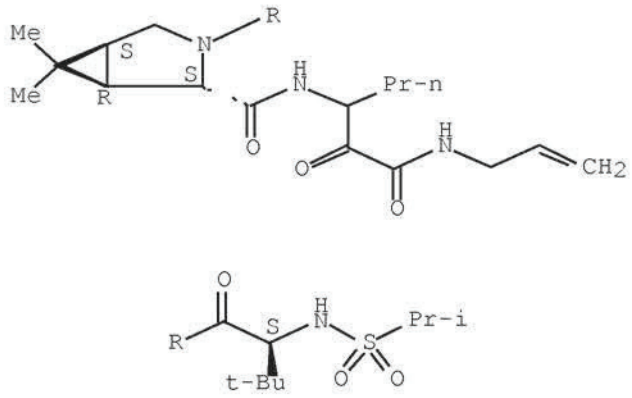
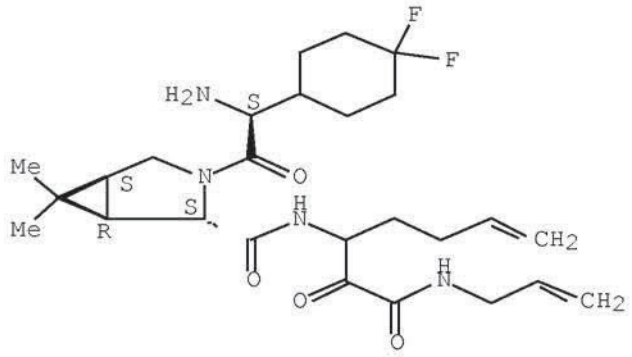


RN 394726-95-5 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carboxamide,

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)

EXHIBIT
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Part 2

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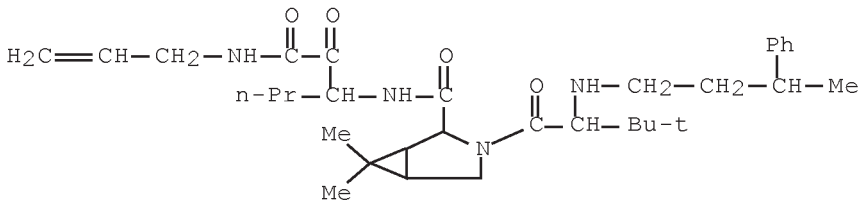
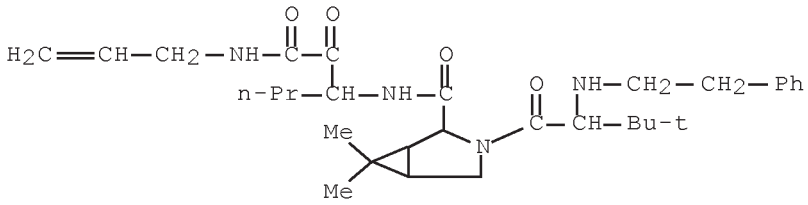


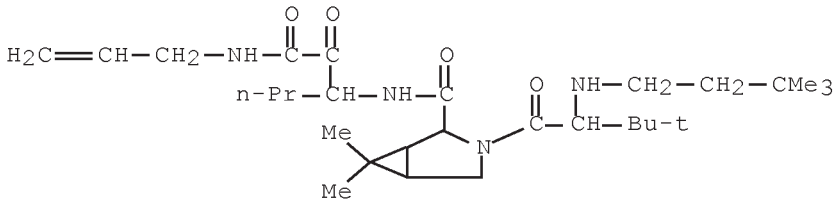
RN 394727-14-1 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carboxamide,

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



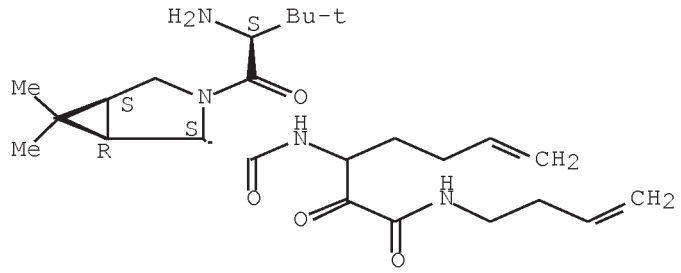
RN 394727-15-2 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carboxamide,

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

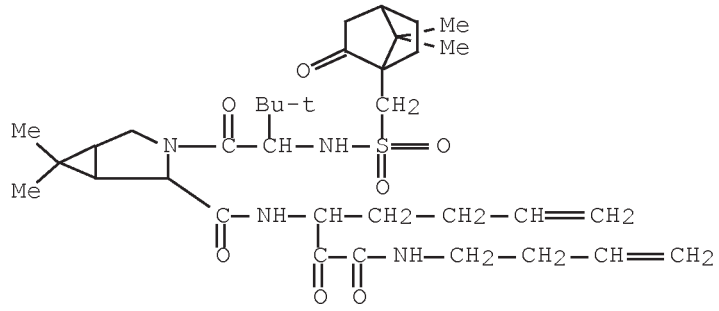


RN 394727-18-5 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carboxamide,
3-[(2S)-2-amino-3,3-dimethyl-1-oxobutyl]-N-[1-[2-(3-buten-1-ylamino)-2-oxoacetyl]-4-penten-1-yl]-6,6-dimethyl-, (1R,2S,5S)- (CA INDEX NAME)

Absolute stereochemistry.

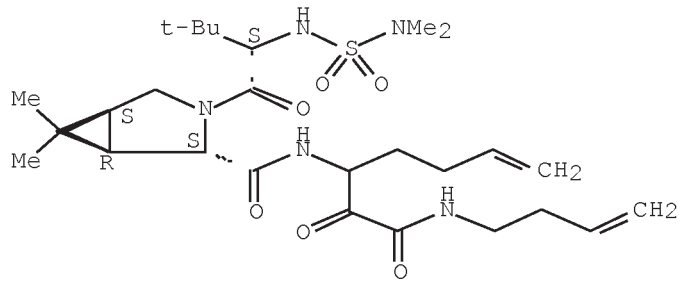


RN 394727-36-7 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carboxamide, N-[1-[2-(3-buten-1-ylamino)-2-oxoacetyl]-4-penten-1-yl]-3-[(2S)-2-[[[[(1R,4S)-7,7-dimethyl-2-oxobicyclo[2.2.1]hept-1-yl]methyl]sulfonyl]amino]-3,3-dimethyl-1-oxobutyl]-6,6-dimethyl-, (1R,2S,5S)- (CA INDEX NAME)



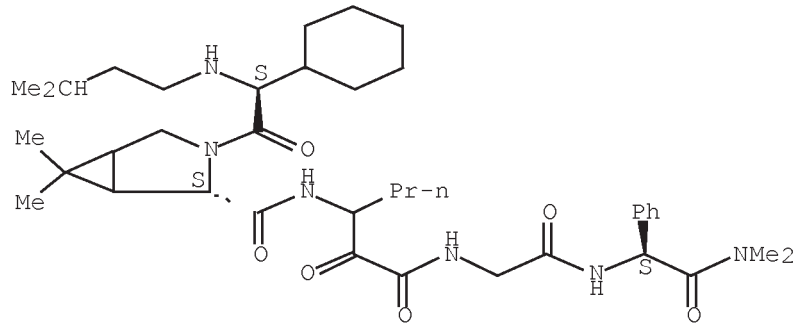
RN 394727-38-9 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carboxamide, N-[1-[2-(3-buten-1-ylamino)-2-oxoacetyl]-4-penten-1-yl]-3-[(2S)-2-[[(dimethylamino)sulfonyl]amino]-3,3-dimethyl-1-oxobutyl]-6,6-dimethyl-, (1R,2S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



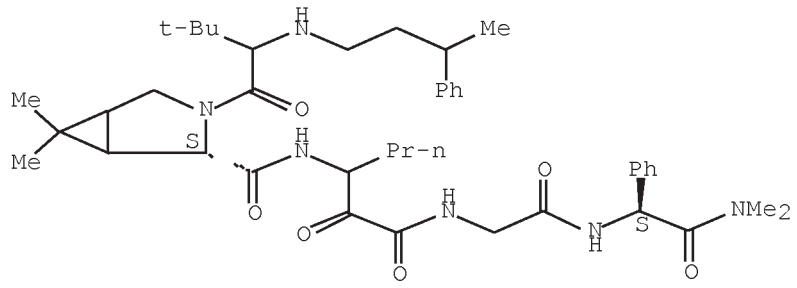
RN 395649-30-6 HCAPLUS
CN Glycinamide,
(2S)-2-cyclohexyl-N-(3-methylbutyl)glycyl-(2S)-6,6-dimethyl-3-azabicyclo[3.1.0]hexane-2-carbonyl-3-amino-2-oxohexanoylglycyl-N,N-dimethyl-2-phenyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



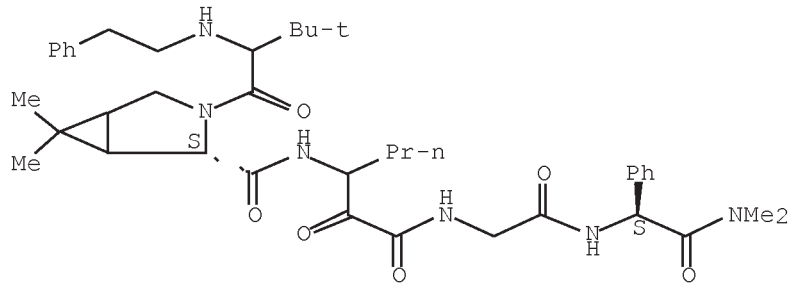
RN 395649-34-0 HCAPLUS
CN Glycinamide, 3-methyl-N-(3-phenylbutyl)valyl-(2S)-6,6-dimethyl-3-azabicyclo[3.1.0]hexane-2-carbonyl-3-amino-2-oxohexanoylglycyl-N,N-dimethyl-2-phenyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



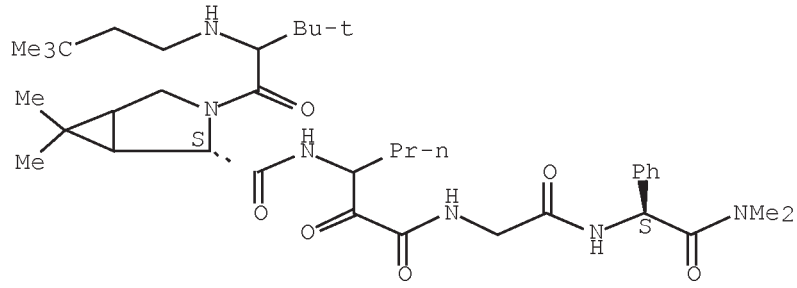
RN 395649-35-1 HCAPLUS
CN Glycinamide, 3-methyl-N-(2-phenylethyl)valyl-(2S)-6,6-dimethyl-3-azabicyclo[3.1.0]hexane-2-carbonyl-3-amino-2-oxohexanoylglycyl-N,N-dimethyl-2-phenyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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

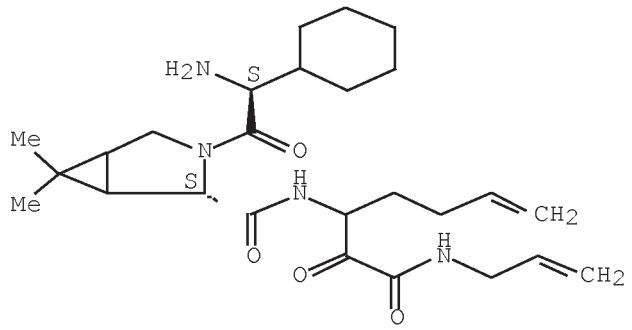
Absolute stereochemistry.



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

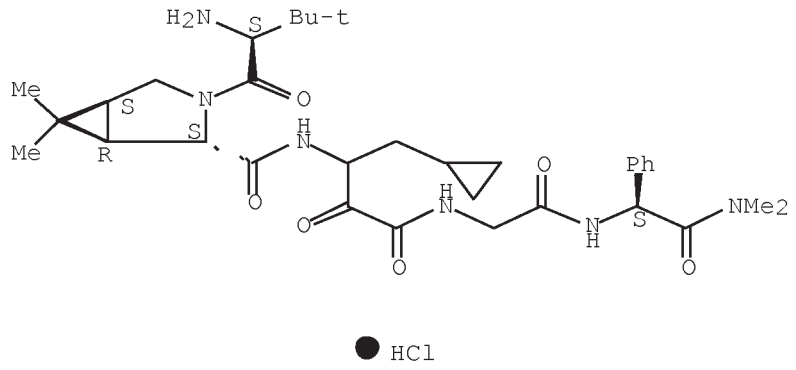
3-[(2S)-2-amino-2-cyclohexylacetyl]-6,6-dimethyl-N-[1-[2-oxo-2-(2-propen-1-ylamino)acetyl]-4-penten-1-yl]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



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

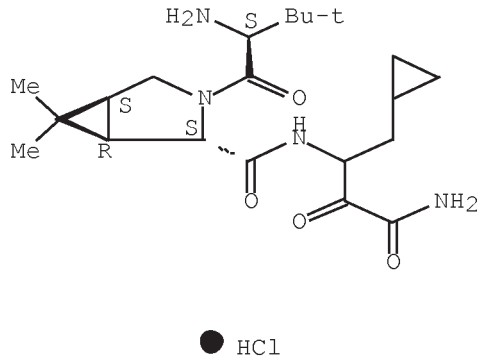
Absolute stereochemistry.



● HCl

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

Absolute stereochemistry.



● HCl

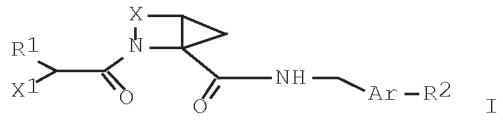
OS.CITING REF COUNT: 35 THERE ARE 35 CAPLUS RECORDS THAT CITE THIS RECORD (40 CITINGS)

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

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

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

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



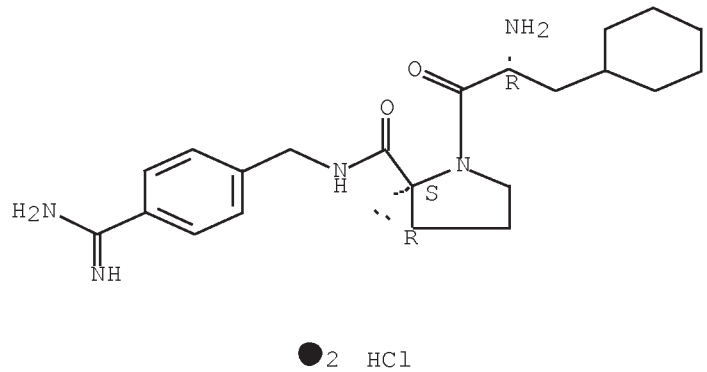
I

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

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

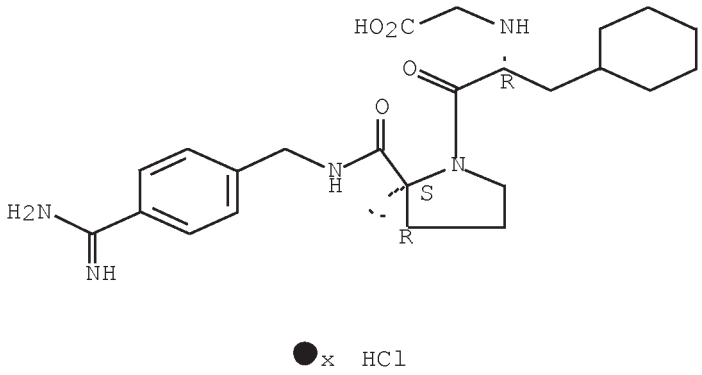
IT 304910-16-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 2,3-methano-amino acid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

Absolute stereochemistry.



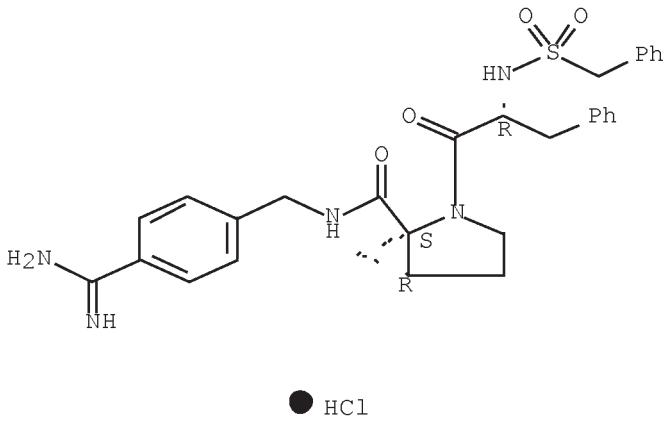
IT 304910-17-6P 304910-19-8P 304910-20-1P
304910-21-2P 304910-22-3P 304910-23-4P
304910-24-5P 304910-26-7P 304910-27-8P
304910-28-9P 304910-29-0P 304910-71-2P
304910-72-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU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

Absolute stereochemistry.



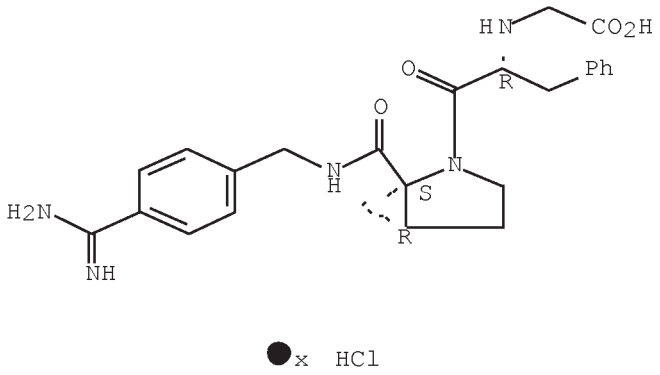
RN 304910-19-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-1-carboxamide, N-[[4-(aminoiminomethyl)phenyl]methyl]-2-[(2R)-1-oxo-3-phenyl-2-[[(phenylmethyl)sulfonyl]amino]propyl]-, hydrochloride (1:1), (1S,5R)-(CA INDEX NAME)

Absolute stereochemistry.



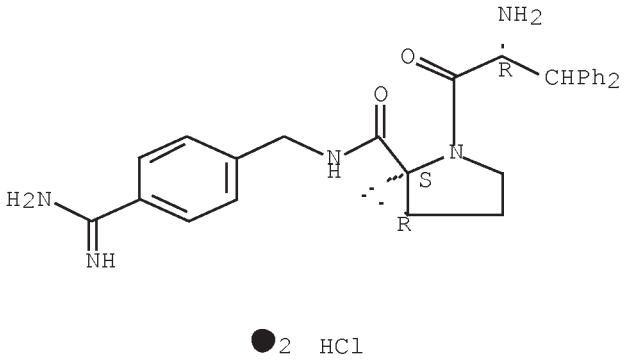
RN 304910-20-1 HCAPLUS
CN Glycine, N-[(1R)-2-[(1S,5R)-1-[[[[4-(aminoiminomethyl)phenyl]methyl]amino]carbonyl]-2-azabicyclo[3.1.0]hex-2-yl]-2-oxo-1-(phenylmethyl)ethyl]-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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)

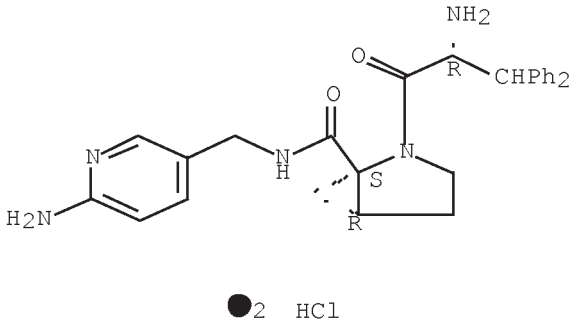
Absolute stereochemistry.



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)

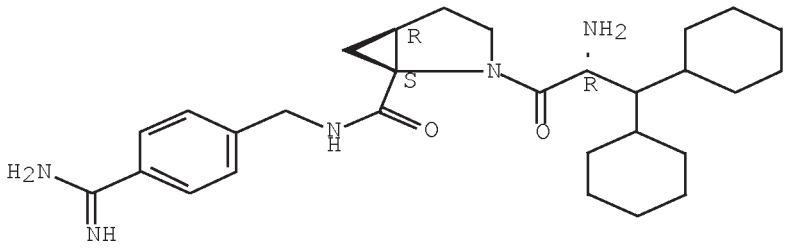
Absolute stereochemistry.



●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)

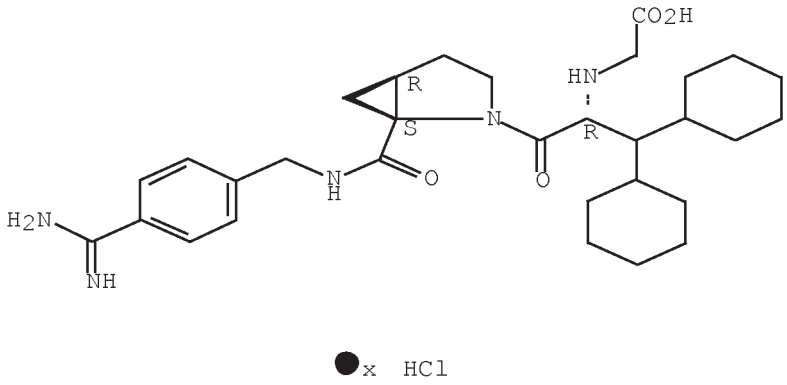
Absolute stereochemistry.



●2 HCl

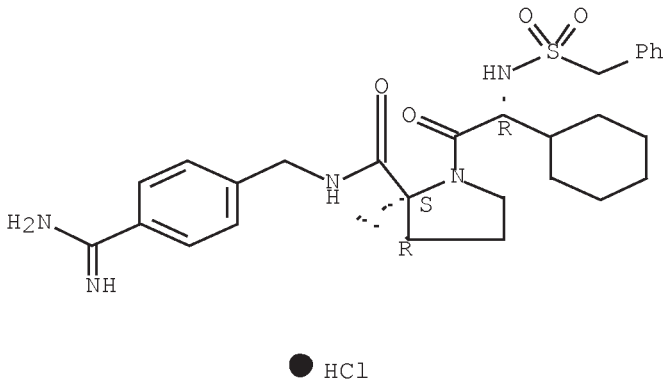
RN 304910-24-5 HCAPLUS
CN Glycine, N-[(1R)-2-[(1S,5R)-1-[[[[4-(aminoiminomethyl)phenyl]methyl]amino]carbonyl]-2-azabicyclo[3.1.0]hex-2-yl]-1-(dicyclohexylmethyl)-2-oxoethyl]-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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)

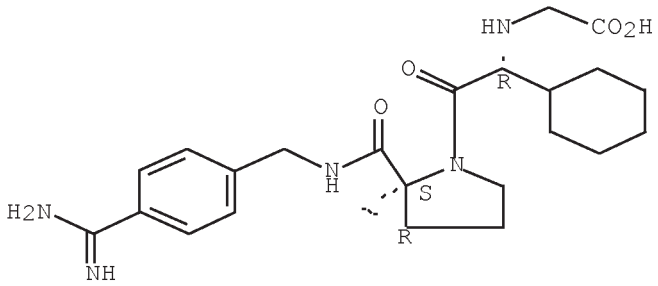
Absolute stereochemistry.



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.

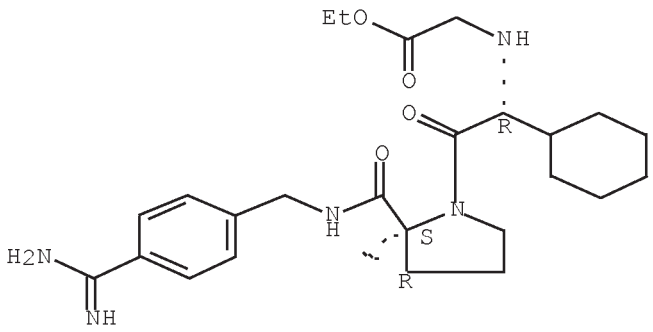


●x HCl

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.

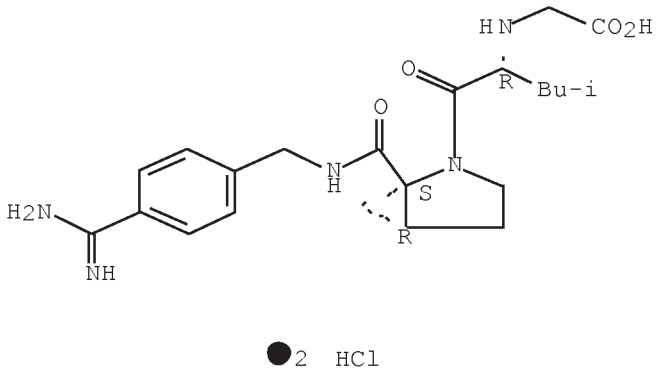


●2 HCl

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

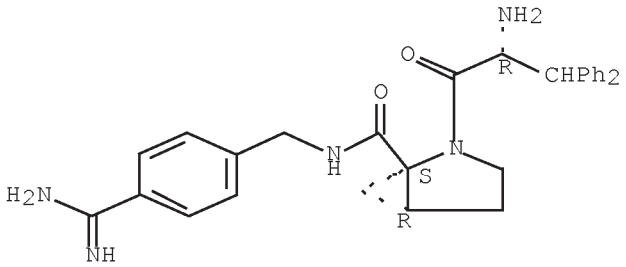
(aminoiminomethyl)phenyl]methyl]amino]carbonyl]-2-azabicyclo[3.1.0]hex-2-yl]carbonyl]-3-methylbutyl]-, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



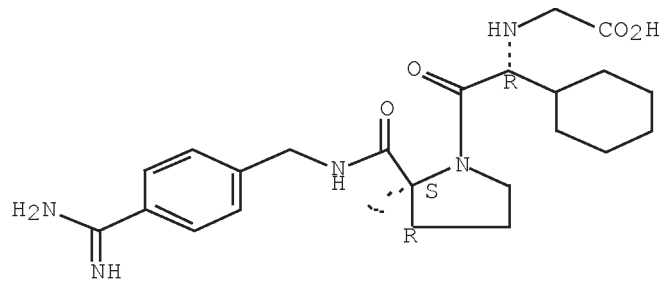
RN 304910-71-2 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-1-carboxamide, N-[[4-(aminoiminomethyl)phenyl]methyl]-2-[(2R)-2-amino-1-oxo-3,3-diphenylpropyl]-, (1S,5R)- (CA INDEX NAME)

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)

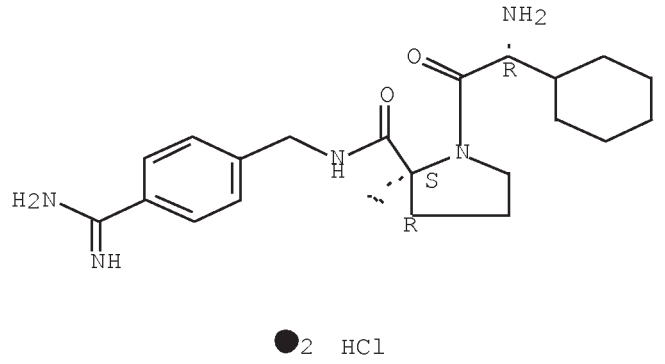
Absolute stereochemistry.



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,

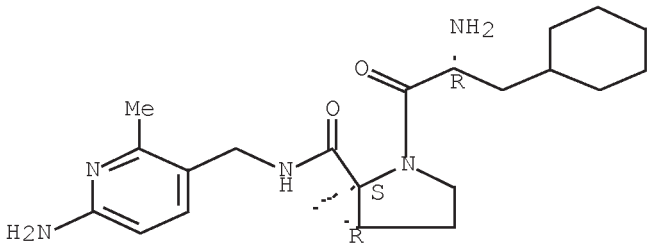
2-[(2R)-2-amino-2-cyclohexylacetyl]-N-[[4-(aminoiminomethyl)phenyl]methyl]-
, hydrochloride (1:2), (1S,5R)- (CA INDEX NAME)

Absolute stereochemistry.



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

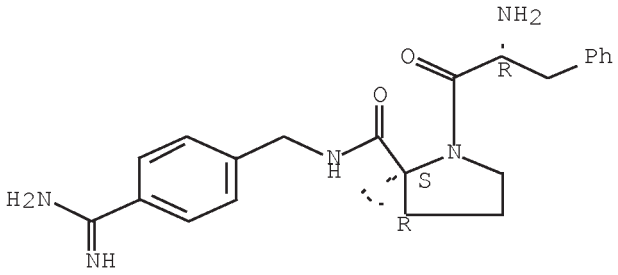
Absolute stereochemistry.



●2 HCl

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

Absolute stereochemistry.



●2 HCl

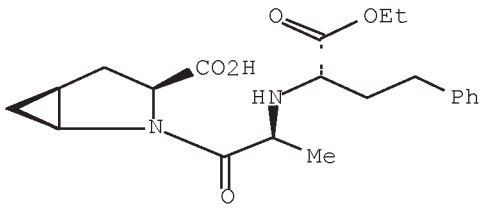
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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

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

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

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

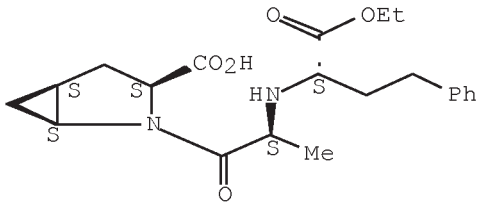


AB The angiotensin-converging enzyme inhibitors R(CH2)nCH(CO2R2)NHCHR1CONR5CHR4CO2R1 (R = H, aliphatic radical, aryl, etc.; R1 = H, aliphatic radical, aryl, heterocyclyl, etc.; R2, R3 = H, aliphatic

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

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

Absolute stereochemistry.



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

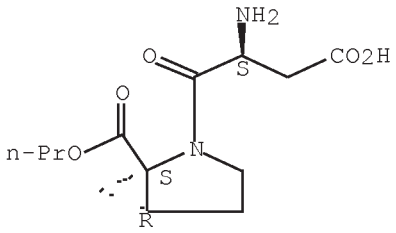
L49 ANSWER 79 OF 87 HCAPLUS COPYRIGHT 2012 ACS on STN
ACCESSION NUMBER: 1991:450274 HCAPLUS Full-text
DOCUMENT NUMBER: 115:50274
ORIGINAL REFERENCE NO.: 115:8757a,8760a
TITLE: Synthesis and conformational analysis of L-aspartylproline and L-aspartyl-2,3-methanoproline propyl esters
AUTHOR(S): Matsui,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

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

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

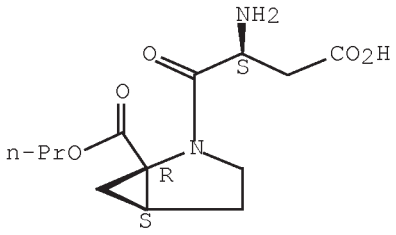
RN 134666-90-3 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-2-butanoic acid, β-amino-γ-oxo-1-(propoxycarbonyl)-, [1S-[1α,2(R*),5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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

Absolute stereochemistry.

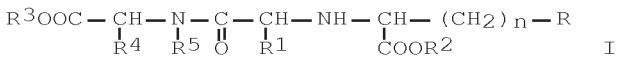


OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

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

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

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



I

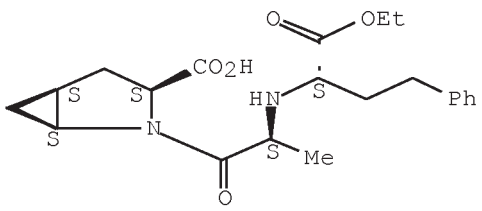
AB ACE inhibitors (I; R = H, optionally substituted C1-8 aliphatic, C3-9 alicyclic, C6-12 aromatic , C7-14 araliph., C7-14 aliphatic-alicyclic hydrocarbyl, SR6, OR6; R1 = H, optionally substituted C1-6 aliphatic, C3-9 alicyclic , C4-13 alicyclic-aliphatic , aryl, C7-16 araliph. hydrocarbyl, C5-12 heteroaryl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

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

RN 99781-97-2 HCAPLUS

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

Absolute stereochemistry.

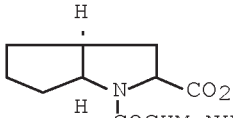


OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

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

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

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



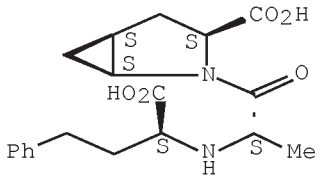
COCHMeNHCH(CO2Et)CH2CH2Ph II

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

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

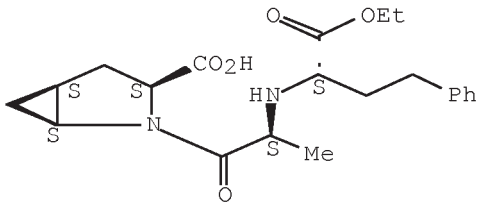
RN 97251-00-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carboxylic acid, 2-[2-[(1-carboxy-3-phenylpropyl)amino]-1-oxopropyl]-, [1S-[1α,2[R*(R*)],3β,5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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

Absolute stereochemistry.

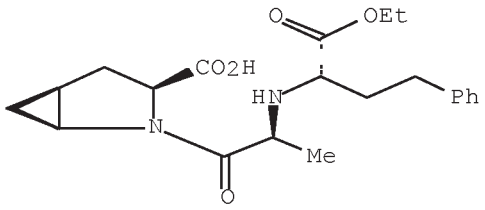


OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)

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

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

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



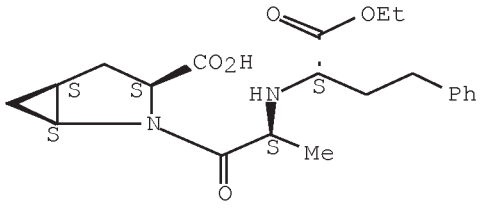
AB The title compds. R3O2CCHR4NR5COCHR1NHCH(CO2R2)(CH2)nR (R = H, alkyl, aryl, R6O, R6S, R6 = alkyl, aryl, etc.; R1 = H, alkyl, aryl, amino acyl, etc.; R2, R3 = H, alkyl, aryl, etc.; R4CHNR5 = heterocyclyl; n = 1, 2) are drugs for the treatment of glaucoma. Thus, tablets were made, containing N-(1-S-carbethoxy-3-phenylpropyl)-S-alanyl-1S,3S,5S-2-azabicyclo[3.3.0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

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

RN 99781-97-2 HCAPLUS

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

Absolute stereochemistry.



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

L49 ANSWER 83 OF 87 HCAPLUS COPYRIGHT 2012 ACS on STN
ACCESSION NUMBER: 1986:207685 HCAPLUS Full-text
DOCUMENT NUMBER: 104:207685
ORIGINAL REFERENCE NO.: 104:32945a,32948a
TITLE: Amino acid derivatives as enzyme inhibitors
INVENTOR(S): Patchett, Arthur A.; Taub, David; Wyvratt, Matthew J. Jr.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: S. African, 81 pp.

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

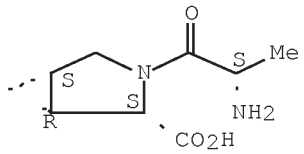
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ZA 8304454	A	19850227	ZA 1983-4454	19830617 <--
PRIORITY APPLN. INFO.:			US 1982-389735 A	19820618 <--

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

CM 1

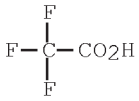
CRN 101952-31-2
CMF C9 H14 N2 O3

Absolute stereochemistry.



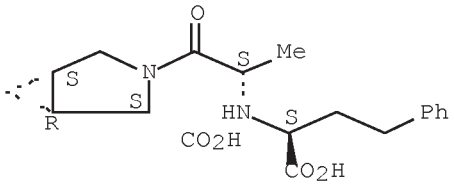
CM 2

CRN 76-05-1
CMF C2 H F3 O2



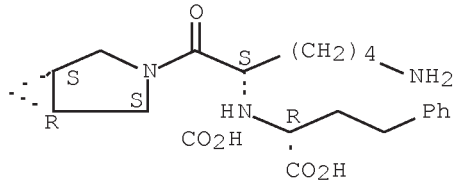
IT 101952-28-7P 101952-30-1P 102044-73-5P
102044-74-6P 102044-75-7P 102044-76-8P
102045-14-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as angiotensin converting enzyme inhibitor)
RN 101952-28-7 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carboxylic acid,
3-[2-[(1-carboxy-3-phenylpropyl)amino]-1-oxopropyl]-,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

Absolute stereochemistry.



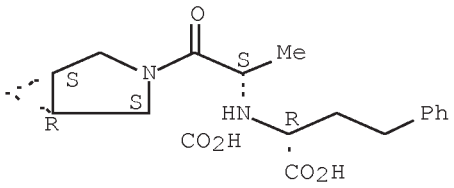
RN 101952-30-1 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carboxylic acid,
3-[6-amino-2-[(1-carboxy-3-phenylpropyl)amino]-1-oxohexyl]-,
[1R-[1α,2β,3[S*(R*)],5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



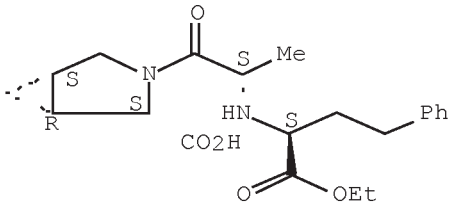
RN 102044-73-5 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carboxylic acid,
3-[2-[(1-carboxy-3-phenylpropyl)amino]-1-oxopropyl]-,
[1R-[1α,2β,3[S*(R*)],5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



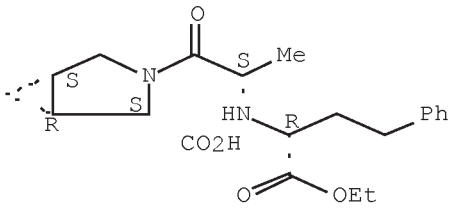
RN 102044-74-6 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carboxylic acid,
3-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-,
[1R-[1α,2β,3[S*(S*)],5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

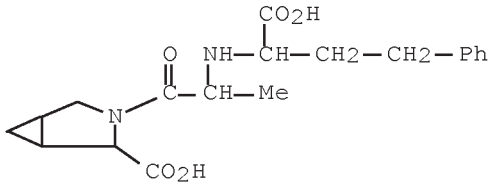


RN 102044-75-7 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carboxylic acid,
3-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-,
[1R-[1α,2β,3[S*(R*)],5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

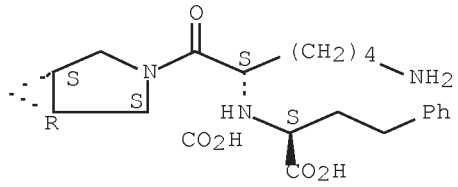


RN 102044-76-8 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carboxylic acid,
3-[2-[(1-carboxy-3-phenylpropyl)amino]-1-oxopropyl]- (CA INDEX NAME)



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

Absolute stereochemistry.

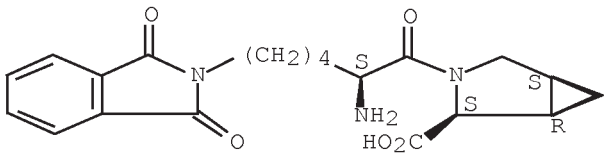


IT 101952-34-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(reductive alkylation of, by glyoxylic acid derivative)
RN 101952-34-5 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carboxylic acid, 3-[2-amino-6-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)-1-oxohexyl]-, [1R-[1α,2β,3(S*),5α]]-, mono(trifluoroacetate)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

CM 1

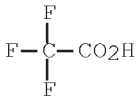
CRN 101952-33-4
CMF C20 H23 N3 O5

Absolute stereochemistry.



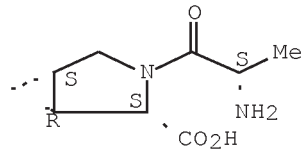
CM 2

CRN 76-05-1
CMF C2 H F3 O2

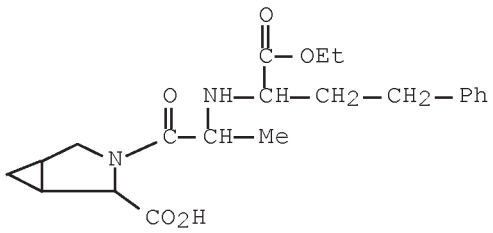


IT 101952-31-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(reductive amination by, of phenyloxobutyric acid)
RN 101952-31-2 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carboxylic acid, 3-(2-amino-1-oxopropyl)-, [1R-[1α,2β,3(S*),5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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

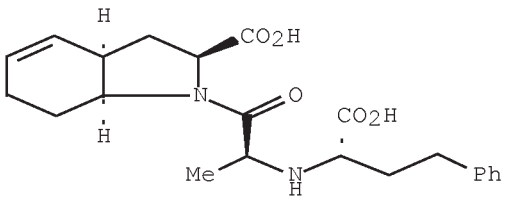


L49 ANSWER 84 OF 87 HCAPLUS COPYRIGHT 2012 ACS on STN
ACCESSION NUMBER: 1986:39761 HCAPLUS Full-text
DOCUMENT NUMBER: 104:39761
ORIGINAL REFERENCE NO.: 104:6423a,6426a
TITLE: Treatment of coronary insufficiency
INVENTOR(S): Henning, Rainer; Urbach, Hansjoerg; Teetz, Volker; Geiger, Rolf; Schoelkens,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

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

PRIORITY APPLN. INFO.: DE 1984-3413710 A 19840412 <--
EP 1985-104028 A 19850403 <--
US 1985-721705 B1 19850410 <--
US 1989-313491 B1 19890222 <--
US 1991-636001 B1 19910103 <--
US 1992-920173 B1 19920727 <--
US 1994-188745 A3 19940131 <--
US 1994-359860 A3 19941220 <--
US 1995-445543 A1 19950522 <--

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 104:39761
ED Entered STN: 08 Feb 1986
GI



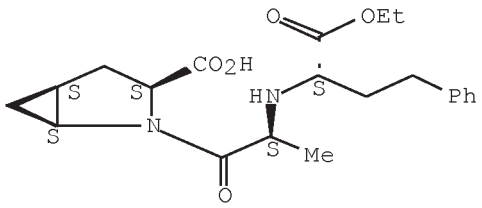
AB The angiotensin-converting enzyme inhibitors R(CH2)nCH(CO2R2)NHCHR1CONR5CHR4CO2R3 [R = H, (un)substituted alkyl, aryl, etc.; R1 = alkyl, cycloalkyl, heterocyclic radical; R2, R3 = H, alkyl, aryl, etc.; R4CHNR2 = heterocyclic radical; n = 1, 2] are drugs for the treatment of cardiac insufficiency.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

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

RN 99781-97-2 HCAPLUS

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

Absolute stereochemistry.



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

L49 ANSWER 85 OF 87 HCAPLUS COPYRIGHT 2012 ACS on STN

ACCESSION NUMBER: 1985:560858 HCAPLUS Full-text

DOCUMENT NUMBER: 103:160858

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

TITLE: N-Alkylated dipeptides and their esters

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

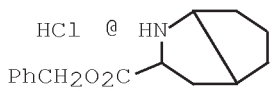
PATENT ASSIGNEE(S): Hoechst A.-G., Fed. Rep. Ger.

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

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

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

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



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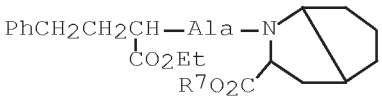


III

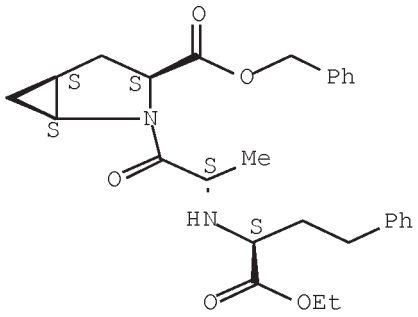
AB Title compds. R3O2CCHR4NR5COCHR1NHCH(CO2R2)(CH2)nR [I; n = 1, 2; R = H, (un)substituted C1-8 aliphatic, C3-9 alicyclic, C6-12 aromatic, C7-14 araliph., or C7-14 alicyclic aliphatic residue, OR6, SR6 [R6 = (un)substituted C1-4 aliphatic, C6-12 aromatic, or heteroarom. residue]; R1 = H, (un)substituted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

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

RN 97250-98-1 HCAPLUS

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

Absolute stereochemistry.



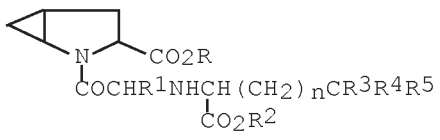
OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

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

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

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

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



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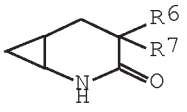

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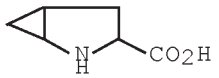
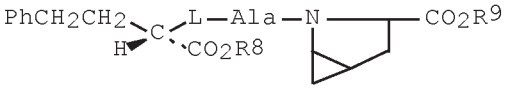


III



IV

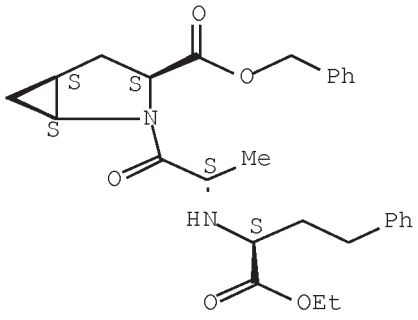
AB Title derivs. I [R = H, C1-6 alkyl, C2-6 alkenyl, (C6-12 aryl)-C1-4 alkyl; R1 = H, (un)substituted C1-6 alkyl, C2-6 alkenyl, C5-9 cycloalkyl, C5-9 cycloalkenyl, etc.; R2 = H, C1-6 alkyl, C2-6 alkenyl, (C6-12 aryl)-C1-4 alkyl; R3 = H, OH, R4 = H; R3R4 = O; R5 = C1-6 alkyl, C2-6 alkenyl, C2-6 alkenyl,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

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

RN 97250-98-1 HCAPLUS

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

Absolute stereochemistry.

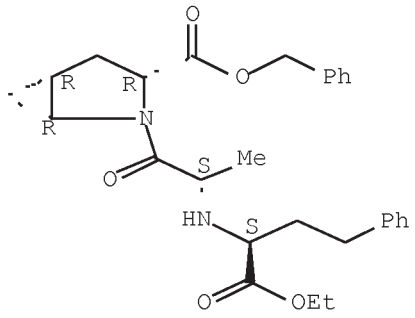


RN 97277-17-3 HCAPLUS

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

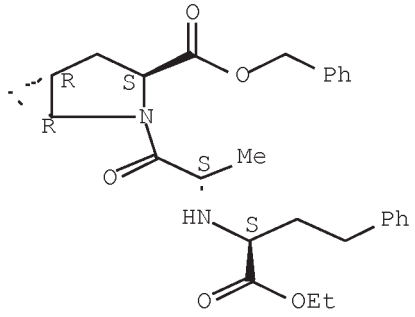
INDEX NAME)

Absolute stereochemistry.



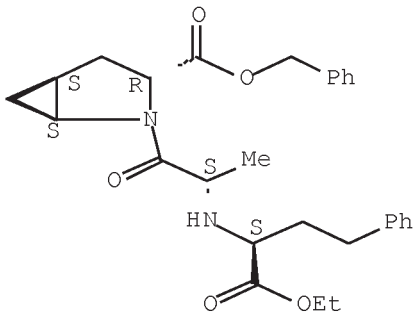
RN 97277-18-4 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-, phenylmethyl ester, [1R-[1α,2[S*(S*)],3α,5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



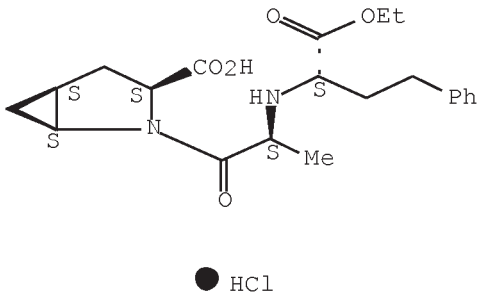
RN 97277-19-5 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-, phenylmethyl ester, [1S-[1α,2[R*(R*)],3α,5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



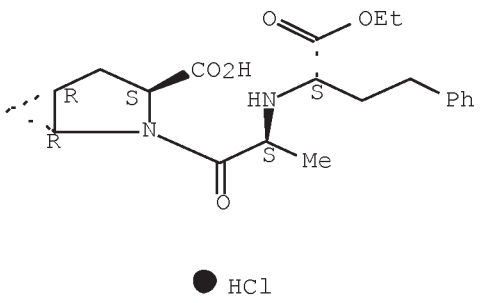
IT 97250-99-2P 97277-21-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and saponification of)
RN 97250-99-2 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-, monohydrochloride,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

Absolute stereochemistry.



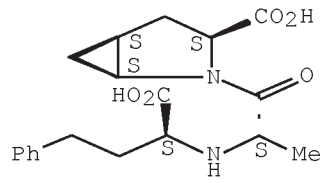
RN 97277-21-9 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-, monohydrochloride, [1R-[1α,2[S*(S*)],3α,5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



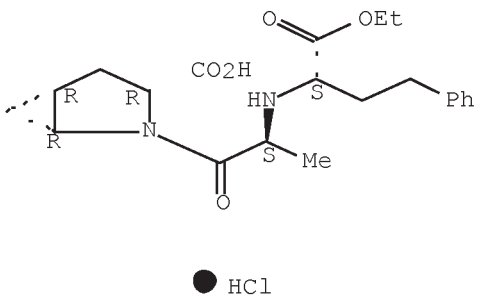
IT 97251-00-8P 97277-20-8P 97277-22-0P
97334-49-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 97251-00-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carboxylic acid,
2-[2-[(1-carboxy-3-phenylpropyl)amino]-1-oxopropyl]-,
[1S-[1α,2[R*(R*)],3β,5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



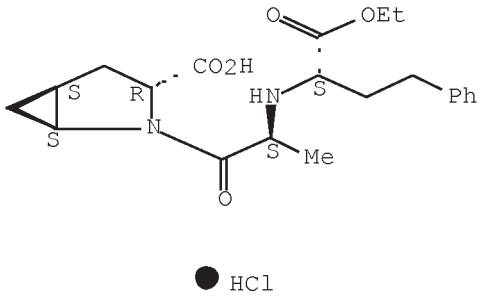
RN 97277-20-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carboxylic acid,
2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-,
monohydrochloride, [1R-[1α,2[S*(S*)],3β,5α]]- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.



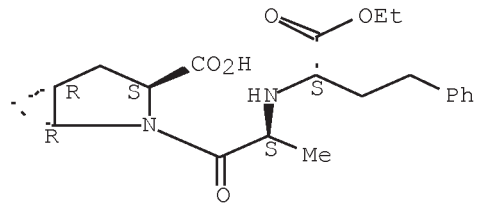
RN 97277-22-0 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-, monohydrochloride, [1S-[1α,2[R*(R*)],3α,5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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

Absolute stereochemistry.

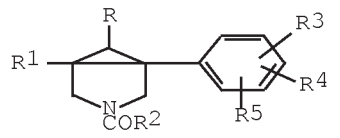


OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)

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

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

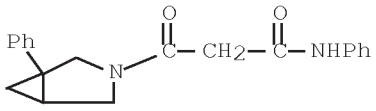
OTHER SOURCE(S): CASREACT 89:129383; MARPAT 89:129383
ED Entered STN: 12 May 1984
GI



I

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

INDEX NAME)



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

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L12              STR
L14         8057 SEA FILE=REGISTRY SSS FUL L12
L17              STR
L19            4 SEA FILE=REGISTRY SUB=L14 SSS FUL L17
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L22         8057 SEA FILE=REGISTRY SUB=L14 SSS FUL L20
L23         8053 SEA FILE=REGISTRY SPE=ON  ABB=ON  PLU=ON  L22 NOT L19
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                 OR L26 OR L27 OR L28 OR L29 OR L30)
L46            0 SEA FILE=HCAPLUS SPE=ON  ABB=ON  PLU=ON  L1 NOT L45
L47           15 SEA FILE=HCAPLUS SPE=ON  ABB=ON  PLU=ON  (L45 OR L46)


=> d his l56

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


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


=> dup rem l47 l56
FILE 'HCAPLUS' ENTERED AT 09:18:09 ON 01 MAY 2012
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE 'EMBASE' ENTERED AT 09:18:09 ON 01 MAY 2012
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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).
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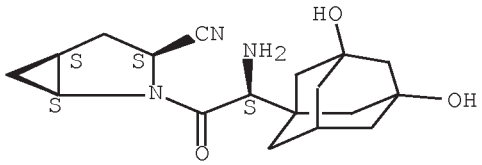
=> d ibib ed abs hitstr 1-15
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, EMBASE' - CONTINUE? (Y)/N:y

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

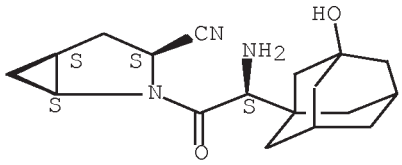
(pharmacokinetics of dipeptidyl peptidase 4 inhibitor saxagliptin in rats, dogs, and monkeys and clin. projections)
RN 841302-24-7 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(3,5-dihydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



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

Absolute stereochemistry.

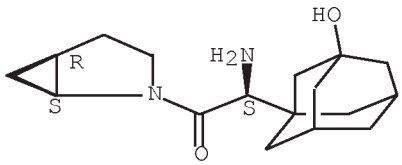


OS.CITING REF COUNT: 20 THERE ARE 20 CAPLUS RECORDS THAT CITE THIS RECORD (20 CITINGS)
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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

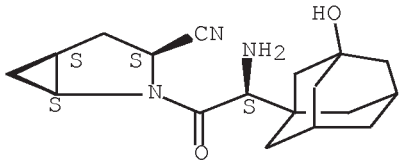
Zhang, Yaqun; Corbett, Martin; Tamura, James K.; He, Bin; Hamann, Lawrence G.; Kirby, Mark S.; Marcinkeviciene, Jovita
CORPORATE SOURCE: Department of Molecular Biosciences, Bristol-Myers Squibb Research and Development, Princeton, NJ, 08543-4000, USA
SOURCE: Protein Science (2008), 17(2), 240-250
CODEN: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

Absolute stereochemistry.



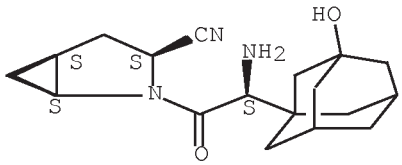
IT 361442-04-8DP, Saxagliptin, complex with dipeptidyl peptidase IV
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation)
(involvement of dipeptidyl peptidase-IV catalytic residues in enzyme-saxagliptin complex formation)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

Absolute stereochemistry.



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

Absolute stereochemistry.



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

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

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

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

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

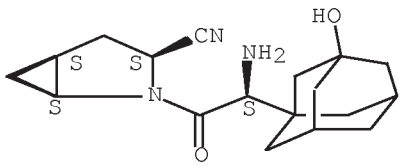
compds. include chemical-modified peptides that not only stimulate insulin secretion in type II diabetics, but also produce other beneficial insulinotropic responses. These synthetic peptide GLP-1 receptor modulators exhibit increased stability to proteolytic cleavage making them ideal therapeutic candidates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

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

RN 361442-04-8 HCAPLUS

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

Absolute stereochemistry.



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

L57 ANSWER 4 OF 16 HCAPLUS COPYRIGHT 2012 ACS on STN DUPLICATE 4

ACCESSION NUMBER: 2007:1279241 HCAPLUS Full-text

DOCUMENT NUMBER: 148:121939

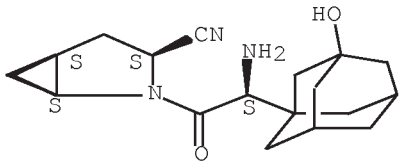
TITLE: Potent non-nitrile dipeptidic dipeptidyl peptidase IV inhibitors

AUTHOR(S): Simpkins, Ligaya M.; Bolton, Scott; Pi, Zulan; Sutton, James C.; Kwon, Chet; Zhao, Guohua; Magnin, David R.; Augeri, David J.; Gungor, Timur; Rotella, David P.; Sun, Zhong; Liu, Yajun; Slusarchyk, William S.; Marcinkeviciene, Jovita; Robertson, James G.; Wang, Aiying; Robl, 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

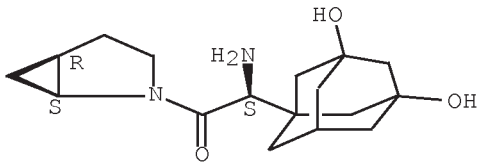
SOURCE: Bioorganic & Medicinal Chemistry Letters (2007), 17(23), 6476-6480
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 148:121939
ED Entered STN: 09 Nov 2007
AB The synthesis and structure-activity relationships of novel dipeptidyl 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[3.3.1.13,7]dec-1-yl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



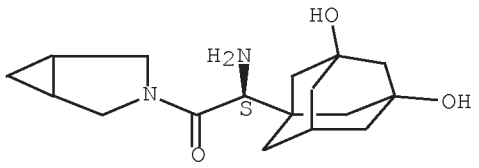
IT 841302-21-4P 841302-27-0P 841302-28-1P
841302-51-0P 1000689-35-9P 1000689-36-0P
1000689-37-1P 1000689-38-2P 1000689-39-3P
1000689-40-6P 1000689-41-7P 1000689-43-9P
1000689-44-0P 1000689-45-1P 1000689-46-2P
1000689-47-3P 1000689-48-4P 1000689-49-5P
1000689-50-8P 1000689-52-0P 1000689-53-1P
1000689-54-2P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

Absolute stereochemistry.



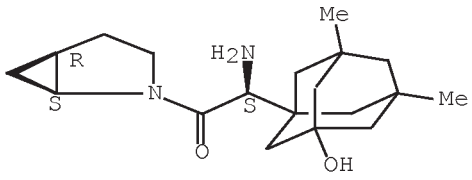
RN 841302-27-0 HCAPLUS
CN Ethanone, 2-amino-1-(3-azabicyclo[3.1.0]hex-3-yl)-2-(3,5-dihydroxytricyclo[3.3.1.13,7]dec-1-yl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



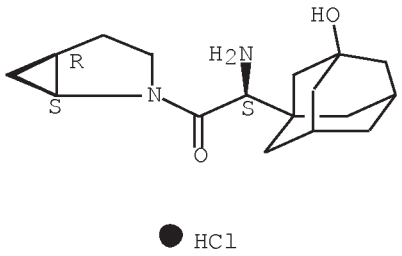
RN 841302-28-1 HCAPLUS
CN Ethanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-2-(3-hydroxy-5,7-dimethyltricyclo[3.3.1.13,7]dec-1-yl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



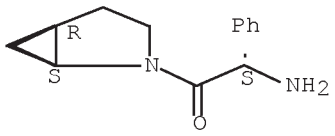
RN 841302-51-0 HCAPLUS
CN Ethanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-2-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)-, hydrochloride (1:1), (2S)- (CA INDEX NAME)

Absolute stereochemistry.



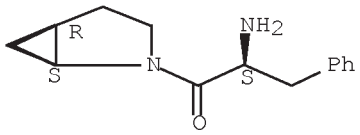
RN 1000689-35-9 HCAPLUS
CN Ethanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-2-phenyl-, (2S)-
(CA INDEX NAME)

Absolute stereochemistry.



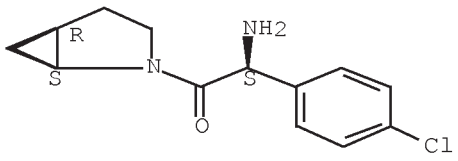
RN 1000689-36-0 HCAPLUS
CN 1-Propanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-3-phenyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



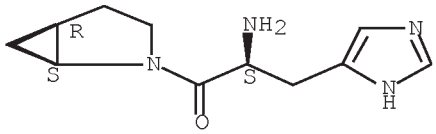
RN 1000689-37-1 HCAPLUS
CN Ethanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-2-(4-chlorophenyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



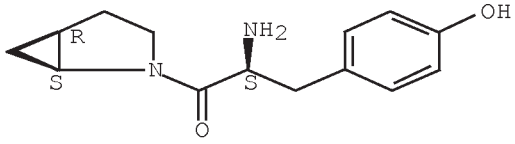
RN 1000689-38-2 HCAPLUS
CN 1-Propanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-3-(1H-imidazol-5-yl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



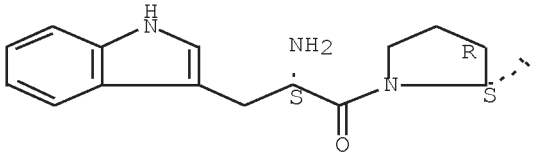
RN 1000689-39-3 HCAPLUS
CN 1-Propanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-3-(4-hydroxyphenyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



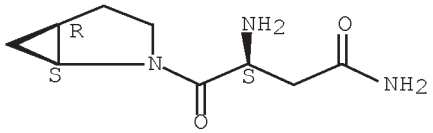
RN 1000689-40-6 HCAPLUS
CN 1-Propanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-3-(1H-indol-3-yl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



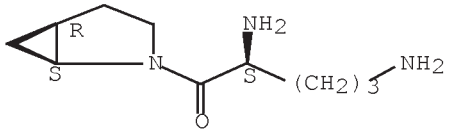
RN 1000689-41-7 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-2-butanamide, β-amino-γ-oxo-, (βS,1S,5R)- (CA INDEX NAME)

Absolute stereochemistry.



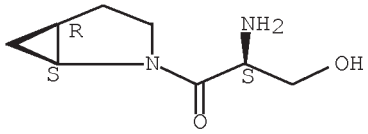
RN 1000689-43-9 HCAPLUS
CN 1-Pentanone, 2,5-diamino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



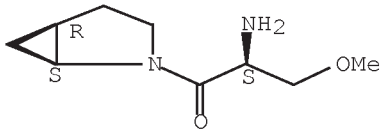
RN 1000689-44-0 HCAPLUS
CN 1-Propanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-3-hydroxy-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



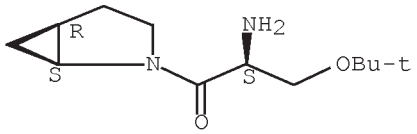
RN 1000689-45-1 HCAPLUS
CN 1-Propanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-3-methoxy-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



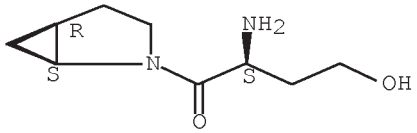
RN 1000689-46-2 HCAPLUS
CN 1-Propanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-3-(1,1-dimethylethoxy)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



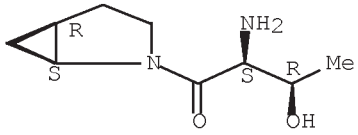
RN 1000689-47-3 HCAPLUS
CN 1-Butanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-4-hydroxy-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



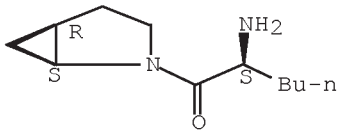
RN 1000689-48-4 HCAPLUS
CN 1-Butanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-3-hydroxy-, (2S,3R)- (CA INDEX NAME)

Absolute stereochemistry.



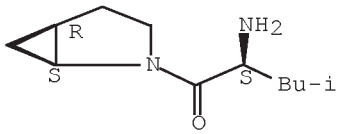
RN 1000689-49-5 HCAPLUS
CN 1-Hexanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



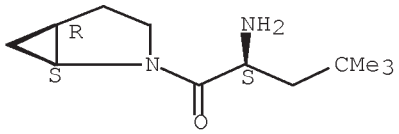
RN 1000689-50-8 HCAPLUS
CN 1-Pentanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



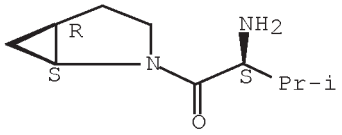
RN 1000689-52-0 HCAPLUS
CN 1-Pentanone,
2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-4,4-dimethyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



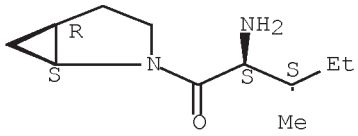
RN 1000689-53-1 HCAPLUS
CN 1-Butanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-3-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



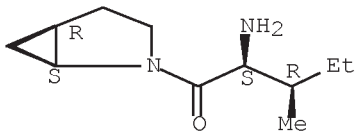
RN 1000689-54-2 HCAPLUS
CN 1-Pentanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-3-methyl-, (2S,3S)- (CA INDEX NAME)

Absolute stereochemistry.



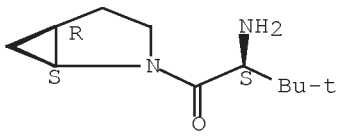
RN 1000689-55-3 HCAPLUS
CN 1-Pentanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-3-methyl-, (2S,3R)- (CA INDEX NAME)

Absolute stereochemistry.



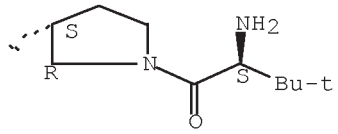
RN 1000689-56-4 HCAPLUS
CN 1-Butanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-3,3-dimethyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



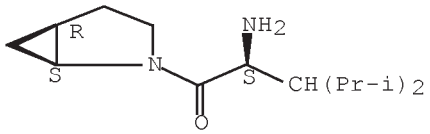
RN 1000689-57-5 HCAPLUS
CN 1-Butanone,
2-amino-1-[(1R,5S)-2-azabicyclo[3.1.0]hex-2-yl]-3,3-dimethyl-,
(2S)- (CA INDEX NAME)

Absolute stereochemistry.



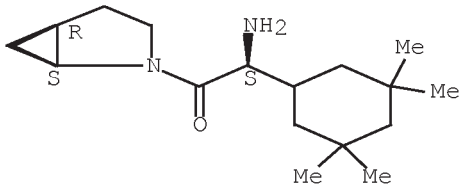
RN 1000689-59-7 HCAPLUS
CN 1-Pentanone,
2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-4-methyl-3-(1-
methylethyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



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

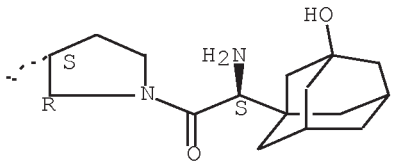
Absolute stereochemistry.



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

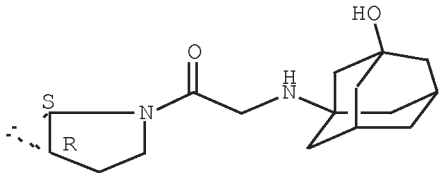
hydroxytricyclo[3.3.1.13,7]dec-1-yl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



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

Absolute stereochemistry.



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

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

ED Entered STN: 30 Dec 2005

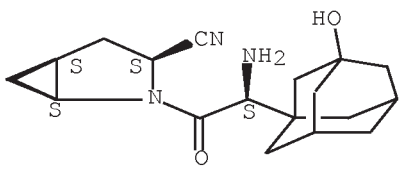
AB Dipeptidyl peptidase-IV (DPP-IV) is a serine protease with a signature Asp-His-Ser motif at the active site. Our pH data suggest that Gly-Pro-pNA cleavage catalyzed by DPP-IV is facilitated by an ionization of a residue with a pK of 7.2±0.1. By analogy to other serine proteases this pK is suggestive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

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

RN 361442-04-8 HCAPLUS

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

Absolute stereochemistry.



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

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

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

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

PRIORITY APPLN. INFO.:
US 2003-523546P P 20031120
US 2004-989138 A 20041115
WO 2004-US39051 W 20041119
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 143:43869
ED Entered STN: 10 Jun 2005
GI

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

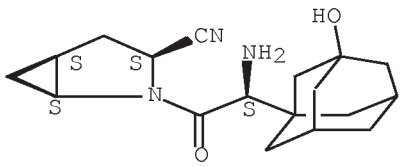
AB Title compds. I [Het = 5- to 8-membered ring including at least one nitrogen atom with provisions; n = 0-1; R1 and R2 independently = H, alkyl, alkenyl, etc.; R3 = H, aryl, cycloalkyl, etc.; R4 and R5 independently = H, alkyl; X = -CR6R7-CR6aR7a-, -CR6=CR7-; R6, R7, R6a and R7a independently = H,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

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

RN 361442-04-8 HCAPLUS

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

Absolute stereochemistry.



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

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

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

ACCESSION NUMBER: 2005:543673 HCAPLUS Full-text

DOCUMENT NUMBER: 143:221803

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

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

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

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

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

PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:221803
ED Entered STN: 24 Jun 2005

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

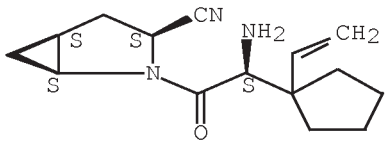
IT 361441-54-5P 361441-75-0P 361441-99-8P
361442-05-9P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(discovery and preclin. profile of saxagliptin (BMS-477118) as highly potent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

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

CM 1

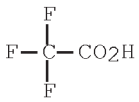
CRN 361441-53-4
CMF C15 H21 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

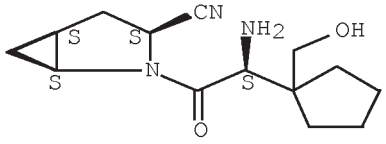


RN 361441-75-0 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-[1-(hydroxymethyl)cyclopentyl]acetyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

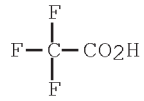
CRN 361441-74-9
CMF C14 H21 N3 O2

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

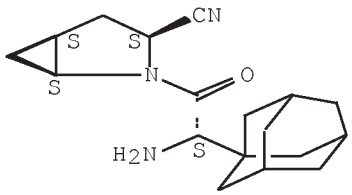


RN 361441-99-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-tricyclo[3.3.1.13,7]dec-1-ylacetyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

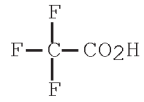
CRN 361441-98-7
CMF C18 H25 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

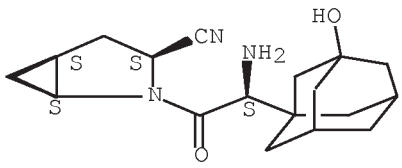


RN 361442-05-9 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-,
(1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

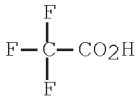
CRN 361442-04-8
CMF C18 H25 N3 O2

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

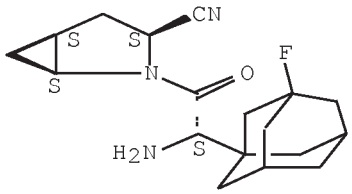


IT 361442-09-3P 361442-44-6P 841302-57-6P
862590-85-0P 862590-86-1P 862590-87-2P
862590-88-3P 862590-89-4P 862590-90-7P
862590-91-8P 862590-93-0P 862590-94-1P
862590-95-2P 862590-96-3P 862590-97-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological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

CM 1

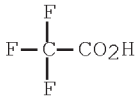
CRN 361442-08-2
CMF C18 H24 F N3 O

Absolute stereochemistry.



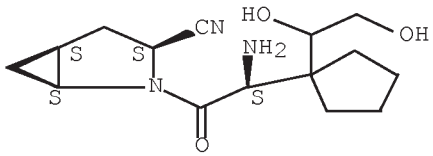
CM 2

CRN 76-05-1
CMF C2 H F3 O2



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

Absolute stereochemistry.

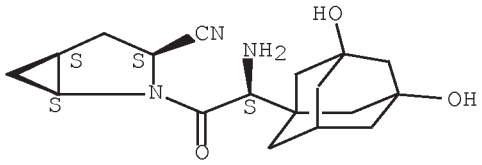


RN 841302-57-6 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(3,5-dihydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-,
(1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

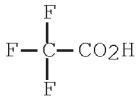
CRN 841302-24-7
CMF C18 H25 N3 O3

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

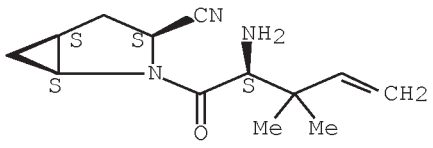


RN 862590-85-0 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-3,3-dimethyl-1-oxo-4-penten-1-yl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

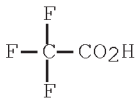
CRN 361441-62-5
CMF C13 H19 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

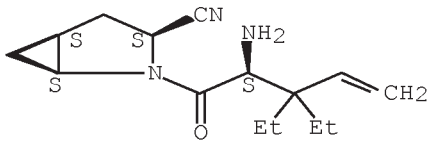


RN 862590-86-1 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-3,3-diethyl-4-methylene-1-oxobutyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361441-63-6
CMF C15 H23 N3 O

Absolute stereochemistry.



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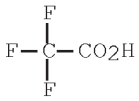
CMF C2 H F3 O2

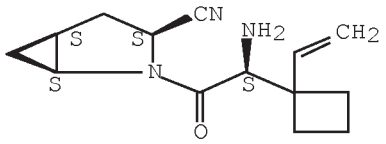


RN 862590-87-2 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(1-ethenylcyclobutyl)acetyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

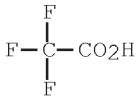
CRN 361441-55-6
CMF C14 H19 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

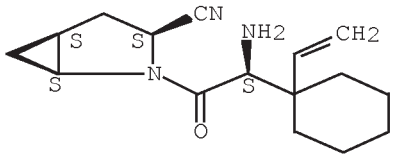


RN 862590-88-3 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(1-ethenylcyclohexyl)acetyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361441-56-7
CMF C16 H23 N3 O

Absolute stereochemistry.



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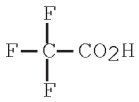
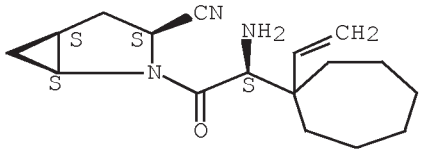


RN 862590-89-4 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(1-ethenylcycloheptyl)acetyl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361441-57-8
CMF C17 H25 N3 O

Absolute stereochemistry.



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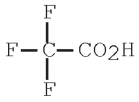
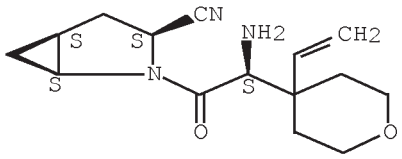


RN 862590-90-7 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(4-ethenyltetrahydro-2H-pyran-4-yl)acetyl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

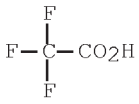
CRN 361441-60-3
CMF C15 H21 N3 O2

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

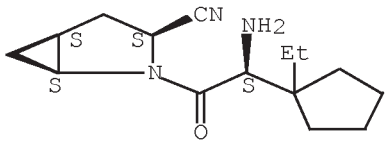


RN 862590-91-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(1-ethylcyclopentyl)acetyl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

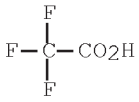
CRN 361441-85-2
CMF C15 H23 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

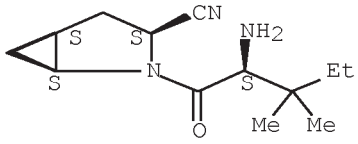


RN 862590-93-0 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-3,3-dimethyl-1-oxopentyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361441-90-9
CMF C13 H21 N3 O

Absolute stereochemistry.



CM 2

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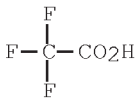


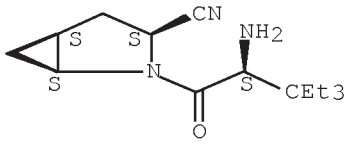
RN 862590-94-1 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-3,3-diethyl-1-oxopentyl]-, (1S,3S,5S)-,

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

CM 1

CRN 361441-91-0
CMF C15 H25 N3 O

Absolute stereochemistry.



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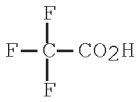

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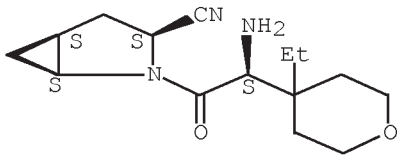
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(4-ethyltetrahydro-2H-pyran-4-yl)acetyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

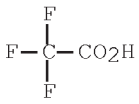
CRN 361441-89-6
CMF C15 H23 N3 O2

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



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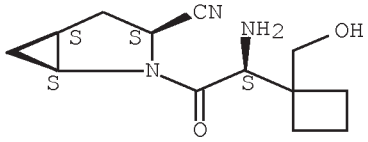
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-[1-(hydroxymethyl)cyclobutyl]acetyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

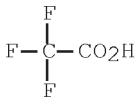
CRN 361441-77-2
CMF C13 H19 N3 O2

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



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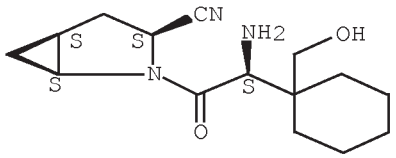
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-[1-(hydroxymethyl)cyclohexyl]acetyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 361441-78-3
CMF C15 H23 N3 O2

Absolute stereochemistry.



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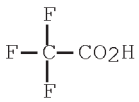

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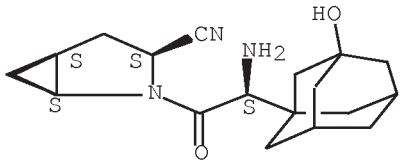
2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-,
(1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



OS.CITING REF COUNT: 205 THERE ARE 205 CAPLUS RECORDS THAT CITE THIS RECORD (206 CITINGS)
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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
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ED   Entered STN:  21 Sep 2001
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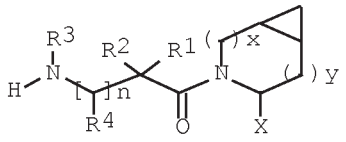

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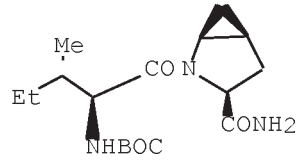

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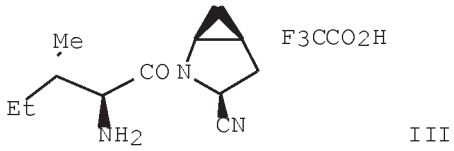


III

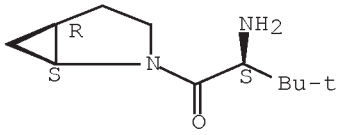
AB Dipeptidyl peptidase IV inhibiting compds. I (x = 0 or 1 and y = 0 or 1 provided that x = 1 when y = 0 and x = 0 when y = 1; n = 0, 1; X = H, CN; R1, R2, R3 and R4 = same or different and independently selected from H, (un)substituted chain or cyclic components) and the pharmaceutically acceptable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

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

RN 1000689-56-4 HCAPLUS

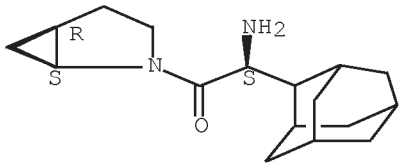
CN 1-Butanone,
2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-3,3-dimethyl-,
(2S)- (CA INDEX NAME)

Absolute stereochemistry.



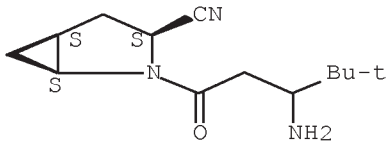
RN 1098535-01-3 HCAPLUS
CN Ethanone, 2-amino-1-(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl-2-tricyclo[3.3.1.13,7]dec-2-yl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



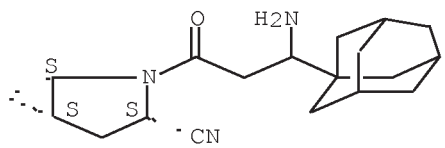
RN 1098535-02-4 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-(3-amino-4,4-dimethyl-1-oxopentyl)-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



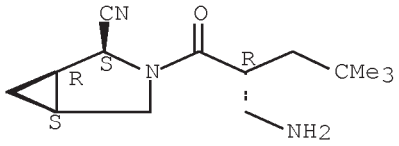
RN 1098535-03-5 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-(3-amino-1-oxo-3-tricyclo[3.3.1.13,7]dec-1-ylpropyl)-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



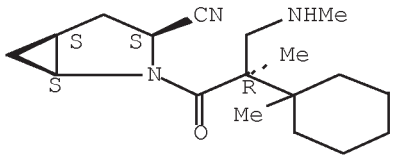
RN 1098535-04-6 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile,
3-[(2R)-2-(aminomethyl)-4,4-dimethyl-1-oxopentyl]-, (1R,2S,5S)- (CA INDEX
NAME)

Absolute stereochemistry.



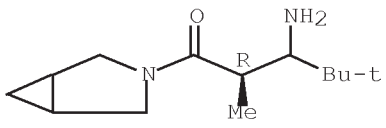
RN 1098535-05-7 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2R)-2-methyl-3-(methylamino)-2-(1-methylcyclohexyl)-1-oxopropyl]-,
(1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



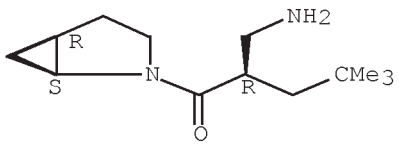
RN 1098535-06-8 HCAPLUS
CN 1-Pentanone, 3-amino-1-(3-azabicyclo[3.1.0]hex-3-yl)-2,4,4-trimethyl-,
(2R)- (CA INDEX NAME)

Absolute stereochemistry.



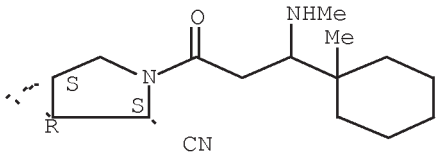
RN 1098535-07-9 HCAPLUS
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



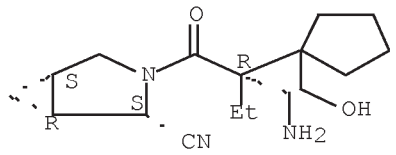
RN 1098535-08-0 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile, 3-[3-(methylamino)-3-(1-methylcyclohexyl)-1-oxopropyl]-, (1R,2S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



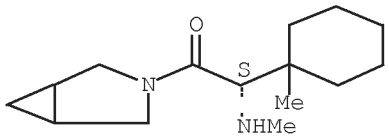
RN 1098535-09-1 HCAPLUS
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



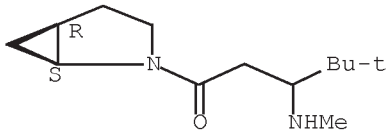
RN 1098535-10-4 HCAPLUS
CN Ethanone, 1-(3-azabicyclo[3.1.0]hex-3-yl)-2-(methylamino)-2-(1-methylcyclohexyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



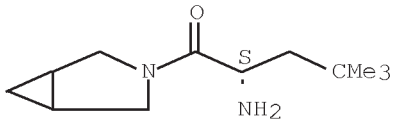
RN 1098535-11-5 HCAPLUS
CN 1-Pentanone, 1-(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl-4,4-dimethyl-3-(methylamino)- (CA INDEX NAME)

Absolute stereochemistry.



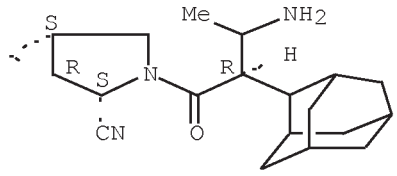
RN 1098535-12-6 HCAPLUS
CN 1-Pentanone, 2-amino-1-(3-azabicyclo[3.1.0]hex-3-yl)-4,4-dimethyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



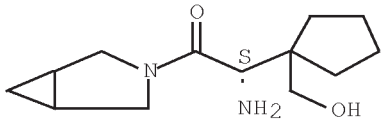
RN 1098535-13-7 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile, 3-[(2R)-3-amino-1-oxo-2-tricyclo[3.3.1.13,7]dec-2-ylbutyl]-, (1R,2S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



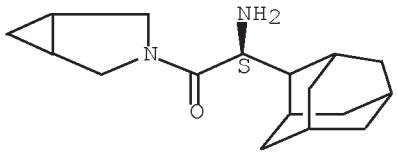
RN 1098535-14-8 HCAPLUS
CN Ethanone, 2-amino-1-(3-azabicyclo[3.1.0]hex-3-yl)-2-[1-(hydroxymethyl)cyclopentyl]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



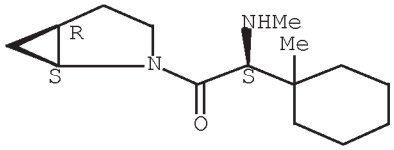
RN 1098535-15-9 HCAPLUS
CN Ethanone, 2-amino-1-(3-azabicyclo[3.1.0]hex-3-yl)-2-tricyclo[3.3.1.13,7]dec-2-yl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



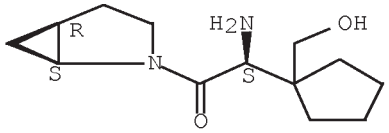
RN 1098535-16-0 HCAPLUS
CN Ethanone, 1-(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl-2-(methylamino)-2-(1-methylcyclohexyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



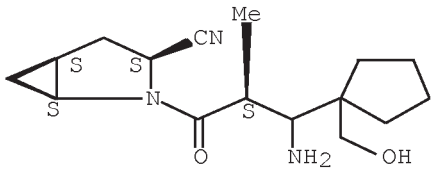
RN 1098535-17-1 HCAPLUS
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



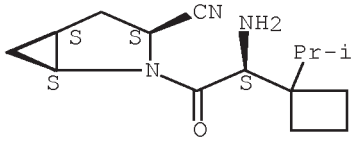
RN 1098535-21-7 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-3-amino-3-[1-(hydroxymethyl)cyclopentyl]-2-methyl-1-oxopropyl]-,
(1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



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
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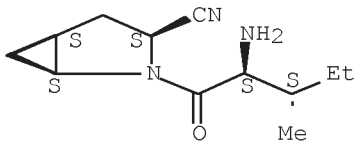
361485-95-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of fused cyclopropylpyrrolidine-based inhibitors of dipeptidyl
peptidase 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.

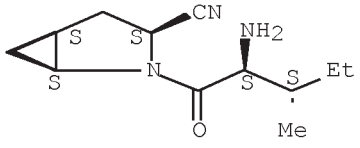


RN 361440-66-6 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

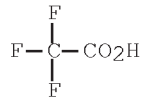
CRN 361440-65-5
CMF C12 H19 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

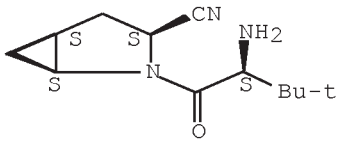


RN 361440-73-5 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-3,3-dimethyl-1-oxobutyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

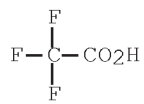
CRN 361440-72-4
CMF C12 H19 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



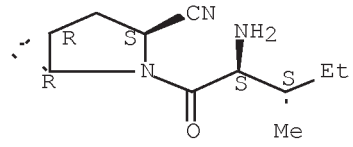
RN 361440-77-9 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,

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

CM 1

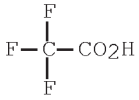
CRN 361440-76-8
CMF C12 H19 N3 O

Absolute stereochemistry.



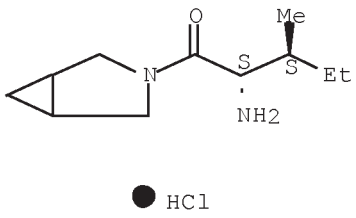
CM 2

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), (2*S*,3S)- (CA INDEX NAME)

Absolute stereochemistry.



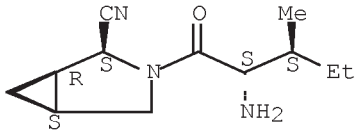
RN 361440-88-2 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile,

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

CM 1

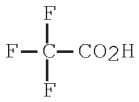
CRN 361440-87-1
CMF C12 H19 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

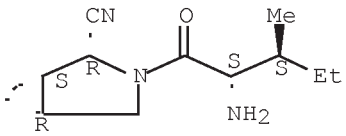


RN 361440-91-7 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile,
3-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]-, (1S,2R,5R)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

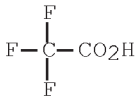
CRN 361440-90-6
CMF C12 H19 N3 O

Absolute stereochemistry.



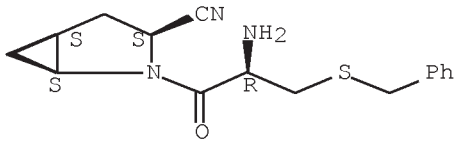
CM 2

CRN 76-05-1
CMF C2 H F3 O2



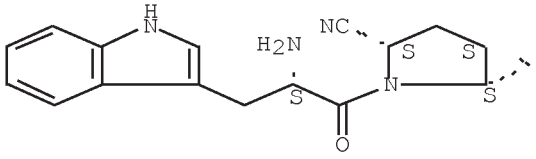
RN 361440-95-1 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2R)-2-amino-1-oxo-3-[(phenylmethyl)thio]propyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



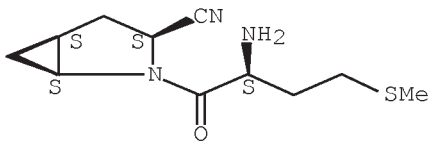
RN 361440-97-3 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-3-(1H-indol-3-yl)-1-oxopropyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



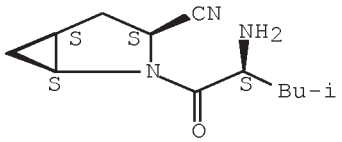
RN 361440-99-5 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-4-(methylthio)-1-oxobutyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



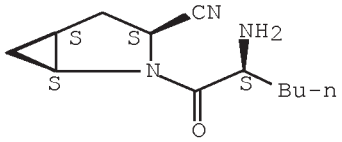
RN 361441-01-2 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-4-methyl-1-oxopentyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



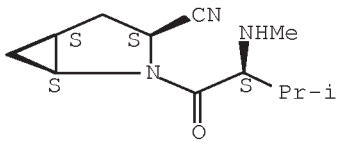
RN 361441-03-4 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-1-oxohexyl]-,
(1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



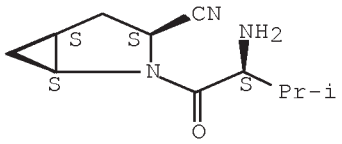
RN 361441-04-5 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-3-methyl-2-(methylamino)-1-oxobutyl]-, (1S,3S,5S)- (CA INDEX
NAME)

Absolute stereochemistry.



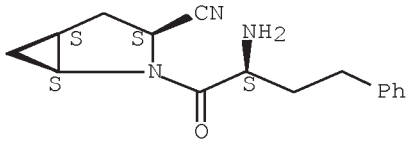
RN 361441-05-6 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-3-methyl-1-oxobutyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



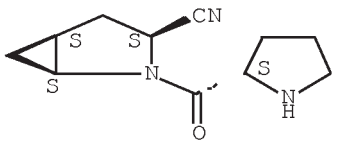
RN 361441-06-7 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-1-oxo-4-phenylbutyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



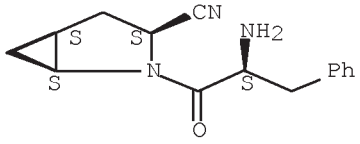
RN 361441-07-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-pyrrolidinylcarbonyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



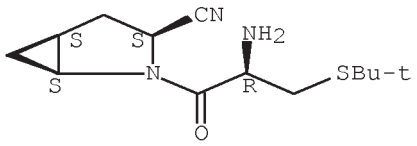
RN 361441-08-9 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-1-oxo-3-phenylpropyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



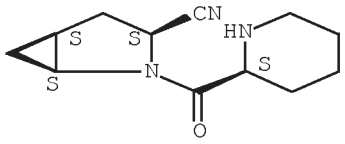
RN 361441-09-0 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2R)-2-amino-3-[(1,1-dimethylethyl)thio]-1-oxopropyl]-, (1S,3S,5S)-
(CA INDEX NAME)

Absolute stereochemistry.



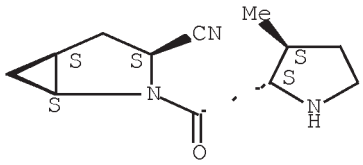
RN 361441-10-3 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-piperidinylcarbonyl]-,
(1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



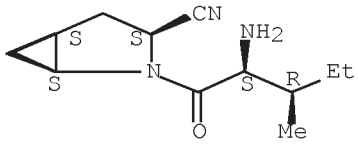
RN 361441-11-4 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[[(2S,3S)-3-methyl-2-pyrrolidinyl]carbonyl]-, (1S,3S,5S)- (CA INDEX
NAME)

Absolute stereochemistry.



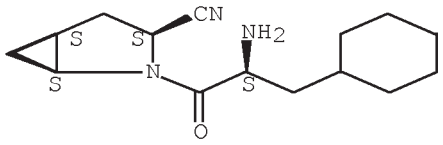
RN 361441-12-5 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S,3R)-2-amino-3-methyl-1-oxopentyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



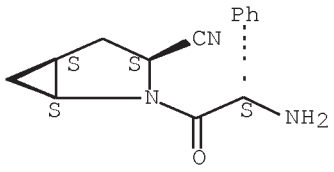
RN 361441-13-6 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-3-cyclohexyl-1-oxopropyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



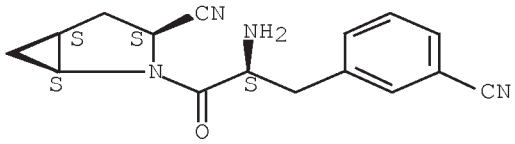
RN 361441-14-7 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-phenylacetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



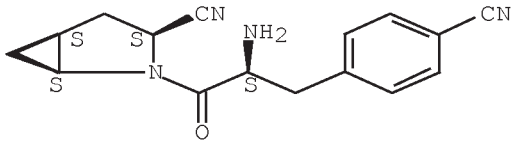
RN 361441-15-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-3-(3-cyanophenyl)-1-oxopropyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



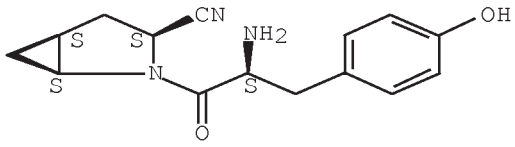
RN 361441-16-9 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-3-(4-cyanophenyl)-1-oxopropyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



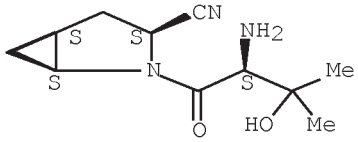
RN 361441-17-0 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-3-(4-hydroxyphenyl)-1-oxopropyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



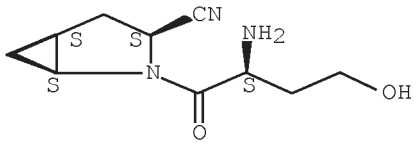
RN 361441-28-3 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-3-hydroxy-3-methyl-1-oxobutyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



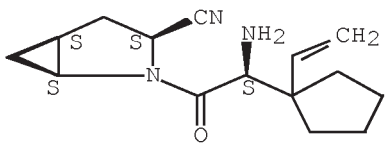
RN 361441-39-6 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-4-hydroxy-1-oxobutyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



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

Absolute stereochemistry.

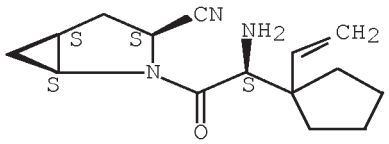


RN 361441-54-5 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(1-ethenylcyclopentyl)acetyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

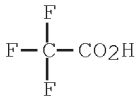
CRN 361441-53-4
CMF C15 H21 N3 O

Absolute stereochemistry.



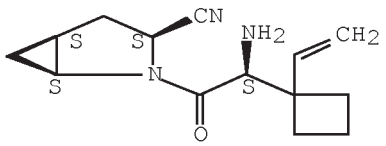
CM 2

CRN 76-05-1
CMF C2 H F3 O2



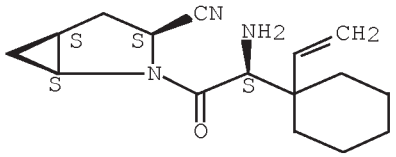
RN 361441-55-6 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(1-ethenylcyclobutyl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



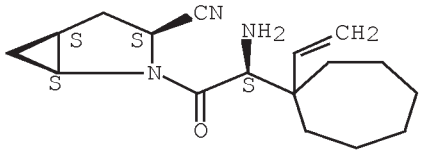
RN 361441-56-7 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(1-ethenylcyclohexyl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



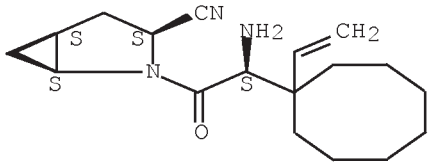
RN 361441-57-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(1-ethenylcycloheptyl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



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

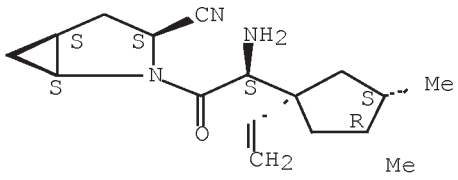
Absolute stereochemistry.



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

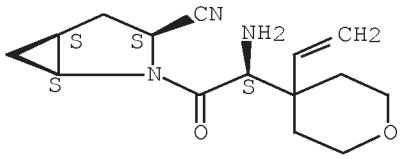
2-[(2S)-2-amino-2-[(3R,4S)-1-ethenyl-3,4-dimethylcyclopentyl]acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



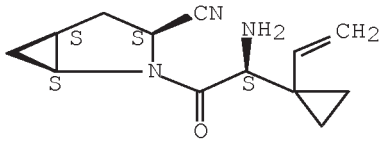
RN 361441-60-3 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(4-ethenyltetrahydro-2H-pyran-4-yl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



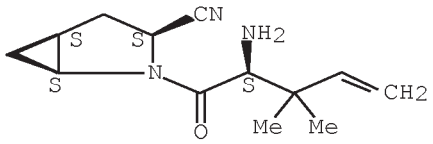
RN 361441-61-4 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(1-ethenylcyclopropyl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



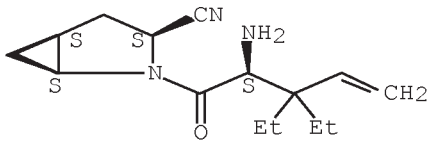
RN 361441-62-5 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-3,3-dimethyl-1-oxo-4-penten-1-yl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



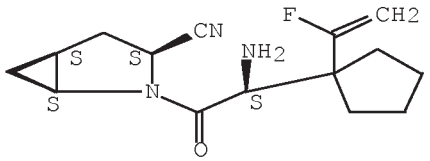
RN 361441-63-6 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-3,3-diethyl-1-oxo-4-pentenyl]-, (1S,3S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



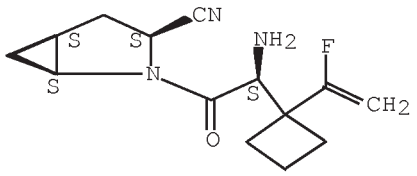
RN 361441-65-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-[1-(1-fluoroethenyl)cyclopentyl]acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



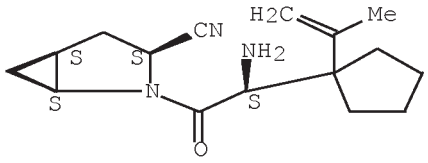
RN 361441-67-0 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-[1-(1-fluoroethenyl)cyclobutyl]acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



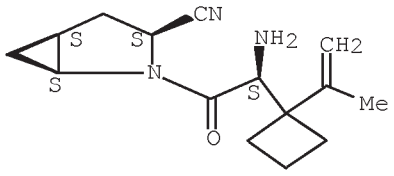
RN 361441-69-2 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-[1-(1-methylethenyl)cyclopentyl]acetyl]-, (1S,3S,5S)-
(CA INDEX NAME)

Absolute stereochemistry.



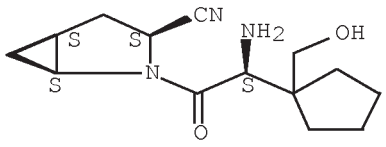
RN 361441-71-6 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-[1-(1-methylethenyl)cyclobutyl]acetyl]-, (1S,3S,5S)-
(CA INDEX NAME)

Absolute stereochemistry.



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

Absolute stereochemistry.

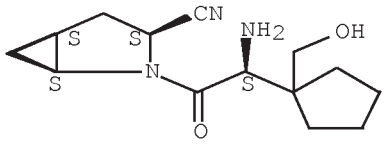


RN 361441-75-0 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-[1-(hydroxymethyl)cyclopentyl]acetyl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

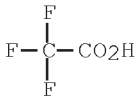
CRN 361441-74-9
CMF C14 H21 N3 O2

Absolute stereochemistry.



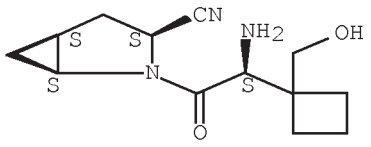
CM 2

CRN 76-05-1
CMF C2 H F3 O2



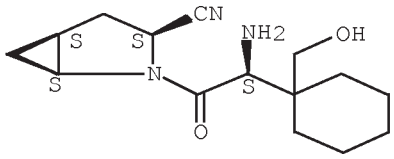
RN 361441-77-2 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-[1-(hydroxymethyl)cyclobutyl]acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



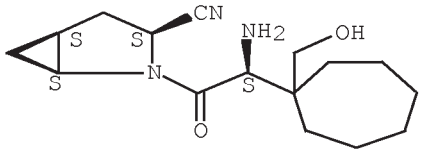
RN 361441-78-3 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-[1-(hydroxymethyl)cyclohexyl]acetyl]-, (1S,3S,5S)- (CA
INDEX NAME)

Absolute stereochemistry.



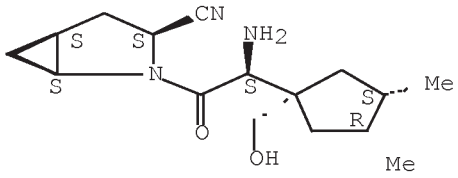
RN 361441-79-4 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-[1-(hydroxymethyl)cycloheptyl]acetyl]-, (1S,3S,5S)-
(CA
INDEX NAME)

Absolute stereochemistry.



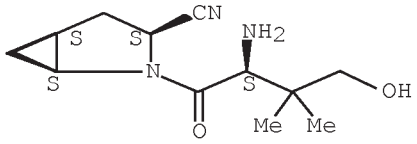
RN 361441-80-7 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-[(3R,4S)-1-(hydroxymethyl)-3,4-
dimethylcyclopentyl]acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



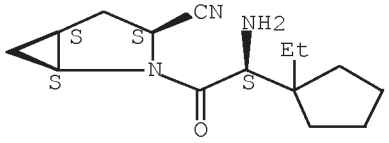
RN 361441-83-0 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-4-hydroxy-3,3-dimethyl-1-oxobutyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



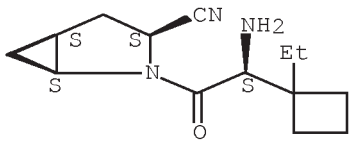
RN 361441-85-2 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(1-ethylcyclopentyl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



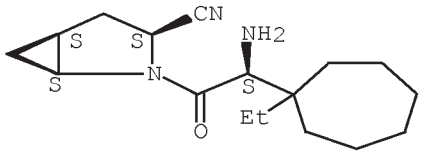
RN 361441-87-4 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(1-ethylcyclobutyl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



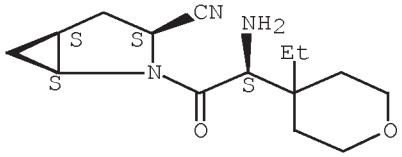
RN 361441-88-5 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(1-ethylcycloheptyl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



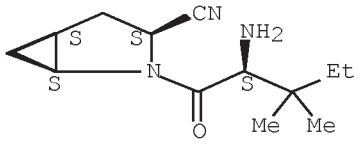
RN 361441-89-6 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(4-ethyltetrahydro-2H-pyran-4-yl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



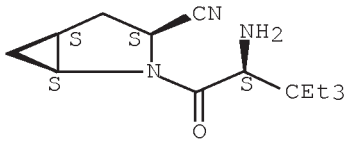
RN 361441-90-9 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-3,3-dimethyl-1-oxopentyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



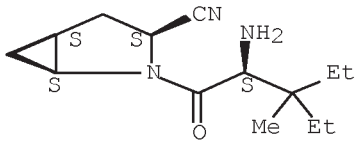
RN 361441-91-0 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-3,3-diethyl-1-oxopentyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



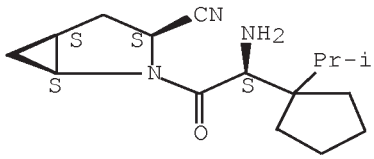
RN 361441-92-1 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-3-ethyl-3-methyl-1-oxopentyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



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

Absolute stereochemistry.



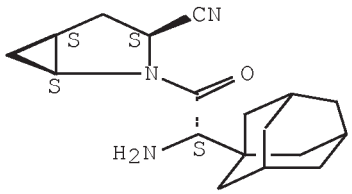
RN 361441-99-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,

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

CM 1

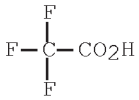
CRN 361441-98-7
CMF C18 H25 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

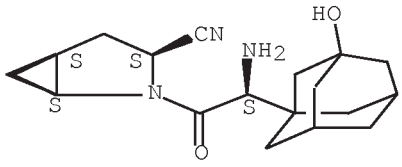


RN 361442-05-9 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-,
(1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

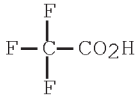
CRN 361442-04-8
CMF C18 H25 N3 O2

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

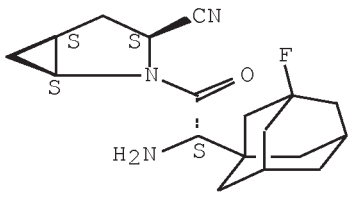


RN 361442-09-3 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(3-fluorotricyclo[3.3.1.13,7]dec-1-yl)acetyl]-,
(1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

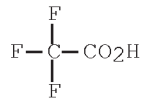
CRN 361442-08-2
CMF C18 H24 F N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

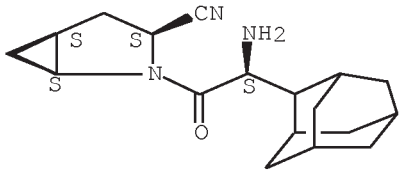


RN 361442-11-7 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-tricyclo[3.3.1.13,7]dec-2-ylacetyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

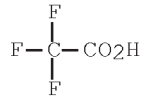
CRN 361442-10-6
CMF C18 H25 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

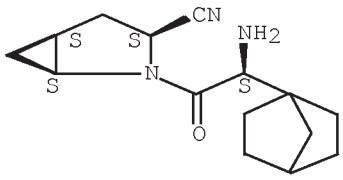


RN 361442-15-1 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-bicyclo[2.2.1]hept-1-ylacetyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

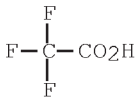
CRN 361442-14-0
CMF C15 H21 N3 O

Absolute stereochemistry.



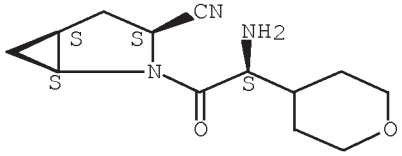
CM 2

CRN 76-05-1
CMF C2 H F3 O2



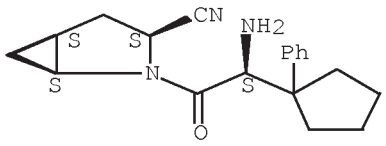
RN 361442-16-2 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(tetrahydro-2H-pyran-4-yl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



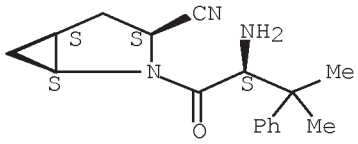
RN 361442-18-4 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(1-phenylcyclopentyl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



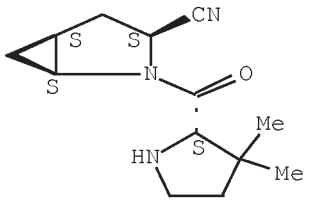
RN 361442-19-5 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-3-methyl-1-oxo-3-phenylbutyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



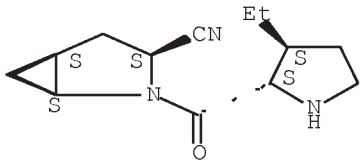
RN 361442-23-1 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[[(2S)-3,3-dimethyl-2-pyrrolidinyl]carbonyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



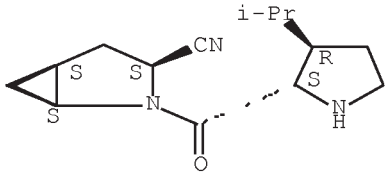
RN 361442-25-3 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[[(2S,3S)-3-ethyl-2-pyrrolidinyl]carbonyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



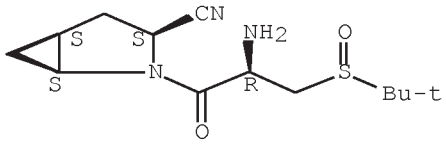
RN 361442-30-0 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[[(2S,3R)-3-(1-methylethyl)-2-pyrrolidinyl]carbonyl]-, (1S,3S,5S)- (CA
INDEX NAME)

Absolute stereochemistry.



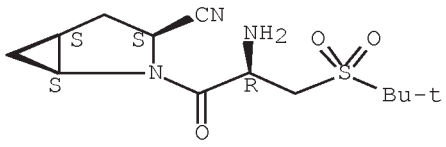
RN 361442-33-3 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2R)-2-amino-3-[(1,1-dimethylethyl)sulfinyl]-1-oxopropyl]-,
(1S,3S,5S)-
(CA INDEX NAME)

Absolute stereochemistry.



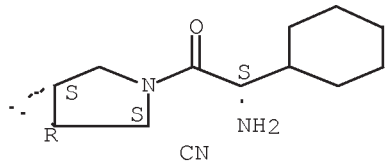
RN 361442-35-5 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2R)-2-amino-3-[(1,1-dimethylethyl)sulfonyl]-1-oxopropyl]-,
(1S,3S,5S)-
(CA INDEX NAME)

Absolute stereochemistry.



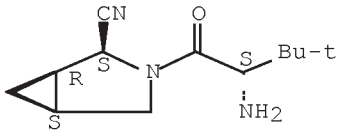
RN 361442-38-8 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile,
3-[(2S)-2-amino-2-cyclohexylacetyl]-, (1R,2S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



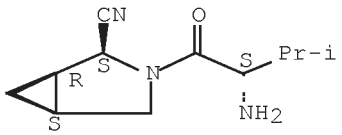
RN 361442-39-9 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile,
3-[(2S)-2-amino-3,3-dimethyl-1-oxobutyl]-, (1R,2S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



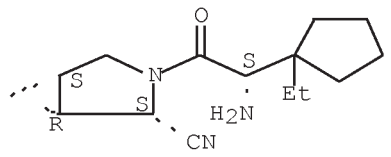
RN 361442-40-2 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile,
3-[(2S)-2-amino-3-methyl-1-oxobutyl]-, (1R,2S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



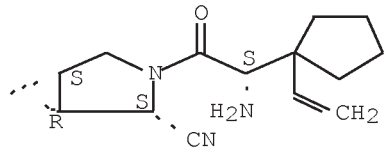
RN 361442-41-3 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile, 3-[(2S)-2-amino-2-(1-ethylcyclopentyl)acetyl]-, (1R,2S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



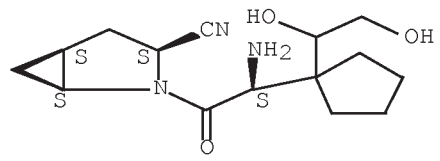
RN 361442-42-4 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile, 3-[(2S)-2-amino-2-(1-ethenylcyclopentyl)acetyl]-, (1R,2S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



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

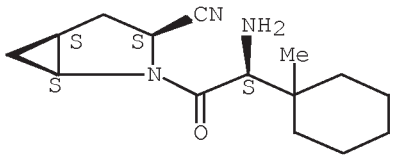
Absolute stereochemistry.



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

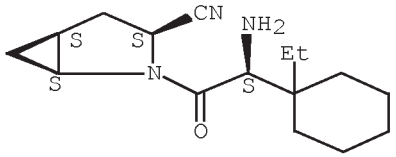
2-[(2S)-2-amino-2-(1-methylcyclohexyl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



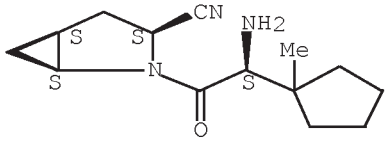
RN 361442-49-1 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(1-ethylcyclohexyl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



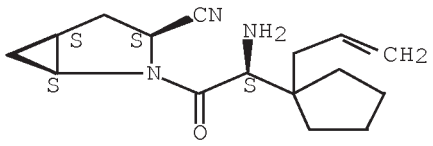
RN 361442-50-4 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(1-methylcyclopentyl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



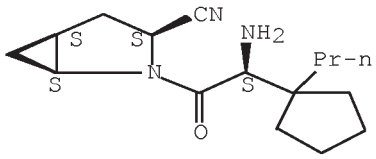
RN 361442-51-5 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-[1-(2-propen-1-yl)cyclopentyl]acetyl]-, (1S,3S,5S)- (CA
INDEX NAME)

Absolute stereochemistry.



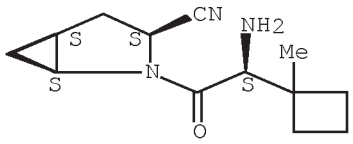
RN 361442-52-6 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(1-propylcyclopentyl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



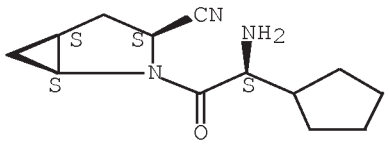
RN 361442-53-7 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(1-methylcyclobutyl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



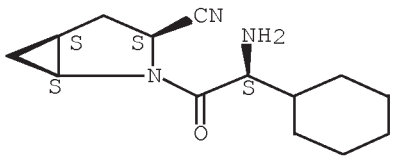
RN 361442-54-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-cyclopentylacetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



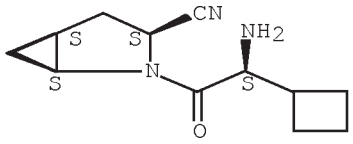
RN 361442-55-9 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-cyclohexylacetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



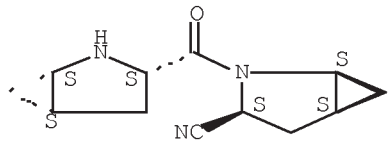
RN 361442-56-0 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-cyclobutylacetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



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

Absolute stereochemistry.

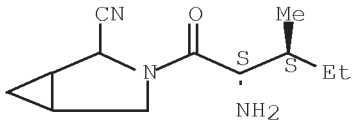


RN 361485-95-2 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile,
3-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]-, 2,2,2-trifluoroacetate (1:1)
(CA INDEX NAME)

CM 1

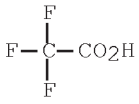
CRN 361485-94-1
CMF C12 H19 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

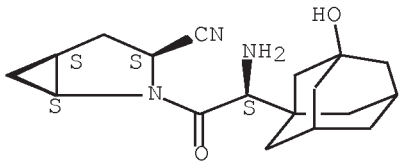


OS.CITING REF COUNT: 36 THERE ARE 36 CAPLUS RECORDS THAT CITE THIS RECORD (61 CITINGS)
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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

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

Absolute stereochemistry.



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

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

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

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

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

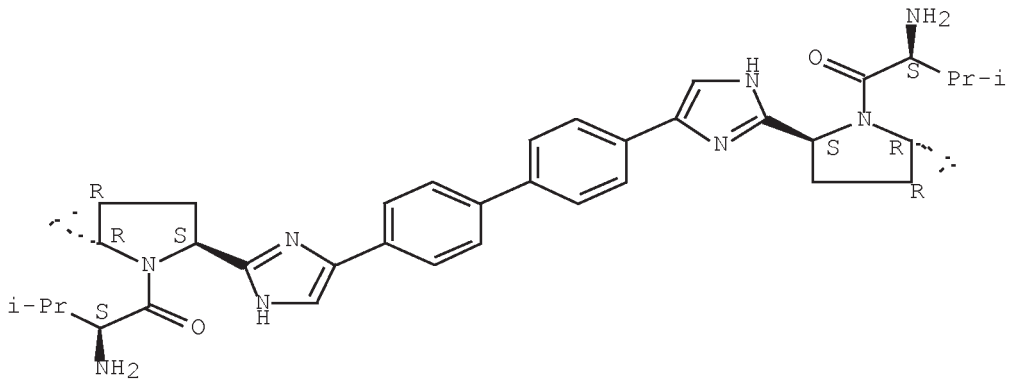
PRIORITY APPLN. INFO.: US 2007-835462 A2 20070808
US 2006-836996P P 20060811
EP 2007-800058 A3 20070809
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 150:330127; MARPAT 150:330127
ED Entered STN: 12 Mar 2009
GI

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

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

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

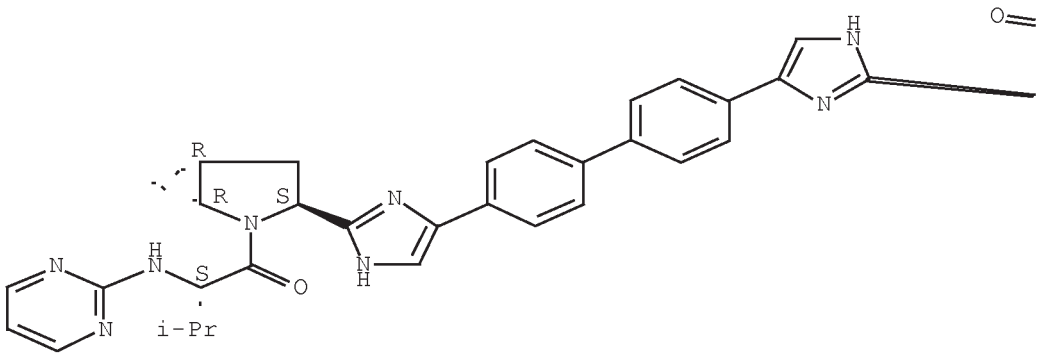
Absolute stereochemistry.



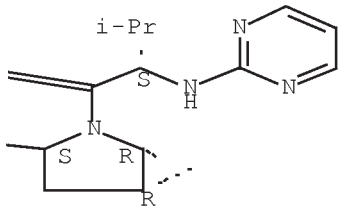
RN 1129634-35-0 HCAPLUS
CN 1-Butanone, 1,1'-[[1,1'-biphenyl]-4,4'-diylbis[1H-imidazole-5,2-diyl(1R,3S,5R)-2-azabicyclo[3.1.0]hexane-3,2-diyl]]bis[3-methyl-2-(2-pyrimidinylamino)-, (2S,2'S)- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



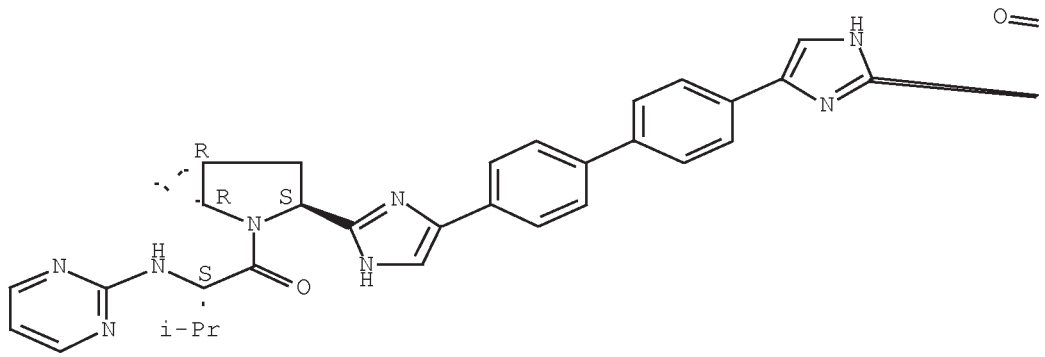
RN 1129634-36-1 HCAPLUS
CN 1-Butanone, 1,1'-[[1,1'-biphenyl]-4,4'-diylbis[1H-imidazole-5,2-diyl(1R,3S,5R)-2-azabicyclo[3.1.0]hexane-3,2-diyl]]bis[3-methyl-2-(2-pyrimidinylamino)-, (2S,2'S)-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

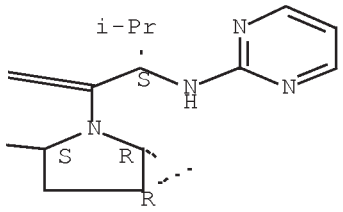
CRN 1129634-35-0
CMF C46 H50 N12 O2

Absolute stereochemistry.

PAGE 1-A

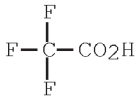


PAGE 1-B



CM 2

CRN 76-05-1
CMF C2 H F3 O2

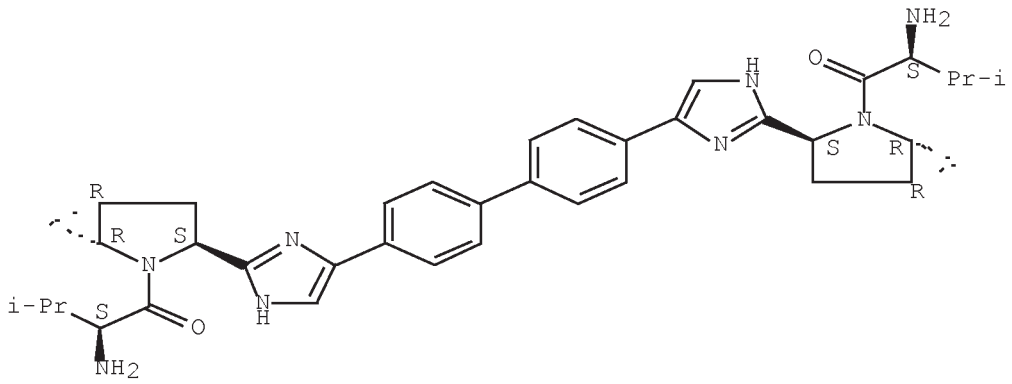


IT 1129634-16-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of biphenyls and biheteroaryls end-capped with amino acid or peptide derivs. as hepatitis c virus inhibitors)
RN 1129634-16-7 HCAPLUS
CN 1-Butanone, 1,1'-[[1,1'-biphenyl]-4,4'-diylbis[1H-imidazole-5,2-diyl-(1R,3S,5R)-2-azabi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

CM 1

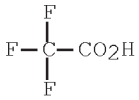
CRN 1129634-15-6
CMF C38 H46 N8 O2

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



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

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

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

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

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

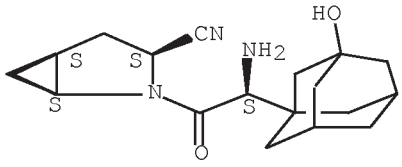
ED Entered STN: 09 Feb 2006

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

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

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

Absolute stereochemistry.



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

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

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

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

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

US 20050038020	A1	20050217	US 2004-899641		20040727
US 6995183	B2	20060207			
EP 1658066	A2	20060524	EP 2004-779352		20040728
EP 1658066	B1	20090930			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR					
JP 2007501231	T	20070125	JP 2006-522608		20040728
EP 1997489	A1	20081203	EP 2008-158967		20040728
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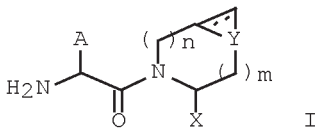
AT 444064	T	20091015	AT 2004-779352		20040728
ES 2332275	T3	20100201	ES 2004-779352		20040728
US 20050228021	A1	20051013	US 2005-149414		20050609
US 20050239839	A1	20051027	US 2005-149408		20050609
NO 2006000479	A	20060220	NO 2006-479		20060130
PRIORITY APPLN. INFO.:			US 2003-491832P	P	20030801
			US 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



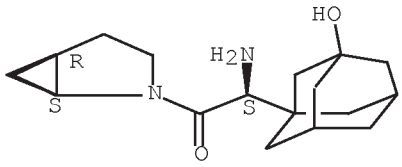
I

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

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

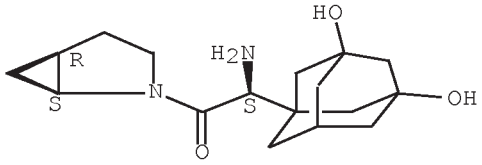
(Uses)
(claimed compound; preparation of adamantyglycinamide inhibitors of dipeptidyl
peptidase IV)
RN 841302-20-3 HCAPLUS
CN Ethanone, 2-amino-1-(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl-2-(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



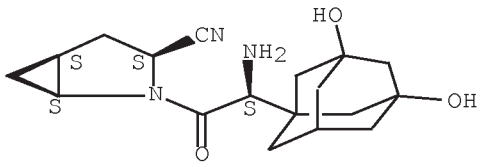
RN 841302-21-4 HCAPLUS
CN Ethanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-2-(3,5-dihydroxytricyclo[3.3.1.13,7]dec-1-yl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



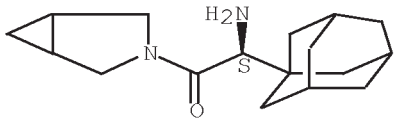
RN 841302-24-7 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(3,5-dihydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



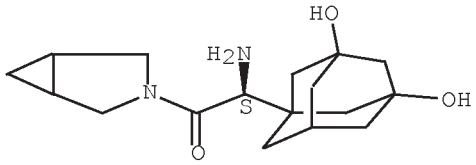
RN 841302-26-9 HCAPLUS
CN Ethanone, 2-amino-1-(3-azabicyclo[3.1.0]hex-3-yl)-2-tricyclo[3.3.1.13,7]dec-1-yl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



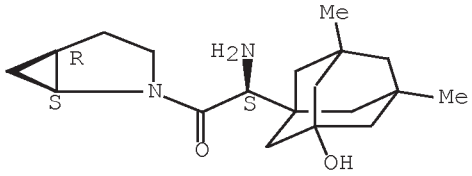
RN 841302-27-0 HCAPLUS
CN Ethanone, 2-amino-1-(3-azabicyclo[3.1.0]hex-3-yl)-2-(3,5-dihydroxytricyclo[3.3.1.13,7]dec-1-yl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



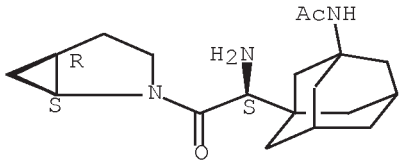
RN 841302-28-1 HCAPLUS
CN Ethanone, 2-amino-1-[(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl]-2-(3-hydroxy-5,7-dimethyltricyclo[3.3.1.13,7]dec-1-yl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



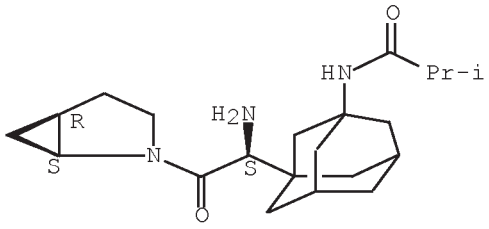
RN 841302-29-2 HCAPLUS
CN Acetamide, N-[3-[(1S)-1-amino-2-(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl-2-oxoethyl]tricyclo[3.3.1.13,7]dec-1-yl]- (CA INDEX NAME)

Absolute stereochemistry.



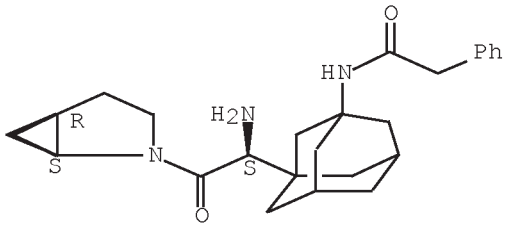
RN 841302-30-5 HCAPLUS
CN Propanamide, N-[3-[(1S)-1-amino-2-(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl-2-oxoethyl]tricyclo[3.3.1.13,7]dec-1-yl]-2-methyl- (CA INDEX NAME)

Absolute stereochemistry.



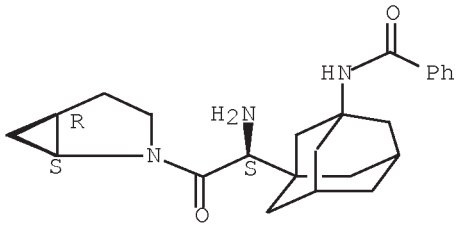
RN 841302-31-6 HCAPLUS
CN Benzeneacetamide, N-[3-[(1S)-1-amino-2-(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl-2-oxoethyl]tricyclo[3.3.1.13,7]dec-1-yl]- (CA INDEX NAME)

Absolute stereochemistry.



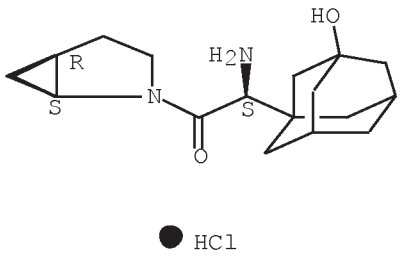
RN 841302-32-7 HCAPLUS
CN Benzamide, N-[3-[(1S)-1-amino-2-(1S,5R)-2-azabicyclo[3.1.0]hex-2-yl-2-oxoethyl]tricyclo[3.3.1.13,7]dec-1-yl]- (CA INDEX NAME)

Absolute stereochemistry.



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

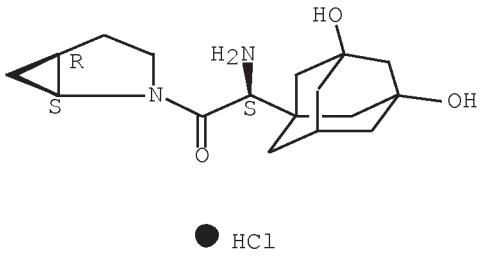
Absolute stereochemistry.



● HCl

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

Absolute stereochemistry.

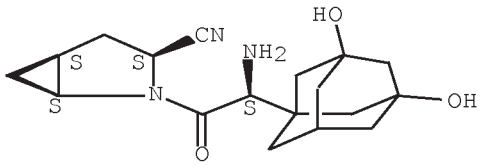


RN 841302-57-6 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-amino-2-(3,5-dihydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

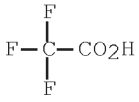
CRN 841302-24-7
CMF C18 H25 N3 O3

Absolute stereochemistry.



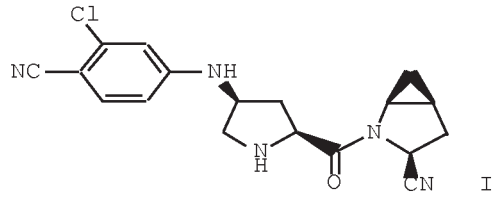
CM 2

CRN 76-05-1
CMF C2 H F3 O2



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

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



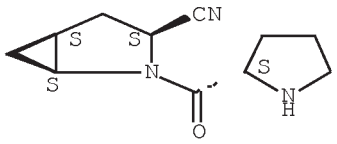
I

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

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

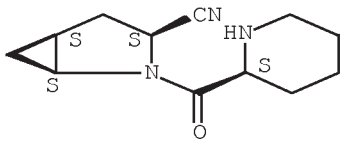
RN 361441-07-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-pyrrolidinylcarbonyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



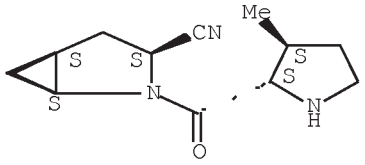
RN 361441-10-3 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-piperidinylcarbonyl]-,
(1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



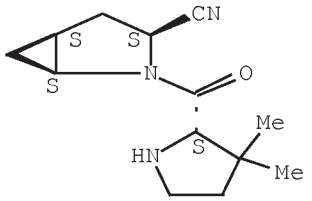
RN 361441-11-4 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[[(2S,3S)-3-methyl-2-pyrrolidinyl]carbonyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



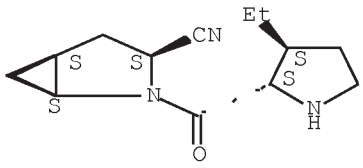
RN 361442-23-1 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[[(2S)-3,3-dimethyl-2-pyrrolidinyl]carbonyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



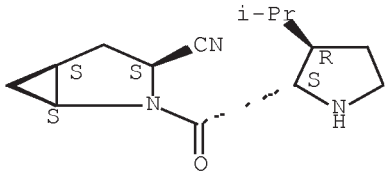
RN 361442-25-3 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[[(2S,3S)-3-ethyl-2-pyrrolidinyl]carbonyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



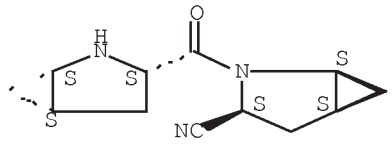
RN 361442-30-0 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[[(2S,3R)-3-(1-methylethyl)-2-pyrrolidinyl]carbonyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



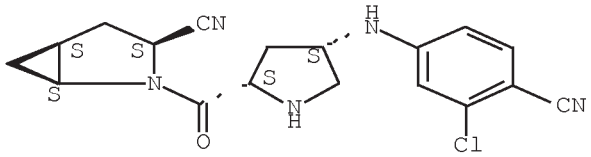
RN 361442-58-2 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(1S,3S,5S)-2-azabicyclo[3.1.0]hex-3-ylcarbonyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



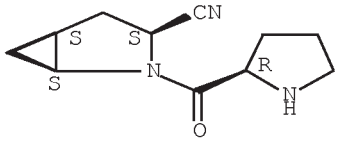
RN 866321-06-4 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[[(2S,4S)-4-[(3-chloro-4-cyanophenyl)amino]-2-pyrrolidinyl]carbonyl]-,
(1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



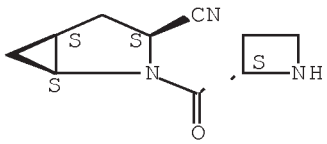
RN 866321-19-9 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2R)-2-pyrrolidinylcarbonyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



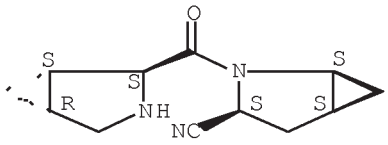
RN 866321-23-5 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-azetidinylcarbonyl]-,
(1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



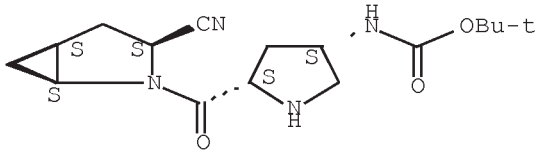
RN 866321-26-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(1S,2S,5R)-3-azabicyclo[3.1.0]hex-2-ylcarbonyl]-, (1S,3S,5S)- (CA INDEX NAME)

Absolute stereochemistry.



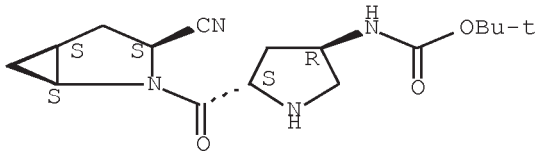
RN 866321-46-2 HCAPLUS
CN Carbamic acid, [(3S,5S)-5-[[(1S,3S,5S)-3-cyano-2-azabicyclo[3.1.0]hex-2-yl]carbonyl]-3-pyrrolidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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

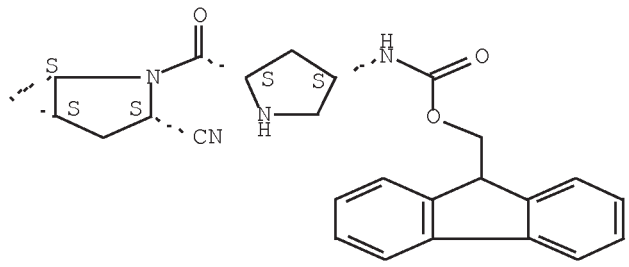
Absolute stereochemistry.



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

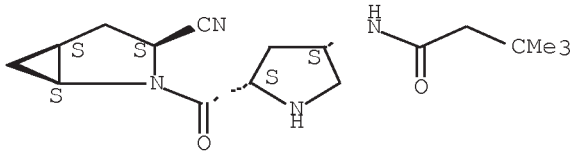
yl]carbonyl]-3-pyrrolidinyl]-, 9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



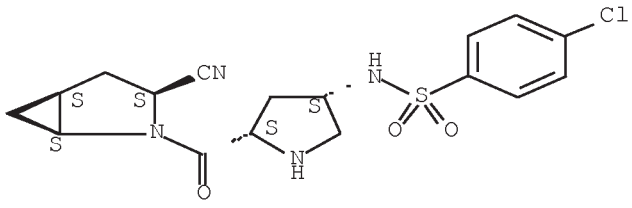
RN 866321-52-0 HCAPLUS
CN Butanamide, N-[(3S,5S)-5-[[(1S,3S,5S)-3-cyano-2-azabicyclo[3.1.0]hex-2-yl]carbonyl]-3-pyrrolidinyl]-3,3-dimethyl- (CA INDEX NAME)

Absolute stereochemistry.



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

Absolute stereochemistry.



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

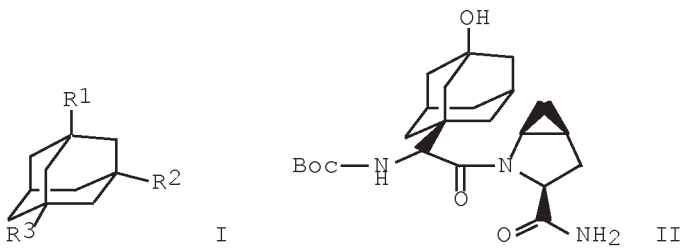
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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

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

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

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



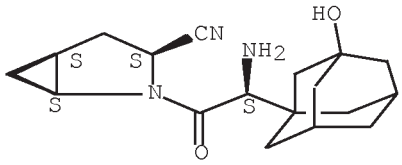
I II

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

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

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

Absolute stereochemistry.

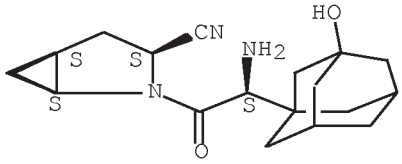


RN 709031-44-7 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-amino(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)acetyl]-,
(1S,3S,5S)-,
monobenzoate (salt) (9CI) (CA INDEX NAME)

CM 1

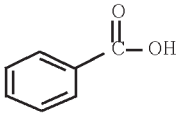
CRN 361442-04-8
CMF C18 H25 N3 O2

Absolute stereochemistry.



CM 2

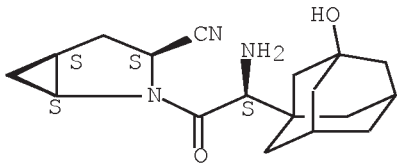
CRN 65-85-0
CMF C7 H6 O2



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

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

Absolute stereochemistry.



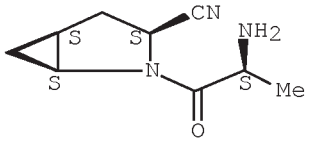
● HCl

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

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

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

Absolute stereochemistry.



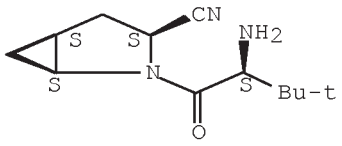
IT 361440-73-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(crystal structure; preparation and biol. activity of methanoprolinenitrile-containing dipeptide mimetics as DPP-IV inhibitors and as antidiabetic agents)
RN 361440-73-5 HCAPLUS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

CM 1

CRN 361440-72-4

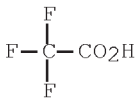
CMF C12 H19 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

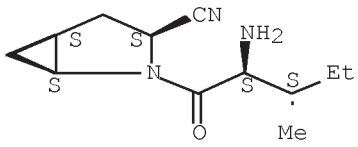


IT 361440-66-6P 361440-77-9P 361440-88-2P
700376-66-5P 700376-67-6P 700376-68-7P
700376-70-1P 700376-71-2P 700376-72-3P
700376-73-4P 700376-74-5P 700376-75-6P
700376-76-7P 700376-77-8P 700376-78-9P
700376-79-0P 700376-80-3P 700376-81-4P
700376-82-5P
RL: PAC (Pharmacological activity); SPN (Synthetic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

CM 1

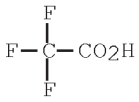
CRN 361440-65-5
CMF C12 H19 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

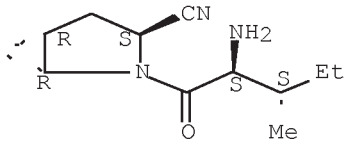


RN 361440-77-9 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]-, (1R,3S,5R)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

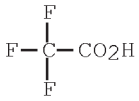
CRN 361440-76-8
CMF C12 H19 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

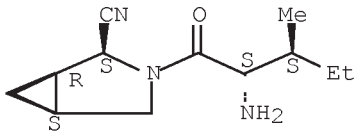


RN 361440-88-2 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile,
3-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]-, (1R,2S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

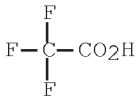
CRN 361440-87-1
CMF C12 H19 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

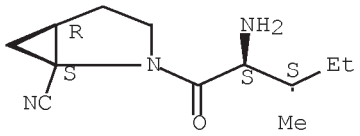


RN 700376-66-5 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-1-carbonitrile,
2-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]-, (1S,5R)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

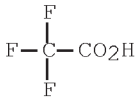
CRN 700376-65-4
CMF C12 H19 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

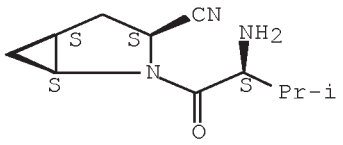


RN 700376-67-6 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-3-methyl-1-oxobutyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate
(1:1) (CA INDEX NAME)

CM 1

CRN 361441-05-6
CMF C11 H17 N3 O

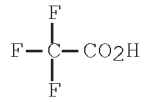
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2

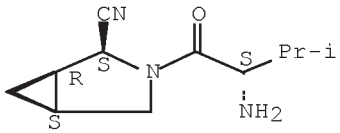


RN 700376-68-7 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile,
3-[(2S)-2-amino-3-methyl-1-oxobutyl]-, (1R,2S,5S)-,
2,2,2-trifluoroacetate
(1:1) (CA INDEX NAME)

CM 1

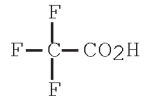
CRN 361442-40-2
CMF C11 H17 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

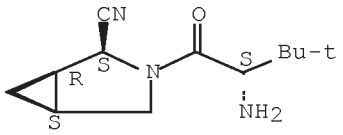


RN 700376-70-1 HCAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2-carbonitrile,
3-[(2S)-2-amino-3,3-dimethyl-1-oxobutyl]-, (1R,2S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

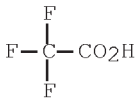
CRN 361442-39-9
CMF C12 H19 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

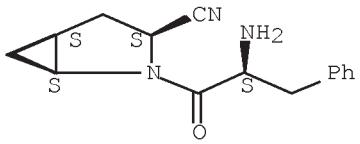


RN 700376-71-2 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-1-oxo-3-phenylpropyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

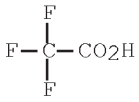
CRN 361441-08-9
CMF C15 H17 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

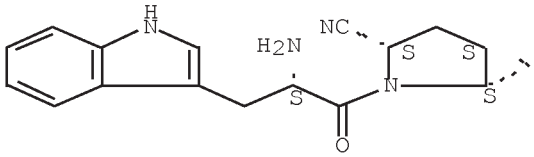


RN 700376-72-3 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-3-(1H-indol-3-yl)-1-oxopropyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

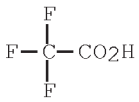
CRN 361440-97-3
CMF C17 H18 N4 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



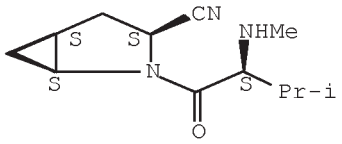
RN 700376-73-4 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-3-methyl-2-(methylamino)-1-oxobutyl]-, (1S,3S,5S)-,

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

CM 1

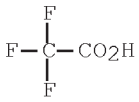
CRN 361441-04-5
CMF C12 H19 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

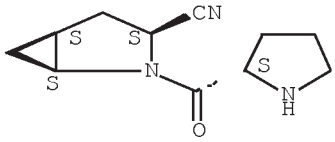


RN 700376-74-5 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile, 2-[(2S)-2-pyrrolidinylcarbonyl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

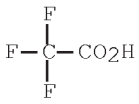
CRN 361441-07-8
CMF C11 H15 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

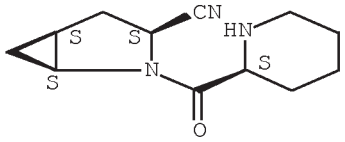


RN 700376-75-6 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-piperidinylcarbonyl]-,
(1S,3S,5S)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

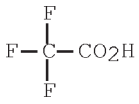
CRN 361441-10-3
CMF C12 H17 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



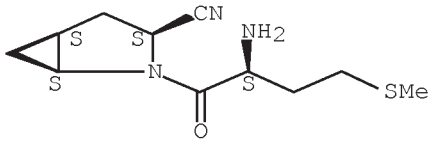
RN 700376-76-7 HCAPLUS

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

CM 1

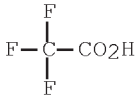
CRN 361440-99-5
CMF C11 H17 N3 O S

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

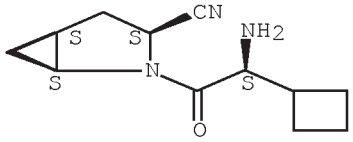


RN 700376-77-8 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-cyclobutylacetyl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate
(1:1) (CA INDEX NAME)

CM 1

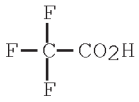
CRN 361442-56-0
CMF C12 H17 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

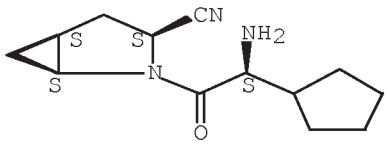


RN 700376-78-9 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-cyclopentylacetyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate
(1:1) (CA INDEX NAME)

CM 1

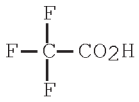
CRN 361442-54-8
CMF C13 H19 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

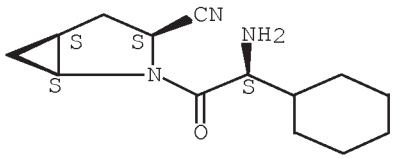


RN 700376-79-0 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-cyclohexylacetyl]-, (1S,3S,5S)-, 2,2,2-trifluoroacetate
(1:1) (CA INDEX NAME)

CM 1

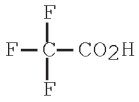
CRN 361442-55-9
CMF C14 H21 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

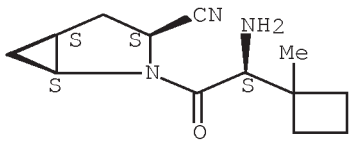


RN 700376-80-3 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(1-methylcyclobutyl)acetyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

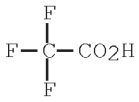
CRN 361442-53-7
CMF C13 H19 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

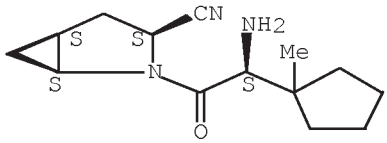


RN 700376-81-4 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(1-methylcyclopentyl)acetyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

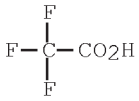
CRN 361442-50-4
CMF C14 H21 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

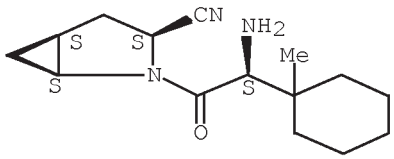


RN 700376-82-5 HCAPLUS
CN 2-Azabicyclo[3.1.0]hexane-3-carbonitrile,
2-[(2S)-2-amino-2-(1-methylcyclohexyl)acetyl]-, (1S,3S,5S)-,
2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

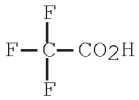
CRN 361442-48-0
CMF C15 H23 N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



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TITLE: Synthesis and SAR of azolopyrimidines as potent and selective dipeptidyl peptidase-4 (DPP4) inhibitors for type 2 diabetes.

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AB Several pyrazolo-, triazolo-, and imidazolopyrimidines were synthesized and evaluated as inhibitors of DPP4. Of these three classes of compounds, the imidazolopyrimidines displayed the greatest potency and demonstrated excellent selectivity over the other dipeptidyl peptidases. SAR evaluation for these scaffolds was described as they may represent potential treatments for type 2 diabetes. .COPYRGT. 2010 Elsevier Ltd. All rights reserved.

CT Medical Descriptors:
animal experiment
animal model
article