The Mechanism of Aromatization of Some Epoxyhydroxysteroids

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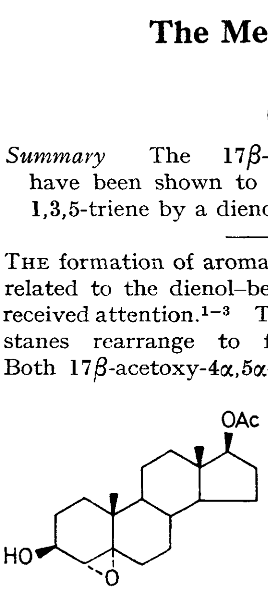
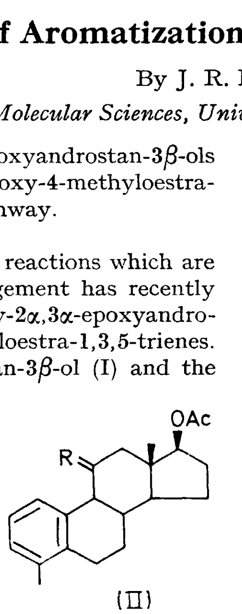
Summary The 17β-acetoxy-4,5-epoxyandrostan-3β-ols have been shown to yield 17β-acetoxy-4-methyloestra-1,3,5-triene by a dienol–benzene pathway.

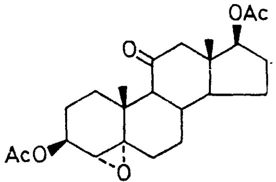
THE formation of aromatic steroids by reactions which are related to the dienol–benzene rearrangement has recently received attention.[1–3] Thus 5α-hydroxy-2α,3α-epoxyandrostanes rearrange to form 4-methyloestra-1,3,5-trienes. Both 17β-acetoxy-4α,5α-epoxyandrostan-3β-ol (I) and the corresponding 4β,5β-epoxide afford 17β-acetoxy-4-methyloestra-1,3,5-triene (II; R = H_2) as the major aromatic product on treatment with HBr in glacial acetic acid under reflux. Even 3β-acetoxy-5α,6α-epoxyandrostan-17-one affords some 4-methyloestra-1,3,5-trien-17-one under these conditions although no attempt has yet been made to optimize the reaction. On the other hand similar treatment of 3β,17β-diacetoxy-4α,5α-epoxyandrostan-11-one (III) gives only a poor yield of 17β-acetoxy-4-methyloestra-1,3,5-trien-11-one (II; R = O), the 11-oxo-group destabilizing as in the dienone–phenol reaction,[4] the formation of the spirocyclic cation.



(I)



(II)



(III)

Two pathways may be envisaged for this reaction. One, a modification of the Westphalen rearrangement, involves the methyl group migrating first to C-5 and then to C-4. The other involves a spirocyclic intermediate as in the dienol–benzene rearrangement in which it is the 9,10-bond which migrates. 17β-Acetoxy-3α-deuterio-4β,5β-epoxyandrostan-3β-ol was prepared and rearranged. This gave 1-deuterio-4-methyloestra-1,3,5-trien-17β-yl acetate which showed an n.m.r. spectrum identical to that of the aromatization product from 17β-acetoxy-3α-deuterio-3β-hydroxyandrosta-1,4-diene. In particular multiplets at τ 3·07 (1H) and 3·19 (2H) in the undeuteriated compound were replaced by a singlet at 3·19 (2H) in the deuteriated products. Had the modified Westphalen pathway been involved, then the hydroxy-epoxide would have given a 3-deuterio-4-methyl aromatic product.

The hydroxy-epoxides are readily prepared from testosterone and the sequence thus provides a simple alternative route to the oestra-1,3,5-trienes.

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[1] J. R. Hanson and T. D. Organ, *J. Chem. Soc.* (*C*), 1970, 513.
[2] J. Libman and Y. Mazur, *Chem. Comm.*, 1971, 729.
[3] J. R. Hanson, *Chem. Comm.*, 1970, 1119.
[4] D. N. Kirk and V. Petrow, *J. Chem. Soc.*, 1960, 4664.