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Characterization of Hydroxyl Groups and the Result of Dehydrogenation of Pseudokobusine

Some time ago, Suginome, *et al.*[1,2] reported the isolation of an aconite alkaloid, pseudokobusine, from *Aconitum yesoensis* NAKAI and *Aconitum luciduscuculum* NAKAI. In one of those papers, they proposed[1] the presence of two alcoholic hydroxyls, one ether linkage, and a C=N type of unsaturation in pseudokobusine.

The present writer isolated the same alkaloid from aconite rhizome collected in Hokkaido and the identity of this sample with that of Suginome's group* was confirmed by mixed melting point determination and comparison of their infrared absorption spectra.

Pseudokobusine (I), $C_{20}H_{27}O_3N$, m.p. 271°(decomp.), is a tertiary base and readily gave its methiodide, m.p. 274°(decomp.) (*Anal.* Calcd. for $C_{20}H_{27}O_3N \cdot CH_3I$: C, 53.50; H, 6.41. Found : C, 53.47; H, 6.13), and the ethiodide, m.p. $>$290°(turning brown) (*Anal.* Calcd. for $C_{20}H_{27}O_3N \cdot C_2H_5I$: C, 54.43; H, 6.65; N, 2.89. Found : C, 54.76; H, 7.35; N, 2.78). One molar equivalent of hydrogen uptake was observed when the double bond determination[3] was carried out on the alkaloid and an infrared absorption band at $900\,cm^{-1}$ suggested that the double bond is an exo-methylene type. One $C-CH_3$ group was found by the Kuhn-Roth method and no methoxyl was detected in pseudokobusine. On treatment with benzoyl chloride in pyridine, tribenzoylpseudokobusine, m.p. 131~136° (*Anal.* Calcd. for $C_{20}H_{24}N \cdot (OCOC_6H_5)_3 \cdot H_2O$: C, 74.64; H, 6.26; C_6H_5CO, 47.79. Found : C, 74.85; H, 6.59; C_6H_5CO, 47.75. After being dried over P_2O_5 at 100~110° *in vacuo* for 1 hour : *Anal.* Calcd. for $C_{20}H_{24}N \cdot (OCOC_6H_5)_3$: C, 76.73; H, 6.13. Found : C, 76.34; H, 6.09) was obtained in a fair yield, supporting that all oxygen functions are hydroxyls.

In order to establish that one of these three hydroxyls is in an allyl alcoholic grouping, which is quite common in nontoxic aconite alkaloids,[4] both oxidation reactions and palladium-catalyzed rearrangement were applied to pseudokobusine. Chromium trioxide-pyridine treatment or manganese dioxide oxidation of (I) afforded pseudokobusinone (II), m.p. 268° (*Anal.* Calcd. for $C_{20}H_{25}O_3N \cdot \frac{1}{2}H_2O$: C, 71.40; H, 7.79. Found : C, 70.84; H, 7.86), whose ultraviolet absorption spectra (λ_{max}^{MeOH} 227 mμ (log ε 3.84)) and infrared absorption bands at 1693 and $1628\,cm^{-1}$ showed the presence of an α,β-unsaturated ketone in (II). When the ethanolic solution of (I) was shaken in hydrogen atmosphere with palladium-carbon, dihydropseudokobusinone (III), m.p. 277~279°, ν^{KBr} $1712\,cm^{-1}$ (*Anal.* Calcd. for $C_{20}H_{27}O_3N \cdot \frac{1}{2}H_2O$: C, 70.97; H, 8.34. Found : C, 71.25; H, 8.46) as the expected rearranged product and dihydropseudokobusine (IV), m.p. 260~261° (*Anal.* Calcd. for $C_{20}H_{29}O_3N \cdot \frac{1}{2}H_2O$: C, 70.55; H, 8.88. Found : C, 70.99; H, 8.78), which was derived from (I) in a high yield by hydrogenation over platinum in acetic acid, were obtained through chromatographic separation. Correlation between (II) and (III) was achieved when (II) was hydrogenated over palladium-carbon in ethanol yielding (III).

Further oxidation reaction of either (III) or (IV) gave informations on characters of the other two hydroxyl groups. Treatment of (III) and (IV) with chromium trioxide in acetic acid resulted in formation of a single oxidation product, oxodihydropseudokobusinone(V), m.p. 276~278° (*Anal.* Calcd. for $C_{20}H_{25}O_3N$: C, 73.36; H, 7.70. Found : C, 73.76;

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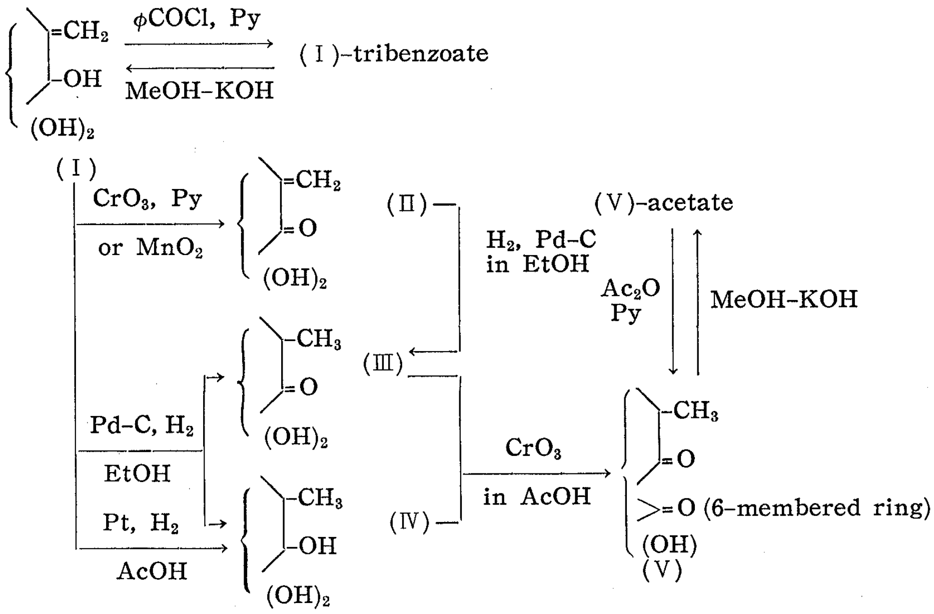
[1] H. Suginome, T. Kōyama, Y. Kunimatsu : J. Fac. Sci., Hokkaido Univ., III, **4**, 16(1950).

[2] H. Suginome, S. Kakimoto, J. Sonoda : *Ibid.*, III, **4**, 25(1950).

[3] K. Tsuda, S. Sakamoto : Yakugaku Zasshi, **57**, 1037(1937).

[4] K. Wiesner, Z. Valenta : Fortschr. Chem. Org. Naturstoffe., **16**, 26(1958), Springer, Vienna; T. Sugasawa : This Bulletin, **4**, 6(1956); S. Sakai : *Ibid.*, **5**, 1(1957); T. Okamoto : *Ibid.*, **7**, 44(1959); E. Ochiai, T. Okamoto : *Ibid.*, **7**, 550(1959).



H, 7.55). It had an infrared absorption band of a new ketone at 1720 cm^{-1} in addition to the original ketone at 1709 cm^{-1}. This fact showed that the second hydroxyl group which was involved in this oxidation is secondary and located in a six-membered ring. The final hydroxyl group seems to be tertiary, since (V) still afforded its acetate, m.p. 217~219° (*Anal.* Calcd. for $C_{20}H_{24}O_2N \cdot OCOCH_3$: C, 71.52; H, 7.37. Found : C, 70.71; H, 7.43) with acetic anhydride in pyridine, whereas (V) was completely inert to the Kiliani reagent and was recovered almost quantitatively.

Selenium dehydrogenation reaction of (I) was examined to make a further structural approach and the same three compounds as obtained from kobusine⁵⁾ were separated from the reaction mixture. A neutral compound, m.p. 84~88°(Kofler), which gave the characteristic ultraviolet absorption spectrum of 1,6,7-trialkylphenanthrenes,⁶⁾ was identified as 1,7-dimethyl-6-propylphenanthrene⁷⁾ and one of two aromatic bases, m.p. 141~143° (Kofler) (λ_{max}^{EtOH} (mμ) : 259, 299, 310, 336~337, 353), was identical with the base of m.p. 142~143° from kobusine by admixture in each case. The second base, though it could not be obtained in crystalline state, clearly showed the same ultraviolet absorption spectrum as that of another aromatic base, m.p. 115~115.5° (λ_{max}^{EtOH} mμ : 221, 267, 318~319, 328~329, 346, 363), derived from kobusine. Therefore, pseudokobusine possibly has the same fundamental structure as kobusine and it would be highly probable that (I) differs from kobusine, $C_{20}H_{27}O_2N$, in having one more tertiary hydroxyl.

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5) M. Natsume : This Bulletin, **7**, 539(1959).
6) E. Ochiai, T. Okamoto, S. Sakai, M. Natsume : *Ibid.*, **5**, 113(1957).
7) E. Ochiai, T. Okamoto, S. Hara, S. Sakai, M. Natsume : *Ibid.*, **6**, 327(1958).