

A Toxic C₁₄ Polyacetylenic Tetrahydropyranyl Alcohol from the Compositae

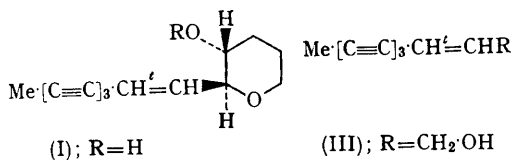
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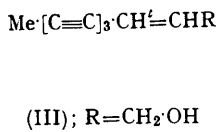
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THE alcohol (I), m.p. 89—90°, $[\alpha]_D^{20} - 40 \pm 1^\circ$ (CHCl₃) and its acetate (II), m.p. 64—64.5°, $[\alpha]_D^{20} + 6.5 \pm 1.5^\circ$, have both been isolated from the leaves and the flowers of *Dahlia coccinea* and

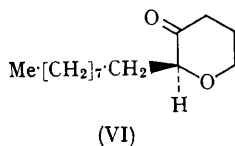
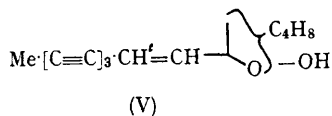
hybrids (Family Compositae, tribe *Heliantheae*) grown in Oxford, and from the leaves of *Ichthyothere terminalis* (Spreng.) Malme (Family Compositae, tribe *Heliantheae*), a small herb frequently encountered amongst the "campos" vegetation of Brazil and the Guyanas, the leaves of which have long been known to be used as a fish poison by natives of the lower Amazon Basin.¹ Minute quantities of either the alcohol (I) or the acetate (II) are extremely toxic to the fish *Lebistes*



(II); R=Ac



(IV); R=CO₂Me



reticulatus confirming that such compounds are at least in part responsible for the toxicity of the leaves of *I. terminalis*; they also kill mice when injected intraperitoneally in doses of 1 mg. in olive oil.

The infrared spectrum of (I) showed strong hydroxyl (3600 cm.⁻¹), disubstituted acetylene (2210 cm.⁻¹), and *trans*-double bond (948 cm.⁻¹) absorption, and a band at 1090 cm.⁻¹ which has proved to be associated with the tetrahydropyranyl oxygen. The ultraviolet absorption spectrum was identical to that of *trans*-dehydromatricarianol² (III).

Attempts to oxidise the alcohol (I) with active manganese dioxide were unsuccessful, but oxidation with 8*N*-chromic acid-acetone at 5° afforded an acidic fraction which after esterification gave *trans*-dehydromatricaria ester (IV) in 12% yield

(crude spectroscopic yield, 25%). This fact combined with the molecular formula of (I), confirmed by its high-resolution mass spectrum,³ requires the partial structure (V).

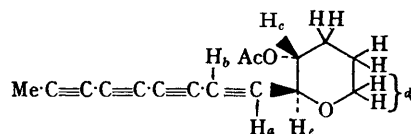
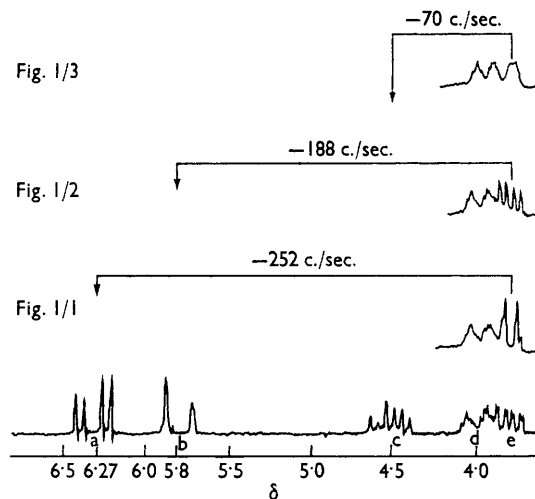


Fig. 1/3

Fig. 1/2

Fig. 1/1



The location of the remaining four carbon atoms and the hydroxyl group was established by nuclear magnetic double resonance studies at 100 Mc./sec. using Johnson's modification⁴ of the method described by Freeman⁵ to permit a detailed assignment of the signals. The results are summarised on the relevant section of the 100 Mc./sec. spectrum⁶ (Figure 1) of the acetate (II). The presence of the acetate allowed identification of H_c 4.5 p.p.m. This signal appears as a pair of overlapping triplets with two large and a small coupling of 9—10 and 4—4.5 c./sec., respectively. H_c is coupled to H_b (Figure 1/3) which in turn is coupled to both vinyl protons (Figures 1/2 and 1/1) (*J*_{eb} 1.5 c./sec. and *J*_{ea} 5.5 c./sec.). This sequence requires structure (II). Furthermore,

¹ J. Baker and A. W. Eichler: "De usu Compositarum Brasiliensum", in C. F. Ph. Martius, "*Flora Brasiliensis*", 1882—1884, 6 (3), 410, Munich.

² J. N. Gardner, E. R. H. Jones, P. R. Leeming, and J. S. Stephenson, *J. Chem. Soc.*, 1960, 691.

³ Determined on an A.E.I. MS9 high-resolution mass spectrometer using a direct probe. Found: *M*, 214.0994 ± 0.0005. C₁₄H₁₄O₂ requires *M*, 214.09937; resolution 15,000, 5% definition.

⁴ L. F. Johnson, "Varian Technical Information Bulletin, 111", No. 3, 1962, p. 5.

⁵ R. Freeman, *Mol. Phys.*, 1960, 3, 435; R. Freeman and D. H. Whiffen, *Proc. Phys. Soc.*, 1962, 79, 794.

⁶ Recorded in CDCl₃ solution with a Varian HR100 spectrometer.

since the coupling of H_c with H_e is of the order of 9—10 c./sec., these two protons are in an axial-axial relationship, the second large coupling of H_c being axial-axial to the other vicinal axial proton and the small one being axial-equatorial to the vicinal equatorial proton, thus establishing the relative stereochemistry of the hydroxyl group and the side chain.

Assuming that the Octant rule⁷ applies equally to tetrahydropyran-3-ones as to cyclohexanones,

then the negative Cotton effect of the saturated ketone (VI) implies the absolute configuration indicated in (I).

Dahlia produce many C_{14} and C_{13} acetylenic compounds closely related in structure to the tetrahydropyran (I).⁸ It may well be derived from an open-chain precursor by epoxidation and cyclisation, through attack by a terminal oxygen function on the epoxide group.

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⁷ I. W. Moffitt, A. Moscovitz, R. B. Woodward, W. Klyne, and C. Djerassi, *J. Amer. Chem. Soc.*, 1961, **83**, 4013.

⁸ Unpublished work at Oxford by S. Safe.