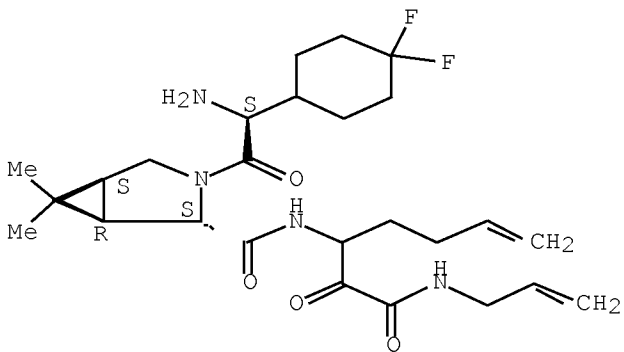


RN 394726-95-5 HCAPLUS
 CN 3-Azabicyclo[3.1.0]hexane-2-carboxamide,

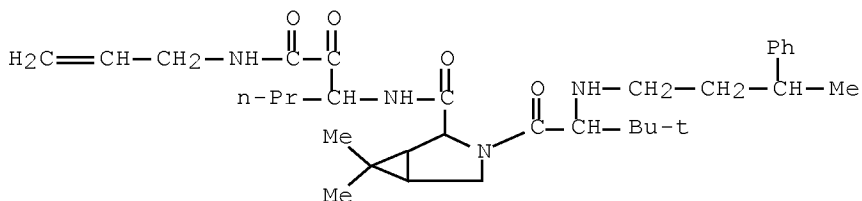
3-[(2S)-2-amino-2-(4,4-difluorocyclohexyl)acetyl]-6,6-dimethyl-N-[1-[2-oxo-2-(2-propen-1-ylamino)acetyl]-4-penten-1-yl]-, (1R,2S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



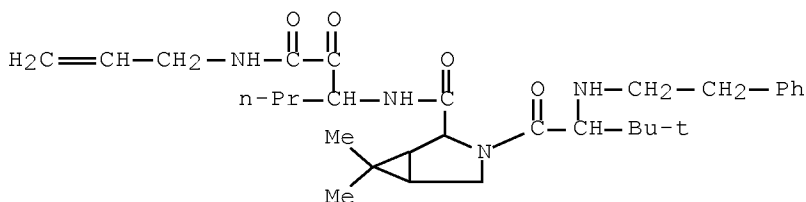
RN 394727-13-0 HCAPLUS
 CN 3-Azabicyclo[3.1.0]hexane-2-carboxamide,

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)



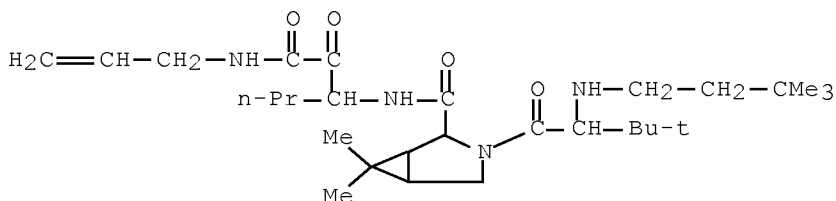
RN 394727-14-1 HCAPLUS
 CN 3-Azabicyclo[3.1.0]hexane-2-carboxamide,

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)



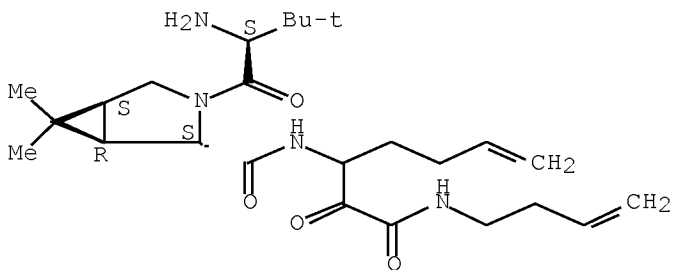
RN 394727-15-2 HCAPLUS
 CN 3-Azabicyclo[3.1.0]hexane-2-carboxamide,

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)

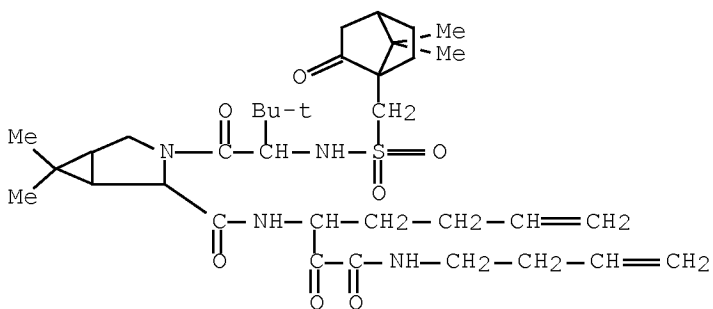


RN 394727-18-5 HCAPLUS
 CN 3-Azabicyclo[3.1.0]hexane-2-carboxamide,
 3-[(2S)-2-amino-3,3-dimethyl-1-oxobutyl]-N-[1-[2-(3-buten-1-ylamino)-2-oxoacetyl]-4-penten-1-yl]-6,6-dimethyl-, (1R,2S,5S)- (CA INDEX NAME)

Absolute stereochemistry.

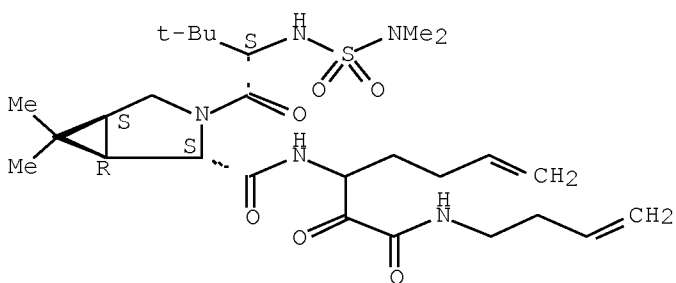


RN 394727-36-7 HCAPLUS
 CN 3-Azabicyclo[3.1.0]hexane-2-carboxamide,
 N-[1-[2-(3-buten-1-ylamino)-2-oxoacetyl]-4-penten-1-yl]-3-[(2S)-2-
 [[[(1R,4S)-7,7-dimethyl-2-oxobicyclo[2.2.1]hept-1-
 yl)methyl]sulfonyl]amino]-3,3-dimethyl-1-oxobutyl]-6,6-dimethyl-,
 (1R,2S,5S)- (CA INDEX NAME)



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.

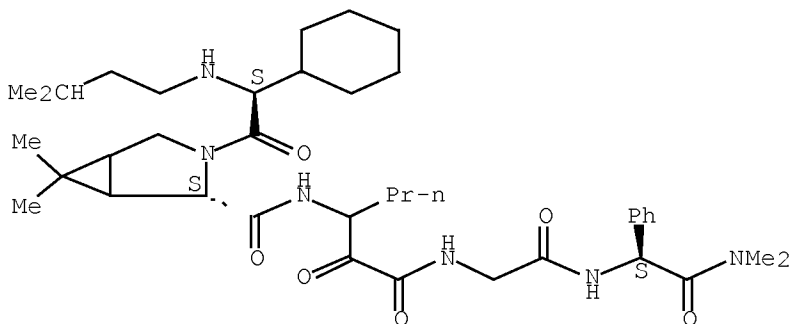


RN 395649-30-6 HCAPLUS

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)

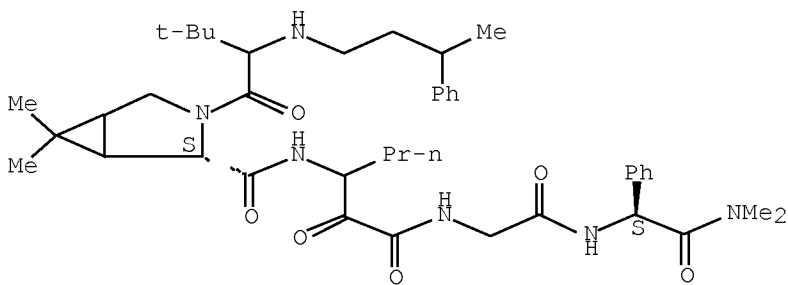
Absolute stereochemistry.



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)

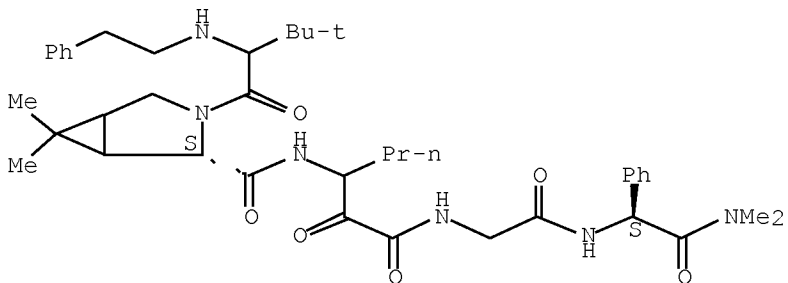
Absolute stereochemistry.



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)

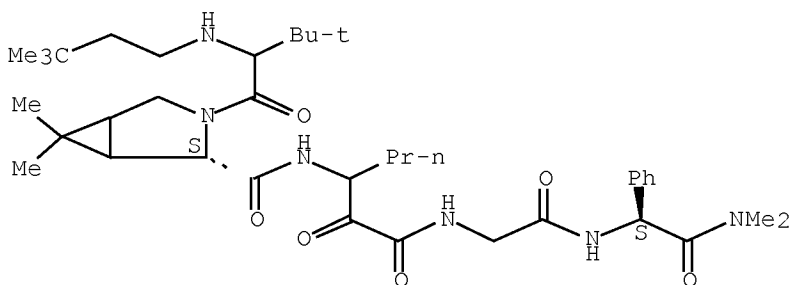
Absolute stereochemistry.



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)

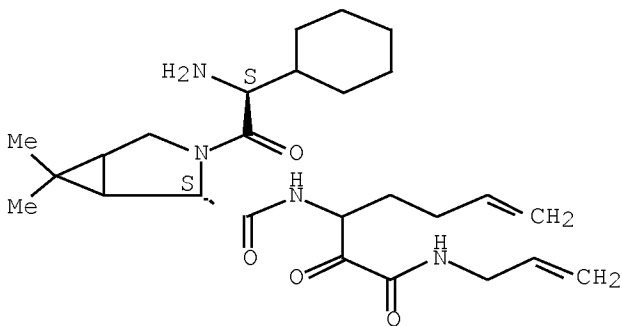
Absolute stereochemistry.



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)

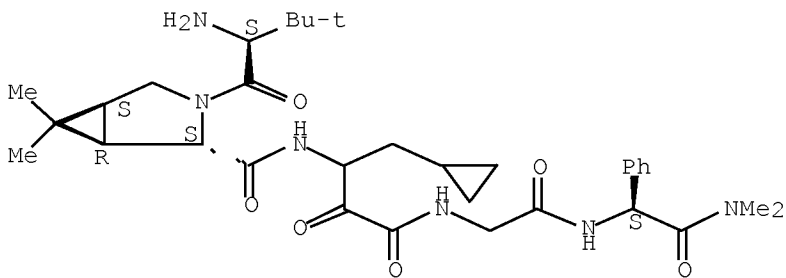
Absolute stereochemistry.



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)

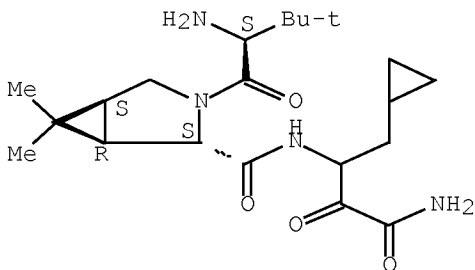
Absolute stereochemistry.



● 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

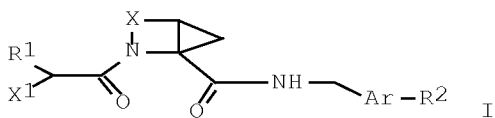
OS.CITING REF COUNT: 35 THERE ARE 35 CAPLUS RECORDS THAT CITE THIS
 RECORD (40 CITINGS)

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 <-- |
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| 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 <-- |
| | | | FR 1999-5601 | A 19990503 <-- |

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



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 304910-16-5F

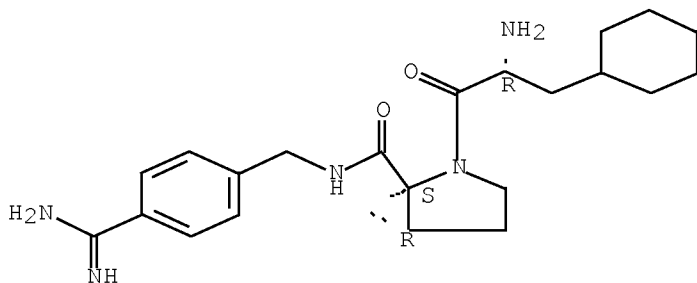
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(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.



● 2 HCl

IT 304910-17-6F 304910-19-8F 304910-20-1F
 304910-21-2F 304910-22-3F 304910-23-4F
 304910-24-5F 304910-26-7F 304910-27-8F
 304910-28-9F 304910-29-0F 304910-71-2F
 304910-72-3F

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)

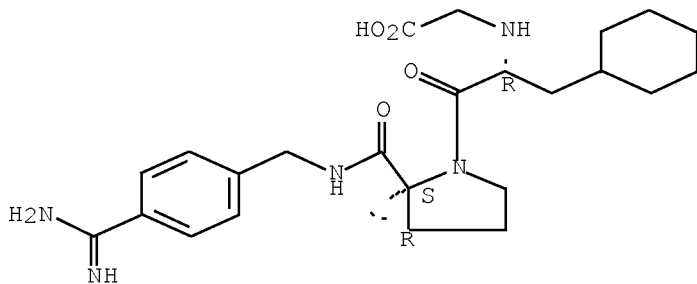
(preparation of 2,3-methano-amino acid derivs. as anticoagulant agents)

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)

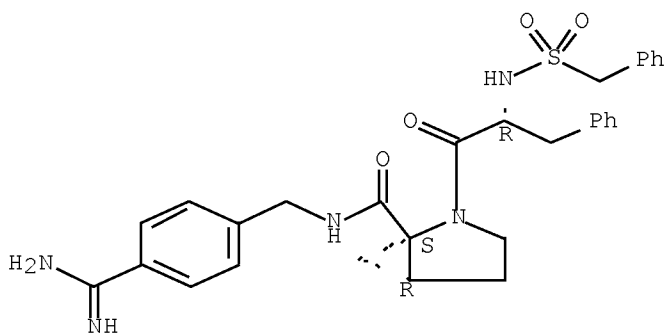
Absolute stereochemistry.



●_x HCl

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)

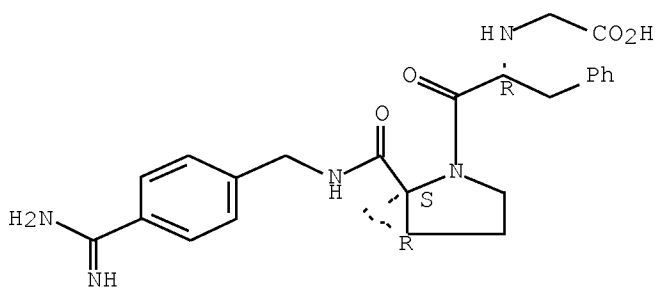
Absolute stereochemistry.



● HCl

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)

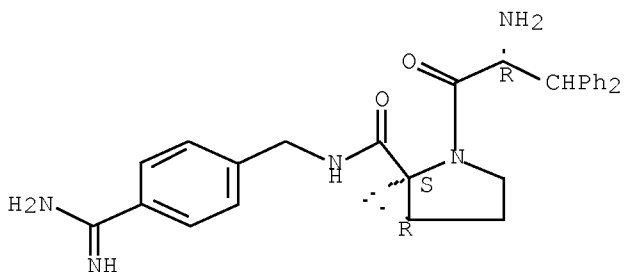
Absolute stereochemistry.



● 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)

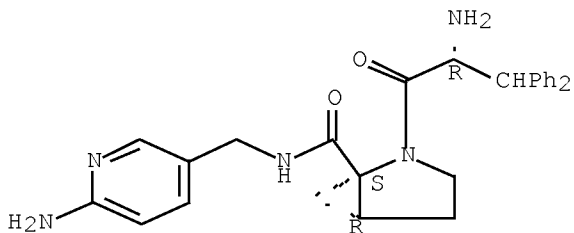
Absolute stereochemistry.



● 2 HCl

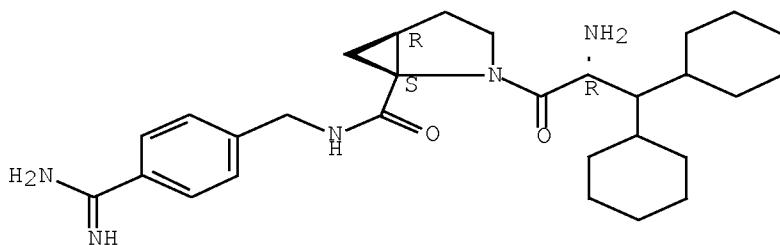
RN 304910-22-3 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-1-carboxamide,
 2-[(2R)-2-amino-1-oxo-3,3-diphenylpropyl]-N-[(6-amino-3-pyridinyl)methyl]-
 , hydrochloride (1:2), (1S,5R)- (CA INDEX NAME)

Absolute stereochemistry.

●₂ HCl

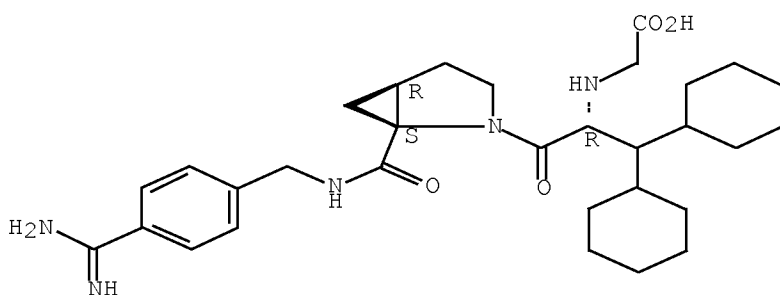
RN 304910-23-4 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-1-carboxamide,
 2-[(2R)-2-amino-3,3-dicyclohexyl-1-oxopropyl]-N-[[4-(aminoiminomethyl)phenyl]methyl]-, hydrochloride (1:2), (1S,5R)- (CA INDEX NAME)

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)

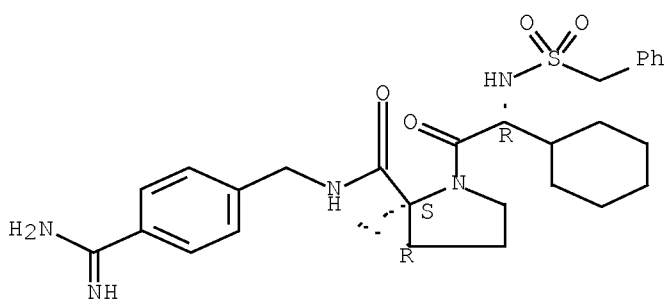
Absolute stereochemistry.



● 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)

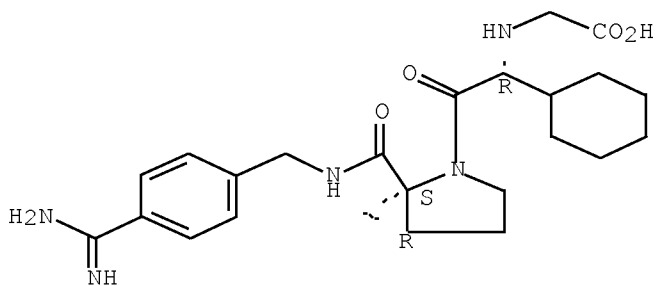
Absolute stereochemistry.



● 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.



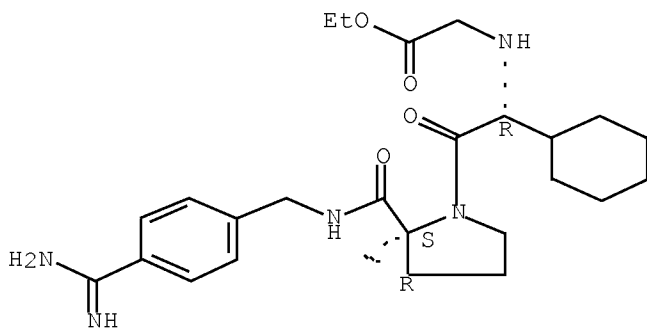
●_x HCl

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.



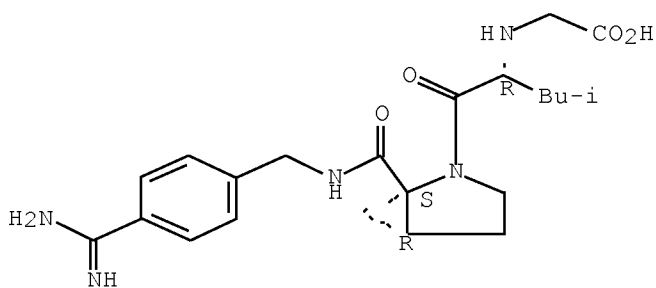
●₂ HCl

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)

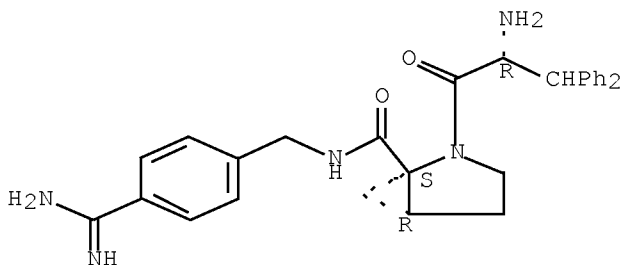
Absolute stereochemistry.



● 2 HCl

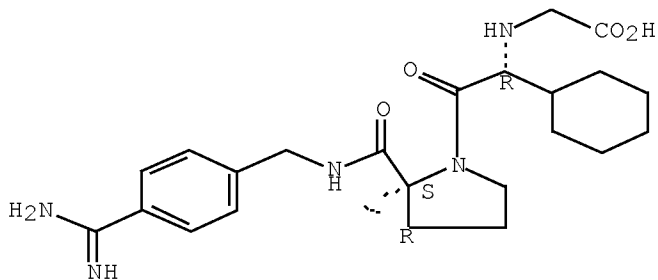
RN 304910-71-2 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-1-carboxamide,
 N-[[4-(aminoiminomethyl)phenyl]methyl]-2-[(2R)-2-amino-1-oxo-3,3-
 diphenylpropyl]-, (1S,5R)- (CA INDEX NAME)

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)

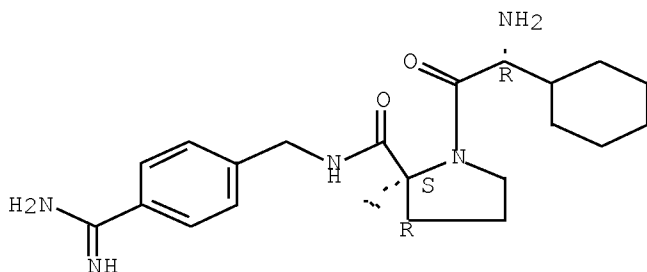
Absolute stereochemistry.



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)

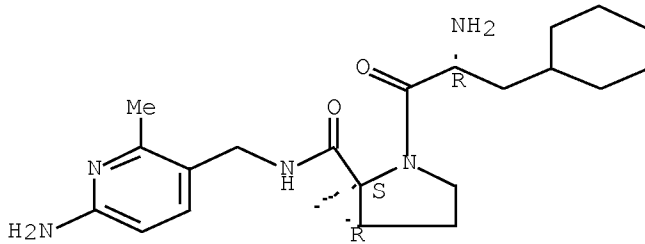
Absolute stereochemistry.



●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)

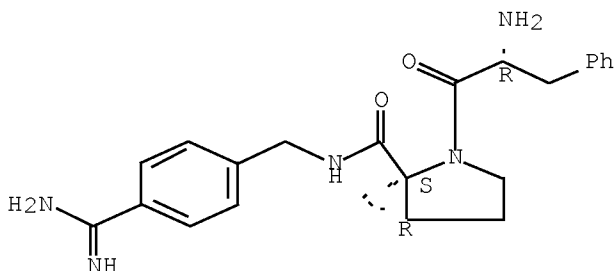
Absolute stereochemistry.



● 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 |

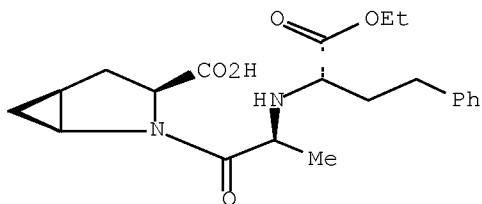
<--

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-converting enzyme inhibitors
 R(CH₂)_nCH(CO₂R₂)NHCHR₁CONR₅CHR₄CO₂R₁ (R = H, aliphatic radical, aryl, etc.;
 R₁ = H, aliphatic radical, aryl, heterocyclyl, etc.; R₂, R₃ = H, aliphatic

148

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

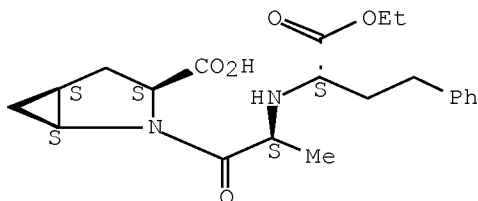
RL: BIOL (Biological study)

(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-[1 α ,2[R*(R*)],3 β ,5 α]]- (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

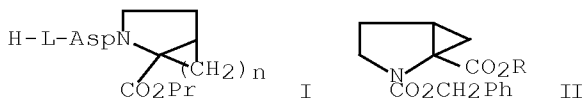
CODEN: IJPPC3; ISSN: 0367-8377

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 (\pm)-II ($R = CMe_3$) via resolution of (\pm)-II ($R = H$). All solid dipeptides had a bitter taste with no indication of sweetness.

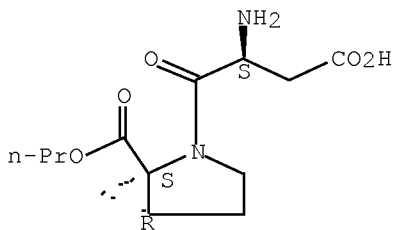
IT 134666-90-3P 134732-59-5P

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-[1 α , 2(R*), 5 α]]- (9CI) (CA INDEX NAME)

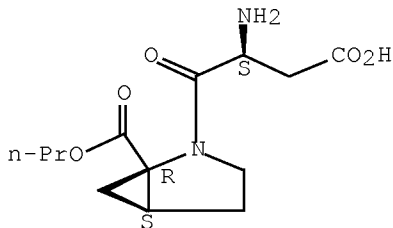
Absolute stereochemistry.



RN 134732-59-5 HCAPLUS

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

Absolute stereochemistry.



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

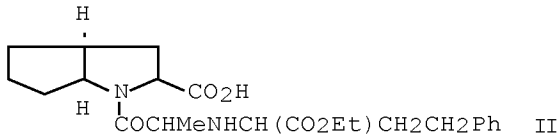
L49 ANSWER 80 OF 87 HCAPLUS COPYRIGHT 2012 ACS on STN
 ACCESSION NUMBER: 1988:516052 HCAPLUS Full-text
 DOCUMENT NUMBER: 109:116052
 ORIGINAL REFERENCE NO.: 109:19241a,19244a
 TITLE: Nootropic pharmaceutical containing
 angiotensin-converting-enzyme inhibitors (ACE
 inhibitors) and their use for the 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 <-- |

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

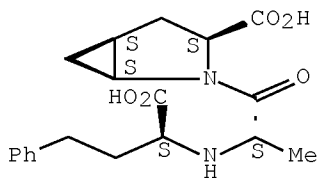
L49 ANSWER 81 OF 87 HCAPLUS COPYRIGHT 2012 ACS on STN
 ACCESSION NUMBER: 1987:591020 HCAPLUS Full-text
 DOCUMENT NUMBER: 107:191020
 ORIGINAL REFERENCE NO.: 107:30449a,30452a
 TITLE: Method and pharmaceutical composition containing an
 angiotensin-converting enzyme inhibitor for treatment
 of atherosclerosis, 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 | | | | |



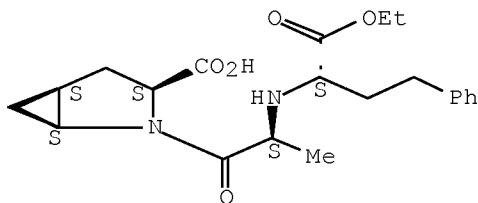
- AB Angiotensin-converting enzyme inhibitors
 $\text{R}_3\text{O}_2\text{CCHR}_4\text{NR}_5\text{COCHR}_1\text{NHCH}(\text{CO}_2\text{R}_2)(\text{CH}_2)_n\text{R}$ (I) [$n = 1, 2$; $\text{R} = \text{H}$, (substituted) hydrocarbyl, alkoxy, alkylthio, etc.; $\text{R}_1 = \text{H}$, (substituted) hydrocarbyl, (substituted) heteroaryl, (protected) amino acid side chain; $\text{R}_2, \text{R}_3 = \text{H}$, (substituted) hydrocarbyl; $\text{R}_4\text{CHNR}_5 = \text{C}_4\text{-15}$ 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-[1 α , 2[R*(R*)], 3 β , 5 α]]- (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-[1 α , 2[R*(R*)], 3 β , 5 α]]- (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

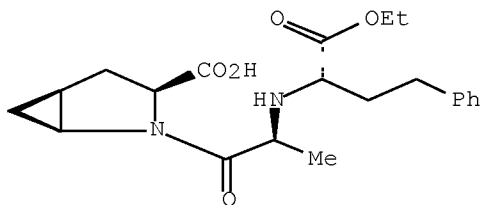
DOCUMENT TYPE: Patent

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. $R_3O_2CCHR_4NR_5COCHR_1NHCH(CO_2R_2)(CH_2)_nR$ ($R = H, \text{ alkyl, aryl, } R_6O, R_6S, R_6 = \text{ alkyl, aryl, etc.}; R_1 = H, \text{ alkyl, aryl, amino acyl, etc.}; R_2, R_3 = H, \text{ alkyl, aryl, etc.}; R_4CHNR_5 = \text{ heterocyclyl}; n = 1, 2$) 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

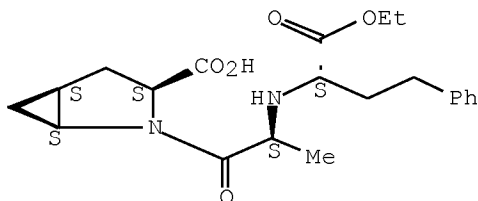
RL: BIOL (Biological study)

(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-[1 α ,2[R*(R*)],3 β ,5 α]]- (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

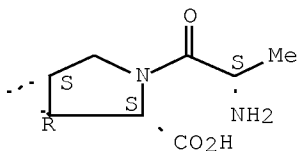
CN 3-Azabicyclo[3.1.0]hexane-2-carboxylic acid, 3-(2-amino-1-oxopropyl)-, [1R-[1 α ,2 β ,3(S*),5 α]]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 101952-31-2

CMF C9 H14 N2 O3

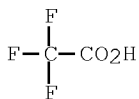
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



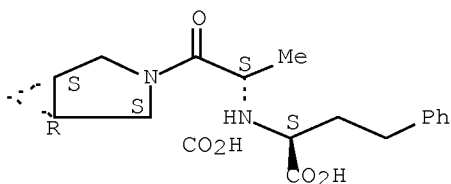
IT 101952-28-7P 101952-30-1P 102044-73-5P
 102044-74-6P 102044-75-7P 102044-76-8P
 102045-14-7P

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-[1 α , 2 β , 3[S*(S*)], 5 α]]- (9CI) (CA INDEX NAME)

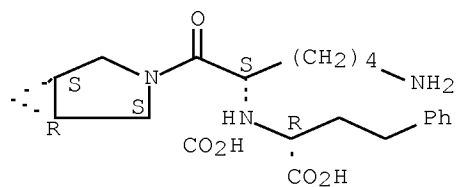
Absolute stereochemistry.



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-[1 α , 2 β , 3[S*(R*)], 5 α]]- (9CI) (CA INDEX NAME)

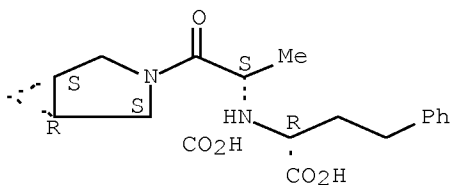
Absolute stereochemistry.



RN 102044-73-5 HCAPLUS

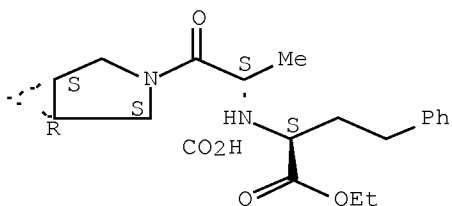
CN 3-Azabicyclo[3.1.0]hexane-2-carboxylic acid,
 3-[2-[(1-carboxy-3-phenylpropyl)amino]-1-oxopropyl]-,
 [1R-[1 α , 2 β , 3[S*(R*)], 5 α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



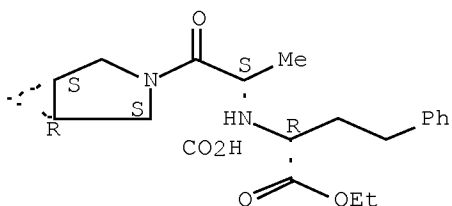
RN 102044-74-6 HCAPLUS
 CN 3-Azabicyclo[3.1.0]hexane-2-carboxylic acid,
 3-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-,
 [1R-[1 α ,2 β ,3[S*(S*)],5 α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

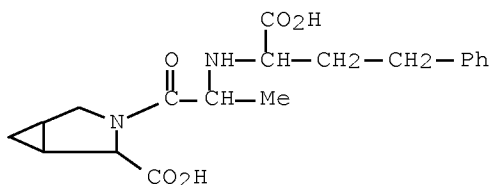


RN 102044-75-7 HCAPLUS
 CN 3-Azabicyclo[3.1.0]hexane-2-carboxylic acid,
 3-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-,
 [1R-[1 α ,2 β ,3[S*(R*)],5 α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

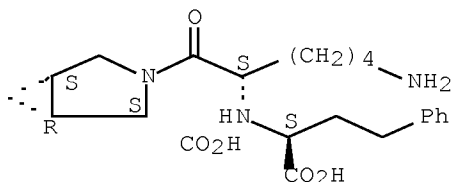


RN 102044-76-8 HCAPLUS
 CN 3-Azabicyclo[3.1.0]hexane-2-carboxylic acid,
 3-[2-[(1-carboxy-3-phenylpropyl)amino]-1-oxopropyl]- (CA INDEX NAME)



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-[1 α ,2 β ,3[S*(S*)],5 α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

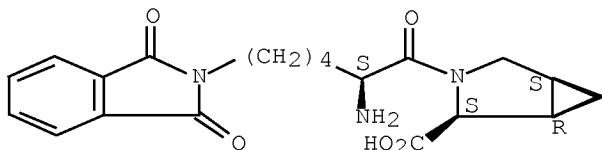


IT 101952-34-5
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (reductive alkylation of, by glyoxylic acid derivative)
 RN 101952-34-5 HCAPLUS
 CN 3-Azabicyclo[3.1.0]hexane-2-carboxylic acid,
 3-[2-amino-6-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)-1-oxohexyl]-,
 [1R-[1 α ,2 β ,3(S*),5 α]]-, mono(trifluoroacetate)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

CM 1

CRN 101952-33-4
 CMF C20 H23 N3 O5

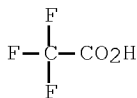
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



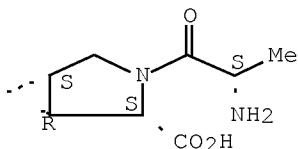
IT 101952-31-2

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-[1 α ,2 β ,3(S*),5 α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

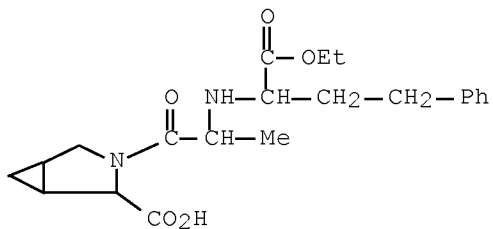


IT 101952-29-8

RL: RCT (Reactant); RACT (Reactant or reagent)
 (saponification of)

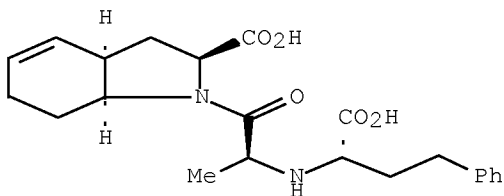
RN 101952-29-8 HCAPLUS

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
 $R(CH_2)_nCH(CO_2R_2)NHCHR_1CONR_5CHR_4CO_2R_3$ [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-carbomethoxy-3-phenylpropyl)-S-alanyl-1S,3S,5S-2-
 azabicyclo[3.3.0]octane-3-carboxylic acid.

IT 99781-97-2

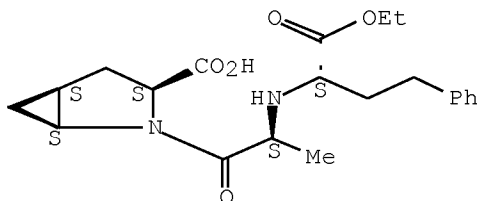
RL: BIOL (Biological study)

(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-[1 α ,2[R*(R*)],3 β ,5 α]]- (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.

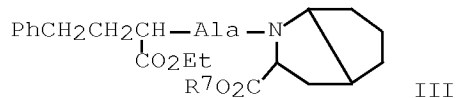
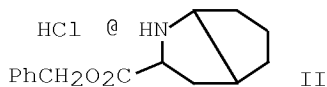
DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| 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

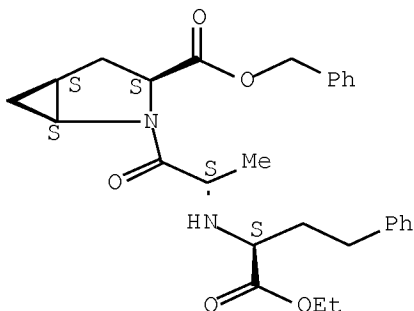


AB Title compds. R3O2CCHR4NR5COCHR1NHCH(CO2R2)(CH2)nR [I; n = 1, 2; R = H, (un)substituted C1-8 aliphatic, C3-9 alicyclic, C6-12 aromatic, C7-14 araliph., or C7-14 alicyclic aliphatic residue, OR6, SR6 [R6 = (un)substituted C1-4 aliphatic, C6-12 aromatic, or heteroarom. residue]; R1 = H, (un)substituted 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-[1 α ,2[R*(R*)],3 β ,5 α]]- (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:

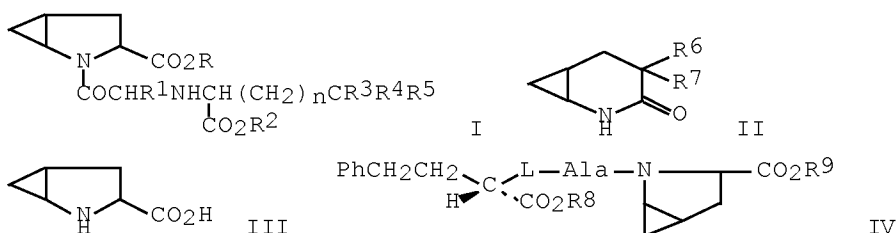
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|-----------------|
| DE 3324263 | A1 | 19850117 | DE 1983-3324263 | 19830706 <-- |
| EP 131226 | A2 | 19850116 | EP 1984-107607 | 19840630 <-- |
| EP 131226 | A3 | 19870826 | | |
| EP 131226 | B1 | 19900530 | | |
| 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

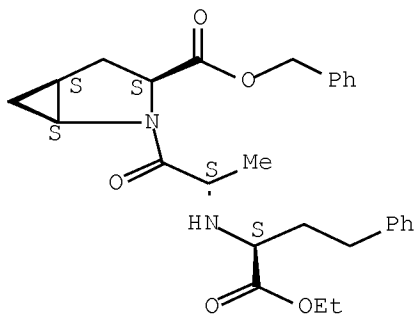
IT 97250-98-1P 97277-17-3P 97277-18-4P
97277-19-5P

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-[1 α ,2[R*(R*)],3 β ,5 α]]- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

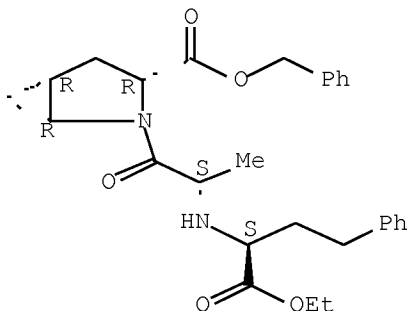


RN 97277-17-3 HCAPLUS

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

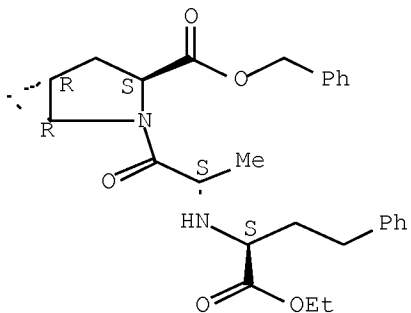
INDEX NAME)

Absolute stereochemistry.



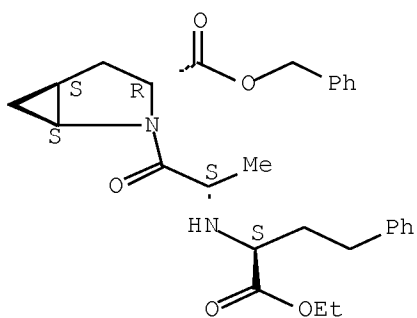
RN 97277-18-4 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carboxylic acid,
 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-,
 phenylmethyl ester, [1R-[1 α ,2[S*(S*)],3 α ,5 α]]- (9CI)
 (CA INDEX NAME)

Absolute stereochemistry.



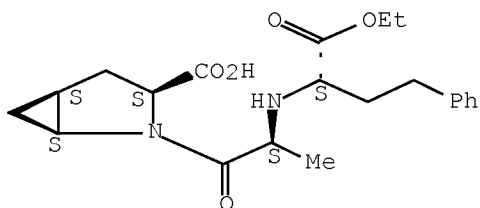
RN 97277-19-5 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carboxylic acid,
 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-,
 phenylmethyl ester, [1S-[1 α ,2[R*(R*)],3 α ,5 α]]- (9CI)
 (CA INDEX NAME)

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-[1 α ,2[R*(R*)],3 β ,5 α]]- (9CI) (CA
 INDEX NAME)

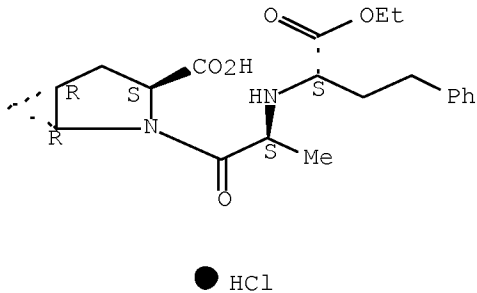
Absolute stereochemistry.



● HCl

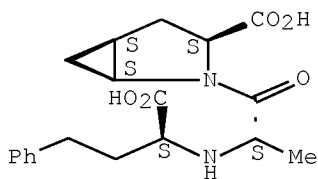
RN 97277-21-9 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carboxylic acid,
 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-,
 monohydrochloride, [1R-[1 α ,2[S*(S*)],3 α ,5 α]]- (9CI) (CA
 INDEX NAME)

Absolute stereochemistry.



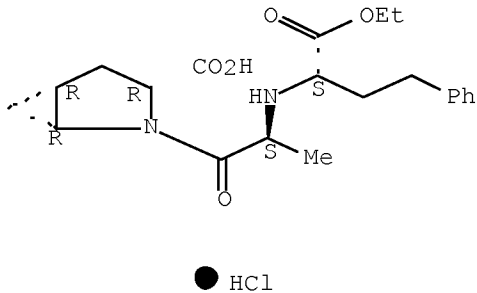
IT 97251-00-8P 97277-20-8P 97277-22-0P
 97334-49-1P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 97251-00-8 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carboxylic acid,
 2-[2-[(1-carboxy-3-phenylpropyl)amino]-1-oxopropyl]-,
 [1S-[1 α ,2[R*(R*)],3 β ,5 α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



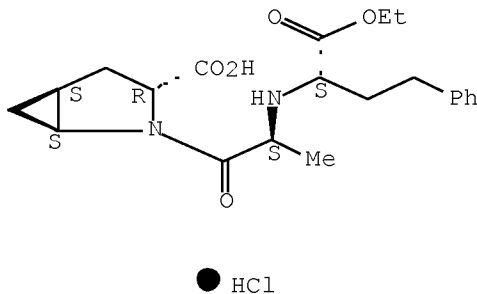
RN 97277-20-8 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carboxylic acid,
 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-,
 monohydrochloride, [1R-[1 α ,2[S*(S*)],3 β ,5 α]]- (9CI) (CA
 INDEX NAME)

Absolute stereochemistry.



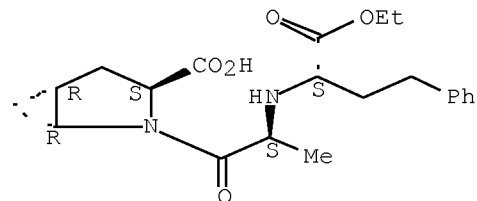
RN 97277-22-0 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carboxylic acid,
 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-,
 monohydrochloride, [1S-[1 α ,2[R*(R*)],3 α ,5 α]]- (9CI) (CA
 INDEX NAME)

Absolute stereochemistry.



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-[1 α ,2[S*(S*)],3 α ,5 α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

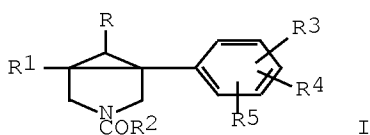


OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD
(7 CITINGS)

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 <-- |
| | | | US 1975-600559 | A1 19750731 <-- |

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



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).

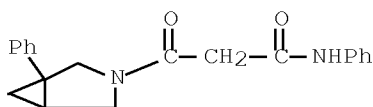
IT 67644-24-0P

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)

=> d que nos 147

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
 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
 L30 QUE SPE=ON ABB=ON PLU=ON BETEBENNER, D?/AU,AUTH,IN
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 L42 1421 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON L23 NOT L41
 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 156

(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 156

L12 STR
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 L17 STR
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 L20 STR
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 L24 QUE SPE=ON ABB=ON PLU=ON ROBL, J?/AU,AUTH,IN
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 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
 L30 QUE SPE=ON ABB=ON PLU=ON BETEBENNER, D?/AU,AUTH,IN
 L39 STR
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 L42 1421 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON L23 NOT L41

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 147 156

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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FILE 'TOXCENTER' ENTERED AT 09:18:09 ON 01 MAY 2012
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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).

=> d ibib ed abs hitstr 1-15

YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, EMBASE' - CONTINUE? (Y)/N:y

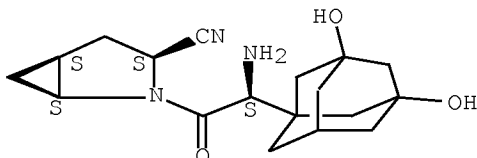
L57 ANSWER 1 OF 16 HCAPLUS COPYRIGHT 2012 ACS on STN DUPLICATE 1
 ACCESSION NUMBER: 2009:672585 HCAPLUS Full-text
 DOCUMENT NUMBER: 151:115551
 TITLE: Pharmacokinetics of the dipeptidyl peptidase 4 inhibitor saxagliptin in rats, dogs, and monkeys and clinical projections
 AUTHOR(S): Fura, Aberra; Khanna, 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 ($\leq 30\%$) 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[3.3.1.1^{3,7}]dec-1-yl)acetyl]-,
(1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



IT 361442-04-8, Saxagliptin

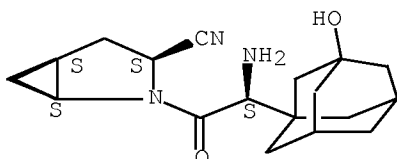
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(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[3.3.1.1^{3,7}]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; Namann, 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 $<1.3 \text{ \AA}$). 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.

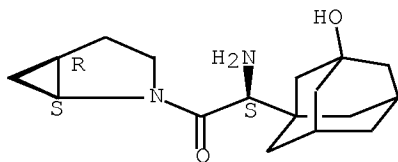
IT 841302-20-3, BMS 538305

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

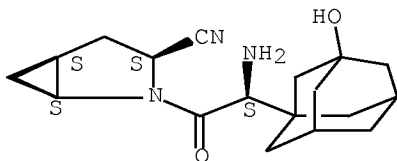
CN Ethanone, 2-amino-1-(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl-2-(3-hydroxytricyclo[3.3.1.1^{3,7}]dec-1-yl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



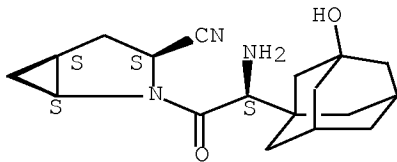
IT 361442-04-8SDP, Saxagliptin, complex with dipeptidyl peptidase IV
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
 PRP (Properties); BIOL (Biological study); PREP (Preparation)
 (involvement of dipeptidyl peptidase-IV catalytic residues in
 enzyme-saxagliptin complex formation)
 RN 361442-04-8 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.1^{3,7}]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[3.3.1.1^{3,7}]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

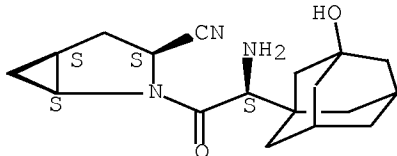
AB The invention provides novel human glucagon-like peptide-1 (GLP-1) receptor modulators Xaa1-Xaa2-Xaa3-Xaa4-Xaa5-Xaa6-Xaa7-Xaa8-Xaa9-Xaa10- Xaa11 [Xaa1-Xaa3, Xaa5-Xaa11 are (certain) naturally or non-naturally occurring amino acid residues; Xaa4 is glycine] that have biol. activity similar or superior to native GLP-1 peptide and thus are useful for the treatment or prevention of diseases or disorders associated with GLP activity. The

comps. include chemical-modified peptides that not only stimulate insulin secretion in type II diabetics, but also produce other beneficial insulintropic 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[3.3.1.1^{3,7}]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, Aiyang; Robl, Jeffrey 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

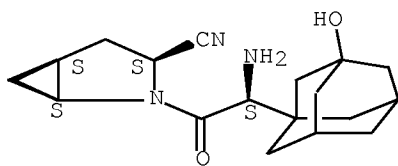
AB The synthesis and structure-activity relationships of novel dipeptidyl
peptidase IV (DDP-IV) inhibitors replacing the classical cyanopyrrolidine
P1 group with other small nitrogen heterocycles are described. A unique
potency enhancement was achieved with β -branched natural and unnatural amino
acids, 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[3.3.1.1^{3,7}]dec-1-yl)acetyl]-,
(1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



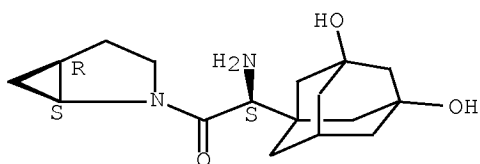
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1000689-37-1P 1000689-38-2P 1000689-39-3P
1000689-40-6P 1000689-41-7P 1000689-43-9P
1000689-44-0P 1000689-45-1P 1000689-46-2P
1000689-47-3P 1000689-48-4P 1000689-49-5P
1000689-50-8P 1000689-52-0P 1000689-53-1P
1000689-54-2P 1000689-55-3P 1000689-56-4P
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[3.3.1.1^{3,7}]dec-1-yl)-, (2S)- (CA INDEX NAME)

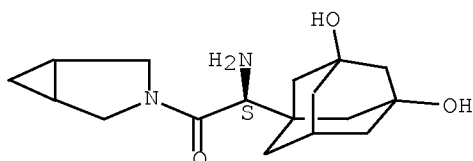
Absolute stereochemistry.



RN 841302-27-0 HCAPLUS

CN Ethanone, 2-amino-1-(3-azabicyclo[3.1.0]hex-3-yl)-2-(3,5-dihydroxytricyclo[3.3.1.1.3,7]dec-1-yl)-, (2S)- (CA INDEX NAME)

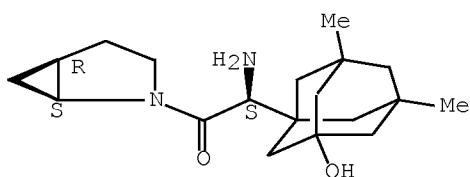
Absolute stereochemistry.



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[3.3.1.1.3,7]dec-1-yl)-, (2S)- (CA INDEX NAME)

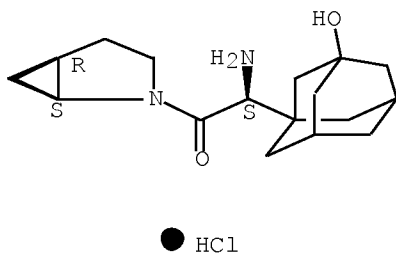
Absolute stereochemistry.



RN 841302-51-0 HCAPLUS

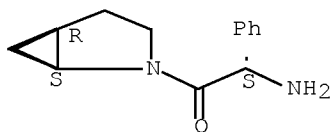
CN Ethanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-2-(3-hydroxytricyclo[3.3.1.1.3,7]dec-1-yl)-, hydrochloride (1:1), (2S)- (CA INDEX NAME)

Absolute stereochemistry.



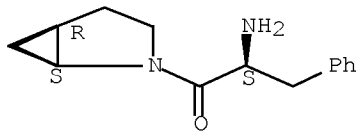
RN 1000689-35-9 HCAPLUS
 CN Ethanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-2-phenyl-,
 (2S)-
 (CA INDEX NAME)

Absolute stereochemistry.



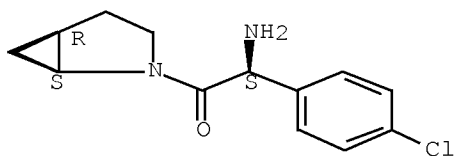
RN 1000689-36-0 HCAPLUS
 CN 1-Propanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-3-phenyl-,
 (2S)- (CA INDEX NAME)

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)

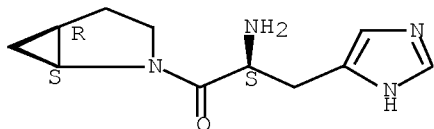
Absolute stereochemistry.



RN 1000689-38-2 HCAPLUS

CN 1-Propanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-3-(4-chlorophenyl)-, (2S)- (CA INDEX NAME)

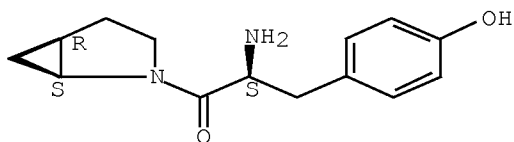
Absolute stereochemistry.



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)

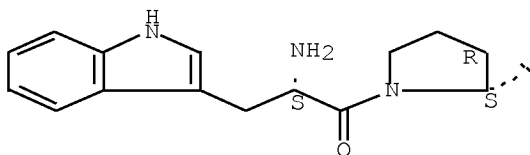
Absolute stereochemistry.



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)

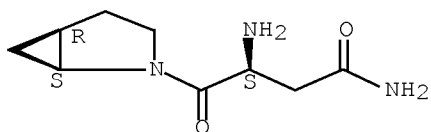
Absolute stereochemistry.



RN 1000689-41-7 HCAPLUS

CN 2-Azabicyclo[3.1.0]hexane-2-butanamide, β -amino- γ -oxo-,
(β S,1S,5R)- (CA INDEX NAME)

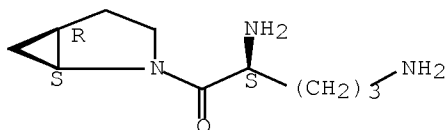
Absolute stereochemistry.



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)

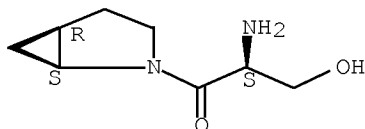
Absolute stereochemistry.



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)

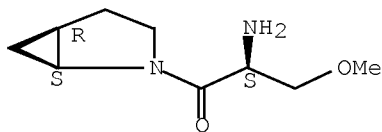
Absolute stereochemistry.



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)

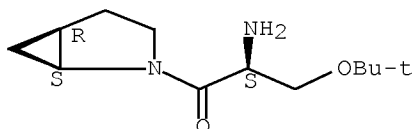
Absolute stereochemistry.



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)

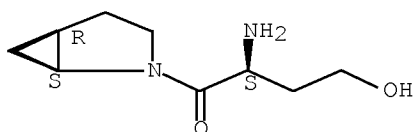
Absolute stereochemistry.



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)

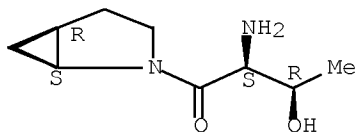
Absolute stereochemistry.



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)

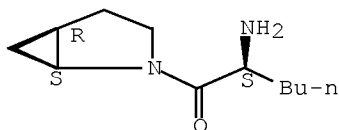
Absolute stereochemistry.



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)

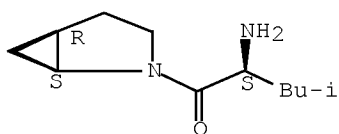
Absolute stereochemistry.



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)

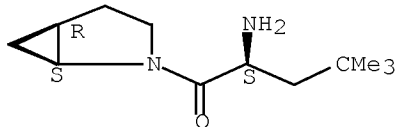
Absolute stereochemistry.



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)

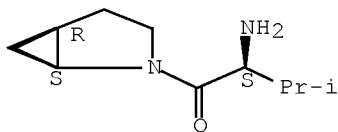
Absolute stereochemistry.



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)

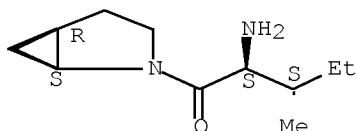
Absolute stereochemistry.



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)

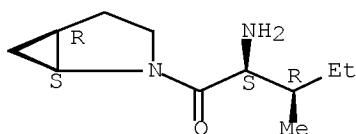
Absolute stereochemistry.



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)

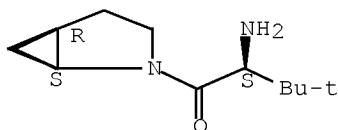
Absolute stereochemistry.



RN 1000689-56-4 HCAPLUS

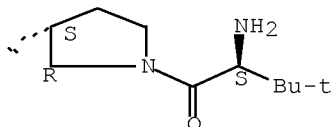
CN 1-Butanone,
2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-3,3-dimethyl-,
(2S)- (CA INDEX NAME)

Absolute stereochemistry.



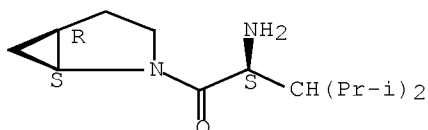
RN 1000689-57-5 HCAPLUS
 CN 1-Butanone,
 2-amino-1-[(1R,5S)-2-azabicyclo[3.1.0]hex-2-yl]-3,3-dimethyl-,
 (2S)- (CA INDEX NAME)

Absolute stereochemistry.



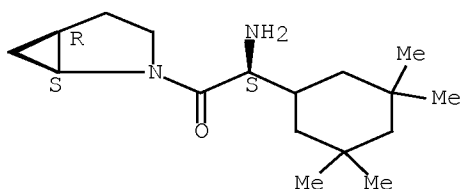
RN 1000689-59-7 HCAPLUS
 CN 1-Pentanone,
 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-4-methyl-3-(1-
 methylethyl)-, (2S)- (CA INDEX NAME)

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)

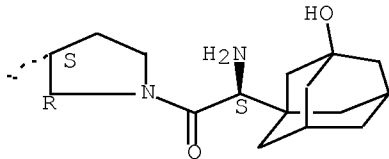
Absolute stereochemistry.



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

hydroxytricyclo[3.3.1.1^{3,7}]dec-1-yl)-, (2S)- (CA INDEX NAME)

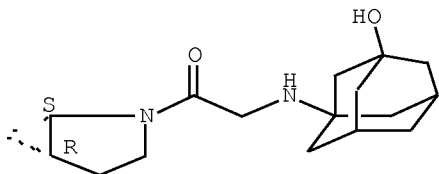
Absolute stereochemistry.



RN 1000689-66-6 HCAPLUS

CN Ethanone, 1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-2-[(3-hydroxytricyclo[3.3.1.1^{3,7}]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.; Ramann, 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 $D_{20}k_{cat}/K_m = 2.9 \pm 0.2$ and a $D_{20}k_{cat} = 1.7 \pm 0.2$ 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 (k_{on}) 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 k_{off} of $(5.5 \pm 0.4) \times 10^{-5} \text{ s}^{-1}$, thus yielding a K^*i (as k_{off}/k_{on}) 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.

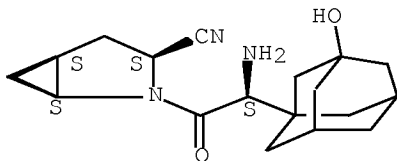
IT 361442-04-8, Saxagliptin

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[3.3.1.1^{3,7}]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

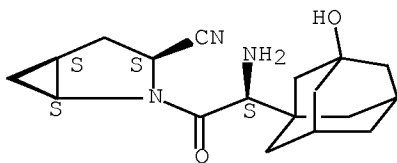
pyridine-based

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[3.3.1.1^{3,7}]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.; Betebanner, David A.; Magnin, David R.; Khanna, Ashish; Robertson, James G.; Wang, Aiyong; 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

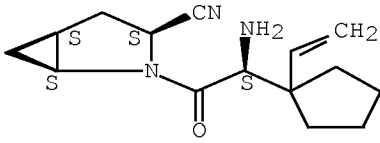
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(1-ethenylcyclopentyl)acetyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361441-53-4

CMF C15 H21 N3 O

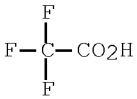
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 361441-75-0 HCAPLUS

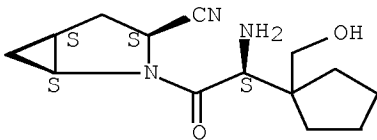
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-[1-(hydroxymethyl)cyclopentyl]acetyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361441-74-9

CMF C14 H21 N3 O2

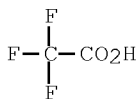
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2

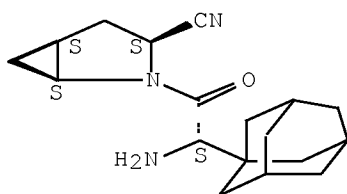


RN 361441-99-8 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-tricyclo[3.3.1.1^{3,7}]dec-1-ylacetyl]-, (1S,3S,5S)-,
 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

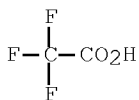
CRN 361441-98-7
 CMF C18 H25 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
 CMF C2 H F3 O2

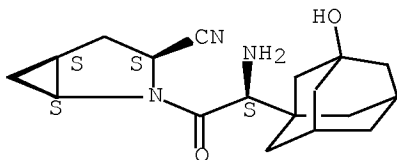


RN 361442-05-9 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.1^{3,7}]dec-1-yl)acetyl]-,
 (1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

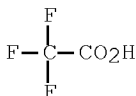
CRN 361442-04-8
 CMF C18 H25 N3 O2

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)

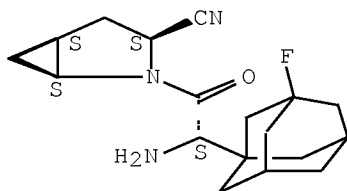
(discovery and preclin. profile of saxagliptin (BMS-477118) as highly potent and long-acting and orally active dipeptidyl peptidase IV inhibitor for treatment of type 2 diabetes)

RN 361442-09-3 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-(3-fluorotricyclo[3.3.1.1^{3,7}]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

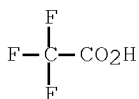
Absolute stereochemistry.



CM 2

CRN 76-05-1

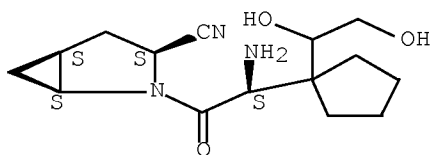
CMF C2 H F3 O2



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

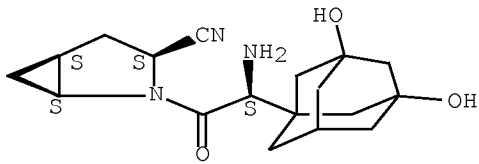
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(3,5-dihydroxytricyclo[3.3.1.1.3,7]dec-1-yl)acetyl]-,
(1S, 3S, 5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 841302-24-7

CMF C18 H25 N3 O3

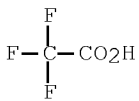
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 862590-85-0 HCAPLUS

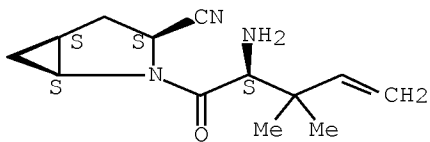
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-3,3-dimethyl-1-oxo-4-penten-1-yl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361441-62-5

CMF C13 H19 N3 O

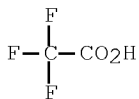
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2

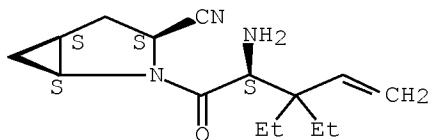


RN 862590-86-1 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-3,3-diethyl-4-methylene-1-oxobutyl]-, (1S,3S,5S)-,
 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

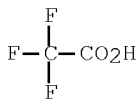
CRN 361441-63-6
 CMF C15 H23 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
 CMF C2 H F3 O2

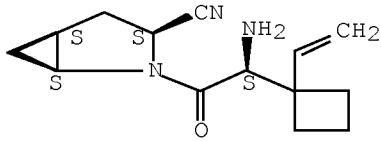


RN 862590-87-2 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-(1-ethenylcyclobutyl)acetyl]-, (1S,3S,5S)-,
 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

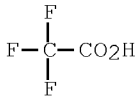
CRN 361441-55-6
 CMF C14 H19 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
 CMF C2 H F3 O2

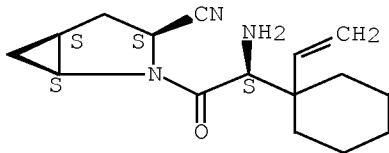


RN 862590-88-3 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-(1-ethenylcyclohexyl)acetyl]-, (1S,3S,5S)-,
 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

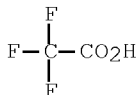
CRN 361441-56-7
 CMF C16 H23 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
 CMF C2 H F3 O2

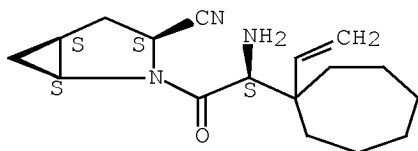


RN 862590-89-4 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-(1-ethenylcycloheptyl)acetyl]-, (1S,3S,5S)-,
 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

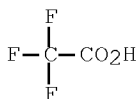
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 CMF C17 H25 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
 CMF C2 H F3 O2



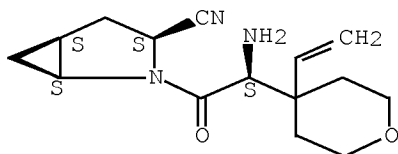
RN 862590-90-7 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-(4-ethenyltetrahydro-2H-pyran-4-yl)acetyl]-,
 (1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361441-60-3

CMF C15 H21 N3 O2

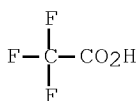
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 862590-91-8 HCAPLUS

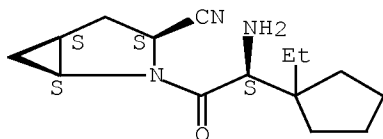
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-(1-ethylcyclopentyl)acetyl]-, (1S,3S,5S)-,
 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361441-85-2

CMF C15 H23 N3 O

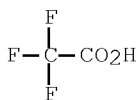
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 862590-93-0 HCAPLUS

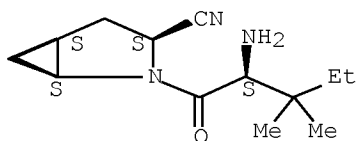
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-3,3-dimethyl-1-oxopentyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361441-90-9

CMF C13 H21 N3 O

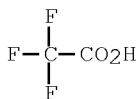
Absolute stereochemistry.



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)-,

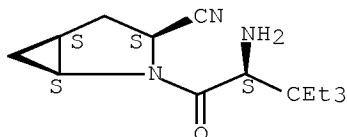
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361441-91-0

CMF C15 H25 N3 O

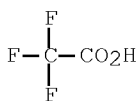
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 862590-95-2 HCAPLUS

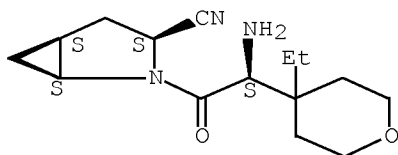
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(4-ethyltetrahydro-2H-pyran-4-yl)acetyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361441-89-6

CMF C15 H23 N3 O2

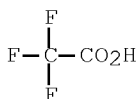
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 862590-96-3 HCAPLUS

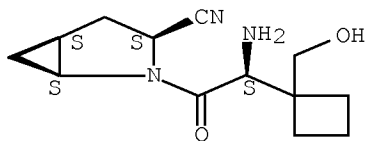
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-[1-(hydroxymethyl)cyclobutyl]acetyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361441-77-2

CMF C13 H19 N3 O2

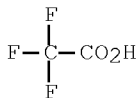
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 862590-97-4 HCAPLUS

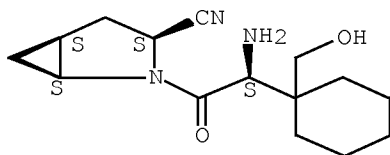
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-[1-(hydroxymethyl)cyclohexyl]acetyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361441-78-3

CMF C15 H23 N3 O2

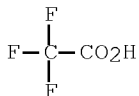
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



IT 361442-04-8, Saxagliptin

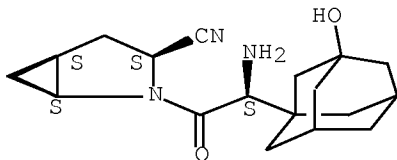
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

(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[3.3.1.1^{3,7}]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 |
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| AU 2001045466 | A | 20010924 | AU 2001-45466 | 20010305 |
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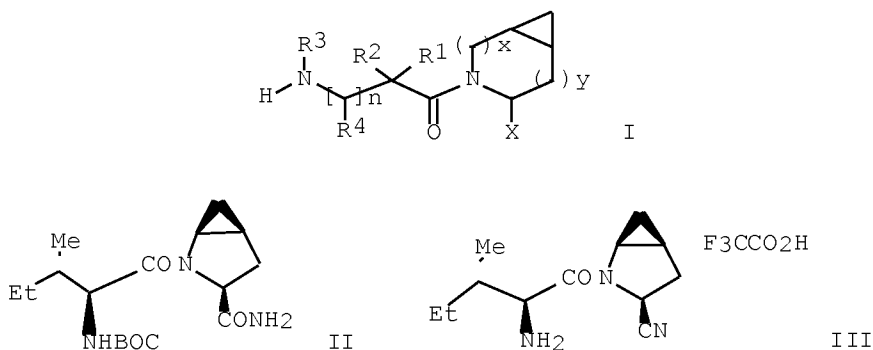
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| HU 2003002792 | A2 | 20031229 | HU 2003-2792 | 20010305 |
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| BR 2001009115 | A | 20031230 | BR 2001-9115 | 20010305 |
| NZ 520821 | A | 20041126 | NZ 2001-520821 | 20010305 |
| AU 2001245466 | B2 | 20050512 | AU 2001-245466 | 20010305 |
| CN 1213028 | C | 20050803 | CN 2001-806315 | 20010305 |
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| 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 |
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| IN 2002MN01154 | A | 20050304 | IN 2002-MN1154 | 20020823 |
| ZA 2002006816 | A | 20031126 | ZA 2002-6816 | 20020826 |
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| NO 324227 | B1 | 20070910 | | |
| KR 754089 | B1 | 20070831 | KR 2002-7011806 | 20020909 |
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| HK 1049330 | A1 | 20081114 | HK 2003-101079 | 20030214 |
| KR 758407 | B1 | 20070914 | KR 2006-7004515 | 20060303 |
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| | | | US 2000-188555P | P 20000310 |
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| | | | 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



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 $y = 1$; $n = 0, 1$; $X = H, CN$; R_1, R_2, R_3 and $R_4 =$ 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)

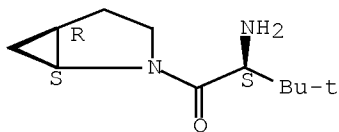
(Preparation of fused cyclopropylpyrrolidine-based inhibitors of dipeptidyl peptidase IV)

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)

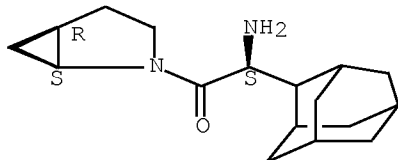
Absolute stereochemistry.



RN 1098535-01-3 HCAPLUS

CN Ethanone, 2-amino-1-(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl-2-tricyclo[3.3.1.1.3,7]dec-2-yl-, (2S)- (CA INDEX NAME)

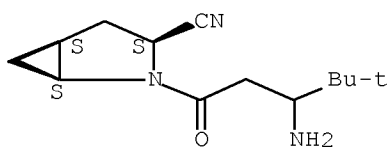
Absolute stereochemistry.



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)

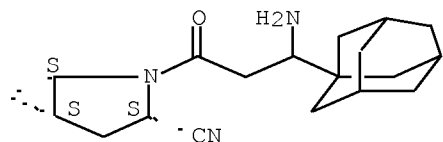
Absolute stereochemistry.



RN 1098535-03-5 HCAPLUS

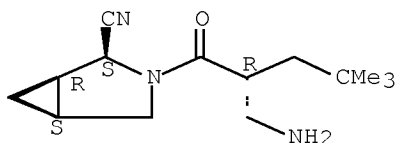
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-(3-amino-1-oxo-3-tricyclo[3.3.1.1.3,7]dec-1-ylpropyl)-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



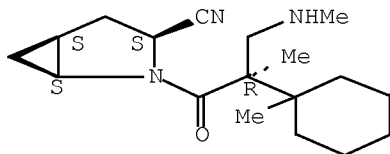
RN 1098535-04-6 HCAPLUS
 CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile,
 3-[(2R)-2-(aminomethyl)-4,4-dimethyl-1-oxopentyl]-, (1R,2S,5S)- (CA
 INDEX
 NAME)

Absolute stereochemistry.



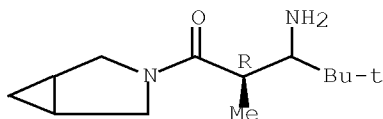
RN 1098535-05-7 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2R)-2-methyl-3-(methylamino)-2-(1-methylcyclohexyl)-1-oxopropyl]-,
 (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



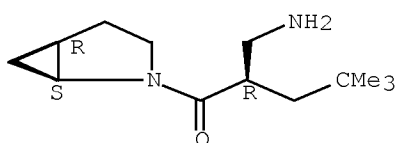
RN 1098535-06-8 HCAPLUS
 CN 1-Pentanone, 3-amino-1-(3-azabicyclo[3.1.0]hex-3-yl)-2,4,4-trimethyl-,
 (2R)- (CA INDEX NAME)

Absolute stereochemistry.



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

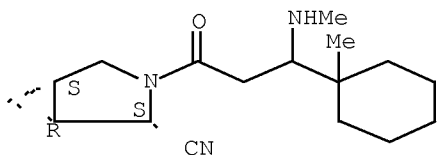
Absolute stereochemistry.



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)

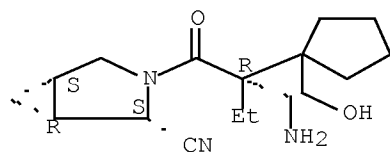
Absolute stereochemistry.



RN 1098535-09-1 HCAPLUS

CN INDEX NAME NOT YET ASSIGNED

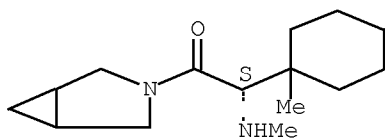
Absolute stereochemistry.



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)

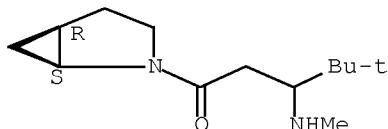
Absolute stereochemistry.



RN 1098535-11-5 HCAPLUS

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

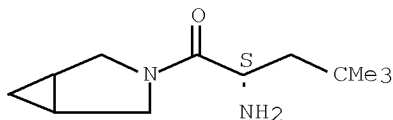
Absolute stereochemistry.



RN 1098535-12-6 HCAPLUS

CN 1-Pentanone, 2-amino-1-(3-azabicyclo[3.1.0]hex-3-yl)-4,4-dimethyl-, (2*S*)- (CA INDEX NAME)

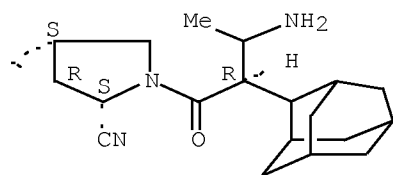
Absolute stereochemistry.



RN 1098535-13-7 HCAPLUS

CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile, 3-[(2*R*)-3-amino-1-oxo-2-tricyclo[3.3.1.1^{3,7}]dec-2-ylbutyl]-, (1*R*,2*S*,5*S*)- (CA INDEX NAME)

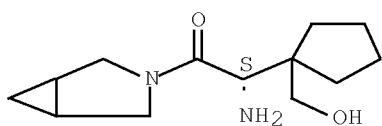
Absolute stereochemistry.



RN 1098535-14-8 HCAPLUS

CN Ethanone, 2-amino-1-(3-azabicyclo[3.1.0]hex-3-yl)-2-[1-(hydroxymethyl)cyclopentyl]-, (2*S*)- (CA INDEX NAME)

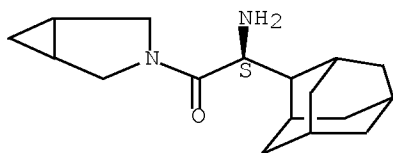
Absolute stereochemistry.



RN 1098535-15-9 HCAPLUS

CN Ethanone, 2-amino-1-(3-azabicyclo[3.1.0]hex-3-yl)-2-tricyclo[3.3.1.1.3,7]dec-2-yl-, (2S)- (CA INDEX NAME)

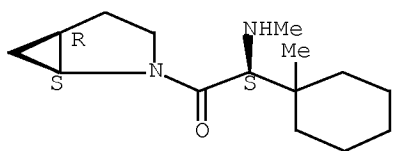
Absolute stereochemistry.



RN 1098535-16-0 HCAPLUS

CN Ethanone, 1-(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl)-2-(1-methylcyclohexyl)-, (2S)- (CA INDEX NAME)

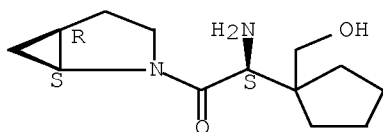
Absolute stereochemistry.



RN 1098535-17-1 HCAPLUS

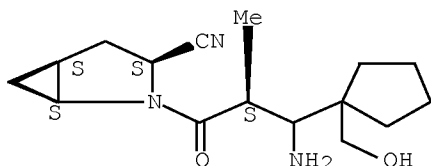
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



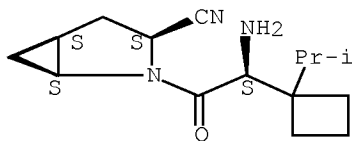
RN 1098535-21-7 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-3-amino-3-[1-(hydroxymethyl)cyclopentyl]-2-methyl-1-oxopropyl]-,
 (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 1098535-23-9 HCAPLUS
 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 |
| | 361440-77-9P | 361440-79-1P | 361440-88-2P |
| | 361440-91-7P | 361440-95-1P | 361440-97-3P |
| | 361440-99-5P | 361441-01-2P | 361441-03-4P |
| | 361441-04-5P | 361441-05-6P | 361441-06-7P |
| | 361441-07-8P | 361441-08-9P | 361441-09-0P |
| | 361441-10-3P | 361441-11-4P | 361441-12-5P |
| | 361441-13-6P | 361441-14-7P | 361441-15-8P |
| | 361441-16-9P | 361441-17-0P | 361441-28-3P |
| | 361441-39-6P | 361441-53-4P | 361441-54-5P |
| | 361441-55-6P | 361441-56-7P | 361441-57-8P |
| | 361441-58-9P | 361441-59-0P | 361441-60-3P |
| | 361441-61-4P | 361441-62-5P | 361441-63-6P |
| | 361441-65-8P | 361441-67-0P | 361441-69-2P |
| | 361441-71-6P | 361441-74-9P | 361441-75-0P |
| | 361441-77-2P | 361441-78-3P | 361441-79-4P |
| | 361441-80-7P | 361441-83-0P | 361441-85-2P |
| | 361441-87-4P | 361441-88-5P | 361441-89-6P |
| | 361441-90-9P | 361441-91-0P | 361441-92-1P |

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 361442-16-2P 361442-18-4P 361442-19-5P
 361442-23-1P 361442-25-3P 361442-30-0P
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 361442-39-9P 361442-40-2P 361442-41-3P
 361442-42-4P 361442-44-6P 361442-48-0P
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 361485-95-2P

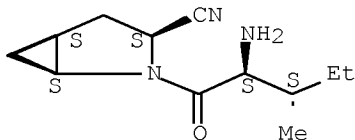
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(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

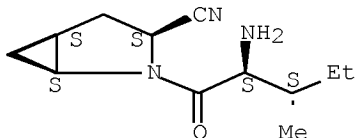
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]-, (1S,3S,5S)-,
 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361440-65-5

CMF C12 H19 N3 O

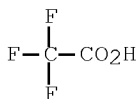
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 361440-73-5 HCAPLUS

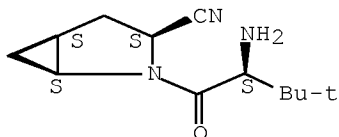
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-3,3-dimethyl-1-oxobutyl]-, (1S,3S,5S)-,
 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361440-72-4

CMF C12 H19 N3 O

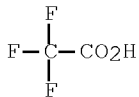
Absolute stereochemistry.



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,

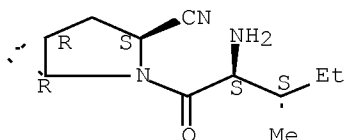
2-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]-, (1R,3S,5R)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361440-76-8

CMF C12 H19 N3 O

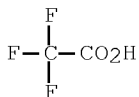
Absolute stereochemistry.



CM 2

CRN 76-05-1

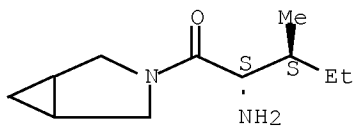
CMF C2 H F3 O2



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.



● HCl

RN 361440-88-2 HCAPLUS

CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile,

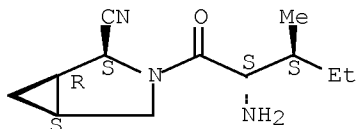
3-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]-, (1R,2S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361440-87-1

CMF C12 H19 N3 O

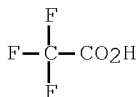
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 361440-91-7 HCAPLUS

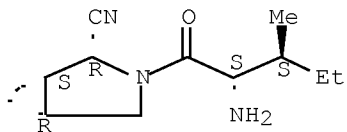
CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile,
3-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]-, (1S,2R,5R)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361440-90-6

CMF C12 H19 N3 O

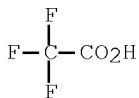
Absolute stereochemistry.



CM 2

CRN 76-05-1

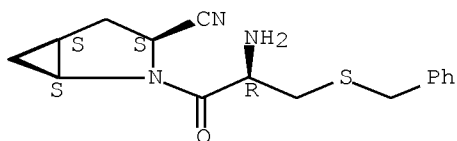
CMF C2 H F3 O2



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)

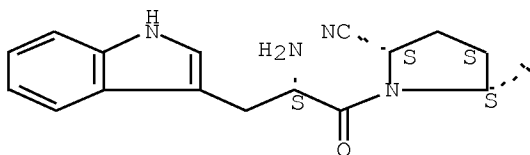
Absolute stereochemistry.



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)

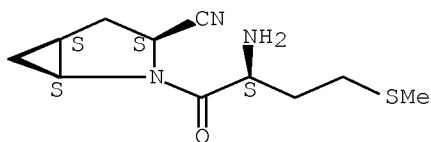
Absolute stereochemistry.



RN 361440-99-5 HCAPLUS

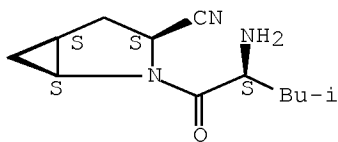
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-4-(methylthio)-1-oxobutyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



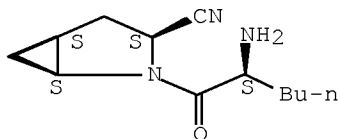
RN 361441-01-2 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-4-methyl-1-oxopentyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



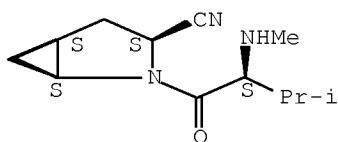
RN 361441-03-4 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-1-oxohexyl]-,
 (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



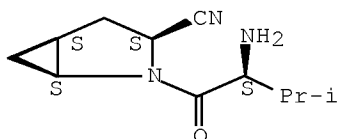
RN 361441-04-5 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-3-methyl-2-(methylamino)-1-oxobutyl]-, (1S,3S,5S)- (CA INDEX
 NAME)

Absolute stereochemistry.



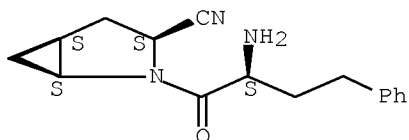
RN 361441-05-6 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-3-methyl-1-oxobutyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



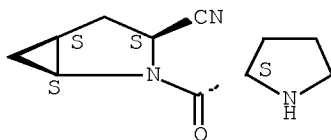
RN 361441-06-7 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-1-oxo-4-phenylbutyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



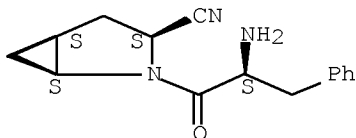
RN 361441-07-8 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-pyrrolidinylcarbonyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



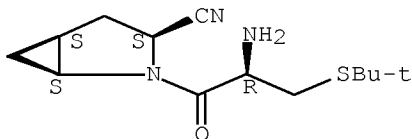
RN 361441-08-9 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-1-oxo-3-phenylpropyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



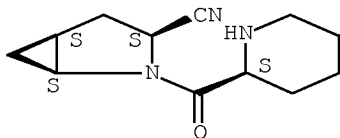
RN 361441-09-0 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2R)-2-amino-3-[(1,1-dimethylethyl)thio]-1-oxopropyl]-, (1S,3S,5S)-
 (CA INDEX NAME)

Absolute stereochemistry.



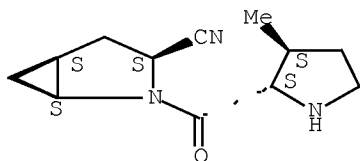
RN 361441-10-3 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-piperidinylcarbonyl]-,
 (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



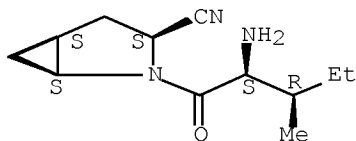
RN 361441-11-4 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[[2-(2S,3S)-3-methyl-2-pyrrolidinyl]carbonyl]-, (1S,3S,5S)- (CA INDEX
 NAME)

Absolute stereochemistry.



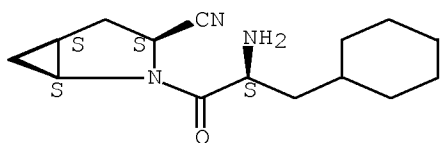
RN 361441-12-5 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S,3R)-2-amino-3-methyl-1-oxopentyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



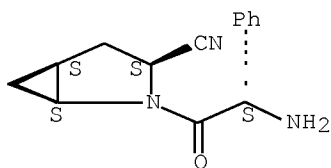
RN 361441-13-6 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-3-cyclohexyl-1-oxopropyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



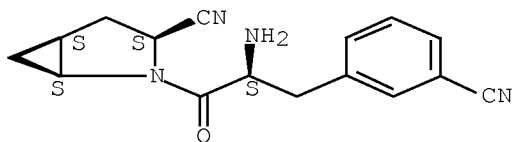
RN 361441-14-7 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-phenylacetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



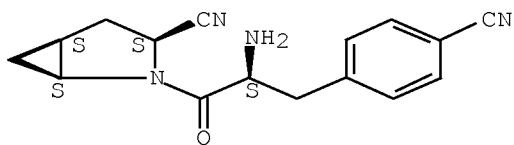
RN 361441-15-8 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-3-(3-cyanophenyl)-1-oxopropyl]-, (1S,3S,5S)- (CA INDEX
 NAME)

Absolute stereochemistry.



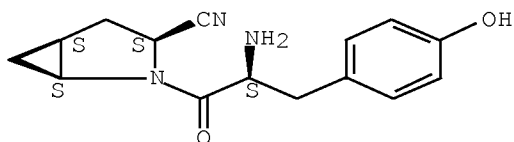
RN 361441-16-9 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-3-(4-cyanophenyl)-1-oxopropyl]-, (1S,3S,5S)- (CA INDEX
 NAME)

Absolute stereochemistry.



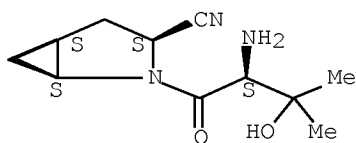
RN 361441-17-0 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-3-(4-hydroxyphenyl)-1-oxopropyl]-, (1S,3S,5S)- (CA INDEX
 NAME)

Absolute stereochemistry.



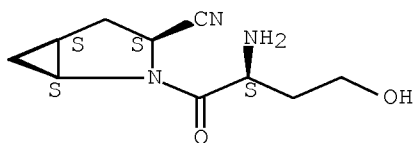
RN 361441-28-3 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-3-hydroxy-3-methyl-1-oxobutyl]-, (1S,3S,5S)- (CA INDEX
 NAME)

Absolute stereochemistry.



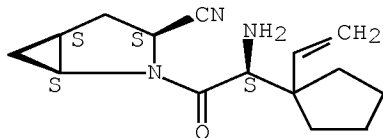
RN 361441-39-6 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-4-hydroxy-1-oxobutyl]-, (1S,3S,5S)- (CA INDEX NAME)

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.

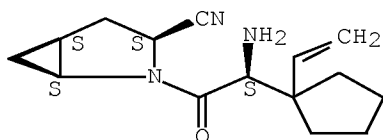


RN 361441-54-5 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-(1-ethenylcyclopentyl)acetyl]-, (1S,3S,5S)-,
 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

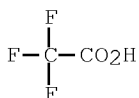
CRN 361441-53-4
 CMF C15 H21 N3 O

Absolute stereochemistry.



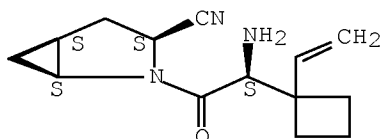
CM 2

CRN 76-05-1
 CMF C2 H F3 O2



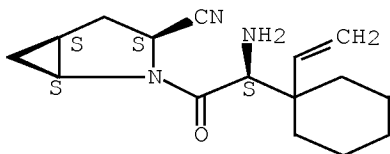
RN 361441-55-6 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-(1-ethenylcyclobutyl)acetyl]-, (1S,3S,5S)- (CA INDEX
 NAME)

Absolute stereochemistry.



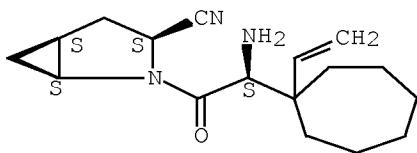
RN 361441-56-7 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-(1-ethenylcyclohexyl)acetyl]-, (1S,3S,5S)- (CA INDEX
 NAME)

Absolute stereochemistry.



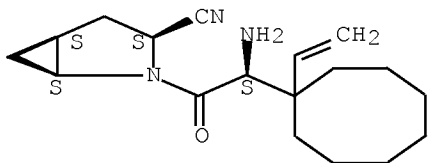
RN 361441-57-8 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-(1-ethenylcycloheptyl)acetyl]-, (1S,3S,5S)- (CA INDEX
 NAME)

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)

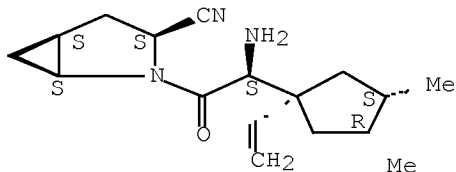
Absolute stereochemistry.



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

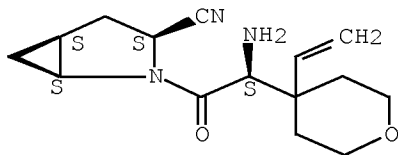
2-[(2S)-2-amino-2-[(3R,4S)-1-ethenyl-3,4-dimethylcyclopentyl]acetyl]-,
(1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



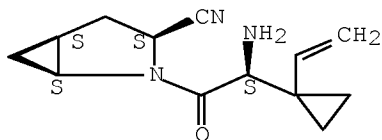
RN 361441-60-3 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(4-ethenyltetrahydro-2H-pyran-4-yl)acetyl]-,
(1S,3S,5S)-
(CA INDEX NAME)

Absolute stereochemistry.



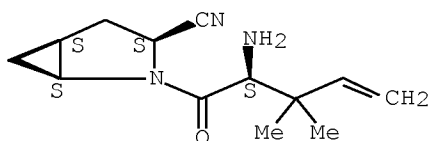
RN 361441-61-4 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(1-ethenylcyclopropyl)acetyl]-, (1S,3S,5S)- (CA INDEX
NAME)

Absolute stereochemistry.



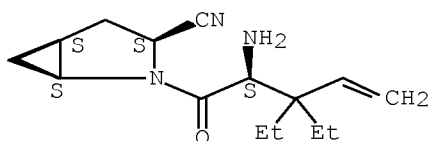
RN 361441-62-5 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-3,3-dimethyl-1-oxo-4-penten-1-yl]-, (1S,3S,5S)- (CA
INDEX
NAME)

Absolute stereochemistry.



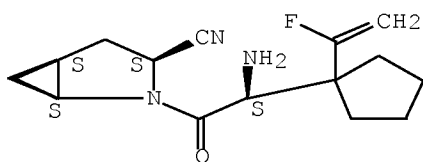
RN 361441-63-6 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-3,3-dimethyl-1-oxo-4-pentenyl]-, (1S,3S,5S)- (9CI) (CA
 INDEX NAME)

Absolute stereochemistry.



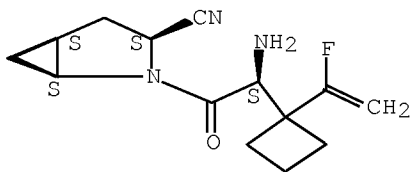
RN 361441-65-8 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-[1-(1-fluoroethenyl)cyclopentyl]acetyl]-, (1S,3S,5S)-
 (CA INDEX NAME)

Absolute stereochemistry.



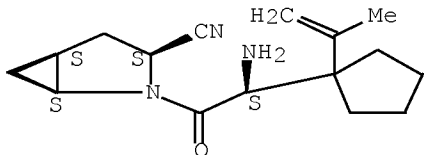
RN 361441-67-0 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-[1-(1-fluoroethenyl)cyclobutyl]acetyl]-, (1S,3S,5S)-
 (CA INDEX NAME)

Absolute stereochemistry.



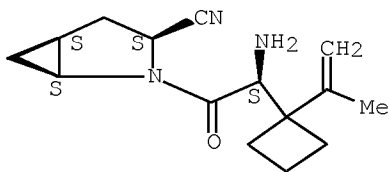
RN 361441-69-2 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-[1-(1-methylethenyl)cyclopentyl]acetyl]-, (1S,3S,5S)-
 (CA INDEX NAME)

Absolute stereochemistry.



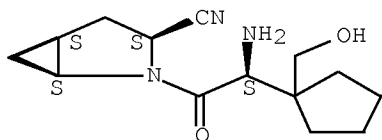
RN 361441-71-6 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-[1-(1-methylethenyl)cyclobutyl]acetyl]-, (1S,3S,5S)-
 (CA INDEX NAME)

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.

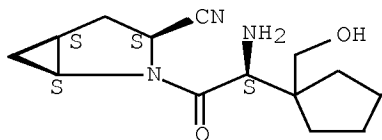


RN 361441-75-0 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-[1-(hydroxymethyl)cyclopentyl]acetyl]-, (1S,3S,5S)-,
 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

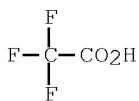
CRN 361441-74-9
 CMF C14 H21 N3 O2

Absolute stereochemistry.



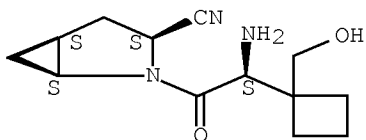
CM 2

CRN 76-05-1
 CMF C2 H F3 O2



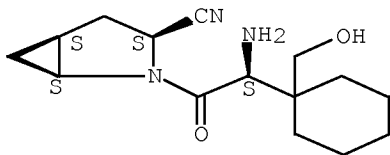
RN 361441-77-2 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-[1-(hydroxymethyl)cyclobutyl]acetyl]-, (1S,3S,5S)- (CA
 INDEX NAME)

Absolute stereochemistry.



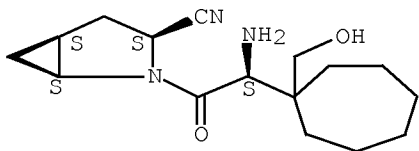
RN 361441-78-3 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-[1-(hydroxymethyl)cyclohexyl]acetyl]-, (1S,3S,5S)- (CA
 INDEX NAME)

Absolute stereochemistry.



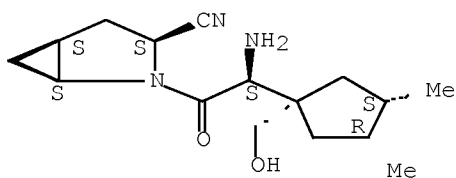
RN 361441-79-4 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-[1-(hydroxymethyl)cycloheptyl]acetyl]-, (1S,3S,5S)-
 (CA
 INDEX NAME)

Absolute stereochemistry.



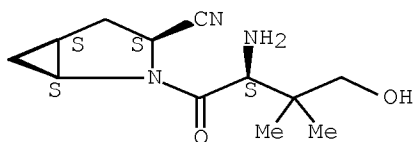
RN 361441-80-7 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-[(3R,4S)-1-(hydroxymethyl)-3,4-
 dimethylcyclopentyl]acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



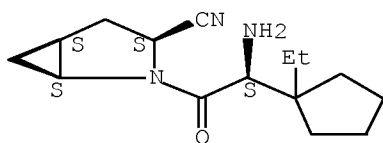
RN 361441-83-0 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-4-hydroxy-3,3-dimethyl-1-oxobutyl]-, (1S,3S,5S)- (CA
 INDEX NAME)

Absolute stereochemistry.



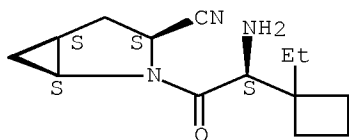
RN 361441-85-2 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-(1-ethylcyclopentyl)acetyl]-, (1S,3S,5S)- (CA INDEX
 NAME)

Absolute stereochemistry.



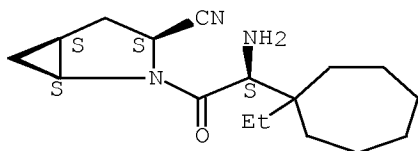
RN 361441-87-4 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-(1-ethylcyclobutyl)acetyl]-, (1S,3S,5S)- (CA INDEX
 NAME)

Absolute stereochemistry.



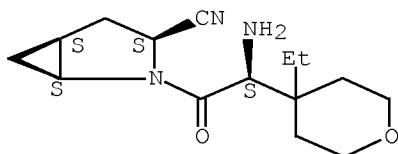
RN 361441-88-5 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-(1-ethylcycloheptyl)acetyl]-, (1S,3S,5S)- (CA INDEX
 NAME)

Absolute stereochemistry.



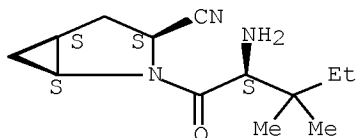
RN 361441-89-6 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-(4-ethyltetrahydro-2H-pyran-4-yl)acetyl]-, (1S,3S,5S)-
 (CA INDEX NAME)

Absolute stereochemistry.



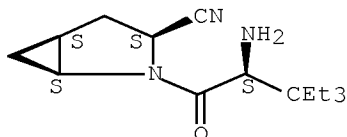
RN 361441-90-9 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-3,3-dimethyl-1-oxopentyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



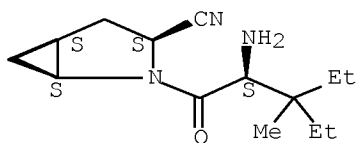
RN 361441-91-0 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-3,3-diethyl-1-oxopentyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



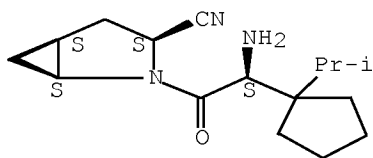
RN 361441-92-1 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-3-ethyl-3-methyl-1-oxopentyl]-, (1S,3S,5S)- (CA INDEX NAME)

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.



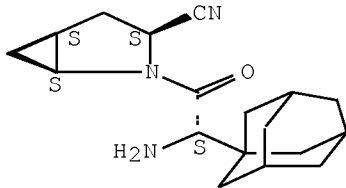
RN 361441-99-8 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,

2-[(2S)-2-amino-2-tricyclo[3.3.1.1^{3,7}]dec-1-ylacetyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

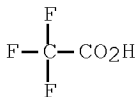
CRN 361441-98-7
CMF C18 H25 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

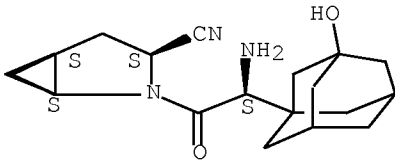


RN 361442-05-9 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.1^{3,7}]dec-1-yl)acetyl]-,
(1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361442-04-8
CMF C18 H25 N3 O2

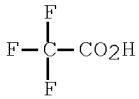
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 361442-09-3 HCAPLUS

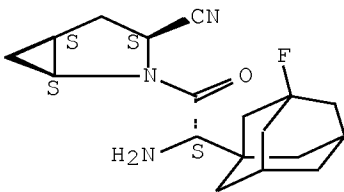
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(3-fluorotricyclo[3.3.1.1.3,7]dec-1-yl)acetyl]-,
(1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361442-08-2

CMF C18 H24 F N3 O

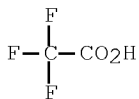
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2

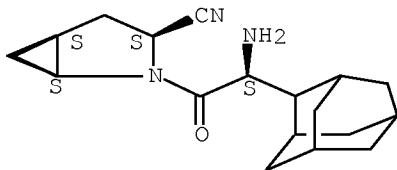


RN 361442-11-7 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-tricyclo[3.3.1.1^{3,7}]dec-2-ylacetyl]-, (1S,3S,5S)-,
 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

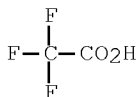
CRN 361442-10-6
 CMF C18 H25 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
 CMF C2 H F3 O2

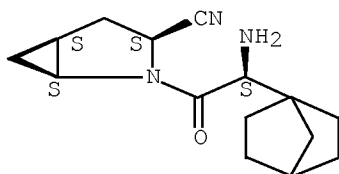


RN 361442-15-1 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-bicyclo[2.2.1]hept-1-ylacetyl]-, (1S,3S,5S)-,
 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

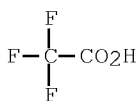
CRN 361442-14-0
 CMF C15 H21 N3 O

Absolute stereochemistry.



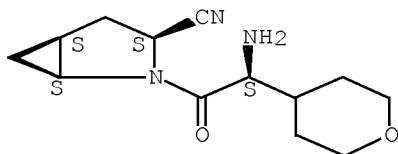
CM 2

CRN 76-05-1
 CMF C2 H F3 O2



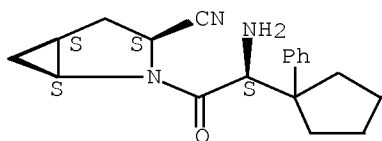
RN 361442-16-2 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-(tetrahydro-2H-pyran-4-yl)acetyl]-, (1S,3S,5S)- (CA
 INDEX NAME)

Absolute stereochemistry.



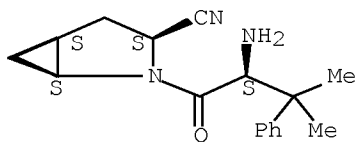
RN 361442-18-4 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-(1-phenylcyclopentyl)acetyl]-, (1S,3S,5S)- (CA INDEX
 NAME)

Absolute stereochemistry.



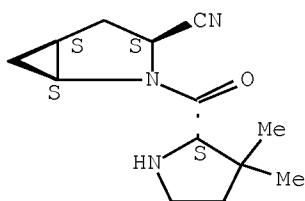
RN 361442-19-5 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-3-methyl-1-oxo-3-phenylbutyl]-, (1S,3S,5S)- (CA INDEX
 NAME)

Absolute stereochemistry.



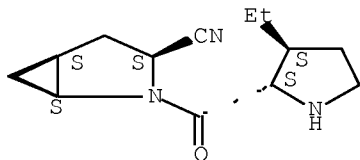
RN 361442-23-1 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[[(2S)-3,3-dimethyl-2-pyrrolidinyl]carbonyl]-, (1S,3S,5S)- (CA INDEX
 NAME)

Absolute stereochemistry.



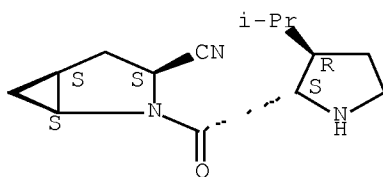
RN 361442-25-3 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[[(2S,3S)-3-ethyl-2-pyrrolidinyl]carbonyl]-, (1S,3S,5S)- (CA INDEX
 NAME)

Absolute stereochemistry.



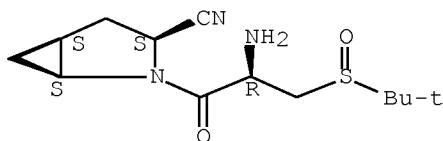
RN 361442-30-0 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[[2-(1-methylethyl)pyrrolidin-2-yl]carbonyl]-, (1S,3S,5S)- (CA
 INDEX NAME)

Absolute stereochemistry.



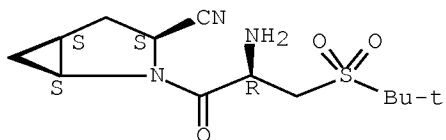
RN 361442-33-3 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2R)-2-amino-3-[(1,1-dimethylethyl)sulfinyl]-1-oxopropyl]-,
 (1S,3S,5S)-
 (CA INDEX NAME)

Absolute stereochemistry.



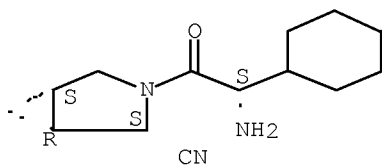
RN 361442-35-5 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2R)-2-amino-3-[(1,1-dimethylethyl)sulfonyl]-1-oxopropyl]-,
 (1S,3S,5S)-
 (CA INDEX NAME)

Absolute stereochemistry.



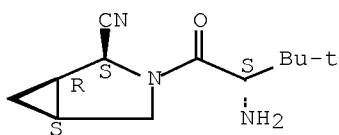
RN 361442-38-8 HCAPLUS
 CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile,
 3-[(2S)-2-amino-2-cyclohexylacetyl]-, (1R,2S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



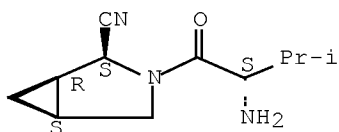
RN 361442-39-9 HCAPLUS
 CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile,
 3-[(2S)-2-amino-3,3-dimethyl-1-oxobutyl]-, (1R,2S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



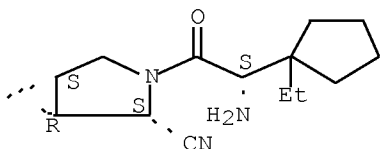
RN 361442-40-2 HCAPLUS
 CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile,
 3-[(2S)-2-amino-3-methyl-1-oxobutyl]-, (1R,2S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



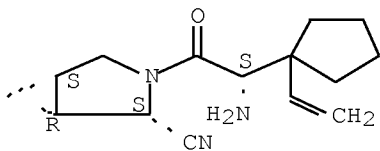
RN 361442-41-3 HCAPLUS
 CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile,
 3-[(2S)-2-amino-2-(1-ethylcyclopentyl)acetyl]-, (1R,2S,5S)- (CA INDEX
 NAME)

Absolute stereochemistry.



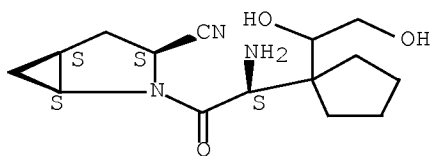
RN 361442-42-4 HCAPLUS
 CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile,
 3-[(2S)-2-amino-2-(1-ethenylcyclopentyl)acetyl]-, (1R,2S,5S)- (CA INDEX
 NAME)

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)

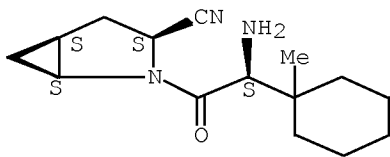
Absolute stereochemistry.



RN 361442-48-0 HCAPLUS
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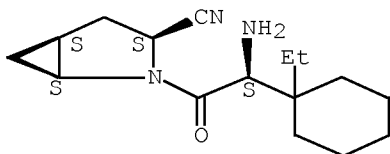
2-[(2S)-2-amino-2-(1-methylcyclohexyl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



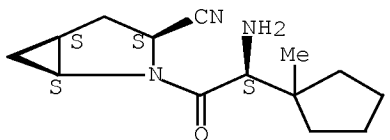
RN 361442-49-1 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-(1-ethylcyclohexyl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



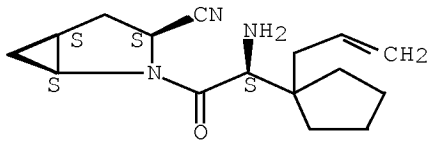
RN 361442-50-4 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-(1-methylcyclopentyl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



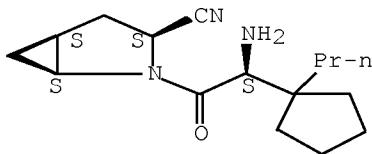
RN 361442-51-5 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-[1-(2-propen-1-yl)cyclopentyl]acetyl]-, (1S,3S,5S)-
 (CA INDEX NAME)

Absolute stereochemistry.



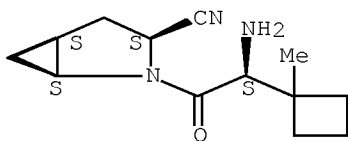
RN 361442-52-6 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-(1-propylcyclopentyl)acetyl]-, (1S,3S,5S)- (CA INDEX
 NAME)

Absolute stereochemistry.



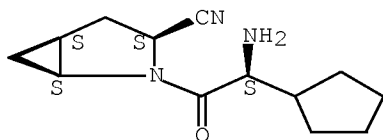
RN 361442-53-7 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-(1-methylcyclobutyl)acetyl]-, (1S,3S,5S)- (CA INDEX
 NAME)

Absolute stereochemistry.



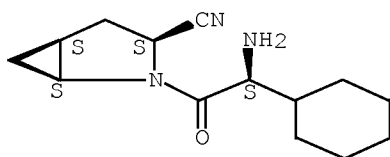
RN 361442-54-8 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-cyclopentylacetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



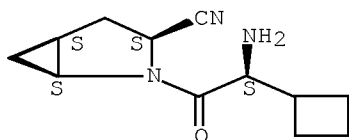
RN 361442-55-9 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-cyclohexylacetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



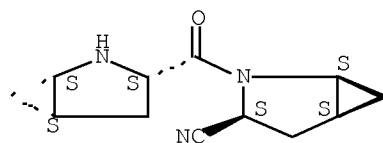
RN 361442-56-0 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-cyclobutylacetyl]-, (1S,3S,5S)- (CA INDEX NAME)

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.

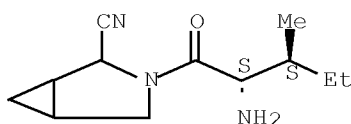


RN 361485-95-2 HCAPLUS
 CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile,
 3-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]-, 2,2,2-trifluoroacetate (1:1)
 (CA INDEX NAME)

CM 1

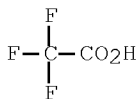
CRN 361485-94-1
 CMF C12 H19 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
 CMF C2 H F3 O2

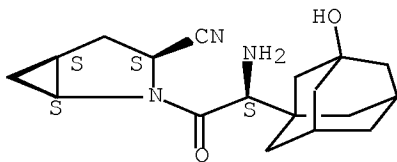


OS.CITING REF COUNT: 36 THERE ARE 36 CAPLUS RECORDS THAT CITE THIS RECORD (61 CITINGS)
 REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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[3.3.1.1^{3,7}]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; Namann, 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

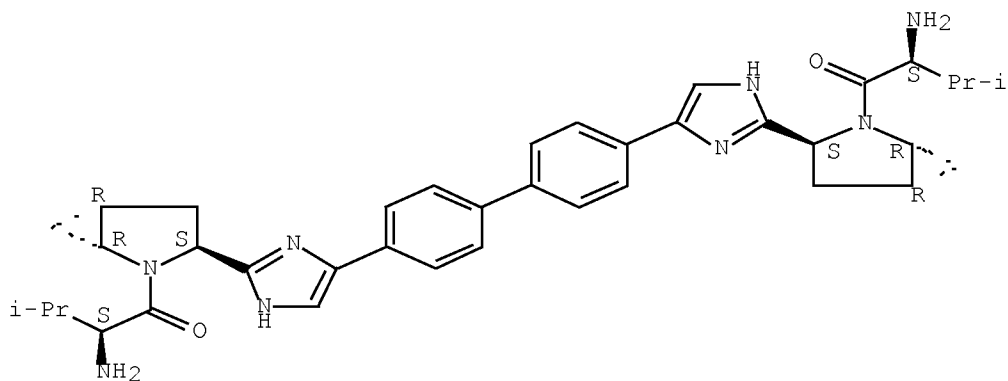
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(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.

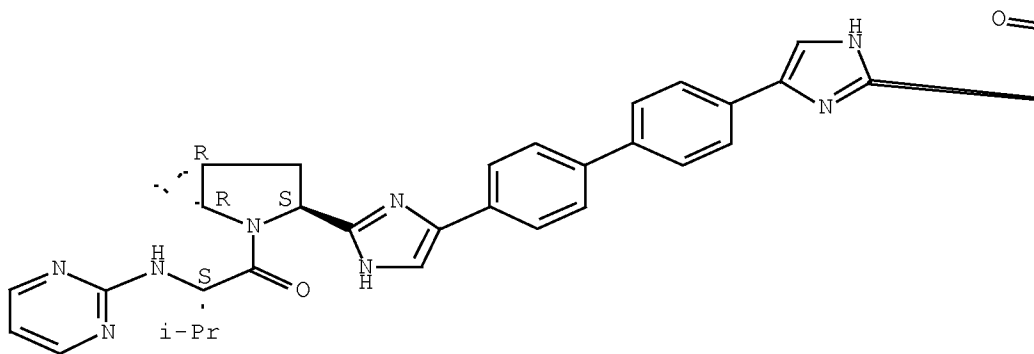


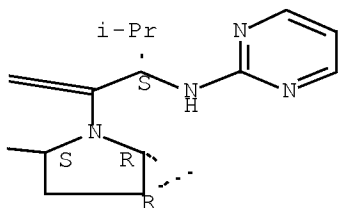
RN 1129634-35-0 HCAPLUS

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



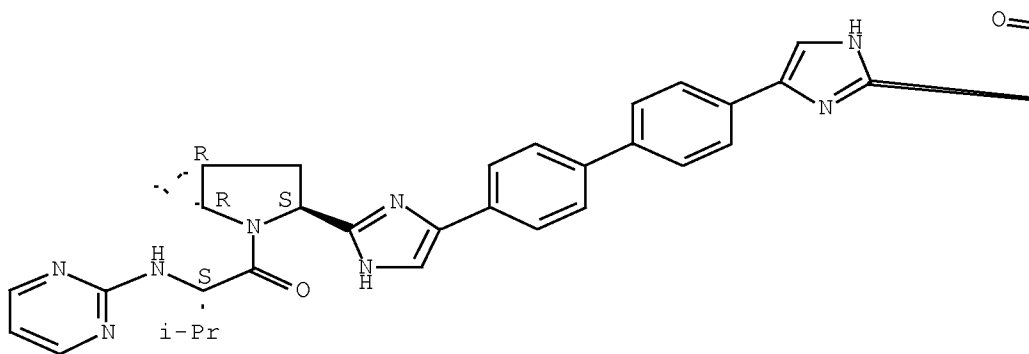


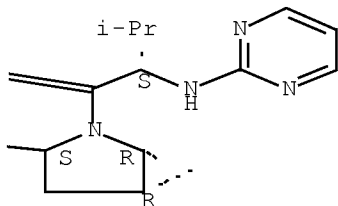
RN 1129634-36-1 HCAPLUS
 CN 1-Butanone, 1,1'-[[[1,1'-biphenyl]-4,4'-diylbis[1H-imidazole-5,2-diyl (1R,3S,5R)-2-azabicyclo[3.1.0]hexane-3,2-diyl]]bis[3-methyl-2-(2-pyrimidinylamino)-, (2S,2'S)-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 1129634-35-0
 CMF C46 H50 N12 O2

Absolute stereochemistry.

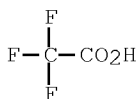




CM 2

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

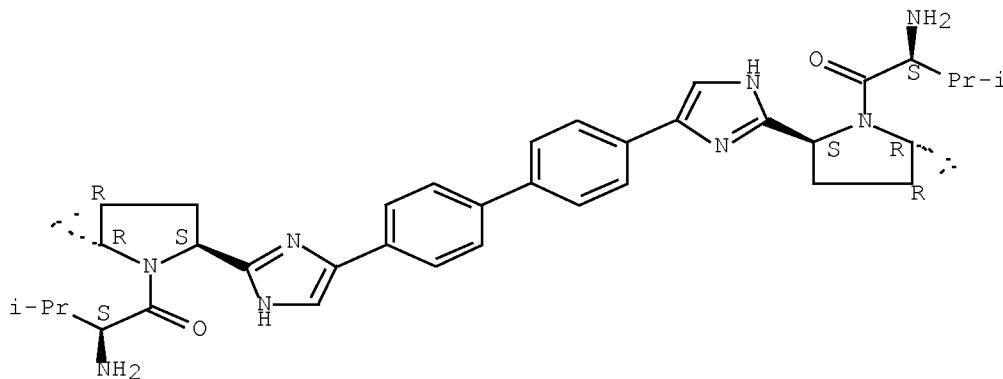
CN 1-Butanone, 1,1'-[[1,1'-biphenyl]-4,4'-diylbis[1H-imidazole-5,2-diyl-(1R,3S,5R)-2-azabicyclo[3.1.0]hexane-3,2-diyl]]bis[2-amino-3-methyl-, (2S,2'S)-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 1129634-15-6

CMF C38 H46 N8 O2

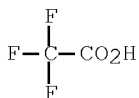
Absolute stereochemistry.



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 |
|------------|------|------|-----------------|------|
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WO 2006014287      A1      20060209      WO 2005-US23076      20050630
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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

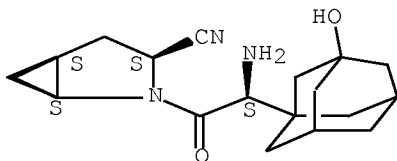
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(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[3.3.1.1^{3,7}]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 adamantylglycinamide 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 | | |

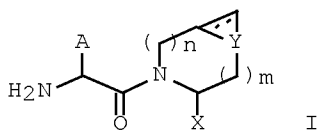
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NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
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 SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
 SN, TD, TG

US 20050038020 A1 20050217 US 2004-899641 20040727
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 EP 1658066 A2 20060524 EP 2004-779352 20040728
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 JP 2007501231 T 20070125 JP 2006-522608 20040728
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 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



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

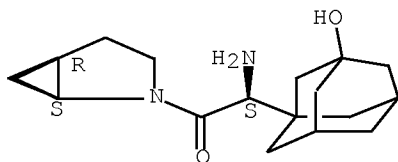
(Uses)

(claimed compound; preparation of adamantylglycinamide 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[3.3.1.1^{3,7}]dec-1-yl)-, (2S)- (CA INDEX NAME)

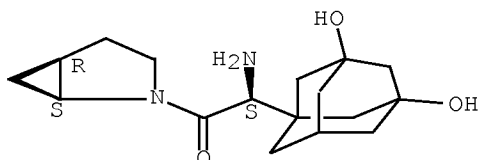
Absolute stereochemistry.



RN 841302-21-4 HCAPLUS

CN Ethanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-2-(3,5-dihydroxytricyclo[3.3.1.1^{3,7}]dec-1-yl)-, (2S)- (CA INDEX NAME)

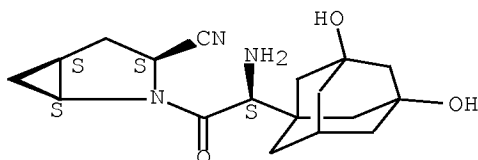
Absolute stereochemistry.



RN 841302-24-7 HCAPLUS

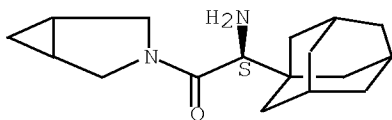
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(3,5-dihydroxytricyclo[3.3.1.1^{3,7}]dec-1-yl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



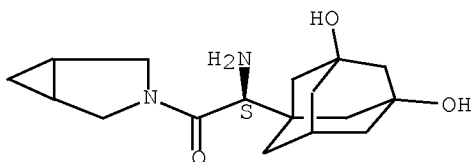
RN 841302-26-9 HCAPLUS
 CN Ethanone, 2-amino-1-(3-azabicyclo[3.1.0]hex-3-yl)-2-
 tricyclo[3.3.1.1^{3,7}]dec-1-yl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



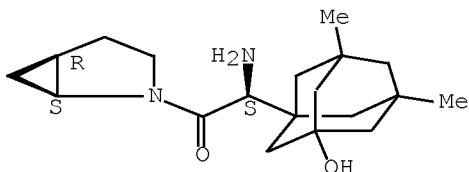
RN 841302-27-0 HCAPLUS
 CN Ethanone, 2-amino-1-(3-azabicyclo[3.1.0]hex-3-yl)-2-(3,5-
 dihydroxytricyclo[3.3.1.1^{3,7}]dec-1-yl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



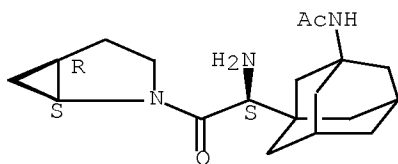
RN 841302-28-1 HCAPLUS
 CN Ethanone,
 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-2-(3-hydroxy-5,7-
 dimethyltricyclo[3.3.1.1^{3,7}]dec-1-yl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



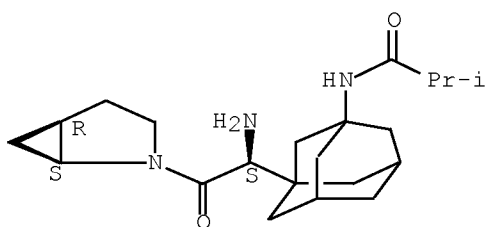
RN 841302-29-2 HCAPLUS
 CN Acetamide, N-[3-[(1S)-1-amino-2-(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-2-
 oxoethyl]tricyclo[3.3.1.1^{3,7}]dec-1-yl]- (CA INDEX NAME)

Absolute stereochemistry.



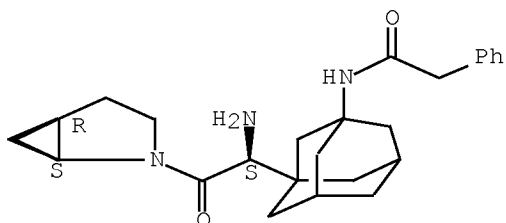
RN 841302-30-5 HCAPLUS
 CN Propanamide, N-[3-[(1S)-1-amino-2-(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-2-oxoethyl]tricyclo[3.3.1.1.3,7]dec-1-yl]-2-methyl- (CA INDEX NAME)

Absolute stereochemistry.



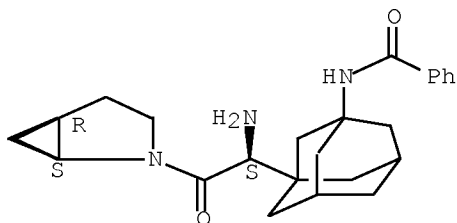
RN 841302-31-6 HCAPLUS
 CN Benzeneacetamide,
 N-[3-[(1S)-1-amino-2-(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-2-oxoethyl]tricyclo[3.3.1.1.3,7]dec-1-yl]- (CA INDEX NAME)

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[3.3.1.1.3,7]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)

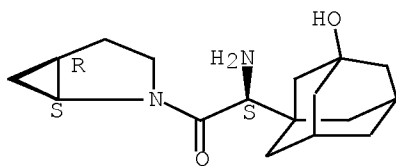
(preparation of adamantylglycinamide inhibitors of dipeptidyl peptidase

IV)

RN 841302-51-0 HCAPLUS

CN Ethanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-2-(3-hydroxytricyclo[3.3.1.1.3,7]dec-1-yl)-, hydrochloride (1:1), (2S)- (CA INDEX NAME)

Absolute stereochemistry.

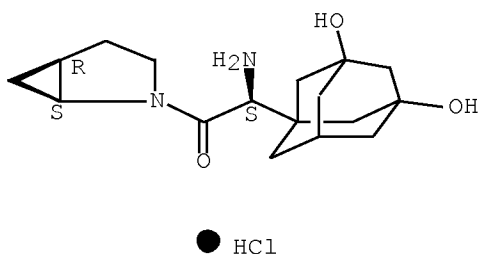


● HCl

RN 841302-52-1 HCAPLUS

CN Ethanone, 2-amino-1-(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl-2-(3,5-dihydroxytricyclo[3.3.1.1.3,7]dec-1-yl)-, hydrochloride (1:1), (2S)- (CA INDEX NAME)

Absolute stereochemistry.

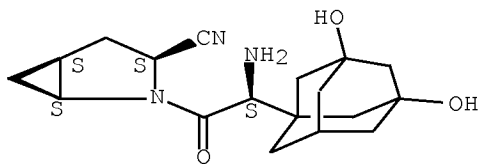


RN 841302-57-6 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-(3,5-dihydroxytricyclo[3.3.1.1.3,7]dec-1-yl)acetyl]-,
 (1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

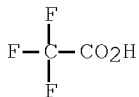
CRN 841302-24-7
 CMF C18 H25 N3 O3

Absolute stereochemistry.



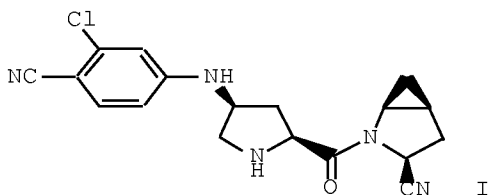
CM 2

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, Aiyang; 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
 GI



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 K_i of 3.6 nM.

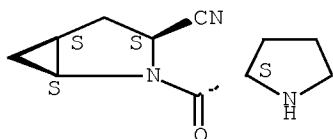
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 866321-23-5P 866321-26-8P 866321-46-2P
 866321-48-4P 866321-50-8P 866321-52-0P
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(diprolyl nitriles as potent dipeptidyl peptidase IV inhibitors)

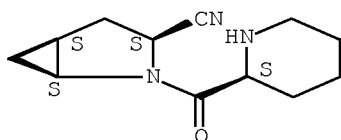
RN 361441-07-8 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-pyrrolidinylcarbonyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



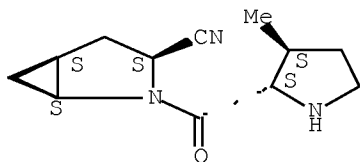
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 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
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Absolute stereochemistry.



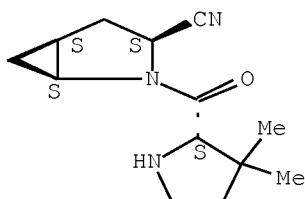
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 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[[2-(2S,3S)-3-methyl-2-pyrrolidinyl]carbonyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



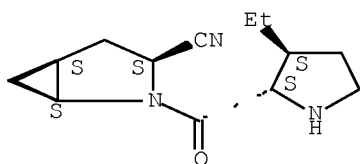
RN 361442-23-1 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[[2-(2S)-3,3-dimethyl-2-pyrrolidinyl]carbonyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



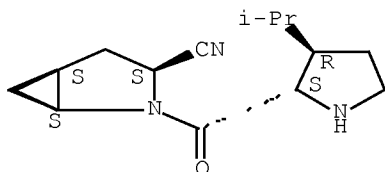
RN 361442-25-3 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[[2S,3S]-3-ethyl-2-pyrrolidinyl]carbonyl]-, (1S,3S,5S)- (CA INDEX
 NAME)

Absolute stereochemistry.



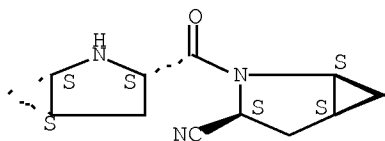
RN 361442-30-0 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[[2S,3R]-3-(1-methylethyl)-2-pyrrolidinyl]carbonyl]-, (1S,3S,5S)- (CA
 INDEX NAME)

Absolute stereochemistry.



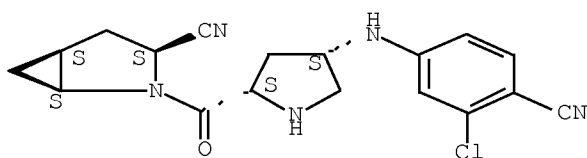
RN 361442-58-2 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(1S,3S,5S)-2-azabicyclo[3.1.0]hex-3-yl]carbonyl]-, (1S,3S,5S)- (CA
 INDEX NAME)

Absolute stereochemistry.



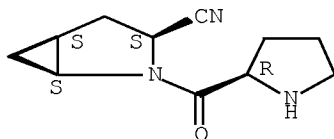
RN 866321-06-4 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[[2-(2S,4S)-4-[(3-chloro-4-cyanophenyl)amino]-2-pyrrolidinyl]carbonyl]-,
 (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



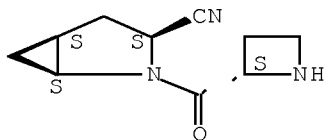
RN 866321-19-9 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2R)-2-pyrrolidinylcarbonyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



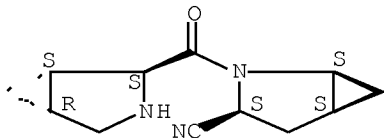
RN 866321-23-5 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-azetidiny carbonyl]-,
 (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



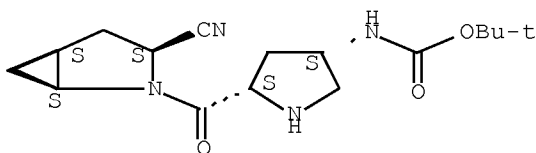
RN 866321-26-8 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(1S,2S,5R)-3-azabicyclo[3.1.0]hex-2-ylcarbonyl]-, (1S,3S,5S)- (CA
 INDEX NAME)

Absolute stereochemistry.



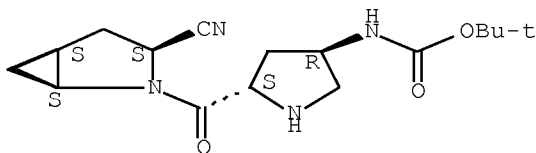
RN 866321-46-2 HCAPLUS
 CN Carbamic acid, [(3S,5S)-5-[[[(1S,3S,5S)-3-cyano-2-azabicyclo[3.1.0]hex-2-yl]carbonyl]-3-pyrrolidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX
 NAME)

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)

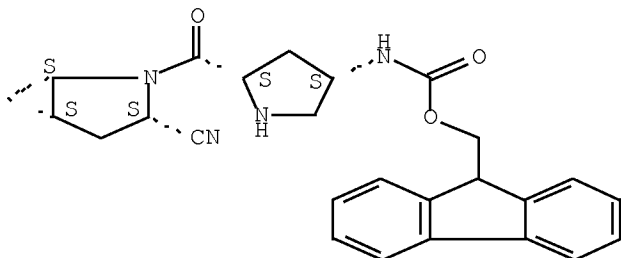
Absolute stereochemistry.



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)

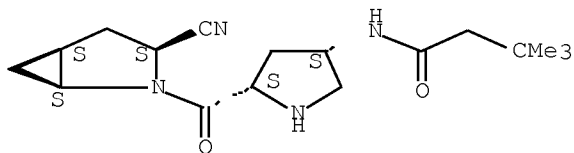
Absolute stereochemistry.



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)

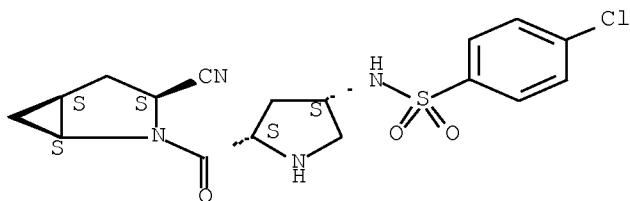
Absolute stereochemistry.



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 |

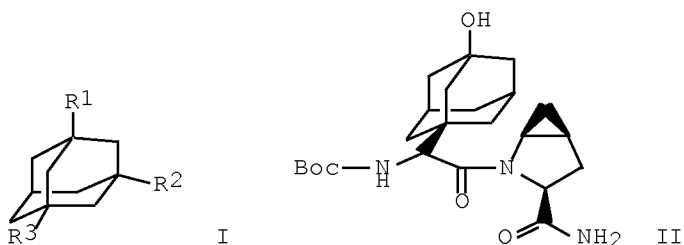
| | | | | |
|------------------------|---|----------|------------------|-------------|
| JP 2011006440 | A | 20110113 | JP 2010-181557 | 20100816 |
| JP 2011006441 | A | 20110113 | JP 2010-181559 | 20100816 |
| PRIORITY APPLN. INFO.: | | | US 2002-431814P | P 20021209 |
| | | | US 2003-716012 | A3 20031118 |
| | | | 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



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 glycine 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

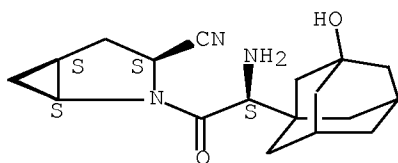
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(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[3.3.1.1^{3,7}]dec-1-yl)acetyl]-,
(1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.

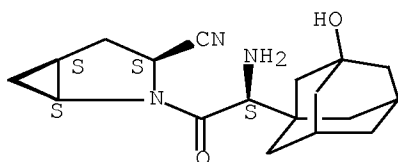


RN 709031-44-7 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-amino(3-hydroxytricyclo[3.3.1.1.3,7]dec-1-yl)acetyl]-,
 (1S,3S,5S)-,
 monobenzoate (salt) (9CI) (CA INDEX NAME)

CM 1

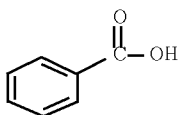
CRN 361442-04-8
 CMF C18 H25 N3 O2

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)

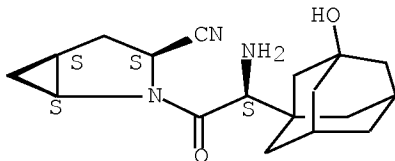
(preparation of cyclopropyl-fused pyrrolidine-based inhibitors of dipeptidyl

peptidase IV)

RN 709031-78-7 HCAPLUS

CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.1^{3,7}]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-methanoproline nitrile-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, Aiyong; 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 Pharmaceuticals, 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

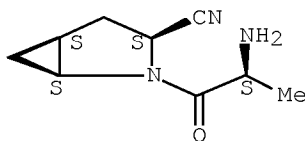
RL: PRP (Properties)

(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

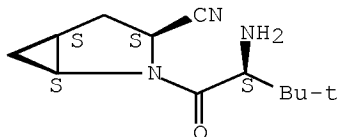
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-3,3-dimethyl-1-oxobutyl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361440-72-4

CMF C12 H19 N3 O

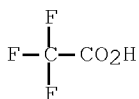
Absolute stereochemistry.



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

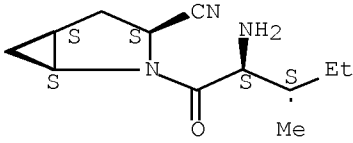
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]-, (1S,3S,5S)-,
 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361440-65-5

CMF C12 H19 N3 O

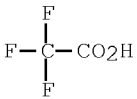
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 361440-77-9 HCAPLUS

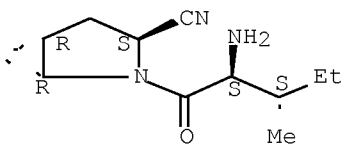
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]-, (1R,3S,5R)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361440-76-8

CMF C12 H19 N3 O

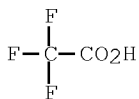
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2

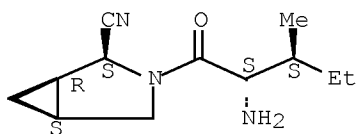


RN 361440-88-2 HCAPLUS
 CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile,
 3-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]-, (1R,2S,5S)-,
 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

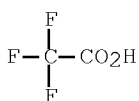
CRN 361440-87-1
 CMF C12 H19 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
 CMF C2 H F3 O2

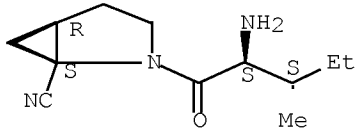


RN 700376-66-5 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-1-carbonitrile,
 2-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]-, (1S,5R)-,
 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 700376-65-4
 CMF C12 H19 N3 O

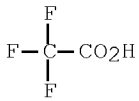
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 700376-67-6 HCAPLUS

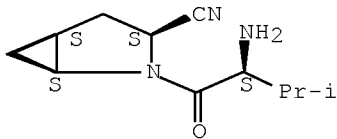
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-3-methyl-1-oxobutyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate
(1:1) (CA INDEX NAME)

CM 1

CRN 361441-05-6

CMF C11 H17 N3 O

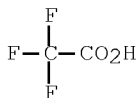
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2

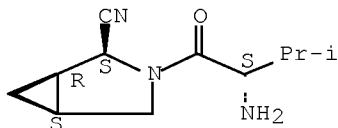


RN 700376-68-7 HCAPLUS
 CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile,
 3-[(2S)-2-amino-3-methyl-1-oxobutyl]-, (1R,2S,5S)-,
 2,2,2-trifluoroacetate
 (1:1) (CA INDEX NAME)

CM 1

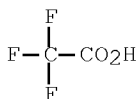
CRN 361442-40-2
 CMF C11 H17 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
 CMF C2 H F3 O2

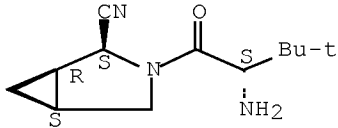


RN 700376-70-1 HCAPLUS
 CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile,
 3-[(2S)-2-amino-3,3-dimethyl-1-oxobutyl]-, (1R,2S,5S)-,
 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

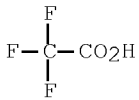
CM 1

CRN 361442-39-9
CMF C12 H19 N3 O

Absolute stereochemistry.



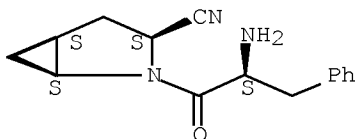
CM 2

CRN 76-05-1
CMF C2 H F3 O2RN 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

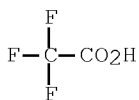
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 700376-72-3 HCAPLUS

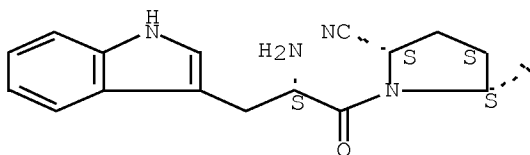
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-3-(1H-indol-3-yl)-1-oxopropyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361440-97-3

CMF C17 H18 N4 O

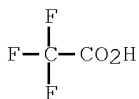
Absolute stereochemistry.



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)-,

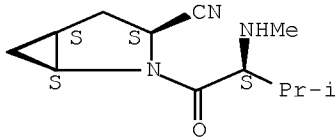
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361441-04-5

CMF C12 H19 N3 O

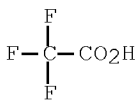
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 700376-74-5 HCAPLUS

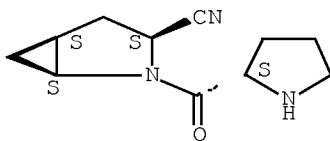
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-pyrrolidinylcarbonyl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate
(1:1) (CA INDEX NAME)

CM 1

CRN 361441-07-8

CMF C11 H15 N3 O

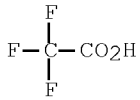
Absolute stereochemistry.



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]-,

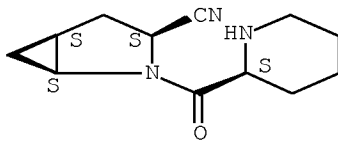
(1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361441-10-3

CMF C12 H17 N3 O

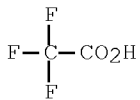
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 700376-76-7 HCAPLUS

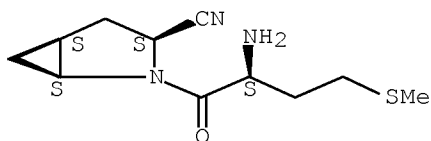
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-4-(methylthio)-1-oxobutyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361440-99-5

CMF C11 H17 N3 O S

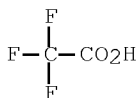
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 700376-77-8 HCAPLUS

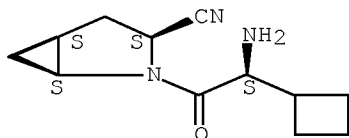
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-cyclobutylacetyl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate
(1:1) (CA INDEX NAME)

CM 1

CRN 361442-56-0

CMF C12 H17 N3 O

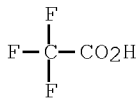
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 700376-78-9 HCAPLUS

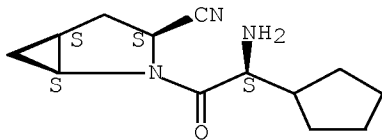
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-cyclopentylacetyl]-, (1S,3S,5S)-,
 2,2,2-trifluoroacetate
 (1:1) (CA INDEX NAME)

CM 1

CRN 361442-54-8

CMF C13 H19 N3 O

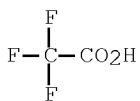
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2

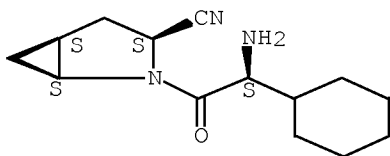


RN 700376-79-0 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-cyclohexylacetyl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate
 (1:1) (CA INDEX NAME)

CM 1

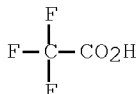
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Absolute stereochemistry.



CM 2

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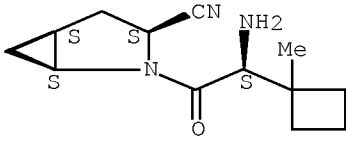


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 2-[(2S)-2-amino-2-(1-methylcyclobutyl)acetyl]-, (1S,3S,5S)-,
 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361442-53-7
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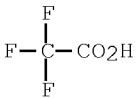
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CMF C2 H F3 O2



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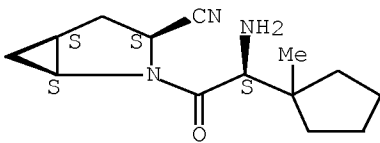
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
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2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361442-50-4

CMF C14 H21 N3 O

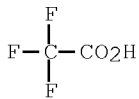
Absolute stereochemistry.



CM 2

CRN 76-05-1

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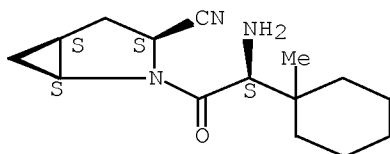


RN 700376-82-5 HCAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-(1-methylcyclohexyl)acetyl]-, (1S,3S,5S)-,
 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

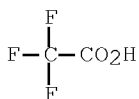
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 CMF C15 H23 N3 O

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, Aiyang; 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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SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 24 Aug 2010
Last Updated on STN: 24 Jan 2011

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Last Updated on STN: 24 Jan 2011

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
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 (vildagliptin) 274901-16-5

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 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

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

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

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

D IBIB ED ABS IND 16

FILE 'STNGUIDE' ENTERED AT 09:19:33 ON 01 MAY 2012
CHARGED TO COST=TC1600

FILE 'STNGUIDE' ENTERED AT 09:19:55 ON 01 MAY 2012
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FILE LAST UPDATED: 30 Apr 2012 (20120430/ED)
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USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2011

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

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FILE LREGISTRY

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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 Library 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.

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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.

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FILE NAPRALERT

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

FILE COVERS 1650 TO 2011

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Beginning in March 2012

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Fields on STN

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Classifications, Current U.S. Classification and Japanese
Legal Status.

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Exposure Toxicity Data
NEWS 29 MAR 12 MARPAT Database Enhanced with Additional Markush Backfile
Content for STN
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March 18, 2012
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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,
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=> fil reg

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STRUCTURE 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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*** YOU HAVE NEW MAIL ***

=> s saxagliptin/cn

L1 1 SAXAGLIPTIN/CN

=> d 11

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[3.3.1.1^{3,7}]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[3.3.1.1^{3,7}]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

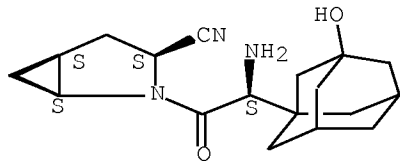
MF C18 H25 N3 O2

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 12 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[3.3.1.1^{3,7}]dec-1-yl)acetyl]-, hydrate
 (1:1), (1S,3S,5S)- (CA INDEX NAME)

OTHER NAMES:

CN Saxagliptin hydrate

FS STEREOSEARCH

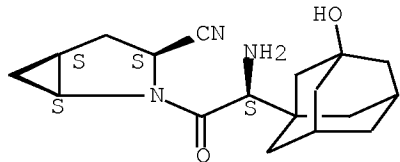
MF C18 H25 N3 O2 . H2 O

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.



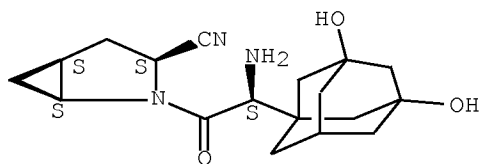
● H2O

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[3.3.1.1^{3,7}]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[3.3.1.1^{3,7}]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.



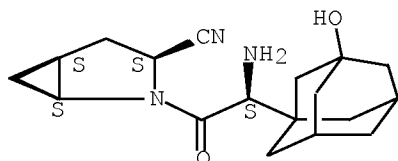
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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[3.3.1.1^{3,7}]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[3.3.1.1^{3,7}]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.

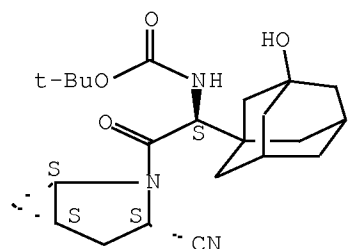


● HCl

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[3.3.1.1^{3,7}]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[3.3.1.1^{3,7}]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.

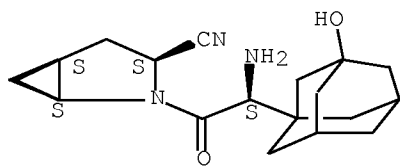


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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[3.3.1.1^{3,7}]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)-2-amino(3-hydroxytricyclo[3.3.1.1^{3,7}]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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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

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/stdoc/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

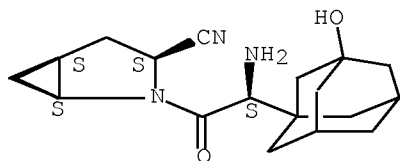
=>

=> 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[3.3.1.1^{3,7}]dec-1-yl)acetyl]-,
(1S,3S,5S)-, (2Z)-2-butenedioate (1:1)
MF C18 H25 N3 O2 . C4 H4 O4

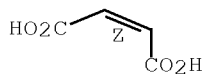
CM 1

Absolute stereochemistry.



CM 2

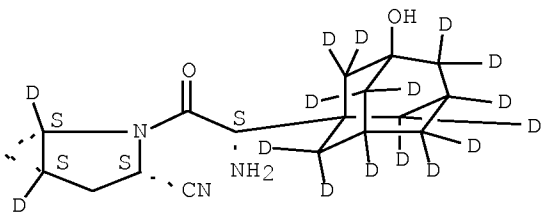
Double bond geometry as shown.



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[3.3.1.1^{3,7}]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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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.

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>

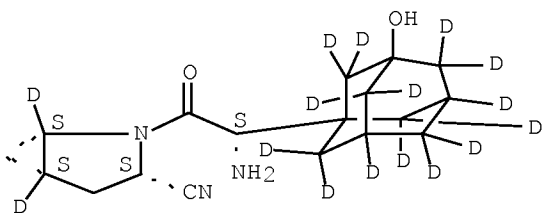
*** YOU HAVE NEW MAIL ***

=> d 14 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[3.3.1.1.3,7]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

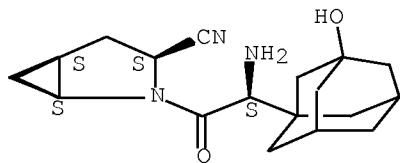
L5 48 361442-04-8/CRN

=> d scan

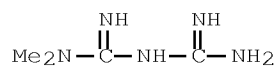
L5 48 ANSWERS REGISTRY COPYRIGHT 2012 ACS on STN
IN Imidodicarbonimidic diamide, N,N-dimethyl-, mixt. with
(1S,3S,5S)-2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.1.3]dec-1-yl)acetyl]-2-azabicyclo[3.1.0]hexane-3-carbonitrile
MF C18 H25 N3 O2 . C4 H11 N5
CI MXS

CM 1

Absolute stereochemistry.



CM 2



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

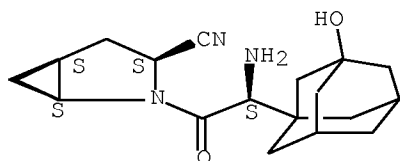
L5 48 ANSWERS REGISTRY COPYRIGHT 2012 ACS on STN

IN Sulfuric acid diammonium salt, compd. with
(1S,3S,5S)-2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.1.3,7]dec-1-yl)acetyl]-2-azabicyclo[3.1.0]hexane-3-carbonitrile (1:1)

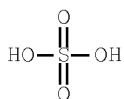
MF C18 H25 N3 O2 . 2 H3 N . H2 O4 S

CM 1

Absolute stereochemistry.



CM 2



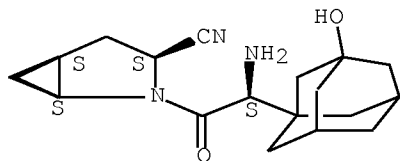
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L5 48 ANSWERS REGISTRY COPYRIGHT 2012 ACS on STN

IN Butanedioic acid, compd. with (1S,3S,5S)-2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.1^{3,7}]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

HO₂C—CH₂—CH₂—CO₂H

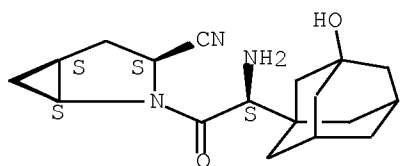
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

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[3.3.1.1^{3,7}]dec-1-yl)acetyl]-, hydrate
(2:1), (1S,3S,5S)-

MF C18 H25 N3 O2 . 1/2 H2 O

Absolute stereochemistry.



● 1/2 H₂O

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

=> 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

=> 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
CA INDEXING COPYRIGHT (C) 2012 AMERICAN CHEMICAL SOCIETY (ACS)

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

=> s 111 and ROBL/IN
L21 0 L11 AND ROBL/IN

=> s 111 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 |
|---------------------|----------------|------|---------------|
| PATENT INFORMATION: | US 20090298794 | A1 | 20091203 |
| | US 7989433 | B2 | 20110802 |
| APPLICATION INFO.: | US 2009-473346 | A1 | 20090528 (12) |

| | NUMBER | DATE |
|-----------------------|---|---------------|
| 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 111 and PRD<20030101

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 | | |

| | | | | |
|------------------------|----|----------|------------------|----------------|
| 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 |
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| 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 | |
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| 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 | |
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| 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 | | |

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

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

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 | |
|---------------------|----------------|------|----------|-----|
| 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.

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L2 5 S SAXAGLIPTIN

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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

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L6 480 S L1

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

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

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=> S 361442-04-8/RN

L27 472 361442-04-8/RN

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L28 26 L27 NOT L11

=> S L28 AND (ROBL JEFFREY A/IN)

L29 0 L28 AND (ROBL JEFFREY A/IN)

=> S L28 AND US6395767/PN

L30 0 L28 AND US6395767/PN

=> S L24 AND L27

L31 0 L24 AND L27

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L32 118 (ROBL JEFFREY A/IN)

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=> S L32 AND PRD<20000311

L36 35 L32 AND PRD<20000311

=> S L32 AND PRD=20000310

L37 2 L32 AND PRD=20000310

=> D L37 IBIB ABS 1-
 YOU HAVE REQUESTED DATA FROM 2 ANSWERS - CONTINUE? Y/(N):Y

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

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| 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

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| 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 <-- |
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| JP 2010077163 | A | 20100408 | JP 2010-6181 | 20100114 <-- |

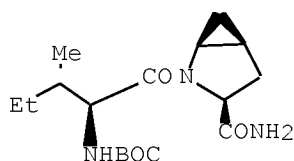
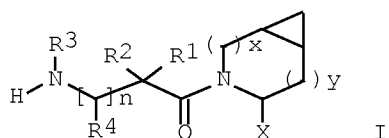
PRIORITY APPLN. INFO.:

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| 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 |

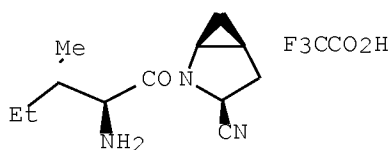
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): MARPAT 135:257147

GI



II



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

329

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.

=> S L37 AND 361442-04-8/RN
L38 0 L37 AND 361442-04-8/RN

=> S L37 AND 361442-04-8
L39 0 L37 AND 361442-04-8

=> 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
L6 480 S L1

FILE 'REGISTRY' ENTERED AT 15:50:53 ON 30 APR 2012
SET SMARTSELECT ON
L7 SEL L1 1- CHEM : 6 TERMS
SET SMARTSELECT OFF

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
L14 0 S L11 AND AD<20000312
L15 0 S L11 AND AD<20010312
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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
 L29 0 S L28 AND (ROBL JEFFREY A/IN)
 L30 0 S L28 AND US6395767/PN
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 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

=> S L37 AND L5
 L40 2 L37 AND L5

=> DUP REMOV L40
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 L41 2 DUP REMOV L40 (0 DUPLICATES REMOVED)

=> 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 |
|---------------------|----------------|------|--------------|
| 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.

IT 361442-05-9P

(preparation of fused cyclopropylpyrrolidine-based inhibitors of dipeptidyl peptidase IV)

RN 361442-05-9 USPATFULL

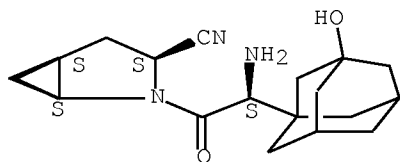
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.1^{3,7}]dec-1-yl)acetyl]-,
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CM 1

CRN 361442-04-8

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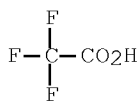
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



=> S L37 AND 361442-04-8/CRN
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'CRN' IS NOT A VALID FIELD CODE
L42 0 L37 AND 361442-04-8/CRN

=> S L37 AND "361442-04-8"
L43 0 L37 AND "361442-04-8"

=> FIL REG

FILE 'REGISTRY' ENTERED AT 16:39:15 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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TSCA INFORMATION NOW CURRENT THROUGH DECEMBER 23, 2011

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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 361442-04-8/RN
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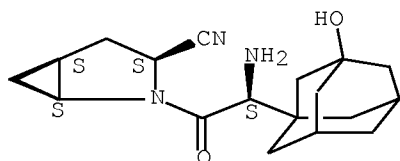
=> D L44

L44 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[3.3.1.1^{3,7}]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[3.3.1.1^{3,7}]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)

=> FIL CAPLUS USPATFUL

FILE 'CAPLUS' ENTERED AT 16:40:05 ON 30 APR 2012
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FILE 'USPATFULL' ENTERED AT 16:40:05 ON 30 APR 2012
CA INDEXING COPYRIGHT (C) 2012 AMERICAN CHEMICAL SOCIETY (ACS)

=> S L44
L45 480 L44

=> S L32 AND PRD<20000311
L46 35 L32 AND PRD<20000311

=> S L32 AND PRD<20000310
L47 33 L32 AND PRD<20000310

=> DUP REMOV L47

PROCESSING COMPLETED FOR L47
L48 31 DUP REMOV L47 (2 DUPLICATES REMOVED)

=> 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; President 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 |
|------------------------|------|----------|-----------------|--------------|
| 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

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

L6 480 S L1

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

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L7 SEL L1 1- CHEM : 6 TERMS

SET SMARTSELECT OFF

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

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L9 454 DUP REMOVE L6 (26 DUPLICATES REMOVED)
L10 1218 DUP REMOVE L8 (24 DUPLICATES REMOVED)
L11 1228 S L9 OR L10
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L13 0 S L11 AND AD<20000309
L14 0 S L11 AND AD<20000312
L15 0 S L11 AND AD<20010312
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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
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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
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L48 31 DUP REMOV L47 (2 DUPLICATES REMOVED)

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

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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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FILE 'REGISTRY' ENTERED AT 15:50:53 ON 30 APR 2012
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FILE 'CAPLUS, USPATFULL' ENTERED AT 15:50:53 ON 30 APR 2012
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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
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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

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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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L37 2 S L32 AND PRD=20000310
L38 0 S L37 AND 361442-04-8/RN
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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)
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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

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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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TSCA INFORMATION NOW CURRENT THROUGH DECEMBER 23, 2011

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

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<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
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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.

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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, tableting.

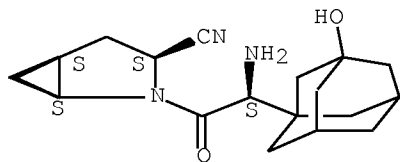
IT 361442-05-9
 RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (oral preparation of saxagliptin)

RN 361442-05-9 CAPLUS
 CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
 2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.1^{3,7}]dec-1-yl)acetyl]-,
 (1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

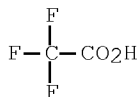
CRN 361442-04-8
 CMF C18 H25 N3 O2

Absolute stereochemistry.



CM 2

CRN 76-05-1
 CMF C2 H F3 O2



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 |
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| 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

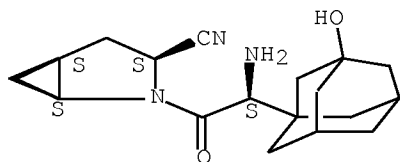
hydrochloride containing 0.75 equiv of H₂O (form H0.75-3) and hydrochloride containing 2 equivs of H₂O (form H2-1), and hydrochloride Pattern P-5, preferably in substantially pure form, and other forms as described herein, pharmaceutical compns. containing these compds. processes for preparing the same, 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[3.3.1.1^{3,7}]dec-1-yl)acetyl]-,
(1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

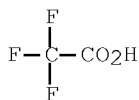
CRN 361442-04-8
CMF C18 H25 N3 O2

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



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, Aiyang; Simpkins, Ligaya M.; Taunk, Prakash;

343

0472

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-methanoproline nitrile 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

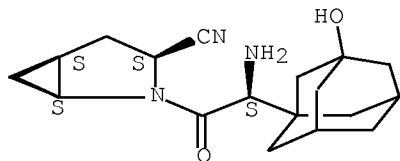
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.1^{3,7}]dec-1-yl)acetyl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361442-04-8

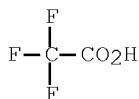
CMF C18 H25 N3 O2

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

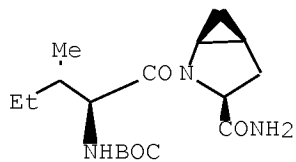
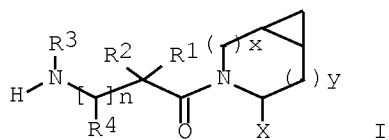


OS.CITING REF COUNT: 205 THERE ARE 205 CAPLUS RECORDS THAT CITE THIS RECORD (206 CITINGS)
REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

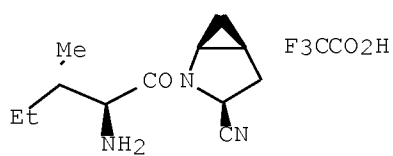
L57 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2012 ACS on STN
ACCESSION NUMBER: 2001:693281 CAPLUS Full-text
DOCUMENT NUMBER: 135:257147
TITLE: Preparation of fused cyclopropylpyrrolidine-based inhibitors of dipeptidyl peptidase IV
INVENTOR(S): Robl, Jeffrey A.; Sulsky, Richard B.; Augeri, David J.; Magnin, David 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 |
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| 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 | | | |
| 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 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 | | |
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| 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 |
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| | | | 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 | | | | |



II



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 $y = 1$; $n = 0, 1$; $X = H, CN$; R_1, R_2, R_3 and $R_4 =$ 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

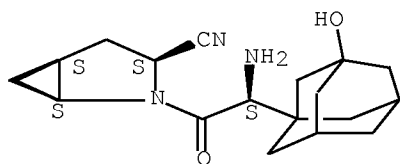
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.1^{3,7}]dec-1-yl)acetyl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361442-04-8

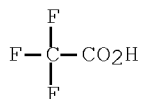
CMF C18 H25 N3 O2

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



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.

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Patent Number: Or U.S. Class: Subclass (optional): Or District Court:

Patent class/subclass definitions

CourtLink search for USP 6,395,767.

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Patent Search 6395767 4/16/2012

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 Term: patno=6395767 (Suggest Terms for My Search)

758173 (09) 6395767 May 28, 2002

UNITED STATES PATENT AND TRADEMARK OFFICE GRANTED PATENT

6395767

[Access PDF of Official Patent *](#)
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[Link to Claims Section](#)

May 28, 2002

Cytosomyl-fused pyridine-based inhibitors of dipeptidyl peptidase IV and method

REISSUE:
 December 1, 2011 - Reissue Application Filed, Ex. Op. 1629; (O.G. February 14, 2012)

INVENTOR: Robl, Jeffrey A. - Newtown, Pennsylvania ; Sulsky, Richard B. - West Trenton, New Jersey ; Augeri, David J. - Princeton, New Jersey ; Magnin, David R. - Hamilton, New Jersey ; Hamann, Lawrence G. - Cherry Hill, New Jersey ; Betekammer, David A. - Lawrenceville, New Jersey

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

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Terms & Connectors 6395767 or 6,395,767 [Suggest terms for my search](#)

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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.

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"6395767 or 6,395,767"

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- 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.

Search View Tutorial
 Select Search Type and Enter Search Terms
 Terms & Connectors 6,395,767 or 6,395,767 Suggest terms for my search

Searched Lexis/Nexis News, All (English, Full Text) database.

FOCUS™ Terms 6395767 or 6,395,767 Search within Original Results (1 - 1) Advanced... view full
 view KWIC # 25 Options 1 of 1
 Edit Search | Save As Alert | More Like This | More Like Selected Text
 Determination of Regulatory Review Period for Purposes of Patent Extension;... (Copy w/ Cite) Page

Source: News & Business > Combined Sources > News, All (English, Full Text) | 1
 Term: 6395767 or 6,395,767 (Suggest Terms for My Search)
 Determination of Regulatory Review Period for Purposes of Patent Extension; ONGLYZA Food and Drug Administration Documents and Publications
 August 31, 2010

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 Food and Drug Administration Documents and Publications
 August 31, 2010

SECTION: FOOD AND DRUG ADMINISTRATION - REGULATORY DOCUMENTS
 LENGTH: 1946 words
 HEADLINE: Determination of Regulatory Review Period for Purposes of Patent Extension; ONGLYZA
 BODY:

... improve glycemic control in adults with type 2 diabetes mellitus. Subsequent to this approval, the Patent and Trademark Office received a patent term restoration application for ONGLYZA (U.S. Patent No. 6,395,767) from Bristol-Myers Squibb Co., and the Patent and Trademark Office requested FDA's assistance in determining this patent's eligibility for patent term restoration. In a letter dated March 3, 2010,

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Tips:

- Don't over-specify: use only the search options you really need.
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Table with 5 columns: APPLICATION NO., FILING DATE, FIRST NAMED INVENTOR, ATTORNEY DOCKET NO., CONFIRMATION NO. Includes application details for Jeffrey A. Robl and examiner information for POLANSKY, GREGG.

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. 13/308,658 | Applicant(s) ROBL ET AL. | |
| | Examiner Gregg Polansky | Art Unit 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
Application No.: 13/308,658
Office Action Dated: May 8, 2012

PATENT

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 PG₁ 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 to cycloheteroalkyl groups as defined above linked through a C atom or heteroatom to a (CH₂)_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 $[(\text{M}+\text{H})^+ = 297]$ 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 $-20^\circ C$ 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 CH₂Cl₂ (4 mL). The tube was sealed under nitrogen atmosphere and treated with 1-[(3-(dimethylamino)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 CH₂Cl₂ (5 mL), 30% methanol in CH₂Cl₂ (5 mL), 50% methanol in CH₂Cl₂ (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 -30⁰C. Slow addition of POCl₃ (0.30 mL, 3.16 mmol) gave after mixing a thick slurry. The slurry was mixed at -30⁰C 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 H₂O, 10% citric acid, brine and dried over Na₂SO₄. 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 re-cooled 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 Et₂O (200 mL) in a separatory funnel, and the layers were separated. The organic layer was then washed with brine (100 mL), dried (Na₂SO₄), and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, CH₂Cl₂ / 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 CH₂Cl₂ at rt was added Step 2 compound (8.61 g, 76.75 mmol, 1.00 equiv) in 20 mL CH₂Cl₂, followed by dicyclohexylcarbodiimide (16.63 g, mmol, 1.05 equiv) in 80 mL CH₂Cl₂. 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 CH₂Cl₂, 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 glycinylnyl 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 ZnCl₂ (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 ZnCl₂ 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 Et₂O, and the resultant organic solution was washed successively with 300 mL 1N HCl and 300 mL brine, dried (Na₂SO₄), and concentrated under reduced pressure. Purification by flash chromatography (silica gel, 3% MeOH in CH₂Cl₂ 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 CH₂Cl₂ 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 OsO₄ (12 mg, catalyst) and NaIO₄ (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 NaHCO₃ solution, dried over MgSO₄ and concentrated to give a dark oil. The oil was diluted with 10 mL of methanol and treated with NaBH₄ (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 NaHCO₃ solution. The mixture was equilibrated and layers separated. The organic fraction was washed with solutions of NaHCO₃ and 0.1 M HCl. The organics were dried (MgSO₄) 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% H_2O -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 NH₄Cl (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 (MgSO₄) 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 Na₂CO₃ 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% KHSO₄ solution. The aqueous phase was washed with ether (2 X 40 mL), the organics dried (MgSO₄), and evaporated to an oil that was purified by silica gel flash chromatography with 8:92 methanol:CH₂Cl₂ 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% NaHCO₃ solution (2x5 mL), brine and dried (MgSO₄). 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 CH₂Cl₂ (30 mL) under argon was added TFA (7.35 mL, 95.3 mmol) dropwise with stirring while maintaining the internal temperature at 25⁰C by means of an ice bath. After stirring for 4 h at rt, the solution was concentrated. The residue was diluted with CH₂Cl₂ (100 mL), then treated with H₂O (50 mL) and solid Na₂CO₃ with vigorous stirring until the mixture was basic. The organic layer was separated, dried (Na₂SO₄), 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°C; 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% NaHCO₃ solution (2x5 mL), brine and dried (MgSO₄). 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-butoxycarbonylglyciny]--(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 Na₂SO₃ and was taken up in EtOAc and washed with H₂O 5 mL, dried (Na₂SO₄), filtered, evaporated and purified by silica gel flash chromatography (5% MeOH/CH₂Cl₂) 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).

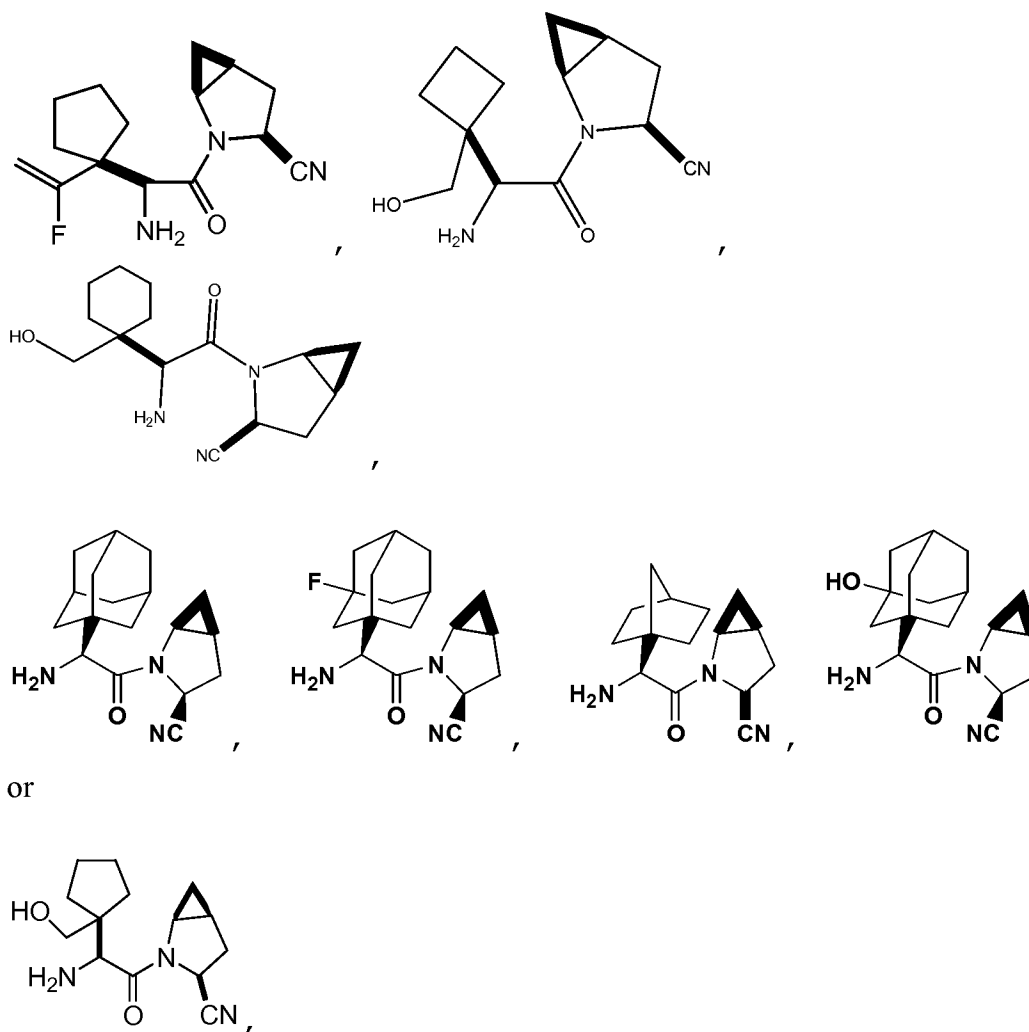
30. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 82, lines 52-67 of the 767 patent:

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 (MgSO₄), 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:

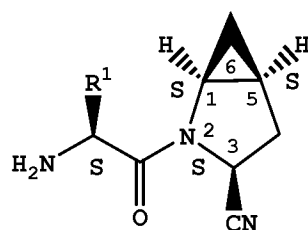
8. A compound having the structure:



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

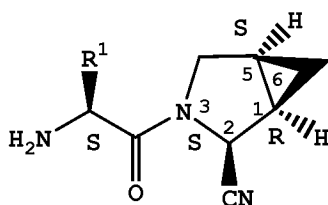


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(1S, 2(2S), 3S, 5S)

wherein R¹ is alkyl, cycloalkyl, bicycloalkyl, tricycloalkyl, alkylcycloalkyl, hydroxyalkyl, hydroxycycloalkyl, hydroxyalkylcycloalkyl, hydroxybicycloalkyl, or hydroxytricycloalkyl,

or



B

(1R, 2S, 3(2S), 5S)

wherein R¹ 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:

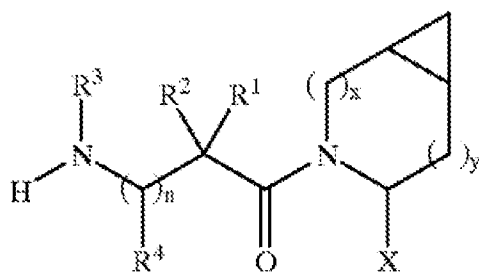
15. The combination as defined in Claim 14 wherein the antidiabetic agent is 1, 2, 3 or more of metformin, glyburide, glimepiride, glipryride, glipizide, chlorpropamide, gliclazide, acarbose, miglitol, pioglitazone, troglitazone, rosiglitazone, insulin, Gl-262570, isaglitazone, JTT-501, NN-2344, L895645, 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

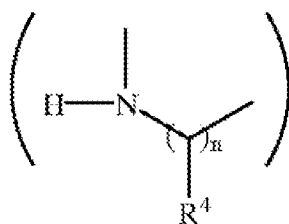
n is 0 or 1;

X is H or CN;

R¹, R², R³ and R⁴ 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,

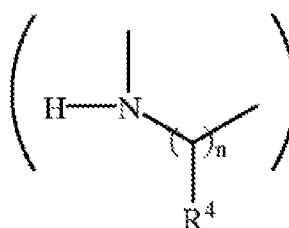
cycloheteroalkyl or cycloheteroalkylalkyl; all optionally substituted through available carbon atoms with 1, 2, 3, 4 or 5 groups selected from hydrogen, halo, alkyl, polyhaloalkyl, alkoxy, haloalkoxy, polyhaloalkoxy, alkoxycarbonyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, polycycloalkyl, heteroarylamino, 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, aryloxy carbonylamino, alkoxycarbonyl, aryloxy carbonyl, 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, aryloxy carbonylamino, alkoxycarbonyl, aryloxy carbonyl, 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 SO₂;

or optionally R¹ and R³ 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 0, and one of R¹ and R² is H and the other is alkyl, then R³ 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:

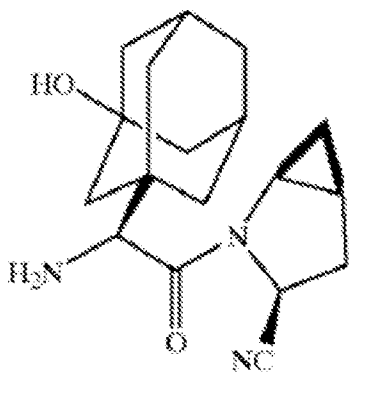
39. The method of claim 38 wherein the antidiabetic agent is metformin.

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



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Application No.: 13/308,658
Office Action Dated: May 8, 2012

PATENT

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.

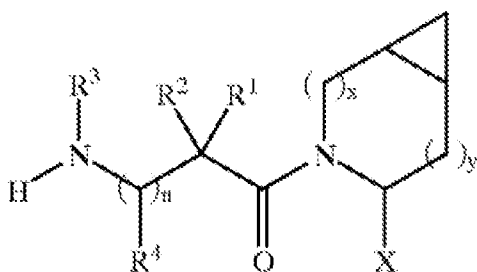
43. The method of any one of claims 41 or 42, wherein the pharmaceutical composition further comprises an antidiabetic agent other than a DP4 inhibitor.

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

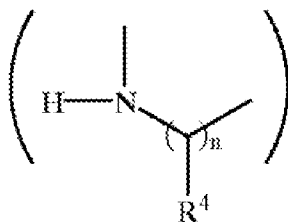
n is 0 or 1;

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, alkoxy carbonyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, polycycloalkyl, heteroaryl amino, aryl amino, cycloheteroalkyl, cycloheteroalkylalkyl, hydroxy, hydroxyalkyl, nitro,

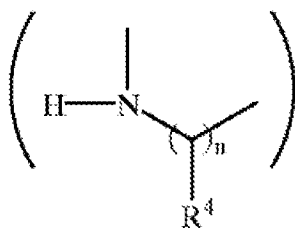
cyano, amino, substituted amino, alkylamino, dialkylamino, thiol, alkylthio, alkylcarbonyl, acyl, alkoxy carbonyl, aminocarbonyl, alkynylaminocarbonyl, alkylaminocarbonyl, alkenylaminocarbonyl, alkylcarbonyloxy, alkylcarbonylamino, arylcarbonylamino, alkylsulfonylamino, alkylaminocarbonylamino, alkoxy carbonylamino, 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, alkoxy carbonylamino, aryloxy carbonylamino, alkoxy carbonyl, aryloxy carbonyl, 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, alkoxy carbonylamino, aryloxy carbonylamino, alkoxy carbonyl, aryloxy carbonyl, 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 SO₂;

or optionally R^1 and R^3 together with



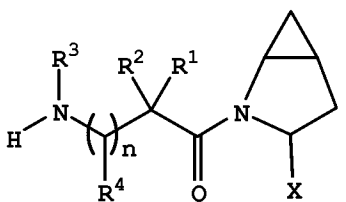
form a 4 to 8 membered cycloheteroalkyl ring wherein the cycloheteroalkyl ring has an optional aryl ring fused thereto or an optional 3 to 7 membered cycloalkyl ring fused thereto;

with the proviso that where x is 1 and y is 0, X is H, n is 0, and one of R¹ and R² is H and the other is alkyl, then R³ is other than pyridyl or substituted pyridyl;

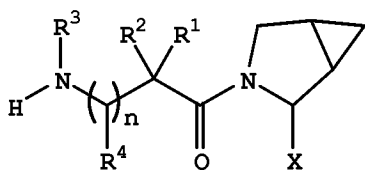
including all stereoisomers thereof;

or [and] a pharmaceutically acceptable salt thereof[, or a prodrug ester thereof], and all stereoisomers thereof.

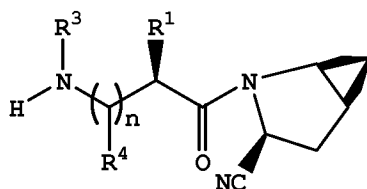
2. (Original) The compound as defined in claim 1 having the structure:



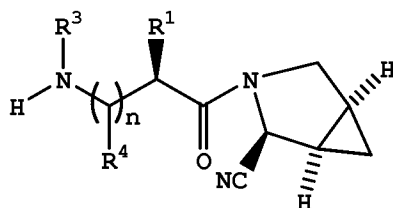
3. (Original) The compound as defined in claim 1 having the structure:



4. (Original) The compound as defined in claim 1 having the structure:



5. (Original) The compound as defined in claim 1 having the structure:



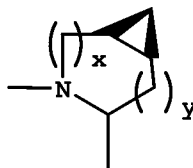
6. (Original) The compound as defined in claim 1 wherein:

R^3 is H, R^1 is H, alkyl, cycloalkyl, bicycloalkyl, tricycloalkyl, alkylcycloalkyl, hydroxyalkyl, hydroxyalkylcycloalkyl, hydroxycycloalkyl hydroxybicycloalkyl, or hydroxytricycloalkyl,

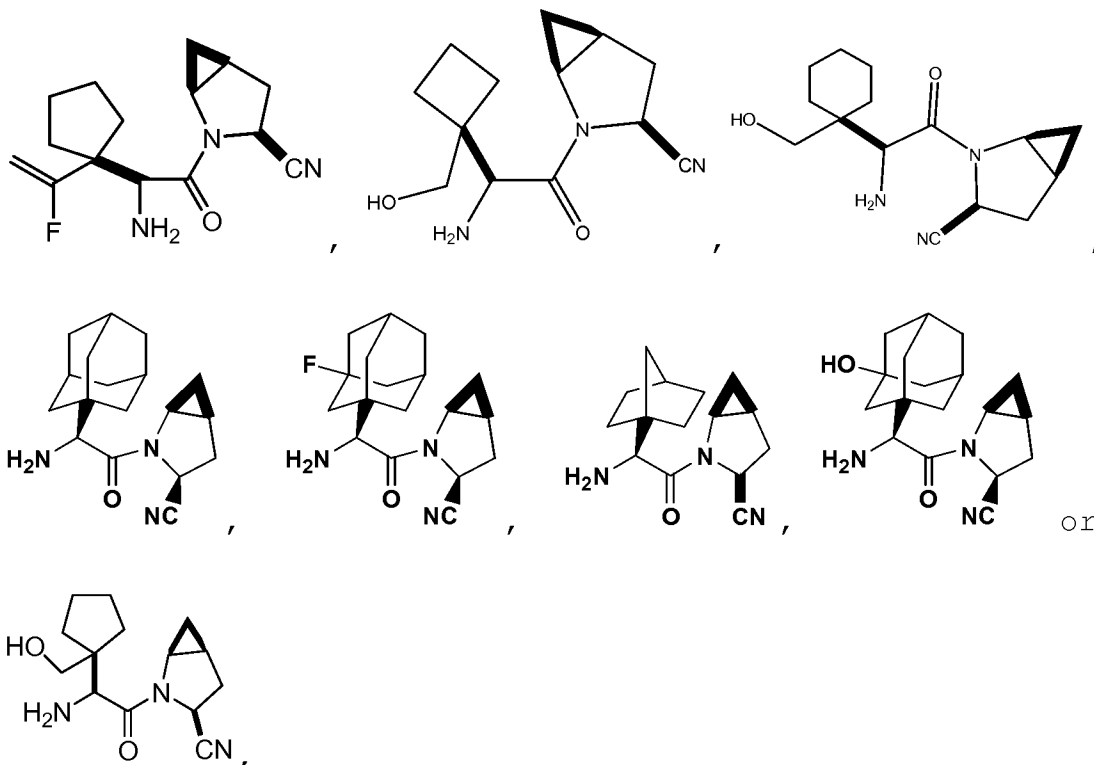
R^2 is H or alkyl, n is 0,

X is CN.

7. (Original) The compound as defined in claim 1 wherein the cyclopropyl fused to the pyrrolidine has the configuration:



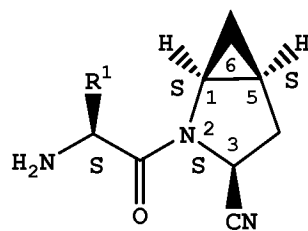
8. (Original) A compound having the structure:



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

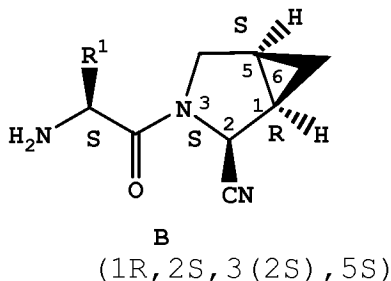


A

(1S, 2(2S), 3S, 5S)

wherein R^1 is alkyl, cycloalkyl, bicycloalkyl, tricycloalkyl, alkylcycloalkyl, hydroxyalkyl, hydroxycycloalkyl, hydroxyalkylcycloalkyl, hydroxybicycloalkyl, or hydroxytricycloalkyl,

or



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 α 2 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, glipyrice, 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 lipoxxygenase 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.

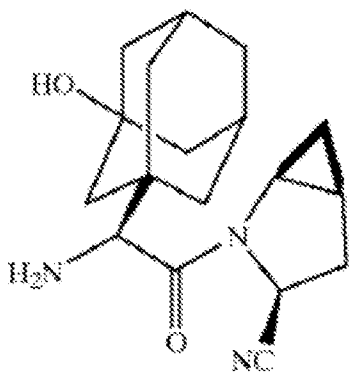
21. (Amended) The combination as defined in claim 19 wherein the compound as defined in claim 1 [DP4 inhibitor] is present in a weight ratio to the lipid-modulating agent within the range from about 0.01 to about 100:1.

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.

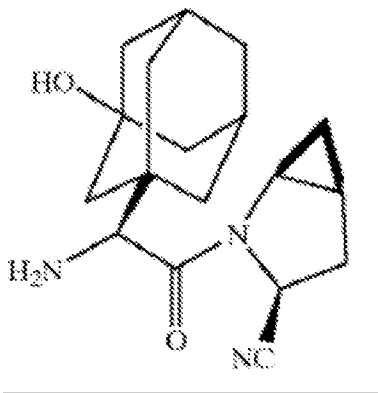
28. (New) A pharmaceutical composition comprising the compound of claim 26 and a pharmaceutically acceptable carrier therefor.

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)

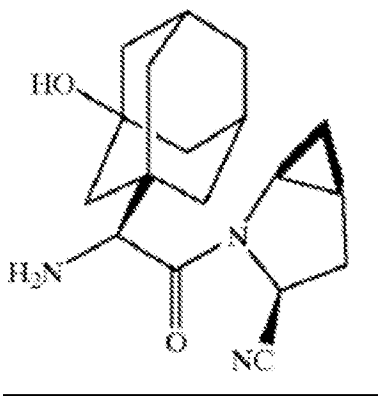
37. (Canceled)

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.

DOCKET NO.: BMS-2856
Application No.: 13/308,658
Office Action Dated: May 8, 2012

PATENT

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 PG₁ 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 to cycloheteroalkyl groups as defined above linked through a C atom or heteroatom to a (CH₂)_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 $[(\text{M}+\text{H})^+ = 297]$ 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 $-20^\circ C$ 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 CH₂Cl₂ (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 CH₂Cl₂ (5 mL), 30% methanol in CH₂Cl₂ (5 mL), 50% methanol in CH₂Cl₂ (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 -30⁰C. Slow addition of POCl₃ (0.30 mL, 3.16 mmol) gave after mixing a thick slurry. The slurry was mixed at -30⁰C 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 H₂O, 10% citric acid, brine and dried over Na₂SO₄. 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 re-cooled 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 Et₂O (200 mL) in a separatory funnel, and the layers were separated. The organic layer was then washed with brine (100 mL), dried (Na₂SO₄), and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, CH₂Cl₂ / 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 CH₂Cl₂ at rt was added Step 2 compound (8.61 g, 76.75 mmol, 1.00 equiv) in 20 mL CH₂Cl₂, followed by dicyclohexylcarbodiimide (16.63 g, mmol, 1.05 equiv) in 80 mL CH₂Cl₂. 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 CH₂Cl₂, 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 glycinylnyl 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 ZnCl₂ (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 ZnCl₂ 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 Et₂O, and the resultant organic solution was washed successively with 300 mL 1N HCl and 300 mL brine, dried (Na₂SO₄), and concentrated under reduced pressure. Purification by flash chromatography (silica gel, 3% MeOH in CH₂Cl₂ 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 CH₂Cl₂ 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 OsO₄ (12 mg, catalyst) and NaIO₄ (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 NaHCO₃ solution, dried over MgSO₄ and concentrated to give a dark oil. The oil was diluted with 10 mL of methanol and treated with NaBH₄ (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 NaHCO₃ solution. The mixture was equilibrated and layers separated. The organic fraction was washed with solutions of NaHCO₃ and 0.1 M HCl. The organics were dried (MgSO₄) 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 CH₂Cl₂, 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% H₂O -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 CH₂Cl₂ (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 H₂O (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/CH₂Cl₂ 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 Et₂O (100 mL) was added. The mixture was washed with 10% aq NaHSO₃ (50 mL), H₂O (2x50 mL), and brine (25 mL). The ether fraction was dried (Na₂SO₄), filtered and concentrated by rotary evaporation. The product was purified by flash column chromatography on silica gel (5x15 cm) with 2% to 4% MeOH/CH₂Cl₂ +

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 NH₄Cl (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 (MgSO₄) 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 Na₂CO₃ 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% KHSO₄ solution. The aqueous phase was washed with ether (2 X 40 mL), the organics dried (MgSO₄), and evaporated to an oil that was purified by silica gel flash chromatography with 8:92 methanol:CH₂Cl₂ 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% NaHCO₃ solution (2x5 mL), brine and dried (MgSO₄). 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 CH₂Cl₂ (30 mL) under argon was added TFA (7.35 mL, 95.3 mmol) dropwise with stirring while maintaining the internal temperature at 25⁰C by means of an ice bath. After stirring for 4 h at rt, the solution was concentrated. The residue was diluted with CH₂Cl₂ (100 mL), then treated with H₂O (50 mL) and solid Na₂CO₃ with vigorous stirring until the mixture was basic. The organic layer was separated, dried (Na₂SO₄), 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°C; 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% NaHCO₃ solution (2x5 mL), brine and dried (MgSO₄). 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-butoxycarbonylglyciny]--(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 Na₂SO₃ and was taken up in EtOAc and washed with H₂O 5 mL, dried (Na₂SO₄), filtered, evaporated and purified by silica gel flash chromatography (5% MeOH/CH₂Cl₂) 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).

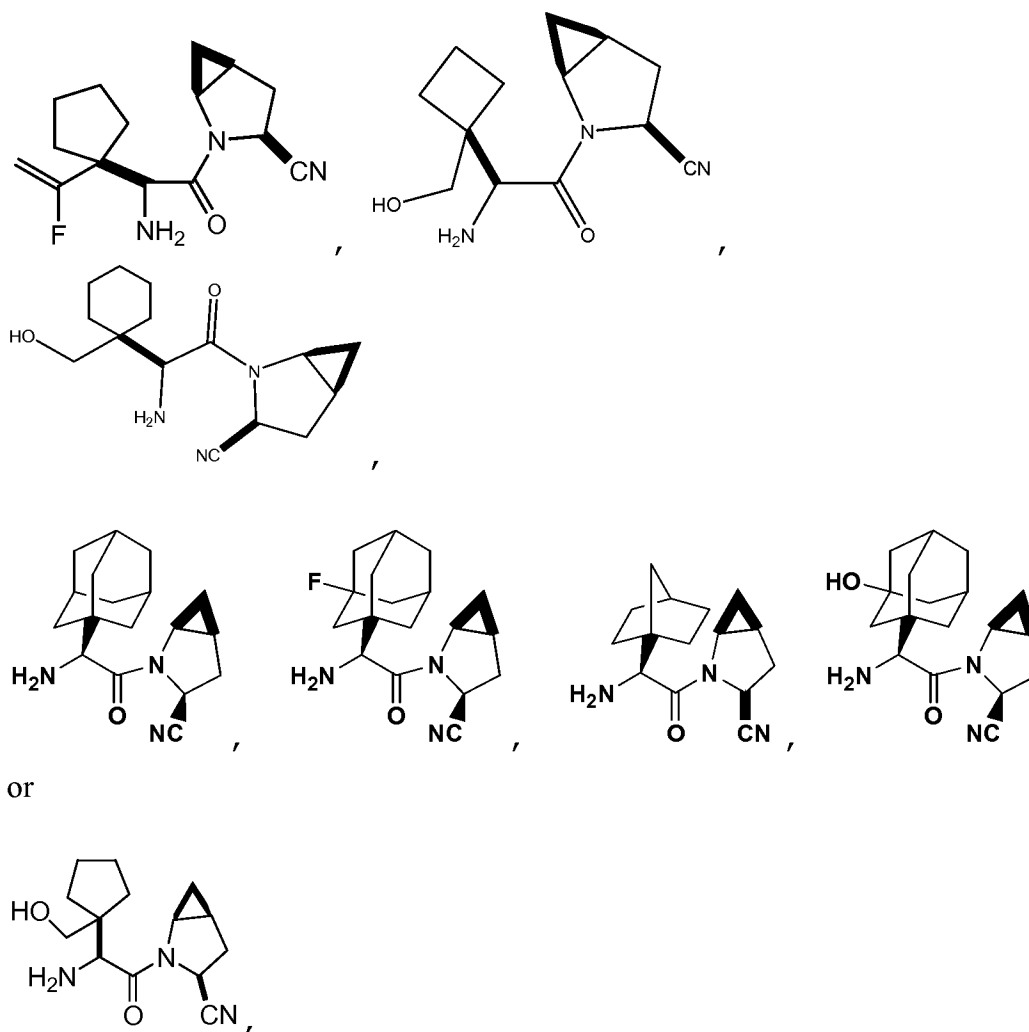
30. As indicated by the Certificate of Correction, please substitute the following paragraph for the paragraph at col. 82, lines 52-67 of the 767 patent:

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 (MgSO₄), 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:

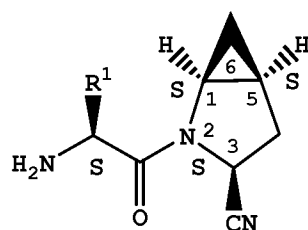


or

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

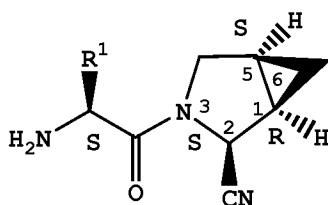


A

(1S, 2(2S), 3S, 5S)

wherein R¹ is alkyl, cycloalkyl, bicycloalkyl, tricycloalkyl, alkylcycloalkyl, hydroxyalkyl, hydroxycycloalkyl, hydroxyalkylcycloalkyl, hydroxybicycloalkyl, or hydroxytricycloalkyl,

or



B

(1R, 2S, 3(2S), 5S)

wherein R¹ 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:

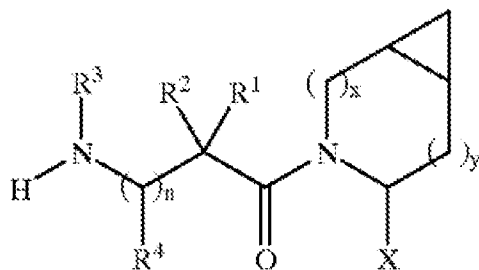
15. The combination as defined in Claim 14 wherein the antidiabetic agent is 1, 2, 3 or more of metformin, glyburide, glimepiride, glipryride, glipizide, chlorpropamide, gliclazide, acarbose, miglitol, pioglitazone, troglitazone, rosiglitazone, insulin, Gl-262570, isaglitazone, JTT-501, NN-2344, L895645, 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

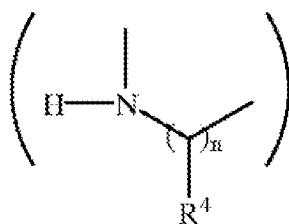
n is 0 or 1;

X is H or CN;

R¹, R², R³ and R⁴ 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,

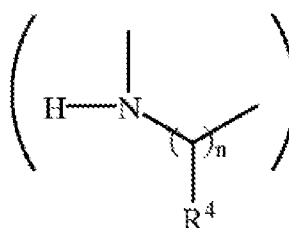
cycloheteroalkyl or cycloheteroalkylalkyl; all optionally substituted through available carbon atoms with 1, 2, 3, 4 or 5 groups selected from hydrogen, halo, alkyl, polyhaloalkyl, alkoxy, haloalkoxy, polyhaloalkoxy, alkoxycarbonyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, polycycloalkyl, heteroaryl amino, aryl amino, cycloheteroalkyl, cycloheteroalkylalkyl, hydroxy, hydroxyalkyl, nitro, cyano, amino, substituted amino, alkyl amino, dialkyl amino, 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, aryloxy carbonylamino, alkoxycarbonyl, aryloxy carbonyl, 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, aryloxy carbonylamino, alkoxycarbonyl, aryloxy carbonyl, 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 SO₂;

or optionally R¹ and R³ 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 0, and one of R¹ and R² is H and the other is alkyl, then R³ 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:

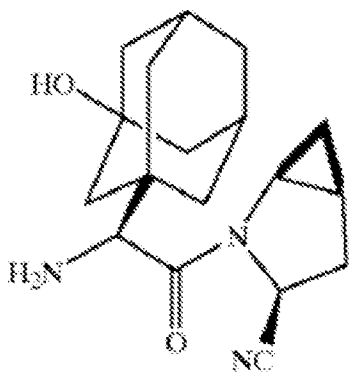
39. The method of claim 38 wherein the antidiabetic agent is metformin.

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.

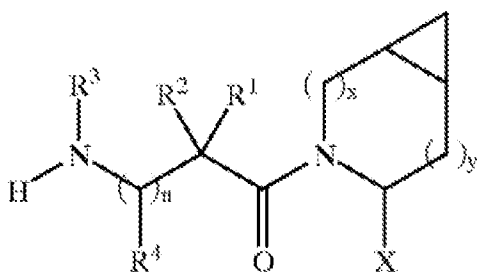
43. The method of any one of claims 41 or 42, wherein the pharmaceutical composition further comprises an antidiabetic agent other than a DP4 inhibitor.

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

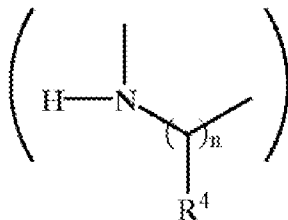
n is 0 or 1;

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, alkoxy carbonyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, polycycloalkyl, heteroaryl amino, aryl amino, cycloheteroalkyl, cycloheteroalkylalkyl, hydroxy, hydroxyalkyl, nitro,

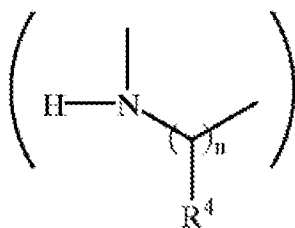
cyano, amino, substituted amino, alkylamino, dialkylamino, thiol, alkylthio, alkylcarbonyl, acyl, alkoxy carbonyl, aminocarbonyl, alkynylaminocarbonyl, alkylaminocarbonyl, alkenylaminocarbonyl, alkylcarbonyloxy, alkylcarbonylamino, arylcarbonylamino, alkylsulfonylamino, alkylaminocarbonylamino, alkoxy carbonylamino, 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, alkoxy carbonylamino, aryloxy carbonylamino, alkoxy carbonyl, aryloxy carbonyl, 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, alkoxy carbonylamino, aryloxy carbonylamino, alkoxy carbonyl, aryloxy carbonyl, 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 SO₂;

or optionally R^1 and R^3 together with



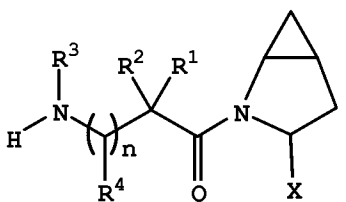
form a 4 to 8 membered cycloheteroalkyl ring wherein the cycloheteroalkyl ring has an optional aryl ring fused thereto or an optional 3 to 7 membered cycloalkyl ring fused thereto;

with the proviso that where x is 1 and y is 0, X is H, n is 0, and one of R¹ and R² is H and the other is alkyl, then R³ is other than pyridyl or substituted pyridyl;

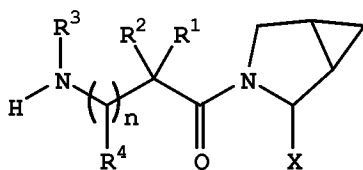
including all stereoisomers thereof;

or [and] a pharmaceutically acceptable salt thereof[, or a prodrug ester thereof], and all stereoisomers thereof.

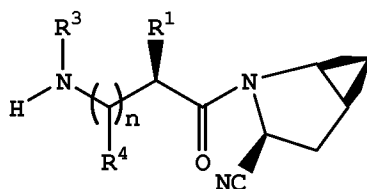
2. (Original) The compound as defined in claim 1 having the structure:



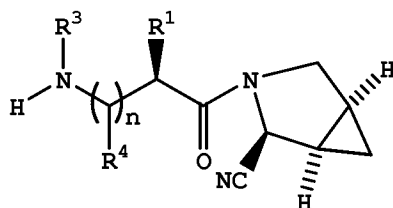
3. (Original) The compound as defined in claim 1 having the structure:



4. (Original) The compound as defined in claim 1 having the structure:



5. (Original) The compound as defined in claim 1 having the structure:



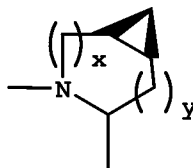
6. (Original) The compound as defined in claim 1 wherein:

R^3 is H, R^1 is H, alkyl, cycloalkyl, bicycloalkyl, tricycloalkyl, alkylcycloalkyl, hydroxyalkyl, hydroxyalkylcycloalkyl, hydroxycycloalkyl hydroxybicycloalkyl, or hydroxytricycloalkyl,

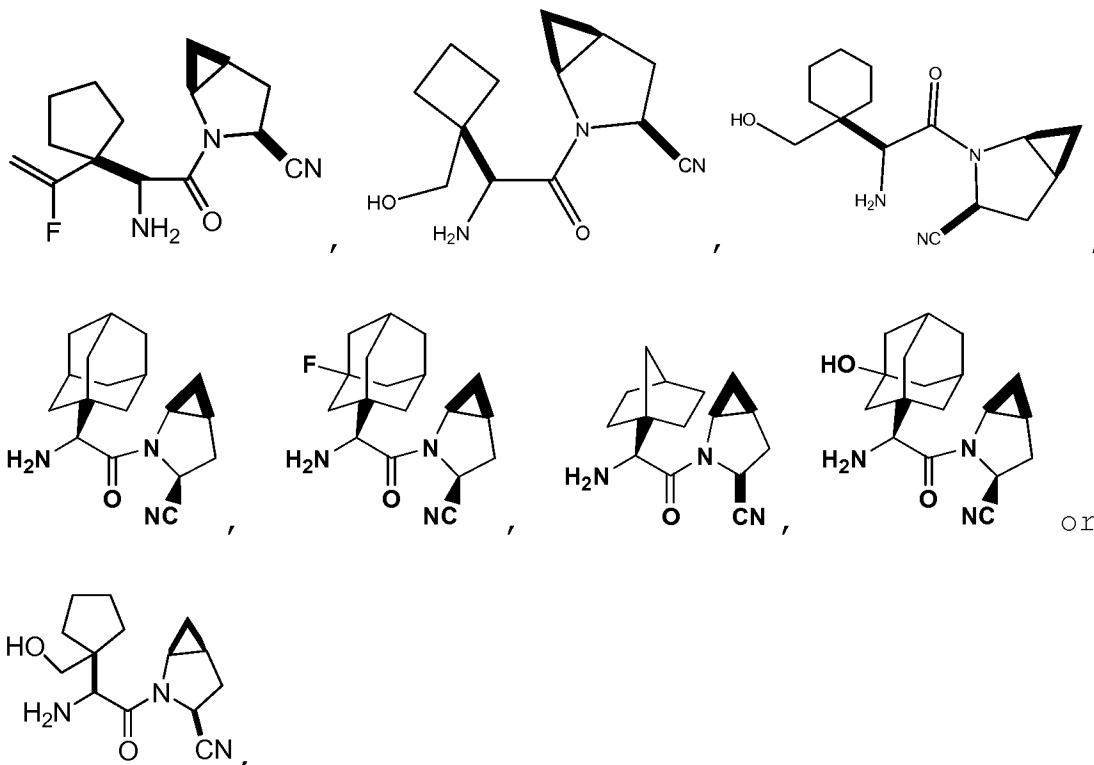
R^2 is H or alkyl, n is 0,

X is CN.

7. (Original) The compound as defined in claim 1 wherein the cyclopropyl fused to the pyrrolidine has the configuration:



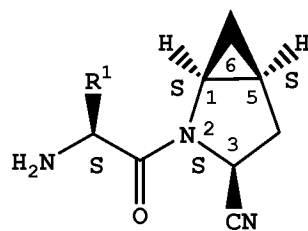
8. (Original) A compound having the structure:



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

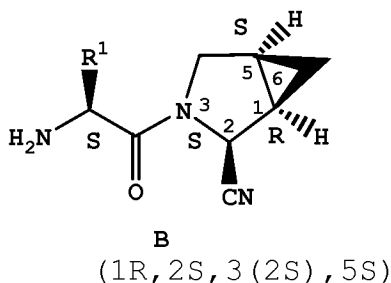


A

(1S, 2(2S), 3S, 5S)

wherein R^1 is alkyl, cycloalkyl, bicycloalkyl, tricycloalkyl, alkylcycloalkyl, hydroxyalkyl, hydroxycycloalkyl, hydroxyalkylcycloalkyl, hydroxybicycloalkyl, or hydroxytricycloalkyl,

or



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 α P2 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, glipyrice, 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.

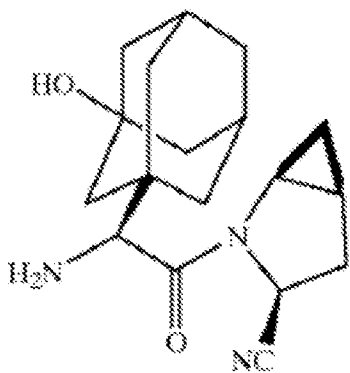
21. (Amended) The combination as defined in claim 19 wherein the compound as defined in claim 1 [DP4 inhibitor] is present in a weight ratio to the lipid-modulating agent within the range from about 0.01 to about 100:1.

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.

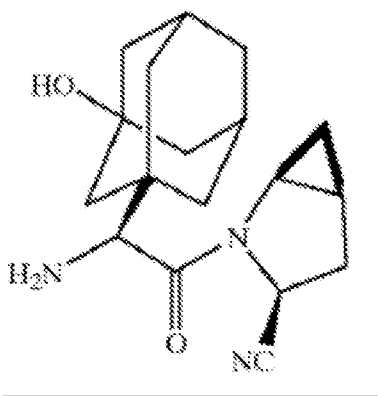
28. (New) A pharmaceutical composition comprising the compound of claim 26 and a pharmaceutically acceptable carrier therefor.

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)

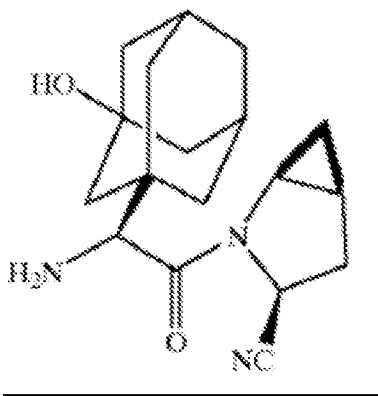
37. (Canceled)

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.

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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.

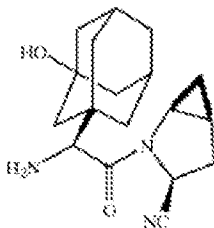
After entry of the present amendments, claims 1-22, 25-35, and 38-45 will remain pending.

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:



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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.

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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
Telephone: (215) 568-3100
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:

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)

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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 85b8b25bcf56ed3f67b7e901298ecc992ee cdee | 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.

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.

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.

| | | |
|--|------------------------|------------------|
| <h1>TRANSMITTAL FORM</h1> <p><i>(to be used for all correspondence after initial filing)</i></p> | Application Number | 13/308,658 |
| | Filing Date | December 1, 2011 |
| | First Named Inventor | Jeffrey A. Robl |
| | Art Unit | 1629 |
| | Examiner Name | Gregg Polansky |
| Total Number of Pages in This Submission | Attorney Docket Number | BMS-2856 |

| ENCLOSURES (Check all that apply) | | |
|---|--|---|
| <input type="checkbox"/> Fee Transmittal Form <input type="checkbox"/> Fee Attached <input checked="" type="checkbox"/> Amendment/Reply <input type="checkbox"/> After Final <input type="checkbox"/> Affidavits/declaration(s) <input type="checkbox"/> Extension of Time Request <input type="checkbox"/> Express Abandonment Request <input type="checkbox"/> Information Disclosure Statement <input type="checkbox"/> Certified Copy of Priority Document(s) <input type="checkbox"/> Reply to Missing Parts/ Incomplete Application <input type="checkbox"/> Reply to Missing Parts under 37 CFR 1.52 or 1.53 | <input type="checkbox"/> Drawing(s) <input type="checkbox"/> Licensing-related Papers <input type="checkbox"/> Petition <input type="checkbox"/> Petition to Convert to a Provisional Application <input type="checkbox"/> Power of Attorney, Revocation <input type="checkbox"/> Change of Correspondence Address <input type="checkbox"/> Terminal Disclaimer <input type="checkbox"/> Request for Refund <input type="checkbox"/> CD, Number of CD(s) _____ <input type="checkbox"/> Landscape Table on CD | <input type="checkbox"/> After Allowance Communication to TC <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences <input type="checkbox"/> Appeal Communication to TC (Appeal Notice, Brief, Reply Brief) <input type="checkbox"/> Proprietary Information <input type="checkbox"/> Status Letter <input checked="" type="checkbox"/> Other Enclosure(s) (please identify below): Supplemental Reissue Declaration |
| Remarks <input style="width: 100%;" type="text"/> | | |

| 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 | <input style="width: 100%;" type="text"/> | | |
| Typed or printed name | <input style="width: 50%;" type="text"/> | Date | <input style="width: 20%;" type="text"/> |

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 and 1.14. 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.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

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.

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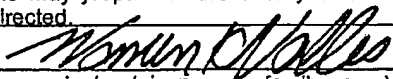
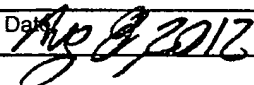
| | | | |
|---|--|--|--|
| REISSUE APPLICATION DECLARATION BY THE ASSIGNEE | | Docket Number (optional) BMS-2856 | |
| I hereby declare that: The residence, mailing address and citizenship of the inventors are stated below. I am authorized to act on behalf of the following assignee: <u>Bristol-Myers Squibb Company</u> and the title of my position with said assignee is: <u>Assistant General Counsel</u> The entire title to the patent identified below is vested in said assignee. | | | |
| Inventor <u>Jeffrey A. Robl</u> | | Citizenship <u>United States</u> | |
| Residence/Mailing Address <u>7 Tulp Drive, Newtown, PA 18940</u> | | | |
| Inventor <u>Richard B. Sulsky</u> | | Citizenship <u>United States</u> | |
| Residence/Mailing Address <u>311 Pennington-Rocky Hill Road, Pennington, NJ 08534</u> | | | |
| <input checked="" type="checkbox"/> Additional Inventors are named on separately numbered sheets attached hereto. | | | |
| Patent Number <u>6,395,767</u> | | Date of Patent Issued <u>May 28, 2002</u> | |
| 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: <div style="border: 1px solid black; padding: 5px; margin: 5px 0;"><u>Cyclopropyl-Fused Pyrrolidine-Based Inhibitors of Dipeptidyl Peptidase IV and Method</u></div> the specification of which <input type="checkbox"/> is attached hereto. <input checked="" type="checkbox"/> was filed on <u>December 1, 2011</u> as reissue application number <u>13</u> / <u>308,658</u> and was amended on <u>12/1/2011 and 8/8/2012</u> (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. <input type="checkbox"/> 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.) <input type="checkbox"/> by reason of a defective specification or drawing. <input checked="" type="checkbox"/> by reason of the patentee claiming more or less than he had the right to claim in the patent. <input type="checkbox"/> by reason of other errors. | | | |

[Page 1 of 2]

This collection of information is required by 37 CFR 1.175. 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 and 1.14. This collection is estimated to take 30 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, 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.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

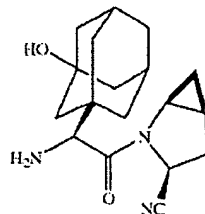
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

| | | | |
|--|---|-----------------------------------|--|
| 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: | | | |
| <input checked="" type="checkbox"/> Practitioners associated with Customer Number: | | 23377 | |
| OR | | | |
| <input type="checkbox"/> 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: | | | |
| <input checked="" type="checkbox"/> The address associated with Customer Number: | | 23377 | |
| OR | | | |
| <input type="checkbox"/> 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  |
| 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

David J. Augeri

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3 Easton Court

Lawrenceville, NJ 08648



UNITED STATES PATENT AND TRADEMARK OFFICE


UNITED STATES DEPARTMENT OF COMMERCE
U.S. Patent and Trademark Office

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Alexandria, Virginia 22313-1450
www.uspto.gov

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

| | | |
|---|--------------------------------------|------------------------------------|
| 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




UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
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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

| | | |
|---|---------------------------------------|-------------------------------------|
| 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
Application No.: 13/308,658
Office Action Dated: May 8, 2012

PATENT

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

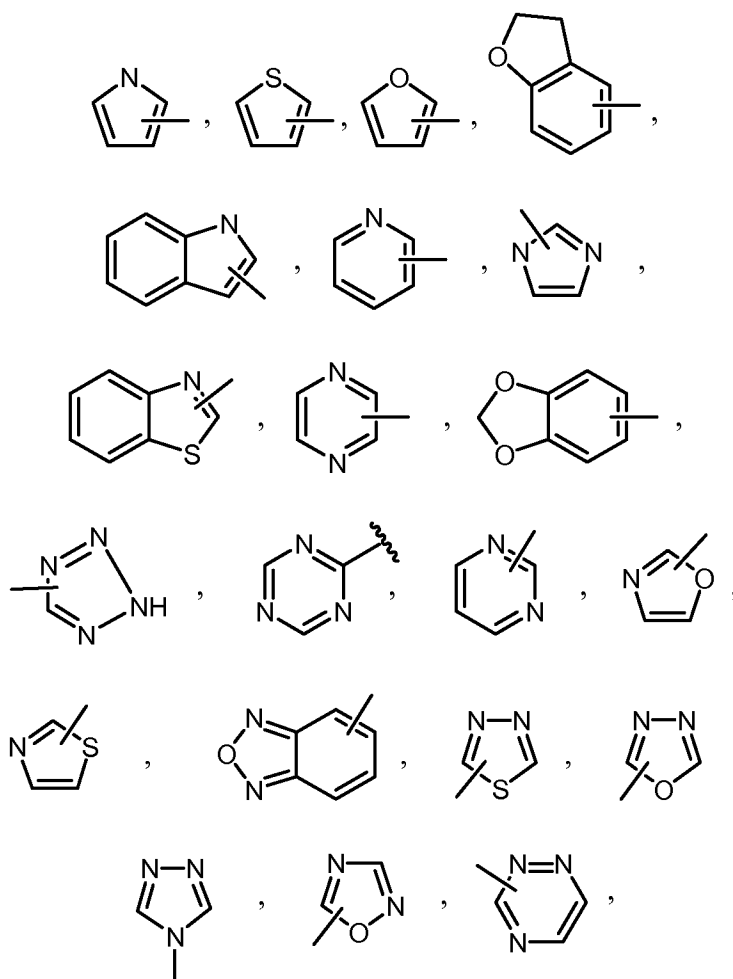
In further response to the Official Action dated **May 8, 2012**, reconsideration is respectfully requested in view of the amendments and/or remarks as indicated below:

- 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 1 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:

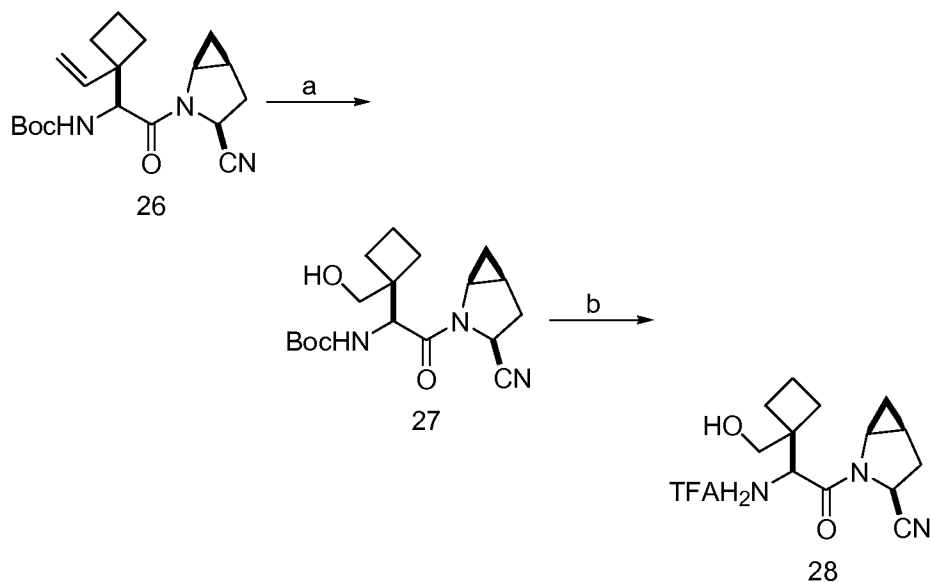
The term "cycloheteroalkylalkyl" as used herein alone or as part of another group refers to cycloheteroalkyl groups as defined above linked through a C atom or heteroatom to a (CH₂)_r chain.

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:

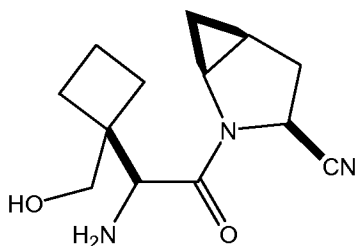
To a flame-dried 500-mL round-bottomed flask containing cyclopentylideneacetic acid ethyl ester (17.5 g, 113 mmol) in 100 mL anhydrous toluene at -78°C under argon was added DIBAL-H (189 mL of a 1.5 M solution in toluene, 284 mmol, 2.50 equiv) dropwise over a 30 min period through an addition funnel, and the mixture was then allowed to warm to rt, stirring for 18 h. The reaction mixture was then re-cooled 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 Et₂O (200 mL) in a separatory funnel, and the layers were separated. The organic layer was then washed with brine (100 mL), dried (Na₂SO₄), and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, CH₂Cl₂ / 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:

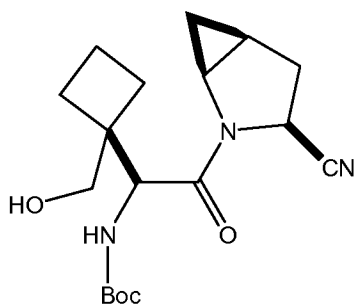
Scheme 7
General Method E, Examples 45-47



a. OsO₄, THF:H₂O, 1:1; NaIO₄; workup, then NaBH₄, MeOH, RT. 56%
b. TFA:CH₂Cl₂, 1:2, 0 degrees C to RT.

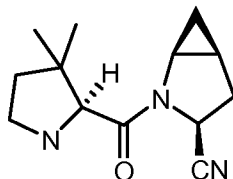


Step 1



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:

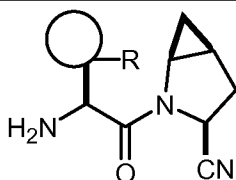
EXAMPLE 67



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 |

DOCKET NO.: BMS-2856
Application No.: 13/308,658
Office Action Dated: May 8, 2012

PATENT

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
2929 Arch Street, 12th Floor
Philadelphia, PA 19104-2891
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) |

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| Document Number | Document Description | File Name | File Size(Bytes)/ Message Digest | Multi Part /.zip | Pages (if appl.) |
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| 1 | Transmittal Letter | BMS-2856_transmittal.PDF | 262602 8e5106d1ec81a16c38e02e973075a62abfcdd811 | no | 2 |

Warnings:

Information:

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|---|--|---|---|-----|---|
| 2 | | BMS-2856_supplemental_response_to_OA_dtd_05-08-2012.PDF | 136534 <small>1c40d87f232354c96586a5ba11ee6350365d5654</small> | 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 | | |
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| TRANSMITTAL FORM <i>(to be used for all correspondence after initial filing)</i> | Application Number | 13/308,658 |
| | Filing Date | December 1, 2011 |
| | First Named Inventor | Jeffrey A. Robol |
| | Art Unit | 1629 |
| | Examiner Name | Gregg Polansky |
| Total Number of Pages in This Submission | 8 | Attorney Docket Number BMS-2856 |

| ENCLOSURES (Check all that apply) | | |
|---|--|--|
| <input type="checkbox"/> Fee Transmittal Form <input type="checkbox"/> Fee Attached <input checked="" type="checkbox"/> Amendment/Reply <input type="checkbox"/> After Final <input type="checkbox"/> Affidavits/declaration(s) <input type="checkbox"/> Extension of Time Request <input type="checkbox"/> Express Abandonment Request <input type="checkbox"/> Information Disclosure Statement <input type="checkbox"/> Certified Copy of Priority Document(s) <input type="checkbox"/> Reply to Missing Parts/ Incomplete Application <input type="checkbox"/> Reply to Missing Parts under 37 CFR 1.52 or 1.53 | <input type="checkbox"/> Drawing(s) <input type="checkbox"/> Licensing-related Papers <input type="checkbox"/> Petition <input type="checkbox"/> Petition to Convert to a Provisional Application <input type="checkbox"/> Power of Attorney, Revocation <input type="checkbox"/> Change of Correspondence Address <input type="checkbox"/> Terminal Disclaimer <input type="checkbox"/> Request for Refund <input type="checkbox"/> CD, Number of CD(s) _____ <input type="checkbox"/> Landscape Table on CD | <input type="checkbox"/> After Allowance Communication to TC <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences <input type="checkbox"/> Appeal Communication to TC (Appeal Notice, Brief, Reply Brief) <input type="checkbox"/> Proprietary Information <input type="checkbox"/> Status Letter <input type="checkbox"/> Other Enclosure(s) (please identify below): |
| Remarks <input style="width: 100px;" type="text"/> 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 |

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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.
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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.



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CIRA CENTRE, 12TH FLOOR
2929 ARCH STREET
PHILADELPHIA, PA 19104-2891

EXAMINER
POLANSKY, GREGG
ART UNIT PAPER NUMBER

1629
DATE MAILED: 02/13/2013

Table with 5 columns: 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

Table with 7 columns: 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.

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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

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Please check the appropriate assignee category or categories (will not be printed on the patent) : Individual Corporation or other private group entity Government

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5. Change in Entity Status (from status indicated above)

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Values: 13/308,658, 12/01/2011, Jeffrey A. Robl, BMS-2856, 7781

23377 7590 02/13/2013
WOODCOCK WASHBURN LLP
CIRA CENTRE, 12TH FLOOR
2929 ARCH STREET
PHILADELPHIA, PA 19104-2891

Table with 2 columns: EXAMINER, ART UNIT, PAPER NUMBER
Values: POLANSKY, GREGG, 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.

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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.
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| | | |
|------------------------|---------------------|--|
| 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. <input type="checkbox"/> Notice of References Cited (PTO-892) | 5. <input type="checkbox"/> Examiner's Amendment/Comment |
| 2. <input type="checkbox"/> Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____ | 6. <input type="checkbox"/> Examiner's Statement of Reasons for Allowance |
| 3. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit of Biological Material | 7. <input type="checkbox"/> Other _____. |
| 4. <input type="checkbox"/> Interview Summary (PTO-413), Paper No./Mail Date _____ . | |

/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. 13308658 | Applicant(s) 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: <input checked="" type="checkbox"/> up to date. <input type="checkbox"/> not required. |
| This reissue patent is subject to A Terminal Disclaimer that: <input type="checkbox"/> was filed during the prosecution of the reissue application. <input type="checkbox"/> was of record prior to the filing of the reissue application. | | |
| Physical surrender of the letters patent <input type="checkbox"/> was made. <input type="checkbox"/> was not made, but a statement of loss/inaccessibility was provided. <input checked="" type="checkbox"/> is not required | | |

| |
|--------------------------|
| Final SPRE Review |
| BC <hr/> (INITIALS) |
| 2/7/2013 <hr/> (DATE) |

U.S. Patent and Trademark Office

| | | |
|--|--|---|
| Search Notes  | Application/Control No. 13308658 | Applicant(s)/Patent Under Reexamination ROBL ET AL. |
| | Examiner GREGG POLANSKY | Art Unit 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. 13308658 | Applicant(s)/Patent Under Reexamination ROBL ET AL. |
| | Examiner GREGG POLANSKY | Art Unit 1629 |

| <input type="checkbox"/> Claims renumbered in the same order as presented by applicant | | | | | | | | | | | | | | | | <input type="checkbox"/> CPA | | <input type="checkbox"/> T.D. | | <input type="checkbox"/> 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 (Assistant Examiner) | 1/24/2013 (Date) | Total Claims Allowed: 41 | |
| (Primary Examiner) | (Date) | O.G. Print Claim(s) 1 | O.G. Print Figure 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. BMS-2856 | |
|---|---|-------------------------------|---|------------------------------------|--------------------------------|
| 13/308,658 | 12/01/2011 | 514 | 1629 | | |
| 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 <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No 35 USC 119(a-d) conditions met <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No Verified and Acknowledged <u>/GREGG POLANSKY/</u> Examiner's Signature | <input type="checkbox"/> Met after Allowance Initials | STATE OR COUNTRY PA | SHEETS DRAWINGS | TOTAL CLAIMS 40 | INDEPENDENT CLAIMS 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: | | <input type="checkbox"/> All Fees <input type="checkbox"/> 1.16 Fees (Filing) <input type="checkbox"/> 1.17 Fees (Processing Ext. of time) <input type="checkbox"/> 1.18 Fees (Issue) <input type="checkbox"/> Other _____ <input type="checkbox"/> Credit | | |

| | | |
|---|--|---|
| Index of Claims  | Application/Control No. 13308658 | Applicant(s)/Patent Under Reexamination ROBL ET AL. |
| | Examiner GREGG POLANSKY | Art Unit 1629 |

| | |
|---|-----------------|
| ✓ | Rejected |
| = | Allowed |

| | |
|---|-------------------|
| - | Cancelled |
| ÷ | Restricted |

| | |
|---|---------------------|
| N | Non-Elected |
| I | Interference |

| | |
|---|-----------------|
| A | Appeal |
| 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 | ✓ | = | | | | | | |
| 8 | 8 | ✓ | = | | | | | | |
| 9 | 9 | ✓ | = | | | | | | |
| 10 | 10 | ✓ | = | | | | | | |
| 11 | 11 | ✓ | = | | | | | | |
| 12 | 12 | ✓ | = | | | | | | |
| 13 | 13 | ✓ | = | | | | | | |
| 14 | 14 | ✓ | = | | | | | | |
| 15 | 15 | ✓ | = | | | | | | |
| 16 | 16 | ✓ | = | | | | | | |
| 17 | 17 | ✓ | = | | | | | | |
| 18 | 18 | ✓ | = | | | | | | |
| 19 | 19 | ✓ | = | | | | | | |
| 20 | 20 | ✓ | = | | | | | | |
| 21 | 21 | ✓ | = | | | | | | |
| 22 | 22 | ✓ | = | | | | | | |
| 23 | 23 | - | - | | | | | | |
| 24 | 24 | - | - | | | | | | |
| 25 | 25 | ✓ | = | | | | | | |
| 26 | 26 | ✓ | = | | | | | | |
| 27 | 27 | ✓ | = | | | | | | |
| 28 | 28 | ✓ | = | | | | | | |
| 29 | 29 | ✓ | = | | | | | | |
| 30 | 30 | ✓ | = | | | | | | |
| 31 | 31 | ✓ | = | | | | | | |
| 32 | 32 | ✓ | = | | | | | | |
| 33 | 33 | ✓ | = | | | | | | |
| 34 | 34 | ✓ | = | | | | | | |
| 35 | 35 | ✓ | = | | | | | | |
| | 36 | ✓ | - | | | | | | |

| | | |
|--|--|---|
| <i>Index of Claims</i>  | Application/Control No. 13308658 | Applicant(s)/Patent Under Reexamination ROBL ET AL. |
| | Examiner GREGG POLANSKY | Art Unit 1629 |

| | |
|---|-----------------|
| ✓ | Rejected |
| = | Allowed |

| | |
|---|-------------------|
| - | Cancelled |
| ÷ | Restricted |

| | |
|---|---------------------|
| N | Non-Elected |
| I | Interference |

| | |
|---|-----------------|
| A | Appeal |
| 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 | | | | | | |
| | 37 | ✓ | - | | | | | | |
| 36 | 38 | ✓ | = | | | | | | |
| 37 | 39 | ✓ | = | | | | | | |
| 38 | 40 | ✓ | = | | | | | | |
| 39 | 41 | | = | | | | | | |
| 40 | 42 | | = | | | | | | |
| 41 | 43 | | = | | | | | | |
| 42 | 44 | | = | | | | | | |
| 43 | 45 | | = | | | | | | |

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450**
or Fax **(571)-273-2885**

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.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

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.

23377 7590 02/13/2013
WOODCOCK WASHBURN LLP
CIRA CENTRE, 12TH FLOOR
2929 ARCH STREET
PHILADELPHIA, PA 19104-2891

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

| | |
|---|--|
| <p>1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).</p> <p><input type="checkbox"/> Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.</p> <p><input type="checkbox"/> "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.</p> | <p>2. For printing on the patent front page, list</p> <p>(1) the names of up to 3 registered patent attorneys or agents OR, alternatively, 1 _____</p> <p>(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. 2 <u>Woodcock Washburn LLP</u></p> <p>3 _____</p> |
|---|--|

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)

Bristol-Myers Squibb Company **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

| | |
|--|--|
| <p>4a. The following fee(s) are submitted:</p> <p><input checked="" type="checkbox"/> Issue Fee</p> <p><input type="checkbox"/> Publication Fee (No small entity discount permitted)</p> <p><input type="checkbox"/> Advance Order - # of Copies _____</p> | <p>4b. Payment of Fee(s); (Please first reapply any previously paid issue fee shown above)</p> <p><input type="checkbox"/> A check is enclosed.</p> <p><input type="checkbox"/> Payment by credit card. Form PTO-2038 is attached.</p> <p><input checked="" type="checkbox"/> The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number <u>233050</u> (enclose an extra copy of this form).</p> |
|--|--|

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:

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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;

The United States represents the largest, most dynamic marketplace in the world and is an unparalleled location for business investment, innovation, and commercialization of new technologies. The USA offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to encourage and facilitate business investment. To learn more about why the USA is the best country in the world to develop technology, manufacture products, and grow your business, visit SelectUSA.gov.

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.

DOCKET NO.: BMS-2856

PATENT

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 "butoxycarbonyl-iso-leucine" and insert -- butoxycarbonyl-iso-leucine --.

Column 33,

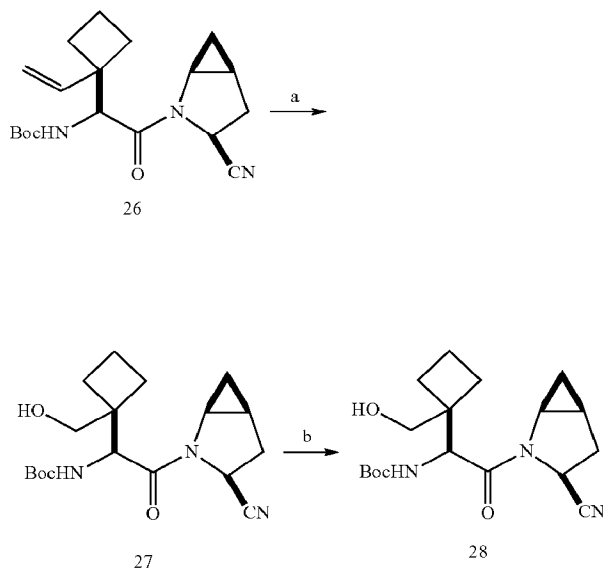
Lines 38-39, delete "1-[(3-dimethylamino)propyl]" and insert -- 1-[(3-dimethylamino)propyl] --.

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



a. OsO₄, THF:H₂O, 1:1; NaIO₄; workup, then NaBH₄, MeOH, RT. 56%
b. TFA:CH₂Cl₂, 1:2, 0 degrees C. to RT.

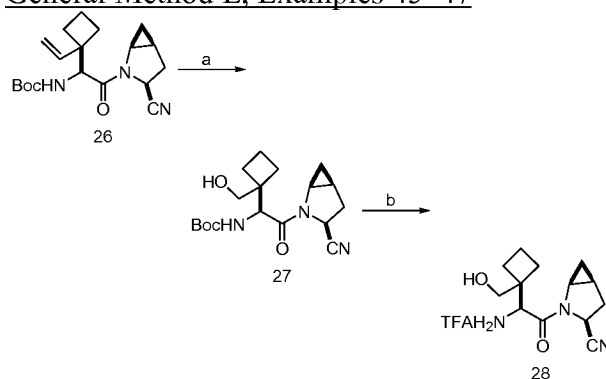
22

**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. OsO₄, THF:H₂O, 1:1; NaIO₄; workup, then NaBH₄, MeOH, RT, 56%
 b. TFA:CH₂Cl₂, 1:2, 0 degrees C to RT.

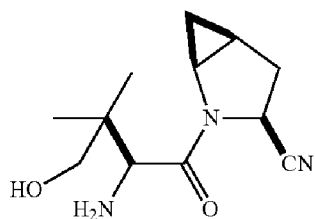
--.

Column 51,
 Line 54, delete "OsO4" and insert -- OsO₄ --.

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

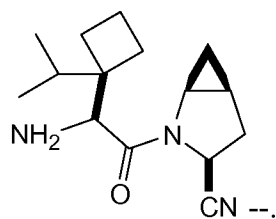
PATENT NO : RE44,186 E
APPLICATION NO. : 13/308,658
ISSUE DATE : April 30, 2013
INVENTOR(S) : Jeffrey A. Robl; Richard B. Sulsky; David J. Augeri; David R. Magnin;
Lawrence G. Hamann; David A. Betebenner

Column 55,
Lines 19-31, EXAMPLE 57, delete “



”

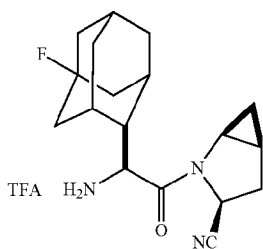
and insert --



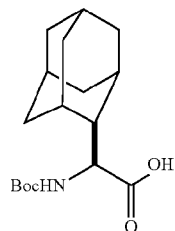
UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

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

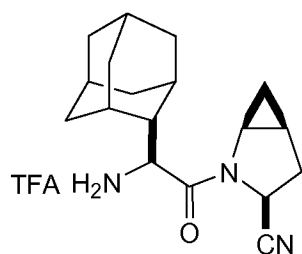


”

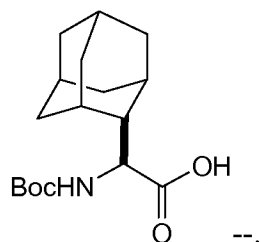
UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

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 "NaHSO₃" and insert -- NaHSO₃ --.

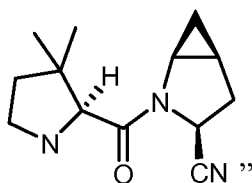
UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

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 “

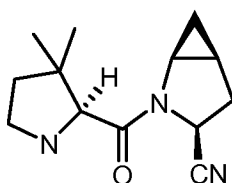
EXAMPLE 67

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 -- R⁴ --.

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:

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| 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 <small>737646480d28b903831e03b6cac6fb353f3ca960</small> | no | 2 |

Warnings:

Information:

| | | | | | |
|---|---------------------------------------|-------------------------|--|----|---|
| 2 | Request for Certificate of Correction | BMS-2856ReqCertCorr.PDF | 79227 | no | 2 |
| | | | 213fd4d2d20f04bd0a7d68fb5ba2c2aa8db7a560 | | |

Warnings:

Information:

| | | | | | |
|---|---------------------------------------|----------------------|---------------------------------------|----|---|
| 3 | Request for Certificate of Correction | BMS-2856CertCorr.PDF | 137994 | no | 8 |
| | | | 97e3cffe5eb7df3ce58ae7eae4e54e2adb3ae | | |

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|-------------------------------------|--|--|--------|--|--|
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New Applications Under 35 U.S.C. 111

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National Stage of an International Application under 35 U.S.C. 371

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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.

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| | | |
|--|----------------------|------------------------------------|
| TRANSMITTAL FORM <i>(to be used for all correspondence after initial filing)</i> | Application Number | 13/308,658 |
| | Filing Date | December 1, 2011 |
| | First Named Inventor | Jeffrey A. Robl |
| | Art Unit | 1629 |
| | Examiner Name | Gregg Polansky |
| Total Number of Pages in This Submission | 12 | Attorney Docket Number BMS-2856 |

| ENCLOSURES (Check all that apply) | | |
|--|--|---|
| <input type="checkbox"/> Fee Transmittal Form <input type="checkbox"/> Fee Attached <input type="checkbox"/> Amendment/Reply <input type="checkbox"/> After Final <input type="checkbox"/> Affidavits/declaration(s) <input type="checkbox"/> Extension of Time Request <input type="checkbox"/> Express Abandonment Request <input type="checkbox"/> Information Disclosure Statement <input type="checkbox"/> Certified Copy of Priority Document(s) <input type="checkbox"/> Reply to Missing Parts/ Incomplete Application <input type="checkbox"/> Reply to Missing Parts under 37 CFR 1.52 or 1.53 | <input type="checkbox"/> Drawing(s) <input type="checkbox"/> Licensing-related Papers <input type="checkbox"/> Petition <input type="checkbox"/> Petition to Convert to a Provisional Application <input type="checkbox"/> Power of Attorney, Revocation <input type="checkbox"/> Change of Correspondence Address <input type="checkbox"/> Terminal Disclaimer <input type="checkbox"/> Request for Refund <input type="checkbox"/> CD, Number of CD(s) _____ <input type="checkbox"/> Landscape Table on CD | <input type="checkbox"/> After Allowance Communication to TC <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences <input type="checkbox"/> Appeal Communication to TC (Appeal Notice, Brief, Reply Brief) <input type="checkbox"/> Proprietary Information <input type="checkbox"/> Status Letter <input checked="" type="checkbox"/> Other Enclosure(s) (please identify below): Request for Certificate of Correction (2 pages) Certificate of Correction (8 pages) |
| <input type="text"/> 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 | | | |
|---|--|------|--|
| 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 | |

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 and 1.14. 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.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

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.

- | | |
|--|---|
| <input type="checkbox"/> Approved | All changes apply. |
| <input type="checkbox"/> Approved in Part | Specify below which changes do not apply. |
| <input type="checkbox"/> 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

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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.

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**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: _____

/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.

Page 1 of 4

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 “butoxycarbonyl-iso-leucine” and insert
-- butoxycarbonyl-iso-leucine --.

Column 33,

Lines 38-39, delete “1-[(3-dimethylamino)propyl]” and insert
-- 1-[(3-dimethyl)amino]propyl] --.

Signed and Sealed this
Eighth Day of October, 2013

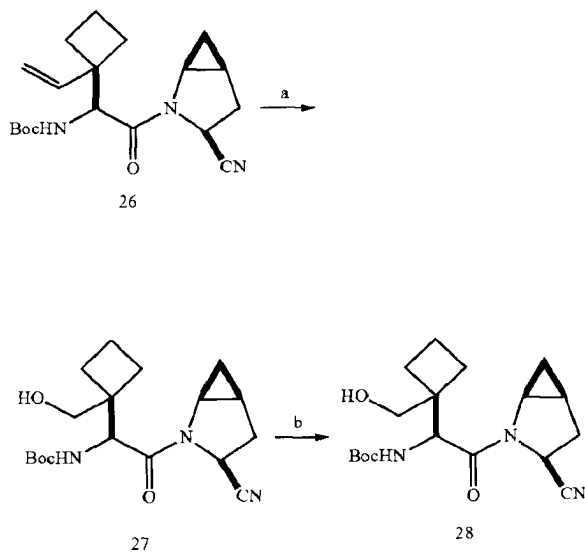


Teresa Stanek Rea
Deputy Director of the United States Patent and Trademark Office

In the Specifications:

Column 51,

Scheme 7
General Method E, Examples 45-47



a. OsO₄, THF:H₂O, 1:1; NaIO₄; workup, then NaBH₄, MeOH, RT. 56%
b. TFA:CH₂Cl₂, 1:2, 0 degrees C. to RT.

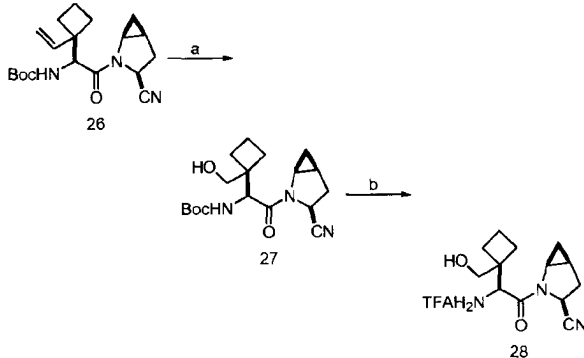
Lines 1-30, delete “

”

and insert

--Scheme 7

General Method E, Examples 45-47



a. OsO₄, THF:H₂O, 1:1; NaIO₄; workup, then NaBH₄, MeOH, RT. 56%
b. TFA:CH₂Cl₂, 1:2, 0 degrees C to RT.

--.

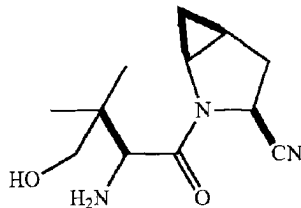
Column 51,

Line 54, delete “OsO₄” and insert -- OsO₄ --.

In the Specifications:

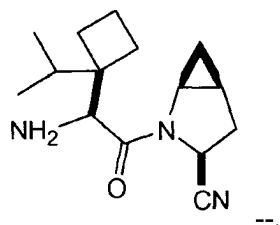
Column 55,

Step 3



Lines 19-31, EXAMPLE 57, delete “

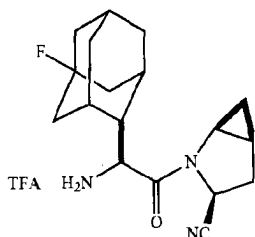
” and



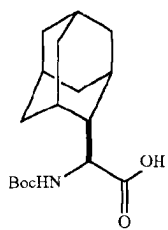
insert --

--.

Column 63,

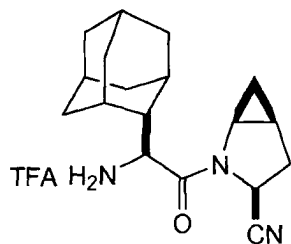


Step 1

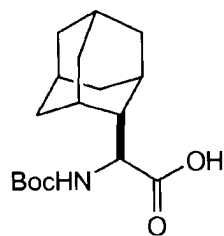


Lines 25-46, EXAMPLE 62, delete “

” and



Step 1



insert --

--.

In the Specifications:

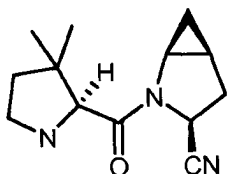
Column 64,

Line 31, delete "NaHSO₃" and insert -- NaHSO₃ --.

Column 69,

EXAMPLE 67

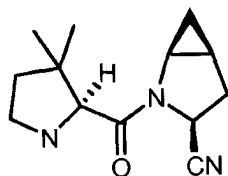
Step 1



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 -- R⁴ --.

Column 92,

Line 21, Claim 36, delete "any one of claim" and insert -- any one of claims --.

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Trademarks or Patents. (the patent action involves 35 U.S.C. § 292.):

| | | |
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| 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 | | |
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In the above—entitled case, the following patent(s)/ trademark(s) have been included:

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| DATE INCLUDED | INCLUDED BY <input type="checkbox"/> Amendment <input type="checkbox"/> Answer <input type="checkbox"/> Cross Bill <input type="checkbox"/> Other Pleading |
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 ___ Trademarks or Patents. (___ the patent action involves 35 U.S.C. § 292.)

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| DOCKET NO. 3:14-cv-03552-MLC-DEA | DATE FILED 6/3/2014 | U.S. DISTRICT COURT TRENTON, NJ |
| PLAINTIFF ASTRAZENECA AB | | DEFENDANT 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 | | |
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In the above—entitled case, the following patent(s)/ trademark(s) have been included:

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| 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:

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| CLERK William T. Walsh | (BY) DEPUTY CLERK s/ Marlene Kalbach | DATE 6/3/2014 |
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Trademarks or Patents. (the patent action involves 35 U.S.C. § 292.):

| | | |
|-----------------------------|-----------------------------|--|
| DOCKET NO. | DATE FILED 6/2/2014 | U.S. DISTRICT COURT District of Delaware |
| PLAINTIFF ASTRAZENECA AB | | DEFENDANT 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 |
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| DOCKET NO. | DATE FILED 6/2/2014 | U.S. DISTRICT COURT District of Delaware |
| PLAINTIFF ASTRAZENECA AB | | DEFENDANT 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 |
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| DOCKET NO. | DATE FILED 6/2/2014 | U.S. DISTRICT COURT District of Delaware |
| PLAINTIFF ASTRAZENECA AB | | DEFENDANT 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 |
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| DOCKET NO. | DATE FILED 6/3/2014 | U.S. DISTRICT COURT Northern District of West Virginia |
| PLAINTIFF ASTRAZENECA AB | | DEFENDANT MYLAN PHARMACEUTICALS, INC. |
| JUN 3 2014 U.S. DISTRICT COURT-WVA WHEELING, WV 26003 | | |
| 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 |
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| DOCKET NO. | DATE FILED 8/15/2014 | U.S. DISTRICT COURT for the District of Delaware |
| PLAINTIFF ASTRAZENECA AB | | DEFENDANT 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 |
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 ___ Trademarks or Patents. (___ the patent action involves 35 U.S.C. § 292.)

| | | |
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| DOCKET NO. 3:14-cv-03552-MLC-DEA | DATE FILED 6/3/2014 | U.S. DISTRICT COURT TRENTON, NJ |
| PLAINTIFF ASTRAZENECA AB | | DEFENDANT 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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| | | |
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| DOCKET NO. 14-cv-5513 (KSH) | DATE FILED 9/3/2014 | U.S. DISTRICT COURT District of New Jersey |
| PLAINTIFF LifePort Sciences LLC | | DEFENDANT 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 |
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| CLERK WILLIAM T. WALSH | (BY) DEPUTY CLERK LEROY DUNBAR | DATE 9/3/2014 |
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| | | |
|---------------------------------|-----------------------------|---|
| DOCKET NO. | DATE FILED 10/31/2014 | U.S. DISTRICT COURT for the District of Delaware |
| PLAINTIFF ASTRAZENECA AB | | DEFENDANT 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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| 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 |
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In the above—entitled case, the following decision has been rendered or judgement issued:

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| DECISION/JUDGEMENT |
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| CLERK | (BY) DEPUTY CLERK | DATE |
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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