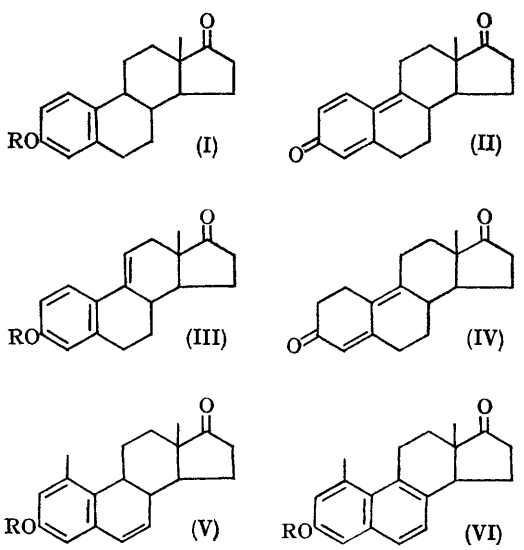
Dehydrogenation of Steroidal Phenols *via* Quinone Methides

By W. BROWN, J. W. A. FINDLAY, and A. B. TURNER*
(*Chemistry Department, University of Aberdeen, Scotland*)

2,3-DICHLORO-5,6-DICYANOBENZOQUINONE (DDQ) is a powerful oxidising agent for phenols.[1] In most of the recorded cases the major products are dimers resulting from C–C or C–O coupling. We now report examples of phenol oxidation in which simple dehydrogenation occurs.

The oxidation of oestrone (I; R = H) has been investigated as a possible route to the quinone methide (II). The phenol is rapidly oxidised by DDQ at room temperature in dioxan to 9(11)-dehydro-oestrone (III; R = H) in 67% yield, thereby providing a convenient direct route to this compound. The same product was obtained when the reaction was carried out in methanol.[2] It thus appears that, even under these mild conditions, addition of the alcohol competes unfavourably with tautomerization of the quinone methide (II), reflecting the extreme instability of this chromophore in a rigid ring system.[3] In Becker's oxidations,[2] the simple quinone methide intermediates, being unable to tautomerize to phenols,



suffer nucleophilic attack by methanol in order to attain aromatic stability. We have obtained some confirmation of these conclusions from DDQ dehydrogenation of oestra-4,9-diene-3,17-dione (IV). This requires heating under reflux with dioxan, which also leads to formation of the phenol (III; R = H).[4] As the ketone (IV) is stable in dioxan under reflux, the high-potential quinone effects 1,2-dehydrogenation[5] to give the intermediate (II). This quinone methide is probably also involved in the high-temperature dehydrochlorination of 10β-chloro-oestra-1,4-dien-3-one, which again leads to the phenol (III; R = H).[6]

Oestrone methyl ether (I; R = Me) also reacts rapidly with DDQ at room temperature, giving the 9(11)-dehydro-derivative (III; R = Me) in 70% yield.[7] The corresponding acetate (I; R = Ac) reacts very slowly at room temperature.

This reaction has been extended to the preparation of A/B-aromatic steroids from styrenes of type (V) under mild conditions. In this series both the free phenol (V; R = H) and its acetate (V; R = Ac) are rapidly oxidised by DDQ at room temperature, giving the naphthalenes (VI; R = H and Ac), respectively, in 80—85% yields. We are investigating the possibility that these reactions can be rationalized by mechanisms involving overall hydride abstraction from different positions in the steroid nucleus.

(*Received, November* 13*th*, 1967; *Com.* 1223.)

[1] D. Walker and J. D. Hiebert, *Chem. Rev.*, 1967, **67**, 153.
[2] H.-D. Becker, *J. Org. Chem.*, 1965, **30**, 982.
[3] A. B. Turner, *Quart. Rev.*, 1964, **18**, 347; *Fortschr. Chem. Org. Naturstoffe*, 1966, **24**, 288.
[4] *cf.*, M. Heller, R. H. Lenhard, and S. Bernstein, *Steroids*, 1967, **10**, 211.
[5] A. B. Turner and H. J. Ringold, *J. Chem. Soc.* (*C*), 1967, 1720.
[6] J. S. Mills, J. Barrera, E. Olivares, and H. Garcia, *J. Amer. Chem. Soc.*, 1960, **82**, 5882.
[7] *cf.*, A. D. Cross, H. Carpio, and P. Crabbe, *J. Chem. Soc.*, 1963, 5539; S. G. Boots and W. S. Johnson, *J. Org. Chem.*, 1966, **31**, 1285.