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# PHOTOCHEMICAL REACTIONS - III.*

# THE PHOTOCHEMICAL FRAGMENTATION OF A STEROIDAL N-CHLOROAMINE

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IN previous papers* we reported the conversion of (22R:25S)- and (22S:25R)-22.26-imino-5α-cholestane-3ß-ol into the <u>Solanum</u> steroidal alkaloid demissidine ((22R:25S)-5α-solanidane-3ß-ol) and its (22S:25R)-stereoisomer. The cyclizations to the tertiary bases were effected using the Hofmann-Löffler-Freytag reaction[1] by UV irradiation of the corresponding N-chloro derivatives and subsequent alkaline treatment of the photochemically derived 16-chloro compounds. In an attempt to apply this reaction sequence to (22S:25S)-22.26-imino-5α-cholestane-3ß-ol (I)[2] a different reaction course has been observed which represents a new type of photochemical fragmentation.

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* For communications I and II of this series, see G. Adam and K. Schreiber, <u>Tetrahedron Letters</u> 943 (1963); <u>Tetrahedron</u> 20, 1719 (1964).

[1] See, M.E. Wolff, <u>Chem. Reviews</u> 63, 55 (1963).

[2] K. Schreiber and G. Adam, <u>Tetrahedron</u> 20, 1707 (1964).

Reaction of I with one equivalent N-chlorosuccinimide in methylene dichloride at -5° gave a nearly quantitative yield of the N-chloro derivative II, m.p. 242-244° dec., $[\alpha]_D^{22}$ -64.5° [*]. Irradiation of this substance dissolved in trifluoroacetic acid in a quartz vessel at 20-30° under argon using a 500-watt high pressure mercury lamp caused rapid disappearance of positive halogen (after 8 min.). Alkaline treatment of the photolysis product and chromatography on alumina (grade 3) furnished not the expected (22S:25S)-5α-solanidane-3ß-ol (III) but instead a nitrogen-free halogen-containing compound (52 %) which appeared homogenous on thin-layer chromatography ($R_F$ 0.21)[**] but melted over the range 147-153°, $[\alpha]_D^{20}$ +7.2°. Elementary analysis indicated the composition $C_{21}H_{35}ClO$, and the molecular mass spectrum (negative ionization) showed a double peak at mass numbers 337 and 339 (= M-1 with $^{35}Cl$ and $^{37}Cl$, respectively); infrared band at 3330 $cm^{-1}$ (hydroxyl). Acetylation with acetic anhydride-pyridine at 20° for 16 hr. gave an acetyl derivative, m.p. 120-126°, $[\alpha]_D^{20}$ -1.2°, $R_F$ 0.62, infrared band at 1732 $cm^{-1}$ (acetoxy). These results suggest that UV irradiation of II causes loss of the piperidine ring to form a chloro-5α-pregnane-3ß-ol

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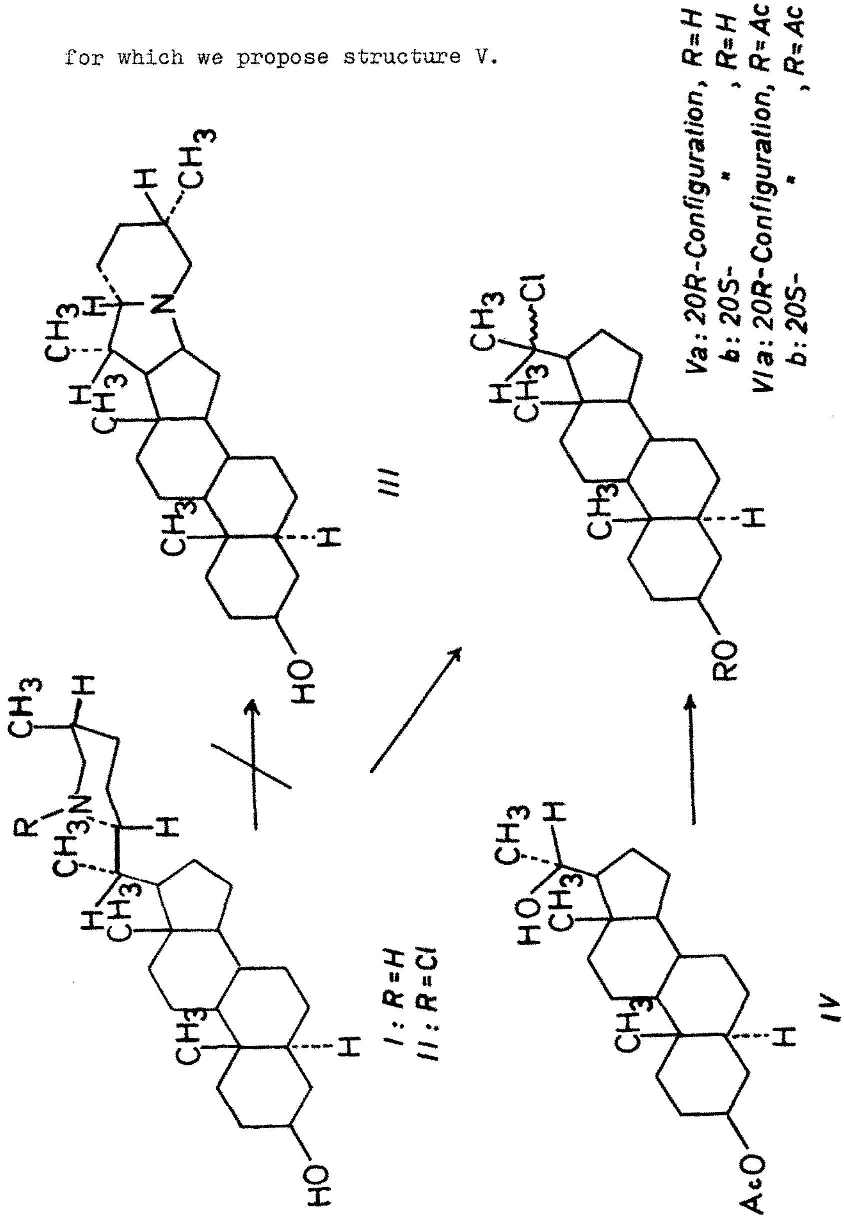
[*] Melting points are corrected. All rotations in chloroform (c ~0.5). Satisfactory analytical data have been secured for all new compounds described in this communication. We are indebted to Dr. K. Heller, Jena, and to Dr. R. Tümmler, Dresden, for infrared measurements and molecular mass spectra, respectively. We wish to thank Dr. Martin-Smith and Dr. C.J. W. Brooks, Glasgow, for the gas chromatograms.

[**] On silica gel G Merck using chloroform for development, detection with Ce(IV)-sulphate in 50 % sulfuric acid.

for which we propose structure V.



I : R=H
II : R=Cl

III

IV

Va : 20R-Configuration, R=H
b : 20S- " , R=H
VIa : 20R-Configuration, R=Ac
b : 20S- " , R=Ac

In order to confirm this and to determine the stereochemistry at C-20, the pairs of stereoisomeric 20-chloro pregnanes VI a, b and V a, b, have been synthesized, starting from (20R)-3ß-acetoxy-5α-pregnane-20-ol IV.[3] Reaction of IV with either phosphorus pentachloride in chloroform (in presence of calcium carbonate) or sulfuryl chloride in pyridine[4] for 1 hr. at 0 to 20$^{\circ}$ furnished mainly a 20-chloro-3ß-acetoxy-pregnane of m.p. 160-165$^{\circ}$ and $[\alpha]_D^{22}$ -5.5$^{\circ}$; and the corresponding 3ß-hydroxy compound of m.p. 211-215$^{\circ}$ and $[\alpha]_D^{20}$ -0.3$^{\circ}$ was obtained after saponification with refluxing 2 % methanolic potassium hydroxide for 1 hr. On the other hand by treating with thionyl chloride for 15 hr. at 20$^{\circ}$ we obtained nearly exclusively the isomeric 20-chloro-3ß-acetoxy-pregnane of m.p. 142-144$^{c}$ and $[\alpha]_D^{21}$ +1.7$^{\circ}$, and after hydrolysis, the corresponding hydroxy derivative of m.p. 163-165$^{\circ}$ and $[\alpha]_D^{22}$ +9.7$^{\circ}$. For the reaction with thionyl chloride under the applied conditions an $S_N$i-machanism is to be expected giving retention of configuration at C-20 so that (20R)-configuration can be assigned to the 20-chloro pregnane with m.p. 142-144$^{\circ}$ (formula VI a). On the other hand the compound of m.p. 160-165$^{\circ}$, obtained with phosphorus pentachloride or sulfuryl chloride, probably has (20S)-configuration, as a result of inversion at C-20 (formula VI b).

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

[4] H. Mori and S. Wada, *Chem. Pharmac. Bull.(Tokyo)* *11*, 1409 (1963).

Both stereoisomeric 20-chloro-3ß-acetoxy-5α-pregnanes (VI a,b) and the corresponding photolysis product VI of m.p. 120-126° appeared identical on thin-layer chromatography ($R_F$ 0.62), in molecular mass spectrography (main peaks at mass numbers 379 and 381 = M-1 with $^{35}Cl$ and $^{37}Cl$, respectively) and on gas chromatography.* However, VI a and VI b differ markedly in the fingerprint region of their infrared spectra. A 1:1 mixture of VI a and VI b (like VI obtained via photolysis) crystallised in plates having a melting **range** 116-125°. There was no mixed m.p. depression and the infrared spectra were very similar. Comparable results were obtained in the

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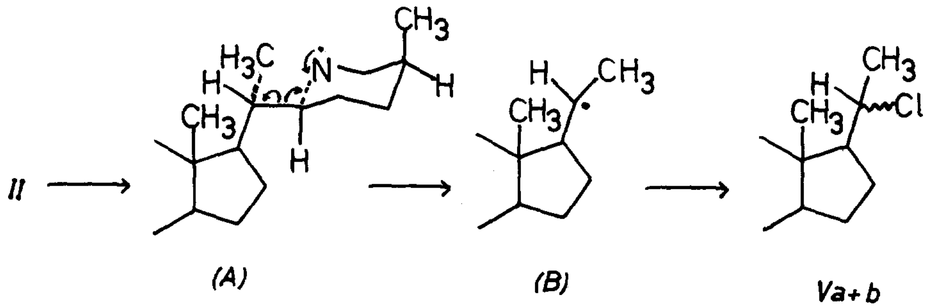
* Retention time 1.17 (on 1 % S.W.-30) or 3.30 (on 1 % QF-1) at 225°, referred to 5α-cholestane = 1. In all cases a second peak of retention time 0.55 and 1.2, respectively, appeared which is probably due to a product formed by thermal elimination of HCl.

3ß-hydroxy series. These results suggest that the photolysis product V and its acetyl derivative VI consist of a mixture of unseparable stereoisomeric 20-chloro pregnanes V a, b (and VI a, b, respectively).

The following mechanism may be proposed for this photolytic fragmentation. As in the Hofmann-Löffler-Freytag reaction initial homolysis of the N-Cl bond leads to a nitrogen radical. In the (22S:25S)-series in question for stereochemical reasons this radical is not able to produce hydrogen abstraction but undergoes stabilization via (A) by carbon-carbon fission producing the trigonal carbon radical (B) which recombines with chlorine to give the stereoisomeric 20-chloro pregnanes V a and b.



Similar fragmentation processes have been found by Barton and coworkers in the photolysis of α-hydroxy substituted 20-nitrite esters of the pregnane series[5] as well as of 17-nitrite esters.[6,7]

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[5] A.L. Nussbaum, S.P. Yuan, C.H. Robinson, H. Mitchell, E.P. Oliveto, J.M. Blaton and D.H.R. Barton, J. Org. Chemistry 27, 20 (1962).

[6] C.H. Robinson, O. Gnoj, A. Mitchell, R. Wayne, E. Townsley, P. Kabasakalian and D.H.R. Barton, J. Amer. Chem. Soc. 83, 1771 (1961).

[7] See also, K. Heusler and J. Kalvoda, Angew. Chem. 76, 518 (1964).