# A Degradation of the Solonidane Skeleton

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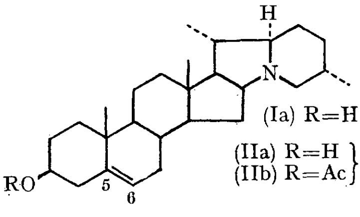
ALTHOUGH the structures as well as the absolute configurations of the solanidane-derived steroidal alkaloids are completely established,[1] degradation experiments on the solanidane skeleton were initiated with the intention of opening ring E so that an array of synthetic intermediates could be obtained perhaps more readily than had been possible previously.[2]

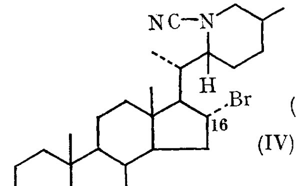
Owing to the early successful synthesis of the solanidane ring system[3] extensive degradative schemes were never carried out, but recently, however, ring F of demissidine (IIa) has been cleaved by a set of oxidative reactions.[4] The E-ring, nevertheless, has had a discouraging stability, and its scission has not until now been reported.

Early workers[5] found that the methiodide of solanidine (Ia) resisted the Hofmann reaction, and likewise the acetates of solanidine (Ib) and its dihydro-derivative, demissidine (IIb), failed to undergo the von Braun degradation. In support of the apparently inert locus of the nitrogen atom of the solanidanes we have found that exposure of solanidine methiodide to the reducing medium of sodium in liquid ammonia gave solanidine in good yield. On the other hand, a re-examination of the von Braun reaction on (Ib) with cyanogen bromide in refluxing chloroform gave the crystalline bromo-cyanamide derivative (III) in excellent yield, m.p. 185° then 245—260° (decomp.);† strong i.r. bands appeared at 2202 ($C{\equiv}N$) and 1733 cm.$^{-1}$ ($C{=}O$). The n.m.r. spectrum showed three complex multiplets due to three protons at $\delta$ 5·38 (6H, olefinic), 4·60 ($3\alpha$-H), and 4·10 ($16\beta$-H). The bromo-cyanamide did not give an immediate precipitate with $AgNO_3$ in aqueous ethanol. Mechanistic[6] reasoning prompts us to suggest a $16\alpha$-orientation for the bromine atom of (III).



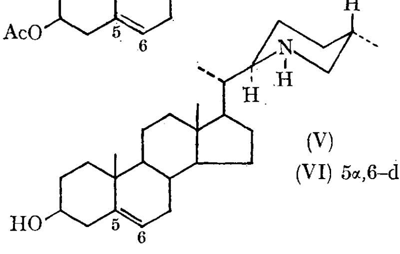
(Ia) R=H, (Ib) R=Ac

(IIa) R=H, (IIb) R=Ac } 5α,6-dihydro



(III)

(IV) 5α,6-dihydro



(V)

(VI) 5α,6-dihydro

Thus, frontside addition of the elements of cyanide to the nitrogen lone-pair of electrons in the *S*-configuration[1] followed by a rearside nucleophilic displacement of the quaternary amine group by bromide ion would result in the cleavage of ring

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† All new compounds gave satisfactory elemental analyses.

E and the substitution of a 16α-bromine atom. T.l.c. indicated only a single compound.

Similarly, (IIb) with cyanogen bromide in refluxing chloroform gave an excellent yield of product, m.p. 155°, then slow decomposition over 250—280°; strong bands in the i.r. appeared at 2205 ($C\equiv N$) and 1716 cm.$^{-1}$ ($C=O$). The n.m.r. showed two complex signals, each integrating for one proton, at 4·63 (3α-H) and 4·02 δ (16β-H). A negative test was given for ionic halogen.

The site of bond rupture leading to the ring-opened products arising from (Ib) and (IIb) was established by a $LiAlH_4$ reduction of the von Braun adducts, (III) and (IV). Accordingly, reduction of (IV) gave a product which when analyzed by g.l.c.‡ revealed the presence of (VI) (49%), an unidentified material (27%), and (IIa) (24%). The demissidine {(IIa), identified by g.l.c., t.l.c., i.r., $[\alpha]_D$, and m.p.} could be readily separated from the mixture by column chromatography on alumina, and (VI) could be separated from the unidentified product (noncrystallizable) by recrystallization. The structure assignment of (VI) was made by comparison of m.p., $[\alpha]_D$, and i.r. with the literature values.[2c] In addition, the mass spectrum showed a very strong peak at *m/e* 98 due to the 4-methyltetrahydropyridine ion, and a high resolution measurement at *m/e* 401 required a composition of $C_{27}H_{47}NO$. The *NO*-diacetyl derivative of (VI) was identical in physical properties with an authentic sample.[2c] §

In the same way reduction of (III) gave a mixture of (V) (47%), an unidentified component (18%), and (Ia) (35%). As before, the mixture was separated by chromatography and crystallization. The piperidyl-steroid (V) so obtained melted at 218—219°, $[\alpha]_D$ −45° ($CHCl_3$). The i.r. spectrum was consistent with structure (V). High resolution mass spectrometry confirmed the presence of $C_{27}H_{45}NO^+$ at *m/e* 399 while the low resolution spectrum was characterized by a very strong peak at *m/e* 98.

(*Received, June 14th,* 1968; *Com.* 780.)

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‡ The nickel column (0·25 in. × 10 ft.) used contained 1% SE-20 on Chromosorb and was operated at 230°.

§ Kindly provided by Professor K. Schreiber, Berlin, D.D.R.

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[3] (a) F. C. Uhle and W. A. Jacobs, *J. Biol. Chem.*, 1945, **160**, 243; (b) V. Prelog and S. Szpilfogel, *Helv. Chim. Acta*, 1944, **27**, 390.

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[6] For a discussion of the von Braun reaction mechanism see H. A. Hageman, *Org. Reactions*, 1953, **7**, 202.