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Neighbouring Group Participation in the Tetracyanoethylene Catalysed Methanolysis of some Steroidal Hydroxy-epoxides

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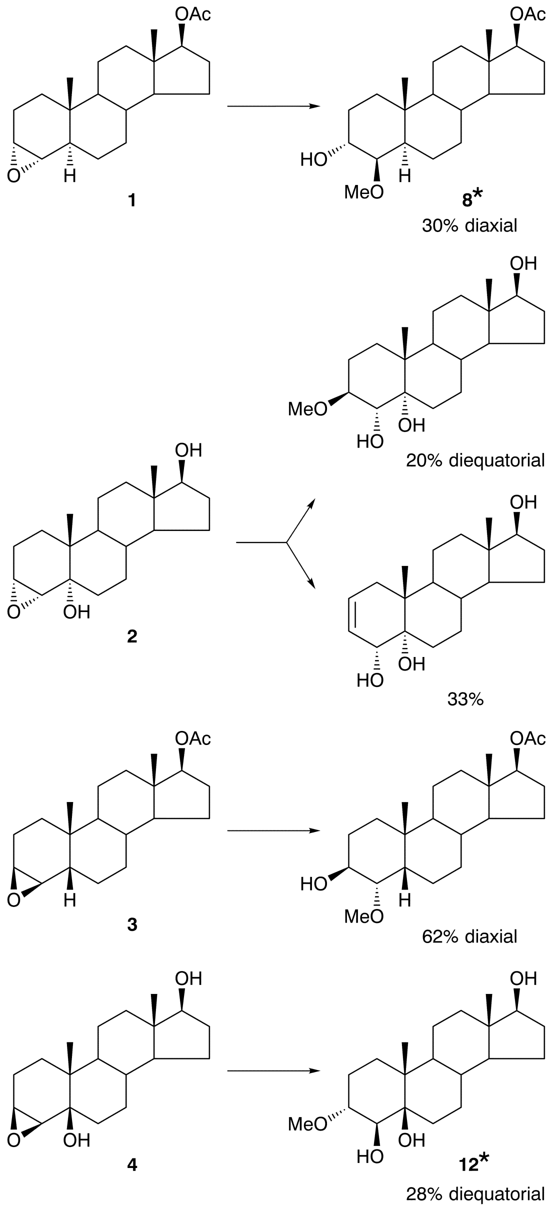
An adjacent *cis* 5-hydroxy group changes the regio- and stereo-chemistry of the TCNE-catalysed methanolysis of steroidal 3,4-epoxides from *trans* diaxial to diequatorial cleavage; the stereochemistry of the two products is established by X-ray crystallography.



* Structures confirmed by X-ray crystallography

Scheme Methanolysis of expoxides

Tetracyanoethylene has attracted interest recently as a mild catalyst for the hydrolysis of epoxides.[1,2] It may exert its catalysis through a single electron transfer mechanism. Methanolysis of the epimeric steroidal 4,5- and 5,6-epoxides catalysed by TCNE has a regiochemistry dominated by the *trans*-anti-periplanar relationship between the resultant alkoxy and hydroxy groups.[3] An adjacent hydroxy group modifies the regiochemistry of the acid-catalysed cleavage of epoxides and in the case of the reaction of 3α,4α-epoxy-5α-hydroxy- and 3β,4β-epoxy-5β-hydroxycholestanes with hydrogen bromide, this leads to diequatorial products.[5] Here we compare the TCNE catalysed methanolysis of 17β-acetoxy-3α,4α-epoxy-5α-hydroxyandrostane (**2**) and 17β-acetoxy-3β,4β-epoxy-5β-hydroxyandrostane (**4**) with their corresponding 5-desoxy analogues (**1**) and (**3**). The results are shown in the scheme.

The methanolysis reactions of the hydroxy-epoxides were slower than those of the unsubstituted epoxides allowing hydrolysis of the 17β-acetate to take place. There was a complete change to diequatorial opening in the presence of the neighbouring hydroxy group. The results may be interpreted in terms of hydrogen bonding between the hydroxy group and the cyano group of the reagent orienting the tetracyanoethylene to favour the diequatorial opening.

Crystallographic Data and Structure Determination.—Compound **8**. $C_{22}H_{36}O_4$, M_r 364.5, monoclinic, space group $P2_1$ (no. 4), $a = 7.590(4)$, $b = 25.326(9)$, $c = 10.673(7)$ Å, $\alpha = \gamma = 90°$, $\beta = 91.97(5)°$, $V = 2050(2)$ Å^3, $Z = 4$, $D_{calc.} = 1.18$ g cm^{-3}, $F(000)$ 800, monochromated MoKα radiation $\lambda = 0.71073$ Å, $\mu = 0.079$ mm^{-1}. Data were collected using a crystal of size *ca.* $0.4 \times 0.4 \times 0.2$ mm on an Enraf-Nonius CAD4 diffractometer. A total of 3956 reflections were collected for $2 < \theta < 25°$ and $-1 < h < 9$, $0 < k < 30$, $-12 < l < 12$. 2421 Reflections with $I > 2\sigma(I)$ were used in the refinement. There was no crystal decay and no absorption correction was applied.

The structure was solved by direct methods using SHELXS-86[11] and SHELXL-93.[12] The non-hydrogen atoms were refined anisotropically by full matrix least squares. Hydrogen atoms were included in the riding mode with $U_{iso}(H) = 1.2\ U_{eq}(C)$ or $1.5\ U_{eq}(C)$ for methyl groups except for hydrogen atoms of hydroxy groups which were located on a difference map and freely refined isotropically. The final R indices were: $R_1 = 0.052$, w$R_2 = 0.134$ and R indices (all data) $R_1 = 0.090$, w$R_2 = 0.165$. The goodness of fit on F^2 was 0.936 and the maximum shift/e.s.d. was 0.04. There were two independent molecules in the asymmetric unit.

Compound **12**. $C_{20}H_{38}O_6$, M_r 374.5, orthorhombic, space group $P2_12_12_1$ (no. 19), $a = 6.763(2)$, $b = 12.349(4)$, $c = 24.493(8)$ Å, $\alpha = \beta = \gamma = 90°$, $V = 2045(11)$ Å^3, $Z = 4$, $D_{calc.} = 1.22$ g cm^{-3}, $F(000)$ 824, monochromated MoKα radiation $\lambda = 0.71073$ Å, $\mu = 0.09$ mm^{-1}. Data were collected using a crystal of size ca. $0.4 \times 0.4 \times 0.3$ mm on an Enraf-Nonius CAD4 diffractometer. A total of 2083 reflections were collected for $2 < \theta < 25°$ and $0 < h < 8$, $0 < k < 14$, $0 < l < 29$. 1691 Reflections with $I > 2\sigma(I)$ were used in the

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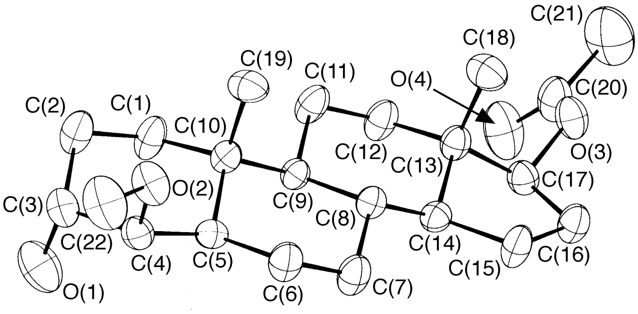

Fig. 1 X-Ray crystal structure of compound **8**

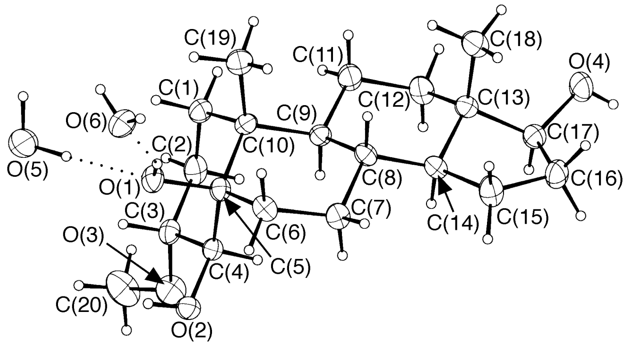

Fig. 2 X-Ray crystal structure of compound **12**

refinement. There was no crystal decay and no absorption correction was applied.

The structure was solved by direct methods using SHELXS-86[11] and SHELXL-93.[12] The non-hydrogen atoms were refined anisotropically by full matrix least squares. Hydrogen atoms were included in the riding mode with $U_{\mathrm{iso}}(\mathrm{H}) = 1.2\,U_{\mathrm{eq}}(\mathrm{C})$ or $1.5\,U_{\mathrm{eq}}(\mathrm{C})$ for methyl groups except for hydrogen atoms of hydroxy groups and water molecules which were located on a difference map and freely refined isotropically. The final R indices were: $R_1 = 0.042$, $wR_2 = 0.097$ and R indices (all data) $R_1 = 0.057$, $wR_2 = 0.110$. The goodness of fit on F^2 was 0.962 and the maximum shift/e.s.d. was 0.001.

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

References: 12

Appendix: Crystal data for **8** and **12**

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