The Functional Groups of Sachaconitine

By Nobukatsu KATSUI and Gen HASEGAWA

(Received December 25, 1959)

In a previous paper[1] the extended formula of sachaconitine (I) ($C_{23}H_{37}O_4N$), one of the alkaloids of *Aconitium miyabei* Nakai, was given as follows:

$$C_{19}H_{24}\left\{\begin{array}{l}(OH)_2\\(OCH_3)_2\\N\text{-}C_2H_5\end{array}\right.$$

Experiments for characterizing the functional groups of "compound I" have been carried out, and the results are here comunicated.

Oxidation of "compound I" with potassium permanganate in acetone gave a mixture of (a) a neutral compound (II), m. p. 194~196°C, $[\alpha]_D$ −37.8 (EtOH) (Found: C, 67.92; H, 8.71; N, 3.51. Calcd. for $C_{23}H_{35}O_5N$: C, 68.12; H, 8.70; N, 3.45%), and (b) a basic compound (III), m. p. 230~231°C, $[\alpha]_D$ +17.1° (EtOH), pK_a 9.8, ν_{max} 3545, 3447 cm^{-1} (OH), 3230 cm^{-1} (NH) (Found: C, 69.30; H, 8.97; N, 4.04. Calcd. for $C_{21}H_{33}O_4N$: C, 69.39; H, 9.15; N, 3.85%).

"Compound II" was characterized as the lactam, oxosachaconitine, by its infrared spectrum, ν_{max} 3537, 3447 cm^{-1} (OH), 1635 cm^{-1} (lactam), and by treatment with lithium aluminum hydride, which converted it into "compound I".

"Base III" was shown to be *N*-desethylsachaconitine by treatment with ethyl iodide, which also reverted to "compound I", thus firmly establishing the presence of an *N*-ethyl group in the alkaloid. Treatment of "compound II" with acetylchloride gave diacetyloxosachaconitine, m. p. 149~151°C, ν_{max} 1725 cm^{-1} (ester carbonyl), 1625 cm^{-1} (lactam) (Found: C, 64.15; H, 8.00; N, 3.01. Calcd. for $C_{27}H_{39}O_7N$: C, 64.49; H, 8.44; N, 3.01%). On the same treatment, "compound III" gave a neutral product in very poor yield, which could not be purified. Hence "compound III" was treated with acetic anhydride in pyridine at room temperature, and then a neutral product, m. p. 175~176°C, was yielded. In the infrared spectrum this product showed an amide band at 1635 cm^{-1}, hydroxyl bands at 3487 and 3331 cm^{-1}, but no ester carbonyl band. With the same reagent "compound I" or "II" were recovered without change, and thus it was suggested that the hydroxyls of the alkaloid resisted acetylation with acetic anhydride at room temperature. Oxidation of "compound I" with chromic acid—pyridine complex or with potassium permanganate in acetone-acetic acid produced again two products: one was a neutral compound (IV), m. p. 237~239°C, $[\alpha]_D$ +35.7° (EtOH), λ_{max} 290 mμ (ε 40) (Found: C, 68.46; H, 8.25; N, 3.62. Calcd. for $C_{23}H_{35}O_5N$: C, 68.46; H, 8.24; N, 3.47%), the second was a base (V), m. p. 275~277°C, $[\alpha]_D$ +107° (EtOH), pK_a 8.3 (Found: C, 70.35; H, 8.00; N, 4.04. Calcd. for $C_{21}H_{29}O_4N$: C, 70.17; N, 8.13; N, 3.90%). "Compound IV", also obtainable from "compound II" by oxidation with chromic acid in acetone, showed a hydroxyl band at 3470 cm^{-1} a lactam band at 1619 cm^{-1} and a five-membered carbonyl band at 1745 cm^{-1} in infrared. Reduction of "compound IV" with sodium borohydride produced "compound II", and with lithium aluminium hydride gave back "compound I". Thus "compound IV" is a keto-lactam, oxosachaconitinone, and also it is indicated, that one of the two hydroxyls in "compound I" or "II" is a secondary one in a five-membered ring.

"Base V" showed a band at 1741 cm^{-1} due to the five-membered ketone carbonyl, a band at 3300 cm^{-1} and no double bond band in infrared, and in ultraviolet spectrum this base contained two maxima at 290 mμ (ε 70) and 250mμ (ε 210) due to ketone carbonyl respectively. Confirmation of base V as a *N*-desethyl base was supported by the facts that the base gave "compound III" on reduction with sodium borohydride and was obtained also from "compound III" by oxidation with chromic acid in acetone; accordingly the above noted band at 3300 cm^{-1} may be due to N–H group. Thus the results of ultraviolet and infrared absorptions give the assumption, that in "base V" two hydroxyls of "compound III" were oxidized to diketo groups both being five-membered cyclic ketones without more free hydroxyl present.

This consideration was further tested by treatment of "base V" with acetic anhydride in pyridine at room temperature, which as above mentioned, is not capable of acetylating the hydroxyls of the alkaloid. The neutral product obtained, m. p. 222~224°C, showed

---

[1] H. Suginome, N. Katsui and G. Hasegawa, This Bulletin 32, 604 (1959).

a band at 1755 cm^{-1} (carbonyl) and 1616 cm^{-1} (amide), but no hydroxyl band in infrared. On the other hand, one maximum(290 mμ, ε 70) in ultraviolet of " base V " is normal and may be caused by the same carbonyl as that of "compound IV", but the second (250 mμ, ε 210) is abnormal. The same abnormality in ultraviolet has been already shown in dehydrodelpheline[2] (250 mμ, ε 200), obtainable by oxidation of the delphinium alkaloid, delpheline, having the same skeletal formula ($C_{21}H_{33}N$) as sachaconitine.

Furthermore the decrease of pK_a in the conversion from " compound I " (pK_a 9.7) or " compound III " (pK_a 9.8) to " compound V " (pK_a 8.3) has been also observed analogously in the change of parent alkaloid to a dehydroderivative. Then it may be assumed, that in " compound V " a carbonyl is present at the analogous position with dehydrodelpheline. Thus "compound V" is assigned the name, *N*-desethyldehydrosachaconitinone; the environment of the ring containing nitrogen in " compound I " is considered to resemble that of delcosine[3], one of the delphinum alkaloids, because the *N*-ethyl group of the former is more readily oxidized as well as the latter to a *N*-desethyl derivative than the other delphinum or aconitum alkaloids.

But it may be more plausible to assume, that the position of a carbonyl in " compound V " is not the same with didehydrodelcosine[4] but with dehydrodelpheline[5], since the carbonyl is a five-membered ring ketone.

Investigation concerning the methoxyl functions of the alkaloid is in progress and will be reported later.

The authors are grateful to Professor Harusada Suginome, President of Hokkaido University, for his exceedingly kind direction throughout this work.

Department of Chemistry
Faculty of Science
Hokkaido University
Sapporo

---

[2] R. C. Cookson and M. E. Trevett, *Chem. and Ind.*, 1324 (1954), *J. Chem. Soc.*, **1956**, 2689.

[3] R. Anet, D. W. Clayton and L. Marion, *Can. J. Chem.*, 35, 397 (1957).

[4] V. Skaric and L. Marion, *J. Am. Chem. Soc.*, **80**, 4434 (1958).

[5] R. C. Cookson and M. E. Trevett, *J. Chem. Soc.*, **1956**, 3121.