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ALKALOIDS OF ACONITUM PALMATUM : CARBON SKELETON OF VAKOGNAVINE

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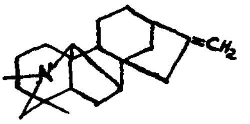
In an earlier communication[1], isolation and characterisation of five new alkaloids was reported. One of these alkaloids, Vakognavine was formulated as $C_{35}H_{41}O_{10}N$ and was found to have one benzoate group and three acetate groups as substituents.

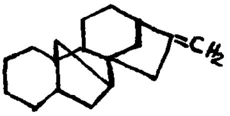
With an objective to elucidate the structural framework of Vakognavine, the base was dehydrogenated by heating with excess selenium for 7 hours at 300°. The acid fraction was found to contain benzoic acid. The neutral fraction was separated by chromatography on alumina column to give a small quantity of an aromatic hydrocarbon which was identified by direct comparison (UV spectrum and melting points of TNB-adduct and the picrate) with an authentic sample kindly placed at our disposal by Prof. Okamoto to be, 1,8-dimethyl-7 ethyl phenanthrene, thus indicating that Vakognavine belongs to the atisine group of diterpene alkaloids.

The basic fraction did not yield any pure product. The yields of the aromatic products in the dehydrogenation of the alkaloid were very poor, because of the high substitution of the skeleton by oxygen functions. Vakognavine thus like songorine has the carbon skeleton (II) and in analogy with other diterpene alkaloids would have the structural framework (I).

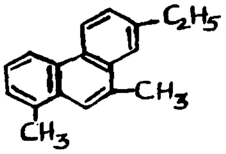
It is rather unusual that alkaloids of atisine group should be so highly substituted by oxygen functions. The NMR spectrum 100 MC confirmed the presence of one $C-CH_3$ ($8.9\,\tau$ -3H), one benzene ring ($2.64\,\tau$ -5H), three acetates and one $N-CH_3$ groups ($7.67\,\tau$-3H, $7.83\,\tau$ -3H, $7.93\,\tau$ -6H). The nitrogen atom thus would bear methyl and not ethyl group and Vakognavine would be formulated as C_{34} and not C_{35} compound. The molecular formula of vakognavine is thus corrected to $C_{34}H_{37}O_{10}N$. On catalytic reduction with Adams catalyst, it gave hexahydro compound $C_{34}H_{43}O_{10}N$, in which the exo-cyclic methylene group and both the carbonyl groups are reduced.



I



II



III

Selenium Dehydrogenation of Vakognavine

In a 100 ml. long necked flask was placed 15 g. of vakognavine and 45 g. of powered gray selenium. The air in the flask was replaced by dry pure nitrogen gas. The flask was inserted into a metal bath at 185° and the tempt. was raised over a period of 30 mins. to 275°, while a slow stream of nitrogen was passed through the apparatus. Over the course of the next 30 mins. the bath tempt. was raised to 300°, where it was maintained for 6½ hours. After cooling the contents of the flask were ground to a fine powder and extracted with chloroform in a continuous extracter. Chloroform was removed to yield a waxy solid which was dissolved in ether and separated into the following fractions by successive washing with 3% sulphuric acid and dilute sodium hydroxide.

1. Basic fraction, 0.1 g.; 2. Acid fraction, 0.9 g.;
3. Neutral fraction, 1.9 g..

Basic fraction:-

The material was chromatographed in petroleum ether over neutral alumina into seven fractions, the first three with petroleum ether (25 ml each fraction) neat and the next three with petroleum ether-benzene mixture, the proportion of benzene rising from 5 to 50 percent and the last with neat benzene. None of these fractions which totalled up 0.06 g. gave a picrate, nor was any fluorescence observed, indicating no evidence of an azaphenanthrene. The dilute hydrochloric acid trap to collect the volatile basic component did not yield any pure product.

Acid fraction:-

This material was found to be essentially benzoic acid as identified by its mixed m.p with an authentic sample.

Neutral fraction:-

The 1.9 g. of neutral material was chromatographed in petroleum ether over neutral alumina. The first four fractions (25 ml each) were eluted with neat petroleum ether and the next seven fractions (25 ml each) with petroleum ether-benzene (20 : 1) and the last fraction, with petroleum ether-benzene (1:1). The total eluent consisted of 0.7 g. of material. Only fractions second (0.036 g.) and third (0.028 g.) were semicrystalline and gave fluorescence and yielded picrates.

1,9-dimethyl-7 ethylphenanthrene:-

The second fraction was converted to a picrate m.p.115° which on recrystallization from methanol gave crystals of m.p.121-122°(52 mg.). It was recrystallized twice from methanol to give material (32 mg.) of constant melting point, 124-125°.

The third fraction was converted to a picrate m.p. 115° which was found to be identical with picrate from fraction second. A benzene solution of the picrate was passed over a short column of alumina to liberate the hydrocarbon, 28 mg. This was converted to a trinitrobenzene adduct, m.p. 140-146° (32 mg). It was recrystallized twice from methanol to yield material (6 mg) of constant melting point, 151-52°. Anal. Calcd. for $C_{18}H_{18}.C_6H_3N_3O_6$: C,64.3;H,4.7 Found: C,63.0;H,5.0.

The ultraviolet spectrum of the hydrocarbon liberated from the picrate indicated that it was trisubstituted phenanthrene[3]. Japanese workers were requested to send us the samples of the alkylphenathrenes suspected. Prof.Okamoto kindly supplied the samples of 1-methyl-6-ethyl phenanthrene; 1,9-dimethyl-7-ethylphenanthrene; 1,9-dimethyl-7-isopropyl phenanthrene; and 1,7-dimethyl-6-n. propylphenanthrene. The melting point of the picrate (125°) of the given hydrocarbon was depressed to 120° on admixture with the picrate of 1, methyl-6-ethylphenanthrene (133°) and the melting point of the TNB.adduct (151-2°) was depressed to 140-42° on mixing with TNB-adduct of 1,7-dimethyl-6n propylphenanthrene (158-9°)

and to 140-42° on admixture with TNB-adduct of alkylphenathrene, (m.p.151-52°) isolated from Selenium dehydrogenation of Vakatisine, another alkaloid from A. palmatum and which appears to be 1,7-dimethyl-6-ethylphenanthrene; and to 115° on admixture with TNB-adduct of 1,9-dimethyl-7-isoprophenanthrene (145°). The sample of 1,9-dimethyl-7-isopropylphenanthrene supplied was crude and melted at 117°. It was purified by elution on the alumina column to give crystals m.p. 145° (Lit.m.p. 153-4°). The sample (18 mg) of 1,9-dimethyl-7-ethylphenanthrene supplied by Prof.Okamoto was also crude and melted at 115°. It was recrystallized for purification twice (8 mg m.p. 125°; 4 mg m.p. 140°) and at each stage mixed melting point was taken with the unknown material. The mixed melting point remained undepressed at all the three stages. The ultra-violet spectrum given as under supports the identify of the neutral hydrocarbon as 1,9-dimethyl-7-ethylphenanthrene. Infrared spectrum indicated the bands 12,9 and 13.4 μ (Lit. 12.62 and 13.34 μ).

Alkylphenanthrene	U.V.Spectrum λmax .mμ (log ε)
1. $C_{18}H_{18}$ (authors)	260(4.69),281(4.10).291(4.24),303(4.02), 328(2.74), 335(2.60), 352(2.35).
2. 1,9-Dimethyl-7-ethylphenanthrene	260(4.70), 281(4.16),291(3.96),303(4.01), 328(2.42), 335(2.53),352(2.24).
3. 1,9-Dimethyl-7-isopropylphenanthrene	260(4.91), 282(4.23), 291(4.11),303(4.15), 337(2.46), 352(2.15).

Acknowledgement

Our thanks are due to Prof. Okamoto of the University of Tokyo for sending us the samples of the four alkylphenanthrene noted in the text.

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