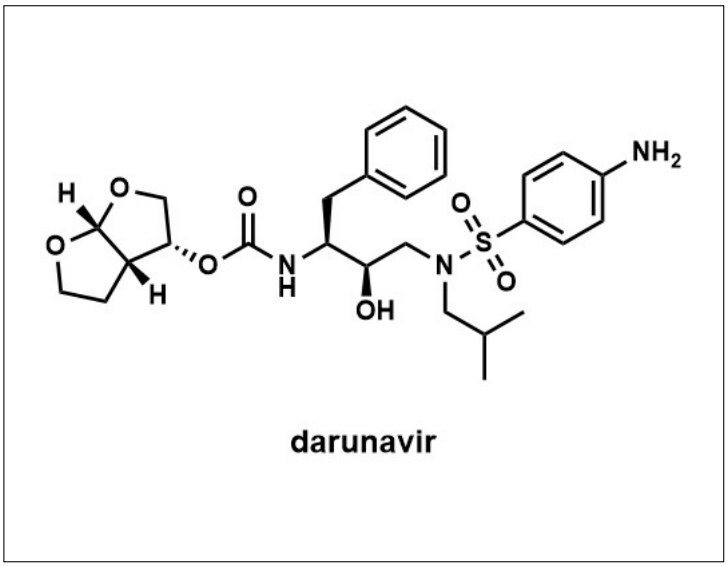
Darunavir



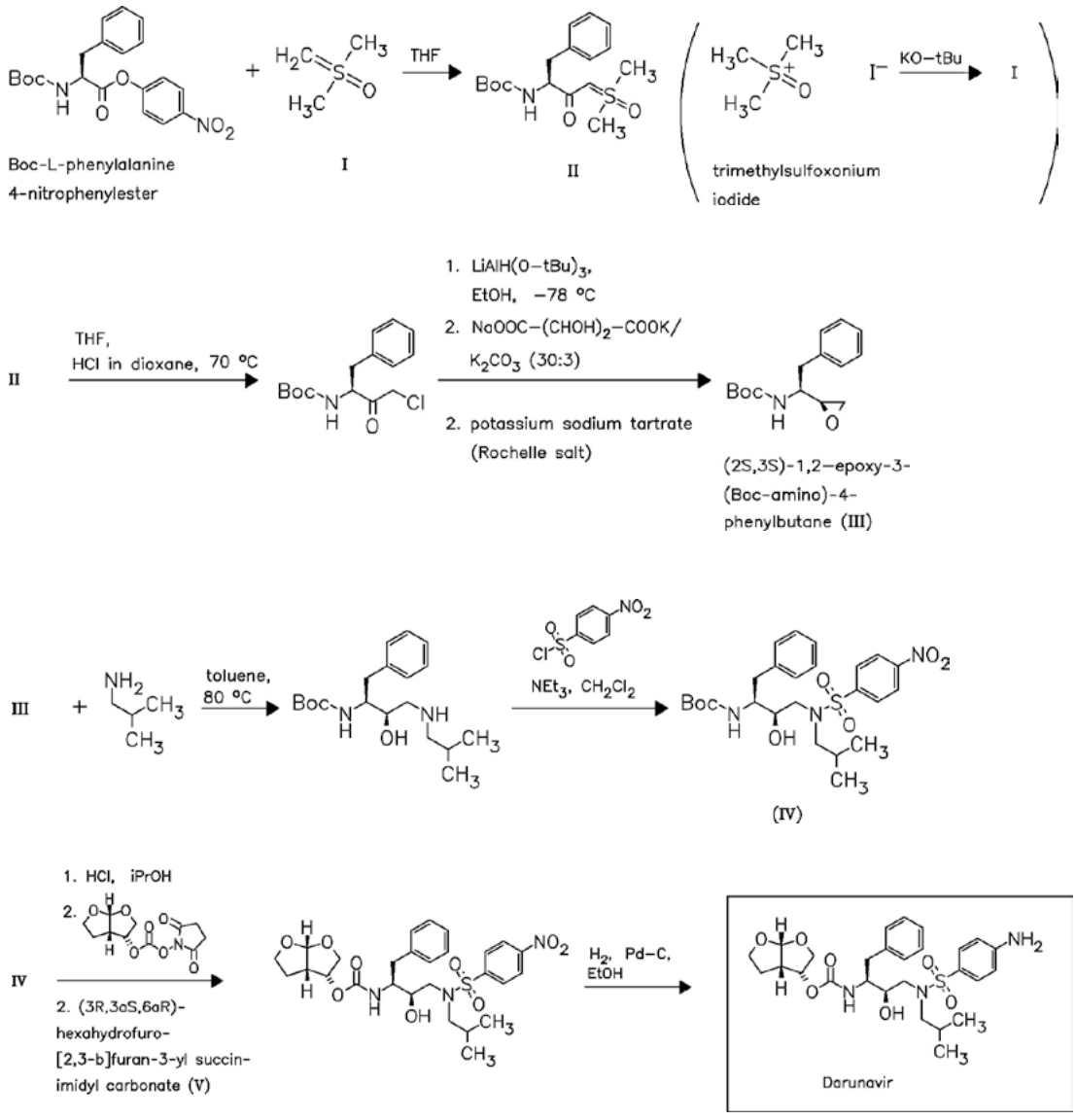
darunavir

Related reviews in Science of Synthesis

- β-Amino Alcohols
- Carbamic Acid Esters
- Arenesulfonamides
- Asymmetric Cross-Aldol Reaction for Key Intermediate

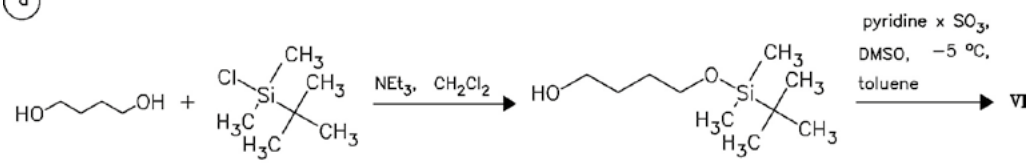
Synonyms: TMC-114, UIC-94017
ATC: J05AE10
Use: antiviral, HIV-protease inhibitor
Chemical name: [(1*S*,2*R*)-3-[[(4-aminophenyl)sulfonyl](2-methylpropyl)amino]-2-hydroxy-1-(phenylmethyl)propyl]carbamic acid (3*R*,3a*S*,6a*R*)-hexahydrofuro[2,3-*b*]furan-3-yl ester
Formula: $C_{27}H_{37}N_3O_7S$
MW: 547.67 g/mol
CAS-RN: 206361-99-1
InChI Key: CJBJHOAVZSMMDJ-HEXNFIEUSA-N
InChI: InChI=1S/C27H37N3O7S/c1-18(2)15-30(38(33,34)21-10-8-20(28)9-11-21)16-24(31)23(14-19-6-4-3-5-7-19)29-27(32)37-25-17-36-26-22(25)12-13-35-26/h3-11,18,22-26,31H,12-17,28H2,1-2H3,(H,29,32)/t22-,23-,24+,25-,26+/m0/s1

Synthesis Path

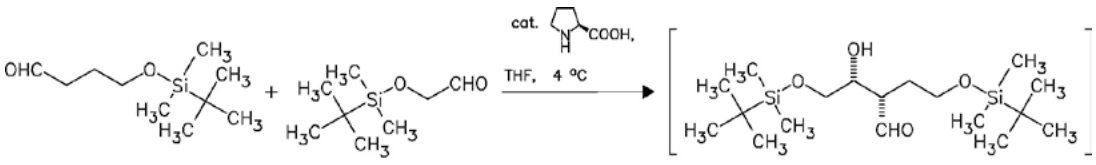


preparation of V

a



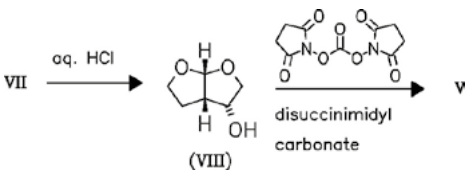
1,4-butanediol



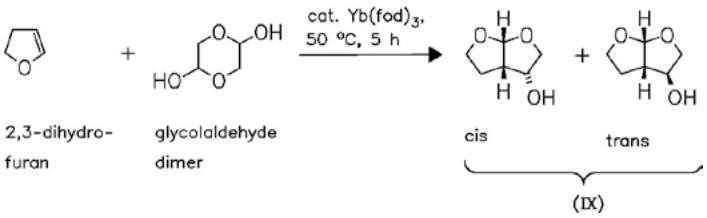
4-(tert-butyldimethylsilyloxy)-butyraldehyde (VI)

(tert-butyldimethylsilyloxy)-acetaldehyde

major diastereomer (VII)

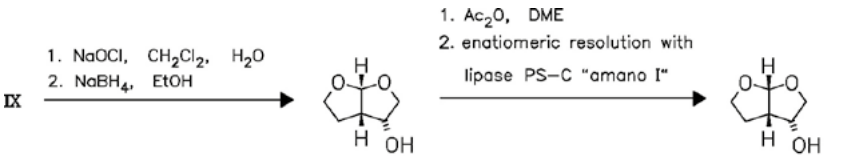


b Gilead's route



2,3-dihydro-furan

glycolaldehyde dimer



cis-rac

(3R,3aS,6aR)-hexahydrofuro-[2,3-b]furan-3-ol (VIII)

Substances Referenced in Synthesis Path

CAS-RN	Formula	Chemical Name	CAS Index Name
7535-56-0	$C_{20}H_{22}N_2O_6$	Boc-L-phenylalanine 4-nitrophenyl ester	
110-63-4	$C_4H_{10}O_2$	1,4-butanediol	1,4-Butanediol
18162-48-6	$C_6H_{15}ClSi$	*tert*-butyldimethylsilyl chloride	Silane, chloro(1,1-dimethylethyl)dimethyl-
102191-92-4	$C_8H_{18}OSi$	(*tert*-butyldimethylsilyloxy)acetaldehyde	
87184-81-4	$C_{10}H_{22}OSi$	4-(*tert*-butyldimethylsilyloxy)butyraldehyde	
160232-08-6	$C_{19}H_{32}N_2O_3$	*tert*-butyl [(1*S*,2*R*)-2-hydroxy-3-[(2-methylpropyl)amino]-1-(phenylmethyl)propyl]carbamate	Carbamic acid, [(1S,2R)-2-hydroxy-3-[(2-methylpropyl)amino]-1-(phenylmethyl)propyl]-, 1,1-dimethylethyl ester
191226-98-9	$C_{25}H_{35}N_3O_7S$	*tert*-butyl [(1*S*,2*R*)-2-hydroxy-3-[(2-methylpropyl)[(4-nitrophenyl)sulfonyl]amino]-1-(phenylmethyl)propyl]carbamate	Carbamic acid, [(1S,2R)-2-hydroxy-3-[(2-methylpropyl)[(4-nitrophenyl)sulfonyl]amino]-1-(phenylmethyl)propyl]-, 1,1-dimethylethyl ester
74124-79-1	$C_9H_8N_2O_7$	1,1'-[carbonylbis(oxy)]bis[2,5-pyrrolidinedione]	
1191-99-7	C_4H_6O	2,3-dihydrofuran	Furan, 2,3-dihydro-
	$C_{17}H_{25}NO_4S$	[(3*S*)-3-[[(1,1-dimethylethoxy)carbonyl]amino]-2-oxo-4-phenylbutylidene]dimethyloxosulfur(VI)	
102123-74-0	$C_{15}H_{20}ClNO_3$	1,1-dimethylethyl [(1*S*)-3-chloro-2-oxo-1-(phenylmethyl)propyl]carbamate	
87184-99-4	$C_{10}H_{24}OSi$	4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-butanol	
	$C_{15}H_{19}NO_3$	1,1-dimethylethyl [(1*S*)-1-[(1*S*)-oxiranyl]-2-phenylethyl]carbamate	
5367-24-8	C_3H_8OS	dimethylsulfoxonium methylide	
	$C_{11}H_{13}NO_7$	(2,5-dioxopyrrolidin-1-yl) [(3*R*,3a*R*,6a*R*)-hexahydrofuro[2,3-*b*]furan-2-yl] carbonate	
23147-58-2	$C_4H_8O_2$	glycolaldehyde dimer	
156928-09-5	$C_6H_{10}O_3$	(3*R*,3a*S*,6a*R*)-hexahydrofuro[2,3-*b*]furan-3-ol	
	$C_6H_{10}O_3$	*rel*-(3*R*,3a*R*,6a*S*)-hexahydrofuro[2,3-*b*]furan-3-ol	
	$C_6H_{10}O_3$	*rel*-(3*R*,3a*S*,6a*R*)-hexahydrofuro[2,3-*b*]furan-3-ol	
	$C_{27}H_{35}N_3O_9S$	(3*R*,3a*S*,6a*R*)-hexahydrofuro[2,3-*b*]furan-3-yl [(1*S*,2*R*)-2-hydroxy-3-[(2-methylpropyl)[(4-nitrophenyl)sulfonyl]amino]-1-(phenylmethyl)propyl]carbamate	
	$C_{18}H_{40}O_4Si_2$	(2*S*,3*R*)-3-hydroxy-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-[2-[[(1,1-dimethylethyl)dimethylsilyl]oxy]ethyl]butanal	
78-81-9	$C_4H_{11}N$	isobutylamine	1-Propanamine, 2-methyl-
98-74-8	$C_6H_4ClNO_4S$	4-nitrobenzenesulfonyl chloride	Benzenesulfonyl chloride, 4-nitro-
18162-48-6	$C_6H_{15}ClSi$	TBDMS chloride	Silane, chloro(1,1-dimethylethyl)dimethyl-
18162-48-6	$C_6H_{15}ClSi$	TBDMS-Cl	Silane, chloro(1,1-dimethylethyl)dimethyl-
1774-47-6	C_3H_9IOS	trimethylsulfoxonium iodide	Sulfoxonium, trimethyl-, iodide

Trade Names

Country	Trade Name	Vendor
D	Prezista	Janssen-Cilag, 2007
I	Prezista	Janssen-Cilag, 2007
USA	Prezista	Tibotec, 2006

Formulations

tabl. 75 mg, 300 mg, 400 mg, 600 mg

References

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Surleraux, D. L. N. G. et al.: J. Med. Chem. (JMCMAR) **48**, 1813 (2005).
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