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THE STRUCTURE OF PSEUDOASCARIDOLE AND SOME OF ITS CHEMISTRY

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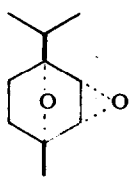
The recent, mutually contradictory, reports of Danilova et.al.[1] on the chemistry of compounds obtained from treatment of pseudoascaridole with hydrogen chloride prompts us to record our results on these reactions.

Pseudoascaridole has been formulated as 1,4;2,3-diepoxy-p-menthane(1)[2] or more recently as cis-1,2;3,4-diepoxy-p-menthane(2)[1,3,5] although the latter structure has been criticised[4]. Lithium aluminium hydride reduction gives initially cis-1-hydroxy-3,4-epoxy-p-menthane(3)* b.p.50-51°C/0.15mm., which on prolonged reduction gives a mixture of cis-p-menthane 1,4-diol m.p.119-120°C (19%) and cis-p-menthane-1,3-diol, m.p.42-43°C (72%). These experiments prove that pseudoascaridole has the structure (2).



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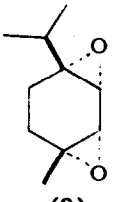

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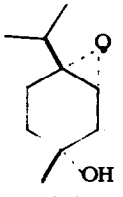

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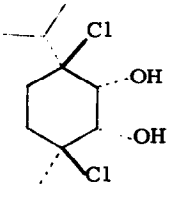


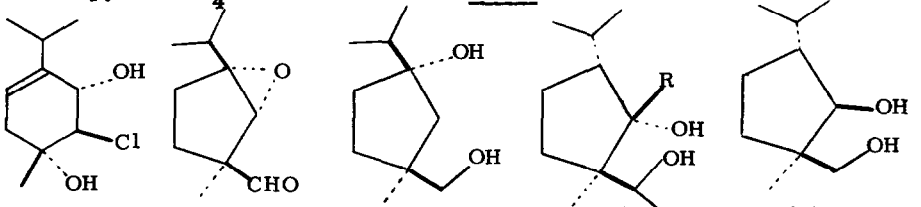
(4)

The treatment of pseudoascaridole with hydrogen chloride in ether yields 1β, 4β-dichloro-2α, 3α-dihydroxy-p-menthane(4) m.p.98-99°C (48%)

*This was synthesised by epoxidation of 1-hydroxy-p-menth-3-ene, and hydrolysis of the epoxide ring could explain the reported isolation of a triol from the lithium aluminium hydride reduction[5].

and 2β-chloro-1α, 3α-dihydroxy-p-menth-4-ene(5)(22%) as an oil. Structure (4) was confirmed by N.M.R. which showed a singlet methyl group at 8.3τ on a carbon bearing a chlorine atom and not an hydroxyl group. The DMSO/DMSO-D_2O N.M.R.[6] showed clearly the presence of two secondary hydroxyl groups.

The treatment of the bis-chlorohydrin(4) with methanolic potassium hydroxide yields, in addition to the reported pseudoascaridole[1], (2) (58%), an isomeric aldehyde, 2α, 3α-epoxy-1α-methyl-3β-isopropyl-cyclopentanal(6)(42%). Lithium aluminium hydride reduction of (6) gives 1β-hydroxymethyl-1α-methyl-3α-hydroxy-3β-isopropylcyclopentane (7)(91%). The N.M.R. of (7) in $CDCl_3$ shows a singlet methyl group at 8.86τ, the hydroxy-methylene protons at 6.73τ(singlet) and a geminal AB quartet at 8.51τ (J=(-)14 cps). The DMSO/DMSO-D_2O N.M.R. shows primary and tertiary hydroxyl groups and dilution I.R. spectroscopy in CCl_4[7] indicates their trans orientation (3617cm^{-1}).



(5) (6) (7) (8) (9)

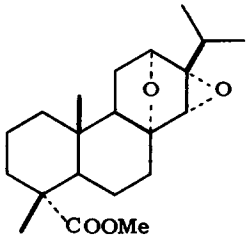
The reduction of the bis-chlorohydrin(4) or its diacetate with lithium aluminium hydride gives two diols, 1α-hydroxymethyl-1β-methyl-2β-hydroxy-3βisopropylcyclopentane (8,R=H), m.p.106-107°C[1](44%) and its 2α-hydroxy isomer (9) m.p.51-52°C(22%). The N.M.R. of both compounds in DMSO/DMSO-D_2O[6] indicates one primary and one secondary hydroxyl group and their trans/cis orientation is indicated by their dilution I.R. spectra[7] which shows a band at 3612cm^{-1} for (8) and bands at 3638 and 3565 cm^{-1} for (9).

Reduction of (4) with lithium aluminium deuteride gives (8((R=D).

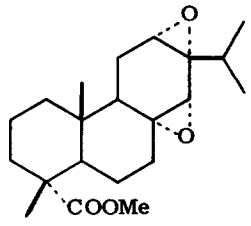
Although the proton at C-3 could not be seen in the N.M.R., comparison of the mass spectral cracking patterns of the deuterated and undeuterated diols eliminated a trideutero compound, even though the molecular ions could not be detected.

It follows from the above reactions that the 1,2 epoxide in (2) is considerably more reactive than the 3,4 epoxide. The isolation of (4) and (5) in the hydrogen cloride reaction suggests a conformational equilibrium for pseudoascaridole, and that if opening of the 1,2-epoxide gives rise to a 1-hydroxy-2-chloro-compound, approach of Cl^- to the 3,4-epoxide is prevented by dipolar repulsion from the 2-chloro atom to such an extent that opening by cis elimination is preferred.

It has recently been reported [4] that levopimaric acid peroxide yields on heating the dioxide (10), and not (11) as expected by analogy with ascaridole. The assignment of structure (10) was based on its reactions with hydrogen chloride and aqueous acid. However, the application of the above arguments to the conformationally rigid



(10)



(11)

structure (11) explains equally well the reported chemistry and eliminates the mechanistic difficulty in formation of (10).

Further discussion of the interesting conformational and mechanistic implications of the above and other related reactions is deferred for a full publication.

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