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(2*S*)-2-Benzyl-1-[(4*R*)-4-benzyl-2,2-dimethyl-1,3-oxazolan-3-yl]pent-4-en-1-one

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Key indicators

Single-crystal X-ray study
T = 273 K
Mean σ(C–C) = 0.004 Å
Disorder in main residue
R factor = 0.038
wR factor = 0.101
Data-to-parameter ratio = 7.8

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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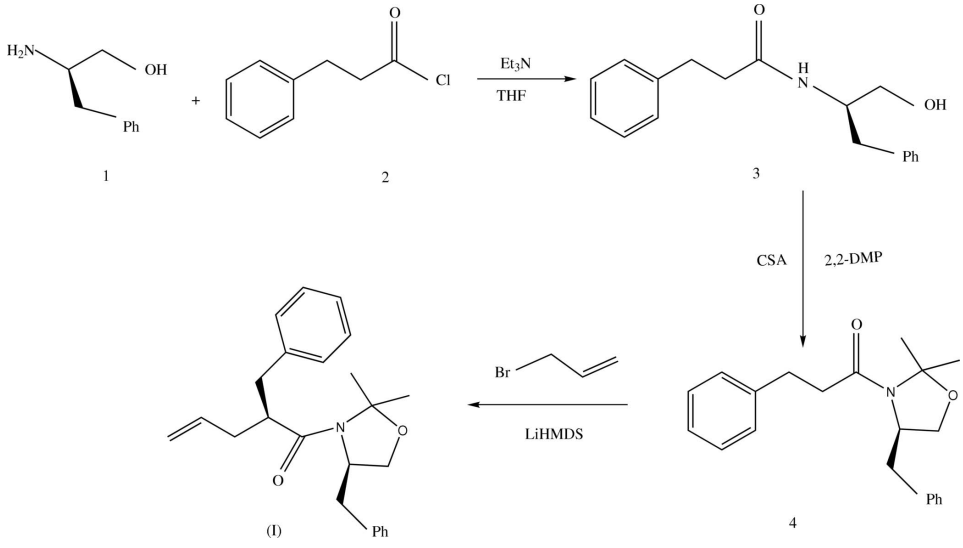
The title compound, $C_{24}H_{29}NO_2$, is one of the intermediates of the potent HIV protease inhibitor Indinavir. The oxazolidine ring adopts an envelope conformation. The orientation of the benzyl groups facilitates C—H$\cdots\pi$ interactions, forming molecular chains along the *a* axis.

Comment

Indinavir is one of the most efficacious protease inhibitors currently available. Several HIV protease inhibitors, including Indinavir, have been approved by the FDA as key therapeutic agents for the treatment of HIV infections and AIDS (Kempf & Sham, 1996). Indinavir analogues with blocked metabolism sites show highly improved pharmacokinetic profiles in animals (Cheng *et al.*, 2002). The title compound (I) is an intermediate of Indinavir and its chemical structure was suggested by IR, ^{1}H NMR and ^{13}C NMR spectroscopic analysis. In order to confirm the assigned structure, an X-ray crystallographic analysis was undertaken and the results are reported here.



The structure of (I) with the atom numbering is shown in Fig. 1. Bond lengths and angles are unexceptional and in accord with anticipated values (Cambridge Structural Database, *MOGUL* Version 1.8; Allen, 2002). The molecule is U-shaped, with the two benzyl rings facing each other in a twisted manner. The 'bridge' connecting these two ring systems is formed by atoms C4/C3/N1/C11/C12/C13 and contains the oxazolidine ring. The terminal C atoms (C23 and C24) of the butenyl chain are disordered over two positions with site occupancies of 0.58 (1) and 0.42 (1), respectively.

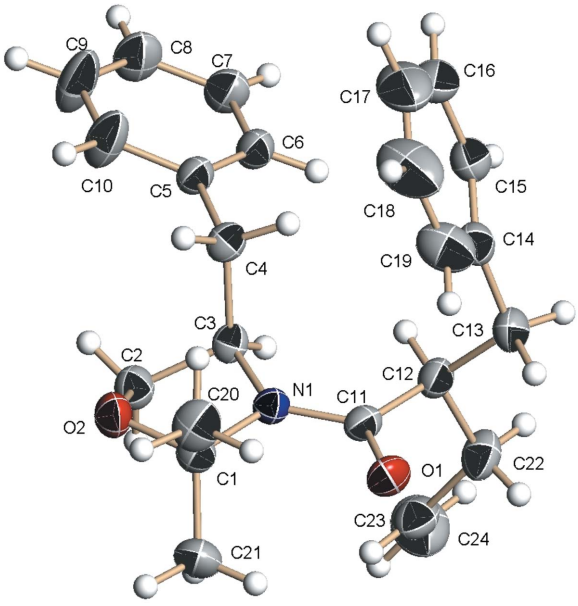


Figure 1
The molecular structure of (I), with the atom-numbering scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii. Only the major component of the disordered butenyl chain is shown.

The oxazolidine ring adopts an envelope conformation [asymmetry parameter ΔC_s(C2) = 0.013 (1) (Nardelli, 1983)], with atom C2 displaced by 0.583 (3) Å from the mean plane defined by atoms N1/C1/O2/C3. The benzyl substituent at C3 is in an antiperiplanar conformation [N1—C3—C4—C5 = 173.2 (2)°]. Atoms O1 and C11 of the carbonyl group are displaced by 0.033 (2) and 0.003 (2) Å, respectively, from the plane through atoms N1/C1/O2/C3 of the oxazolidine ring [maximum deviation 0.007 (2) Å for C1]. The disordered butenyl side chain is in an anticlinal conformation [C12—C22—C23—C24 = 121.6 (10) and −122.4 (14)° for the major and minor components, respectively]. The orientation of the two benzyl groups allows the formation of intramolecular C—H···π interactions (Table 1). The dihedral angle between the phenyl rings is 50.7 (1)°.

In the absence of classical hydrogen bonds, the crystal structure is stabilized by van der Waals interactions and by a weak C—H···π intermolecular interaction (Table 1), forming molecular chains along the *a* axis (Fig. 2).

Experimental

The title compound was prepared *via* a reaction sequence (Kiran kumar Reddy, 2004), starting with D-phenylalaninol, (1) (10 g, 62.2 mmol), acylated with 3-phenylpropionyl chloride, (2) (9.9 ml, 62.2 mmol), to yield the hydroxyl amide intermediate (3), which was treated with 2,2-methoxypropane (3.3 ml, 26.5 mmol) in the presence of a catalytic amount of camphor-10-sulfonic acid to yield the acetonide intermediate (4). Compound (4) (4 g, 12.4 mmol) was further alkylated with allyl bromide (1.1 5 ml, 13.6 mmol) at 248 K using lithium bis(trimethylsilyl)amide (10.8 ml, 14.9 mmol) as a base to yield the title compound. Crystals of (I) suitable for X-ray analysis were obtained by slow evaporation of a methanol solution. Analysis calculated for $C_{24}H_{29}NO_2$: C 79.22, H 8.12, N 3.90; found: C 79.22, H 8.04, N 3.90.

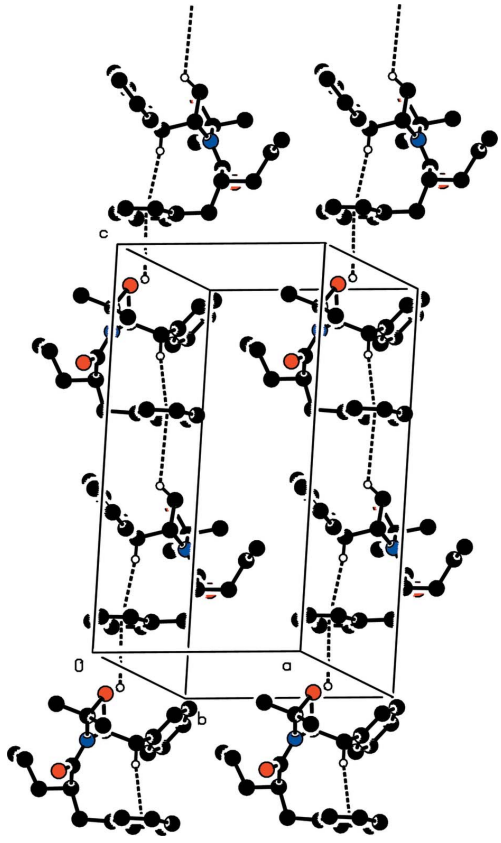


Figure 2
Part of the crystal packing of (I), showing the C—H···π interactions as dashed lines. H atoms not involved in the interactions and the minor component of the disordered butenyl chain have been omitted for clarity.

Crystal data

$C_{24}H_{29}NO_2$
M_r = 363.48
Orthorhombic, $P2_12_12_1$
a = 10.0061 (12) Å
b = 11.5146 (14) Å
c = 18.602 (2) Å
V = 2143.3 (4) Å^3
Z = 4
D_x = 1.126 Mg m^{-3}
Mo $K\alpha$ radiation
μ = 0.07 mm^{-1}
T = 273 (2) K
Block, colourless
0.19 × 0.13 × 0.09 mm

Data collection

Bruker SMART APEX CCD area-detector diffractometer
ω scans
Absorption correction: none
10985 measured reflections
2069 independent reflections
1832 reflections with $I > 2\sigma(I)$
R_{int} = 0.025
θ_{max} = 25.0°

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.038
$wR(F^2)$ = 0.101
S = 1.05
2069 reflections
265 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0558P)^2 + 0.202P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.11 e Å^{-3}
$\Delta\rho_{min}$ = −0.18 e Å^{-3}

Table 1
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
C13—H13A···O1	0.97	2.56	2.881 (4)	100
C20—H20C···O1	0.96	2.50	3.032 (4)	115
C21—H21C···O1	0.96	2.45	3.015 (4)	117
C4—H4B···$Cg1$	0.97	2.88	3.815 (2)	163
C2—H2A···$Cg1^{i}$	0.97	3.23	3.896 (2)	128

Symmetry code: (i) $-x+\frac{3}{2}, -y+2, z+\frac{1}{2}$. $Cg1$ is the centroid of the C14–C19 phenyl ring.

The site-occupation factors of the disordered atoms (C23 and C24) were refined to 0.58 (1) and 0.42 (1). The geometries about the disordered atoms were restrained with C22—C23 = C23—C23A = 1.55 (1) Å and C23—C24 = C23A—C24A = 1.24 (10) Å. H atoms were positioned geometrically and treated as riding atoms, with C—H = 0.93–0.98 Å and U_{iso}(H) = 1.5U_{eq}(methyl C) or 1.2U_{eq}(C). The methyl groups were allowed to rotate but not to tip. In the absence of significant anomalous scattering effects, Friedel pairs were merged. The absolute configuration was assigned from the known configuration of the starting material.

Data collection: *SMART* (Bruker, 2001); cell refinement: *SAINT* (Bruker, 2001); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL/PC* (Sheldrick, 1990) and *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXL97*.

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