Synthesis of 9-Hydroxy-HEOD, a Major Mammalian Metabolite of HEOD (Dieldrin)

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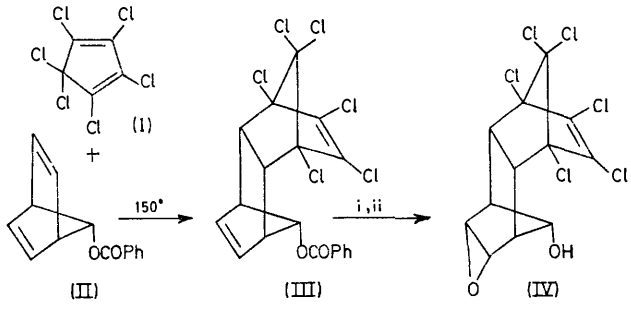
Summary The first synthesis of a 9-hydroxylated derivative of HEOD (dieldrin) has been accomplished in three steps starting from hexachlorocyclopentadiene and 7-benzoyloxybicyclo[2,2,1]hepta-2,5-diene.

THE title compound (IV) is a metabolite of HEOD (dieldrin)† in the rat,[1] mouse,[2] and sheep,[3] and also in man.[4] We record here the first synthesis of this compound.

The bicycloheptadiene (II), prepared according to the literature,[5] was heated under nitrogen with hexachlorocyclopentadiene (I) (1 mol. equiv.) for 6 h at 150°. The crude syrupy product was saponified with aqueous alcoholic NaOH, and the neutral fraction therefrom was oxidised with *m*-chloroperoxybenzoic acid in methylene dichloride. Chromatography over silica gel in hexane–benzene of the alkali-washed oxidation product yielded the title compound (IV), which formed white crystals (12%) from methanol, m.p. 173—175°, and was identical in all respects (m.p. and mixed m.p., t.l.c., g.l.c., i.r., n.m.r., and mass spectra) with the natural metabolite isolated from rat faeces.[1]



Reagents: i, NaOH; ii, *m*-chloroperoxybenzoic acid.

Further work is in hand to isolate and identify the major primary condensation product, presumably the benzoate (III), and its saponification product. A by-product of the synthesis, which appears from t.l.c. and g.l.c. analysis to be a related, probably isomeric, alcohol is also being investigated.

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† Dieldrin contains not less than 85% of the compound 1,2,3,4,10,10-hexachloro-6,7-epoxy-1,4,4a,5,6,7,8,8a-octahydro-*exo*-1,4-*endo*-5,8-dimethanonaphthalene (HEOD).

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