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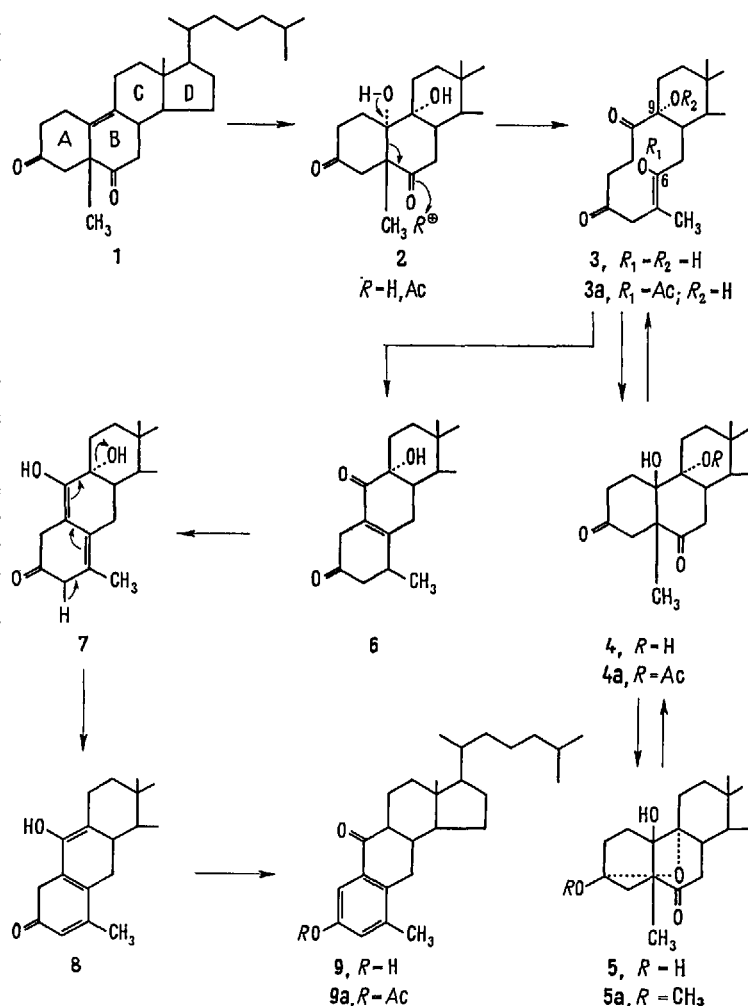
Retroaldol Transformations in the Westphalen Diol Series

Studies on the hydroxylation of the Westphalen diketone **1** have revealed a rearrangement sequence initiated by a retroaldolization process leading to what is in all probability the anthrasteroid **9**. Hydroxylation of **1**¹ with osmium tetroxide afforded the *cis* α -diol **2** (A/B *trans*), m.p. 172–174°, $\lambda_{\max}^{\text{Chf}}$ 2.9–3.0 μ (OH), 5.86 μ (C=O) (Found: C, 74.97; H, 10.47. Calc for C₂₇H₄₄O₄: C, 74.96; H, 10.25), which by its very nature is constrained in a B-ring boat conformation. The latter fact doubtlessly contributes to the ease of retroaldol isomerization of **2** in the presence of warm alkali to give the more stable isomer **4** (A/B *cis*) isolated as the transannular oxide tautomer **5**, m.p. 231–232°, $\lambda_{\max}^{\text{Chf}}$ 2.7, 2.85 μ (OH), 5.84 μ (C=O), 9.75 μ (C–O–C) (Found: C, 74.96; H, 10.41. Calc for C₂₇H₄₄O₄: C, 74.96; H, 10.25). On the other hand, acetylation of the *cis* α -diol **2** with acetic anhydride in hot pyridine appears to intercept **4** as its 9-acetate **4a**, m.p. 160–161°, $\lambda_{\max}^{\text{Chf}}$ 2.76 μ (OH), 5.84 μ (C=O), 5.73 and 7.95–8.0 μ (OAc) (Found: C, 73.25; H, 9.50. Calc for C₂₉H₄₆O₅: C, 73.30; H, 9.77). The formation of **4a** apparently occurs in virtue of transannular acyl transfer (C₆–O \rightarrow C₉–O) in the dealdolized intermediate **3** probably present initially as its enol acetate (**3a**). This acetate derivative is different from the non-crystalline product derived from acetylation of **5**. Treatment of **4a** with hydrogen chloride in aqueous acetone at room temperature readily converts it to **5**; under these same conditions the *cis* α -diol, **2**, is unaffected. Characteristic of hemiketal groupings, the isomer **5** readily provides a methyl ether **5a** with methanolic hydrogen chloride, m.p. 127–128° (Found: C, 75.32; H, 10.16; CH₃O, 7.21. Calc for C₂₈H₄₆O₄: C, 75.28; H, 10.38; CH₃O, 6.95). This methyl ether exchanges two hydrogen atoms for deuterium (Found, 1.95) in alkaline deuterium butoxide solution thereby providing additional confirmation of structure **5a**.

Under more drastic alkaline conditions (hot 30% methanolic potassium hydroxide for 18 h) **5** undergoes further rearrangement, ostensibly by way of the same dealdolized intermediate **3** to give the phenolic ketone **9** (compare **5** \rightarrow **9**), m.p. 206–207°, $\lambda_{\max}^{\text{CH}_2\text{OH}}$ 258 m μ ($\epsilon = 8,140$) and 324 m μ ($\epsilon = 2,760$); $\lambda_{\max}^{\text{Chf}}$ 2.78 and 3.0 μ (OH), 5.98 μ (ar-conj. C=O), 6.18 μ (C=C) (Found: C, 81.75; H, 10.16); Acetate derivative **9a**; m.p. 133–134° (Found: C, 79.19; H, 9.54. Calc for C₂₉H₄₂O₃: C, 79.41; H, 9.65). The UV spectrum of the phenolic ketone **9** is essentially identical with that of 6-keto estrone. The N.M.R. spectrum of **9** confirms this structure as a phenol ($\tau = 3.45$) having an aromatic methyl group ($\tau = 7.74$) and bearing two *meta* disposed hydrogens ($\tau = 2.62$ and 3.05)².

Zusammenfassung. Durch Behandlung mit Kalilauge erleidet 5 β -methyl-19-norcholestan-9 α ,10 α -diol-3,6-dione eine Retroaldolisomerisierung unter Bildung des 10 β -Hy-

droxy-Isomers. Letzteres wurde als Hemiketalderivat isoliert. Bei drastischer Behandlung mit Alkali gehen beide Isomere in ein Anthrasteroid über.



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¹ First prepared by V. PETROW, O. ROSENHEIM, and W. W. STARLING, J. chem. Soc. 671 (1938).

² The nuclear magnetic spectrum was carried out with a 60 megacycle Varian Model 4300-B spectrometer with benzene as external reference and deuteriochloroform as solvent. Resonances are reported as shielding value numbers (τ). The authors are indebted to Dr. N. R. TRENNER and Mr. B. ARISON for the determination and interpretation of this spectrum.