The Tetracyanoethylene Catalysed Methanolysis of Androstane 2,3-Epoxides

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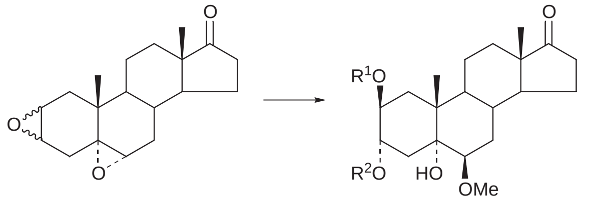
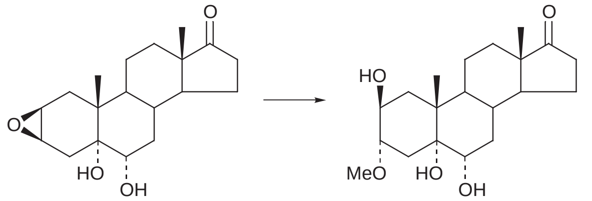
Unlike other acidic systems, the tetracyanoethylene catalysed methanolysis of androstane 2,3-epoxides proceeds normally without giving products arising from the transannular participation of a 5α,6α-epoxide, a 5α-hydroxy group or a 5(6)-ene.

Tetracyanoethylene (TCNE) is a mild π-acid catalyst for the cleavage of epoxides.[1] Although the methanolysis of isolated cyclic epoxides catalysed by TCNE proceeded with a normal *trans*-diaxial stereochemistry,[2] neighbouring group effects in vicinal diepoxides[3] and hydroxyepoxides[4] have led to the formation of abnormal products. In the sesquiterpenoid caryophyllene series, the transannular participation of an alkene in the methanolysis of an epoxide led to the formation of cyclic products.[5] The transannular participation of hydroxy groups in the cleavage of steroidal ring A epoxides under acid-catalysed conditions, has been observed[6] and in particular, an androstane 5α-hydroxy-2α,3α-epoxide has been reported[7] to give a 2α,5α-oxide *via* a 2β,3α-bromohydrin. Under more vigorous conditions aromatic products are formed.[8] Here, we report investigations directed at examining the possible participation of a 5α,6α-epoxide, a 5α-hydroxy group and a 5(6)-ene in the TCNE catalysed methanolysis of androstane-2,3-epoxides.



3 2α, 3α-epoxide
5 2β, 3β-epoxide

4 R^1 = Me, R^2 = H
6 R^1 = H, R^2 = Me



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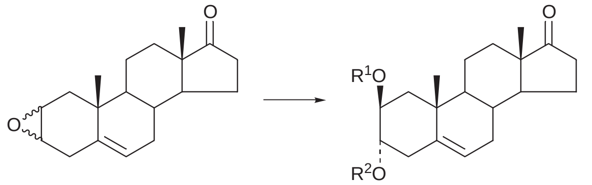

9 2α, 3α-epoxide
11 2β, 3β-epoxide

10 R^1 = Me, R^2 = H
12 R^1 = H, R^2 = Me

Table 1 Methanolysis of androstane-2,3-epoxides

Substrate	Product	Yield(%)
2α,3α;5α,6α-Diepoxyandrostan-17-one	3α,5α-Dihydroxy-2β,6β-dimethoxyandrostan-17-one	70
2β,3β;5α,6α-Diepoxyandrostan-17-one	2β,5α-Dihydroxy-3α,6β-dimethoxyandrostan-17-one	78
5α,6α-Dihydroxy-2β,3β-epoxyandrostan-17-one	3α-Methoxy-2β,5α,6α-trihydroxyandrostan-17-one	82
2α,3α-Epoxyandrost-5-en-17-one	3α-Hydroxy-2β-methoxyandrost-5-en-17-one	75
2β,3β-Epoxyandrost-5-en-17-one	2β-Hydroxy-3α-methoxyandrost-5-en-17-one	77

Treatment of 2α,3α;5α,6α- and 2β,3β;5α,6α-diepoxyandrostan-17-one, **3** and **5**,[9] 5α,6α-dihydroxy-2β,-3β-epoxyandrostan-17-one **7** and 2α,3α- and 2β,3β-epoxyandrost-5-en-17-one, **9** and **11**, with a catalytic amount of TCNE in methanol gave the products of simple methanolysis of the epoxides, **4**, **6**, **8**, **10** and **12**, respectively (Table 1).

The structure and stereochemistry of the products were established by a combination of ^{1}H NMR nuclear Overhauser effect and spin decoupling experiments. The strategy involved locating the H-4 proton resonances, the protons coupled to them and the NOE enhancements that they received.

The products obtained from these experiments unlike those from more vigorous acid-catalysed reactions, do not show any evidence for the participation of a 5α-substituent or a 5(6)-double bond in the TCNE catalysed methanolysis of androstane-2,3-epoxides.

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Techniques used: IR, ^{1}H NMR, chromatography.

References: 11

Tables: 2

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