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# *tert*-Butoxycarbonyl-L-leucyl-L-valine trichloroethyl ester (Boc-L-Leu-L-Val-OTce)

**Hiroyuki Oku,* Teruya Endo, Keiichi Yamada and Ryoichi Katakai**

Department of Chemistry, Gunma University, Kiryu, Gunma 376-8515, Japan

Correspondence e-mail: oku@chem.gunma-u.ac.jp

**Key indicators**

Single-crystal X-ray study
*T* = 173 K
Mean σ(C–C) = 0.007 Å
*R* factor = 0.035
*wR* factor = 0.087
Data-to-parameter ratio = 15.3

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



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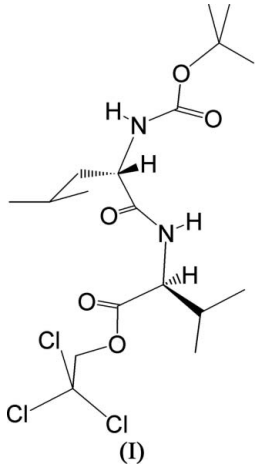
The title compound, $C_{18}H_{31}Cl_3N_2O_5$, an enantiopure dipeptide trichloroethyl ester, is one of two starting fragments in the synthesis of cyclosporin O analogs. In the crystal structure, molecules are linked by N—H···O=C hydrogen bonds, forming a β-spiral assembly along the *c* axis.

## Comment

Cyclosporins are naturally occurring physiologically active peptides containing *N*-methyl amino acid residues, which are potent chemotherapeutic agents (Humpherey & Chamberlin, 1997; Walgate, 1985; Stiller *et al.*, 1984). The 2,2,2-trichloroethyl group (–OTce) is widely employed for carboxyl protection, and the compound (I) is one of two starting –OTce protected fragments in our synthetic study of cyclosporin O derivatives (Endo *et al.*, 2003). We have recently reported the crystal structure of the other fragment, Boc-L-Leu-L-Ala-OTce (II) (Oku, *et al.*, 2005). In this paper, we have studied the structure of (I) to assess the enantiopurity and crystallinity.




(I)

The molecular structure of (I) and the packing viewed along the *c* and *a* axes are shown in Figs. 1, 2 and 3, respectively. The crystal structure of (I) is isostructural to that of (II) (space group $P6_5$; Oku *et al.*, 2005). The cell lengths *a* and *c* are longer than those of (II) by 0.140 (5) and 0.477 (13) Å, respectively. The main chain torsion angles of (I) deviate by only 2.0–5.3° from those of (II). As observed in (II), the structure of (I) adopts an extended β-sheet conformation (Table 1) and molecules are tightly linked together by N—H···O=C hydrogen bonds (Table 2), forming a β-spiral assembly along the *c* axis (Fig. 3). The melting point of (I) is 38 K lower than that of (II). This probably corresponds to the relatively high thermal motion of the Val side chain (atoms C33/C34/C35) of (I).

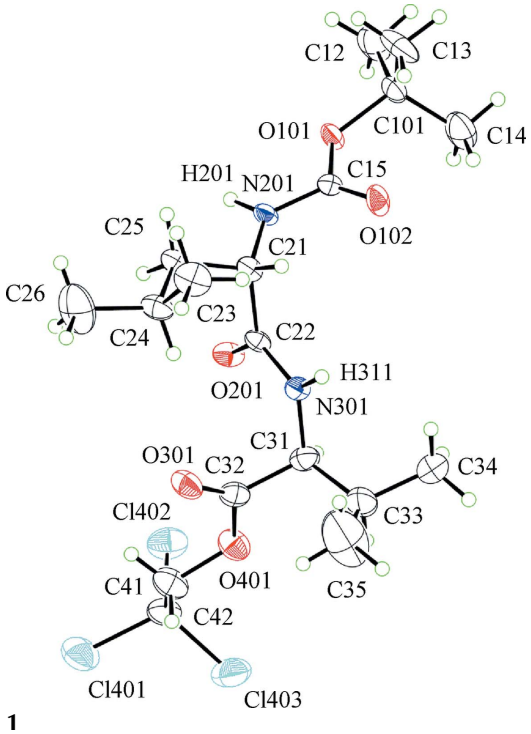



**Figure 1**
A view of (I) with the atomic numbering scheme. Displacement ellipsoids are drawn at the 20% probability level.

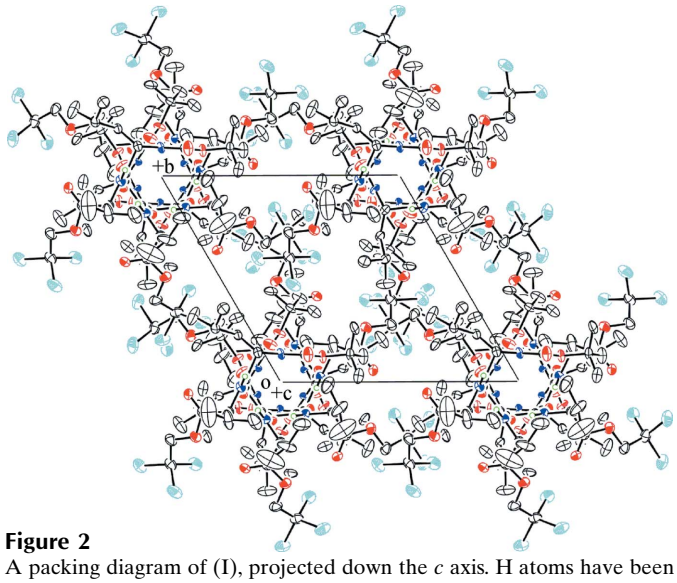



**Figure 2**
A packing diagram of (I), projected down the *c* axis. H atoms have been omitted except for those of NH groups.

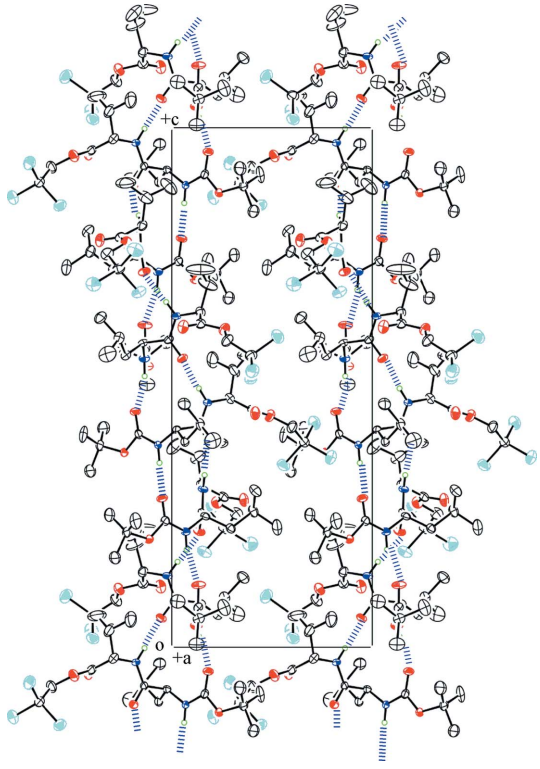



**Figure 3**
A packing diagram of (I), projected down the *a* axis. $\beta$-Spiral colums are formed along the *c* axis. H atoms have been omitted except for those of NH groups. Dashed lines indicate hydrogen bonds.

## Experimental

The title peptide, (I), was prepared by the coupling of Boc-Leu-OH·-0.5$H_2O$ (4.5 g, 18 mmol) and HCl·Val-OTce (4.3 g, 15 mmol) in a solution-phase synthesis; yield 6.1 g (87%). Colorless needle crystals of (I) were grown by slow diffusion of hexane vapor into a solution in ethyl acetate. Analytical data (melting point, $^1$H NMR, ESI–MS, and $[\alpha]_D^{20}$) are in accordance with the expected structure; $[\alpha]_D^{20} = -47.6°$ ($c$ = 0.1, methanol), m.p. 377–379 K.

*Crystal data*

$C_{18}H_{31}Cl_3N_2O_5$
$M_r$ = 461.81
Hexagonal, $P6_5$
$a$ = 12.245 (5) Å
$c$ = 27.416 (13) Å
$V$ = 3560 (3) Å$^3$
$Z$ = 6
$D_x$ = 1.292 Mg m$^{-3}$
Cu $K\alpha$ radiation
$\mu$ = 3.75 mm$^{-1}$
$T$ = 173.1 K
Needle, colorless
0.20 × 0.01 × 0.01 mm

*Data collection*

Rigaku R-AXIS RAPID diffractometer
$\omega$ scans
Absorption correction: none
32841 measured reflections
4352 independent reflections
1558 reflections with $F^2 > 2\sigma(F^2)$
$R_{int}$ = 0.068
$\theta_{max}$ = 68.2°

*Refinement*

Refinement on $F^2$
$R[F^2 > 2\sigma(F^2)]$ = 0.035
$wR(F^2)$ = 0.087
$S$ = 0.97
4352 reflections
285 parameters
All H-atom parameters refined
$w = 4F_o^2/[0.0002F_o^2 + 0.2\sigma(F_o^2) + 0.1]$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 1.17 e Å$^{-3}$
$\Delta\rho_{min}$ = −0.93 e Å$^{-3}$
Absolute structure: Flack (1983), 2123 Friedel pairs
Flack parameter: 0.015 (15)

**Table 1**
Selected torsion angles (°).

| | | | |
|---|---|---|---|
| C32—O401—C41—C42 | 154.9 (4) | C22—N301—C31—C32 | −63.9 (4) |
| C41—O401—C32—C31 | −179.8 (3) | C31—N301—C22—C21 | 177.7 (3) |
| C15—N201—C21—C22 | −96.9 (4) | N201—C21—C22—N301 | 128.6 (3) |
| C21—N201—C15—O101 | 178.5 (4) | N301—C31—C32—O401 | 155.1 (3) |

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

| $D$—H···$A$ | $D$—H | H···$A$ | $D$···$A$ | $D$—H···$A$ |
|---|---|---|---|---|
| N201—H201···O102$^{i}$ | 0.95 | 1.98 | 2.902 (4) | 162 |
| N301—H301···O201$^{ii}$ | 0.94 | 2.01 | 2.947 (4) | 177 |

Symmetry codes: (i) $x-y+1, x, z-\frac{1}{6}$; (ii) $y, -x+y+1, z+\frac{1}{6}$.

The ratio of observed/unique reflections was relatively low (36%), although the X-ray measurement was carried out at 173 K with Cu $K\alpha$ radiation. H atoms were positioned geometrically, with C—H and N—H = 0.95 Å, and refined using a riding model, with $U_{iso}$(H) assigned to be $1.2U_{eq}$(carrier atom). The absolute configuration of (I) agrees with the fact that the $^1$H NMR spectroscopic data detected no racemization in the preparation.

Data collection: *RAPID-AUTO* (Rigaku, 2003); cell refinement: *RAPID-AUTO*; data reduction: *CrystalStructure* (Rigaku, 2003); program(s) used to solve structure: *SIR2002* (Burla *et al.*, 2003); program(s) used to refine structure: *CRYSTALS* (Betteridge *et al.*, 2003); molecular graphics: *ORTEP* (Johnson, 1965); software used to prepare material for publication: *CrystalStructure*.

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