

Formation of Oestratrienes from Ring B Hydroxy-epoxides

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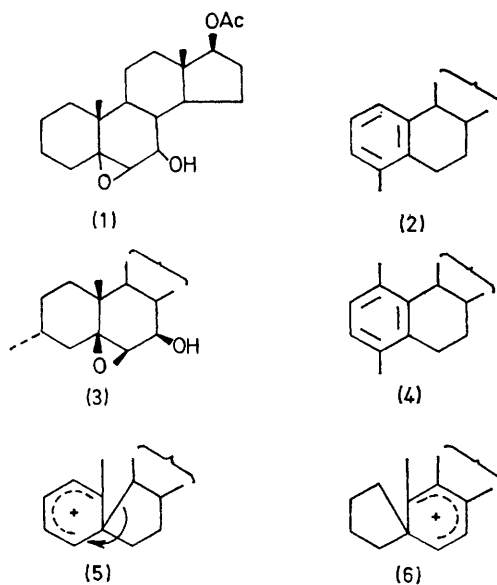
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Summary Treatment of 5,6-epoxy-7-hydroxyandrostanes with hydrogen bromide in acetic acid unexpectedly affords 4-methyloestratrienes *via* a spiranic intermediate. We have shown¹ that steroids containing hydroxy-epoxides on ring A undergo aromatization with rearrangement *via* a spiranic intermediate to form 4-methyloestratrienes. We

expected that ring B hydroxy-epoxides would form anthra-steroids by an analogous spiro-diene pathway.² Treatment of 17 β -acetoxy-5 α ,6 α -epoxy-7 α -hydroxyandrostane, 17 β -acetoxy-5 β ,6 β -epoxy-7 β -hydroxyandrostane and 17 β -acetoxy-5 α ,6 α -epoxy-7 β -hydroxyandrostane (1) with hydrobromic acid in refluxing glacial acetic acid gave (2) (30–40% yield) and the corresponding 17-bromo-steroid (4–5% yield) as the aromatic products. Under similar conditions 17 β -acetoxy-4 β ,5 β -epoxy-6 β -hydroxyandrostane gave (2) (13%), the 17-bromo-4-methyloestratriene (4%) and 17 β -acetoxyandrost-4-en-6-one (4%), *i.e.* ring A aromatic products.

In order to show that the reaction followed a spiro-diene pathway, (3) was treated with hydrobromic acid in glacial acetic acid. The aromatic product was (4)³ in which the methyl groups have retained their 1,4-relationship characteristic of a skeletal rather than a methyl group, rearrangement.

These reactions are particularly unexpected for a steroid possessing a 5 β -epoxide which is suitably oriented for migration of the C-1–C-10 bond, and the reactions contrast with the report of Libman and Mazur⁴ on anthrasteroid formation from bromo-steroids. A possible stereochemical explanation for the formation of ring A aromatic products lies in the different stereochemical interactions in the transition states. In the spiro-diene carbonium ion (5) leading to the aromatization of ring A there is release of the C-1–C-11 compression. On the other hand in the spiro-diene carbonium ion (6) for aromatization of ring B, as C-10 changes from an sp³ to an sp² hybridization, interactions are introduced between the



C-19 methyl group and C-11 and subsequently the new C-1.

The synthesis of the substrates will be reported in our full paper.

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¹ D. Baldwin and J. R. Hanson, *J.C.S. Perkin I*, 1972, 1889.

² D. N. Kirk and M. P. Hartshorn, 'Steroid Reaction Mechanisms', Elsevier, Amsterdam, 1968, p. 288–290.

³ H. Dannenberg and H. G. Neumann, *Annalen*, 1961, **646**, 148.

⁴ J. Libman and Y. Mazur, *Chem. Comm.*, 1971, 730.