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O-Benzyl-*N*-*tert*-butoxycarbonyl-L-threonyl-L-proline trichloroethyl ester [Boc-L-Thr(Bzl)-L-Pro-OTce]

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Key indicators

Single-crystal X-ray study
T = 173 K
Mean σ(C–C) = 0.009 Å
R factor = 0.063
wR factor = 0.145
Data-to-parameter ratio = 13.7

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

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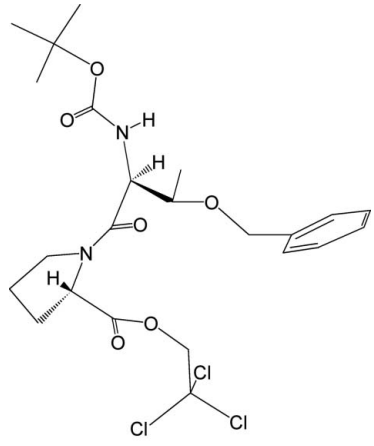
The title peptide compound, $C_{23}H_{31}Cl_3N_2O_6$, is a synthetic intermediate as a plasmodium falciparum blood-stage antigen. There is an intramolecular N—H···O hydrogen bond between the urethane and benzyl ether groups. The relatively low melting point is attributed to the lack of an intermolecular hydrogen-bond network.

Comment

The title compound, (I) is a key starting material (Omi *et al.*, 2005) in our continuing studies of synthetic antigens for falciparum malaria (Karasawa *et al.*, 2000; Ishiguro *et al.*, 2001; Kokubo *et al.*, 2002; Noi *et al.*, 2003.



Boc-L-Thr(Bzl)-L-Pro-OTce

(I)

Generally, in peptide synthesis, the 2,2,2-trichloroethyl group (—OTce) is useful for carboxyl protection and can be removed simply by treating the peptide with zinc powder in acetic acid (Marinier *et al.*, 1973; Olsen *et al.*, 1986; Pastuszak *et al.*, 1982; Yamada *et al.*, 2003; Endo *et al.*, 2003; Oku *et al.*, 2005). We often encounter oily products and poor crystallinity when we prepare *N*-protected peptide trichloroethyl esters, such as *Z*-Ala-OTce (Dhaon *et al.*, 1982), *Z*-Leu-Ala-OTce (Marinier *et al.*, 1973), Boc-Val-Leu-OTce (Yamada *et al.*, 2003) and Boc-Asp(OBzl)-Leu-OTce (Omi *et al.*, 2005). Therefore, in this paper, to assess the enantiopurity and crystallinity, we have studied the solid-state structure of (I) by X-ray crystallography.

There is one molecule in the asymmetric unit (Fig. 1). An N—H···O hydrogen bond (Table 2) is found between O202 of the benzyl ether and N201—H1 of the urethane group. There is no intermolecular hydrogen bond and molecules are probably connected together by van der Waals forces and dipole–dipole interactions (Fig. 2). The relatively low melting point of

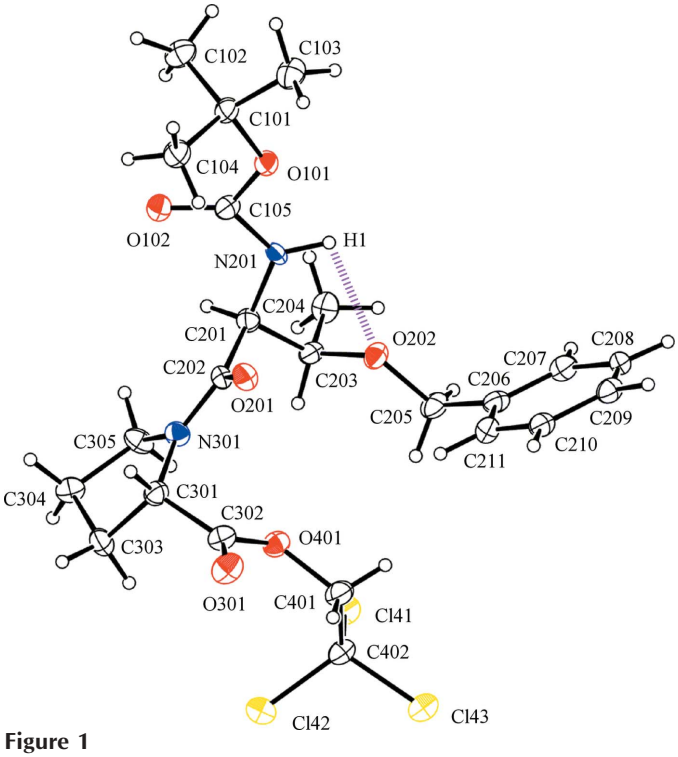


Figure 1
A view of (I) with the atomic numbering scheme. Displacement ellipsoids are drawn at the 20% probability level. The dashed line indicates a hydrogen bond.

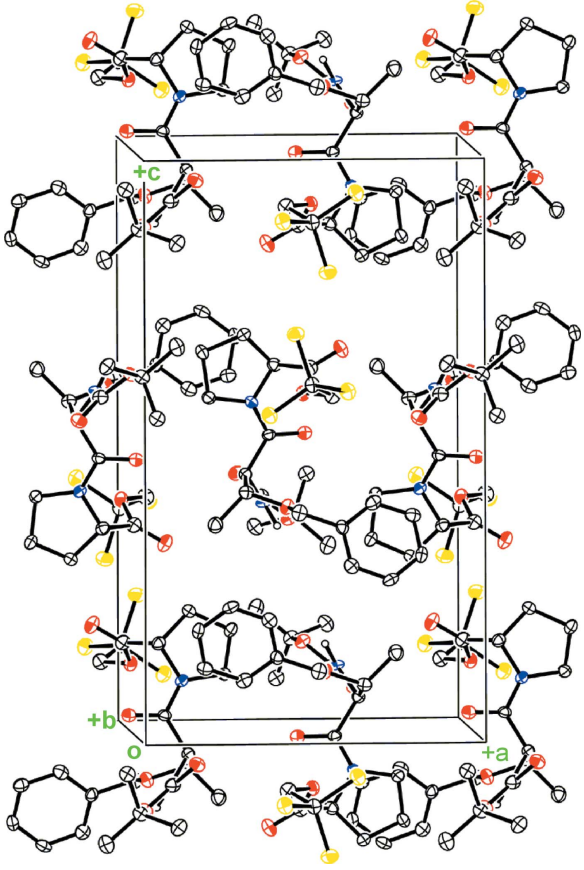


Figure 2
A packing diagram of (I). H atoms have been omitted for clarity, except for those of NH groups.

(I) is attributed to the lack of an intermolecular hydrogen-bond network, which is an important crystallizing force for short-peptide compounds (Oku *et al.*, 2003, 2003*a*,*b*; Antolic *et al.*, 1999; Ashida *et al.*, 1981; Cruse *et al.*, 1982). Thus, the weak intermolecular association in the crystal structure and the thermal mobility, especially at Boc-Thr(Bzl), probably lowers the melting point of (I).

Experimental

The title compound, (I), was prepared by the coupling of Boc-Thr(Bzl)-OH (5.10 g, 16.5 mmol) and HCl·Pro-OTce (4.24 g, 15.0 mmol) as a solution-phase synthesis. Dicyclohexylcarbodiimide (3.41 g, 15.0 mmol) was used as a coupling reagent (yield 6.55 g, 81%). Crystals of (I) were successfully grown from an oil by the addition of diethyl ether or n-hexane and stored below 277 K overnight. The fine platelets have shown relatively low melting point, 381–382 K. Analytical data (melting point, ^{1}H NMR, ESI–MS and $[\alpha]_D^{20}$) are in accordance with the expected structure; $[\alpha]_D^{20} = -49.4^\circ$ (*c* 0.1, methanol).

Crystal data

$C_{23}H_{31}Cl_3N_2O_6$
$M_r = 537.87$
Orthorhombic, $P2_12_12_1$
$a = 11.311$ (9) Å
$b = 11.693$ (7) Å
$c = 19.417$ (12) Å
$V = 2568$ (3) Å^3
$Z = 4$
$D_x = 1.391$ Mg m^{-3}
Cu $K\alpha$ radiation
Cell parameters from 20848 reflections
$\theta = 3.9$–67.2°
$\mu = 3.58$ mm^{-1}
$T = 173.1$ K
Platelet, colorless
0.05 × 0.02 × 0.01 mm

Data collection

Rigaku R-AXIS RAPID diffractometer
ω scans
20848 measured reflections
4647 independent reflections
2140 reflections with $F^2 > 2\sigma(F^2)$
$R_{int} = 0.071$
$\theta_{max} = 68.2^\circ$
$h = -13 \rightarrow 13$
$k = -14 \rightarrow 14$
$l = -23 \rightarrow 23$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.063$
$wR(F^2) = 0.145$
$S = 0.97$
4647 reflections
339 parameters
H-atom parameters constrained
$w = 4F_o^2/[0.0008F_o^2 + \sigma(F_o^2)]$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.74$ e Å^{-3}
$\Delta\rho_{min} = -1.01$ e Å^{-3}
Absolute structure: Flack (1983), 1983 Friedel pairs
Flack parameter: 0.16 (2)

Table 1
Selected geometric parameters (°).

C101—O101—C105—N201	−177.5 (5)	C202—N301—C301—C302	−63.5 (7)
C401—O401—C302—C301	−172.5 (5)	C301—N301—C202—C201	174.6 (5)
C105—N201—C201—C202	−68.8 (6)	N201—C201—C202—N301	164.0 (5)
C201—N201—C105—O101	162.6 (5)	N301—C301—C302—O401	−33.3 (7)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N201—H1···O202	0.95	2.25	2.601 (6)	101

H atoms were positioned geometrically and refined using a riding model, with N—H = C—H = 0.95Å and U_{iso}(H) = 1.2U_{eq}(N,C). 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/MSC, 2003); cell refinement: *RAPID-AUTO*; data reduction: *CrystalStructure* (Rigaku/MSC, 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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