ORGANIC COMPOUNDS

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8,9-Dimethoxybenzo[*b*]carbazole

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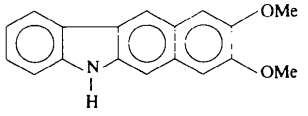
Abstract

The molecules of $C_{18}H_{15}NO_2$ are highly planar and similar to those of ellipticine [Courseille, Busetta & Hospital (1974). *Acta Cryst.* B**30**, 2628–2631], which is a DNA-intercalating molecule. Molecular association occurs through van der Waals interactions.

Comment

Preliminary biological studies of carbazole derivatives showed that the presence of oxygenated substituents on the carbazole ring increases the biological activity (Hewlings, Oliveira-Campos & Shannon, 1984). The structures of these derivatives are analogous to that of ellipticine, a plant alkaloid having pronounced antitumor activity (Hartwell & Abbott, 1969), and are found to have DNA-intercalating properties (Courseille, Busetta & Hospital, 1974; Neidle, 1979; Gale, Cundliffe, Reynolds, Richmond & Waring, 1981; Aggarwal, Neidle & Sainsbury, 1983). The title compound, (I), was one of the carbazole derivatives produced with a view to obtaining molecules similar to ellipticine by a reductive condensation method (Rajeswaran & Srinivasan, 1994). The structural details are given in this paper.



(I)

A perspective view of the title molecule is shown in Fig. 1. The molecule is very similar to that of 1,4-dimethoxybenzocarbazole (Seetharaman & Rajan, 1995). The mean C_{sp^2}—C_{sp^2} bond distance is 1.401 (2) Å. This agrees well with corresponding values in related compounds (Noriaki, Takao & Kunikatsu, 1986). The substituted methoxy groups at atoms C2 and C3 are twisted from planarity by angles of 8.5 (7) (C4—C3—O20—C21) and 7.3 (7)° (C1—C2—O18—C19), respectively. The molecules are highly planar, similar to other ellipticine derivatives such as 7-methylellipticine (Kuroda & Sainsbury, 1984), 5-*n*-butyl-11-dimethoxyellipticine and 9-methoxyellipticine (Aggarwal *et al.*, 1983), and ellipticine-iodoCpG$^+$ (Jain, Bhandary & Sobell, 1979). This planarity is said to be essential for DNA intercalation (Neidle, 1979; Gale *et al.*, 1981; Aggarwal *et al.*, 1983). All the individual rings are planar, with a maximum deviation of −0.020 (5) Å occurring for atom C2. A stereoview of the molecular packing is shown in Fig. 2. It should be noted that unlike most DNA-intercalating molecules, the molecules in this study are not stacked one over the other, in spite of their planar conformation. The crystal structure is stabilized by van der Waals interactions

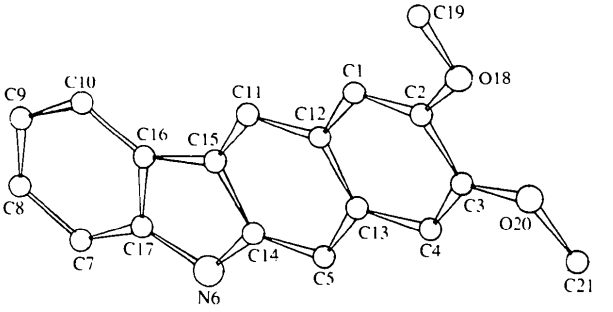


Fig. 1. *PLUTO* (Motherwell & Clegg, 1976) plot of the title molecule showing the atom-numbering scheme.

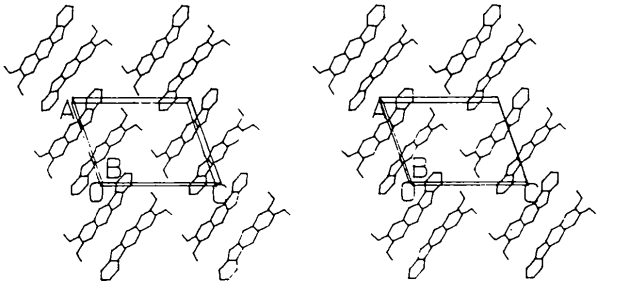


Fig. 2. Stereoview of the unit-cell packing of the title molecules.

Experimental

The title compound was synthesized by means of a reductive condensation method and crystallized from acetone–water solution. The density D_m was measured by flotation in water.

Crystal data

$C_{18}H_{15}NO_2$
M_r = 277.31

Cu $K\alpha$ radiation
λ = 1.54184 Å

† DCB contribution No. 852.

Monoclinic
$P2_1$
$a = 9.625\ (2)$ Å
$b = 5.805\ (1)$ Å
$c = 12.665\ (3)$ Å
$\beta = 109.63\ (5)°$
$V = 666\ (3)$ Å^3
$Z = 2$
$D_x = 1.566\ (3)$ Mg m^{-3}
$D_m = 1.581$ Mg m^{-3}

Cell parameters from 20 reflections
$\theta = 15–25°$
$\mu = 0.88$ mm^{-1}
$T = 293$ K
Rectangular block
0.35 × 0.25 × 0.20 mm
Colourless

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: ψ scan (North, Phillips & Mathews, 1968)
$T_{min} = 0.72$, $T_{max} = 0.87$
1401 measured reflections
1293 independent reflections
864 observed reflections [$I > 3\sigma(I)$]

$R_{int} = 0.009$
$\theta_{max} = 70°$
$h = 0 \rightarrow 11$
$k = -7 \rightarrow 7$
$l = 0 \rightarrow 15$
2 standard reflections monitored every 100 reflections
intensity decay: <2%

Refinement

Refinement on F
$R = 0.056$
$wR = 0.063$
$S = 1.01$
864 reflections
250 parameters
All H-atom parameters refined

$w = 1/[\sigma^2(F) + 0.00584F^2]$
$(\Delta/\sigma)_{max} = 0.089$
$\Delta\rho_{max} = 0.30$ e Å^{-3}
$\Delta\rho_{min} = -0.20$ e Å^{-3}
Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV)

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters* (Å^2)

$U_{eq} = (1/3)\Sigma_i\Sigma_j U_{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j.$

	x	y	z	U_{eq}
C1	0.4862 (5)	0.0196 (5)	0.2715 (4)	0.038 (3)
C2	0.6123 (6)	−0.0456 (6)	0.3507 (4)	0.039 (3)
C3	0.6884 (6)	−0.2487 (5)	0.3332 (4)	0.036 (3)
C4	0.6296 (6)	−0.3797 (5)	0.2392 (4)	0.035 (3)
C5	0.4303 (6)	−0.4577 (4)	0.0615 (4)	0.038 (3)
N6	0.2134 (5)	−0.4950 (5)	−0.1138 (4)	0.041 (3)
C7	−0.0264 (6)	−0.4029 (4)	−0.2650 (5)	0.044 (3)
C8	−0.1406 (6)	−0.2461 (6)	−0.2973 (5)	0.052 (4)
C9	−0.1393 (6)	−0.0512 (6)	−0.2318 (5)	0.048 (4)
C10	−0.0247 (6)	−0.0078 (5)	−0.1329 (5)	0.040 (3)
C11	0.2865 (6)	−0.0432 (5)	0.0900 (4)	0.033 (3)
C12	0.4212 (5)	−0.1110 (5)	0.1718 (4)	0.035 (3)
C13	0.4925 (5)	−0.3169 (6)	0.1565 (4)	0.036 (3)
C14	0.2978 (5)	−0.3880 (6)	−0.0161 (4)	0.033 (3)
C15	0.2252 (6)	−0.1808 (5)	−0.0038 (5)	0.035 (3)
C16	0.0913 (5)	−0.1669 (5)	−0.0990 (4)	0.036 (3)
C17	0.0877 (6)	−0.3653 (4)	−0.1657 (4)	0.039 (3)
O18	0.6816 (4)	0.0626 (5)	0.4509 (3)	0.047 (2)
C19	0.6055 (6)	0.2483 (6)	0.4803 (5)	0.049 (3)
O20	0.8158 (4)	−0.2941 (4)	0.4182 (3)	0.044 (2)
C21	0.9058 (6)	−0.4787 (5)	0.4011 (5)	0.047 (3)

Table 2. *Selected geometric parameters* (Å, °)

C1—C2	1.343 (6)	C7—C17	1.381 (7)
C1—C12	1.425 (6)	C8—C9	1.400 (7)
C2—C3	1.444 (6)	C9—C10	1.386 (7)
C2—O18	1.371 (5)	C10—C16	1.401 (6)
C3—C4	1.365 (6)	C11—C12	1.417 (6)
C3—O20	1.358 (5)	C11—C15	1.388 (6)
C4—C13	1.429 (6)	C12—C13	1.423 (6)
C5—C13	1.411 (6)	C14—C15	1.426 (6)
C5—C14	1.383 (6)	C15—C16	1.441 (6)
N6—C14	1.379 (6)	C16—C17	1.422 (5)
N6—C17	1.389 (6)	O18—C19	1.421 (6)
C7—C8	1.379 (6)	O20—C21	1.439 (6)
C2—C1—C12	122.0 (3)	C5—C13—C12	121.1 (4)
C1—C2—O18	126.8 (4)	C4—C13—C12	118.9 (4)
C1—C2—C3	119.5 (4)	C4—C13—C5	120.0 (3)
C3—C2—O18	113.7 (4)	C5—C14—N6	129.1 (3)
C2—C3—O20	114.0 (3)	N6—C14—C15	108.4 (4)
C2—C3—C4	120.4 (4)	C5—C14—C15	122.5 (4)
C4—C3—O20	125.6 (3)	C11—C15—C14	119.7 (5)
C3—C4—C13	120.5 (3)	C14—C15—C16	106.8 (3)
C13—C5—C14	117.5 (3)	C11—C15—C16	133.4 (3)
C14—N6—C17	109.7 (3)	C10—C16—C15	133.6 (3)
C8—C7—C17	118.5 (3)	C15—C16—C17	106.7 (3)
C7—C8—C9	120.6 (5)	C10—C16—C17	119.6 (4)
C8—C9—C10	121.9 (4)	C7—C17—C16	121.5 (4)
C9—C10—C16	117.9 (4)	N6—C17—C16	108.3 (4)
C12—C11—C15	119.2 (3)	N6—C17—C7	130.2 (3)
C1—C12—C11	121.5 (3)	C2—O18—C19	117.2 (4)
C11—C12—C13	119.9 (4)	C3—O20—C21	117.0 (3)
C1—C12—C13	118.6 (4)		

The structure was solved by direct methods. All H atoms were located from a difference Fourier map and refined for one cycle. Refinement was by full-matrix least squares with anisotropic displacement parameters for all non-H atoms and isotropic displacement parameters for H atoms.

Data collection, cell refinement and data reduction: *SDP* (Frenz, 1978). Structure solution: *SHELXS*86 (Sheldrick, 1985). Structure refinement: *SHELX*76 (Sheldrick, 1976). Molecular graphics: *PLUTO* (Motherwell & Clegg, 1976). Preparation of material for publication: *PARST* (Nardelli, 1983).

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Lists of structure factors, anisotropic displacement parameters, H-atom coordinates, complete geometry and least-squares-planes data have been deposited with the IUCr (Reference: PT1011). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Acetyl-L-carnitine Hydrochloride

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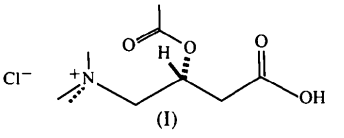
Abstract

The title compound, 2-acetoxy-3-carboxy-*N*,*N*,*N*-trimethyl-1-propanaminium chloride, $C_9H_{18}NO_4^+.Cl^-$, represents a source of activated acetyl groups which are efficiently used for biosynthetic purposes. The crystal structure reported here confirms the extended conformation of the compound predicted from solid-state NMR studies and differs from that previously reported in the literature.

Comment

Acetyl-L-carnitine is involved in the reversible transfer of acetyl groups between carnitine and coenzyme A through the activity of carnitine acetyltransferase (CAT; EC 2.3.1.7). There is considerable interest in the active conformation of acetyl-L-carnitine and it has been suggested that CAT requires the extended conformation of L-carnitine for the forward reaction, and that acetyl-L-carnitine, formed upon acetylation, adopts a folded conformation. These assumptions were supported by X-ray crystallographic data on both compounds (Gandour, Colucci & Fronczek, 1985). However, a recent NMR investigation of carnitine and acetylcarnitine in aqueous solution suggested that the extended conformation predominates for both compounds (Brewster, Hermann & Englard, 1990). A solid-state NMR study (Anderson *et al.*, 1995) of acetyl-L-carnitine, using the REDOR technique (Gullion & Schaefer, 1989*a*,*b*), led to the conclusion that the C(1)···N distance lies between 4.98 and 5.05 Å, clearly indicating an extended conformation of the compound.

Before extending the NMR study to a determination of the CAT-bound conformation of acetyl-L-carnitine, an X-ray analysis of the same crystalline material was performed to check the results of the REDOR-NMR investigation. The present X-ray analysis of acetyl-L-carnitine hydrochloride, (I), found a C(1)···N distance of 5.06 Å, which is in excellent agreement with the NMR results.



(I)

The crystalline molecular conformation of (I) is shown in Fig. 1. The carboxy group is eclipsed with respect to the C(2)—C(3) bond and the ester carbonyl group is in an eclipsed conformation with respect to the C(3)—H bond. All other torsion angles correspond to staggered conformations. There is a hydrogen bond from the carboxy OH group to the Cl^- ion at $(x-\frac{1}{2}, \frac{1}{2}-y, 1-z)$ [H···Cl^- 2.11 (1), O(1*B*)···Cl^- 2.988 (3) Å, O(1*B*)—H···Cl^- 167 (1)°].

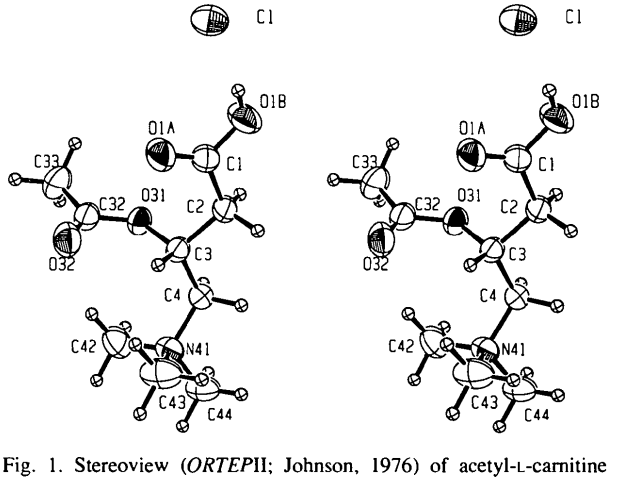


Fig. 1. Stereoview (*ORTEP*II; Johnson, 1976) of acetyl-L-carnitine showing the atomic numbering scheme, the molecular conformation and 50% probability ellipsoids for the non-H atoms. H atoms are shown with constant radii of 0.1 Å.