

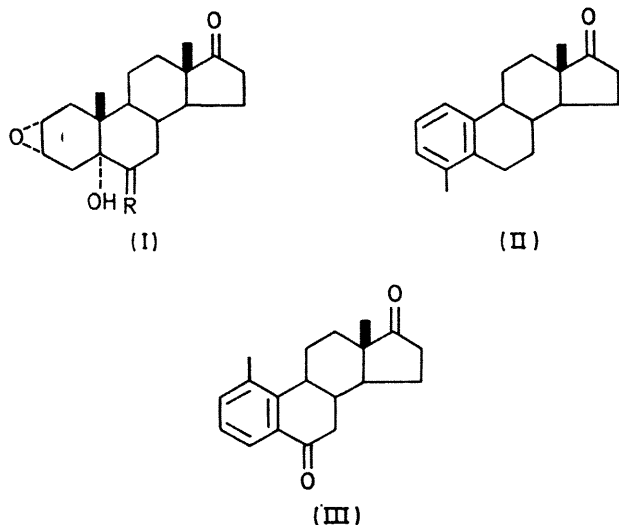
Novel Steroidal Aromatization Reactions

By J. R. HANSON

(The School of Molecular Sciences, University of Sussex, Brighton, Sussex BN1 9QJ)

Summary $2\alpha,3\alpha$ -Epoxy- 5α -hydroxyandrost-17-one undergoes rearrangement to form 4-methyloestra-1,3,5(10)-trien-17-one whilst the corresponding 6-ketone affords 1-methyloestra-1,3,5(10)-triene-6,17-dione on treatment with HBr in glacial acetic acid.

REARRANGEMENTS leading to aromatization require the juxtaposition of two double-bond equivalents and a carbonium ion source. The cationic spiro-diene intermediate



which is characteristic of the dienol-benzene rearrangement of steroids,¹ may be derived in theory from a range of compounds, for example ring-A hydroxy-epoxides. On the

other hand the formation of a C-5 carbonium ion implicit in such reactions, can also lead to products typical of Westphalen and backbone rearrangements.

$2\alpha,3\alpha$ -Epoxy- 5α -hydroxyandrost-17-one (I; R = H)² satisfies the first proposition and yet contains a 5α -hydroxy-group. On treatment with HBr in glacial acetic acid, it gave 4-methyloestra-1,3,5(10)-trien-17-one (II)³ as the major isolable product. Under the same conditions, 17β -acetoxy- $4\alpha,5\alpha$ -epoxy- 3β -hydroxyandrostane gave the corresponding aromatic 17β -acetate again as the major product. Similarly 4-methyloestra-1,3,5(10)-trien-17-one (II) was obtained from reaction of $5\alpha,6\alpha$ -epoxyandrost-2-en-17-one. On the other hand treatment of $2\alpha,3\alpha$ -epoxy- 5α -hydroxyandrost-6,17-dione (I; R = O) and its 17β -acetoxy-compound with HBr and glacial acetic acid gave 1-methyloestra-1,3,5(10)-triene-6,17-dione (III) and the 17β -acetoxy-compound and not the 4-methyl-steroid. Authentic samples of both 1-methyloestra-1,3,5(10)-triene-6,17-dione and 4-methyloestra-1,3,5(10)-trien-17-one were prepared by the chromium trioxide oxidation of 1-methyl- and 4-methyl-oestra-1,3,5(10)-trien-17-one. Similar aromatic compounds have also been obtained on treatment of Δ^2 -4-bromo- 5α -hydroxy-steroids with HBr in glacial acetic acid.

I therefore conclude that the dienol-benzene rearrangement is one example of a wider class of reaction, some other examples of which are presented above. Furthermore the presence of a 6-carbonyl function serves, as in the dienone-phenol rearrangement, to destabilize a C-5 carbonium ion and prevents the formation of spirocyclic intermediates. This leads to aromatization *via* the alternative pathway of a C-10 \rightarrow C-1 methyl migration.

(Received, July 12th, 1971: Com. 1194.)

¹ See D. N. Kirk and M. P. Hartshorn, "Steroid Reaction Mechanisms," Elsevier, London, 1968.

² The preparation of the hydroxy-epoxides followed standard procedures which will be described in the full paper.

³ J. R. Hanson and T. D. Organ, *J. Chem. Soc. (C)*, 1970, 513.