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THE STRUCTURE OF VINCAMININE AND VINCININE[1]

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Some time ago, we were able to separate[2,3] the "vincamine fraction"[4] of *Vinca minor L.* into its four alkaloid components: vincamine[5], vincine[3,6], vincaminine[2,3] (= vincareine[7]), and vincinine[2,3]. Later, the structures Ia and Ib were deduced for vincamine[8-10] and vincine[1,11]

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[1] Part XI. For paper X see O. Štrouf and J. Trojánek, Coll. Czech. Chem. Comm. (in press).

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[4] J. Trojánek, J. Hoffmannova, O. Štrouf and Z. Čekan, Coll. Czech. Chem. Comm. 24, 526 (1959).

[5] E. Schlittler and A. Furlenmeier, Helv. Chim. Acta 36, 2017 (1953).

[6] J. Trojánek, K. Kavková, O. Štrouf and Z. Čekan, Coll. Czech. Chem. Comm. 26, 867 (1961).

[7] J. Mokrý, I. Kompiš, O. Bauerová, J. Tomko and S. Bauer, Experientia 17, 354 (1961).

[8] J. Trojánek, O. Štrouf, J. Holubek and Z. Čekan, Tetrahedron Letters 20, 702 (1961).

[9] J. Trojánek, O. Štrouf, J. Holubek and Z. Čekan, Coll. Czech. Chem. Comm. (in press).

[10] M. Plat, D. D. Manh, J. LeMen, M.-M. Janot, H. Budzikiewicz, J. M. Wilson, L. J. Durham and C. Djerassi, Bull. soc. chim. France 1082 (1962).

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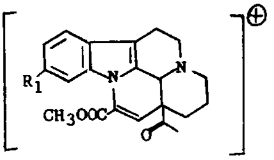
(= 11-methoxy vincamine[10]), respectively. The two remaining alkaloids--vincaminine and vincinine--appeared to be, on the basis of molecular formulas, functional group analyses and spectral (U.V., I.R.) evidence, the oxo-analogues of Ia and Ib, respectively. We assigned[12] the position C_{20} to the carbonyl group in vincaminine and vincinine on the basis of the formation of acetic acid in the modified chromic acid micro-oxidation and on the basis of an I.R. band at 1720 cm^{-1} (chloroform)[3]. Now, in this communication, we present N.M.R., mass spectral and chemical data which confirm the structures Ic and Id for vincaminine and vincinine, respectively.

Vincaminine, $C_{21}H_{24}N_2O_4$, gives a strongly positive iodoform reaction, thereby indicating the presence of a methyl ketone function in the molecule. It forms a hydrazone, m.p. 222-224° (decomp.), I.R. bands in nujol: 1750 cm^{-1} (ester), 1655 cm^{-1} (weak)(C=N) and no band for ketone. The structure of vincaminine is further elucidated by its N.M.R. spectrum. An unsplit methyl peak at 7.61τ indicates a methyl ketone group. Furthermore, the N.M.R. spectra of this alkaloid resemble very closely that of vincamine (Ia)[9,10] except that the above unsplit peak ($\underline{CH_3}$-CO-) is replaced by a triplet ($\underline{CH_3}$-CH_2-) centered at 9.10τ in the latter. The overall pattern due to the aromatic protons (2.4-3.0τ) is identical in vincamine and vincaminine. The methyl protons of the ester group appear at 6.22τ in both alkaloids.



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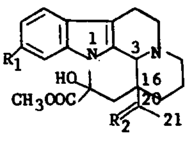
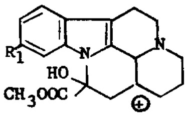


I



D

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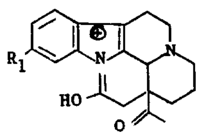
[12] Presented by O. Štrouf in the 2nd International Symposium on the Chemistry of Natural Products, Prague on August 31, 1962.



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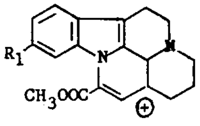

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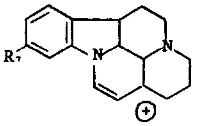

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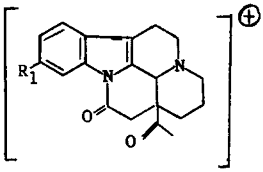

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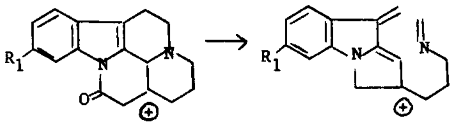

G H

a: R_1=H, R_2=2H ; b: R_1=OCH_3, R_2=2H ; c: R_1=H, R_2=O ; d: R_1=OCH_3, R_2=O

The mass spectrum of vincaminine shows the molecular peak at m/e 368 which proves the correctness of the molecular formula. In the mass spectrum there are a number of peaks (M^+, A, B and C), which correspond to those found in the vincamine spectrum[10] except for an increase of 14 mass units (e.g., CH_2 replaced by CO). Of significance in this connection is the occurence of identical peaks (D-H) in the spectra of both vincamine[10] and vincaminine (table 1). This proves on one hand the skeletal identity of both alkaloids and on the other hand reveals that the two structures differ only in the angular two carbon atom chain. This leads to structure Ic for vincaminine.

Similar analogies were also found in the mass spectra of vincinine, $C_{22}H_{26}N_2O_5$, and vincine (Ib)[10], the corresponding peaks in the former having been shifted again by an increase of 14 mass units (table 1). In this case, however, the molecular peak and the peak due to the fragment ion $(M - COCH_3)^+$ were not detected, though the corresponding dehydrated ions (A and E) were found to be present[14]. This clearly

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13. H. K. Schnoes, A. L. Burlingame and K. Biemann, Tetrahedron Letters 22, 993 (1962).

Table 1

Ion	Vincamine[10] (Ia)	Vincaminine (Ic)	Vincine[10] (Ib)	Vincinine (Id)
M^+	354	368	384	---
A	336	350	366	380
B	295	309	325	(339)
C	294	308	324	338
D	325	325	355	---
E	307	307	337	337
F	249	249	279	279
G	265	265	295	295
H^*	237	237	267	267

* The ion H is typical for the eburnamonine type structure and arises from ion G by retro Diels-Alder cleavage of ring C followed by the loss of C=O[13]. The ion F is prominent in the mass spectrum of eburnamine.

points out the relation between the structures of the above two alkaloids and also confirms the previously[12] assigned structure Id for vincinine.

We are thankful to Dr. J. Fried and Prof. C. Djerassi for the mass spectra of vincaminine and vincinine.

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[14] 14. Similar behavior was observed in the case of eburnamine, too[10].