

CYCLOPROPANE RING FORMATION IN THE DEAMINATION OF 18-AMINOSTEROIDS

J. Hora, V. Černý and F. Šorm

Institute of Organic Chemistry and Biochemistry

Czechoslovak Academy of Science, Prague, Czechoslovakia

(Received 27 April 1962)

RECENTLY, it has been found in this laboratory that deamination of 18-amino-5 α -pregnane-3 β ,20 ζ -diol (I) leads to a compound C₂₁H₃₄O₂ (IIa).¹ Similarly, deamination of N-desmethylconan-5,N(20)-dien-3 β -ol (III) affords a product C₂₁H₃₀O₂ (IV) of the same type.² The composition of these substances indicated that the reaction involves a Demyanov rearrangement.¹

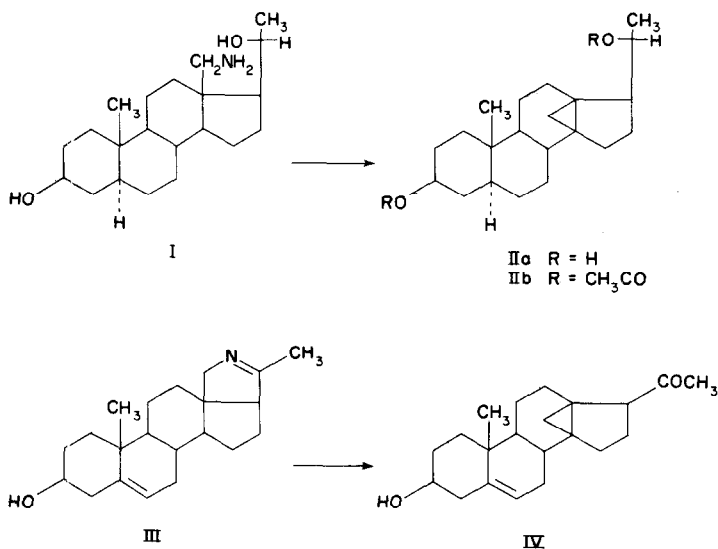
We have now proved that the reaction proceeds under formation of a cyclopropane ring. The compound IIb does not contain a double bond; it is resistant towards osmium tetroxide, perbenzoic acid and hydrogenation. The presence of a double bond could not be proved in the 190-205 μ region of the ultra-violet spectrum. A maximum at 3050 cm⁻¹ in the infrared spectrum indicated the presence of a cyclopropane ring. The NMR spectrum contains doublets at 9.42 τ and 9.95 τ characteristic for a cyclopropane ring. On treatment with hydrogen chloride in chloroform solution, the diacetate IIb isomerizes to 3 β ,20 β -diacetoxo-5 α -pregn-14-ene (V; m.p. 150-151 $^{\circ}$, $[\alpha]_D^{20}$ +42 $^{\circ}$; Found: C, 74.58; H, 9.59. C₂₅H₃₈O₄ requires: C, 74.59; H, 9.52) which on hydrolysis and subsequent oxidation affords the known 5 α -pregn-14-en-3,20-dione (VI; m.p. 184-186 $^{\circ}$, $[\alpha]_D^{20}$ +94 $^{\circ}$; Found: C, 80.17; H, 9.71. C₂₁H₃₀O₂ requires: C, 80.21; H, 9.62. The literature³ reports m.p.

¹ V. Černý and F. Šorm, Coll. Czech. Chem. Comm. **25**, 2841 (1960).

² J. Hora and V. Černý, Coll. Czech. Chem. Comm. **26**, 2217 (1961).

³ H. Heusser, M. Roth, O. Rohr and R. Anliker, Helv. Chim. Acta **38**, 1178 (1955).

186-187°, $[\alpha]_D^{20} +77^\circ$; the infra-red spectrum was identical with that of the authentic sample). On hydrogenation, the unsaturated diacetate V yields the known $3\beta,20\beta$ -diacetoxy-5 α -pregnane (VII; m.p. 142-143°, $[\alpha]_D^{20} +25^\circ$; Found: C, 74.09; H, 9.94. $C_{25}H_{40}O_4$ requires: C, 74.21; H, 9.97. The literature⁴ reports m.p. 141-142°, $[\alpha]_D^{20} +22^\circ$; the substance melted undepressed on



admixture of the authentic sample, the infra-red spectra were identical). In view of the formation of VII, the configuration of the hydroxyl group in I and II must be 20 β .

From the above facts the structure of 14 $\beta,18$ -cyclo-5 α -pregnane-3 $\beta,20\beta$ -diol follows unambiguously for the deamination product IIa. The deamination product of the pyrroline III has already been correlated² with substance II and therefore has the structure of 14 $\beta,18$ -cyclopregn-5-en-3 β -ol-20-one (IV).

The deamination of steroid pyrrolines of this type has already been used for the preparation of 18-hydroxy-20-oxo-pregnane derivatives;^{2,5}

⁴ W. Klyne and D.H.R. Barton, *J. Amer. Chem. Soc.* **71**, 1500 (1949).

⁵ F. Buzetti, W. Wicki, J. Kalvoda and O. Jeger, *Helv. Chim. Acta* **42**, 388 (1959).

in this reaction, however, the latter compounds are formed as by-products only, whereas the 14 β ,18-cyclopregnane derivatives always predominate in the reaction mixture.² The formation of cyclopropane derivatives as products of the deamination of primary amines has been observed only recently.⁶ The comparatively high yields achieved with 18-substituted steroids^{1,2} indicate that the steric arrangement of the centers involved significantly affects the reaction course.

The authors express their gratitude to Professor A.K. Bose from the Stevens Institute of Technology, Hoboken, New Jersey, for the measuring and interpretation of the NMR spectrum of the substance IIb, and to Dr. R. Anliker from Ciba A.G. Basel for his kind help in providing the infra-red spectrum of substance III.

⁶ M.S. Silver, J. Amer. Chem. Soc. 82, 2971 (1960); P.S. Skell and I. Starer, J. Amer. Chem. Soc. 82, 2971 (1960); O.E. Edwards and M. Lesage, Chem. & Ind. 1107 (1960).