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The Oxidation of Some Steroidal Dienes by Potassium Permanganate:Copper Sulfate

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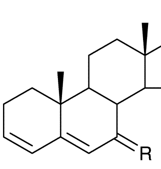
Oxidation of androsta-3,5- and 4,6-dienes by the biphasic system potassium permanganate:copper sulfate afforded the 3α,4α-epoxy-5α-hydroxy-6-ketone and the 5α,6α-epoxy-4β-hydroxy-7-ketone respectively as the major products whilst the androsta-3,5-dien-7-one and androsta-4,6-dien-3-one gave the 3α,4α- and 6α,7α-epoxides as the major products.

The products of oxidation of steroidal alkenes by the biphasic system, potassium permanganate:copper sulfate differ from those of homogeneous oxidation using potassium permanganate.[1–6] Other metal sulfates such as ferric sulfate have also been used in the biphasic system.[7] Some relatively inaccessible β-oriented epoxides, rather than vicinal diols, have been obtained from steroidal alkenes using these systems. We have rationalized the stereochemical results in terms of an initial pseudo-axial attack by the electron-deficient manganese on the alkene followed by the formation and subsequent decomposition of a manganate to produce the epoxide, the latter step being facilitated by the metal sulfate.[5,6] However this view has recently been challenged[8] with the suggestion that the stereochemistry is determined by the initial formation of a π-complex with the copper on the less-hindered face of the alkene directing the subsequent attack of the permanganate to the more hindered face. If our reasoning were to be applied to the oxidation of a diene, it would suggest that the initial attack of the manganese would take place on the pseudo-axial terminal position of the diene to allow any carbocationic character to be stabilized by the adjacent double bond. The stereochemistry of the products would be determined by the orientation of this position. In the case of a dienone, the presence of the ketone would direct the initial attack to the γδ-double bond. We have therefore examined the oxidation of two heteroannular dienes, androsta-3,5-dien-17-one **1**[9] and 17β-acetoxyandrosta-4,6-diene **3**[10] together with their related C-7 and C-3 ketones, **2**[11], **4**[12] and **5**[12] by this system. The results are given in Table 1.

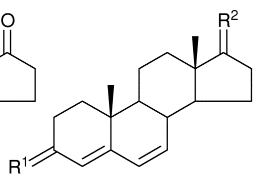
Table 1 Products of potassium permanganate oxidation of dienes

Substrate	Product	% Yield
Androsta-3,5-diene-17-one **1**	**6**	42
	7	19
17β-Acetoxyandrosta-4,6-diene **3**	**8**	3
	9	5
	10	12
	11	39
17β-Acetoxyandrosta-4,6-dien-3-one **4**	**12**	25
	14	12
Androsta-4,6-diene-3,17-dione **5**	**13**	33
	15	19
Androsta-3,5-diene-7,17-dione **2**	**16**	30
	17	20

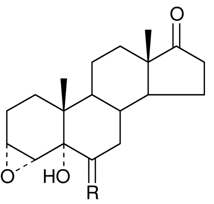
The structures of the products were established by a combination of spectroscopic and crystallographic methods. The formation of these oxidation products (Figs. 1–3) from the 3,5- and 4,6-dienes may be rationalized in terms of the formation of diepoxides based on the pseudo-axial attack of the reagent at C-3α and C-6β in the case of the 3,5-diene and C-4β and C-7α in the case of the 4,6-diene. The diepoxidation may be followed by partial hydrolysis to afford the trans diols or with oxidation, the α-ketols. The hydroxy-



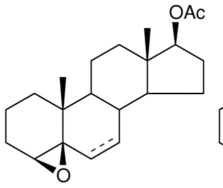
1 R = H$_2$
2 R = O



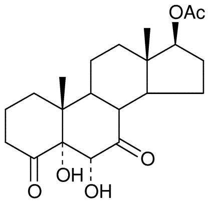
3 R^1 = H$_2$, R^2 = α-H, β-OAc
4 R^1 = O, R^2 = α-H, β-OAc
5 R^1 = R^2 = O



6 R = O
7 R = α-H, β-OH



8 6,7-ene
9 6α, 7α-epoxide



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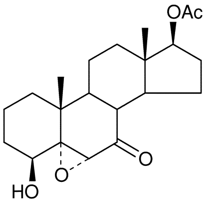

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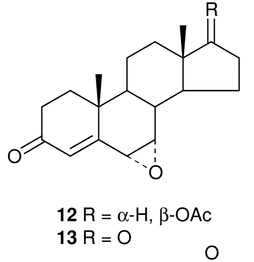
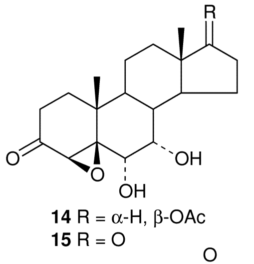
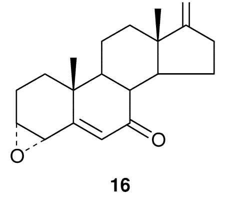


12 R = α-H, β-OAc
13 R = O



14 R = α-H, β-OAc
15 R = O



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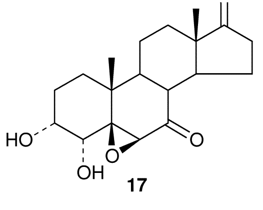

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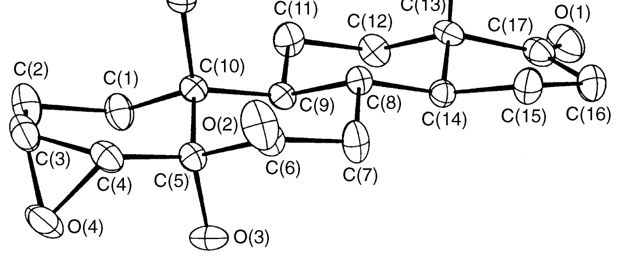

Fig. 1 X-Ray crystal structure of compound **6**

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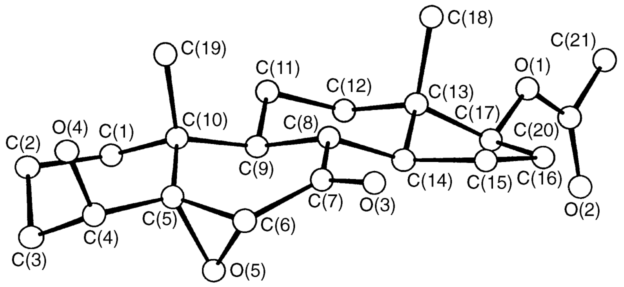

Fig. 2 X-Ray crystal structure of compound **11**

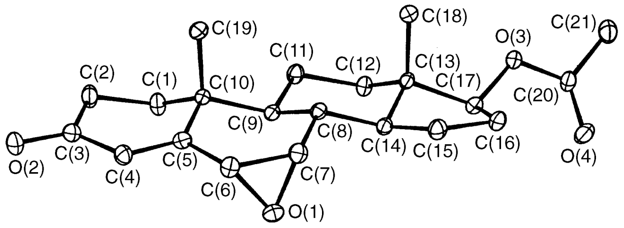

Fig. 3 X-Ray crystal structure of compound **12**

epoxide **11** may be formed *via* **9** by an oxidative hydrolysis and Payne rearrangement.[17] As anticipated, oxidation of the dienones takes place at the $\gamma\delta$-double bond first and follows the same pattern. If the stereochemistry of the products were to be determined by the initial formation of a copper π-complex on the less-hindered face of the alkene directing attack of the permanganate to the more hindered face, it would be difficult to explain the formation of the $3\alpha,4\alpha$- and $6\alpha,7\alpha$-epoxides and products derived from them.

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Techniques used: ^{1}H NMR, IR, X-ray crystallography

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Appendix: Crystallographic data for compounds **6**, **11** and **12**

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