Aconite Alkaloids.—On Pyrolytic Products of Aconitine, Oxonitine, and their Derivatives

By Takeo SHIMA and Takashi AMIYA

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It is well known that the pyrolysis of aconitine I ($C_{34}H_{47}O_{11}N$) at or above its melting point results in the internal loss of a molecule of acetic acid whereupon pyraconitine II ($C_{32}H_{43}O_9N$) is formed. Little is known, however, about the mode of elimination of acetic acid. Stern[1] mentioned that epoxide-formation occurred between the acetoxy group and an adjacent hydroxyl group or that a new ethylenic

1) R. H. F. Manske and H. L. Holmes, "The Alkaloids", Vol. IV, Academic Press Inc. New York, (1954), p. 292.

kage was introduced by this pyrolysis. cently on the ground of the observation the infrared spectra Schneider[2] sug- ested that a new ethylenic linkage was ntroduced in the conjugated position to an inert ethylenic linkage initially present in compound I during pyrolysis of compound I by abstraction of a molecule of acetic acid between the acetoxy group and a hydrogen atom from a neighboring carbon atom. This mechanism was supported by Nath and Dasgupta[3,3a] although it had been previously denied by Edwards and Marion[4]. Attempts were made therefore to re-investigate pyrolytic reactions of compound I, oxonitine, and their derivatives by means of an examination of both ultraviolet and infrared spectra.

Thus, it was found that on pyrolysis of each of these alkaloids a new carbonyl group was formed by the splitting of a molecule of acetic acid between the acetoxy group and the hydroxyl group on a carbon atom near the acetoxy group.

Results were as follows:

Pyraconitine hydroperchlorate (III) ($C_{32}H_{43}O_9N \cdot HClO_4 \cdot H_2O$)[5,*]: infrared spectrum (nujol), >C=O and ester carbonyl 5.83 μ**; OH 3.01 μ: ultraviolet spectrum (methanol), λ_{max} 230 mμ, log ε 4.15; λ_{max} 275 mμ, log ε 3.03***.

Diacetyl pyraconitine (IV) ($C_{36}H_{47}O_{11}N \cdot C_2H_5OH$)[6,*]: infrared spectrum (nujol), >C=O 5.85 μ; ester carbonyl 5.76 μ; no-OH.

Pyroxonitine(V) ($C_{30}H_{37}O_{10}N$)[1]: infrared spectrum (nujol), lactam carbonyl 6.06 μ; >C=O and ester carbonyl 5.83 μ**; OH 3.01 μ: ultraviolet spectrum (methanol), λ_{max} 230 mμ, log ε 4.26; λ_{max} 275 mμ, log ε 3.03.

Diacetyl pyroxonitine(VI) ($C_{34}H_{41}O_{12}N \cdot C_2H_5OH \cdot H_2O$)[7,*]: infrared spectrum (nujol), lactam carbonyl 5.98 μ; >C=O 5.88 μ; ester carbonyl 5.80 μ; no-OH.

Pyraconine(VII) ($C_{25}H_{39}O_8N$)[8,****]: infrared spectrum (nujol), >C=O 5.88 μ; OH 2.94 μ: ultraviolet spectrum (methanol), λ_{max} 275 mμ, log ε 1.66.

Pyraconine hydrochloride(VIII) ($C_{25}H_{39}O_8N \cdot HCl \cdot 2.5H_2O$)*****,[8]: infrared spectrum (nujol), >C=O 5.94 μ; OH 2.94, 2.89, 2.87 μ: ultraviolet spectrum (methanol), λ_{max} 320 mμ, log ε 1.64.

Pyraconine hydroiodide(IX) ($C_{25}H_{39}O_8N \cdot HI \cdot H_2O$)[6]: infrared spectrum (nujol), >C=O 5.94 μ; OH 3.01, 2.88, 2.80 μ: ultraviolet spectrum (methanol), λ_{max} 220 mμ, log ε 4.11; λ_{max} 310 mμ, log ε 1.99.

Aconine(X) ($C_{25}H_{41}O_9N$)[8,****]: infrared spectrum (nujol), OH 2.88 μ: ultraviolet spectrum (methanol), no λ_{max} at wave lengths 210~350 mμ.

Aconine hydrochloride(XI) ($C_{25}H_{41}O_9N \cdot HCl \cdot 2H_2O$)[8,****]: infrared spectrum (nujol), H_2O 6.08 μ; OH 2.98 μ: ultraviolet spectrum (methanol), no λ_{max} at wave lengths 210~350 mμ.

Pyroxonine(XII) ($C_{23}H_{33}O_9N$)[1]: infrared spectrum (nujol), lactam carbonyl 6.08 μ, >C=O 5.87 μ; OH 3.01, 2.91 μ: ultraviolet spectrum (methanol), λ_{max} 305 mμ, log ε 1.64.

Oxonine(XIII) ($C_{23}H_{35}O_{10}N$)[1]: infrared spectrum (nujol), lactam carbonyl 6.02~6.07 μ; OH 2.9 μ.

Pyrodesmethanol aconitinone hydroperchlorate(XIV) ($C_{31}H_{37}O_8N \cdot HClO_4 \cdot H_2O$)[8]: ultraviolet spectrum (methanol), λ_{max} 233 mμ, log ε 4.39*.

Desmethanol aconitinone(XV) ($C_{33}H_{41}O_{10}N$)[8]: ultraviolet spectrum (methanol), λ_{max} 233 mμ, log ε 4.38[3a].

According to the above data there are marked differences between the absorption bands of compounds VII and VIII and those of compounds X and XI in the ultraviolet spectra and the infrared spectra. Also there was a marked difference in the infrared spectrum between the absorption bands of compound XII and those of compound XIII. Thus compounds VII, VIII and XII are believed to possess carbonyl groups newly formed by pyrolyses. Compounds IV and VI showed no bands at wave length 2.6~3.2 μ characteristic of hydroxyl group. This fact sug-

2) W. Schneider, *Ber.*, **89**, 768 (1956).
3) B. Nath, *J. Sci. Ind. Res., India*, **16, B**, 159 (1957).
3a) S. Dasgupta and B. Nath, *J. Ind. Chem. Soc.*, **34**, 204 (1957).
4) O. E. Edwards and L. Marion, *Can. J. Chem.*, **30**, 627 (1952).
5) H. Schulze and A. Liebner, *Arch. Pharm.*, **251**, 453 (1913).
* The infrared absorption spectra of these compounds were determined after drying in vacuo.
** This absorption band is broad.
*** The ultraviolet spectrum of compound III is nearly identical with that of pyraconitine.
6) H. Schulze and A. Liebner, *Arch. Pharm.*, **254**, 567 (1916).
7) K. Tamura, *Ann.*, **533**, 183 (1938).
8) T. A. Henry, "The Plant Alkaloids", J. & A. Churchill Ltd., London, (1949), p. 673.

**** Compounds VII, X and XI consume one mole each of periodic acid respectively. This fact suggests that the α-glycol of aconine X is not concerned in the pyrolytic reaction.
***** When aconine hydrochloride XI was heated at 180°C for 10 minutes pyraconine hydrochloride VIII was obtained. This compound VIII, which was crystallized from water, was identical with pyraconine hydrochloride which was prepared from pyraconitine by hydrolysis[1] (m. p. and analysis). *Anal.* Found: C, 54.01; H, 8.16. Calcd. for $C_{25}H_{45}O_{10.5}NCl$: C, 54.01; H, 8.18%.
* The ultraviolet spectrum of compound XIV was nearly identical with that of pyrodesmethanol aconitinone.

gests that a new carbonyl group was introduced by abstraction of a molecule of acetic acid between the acetoxy group and the hydroxyl group on a carbon atom near the acetoxy group. On the other hand there was no marked difference between the ultraviolet spectrum of compound III and that[9] of compound I at wave lengths 210~280 mμ. Hence, just as the former investigators[4] stated, no conjugated unsaturation results from pyrolysis. Reduction of compound VII with lithium aluminum hydride gave an amorphous base which the present workers named "pyraconiol". This base formed a hydroiodide which crystallized from water. Pyroconinol hydroiodide XVI ($C_{25}H_{41}O_8N \cdot HI \cdot 1.5H_2O$) showed m. p. 185°C (*Anal.* Found: C, 47.33; H, 7.23; H_2O, 4.25. Calc. for $C_{25}H_{45}O_{9.5}NI$: C, 47.20; H, 7.10; H_2O, 4.25%). The infrared absorption spectrum of compound XVI lacks the band corresponding to that (5.94 μ) of compound IX in the carbonyl region. Also the ultraviolet spectrum of compound XVI (λ_{max} 220 mμ, log ε 4.03) in methanol lacks a maximum corresponding to that (310 mμ) of compound IX in the carbonyl region. From the above data, it is suggested that the carbonyl group does not exist in compound XVI. The ultraviolet spectra of compound XIV and compound XV were rather similar at wave lengths 210~280 mμ. This fact suggests that the carbonyl group newly formed by pyrolysis in compound XIV is not conjugated to the α, β-unsaturated ketone which has been present in compound XV.

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Department of Chemistry,
Faculty of Science,
Hokkaido University, Sapporo

9) E. Ochiai, T. Okamoto and S. Sakai, *J. Pharm. Soc. Japan* (*Yakugaku Zasshi*), **75**, 545 (1955).