The Mechanism of a Steroidal Aromatization Reaction

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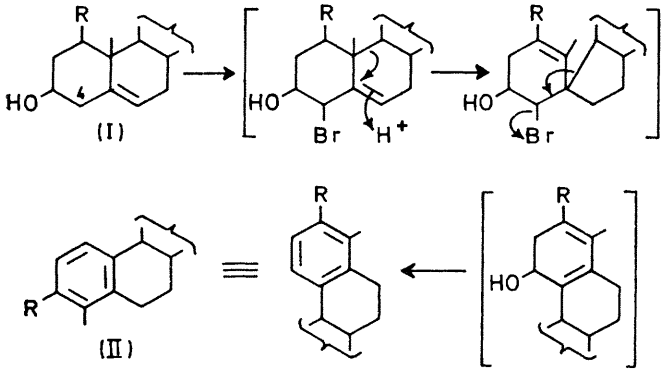
Summary The aromatization of 3β-hydroxyandrost-5-en-17-one with *NN*-dibromo-5,5-dimethylhydantoin has been shown to be of the dienol–benzene type.

WE have recently described[1] an unusual rearrangement in which 3β-hydroxyandrost-5-en-17-one (I; R = H) was converted into a mixture of 4-methyloestra-1,3,5(10)-trien-17-one (II; R = H) and androst-5-ene-3,17-dione by the



action of *NN*-dibromo-5,5-dimethylhydantoin or *N*-bromosuccinimide. Assuming that bromination is directed to C-4 by the hydroxy-group, two possible pathways exist for the rearrangement.[2] Either a Westphalen type of rearrangement may occur in which the methyl group migrates from C-10 to C-5 and thence to C-4, or the C-9 carbon may migrate in a dienol–benzene type of rearrangement as shown. There are a number of variations within each pathway depending upon the order of the various stages. However we have distinguished between the two main pathways. 3β,17β-Dihydroxy-1β-methylandrost-5-ene (I; R = Me) was prepared by deconjugation[3] and lithium aluminium hydride reduction[4] of 17β-hydroxy-1β-methylandrost-4-en-3-one.[5,6] This compound was treated with *NN*-dibromo-5-dimethylhydantoin and the crude product purified by acetylation to give the 17β-acetate of 3,4-dimethyloestra-1,3,5(10)-trien-17β-ol (II; R = Me). This compound was identical with authentic material prepared[7] from the acetate of 17β-hydroxy-4,4-dimethyl-19-norandrost-5-en-3-one and differed from the acetate of 1,4-dimethyloestra-1,3,5(10)-trien-17β-ol. The authentic sample of the latter was prepared[8] by the action of methylmagnesium iodide on 17β-hydroxyandrosta-1,4-dien-3-one. Since the two methyl groups remain adjacent to one another, the reaction must follow the dienol–benzene pathway.

In support of the intervention of a 4-bromo-compound, 4β-bromo-5α,6α-epoxyandrost-2-en-17-one underwent aromatization when treated with a zinc–copper couple in acetic acid to afford 4-methyloestra-1,3,5(10)-trien-17-one.

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[1] J. R. Hanson and T. D. Organ, *J. Chem. Soc.* (*C*), 1970, 513.
[2] D. N. Kirk and M. P. Hartshorn, "Steroid Reaction Mechanisms," Elsevier, London, 1968, pp. 277, 291—293.
[3] H. J. Ringold and S. K. Malhotra, *Tetrahedron Letters*, 1962, 669.
[4] R. Beugelmans, *Bull. Soc. chim. France*, 1967, 244.
[5] H. Mori, *Chem. and Pharm. Bull.* (*Japan*), 1962, **10**, 386.
[6] W. J. Wechter, G. Slomp, F. A. MacKellar, R. Wiechert, and U. Kerb, *Tetrahedron*, 1965, **21**, 1625.
[7] P. Bey, F. Lederer, and G. Ourisson, *Chem. and Pharm. Bull.* (*Japan*), 1965, **13**, 1140.
[8] H. Dannenberg and H. G. Neumann, *Annalen*, 1961, **646**, 148.