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Ethyl 6-acetylamino-6,7-dihydro-5*H*-dibenzo[*a*,*c*]cycloheptene-6-carboxylate

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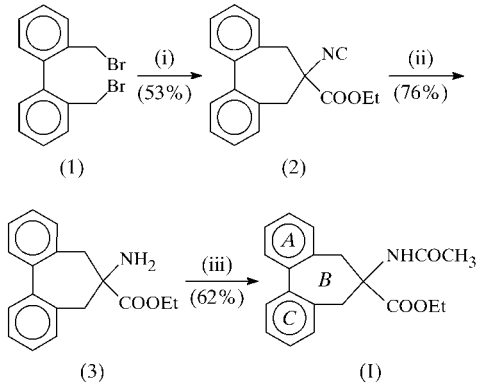
The title compound, $C_{20}H_{21}NO_3$, is a derivative of Aib (α-aminoisobutyric acid) and is cyclized at the C^{α} position by biphenyl rings. The seven-membered ring possesses *C*2 symmetry. The C^{α} cyclization causes the backbone to assume a helical conformation in the crystal structure. The packing of the molecules is stabilized by intermolecular C—H···O, C—H···π and N—H···O hydrogen bonds.

Comment

In recent years, the synthesis and structural analysis of peptide fragments incorporating α,α-disubstituted glycines have attracted considerable attention (Heimgartner, 1991; Toniolo *et al.*, 1993; Smythe *et al.*, 1995; Crisma *et al.*, 1991; Prasad *et al.*, 1994; Valle *et al.*, 1991), and α-aminoisobutyric acid (Aib or α-methyl alanine) is the best studied member of this family. However, its analogue, α,α-dibenzylglycine (Dbzg), has not been studied extensively (Kotha *et al.*, 2002). We believe that the main reason for this is the non-availability of simple



preparative methods for these α,α-disubstituted amino acid derivatives (Kotha *et al.*, 2001, 2000; Formaggio *et al.*, 2000; Ridvan *et al.*, 1999). The unique stereochemistry of peptides containing these conformationally restricted amino acids provides a useful spectroscopic probe for the study of conformation–activity relationships (Karle & Balaram, 1990; Polese *et al.*, 1996; Kotha & Brahmachary, 2000). Here, we present the crystal structure of the title compound, (I), a derivative of Aib.

The structure of (I) is shown in Fig. 1. The bond distances and angles are close to normal values (Allen *et al.*, 1979). Atoms C20 and C7 are coplanar with rings *A* and *C*, respectively. The angle between the biphenyl rings *A* and *C* is 49.2 (2)°. The seven-membered ring *B* has *C*2 symmetry, and

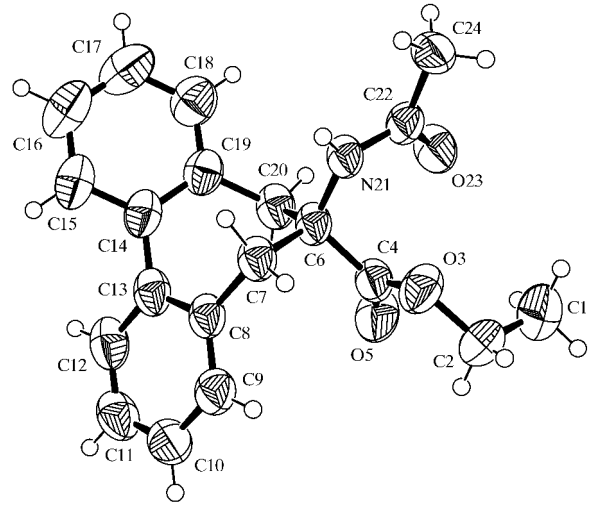


Figure 1
The molecular structure of (I) with the atomic numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

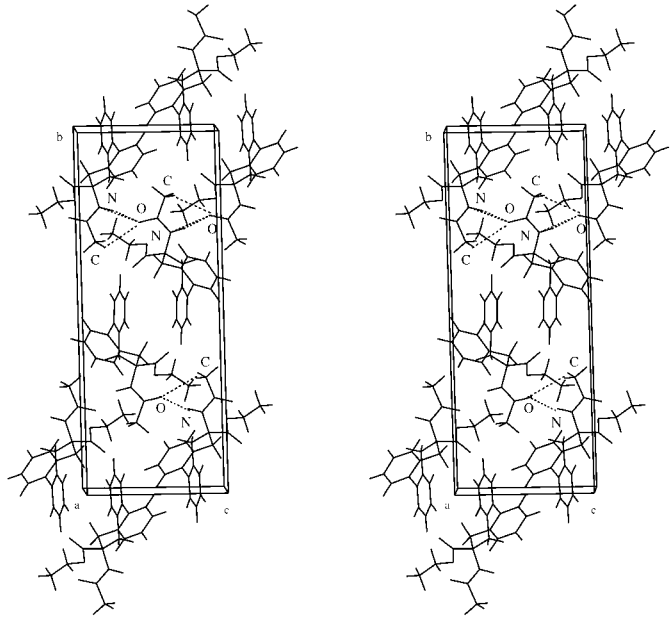


Figure 2
A stereoview of the packing of the molecules in (I), showing the C—H···O and N—H···O interactions.

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the symmetry axis passes through atom C6 and the C13—C14 bond. The amide unit is planar and the backbone torsion angles φ and ψ (C22—N21—C6—C4 and N21—C6—C4—O3) are 48.0 (4) and 44.6 (4)°, respectively, indicating a near α-helical conformation (Ramesh & Balaram, 1999).

The packing in (I) is stabilized by intermolecular C—H···O, N—H···O and C—H···π (Desiraju, 1989) hydrogen bonds, shown in Fig. 2 and Table 1. Carbonyl atom O23 forms a bifurcated hydrogen bond with atoms N21 and C24 (Fig. 2).

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

*Cg*1 and *Cg*2 are the centroids of rings *C* and *A*, respectively.

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N21—H21···O23^{i}	0.86	2.01	2.863 (3)	169
C24—H24*A*···O23^{i}	0.96	2.46	3.316 (4)	148
C9—H9···*Cg*2^{ii}	0.93	3.30	3.926 (4)	127
C15—H15···*Cg*1^{iii}	0.93	3.03	3.785 (4)	140

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

Experimental

The *Scheme* in the *Comment* shows the synthesis of (I) under phase-transfer conditions (PTC), using ethyl isocyanoacetate as a glycine equivalent. Thus, treatment of 2,2′-bis(bromomethyl)-1,1′-biphenyl, (1), with ethyl isocyanoacetate in acetonitrile in the presence of K_2CO_3 and tetrabutylammonium hydrogen sulfate at room temperature [step (i) in the *Scheme*] gave the isonitrile compound, (2). Hydrolysis of the coupling product was achieved by treating (2) in ethanolic HCl at room temperature for a few hours [step (ii) in the *Scheme*]. The free amino group in (3) was protected with acetic anhydride in dichloromethane in the presence of a catalytic amount of 4-(dimethylamino)pyridine [step (iii) in the *Scheme*], giving (I) (m.p. 431–433 K).

Crystal data

$C_{20}H_{21}NO_3$
M_r = 323.38
Monoclinic, $P2_1/c$
a = 7.837 (2) Å
b = 24.074 (9) Å
c = 9.543 (2) Å
β = 102.87 (2)°
V = 1755.2 (9) Å^3
Z = 4
D_x = 1.224 Mg m^{-3}
Cu $K\alpha$ radiation
Cell parameters from 25 reflections
θ = 7.6–28.4°
μ = 0.66 mm^{-1}
T = 293 (2) K
Rectangular block, colourless
0.35 × 0.13 × 0.10 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
Non-profiled $\omega/2\theta$ scans
Absorption correction: ψ scan (North *et al.*, 1968)
T_{min} = 0.802, T_{max} = 0.922
3522 measured reflections
3312 independent reflections
1976 reflections with $I > 2\sigma(I)$
R_{int} = 0.047
θ_{max} = 71.9°
$h = -9 \rightarrow 9$
$k = 0 \rightarrow 29$
$l = -11 \rightarrow 10$
3 standard reflections
frequency: 120 min
intensity decay: 16%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.080
$wR(F^2)$ = 0.262
S = 1.05
3312 reflections
219 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.1621P)^2 + 0.1670P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.046
$\Delta\rho_{max}$ = 0.24 e Å^{-3}
$\Delta\rho_{min}$ = −0.28 e Å^{-3}

H atoms were fixed geometrically at calculated positions, with C—H = 0.93–0.96 Å and N—H = 0.86 Å, and treated as riding, with $U_{iso}(H) = 1.2U_{eq}(C)$.

Data collection: *CAD*-4 *EXPRESS* (Enraf–Nonius, 1994); cell refinement: *CAD*-4 *EXPRESS*; data reduction: *XCAD*4 (Harms & Wocadlo, 1995); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*-3 (Farrugia, 1997).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: DE1181). Services for accessing these data are described at the back of the journal.

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