

## Fungal Metabolites. Part 8.<sup>1</sup> Isolation of 2-Methoxy-6-(3,4-dihydroxyhepta-1,5-dienyl)benzyl Alcohol

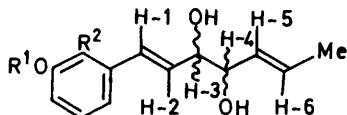
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A new metabolite of *Aspergillus varicolor* has been isolated and identified as having the structure (1) of the title compound.

THE isolation of several metabolites from static culture of the fungus *Aspergillus varicolor* has been described.<sup>1-3</sup> During these isolations, terrein<sup>2</sup> and an unknown substance (X)<sup>1</sup> were separated by continuous-elution thin layer chromatography.

Compound (X) was optically active and elemental analysis suggested the formula C<sub>15</sub>H<sub>20</sub>O<sub>4</sub>, but no molecular ion corresponding to this was observed in the electron-impact mass spectrum. Field-desorption mass spectrometry revealed a cluster ion, C<sub>30</sub>H<sub>41</sub>O<sub>8</sub> (2M + H)<sup>+</sup>. The i.r. spectrum showed strong OH stretching absorptions at 3 300 and, unusually, also at 2 450 cm<sup>-1</sup>. Such bands as the latter are observed in cases of very strong hydrogen bonding.<sup>4</sup> Heating compound (X) at 60 °C for several hours *in vacuo* caused the disappearance of the lower frequency band but no change in the elemental analysis or other spectroscopic properties (u.v., <sup>1</sup>H n.m.r., and mass spectra). Presumably, the change was due to rearrangement of the crystal structure.

The <sup>1</sup>H n.m.r. spectrum, with double-resonance experiments, enabled most of the structural features of the compound [2-methoxy-6-(3,4-dihydroxyhepta-1,5-dienyl)benzyl alcohol (1)] to be elucidated. Two *trans*-olefinic protons (H-5 and H-6; *J* 15 Hz) appear at δ 5.45



(1) R<sup>1</sup> = Me; R<sup>2</sup> = CH<sub>2</sub>OH

(2) R<sup>1</sup> = H; R<sup>2</sup> = CHO

and 5.74, and one of these (H-6) is coupled further (doublet of quartets) to a methyl group (δ 1.69, d, *J* 6 Hz). The second proton (H-5) is also coupled (d of d; *J* 6 Hz) to H-4. A second pair of *trans*-olefinic protons (H-2 and H-1) appears at δ 6.06 and 6.94 (*J* 16 Hz) and, from the chemical shifts, must form part of a conjugated system. One of these protons (H-2; d of d) lies next to H-3. Because of their chemical shifts, protons H-3 and H-4 must lie on carbon atoms attached to oxygen and, although at 100 MHz only one complex multiplet (δ 4.18) is observed for them, at 220 MHz this splits to give two similar multiplets. Irradiation at H-5 caused a marked change in the multiplet structure of H-4 at δ 4.12 and the two must be coupled. Similarly,

irradiation at H-5 caused the structure at δ 5.74 to change to a quartet. Irradiation at H-2 caused a marked change in the multiplet structure of H-3 centred at δ 4.24. Finally, two of the three hydroxy-protons (δ 2.68 and 3.00br; 2 H and 1 H, respectively; exchanged with D<sub>2</sub>O) must lie in this chain because of the chemical shifts and secondary natures of the protons H-3 and H-4.

The conjugated double-bond (H-1-H-2), the u.v. spectrum, and the n.m.r. absorptions of the three protons between δ 6.76 and 7.18 indicate that the side-chain is attached to a trisubstituted aromatic ring having also a methoxy (δ 3.80; s) and a hydroxymethylene group (δ 4.72; s). That the three aromatic hydrogens are adjacent is apparent from their couplings (two doublets and a triplet). The positions of the two doublets [δ 6.76 (*J* 8 Hz) and 7.00 (*J* 8 Hz)] indicate that these hydrogens lie *ortho* and *para* to the methoxy-group, whilst the triplet at δ 7.18 (*J* 8 Hz), shows that a hydrogen is *para* to it.<sup>5</sup>

The above data afford structure (1) for compound (X) and, although the unsaturated side-chain and the hydroxymethylene groups might be interchanged, three pieces of evidence indicate the correctness of structure (1). A similar heptaketide, pyriculol (2),<sup>6</sup> has adjacent phenolic OH and aromatic aldehyde groups corresponding to the methoxy and hydroxymethylene groups in (1). The chemical shifts and multiplicities in the <sup>13</sup>C n.m.r. spectrum of compound (X) help to confirm the above assignments,<sup>7</sup> and the chemical shifts for the aromatic <sup>13</sup>C and <sup>1</sup>H nuclei fit those predicted by additivity rules.<sup>5,7</sup> The u.v. spectrum provides convincing evidence for structure (1). Styrene-type molecules in which the double-bond is fully co-planar with the benzene ring have u.v. maxima near 260 nm with log ε values of 4.0–4.3 and subsidiary maxima near 285–295 nm (log ε 2.0–2.3).<sup>8</sup> If the double-bond cannot conjugate fully with the benzene ring, the u.v. bands are shifted hypsochromically, with the one at shorter wavelength disappearing completely in sterically difficult cases. For example, with *o*-methylisopropenylbenzene, in which the double-bond is prevented sterically from becoming co-planar with the ring, no shorter-wavelength maximum is observed.<sup>9</sup> Phenol and anisole give maxima near 270–280 nm which are not much affected by the presence of *ortho*-, *meta*-, or *para*-alkyl groups,<sup>10</sup> and *ortho*- or *meta*-hydroxy- or methoxy-groups have little effect in styrenes on the positions of the bands at 260 and 285–295 nm.<sup>11</sup>

Thus, where the double-bond of styrene-like molecules can conjugate with the benzene ring, two absorption bands are observed but, when conjugation is prevented, only simple substituted benzenoid bands near 270–280 nm are observed.<sup>12</sup> Compound (X) has absorption bands at 250 and 292 nm ( $\log \epsilon$  4.14 and 3.42 respectively) showing that the side-chain double-bond conjugates effectively with the benzene ring and cannot be placed between the methoxy and hydroxymethyl groups since these would prevent co-planarity.

The absolute configurations about the hydroxylic centres remain unresolved for lack of material. Similarly, the absolute configuration of pyriculol (2) remains undetermined.

#### EXPERIMENTAL

Compound (X) was isolated in a yield of 1.7 mg l<sup>-1</sup> of fungal culture liquors,<sup>3</sup> m.p. 132–133° (from CHCl<sub>3</sub>) (Found: C, 68.2; H, 7.6%. C<sub>15</sub>H<sub>20</sub>O<sub>4</sub> requires C, 68.2; H, 7.6%), partial mass spectrum (electron-impact; 70 eV) *m/e* 199.113 8 (normalized abundance 10%, C<sub>14</sub>H<sub>15</sub>O<sub>3</sub>; M<sup>+</sup> – H<sub>2</sub>O – CH<sub>3</sub> from unobserved molecular ion at *m/e* 264), 176.084 4 (25, C<sub>11</sub>H<sub>12</sub>O<sub>2</sub>), and 175.076 7 (100, C<sub>11</sub>H<sub>11</sub>O<sub>2</sub>, M<sup>+</sup> – H<sub>2</sub>O – C<sub>4</sub>H<sub>7</sub> from side-chain cleavage of 1,2-diol);  $[\alpha]_D^{27} + 20.2$  (*c* 0.98, EtOH),  $[\alpha]_D^{24.5} + 42.7$  (*c* 0.22, CHCl<sub>3</sub>);  $\nu_{\max}$  (Nujol) 3 300, 2 450, 1 580, 1 470, and 962 cm<sup>-1</sup>;  $\delta_C$  (CDCl<sub>3</sub>) 18.0 (q), 55.5 (t), 56.0 (q), 76.8 (d), 110.6 (d), 119.6 (d), 127.0 (s), 128.8 (d), 129.7 (d), 130.0 (d), 131.5 (d), 132.8 (d), 139.6 (s), and 159.2 (s).

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#### REFERENCES

- <sup>1</sup> Part 7, A. W. Dunn, R. A. W. Johnstone, T. J. King, L. Lessinger, and B. Sklarz, *J.C.S. Perkin I*, 1979, 2113.
- <sup>2</sup> A. W. Dunn, I. D. Entwistle, and R. A. W. Johnstone, *Phytochemistry*, 1975, **14**, 2081.
- <sup>3</sup> A. W. Dunn, R. A. W. Johnstone, T. J. King, L. Lessinger, and B. Sklarz, *J.C.S. Chem. Comm.*, 1978, 533.
- <sup>4</sup> For leading references, see L. J. Bellamy, 'Advances in Infrared Group Frequencies,' Methuen, London, 1968, p. 277.
- <sup>5</sup> For leading references and tables of chemical shifts, see L. M. Jackman and S. Sternhell, 'Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry,' Pergamon, London, 1969, pp. 202–204.
- <sup>6</sup> S. Iwasaki, S. Nozoe, S. Okuda, Z. Sata, and T. Kozaka, *Tetrahedron Letters*, 1969, 3977.
- <sup>7</sup> See *e.g.*, G. C. Levy and G. L. Nelson, 'Carbon-13 Nuclear Magnetic Resonance for Organic Chemists,' Wiley, New York, 1972, pp. 65–66 and 79–93.
- <sup>8</sup> R. A. Morton and A. J. A. de Gouveia, *J. Chem. Soc.*, 1934, 916; A. I. Scott, 'Interpretation of the Ultraviolet Spectra of Natural Products,' Pergamon, Oxford, 1964, pp. 96–100.
- <sup>9</sup> P. Ramart and M. J. Hoch, *Bull. Soc. chim. France*, 1938, **5**, 848; J. Gripenberg and T. Hase, *Acta Chem. Scand.*, 1966, **20**, 1561; O. H. Wheeler and C. B. Covarrubias, *Canad. J. Chem.*, 1962, **40**, 1224.
- <sup>10</sup> R. A. Friedel and M. Orchin, 'Ultraviolet Spectra of Aromatic Compounds,' Wiley, New York, 1951.
- <sup>11</sup> R. Ya. Levina, Yu. S. Shabarov, M. G. Kuz'min, N. I. Vasil'ev, S. I. Pokraka, and E. G. Treshchova, *J. Gen. Chem. U.S.S.R.*, 1959, **29**, 3504; A. E. Lutskii and A. F. Soldatova, *ibid.*, 1965, **35**, 2088; see also refs. 9 and 10 and E. Spinner, *Spectrochim. Acta*, 1961, **17**, 545.
- <sup>12</sup> Y-R. Naves, *Bull. Soc. chim. France*, 1959, 1871.