Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

tert-Butyl 4,4-dimethyl-5-oxo-1,3-oxazolidine-3-carboxylate

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Key indicators

Single-crystal X-ray study
T = 100 K
Mean σ(C–C) = 0.001 Å
R factor = 0.034
wR factor = 0.086
Data-to-parameter ratio = 18.6

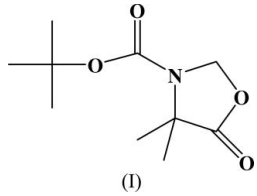
For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Received 10 October 2005
Accepted 2 November 2005
Online 16 November 2005

In the title compound, $C_{10}H_{17}NO_4$, the urethane group is planar and the oxazolidinone ring adopts an envelope conformation. Intermolecular C—H···O interactions link the screw- and glide-related molecules into a two-dimensional network parallel to (101).

Comment

N-Methylamino acid-containing peptides are increasingly recognized as potentially useful therapeutics (Fairlie *et al.*, 1995). *N*-Methylation has been shown to improve pharmacokinetically useful parameters, such as membrane permeability, proteolytic stability and conformational rigidity (Cody *et al.*, 1997). *N*-Methylamino acids are useful for obtaining information about the backbone conformations and structure–activity relationships of peptides. N^{α}-Urethane-protected 5-oxazolidinones are key intermediates, serving as useful synthons in the synthesis of *N*-methylamino acids (Freidinger *et al.*, 1983). They are also utilized for the direct preparation of dipeptides containing *N*-methylamino acids (Dorow & Gingrich, 1999) and for the synthesis of angiotensin-II analogues with full agonistic activity at the AT receptor (Johannesson *et al.*, 1999, 2002). α-Aminoisobutyric acid (Aib) is an unusual amino acid, in which the α-H atom of L-alanine is replaced by a methyl group. This substitution makes the residue achiral and introduces severe stereochemical constraints. Several Aib-containing microbial peptides (*e*.g. alamethacin, zervamicin, emerimicin, *etc*.) possess the ability to modify the permeability properties of phospholipid bilayer membranes and also form transmembrane channels. Boc-amino acids and peptides are often used as substrates, substrate analogues or competitive inhibitors of proteolytic enzymes (Benedetti *et al.*, 1980). We report here the crystal structure of the title compound, (I).



(I)

In the Boc group, the *tert*-butyl group is staggered with respect to the O1—C5 bond (Fig. 1). The torsion angles C5—O1—C4—C1 [59.3 (1)°], C5—O1—C4—C2 [176.8 (1)°] and C5—O1—C4—C3 [−65.4 (1)°] are close to the ideal values of 60, 180 and −60°, respectively. The torsion angle C4—O1—C5—O2 [4.7 (2)°] indicates that the C4—O1 and C5—O2 bonds are in a *cis* conformation. The bond angle O1—C4—C2 [101.6 (1)°] is smaller while C3—C4—C1 [112.4 (1)°] is larger

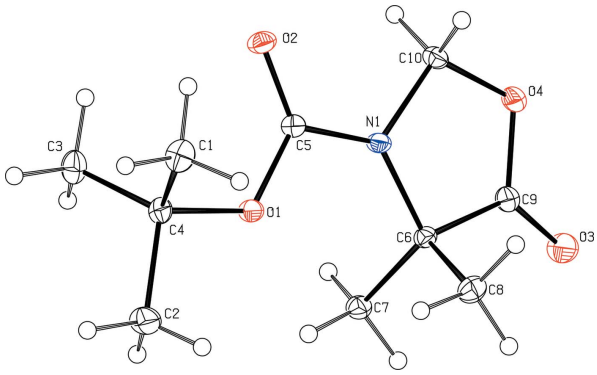


Figure 1
The molecular structure of (I), showing 30% probability displacement ellipsoids.

than the tetrahedral value. The C4—O1—C5 angle is 121.2 (1)° and it deviates from the usual value of 116.0° observed in ester groups (Karlsson *et al.*, 1979). These deviations are mainly due to the non-bonded repulsion between O2 and two of the methyl groups (C1 and C3) in the Boc moiety (Marsh *et al.*, 1977).

The urethane group is planar and the angle O1—C5—N1 [111.4 (1)°] is lower by about 5.2° than the corresponding value (116.6°; Benedetti *et al.*, 1980) observed in *trans* peptides. This is because the repulsion between the trigonal O atom in the urethane and the nearest substituent on the N1 atom is smaller than the corresponding repulsion between the tetrahedral C^{α} atom in the peptide group and the nearest substituent on the peptide N atom. The N1—C5—O1—C4 and O1—C5—N1—C6 torsion angles are −175.42 (8) −2.9 (1)°, respectively.

The atom C6 deviates by 0.134 (1) Å from the mean plane through atoms C9/O4/C10/N1. The puckering parameters (Cremer & Pople, 1975) and smallest displacement asymmetry parameters (Nardelli, 1983) for the ring (involving atoms C9/O4/C10/N1/C6), $q2 = 0.082$ (1) Å, $\varphi = 146.3$ (1)° and Δ_s (C6) = 0.003 (1), show that it adopts an envelope conformation, with flap atom C6. The molecular structure is stabilized by three C—H···O intramolecular interactions. The crystal packing is stabilized by two C—H···O intermolecular interactions (Table 2). The C10—H10*B*···O2^{ii} interaction links screw-related molecules into chains along the *b* axis. Glide-related molecules in adjacent chains are linked by intermolecular C2—H2*C*···O3^{i} interactions (symmetry codes are given in Table 2), forming a two-dimensional network parallel to (101) (Fig. 2).

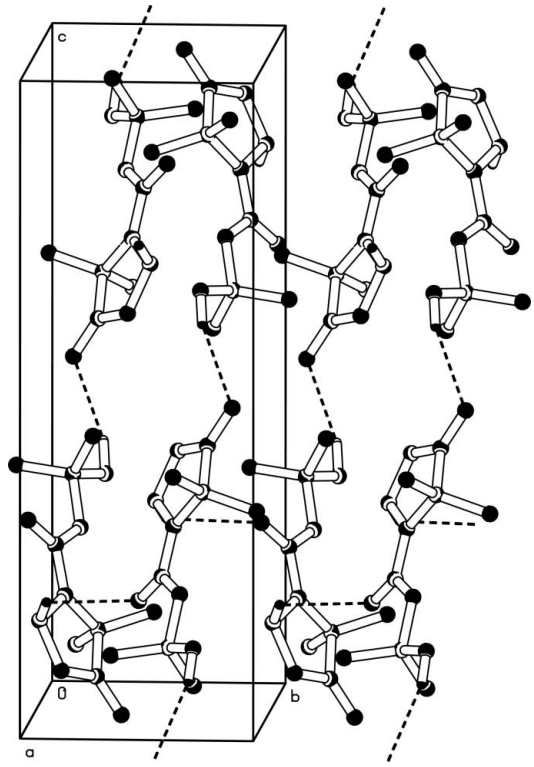
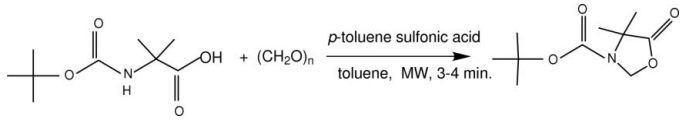


Figure 2
The crystal packing of (I), viewed approximately down the *a* axis. For clarity, only H atoms involved in the hydrogen bonds (dashed lines) are shown.

Experimental

A slurry of *tert*-butoxycarbonylisobutyric acid (2.033 g, 10 mmol), paraformaldehyde (2 g) and *p*-toluenesulfonic acid (100 mg, 0.52 mmol) in toluene (5 ml) was exposed to microwave irradiation. The reaction mixture was diluted with ethyl acetate (15 ml), washed with water (2 × 10 ml), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The resulting residue was recrystallized using dichloromethane and hexane (1:3 *v*/*v*) [yield: 1.65 g (76.7%), m.p. 340 K]. IR cm^{-1} ($CHCl_3$): 1692, 1806; ^{1}H NMR ($CDCl_3$, δ): 1.4 (9H, *s*), 1.52 (6H, *s*), 5.12 (2H, *s*). Analysis calculated for $C_{10}H_{17}NO_4$: C 55.80, H 7.96, N 6.51%; found: C 55.75, H 7.90, N 6.45%.



Crystal data

$C_{10}H_{17}NO_4$
$M_r = 215.25$
Monoclinic, $P2_1/n$
$a = 10.8869$ (9) Å
$b = 6.1138$ (5) Å
$c = 17.3497$ (14) Å
$\beta = 90.182$ (7)°
$V = 1154.80$ (16) Å^3
$Z = 4$
$D_x = 1.238$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 2624 reflections
$\theta = 4.5$–27.6°
$\mu = 0.10$ mm^{-1}
$T = 100$ K
Block, colourless
0.45 × 0.30 × 0.26 mm

Data collection

Oxford Diffraction Xcalibur3 CCD area-detector diffractometer
ω scans
Absorption correction: none
8044 measured reflections
2624 independent reflections
2419 reflections with $I > 2\sigma(I)$
$R_{int} = 0.012$
$\theta_{max} = 27.6°$
$h = -13 \rightarrow 14$
$k = -7 \rightarrow 7$
$l = -22 \rightarrow 20$

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0384P)^2 + 0.3972P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)] = 0.034$	$(\Delta/\sigma)_{max} = 0.001$
$wR(F^2) = 0.086$	$\Delta\rho_{max} = 0.32$ e Å^{-3}
$S = 1.06$	$\Delta\rho_{min} = -0.19$ e Å^{-3}
2624 reflections	
141 parameters	
H-atom parameters constrained	

Table 1
Selected geometric parameters (Å, °).

C4—O1	1.483 (1)	C9—O3	1.197 (1)
C5—O2	1.219 (1)	C9—O4	1.350 (1)
C5—O1	1.341 (1)	C10—O4	1.4273 (12)
C5—N1	1.351 (1)	C10—N1	1.457 (1)
C6—N1	1.4643 (11)		
O2—C5—O1	126.40 (9)	C5—N1—C6	129.59 (8)
O1—C5—N1	111.4 (1)	C10—N1—C6	112.26 (7)
C5—N1—C10	118.13 (8)		

Table 2
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
C1—H1*A*···O2	0.96	2.46	3.015 (1)	116
C2—H2*C*···O3^{i}	0.96	2.47	3.404 (2)	164
C3—H3*C*···O2	0.96	2.50	3.057 (1)	117
C7—H7*C*···O1	0.96	2.46	2.962 (1)	112
C10—H10*B*···O2^{ii}	0.97	2.48	2.995 (1)	113

Symmetry codes: (i) $x+\frac{1}{2}, -y+\frac{3}{2}, z-\frac{1}{2}$; (ii) $-x+\frac{1}{2}, y-\frac{1}{2}, -z+\frac{3}{2}$.

H atoms were positioned geometrically and allowed to ride on their parent C atoms, with C—H = 0.96 or 0.97 Å and U_{iso}(H) = 1.2–1.5U_{eq}(C).

Data collection: *CrysAlis CCD* (Oxford Diffraction, 2005); cell refinement: *CrysAlis CCD*; data reduction: *CrysAlis RED* (Oxford Diffraction, 2005); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXL97* and *PARST* (Nardelli, 1995).

Financial support from the University Grants Commission (UGC–SAP) and the Department of Science & Technology (DST-FIST), Government of India, is acknowledged for providing facilities to the department. DG thanks the University Grants Commission for a fellowship and DV thanks the Council of Scientific Industrial Research (CSIR), India, for funding. Oxford Diffraction is greatfully acknowledged for providing the X-ray data. VVSB thanks the Department of Biotechnology, Government of India, for financial assistance.

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