2-amino-3-[(1,1-dimethylethyl)sulfonyl]-1-oxopropyl]-,
(1S,3S,5S)-
(CA INDEX NAME)

Absolute stereochemistry.



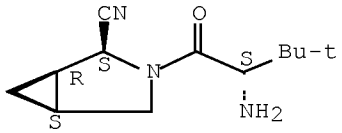
RN 361442-38-8 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile,
3-[(2S)-2-amino-2-cyclohexylacetyl]-, (1R,2S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



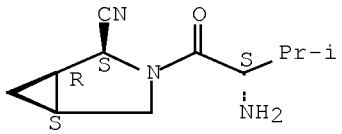
RN 361442-39-9 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile,
3-[(2S)-2-amino-3,3-dimethyl-1-oxobutyl]-, (1R,2S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



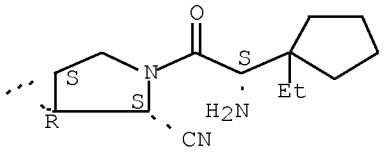
RN 361442-40-2 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile,
3-[(2S)-2-amino-3-methyl-1-oxobutyl]-, (1R,2S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



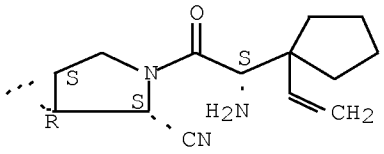
RN 361442-41-3 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile, 3-[(2S)-2-amino-2-(1-ethylcyclopentyl)acetyl]-, (1R,2S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



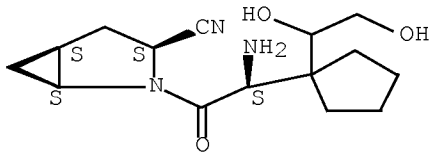
RN 361442-42-4 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile, 3-[(2S)-2-amino-2-(1-ethenylcyclopentyl)acetyl]-, (1R,2S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 361442-44-6 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-[1-(1,2-dihydroxyethyl)cyclopentyl]acetyl]-, (1S,3S,5S)-
(CA INDEX NAME)

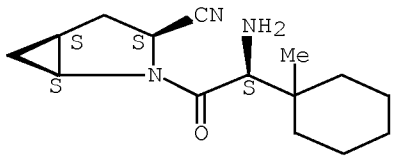
Absolute stereochemistry.



RN 361442-48-0 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,

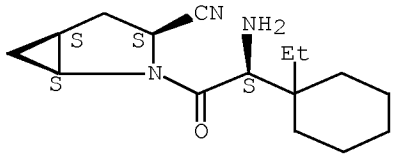
2-[(2S)-2-amino-2-(1-methylcyclohexyl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



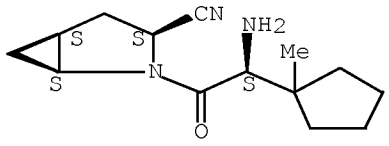
RN 361442-49-1 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(1-ethylcyclohexyl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



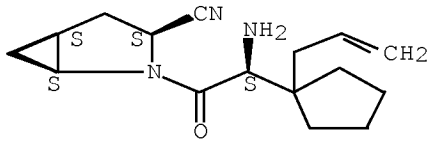
RN 361442-50-4 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(1-methylcyclopentyl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



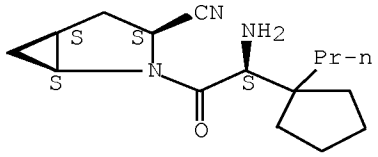
RN 361442-51-5 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-[1-(2-propen-1-yl)cyclopentyl]acetyl]-, (1S,3S,5S)- (CA
INDEX NAME)

Absolute stereochemistry.



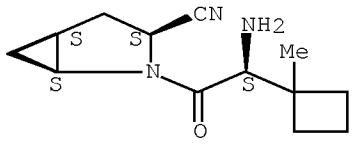
RN 361442-52-6 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(1-propylcyclopentyl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



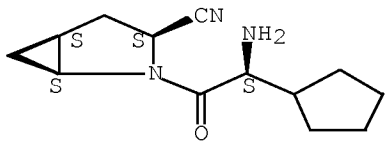
RN 361442-53-7 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(1-methylcyclobutyl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



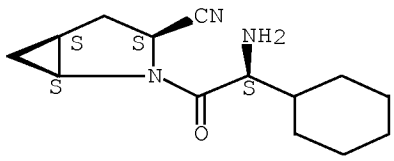
RN 361442-54-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-cyclopentylacetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



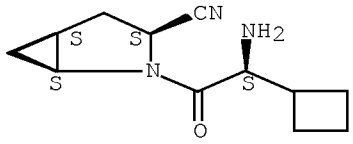
RN 361442-55-9 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-cyclohexylacetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



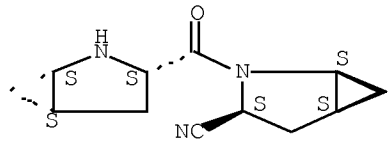
RN 361442-56-0 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-cyclobutylacetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 361442-58-2 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(1S,3S,5S)-2-azabicyclo[3.1.0]hex-3-ylcarbonyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.

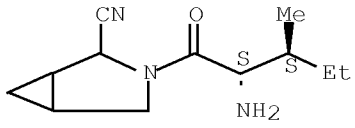


RN 361485-95-2 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile, 3-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

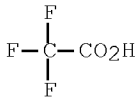
CRN 361485-94-1
CMF C12 H19 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

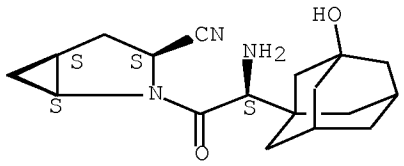


OS.CITING REF COUNT: 36 THERE ARE 36 CAPLUS RECORDS THAT CITE THIS RECORD (61 CITINGS)
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L57 ANSWER 9 OF 16 HCAPLUS COPYRIGHT 2012 ACS on STN
ACCESSION NUMBER: 2010:1573900 HCAPLUS Full-text
DOCUMENT NUMBER: 155:171960
TITLE: The discovery of the dipeptidyl peptidase-4 (DPP4) inhibitor onglyza: from concept to market
AUTHOR(S): Robl, Jeffrey A.; Hamann, Lawrence G.
CORPORATE SOURCE: Bristol-Myers Squibb Research & Development, Department of Discovery Chemistry - Metabolic Diseases, Princeton, NJ, 08543, USA
SOURCE: RSC Drug Discovery Series (2011), 4(Accounts in Drug Discovery), 1-24

CODEN: RDDSA7; ISSN: 2041-3203
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ED Entered STN: 20 Dec 2010
AB A review. The modulation of glucagon like peptide-1 in the treatment of diabetes, role of dipeptidyl peptidase-4 (DPP4) as a target for diabetes treatment, early inhibitors of DPP4, design of Bristol-Myers Squibb's DPP4 medicinal chemical program, and design of cyclopropyl-fused nitrilo-pyrrolidines are briefly described. Structure-activity relationship optimization leading to the discovery of saxagliptin, binding of saxagliptin to human DPP4, chemical stability of saxagliptin and analogs, in vivo efficacy of saxagliptin, peptidase selectivity of saxagliptin, synthesis of saxagliptin, and saxagliptin development are also shown.
IT 361442-04-8, Onglyza
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(understanding biol. function of target, ability to design small mol. to interact with critical element of target active site may lead to discovery of Onglyza which may be effective for treatment of patient with diabetes)
RN 361442-04-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L57 ANSWER 10 OF 16 HCAPLUS COPYRIGHT 2012 ACS on STN
ACCESSION NUMBER: 2009:288826 HCAPLUS Full-text
DOCUMENT NUMBER: 150:330127
TITLE: Preparation of biphenyls and biheteroaryls end-capped with amino acid or peptide derivatives as hepatitis c virus inhibitors
INVENTOR(S): Bachand, Carol; Belema, Makonen; Deon, Daniel H.; Good, Andrew C.; Goodrich, Jason; James, Clint A.; Lavoie, Rico; Lopez, Omar D.; Martel, Alain; Meanwell, Nicholas A.; Nguyen, Van N.; Romine, Jeffrey Lee; Ruediger, Edward H.; Snyder, Lawrence B.; St. Laurent, Denis R.; Yang, Fukang; Langley, David R.; Wang, Gan; Hamann, Lawrence G.

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: U.S. Pat. Appl. Publ., 515pp., Cont.-in-part of U.S. Ser. No. 835,462.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20090068140	A1	20090312	US 2008-30232	20080213
US 20080050336	A1	20080228	US 2007-835462	20070808
EP 2385048	A1	20111109	EP 2011-171390	20070809

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, HR

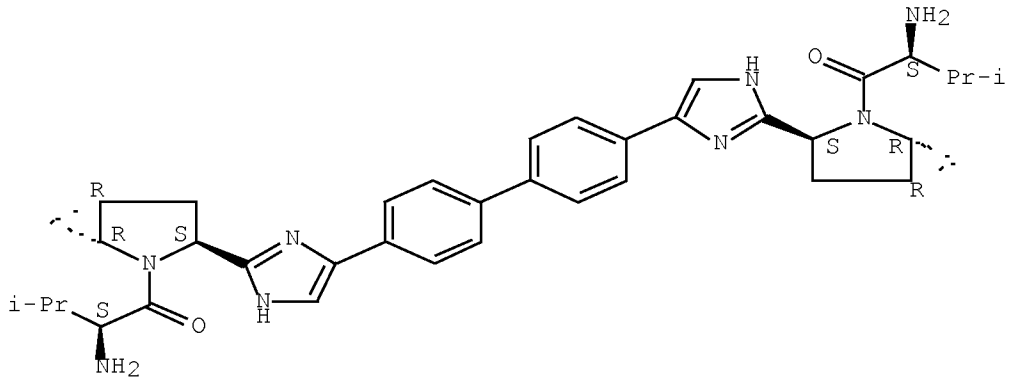
PRIORITY APPLN. INFO.: US 2007-835462 A2 20070808
US 2006-836996P P 20060811
EP 2007-800058 A3 20070809
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 150:330127; MARPAT 150:330127
ED Entered STN: 12 Mar 2009
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention is related to 4,4'-disubstituted biphenyls and biheteroaryls in which the substituents in 4 and 4' positions contain structures associated with amino acids and peptides, e.g., I, their pharmaceutical acceptable salts, pharmaceutical compns. and methods for the treatment of hepatitis C virus (HCV) infection. Thus, Pd-coupling of bromide II (preparation given) with boronate III (preparation given), hydrogenolysis, cleavage of the tert-butoxycarbonyl groups and coupling with N-(methoxycarbonyl)-L-valine gave I as an acetate salt. Compds. of the invention were active in an HCV replicon assay.

IT 1129634-15-6P 1129634-35-0P 1129634-36-1P
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of biphenyls and biheteroaryls end-capped with
amino acid or peptide derivs. as hepatitis c virus inhibitors)
RN 1129634-15-6 HCAPLUS
CN 1-Butanone, 1,1'-[[1,1'-biphenyl]-4,4'-diylbis[1H-imidazole-5,2-diyl-(1R,3S,5R)-2-azabicyclo[3.1.0]hexane-3,2-diyl]]bis[2-amino-3-methyl-, (2S,2'S)- (CA INDEX NAME)

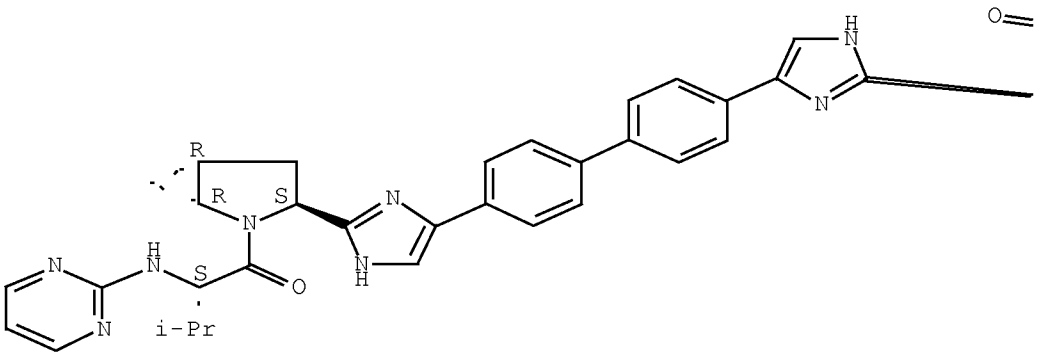
Absolute stereochemistry.



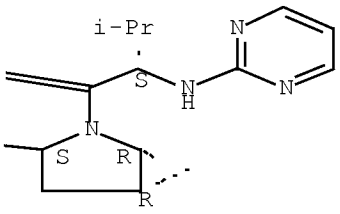
RN 1129634-35-0 HCAPLUS
CN 1-Butanone, 1,1'-[[1,1'-biphenyl]-4,4'-diylbis[1H-imidazole-5,2-diyl(1R,3S,5R)-2-azabicyclo[3.1.0]hexane-3,2-diyl]]bis[3-methyl-2-(2-pyrimidinylamino)-, (2S,2'S)- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



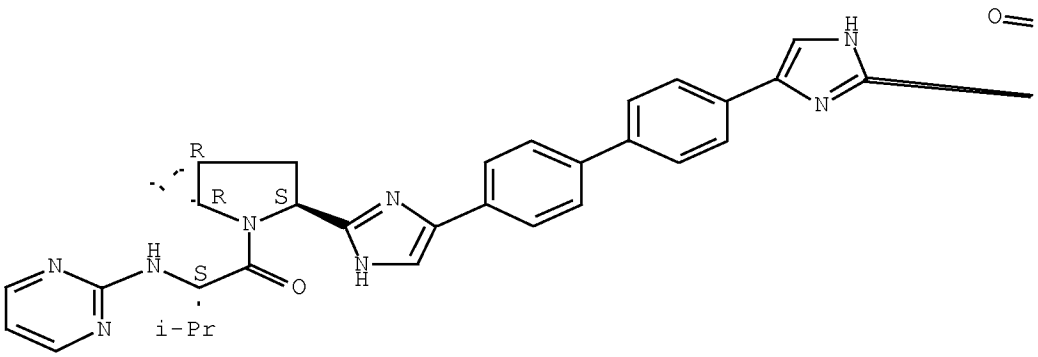
RN 1129634-36-1 HCAPLUS
CN 1-Butanone, 1,1'-[[1,1'-biphenyl]-4,4'-diylbis[1H-imidazole-5,2-diyl(1R,3S,5R)-2-azabicyclo[3.1.0]hexane-3,2-diyl]]bis[3-methyl-2-(2-pyrimidinylamino)-, (2S,2'S)-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

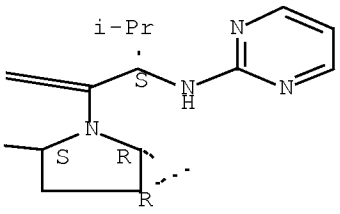
CRN 1129634-35-0
CMF C46 H50 N12 O2

Absolute stereochemistry.

PAGE 1-A

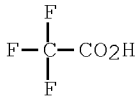


PAGE 1-B



CM 2

CRN 76-05-1
CMF C2 H F3 O2

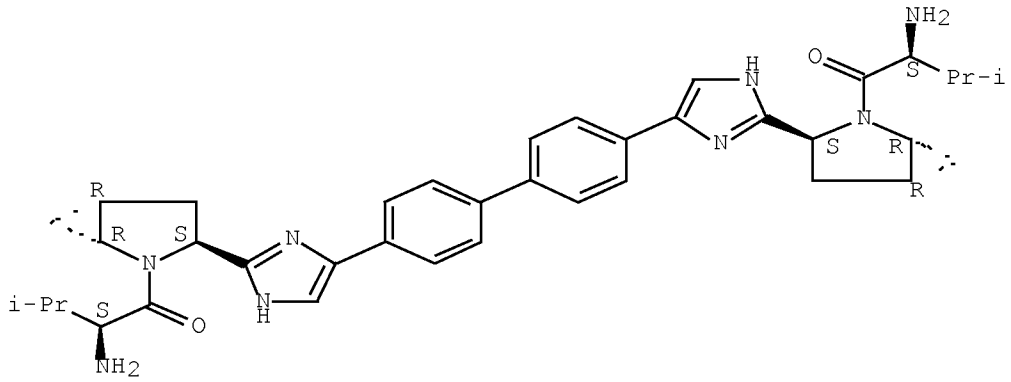


IT 1129634-16-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of biphenyls and biheteroaryls end-capped with amino acid or peptide derivs. as hepatitis c virus inhibitors)
RN 1129634-16-7 HCAPLUS
CN 1-Butanone, 1,1'-[[1,1'-biphenyl]-4,4'-diylbis[1H-imidazole-5,2-diyl-(1R,3S,5R)-2-azabicyclo[3.1.0]hexane-3,2-diyl]]bis[2-amino-3-methyl-, (2S,2'S)-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

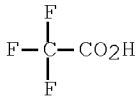
CRN 1129634-15-6
CMF C38 H46 N8 O2

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)

L57 ANSWER 11 OF 16 HCAPLUS COPYRIGHT 2012 ACS on STN
ACCESSION NUMBER: 2006:119838 HCAPLUS Full-text
DOCUMENT NUMBER: 144:213022
TITLE: Preparation of human glucagon-like-peptide-1 modulators and their use in the treatment of diabetes and related conditions
INVENTOR(S): Ewing, William R.; Mapelli, Claudio; Sulsky, Richard B.; Haque, Tasir S.; Lee, Ving G.; Riexinger, Douglas James; Martinez, Rogelio L.; Zhu, Yeheng
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 236 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2006014287	A1	20060209	WO 2005-US23076	20050630
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2571794	A1	20060209	CA 2005-2571794	20050630
EP 1773877	A1	20070418	EP 2005-763871	20050630
EP 1773877	B1	20100317		
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, HR, LV, MK, YU				
CN 101010339	A	20070801	CN 2005-80029543	20050630
CN 101010339	B	20111109		
BR 2005011393	A	20071204	BR 2005-11393	20050630
JP 2008505899	T	20080228	JP 2007-520360	20050630
AT 461218	T	20100415	AT 2005-763871	20050630
ES 2340181	T3	20100531	ES 2005-763871	20050630
AR 49572	A1	20060816	AR 2005-102778	20050704
MX 2006015193	A	20070228	MX 2006-15193	20061220
ZA 2006010786	A	20081231	ZA 2006-10786	20061220
IN 2006DN07816	A	20070817	IN 2006-DN7816	20061222
AU 2005270129	A1	20060209	AU 2005-270129	20070102
NO 2007000614	A	20070327	NO 2007-614	20070201
KR 2007042162	A	20070420	KR 2007-7002645	20070201
PRIORITY APPLN. INFO.:			US 2004-585358P P	20040702
			US 2005-684805P P	20050526
			WO 2005-US23076 W	20050630

OTHER SOURCE(S): CASREACT 144:213022; MARPAT 144:213022

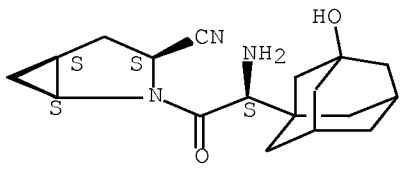
ED Entered STN: 09 Feb 2006

AB The invention provides novel human glucagon-like peptide-1 (GLP-1)-receptor modulators Xaa1-Xaa2-Xaa3-Xaa4-Xaa5-Xaa6-Xaa7-Xaa8-Xaa9- Xaa10-Xaa11 [Xaa1-Xaa3, Xaa5-Xaa11 are (certain) naturally or non-naturally occurring amino acid residues; Xaa4 is glycine] that have biol. activity similar or superior to native GLP-1 peptide and thus are useful for the treatment or prevention of diseases or disorders associated with GLP activity. The novel, chemical modified peptides not only stimulate insulin secretion in type II diabetics, but also produce other beneficial insulinotropic responses. These synthetic peptide GLP-1 receptor modulators exhibit increased stability to proteolytic cleavage making them ideal therapeutic candidates for oral or parenteral administration. Peptides of the invention show desirable pharmacokinetic properties and desirable potency in efficacy models of diabetes. Thus, claimed peptide H-H-Aib-EGT-L-α-MePhe(2-fluoro)-TSD-Bip(2'-Et-4'-OMe)-4-(2'-methylphenyl)-3-pyridylalanine-NH2 (H, E, G, T, S and D are one-letter amino acid symbols, Aib = α-aminoisobutyric acid residue, Bip = biphenylalanine

residue) was prepared by the solid-phase method and shown to produce a time-dependent statistically significant decrease in postprandial plasma glucose following s.c. administration in ob/ob mice.

IT 361442-04-8, Saxagliptin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of human glucagon-like-peptide-1 modulators and their use in
treatment of diabetes and related conditions)
RN 361442-04-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L57 ANSWER 12 OF 16 HCAPLUS COPYRIGHT 2012 ACS on STN
ACCESSION NUMBER: 2005:120884 HCAPLUS Full-text
DOCUMENT NUMBER: 142:219555
TITLE: Preparation of adamantyglycinamide inhibitors of dipeptidyl peptidase IV
INVENTOR(S): Hamann, Lawrence G.; Khanna, Ashish; Kirby, Mark S.; Magnin, David R.; Simpkins, Ligaya M.; Sutton, James C.; Robl, Jeffrey
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005012249	A2	20050210	WO 2004-US24257	20040728
WO 2005012249	A3	20050506		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,

NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG

US 20050038020	A1	20050217	US 2004-899641	20040727
US 6995183	B2	20060207		
EP 1658066	A2	20060524	EP 2004-779352	20040728
EP 1658066	B1	20090930		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR

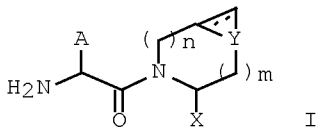
JP 2007501231	T	20070125	JP 2006-522608	20040728
EP 1997489	A1	20081203	EP 2008-158967	20040728

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, HR, LT, LV, MK

AT 444064	T	20091015	AT 2004-779352	20040728
ES 2332275	T3	20100201	ES 2004-779352	20040728
US 20050228021	A1	20051013	US 2005-149414	20050609
US 20050239839	A1	20051027	US 2005-149408	20050609
NO 2006000479	A	20060220	NO 2006-479	20060130

PRIORITY APPLN. INFO.:	US 2003-491832P	P	20030801
	US 2004-899641	A	20040727
	EP 2004-779352	A3	20040728
	WO 2004-US24257	W	20040728

OTHER SOURCE(S): CASREACT 142:219555; MARPAT 142:219555
ED Entered STN: 11 Feb 2005
GI



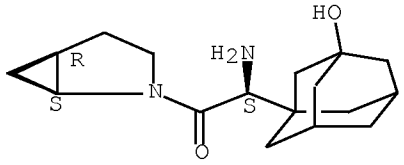
I

AB Title compds. [I; m, n = 0-2; m+n ≤2; dashed bonds form a cyclopropyl ring when Y = CH; X = H, CN; Y = CH, CH2, CHF, CF2, O, S, SO, SO2; A = (substituted) adamantyl], were prepared Thus, (S)-(3-hydroxy-5,7-dimethyladamantan-1-yl)glycine pyrrolidinamide (preparation from 3,5-dimethyladamantane-1-carboxylic acid given) at 3 μmol/kg orally in rats gave a 39% reduction in serum glucose after 4 h.

IT 841302-20-3P 841302-21-4P 841302-24-7P
841302-26-9P 841302-27-0P 841302-28-1P
841302-29-2P 841302-30-5P 841302-31-6P
841302-32-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

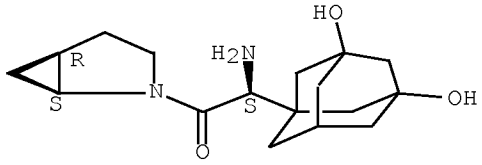
(Uses)
(claimed compound; preparation of adamantyglycinamide inhibitors of dipeptidyl
peptidase IV)
RN 841302-20-3 HCAPLUS
CN Ethanone, 2-amino-1-(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl-2-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



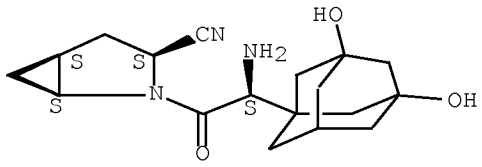
RN 841302-21-4 HCAPLUS
CN Ethanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-2-(3,5-dihydroxytricyclo[3.3.1.13,7]dec-1-yl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



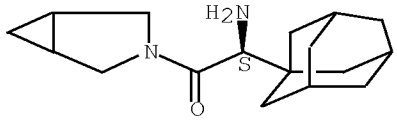
RN 841302-24-7 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(3,5-dihydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



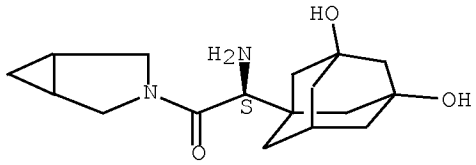
RN 841302-26-9 HCAPLUS
CN Ethanone, 2-amino-1-(3-azabicyclo[3.1.0]hex-3-yl)-2-tricyclo[3.3.1.13,7]dec-1-yl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



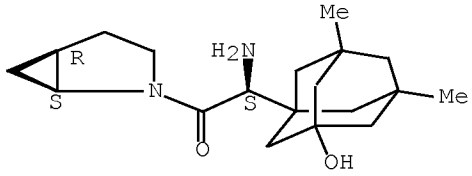
RN 841302-27-0 HCAPLUS
CN Ethanone, 2-amino-1-(3-azabicyclo[3.1.0]hex-3-yl)-2-(3,5-dihydroxytricyclo[3.3.1.13,7]dec-1-yl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



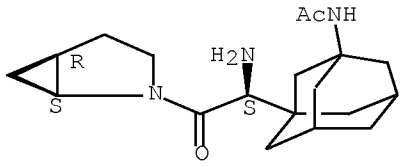
RN 841302-28-1 HCAPLUS
CN Ethanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-2-(3-hydroxy-5,7-dimethyltricyclo[3.3.1.13,7]dec-1-yl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



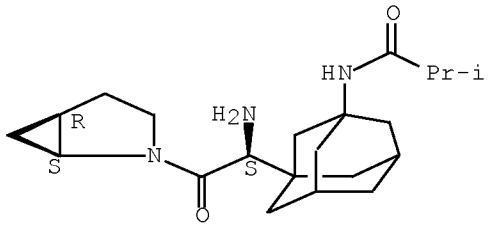
RN 841302-29-2 HCAPLUS
CN Acetamide, N-[3-[(1S)-1-amino-2-(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl-2-oxoethyl]tricyclo[3.3.1.13,7]dec-1-yl]- (CA INDEX NAME)

Absolute stereochemistry.



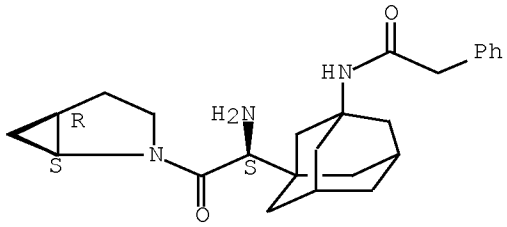
RN 841302-30-5 HCAPLUS
CN Propanamide, N-[3-[(1S)-1-amino-2-(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl-2-oxoethyl]tricyclo[3.3.1.13,7]dec-1-yl]-2-methyl- (CA INDEX NAME)

Absolute stereochemistry.



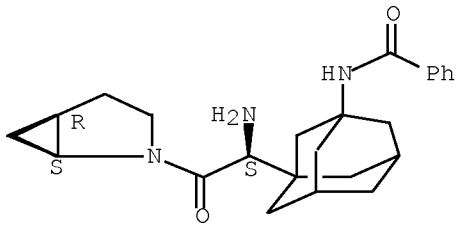
RN 841302-31-6 HCAPLUS
CN Benzeneacetamide, N-[3-[(1S)-1-amino-2-(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl-2-oxoethyl]tricyclo[3.3.1.13,7]dec-1-yl]- (CA INDEX NAME)

Absolute stereochemistry.



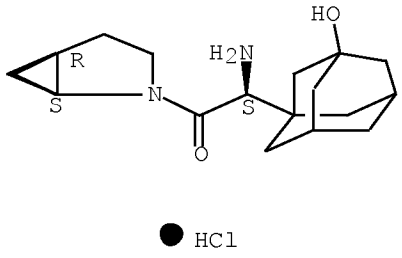
RN 841302-32-7 HCAPLUS
CN Benzamide, N-[3-[(1S)-1-amino-2-(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl-2-oxoethyl]tricyclo[3.3.1.13,7]dec-1-yl]- (CA INDEX NAME)

Absolute stereochemistry.



IT 841302-51-0P 841302-52-1P 841302-57-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of adamantyglycinamide inhibitors of dipeptidyl peptidase IV)
RN 841302-51-0 HCAPLUS
CN Ethanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-2-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)-, hydrochloride (1:1), (2S)- (CA INDEX NAME)

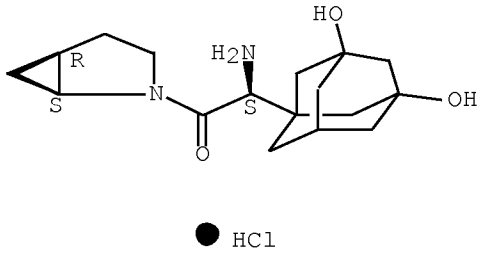
Absolute stereochemistry.



● HCl

RN 841302-52-1 HCAPLUS
CN Ethanone, 2-amino-1-(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl-2-(3,5-dihydroxytricyclo[3.3.1.13,7]dec-1-yl)-, hydrochloride (1:1), (2S)- (CA INDEX NAME)

Absolute stereochemistry.

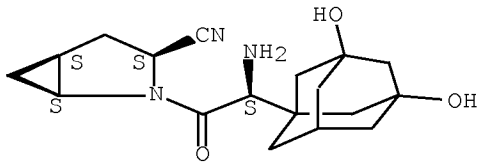


RN 841302-57-6 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(3,5-dihydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

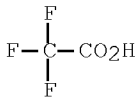
CRN 841302-24-7
CMF C18 H25 N3 O3

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



OS.CITING REF COUNT: 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L57 ANSWER 13 OF 16 HCAPLUS COPYRIGHT 2012 ACS on STN
ACCESSION NUMBER: 2005:760338 HCAPLUS Full-text
DOCUMENT NUMBER: 143:367574
TITLE: Diprolyl nitriles as potent dipeptidyl peptidase IV inhibitors
AUTHOR(S): Zhao, Guohua; Taunk, Prakash C.; Magnin, David R.; Simpkins, Ligaya M.; Robl, Jeffrey A.; Wang, Aiying; Robertson, James G.; Marcinkeviciene, Jovita; Sitkoff, Doree F.; Parker, Rex A.; Kirby, Mark S.; Hamann, Lawrence G.
CORPORATE SOURCE: Department of Discovery Chemistry, Pharmaceutical Research Institute, Bristol-Myers Squibb, Princeton, NJ, 08543-5400, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2005), 15(18), 3992-3995
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:367574
ED Entered STN: 15 Aug 2005
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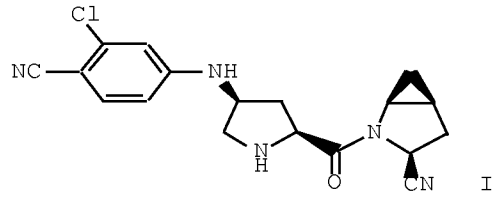


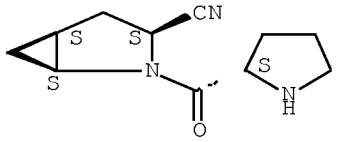
I

AB Dipeptidyl peptidase IV (DPP4) is a multifunctional type II transmembrane serine peptidase which regulates various physiol. processes, most notably plasma glucose homeostasis by cleaving peptide hormones glucagon-like peptide-1 and glucose-dependent insulinotropic polypeptide. Inhibition of DPP4 is a potentially valuable therapy for type 2 diabetes. Synthesis and structure-activity relationships of a series of substituted diprolyl nitriles are described, leading to the identification of compound I with a measured DPP4 Ki of 3.6 nM.

IT 361441-07-8P 361441-10-3P 361441-11-4P
361442-23-1P 361442-25-3P 361442-30-0P
361442-58-2P 866321-06-4P 866321-19-9P
866321-23-5P 866321-26-8P 866321-46-2P
866321-48-4P 866321-50-8P 866321-52-0P
866321-54-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(diprolyl nitriles as potent dipeptidyl peptidase IV inhibitors)

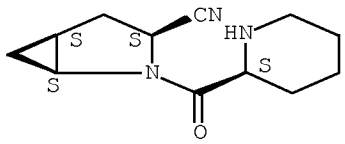
RN 361441-07-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-pyrrolidinylcarbonyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



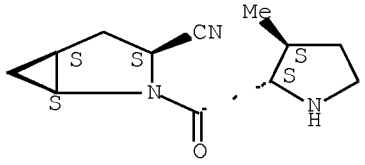
RN 361441-10-3 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-piperidinylcarbonyl]-,
(1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



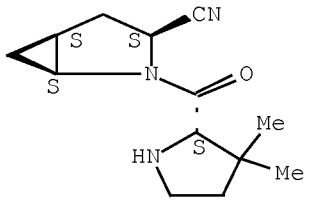
RN 361441-11-4 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[[(2S,3S)-3-methyl-2-pyrrolidinyl]carbonyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



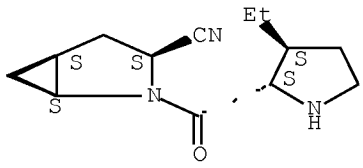
RN 361442-23-1 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[[(2S)-3,3-dimethyl-2-pyrrolidinyl]carbonyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



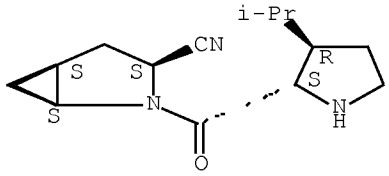
RN 361442-25-3 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[[(2S,3S)-3-ethyl-2-pyrrolidinyl]carbonyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



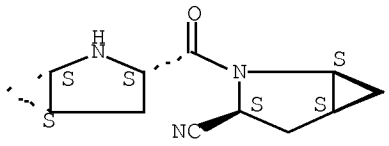
RN 361442-30-0 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[[(2S,3R)-3-(1-methylethyl)-2-pyrrolidinyl]carbonyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



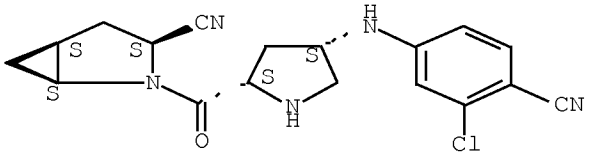
RN 361442-58-2 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(1S,3S,5S)-2-azabicyclo[3.1.0]hex-3-ylcarbonyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



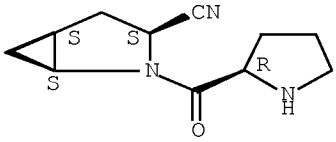
RN 866321-06-4 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[[(2S,4S)-4-[(3-chloro-4-cyanophenyl)amino]-2-pyrrolidinyl]carbonyl]-,
(1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



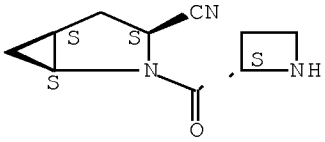
RN 866321-19-9 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2R)-2-pyrrolidinylcarbonyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



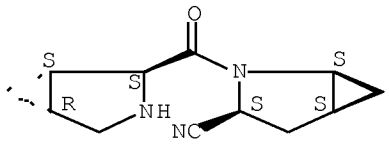
RN 866321-23-5 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-azetidinylcarbonyl]-,
(1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



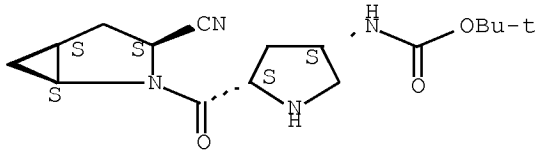
RN 866321-26-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(1S,2S,5R)-3-azabicyclo[3.1.0]hex-2-ylcarbonyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



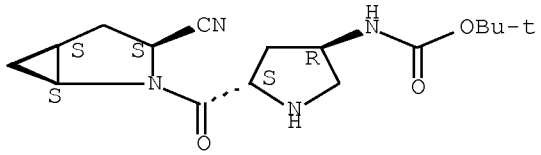
RN 866321-46-2 HCAPLUS
CN Carbamic acid, [(3S,5S)-5-[[(1S,3S,5S)-3-cyano-2-azabicyclo[3.1.0]hex-2-yl]carbonyl]-3-pyrrolidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 866321-48-4 HCAPLUS
CN Carbamic acid, [(3R,5S)-5-[[(1S,3S,5S)-3-cyano-2-azabicyclo[3.1.0]hex-2-yl]carbonyl]-3-pyrrolidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

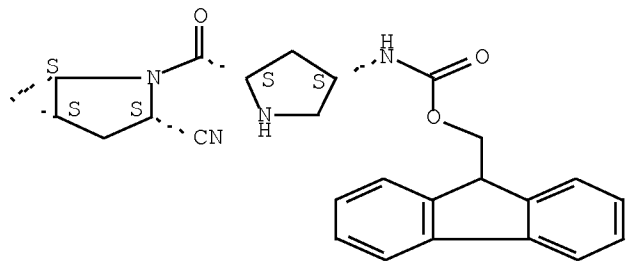
Absolute stereochemistry.



RN 866321-50-8 HCAPLUS
CN Carbamic acid, [(3S,5S)-5-[[(1S,3S,5S)-3-cyano-2-azabicyclo[3.1.0]hex-2-

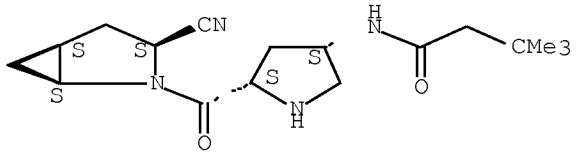
yl]carbonyl]-3-pyrrolidinyl]-, 9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



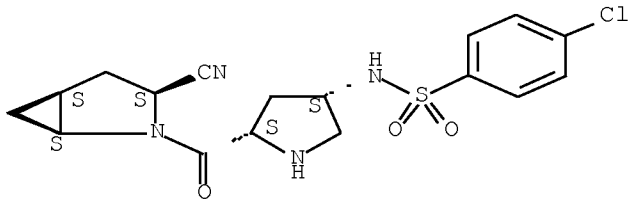
RN 866321-52-0 HCAPLUS
CN Butanamide, N-[(3S,5S)-5-[[(1S,3S,5S)-3-cyano-2-azabicyclo[3.1.0]hex-2-yl]carbonyl]-3-pyrrolidinyl]-3,3-dimethyl- (CA INDEX NAME)

Absolute stereochemistry.



RN 866321-54-2 HCAPLUS
CN Benzenesulfonamide, 4-chloro-N-[(3S,5S)-5-[[(1S,3S,5S)-3-cyano-2-azabicyclo[3.1.0]hex-2-yl]carbonyl]-3-pyrrolidinyl]- (CA INDEX NAME)

Absolute stereochemistry.



OS.CITING REF COUNT: 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS

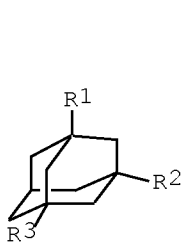
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L57 ANSWER 14 OF 16 HCAPLUS COPYRIGHT 2012 ACS on STN
ACCESSION NUMBER: 2004:515478 HCAPLUS Full-text
DOCUMENT NUMBER: 141:54618
TITLE: Preparation of cyclopropyl-fused pyrrolidine-based inhibitors of dipeptidyl peptidase IV
INVENTOR(S): Vu, Truc Chi; Brzozowski, David B.; Fox, Rita; Godfrey, Jollie Duaine, Jr.; Hanson, Ronald L.; Kolotuchin, Sergei V.; Mazzullo, John A., Jr.; Patel, Ramesh N.; Wang, Jianji; Wong, Kwok; Yu, Jurong; Zhu, Jason; Magnin, David R.; Augeri, David J.; Hamann, Lawrence G.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004052850	A2	20040624	WO 2003-US38558	20031204
WO 2004052850	A3	20060302		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 20050090539	A1	20050428	US 2003-716012	20031118
US 7420079	B2	20080902		
CA 2508619	A1	20040624	CA 2003-2508619	20031204
AU 2003297647	A1	20040630	AU 2003-297647	20031204
EP 1581487	A2	20051005	EP 2003-812799	20031204
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003017139	A	20051129	BR 2003-17139	20031204
CN 1791401	A	20060621	CN 2003-80109631	20031204
JP 2006516121	T	20060622	JP 2004-559282	20031204
JP 4886193	B2	20120229		
CN 102070451	A	20110525	CN 2010-10260709	20031204
IN 2005DN02279	A	20090123	IN 2005-DN2279	20050530
IN 244388	A1	20101210		
MX 2005005970	A	20050818	MX 2005-5970	20050603
IN 2008DN00420	A	20080215	IN 2008-DN420	20080115
US 20090018311	A1	20090115	US 2008-181216	20080728
US 7705033	B2	20100427		
US 20100274025	A1	20101028	US 2010-712958	20100225

JP 2011006440	A	20110113	JP 2010-181557	20100816
JP 2011006441	A	20110113	JP 2010-181559	20100816
PRIORITY APPLN. INFO.:			US 2002-431814P	P 20021209
			US 2003-716012	A3 20031118
			CN 2003-80109631	A3 20031204
			JP 2004-559282	A3 20031204
			WO 2003-US38558	W 20031204
			IN 2005-DN2279	A3 20050530
			US 2008-181216	A3 20080728

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 141:54618; MARPAT 141:54618
ED Entered STN: 27 Jun 2004
GI



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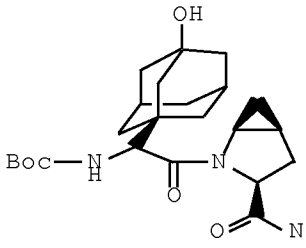


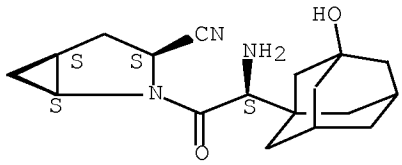
II

AB The invention provides methods and compds. for the production of cyclopropyl-fused pyrrolidine-based inhibitors of dipeptidyl peptidase IV. Also described are methods for the asym. reductive amination of (3-hydroxyadamantan-1-yl)oxoacetic acid. Adamantane derivs. I [R1 is H or OH; R2 is C(O)COR4, C(O)NR5R6, C(X)nCOR4 or C(NR7R8)COR4, where X is halo, n is 1-2, R4 is alkoxy, NH2 or OH, and R5-R8 are H or carbalkoxy; R3 is H, OH or NR9C(O)R10, where R9 is carboxy-substituted alkyl or aryl and R10 is 3-cyano-2-azabicyclo[3.1.0]hex-2-yl] or their pharmaceutically-acceptable salts are claimed. Thus, adamantyl-substituted glycinamide derivative II (Boc = tert-butoxycarbonyl) was prepared via amidation of Boc-protected (S)-α-amino-3-hydroxy-1-adamantaneacetic acid.

IT 361442-04-8P 709031-44-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cyclopropyl-fused pyrrolidine-based inhibitors of dipeptidyl peptidase IV)

RN 361442-04-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.

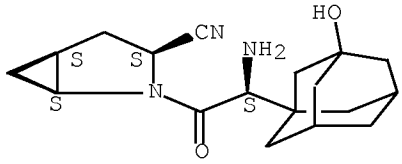


RN 709031-44-7 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-amino(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-,
(1S,3S,5S)-,
monobenzoate (salt) (9CI) (CA INDEX NAME)

CM 1

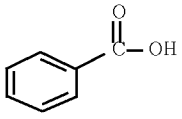
CRN 361442-04-8
CMF C18 H25 N3 O2

Absolute stereochemistry.



CM 2

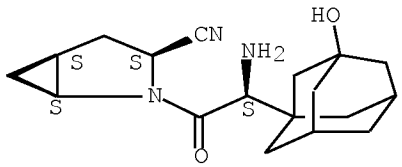
CRN 65-85-0
CMF C7 H6 O2



IT 709031-78-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of cyclopropyl-fused pyrrolidine-based inhibitors of dipeptidyl
peptidase IV)
RN 709031-78-7 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-,
hydrochloride (1:1), (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



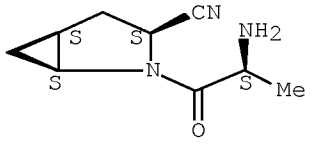
● HCl

OS.CITING REF COUNT: 25 THERE ARE 25 CAPLUS RECORDS THAT CITE THIS RECORD (35 CITINGS)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L57 ANSWER 15 OF 16 HCAPLUS COPYRIGHT 2012 ACS on STN
ACCESSION NUMBER: 2004:300939 HCAPLUS Full-text
DOCUMENT NUMBER: 141:23891
TITLE: Synthesis of Novel Potent Dipeptidyl Peptidase IV Inhibitors with Enhanced Chemical Stability: Interplay between the N-Terminal Amino Acid Alkyl Side Chain and the Cyclopropyl Group of α-Aminoacyl-L-cis-4,5-methanoprolinenitrile-Based Inhibitors
AUTHOR(S): Magnin, David R.; Robl, Jeffrey A.; Sulsky, Richard B.; Augeri, David J.; Huang, Yanting; Simpkins, Ligaya M.; Taunk, Prakash C.; Betebenner, David A.; Robertson, James G.; Abboa-Offei, Benoni E.; Wang, Aiying; Cap, Michael; Xin, Li; Tao, Li; Sitkoff, Doree F.; Malley, Mary F.; Gougoutas, Jack Z.; Khanna, Ashish; Huang, Qi; Han, Song-Ping; Parker, Rex A.; Hamann, Lawrence G.
CORPORATE SOURCE: Departments of Discovery Chemistry, Metabolic Research, Exploratory Pharmaceutics, Computer-Assisted Drug Design, Solid State Chemistry and Pharmaceutical Candidate Optimization, Bristol-Myers Squibb Pharmaceutical Research Institute, Princeton, NJ, 08543-5400, USA
SOURCE: Journal of Medicinal Chemistry (2004), 47(10), 2587-2598
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:23891
ED Entered STN: 14 Apr 2004
AB A series of methanoprolinenitrile-containing dipeptide mimetics were synthesized and evaluated as inhibitors of the N-terminal sequence-specific serine protease dipeptidyl peptidase IV (DPP-IV). The catalytic action of DPP-IV is the principle means of degradation of glucagon-like peptide-1 (a key mediator of glucose-stimulated insulin secretion) and DPP-IV inhibition shows clin. benefit as a novel mechanism for treatment of type 2 diabetes. However, many of the reversible inhibitors to date suffer from chemical instability stemming from an amine to nitrile intramol. cyclization. Installation of a cyclopropyl moiety at either the 3,4- or 4,5-position of traditional 2-cyanopyrrolidide proline mimetics led to compds. with potent inhibitory activity against the enzyme. Addnl., cis-4,5-methanoprolinenitriles with β-branching in the N-terminal amino acid provided enhanced chemical stability and high inhibitory potency. This class of inhibitors also exhibited the ability to suppress prandial glucose elevations after an oral glucose challenge in male Zucker rats.
IT 700376-83-6
RL: PRP (Properties)
(calcns. of energy barrier toward adopting the conformation required for intramol. cyclization by dipeptidyl prolinenitrile and methanoprolinenitrile)
RN 700376-83-6 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-1-oxopropyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



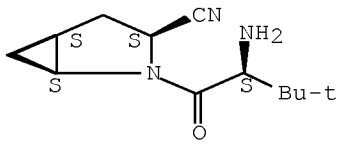
IT 361440-73-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(crystal structure; preparation and biol. activity of methanoprolinenitrile-containing dipeptide mimetics as DPP-IV inhibitors and as antidiabetic agents)
RN 361440-73-5 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-3,3-dimethyl-1-oxobutyl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361440-72-4

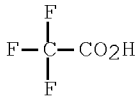
CMF C12 H19 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

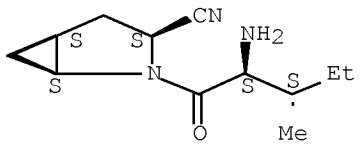


IT 361440-66-6P 361440-77-9P 361440-88-2P
700376-66-5P 700376-67-6P 700376-68-7P
700376-70-1P 700376-71-2P 700376-72-3P
700376-73-4P 700376-74-5P 700376-75-6P
700376-76-7P 700376-77-8P 700376-78-9P
700376-79-0P 700376-80-3P 700376-81-4P
700376-82-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and biol. activity of methanoprolinenitrile-containing dipeptide
mimetics as DPP-IV inhibitors and as antidiabetic agents)
RN 361440-66-6 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

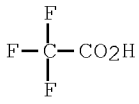
CRN 361440-65-5
CMF C12 H19 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

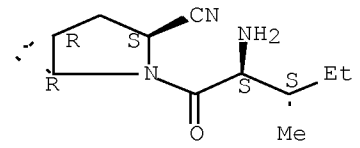


RN 361440-77-9 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]-, (1R,3S,5R)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

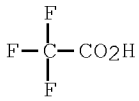
CRN 361440-76-8
CMF C12 H19 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

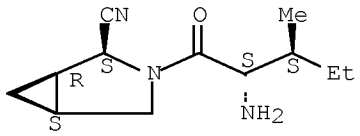


RN 361440-88-2 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile,
3-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]-, (1R,2S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

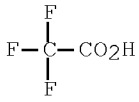
CRN 361440-87-1
CMF C12 H19 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

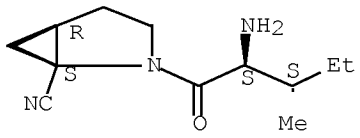


RN 700376-66-5 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-1-carbonitrile,
2-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]-, (1S,5R)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

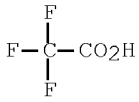
CRN 700376-65-4
CMF C12 H19 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

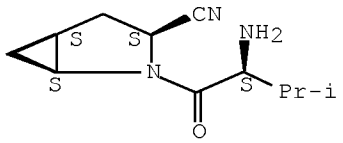


RN 700376-67-6 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-3-methyl-1-oxobutyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate
(1:1) (CA INDEX NAME)

CM 1

CRN 361441-05-6
CMF C11 H17 N3 O

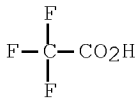
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2

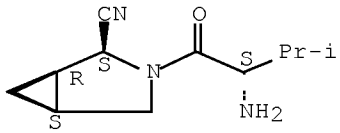


RN 700376-68-7 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile,
3-[(2S)-2-amino-3-methyl-1-oxobutyl]-, (1R,2S,5S)-,
2,2,2-trifluoroacetate
(1:1) (CA INDEX NAME)

CM 1

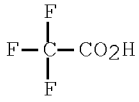
CRN 361442-40-2
CMF C11 H17 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

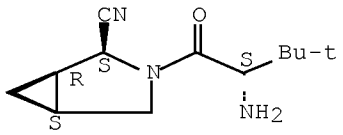


RN 700376-70-1 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile,
3-[(2S)-2-amino-3,3-dimethyl-1-oxobutyl]-, (1R,2S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

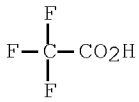
CRN 361442-39-9
CMF C12 H19 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

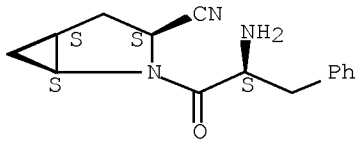


RN 700376-71-2 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-1-oxo-3-phenylpropyl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

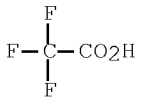
CRN 361441-08-9
CMF C15 H17 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

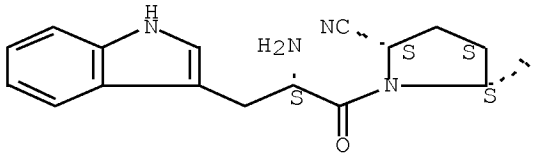


RN 700376-72-3 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-3-(1H-indol-3-yl)-1-oxopropyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

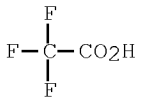
CRN 361440-97-3
CMF C17 H18 N4 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



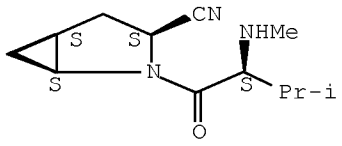
RN 700376-73-4 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-3-methyl-2-(methylamino)-1-oxobutyl]-, (1S,3S,5S)-,

2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

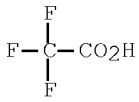
CRN 361441-04-5
CMF C12 H19 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

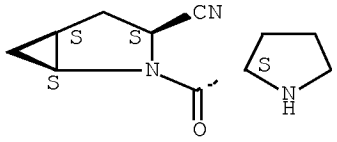


RN 700376-74-5 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-pyrrolidinylcarbonyl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

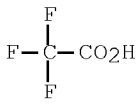
CRN 361441-07-8
CMF C11 H15 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

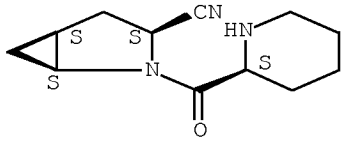


RN 700376-75-6 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-piperidinylcarbonyl]-,
(1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

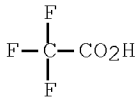
CRN 361441-10-3
CMF C12 H17 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



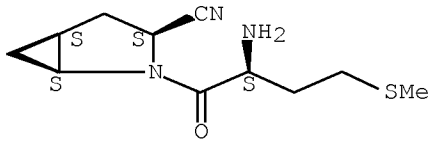
RN 700376-76-7 HCAPLUS

CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-4-(methylthio)-1-oxobutyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

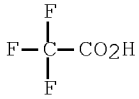
CRN 361440-99-5
CMF C11 H17 N3 O S

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

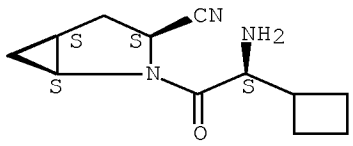


RN 700376-77-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-cyclobutylacetyl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate
(1:1) (CA INDEX NAME)

CM 1

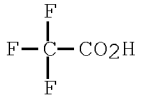
CRN 361442-56-0
CMF C12 H17 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

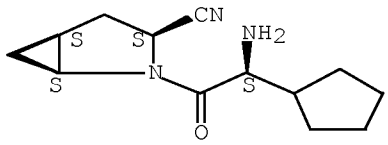


RN 700376-78-9 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-cyclopentylacetyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate
(1:1) (CA INDEX NAME)

CM 1

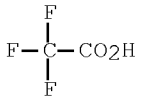
CRN 361442-54-8
CMF C13 H19 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

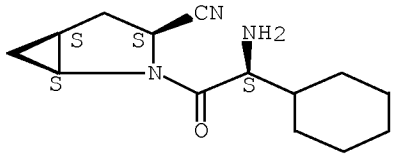


RN 700376-79-0 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-cyclohexylacetyl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate
(1:1) (CA INDEX NAME)

CM 1

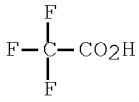
CRN 361442-55-9
CMF C14 H21 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

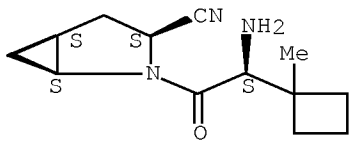


RN 700376-80-3 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(1-methylcyclobutyl)acetyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361442-53-7
CMF C13 H19 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
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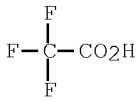

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CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(1-methylcyclopentyl)acetyl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

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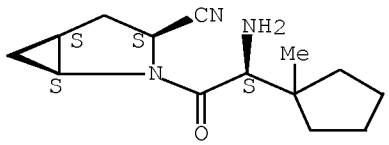
CRN 361442-50-4
CMF C14 H21 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
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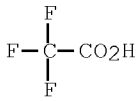
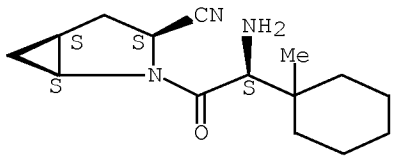


RN 700376-82-5 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(1-methylcyclohexyl)acetyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

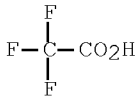
CRN 361442-48-0
CMF C15 H23 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



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ACCESSION NUMBER: 2010425818 EMBASE Full-text
TITLE: Synthesis and SAR of azolopyrimidines as potent and selective dipeptidyl peptidase-4 (DPP4) inhibitors for type 2 diabetes.
AUTHOR: Brigance, Robert P.; Meng, Wei; Zahler, Robert; Hamann, Lawrence G.
CORPORATE SOURCE: Department of Discovery Chemistry, Bristol-Myers Squibb, Research and Development, PO Box 5400, Princeton, NJ 08543-5400, United States. robert.brigance@bms.com; wei.meng@bms.com
AUTHOR: Fura, Aberra
CORPORATE SOURCE: Department of Pharmaceutical Candidate Optimization, Bristol-Myers Squibb, Research and Development, PO Box 5400, Princeton, NJ 08543-5400, United States.
AUTHOR: Harrity, Thomas; Wang, Aiying; Kirby, Mark S.
CORPORATE SOURCE: Department of Metabolic Diseases, Bristol-Myers Squibb, Research and Development, PO Box 5400, Princeton, NJ 08543-5400, United States.
AUTHOR: Brigance, R. P. (correspondence)
CORPORATE SOURCE: Department of Discovery Chemistry, Bristol-Myers Squibb, Research and Development, PO Box 5400, Princeton, NJ 08543-5400, United States. robert.brigance@bms.com
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AB Several pyrazolo-, triazolo-, and imidazolopyrimidines were synthesized and evaluated as inhibitors of DPP4. Of these three classes of compounds, the imidazolopyrimidines displayed the greatest potency and demonstrated excellent selectivity over the other dipeptidyl peptidases. SAR evaluation for these scaffolds was described as they may represent potential treatments for type 2 diabetes. .COPYRGT. 2010 Elsevier Ltd. All rights reserved.

CT Medical Descriptors:
animal experiment
animal model
article

```
     drug potency
     drug selectivity
     drug synthesis
     mouse
     *non insulin dependent diabetes mellitus
     nonhuman
     *structure activity relation
CT   Drug Descriptors:
     alogliptin: AN, drug analysis
     alogliptin: PD, pharmacology
     *azolopyrimidine: AN, drug analysis
     *azolopyrimidine: PD, pharmacology
     *dipeptidyl peptidase IV inhibitor: AN, drug analysis
     *dipeptidyl peptidase IV inhibitor: PD, pharmacology
     linagliptin: AN, drug analysis
     linagliptin: PD, pharmacology
     saxagliptin: AN, drug analysis
     saxagliptin: PD, pharmacology
     sitagliptin: AN, drug analysis
     sitagliptin: PD, pharmacology
     unclassified drug
     vildagliptin: AN, drug analysis
     vildagliptin: PD, pharmacology
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     (vildagliptin) 274901-16-5


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                1098535-23-9/BI OR 1098535-24-0/BI OR 1191-95-3/BI OR 120-92-3/
                BI OR 13031-04-4/BI OR 13139-16-7/BI OR 13433-00-6/BI OR
                13837-45-1/BI OR 14328-51-9/BI OR 143979-40-2/BI OR 144643-84-5
                /BI OR 144978-12-1/BI OR 15023-45-7/BI OR 1576-87-0/BI OR
                173724-30-6/BI OR 173724-34-0/BI OR 178172-26-4/BI OR 179015-57
                -7/BI OR 179015-58-8/BI OR 18928-91-1/BI OR 1903-22-6/BI OR
                191655-45-5/BI OR 19550-72-2/BI OR 197142-36-2/BI OR 200424-69-
                7/BI OR 20859-02-3/BI OR 2094-74-8/BI OR 2130-96-3/BI OR
                214193-10-9/BI OR 214193-11-0/BI OR 214193-13-2/BI OR 21573-69-
                3/BI OR 2356-16-3/BI OR 2534-90-9/BI OR 3005-66-1/BI OR
                35264-06-3/BI OR 361440-58-6/BI OR 361440-61-1/BI OR 361440-62-
                2/BI OR 361440-63-3/BI OR 361440-64-4/BI OR 361440-65-5/BI OR
                361440-66-6/BI OR 361440-67-7/BI OR 361440-69-9/BI OR 361440-70
                -2/BI OR 361440-71-3/BI OR 361440-73-5/BI OR 361440-77-9/BI OR
                361440-78-0/BI OR 361440-79-1/BI OR 361440-88-2/BI OR 361440-91
                -7/BI OR 361440-95-1/BI OR 361440-97-3/BI OR 361440-99-5/BI OR
                361441-01-2/BI OR 361441-03-4/BI OR 361441-04-5/BI OR 361441-05
                -6/BI OR 361441-06-7/BI OR 361441-07-8/BI OR 361441-08-9/BI OR
                361441-09-0/BI OR 361441-10-3/BI OR 361441-11-4/BI OR 361441-12
                -5/BI OR 361441-13-6/BI OR 361441-14-7/BI OR 361441-15-8/BI
L3           150 SEA SPE=ON  ABB=ON  PLU=ON  L2 AND C3-NC4/ES

     FILE 'LREGISTRY' ENTERED AT 08:10:11 ON 01 MAY 2012
CHARGED TO COST=TC1600
L4              STR
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     FILE 'REGISTRY' ENTERED AT 08:15:03 ON 01 MAY 2012
CHARGED TO COST=TC1600
L5           50 SEA SSS SAM L4

     FILE 'LREGISTRY' ENTERED AT 08:15:38 ON 01 MAY 2012
CHARGED TO COST=TC1600
L6              STR L4

     FILE 'REGISTRY' ENTERED AT 08:16:15 ON 01 MAY 2012
CHARGED TO COST=TC1600
L7           50 SEA SSS SAM L6

     FILE 'STNGUIDE' ENTERED AT 08:16:57 ON 01 MAY 2012
CHARGED TO COST=TC1600

     FILE 'LREGISTRY' ENTERED AT 08:17:39 ON 01 MAY 2012
CHARGED TO COST=TC1600
L8              STR L6

     FILE 'REGISTRY' ENTERED AT 08:17:51 ON 01 MAY 2012
CHARGED TO COST=TC1600
L9           50 SEA SSS SAM L8

     FILE 'STNGUIDE' ENTERED AT 08:18:53 ON 01 MAY 2012
CHARGED TO COST=TC1600

     FILE 'REGISTRY' ENTERED AT 08:19:58 ON 01 MAY 2012
CHARGED TO COST=TC1600

     FILE 'LREGISTRY' ENTERED AT 08:20:31 ON 01 MAY 2012
CHARGED TO COST=TC1600
L10             STR L8

     FILE 'REGISTRY' ENTERED AT 08:21:03 ON 01 MAY 2012
CHARGED TO COST=TC1600
L11          50 SEA SSS SAM L10

     FILE 'STNGUIDE' ENTERED AT 08:21:56 ON 01 MAY 2012
CHARGED TO COST=TC1600
                D QUE STAT

     FILE 'LREGISTRY' ENTERED AT 08:28:12 ON 01 MAY 2012
CHARGED TO COST=TC1600
L12             STR L10

     FILE 'REGISTRY' ENTERED AT 08:29:43 ON 01 MAY 2012
CHARGED TO COST=TC1600
L13          50 SEA SSS SAM L12

     FILE 'STNGUIDE' ENTERED AT 08:30:11 ON 01 MAY 2012
CHARGED TO COST=TC1600
                D QUE STAT

     FILE 'REGISTRY' ENTERED AT 08:32:40 ON 01 MAY 2012
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CHARGED TO COST=TC1600
L14        8057 SEA SSS FUL L12
                SAVE TEMP L14 POL658PSET1/A
L15          15 SEA SPE=ON  ABB=ON  PLU=ON  L3 NOT L14
                D SCAN

     FILE 'STNGUIDE' ENTERED AT 08:33:40 ON 01 MAY 2012
CHARGED TO COST=TC1600

     FILE 'REGISTRY' ENTERED AT 08:35:08 ON 01 MAY 2012
CHARGED TO COST=TC1600
L16         135 SEA SPE=ON  ABB=ON  PLU=ON  L2 AND L14

     FILE 'STNGUIDE' ENTERED AT 08:35:23 ON 01 MAY 2012
CHARGED TO COST=TC1600

     FILE 'LREGISTRY' ENTERED AT 08:38:02 ON 01 MAY 2012
CHARGED TO COST=TC1600
L17             STR

     FILE 'REGISTRY' ENTERED AT 08:41:44 ON 01 MAY 2012
CHARGED TO COST=TC1600
L18           0 SEA SUB=L14 SSS SAM L17
                D QUE STAT
L19           4 SEA SUB=L14 SSS FUL L17
                SAVE TEMP L19 POL658NSET1/A
                D SCAN

     FILE 'LREGISTRY' ENTERED AT 08:44:15 ON 01 MAY 2012
CHARGED TO COST=TC1600
L20             STR L12

     FILE 'REGISTRY' ENTERED AT 08:46:21 ON 01 MAY 2012
CHARGED TO COST=TC1600
L21          50 SEA SUB=L14 SSS SAM L20
                D QUE STAT
L22        8057 SEA SUB=L14 SSS FUL L20
                SAVE TEMP L22 POL658RSET1/A
L23        8053 SEA SPE=ON  ABB=ON  PLU=ON  L22 NOT L19
                SAVE TEMP L23 POL658CROSS/A
                D SCAN L19

     FILE 'STNGUIDE' ENTERED AT 08:48:55 ON 01 MAY 2012
CHARGED TO COST=TC1600
                D SAVED

     FILE 'ZCAPLUS' ENTERED AT 08:49:36 ON 01 MAY 2012
CHARGED TO COST=TC1600
L24             QUE SPE=ON  ABB=ON  PLU=ON  ROBL, J?/AU,AUTH,IN
L25             QUE SPE=ON  ABB=ON  PLU=ON  SULSKY, R?/AU,AUTH,IN
L26             QUE SPE=ON  ABB=ON  PLU=ON  SULSKY, D?/AU,AUTH,IN
L27             QUE SPE=ON  ABB=ON  PLU=ON  AUGERI, D?/AU,AUTH,IN
L28             QUE SPE=ON  ABB=ON  PLU=ON  MAGNIN, D?/AU,AUTH,IN
L29             QUE SPE=ON  ABB=ON  PLU=ON  HAMANN, L?/AU,AUTH,IN
```

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L30             QUE SPE=ON  ABB=ON  PLU=ON  BETEBENNER, D?/AU,AUTH,IN

     FILE 'HCAPLUS' ENTERED AT 08:50:44 ON 01 MAY 2012
CHARGED TO COST=TC1600
L31           1 SEA SPE=ON  ABB=ON  PLU=ON  L1 AND (L24 OR L25 OR L26 OR L27
                OR L28 OR L29 OR L30)
                D BIB

     FILE 'ZCAPLUS' ENTERED AT 08:51:00 ON 01 MAY 2012
CHARGED TO COST=TC1600
L32             QUE SPE=ON  ABB=ON  PLU=ON  AY<2001 OR PY<2001 OR PRY<2001 OR
                MY<2001 OR REVIEW/DT

     FILE 'HCAPLUS' ENTERED AT 08:51:58 ON 01 MAY 2012
CHARGED TO COST=TC1600
L33         725 SEA SPE=ON  ABB=ON  PLU=ON  L23
L34          26 SEA SPE=ON  ABB=ON  PLU=ON  L33 AND (L24 OR L25 OR L26 OR L27
                OR L28 OR L29 OR L30)
L35           0 SEA SPE=ON  ABB=ON  PLU=ON  L1 NOT L34
L36          26 SEA SPE=ON  ABB=ON  PLU=ON  (L34 OR L35)
L37         699 SEA SPE=ON  ABB=ON  PLU=ON  L33 NOT L36
L38         142 SEA SPE=ON  ABB=ON  PLU=ON  L37 AND L32

     FILE 'STNGUIDE' ENTERED AT 08:53:26 ON 01 MAY 2012
CHARGED TO COST=TC1600

     FILE 'LREGISTRY' ENTERED AT 08:55:08 ON 01 MAY 2012
CHARGED TO COST=TC1600
L39             STR L12

     FILE 'REGISTRY' ENTERED AT 08:55:41 ON 01 MAY 2012
CHARGED TO COST=TC1600
L40          50 SEA SUB=L14 SSS SAM L39

     FILE 'STNGUIDE' ENTERED AT 08:56:21 ON 01 MAY 2012
CHARGED TO COST=TC1600
                D QUE STAT

     FILE 'REGISTRY' ENTERED AT 08:59:05 ON 01 MAY 2012
CHARGED TO COST=TC1600
L41        6632 SEA SUB=L14 SSS FUL L39
                SAVE TEMP L41 POL658NSET2/A
L42        1421 SEA SPE=ON  ABB=ON  PLU=ON  L23 NOT L41
                SAVE TEMP L42 POL658CROSS2/A

     FILE 'STNGUIDE' ENTERED AT 09:00:19 ON 01 MAY 2012
CHARGED TO COST=TC1600
                D SAVED

     FILE 'HCAPLUS' ENTERED AT 09:00:54 ON 01 MAY 2012
CHARGED TO COST=TC1600

     FILE 'REGISTRY' ENTERED AT 09:01:03 ON 01 MAY 2012
CHARGED TO COST=TC1600
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L43          27 SEA SPE=ON  ABB=ON  PLU=ON  L16 NOT L42

     FILE 'HCAPLUS' ENTERED AT 09:02:03 ON 01 MAY 2012
CHARGED TO COST=TC1600
L44         427 SEA SPE=ON  ABB=ON  PLU=ON  L42
L45          15 SEA SPE=ON  ABB=ON  PLU=ON  L44 AND (L24 OR L25 OR L26 OR L27
                OR L28 OR L29 OR L30)
L46           0 SEA SPE=ON  ABB=ON  PLU=ON  L1 NOT L45
L47          15 SEA SPE=ON  ABB=ON  PLU=ON  (L45 OR L46)
L48         412 SEA SPE=ON  ABB=ON  PLU=ON  L44 NOT L47
L49          87 SEA SPE=ON  ABB=ON  PLU=ON  L48 AND L32

     FILE 'REGISTRY' ENTERED AT 09:03:44 ON 01 MAY 2012
CHARGED TO COST=TC1600

     FILE 'HCAPLUS' ENTERED AT 09:03:55 ON 01 MAY 2012
CHARGED TO COST=TC1600
L50             TRA PLU=ON  L49 1- RN HIT :      74 TERMS

     FILE 'REGISTRY' ENTERED AT 09:04:00 ON 01 MAY 2012
CHARGED TO COST=TC1600
L51          74 SEA SPE=ON  ABB=ON  PLU=ON  L50
L52          74 SEA SPE=ON  ABB=ON  PLU=ON  L51 NOT L2
                E SAXAGLIPTIN/CN
L53           1 SEA SPE=ON  ABB=ON  PLU=ON  SAXAGLIPTIN/CN
                D SCAN

     FILE 'STNGUIDE' ENTERED AT 09:08:27 ON 01 MAY 2012
CHARGED TO COST=TC1600

     FILE 'REGISTRY' ENTERED AT 09:08:58 ON 01 MAY 2012
CHARGED TO COST=TC1600
L54         961 SEA SPE=ON  ABB=ON  PLU=ON  L42 AND (MEDLINE OR BIOSIS OR
                EMBASE OR CABA OR BIOTECHNO OR DRUGU OR VETU OR TOXCENTER OR
                NAPRALERT)/LC

     FILE 'MEDLINE, BIOSIS, EMBASE, CABA, BIOTECHNO, DRUGU, VETU, TOXCENTER,
     NAPRALERT' ENTERED AT 09:09:45 ON 01 MAY 2012
CHARGED TO COST=TC1600
L55         859 SEA SPE=ON  ABB=ON  PLU=ON  L54
L56          10 SEA SPE=ON  ABB=ON  PLU=ON  L55 AND (L24 OR L25 OR L26 OR L27
                OR L28 OR L29 OR L30)

     FILE 'STNGUIDE' ENTERED AT 09:10:15 ON 01 MAY 2012
CHARGED TO COST=TC1600
                D QUE STAT L14
                D QUE STAT L19
                D QUE STAT L22
                D QUE STAT L23
                D QUE STAT L41
                D QUE STAT L42
                D QUE NOS L49

     FILE 'HCAPLUS' ENTERED AT 09:12:53 ON 01 MAY 2012
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CHARGED TO COST=TC1600
                SAVE TEMP L49 POL658MAINB/A

     FILE 'STNGUIDE' ENTERED AT 09:13:17 ON 01 MAY 2012
CHARGED TO COST=TC1600

     FILE 'EMBASE, TOXCENTER' ENTERED AT 09:14:16 ON 01 MAY 2012
CHARGED TO COST=TC1600

     FILE 'STNGUIDE' ENTERED AT 09:14:23 ON 01 MAY 2012
CHARGED TO COST=TC1600

     FILE 'HCAPLUS' ENTERED AT 09:14:48 ON 01 MAY 2012
CHARGED TO COST=TC1600
                D L49 IBIB ED ABS HITSTR 1-30

     FILE 'STNGUIDE' ENTERED AT 09:14:51 ON 01 MAY 2012
CHARGED TO COST=TC1600

     FILE 'HCAPLUS' ENTERED AT 09:15:22 ON 01 MAY 2012
CHARGED TO COST=TC1600
                D L49 IBIB ED ABS HITSTR 31-60

     FILE 'STNGUIDE' ENTERED AT 09:15:25 ON 01 MAY 2012
CHARGED TO COST=TC1600

     FILE 'HCAPLUS' ENTERED AT 09:15:39 ON 01 MAY 2012
CHARGED TO COST=TC1600
                D L49 IBIB ED ABS HITSTR 61-87

     FILE 'STNGUIDE' ENTERED AT 09:15:51 ON 01 MAY 2012
CHARGED TO COST=TC1600
                D QUE NOS L47
                D QUE NOS L56

     FILE 'HCAPLUS, EMBASE, TOXCENTER' ENTERED AT 09:18:09 ON 01 MAY 2012
CHARGED TO COST=TC1600
L57          16 DUP REM L47 L56 (9 DUPLICATES REMOVED)
                     ANSWERS '1-15' FROM FILE HCAPLUS
                     ANSWER '16' FROM FILE EMBASE
                SAVE TEMP L57 POL658INV/A

     FILE 'STNGUIDE' ENTERED AT 09:18:22 ON 01 MAY 2012
CHARGED TO COST=TC1600

     FILE 'HCAPLUS, EMBASE' ENTERED AT 09:18:58 ON 01 MAY 2012
CHARGED TO COST=TC1600
                D IBIB ED ABS HITSTR 1-15

     FILE 'STNGUIDE' ENTERED AT 09:19:17 ON 01 MAY 2012
CHARGED TO COST=TC1600

     FILE 'HCAPLUS, EMBASE' ENTERED AT 09:19:32 ON 01 MAY 2012
CHARGED TO COST=TC1600
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D IBIB ED ABS IND 16

FILE 'STNGUIDE' ENTERED AT 09:19:33 ON 01 MAY 2012
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FILE 'STNGUIDE' ENTERED AT 09:19:55 ON 01 MAY 2012
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FILE HOME

FILE ZCAPLUS

FILE COVERS 1907 - 1 May 2012 VOL 156 ISS 19
FILE LAST UPDATED: 30 Apr 2012 (20120430/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2011
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2011

ZCAplus now includes complete International Patent Classification (IPC) reclassification data for the fourth quarter of 2011.

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FILE HCAPLUS

FILE COVERS 1907 - 1 May 2012 VOL 156 ISS 19
FILE LAST UPDATED: 30 Apr 2012 (20120430/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2011
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2011

HCAplus now includes complete International Patent Classification (IPC) reclassification data for the fourth quarter of 2011.

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FILE REGISTRY
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STRUCTURE FILE UPDATES: 30 APR 2012 HIGHEST RN 1371687-07-8
DICTIONARY FILE UPDATES: 30 APR 2012 HIGHEST RN 1371687-07-8

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TSCA INFORMATION NOW CURRENT THROUGH DECEMBER 23, 2011

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FILE LREGISTRY
LREGISTRY IS A STATIC LEARNING FILE

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FILE STNGUIDE
FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Apr 27, 2012 (20120427/UP).

FILE MEDLINE
FILE LAST UPDATED: 28 Apr 2012 (20120428/UP). FILE COVERS 1946 TO DATE.

MEDLINE(R) is a registered trademark of the U.S. National Library of Medicine (NLM).

MEDLINE and LMEDLINE have been updated with the 2012 Medical Subject Headings (MeSH) vocabulary and tree numbers from the U.S. National Libra of Medicine (NLM). Additional information is available at:

http://www.nlm.nih.gov/pubs/techbull/nd11/nd11_medline_data_changes_2012.

The 2012 Medline reload was completed on January 29, 2012.
See HELP RLOAD for details.

Get the Content You Need Sooner with ePub Ahead of Print Records
Available in MEDLINE on STN! See NEWS for details.

This file contains CAS Registry Numbers for easy and accurate
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See HELP RANGE before carrying out any RANGE search.

FILE BIOSIS
FILE COVERS 1926 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1926 TO DATE.

RECORDS LAST ADDED: 26 April 2012 (20120426/ED)

BIOSIS has been augmented with 1.8 million archival records from 1926
through 1968. These records have been re-indexed to match current
BIOSIS indexing.

FILE EMBASE
FILE COVERAGE: EMBASE-originated material 1947 to 30 Apr 2012 (20120430/E
Unique MEDLINE content 1948 to present

EMBASE is now updated daily. SDI frequency remains weekly (default)
and biweekly.

This file contains CAS Registry Numbers for easy and accurate
substance identification.

For further assistance, please contact your local helpdesk.

FILE CABA
FILE LAST UPDATED: 25 APR 2012 <20120425/UP>
FILE COVERS 1973 TO DATE

<<< SIMULTANEOUS LEFT AND RIGHT TRUNCATION IS AVAILABLE IN
THE BASIC INDEX (/BI), ABSTRACT (/AB), AND TITLE (/TI) FIELDS >>>

FILE BIOTECHNO
FILE LAST UPDATED: 7 JAN 2004 <20040107/UP>
FILE COVERS 1980 TO 2003.
THIS FILE IS A STATIC FILE WITH NO UPDATES

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION AVAILABLE IN
/CT AND BASIC INDEX <<<

FILE DRUGU

FILE LAST UPDATED: 30 APR 2012 <20120430/UP>
>>> DERWENT DRUG FILE (SUBSCRIBER) <<<

>>> FILE COVERS 1983 TO DATE <<<

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION HAS BEEN ADDED TO
THE BASIC INDEX (/BI) FIELD <<<

FILE VETU
FILE LAST UPDATED: 2 JAN 2002 <20020102/UP>
FILE COVERS 1983-2001

FILE TOXCENTER

FILE COVERS 1907 TO 1 May 2012 (20120501/ED)

MEDLINE was last reloaded on January 29, 2011.

See HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE NAPRALERT

On March 30, the NAPRALERT database was updated with additional content indexed between 2006 and 2011.

FILE COVERS 1650 TO 2011

This file contains CAS Registry Numbers for easy and accurate substance identification.

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 NEWS  1  FEB  1  Instructor-led and on-demand STN training options available
                  from CAS
 NEWS  2  JUL 25  STN adds Australian patent full-text database,
                  AUPATFULL, including the new numeric search feature.
 NEWS  3  AUG 01  CA Sections Added to ACS Publications Web Editions
                  Platform
 NEWS  4  AUG 16  INPADOC: Coverage of German Patent Data resumed,
                  enhanced legal status
 NEWS  5  AUG 18  Upgrade now to STN Express, Version 8.5
 NEWS  6  SEP 01  CAS Journal Coverage Now Includes Ahead-of-Print
                  Articles for More Than 100 Journal Titles
 NEWS  7  SEP 01  Older Versions of STN Express to be Discontinued
                  Beginning in March 2012
 NEWS  8  SEP 09  USAN Database Updates Offer Superior Currency on STN(R)
 NEWS  9  SEP 26  STN Adds Canadian Patent Full-text Database - CANPATFULL
 NEWS 10  SEP 26  GEOREF and ENCOMPLIT databases were reloaded on
                  September 24, 2011.
 NEWS 11  SEP 26  Updates to the IFIPAT/IFIUDB/IFICDB databases have resumed.
 NEWS 12  SEP 26  ECLA Thesaurus in CA/CAplus Improves Patent Searching on STN
 NEWS 13  SEP 26  Access AUPATFULL and CANPATFULL databases with STN Viewer
 NEWS 14  OCT 26  New STN Revolutionizes Patent Searching for Professionals
 NEWS 15  DEC  1  CA/CAplus Now Includes Examiner Citations for Japanese Patents
 NEWS 16  DEC  1  CAS Expands Global Patent Coverage - Intellectual Property
                  Corporation of Malaysia Becomes 62nd Authority on CA/CAplus
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                  Microsoft Windows 7
 NEWS 18  DEC 14  Removal of ITRD and PATIPC databases from STN
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 NEWS 20  JAN 12  Structure Graphics Have Been Added to Abstracts for
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 NEWS 24  FEB  1  INPADOC Databases Enhanced with Japanese Patent
                  Classifications, Current U.S. Classification and Japanese
                  Legal Status.
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 NEWS 25  FEB  3  Access More Than 32,000 Harmonized Tariff Codes Now in
                  CHEMLIST on STN
 NEWS 26  FEB 13  PCTFULL Documents with Non-Latin Filing Language Enhanced
                  with English Machine Translations
 NEWS 27  FEB 28  REACH List of Registered Substances Now in CHEMLIST on STN
 NEWS 28  MAR 12  RTECS Database on STN Enhanced with Aquatic and In Vitro
                  Exposure Toxicity Data
 NEWS 29  MAR 12  MARPAT Database Enhanced with Additional Markush Backfile
                  Content for STN
 NEWS 30  MAR 19  The 1MOBILITY and 2MOBILITY databases were reloaded on
                  March 18, 2012
 NEWS 31  MAR 19  STN Adds Chinese Patent Full Text Database - CNFULL
 NEWS 32  MAR 19  Get the Content You Need Sooner with ePub Ahead of Print
                  Records Available in MEDLINE on STN!
 NEWS 33  MAR 30  NAPRALERT Updated with More Natural Products Information
 NEWS 34  APR  9  CAS Expands Global Patent Coverage - The Eurasian Patent
                  Organization Becomes 63rd Authority on CA/CAplus
 NEWS 35  APR 16  DWPI Database (WPINDEX, WPIDS, WPIX) Enhanced with
                  Numerical Property Search Feature
 NEWS 36  APR 23  RSS Delivery for STN Alerts (SDIs) is Now Available on STN

 NEWS EXPRESS 18 AUGUST 2011 CURRENT WINDOWS VERSION IS V8.5,
              AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2011.

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STRUCTURE FILE UPDATES:   29 APR 2012  HIGHEST RN 1371145-50-4
DICTIONARY FILE UPDATES:  29 APR 2012  HIGHEST RN 1371145-50-4
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  Please note that search-term pricing does apply when
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REGISTRY includes numerically searchable data for experimental and
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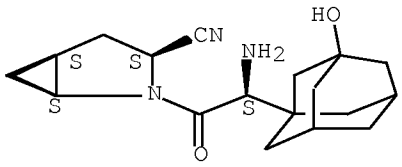
*** YOU HAVE NEW MAIL ***

=> s saxagliptin/cn
L1   1 SAXAGLIPTIN/CN

=> d l1

L1   ANSWER 1 OF 1 REGISTRY COPYRIGHT 2012 ACS on STN
RN   361442-04-8 REGISTRY
ED   Entered STN: 11 Oct 2001
CN   2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
     2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-,
     (1S,3S,5S)- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
     2-[(2S)-amino(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-, (1S,3S,5S)-
     (9CI)
OTHER NAMES:
CN   BMS 477118
CN   BMS 477118-11
CN   Onglyza
CN   Saxagliptin
FS   STEREOSEARCH
DR   1339955-48-4
MF   C18 H25 N3 O2
CI   COM
SR   CA
LC   STN Files: ADISINSIGHT, ANABSTR, CA, CAPLUS, CASREACT, CBNB, CHEMCATS,
       CHEMLIST, DDFU, DRUGU, EMBASE, IMSPATENTS, IMSRESEARCH, IPA, MRCK*,
       PATDPASPC, PS, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL
         (*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

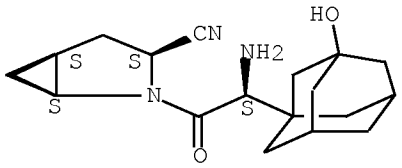
313 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
330 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> s saxagliptin
L2 5 SAXAGLIPTIN

=> d l2 1-
YOU HAVE REQUESTED DATA FROM 5 ANSWERS - CONTINUE? Y/(N):y

L2 ANSWER 1 OF 5 REGISTRY COPYRIGHT 2012 ACS on STN
RN 945667-22-1 REGISTRY
ED Entered STN: 28 Aug 2007
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-, hydrate
(1:1), (1S,3S,5S)- (CA INDEX NAME)
OTHER NAMES:
CN Saxagliptin hydrate
FS STEREOSEARCH
MF C18 H25 N3 O2 . H2 O
SR CAS Client Services
LC STN Files: ADISINSIGHT, CA, CAPLUS, CASREACT, CHEMCATS, EMBASE,
IMSPATENTS, IMSRESEARCH, IPA, MRCK*, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
CRN (361442-04-8)

Absolute stereochemistry.



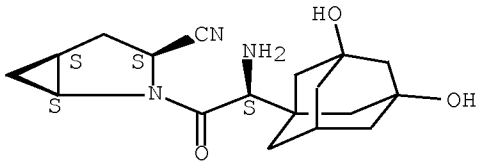
● H2O

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 2 OF 5 REGISTRY COPYRIGHT 2012 ACS on STN
RN 841302-24-7 REGISTRY
ED Entered STN: 03 Mar 2005
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(3,5-dihydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-,
(1S,3S,5S)- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-amino(3,5-dihydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-,
(1S,3S,5S)- (9CI)
OTHER NAMES:
CN 5-Hydroxy saxagliptin
CN BMS 510849
CN M2 saxagliptin hydroxylated metabolite
FS STEREOSEARCH
MF C18 H25 N3 O3
CI COM
SR CA
LC STN Files: CA, CAPLUS, CASREACT, CHEMCATS, TOXCENTER, USPAT2, USPATFULL

Absolute stereochemistry.



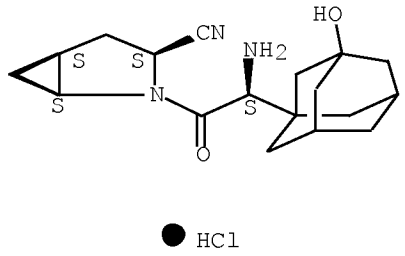
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

6 REFERENCES IN FILE CA (1907 TO DATE)
7 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 3 OF 5 REGISTRY COPYRIGHT 2012 ACS on STN
RN 709031-78-7 REGISTRY
ED Entered STN: 13 Jul 2004
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-,
hydrochloride (1:1), (1S,3S,5S)- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-amino(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-,
monohydrochloride, (1S,3S,5S)- (9CI)
OTHER NAMES:
CN Saxagliptin hydrochloride
FS STEREOSEARCH
MF C18 H25 N3 O2 . Cl H
SR CA

LC STN Files: CA, CAPLUS, CASREACT, CHEMCATS, PATDPASPC, TOXCENTER, USPAT2, USPATFULL
CRN (361442-04-8)

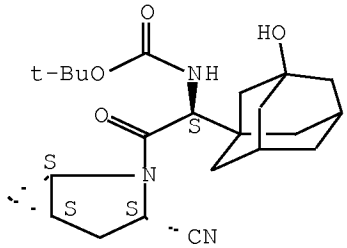
Absolute stereochemistry.



12 REFERENCES IN FILE CA (1907 TO DATE)
12 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 4 OF 5 REGISTRY COPYRIGHT 2012 ACS on STN
RN 709031-43-6 REGISTRY
ED Entered STN: 13 Jul 2004
CN Carbamic acid, N-[(1S)-2-[(1S,3S,5S)-3-cyano-2-azabicyclo[3.1.0]hex-2-yl]-1-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)-2-oxoethyl]-, 1,1-dimethylethyl ester (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Carbamic acid, [(1S)-2-[(1S,3S,5S)-3-cyano-2-azabicyclo[3.1.0]hex-2-yl]-1-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)-2-oxoethyl]-, 1,1-dimethylethyl ester (9CI)
OTHER NAMES:
CN Boc-saxagliptin
FS STEREOSEARCH
MF C23 H33 N3 O4
CI COM
SR CA
LC STN Files: CA, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, TOXCENTER, USPAT2, USPATFULL

Absolute stereochemistry.

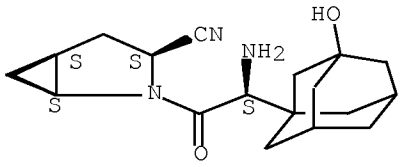


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

14 REFERENCES IN FILE CA (1907 TO DATE)
14 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 5 OF 5 REGISTRY COPYRIGHT 2012 ACS on STN
RN 361442-04-8 REGISTRY
ED Entered STN: 11 Oct 2001
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-,
(1S,3S,5S)- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-amino(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-, (1S,3S,5S)-
(9CI)
OTHER NAMES:
CN BMS 477118
CN BMS 477118-11
CN Onglyza
CN Saxagliptin
FS STEREOSEARCH
DR 1339955-48-4
MF C18 H25 N3 O2
CI COM
SR CA
LC STN Files: ADISINSIGHT, ANABSTR, CA, CAPLUS, CASREACT, CBNB, CHEMCATS,
CHEMLIST, DDFU, DRUGU, EMBASE, IMSPATENTS, IMSRESEARCH, IPA, MRCK*,
PATDPASPC, PS, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

313 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
330 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> display set notice

```
SET PARAMETER CURRENT  PERMANENT LOGIN  DEFAULT
------------- -------  --------- ------ -------
NOTICE (USD)
  DISPLAY     'OFF'              'OFF'  '100'
  SEARCH      '1000'             '1000' '1000'


=>  FILE REG


FILE 'REGISTRY' ENTERED AT 15:46:17 ON 30 APR 2012
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DICTIONARY FILE UPDATES:  29 APR 2012  HIGHEST RN 1371145-50-4

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TSCA INFORMATION NOW CURRENT THROUGH DECEMBER 23, 2011

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REGISTRY includes numerically searchable data for experimental and
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experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> STR 361442-04-8

:END

L3   STRUCTURE CREATED

=> S L3 FAM SAM

SAMPLE SEARCH INITIATED 15:46:20 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -       12 TO ITERATE

100.0% PROCESSED       12 ITERATIONS                              2 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:           33 TO      447
PROJECTED ANSWERS:               2 TO      124
```

L4 2 SEA FAM SAM L3

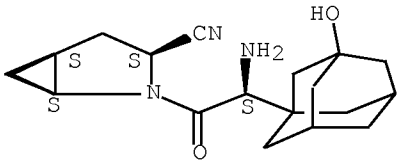
=>

=> D SCAN

L4 2 ANSWERS REGISTRY COPYRIGHT 2012 ACS on STN
IN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-,
(1S,3S,5S)-, (2Z)-2-butenedioate (1:1)
MF C18 H25 N3 O2 . C4 H4 O4

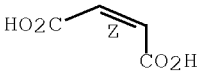
CM 1

Absolute stereochemistry.



CM 2

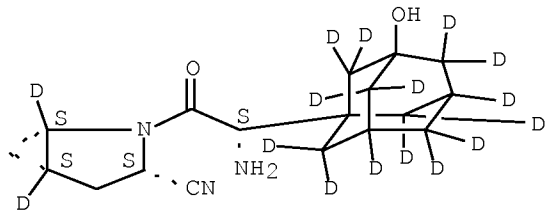
Double bond geometry as shown.



HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L4 2 ANSWERS REGISTRY COPYRIGHT 2012 ACS on STN
IN 2-Azabicyclo[3.1.0]hexane-1,5-d2-3-carbonitrile,
2-[(2S)-2-amino-2-(7-hydroxytricyclo[3.3.1.13,7]dec-1-yl-
2,2,3,4,4,5,6,6,8,8,9,9,10,10-d14)acetyl]-, (1S,3S,5S)-
MF C18 H9 D16 N3 O2

Absolute stereochemistry.



ALL ANSWERS HAVE BEEN SCANNED

=> fil REGISTRY

FILE 'REGISTRY' ENTERED AT 15:46:33 ON 30 APR 2012
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STRUCTURE FILE UPDATES: 29 APR 2012 HIGHEST RN 1371145-50-4
DICTIONARY FILE UPDATES: 29 APR 2012 HIGHEST RN 1371145-50-4

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  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

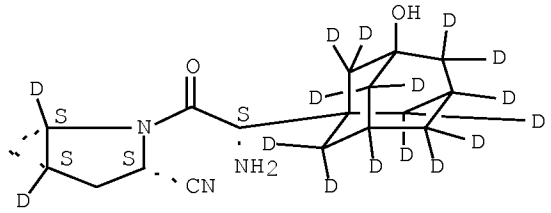
*** YOU HAVE NEW MAIL ***

=> d l4 2

L4   ANSWER 2 OF 2 REGISTRY COPYRIGHT 2012 ACS on STN
RN   1227074-04-5 REGISTRY
ED   Entered STN: 07 Jun 2010
CN   2-Azabicyclo[3.1.0]hexane-1,5-d2-3-carbonitrile,
     2-[(2S)-2-amino-2-(7-hydroxytricyclo[3.3.1.13,7]dec-1-yl-
     2,2,3,4,4,5,6,6,8,8,9,9,10,10-d14)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)
FS   STEREOSEARCH
MF   C18 H9 D16 N3 O2

SR   CA
LC   STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> d hist

(FILE 'HOME' ENTERED AT 15:43:05 ON 30 APR 2012)

FILE 'REGISTRY' ENTERED AT 15:43:22 ON 30 APR 2012
L1   1 S SAXAGLIPTIN/CN
L2   5 S SAXAGLIPTIN

FILE 'REGISTRY' ENTERED AT 15:46:17 ON 30 APR 2012
L3   STR 361442-04-8
L4   2 S L3 FAM SAM

FILE 'REGISTRY' ENTERED AT 15:46:33 ON 30 APR 2012

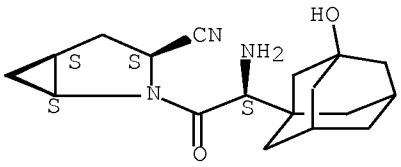
=> s 361442-04-8/crn
L5   48 361442-04-8/CRN

=> d scan

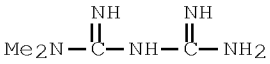
L5   48 ANSWERS   REGISTRY COPYRIGHT 2012 ACS on STN
IN   Imidodicarbonimidic diamide, N,N-dimethyl-, mixt. with
     (1S,3S,5S)-2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.13,7]dec-1-
     yl)acetyl]-2-azabicyclo[3.1.0]hexane-3-carbonitrile
MF   C18 H25 N3 O2 . C4 H11 N5
CI   MXS

     CM   1

Absolute stereochemistry.



CM 2

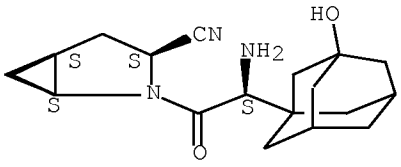


HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

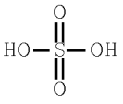
L5 48 ANSWERS REGISTRY COPYRIGHT 2012 ACS on STN
IN Sulfuric acid diammonium salt, compd. with (1S,3S,5S)-2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-2-azabicyclo[3.1.0]hexane-3-carbonitrile (1:1)
MF C18 H25 N3 O2 . 2 H3 N . H2 O4 S

CM 1

Absolute stereochemistry.



CM 2



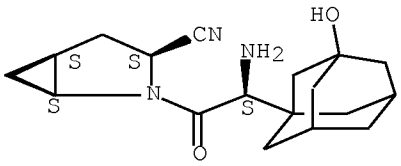
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L5 48 ANSWERS REGISTRY COPYRIGHT 2012 ACS on STN

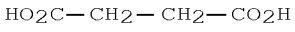
IN Butanedioic acid, compd. with (1S,3S,5S)-2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-2-azabicyclo[3.1.0]hexane-3-carbonitrile (1:1)
MF C18 H25 N3 O2 . C4 H6 O4

CM 1

Absolute stereochemistry.



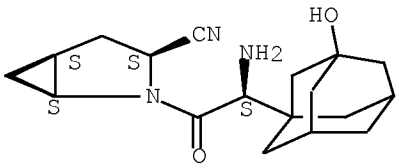
CM 2

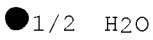


HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L5 48 ANSWERS REGISTRY COPYRIGHT 2012 ACS on STN
IN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-, hydrate (2:1), (1S,3S,5S)-
MF C18 H25 N3 O2 . 1/2 H2 O

Absolute stereochemistry.





HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> d hist

(FILE 'HOME' ENTERED AT 15:43:05 ON 30 APR 2012)

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     FILE 'REGISTRY' ENTERED AT 15:43:22 ON 30 APR 2012
L1             1 S SAXAGLIPTIN/CN
L2             5 S SAXAGLIPTIN

     FILE 'REGISTRY' ENTERED AT 15:46:17 ON 30 APR 2012
L3               STR 361442-04-8
L4             2 S L3 FAM SAM

     FILE 'REGISTRY' ENTERED AT 15:46:33 ON 30 APR 2012
L5            48 S 361442-04-8/CRN

=> fil caplus uspatful

FILE 'CAPLUS' ENTERED AT 15:50:20 ON 30 APR 2012
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FILE 'USPATFULL' ENTERED AT 15:50:20 ON 30 APR 2012
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=> s l1
L6          480 L1

=> s l1<chem>

   SmartSELECT INITIATED
New TRANSFER and ANALYZE Commands Now Available
See HELP TRANSFER and HELP ANALYZE for Details



FILE 'REGISTRY' ENTERED AT 15:50:53 ON 30 APR 2012
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*** YOU HAVE NEW MAIL ***

SET SMARTSELECT ON
SET COMMAND COMPLETED

SEL L1 1- CHEM
L7           SEL L1 1- CHEM :       6 TERMS

SET SMARTSELECT OFF
SET COMMAND COMPLETED



FILE 'CAPLUS' ENTERED AT 15:50:53 ON 30 APR 2012
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```

```
FILE 'USPATFULL' ENTERED AT 15:50:53 ON 30 APR 2012
CA INDEXING COPYRIGHT (C) 2012 AMERICAN CHEMICAL SOCIETY (ACS)

S L7
L8        1242 L7

=> dup remove l6
PROCESSING COMPLETED FOR L6
L9         454 DUP REMOVE L6 (26 DUPLICATES REMOVED)

=> dup remove l8
PROCESSING COMPLETED FOR L8
L10       1218 DUP REMOVE L8 (24 DUPLICATES REMOVED)

=> s l9 or l10
L11       1228 L9 OR L10

=> s l11 and PD<20000309
L12          0 L11 AND PD<20000309

=> s l11 and AD<20000309
L13          0 L11 AND AD<20000309

=> s l11 and AD<20000312
L14          0 L11 AND AD<20000312

=> s l11 and AD<20010312
L15          0 L11 AND AD<20010312

=> s l11 and AD<20020312
L16          0 L11 AND AD<20020312

=> s l11 and AY<2002
L17          0 L11 AND AY<2002

=> s l11 and AY>2002
L18       1071 L11 AND AY>2002

=> s l11 and AY>2000
L19       1071 L11 AND AY>2000

=> s l11 and PRD<20020312
L20          1 L11 AND PRD<20020312

=> D IBIB ABS L20

L20  ANSWER 1 OF 1  USPATFULL on STN
ACCESSION NUMBER:       2009:320331  USPATFULL Full-text
TITLE:                  Amide Compounds
INVENTOR(S):            Kitamura, Shuji, Osaka, JAPAN
                        Aicher, Thomas Daniel, Superior, CO, UNITED STATES
                        Gonzales, Steve, Media, PA, UNITED STATES
                        Le Huerou, Yvan, Boulder, CO, UNITED STATES
                        Pratt, Scott Alan, Longmont, CO, UNITED STATES
                        Turner, Tim, Longmont, CO, UNITED STATES
                        Nakada, Yoshihisa, Osaka, JAPAN
```

PATENT ASSIGNEE(S): TAKEDA PHARMACEUTICAL COMPANY LIMITED, OSAKA, JAPAN
(non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 20090286791	A1	20091119	
APPLICATION INFO.:	US 2007-309493	A1	20070720	(12)
	WO 2007-US16425		20070720	
			20090414	PCT 371 date

	NUMBER	DATE	
PRIORITY INFORMATION:	EP 2001-127442	20011127	<--
	US 2006-832115P	20060721	(60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: WENDEROTH, LIND & PONACK, L.L.P., 1030 15th Street, N.W.,, Suite 400 East, Washington, DC, 20005-1503, US
NUMBER OF CLAIMS: 29
EXEMPLARY CLAIM: 1
LINE COUNT: 7740
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides compounds represented by the formula (Ia):

##STR1##

the formula (Ib):

##STR2##

the formula (Ic):

##STR3##

and the formula (Id):

##STR4##

wherein each symbol is as defined in the specification.

According to the present invention, these compounds have a DGAT inhibitory activity and are useful for the prophylaxis, treatment or improvement of diseases or pathologies caused by high expression or high activation of DGAT.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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=> s l11 and ROBL/IN
L21          0 L11 AND ROBL/IN

=> s l11 and (ROBL JEFFREY A/IN)
L22          3 L11 AND (ROBL JEFFREY A/IN)

=> D TI L22 1-
YOU HAVE REQUESTED DATA FROM 3 ANSWERS - CONTINUE? Y/(N):Y

L22  ANSWER 1 OF 3  USPATFULL on STN
TI     HYDROXY SUBSTITUTED THIENO PYRIMIDINONES AS MELANIN CONCENTRATING
       HORMONE RECEPTOR-1 ANTAGONISTS

L22  ANSWER 2 OF 3  USPATFULL on STN
TI     HMG-CoA reductase inhibitors

L22  ANSWER 3 OF 3  USPATFULL on STN
TI     HMG-CoA reductase inhibitors and method


=> D IBIB L22 1-
YOU HAVE REQUESTED DATA FROM 3 ANSWERS - CONTINUE? Y/(N):Y

L22  ANSWER 1 OF 3  USPATFULL on STN
ACCESSION NUMBER:       2009:333876  USPATFULL Full-text
TITLE:                  HYDROXY SUBSTITUTED THIENO PYRIMIDINONES AS MELANIN
                        CONCENTRATING HORMONE RECEPTOR-1 ANTAGONISTS
INVENTOR(S):            Washburn, William N., Titusville, NJ, UNITED STATES
                        Ahmad, Saleem, Wall, NJ, UNITED STATES
                        Devasthale, Pratik, Plainsboro, NJ, UNITED STATES
                        Robl, Jeffrey A., Newtown, PA, UNITED STATES
                        Goswami, Animesh, Plainsboro, NJ, UNITED STATES
                        Guo, Zhiwei, Franklin Park, NJ, UNITED STATES
                        Patel, Ramesh N., Bridgewater, NJ, UNITED STATES
PATENT ASSIGNEE(S):     Bristol-Myers Squibb Company (U.S. corporation)

                             NUMBER       KIND    DATE
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PATENT INFORMATION:     US 20090298794     A1   20091203
                        US 7989433         B2   20110802
APPLICATION INFO.:      US 2009-473346     A1   20090528  (12)

                               NUMBER             DATE
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PRIORITY INFORMATION:   US 2008-56949P          20080529 (61)
DOCUMENT TYPE:          Utility
FILE SEGMENT:           APPLICATION
LEGAL REPRESENTATIVE:   LOUIS J. WILLE, BRISTOL-MYERS SQUIBB COMPANY, PATENT
                        DEPARTMENT, P O BOX 4000, PRINCETON, NJ, 08543-4000, US
NUMBER OF CLAIMS:       23
EXEMPLARY CLAIM:        1
LINE COUNT:             2167
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L22  ANSWER 2 OF 3  USPATFULL on STN
```

ACCESSION NUMBER: 2007:285027 USPATFULL Full-text
TITLE: HMG-CoA reductase inhibitors
INVENTOR(S): Stein, Philip D., Pennington, NJ, UNITED STATES
Seitz, Steven P., Swarthmore, PA, UNITED STATES
Carini, David J., Wallingford, CT, UNITED STATES
Shi, Yan, Flourtown, PA, UNITED STATES
Robl, Jeffrey A., Newtown, PA, UNITED STATES
Markwalder, Jay A., New London, PA, UNITED STATES
He, Chunhong, Boothwyn, PA, UNITED STATES
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 20070249583	A1	20071025
	US 7659281	B2	20100209
APPLICATION INFO.:	US 2007-789335	A1	20070424 (11)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2006-794733P	20060425 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: LOUIS J. WILLE, BRISTOL-MYERS SQUIBB COMPANY, PATENT DEPARTMENT, P O BOX 4000, PRINCETON, NJ, 08543-4000, US
NUMBER OF CLAIMS: 24
EXEMPLARY CLAIM: 1
LINE COUNT: 8226
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L22 ANSWER 3 OF 3 USPATFULL on STN
ACCESSION NUMBER: 2005:99578 USPATFULL Full-text
TITLE: HMG-CoA reductase inhibitors and method
INVENTOR(S): Ahmad, Saleem, Wall, NJ, UNITED STATES
Robl, Jeffrey A., Newtown, PA, UNITED STATES
Ngu, Khehyong, Pennington, NJ, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 20050085497	A1	20050421
	US 7371759	B2	20080513
APPLICATION INFO.:	US 2004-946055	A1	20040921 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2003-505893P	20030925 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: STEPHEN B. DAVIS, BRISTOL-MYERS SQUIBB COMPANY, PATENT DEPARTMENT, P O BOX 4000, PRINCETON, NJ, 08543-4000, US
NUMBER OF CLAIMS: 25
EXEMPLARY CLAIM: 1
LINE COUNT: 2114
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> s l11 and PRD<20030101

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L23          5 L11 AND PRD<20030101

=> D IBIB L23 1-
YOU HAVE REQUESTED DATA FROM 5 ANSWERS - CONTINUE? Y/(N):Y

L23  ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2012 ACS on STN
ACCESSION NUMBER:         2004:515478  CAPLUS Full-text
DOCUMENT NUMBER:          141:54618
TITLE:                    Preparation of cyclopropyl-fused pyrrolidine-based
                          inhibitors of dipeptidyl peptidase IV
INVENTOR(S):              Vu, Truc Chi; Brzozowski, David B.; Fox, Rita;
                          Godfrey, Jollie Duaine, Jr.; Hanson, Ronald L.;
                          Kolotuchin, Sergei V.; Mazzullo, John A., Jr.; Patel,
                          Ramesh N.; Wang, Jianji; Wong, Kwok; Yu, Jurong; Zhu,
                          Jason; Magnin, David R.; Augeri, David J.; Hamann,
                          Lawrence G.
PATENT ASSIGNEE(S):       Bristol-Myers Squibb Company, USA
SOURCE:                   PCT Int. Appl., 101 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ---------------     ----   --------    --------------------   --------
     WO 2004052850        A2    20040624    WO 2003-US38558        20031204 <--
     WO 2004052850        A3    20060302
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
             GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
             LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
             OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
             TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
             ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
             TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     US 20050090539       A1    20050428    US 2003-716012         20031118 <--
     US 7420079           B2    20080902
     CA 2508619           A1    20040624    CA 2003-2508619        20031204 <--
     AU 2003297647        A1    20040630    AU 2003-297647         20031204 <--
     EP 1581487           A2    20051005    EP 2003-812799         20031204 <--
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
     BR 2003017139        A     20051129    BR 2003-17139          20031204 <--
     CN 1791401           A     20060621    CN 2003-80109631       20031204 <--
     JP 2006516121        T     20060622    JP 2004-559282         20031204 <--
     JP 4886193           B2    20120229
     CN 102070451         A     20110525    CN 2010-10260709       20031204 <--
     IN 2005DN02279       A     20090123    IN 2005-DN2279         20050530 <--
     IN 244388            A1    20101210
     MX 2005005970        A     20050818    MX 2005-5970           20050603 <--
     IN 2008DN00420       A     20080215    IN 2008-DN420          20080115 <--
     US 20090018311       A1    20090115    US 2008-181216         20080728 <--
     US 7705033           B2    20100427
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US 20100274025	A1	20101028	US 2010-712958		20100225 <--
JP 2011006440	A	20110113	JP 2010-181557		20100816 <--
JP 2011006441	A	20110113	JP 2010-181559		20100816 <--
PRIORITY APPLN. INFO.:			US 2002-431814P	P	20021209 <--
			US 2003-716012	A3	20031118
			CN 2003-80109631	A3	20031204
			JP 2004-559282	A3	20031204
			WO 2003-US38558	W	20031204
			IN 2005-DN2279	A3	20050530
			US 2008-181216	A3	20080728

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 141:54618; MARPAT 141:54618
OS.CITING REF COUNT: 25 THERE ARE 25 CAPLUS RECORDS THAT CITE THIS RECORD (35 CITINGS)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 2 OF 5 USPATFULL on STN
ACCESSION NUMBER: 2010:307761 USPATFULL Full-text
TITLE: METHODS AND COMPOUNDS FOR PRODUCING DIPEPTIDYL PEPTIDASE IV INHIBITORS AND INTERMEDIATES THEREOF
INVENTOR(S): Vu, Truc Chi, Watchung, NJ, UNITED STATES
Brzozowski, David B., Pattersonville, NY, UNITED STATES
Fox, Rita, Princeton, NJ, UNITED STATES
Godfrey, JR., Jollie Duaine, Ewing, NJ, UNITED STATES
Hanson, Ronald L., Morris Plains, NJ, UNITED STATES
Kolotuchin, Sergei V., Roselle Park, NJ, UNITED STATES
Mazzullo, John A., Florence, SC, UNITED STATES
Patel, Ramesh N., Bridgewater, NJ, UNITED STATES
Wang, Jianji, Dayton, NJ, UNITED STATES
Wong, Kwok, Lawrenceville, NJ, UNITED STATES
Yu, Jurong, Dayton, NJ, UNITED STATES
Zhu, Jason J., East Brunswick, NJ, UNITED STATES
Magnin, David R., Sumter, SC, UNITED STATES
Augeri, David J., Princeton, NJ, UNITED STATES
Hamann, Lawrence G., North Grafton, MA, UNITED STATES
PATENT ASSIGNEE(S): BRISTOL-MYERS SQUIBB COMPANY, Princeton, NJ, UNITED STATES (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 20100274025	A1	20101028
APPLICATION INFO.:	US 2010-712958	A1	20100225 (12)

RELATED APPLN. INFO.: Division of Ser. No. US 2008-181216, filed on 28 Jul 2008, Pat. No. US 7705033 Division of Ser. No. US 2003-716012, filed on 18 Nov 2003, Pat. No. US 7420079

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2002-431814P	20021209 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: McDonnell Boehnen Hulbert & Berghoff LLP, Bristol-Myers Squibb, 300 South Wacker Drive, Chicago, IL, 60606, US
NUMBER OF CLAIMS: 22
EXEMPLARY CLAIM: 1

LINE COUNT: 2619
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L23 ANSWER 3 OF 5 USPATFULL on STN
ACCESSION NUMBER: 2009:320331 USPATFULL Full-text
TITLE: Amide Compounds
INVENTOR(S): Kitamura, Shuji, Osaka, JAPAN
Aicher, Thomas Daniel, Superior, CO, UNITED STATES
Gonzales, Steve, Media, PA, UNITED STATES
Le Huerou, Yvan, Boulder, CO, UNITED STATES
Pratt, Scott Alan, Longmont, CO, UNITED STATES
Turner, Tim, Longmont, CO, UNITED STATES
Nakada, Yoshihisa, Osaka, JAPAN
PATENT ASSIGNEE(S): TAKEDA PHARMACEUTICAL COMPANY LIMITED, OSAKA, JAPAN
(non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 20090286791	A1	20091119	
APPLICATION INFO.:	US 2007-309493	A1	20070720	(12)
	WO 2007-US16425		20070720	
			20090414	PCT 371 date

	NUMBER	DATE	
PRIORITY INFORMATION:	EP 2001-127442	20011127	<--
	US 2006-832115P	20060721	(60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: WENDEROTH, LIND & PONACK, L.L.P., 1030 15th Street, N.W.,, Suite 400 East, Washington, DC, 20005-1503, US
NUMBER OF CLAIMS: 29
EXEMPLARY CLAIM: 1
LINE COUNT: 7740
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L23 ANSWER 4 OF 5 USPATFULL on STN
ACCESSION NUMBER: 2009:19680 USPATFULL Full-text
TITLE: METHODS AND COMPOUNDS FOR PRODUCING DIPEPTIDYL PEPTIDASE IV INHIBITORS AND INTERMEDIATES THEREOF
INVENTOR(S): Vu, Truc Chi, Watchung, NJ, UNITED STATES
Brzozowski, David B., Pattersonville, NY, UNITED STATES
Fox, Rita, Princeton, NJ, UNITED STATES
Godfrey, JR., Jollie Duaine, Ewing, NJ, UNITED STATES
Hanson, Ronald L., Morris Plains, NJ, UNITED STATES
Kolotuchin, Sergei V., Roselle Park, NJ, UNITED STATES
Mazzullo, John A., Florence, SC, UNITED STATES
Patel, Ramesh N., Bridgewater, NJ, UNITED STATES
Wang, Jianji, Dayton, NJ, UNITED STATES
Wong, Kwok, Lawrenceville, NJ, UNITED STATES
Yu, Jurong, Dayton, NJ, UNITED STATES
Zhu, Jason J., East Brunswick, NJ, UNITED STATES
Magnin, David R., Sumter, SC, UNITED STATES
Augeri, David J., Princeton, NJ, UNITED STATES
Hamann, Lawrence G., North Grafton, MA, UNITED STATES
PATENT ASSIGNEE(S): BRISTOL-MYERS SQUIBB COMPANY, Princeton, NJ, UNITED

STATES (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 20090018311	A1	20090115
	US 7705033	B2	20100427
APPLICATION INFO.:	US 2008-181216	A1	20080728 (12)

RELATED APPLN. INFO.: Division of Ser. No. US 2003-716012, filed on 18 Nov 2003, Pat. No. US 7420079

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-431814P	20021209 (60) <--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: McDonnell Boehnen Hulbert & Berghoff LLP, Bristol-Myers Squibb, 300 South Wacker Drive, Chicago, IL, 60606, US
NUMBER OF CLAIMS: 25
EXEMPLARY CLAIM: 1
LINE COUNT: 2646
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L23 ANSWER 5 OF 5 USPATFULL on STN
ACCESSION NUMBER: 2005:105601 USPATFULL Full-text
TITLE: Methods and compounds for producing dipeptidyl peptidase IV inhibitors and intermediates thereof
INVENTOR(S): Vu, Truc Chi, Watchung, NJ, UNITED STATES
Brzozowski, David B., Island Lake, IL, UNITED STATES
Fox, Rita, Princeton, NJ, UNITED STATES
Godfrey, Jollie Duaine JR., Ewing, NJ, UNITED STATES
Hanson, Ronald L., Morris Plains, NJ, UNITED STATES
Kolotuchin, Sergei V., Roselle Park, NJ, UNITED STATES
Mazzullo, John A., Florence, SC, UNITED STATES
Patel, Ramesh N., Bridgewater, NJ, UNITED STATES
Wang, Jianji, Dayton, NJ, UNITED STATES
Wong, Kwok, Lawrenceville, NJ, UNITED STATES
Yu, Jurong, Dayton, NJ, UNITED STATES
Zhu, Jason J., East Brunswick, NJ, UNITED STATES
Magnin, David R., Hamilton, NJ, UNITED STATES
Augeri, David J., Princeton, NJ, UNITED STATES
Hamann, Lawrence G., Cherry Hill, NJ, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 20050090539	A1	20050428
	US 7420079	B2	20080902
APPLICATION INFO.:	US 2003-716012	A1	20031118 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-431814P	20021209 (60) <--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: STEPHEN B. DAVIS, BRISTOL-MYERS SQUIBB COMPANY, PATENT DEPARTMENT, P O BOX 4000, PRINCETON, NJ, 08543-4000, US
NUMBER OF CLAIMS: 31

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EXEMPLARY CLAIM:        1
LINE COUNT:             2603
CAS INDEXING IS AVAILABLE FOR THIS PATENT.


=> D US6395767/PN
'US6395767' MUST END IN '/Q', '/A', '/L', '/S' OR '/B'
The saved name for a query (or structure or screen set) must end with
'/Q'.  The saved name for an answer set must end with '/A'.  The saved
name for an L# list must end with '/L'.  SDI request names must end
with '/S'.  To see a list of all saved query, answer set,, and L# list
names for this loginid, enter "DISPLAY SAVED" at an arrow
prompt (=>).  Enter "DISPLAY SAVED/S" to see a list of SDI request
names.  Enter "DISPLAY SAVED/B" to see a list of BATCH search
requests.

=> S US6395767/PN
L24          2 US6395767/PN

=> DUP REMOV L24
PROCESSING COMPLETED FOR L24
L25           2 DUP REMOV L24 (0 DUPLICATES REMOVED)

=> D IBIB L24 1-
YOU HAVE REQUESTED DATA FROM 2 ANSWERS - CONTINUE? Y/(N):Y

L24  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2012 ACS on STN
ACCESSION NUMBER:        2001:693281  CAPLUS Full-text
DOCUMENT NUMBER:         135:257147
TITLE:                   Preparation of fused cyclopropylpyrrolidine-based
                         inhibitors of dipeptidyl peptidase IV
INVENTOR(S):             Robl, Jeffrey A.; Sulsky, Richard B.; Augeri, David
                         J.; Magnin, David R.; Hamann, Lawrence G.; Betebenner,
                         David A.
PATENT ASSIGNEE(S):      Bristol-Myers Squibb Co., USA
SOURCE:                  PCT Int. Appl., 135 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ---------------     ----   --------    --------------------   --------
     WO 2001068603        A2    20010920    WO 2001-US7151         20010305
     WO 2001068603        A3    20020214
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,
             CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
             ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
             LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
             SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     US 20020019411       A1    20020214    US 2001-788173         20010216
     US 6395767           B2    20020528                                  <--
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CA 2402894	A1	20010920	CA 2001-2402894	20010305
CA 2402894	C	20120417		
AU 2001045466	A	20010924	AU 2001-45466	20010305
EP 1261586	A2	20021204	EP 2001-918383	20010305
EP 1261586	B1	20080521		
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JP 2003531118	T	20031021	JP 2001-567699	20010305
JP 4460205	B2	20100512		
HU 2003002792	A2	20031229	HU 2003-2792	20010305
HU 2003002792	A3	20070328		
BR 2001009115	A	20031230	BR 2001-9115	20010305
NZ 520821	A	20041126	NZ 2001-520821	20010305
AU 2001245466	B2	20050512	AU 2001-245466	20010305
CN 1213028	C	20050803	CN 2001-806315	20010305
EP 1559710	A2	20050803	EP 2005-5368	20010305
EP 1559710	A3	20090722		
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CN 1698601	A	20051123	CN 2005-10078518	20010305
TW 258468	B	20060721	TW 2001-104965	20010305
RU 2286986	C2	20061110	RU 2002-125491	20010305
AT 396176	T	20080615	AT 2001-918383	20010305
PT 1261586	E	20080804	PT 2001-918383	20010305
ES 2305062	T3	20081101	ES 2001-918383	20010305
SG 152030	A1	20090529	SG 2004-5783	20010305
IL 151372	A	20091224	IL 2001-151372	20010305
IL 177018	A	20100328	IL 2001-177018	20010305
PL 207041	B1	20101029	PL 2001-365520	20010305
EP 2272825	A2	20110112	EP 2010-178907	20010305
EP 2272825	A3	20110504		
R: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE, TR				
IN 2002MN01154	A	20050304	IN 2002-MN1154	20020823
ZA 2002006816	A	20031126	ZA 2002-6816	20020826
NO 2002004295	A	20021106	NO 2002-4295	20020909
NO 324227	B1	20070910		
KR 754089	B1	20070831	KR 2002-7011806	20020909
MX 2002008837	A	20030425	MX 2002-8837	20020910
HK 1049330	A1	20081114	HK 2003-101079	20030214
KR 758407	B1	20070914	KR 2006-7004515	20060303
IN 2007MN00184	A	20080215	IN 2007-MN184	20070205
JP 2010077163	A	20100408	JP 2010-6181	20100114
PRIORITY APPLN. INFO.:			US 2000-188555P	P 20000310
			CN 2001-806315	A3 20010305
			EP 2001-918383	A3 20010305
			EP 2005-5368	A3 20010305
			IL 2001-151372	A3 20010305
			JP 2001-567699	A3 20010305
			WO 2001-US7151	W 20010305
			IN 2002-MN1154	A3 20020823
			KR 2002-7011806	A3 20020909

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 135:257147
OS.CITING REF COUNT: 35 THERE ARE 35 CAPLUS RECORDS THAT CITE THIS RECORD (60 CITINGS)

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REFERENCE COUNT:          11    THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24  ANSWER 2 OF 2  USPATFULL on STN
ACCESSION NUMBER:       2002:32589  USPATFULL Full-text
TITLE:                  Cyclopropyl-fused pyrrolidine-based inhibitors of
                        dipeptidyl peptidase IV and method
INVENTOR(S):            Robl, Jeffrey A., Newtown, PA, UNITED STATES
                        Sulsky, Richard B., West Trenton, NJ, UNITED STATES
                        Augeri, David J., Princeton, NJ, UNITED STATES
                        Magnin, David R., Hamilton, NJ, UNITED STATES
                        Hamann, Lawrence G., Cherry Hill, NJ, UNITED STATES
                        Betebenner, David A., Lawrenceville, NJ, UNITED STATES

                             NUMBER       KIND    DATE
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PATENT INFORMATION:     US 20020019411     A1   20020214
                        US 6395767         B2   20020528            <--
APPLICATION INFO.:      US 2001-788173     A1   20010216  (9)

                               NUMBER             DATE
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PRIORITY INFORMATION:   US 2000-188555P         20000310 (60)
DOCUMENT TYPE:          Utility
FILE SEGMENT:           APPLICATION
LEGAL REPRESENTATIVE:   MARLA J MATHIAS, BRISTOL-MYERS SQUIBB COMPANY, PATENT
                        DEPARTMENT, P O BOX 4000, PRINCETON, NJ, 08543-4000
NUMBER OF CLAIMS:       24
EXEMPLARY CLAIM:        1
LINE COUNT:             2767
CAS INDEXING IS AVAILABLE FOR THIS PATENT.


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L4             2 S L3 FAM SAM

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=> D L37 IBIB ABS 1-
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L37 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2012 ACS on STN
ACCESSION NUMBER: 2001:693281 CAPLUS Full-text
DOCUMENT NUMBER: 135:257147
TITLE: Preparation of fused cyclopropylpyrrolidine-based inhibitors of dipeptidyl peptidase IV
INVENTOR(S): Robl, Jeffrey A.; Sulsky, Richard B.; Augeri, David J.; Magnin, David R.; Hamann, Lawrence G.; Betebenner, David A.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Co., USA
SOURCE: PCT Int. Appl., 135 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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			JP 2001-567699	A3	20010305
			WO 2001-US7151	W	20010305
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ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 135:257147
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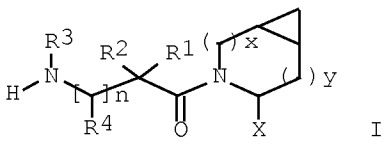

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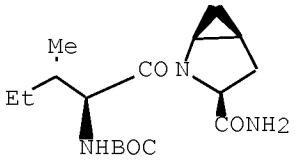

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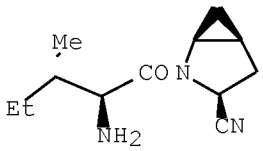

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III

AB Dipeptidyl peptidase IV inhibiting compds. I (x = 0 or 1 and y = 0 or 1 provided that x = 1 when y = 0 and x = 0 when y = 1; n = 0, 1; X = H, CN; R1, R2, R3 and R4 = same or different and independently selected from H, (un)substituted chain or cyclic components) and the pharmaceutically acceptable salts or prodrugs (no data) were prepared Thus L-pyroglutamic acid Et ester was protected, cyclopropanated and reacted further with (S)-N-BOC-isoleucine providing an

intermediate II which reacted further to yield the fused cyclopropylpyrrolidine III in 57% yield. A method is also provided for treating diabetes and related diseases, especially Type II diabetes, and other diseases by employing a title DP 4 inhibitor or a combination of DP 4 inhibitor and one or more of another antidiabetic agent such as metformin, glyburide, troglitazone, pioglitazone, rosiglitazone and/or insulin and/or one or more of a hypolipidemic agent and/or anti-obesity agent and/or other therapeutic agent.

OS.CITING REF COUNT: 35 THERE ARE 35 CAPLUS RECORDS THAT CITE THIS RECORD (60 CITINGS)

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 2 OF 2 USPATFULL on STN

ACCESSION NUMBER: 2002:32589 USPATFULL Full-text

TITLE: Cyclopropyl-fused pyrrolidine-based inhibitors of dipeptidyl peptidase IV and method

INVENTOR(S): Robl, Jeffrey A., Newtown, PA, UNITED STATES
Sulsky, Richard B., West Trenton, NJ, UNITED STATES
Augeri, David J., Princeton, NJ, UNITED STATES
Magnin, David R., Hamilton, NJ, UNITED STATES
Hamann, Lawrence G., Cherry Hill, NJ, UNITED STATES
Betebenner, David A., Lawrenceville, NJ, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 20020019411	A1	20020214
	US 6395767	B2	20020528
APPLICATION INFO.:	US 2001-788173	A1	20010216 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-188555P	20000310 (60) <--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MARLA J MATHIAS, BRISTOL-MYERS SQUIBB COMPANY, PATENT DEPARTMENT, P O BOX 4000, PRINCETON, NJ, 08543-4000
NUMBER OF CLAIMS: 24
EXEMPLARY CLAIM: 1
LINE COUNT: 2767
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Dipeptidyl peptidase IV (DP 4) inhibiting compounds are provided having the formula ##STR1##

where x is 0 or 1 and y is 0 or 1 (provided that x=1 when y=0 and x=0 when y=1);

n is 0 or 1; X is H or CN;

and wherein R.sup.1, R.sup.2, R.sup.3 and R.sup.4 are as described herein.

A method is also provided for treating diabetes and related diseases, especially Type II diabetes, and other diseases as set out herein, employing such DP 4 inhibitor or a combination of such DP 4 inhibitor and one or more of another

antidiabetic agent such as metformin, glyburide, troglitazone, pioglitazone, rosiglitazone and/or insulin and/or one or more of a hypolipidemic agent and/or anti-obesity agent and/or other therapeutic agent.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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=> S  L37 AND 361442-04-8
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L5           48 S 361442-04-8/CRN

     FILE 'CAPLUS, USPATFULL' ENTERED AT 15:50:20 ON 30 APR 2012
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L23            5 S L11 AND PRD<20030101
L24            2 S US6395767/PN
L25            2 DUP REMOV L24 (0 DUPLICATES REMOVED)
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=> D IBIB ABS HITSTR

L41  ANSWER 1 OF 2  USPATFULL on STN
ACCESSION NUMBER:       2002:32589  USPATFULL Full-text
TITLE:                  Cyclopropyl-fused pyrrolidine-based inhibitors of
                        dipeptidyl peptidase IV and method
INVENTOR(S):            Robl, Jeffrey A., Newtown, PA, UNITED STATES
                        Sulsky, Richard B., West Trenton, NJ, UNITED STATES
                        Augeri, David J., Princeton, NJ, UNITED STATES
                        Magnin, David R., Hamilton, NJ, UNITED STATES
                        Hamann, Lawrence G., Cherry Hill, NJ, UNITED STATES
                        Betebenner, David A., Lawrenceville, NJ, UNITED STATES

                             NUMBER       KIND    DATE
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PATENT INFORMATION:     US 20020019411     A1   20020214
                        US 6395767         B2   20020528
APPLICATION INFO.:      US 2001-788173     A1   20010216  (9)

                               NUMBER             DATE
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PRIORITY INFORMATION:   US 2000-188555P         20000310 (60)       <--
DOCUMENT TYPE:          Utility
FILE SEGMENT:           APPLICATION
LEGAL REPRESENTATIVE:   MARLA J MATHIAS, BRISTOL-MYERS SQUIBB COMPANY, PATENT
                        DEPARTMENT, P O BOX 4000, PRINCETON, NJ, 08543-4000
NUMBER OF CLAIMS:       24
EXEMPLARY CLAIM:        1
LINE COUNT:             2767
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB      Dipeptidyl peptidase IV (DP 4) inhibiting compounds are provided having the
        formula   ##STR1##
```

where x is 0 or 1 and y is 0 or 1 (provided that x=1 when y=0 and x=0 when y=1);

n is 0 or 1; X is H or CN;

and wherein R.sup.1, R.sup.2, R.sup.3 and R.sup.4 are as described herein.

A method is also provided for treating diabetes and related diseases, especially Type II diabetes, and other diseases as set out herein, employing such DP 4 inhibitor or a combination of such DP 4 inhibitor and one or more of another antidiabetic agent such as metformin, glyburide, troglitazone, pioglitazone, rosiglitazone and/or insulin and/or one or more of a hypolipidemic agent and/or anti-obesity agent and/or other therapeutic agent.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 361442-05-9P
(preparation of fused cyclopropylpyrrolidine-based inhibitors of dipeptidyl peptidase IV)
RN 361442-05-9 USPATFULL
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-,
(1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

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CMF C18 H25 N3 O2

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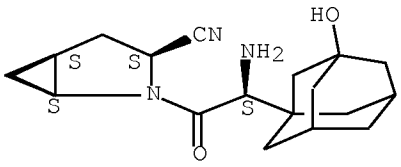

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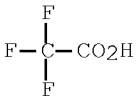

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=> S  L37 AND "361442-04-8"
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USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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STRUCTURE FILE UPDATES:   29 APR 2012  HIGHEST RN 1371145-50-4
DICTIONARY FILE UPDATES:  29 APR 2012  HIGHEST RN 1371145-50-4

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy.html

TSCA INFORMATION NOW CURRENT THROUGH DECEMBER 23, 2011

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

*** YOU HAVE NEW MAIL ***

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L44          1 361442-04-8/RN

=> D L44

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     2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-,
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OTHER CA INDEX NAMES:
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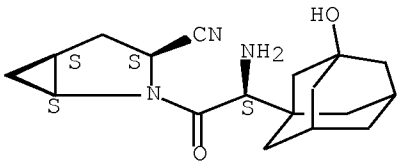
Absolute stereochemistry.



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4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
330 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> FIL CAPLUS USPATFUL

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USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE 'USPATFULL' ENTERED AT 16:40:05 ON 30 APR 2012

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=> D IBIB ABS HITSTR

L48  ANSWER 1 OF 31  CAPLUS  COPYRIGHT 2012 ACS on STN
ACCESSION NUMBER:         2008:764140  CAPLUS Full-text
DOCUMENT NUMBER:          149:96035
TITLE:                    Method for treating diabetes employing an aP2
                          inhibitor and combination
INVENTOR(S):              Robl, Jeffrey A.; Parker, Rex A.; Biller, Scott A.;
                          Jamil, Haris; Jacobson, Bruce L.; Kodukula, Krishna
PATENT ASSIGNEE(S):       Bristol-Myers Squibb Company, USA; Pesident and
                          Fellows of Harvard College
SOURCE:                   U.S., 19pp.
                          CODEN: USXXAM
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
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     US 7390824            B1    20080624    US 1999-391053          19990907 <--
PRIORITY APPLN. INFO.:                       US 1999-391053          19990907 <--
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S):          MARPAT 149:96035
AB    A method is provided for treating diabetes and related diseases, esp. Type II
      diabetes, employing an aP2 inhibitor or a combination of an aP2 inhibitor and
      another antidiabetic agent such as metformin, glyburide, troglitazone and/or
      insulin.
REFERENCE COUNT:          27    THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> D HIST

     (FILE 'HOME' ENTERED AT 15:43:05 ON 30 APR 2012)

     FILE 'REGISTRY' ENTERED AT 15:43:22 ON 30 APR 2012
L1             1 S SAXAGLIPTIN/CN
L2             5 S SAXAGLIPTIN

     FILE 'REGISTRY' ENTERED AT 15:46:17 ON 30 APR 2012
L3               STR 361442-04-8
L4             2 S L3 FAM SAM

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L5            48 S 361442-04-8/CRN

     FILE 'CAPLUS, USPATFULL' ENTERED AT 15:50:20 ON 30 APR 2012
L6           480 S L1

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                SET SMARTSELECT ON
L7           SEL L1 1- CHEM :       6 TERMS
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     FILE 'CAPLUS, USPATFULL' ENTERED AT 15:50:53 ON 30 APR 2012
L8          1242 S L7
L9           454 DUP REMOVE L6 (26 DUPLICATES REMOVED)
L10         1218 DUP REMOVE L8 (24 DUPLICATES REMOVED)
L11         1228 S L9 OR L10
L12            0 S L11 AND PD<20000309
L13            0 S L11 AND AD<20000309
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L15            0 S L11 AND AD<20010312
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L17            0 S L11 AND AY<2002
L18         1071 S L11 AND AY>2002
L19         1071 S L11 AND AY>2000
L20            1 S L11 AND PRD<20020312
L21            0 S L11 AND ROBL/IN
L22            3 S L11 AND (ROBL JEFFREY A/IN)
L23            5 S L11 AND PRD<20030101
L24            2 S US6395767/PN
L25            2 DUP REMOV L24 (0 DUPLICATES REMOVED)
L26            0 S L11 AND L25
L27          472 S  361442-04-8/RN
L28           26 S L27 NOT L11
L29            0 S L28 AND (ROBL JEFFREY A/IN)
L30            0 S L28 AND US6395767/PN
L31            0 S L24 AND L27
L32          118 S (ROBL JEFFREY A/IN)
L33           56 S L32 AND PRD<20030101
L34           56 S L32 AND PRD<20020101
L35           48 S L32 AND PRD<20010101
L36           35 S L32 AND PRD<20000311
L37            2 S L32 AND PRD=20000310
L38            0 S  L37 AND 361442-04-8/RN
L39            0 S  L37 AND 361442-04-8
L40            2 S  L37 AND L5
L41            2 DUP REMOV L40 (0 DUPLICATES REMOVED)
L42            0 S  L37 AND 361442-04-8/CRN
L43            0 S  L37 AND "361442-04-8"

     FILE 'REGISTRY' ENTERED AT 16:39:15 ON 30 APR 2012
L44            1 S 361442-04-8/RN

     FILE 'CAPLUS, USPATFULL' ENTERED AT 16:40:05 ON 30 APR 2012
L45          480 S L44
L46           35 S L32 AND PRD<20000311
L47           33 S L32 AND PRD<20000310
L48           31 DUP REMOV L47 (2 DUPLICATES REMOVED)

=> S L45 AND PRD<20000310
L49            0 L45 AND PRD<20000310

=> S L45 AND PRD<20000311
L50            0 L45 AND PRD<20000311

=> S L44 AND PRD<20000311
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L52          0 L44 AND PRD<20010311

=> S L44 AND PRD=<20000310
L53          0 L44 AND PRD=<20000310

=> S L45 AND(ROBL JEFFREY A/IN)
L54          0 L45 AND(ROBL JEFFREY A/IN)

=> D HIST

     (FILE 'HOME' ENTERED AT 15:43:05 ON 30 APR 2012)

     FILE 'REGISTRY' ENTERED AT 15:43:22 ON 30 APR 2012
L1            1 S SAXAGLIPTIN/CN
L2            5 S SAXAGLIPTIN

     FILE 'REGISTRY' ENTERED AT 15:46:17 ON 30 APR 2012
L3              STR 361442-04-8
L4            2 S L3 FAM SAM

     FILE 'REGISTRY' ENTERED AT 15:46:33 ON 30 APR 2012
L5           48 S 361442-04-8/CRN

     FILE 'CAPLUS, USPATFULL' ENTERED AT 15:50:20 ON 30 APR 2012
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     FILE 'CAPLUS, USPATFULL' ENTERED AT 15:50:53 ON 30 APR 2012
L8          1242 S L7
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L10         1218 DUP REMOVE L8 (24 DUPLICATES REMOVED)
L11         1228 S L9 OR L10
L12            0 S L11 AND PD<20000309
L13            0 S L11 AND AD<20000309
L14            0 S L11 AND AD<20000312
L15            0 S L11 AND AD<20010312
L16            0 S L11 AND AD<20020312
L17            0 S L11 AND AY<2002
L18         1071 S L11 AND AY>2002
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L22            3 S L11 AND (ROBL JEFFREY A/IN)
L23            5 S L11 AND PRD<20030101
L24            2 S US6395767/PN
L25            2 DUP REMOV L24 (0 DUPLICATES REMOVED)
L26            0 S L11 AND L25
L27          472 S  361442-04-8/RN
L28           26 S L27 NOT L11
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L29           0 S L28 AND (ROBL JEFFREY A/IN)
L30           0 S L28 AND US6395767/PN
L31           0 S L24 AND L27
L32         118 S (ROBL JEFFREY A/IN)
L33          56 S L32 AND PRD<20030101
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L35          48 S L32 AND PRD<20010101
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L40           2 S  L37 AND L5
L41           2 DUP REMOV L40 (0 DUPLICATES REMOVED)
L42           0 S  L37 AND 361442-04-8/CRN
L43           0 S  L37 AND "361442-04-8"

     FILE 'REGISTRY' ENTERED AT 16:39:15 ON 30 APR 2012
L44           1 S 361442-04-8/RN

     FILE 'CAPLUS, USPATFULL' ENTERED AT 16:40:05 ON 30 APR 2012
L45         480 S L44
L46          35 S L32 AND PRD<20000311
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L48          31 DUP REMOV L47 (2 DUPLICATES REMOVED)
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L51           0 S L44 AND PRD<20000311
L52           0 S L44 AND PRD<20010311
L53           0 S L44 AND PRD=<20000310
L54           0 S L45 AND(ROBL JEFFREY A/IN)

=> F REG
L55      30092 REG

=> FIL REG

FILE 'REGISTRY' ENTERED AT 16:46:53 ON 30 APR 2012
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   29 APR 2012  HIGHEST RN 1371145-50-4
DICTIONARY FILE UPDATES:  29 APR 2012  HIGHEST RN 1371145-50-4

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http://www.cas.org/legal/infopolicy.html

TSCA INFORMATION NOW CURRENT THROUGH DECEMBER 23, 2011

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.
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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

*** YOU HAVE NEW MAIL ***

=> S 361442-05-9/RN
L56 1 361442-05-9/RN

=> FIL CAPLUS

FILE 'CAPLUS' ENTERED AT 16:47:11 ON 30 APR 2012
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 30 Apr 2012 VOL 156 ISS 19
FILE LAST UPDATED: 29 Apr 2012 (20120429/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2011
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2011

CAplus now includes complete International Patent Classification (IPC) reclassification data for the fourth quarter of 2011.

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy.html

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> S L56
L57 4 L56

=> D IBIB ABS HITSTR 1-
YOU HAVE REQUESTED DATA FROM 4 ANSWERS - CONTINUE? Y/(N):Y

L57 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2012 ACS on STN
ACCESSION NUMBER: 2012:439526 CAPLUS Full-text
DOCUMENT NUMBER: 156:432112
TITLE: Oral preparation of saxagliptin
INVENTOR(S): Lin, Fei

PATENT ASSIGNEE(S): Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 18pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 102379869	A	20120321	CN 2010-10267175	20100831
PRIORITY APPLN. INFO.:			CN 2010-10267175	20100831

AB Application(for treating diabetes or the related diseases) of the invention should be covered in the abstract The title preparation contains saxagliptin 1-40 mg and the carrier. The title preparation contains saxagliptin hydrochloride 0.1-50% and the carrier 50-99.9%. The preparation method of dispersible tablet consists of pulverizing the saxagliptin hydrochloride, pulverizing the carrier, adding the loading agent, disintegrant, surfactant, flavoring, aromatic substance and colorant, mixing, adding the powder of saxagliptin hydrochloride, mixing, preparing the 2-15% bond solution with bond and water or ethanol-water, adding the bond to make the damp mass, pelletizing, parching, adding the glidant, lubricant and disintegrant, mixing, tabletting.

IT 361442-05-9
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral preparation of saxagliptin)

RN 361442-05-9 CAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

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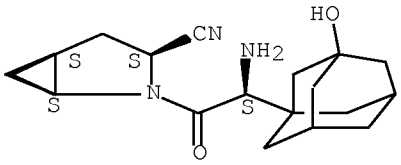
CRN 361442-04-8
CMF C18 H25 N3 O2

Absolute stereochemistry.



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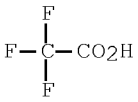
CRN 76-05-1
CMF C2 H F3 O2



L57 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2012 ACS on STN
ACCESSION NUMBER: 2008:1300536 CAPLUS Full-text
DOCUMENT NUMBER: 149:519052
TITLE: Preparation of crystal forms of saxagliptin
INVENTOR(S): Gougoutas, Jack Z.; Malley, Mary F.; DiMarco, John D.; Yin, Xiaotian S.; Wei, Chenkou; Yu, Jurong; Vu, Truc Chi; Jones, Gregory Scott; Savage, Scott A.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 134pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008131149	A2	20081030	WO 2008-US60711	20080418
WO 2008131149	A3	20090625		
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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
US 20090054303	A1	20090226	US 2008-105316	20080418
US 7943656	B2	20110517		
AR 66130	A1	20090722	AR 2008-101632	20080418
EP 2137149	A2	20091230	EP 2008-746183	20080418
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, MK, RS				
JP 2010524966	T	20100722	JP 2010-504258	20080418
IN 2009DN06560	A	20100611	IN 2009-DN6560	20091014
CN 101687793	A	20100331	CN 2008-80021025	20091221
US 20110257085	A1	20111020	US 2011-81341	20110406
PRIORITY APPLN. INFO.:			US 2007-912950P P	20070420
			US 2008-105316 A3	20080418
			WO 2008-US60711 W	20080418

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Phys. crystal structures of saxagliptin are provided including the free base monohydrate thereof (form H-1) and the hydrochloride thereof, including

hydrochlorde containing 0.75 equiv of H2O (form H0.75-3) and hydrochloride containing 2 equivs of H2O (form H2-1), and hydrochlorde Pattern P-5, preferably in substantially pure form, and other forms as described herein, pharmaceutical compns. containing these compds. processes for preparing the same, and methods of treating diseases such as diabetes.

IT 361442-05-9
RL: PRP (Properties); RCT (Reactant); RACT (Reactant or reagent)
(preparation of crystal forms of saxagliptin)

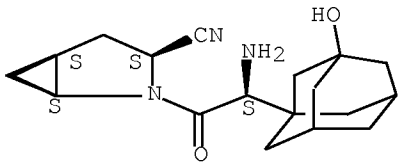
RN 361442-05-9 CAPLUS

CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361442-04-8
CMF C18 H25 N3 O2

Absolute stereochemistry.



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CRN 76-05-1
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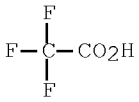


OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

L57 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2012 ACS on STN
ACCESSION NUMBER: 2005:543673 CAPLUS Full-text
DOCUMENT NUMBER: 143:221803
TITLE: Discovery and Preclinical Profile of Saxagliptin (BMS-477118): A Highly Potent, Long-Acting, Orally Active Dipeptidyl Peptidase IV Inhibitor for the Treatment of Type 2 Diabetes
AUTHOR(S): Augeri, David J.; Robl, Jeffrey A.; Betebenner, David A.; Magnin, David R.; Khanna, Ashish; Robertson, James G.; Wang, Aiying; Simpkins, Ligaya M.; Taunk, Prakash;

Huang, Qi; Han, Song-Ping; Abboa-Offei, Benoni; Cap, Michael; Xin, Li; Tao, Li; Tozzo, Effie; Welzel, Gustav E.; Egan, Donald M.; Marcinkeviciene, Jovita; Chang, Shu Y.; Biller, Scott A.; Kirby, Mark S.; Parker, Rex A.; Hamann, Lawrence G.
CORPORATE SOURCE: Department of Discovery Chemistry, Bristol-Myers Squibb, Princeton, NJ, 08543-5400, USA
SOURCE: Journal of Medicinal Chemistry (2005), 48(15), 5025-5037
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:221803
AB Efforts to further elucidate structure-activity relationships (SAR) within the authors previously disclosed series of β-quaternary amino acid linked L-cis-4,5-methanoprolinenitrile dipeptidyl peptidase IV (DPP-IV) inhibitors led to the investigation of vinyl substitution at the β-position of α-cycloalkyl-substituted glycines. Despite poor systemic exposure, vinyl-substituted compds. showed extended duration of action in acute rat ex vivo plasma DPP-IV inhibition models. Oxygenated putative metabolites were prepared and were shown to exhibit the potency and extended duration of action of their precursors in efficacy models measuring glucose clearance in Zuckerfa/fa rats. Extension of this approach to adamantylglycine-derived inhibitors led to the discovery of highly potent inhibitors, including hydroxyadamantyl compound BMS-477118 (saxagliptin), a highly efficacious, stable, and long-acting DPP-IV inhibitor, which is currently undergoing clin. trials for treatment of type 2 diabetes.

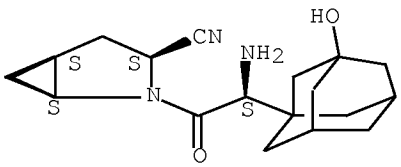
IT 361442-05-9P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(discovery and preclin. profile of saxagliptin (BMS-477118) as highly potent and long-acting and orally active dipeptidyl peptidase IV inhibitor for treatment of type 2 diabetes)

RN 361442-05-9 CAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361442-04-8
CMF C18 H25 N3 O2

Absolute stereochemistry.



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CRN 76-05-1
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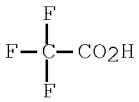

OS.CITING REF COUNT: 205 THERE ARE 205 CAPLUS RECORDS THAT CITE THIS RECORD (206 CITINGS)
REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L57 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2012 ACS on STN
ACCESSION NUMBER: 2001:693281 CAPLUS Full-text
DOCUMENT NUMBER: 135:257147
TITLE: Preparation of fused cyclopropylpyrrolidine-based inhibitors of dipeptidyl peptidase IV
INVENTOR(S): Robl, Jeffrey A.; Sulsky, Richard B.; Augeri, David J.; Magnin, David R.; Hamann, Lawrence G.; Betebenner, David A.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Co., USA
SOURCE: PCT Int. Appl., 135 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001068603	A2	20010920	WO 2001-US7151	20010305
WO 2001068603	A3	20020214		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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US 6395767	B2	20020528		
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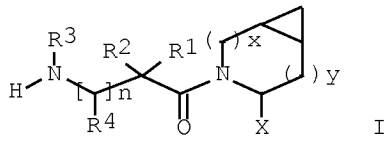
EP 2272825	A3	20110504			

R: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE, TR

IN 2002MN01154	A	20050304	IN 2002-MN1154		20020823
ZA 2002006816	A	20031126	ZA 2002-6816		20020826
NO 2002004295	A	20021106	NO 2002-4295		20020909
NO 324227	B1	20070910			
KR 754089	B1	20070831	KR 2002-7011806		20020909
MX 2002008837	A	20030425	MX 2002-8837		20020910
HK 1049330	A1	20081114	HK 2003-101079		20030214
KR 758407	B1	20070914	KR 2006-7004515		20060303
IN 2007MN00184	A	20080215	IN 2007-MN184		20070205
JP 2010077163	A	20100408	JP 2010-6181		20100114
PRIORITY APPLN. INFO.:			US 2000-188555P	P	20000310
			CN 2001-806315	A3	20010305
			EP 2001-918383	A3	20010305
			EP 2005-5368	A3	20010305
			IL 2001-151372	A3	20010305
			JP 2001-567699	A3	20010305
			WO 2001-US7151	W	20010305
			IN 2002-MN1154	A3	20020823
			KR 2002-7011806	A3	20020909

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 135:257147
GI



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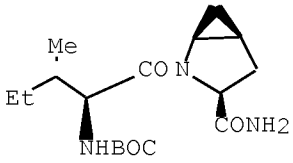

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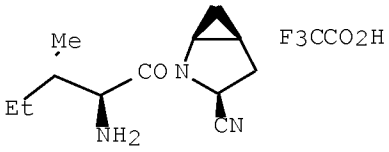


III

AB Dipeptidyl peptidase IV inhibiting compds. I (x = 0 or 1 and y = 0 or 1 provided that x = 1 when y = 0 and x = 0 when y = 1; n = 0, 1; X = H, CN; R1, R2, R3 and R4 = same or different and independently selected from H, (un)substituted chain or cyclic components) and the pharmaceutically acceptable salts or prodrugs (no data) were prepared Thus L-pyroglutamic acid Et ester was protected, cyclopropanated and reacted further with (S)-N-BOC-isoleucine providing an intermediate II which reacted further to yield the fused cyclopropylpyrrolidine III in 57% yield. A method is also provided for treating diabetes and related diseases, especially Type II diabetes, and other diseases by employing a title DP 4 inhibitor or a combination of DP 4 inhibitor and one or more of another antidiabetic agent such as metformin, glyburide, troglitazone, pioglitazone, rosiglitazone and/or insulin and/or one or more of a hypolipidemic agent and/or anti-obesity agent and/or other therapeutic agent.

IT 361442-05-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of fused cyclopropylpyrrolidine-based inhibitors of dipeptidyl peptidase IV)

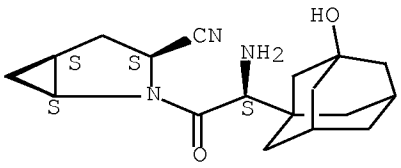
RN 361442-05-9 CAPLUS

CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361442-04-8
CMF C18 H25 N3 O2

Absolute stereochemistry.



CM 2

CRN 76-05-1
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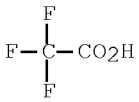
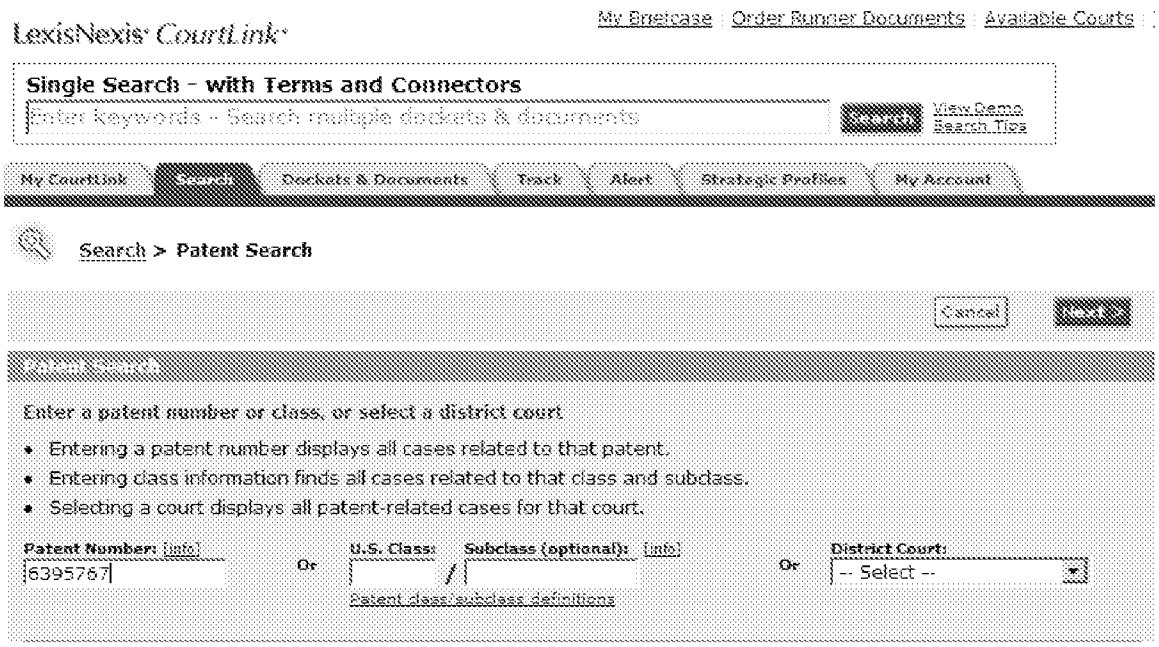


OS.CITING REF COUNT: 35 THERE ARE 35 CAPLUS RECORDS THAT CITE THIS RECORD (60 CITINGS)
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> LOGOFF HOLD

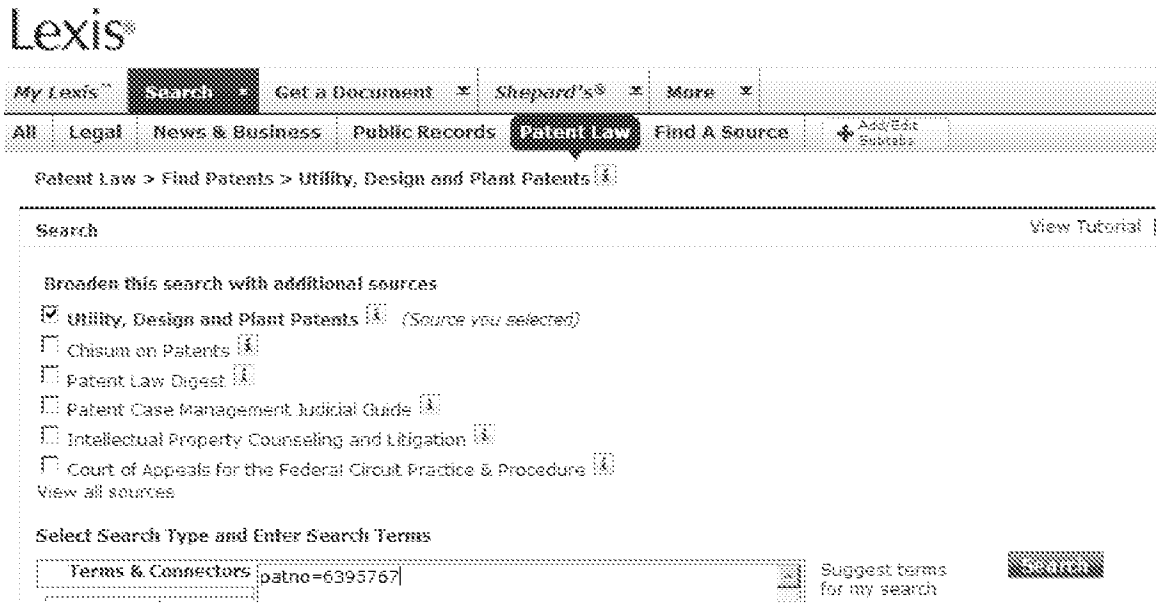
SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 16:48:32 ON 30 APR 2012

CourtLink, Lexis/Nexis and Dialog Litigation search for USP 6,395,767. Case 13/308,658.

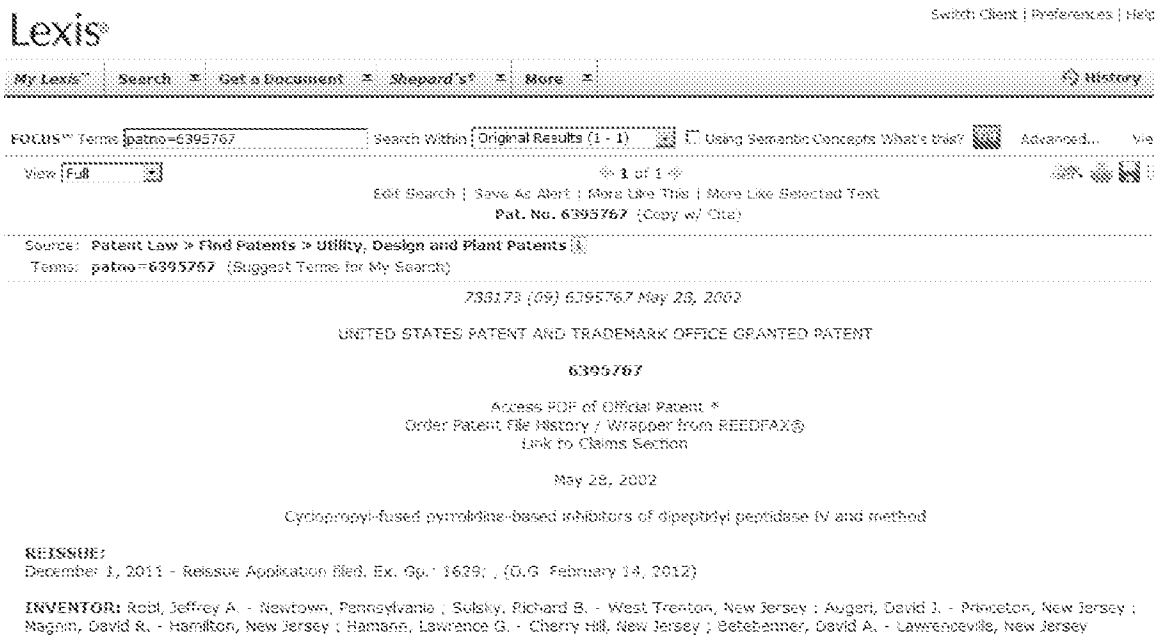


CourtLink search for USP 6,395,767.

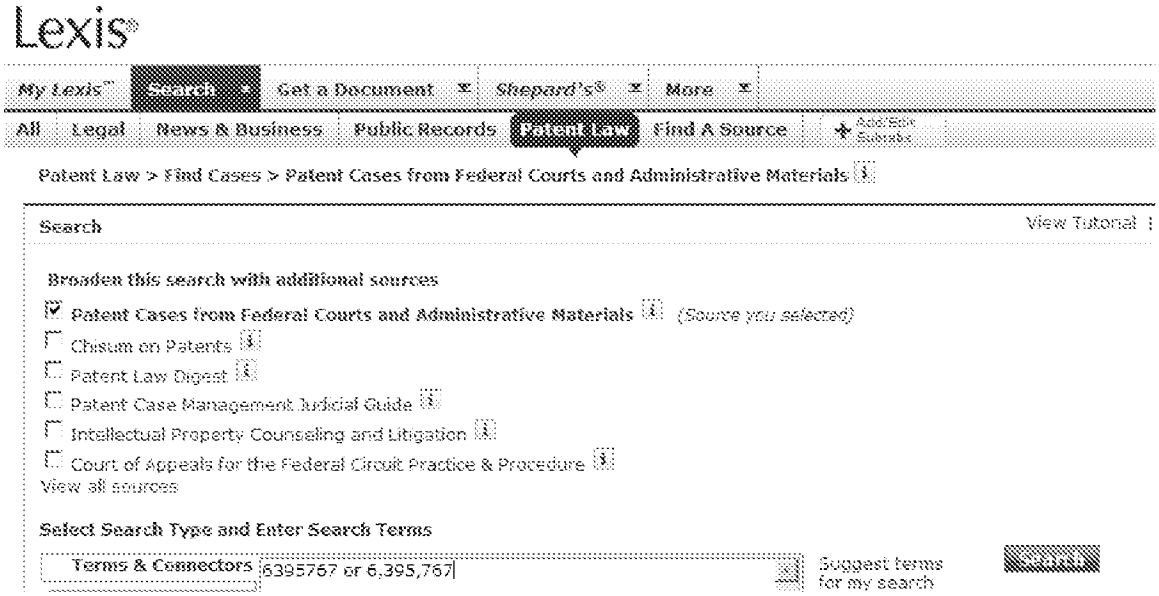
No Cases found in CourtLink Search.



Searched the Utility, Design and Plant Patents database.



Lexis lists litigation at the top of its patents: No litigation listed.



Searched the Patent Cases from Federal Courts and Administrative Materials Database.

No Documents Found

No documents were found for your search terms
"6395767 or 6,395,767"

Click "Save this search as an Alert" to schedule your search to run in the future.

- OR -
Click "Search Using Natural Language" to run your search as Natural Language search.

- OR -

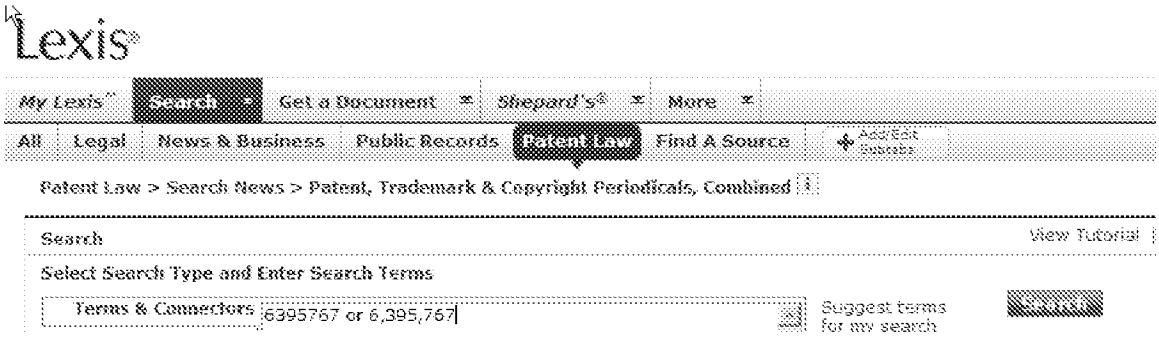
Click "Edit Search" to return to the search form and modify your search.

Suggestions:

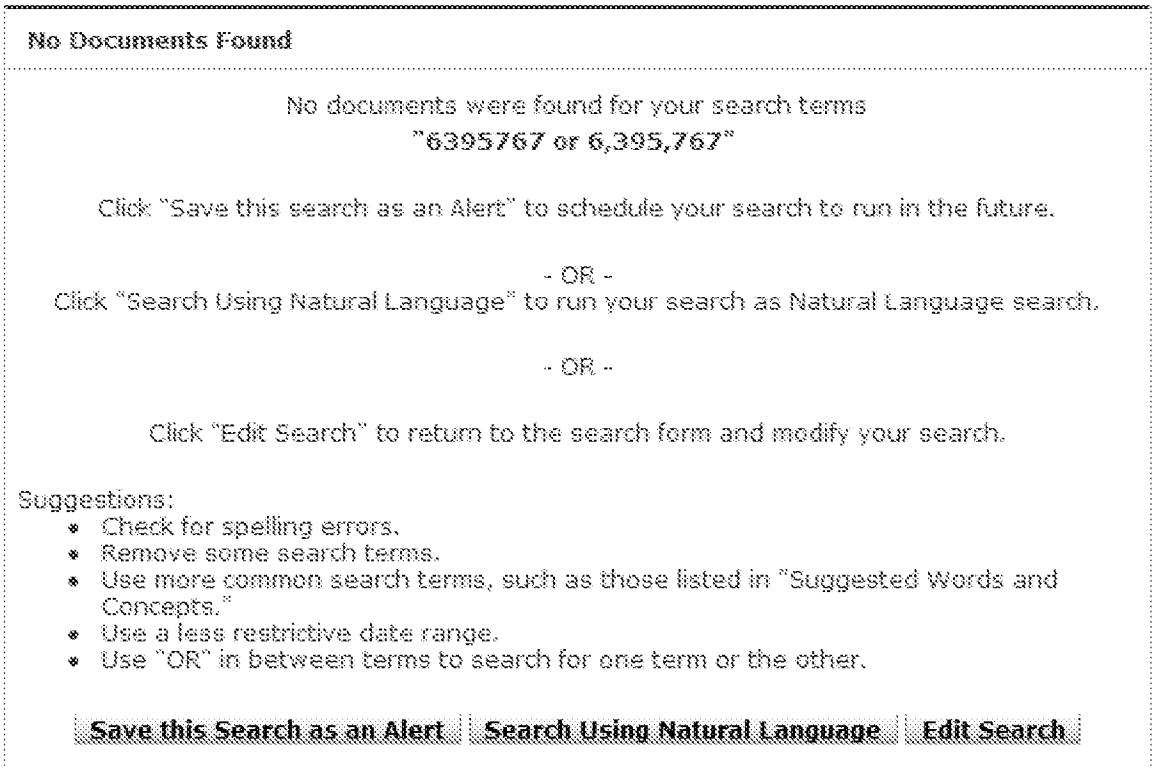
- Check for spelling errors.
- Remove some search terms.
- Use more common search terms, such as those listed in "Suggested Words and Concepts."
- Use a less restrictive date range.
- Use "OR" in between terms to search for one term or the other.

Save this Search as an Alert | **Search Using Natural Language** | **Edit Search**

No documents found.



Searched the Patent, Trademark & Copyright Periodicals, Combined database.



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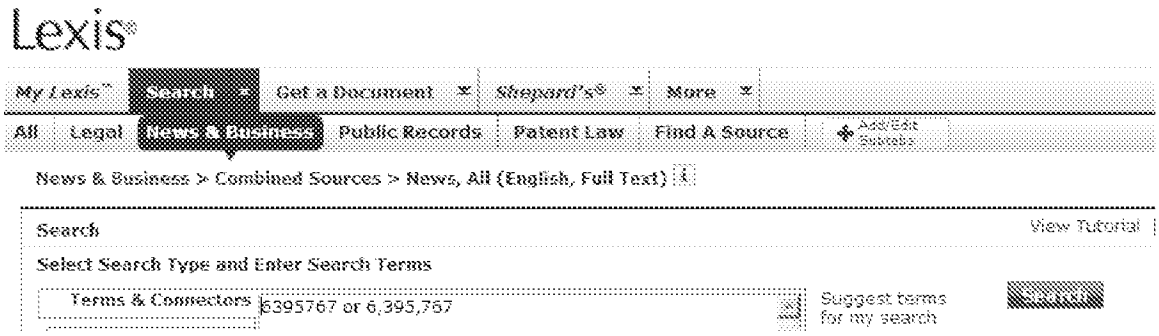

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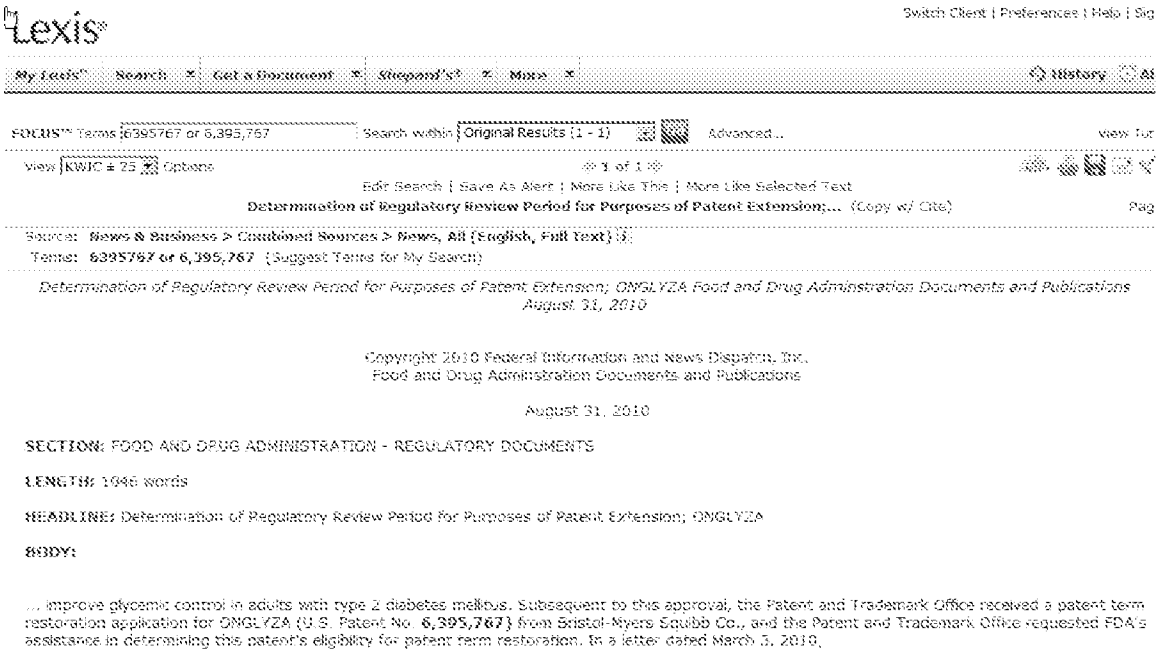
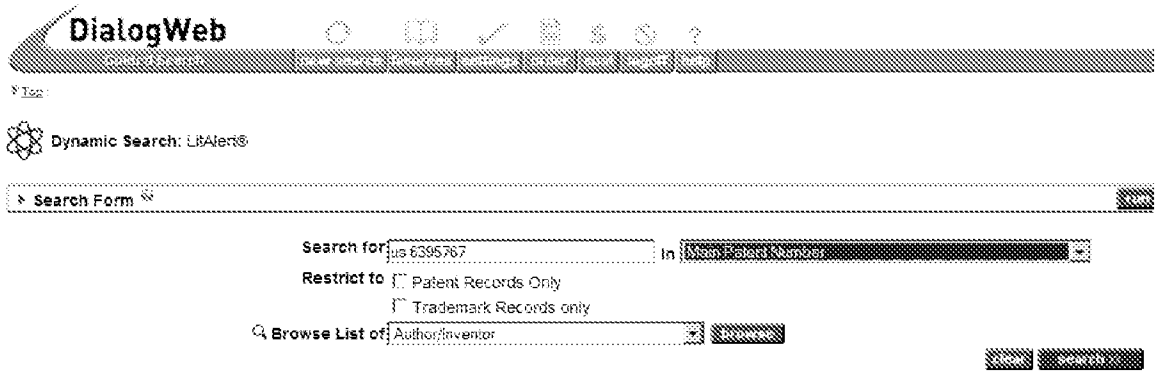


One article found. No litigation is mentioned.



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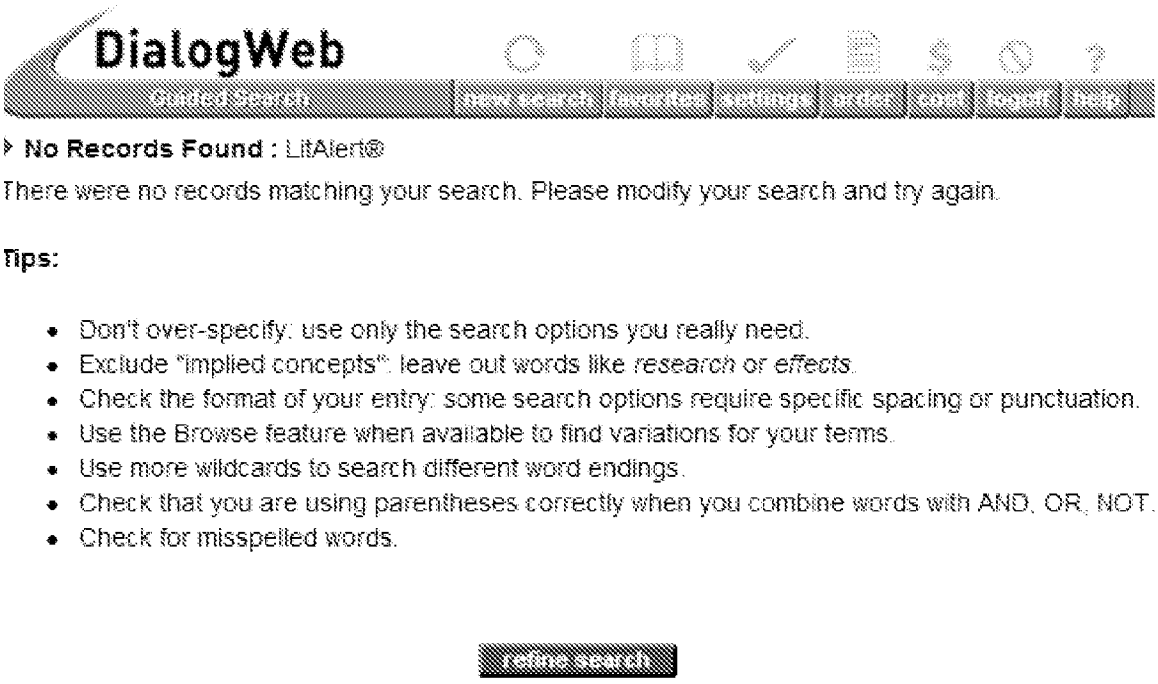


UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/308,658	12/01/2011	Jeffrey A. Robl	BMS-2856	7781

23377 7590 05/30/2012

WOODCOCK WASHBURN LLP
CIRA CENTRE, 12TH FLOOR
2929 ARCH STREET
PHILADELPHIA, PA 19104-2891

EXAMINER	
POLANSKY, GREGG	
ART UNIT	PAPER NUMBER
1629	

NOTIFICATION DATE	DELIVERY MODE
05/30/2012	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

eofficemonitor@woodcock.com

Applicant-Initiated Interview Summary	Application No.	Applicant(s)	
	13/308,658	ROBL ET AL.	
	Examiner	Art Unit	
	Gregg Polansky	1629	

All participants (applicant, applicant's representative, PTO personnel):

(1) *Gregg Polansky*. (3) *Maurice Valla*.

(2) *James Anderson*. (4)_____.

Date of Interview: *22 May 2012*.

Type: ☒ Telephonic ☐ Video Conference
☐ Personal [copy given to: ☐ applicant ☐ applicant's representative]

Exhibit shown or demonstration conducted: ☐ Yes ☒ No.
If Yes, brief description: _____.

Issues Discussed ☐101 ☐112 ☐102 ☐103 ☒Others
(For each of the checked box(es) above, please describe below the issue and detailed description of the discussion)

Claim(s) discussed: *pending claims*.

Identification of prior art discussed: *none*.

Substance of Interview
(For each issue discussed, provide a detailed description and indicate if agreement was reached. Some topics may include: identification or clarification of a reference or a portion thereof, claim interpretation, proposed amendments, arguments of any applied references etc...)

Discussed the objections and rejections set forth in the Office action mailed on 5/08/2012. Attorney Valla spoke to his understanding of the issues presented in the Office action and the means to overcome them. The Examiner's provided clarification with regard to problems with Applicants' Oath and the incorporation of corrections provided by the Certificate of Correction in the original patent .

Applicant recordation instructions: The formal written reply to the last Office action must include the substance of the interview. (See MPEP section 713.04). If a reply to the last Office action has already been filed, applicant is given a non-extendable period of the longer of one month or thirty days from this interview date, or the mailing date of this interview summary form, whichever is later, to file a statement of the substance of the interview

Examiner recordation instructions: Examiners must summarize the substance of any interview of record. A complete and proper recordation of the substance of an interview should include the items listed in MPEP 713.04 for complete and proper recordation including the identification of the general thrust of each argument or issue discussed, a general indication of any other pertinent matters discussed regarding patentability and the general results or outcome of the interview, to include an indication as to whether or not agreement was reached on the issues raised.

☐ Attachment

/JAMES D ANDERSON/ Primary Examiner, Art Unit 1629	/Gregg Polansky/ Examiner, Art Unit 1629

Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record
A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews
Paragraph (b)

In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

37 CFR §1.2 Business to be transacted in writing.
All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:
- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case. It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:
1) A brief description of the nature of any exhibit shown or any demonstration conducted,
2) an identification of the claims discussed,
3) an identification of the specific prior art discussed,
4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
5) a brief identification of the general thrust of the principal arguments presented to the examiner,
   (The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
6) a general indication of any other pertinent matters discussed, and
7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.

DOCKET NO.: BMS-2856 **PATENT**
Application No.: 13/308,658
Office Action Dated: May 8, 2012

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: **Jeffrey A. Robl**	Confirmation No.: **7781**
Application No.: **13/308,658**	Group Art Unit: **1629**
Filing Date: **December 1, 2011**	Examiner: **Gregg Polansky**

For: **Cyclopropyl-Fused Pyrrolidine-Based Inhibitors of Dipeptidyl Peptidase IV and Method**

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Commissioner:

REPLY PURSUANT TO 37 CFR § 1.111

In response to the Official Action dated **May 8, 2012**, reconsideration is respectfully requested in view of the amendments and/or remarks as indicated below:

☒ **A Listing of Prior Changes to U.S. 6,395,767 ("the 767 patent") Made By Certificate of Correction** begin on page 2 of this paper.

☒ **Amendments to the Claims of the 767 Patent** begin on page 16 of this paper.

☒ **A Complete Listing of the Claims as Amended**, with status identifiers, begins on page 22 of this paper.

☒ **Remarks** begin on page 33 of this paper.

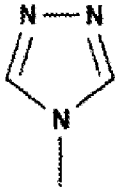
☒ The Commissioner is hereby authorized to charge any fee deficiency, charge any additional fees, or credit any overpayment of fees, associated with this application in connection with this filing, or any future filing, submitted to the U.S. Patent and Trademark Office during the pendency of this application, to Deposit Account No. 23-3050.

Changes to 767 Patent Previously Entered by Certificate of Correction

1. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 7, line 4-col. 8, line 7 of the 767 patent:

Alternately, the carboxamide group in 8 may be converted to the nitrile as described above to give compound 9. Deprotection of PG_1 affords 10 which may be subject to standard peptide coupling conditions to afford 7, an intermediate in the synthesis of Ib. Compound 10 may also be generated by oxidation of the amine 2 (e.g. NCS) followed by hydrolysis and subsequent cyanide treatment. Compound 10 may be obtained as a mixture of stereoisomers or a single isomer/diastereomer which may be epimerized (employing conventional procedures) to afford a mixture of stereoisomers.

2. As indicated by the Certificate of Correction, please insert the following structure at col. 14, line 50 of the 767 patent:



3. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 14, lines 55-58 of the 767 patent:

The term "cycloheteroalkylalkyl" as used herein alone or as part of another group refers tocycloheteroalkyl groups as defined above linked through a C atom or heteroatom to a $(CH_2)_r$ chain.

4. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 15, lines 49-56 of the 767 patent:

The other antidiabetic agent may also preferably be a sulfonyl urea such as glyburide (also known as glibenclamide), glimepiride (disclosed in U.S. Pat. No. 4,379,785), glipizide, gliclazide or chlorpropamide, other known sulfonylureas or other

antihyperglycemic agents which act on the ATP-dependent channel of the β-cells, with glyburide and glipizide being preferred, which may be administered in the same or in separate oral dosage forms.

5. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 20, lines 57-62 of the 767 patent:

The other type of therapeutic agent which may be optionally employed with the DP4 inhibitor of formula I may be 1, 2, 3 or more of an anti-obesity agent including a beta 3 adrenergic agonist, a lipase inhibitor, a serotonin (and dopamine) reuptake inhibitor, a thyroid receptor beta drug, an anorectic agent and/or a fatty acid oxidation upregulator.

6. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 29, lines 15-29 of the 767 patent:

To a stirred solution of (S)-N-tert-butoxycarbonyl-isoleucine (231 mg, 1 mmol) and benzotriazol-1-yloxytripyrrolidinophosphonium hexafluorophosphate (780 mg, 1.5 mmol) in CH_2Cl_2 (6 mL) under nitrogen at rt was added 4-methylmorpholine (0.33 mL, 3 mmol). After 5 min, Step 1 compound (120 mg, 1 mmol) was added in one portion. The reaction mixture was stirred under nitrogen at rt overnight and then diluted with CH_2Cl_2 (30 mL), washed with 4.1% $KHSO_4$ (10 mL)), aqueous $NaHCO_3$ (10 mL), brine (10 mL), dried (Na_2SO_4) and evaporated. Purification by flash chromatography on silica gel (2.4x20 cm column, 1:3 EtOAc/hexane) gave the title compound as a colorless oil, 290 mg, 90% yield. LC/MS gave the correct molecular ion [$(M+H)^+$ =297] for the desired compound.

7. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 29, line 40-col. 30, line 3 of the 767 patent:

The reaction mixture of Step 2 compound (220 mg, 0.74 mmol) and 4 M HCl in dioxane (1.5 mL, 6 mmol) was stirred at rt for 2 h and evaporated under reduced pressure. Et_2O was added to the residue and a precipitate was formed. Et_2O was decanted and this was

done three times. The precipitate was dried *in vacuo* to give the title compound as a white powder, 130 mg (76% yield), mp 205-206°C. LC/MS gave the correct molecular ion [$(M+H)^+$ = 197] for the desired compound.

8. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 32, lines 54-63 of the 767 patent:

To a stirred solution of Step 2 compounds (104 mg, 0.32 mmol) in CH_2Cl_2 (1 mL) at rt was added TFA (1 mL). The reaction mixture was stirred at rt for 2 h. The reaction mixture was added slowly to a precooled slurry of $NaHCO_3$ (2 g) in H_2O (2 mL). The mixture was extracted with CH_2Cl_2 (4 mL x 4), and combined CH_2Cl_2 layers were evaporated and purified by preparative HPLC to give the title compound Example 5 (36 mg) and Example 5A (36 mg). LC/MS gave the correct molecular ion [$(M+H)^+$ = 222] for the desired compounds..

9. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 32, line 66-col. 33, line 12 of the 767 patent:

General Method A: Parallel array synthesis methods for preparation of inhibitors from commercially available amino acids. As shown in Scheme 3, the ester 11, described in Example 1 Step 1, was saponified to the acid with LiOH in THF/H_2O and converted to the amide 12 by treatment with isobutyl chloroformate/NMM followed by ammonia in dioxane. The Boc protecting group was removed under acidic conditions using TFA in methylene chloride to give 13. The TFA salt was coupled to Boc-*t*-butylglycine using either EDAC/HOBT/DMF or EDAC/DMAP/CH_2Cl_2 to give 14. The amide was dehydrated to the nitrile 15 using $POCl_3$/imidazole in pyridine at –20°C and finally deprotected with TFA in CH_2Cl_2 at ambient temperature to afford the target 16. SCHEME 3, GENERAL METHOD A (EXAMPLES 6-27)

10. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 34, line 59-col. 35, line 13 of the 767 patent:

An oven-dried 15-mL test tube was charged with Step 3 compound (56 mg, 0.22 mmol), N-*tert*-butoxycarbonyl-(L)-*tert*-leucine (53 mg, 0.23 mmol), dimethylaminopyridine (0.11 g, 0.88 mmol), and CH_2Cl_2 (4 mL). The tube was sealed under nitrogen atmosphere and treated with 1-[(3-(dimethyl)amino)propyl]-3-ethylcarbodiimide (84 mg, 0.44 mmol). The mixture was placed in a shaker and vortexed overnight. The product was purified by solid phase extraction using a United Technology SCX column (2 g of sorbent in a 6 mL column) by loading the material on a SCX ion exchange column and successively washing with CH_2Cl_2 (5 mL), 30% methanol in CH_2Cl_2 (5 mL), 50% methanol in CH_2Cl_2 (5 mL) and methanol (10 mL). The product containing fractions were concentrated under reduced pressure to give the desired amide. Further purification by reverse phase preparative column chromatography on a YMC S5 ODS 20 x 250 mm column gave the title compound, 50 mg (68% yield). Purification conditions: Gradient elution from 30% methanol/water/0.1 TFA to 90% methanol/water/0.1 TFA over 15 min. 5 min. hold at 90% methanol/water/0.1 TFA. Flow rate: 20 mL/min. Detection wavelength: 220. Retention Time: 14 min.

11. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 41, lines 36-46 of the 767 patent:

An oven-dried 10-mL round bottomed flask was charged with Step 2 compound (350 mg, 0.79 mmol), imidazole (108 mg, 1.58 mmol), pyridine (3 mL). The flask under argon was cooled to -30^0C. Slow addition of $POCl_3$ (0.30 mL, 3.16 mmol) gave after mixing a thick slurry. The slurry was mixed at -30^0C for 3 h and the volatiles evaporated. Dichloromethane (5 mL) was then added and the insoluble solid was removed by filtration. The organic layer was washed with H_2O, 10% citric acid, brine and dried over Na_2SO_4. Removal of solvent gave crude desired nitrile (330 mg) (LC/Mass, + ion): 424 (M+H).

12. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 43, lines 20-29 of the 767 patent:

To a flame-dried 500-mL round-bottomed flask containing cyclopentylideneacetic acid ethyl ester (17.5 g, 113 mmol) in 100 mL anhydrous toluene at -78°C under argon was added DIBAL-H (189 mL of a 1.5 M solution in toluene, 284 mmol, 2.50 equiv) dropwise over a 30 min period through an addition funnel, and the mixture was then allowed to warm to rt, stirring for 18 h. The reaction mixture was then recooled to -78°C, and quenched by the careful addition of 30 mL anhydrous MeOH. Upon warming to rt, 1 N Rochelle's salt (100 mL) was added, and the mixture was stirred 90 min. The biphasic reaction mixture was then diluted with Et_2O (200 mL) in a separatory funnel, and the layers were separated. The organic layer was then washed with brine (100 mL), dried (Na_2SO_4), and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, CH_2Cl_2 / EtOAc, 10:1) gave 11.6 g (92%) of the desired allylic alcohol as a colorless oil.

13. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 43, lines 53-67 of the 767 patent:

To a flame-dried 500-mL round-bottomed flask containing N-(*tert*-butyloxycarbonyl)glycine (13.45 g, 76.75 mmol) in 100 mL CH_2Cl_2 at rt was added Step 2 compound (8.61 g, 76.75 mmol, 1.00 equiv) in 20 mL CH_2Cl_2, followed by dicyclohexylcarbodiimide (16.63 g, mmol, 1.05 equiv) in 80 mL CH_2Cl_2. To this reaction mixture was then added 4-dimethylaminopyridine (0.94 mg, mmol, 0.10 equiv), and the mixture was allowed to stir overnight. The reaction mixture was then filtered through a medium sintered-glass funnel, rinsing with 100 mL CH_2Cl_2, and concentrated under reduced pressure. The crude product was then purified by flash chromatography (silica gel, hexanes/EtOAc, 20:1 to 1:1 gradient) to give 19.43 g (94%) of the desired glycinyl ester as a colorless oil.

14. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 44, lines 19-45 of the 767 patent:

A flame-dried 500-mL round-bottomed flask under argon was charged with $ZnCl_2$ (11.8 g, mmol, 1.20 equiv) and 20 mL toluene. The mixture was heated under vacuum with vigorous stirring to azeotrope off any traces of moisture with the distilling toluene, repeating this process (2 x). The flask was then cooled to rt under argon, (2-cyclopentylideneethyl) N-(*tert*-butyloxycarbonyl)glycinate (19.36 g, 71.88 mmol) was added via cannula as a solution in 180 mL THF, and the mixture was then cooled to -78°C. In a separate flame-dried 200-mL round-bottomed flask containing diisopropylamine (26.3 mL, mmol, 2.60 equiv) in 90 mL THF at -78°C was added n-butyllithium (71.89 mL of a 2.5 M solution in hexanes, mmol, 2.5 equiv), and the mixture was allowed to warm to 0°C for 30 min before recooling to -78°C. The lithium diisopropylamine thus generated was then added via cannula to the $ZnCl_2$ ester mixture dropwise at a steady rate over 40 min, and the resultant reaction mixture was allowed to slowly warm to rt and stir overnight. The yellow reaction mixture was then poured into a separatory funnel, diluted with 300 mL Et_2O, and the resultant organic solution was washed successively with 300 mL 1N HCl and 300 mL brine, dried (Na_2SO_4), and concentrated under reduced pressure. Purification by flash chromatography (silica gel, 3% MeOH in CH_2Cl_2 with 0.5% HOAc) gave 17.8 g (92%) of the desired amino acid product as a white solid. (FAB MH+ 270).

15. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col 46, lines 48-59 of the 767 patent:

Step 2 compound (32 mg, 0.09 mmol) was dissolved in 1 mL of CH_2Cl_2 and 1 mL of TFA was added and the reaction stirred for 30 min at rt and was evaporated to dryness. The product was purified by reverse phase preparative column chromatography on a YMC S5 ODS 20 X 250 mm column to give 12 mg of the TFA salt (lyophilized from water or isolated after evaporation of eluent and trituration with ether) the title compound. Purification conditions: gradient elution from 10% methanol/water/0.1 TFA

to 90% methanol/water/0.1 TFA over 18 min; 5 min. hold at 90% methanol/water/0.1 trifluoroacetic acid. Flow rate: 20 mL/min. Detection wavelength: 220.

16. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 46, lines 61-67 of the 767 patent:

Examples 30–39 were prepared by the methods outlined in General Method B and General Method C starting from cyclopentanone, cyclobutanone, cyclohexanone, cycloheptanone, cyclooctanone, cis-3,4-dimethylcyclopentanone, and 4-pyranone, cyclopropaneethylhemiacetal, acetone, and 3-pentanone respectively.

17. As indicated by the Certificate of Correction, at col. 52, line 64 of the 767 patent, change "25" to ---28--.

18. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 53, lines 28-45 of the 767 patent:

N-Boc protected cyclobutylvinyl compound (Example 31, prepared by general method C) (0.16 g, 0.46 mmol) was dissolved in 10 mL of a 1:1 mixture of THF:water and treated with OsO_4 (12 mg, catalyst) and $NaIO_4$ (0.59 g, 2.76 mmol, 6 equiv). After 2 h, the reaction mixture was diluted with 50 mL of ether and 10 mL of water. The layers were equilibrated and the organic fraction was washed one time with $NaHCO_3$ solution, dried over $MgSO_4$ and concentrated to give a dark oil. The oil was diluted with 10 mL of methanol and treated with $NaBH_4$ (0.08 g, 2.0 mmol). The mixture turned very dark and after 30 min was diluted with ether and the reaction was quenched with aqueous $NaHCO_3$ solution. The mixture was equilibrated and layers separated. The organic fraction was washed with solutions of $NaHCO_3$ and 0.1 M HCl. The organics were dried ($MgSO_4$) and concentrated to give 90 mg (56%) of the Step 1 compound as a dark oil.

19. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 53, lines 59-67 of the 767 patent:

Step 1 compound (90 mg, 0.26 mmol) was dissolved in 3 mL of CH_2Cl_2, cooled to 0°C and treated with 3 mL of freshly distilled TFA. The reaction was complete in 80 min and evaporated to dryness and purified by preparative HPLC (YMC S5 ODS 30 x 100 mm, 10 minute gradient 100%A to 100%B, Solvent A = 10% MeOH-90%H2O-0.1% TFA, Solvent B = 90% MeOH-10% H_2O -0.1% TFA, to give, after removal of water, 50 mg (60%) of title compound. (MH+250).

20. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 62, lines 56-67 of the 767 patent:

The Step 2 compound (95 mg, 0.22 mmol, 1 equiv) was dissolved in anhydrous CH_2Cl_2 (2.5 mL) under argon and cooled to –78°C. The mixture was treated with diisopropylethylamine (65 μL, 0.37 mmol, 1.7 equiv), and triethylsilyl triflate (75 μL, 0.33 mmol, 1.5 equiv), and stirred at 0°C for 1.5 h. The reaction was mixed with MeOH (0.5 mL), silica gel (200 mg) and H_2O (2 drops) and stirred at rt for 18 h. The solvent was removed by rotary evaporation and the residue purified flash column chromatography on silica gel(2.5x10 cm) with 4% MeOH/CH_2Cl_2 to afford the product (92 mg, 0.17 mmol, 77%): MS m/e 540 $(m+H)^+$.

21. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 66, lines 11-27 of the 767 patent:

An oven-dried flask equipped with a condenser and drying tube was charged with norbornane-2-carboxylic acid (4.92 g, 35 mmol, 1 equiv) and treated with bromine (2.1 mL, 41 mmol, 1.15 equiv) and phosphorous trichloride (0.153 mL, 1.8 mmol, 0.05 equiv). The mixture was heated at 85°C for 7 h protected from light. Additional bromine (0.4 mL, 7.8 mmol, 0.22 equiv) was added with continued heating for 1 h. The mixture was cooled to rt, and Et_2O (100 mL) was added. The mixture was washed with 10% aq $NaHSO_3$ (50 mL), H_2O (2x50 mL), and brine (25 mL). The ether fraction was dried (Na_2SO_4), filtered and concentrated by rotary evaporation. The product was purified by flash column chromatography on silica gel (5x15 cm) with 2% to 4% MeOH/CH_2Cl_2 +

0.5% HOAc. The product was chased with hexanes to remove residual HOAc. The isolated material consists of two inseparable materials (4.7 g), which was used without further purification in the next step.

22. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 69, lines 20-27 of the 767 patent:

To a 50-mL round-bottomed flask containing Step 2 compound (0.72 g, 4.20 mmol) in 8 mL of water at rt was added NaCN (0.20 g, 4.20 mmol) followed by NH_4Cl (0.20 g, 5.00 mmol). To this reaction mixture was then added methanol (8 mL) and the mixture was allowed to stir overnight. The reaction mixture was then extracted with ether (2x15 mL), dried ($MgSO_4$) and concentrated under reduced pressure to give the crude Strecker product.

23. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 69, lines 28-44 of the 767 patent:

To a 100-mL round-bottomed flask containing the crude Strecker product was added 10 mL of HOAc and 10 mL of conc. HCl. The mixture was refluxed overnight. The mixture was concentrated under reduced pressure to give a yellow solid. The solid was triturated with 5 mL of 1:1 mixture of ether and hexanes. The white solid was treated with triethylamine (1.4 mL, 9.99 mmol) and di-*tert*-butyldicarbonate (1.00 g, 4.60 mmol) in 50 mL DMF. After 4 h the pH of the mixture was adjusted to 9 with saturated Na_2CO_3 soln. After an additional 3 h of stirring the mixture was extracted with 1:1 ether and hexanes and the aqueous fraction acidified to pH 2 with 5% $KHSO_4$ solution. The aqueous phase was washed with ether (2 X 40 mL), the organics dried ($MgSO_4$), and evaporated to an oil that was purified by silica gel flash chromatography with 8:92 methanol:CH_2Cl_2 to give 0.3 g (23%) of the Boc-protected amino acid as a light oil (M-H, 318).

24. As indicated by the Certificate of Correction, please move "Step 1" at col. 70, line 56 of the 767 patent to col. 70, line 65.

25. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 72, lines 30-49 of the 767 patent:

Sodium ethoxide (940 mg of 21 wt% solution in ethanol, 2.9 mmol) in ethanol (2 mL) was added to a stirred solution of diethyl acetamidomalonate (4.31g, 19.8 mmol) in EtOH (23 mL) at rt under argon. The reaction mixture was cooled to 0°C; and trans-2-pentenal (1.51 g, 18.0 mmol) was added dropwise maintaining the reaction temperature at < 5°C. After the addition, the reaction was allowed to warm to rt, stirred for 4 h, then quenched with acetic acid (460 μl). The solution was concentrated *in vacuo*, and the residue dissolved in EtOAc (25 mL), washed with 10% $NaHCO_3$ solution (2x5 mL), brine and dried ($MgSO_4$). The solution was filtered and concentrated to a 10 mL volume, then heated to reflux and diluted with hexane (20 mL). Upon cooling to rt, the title compound precipitated and was collected to give 3.0 g (50%) of the Step 1 compound (mp 106-109°C; LC/Mass: + ions, 324 M+Na).

26. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 72, line 64-col. 73, line 8 of the 767 patent:

To a solution of Step 1 compound (2.87 g, 9.5 mmol) and triethylsilane (2.28 mL, 14.3 mmol) in CH_2Cl_2 (30 mL) under argon was added TFA (7.35 mL, 95.3 mmol) dropwise with stirring while maintaining the internal temperature at 25^0C by means of an ice bath. After stirring for 4 h at rt, the solution was concentrated. The residue was diluted with CH_2Cl_2 (100 mL), then treated with H_2O (50 mL) and solid Na_2CO_3 with vigorous stirring until the mixture was basic. The organic layer was separated, dried (Na_2SO_4), filtered, then concentrated to give the Step 2 compound as a yellow oil which was used without further purification (LC/Mass: + ions, 308 M+Na).

27. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 73, lines 22-27 of the 767 patent:

Step 2 compound (3.73 g, 9.5 mmol) was suspended in 6 N HCl (20 mL) and HOAc (5 mL) and heated at reflux for 20 h. The reaction mixture was then cooled, washed with EtOAc (20 mL), then concentrated to give an oil which crystallized upon trituration with ether to give the title compound (1.2 g, 70.6%) (LC/Mass, + ion): 144 (M+H).

28. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 74, lines 26-41 of the 767 patent:

Sodium ethoxide (940 mg, 2.9 mmol; 21% w/w solution in ethanol) in ethanol (2 mL) was added to a stirred solution of diethyl acetamidomalonate (4.31 g, 19.8 mmol) in EtOH (23 mL) at rt under argon. The reaction mixture was cooled to 0^0C; and 4-methyl-2-pentenal (1.77 g, 18.0 mmol)was added dropwise maintaining the reaction temperature at < 5°C. After the addition, the reaction was allowed to warm to rt, stirred for 4 h, then quenched with acetic acid (460 μl). The solution was concentrated and the remainder dissolved in EtOAc (25 mL). The organics were washed with 10% $NaHCO_3$ solution (2x5 mL), brine and dried ($MgSO_4$). The solution was filtered and concentrated to 10 mL volume, then heated to reflux and treated with hexane (20 mL). On cooling, the Step 1 compound precipitated and was collected (3.3 g) (LC/Mass, + ion): 338 (M+Na).

29. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 79, lines 54-67 of the 767 patent:

N-[((S)-cyclopentylvinyl)-N-tert-butoxycarbonylglycinyl]-(2S,4S,5S)-2-cyano-4,5-methano-L-prolylamide (70 mg, 0.19 mmol) described in General Method C, Step 2 was dissolved in a mixture of 2 mL *t*-BuOH / 3 mL THF and N-methylmorpholine-N-oxide (33mg, 0.28 mmol) was added followed by osmium tetroxide (0.1 mmol, 50 mol%). The reaction was quenched with 1 mL of 10% aqueous Na_2SO_3 and was taken up in EtOAc and washed with H_2O 5 mL, dried (Na_2SO_4), filtered, evaporated and purified by silica gel flash chromatography (5% MeOH/CH_2Cl_2) to give 41 mg (55%) of the protected diol

as an oil. The title compound was obtained by deprotection of the amine functionality with TFA according to General Method C (FAB MH+ 294).

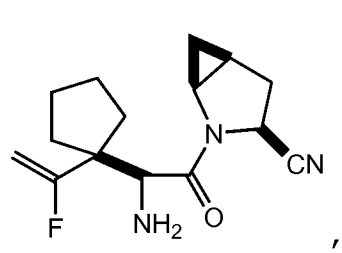
30. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 82, lines 52-67 of the 767 patent:

According to literature (J. Org. Chem 1994, 59, 8215), a solution of Step 3 compound (0.875 g, 3.83 mmol) in dry benzene (4.0 mL) was treated with triethylamine (0.52 mL, 3.83 mmol) and diphenylphosphoryl azide (0.85 mL, 3.83 mmol), refluxed under nitrogen for 1 h and cooled to rt. The solution was treated with benzyl alcohol (0.60 mL, 5.75 mmol or 1.5 equiv), refluxed for 17 h, cooled then diluted with ether (40 mL). The solution was washed with 10% aqueous citric acid (2x3 mL),back-extracting the citric acid wash with ether (40 mL). The combined organic extracts were washed with 5% sodium bicarbonate (2x3 mL), dried ($MgSO_4$), filtered, and concentrated. Flash chromatography on silica gel of the crude product with 10% EtOAc in hexane (1.0 L) gave step 4 compound as a clear thick syrup. Yield: 1.15 g (90%). MS(M+H) 334.

31. As indicated by the Certificate of Correction, at col. 84, line 34 of the 767 patent, please replace "NS" with --MS--.

32. As indicated by the Certificate of Correction, please replace claim 8 at col. 91, lines 9-49 with the following corrected claim:

8. A compound having the structure:



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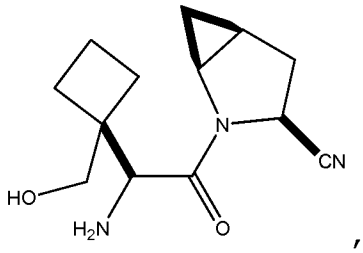

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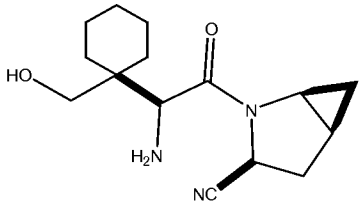

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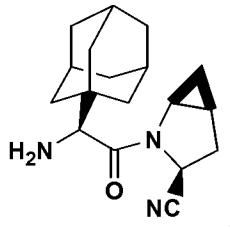

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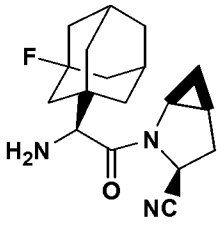

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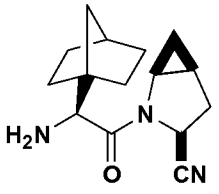

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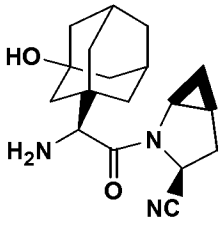

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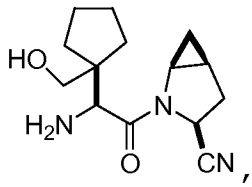
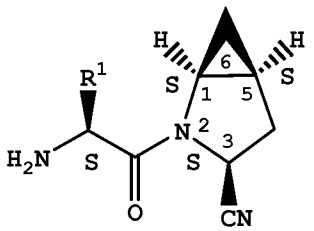


,

or a pharmaceutically acceptable salt thereof.

33. As indicated by the Certificate of Correction, please replace claim 10 at col. 91, line 54-col. 92, line 18 with the following corrected claim:

10. A compound which is

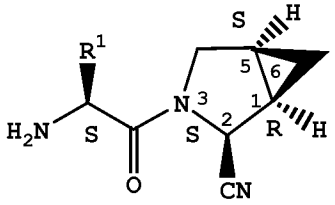


A

(1S,2(2S),3S,5S)

wherein R^1 is alkyl, cycloalkyl, bicycloalkyl, tricycloalkyl, alkylcycloalkyl, hydroxyalkyl, hydroxycycloalkyl, hydroxyalkylcycloalkyl, hydroxybicycloalkyl, or hydroxytricycloalkyl,

or



B

(1R,2S,3(2S),5S)

wherein R^1 is alkyl, cycloalkyl, bicycloalkyl, tricycloalkyl, alkylcycloalkyl, hydroxyalkyl, hydroxycycloalkyl, hydroxyalkylcycloalkyl, hydroxybicycloalkyl, or hydroxytricycloalkyl.

34. As indicated by the Certificate of Correction, please replace claim 15 at col. 92, lines 36 to 44 of the 767 patent with the following corrected claim:

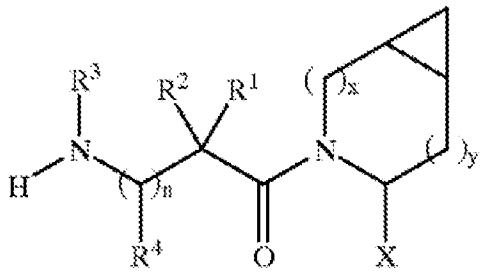
15. The combination as defined in Claim 14 wherein the antidiabetic agent is 1, 2, 3 or more of metformin, glyburide, glimepiride, glipyride, glipizide, chlorpropamide, gliclazide, acarbose, miglitol, pioglitazone, troglitazone, rosiglitazone, insulin, Gl-262570, isaglitazone, JTT-501, NN-2344, L895645, YM-440, R-119702, AJ9677, repaglinide, nateglinide, KAD1129, AR-HO39242, GW-409544, KRP297, AC2993, Exendin-4, LY307161, NN2211, and/or LY315902.

Amendments to the Claims of the 767 Patent:

Please further amend the claims of the 767 patent as shown below (deletions and additions are shown relative to the claims as issued in the 767 patent):

Amend claim 1 as follows:

1. A compound having the structure



wherein x is 0 or 1 and y is 0 or 1, provided that

x=1 when y=0 and

x=0 when y=1; and wherein

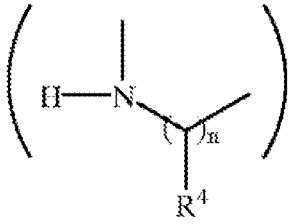
n is 0 or 1;

X is H or CN;

R^1, R^2, R^3 and R^4 are the same or different and are independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, bicycloalkyl, tricycloalkyl, alkylcycloalkyl, hydroxyalkyl, hydroxyalkylcycloalkyl, hydroxycycloalkyl, hydroxybicycloalkyl, hydroxytricycloalkyl, bicycloalkylalkyl, alkylthioalkyl, arylalkylthioalkyl, cycloalkenyl, aryl, aralkyl, heteroaryl, heteroarylalkyl,

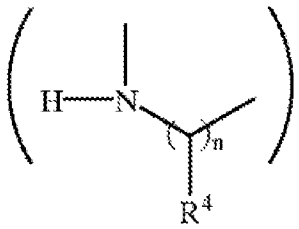
cycloheteroalkyl or cycloheteroalkylalkyl; all optionally substituted through available carbon atoms with 1, 2, 3, 4 or 5 groups selected from hydrogen, halo, alkyl, polyhaloalkyl, alkoxy, haloalkoxy, polyhaloalkoxy, alkoxycarbonyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, polycycloalkyl, heteroarylamino, arylamino, cycloheteroalkyl, cycloheteroalkylalkyl, hydroxy, hydroxyalkyl, nitro, cyano, amino, substituted amino, alkylamino, dialkylamino, thiol, alkylthio, alkylcarbonyl, acyl, alkoxycarbonyl, aminocarbonyl, alkynylaminocarbonyl, alkylaminocarbonyl, alkenylaminocarbonyl, alkylcarbonyloxy, alkylcarbonylamino, arylcarbonylamino, alkylsulfonylamino, alkylaminocarbonylamino, alkoxycarbonylamino, alkylsulfonyl, aminosulfinyl, aminosulfonyl, alkylsulfinyl, sulfonamido or sulfonyl;

and R^1 and R^3 may optionally be taken together to form $(CR^5R^6)_m$ where m is 2 to 6, and R^5 and R^6 are the same or different and are independently selected from hydroxy, alkoxy, H, alkyl, alkenyl, alkynyl, cycloalkyl, halo, amino, substituted amino, cycloalkylalkyl, cycloalkenyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloheteroalkyl, cycloheteroalkylalkyl, alkylcarbonylamino, arylcarbonylamino, alkoxycarbonylamino, aryloxycarbonylamino, alkoxycarbonyl, aryloxycarbonyl, or alkylaminocarbonylamino, or R^1 and R^4 may optionally be taken together to form $(CR^7R^8)_p$ wherein p is 2 to 6, and R^7 and R^8 are the same or different and are independently selected from hydroxy, alkoxy, cyano, H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, halo, amino, substituted amino, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloheteroalkyl, cycloheteroalkylalkyl, alkylcarbonylamino, arylcarbonylamino, alkoxycarbonylamino, aryloxycarbonylamino, alkoxycarbonyl, aryloxycarbonyl, or alkylaminocarbonylamino, or optionally R^1 and R^3 together with



form a 5 to 7 membered ring containing a total of 2 to 4 heteroatoms selected from N, O, S, SO, or SO_2;

or optionally R^1 and R^3 together with



form a 4 to 8 membered cycloheteroalkyl ring wherein the cycloheteroalkyl ring has an optional aryl ring fused thereto or an optional 3 to 7 membered cycloalkyl ring fused thereto;

with the proviso that where x is 1 and y is 0, X is H, n is o, and one of R^1 and R^2 is H and the other is alkyl, then R^3 is other than pyridyl or substituted pyridyl;

including all stereoisomers thereof;

or [and] a pharmaceutically acceptable salt thereof[, or a prodrug ester thereof], and all stereoisomers thereof.

Amend claim 12 as follows:

12. A pharmaceutical combination comprising a [DP4 inhibitor] compound as defined in claim 1 and an antidiabetic agent other than a DP4 inhibitor for treating diabetes and related diseases, an anti-obesity agent and/or a lipid-modulating agent.

Amend claim 13 as follows:

13. The pharmaceutical combination as defined in claim 12 comprising said [DP4 inhibitor] compound as defined in claim 1 and [an] the antidiabetic agent other than a DP4 inhibitor.

Amend claim 16 as follows:

16. The combination as defined in claim 13 wherein the compound as defined in claim 1 is present in a weight ratio to the antidiabetic agent within the range from about 0.01 to about 100:1.

Amend claim 17 as follows:

17. The combination as defined in claim 12 wherein the anti-obesity agent is a beta 3 adrenergic agonist, a lipase inhibitor, [a serotonin (and dopamine) reuptake inhibitor,] a thyroid receptor beta compound, an anorectic agent, and/or a fatty acid oxidation upregulator.

Amend claim 21 as follows:

21. The combination as defined in claim 19 wherein the compound as defined in claim 1 [DP4 inhibitor] is present in a weight ratio to the lipid-modulating agent within the range from about 0.01 to about 100:1.

Amend claim 22 as follows:

22. A pharmaceutical combination comprising a [DP4 inhibitor] compound as defined in claim 1 and an agent for treating infertility, an agent for treating polycystic ovary syndrome, an agent for treating a growth disorder and/or frailty, an anti-arthritis agent, an agent for preventing or inhibiting allograft rejection in transplantation, an agent for treating autoimmune disease, an anti-AIDS agent, an agent for treating inflammatory bowel disease/syndrome, an agent for treating anorexia nervosa, an anti-osteoporosis agent and/or an anti-obesity agent.

Amend added claim 29 to read as follows:

29. The composition of claim 27 or 28 further comprising an antidiabetic agent other than a DP4 inhibitor.

Amend added claim 30 to read as follows:

30. The composition of claim 29 wherein the antidiabetic agent is metformin.

Amend added claim 31 to read as follows:

31. The composition of claim 29 wherein the antidiabetic agent is a SGLT2 inhibitor.

Cancel added claims 36 and 37.

Amend added claim 38 to read as follows:

38. The method of any one of claims 32, 33, 34, or 35, wherein the pharmaceutical composition further comprises an antidiabetic agent other than a DP4 inhibitor.

Amend added claim 39 to read as follows:

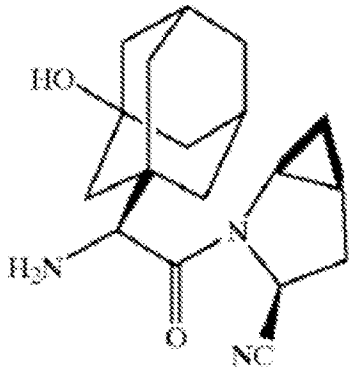
39. The method of claim 38 wherein the antidiabetic agent is metformin.

Amend added claim 40 to read as follows:\

40. The method of claim 38 wherein the antidiabetic agent is a SGLT2 inhibitor.

Add new claims 41 to 45 to read as follows:

41. A method for treating type II diabetes in a mammal comprising administering to the mammal a pharmaceutical composition comprising a compound that is



or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier therefor.

42. The method of claim 41, wherein the pharmaceutically acceptable salt is the hydrochloride salt.

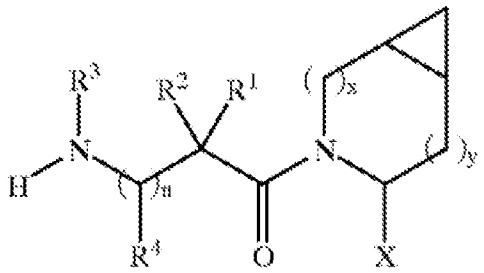
43. The method of any one of claims 41 or 42, wherein the pharmaceutical composition further comprises an antidiabetic agent other than a DP4 inhibitor.

44. The method of claim 43, wherein the antidiabetic agent is metformin.

45. The method of claim 43, wherein the antidiabetic agent is a SGLT2 inhibitor.

Complete Listing of Claims As Amended (including status identifiers):

1. (Amended) A compound having the structure



wherein x is 0 or 1 and y is 0 or 1, provided that

x=1 when y=0 and

x=0 when y=1; and wherein

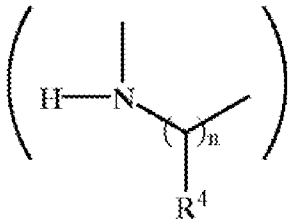
n is 0 or 1;

X is H or CN;

R^1, R^2, R^3 and R^4 are the same or different and are independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, bicycloalkyl, tricycloalkyl, alkylcycloalkyl, hydroxyalkyl, hydroxyalkylcycloalkyl, hydroxycycloalkyl, hydroxybicycloalkyl, hydroxytricycloalkyl, bicycloalkylalkyl, alkylthioalkyl, arylalkylthioalkyl, cycloalkenyl, aryl, aralkyl, heteroaryl, heteroarylalkyl, cycloheteroalkyl or cycloheteroalkylalkyl; all optionally substituted through available carbon atoms with 1, 2, 3, 4 or 5 groups selected from hydrogen, halo, alkyl, polyhaloalkyl, alkoxy, haloalkoxy, polyhaloalkoxy, alkoxycarbonyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, polycycloalkyl, heteroarylamino, arylamino, cycloheteroalkyl, cycloheteroalkylalkyl, hydroxy, hydroxyalkyl, nitro,

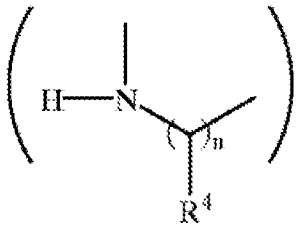
cyano, amino, substituted amino, alkylamino, dialkylamino, thiol, alkylthio, alkylcarbonyl, acyl, alkoxycarbonyl, aminocarbonyl, alkynylaminocarbonyl, alkylaminocarbonyl, alkenylaminocarbonyl, alkylcarbonyloxy, alkylcarbonylamino, arylcarbonylamino, alkylsulfonylamino, alkylaminocarbonylamino, alkoxycarbonylamino, alkylsulfonyl, aminosulfinyl, aminosulfonyl, alkylsulfinyl, sulfonamido or sulfonyl;

and R^1 and R^3 may optionally be taken together to form $(CR^5R^6)_m$ where m is 2 to 6, and R^5 and R^6 are the same or different and are independently selected from hydroxy, alkoxy, H, alkyl, alkenyl, alkynyl, cycloalkyl, halo, amino, substituted amino, cycloalkylalkyl, cycloalkenyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloheteroalkyl, cycloheteroalkylalkyl, alkylcarbonylamino, arylcarbonylamino, alkoxycarbonylamino, aryloxycarbonylamino, alkoxycarbonyl, aryloxycarbonyl, or alkylaminocarbonylamino, or R^1 and R^4 may optionally be taken together to form $(CR^7R^8)_p$ wherein p is 2 to 6, and R^7 and R^8 are the same or different and are independently selected from hydroxy, alkoxy, cyano, H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, halo, amino, substituted amino, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloheteroalkyl, cycloheteroalkylalkyl, alkylcarbonylamino, arylcarbonylamino, alkoxycarbonylamino, aryloxycarbonylamino, alkoxycarbonyl, aryloxycarbonyl, or alkylaminocarbonylamino, or optionally R^1 and R^3 together with



form a 5 to 7 membered ring containing a total of 2 to 4 heteroatoms selected from N, O, S, SO, or SO_2;

or optionally R^1 and R^3 together with



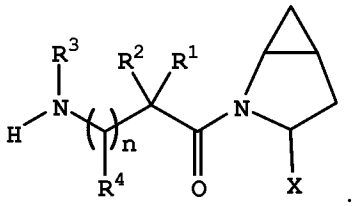
form a 4 to 8 membered cycloheteroalkyl ring wherein the cycloheteroalkyl ring has an optional aryl ring fused thereto or an optional 3 to 7 membered cycloalkyl ring fused thereto;

with the proviso that where x is 1 and y is 0, X is H, n is o, and one of R^1 and R^2 is H and the other is alkyl, then R^3 is other than pyridyl or substituted pyridyl;

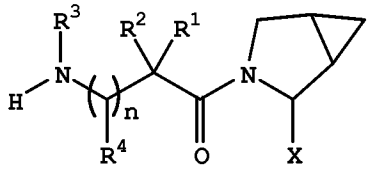
including all stereoisomers thereof;

or [and] a pharmaceutically acceptable salt thereof[, or a prodrug ester thereof], and all stereoisomers thereof.

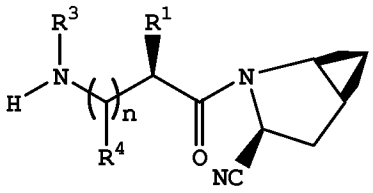
2. (Original) The compound as defined in claim 1 having the structure:



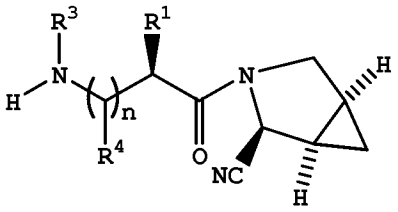
3. (Original) The compound as defined in claim 1 having the structure:



4. (Original) The compound as defined in claim 1 having the structure:



5. (Original) The compound as defined in claim 1 having the structure:



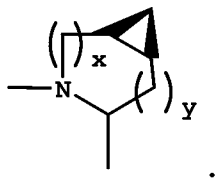
6. (Original) The compound as defined in claim 1 wherein:

R^3 is H, R^1 is H, alkyl, cycloalkyl, bicycloalkyl, tricycloalkyl, alkylcycloalkyl, hydroxyalkyl, hydroxyalkylcycloalkyl, hydroxycycloalkyl hydroxybicycloalkyl, or hydroxytricycloalkyl,

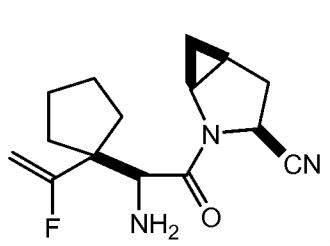
R^2 is H or alkyl, n is 0,

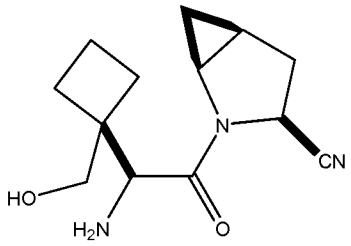
X is CN.

7. (Original) The compound as defined in claim 1 wherein the cyclopropyl fused to the pyrrolidine has the configuration:



8. (Original) A compound having the structure:



,


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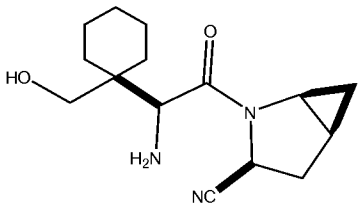
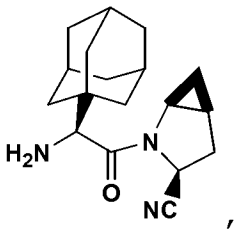
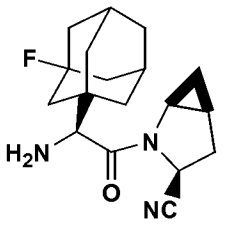


,


,


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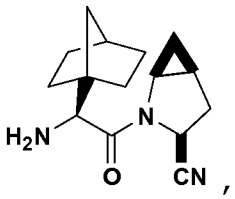

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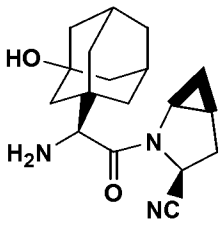
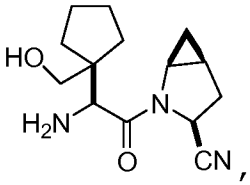


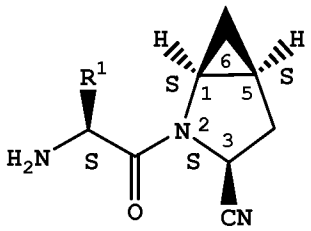
or


,

or a pharmaceutically acceptable salt thereof.

9. (Original) The compound as defined in claim 8 wherein the pharmaceutically acceptable salt is the hydrochloride salt or the trifluoroacetic acid salt.

10. (Original) A compound which is

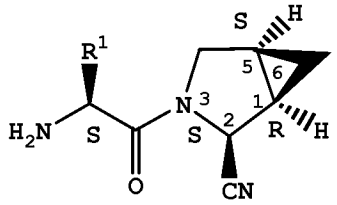


A

(1S,2(2S),3S,5S)

wherein R^1 is alkyl, cycloalkyl, bicycloalkyl, tricycloalkyl, alkylcycloalkyl, hydroxyalkyl, hydroxycycloalkyl, hydroxyalkylcycloalkyl, hydroxybicycloalkyl, or hydroxytricycloalkyl,

or



B

(1R,2S,3(2S),5S)

wherein R^1 is alkyl, cycloalkyl, bicycloalkyl, tricycloalkyl, alkylcycloalkyl, hydroxyalkyl, hydroxycycloalkyl, hydroxyalkylcycloalkyl, hydroxybicycloalkyl, or hydroxytricycloalkyl.

11. (Original) A pharmaceutical composition comprising a compound as defined in claim 1 and a pharmaceutically acceptable carrier therefor.

12. (Amended) A pharmaceutical combination comprising a [DP4 inhibitor] compound as defined in claim 1 and an antidiabetic agent other than a DP4 inhibitor for treating diabetes and related diseases, an anti-obesity agent and/or a lipid-modulating agent.

13. (Twice Amended) The pharmaceutical combination as defined in claim 12 comprising said [DP4 inhibitor] compound as defined in claim 1 and [an] the antidiabetic agent other than a DP4 inhibitor.

14. (Original) The combination as defined in claim 13 wherein the antidiabetic agent is 1, 2, 3 or more of a biguanide, a sulfonyl urea, a glucosidase inhibitor, a PPAR agonist, a PPAR / dual agonist, an SGLT2 inhibitor, an aP2 inhibitor, a glycogen phosphorylase inhibitor, an AGE inhibitor, an insulin sensitizer, a glucagon-like peptide-1 (GLP-1) or mimetic thereof, insulin and/or a meglitinide.

15. (Original) The combination as defined in Claim 14 wherein the antidiabetic agent is 1, 2, 3 or more of metformin, glyburide, glimepiride, glipyride, glipizide, chlorpropamide, gliclazide, acarbose, miglitol, pioglitazone, troglitazone, rosiglitazone, insulin, Gl-262570, isaglitazone, JTT-501, NN-2344, L895645, YM-440, R-119702, AJ9677, repaglinide, nateglinide, KAD1129, AR-HO39242, GW-409544, KRP297, AC2993, Exendin-4, LY307161, NN2211, and/or LY315902.

16. (Amended) The combination as defined in claim 13 wherein the compound as defined in claim 1 is present in a weight ratio to the antidiabetic agent within the range from about 0.01 to about 100:1.

17. (Amended) The combination as defined in claim 12 wherein the anti-obesity agent is a beta 3 adrenergic agonist, a lipase inhibitor, [a serotonin (and dopamine) reuptake inhibitor,] a thyroid receptor beta compound, an anorectic agent, and/or a fatty acid oxidation upregulator.

18. (Original) The combination as defined in claim 17 wherein the anti-obesity agent is orlistat, ATL-962, AJ9677, L750355, CP331648, sibutramine, topiramate, axokine, dexamphetamine, phentermine, phenylpropanolamine, famoxin, and/or mazindol.

19. (Original) The combination as defined in claim 12 wherein the lipid modulating agent is an MTP inhibitor, an HMG CoA reductase inhibitor, a squalene synthetase inhibitor, a fibric acid derivative, an upregulator of LDL receptor activity, a lipoxygenase inhibitor, an ACAT inhibitor, a cholesteryl ester transfer protein inhibitor, or an ATP citrate lyase inhibitor.

20. (Original) The combination as defined in claim 19 wherein the lipid modulating agent is pravastatin, lovastatin, simvastatin, atorvastatin, cerivastatin, fluvastatin, nisvastatin, visastatin, fenofibrate, gemfibrozil, clofibrate, implitapide, CP-529,414, avasimibe, TS-962, MD-700, and/or LY295427.

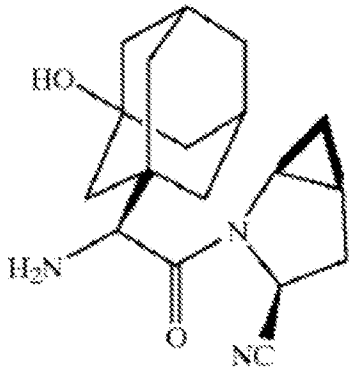
21. (Amended) The combination as defined in claim 19 wherein the compound as defined in claim 1 [DP4 inhibitor] is present in a weight ratio to the lipid-modulating agent within the range from about 0.01 to about 100:1.

22. (Amended) A pharmaceutical combination comprising a [DP4 inhibitor] compound as defined in claim 1 and an agent for treating infertility, an agent for treating polycystic ovary syndrome, an agent for treating a growth disorder and/or frailty, an anti-arthritis agent, an agent for preventing or inhibiting allograft rejection in transplantation, an agent for treating autoimmune disease, an anti-AIDS agent, an agent for treating inflammatory bowel disease/syndrome, an agent for treating anorexia nervosa, an anti-osteoporosis agent and/or an anti-obesity agent.

23. (Canceled)

24. (Canceled)

25. (New) A compound that is



; or a pharmaceutically acceptable salt thereof.

26. (New) The compound as defined in claim 25, wherein the pharmaceutically acceptable salt is the hydrochloride salt.

27. (New) A pharmaceutical composition comprising the compound of claim 25 and a pharmaceutically acceptable carrier therefor.

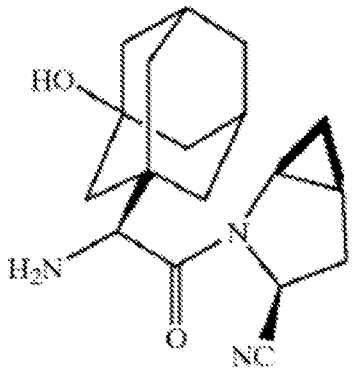
28. (New) A pharmaceutical composition comprising the compound of claim 26 and a pharmaceutically acceptable carrier therefor.

29. (New/Amended) The composition of claim 27 or 28 further comprising an antidiabetic agent other than a DP4 inhibitor.

30. (New/Amended) The composition of claim 29 wherein the antidiabetic agent is metformin.

31. (New/Amended) The composition of claim 29, wherein the antidiabetic agent is a SGLT2 inhibitor.

32. (New) A method for treating diabetes, insulin resistance, hyperglycemia, hyperinsulinemia, impaired glucose homeostasis, or impaired glucose tolerance in a mammal comprising administering to the mammal a pharmaceutical composition comprising a compound that is



or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier therefor.

33. (New) The method of claim 32, wherein the pharmaceutically acceptable salt is the hydrochloride salt.

34. (New) The method of claim 32, for treating diabetes.

35. (New) The method of claim 33, for treating diabetes.

36. (Canceled)

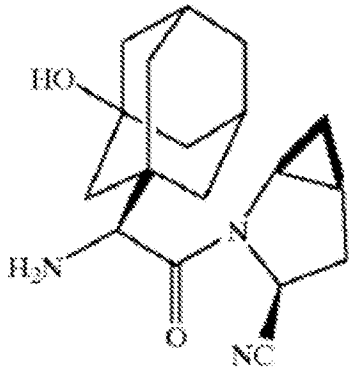
37. (Canceled)

38. (New/Amended) The method of any one of claims 32, 33, 34, or 35 wherein the pharmaceutical composition further comprises an antidiabetic agent other than a DP4 inhibitor.

39. (New/Amended) The method of claim 38, wherein the antidiabetic agent is metformin.

40. (New/Amended) The method of claim 38, wherein the antidiabetic agent is a SGLT2 inhibitor.

41. (New) A method for treating type II diabetes in a mammal comprising administering to the mammal a pharmaceutical composition comprising a compound that is



or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier therefor.

42. (New) The method of claim 41, wherein the pharmaceutically acceptable salt is the hydrochloride salt.

43. (New) The method of any one of claims 41 or 42, wherein the pharmaceutical composition further comprises an antidiabetic agent other than a DP4 inhibitor.

44. (New) The method of claim 43, wherein the antidiabetic agent is metformin.

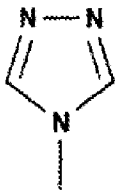
45. (New) The method of claim 43, wherein the antidiabetic agent is a SGLT2 inhibitor.

Changes to 767 Patent Previously Entered by Certificate of Correction

1. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 7, line 4-col. 8, line 7 of the 767 patent:

Alternately, the carboxamide group in 8 may be converted to the nitrile as described above to give compound 9. Deprotection of PG_1 affords 10 which may be subject to standard peptide coupling conditions to afford 7, an intermediate in the synthesis of Ib. Compound 10 may also be generated by oxidation of the amine 2 (e.g. NCS) followed by hydrolysis and subsequent cyanide treatment. Compound 10 may be obtained as a mixture of stereoisomers or a single isomer/diastereomer which may be epimerized (employing conventional procedures) to afford a mixture of stereoisomers.

2. As indicated by the Certificate of Correction, please insert the following structure at col. 14, line 50 of the 767 patent:



3. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 14, lines 55-58 of the 767 patent:

The term "cycloheteroalkylalkyl" as used herein alone or as part of another group refers tocycloheteroalkyl groups as defined above linked through a C atom or heteroatom to a $(CH_2)_r$ chain.

4. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 15, lines 49-56 of the 767 patent:

The other antidiabetic agent may also preferably be a sulfonyl urea such as glyburide (also known as glibenclamide), glimepiride (disclosed in U.S. Pat. No. 4,379,785), glipizide, gliclazide or chlorpropamide, other known sulfonylureas or other

antihyperglycemic agents which act on the ATP-dependent channel of the β-cells, with glyburide and glipizide being preferred, which may be administered in the same or in separate oral dosage forms.

5. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 20, lines 57-62 of the 767 patent:

The other type of therapeutic agent which may be optionally employed with the DP4 inhibitor of formula I may be 1, 2, 3 or more of an anti-obesity agent including a beta 3 adrenergic agonist, a lipase inhibitor, a serotonin (and dopamine) reuptake inhibitor, a thyroid receptor beta drug, an anorectic agent and/or a fatty acid oxidation upregulator.

6. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 29, lines 15-29 of the 767 patent:

To a stirred solution of (S)-N-tert-butoxycarbonyl-isoleucine (231 mg, 1 mmol) and benzotriazol-1-yloxytripyrrolidinophosphonium hexafluorophosphate (780 mg, 1.5 mmol) in CH_2Cl_2 (6 mL) under nitrogen at rt was added 4-methylmorpholine (0.33 mL, 3 mmol). After 5 min, Step 1 compound (120 mg, 1 mmol) was added in one portion. The reaction mixture was stirred under nitrogen at rt overnight and then diluted with CH_2Cl_2 (30 mL), washed with 4.1% $KHSO_4$ (10 mL)), aqueous $NaHCO_3$ (10 mL), brine (10 mL), dried (Na_2SO_4) and evaporated. Purification by flash chromatography on silica gel (2.4x20 cm column, 1:3 EtOAc/hexane) gave the title compound as a colorless oil, 290 mg, 90% yield. LC/MS gave the correct molecular ion [$(M+H)^+$ =297] for the desired compound.

7. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 29, line 40-col. 30, line 3 of the 767 patent:

The reaction mixture of Step 2 compound (220 mg, 0.74 mmol) and 4 M HCl in dioxane (1.5 mL, 6 mmol) was stirred at rt for 2 h and evaporated under reduced pressure. Et_2O was added to the residue and a precipitate was formed. Et_2O was decanted and this was

done three times. The precipitate was dried *in vacuo* to give the title compound as a white powder, 130 mg (76% yield), mp 205-206°C. LC/MS gave the correct molecular ion [$(M+H)^+$ = 197] for the desired compound.

8. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 32, lines 54-63 of the 767 patent:

To a stirred solution of Step 2 compounds (104 mg, 0.32 mmol) in CH_2Cl_2 (1 mL) at rt was added TFA (1 mL). The reaction mixture was stirred at rt for 2 h. The reaction mixture was added slowly to a precooled slurry of $NaHCO_3$ (2 g) in H_2O (2 mL). The mixture was extracted with CH_2Cl_2 (4 mL x 4), and combined CH_2Cl_2 layers were evaporated and purified by preparative HPLC to give the title compound Example 5 (36 mg) and Example 5A (36 mg). LC/MS gave the correct molecular ion [$(M+H)^+$ = 222] for the desired compounds..

9. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 32, line 66-col. 33, line 12 of the 767 patent:

General Method A: Parallel array synthesis methods for preparation of inhibitors from commercially available amino acids. As shown in Scheme 3, the ester 11, described in Example 1 Step 1, was saponified to the acid with LiOH in THF/H_2O and converted to the amide 12 by treatment with isobutyl chloroformate/NMM followed by ammonia in dioxane. The Boc protecting group was removed under acidic conditions using TFA in methylene chloride to give 13. The TFA salt was coupled to Boc-*t*-butylglycine using either EDAC/HOBT/DMF or EDAC/DMAP/CH_2Cl_2 to give 14. The amide was dehydrated to the nitrile 15 using $POCl_3$/imidazole in pyridine at –20°C and finally deprotected with TFA in CH_2Cl_2 at ambient temperature to afford the target 16. SCHEME 3, GENERAL METHOD A (EXAMPLES 6-27)

10. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 34, line 59-col. 35, line 13 of the 767 patent:

An oven-dried 15-mL test tube was charged with Step 3 compound (56 mg, 0.22 mmol), N-*tert*-butoxycarbonyl-(L)-*tert*-leucine (53 mg, 0.23 mmol), dimethylaminopyridine (0.11 g, 0.88 mmol), and CH_2Cl_2 (4 mL). The tube was sealed under nitrogen atmosphere and treated with 1-[(3-(dimethyl)amino)propyl]-3-ethylcarbodiimide (84 mg, 0.44 mmol). The mixture was placed in a shaker and vortexed overnight. The product was purified by solid phase extraction using a United Technology SCX column (2 g of sorbent in a 6 mL column) by loading the material on a SCX ion exchange column and successively washing with CH_2Cl_2 (5 mL), 30% methanol in CH_2Cl_2 (5 mL), 50% methanol in CH_2Cl_2 (5 mL) and methanol (10 mL). The product containing fractions were concentrated under reduced pressure to give the desired amide. Further purification by reverse phase preparative column chromatography on a YMC S5 ODS 20 x 250 mm column gave the title compound, 50 mg (68% yield). Purification conditions: Gradient elution from 30% methanol/water/0.1 TFA to 90% methanol/water/0.1 TFA over 15 min. 5 min. hold at 90% methanol/water/0.1 TFA. Flow rate: 20 mL/min. Detection wavelength: 220. Retention Time: 14 min.

11. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 41, lines 36-46 of the 767 patent:

An oven-dried 10-mL round bottomed flask was charged with Step 2 compound (350 mg, 0.79 mmol), imidazole (108 mg, 1.58 mmol), pyridine (3 mL). The flask under argon was cooled to -30^0C. Slow addition of $POCl_3$ (0.30 mL, 3.16 mmol) gave after mixing a thick slurry. The slurry was mixed at -30^0C for 3 h and the volatiles evaporated. Dichloromethane (5 mL) was then added and the insoluble solid was removed by filtration. The organic layer was washed with H_2O, 10% citric acid, brine and dried over Na_2SO_4. Removal of solvent gave crude desired nitrile (330 mg) (LC/Mass, + ion): 424 (M+H).

12. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 43, lines 20-29 of the 767 patent:

To a flame-dried 500-mL round-bottomed flask containing cyclopentylideneacetic acid ethyl ester (17.5 g, 113 mmol) in 100 mL anhydrous toluene at -78°C under argon was added DIBAL-H (189 mL of a 1.5 M solution in toluene, 284 mmol, 2.50 equiv) dropwise over a 30 min period through an addition funnel, and the mixture was then allowed to warm to rt, stirring for 18 h. The reaction mixture was then recooled to -78°C, and quenched by the careful addition of 30 mL anhydrous MeOH. Upon warming to rt, 1 N Rochelle's salt (100 mL) was added, and the mixture was stirred 90 min. The biphasic reaction mixture was then diluted with Et_2O (200 mL) in a separatory funnel, and the layers were separated. The organic layer was then washed with brine (100 mL), dried (Na_2SO_4), and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, CH_2Cl_2 / EtOAc, 10:1) gave 11.6 g (92%) of the desired allylic alcohol as a colorless oil.

13. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 43, lines 53-67 of the 767 patent:

To a flame-dried 500-mL round-bottomed flask containing N-(*tert*-butyloxycarbonyl)glycine (13.45 g, 76.75 mmol) in 100 mL CH_2Cl_2 at rt was added Step 2 compound (8.61 g, 76.75 mmol, 1.00 equiv) in 20 mL CH_2Cl_2, followed by dicyclohexylcarbodiimide (16.63 g, mmol, 1.05 equiv) in 80 mL CH_2Cl_2. To this reaction mixture was then added 4-dimethylaminopyridine (0.94 mg, mmol, 0.10 equiv), and the mixture was allowed to stir overnight. The reaction mixture was then filtered through a medium sintered-glass funnel, rinsing with 100 mL CH_2Cl_2, and concentrated under reduced pressure. The crude product was then purified by flash chromatography (silica gel, hexanes/EtOAc, 20:1 to 1:1 gradient) to give 19.43 g (94%) of the desired glycinyl ester as a colorless oil.

14. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 44, lines 19-45 of the 767 patent:

A flame-dried 500-mL round-bottomed flask under argon was charged with $ZnCl_2$ (11.8 g, mmol, 1.20 equiv) and 20 mL toluene. The mixture was heated under vacuum with vigorous stirring to azeotrope off any traces of moisture with the distilling toluene, repeating this process (2 x). The flask was then cooled to rt under argon, (2-cyclopentylideneethyl) N-(*tert*-butyloxycarbonyl)glycinate (19.36 g, 71.88 mmol) was added via cannula as a solution in 180 mL THF, and the mixture was then cooled to -78°C. In a separate flame-dried 200-mL round-bottomed flask containing diisopropylamine (26.3 mL, mmol, 2.60 equiv) in 90 mL THF at -78°C was added n-butyllithium (71.89 mL of a 2.5 M solution in hexanes, mmol, 2.5 equiv), and the mixture was allowed to warm to 0°C for 30 min before recooling to -78°C. The lithium diisopropylamine thus generated was then added via cannula to the $ZnCl_2$ ester mixture dropwise at a steady rate over 40 min, and the resultant reaction mixture was allowed to slowly warm to rt and stir overnight. The yellow reaction mixture was then poured into a separatory funnel, diluted with 300 mL Et_2O, and the resultant organic solution was washed successively with 300 mL 1N HCl and 300 mL brine, dried (Na_2SO_4), and concentrated under reduced pressure. Purification by flash chromatography (silica gel, 3% MeOH in CH_2Cl_2 with 0.5% HOAc) gave 17.8 g (92%) of the desired amino acid product as a white solid. (FAB MH+ 270).

15. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col 46, lines 48-59 of the 767 patent:

Step 2 compound (32 mg, 0.09 mmol) was dissolved in 1 mL of CH_2Cl_2 and 1 mL of TFA was added and the reaction stirred for 30 min at rt and was evaporated to dryness. The product was purified by reverse phase preparative column chromatography on a YMC S5 ODS 20 X 250 mm column to give 12 mg of the TFA salt (lyophilized from water or isolated after evaporation of eluent and trituration with ether) the title compound. Purification conditions: gradient elution from 10% methanol/water/0.1 TFA

to 90% methanol/water/0.1 TFA over 18 min; 5 min. hold at 90% methanol/water/0.1 trifluoroacetic acid. Flow rate: 20 mL/min. Detection wavelength: 220.

16. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 46, lines 61-67 of the 767 patent:

Examples 30–39 were prepared by the methods outlined in General Method B and General Method C starting from cyclopentanone, cyclobutanone, cyclohexanone, cycloheptanone, cyclooctanone, cis-3,4-dimethylcyclopentanone, and 4-pyranone, cyclopropaneethylhemiacetal, acetone, and 3-pentanone respectively.

17. As indicated by the Certificate of Correction, at col. 52, line 64 of the 767 patent, change "25" to ---28--.

18. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 53, lines 28-45 of the 767 patent:

N-Boc protected cyclobutylvinyl compound (Example 31, prepared by general method C) (0.16 g, 0.46 mmol) was dissolved in 10 mL of a 1:1 mixture of THF:water and treated with OsO_4 (12 mg, catalyst) and $NaIO_4$ (0.59 g, 2.76 mmol, 6 equiv). After 2 h, the reaction mixture was diluted with 50 mL of ether and 10 mL of water. The layers were equilibrated and the organic fraction was washed one time with $NaHCO_3$ solution, dried over $MgSO_4$ and concentrated to give a dark oil. The oil was diluted with 10 mL of methanol and treated with $NaBH_4$ (0.08 g, 2.0 mmol). The mixture turned very dark and after 30 min was diluted with ether and the reaction was quenched with aqueous $NaHCO_3$ solution. The mixture was equilibrated and layers separated. The organic fraction was washed with solutions of $NaHCO_3$ and 0.1 M HCl. The organics were dried ($MgSO_4$) and concentrated to give 90 mg (56%) of the Step 1 compound as a dark oil.

19. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 53, lines 59-67 of the 767 patent:

Step 1 compound (90 mg, 0.26 mmol) was dissolved in 3 mL of CH_2Cl_2, cooled to 0°C and treated with 3 mL of freshly distilled TFA. The reaction was complete in 80 min and evaporated to dryness and purified by preparative HPLC (YMC S5 ODS 30 x 100 mm, 10 minute gradient 100%A to 100%B, Solvent A = 10% MeOH-90%H2O-0.1% TFA, Solvent B = 90% MeOH-10% H_2O -0.1% TFA, to give, after removal of water, 50 mg (60%) of title compound. (MH+250).

20. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 62, lines 56-67 of the 767 patent:

The Step 2 compound (95 mg, 0.22 mmol, 1 equiv) was dissolved in anhydrous CH_2Cl_2 (2.5 mL) under argon and cooled to –78°C. The mixture was treated with diisopropylethylamine (65 μL, 0.37 mmol, 1.7 equiv), and triethylsilyl triflate (75 μL, 0.33 mmol, 1.5 equiv), and stirred at 0°C for 1.5 h. The reaction was mixed with MeOH (0.5 mL), silica gel (200 mg) and H_2O (2 drops) and stirred at rt for 18 h. The solvent was removed by rotary evaporation and the residue purified flash column chromatography on silica gel(2.5x10 cm) with 4% MeOH/CH_2Cl_2 to afford the product (92 mg, 0.17 mmol, 77%): MS m/e 540 $(m+H)^+$.

21. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 66, lines 11-27 of the 767 patent:

An oven-dried flask equipped with a condenser and drying tube was charged with norbornane-2-carboxylic acid (4.92 g, 35 mmol, 1 equiv) and treated with bromine (2.1 mL, 41 mmol, 1.15 equiv) and phosphorous trichloride (0.153 mL, 1.8 mmol, 0.05 equiv). The mixture was heated at 85°C for 7 h protected from light. Additional bromine (0.4 mL, 7.8 mmol, 0.22 equiv) was added with continued heating for 1 h. The mixture was cooled to rt, and Et_2O (100 mL) was added. The mixture was washed with 10% aq $NaHSO_3$ (50 mL), H_2O (2x50 mL), and brine (25 mL). The ether fraction was dried (Na_2SO_4), filtered and concentrated by rotary evaporation. The product was purified by flash column chromatography on silica gel (5x15 cm) with 2% to 4% MeOH/CH_2Cl_2 +

0.5% HOAc. The product was chased with hexanes to remove residual HOAc. The isolated material consists of two inseparable materials (4.7 g), which was used without further purification in the next step.

22. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 69, lines 20-27 of the 767 patent:

To a 50-mL round-bottomed flask containing Step 2 compound (0.72 g, 4.20 mmol) in 8 mL of water at rt was added NaCN (0.20 g, 4.20 mmol) followed by NH_4Cl (0.20 g, 5.00 mmol). To this reaction mixture was then added methanol (8 mL) and the mixture was allowed to stir overnight. The reaction mixture was then extracted with ether (2x15 mL), dried ($MgSO_4$) and concentrated under reduced pressure to give the crude Strecker product.

23. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 69, lines 28-44 of the 767 patent:

To a 100-mL round-bottomed flask containing the crude Strecker product was added 10 mL of HOAc and 10 mL of conc. HCl. The mixture was refluxed overnight. The mixture was concentrated under reduced pressure to give a yellow solid. The solid was triturated with 5 mL of 1:1 mixture of ether and hexanes. The white solid was treated with triethylamine (1.4 mL, 9.99 mmol) and di-*tert*-butyldicarbonate (1.00 g, 4.60 mmol) in 50 mL DMF. After 4 h the pH of the mixture was adjusted to 9 with saturated Na_2CO_3 soln. After an additional 3 h of stirring the mixture was extracted with 1:1 ether and hexanes and the aqueous fraction acidified to pH 2 with 5% $KHSO_4$ solution. The aqueous phase was washed with ether (2 X 40 mL), the organics dried ($MgSO_4$), and evaporated to an oil that was purified by silica gel flash chromatography with 8:92 methanol:CH_2Cl_2 to give 0.3 g (23%) of the Boc-protected amino acid as a light oil (M-H, 318).

24. As indicated by the Certificate of Correction, please move "Step 1" at col. 70, line 56 of the 767 patent to col. 70, line 65.

25. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 72, lines 30-49 of the 767 patent:

Sodium ethoxide (940 mg of 21 wt% solution in ethanol, 2.9 mmol) in ethanol (2 mL) was added to a stirred solution of diethyl acetamidomalonate (4.31g, 19.8 mmol) in EtOH (23 mL) at rt under argon. The reaction mixture was cooled to 0°C; and trans-2-pentenal (1.51 g, 18.0 mmol) was added dropwise maintaining the reaction temperature at < 5°C. After the addition, the reaction was allowed to warm to rt, stirred for 4 h, then quenched with acetic acid (460 μl). The solution was concentrated *in vacuo*, and the residue dissolved in EtOAc (25 mL), washed with 10% $NaHCO_3$ solution (2x5 mL), brine and dried ($MgSO_4$). The solution was filtered and concentrated to a 10 mL volume, then heated to reflux and diluted with hexane (20 mL). Upon cooling to rt, the title compound precipitated and was collected to give 3.0 g (50%) of the Step 1 compound (mp 106-109°C; LC/Mass: + ions, 324 M+Na).

26. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 72, line 64-col. 73, line 8 of the 767 patent:

To a solution of Step 1 compound (2.87 g, 9.5 mmol) and triethylsilane (2.28 mL, 14.3 mmol) in CH_2Cl_2 (30 mL) under argon was added TFA (7.35 mL, 95.3 mmol) dropwise with stirring while maintaining the internal temperature at 25^0C by means of an ice bath. After stirring for 4 h at rt, the solution was concentrated. The residue was diluted with CH_2Cl_2 (100 mL), then treated with H_2O (50 mL) and solid Na_2CO_3 with vigorous stirring until the mixture was basic. The organic layer was separated, dried (Na_2SO_4), filtered, then concentrated to give the Step 2 compound as a yellow oil which was used without further purification (LC/Mass: + ions, 308 M+Na).

27. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 73, lines 22-27 of the 767 patent:

Step 2 compound (3.73 g, 9.5 mmol) was suspended in 6 N HCl (20 mL) and HOAc (5 mL) and heated at reflux for 20 h. The reaction mixture was then cooled, washed with EtOAc (20 mL), then concentrated to give an oil which crystallized upon trituration with ether to give the title compound (1.2 g, 70.6%) (LC/Mass, + ion): 144 (M+H).

28. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 74, lines 26-41 of the 767 patent:

Sodium ethoxide (940 mg, 2.9 mmol; 21% w/w solution in ethanol) in ethanol (2 mL) was added to a stirred solution of diethyl acetamidomalonate (4.31 g, 19.8 mmol) in EtOH (23 mL) at rt under argon. The reaction mixture was cooled to 0^0C; and 4-methyl-2-pentenal (1.77 g, 18.0 mmol)was added dropwise maintaining the reaction temperature at < 5°C. After the addition, the reaction was allowed to warm to rt, stirred for 4 h, then quenched with acetic acid (460 μl). The solution was concentrated and the remainder dissolved in EtOAc (25 mL). The organics were washed with 10% $NaHCO_3$ solution (2x5 mL), brine and dried ($MgSO_4$). The solution was filtered and concentrated to 10 mL volume, then heated to reflux and treated with hexane (20 mL). On cooling, the Step 1 compound precipitated and was collected (3.3 g) (LC/Mass, + ion): 338 (M+Na).

29. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 79, lines 54-67 of the 767 patent:

N-[((S)-cyclopentylvinyl)-N-tert-butoxycarbonylglycinyl]-(2S,4S,5S)-2-cyano-4,5-methano-L-prolylamide (70 mg, 0.19 mmol) described in General Method C, Step 2 was dissolved in a mixture of 2 mL *t*-BuOH / 3 mL THF and N-methylmorpholine-N-oxide (33mg, 0.28 mmol) was added followed by osmium tetroxide (0.1 mmol, 50 mol%). The reaction was quenched with 1 mL of 10% aqueous Na_2SO_3 and was taken up in EtOAc and washed with H_2O 5 mL, dried (Na_2SO_4), filtered, evaporated and purified by silica gel flash chromatography (5% MeOH/CH_2Cl_2) to give 41 mg (55%) of the protected diol

as an oil. The title compound was obtained by deprotection of the amine functionality with TFA according to General Method C (FAB MH+ 294).

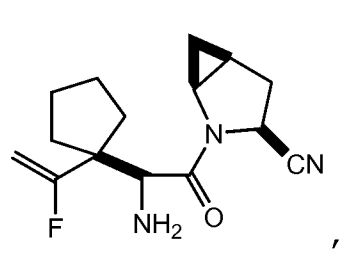
30. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 82, lines 52-67 of the 767 patent:

According to literature (J. Org. Chem 1994, 59, 8215), a solution of Step 3 compound (0.875 g, 3.83 mmol) in dry benzene (4.0 mL) was treated with triethylamine (0.52 mL, 3.83 mmol) and diphenylphosphoryl azide (0.85 mL, 3.83 mmol), refluxed under nitrogen for 1 h and cooled to rt. The solution was treated with benzyl alcohol (0.60 mL, 5.75 mmol or 1.5 equiv), refluxed for 17 h, cooled then diluted with ether (40 mL). The solution was washed with 10% aqueous citric acid (2x3 mL),back-extracting the citric acid wash with ether (40 mL). The combined organic extracts were washed with 5% sodium bicarbonate (2x3 mL), dried ($MgSO_4$), filtered, and concentrated. Flash chromatography on silica gel of the crude product with 10% EtOAc in hexane (1.0 L) gave step 4 compound as a clear thick syrup. Yield: 1.15 g (90%). MS(M+H) 334.

31. As indicated by the Certificate of Correction, at col. 84, line 34 of the 767 patent, please replace "NS" with --MS--.

32. As indicated by the Certificate of Correction, please replace claim 8 at col. 91, lines 9-49 with the following corrected claim:

8. A compound having the structure:



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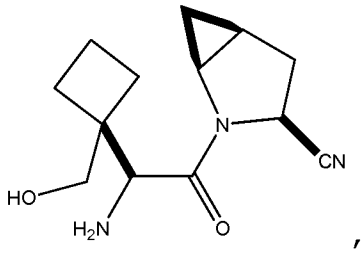

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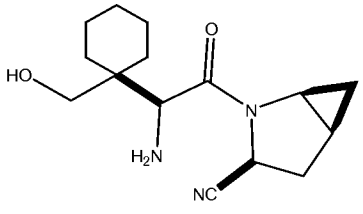

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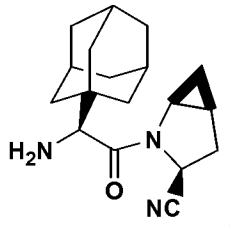

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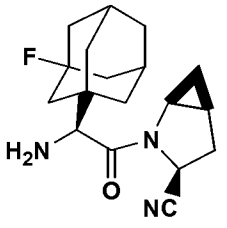

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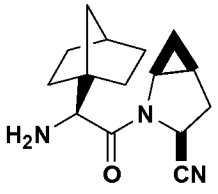

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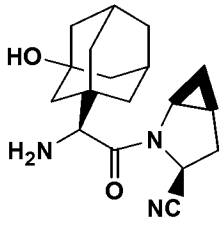
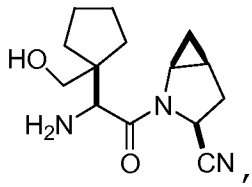


or

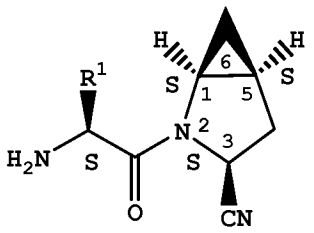


,

or a pharmaceutically acceptable salt thereof.

33. As indicated by the Certificate of Correction, please replace claim 10 at col. 91, line 54-col. 92, line 18 with the following corrected claim:

10. A compound which is

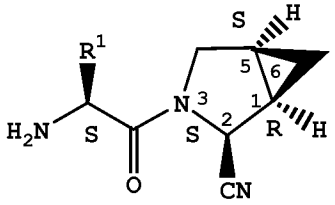


A

(1S,2(2S),3S,5S)

wherein R^1 is alkyl, cycloalkyl, bicycloalkyl, tricycloalkyl, alkylcycloalkyl, hydroxyalkyl, hydroxycycloalkyl, hydroxyalkylcycloalkyl, hydroxybicycloalkyl, or hydroxytricycloalkyl,

or



B

(1R,2S,3(2S),5S)

wherein R^1 is alkyl, cycloalkyl, bicycloalkyl, tricycloalkyl, alkylcycloalkyl, hydroxyalkyl, hydroxycycloalkyl, hydroxyalkylcycloalkyl, hydroxybicycloalkyl, or hydroxytricycloalkyl.

34. As indicated by the Certificate of Correction, please replace claim 15 at col. 92, lines 36 to 44 of the 767 patent with the following corrected claim:

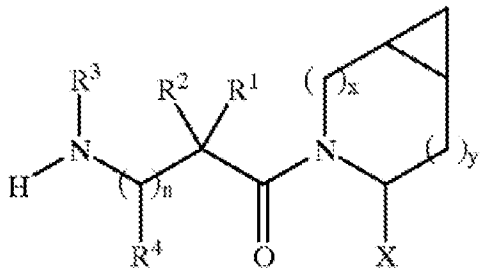
15. The combination as defined in Claim 14 wherein the antidiabetic agent is 1, 2, 3 or more of metformin, glyburide, glimepiride, glipyride, glipizide, chlorpropamide, gliclazide, acarbose, miglitol, pioglitazone, troglitazone, rosiglitazone, insulin, Gl-262570, isaglitazone, JTT-501, NN-2344, L895645, YM-440, R-119702, AJ9677, repaglinide, nateglinide, KAD1129, AR-HO39242, GW-409544, KRP297, AC2993, Exendin-4, LY307161, NN2211, and/or LY315902.

Amendments to the Claims of the 767 Patent:

Please further amend the claims of the 767 patent as shown below (deletions and additions are shown relative to the claims as issued in the 767 patent):

Amend claim 1 as follows:

1. A compound having the structure



wherein x is 0 or 1 and y is 0 or 1, provided that

x=1 when y=0 and

x=0 when y=1; and wherein

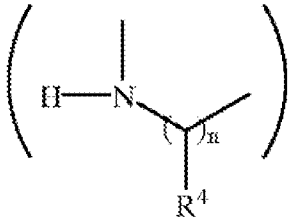
n is 0 or 1;

X is H or CN;

R^1, R^2, R^3 and R^4 are the same or different and are independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, bicycloalkyl, tricycloalkyl, alkylcycloalkyl, hydroxyalkyl, hydroxyalkylcycloalkyl, hydroxycycloalkyl, hydroxybicycloalkyl, hydroxytricycloalkyl, bicycloalkylalkyl, alkylthioalkyl, arylalkylthioalkyl, cycloalkenyl, aryl, aralkyl, heteroaryl, heteroarylalkyl,

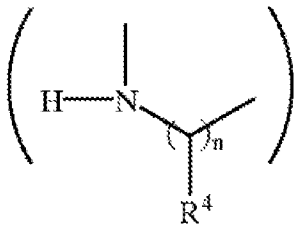
cycloheteroalkyl or cycloheteroalkylalkyl; all optionally substituted through available carbon atoms with 1, 2, 3, 4 or 5 groups selected from hydrogen, halo, alkyl, polyhaloalkyl, alkoxy, haloalkoxy, polyhaloalkoxy, alkoxycarbonyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, polycycloalkyl, heteroarylamino, arylamino, cycloheteroalkyl, cycloheteroalkylalkyl, hydroxy, hydroxyalkyl, nitro, cyano, amino, substituted amino, alkylamino, dialkylamino, thiol, alkylthio, alkylcarbonyl, acyl, alkoxycarbonyl, aminocarbonyl, alkynylaminocarbonyl, alkylaminocarbonyl, alkenylaminocarbonyl, alkylcarbonyloxy, alkylcarbonylamino, arylcarbonylamino, alkylsulfonylamino, alkylaminocarbonylamino, alkoxycarbonylamino, alkylsulfonyl, aminosulfinyl, aminosulfonyl, alkylsulfinyl, sulfonamido or sulfonyl;

and R^1 and R^3 may optionally be taken together to form $(CR^5R^6)_m$ where m is 2 to 6, and R^5 and R^6 are the same or different and are independently selected from hydroxy, alkoxy, H, alkyl, alkenyl, alkynyl, cycloalkyl, halo, amino, substituted amino, cycloalkylalkyl, cycloalkenyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloheteroalkyl, cycloheteroalkylalkyl, alkylcarbonylamino, arylcarbonylamino, alkoxycarbonylamino, aryloxycarbonylamino, alkoxycarbonyl, aryloxycarbonyl, or alkylaminocarbonylamino, or R^1 and R^4 may optionally be taken together to form $(CR^7R^8)_p$ wherein p is 2 to 6, and R^7 and R^8 are the same or different and are independently selected from hydroxy, alkoxy, cyano, H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, halo, amino, substituted amino, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloheteroalkyl, cycloheteroalkylalkyl, alkylcarbonylamino, arylcarbonylamino, alkoxycarbonylamino, aryloxycarbonylamino, alkoxycarbonyl, aryloxycarbonyl, or alkylaminocarbonylamino, or optionally R^1 and R^3 together with



form a 5 to 7 membered ring containing a total of 2 to 4 heteroatoms selected from N, O, S, SO, or SO_2;

or optionally R^1 and R^3 together with



form a 4 to 8 membered cycloheteroalkyl ring wherein the cycloheteroalkyl ring has an optional aryl ring fused thereto or an optional 3 to 7 membered cycloalkyl ring fused thereto;

with the proviso that where x is 1 and y is 0, X is H, n is o, and one of R^1 and R^2 is H and the other is alkyl, then R^3 is other than pyridyl or substituted pyridyl;

including all stereoisomers thereof;

or [and] a pharmaceutically acceptable salt thereof[, or a prodrug ester thereof], and all stereoisomers thereof.

Amend claim 12 as follows:

12. A pharmaceutical combination comprising a [DP4 inhibitor] compound as defined in claim 1 and an antidiabetic agent other than a DP4 inhibitor for treating diabetes and related diseases, an anti-obesity agent and/or a lipid-modulating agent.

Amend claim 13 as follows:

13. The pharmaceutical combination as defined in claim 12 comprising said [DP4 inhibitor] compound as defined in claim 1 and [an] the antidiabetic agent other than a DP4 inhibitor.

Amend claim 16 as follows:

16. The combination as defined in claim 13 wherein the compound as defined in claim 1 is present in a weight ratio to the antidiabetic agent within the range from about 0.01 to about 100:1.

Amend claim 17 as follows:

17. The combination as defined in claim 12 wherein the anti-obesity agent is a beta 3 adrenergic agonist, a lipase inhibitor, [a serotonin (and dopamine) reuptake inhibitor,] a thyroid receptor beta compound, an anorectic agent, and/or a fatty acid oxidation upregulator.

Amend claim 21 as follows:

21. The combination as defined in claim 19 wherein the compound as defined in claim 1 [DP4 inhibitor] is present in a weight ratio to the lipid-modulating agent within the range from about 0.01 to about 100:1.

Amend claim 22 as follows:

22. A pharmaceutical combination comprising a [DP4 inhibitor] compound as defined in claim 1 and an agent for treating infertility, an agent for treating polycystic ovary syndrome, an agent for treating a growth disorder and/or frailty, an anti-arthritis agent, an agent for preventing or inhibiting allograft rejection in transplantation, an agent for treating autoimmune disease, an anti-AIDS agent, an agent for treating inflammatory bowel disease/syndrome, an agent for treating anorexia nervosa, an anti-osteoporosis agent and/or an anti-obesity agent.

Amend added claim 29 to read as follows:

29. The composition of claim 27 or 28 further comprising an antidiabetic agent other than a DP4 inhibitor.

Amend added claim 30 to read as follows:

30. The composition of claim 29 wherein the antidiabetic agent is metformin.

Amend added claim 31 to read as follows:

31. The composition of claim 29 wherein the antidiabetic agent is a SGLT2 inhibitor.

Cancel added claims 36 and 37.

Amend added claim 38 to read as follows:

38. The method of any one of claims 32, 33, 34, or 35, wherein the pharmaceutical composition further comprises an antidiabetic agent other than a DP4 inhibitor.

Amend added claim 39 to read as follows:

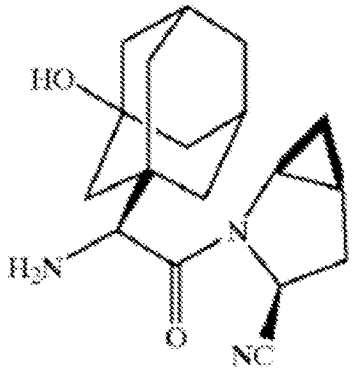
39. The method of claim 38 wherein the antidiabetic agent is metformin.

Amend added claim 40 to read as follows:\

40. The method of claim 38 wherein the antidiabetic agent is a SGLT2 inhibitor.

Add new claims 41 to 45 to read as follows:

41. A method for treating type II diabetes in a mammal comprising administering to the mammal a pharmaceutical composition comprising a compound that is



or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier therefor.

42. The method of claim 41, wherein the pharmaceutically acceptable salt is the hydrochloride salt.

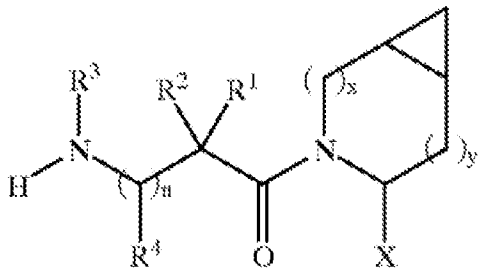
43. The method of any one of claims 41 or 42, wherein the pharmaceutical composition further comprises an antidiabetic agent other than a DP4 inhibitor.

44. The method of claim 43, wherein the antidiabetic agent is metformin.

45. The method of claim 43, wherein the antidiabetic agent is a SGLT2 inhibitor.

Complete Listing of Claims As Amended (including status identifiers):

1. (Amended) A compound having the structure



wherein x is 0 or 1 and y is 0 or 1, provided that

x=1 when y=0 and

x=0 when y=1; and wherein

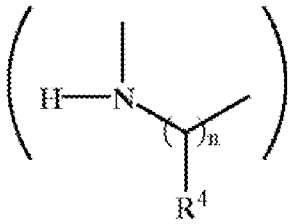
n is 0 or 1;

X is H or CN;

R^1, R^2, R^3 and R^4 are the same or different and are independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, bicycloalkyl, tricycloalkyl, alkylcycloalkyl, hydroxyalkyl, hydroxyalkylcycloalkyl, hydroxycycloalkyl, hydroxybicycloalkyl, hydroxytricycloalkyl, bicycloalkylalkyl, alkylthioalkyl, arylalkylthioalkyl, cycloalkenyl, aryl, aralkyl, heteroaryl, heteroarylalkyl, cycloheteroalkyl or cycloheteroalkylalkyl; all optionally substituted through available carbon atoms with 1, 2, 3, 4 or 5 groups selected from hydrogen, halo, alkyl, polyhaloalkyl, alkoxy, haloalkoxy, polyhaloalkoxy, alkoxycarbonyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, polycycloalkyl, heteroarylamino, arylamino, cycloheteroalkyl, cycloheteroalkylalkyl, hydroxy, hydroxyalkyl, nitro,

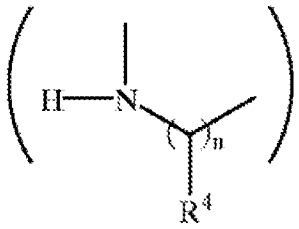
cyano, amino, substituted amino, alkylamino, dialkylamino, thiol, alkylthio, alkylcarbonyl, acyl, alkoxycarbonyl, aminocarbonyl, alkynylaminocarbonyl, alkylaminocarbonyl, alkenylaminocarbonyl, alkylcarbonyloxy, alkylcarbonylamino, arylcarbonylamino, alkylsulfonylamino, alkylaminocarbonylamino, alkoxycarbonylamino, alkylsulfonyl, aminosulfinyl, aminosulfonyl, alkylsulfinyl, sulfonamido or sulfonyl;

and R^1 and R^3 may optionally be taken together to form $(CR^5R^6)_m$ where m is 2 to 6, and R^5 and R^6 are the same or different and are independently selected from hydroxy, alkoxy, H, alkyl, alkenyl, alkynyl, cycloalkyl, halo, amino, substituted amino, cycloalkylalkyl, cycloalkenyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloheteroalkyl, cycloheteroalkylalkyl, alkylcarbonylamino, arylcarbonylamino, alkoxycarbonylamino, aryloxycarbonylamino, alkoxycarbonyl, aryloxycarbonyl, or alkylaminocarbonylamino, or R^1 and R^4 may optionally be taken together to form $(CR^7R^8)_p$ wherein p is 2 to 6, and R^7 and R^8 are the same or different and are independently selected from hydroxy, alkoxy, cyano, H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, halo, amino, substituted amino, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloheteroalkyl, cycloheteroalkylalkyl, alkylcarbonylamino, arylcarbonylamino, alkoxycarbonylamino, aryloxycarbonylamino, alkoxycarbonyl, aryloxycarbonyl, or alkylaminocarbonylamino, or optionally R^1 and R^3 together with



form a 5 to 7 membered ring containing a total of 2 to 4 heteroatoms selected from N, O, S, SO, or SO_2;

or optionally R^1 and R^3 together with



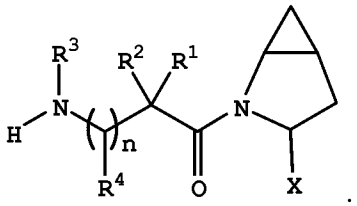
form a 4 to 8 membered cycloheteroalkyl ring wherein the cycloheteroalkyl ring has an optional aryl ring fused thereto or an optional 3 to 7 membered cycloalkyl ring fused thereto;

with the proviso that where x is 1 and y is 0, X is H, n is o, and one of R^1 and R^2 is H and the other is alkyl, then R^3 is other than pyridyl or substituted pyridyl;

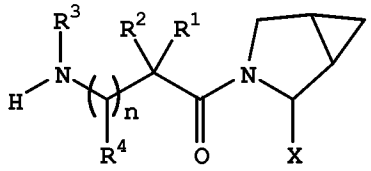
including all stereoisomers thereof;

or [and] a pharmaceutically acceptable salt thereof[, or a prodrug ester thereof], and all stereoisomers thereof.

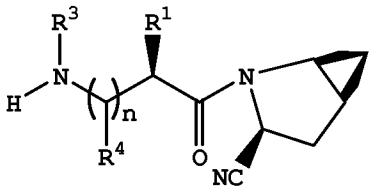
2. (Original) The compound as defined in claim 1 having the structure:



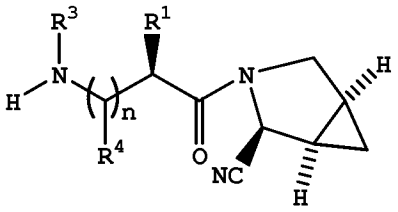
3. (Original) The compound as defined in claim 1 having the structure:



4. (Original) The compound as defined in claim 1 having the structure:



5. (Original) The compound as defined in claim 1 having the structure:



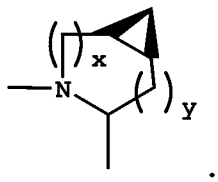
6. (Original) The compound as defined in claim 1 wherein:

R^3 is H, R^1 is H, alkyl, cycloalkyl, bicycloalkyl, tricycloalkyl, alkylcycloalkyl, hydroxyalkyl, hydroxyalkylcycloalkyl, hydroxycycloalkyl hydroxybicycloalkyl, or hydroxytricycloalkyl,

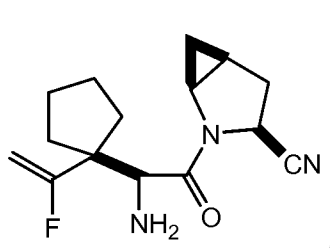
R^2 is H or alkyl, n is 0,

X is CN.

7. (Original) The compound as defined in claim 1 wherein the cyclopropyl fused to the pyrrolidine has the configuration:



8. (Original) A compound having the structure:



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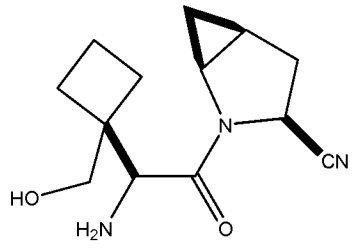

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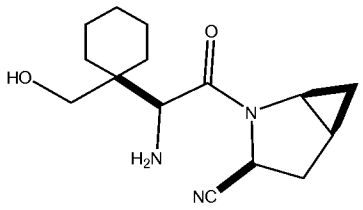

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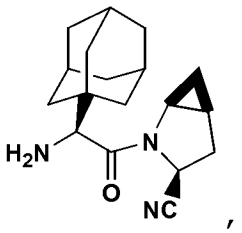

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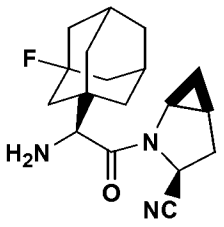

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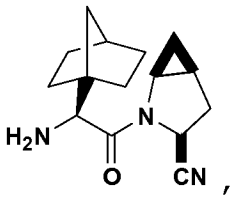

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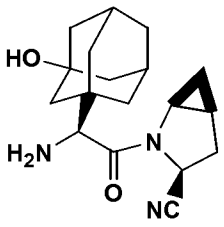
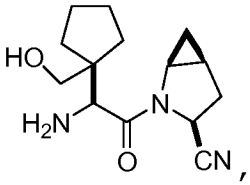


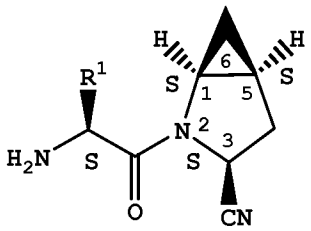
or


,

or a pharmaceutically acceptable salt thereof.

9. (Original) The compound as defined in claim 8 wherein the pharmaceutically acceptable salt is the hydrochloride salt or the trifluoroacetic acid salt.

10. (Original) A compound which is

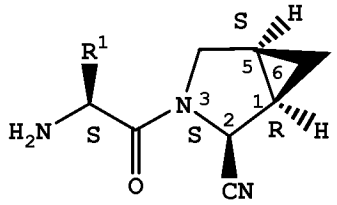


A

(1S,2(2S),3S,5S)

wherein R^1 is alkyl, cycloalkyl, bicycloalkyl, tricycloalkyl, alkylcycloalkyl, hydroxyalkyl, hydroxycycloalkyl, hydroxyalkylcycloalkyl, hydroxybicycloalkyl, or hydroxytricycloalkyl,

or



B

(1R,2S,3(2S),5S)

wherein R^1 is alkyl, cycloalkyl, bicycloalkyl, tricycloalkyl, alkylcycloalkyl, hydroxyalkyl, hydroxycycloalkyl, hydroxyalkylcycloalkyl, hydroxybicycloalkyl, or hydroxytricycloalkyl.

11. (Original) A pharmaceutical composition comprising a compound as defined in claim 1 and a pharmaceutically acceptable carrier therefor.

12. (Amended) A pharmaceutical combination comprising a [DP4 inhibitor] compound as defined in claim 1 and an antidiabetic agent other than a DP4 inhibitor for treating diabetes and related diseases, an anti-obesity agent and/or a lipid-modulating agent.

13. (Twice Amended) The pharmaceutical combination as defined in claim 12 comprising said [DP4 inhibitor] compound as defined in claim 1 and [an] the antidiabetic agent other than a DP4 inhibitor.

14. (Original) The combination as defined in claim 13 wherein the antidiabetic agent is 1, 2, 3 or more of a biguanide, a sulfonyl urea, a glucosidase inhibitor, a PPAR agonist, a PPAR / dual agonist, an SGLT2 inhibitor, an aP2 inhibitor, a glycogen phosphorylase inhibitor, an AGE inhibitor, an insulin sensitizer, a glucagon-like peptide-1 (GLP-1) or mimetic thereof, insulin and/or a meglitinide.

15. (Original) The combination as defined in Claim 14 wherein the antidiabetic agent is 1, 2, 3 or more of metformin, glyburide, glimepiride, glipyride, glipizide, chlorpropamide, gliclazide, acarbose, miglitol, pioglitazone, troglitazone, rosiglitazone, insulin, Gl-262570, isaglitazone, JTT-501, NN-2344, L895645, YM-440, R-119702, AJ9677, repaglinide, nateglinide, KAD1129, AR-HO39242, GW-409544, KRP297, AC2993, Exendin-4, LY307161, NN2211, and/or LY315902.

16. (Amended) The combination as defined in claim 13 wherein the compound as defined in claim 1 is present in a weight ratio to the antidiabetic agent within the range from about 0.01 to about 100:1.

17. (Amended) The combination as defined in claim 12 wherein the anti-obesity agent is a beta 3 adrenergic agonist, a lipase inhibitor, [a serotonin (and dopamine) reuptake inhibitor,] a thyroid receptor beta compound, an anorectic agent, and/or a fatty acid oxidation upregulator.

18. (Original) The combination as defined in claim 17 wherein the anti-obesity agent is orlistat, ATL-962, AJ9677, L750355, CP331648, sibutramine, topiramate, axokine, dexamphetamine, phentermine, phenylpropanolamine, famoxin, and/or mazindol.

19. (Original) The combination as defined in claim 12 wherein the lipid modulating agent is an MTP inhibitor, an HMG CoA reductase inhibitor, a squalene synthetase inhibitor, a fibric acid derivative, an upregulator of LDL receptor activity, a lipoxygenase inhibitor, an ACAT inhibitor, a cholesteryl ester transfer protein inhibitor, or an ATP citrate lyase inhibitor.

20. (Original) The combination as defined in claim 19 wherein the lipid modulating agent is pravastatin, lovastatin, simvastatin, atorvastatin, cerivastatin, fluvastatin, nisvastatin, visastatin, fenofibrate, gemfibrozil, clofibrate, implitapide, CP-529,414, avasimibe, TS-962, MD-700, and/or LY295427.

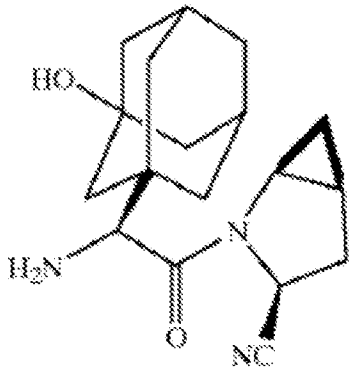
21. (Amended) The combination as defined in claim 19 wherein the compound as defined in claim 1 [DP4 inhibitor] is present in a weight ratio to the lipid-modulating agent within the range from about 0.01 to about 100:1.

22. (Amended) A pharmaceutical combination comprising a [DP4 inhibitor] compound as defined in claim 1 and an agent for treating infertility, an agent for treating polycystic ovary syndrome, an agent for treating a growth disorder and/or frailty, an anti-arthritis agent, an agent for preventing or inhibiting allograft rejection in transplantation, an agent for treating autoimmune disease, an anti-AIDS agent, an agent for treating inflammatory bowel disease/syndrome, an agent for treating anorexia nervosa, an anti-osteoporosis agent and/or an anti-obesity agent.

23. (Canceled)

24. (Canceled)

25. (New) A compound that is



; or a pharmaceutically acceptable salt thereof.

26. (New) The compound as defined in claim 25, wherein the pharmaceutically acceptable salt is the hydrochloride salt.

27. (New) A pharmaceutical composition comprising the compound of claim 25 and a pharmaceutically acceptable carrier therefor.

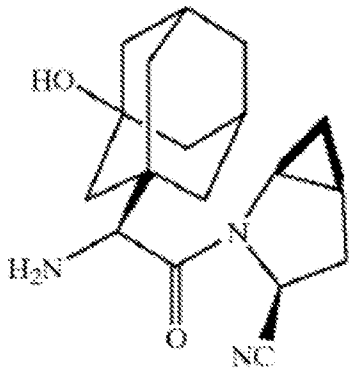
28. (New) A pharmaceutical composition comprising the compound of claim 26 and a pharmaceutically acceptable carrier therefor.

29. (New/Amended) The composition of claim 27 or 28 further comprising an antidiabetic agent other than a DP4 inhibitor.

30. (New/Amended) The composition of claim 29 wherein the antidiabetic agent is metformin.

31. (New/Amended) The composition of claim 29, wherein the antidiabetic agent is a SGLT2 inhibitor.

32. (New) A method for treating diabetes, insulin resistance, hyperglycemia, hyperinsulinemia, impaired glucose homeostasis, or impaired glucose tolerance in a mammal comprising administering to the mammal a pharmaceutical composition comprising a compound that is



or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier therefor.

33. (New) The method of claim 32, wherein the pharmaceutically acceptable salt is the hydrochloride salt.

34. (New) The method of claim 32, for treating diabetes.

35. (New) The method of claim 33, for treating diabetes.

36. (Canceled)

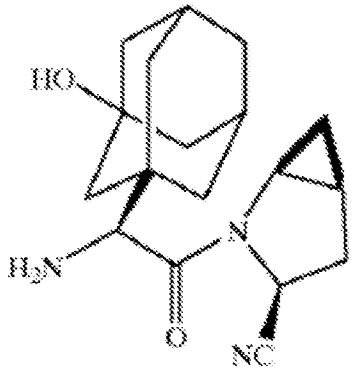
37. (Canceled)

38. (New/Amended) The method of any one of claims 32, 33, 34, or 35 wherein the pharmaceutical composition further comprises an antidiabetic agent other than a DP4 inhibitor.

39. (New/Amended) The method of claim 38, wherein the antidiabetic agent is metformin.

40. (New/Amended) The method of claim 38, wherein the antidiabetic agent is a SGLT2 inhibitor.

41. (New) A method for treating type II diabetes in a mammal comprising administering to the mammal a pharmaceutical composition comprising a compound that is



or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier therefor.

42. (New) The method of claim 41, wherein the pharmaceutically acceptable salt is the hydrochloride salt.

43. (New) The method of any one of claims 41 or 42, wherein the pharmaceutical composition further comprises an antidiabetic agent other than a DP4 inhibitor.

44. (New) The method of claim 43, wherein the antidiabetic agent is metformin.

45. (New) The method of claim 43, wherein the antidiabetic agent is a SGLT2 inhibitor.

REMARKS

Claims 1, 12, 13, 16, 17, 21, 22, 29, 30, 31, 38, 39, and 40 are amended herein. Claims 36 and 37 are canceled and new claims 41 to 45 are added herein. Support for each of the new claims and/or amendments is implicit in the prior versions of the claims, or is set forth in the chart that was submitted with the preliminary amendment filed December 1, 2011. No new matter is added.

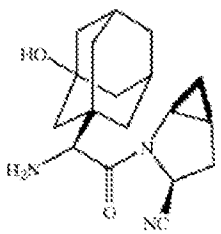
After entry of the present amendments, claims 1-22, 25-35, and 38-45 will remain pending.

Summary of the Interview

The undersigned thanks Examiners Polansky and Anderson for the courtesy of the telephonic interview conducted on May 22, 2012. The pending claims were discussed, as well as the objections and alleged rejections set forth in the May 8, 2012 Office Action. In particular, the undersigned thanks the Examiners for clarifying the objections to the Applicants' reissue declaration, the incorporation of corrections provided in the Certificates of Correction for the original patent, and the procedures to be followed to remedy any perceived errors.

Reissue Oath/Declaration

The Office alleges that the reissue declaration is defective because it fails to identify at least one specific error which is relied upon to support the reissue application. Without conceding the propriety of this assertion and in the interest of advancing prosecution of the application, a supplemental declaration is filed herewith, which states that the specific error relied upon is that, while the patent included claims encompassing the compound below, the patentee failed to include claims that are specifically directed to the compound:



or a pharmaceutical salt thereof, as set forth in added claims 25 to 35 and 38 to 45.

The supplemental declaration also sets forth the mailing addresses and residences of the inventors. Patent Owner asserts that the supplemental reissue declaration complies with 37 C.F.R. 1.175.

Certificates of Correction

The Office has noted that changes to the specification and claims made via the Certificates of Correction for the original patent should be incorporated into the reissue patent. Said changes have been effected by the Patent Owner according to the procedure described in the Office Action. *See* MPEP 1453.VI.(C).

Claim Objections

The Office objects to added claim 38 for reciting, "The method of any one of claims 32, 33, 34, **25**, **26**, or 37…" Added claim 38 has been amended to recite "The method of any one of claims 32, 33, 34, or **35** …" Withdrawal of the objection is requested.

The Office objects to claim 38 for reciting "an agent for preventing inhibiting allograft rejection in transplantation…" As discussed in the telephonic interview, claim 22, not claim 38, recites the identified language. Claim 22 has accordingly been amended to recite, "an agent for preventing **or** inhibiting allograft rejection in transplantation." Withdrawal of the objection is requested.

Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 1-7, 11-22, 29-31, and 38-40 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. In light of the present claim amendments, withdrawal of the rejections is requested.

Claim 1 has been amended to more clearly identify pharmaceutically acceptable salts as an alternative, *i.e.,* "**or** a pharmaceutically acceptable salt thereof." The rejection of claim 1 therefore is considered moot.

Claim 12 has been amended to recite "a [DP4 inhibitor] compound as defined in claim 1." Claim 13 has been similarly amended. The rejection of claims 12 and 13 is considered moot.

Claim 22 has been amended to recite "A pharmaceutical combination comprising a [DP4 inhibitor] compound as defined in claim 1." The rejection of claim 22 is considered moot. Patent Owner notes that claim 21 has been amended to recite, "The combination as defined in claim 19 wherein the compound as defined in claim 1 [DP4 inhibitor] is present in a weight ratio to the lipid-modulating agent within the range from about 0.01 to about 100:1." Claim 16 has been amended similarly to claim 21.

Claim 17 has been amended to delete the limitation, "a serotonin (and dopamine) reuptake inhibitor." The rejection of claim 17 is considered moot.

Claim 29 has been amended to recite, "The composition of claim 27 or 28 further comprising **an** antidiabetic agent other than a DP4 inhibitor." The rejection of claim 29 is considered moot. Dependent claims 30 and 31 have been amended to recite, "wherein the antidiabetic agent is . . ."

Claim 38 has been amended to recite, "The method of any one of claims 32, 33, 34, or **35**." The rejection is considered moot. . Claim 38 has also been amended to recite, "wherein the pharmaceutical composition further comprises an antidiabetic agent other than a DP4 inhibitor." Dependent claims 39 and 40 have been amended to recite "wherein the antidiabetic agent is…" Dependent claim 40 has also been amended to recite "The method of claim 38…"

Rejections under 35 U.S.C. § 112, First Paragraph

Claims 1-7 and 11-22 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly not complying with the written description requirement for reciting the "prodrug esters" of the compounds of claim 1. While not conceding the propriety of the rejection, the term "prodrug ester thereof" has been deleted from claim 1 to advance prosecution. Withdrawal of the rejection is requested.

CONCLUSION

Patent Owner believes that the foregoing addresses all issues raised in the Office Action dated May 8, 2012, and that the application is now in condition for allowance. If any further issues remain, the Examiner is invited to contact Patent Owner's undersigned representative at the contact number listed below.

Date: August 8, 2012

/S. Maurice Valla/
S. Maurice Valla
Registration No. 43,966

Woodcock Washburn LLP
Cira Centre
2929 Arch Street, 12th Floor
Philadelphia, PA 19104-2891
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Facsimile: (215) 568-3439

Electronic Patent Application Fee Transmittal

Application Number:	13308658
Filing Date:	01-Dec-2011
Title of Invention:	Cyclopropyl-Fused Pyrrolidine-Based Inhibitors Of Dipeptidyl Peptidase IV And Method
First Named Inventor/Applicant Name:	Jeffrey A. Robl
Filer:	SAMUEL VALLA/D. McCarty
Attorney Docket Number:	BMS-2856

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Claims in excess of 20	1202	3	60	180
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
			Total in USD ($)	**180**

Electronic Acknowledgement Receipt

EFS ID:	13444151
Application Number:	13308658
International Application Number:	
Confirmation Number:	7781
Title of Invention:	Cyclopropyl-Fused Pyrrolidine-Based Inhibitors Of Dipeptidyl Peptidase IV And Method
First Named Inventor/Applicant Name:	Jeffrey A. Robl
Customer Number:	23377
Filer:	SAMUEL VALLA/D. McCarty
Filer Authorized By:	SAMUEL VALLA
Attorney Docket Number:	BMS-2856
Receipt Date:	08-AUG-2012
Filing Date:	01-DEC-2011
Time Stamp:	11:20:56
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$180
RAM confirmation Number	8914
Deposit Account	233050
Authorized User	

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

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Charge any Additional Fees required under 37 C.F.R. Section 1.20 (Post Issuance fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.21 (Miscellaneous fees and charges)

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Transmittal Letter	BMS-2856-Transmittal-reply-to-05-08-12.PDF	262560 f5c75d475478a99889c129e8444656fa3c189c57	no	2
Warnings:					
Information:					
2		BMS-2856-reply-to-05-08-12.PDF	359181 85b8b25bcf56ed3f67b7e901298ecc99f2eecdee	yes	36

	Multipart Description/PDF files in .zip description		
	Document Description	**Start**	**End**
	Amendment/Req. Reconsideration-After Non-Final Reject	1	1
	Claims	2	32
	Applicant Arguments/Remarks Made in an Amendment	33	36

Warnings:					
Information:					
3	Oath or Declaration filed	BMS-2856-Supplemental-Declaration.PDF	86103 d141ce311b111da19ff431467fc6fd89f40c777f	no	4
Warnings:					
Information:					
4	Fee Worksheet (SB06)	fee-info.pdf	30247 a92269519b1df66b248102c534e402d4b530cadc	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	738091		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

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If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Doc Code: TRAN.LET

Document Description: Transmittal Letter

PTO/SB/21 (07-09)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Total Number of Pages in This Submission	

Application Number	13/308,658
Filing Date	December 1, 2011
First Named Inventor	Jeffrey A. Robl
Art Unit	1629
Examiner Name	Gregg Polansky
Attorney Docket Number	BMS-2856

ENCLOSURES (*Check all that apply*)

- ☐ Fee Transmittal Form
  - ☐ Fee Attached
- ☑ Amendment/Reply
  - ☐ After Final
  - ☐ Affidavits/declaration(s)
- ☐ Extension of Time Request
- ☐ Express Abandonment Request
- ☐ Information Disclosure Statement
- ☐ Certified Copy of Priority Document(s)
- ☐ Reply to Missing Parts/ Incomplete Application
  - ☐ Reply to Missing Parts under 37 CFR 1.52 or 1.53
- ☐ Drawing(s)
- ☐ Licensing-related Papers
- ☐ Petition
- ☐ Petition to Convert to a Provisional Application
- ☐ Power of Attorney, Revocation
- ☐ Change of Correspondence Address
- ☐ Terminal Disclaimer
- ☐ Request for Refund
- ☐ CD, Number of CD(s) _____
  - ☐ Landscape Table on CD
- ☐ After Allowance Communication to TC
- ☐ Appeal Communication to Board of Appeals and Interferences
- ☐ Appeal Communication to TC **(Appeal Notice, Brief, Reply Brief)**
- ☐ Proprietary Information
- ☐ Status Letter
- ☑ Other Enclosure(s) (please Identify below):

Supplemental Reissue Declaration

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	Woodcock Washburn, LLP		
Signature	/S. Maurice Valla/		
Printed name	S. Maurice Valla		
Date	August 8, 2012	Reg. No.	43,966

CERTIFICATE OF TRANSMISSION/MAILING

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below:

Signature			
Typed or printed name		Date	

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The **Privacy Act of 1974 (P.L. 93-579)** requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (*i.e.*, GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

PTO/SB/52 (05-08)
Approved for use through 08/31/2013. OMB 0651-0033
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

REISSUE APPLICATION DECLARATION BY THE ASSIGNEE	Docket Number (optional) BMS-2856

I hereby declare that:

The residence, mailing address and citizenship of the inventors are stated below.

I am authorized to act on behalf of the following assignee: Bristol-Myers Squibb Company

and the title of my position with said assignee is: Assistant General Counsel

The entire title to the patent identified below is vested in said assignee.

Inventor Jeffrey A. Robl	Citizenship United States
Residence/Mailing Address 7 Tulip Drive, Newtown, PA 18940	
Inventor Richard B. Sulsky	Citizenship United States
Residence/Mailing Address 311 Pennington-Rocky Hill Road, Pennington, NJ 08534	
☑ Additional Inventors are named on separately numbered sheets attached hereto.	
Patent Number 6,395,767	Date of Patent Issued May 28, 2002

I believe said inventor(s) to be the original and first inventor(s) of the subject matter which is described and claimed in said patent, for which a reissue patent is sought on the invention entitled:

Cyclopropyl-Fused Pyrrolidine-Based Inhibitors of Dipeptidyl Peptidase IV and Method

the specification of which

☐ is attached hereto.

☑ was filed on December 1, 2011 as reissue application number 13 / 308,658

and was amended on 12/1/2011 and 8/8/2012 (If applicable)

I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR 1.56.

☐ I hereby claim foreign priority benefits under 35 U.S.C. 119(a)-(d) or (f), or 365(b). Attached is form PTO/SB/02B (or equivalent) listing the foreign applications.

I verily believe the original patent to be wholly or partly inoperative or invalid, for the reasons described below. (Check all boxes that apply.)

☐ by reason of a defective specification or drawing.

☑ by reason of the patentee claiming more or less than he had the right to claim in the patent.

☐ by reason of other errors.

PTO/SB/52 (05-08)
Approved for use through 08/31/2013. OMB 0651-0033
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

REISSUE APPLICATION DECLARATION BY THE ASSIGNEE	Docket Number (Optional) BMS-2856

At least one error upon which reissue is based is described as follows:

See attached sheet

[Attach additional sheets, if needed.]

All errors corrected in this reissue application arose without any deceptive intention on the part of the applicant.

I hereby appoint:

☑ Practitioners associated with Customer Number: 23377

OR

☐ Practitioner(s) named below:

Name	Registration Number

as my/our attorney(s) or agent(s) to prosecute the application identified above, and to transact all business in the United States Patent and Trademark Office connected therewith.

Correspondence Address: Direct all communications about the application to:

☑ The address associated with Customer Number: 23377

OR

☐ Firm or Individual Name					
Address					
City		State		Zip	
Country					
Telephone		Email			

WARNING:

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

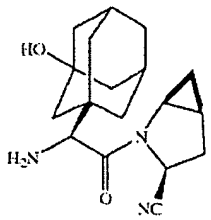
I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this declaration is directed.

Signature	Date Aug 8, 2012
Full name of person signing (given name, family name) Warren K. Volles	
Address of Assignee Bristol-Myers Squibb Co.; Patent Department; P.O. Box 4000; Princeton, NJ 08543-4000	

Supplemental Declaration Additional Sheet

At least one error upon which reissue is based is described as follows:

While the patent included claims encompassing the compound below, the patent failed to include



claims that are specifically directed to the compound or a pharmaceutical salt thereof, as set forth in added claims 25 to 35 and 38 to 45.

ADDITIONAL INVENTORS
Page 1 of 1

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23377 e 2012-08-13

WOODCOCK WASHBURN LLP
CIRA CENTRE, 12TH FLOOR
2929 ARCH STREET
PHILADELPHIA, PA 19104-2891

Paper No.

Application No.:	**13/308,658**	**Date Mailed:**	**2012-08-13**
First Named Inventor:	Robl, Jeffrey, A.	Examiner:	POLANSKY, GREGG
Attorney Docket No.:	BMS-2856	Art Unit:	1629
Confirmation No.:	7781	Filing Date:	2011-12-01

Please find attached an Office communication concerning this application or proceeding.

Commissioner for Patents

PTO-90c (Rev.08-06)

Notice of Non-Compliant Amendment (37 CFR 1.121)	Application No. 13/308,658	Applicant(s) ROBL ET AL.
		Art Unit 1700

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

The amendment document filed on *08 August, 2012* is considered non-compliant because it has failed to meet the requirements of 37 CFR 1.121 or 1.4. In order for the amendment document to be compliant, correction of the following item(s) is required.

THE FOLLOWING MARKED (X) ITEM(S) CAUSE THE AMENDMENT DOCUMENT TO BE NON-COMPLIANT:

- ☐ 1. Amendments to the specification:
  - ☐ A. Amended paragraph(s) do not include markings.
  - ☐ B. New paragraph(s) should not be underlined.
  - ☐ C. Other _____.
- ☐ 2. Abstract:
  - ☐ A. Not presented on a separate sheet. 37 CFR 1.72.
  - ☐ B. Other _____.
- ☐ 3. Amendments to the drawings:
  - ☐ A. The drawings are not properly identified in the top margin as "Replacement Sheet," "New Sheet," or "Annotated Sheet" as required by 37 CFR 1.121(d).
  - ☐ B. The practice of submitting proposed drawing correction has been eliminated. Replacement drawings showing amended figures, without markings, in compliance with 37 CFR 1.84 are required.
  - ☐ C. Other _____.
- ☒ 4. Amendments to the claims:
  - ☐ A. A complete listing of all of the claims is not present.
  - ☐ B. The listing of claims does not include the text of all pending claims (including withdrawn claims)
  - ☒ C. Each claim has not been provided with the proper status identifier, and as such, the individual status of each claim cannot be identified. Note: the status of every claim must be indicated after its claim number by using one of the following status identifiers: (Original), (Currently amended), (Canceled), (Previously presented), (New), (Not entered), (Withdrawn) and (Withdrawn-currently amended).
  - ☐ D. The claims of this amendment paper have not been presented in ascending numerical order.
  - ☐ E. Other: _____.
- ☐ 5. Other (e.g., the amendment is unsigned or not signed in accordance with 37 CFR 1.4): For further explanation of the amendment format required by 37 CFR 1.121, see MPEP § 714.

TIME PERIODS FOR FILING A REPLY TO THIS NOTICE:

1. Applicant is given **no new time period if the non-compliant amendment is an** after-final amendment or an amendment filed after allowance, or a drawing submission (only) If applicant wishes to resubmit the non-compliant after-final amendment with corrections, the **entire corrected amendment** must be resubmitted.

2. Applicant is given **one month**, or thirty (30) days, whichever is longer, from the mail date of this notice to supply the correction, if the non-compliant amendment is one of the following: a preliminary amendment, a non-final amendment (including a submission for a request for continued examination (RCE) under 37 CFR 1.114), a supplemental amendment filed within a suspension period under 37 CFR 1.103(a) or (c), and an amendment filed in response to a Quayle action. If any of above boxes 1 to 4 are checked, the correction required is only the corrected section of the non-compliant amendment in compliance with 37 CFR 1.121.

Extensions of time are available under 37 CFR 1.136(a) only if the non-compliant amendment is a non-final amendment or an amendment filed in response to a *Quayle* action.

Failure to timely respond to this notice will result in:

Abandonment of the application if the non-compliant amendment is a non-final amendment or an amendment filed in response to a *Quayle* action; or

Non-entry of the amendment if the non-compliant amendment is a preliminary amendment or supplemental amendment.

Legal Instruments Examiner (LIE), if applicable /BRUCE HARRISON/ Telephone No: (571)272-1016

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23377 e 2012-08-21

WOODCOCK WASHBURN LLP
CIRA CENTRE, 12TH FLOOR
2929 ARCH STREET
PHILADELPHIA, PA 19104-2891

Paper No.

Application No.:	**13/308,658**	**Date Mailed:**	**2012-08-21**
First Named Inventor:	Robl, Jeffrey, A.	Examiner:	POLANSKY, GREGG
Attorney Docket No.:	BMS-2856	Art Unit:	1629
Confirmation No.:	7781	Filing Date:	2011-12-01

Please find attached an Office communication concerning this application or proceeding.

Commissioner for Patents

PTO-90c (Rev.08-06)

Letter Withdrawing a Notice of Non-Compliant Amendment	Application No.: 13/308,658	Applicant(s): ROBL ET AL.
		Art Unit: 1700

The Notice of Non-Compliant Amendment mailed on 13 August, 2012 was sent in error, and is hereby withdrawn. The application is being forwarded to the examiner for appropriate action. (Note: this letter does not apply to any Notice of Non-Compliant Amendment where the amendment was a reply to a final Office action.)

Legal Instruments Examiner (LIE):	Telephone Number:
/BRUCE HARRISON/	(571)272-1016

DOCKET NO.: BMS-2856 **PATENT**
Application No.: 13/308,658
Office Action Dated: May 8, 2012

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Jeffrey A. Robl

Confirmation No.: **7781**

Application No.: **13/308,658**

Group Art Unit: **1629**

Filing Date: **December 1, 2011**

Examiner: **Gregg Polansky**

For: **Cyclopropyl-Fused Pyrrolidine-Based Inhibitors of Dipeptidyl Peptidase IV and Method**

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Commissioner:

SUPPLEMENTAL REPLY PURSUANT TO 37 CFR § 1.111

In further response to the Official Action dated **May 8, 2012**, reconsideration is respectfully requested in view of the amendments and/or remarks as indicated below:

☒ **A Listing of Prior Changes to U.S. 6,395,767 ("the 767 patent") Made By Certificate of Correction** begin on page 2 of this paper.

☐ **Amendments to the Claims** are reflected in the listing of the claims which begins on page of this paper.

☐ **Amendments to the Drawings** begin on page of this paper and include an attached replacement sheet.

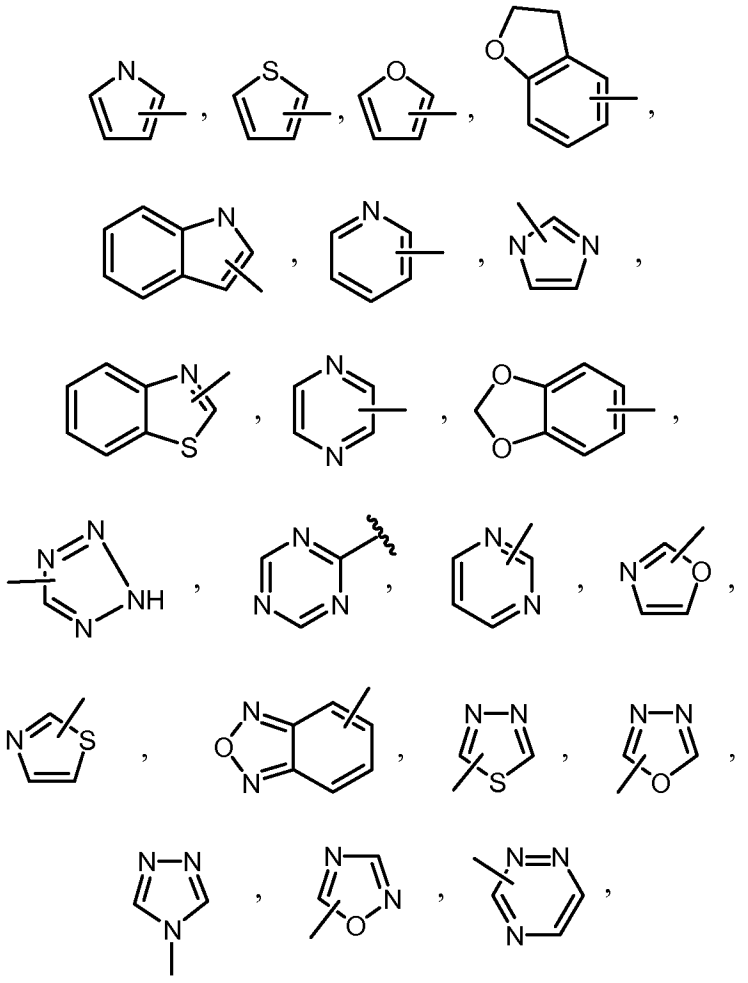
☒ **Remarks** begin on page 6 of this paper.

☒ The Commissioner is hereby authorized to charge any fee deficiency, charge any additional fees, or credit any overpayment of fees, associated with this application in connection with this filing, or any future filing, submitted to the U.S. Patent and Trademark Office during the pendency of this application, to Deposit Account No. 23-3050.

Changes to 767 Patent Previously Entered by Certificate of Correction

1. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 14, lines 13-54 of the 767 patent:

Unless otherwise indicated, the term "heteroaryl" as used herein alone or as part of another group refers to a 5- or 6- membered aromatic ring which includes 1, 2, 3 or 4 hetero atoms such as nitrogen, oxygen or sulfur, and such rings fused to an aryl, cycloalkyl, heteroaryl or cycloheteroalkyl ring (e.g. benzothiophenyl, indolyl), and includes possible N-oxides. The heteroaryl group may optionally include l to 4 substituents such as any of the substituents set out above for alkyl. Examples of heteroaryl groups include the following:



and the like.

2. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 14, lines 55-58 of the 767 patent:

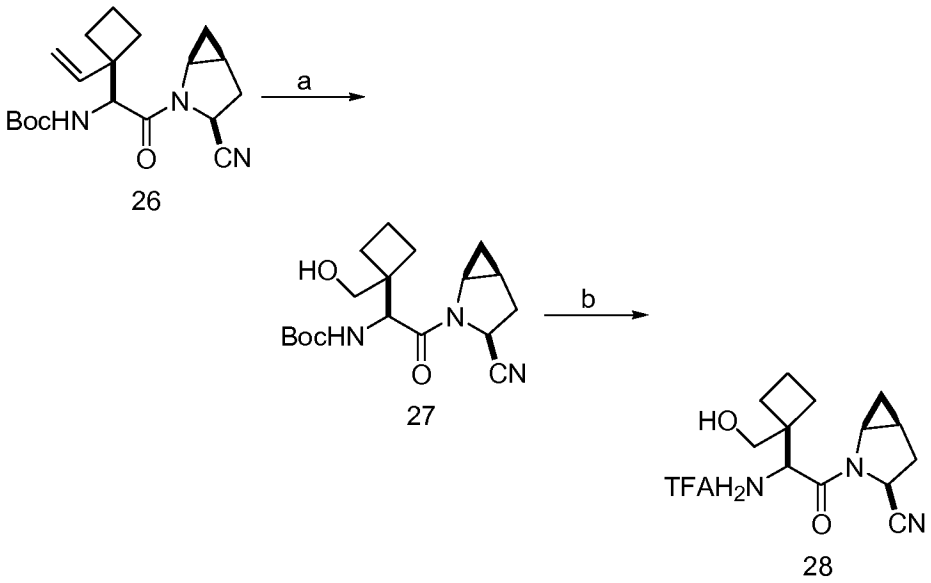
The term "cycloheteroalkylalkyl" as used herein alone or as part of another group refers to cycloheteroalkyl groups as defined above linked through a C atom or heteroatom to a $(CH_2)_r$ chain.

3. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 43, lines 20-38 of the 767 patent:

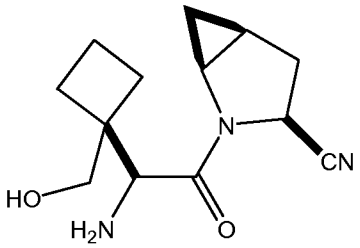
To a flame-dried 500-mL round-bottomed flask containing cyclopentylideneacetic acid ethyl ester (17.5 g, 113 mmol) in 100 mL anhydrous toluene at -78°C under argon was added DIBAL-H (189 mL of a 1.5 M solution in toluene, 284 mmol, 2.50 equiv) dropwise over a 30 min period through an addition funnel, and the mixture was then allowed to warm to rt, stirring for 18 h. The reaction mixture was then recooled to -78°C, and quenched by the careful addition of 30 mL anhydrous MeOH. Upon warming to rt, 1 N Rochelle's salt (100 mL) was added, and the mixture was stirred 90 min. The biphasic reaction mixture was then diluted with Et_2O (200 mL) in a separatory funnel, and the layers were separated. The organic layer was then washed with brine (100 mL), dried (Na_2SO_4), and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, CH_2Cl_2 / EtOAc, 10:1) gave 11.6 g (92%) of the desired allylic alcohol as a colorless oil.

4. As indicated by the Certificate of Correction, please substitute the following Scheme 7 for the Scheme 7 at col. 52, line 37- col. 53, line 25 of the 767 patent:

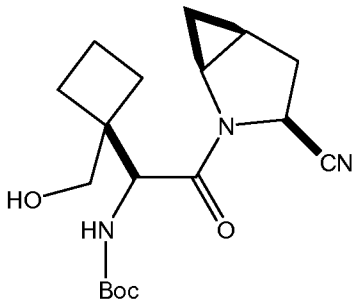
Scheme 7
General Method E, Examples 45 47



a.OsO_4, THF:H_2O, 1:1; $NaIO_4$; workup,then $NaBH_4$, MeOH, RT. 56%
b. TFA:CH_2Cl_2, 1:2, 0 degrees C to RT.

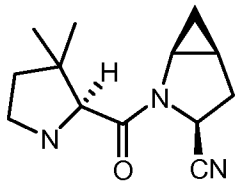


Step 1



5. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 70, lines 55-65 of the 767 patent:

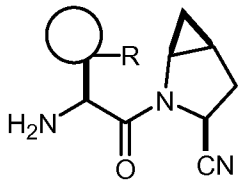
EXAMPLE 67



Step 1

6. As indicated by the Certificate of Correction, please substitute the following Table 5 for the Table 5 at col. 84, lines 23-42 of the 767 patent:

TABLE 5



Example #	Cycloalkane	R	MS Data M+H
79	cyclohexane	Methyl	262
80	cyclohexane	Ethyl	276
81	cyclopentane	Methyl	248
82	cyclopentane	Allyl	274
83	cyclopentane	Propyl	276
84	cyclobutane	Methyl	234

REMARKS

The Patent Owner thanks the examiner for the courtesy of the telephonic interview conducted on January 10, 2013 with Stephanie A. Barbosa, attorney for Patent Owner. Examiner Polansky requested that the Patent Owner file a supplemental response that addresses certain changes to U.S. 6,395,767 that were previously entered by certificate of correction. In particular, Examiner Polansky identified that all changes must be set forth *via* entire paragraph, scheme, and table replacements rather than single line replacements. This supplemental response also includes the changes from the Certificate of Correction for col. 14, lines 55-58 and col. 43, lines 20-38 to correct typographical errors from the previous reply. This supplemental paper is filed in response to the Examiner's request.

Date: January 18, 2013

/S. Maurice Valla/
S. Maurice Valla
Registration No. 43,966

Woodcock Washburn LLP
Cira Centre
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Telephone: (215) 568-3100
Facsimile: (215) 568-3439

Electronic Acknowledgement Receipt

EFS ID:	14735292
Application Number:	13308658
International Application Number:	
Confirmation Number:	7781
Title of Invention:	Cyclopropyl-Fused Pyrrolidine-Based Inhibitors Of Dipeptidyl Peptidase IV And Method
First Named Inventor/Applicant Name:	Jeffrey A. Robl
Customer Number:	23377
Filer:	SAMUEL VALLA/Joanne Gallagher
Filer Authorized By:	SAMUEL VALLA
Attorney Docket Number:	BMS-2856
Receipt Date:	18-JAN-2013
Filing Date:	01-DEC-2011
Time Stamp:	11:44:20
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Transmittal Letter	BMS-2856_transmittal.PDF	262602 8e5106d1ec81a16c38e02e973075a62abfcdd811	no	2

Warnings:	
Information:	

2		BMS-2856_supplemental_response_to_OA_dtd_05-08-2012.PDF	136534 1c40d87f232354c96586a5ba11ee6350365d5654	yes	6

Multipart Description/PDF files in .zip description		
Document Description	**Start**	**End**
Supplemental Response or Supplemental Amendment	1	1
Claims	2	5
Applicant Arguments/Remarks Made in an Amendment	6	6

Warnings:	
Information:	
Total Files Size (in bytes):	399136

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Doc Code: TRAN.LET

Document Description: Transmittal Letter

PTO/SB/21 (07-09)
Approved for use through 07/31/2012. OMB 0651-0031
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TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Total Number of Pages in This Submission	8

Application Number	13/308,658
Filing Date	December 1, 2011
First Named Inventor	Jeffrey A. Robol
Art Unit	1629
Examiner Name	Gregg Polansky
Attorney Docket Number	BMS-2856

ENCLOSURES (*Check all that apply*)

- ☐ Fee Transmittal Form
  - ☐ Fee Attached
- ☑ Amendment/Reply
  - ☐ After Final
  - ☐ Affidavits/declaration(s)
- ☐ Extension of Time Request
- ☐ Express Abandonment Request
- ☐ Information Disclosure Statement
- ☐ Certified Copy of Priority Document(s)
- ☐ Reply to Missing Parts/ Incomplete Application
  - ☐ Reply to Missing Parts under 37 CFR 1.52 or 1.53
- ☐ Drawing(s)
- ☐ Licensing-related Papers
- ☐ Petition
- ☐ Petition to Convert to a Provisional Application
- ☐ Power of Attorney, Revocation
- ☐ Change of Correspondence Address
- ☐ Terminal Disclaimer
- ☐ Request for Refund
- ☐ CD, Number of CD(s) _____
  - ☐ Landscape Table on CD
- ☐ After Allowance Communication to TC
- ☐ Appeal Communication to Board of Appeals and Interferences
- ☐ Appeal Communication to TC **(Appeal Notice, Brief, Reply Brief)**
- ☐ Proprietary Information
- ☐ Status Letter
- ☐ Other Enclosure(s) (please Identify below):

Remarks

Supplemental Reply

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	Woodcock Washburn LLP		
Signature	/S. Maurice Valla/		
Printed name	S. Maurice Valla		
Date	January 18, 2013	Reg. No.	43,966

CERTIFICATE OF TRANSMISSION/MAILING

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below:

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Typed or printed name		Date	

This collection of information is required by 37 CFR 1.5. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and1.14. This collection is estimated to 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
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8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

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NOTICE OF ALLOWANCE AND FEE(S) DUE

23377 7590 02/13/2013

WOODCOCK WASHBURN LLP
CIRA CENTRE, 12TH FLOOR
2929 ARCH STREET
PHILADELPHIA, PA 19104-2891

EXAMINER
POLANSKY, GREGG

ART UNIT	PAPER NUMBER
1629	

DATE MAILED: 02/13/2013

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/308,658	12/01/2011	Jeffrey A. Robl	BMS-2856	7781

TITLE OF INVENTION: Cyclopropyl-Fused Pyrrolidine-Based Inhibitors Of Dipeptidyl Peptidase IV And Method

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	$1770	$0	$0	$1770	05/13/2013

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

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B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
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INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

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23377 7590 02/13/2013
WOODCOCK WASHBURN LLP
CIRA CENTRE, 12TH FLOOR
2929 ARCH STREET
PHILADELPHIA, PA 19104-2891

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission
I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/308,658	12/01/2011	Jeffrey A. Robl	BMS-2856	7781

TITLE OF INVENTION: Cyclopropyl-Fused Pyrrolidine-Based Inhibitors Of Dipeptidyl Peptidase IV And Method

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	$1770	$0	$0	$1770	05/13/2013

EXAMINER	ART UNIT	CLASS-SUBCLASS
POLANSKY, GREGG	1629	514-252190

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).
- ❑ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
- ❑ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
(1) the names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.
1 _____
2 _____
3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ❑ Individual ❑ Corporation or other private group entity ❑ Government

4a. The following fee(s) are submitted:
- ❑ Issue Fee
- ❑ Publication Fee (No small entity discount permitted)
- ❑ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**
- ❑ A check is enclosed.
- ❑ Payment by credit card. Form PTO-2038 is attached.
- ❑ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)
- ❑ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27.
- ❑ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

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2929 ARCH STREET
PHILADELPHIA, PA 19104-2891

EXAMINER	
POLANSKY, GREGG	
ART UNIT	PAPER NUMBER
1629	

DATE MAILED: 02/13/2013

Determination of Patent Term Extension or Adjustment under 35 U.S.C. 154 (b)

A reissue patent is for "the unexpired part of the term of the original patent." See 35 U.S.C. 251. Accordingly, the above-identified reissue application is not eligible for Patent Term Extension or Adjustment under 35 U.S.C. 154(b).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Notice of Allowability	Application No.	Applicant(s)	
	13/308,658	ROBL ET AL.	
	Examiner	Art Unit	
	Gregg Polansky	1629	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *papers filed 8/08/2012 & 1/18/2013*.

2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

3. ☒ The allowed claim(s) is/are *1-22,25-35 and 38-45*. As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov .

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.

   ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
4. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
5. ☐ Examiner's Amendment/Comment
6. ☐ Examiner's Statement of Reasons for Allowance
7. ☐ Other _____.

/SAVITHA RAO/ Primary Examiner, Art Unit 1629	/Gregg Polansky/ Examiner, Art Unit 1629

EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L2	2	("6395767").PN.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2013/01/24 17:16
L3	10	onglyza	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	ON	2013/01/24 17:16
L4	1478	saxagliptin	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	ON	2013/01/24 17:16
L5	1480	L3 or L4	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	ON	2013/01/24 17:16
L6	375	BMS-477118	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	ON	2013/01/24 17:16
L7	476	BMS adj "477118"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	ON	2013/01/24 17:16
L8	476	BMS adj2 "477118"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	ON	2013/01/24 17:16
L9	476	L6 or L7	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	ON	2013/01/24 17:16
L10	0	"361442-05-9"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	ON	2013/01/24 17:16
L11	808	548/452.ccls.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	ON	2013/01/24 17:20
L12	1048	514/412.ccls.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	ON	2013/01/24 17:20

EAST Search History (Interference)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L13	464	514/412.ccls.	USPAT; UPAD	AND	ON	2013/01/24 17:20
L14	506	548/452.ccls.	USPAT; UPAD	AND	ON	2013/01/24 17:21

1/24/2013 5:21:49 PM
C:\Users\gpolansky\Documents\EAST\Workspaces\13308658 Reissue of US 6395767.wsp

Application Number	Application No.	Applicant(s)
	13308658	Robl et al.
	Notice of Reissue Published in OG on 02/14/2012	

Original Patent Number of Patent To Be Reissued is 6395767	The Maintenance fee status is: ☒ up to date. ☐ not required.

This reissue patent is subject to A Terminal Disclaimer that:

☐ was filed during the prosecution of the reissue application.
☐ was of record prior to the filing of the reissue application.

Physical surrender of the letters patent

☐ was made.
☐ was not made, but a statement of loss/inaccessibility was provided.
☒ is not required

Final SPRE Review

BC
(INITIALS)

2/7/2013
(DATE)

U.S. Patent and Trademark Office

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13308658	ROBL ET AL.
	Examiner	Art Unit
	GREGG POLANSKY	1629

CPC- SEARCHED		
Symbol	Date	Examiner

CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner
514	412	1/24/2013	GP
548	452	1/24/2013	GP

SEARCH NOTES		
Search Notes	Date	Examiner
EAST Search: see EAST Search Histroy	5/2/2012	GP
STN Search: see STN Search History	5/2/2012	GP
Litigation Search: see Litigation Search History	5/2/2012	GP
PALM Inventor Search	5/2/2012	GP
EAST Search: see EAST Search Histroy	1/24/2013	GP
Reviewed previous STN Search History	1/24/2013	GP
PALM Inventor Search	1/24/2013	GP

INTERFERENCE SEARCH			
US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner
514	412	1/24/2013	GP
548	452	1/24/2013	GP

/GREGG POLANSKY/ Examiner.Art Unit 1629	/SAVITHA RAO/ Primary Examiner, Art Unit 1629

Issue Classification

Application/Control No.	Applicant(s)/Patent Under Reexamination
13308658	ROBL ET AL.
Examiner	**Art Unit**
GREGG POLANSKY	1629

CPC						
Symbol					**Type**	**Version**
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CPC Combination Sets							
Symbol				**Type**	**Set**	**Ranking**	**Version**
			/				
			/				

US ORIGINAL CLASSIFICATION		INTERNATIONAL CLASSIFICATION										
CLASS	**SUBCLASS**	**CLAIMED**					**NON-CLAIMED**					
514	412	C	0	7	D	209 / 02 (2006.01.01)						
CROSS REFERENCE(S)		A	6	1	K	31 / 403 (2006.01.01)						
CLASS	**SUBCLASS (ONE SUBCLASS PER BLOCK)**											
548	452											

/GREGG POLANSKY/ Examiner.Art Unit 1629	1/24/2013	**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	41	
		O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	NONE

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13308658	ROBL ET AL.
	Examiner	**Art Unit**
	GREGG POLANSKY	1629

/GREGG POLANSKY/ Examiner.Art Unit 1629	1/24/2013	**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	41	
		O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	NONE

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	13308658	ROBL ET AL.
	Examiner	**Art Unit**
	GREGG POLANSKY	1629

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original
1	1	17	17	33	33										
2	2	18	18	34	34										
3	3	19	19	35	35										
4	4	20	20		36										
5	5	21	21		37										
6	6	22	22	36	38										
7	7	23	23	37	39										
8	8	24	24	38	40										
9	9	25	25	39	41										
10	10	26	26	40	42										
11	11	27	27	41	43										
12	12	28	28	42	44										
13	13	29	29	43	45										
14	14	30	30												
15	15	31	31												
16	16	32	32												

/GREGG POLANSKY/ Examiner.Art Unit 1629	1/24/2013	**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	41	
		O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	NONE

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BIB DATA SHEET

CONFIRMATION NO. 7781

SERIAL NUMBER	FILING or 371(c) DATE RULE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
13/308,658	12/01/2011	514	1629	BMS-2856

APPLICANTS

Jeffrey A. Robl, Newtown, PA;
Richard B. Sulsky, West Trenton, NJ;
David J. Augeri, Princeton, NJ;
David R. Magnin, Hamilton, NJ;
Lawrence G. Hamann, Cherry Hill, NJ;
David A. Betebenner, Lawrenceville, NJ;

**** CONTINUING DATA ***************************

This application is a REI of 09/788,173 02/16/2001 PAT 6,395,767
which claims benefit of 60/188,555 03/10/2000

**** FOREIGN APPLICATIONS ***************************

**** IF REQUIRED, FOREIGN FILING LICENSE GRANTED ****

12/06/2011

Foreign Priority claimed ☐ Yes ☑ No 35 USC 119(a-d) conditions met ☐ Yes ☑ No Verified and Acknowledged /GREGG POLANSKY/ Examiner's Signature	☐ Met after Allowance Initials	STATE OR COUNTRY	SHEETS DRAWINGS	TOTAL CLAIMS	INDEPENDENT CLAIMS
		PA		40	3

ADDRESS

WOODCOCK WASHBURN LLP
CIRA CENTRE, 12TH FLOOR
2929 ARCH STREET
PHILADELPHIA, PA 19104-2891
UNITED STATES

TITLE

Cyclopropyl-Fused Pyrrolidine-Based Inhibitors Of Dipeptidyl Peptidase IV And Method

FILING FEE RECEIVED		
3130	FEES: Authority has been given in Paper No._____ to charge/credit DEPOSIT ACCOUNT No._____ for following:	☐ All Fees ☐ 1.16 Fees (Filing) ☐ 1.17 Fees (Processing Ext. of time) ☐ 1.18 Fees (Issue) ☐ Other _____ ☐ Credit

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13308658	ROBL ET AL.
	Examiner	Art Unit
	GREGG POLANSKY	1629

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	05/01/2012	02/06/2013							
1	1	✓	=							
2	2	✓	=							
3	3	✓	=							
4	4	✓	=							
5	5	✓	=							
6	6	✓	=							
7	7	✓	=							
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31	31	✓	=							
32	32	✓	=							
33	33	✓	=							
34	34	✓	=							
35	35	✓	=							
	36	✓	-							

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
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CLAIM		DATE								
Final	Original	05/01/2012	02/06/2013							
	37	✓	-							
36	38	✓	=							
37	39	✓	=							
38	40	✓	=							
39	41		=							
40	42		=							
41	43		=							
42	44		=							
43	45		=							

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(Depositor's name)
(Signature)
(Date)

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TITLE OF INVENTION: Cyclopropyl-Fused Pyrrolidine-Based Inhibitors Of Dipeptidyl Peptidase IV And Method

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nonprovisional	NO	$1770	$0	$0	$1770	05/13/2013

EXAMINER	ART UNIT	CLASS-SUBCLASS
POLANSKY, GREGG	1629	514-252190

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).
- ☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
- ☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
(1) the names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 _____
2 Woodcock Washburn LLP
3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE: Bristol-Myers Squibb Company

(B) RESIDENCE: (CITY and STATE OR COUNTRY): Princeton, NJ

Please check the appropriate assignee category or categories (will not be printed on the patent) : ☐ Individual ☒ Corporation or other private group entity ☐ Government

4a. The following fee(s) are submitted:
- ☒ Issue Fee
- ☐ Publication Fee (No small entity discount permitted)
- ☐ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**
- ☐ A check is enclosed.
- ☐ Payment by credit card. Form PTO-2038 is attached.
- ☒ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number 233050 (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)
- ☐ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27.
- ☐ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature /S. Maurice Valla/ Date February 15, 2013

Typed or printed name S. Maurice Valla Registration No. 43,966

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Electronic Patent Application Fee Transmittal

Application Number:	13308658
Filing Date:	01-Dec-2011
Title of Invention:	Cyclopropyl-Fused Pyrrolidine-Based Inhibitors Of Dipeptidyl Peptidase IV And Method
First Named Inventor/Applicant Name:	Jeffrey A. Robl
Filer:	SAMUEL VALLA/Ann Trevisani
Attorney Docket Number:	BMS-2856

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Utility Appl issue fee	1501	1	1770	1770
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
			Total in USD ($)	**1770**

Electronic Acknowledgement Receipt

EFS ID:	14971738
Application Number:	13308658
International Application Number:	
Confirmation Number:	7781
Title of Invention:	Cyclopropyl-Fused Pyrrolidine-Based Inhibitors Of Dipeptidyl Peptidase IV And Method
First Named Inventor/Applicant Name:	Jeffrey A. Robl
Customer Number:	23377
Filer:	SAMUEL VALLA/Ann Trevisani
Filer Authorized By:	SAMUEL VALLA
Attorney Docket Number:	BMS-2856
Receipt Date:	15-FEB-2013
Filing Date:	01-DEC-2011
Time Stamp:	14:29:16
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$1770
RAM confirmation Number	897
Deposit Account	233050
Authorized User	

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

Charge any Additional Fees required under 37 C.F.R. Section 1.16 (National application filing, search, and examination fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.19 (Document supply fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.20 (Post Issuance fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.21 (Miscellaneous fees and charges)

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Issue Fee Payment (PTO-85B)	Issue_Fee_Transmittal.PDF	1027096 48570b69ef33e9f3be16d22f5b113851e67190a1	no	1
Warnings:					
Information:					
2	Fee Worksheet (SB06)	fee-info.pdf	30083 39951163a67f4d4a649a4c2438c239a98d3eca4d	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	1057179		

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New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	ISSUE DATE	PATENT NO.	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/308,658	04/30/2013	RE44186	BMS-2856	7781

23377 7590 04/10/2013

WOODCOCK WASHBURN LLP
CIRA CENTRE, 12TH FLOOR
2929 ARCH STREET
PHILADELPHIA, PA 19104-2891

ISSUE NOTIFICATION

The projected patent number and issue date are specified above.

Determination of Patent Term Extension or Adjustment under 35 U.S.C. 154 (b)

A reissue patent is for "the unexpired part of the term of the original patent." See 35 U.S.C. 251. Accordingly, the above-identified reissue application is not eligible for Patent Term Extension or Adjustment under 35 U.S.C. 154(b).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Application Assistance Unit (AAU) of the Office of Data Management (ODM) at (571)-272-4200.

APPLICANT(s) (Please see PAIR WEB site http://pair.uspto.gov for additional applicants):

Jeffrey A. Robl, Newtown, PA;
Richard B. Sulsky, West Trenton, NJ;
David J. Augeri, Princeton, NJ;
David R. Magnin, Hamilton, NJ;
Lawrence G. Hamann, Cherry Hill, NJ;
David A. Betebenner, Lawrenceville, NJ;

DOCKET NO.: BMS-2856 **PATENT**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

Jeffrey A. Robl; Richard B. Sulsky; David J. Augeri; David R. Magnin; Lawrence G. Hamann; David A. Betebenner

Confirmation No.: 7781

Patent No.: RE44,186 E

Issued: April 30, 2013

Application No.: 13/308,658

Filing Date: December 1, 2011

For: CYCLOPROPYL-FUSED PYRROLIDINE-BASED INHIBITORS OF DIPEPTIDYL PEPTIDASE IV AND METHOD

Commissioner for Patents
Attn: Certificate of Correction Branch
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

REQUEST FOR CERTIFICATE OF CORRECTION OF PATENT FOR PTO MISTAKE PURSUANT TO 37 CFR § 1.322(a)

It is respectfully requested that a Certificate of Correction be issued for the above-identified patent. In accordance with 37 CFR § 1.322(a), the patent has errors in it that occurred through the fault of the Patent and Trademark Office as clearly disclosed by the records and files of the office.

Enclosed herewith please find a completed Certificate of Correction form.

Since the errors are not due to applicants' mistake, no correction fee is due. Please charge any fees for copies and any additional fees to our Deposit Account No. 23-3050.

Date: July 3, 2013

/Stephanie A. Lodise/
Stephanie A. Lodise
Registration No. 51,430

Woodcock Washburn LLP
Cira Centre
2929 Arch Street, 12th Floor
Philadelphia, PA 19104-2891
Telephone: (215) 568-3100
Facsimile: (215) 568-3439

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO	:	RE44,186 E
APPLICATION NO.	:	13/308,658
ISSUE DATE	:	April 30, 2013
INVENTOR(S)	:	Jeffrey A. Robl; Richard B. Sulsky; David J. Augeri; David R. Magnin; Lawrence G. Hamann; David A. Betebenner

It is certified that errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 4,
Line 56, delete "alkylcyclo alkyl," and insert -- alkylcycloalkyl, --.
Line 56, delete "hydroxytricyclo alkyl," and insert -- hydroxytricycloalkyl, --.

Column 17,
Line 48, delete "a-phosphono-sulfonates" and insert -- α-phosphono-sulfonates --.

Column 19,
Line 51, delete "lipoxygevase" and insert -- lipoxygenase --.

Column 28,
Lines 16-17, delete "butoxycarbonylisoleucine" and insert -- butoxycarbonyl-isoleucine --.

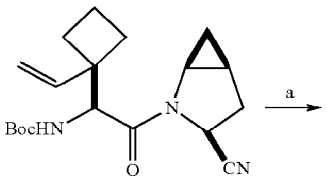
Column 33,
Lines 38-39, delete "1-[(3-dimethypamino)propyl]" and insert -- 1-[(3-dimethyl)amino)propyl] --.

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

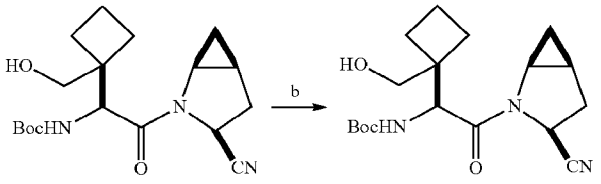
PATENT NO	:	RE44,186 E
APPLICATION NO.	:	13/308,658
ISSUE DATE	:	April 30, 2013
INVENTOR(S)	:	Jeffrey A. Robl; Richard B. Sulsky; David J. Augeri; David R. Magnin; Lawrence G. Hamann; David A. Betebenner

Column 51,
Lines 1-30, delete "

Scheme 7
General Method E, Examples 45 47



26



27 28

a. OsO_4, THF:H_2O, 1:1; $NaIO_4$; workup, then $NaBH_4$, MeOH, RT. 56%
b. TFA:CH_2Cl_2, 1:2, 0 degrees C. to RT.

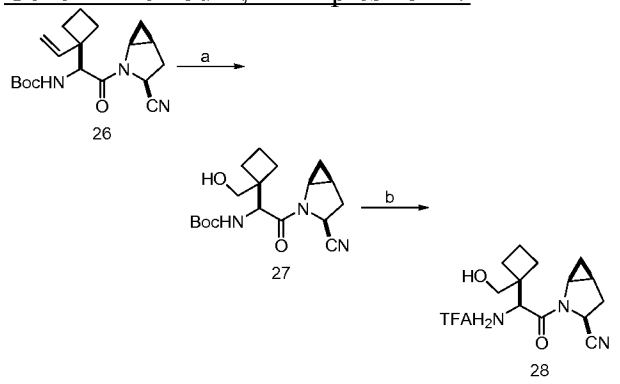
"

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO	:	RE44,186 E
APPLICATION NO.	:	13/308,658
ISSUE DATE	:	April 30, 2013
INVENTOR(S)	:	Jeffrey A. Robl; Richard B. Sulsky; David J. Augeri; David R. Magnin; Lawrence G. Hamann; David A. Betebenner

and insert --

Scheme 7
General Method E, Examples 45 47



a.OsO_4, THF:H_2O, 1:1; $NaIO_4$; workup,then $NaBH_4$, MeOH, RT. 56%
b. TFA:CH_2Cl_2, 1:2, 0 degrees C to RT.

--.

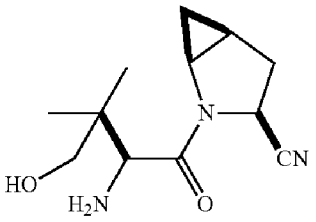
Column 51,
Line 54, delete "OsO4" and insert -- OsO_4 --.

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO	:	RE44,186 E
APPLICATION NO.	:	13/308,658
ISSUE DATE	:	April 30, 2013
INVENTOR(S)	:	Jeffrey A. Robl; Richard B. Sulsky; David J. Augeri; David R. Magnin; Lawrence G. Hamann; David A. Betebenner

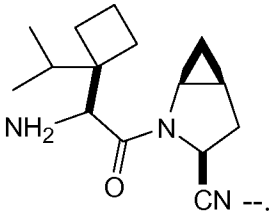
Column 55,
Lines 19-31, EXAMPLE 57, delete "

Step 3



"

and insert --

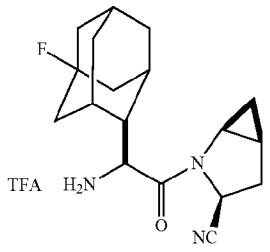


--.

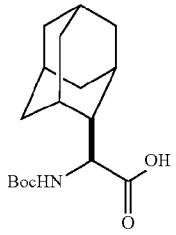
UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO	:	RE44,186 E
APPLICATION NO.	:	13/308,658
ISSUE DATE	:	April 30, 2013
INVENTOR(S)	:	Jeffrey A. Robl; Richard B. Sulsky; David J. Augeri; David R. Magnin; Lawrence G. Hamann; David A. Betebenner

Column 63,
Lines 25-46, EXAMPLE 62, delete "



Step 1

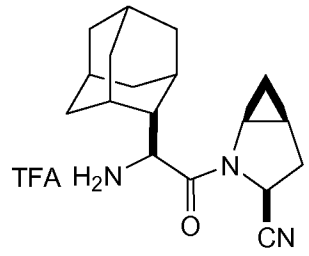


"

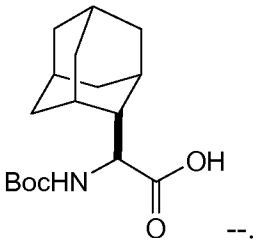
UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO	:	RE44,186 E
APPLICATION NO.	:	13/308,658
ISSUE DATE	:	April 30, 2013
INVENTOR(S)	:	Jeffrey A. Robl; Richard B. Sulsky; David J. Augeri; David R. Magnin; Lawrence G. Hamann; David A. Betebenner

and insert --



Step 1



--.

Column 64,
Line 31, delete "$NaHS0_3$" and insert -- $NaHSO_3$ --.

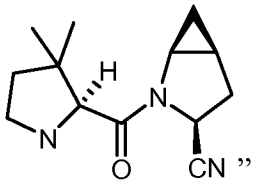
UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO	:	RE44,186 E
APPLICATION NO.	:	13/308,658
ISSUE DATE	:	April 30, 2013
INVENTOR(S)	:	Jeffrey A. Robl; Richard B. Sulsky; David J. Augeri; David R. Magnin; Lawrence G. Hamann; David A. Betebenner

Column 69,
Lines 20-32, delete "

EXAMPLE 67

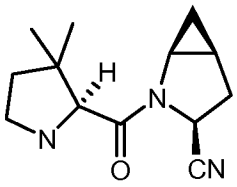
Step 1



"

and insert --

EXAMPLE 67



Step 1--.

Column 70,
Line 59, delete "19,8 mmol" and insert -- 19.8 mmol --.

Column 82,
Line 27, after "30 min" insert -- . --.

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO	:	RE44,186 E
APPLICATION NO.	:	13/308,658
ISSUE DATE	:	April 30, 2013
INVENTOR(S)	:	Jeffrey A. Robl; Richard B. Sulsky; David J. Augeri; David R. Magnin; Lawrence G. Hamann; David A. Betebenner

Column 87,
Line 7, Claim 1, delete "R4" and insert -- R^4 --.

Column 92,
Line 21, Claim 36, delete "any one of claim" and insert -- any one of claims --.

MAILING ADDRESS OF SENDER (Please do not use customer number below):

Woodcock Washburn LLP
Cira Centre
2929 Arch Street, 12th Floor
Philadelphia, PA 19104-2891

Electronic Acknowledgement Receipt

EFS ID:	16226296
Application Number:	13308658
International Application Number:	
Confirmation Number:	7781
Title of Invention:	Cyclopropyl-Fused Pyrrolidine-Based Inhibitors Of Dipeptidyl Peptidase IV And Method
First Named Inventor/Applicant Name:	Jeffrey A. Robl
Customer Number:	23377
Filer:	Stephanie A. Barbosa/Laura Taylor
Filer Authorized By:	Stephanie A. Barbosa
Attorney Docket Number:	BMS-2856
Receipt Date:	03-JUL-2013
Filing Date:	01-DEC-2011
Time Stamp:	10:47:07
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Miscellaneous Incoming Letter	BMS-2856Transmittal.PDF	262282 737646480d28b903831e03b6cac6fb353f3ca960	no	2

Warnings:	
Information:	

2	Request for Certificate of Correction	BMS-2856ReqCertCorr.PDF	79227 213fd4d2d20f04bd0a7d68fb5ba2c2aa8db7a560	no	2
Warnings:					
Information:					
3	Request for Certificate of Correction	BMS-2856CertCorr.PDF	137994 97e3cffefa5eb7df3ce58ae7eaee4e54e2adb3ae	no	8
Warnings:					
Information:					
			Total Files Size (in bytes):	479503	

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New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

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New International Application Filed with the USPTO as a Receiving Office
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Doc Code: TRAN.LET

Document Description: Transmittal Letter

PTO/SB/21 (07-09)
Approved for use through 07/31/2012. OMB 0651-0031
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TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Total Number of Pages in This Submission	12

Application Number	13/308,658
Filing Date	December 1, 2011
First Named Inventor	Jeffrey A. Robl
Art Unit	1629
Examiner Name	Gregg Polansky
Attorney Docket Number	BMS-2856

ENCLOSURES (*Check all that apply*)

- ☐ Fee Transmittal Form
  - ☐ Fee Attached
- ☐ Amendment/Reply
  - ☐ After Final
  - ☐ Affidavits/declaration(s)
- ☐ Extension of Time Request
- ☐ Express Abandonment Request
- ☐ Information Disclosure Statement
- ☐ Certified Copy of Priority Document(s)
- ☐ Reply to Missing Parts/ Incomplete Application
  - ☐ Reply to Missing Parts under 37 CFR 1.52 or 1.53
- ☐ Drawing(s)
- ☐ Licensing-related Papers
- ☐ Petition
- ☐ Petition to Convert to a Provisional Application
- ☐ Power of Attorney, Revocation
- ☐ Change of Correspondence Address
- ☐ Terminal Disclaimer
- ☐ Request for Refund
- ☐ CD, Number of CD(s) _____
  - ☐ Landscape Table on CD
- ☐ After Allowance Communication to TC
- ☐ Appeal Communication to Board of Appeals and Interferences
- ☐ Appeal Communication to TC **(Appeal Notice, Brief, Reply Brief)**
- ☐ Proprietary Information
- ☐ Status Letter
- ☑ Other Enclosure(s) (please Identify below):
  - Request for Certificate of Correction (2 pages)
  - Certificate of Correction (8 pages)

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	Woodcock Washburn LLP		
Signature	/Stephanie A. Lodise/		
Printed name	Stephanie A. Lodise		
Date	July 3, 2013	Reg. No.	51430

CERTIFICATE OF TRANSMISSION/MAILING

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Signature			
Typed or printed name		Date	

Privacy Act Statement

The **Privacy Act of 1974 (P.L. 93-579)** requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (*i.e.*, GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

SPE RESPONSE FOR CERTIFICATE OF CORRECTION

Paper No.: _____

DATE : July 18, 2013

TO SPE OF : ART UNIT 1629

SUBJECT : Request for Certificate of Correction for Appl. No.: 13308658 Patent No.: RE44186

COCIN mailroom date: July 3, 2013

Please respond to this request for a certificate of correction within 7 days.

FOR IFW FILES:

Please review the requested changes/corrections as shown in the **COCIN** document(s) in the IFW application image. No new matter should be introduced nor should the scope or meaning of the claims be changed.

Please complete the response (see below) and forward the completed response to scanning using document code **COCX**.

FOR PAPER FILES:

Please review the requested changes/corrections as shown in the attached certificate of correction. Please complete this form (see below) and forward it with the file to:

Certificates of Correction Branch (CofC)
Randolph Square – 9D10-A
Palm Location 7580

In Particular note:

Valerie Jackson
Certificates of Correction Branch
703-756-1814

Thank You For Your Assistance

The request for issuing the above-identified correction(s) is hereby:
Note your decision on the appropriate box.

- ☐ **Approved** — **All** changes apply.
- ☐ **Approved in Part** — Specify below which changes **do not** apply.
- ☐ **Denied** — State the reasons for denial below.

Comments: _____

SPE RESPONSE FOR CERTIFICATE OF CORRECTION

SPE Art Unit

SPE RESPONSE FOR CERTIFICATE OF CORRECTION

Paper No.: _____

DATE : July 18, 2013

TO SPE OF : ART UNIT 1629

SUBJECT : Request for Certificate of Correction for Appl. No.: 13308658 Patent No.: RE44186

COCIN mailroom date: July 3, 2013

Please respond to this request for a certificate of correction within 7 days.

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Please complete the response (see below) and forward the completed response to scanning using document code **COCX**.

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Please review the requested changes/corrections as shown in the attached certificate of correction. Please complete this form (see below) and forward it with the file to:

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Randolph Square – 9D10-A
Palm Location 7580

In Particular note:

Valerie Jackson
Certificates of Correction Branch
703-756-1814

Thank You For Your Assistance

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Note your decision on the appropriate box.

X Approved	**All** changes apply.
☐ **Approved in Part**	Specify below which changes **do not** apply.
☐ **Denied**	State the reasons for denial below.

Comments: _____

/Jeffrey S. Lundgren/ **1629**

SPE RESPONSE FOR CERTIFICATE OF CORRECTION

SPE

Art Unit

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : RE44,186 E
APPLICATION NO. : 13/308658
DATED : April 30, 2013
INVENTOR(S) : Jeffrey A. Robl et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In the Specifications:

Column 4,
Line 56, delete "alkylcyclo alkyl," and insert -- alkylcycloalkyl, --.
Line 56, delete "hydroxytricyclo alkyl," and insert
-- hydroxytricycloalkyl, --.

Column 17,
Line 48, delete "a-phosphono-sulfonates" and insert -- α-phosphono-sulfonates --.

Column 19,
Line 51, delete "lipoxygevase" and insert -- lipoxygenase --.

Column 28,
Lines 16-17, delete "butoxycarbonylisoleucine" and insert
-- butoxycarbonyl-isoleucine --.

Column 33,
Lines 38-39, delete "1-[(3-dimethypamino)propyl]" and insert
-- 1-[(3-dimethyl)amino)propyl] --.

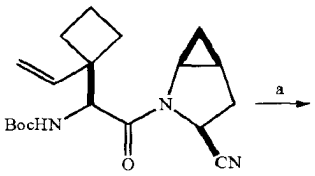
Signed and Sealed this
Eighth Day of October, 2013

Teresa Stanek Rea
Deputy Director of the United States Patent and Trademark Office

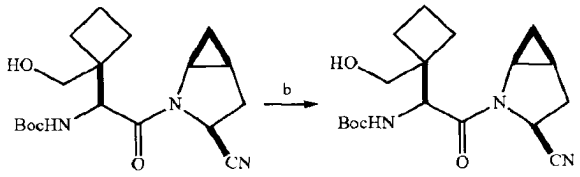
In the Specifications:

Column 51,

Scheme 7
General Method E, Examples 45 47



26

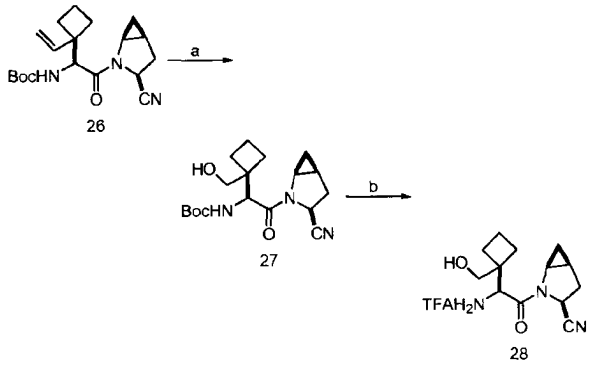


27 28

a. OsO_4, THF:H_2O, 1:1; $NaIO_4$; workup, then $NaBH_4$, MeOH, RT. 56%
b. TFA:CH_2Cl_2, 1:2, 0 degrees C. to RT.

Lines 1-30, delete " "

and insert --Scheme 7
General Method E, Examples 45 47



a.OsO_4, THF:H_2O, 1:1; $NaIO_4$; workup,then $NaBH_4$, MeOH, RT. 56%
b. TFA:CH_2Cl_2, 1:2, 0 degrees C to RT.

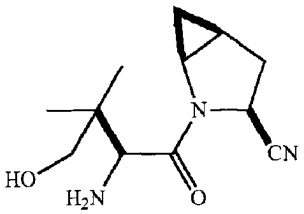
--.

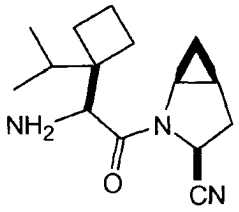
Column 51,
Line 54, delete "OsO4" and insert -- OsO_4 --.

In the Specifications:

Column 55,

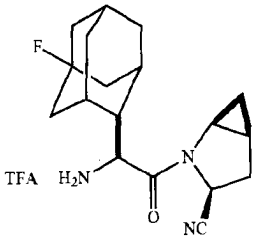
Step 3

Lines 19-31, EXAMPLE 57, delete "  " and

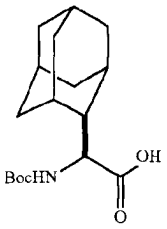


insert -- --.

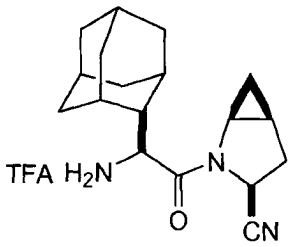
Column 63,



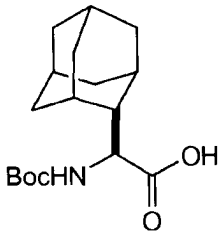
Step 1



Lines 25-46, EXAMPLE 62, delete " " and



Step 1



insert -- --.

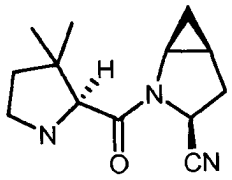
In the Specifications:

Column 64,
Line 31, delete "$NaHS0_3$" and insert -- $NaHSO_3$ --.

Column 69,

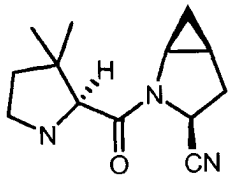
EXAMPLE 67

Step 1



Lines 20-32, delete " " and

EXAMPLE 67



insert -- Step 1 --.

Column 70,
Line 59, delete "19,8 mmol" and insert -- 19.8 mmol --.

Column 82,
Line 27, after "30 min" insert -- . --.

In the Claims:

Column 87,
Line 7, Claim 1, delete "R4" and insert -- R^4 --.

Column 92,
Line 21, Claim 36, delete "any one of claim" and insert -- any one of claims --.

AO 120 (Rev. 08/10)

TO:	REPORT ON THE FILING OR DETERMINATION OF AN ACTION REGARDING A PATENT OR TRADEMARK
Mail Stop 8 Director of the U.S. Patent and Trademark Office P.O. Box 1450 Alexandria, VA 22313-1450	

In Compliance with 35 U.S.C. § 290 and/or 15 U.S.C. § 1116 you are hereby advised that a court action has been filed in the U.S. District Court United States District Court for the District of Delaware on the following

☐ Trademarks or ☒ Patents. (☐ the patent action involves 35 U.S.C. § 292.):

DOCKET NO.	DATE FILED	U.S. DISTRICT COURT United States District Court for the District of Delaware
PLAINTIFF ASTRAZENECA AB		DEFENDANT WOCKHARDT BIO AG and WOCKHARDT USA LLC

	PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
1	RE44,186	April 30, 2013	AstraZeneca AB
2	7,951,400	May 31, 2011	AstraZeneca AB
3			
4			
5			

In the above—entitled case, the following patent(s)/ trademark(s) have been included:

DATE INCLUDED	INCLUDED BY ☐ Amendment ☐ Answer ☐ Cross Bill ☐ Other Pleading	
PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
1		
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In the above—entitled case, the following decision has been rendered or judgement issued:

DECISION/JUDGEMENT

CLERK	(BY) DEPUTY CLERK	DATE

Copy 1—Upon initiation of action, mail this copy to Director **Copy 3—Upon termination of action, mail this copy to Director**
Copy 2—Upon filing document adding patent(s), mail this copy to Director **Copy 4—Case file copy**

AO 120 (Rev. 08/10)

TO:	**Mail Stop 8 Director of the U.S. Patent and Trademark Office P.O. Box 1450 Alexandria, VA 22313–1450**	**REPORT ON THE FILING OR DETERMINATION OF AN ACTION REGARDING A PATENT OR TRADEMARK**

In Compliance with 35 U.S.C. § 290 and/or 15 U.S.C. § 1116 you are hereby advised that a court action has been filed in the **U.S. District Court for the District of New Jersey** on the following:
____ Trademarks or **X** Patents. (____ the patent action involves 35 U.S.C. § 292.)

DOCKET NO.	DATE FILED	U.S. DISTRICT COURT
3:14–cv–03552–MLC–DEA	6/3/2014	TRENTON, NJ

PLAINTIFF	DEFENDANT
ASTRAZENECA AB	SUN PHARMA GLOBAL FZE

PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
1 US RE44,186 E	April 30, 2013	Bristol–Myers Squibb Company
2 US 7,951,400 B2	May 31, 2011	Bristol–Myers Squibb Company
3 US 8,628,799 B2	January 14, 2014	Bristol–Myers Squibb Company
4		
5		

In the above—entitled case, the following patent(s)/ trademark(s) have been included:

DATE INCLUDED	INCLUDED BY ___ Amendment ___ Answer ___ Cross Bill ___ Other Pleading	
PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
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In the above—entitled case, the following decision has been rendered or judgement issued:

DECISION/JUDGEMENT

CLERK	(BY) DEPUTY CLERK	DATE
William T. Walsh	s/ Marlene Kalbach	6/3/2014

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AO 120 (Rev. 08/10)

TO:	REPORT ON THE FILING OR DETERMINATION OF AN ACTION REGARDING A PATENT OR TRADEMARK
Mail Stop 8 **Director of the U.S. Patent and Trademark Office** **P.O. Box 1450** **Alexandria, VA 22313-1450**	

In Compliance with 35 U.S.C. § 290 and/or 15 U.S.C. § 1116 you are hereby advised that a court action has been filed in the U.S. District Court District of Delaware on the following

☐ Trademarks or ☑ Patents. (☐ the patent action involves 35 U.S.C. § 292.):

DOCKET NO.	DATE FILED	U.S. DISTRICT COURT
	6/2/2014	District of Delaware

PLAINTIFF	DEFENDANT
ASTRAZENECA AB	SUN PHARMA GLOBAL FZE, SUN PHARMACEUTICAL INDUSTRIES LTD. and CARACO PHARMACEUTICAL LABORATORIES LTD.

	PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
1	RE44,186	4/30/2013	AstraZeneca AB
2	7,951,400	5/31/2011	AstraZeneca AB
3	8,628,799	1/14/2014	AstraZeneca AB
4			
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In the above—entitled case, the following patent(s)/ trademark(s) have been included:

DATE INCLUDED	INCLUDED BY ☐ Amendment ☐ Answer ☐ Cross Bill ☐ Other Pleading	
PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
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In the above—entitled case, the following decision has been rendered or judgement issued:

DECISION/JUDGEMENT

CLERK	(BY) DEPUTY CLERK	DATE

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AO 120 (Rev. 08/10)

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Mail Stop 8 Director of the U.S. Patent and Trademark Office P.O. Box 1450 Alexandria, VA 22313-1450	

In Compliance with 35 U.S.C. § 290 and/or 15 U.S.C. § 1116 you are hereby advised that a court action has been filed in the U.S. District Court District of Delaware on the following

☐ Trademarks or ☑ Patents. (☐ the patent action involves 35 U.S.C. § 292.):

DOCKET NO.	DATE FILED	U.S. DISTRICT COURT
	6/2/2014	District of Delaware

PLAINTIFF	DEFENDANT
ASTRAZENECA AB	AMNEAL PHARMACEUTICALS LLC

	PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
1	RE44,186	4/30/2013	AstraZeneca AB
2	7,951,400	5/31/2011	AstraZeneca AB
3	8,628,799	1/14/2014	AstraZeneca AB
4			
5			

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PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
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DECISION/JUDGEMENT

CLERK	(BY) DEPUTY CLERK	DATE

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Copy 2—Upon filing document adding patent(s), mail this copy to Director **Copy 4—Case file copy**

AO 120 (Rev. 08/10)

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Mail Stop 8 **Director of the U.S. Patent and Trademark Office** **P.O. Box 1450** **Alexandria, VA 22313-1450**	

In Compliance with 35 U.S.C. § 290 and/or 15 U.S.C. § 1116 you are hereby advised that a court action has been filed in the U.S. District Court District of Delaware on the following

☐ Trademarks or ☑ Patents. (☐ the patent action involves 35 U.S.C. § 292.):

DOCKET NO.	DATE FILED	U.S. DISTRICT COURT
	6/2/2014	District of Delaware

PLAINTIFF	DEFENDANT
ASTRAZENECA AB	MYLAN PHARMACEUTICALS, INC.

	PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
1	RE44,186	4/30/2013	AstraZeneca AB
2	7,951,400	5/31/2011	AstraZeneca AB
3	8,628,799	1/14/2014	AstraZeneca AB
4			
5			

In the above—entitled case, the following patent(s)/ trademark(s) have been included:

DATE INCLUDED	INCLUDED BY ☐ Amendment ☐ Answer ☐ Cross Bill ☐ Other Pleading	
PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
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In the above—entitled case, the following decision has been rendered or judgement issued:

DECISION/JUDGEMENT

CLERK	(BY) DEPUTY CLERK	DATE

Copy 1—Upon initiation of action, mail this copy to Director **Copy 3—Upon termination of action, mail this copy to Director**
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1:14-CV-94

AO 120 (Rev. 08/10)

TO:	REPORT ON THE FILING OR DETERMINATION OF AN ACTION REGARDING A PATENT OR TRADEMARK
Mail Stop 8 Director of the U.S. Patent and Trademark Office P.O. Box 1450 Alexandria, VA 22313-1450	

In Compliance with 35 U.S.C. § 290 and/or 15 U.S.C. § 1116 you are hereby advised that a court action has been filed in the U.S. District Court Northern District of West Virginia on the following

☐ Trademarks or ☑ Patents. (☐ the patent action involves 35 U.S.C. § 292.):

FILED
JUN 3 2014
U.S. DISTRICT COURT-WVN
WHEELING, WV 26003

DOCKET NO.	DATE FILED	U.S. DISTRICT COURT
	6/3/2014	Northern District of West Virginia

PLAINTIFF	DEFENDANT
ASTRAZENECA AB	MYLAN PHARMACEUTICALS, INC.

	PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
1	RE44,186	4/30/2013	AstraZeneca AB
2	7,951,400	5/31/2011	AstraZeneca AB
3	8,628,799	1/14/2014	AstraZeneca AB
4			
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In the above—entitled case, the following patent(s)/ trademark(s) have been included:

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PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
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In the above—entitled case, the following decision has been rendered or judgement issued:

DECISION/JUDGEMENT

CLERK	(BY) DEPUTY CLERK	DATE

Copy 1—Upon initiation of action, mail this copy to Director **Copy 3—Upon termination of action, mail this copy to Director**
Copy 2—Upon filing document adding patent(s), mail this copy to Director **Copy 4—Case file copy**

AO 120 (Rev. 08/10)

TO:	REPORT ON THE FILING OR DETERMINATION OF AN ACTION REGARDING A PATENT OR TRADEMARK
Mail Stop 8 Director of the U.S. Patent and Trademark Office P.O. Box 1450 Alexandria, VA 22313-1450	

In Compliance with 35 U.S.C. § 290 and/or 15 U.S.C. § 1116 you are hereby advised that a court action has been filed in the U.S. District Court for the District of Delaware on the following

☐ Trademarks or ☒ Patents. (☐ the patent action involves 35 U.S.C. § 292.):

DOCKET NO.	DATE FILED	U.S. DISTRICT COURT
	8/15/2014	for the District of Delaware

PLAINTIFF	DEFENDANT
ASTRAZENECA AB	WATSON LABORATORIES, INC., ACTAVIS, INC. and ACTAVIS LLC

	PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
1	RE44,186	4/30/2013	AstraZeneca AB
2			
3			
4			
5			

In the above entitled case, the following patent(s)/ trademark(s) have been included:

DATE INCLUDED	INCLUDED BY ☐ Amendment ☐ Answer ☐ Cross Bill ☐ Other Pleading	
PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
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Copy 2—Upon filing document adding patent(s), mail this copy to Director **Copy 4—Case file copy**

AO 120 (Rev. 08/10)

TO:	**Mail Stop 8** **Director of the U.S. Patent and Trademark Office** **P.O. Box 1450** **Alexandria, VA 22313–1450**	**REPORT ON THE FILING OR DETERMINATION OF AN ACTION REGARDING A PATENT OR TRADEMARK**

In Compliance with 35 U.S.C. § 290 and/or 15 U.S.C. § 1116 you are hereby advised that a court action has been filed in the **U.S. District Court for the District of New Jersey** on the following:
____ Trademarks or **X** Patents. (____ the patent action involves 35 U.S.C. § 292.)

DOCKET NO.	DATE FILED	U.S. DISTRICT COURT
3:14–cv–03552–MLC–DEA	6/3/2014	TRENTON, NJ

PLAINTIFF	DEFENDANT
ASTRAZENECA AB	SUN PHARMA GLOBAL FZE

PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
1 US RE44,186 E	April 30, 2013	Bristol–Myers Squibb Company
2 US 7,951,400 B2	May 31, 2011	Bristol–Myers Squibb Company
3 US 8,628,799 B2	January 14, 2014	Bristol–Myers Squibb Company
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In the above—entitled case, the following patent(s)/ trademark(s) have been included:

DATE INCLUDED	INCLUDED BY ___ Amendment ___ Answer ___ Cross Bill ___ Other Pleading

PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
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In the above—entitled case, the following decision has been rendered or judgement issued:

DECISION/JUDGEMENT

CLERK	(BY) DEPUTY CLERK	DATE
William T. Walsh	s/ Marlene Kalbach	6/3/2014

Copy 1—Upon initiation of action, mail this copy to Director Copy 3—Upon termination of action, mail this copy to Director
Copy 2—Upon filing document adding patent(s), mail this copy to Director Copy 4—Case file copy

AO 120 (Rev. 08/10)

TO:	REPORT ON THE FILING OR DETERMINATION OF AN ACTION REGARDING A PATENT OR TRADEMARK
Mail Stop 8 **Director of the U.S. Patent and Trademark Office** **P.O. Box 1450** **Alexandria, VA 22313-1450**	

In Compliance with 35 U.S.C. § 290 and/or 15 U.S.C. § 1116 you are hereby advised that a court action has been filed in the U.S. District Court District of New Jersey on the following

☐ Trademarks or ☑ Patents. (☐ the patent action involves 35 U.S.C. § 292.):

DOCKET NO.	DATE FILED	U.S. DISTRICT COURT
14-cv-5513 (KSH)	9/3/2014	District of New Jersey

PLAINTIFF	DEFENDANT
LifePort Sciences LLC	C.R. Bard Inc. Bard Peripheral Vascular Inc.

	PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
1	6,673,103	1/6/2004	LifePort Sciences LLC
2			
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In the above—entitled case, the following patent(s)/ trademark(s) have been included:

DATE INCLUDED	INCLUDED BY ☐ Amendment ☐ Answer ☐ Cross Bill ☐ Other Pleading		
	PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
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In the above—entitled case, the following decision has been rendered or judgement issued:

DECISION/JUDGEMENT

CLERK	(BY) DEPUTY CLERK	DATE
WILLIAM T. WALSH	LEROY DUNBAR	9/3/2014

Copy 1—Upon initiation of action, mail this copy to Director **Copy 3—Upon termination of action, mail this copy to Director**
Copy 2—Upon filing document adding patent(s), mail this copy to Director **Copy 4—Case file copy**

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TO:	REPORT ON THE FILING OR DETERMINATION OF AN ACTION REGARDING A PATENT OR TRADEMARK
Mail Stop 8 Director of the U.S. Patent and Trademark Office P.O. Box 1450 Alexandria, VA 22313-1450	

In Compliance with 35 U.S.C. § 290 and/or 15 U.S.C. § 1116 you are hereby advised that a court action has been filed in the U.S. District Court for the District of Delaware on the following

☐ Trademarks or ☒ Patents. (☐ the patent action involves 35 U.S.C. § 292.):

DOCKET NO.	DATE FILED	U.S. DISTRICT COURT
	10/31/2014	for the District of Delaware

PLAINTIFF	DEFENDANT
ASTRAZENECA AB	ACTAVIS LABORATORIES FL, INC. f/k/a WATSON LABORATORIES FL, INC., WATSON LABORATORIES, INC., ACTAVIS, INC., and ACTAVIS LLC,

	PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
1	RE44,186	4/30/2013	AstraZeneca AB
2	8,628,799	1/14/2014	AstraZeneca AB
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In the above—entitled case, the following patent(s)/ trademark(s) have been included:

DATE INCLUDED	INCLUDED BY ☐ Amendment ☐ Answer ☐ Cross Bill ☐ Other Pleading	
PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
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DECISION/JUDGEMENT

CLERK	(BY) DEPUTY CLERK	DATE

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Copy 2—Upon filing document adding patent(s), mail this copy to Director **Copy 4—Case file copy**

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In Compliance with 35 U.S.C. § 290 and/or 15 U.S.C. § 1116 you are hereby advised that a court action has been filed in the U.S. District Court for the District of Delaware on the following

☐ Trademarks or ☒ Patents. (☐ the patent action involves 35 U.S.C. § 292.):

DOCKET NO.	DATE FILED 12/9/2014	U.S. DISTRICT COURT for the District of Delaware
PLAINTIFF ASTRAZENECA AB		DEFENDANT AUROBINDO PHARMA LTD., and AUROBINDO PHARMA U.S.A., INC.

	PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
1	RE 44,186	4/30/2013	AstraZeneca AB
2			
3			
4			
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In the above—entitled case, the following patent(s)/ trademark(s) have been included:

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