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7-Isopropyl-5-methyl-1,3,5-triazepan-2,6-dione deuterated chloroform 0.94-solvate

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Key indicators

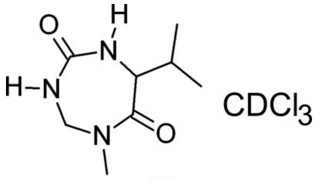
Single-crystal X-ray study
T = 100 K
Mean σ(C–C) = 0.002 Å
Disorder in solvent or counterion
R factor = 0.028
wR factor = 0.073
Data-to-parameter ratio = 24.3

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

The title compound, $C_8H_{15}N_3O_2.0.94CDCl_3$, displays a folded conformation and cocrystallizes with deuterated chloroform molecules. The asymmetric unit contains two triazepan molecules and two solvent molecules with incomplete occupancy. The expected absolute configuration was confirmed from the Flack parameter using anomalous dispersion. Molecules are linked by hydrogen bonds to form infinite planes which are perpendicular to the c axis. The network of these planes is sandwiched by a layer of organic solvent molecules through hydrogen bonds and van der Waals interactions.

Comment

We have recently developed the 1,3,5-triazepan-2,6-dione system as a novel, conformationally restricted, and readily accessible class of dipeptidomimetics (Lena, Lallemand *et al.*, 2006). Because they are structurally diverse and rapidly accessible in a library format from *N*-protected dipeptides, 1,3,5-triazepan-2,6-diones have a strong potential for applications in biology. So far, *in silico* and biological screens led to the identification of compounds with activity against the malaria liver stage (Lena, Lallemand *et al.*, 2006) and to the discovery of inhibitors of secreted phospholipase A2 (sPLA2) (Muller *et al.*, 2006). Moreover, the 1,3,5-triazepan-2,6-dione skeleton is a versatile new supramolecular synthon with unique self-assembly behaviour. For example, we found that 7-benzyl-5-methyl-1,3,5-triazepan-2,6-dione [*i.e.* *cyclo*(Phe-*g*Sar-CO)] aggregates to form unusual hydrogen-bonded helical molecular tapes and a stable helical tubular network large enough to accommodate guest solvent molecules inside channels (Schaffner *et al.*, 2006). To elucidate the role of the benzyl (Phe) side chain and aromatic interactions in the formation and stabilization of helical molecular tapes, we have, therefore, investigated self-assembly in the solid state of 1,3,5-triazepan-2,6-dione lacking an aromatic side chain at the 7-position. Here, we present the X-ray crystal structure of the title compound, (I), the deuterated chloroform 0.94-solvate of *cyclo*(L-Val-*g*Sar-CO).


(I)

The title compound crystallizes in space group $P2_12_12_1$ with two *cyclo*(L-Val-*g*Sar-CO) molecules (labelled *A* and *B*, see

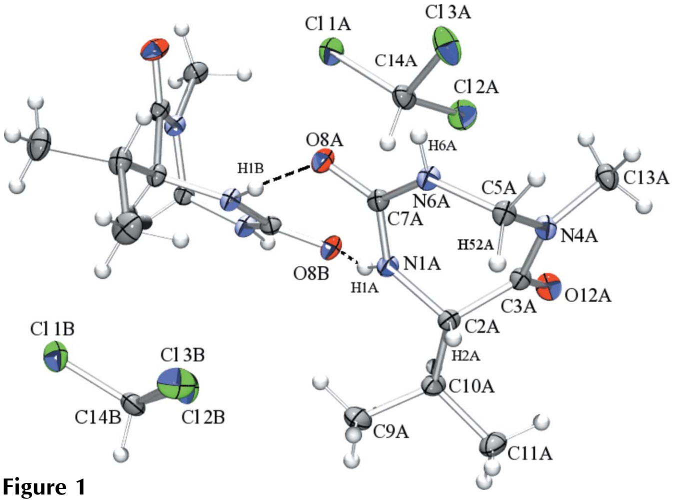


Figure 1
The asymetric unit of the title compound. Atomic displacement ellipsoids are plotted at the 50% probability level. Image rendered with *PovRay* (Persistence of Vision Development Team, 2005). The dashed line indicates a hydrogen bond.

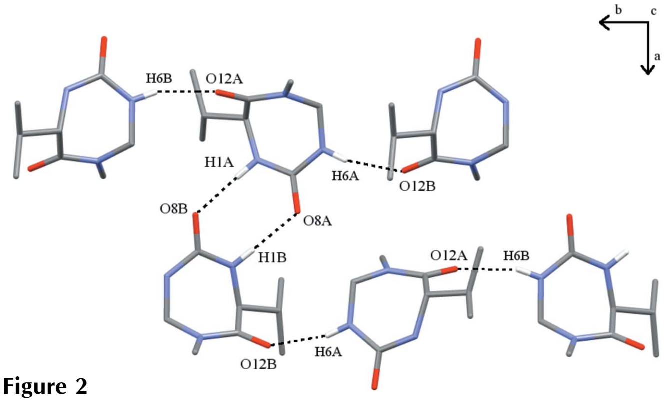


Figure 2
Hydrogen bonding of (I) forms infinite molecular planes perpendicular to the *c* axis (only N—H···O═C hydrogen bonds are displayed as dashed lines and H atoms not involved in these interactions have been omitted for clarity; view along *c* axis).

Fig. 1) and two deuterated chloroform molecules with incomplete occupancy per asymmetric unit. The *S* configuration of the α-C atom of the valine residue was checked using anomalous dispersion arising mainly from the chlorine atoms of the solvent. All interatomic bond distances are consistent with tabulated values (Allen *et al.*, 1995).

Molecules *A* and *B* both consist of nearly planar halves; the first is composed of atoms C2, C3, N4, C5, O12 and C13 with an r.m.s. deviation from planarity equal to 0.043 and 0.075 Å for molecules *A* and *B*, respectively. The second halves of the molecules are composed of atoms C2, N1, C7, N6, C5 and O8 with an r.m.s. deviation from planarity of 0.051 Å for both *A* and *B*. In this part of the molecule, H1 and H6 are obviously displaced from the mean plane [0.32 (2) and 0.32 (2) Å for H1*A* and H1*B*, respectively; 0.11 (2) and 0.22 (2) Å for H6*A* and H6*B*, respectively); this observation is to be related to the hydrogen bonding with neighbouring molecules (see below).

The title compound presents the same structural characteristics as observed in other 1,3,5-triazepan-2,6-diones (Lena, Lallemand *et al.*, 2006; Lena, Wenger *et al.*, 2006; Schaffner *et al.*, 2006): the triazepan ring adopts a twisted boat conformation TB (Boessenkool & Boyens, 1980) with a dihedral angle between the amide and urea planes of 111.27 (4) and 110.81 (4)° in molecules *A* and *B*, respectively. This conformation leads to short (less than 2 Å) intramolecular H2···H52 contacts through the C2(H2)··· C5(H52) axis linking both halves. Molecules of *cyclo*(L-Val-*g*Sar-CO) interact together mainly through N—H···O═C hydrogen bonds (Table 1), forming infinite buckled planes perpendicular to the *c* axis (Fig. 2). Molecules *A* and *B* agregate as $R_2^2(8)$ dimers (Bernstein *et al.*, 1995) [dimers of type I′ according to the nomenclature proposed by Schaffner *et al.* (2006)] that are chained together (Fig. 2). These planes are separated by chloroform molecules and display van der Waals contacts and C—H···O═C interactions with these. The weakness of these *cyclo*(L-Val-*g*Sar-CO)–chloroform interactions may be related to the observed degradation of the crystals with time.

Experimental

The title compound was prepared in four steps from Boc–L-ValSar–OH in 67% overall yield as previously described (Lena, Lallemand *et al.*, 2006) and was crystallized by slow evaporation of a deuterated chloroform solution.

Crystal data

$C_8H_{15}N_3O_2 \cdot 0.94CDCl_3$
$M_r = 298.20$
Orthorhombic, $P2_12_12_1$
$a = 11.8160$ (2) Å
$b = 12.5893$ (3) Å
$c = 18.3033$ (4) Å
$V = 2722.71$ (10) Å^3
$Z = 8$
Mo *K*α radiation
$\mu = 0.63$ mm^{-1}
$T = 100$ (2) K
0.30 × 0.20 × 0.12 mm

Data collection

Bruker–Nonius KappaCCD diffractometer
Absorption correction: multi-scan (*SORTAV*; Blessing, 1995)
$T_{min} = 0.86$, $T_{max} = 0.93$
115224 measured reflections
7948 independent reflections
7592 reflections with $I > 2\sigma(I)$
$R_{int} = 0.043$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.028$
$wR(F^2) = 0.073$
$S = 1.04$
7948 reflections
327 parameters
4 restraints
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max} = 0.65$ e Å^{-3}
$\Delta\rho_{min} = -0.39$ e Å^{-3}
Absolute structure: Flack (1983), 3529 Friedel pairs
Flack parameter: −0.02 (3)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1*A*—H1*A*···O8*B*^{i}	0.859 (9)	2.067 (10)	2.9012 (15)	163.4 (17)
N1*B*—H1*B*···O8*A*^{ii}	0.861 (9)	2.055 (9)	2.9123 (14)	173.7 (17)
N6*A*—H6*A*···O12*B*^{iii}	0.854 (9)	2.129 (10)	2.9600 (15)	164.5 (18)
N6*B*—H6*B*···O12*A*^{iv}	0.858 (9)	2.136 (12)	2.9239 (14)	152.5 (18)
C13*B*—H13*E*···O8*B*^{v}	0.98	2.50	3.4100 (17)	154
C13*A*—H13*B*···O8*A*^{vi}	0.98	2.42	3.3256 (17)	154
C5*A*—H51*A*···O8*A*^{vi}	0.99	2.55	3.4071 (16)	145
C14*A*—D14*A*···O8*B*^{i}	1.00	2.36	3.2024 (18)	142

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

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All H atoms were located in difference Fourier maps, but because of the large deviations of C,N—H bond distances and $U_{\rm iso}$(H) initially observed, the final structure was constructed using riding models for C—H bonds with interatomic distances fixed in the range 0.98–1.00 Å and $U_{\rm iso}$(H) fixed at $1.2U_{\rm eq}$(C) for methine and methylene groups and $1.5U_{\rm eq}$(C) for methyl groups. In order to allow H-atom deviation from the molecular plane, only distance restraints [0.86 (1) Å] and atomic displacement parameter constraints [$1.2U_{\rm eq}$(N)] were used for N—H bonds. Owing to the fact that the measured crystal was not very fresh and was observed to decompose with time (over a period much longer than data collection), partial occupancies were refined for the two independent chloroform molecules [0.933 (2), 0.944 (2)]. However, thanks to the inclusion of these chloroform molecules into the crystal structure, anomalous dispersion was significantly large enough to allow a check of the absolute configuration. At the end of the structure refinement, the Flack parameter was $x = -0.02$ (3), leading to unambiguous confirmation of the *S* configuration of the two crystallographically independent molecules.

Data collection: *COLLECT* (Nonius, 1998); cell refinement: *COLLECT*; data reduction: *HKL* Suite (Otwinowski & Minor, 1997); program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1994); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997); software used to prepare material for publication: *WinGX* (Farrugia, 1999) and *PLATON* (Spek, 2003).

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References

Allen, F. H., Kennard, O., Watson, D. G., Brammer, L., Orpen, A. G. & Taylor, R. (1995). *International Tables for Crystallography*, Vol. C, Section 9.5, pp. 685–706. Kluwer: Dordrecht.

Altomare, A., Cascarano, G., Giacovazzo, C., Guagliardi, A., Burla, M. C., Polidori, G. & Camalli, M. (1994). *J. Appl. Cryst.* **27**, 435.

Bernstein, J., Davis, R. E., Shimoni, L. & Chang, N.-L. (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 1555–1573.

Blessing, R. H. (1995). *Acta Cryst.* A**51**, 33–38.

Boessenkool, I. K. & Boyens, J. C. A. (1980). *J. Cryst. Mol. Struct.* **10**, 11–18.

Farrugia, L. J. (1997). *J. Appl. Cryst.* **30**, 565.

Farrugia, L. J. (1999). *J. Appl. Cryst.* **32**, 837–838.

Flack, H. D. (1983). *Acta Cryst.* A**39**, 876–881.

Lena, G., Lallemand, E., Gruner, A. C., Boeglin, J., Roussel, S., Schaffner, A.-P., Aubry, A., Franetich, J.-F., Mazier, D., Landau, I., Briand, J.-P., Didierjean, C., Rénia, L. & Guichard, G. (2006). *Chem. Eur. J.* **12**, 8498–8512.

Lena, G., Wenger, E., Guichard, G. & Didierjean, C. (2006). *Acta Cryst.* E**62**, o518–o520.

Muller, P., Lena, G., Boilard, E., Bezzine, S., Lambeau, G., Guichard, G. & Rognan, D. (2006). *J. Med. Chem.* **49**, 6768–6778.

Nonius (1998). *COLLECT*. Nonius BV, Delft, The Netherlands.

Otwinowski, Z. & Minor, W. (1997). *Methods in Enzymology*, Vol. 276, *Macromolecular Crystallography*, Part A, edited by C. W. Carter Jr & R. M. Sweet, pp. 307–326. New York: Academic Press.

Persistence of Vision Development Team (2005). *POVRay - The Persistence of Vision Raytracer.* http://www.povray.org.

Schaffner, A.-P., Lena, G., Roussel, S., Wawrezinieck, A., Aubry, A., Briand, J.-P., Didierjean, C. & Guichard, G. (2006). *Chem. Commun.* pp. 4069–4071.

Sheldrick, G. M. (1997). *SHELXL97*. University of Göttingen, Germany.

Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.

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