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ISOPRENE EPOXIDE AS A HEMITERPENOID SYNTHON

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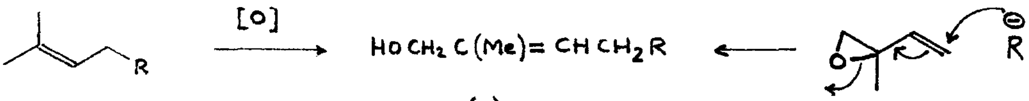
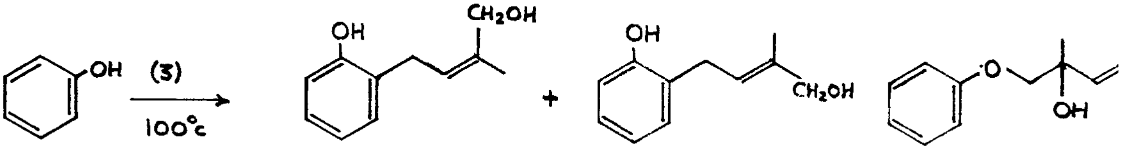
Hemiterpenoid (prenyl) part structures are common in secondary metabolites[1] and it is becoming increasingly clear that terminally oxidised derivatives, of general structures (1), form an important subgroup of hemiterpenoid natural products. The synthesis of structures of type (1) presents considerable problems, largely because available routes either involve a difficult selective oxidation[2] of only one of the terminal methyl groups of part structures (2), or require stepwise formation[3] of (1). Isoprene epoxide (3) is a potential one-step precursor of (1), as shown below, provided that allylic rearrangement accompanies ring-opening, and we describe two examples to show that this can be achieved under appropriate conditions.



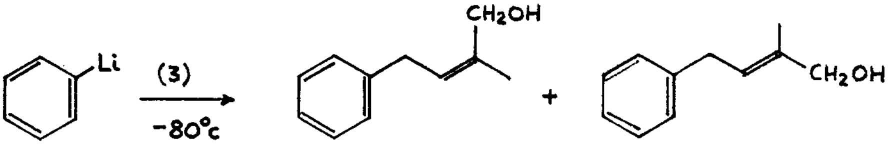
(2) (1) (3)

When isoprene epoxide (3) is solvolysed in phenol in the presence of sodium phenoxide (1 mol. equiv.) at 100°C, ring-opening occurs almost exclusively with allylic rearrangement to give the phenols (4) and (5), together with small amounts of the ether (6). A similar ring-opening occurs when (3) is reacted with phenyllithium in benzene-ether at -80°C, and the mixture is allowed to come to room temperature before work-up. The major product is the alcohol (7), while the geometric isomer (8) is formed to a small extent.

The structures of these aromatic hemiterpenoids follow from microanalysis, i.r., n.m.r. and other data. Typically, the alcohol (7) (b.p. 118-120°C/2.0 m.m) showed $\nu_{\mathrm{max}}^{\mathrm{LF}}$ 3450, 1550, 998, 888 cm^{-1}; m/e 162; $\tau_{\mathrm{CDCl_3}}$ 2.8-3.9 (m, 5H, aryl), 4.75 (b.t., 1H, $>$C=C$\underline{\mathrm{H}}$-CH$_2$), 5.9 (s, 2H, C$\underline{\mathrm{H}}_2$OH), 6.4 (s, 1H, D$_2$O exch., OH), 6.75 (d, 2H, C$\underline{\mathrm{H}}_2$-CH=C$<$), 8.2 (b.s., 3H, CH$_3$). The alcohols (4), (5) and (8) gave similar data. The double bond geometry in (7) was established by a double nuclear Overhauser[4] study which indicated the CH$_3$ and vinyl hydrogens to be *cis*- to each other.



(4) (5) (6)



(7) (8)

These reactions provide a significant contrast to similar ring-opening reactions of allylic epoxides described in the literature. Thus isoprene epoxide (3) has been treated with ethanolic sodium phenoxide,[5] but the products are ethers. Similarly ring-opening of (3) by Grignard reagents[6] and by alkyllithium reagents, has been shown to be difficult to control, and indeed only in very recent work has any degree of regioselectivity or stereoselectivity been achieved in ring-opening of allylic epoxides by organometallic reagents.[7]

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