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Acta Cryst. (1995). C**51**, 1915–1917

Methyl 4-Oxo-*N*-(1-phenylethyl)-10-oxa-3-azatricyclo[5.2.1.$0^{1,5}$]dec-8-ene-6-carboxylate

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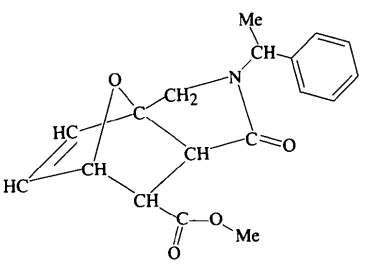
Abstract

The title compound, $C_{18}H_{19}NO_4$, is a precursor for numerous pharmacologically active compounds, the stereocontrol of the synthesis of which is of great importance.

Comment

The pyrrolidone ring is found in numerous natural products and a variety of pharmacologically active compounds (Marson, Grabowska, Walsgrove, Eggleston & Baurs, 1994). For example, pyrrolidone derivatives are used in the treatment of arteriosclerosis (Diaz, Monreal & Lucas, 1990). These molecules may act as potent neuroexitatory agents (Woo & Mullins, 1991) or neurotropic drugs (Toja, Gorini, Zirotti, Barzaghi & Galliani, 1987). Stereocontrol in the synthesis of these compounds is very important.

Our studies have demonstrated that stereocontrol can be achieved by the reaction of optically active furfurylamines with maleic anhydride. The mechanism of the reaction has been investigated previously with optically inactive compounds and proceeds by an intramolecular Diels–Alder reaction (Brun, Zylber, Pèpe & Reboul, 1994; Pèpe, Reboul, Brun & Zylber, 1995). With furfuryl *N*-1-phenylethylamine (*S*), the title compound, (I), is obtained as two diastereomeric adducts in a 65/35 ratio. These can be isolated in their pure forms. The cleavage of the oxa bridge of such systems leads to various functionalized disubstituted pyrrolidones with absolute control of the configuration of the different asymmetric centres (Ager & East, 1993).



(I)

The molecular configuration observed in the crystal studied here confirms the stereocontrol of the synthesis. The interatomic distances in the title compound have standard values and the only intermolecular contacts found are of van der Waals nature.

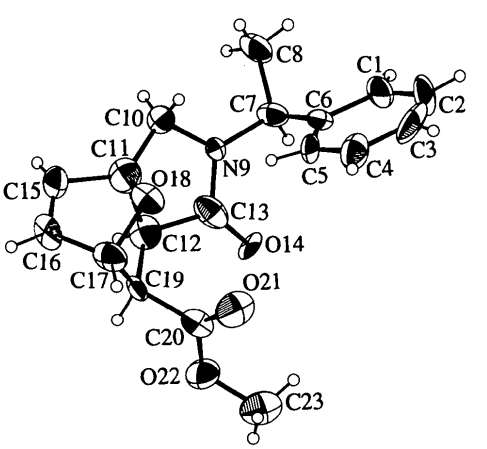


Fig. 1. An *ORTEP*II drawing (Johnson, 1976) of the title compound with displacement ellipsoids at the 50% probability level for non-H atoms. H atoms are drawn as small spheres of arbitrary radii.

Experimental

The crystal used for the X-ray structure analysis was grown from a CH_2Cl_2/Et_2O solution. The density D_m was measured by flotation.

Crystal data

$C_{18}H_{19}NO_4$
$M_r = 313.35$
Monoclinic
$P2_1$
$a = 8.112\ (2)$ Å
$b = 10.142\ (2)$ Å
$c = 10.033\ (2)$ Å
$\beta = 74.49\ (3)°$
$V = 795.3\ (2)$ Å^3
$Z = 2$
$D_x = 1.31$ Mg m^{-3}
$D_m = 1.30\ (2)$ Mg m^{-3}
Cu $K\alpha$ radiation
$\lambda = 1.5418$ Å
Cell parameters from 25 reflections
$\theta = 7.5–22.5°$
$\mu = 0.72$ mm^{-1}
$T = 293$ K
Square prism
0.3 × 0.2 × 0.2 mm
Colourless

Data collection

Nonius CAD-4 diffractometer
θ scans
Absorption correction: none
1920 measured reflections
1816 independent reflections
1720 observed reflections [$I > 2\sigma(I)$]
$R_{int} = 0.025$
$\theta_{max} = 22.5°$
$h = -9 \rightarrow 9$
$k = 0 \rightarrow 11$
$l = 0 \rightarrow 11$
4 standard reflections
frequency: 60 min
intensity decay: none

Refinement

Refinement on F
$R = 0.0362$
$wR = 0.0362$
$S = 0.52$
1720 reflections
264 parameters
H-atom coordinates refined from calculated positions; U_{iso} fixed at 0.05 Å^2
Unit weights applied
$(\Delta/\sigma)_{max} = 0.13$
$\Delta\rho_{max} = 0.20$ e Å^{-3}
$\Delta\rho_{min} = -0.18$ e Å^{-3}
Extinction correction: none
Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV, Table 2.2B)

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

$B_{eq} = (4/3)\sum_i\sum_j\beta_{ij}\mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	B_{eq}
C1	−0.2841 (4)	0.7040	0.3080 (3)	5.44 (18)
C2	−0.4116 (4)	0.6117 (7)	0.3099 (4)	5.8 (2)
C3	−0.4582 (5)	0.5263 (7)	0.4133 (5)	6.5 (2)
C4	−0.3792 (4)	0.5220 (6)	0.5249 (4)	4.60 (16)
C5	−0.2493 (3)	0.6127 (6)	0.5204 (3)	2.90 (11)
C6	−0.1977 (3)	0.7024 (6)	0.4166 (2)	3.26 (12)
C7	−0.0584 (4)	0.8074 (6)	0.4074 (2)	3.79 (17)
C8	0.0966 (5)	0.7886 (7)	0.2724 (3)	5.20 (19)
N9	0.0121 (3)	0.7934 (5)	0.5280 (2)	2.59 (9)
C10	0.1602 (4)	0.7147 (6)	0.5344 (3)	3.47 (12)
C11	0.1426 (4)	0.7143 (6)	0.6881 (3)	5.11 (14)
C12	0.0396 (4)	0.8355 (6)	0.7493 (3)	4.38 (13)
C13	−0.0716 (4)	0.8643 (5)	0.6456 (2)	4.58 (14)
O14	−0.1897 (2)	0.9370 (5)	0.6614 (2)	2.90 (07)
C15	0.2899 (5)	0.6978 (6)	0.7584 (4)	4.99 (15)
C16	0.2060 (6)	0.6641 (6)	0.8856 (4)	5.84 (19)
C17	0.0197 (5)	0.6522 (6)	0.8994 (4)	4.73 (15)
O18	0.0268 (3)	0.6099 (5)	0.7546 (2)	3.56 (9)
C19	−0.0533 (3)	0.7893 (5)	0.8966 (3)	2.57 (10)
C20	−0.2462 (4)	0.7910 (6)	0.9272 (3)	3.47 (13)
O21	−0.3284 (3)	0.7035 (5)	0.8968 (3)	5.43 (12)
O22	−0.3174 (3)	0.8955 (5)	0.9952 (2)	5.02 (11)
C23	−0.5017 (5)	0.9106 (8)	1.0186 (7)	8.2 (3)

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

C1—C2	1.391 (7)	C11—O18	1.454 (7)
C1—C6	1.445 (5)	C12—C13	1.576 (7)
C2—C3	1.326 (7)	C12—C19	1.541 (7)
C3—C4	1.432 (9)	C13—N9	1.393 (6)
C4—C5	1.390 (8)	C13—O14	1.185 (6)
C5—C6	1.362 (7)	C15—C16	1.321 (9)
C6—C7	1.537 (7)	C16—C17	1.485 (9)
C7—C8	1.594 (8)	C17—O18	1.501 (7)
C7—N9	1.477 (6)	C17—C19	1.514 (8)
C10—N9	1.458 (7)	C19—C20	1.512 (7)
C10—C11	1.510 (8)	C20—O22	1.308 (7)
C11—C12	1.520 (8)	C20—O21	1.197 (7)
C11—C15	1.550 (8)	C23—O22	1.458 (9)
C1—C2—C3	120.4 (14)	C11—C12—C13	103.5 (10)
C2—C3—C4	122.5 (15)	C11—C12—C19	102.5 (10)
C3—C4—C5	116.6 (13)	C13—C12—C19	118.0 (10)
C4—C5—C6	122.8 (12)	C12—C13—N9	103.2 (09)
C1—C6—C5	118.2 (10)	C12—C13—O14	127.7 (11)
C1—C6—C7	116.4 (9)	N9—C13—O14	128.9 (11)
C5—C6—C7	125.4 (10)	C11—C15—C16	101.9 (13)
C6—C7—C8	111.6 (10)	C15—C16—C17	111.1 (14)
C6—C7—N9	108.9 (9)	C16—C17—O18	99.1 (11)
C8—C7—N9	107.1 (10)	C16—C17—C19	108.5 (12)
C10—N9—C7	126.4 (10)	C19—C17—O18	99.1 (10)
C10—N9—C13	117.8 (10)	C11—O18—C17	95.1 (10)
C13—N9—C7	115.9 (9)	C12—C19—C17	101.7 (10)
C11—C10—N9	101.1 (10)	C12—C19—C20	113.9 (10)
C10—C11—C12	107.6 (11)	C17—C19—C20	113.3 (10)
C10—C11—C15	126.2 (11)	C19—C20—O21	123.8 (12)
C10—C11—O18	110.0 (10)	C19—C20—O22	113.8 (11)
C12—C11—C15	108.1 (11)	O21—C20—O22	122.3 (13)
C12—C11—O18	100.7 (10)	C20—O22—C23	117.4 (12)
C15—C11—O18	101.2 (10)		

Data collection: CAD-4 diffractometer software (Enraf–Nonius, 1977). Cell refinement: CAD-4 diffractometer software. Data reduction: local program. Program(s) used to solve structure: *MULTAN* (Main *et al.*, 1980). Program(s) used to refine structure: *SHELX*76 (Sheldrick, 1976). Molecular graphics: *ORTEP*II (Johnson, 1976).

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates, bond distances and angles involving non-H atoms, and bond distances involving H atoms have been deposited with the IUCr (Reference: PA1167). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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6-[1-(4-Ethoxyphenyl)ethyl]-5-methoxy-1,3-benzodioxole

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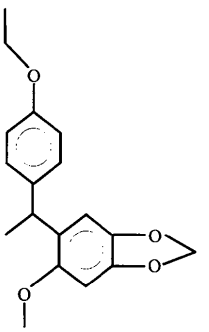
Abstract

The title compound, $C_{18}H_{20}O_4$, is structurally similar to podophyllotoxin. It contains a fused dioxole and phenyl ring system and an unfused phenyl ring which are almost perpendicular to each other. However, this compound lacks the cyclohexyl and lactone rings which are present in podophyllotoxin. In addition, the unfused phenyl ring in podophyllotoxin contains three methoxy groups in the *para* and *meta* positions, whereas the title compound contains only an ethoxy group in the *para* position.

Comment

The title compound, (I), belongs to a series of 6-benzyl-1,3-benzodioxole derivatives that are structurally similar to podophyllotoxin and have podophyllotoxin-like antimitotic activity (Batra, Jurd & Hamel, 1985). These derivatives have been used to study structure–function relationships of podophyllotoxin. For example, tubulin polymerization is inhibited if the 6-benzyl-1,3-benzodioxole derivative contains an intact dioxole ring, a methoxy group at the *para* position of the unfused phenyl ring and a methoxy or ethoxy group at the 5-position of the fused rings (Batra *et al.*, 1985). The title compound contains all these key structural features except that the methoxy group at the *para* position of the unfused phenyl ring is replaced by an ethoxy group, which reduces its potency as an inhibitor of tubulin polymerization by only twofold (Batra *et al.*, 1985).



(I)

The structure determination reveals that the fused dioxole and phenyl rings and the unfused phenyl ring are both planar and almost perpendicular to each other. The relative orientation between these two ring systems is likely to be an important factor that enables the derivative to bind tubulin. The only other report of a crystal structure of a 6-benzyl-1,3-benzodioxole derivative ap-

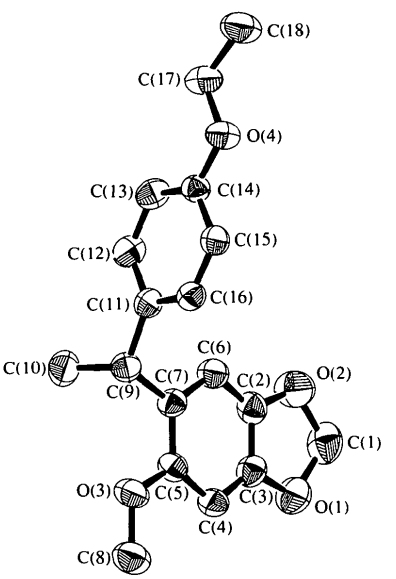


Fig. 1. *ORTEP*II (Johnson, 1976) plot of the molecular structure of the benzyl–benzodioxole derivative (ellipsoids represent 50% probability).

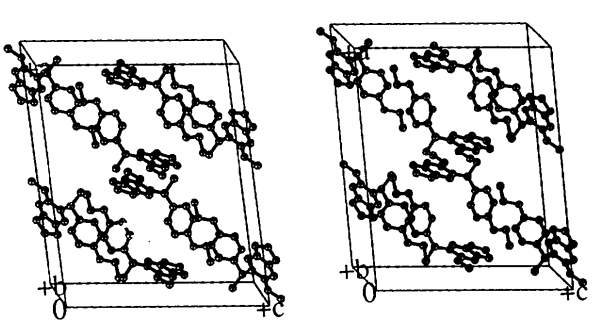


Fig. 2. *PLUTO* (Motherwell & Clegg, 1978) stereoplot of the packing of the benzyl–benzodioxole derivative.