Structure of 5-(2-Hydroxyethoxy)-6-[1-(4-methoxyphenyl)ethyl]-1,3-benzodioxole

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Abstract. $C_{18}H_{20}O_5$, $M_r = 316.35$, orthorhombic, $Pbca$, $a = 16.800$ (2), $b = 20.071$ (2), $c = 9.429$ (1) Å, $V = 3179.4$ (5) Å^3, $Z = 8$, $D_m = 1.36$ (7), $D_x = 1.322$ g cm^{-3}, λ(Cu $K\alpha$) = 1.54178 Å, $\mu = 7.53$ cm^{-1}, $F(000) = 1344$, $T = 296$ K, final $R = 0.045$, $wR = 0.057$ for 1695 unique reflections. This compound structurally resembles podophyllotoxin in that it contains a fused dioxole and phenyl ring system, but lacks the cyclohexyl and lactone rings. Whereas the unfused phenyl ring in podophyllotoxin contains three methoxy groups in the *para* and *meta* positions, the title compound contains only one in the *para* position.

Experimental. The title compound was obtained in crystalline form from the National Cancer Institute, NSC # 352875. A transparent rectangular crystal having approximate dimensions 0.2 × 0.2 × 0.15 mm was mounted on a glass fibre. Crystal density was determined by suspension in an aqueous CsCl solution. Measurements were made on a Rigaku AFC-6R diffractometer with graphite-mono-chromated Cu $K\alpha$ radiation and 12 kW rotating-anode generator. Intensities were measured at 296 K using ω–2θ scans to a maximum 2θ value of 120.2°. Cell constants were obtained from a least-squares refinement of the setting angles of 24 reflections in the range $56.08 < 2\theta < 79.88°$. h,k,l ranged from 0,0,0 to 18,22,10. 2714 reflections were collected; all were unique. The number of unobserved reflections was 673, defined by $I \leq 3.0\sigma(I)$ with 346 systematic absences. The intensities of three representative reflections (141, 02$\bar{2}$ and 04$\bar{1}$) remained constant throughout data collection and thus no decay correction was applied. The data were corrected for Lorentz and polarization effects. An empirical absorption correction (North, Phillips & Mathews, 1968) was applied, based on azimuthal scans of several reflections, with transmission factors ranging from 0.74 to 1.00. The structure was solved by direct methods using *MITHRIL* (Gilmore, 1984). H atoms were generated using optimum bonding geometry and included in F_c. H-atom thermal parameters and positions were not refined. Non-H atoms were refined anisotropically. Parameters were refined on F, with function minimized $\Sigma w(|F_o| - |F_c|)^2$, where

$w = 4F_o^2/\sigma^2(F_o^2)$, $\sigma^2(F_o^2) = [S^2(C + R^2B) + (pF_o^2)^2]/$ (Lp)^2, S = scan rate, C = total integrated peak count, R = ratio of scan time to background counting time, B = total background count, Lp = Lorentz–polarization factor, p = ignorance factor, set to a default setting of 0.03. The final cycle of full-matrix least-squares refinement was based on 1695 observed reflections and 288 variable parameters and converged with unweighted and weighted agreement factors of $R = 0.045$ and $wR = 0.057$ (R and wR for all 2368 observations were 0.07 and 0.063, respectively). The maximum shift/e.s.d. in the final cycle was 0.08. The standard deviation, S, of an observation of unit weight was 1.78. Maximum and minimum peaks of 0.20 and -0.26 e Å^{-3}, respectively, were observed on the final difference Fourier map. Anomalous-dispersion effects were included in F_c (Ibers & Hamilton, 1964); the values for f' and f'' were those of Cromer (1974). All calculations were performed using *TEXSAN* (Molecular Structure Corporation, 1985).

Table 1 lists positional parameters and equivalent isotropic temperature factors. Table 2 lists bond lengths and bond angles for non-H atoms. Fig. 1 displays the title compound using an *ORTEP*II (Johnson, 1976) representation. Fig. 2 displays the crystal packing arrangement using *PLUTO* (Mother-well & Clegg, 1978).*

Related literature. Jurd, Fye & Morgan (1979) synthesized derivatives of 6-benzyl-1,3-benzodioxole which acted as insect chemosterilants. These compounds were shown to exhibit antifertility effects (Rawlins, Jurd & Snow, 1979), some of which showed a strong and direct anti-juvenile hormone effect (van Mellaert, De Loof & Jurd, 1983). Structure–activity studies with derivatives of 6-benzyl-1,3-benzodioxole carried out by Batra, Jurd & Hamel (1985) demonstrated the antimitotic

$C_{18}H_{20}O_5$.

Table 1. Positional parameters and equivalent isotropic temperature factors (Å²)

$$B_{eq} = (8\pi^2/3)\sum_{i=1}^{3}\sum_{j=1}^{3} U_{ij}a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	B_{eq}
O(19)	0.2886 (1)	0.19862 (9)	0.4709 (2)	4.5 (1)
O(20)	0.1803 (1)	0.1449 (1)	0.3721 (2)	4.2 (1)
O(21)	0.3997 (1)	−0.0111 (1)	0.6424 (2)	3.59 (8)
O(22)	0.4847 (2)	−0.0595 (1)	0.8882 (3)	7.9 (2)
O(23)	0.5132 (1)	−0.2216 (1)	0.2186 (2)	5.1 (1)
C(1)	0.2230 (2)	0.2055 (2)	0.3763 (4)	5.5 (2)
C(2)	0.2320 (2)	0.0984 (1)	0.4315 (3)	3.2 (1)
C(3)	0.2230 (2)	0.0308 (1)	0.4399 (3)	3.3 (1)
C(4)	0.2813 (1)	−0.0059 (1)	0.5117 (3)	2.8 (1)
C(5)	0.3461 (1)	0.0279 (1)	0.5719 (3)	2.9 (1)
C(6)	0.3543 (2)	0.0974 (1)	0.5621 (3)	3.3 (1)
C(7)	0.2960 (2)	0.1305 (1)	0.4906 (3)	3.2 (1)
C(8)	0.4703 (2)	0.0193 (1)	0.6955 (3)	3.8 (1)
C(9)	0.5187 (2)	−0.0338 (2)	0.7651 (4)	4.8 (2)
C(10)	0.2762 (2)	−0.0813 (1)	0.5285 (3)	3.3 (1)
C(11)	0.1944 (2)	−0.1104 (2)	0.4910 (4)	4.8 (2)
C(12)	0.3409 (2)	−0.1179 (1)	0.4468 (3)	2.9 (1)
C(13)	0.3952 (2)	−0.1585 (1)	0.5161 (3)	3.4 (1)
C(14)	0.4526 (2)	−0.1946 (1)	0.4441 (3)	3.4 (1)
C(15)	0.4568 (2)	−0.1897 (1)	0.2992 (3)	3.4 (1)
C(16)	0.4039 (2)	−0.1490 (1)	0.2261 (3)	3.7 (1)
C(17)	0.3463 (2)	−0.1137 (1)	0.2995 (3)	3.3 (1)
C(18)	0.5607 (2)	−0.2709 (2)	0.2861 (4)	6.3 (2)

Fig. 1. ORTEPII (Johnson, 1976) plot of the molecular structure of the title benzyl-benzodioxole derivative with coordinate atom labelling.

Table 2. Intramolecular bond distances (Å) and angles (°)

O(19)—C(1)	1.424 (4)	C(4)—C(10)	1.524 (4)
O(19)—C(7)	1.386 (3)	C(5)—C(6)	1.405 (4)
O(20)—C(1)	1.414 (4)	C(6)—C(7)	1.362 (4)
O(20)—C(2)	1.393 (3)	C(8)—C(9)	1.492 (4)
O(21)—C(5)	1.366 (3)	C(10)—C(11)	1.535 (4)
O(21)—C(8)	1.424 (3)	C(10)—C(12)	1.522 (4)
O(22)—C(9)	1.393 (4)	C(12)—C(13)	1.386 (4)
O(23)—C(15)	1.373 (3)	C(12)—C(17)	1.395 (4)
O(23)—C(18)	1.421 (4)	C(13)—C(14)	1.384 (4)
C(2)—C(3)	1.368 (4)	C(14)—C(15)	1.372 (4)
C(2)—C(7)	1.371 (4)	C(15)—C(16)	1.391 (4)
C(3)—C(4)	1.400 (4)	C(16)—C(17)	1.385 (4)
C(4)—C(5)	1.402 (4)		

C(1)—O(19)—C(7)	104.4 (2)	O(19)—C(7)—C(6)	127.7 (2)
C(1)—O(20)—C(2)	104.3 (2)	C(2)—C(7)—C(6)	122.5 (2)
C(5)—O(21)—C(8)	118.4 (2)	O(21)—C(8)—C(9)	107.7 (2)
C(15)—O(23)—C(18)	117.6 (2)	O(22)—C(9)—C(8)	114.0 (3)
O(19)—C(1)—O(20)	109.1 (2)	C(4)—C(10)—C(11)	113.9 (2)
O(20)—C(2)—C(3)	128.2 (2)	C(4)—C(10)—C(12)	112.7 (2)
O(20)—C(2)—C(7)	109.8 (2)	C(11)—C(10)—C(12)	109.8 (2)
C(3)—C(2)—C(7)	121.9 (2)	C(10)—C(12)—C(13)	121.0 (2)
C(2)—C(3)—C(4)	118.2 (2)	C(10)—C(12)—C(17)	121.4 (2)
C(3)—C(4)—C(5)	119.0 (2)	C(13)—C(12)—C(17)	117.6 (2)
C(3)—C(4)—C(10)	122.2 (2)	C(12)—C(13)—C(14)	122.3 (2)
C(5)—C(4)—C(10)	118.8 (2)	C(13)—C(14)—C(15)	119.2 (3)
O(21)—C(5)—C(4)	115.6 (2)	O(23)—C(15)—C(14)	123.6 (2)
O(21)—C(5)—C(6)	122.4 (2)	O(23)—C(15)—C(16)	116.2 (2)
C(4)—C(5)—C(6)	122.0 (2)	C(14)—C(15)—C(16)	120.2 (3)
C(5)—C(6)—C(7)	116.4 (2)	C(15)—C(16)—C(17)	120.0 (3)
O(19)—C(7)—C(2)	109.8 (2)	C(12)—C(17)—C(16)	120.8 (2)

Fig. 2. PLUTO (Motherwell & Clegg, 1978) stereo plot of packing diagram; unit-cell axes and origin are labeled.

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properties of this class of compounds and structural similarities with podophyllotoxin. Using cultured Chinese Hamster Ovary (CHO) cells selected for resistance to podophyllotoxin, Gupta (1992) has shown that these compounds exhibit podophyllotoxin-like antimitotic activity. Recently the crystal structures of two podophyllotoxin derivatives showing antimitotic activity have been reported (Sicheri, Derry, Gupta & Yang, 1991, 1992). This information should prove useful in determining the structure–activity relationships of these compounds.
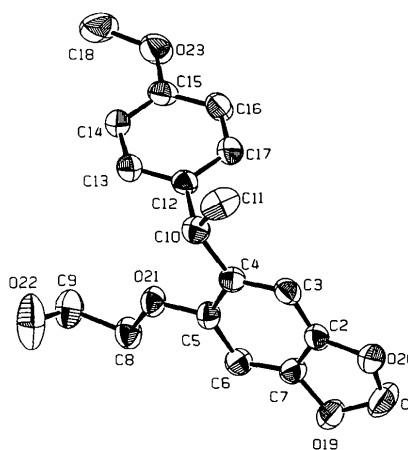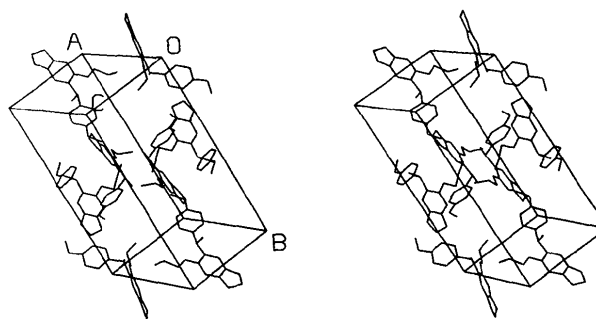
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syn-2-Benzyl-1,3-dithiane 1-Oxide

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Abstract. $C_{11}H_{14}OS_2$, $M_r = 226.35$, orthorhombic, $P2_12_12_1$, $a = 7.598$ (3), $b = 25.635$ (2), $c = 5.774$ (3) Å, $V = 1124.6$ Å^3, $Z = 4$, $D_x = 1.337$ g cm^{-3}, Mo $K\alpha$ radiation, $\lambda = 0.71069$ Å, $\mu = 4.20$ cm^{-1}, $F(000) = 480$, room temperature, $R = 0.033$ for 913 reflections with $I > 3\sigma(I)$. Bond lengths and angles are normal. Structure determination confirmed the constitution of a material prepared with 94% enantiomeric excess, by the sequential asymmetric oxidation and deacylation of 2-acetyl-2-benzyl-1,3-dithiane [Page & Namwindwa (1991). *Synth. Lett.* pp. 80–83].

Experimental. A yellow crystal, $0.15 \times 0.35 \times 0.45$ mm, was analyzed using a Rigaku AFC-6S diffractometer with $\omega/2\theta$ scans. Unit-cell parameters were determined from 18 reflections with $20 < 2\theta < 33°$. No absorption correction was applied. $2\theta_{max} = 50°$; $0 < h < 9$, $0 < k < 30$, $0 < l < 6$. Three standard reflections showed no significant change. 1209 reflections were measured (one unique set), of which
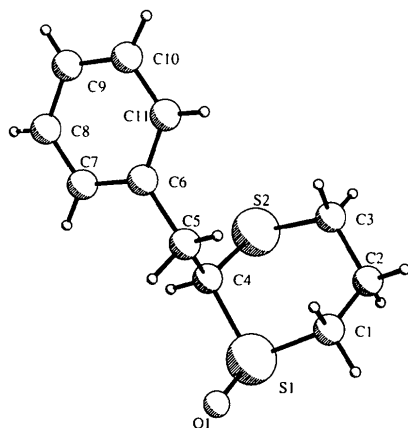

Fig. 1. One molecule of the title compound, illustrating the structure and the atom numbering (*PLUTO*; Motherwell & Clegg, 1978).

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

$$B_{eq} = 8\pi^2 U_{eq} = (8\pi^2/3)\Sigma_i\Sigma_j U_{ij}a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	B_{eq}
S(1)	0.5197 (1)	0.01780 (4)	0.7820 (2)	3.55 (5)
S(2)	0.4527 (2)	0.12721 (5)	0.8792 (2)	4.35 (6)
O(1)	0.6573 (4)	−0.0218 (1)	0.7247 (5)	4.5 (1)
C(1)	0.4237 (6)	0.0344 (2)	0.5054 (9)	3.9 (2)
C(2)	0.2885 (8)	0.0778 (2)	0.511 (1)	4.9 (3)
C(3)	0.3646 (7)	0.1292 (2)	0.588 (1)	4.9 (3)
C(4)	0.6274 (6)	0.0801 (2)	0.8456 (8)	3.3 (2)
C(5)	0.7776 (7)	0.0936 (2)	0.686 (1)	3.9 (2)
C(6)	0.8733 (5)	0.1429 (1)	0.7567 (8)	3.3 (2)
C(7)	0.9636 (7)	0.1459 (2)	0.961 (1)	4.4 (2)
C(8)	1.0527 (8)	0.1901 (2)	1.024 (1)	5.7 (3)
C(9)	1.0533 (8)	0.2328 (2)	0.882 (1)	6.6 (4)
C(10)	0.965 (1)	0.2308 (2)	0.676 (1)	7.0 (4)
C(11)	0.8745 (7)	0.1861 (2)	0.615 (1)	5.1 (3)

Table 2. *Selected bond lengths* (Å) *and angles* (°)

S(1)—O(1)	1.495 (3)	C(5)—C(6)	1.514 (6)
S(1)—C(1)	1.807 (5)	C(6)—C(7)	1.370 (7)
S(1)—C(4)	1.832 (4)	C(6)—C(11)	1.378 (7)
S(2)—C(3)	1.813 (7)	C(7)—C(8)	1.368 (8)
S(2)—C(4)	1.805 (5)	C(8)—C(9)	1.37 (1)
C(1)—C(2)	1.514 (7)	C(9)—C(10)	1.37 (1)
C(2)—C(3)	1.506 (8)	C(10)—C(11)	1.382 (8)
C(4)—C(5)	1.508 (7)		

O(1)—S(1)—C(1)	104.3 (2)	C(4)—C(5)—C(6)	112.9 (4)
O(1)—S(1)—C(4)	108.9 (2)	C(5)—C(6)—C(7)	121.5 (4)
C(1)—S(1)—C(4)	98.7 (2)	C(5)—C(6)—C(11)	120.8 (4)
C(3)—S(2)—C(4)	101.0 (2)	C(7)—C(6)—C(11)	117.7 (4)
S(1)—C(1)—C(2)	115.3 (4)	C(6)—C(7)—C(8)	121.6 (5)
C(1)—C(2)—C(3)	112.8 (5)	C(7)—C(8)—C(9)	120.3 (6)
S(2)—C(3)—C(2)	112.9 (4)	C(8)—C(9)—C(10)	119.3 (6)
S(1)—C(4)—S(2)	106.0 (2)	C(9)—C(10)—C(11)	119.9 (6)
S(1)—C(4)—C(5)	114.5 (3)	C(6)—C(11)—C(10)	121.2 (6)
S(2)—C(4)—C(5)	118.0 (3)		

912 with $I > 3\sigma(I)$ were used for refinement. Structure solution was by direct methods (*SHELXS*86; Sheldrick 1986) and refinement on F, all within the *TEXSAN* system (Molecular Structure Corporation, 1985); anisotropic vibration parameters for non-H atoms, H atoms located in a difference map and refined with isotropic U values. For 183 parameters