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A RIGOROUS PROOF OF THE SELAGINE STRUCTURE

H. Yoshimura[1], Z. Valenta and K. Wiesner

Organic Chemistry Laboratory, University of New Brunswick
Fredericton, Canada

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THE elucidation of the structure of annotinine, the alkaloid of *Lycopodium annotinum* [2], revealed for the first time the structural type to be expected in other *Lycopodium* alkaloids. The key factor in the deduction of this structure was the identification of dehydrogenation products, and extensive systematic degradation[3]. Since then, structures have been proposed for additional alkaloids of this type, namely, lycopodine[4], selagine[5] and the obscurines[6]. Extensive use of N.M.R. spectroscopy[5], dehydrogenation[4,6]

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[1] N.R.C. postdoctoral fellow on leave from Kyushu University, Japan.

[2] K. Wiesner, Z. Valenta, W.A. Ayer and C. Bankiewicz, *Chem. and Ind.* 1019 (1956); K. Wiesner, W.A. Ayer, L.R. Fowler and Z. Valenta, *Chem. and Ind.* 564 (1957); K. Wiesner, Z. Valenta, W.A. Ayer, L.R. Fowler and J.E. Francis, *Tetrahedron* **4**, 87 (1958).

[3] A complete X-ray analysis (M. Przybylska and F.R. Ahmed, *Acta Cryst.* **11**, 718 (1958)) corroborated the the proposed structure.

[4] D.B. McLean and W.A. Harrison, in the press.

[5] Z. Valenta, H. Yoshimura, E.F. Rogers, M. Ternbah and K. Wiesner, *Tetrahedron Letters* No.10, 26 (1960).

[6] W.A. Ayer and G.G. Iverach, *Tetrahedron Letters* No. 10, 19 (1960).

and skeletal similarities within the Lycopodium group[4,6] were mainly responsible for these structure elucidations.

In no case so far reported was it possible to degrade one of the Lycopodium alkaloids in a series of simple (unrearranging) and predictable steps to a known compound. This has now been achieved with tetrahydroselaginol (II), a simple derivative of selagine (I)[5]. Compound II (8.5 mmols) was oxidized in an aqueous NaOH-K_2CO_3 solution with $NaIO_4$ (102 mmols)-$KMnO_4$ (5 mmols) for 6 hours at room temperature[7]. The chromatography of the mixture of acidic products on silicic acid yielded several crystalline fractions as a 10% ether in benzene eluate. Repeated crystallization from benzene-petroleum ether gave a keto acid, m.p. 135-139° (Found: C, 64.55; H, 8.95; O, 26.63; C-CH_3, 13.3. $C_{10}H_{16}O_3$ requires C, 65.20; H, 8.74; O, 26.06; 2 C-CH_3, 16.3), IR max ($CHCl_3$) 1709 cm^{-1}, IR max (KBr) 1732 and 1682 cm^{-1}. It was further characterized as a 2,4-dinitrophenylhydrazone, m.p. 212-214° (Found: C, 53.15; H, 5.73. $C_{16}H_{20}O_6N_4$ requires C, 52.74; H, 5.53).

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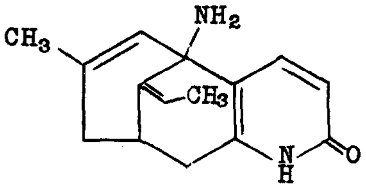
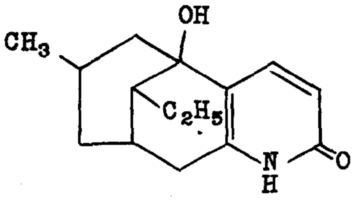
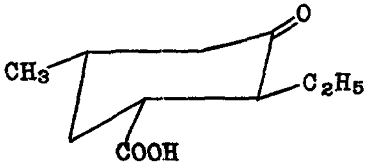
[7] R.U. Lemieux, E. von Rudloff, Can. J. Chem. 33, 1701 (1955).



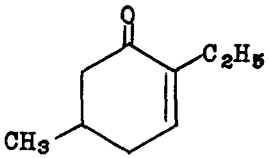
I



II



III



IV

On the basis of the tetrahydroselaginol structure (II), the oxidation product was expected to be 2-ethyl-3-carboxy-5-methyl-*cyclo*hexanone (III).[8] This was confirmed by the following synthesis. The racemic *cyclo*hexenone IV, described previously by Wallach[9], was prepared by the procedure of Nazarov *et al.*[10] from 2-ethyl-5-methyl*cyclo*hexanone[11]. Reflux of IV with KCN in methanol for 4

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[8] The compound could be expected to be equilibrated at the two epimerizable carbon atoms during the basic reaction and the acidic work-up.

[9] O. Wallach, *Ann.* **397**, 181 (1913).

[10] I.N. Nazarov, L.D. Bergel'son, I.V. Torgov and S.N. Ananchenko, *Izvest. Akad. Nauk SSSR.*, *Otdel. Khim. Nauk* **1953**, 889.

[11] A. Kotz, A.Bieber and A.Schwarz, *Ann.* **357**,192 (1907).

hours[12], followed by hydrolysis with boiling conc. HCl for 3 hours, yielded acid III, m.p. 120-123° (Found: C, 65.15; H, 8.59; O, 26.09). Its infrared spectrum in chloroform solution was superimposable with the spectrum of the degradation product. A mixture of the two acids melted at 120-132°. Clearly, the synthetic product is the racemate of the all-equatorial acid III, while the degradation product is one of its enantiomers.

It should be noted that the keto acid III contains all but 5 carbon atoms of the selagine molecule and that its two oxygen functions clearly reveal the double attachment of the α-pyridone ring to the six-membered carboxylic ring. The placement of the two isolated double-bonds into the completely elaborated selagine skeleton presents no difficulties[5].

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[12] E. Adlerová, L. Novák and M. Protiva, Chem. Listy 51, 553 (1957).