An Abnormal Claisen Rearrangement of 3,3-Dimethylallyl Œstrone Ether

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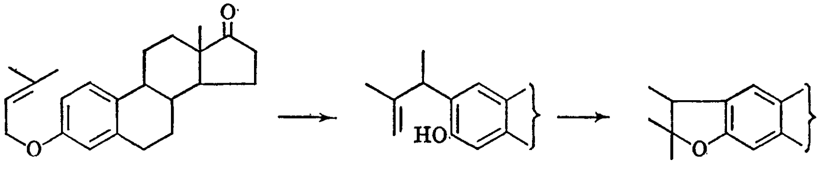
THE nature of the Claisen rearrangement has been extensively investigated,[1] yet it is difficult to predict rearrangement products from 3,3-dimethylallyl aryl ethers.[2] Thus in some cases when normal migration to the *ortho*-position is expected, ether cleavage to yield isoprene and the phenol occurs[3] and in other instances migration to the *para*-position predominates.[4]

Although the rearrangement of allyl œstrone ether gives the expected mixture of 2- and largely 4-allylœstrones,[5] rearrangement of the 3,3-dimethylallyl œstrone ether (I) (m.p. 103°, $[\alpha]_D$ 125°) in dimethylaniline or, better, in diethylaniline, did not yield any of the normal Claisen products (*e.g.*, IV). The n.m.r. spectrum of the product (II), (m.p. 202°, $[\alpha]_D$ 150°) showed that migration occurred only to the 2-position since the aromatic protons at C-1 and C-4 appeared as singlets at τ 2·95 and 3·45 and the signal due to the 3-hydroxyl group at τ 4·65 disappeared when deuterium oxide was added.

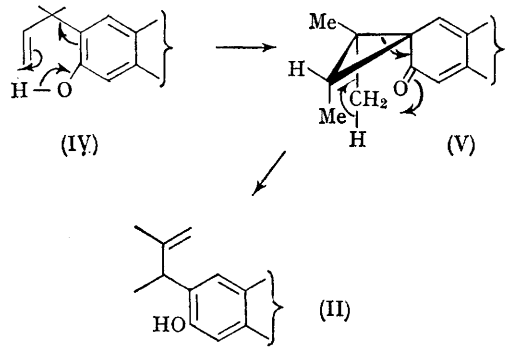
This substitution pattern was confirmed by the infrared spectrum which showed the hydroxyl group at 3400 cm.$^{-1}$, the aromatic nucleus at 1620, 1595, and 1510 cm.$^{-1}$ and the aromatic C–H out-of-plane bending frequency at 880 cm.$^{-1}$ Apart from the signals due to the steroid nucleus, the remainder of the n.m.r. spectrum was consistent with $-CHMe\cdot CMe{=}CH_2$ as the side chain at C-2, showing one methyl group as a doublet centred at τ 8·60 (3H) with the adjacent C–H as a quartet at τ 6·50 (1H), the other methyl group as a singlet at τ 8·37 (3H) and the olefinic methylene group as a broad band at τ 4·90 (2H). The structure of this abnormal Claisen rearrangement product (II) was confirmed by cyclisation in polyphosphoric acid to the furano-steroid (III), (m.p. 160°, $[\alpha]_D$ 160°) which shows the three methyl groups in the furan ring as two singlets at τ 8·73 (3H) and 8·57 (3H) due to the *gem*-dimethyl group and the methyl attached to –CH as a doublet at τ 8·79.



(I) (II) (III)

The formation of the abnormal product (II) could be explained by postulating prior formation of the normal Claisen product (IV) in the less hindered 2-position which then undergoes a further rearrangement through the intermediate spiro-dienone (V) following a mechanism postulated by Marvell *et al.*[6] shown as (IV) → (V) → (II).

However, unlike other work on abnormal Claisen rearrangements our efforts to detect the normal product (IV) were unsuccessful even when the rearrangement was attempted in different solvents. To trap the unstable 1,1-dimethylallyl-phenol intermediate (IV) the rearrangement of the ether (I) was carried out in diethylaniline containing butyric anhydride. The normal Claisen product was thus trapped as its butyric ester (IV; $CH_3\cdot CH_2\cdot CH_2\cdot CO_2$ for OH), m.p. 140—141°, $[\alpha]_D$ 115°. The n.m.r. spectrum of the phenol (IV) m.p. 162°, $[\alpha]_D$ 135° showed the 1,1-dimethylallyl side chain with the three olefinic protons as an AXY system (A, X, and Y centred at τ 3·8, 4·63, and 4·85 respectively), and the *gem*-dimethyl as a singlet at τ 8·6. The normal Claisen product (IV) rapidly isomerised to the abnormal product (II) on heating in diethylaniline, thus supporting the mechanism postulated. This mechanism can similarly account for other unexplained *ortho*-migrations of 3,3-dimethylallyl aryl ethers.[7]



(IV) (V) (II)

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