

X-Ray Structure of Cannabispiran: a Novel *Cannabis* Constituent

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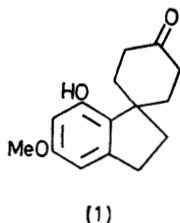
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Summary Cannabispiran, a spiro-compound with a novel skeletal class was isolated from the leaves of *Cannabis sativa* L. and X-ray crystallographic studies indicated that the compound was 7'-hydroxy-5'-methoxyspiro(cyclohexane-1,1'-indan)-4-one (1).

COMBINED gas chromatographic-mass spectrometric analysis of the alcoholic extract of an Indian *Cannabis* (marihuana) variant revealed the presence of a novel constituent which had the same relative retention time¹ as (-)- Δ^8 -trans-tetrahydrocannabinol both before silylation (0.43) and after silylation (0.21). This compound was isolated by adsorption chromatography on silica gel and was obtained as colourless crystals, m.p. 178–179 °C, and was optically inactive. Analysis indicated the formula $C_{16}H_{18}O_3$ which was confirmed by high-resolution mass spectral data.



The i.r. spectrum showed major peaks at ν_{\max} (CHCl_3) 3600, 3335, 1715, 1602, and 1503 cm^{-1} while the $^1\text{H-n.m.r.}$ spectrum (100 MHz; CDCl_3) did not show any resonances due to methyl groups but did reveal a methoxy-singlet at δ 3.75; furthermore, it exhibited a pair of spin-coupled 2H triplets at δ 2.22 and 2.95 (J 7.0 Hz), an 8H multiplet centred at δ 2.56, an exchangeable signal at δ 5.24, and two 1H doublets at δ 6.12 and 6.36 (J 1.8 Hz) which were ascribed to the two aromatic protons.

The paucity of the compound (yields from the plant were ca. 0.002% by dry weight) precluded its structure elucidation by chemical means and thus an X-ray crystallographic study was undertaken. *Crystal data*: space group $Pbca$, orthorhombic, $a = 10.388(5)$, $b = 14.754(7)$, $c = 16.950(8)$ Å, $U = 2597.7(9)$ Å³, $Z = 8$, $F(000) = 1056$. The structure determination was carried out using 852 reflections with $I > 2\sigma(I)$ collected by counter methods, using Mo- K_α -radiation ($2\theta_{\max} = 45$). The phase problem was solved by direct methods.² The structure model was refined to an R factor of 0.15. Inclusion of the hydrogen atoms in calculated positions and full-matrix least-squares refinement of all positional parameters, anisotropic thermal parameters for all non-hydrogen atoms and isotropic thermal parameters for hydrogen atoms, resulted in an R factor

of 0.074 and weighted R_w of 0.054. Atomic parameters and a listing of observed and calculated structure factors are available from the authors upon request. All programs used are part of a local assembly of computer programs for CYBER-74 which have been described.³ A view of the molecule is shown in the Figure. The indan system except for C(8), which deviates by 0.3 Å, is planar. Selected dihedral angles around C(9) are as follows (+ve \equiv right-handed screw): C(7)–C(8)–C(9)–C(2) $-26.0(7)^\circ$, C(1)–C(2)–C(9)–C(10) $135.7(7)^\circ$, and C(1)–C(2)–C(9)–C(14) $-102.6(7)^\circ$.

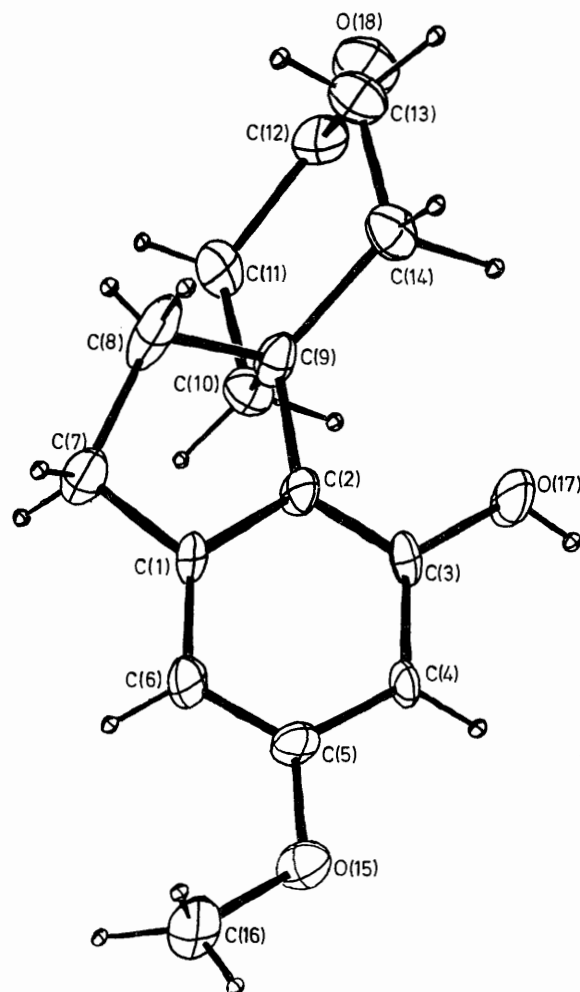


FIGURE. A view of the molecule of (1) down on the plane of the phenyl ring. The thermal ellipsoids are shown with 25% probability. The hydrogen atoms are drawn artificially small.

We have named the compound cannabispiran (**1**) and its structure is related to the synthetic compound spiro(cyclohexane-1,2'-indan)-1',4-dione which was reported to potentiate the estrogenic activity of stilbestrol.⁴

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¹ Gas chromatography was performed on a column of 2% OV-17 on 100/120 mesh Gas Chrom Q at 210 °C using androst-4-ene-3,17-dione as internal standard as described by C. E. Turner and K. Hadley, *J. Pharm. Sci.*, 1973, **62**, 251.

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