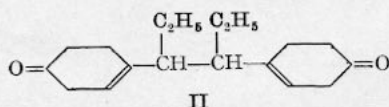
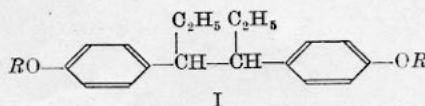


Reduction by Sodium-Ammonia Solutions

REDUCTION of methoxybenzene derivatives by the sodium-ammonia-alcohol reagent followed by acid hydrolysis leads to the formation of a number of hitherto inaccessible unsaturated ketones¹. The process fails with some compounds because of their insolubility in liquid ammonia, a typical example being hexæstrol dimethyl ether (I, $R = \text{CH}_3$). This substance has been treated under a variety of conditions and with admixed solvents, for example, ether or ethylenediamine, but so far without success.



The observation that alcohols are often readily soluble in ammonia has now led us to replace the methyl ethers of phenols by the 2-hydroxyethyl- or glyceryl-ethers. These ethers are, in fact, more readily soluble in ammonia and are easily prepared by the action of the appropriate chloro-compound on the sodium phenoxide in hot aqueous solution. The ether side-chain is lost during acid hydrolysis, so its nature does not affect the final product. A further advantage with these ethers is that any unreduced material present in the product can be removed because of its relatively higher boiling-point.

Hexæstrol (I, $R = \text{H}$) gives rise to a *bis*(2-hydroxyethyl) ether (I, $R = -\text{CH}_2\text{CH}_2\text{OH}$) which crystallizes as colourless plates from benzene, m.p. $90-91^\circ$ (found: C, 73.4; H, 7.9; $\text{C}_{22}\text{H}_{30}\text{O}_4$ requires C, 73.7; H, 8.4 per cent). This is readily reduced and gives after acid hydrolysis 3:4-di(4'-ketocyclohex-1'-enyl)hexane (II), which forms clusters of prisms from ether-light petroleum, m.p. $131-132^\circ$ (shrinks 120°) (found: C, 78.6; H, 9.9; $\text{C}_{18}\text{H}_{26}\text{O}_2$ requires C, 78.5; H,

9.5 per cent) (bis-semicarbazone m.p. 242° (decomp.)). The formulation of (II) as the $\beta\gamma$ -unsaturated ketone rests on the lack of an absorption maximum in the region 2200–2700 Å. It is being tested for possible sex-hormone activity.

The reduction of other phenols, including oestrone, and the synthesis of some natural products are being carried out.

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¹ Birch, *J. Chem. Soc.*, 593 (1946).