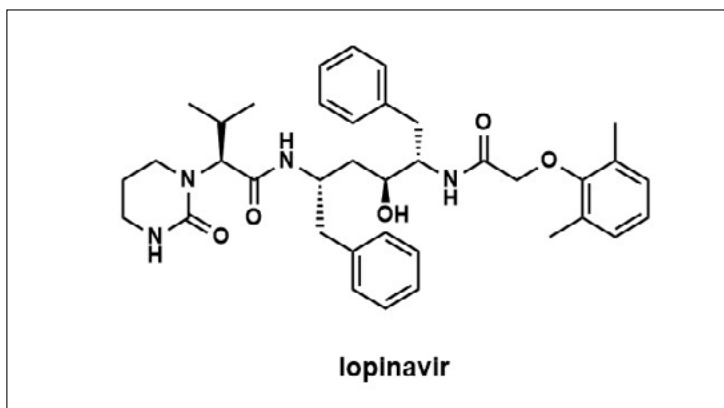


# Lopinavir



**SOS**

## Related reviews in Science of Synthesis

- $\beta$ -Amino Alcohols
- Urea Derivatives
- Reductive Amination Using Sodium Cyanoborohydride

**Synonyms:** A-157378.0, ABT-378, Amviran, RS-346

**ATC:** J05AE06

**Use:** antiviral, AIDS therapeutic, HIV-1-protease inhibitor

**Chemical name:** ( $\alpha S$ )-*N*-[(1*S*,3*S*,4*S*)-4-[[2,6-dimethylphenoxy]acetyl]amino]-3-hydroxy-5-phenyl-1-(phenylmethyl)pentyl]tetrahydro- $\alpha$ -(1-methylethyl)-2-oxo-1(2*H*)-pyrimidineacetamide

**Formula:** C<sub>37</sub>H<sub>48</sub>N<sub>4</sub>O<sub>5</sub>

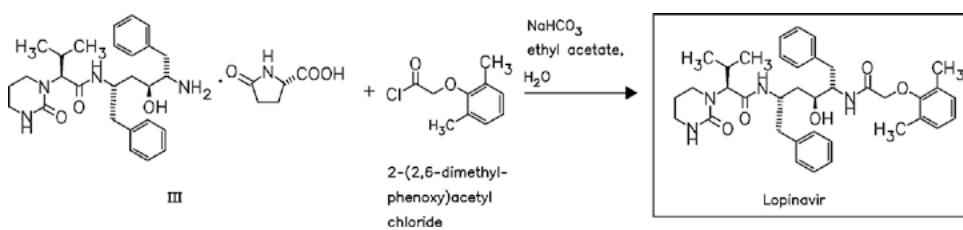
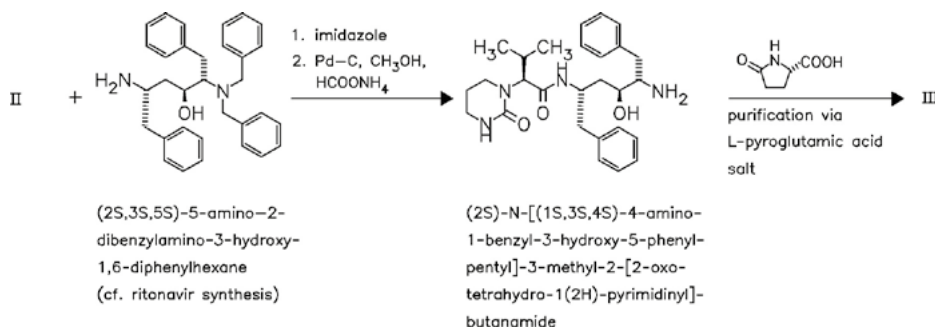
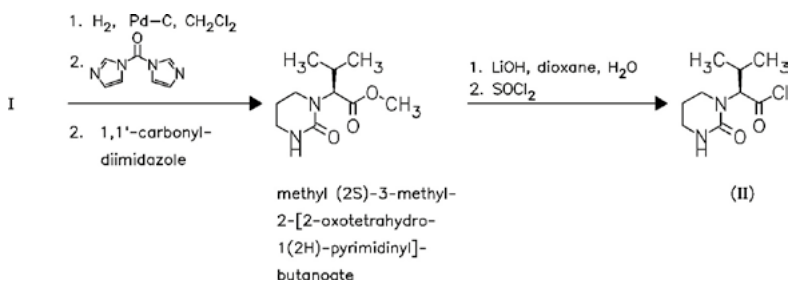
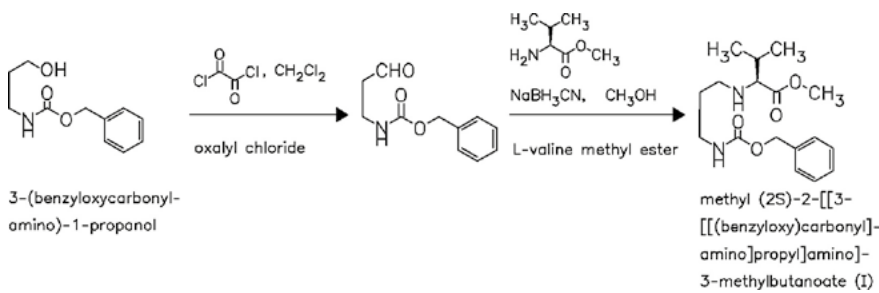
**MW:** 628.81 g/mol

**CAS-RN:** 192725-17-0

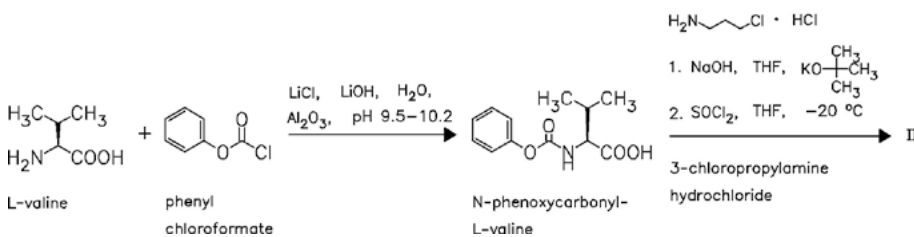
**InChI Key:** KJHKTHWMRKYKJE-SUGCFTRWSA-N

**InChI:** InChI=1S/C37H48N4O5/c1-25(2)34(41-20-12-19-38-37(41)45)36(44)39-30(21-28-15-7-5-8-16-28)23-32(42)31(22-29-17-9-6-10-18-29)40-33(43)24-46-35-26(3)13-11-14-27(35)4/h5-11,13-18,25,30-32,34,42H,12,19-24H2,1-4H3,(H,38,45)(H,39,44)(H,40,43)/t30-,31-,32-,34-/m0/s1

Synthesis Path



alternative synthesis of II



## Substances Referenced in Synthesis Path

CAS-RN	Formula	Chemical Name	CAS Index Name
192726-05-9	C <sub>27</sub> H <sub>38</sub> N <sub>4</sub> O <sub>3</sub>	(2S)-N-[(1S,3S,4S)-4-amino-1-benzyl-3-hydroxy-5-phenylpentyl]-3-methyl-2-[2-oxotetrahydro-1(2H)-pyrimidinyl]butanamide	1(2H)-Pyrimidineacetamide, N-[(1S,3S,4S)-4-amino-3-hydroxy-5-phenyl-1-(phenylmethyl)pentyl]tetrahydro- $\alpha$ -(1-methylethyl)-2-oxo-, ( $\alpha$ S)-
156732-15-9	C <sub>32</sub> H <sub>36</sub> N <sub>2</sub> O	(2S,3S,5S)-5-amino-2-dibenzylamino-3-hydroxy-1,6-diphenylhexane	Benzenebutanol, $\gamma$ -amino- $\alpha$ -[1-bis(phenylmethyl)amino]-2-phenylethyl]-, [ $\alpha$ S- $[\alpha$ R*(R*), $\gamma$ R*]]-
34637-22-4	C <sub>11</sub> H <sub>15</sub> NO <sub>3</sub>	3-(benzyloxycarbonylamino)-1-propanol	Carbamic acid, (3-hydroxypropyl)-, phenylmethyl ester
6276-54-6	C <sub>3</sub> H <sub>9</sub> Cl <sub>2</sub> N	3-chloropropylamine hydrochloride	1-Propanamine, 3-chloro-, hydrochloride
20143-48-0	C <sub>10</sub> H <sub>11</sub> ClO <sub>2</sub>	2-(2,6-dimethylphenoxy)acetyl chloride	Acetyl chloride, (2,6-dimethylphenoxy)-
192725-83-0	C <sub>17</sub> H <sub>26</sub> N <sub>2</sub> O <sub>4</sub>	methyl (2S)-2-[[3-[[[(benzyloxy)carbonyl]amino]propyl]amino]-3-methylbutanoate	L-Valine, N-[3-[[[(phenylmethoxy)carbonyl]amino]propyl]-, methyl ester
192725-85-2	C <sub>10</sub> H <sub>18</sub> N <sub>2</sub> O <sub>3</sub>	methyl (2S)-3-methyl-2-[2-oxotetrahydro-1(2H)-pyrimidinyl]butanoate	1(2H)-Pyrimidineacetic acid, tetrahydro- $\alpha$ -(1-methylethyl)-2-oxo-, methyl ester, ( $\alpha$ S)-
192726-06-0	C <sub>32</sub> H <sub>45</sub> N <sub>5</sub> O <sub>6</sub>	5-oxo-L-proline compd. with ( $\alpha$ S)-N-[(1S,3S,4S)-4-amino-3-hydroxy-5-phenyl-1-(phenylmethyl)pentyl]tetrahydro- $\alpha$ -(1-methylethyl)-2-oxo-1(2H)pyrimidineacetamide (1:1)	L-Proline, 5-oxo-, compd. with ( $\alpha$ S)-N-[(1S,3S,4S)-4-amino-3-hydroxy-5-phenyl-1-(phenylmethyl)pentyl]tetrahydro- $\alpha$ -(1-methylethyl)-2-oxo-1(2H)-pyrimidineacetamide (1:1)
65564-05-8	C <sub>11</sub> H <sub>13</sub> NO <sub>3</sub>	(3-oxopropyl)carbamic acid phenylmethyl ester	Carbamic acid, (3-oxopropyl)-, phenylmethyl ester
126147-70-4	C <sub>12</sub> H <sub>15</sub> NO <sub>4</sub>	N-phenoxy carbonyl-L-valine	L-Valine, N-(phenoxy carbonyl)-
1885-14-9	C <sub>7</sub> H <sub>5</sub> ClO <sub>2</sub>	phenyl chloroformate	Carbonochloridic acid, phenyl ester
98-79-3	C <sub>5</sub> H <sub>7</sub> NO <sub>3</sub>	L-pyroglutamic acid	L-Proline, 5-oxo-
192800-77-4	C <sub>9</sub> H <sub>15</sub> ClN <sub>2</sub> O <sub>2</sub>	( $\alpha$ S)-tetrahydro- $\alpha$ -(1-methylethyl)-2-oxo-1(2H)-pyrimidineacetyl chloride	1(2H)-Pyrimidineacetyl chloride, tetrahydro- $\alpha$ -(1-methylethyl)-2-oxo-, ( $\alpha$ S)-
72-18-4	C <sub>5</sub> H <sub>11</sub> NO <sub>2</sub>	L-valine	
4070-48-8	C <sub>6</sub> H <sub>13</sub> NO <sub>2</sub>	L-valine methyl ester	

## Trade Names

Country	Trade Name	Vendor	Annotation
D	Kaletra	Abbott	comb. with ritonavir
F	Kaletra	Abbott	
GB	Kaletra	Abbott	
I	Kaletra	Abbott	
J	Kaletra	Abbott	comb. with ritonavir
USA	Kaletra	Abbott	comb. with ritonavir

## Formulations

oral sol. 80 mg/ml Lopinavir and 20 mg/ml Ritonavir; soft-gelatin cps. 133.3 mg Lopinavir and 33.3 mg Ritonavir

## References

Stoner, E.J. et al.: Org. Process Res. Dev. (OPRDFK) **3** (2), 145 (1999).

US 5 914 332 (Abbott; 22.6.1999; appl. 21.11.1996; USA-prior. 13.12.1995).

US 5 635 523 (Abbott; 3.6.1997; appl. 6.4.1995; USA-prior. 23.5.1989, 8.9.1989, 22.12.1989, 9.5.1990, 20.11.1990, 15.8.1991, 23.10.1991, 29.12.1992, 2.12.1993).

US 5 541 206 (Abbott; 30.7.1996; appl. 25.4.1995; USA-prior. 23.5.1989, 8.9.1989, 22.12.1989, 9.5.1990, 20.11.1990, 15.8.1991, 23.10.1991, 29.12.1992, 2.12.1993).

US 5 674 882 (Abbott; 7.10.1997; appl. 29.3.1995; USA-prior. 23.5.1989, 8.9.1989, 22.12.1989, 9.5.1990, 20.11.1990, 15.8.1991, 23.10.1991, 29.12.1992, 2.12.1993).

US 5 886 036 (Abbott; 23.3.1999; appl. 20.3.1997; USA-prior. 29.12.1992, 2.12.1993, 28.3.1995).

US 5 846 987 (Abbott; 8.12.1998; appl. 20.3.1997; USA-prior. 29.12.1992, 2.12.1993, 6.4.1995).

US 5 648 497 (Abbott; 15.7.1997; appl. 24.3.1995; USA-prior. 23.5.1989, 8.9.1989, 22.12.1989, 9.5.1990, 20.11.1990, 15.8.1991, 23.10.1991, 14.9.1993, 23.8.1994).

WO 9 721 683 (Abbott; appl. 6.12.1996; USA-prior. 13.12.1995).

WO 9 721 685 (Abbott; appl. 6.12.1996; USA-prior. 13.12.1995).

### **alternative synthesis of I:**

Stoner, E.J. et al.: Org. Process Res. Dev. (OPRDFK) **4** (4), 264 (2000).

Chang, S.-J.; Stuk, T.L.: Synth. Commun. (SYNCAV) **30** (5), 955-961 (2000).

### **solid dispersions:**

WO 2 001 034 119 (Abbott; appl. 10.11.2000; USA-prior. 12.11.1999).

### **liquid compositions:**

US 6 232 333 (Abbott; appl. 7.11.1997; 15.5.2001).