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SHORT SYNTHESES OF CONDURITOLS A AND D, AND DEHYDROCONDURITOLS, FROM BENZENE: THE PHOTO-OXIDATION OF cis-CYCLOHEXA-3,5-DIENE-1,2-DIOL

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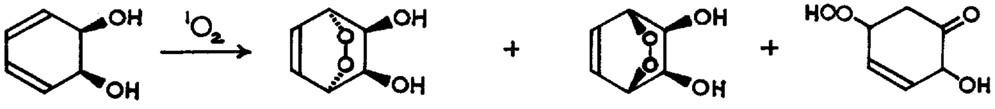
Summary: Diene (1), available by microbial oxidation of benzene, undergoes reaction with singlet oxygen to yield endoperoxides (2) and (3); reduction or rearrangement of these compounds gives conduritols (5) and (6) or dehydroconduritols (8) and (9), respectively.

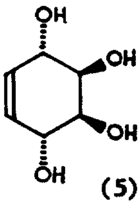
There is no simple chemical reaction which allows the direct oxidation of benzene to alicyclic compounds. However, stereospecific microbial oxidation of benzene using Pseudomonas putida strains has made cis-cyclohexa-3,5-diene-1,2-diol (1) a readily available compound.[1,2] Moreover, there is a need to develop methods for the stereoselective introduction of functional groups into the benzene ring . Thus, the synthesis of cyclic polyols from aromatic compounds could be rewarding, in view of the role of inositol phosphates as secondary messengers in cells.[3] We describe here the reaction of (1) with singlet oxygen, and its potential in synthesis.

Methylene Blue-sensitised photo-oxidation of (1) in dichloromethane solution at -80°C gave two endoperoxide isomers, (2) and (3) in the ratio 2.8:1. The individual crystalline peroxides were easily separable by column chromatography on silica gel.[4] T.l.c. of the crude photo-oxidation product provided evidence for a small amount of an additional unstable compound presumed to be an allylic hydroperoxide (4, drawn in its ketonic form) derived by ene reaction of singlet oxygen, which was converted to catechol (1,2-dihydroxybenzene) on chromatography (3% isolated yield).[5]



(1) (2) (3) (4)

Reduction of the endoperoxide (2) by thiourea in methanol (100% yield)[6] or by sodium borohydride in ethanol (60% yield) gave conduritol A (5),[7] whilst the corresponding reduction of endoperoxide (3) by thiourea/methanol gave the all *cis*-form, conduritol D (6).[8] Hydrogenation (Pt/EtOH) of (2) led to dihydroconduritol A (7)[9,10] in 80% isolated yield. These three-step syntheses of cyclitols from benzene are considerably shorter than the multi-step routes pioneered by Nakajima *et al.*,[11] and the chemistry involved should be applicable to the synthesis of specific stereoisomers of protected inositols.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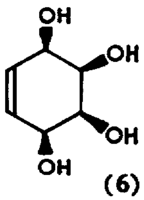
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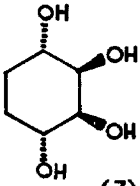
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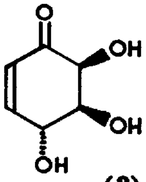
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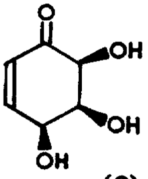
(9)

Interestingly, treatment of acetone or chloroform solutions of endoperoxide (2) with triethylamine (0.1 mol. equiv.) gave base-catalysed rearrangement to hydroxyenone, to yield the sensitive dehydroconduritol A (8), whereas similar treatment of (3) gave dehydroconduritol D (9) in a more rapid reaction.[12] Compounds (8) and (9) have previously been prepared in low yield from oxidation (Pt/O_2) of conduritols,[13] but the simplicity and directness of the present route, starting from benzene as precursor, makes it an attractive alternative.

We thank ICI Fine Chemicals for a supply of compound (1).

References and Notes

1. S.V. Ley, F. Sternfeld and S. Taylor, *Tetrahedron Lett.*, 1987, *28*, 225.
2. D.G.H. Ballard, A. Courtis, I.M. Shirley and S.C. Taylor, *J. Chem. Soc., Chem. Commun.*, 1983, 954.
3. M.J. Berridge, *Ann. Rev. Biochem.*, 1987, *56*, 159.
4. Eluting solvent: 5-10% acetone/95-90% diethyl ether. Isolated yields: (2), 40%; (3), 15%; polymeric material, 40%, see ref. 2. Compound (2): m.p. 125-7°C(decomp.), δ_C (CD_3COCD_3) 65.3, 73.7 and 132.4 p.p.m.; Compound (3): m.p. 109-116°C(decomp.), δ_C (CD_3COCD_3) 61.1, 77.0 and 132.8 p.p.m.
5. cf. R. Atkins and H.A.J. Carless, *Tetrahedron Lett.*, 1987, *28*, 6093.
6. M. Balci, *Chem. Rev.*, 1981, *81*, 91.
7. Compound (5): m.p. 141-3° (lit. 142-3°),[11] δ_C (CD_3OD) 70.6, 74.1 and 130.6 p.p.m.
8. Compound (6): δ_C (CD_3OD) 69.1, 72.0 and 130.4 p.p.m.
9. Compound (7): m.p. 206.5-209°, δ_C (CD_3OD) 27.5, 71.1 and 74.7 p.p.m.
10. Balci has recently described an interesting route to the related cyclohexanetetrols, *via* photo-oxidation of cyclohexa-1,3-diene: N. Akbalut and M. Balci, *J. Org. Chem.*, 1988, *53*, 3338.
11. M. Nakajima, I. Tomida and S. Takei, *Chem. Ber.*, 1959, *92*, 163; *ibid.*, 1957, *90*, 246.
12. Compound (8): δ_C (CD_3COCD_3) 69.4, 74.0, 75.9, 127.8, 147.3 and 206.3 p.p.m.;
    Compound (9): δ_C (CD_3SOCD_3) 68.5, 75.4, 76.4, 125.9, 150.9 and 198.9 p.p.m.
13. K. Heyns, H. Gottschalck and H. Paulsen, *Chem. Ber.*, 1962, *95*, 2660.

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