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10-Methyl-8,9,10,11,11a,12-hexahydro-5*H*,7*H*-isoquinolino[3,2-*g*][1,3,5]triazepine-7,11-dione

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Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.004 Å
R factor = 0.045
wR factor = 0.117
Data-to-parameter ratio = 9.6

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

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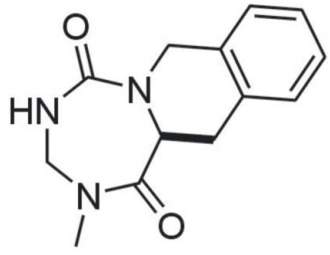
In the title compound, $C_{13}H_{15}N_3O_2$, the triazepane ring adopts a twist–boat conformation and the piperidine ring adopts a boat conformation. The molecular packing is stabilized by N—H···O, C—H···O, C—H···π and van der Waals interactions.

Comment

We recently developed a method of parallel solution-phase synthesis and presented the first biological applications of a small pilot library of structurally diverse 1,3,5-triazepane-2,6-diones, a novel dipeptide-derived skeleton (Lena *et al.*, 2006). Our interest in designing and evaluating the 1,3,5-triazepane-2,6-dione scaffold stemmed from the remarkable biological activities exhibited by molecules with diazepine and triazepine skeletons, including seven-membered cyclic ureas. Here, we present the X-ray crystal structure of the tricyclic title compound, cyclo(L-TicgSar-CO), (I), prepared from Boc-TicSar-OH in only four steps with an overall yield of 45% [Tic is 1,2,3,4-L-tetrahydroisoquinoline-3-carboxylic acid, Sar is sarcosine and g = gem, refers to the 2-alkyl gem-diamino derivative of the corresponding amino acid according to the nomenclature proposed by Chorev & Goodman (1993)].



(I)

Compound (I) crystallizes in the orthorhombic space group $P2_12_12_1$ with two molecules in the asymmetric unit (Fig. 1). Molecule *A* refers to atoms labelled C1*A*–C13*A* and molecule *B* refers to atoms labelled C1*B*–C13*B*. All bond distances and angles fall in normal ranges (Allen *et al.*, 1987) and are in agreement with the geometry of similar 1,3,5-triazepane-2,6-diones (Lena *et al.*, 2006). The *S* configuration of the C atom at the 2-position of the seven-membered ring was assumed from the precursor Boc-L-Tic OH compound.

The most obvious difference between the independent molecules is the planarity of the amide N atom: the distance of atom N2*A* from the plane defined by atoms C2*A*, C3*A* and C4*A* is 0.159 (3) Å in molecule *A*, and the corresponding distance in molecule *B* is 0.031 (3) Å. This difference is probably due to the crystal packing, which affords different

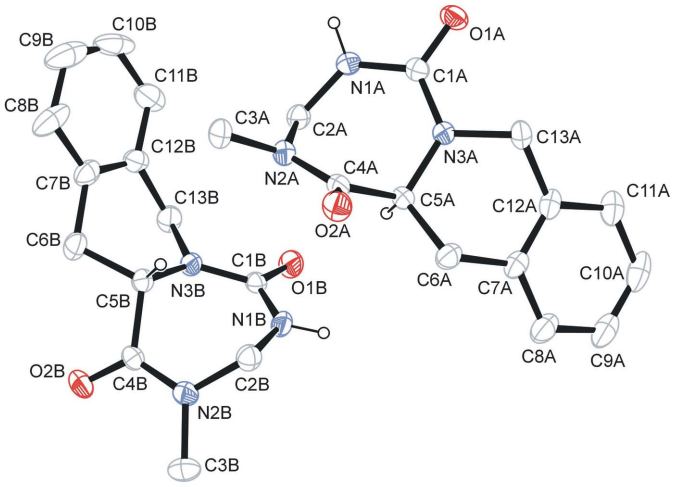


Figure 1
The molecular structures of the two independent molecules of (I), showing the atomic numbering scheme and 25% probability displacement ellipsoids. H atoms, except those of the NH and asymmetric CH groups, have been omitted for clarity.

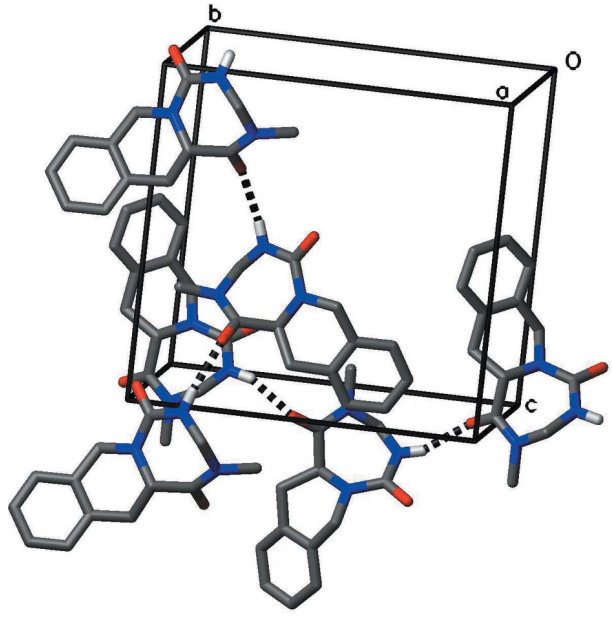


Figure 2
Part of the crystal structure of (I), showing the *C*(6) chains along [100] and [010]. Intermolecular hydrogen bonds are shown as dashed lines. H atoms have been omitted.

neigbours for the amide N atom of molecules *A* and *B*. Indeed, the peptide plane defined by C2*A*/N2*A*/C4*A*/C5*A* is in a stacking interaction with the urea group (defined by N1*B*/C1*B*/O1*B*/N3*B*) of a symmetry-related molecule. In contrast, the equivalent peptide plane (C2*B*/N2*B*/C4*B*/C5*B*) in molecule *B* is sandwiched between a urea group and a benzene ring (defined by N1*A*/C1*A*/O1*A*/N3*A* and C7*A*/C8*A*/C9*A*/C10*A*/C11*A*/C12*A*, respectively) from two symmetry-related molecules.

The triazepane ring adopts a twist–boat conformation, TB (Boessenkool & Boyens, 1980), similar to those observed in the crystal structures of carbazepine (Hempel *et al.*, 2005; Lisgarten *et al.*, 1989). Thus, the seven-menbered ring consists of two nearly planar halves, C2/N2/C4/C5 and C2/N1/C1/N3/C5. In molecule *A*, the r.m.s. deviations of the fitted atoms from these two planes are 0.06 and 0.05 Å, respectively, while in molecule *B*, the equivalent r.m.s. deviations are 0.005 and 0.03 Å, respectively. The dihedral angle between the two halves is 119.1 (1)° in molecule *A* and 119.5 (1)° in molecule *B*. Both independent piperidine rings are in a boat conformation, with atoms C6*A* and C13*A* displaced by 0.570 (4) and 0.401 (4) Å, respectively, from the mean plane defined by N3*A*/C5*A*/C7*A*/C12*A* in molecule *A*, and with atoms C6*B* and C13*B* displaced by 0.561 (4) and 0.631 (4) Å, respectively, from the mean plane defined by N3*B*/C5*B*/C7*B*/C12*B* in molecule *B*.

In the crystal structure of (I), the molecules are linked by C═O···H—N hydrogen bonds (Table 1 and Fig. 2), exhibiting the graph-set motif *C*(6) (Bernstein *et al.*, 1995). Molecules *A* form chains running along the [100] direction and molecules *B* form chains running along the [010] direction. Weak hydrogen bonds of the form C—H···π and C—H···O link chains of molecules *A* with chains of molecules *B*. The shortest interactions are listed in Table 1. All other intermolecular interactions correspond to van der Waals contacts.

Experimental

The title compound was prepared in four steps from Boc-L-TicSar-OH (3.76 g) in 45% overall yield, as previously described by Lena *et al.* (2006), and was crystallized by slow evaporation from a mixture of dichloromethane–diisopropyl ether (5:1 *v*/*v*).

Crystal data

$C_{13}H_{15}N_3O_2$
M_r = 245.28
Orthorhombic, $P2_12_12_1$
a = 12.1766 (2) Å
b = 12.5948 (2) Å
c = 15.4676 (3) Å
V = 2372.14 (7) Å^3
Z = 8
D_x = 1.374 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 14659 reflections
θ = 1.0–27.9°
μ = 0.10 mm^{-1}
T = 293 (2) K
Prism, colourless
0.6 × 0.6 × 0.5 mm

Data collection

Bruker Nonius KappaCCD area-detector diffractometer
ω scans
14659 measured reflections
3144 independent reflections
2706 reflections with $I > 2\sigma(I)$
R_{int} = 0.04
θ_{max} = 27.9°
$h = -16 \rightarrow 16$
$k = -16 \rightarrow 16$
$l = -20 \rightarrow 20$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.045
$wR(F^2)$ = 0.117
S = 1.05
3144 reflections
326 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.061P)^2 + 0.3973P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.17 e Å^{-3}
$\Delta\rho_{min}$ = −0.17 e Å^{-3}

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

Cg is the centroid of the benzene ring of molecule *A*.

D—H···A	D—H	H···A	D···A	D—H···A
N1*A*—H1*A*···O2*A*^{i}	0.86	2.11	2.967 (3)	171
N1*B*—H1*B*···O2*B*^{ii}	0.86	2.02	2.827 (3)	156
C2*B*—H3*B*···O1*A*^{iii}	0.97	2.48	3.239 (3)	135
C3*B*—H4*B*···*Cg*^{iv}	0.97	2.87	3.700 (3)	145

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

Because of the lack of any significant anomalous dispersion effects, the absolute configuration could not be determined from the diffraction experiment and Friedel pairs were merged prior to refinement. All H atoms were placed in calculated positions and refined using a riding model, with C—H distances of 0.93–0.97 Å and an N—H distance of 0.86 Å, and with U_{iso}(H) fixed at $1.2U_{eq}$(C) for aromatic, methine and methylene groups, at $1.2U_{eq}$(N) for the N—H group and at $1.5U_{eq}$(C) for methyl groups.

Data collection: *COLLECT* (Nonius, 1998); cell refinement: *COLLECT*; data reduction: *HKL* (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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