COMMUNICATIONS

The structures of three alkaloids from Fumaria officinalis L.

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Structures are proposed for three alkaloids isolated from *Fumaria officinalis* L. The three alkaloids, with a common ring system, are structurally related to the known ochotensimine. Canadian Journal of Chemistry, 46, 2873 (1968)

In 1938 Manske (1) reported the isolation of alkaloid, F-37 (1), from *F. officinalis*. More recently two related alkaloids, 2 and 3, have been isolated by Manske (2) from the same source. Compound 2, a lower homologue of 1, is converted to 1 with diazomethane. The first clue that 3 has a ring system similar to 1 and 2 came from an examination of the mass spectra of 1, 2, and 4 (the product obtained by reduction of 3 with lithium aluminium hydride). The fragmentation of the three compounds was similar, showing the shifts expected because of the nature of their substituents. Evidence is presented that the alkaloids have structure A.



1 ${}^{1}C_{21}H_{23}NO_{5}$; ${}^{2}R_{1} + R_{2} = H + OH$; $R_{3} = R_{4} = CH_{3}$; m.p. 177°; $[\alpha]_{D} = -31^{\circ} (c = 0.97 \text{ in CHCl}_{3}).$

¹The names fumaricine and fumariline are suggested for 1 and 3, respectively. ²The molecular formulas of the three natural com-

²The molecular formulas of the three natural compounds were assigned on the basis of elemental analysis and high resolution mass spectrometry; in the case of **4** the assignment is based on mass spectrometry alone.

$$2 C_{20}H_{21}NO_5; R_1 + R_2 = H + OH;R_3 + R_4 = H + CH_3; m.p. 157^{\circ}.$$

 $\begin{array}{l} 3 \ \mathrm{C_{20}H_{17}NO_5; R_1 + R_2 = O; R_3 + R_4 = } \\ \mathrm{CH_2; m.p. \ 138^\circ; \ } [\alpha]_{\mathrm{D}} = +138^\circ \ (c = 1.05 \\ \mathrm{in \ CHCl_3).} \end{array}$

$$\begin{array}{l} 4 \text{ } \text{C}_{20}\text{H}_{19}\text{NO}_5; \text{ } \text{R}_1 + \text{R}_2 = \text{H} + \text{OH}; \\ \text{R}_3 + \text{R}_4 = \text{CH}_2; \text{ m.p. 161-166}^\circ \text{ (d)}. \end{array}$$

Because of the paucity of the natural bases and their sensitivity to simple chemical reagents our structural assignment is based primarily on physical evidence. The physical properties of **3** are: λ_{max} (EtOH) 203, 237, 263, 294, and 355 mµ (log ϵ 4.60, 4.31, 4.05, 3.66, and 3.51) and ν_{max} (CHCl₃) 1709 cm⁻¹; of **1**: λ_{max} (EtOH) 207, 235, and 288 mµ (log ϵ 4.74, 3.94, and 3.74), and ν_{max} (CS₂) 3560 cm⁻¹ (unchanged upon dilution). It is noteworthy that the ultraviolet (u.v.) spectrum of **4** was virtually superimposable on that of **1** and that its infrared spectrum showed a similar absorption in the hydroxyl region. The change in u.v. absorption in the transformation, **3** \rightarrow **4**, is indicative of the reduction of a conjugated carbonyl group.

The proton magnetic resonance spectrum (p.m.r.) of **3** shown in Fig. 1*a*, revealed the presence of: (*i*) four aromatic protons, two ortho to each other (δ_{HA} , 7.07, δ_{HB} , 6.86; $J_{AB} = 8.0$ Hz) and two para to each other ($\delta_{HA'}$, 6.54, $\delta_{HB'}$, 6.16; $J_{A'B'} \cong 0$ Hz); (*ii*) two sets of methylenedioxy protons centered at $\delta = 6.12$ and $\delta = 5.80$; (*iii*) six aliphatic protons in the region δ 3.60–2.60 two of which are present in a benzylic AB quartet ($\delta_{HA''}$, 3.50, $\delta_{HB''} = 3.32$; $J_{A'B''} = 18.0$ Hz) while the other four are not readily analyzable;



and finally (iv) a singlet (3H) at $\delta = 2.36$ attributed to an > N-CH₃ group.

In the p.m.r. spectrum of 4 the hydrogen geminal to the hydroxyl group was uncoupled to neighboring aliphatic protons, an observation compatible with the fact that 3 would not exchange hydrogen for deuterium under the usual conditions of exchange of enolizable hydrogens (3). Thus it seems that the carbonyl of 3 is flanked on one side by a phenyl group and on the other by a quaternary center. These data suggest that 3 may have the gross structure A.

In order to substantiate gross structure A and to establish the orientation of the methylenedioxy groups in 3 a detailed comparison of the p.m.r. spectrum of 3 with the synthetic compound 5 (Fig. 1b) of established structure (4) was undertaken. Cursory examination of the spectra of 3and 5 reveals a remarkable similarity particularly in the region of the aliphatic protons (δ 2.6–3.6). In the aromatic region, too, the two spectra exhibit a common pattern and differ appreciably only in the chemical shift of the low field protons of the AB quartet.

These observations imply that 3 and 5 have a common ring system but may differ in substitution pattern as well as in the nature of their substituents. Moreover, the product of hydride reduction of 5, an isomer of 1, has a mass spectrum virtually identical with the natural base 1. lending further support to the assumption of a common ring system in 1, 2, 3, and 5.

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By locating the methylenedioxy group of 3 at C-12 and C-13 instead of at C-10 and C-11 as in 5, the properties of 3 are explicable. H_A in 5 is ortho to the carbonyl group whereas in 3 it is para. The chemical shift difference of H_{A} between 3 and 5 is expected of aromatic protons ortho and para to a carbonyl group (5), respectively. In each case H_B is meta to the carbonyl and absorbs at approximately the same region. H_{A} and H_{B} are long-range coupled to the AB quartet centered near 3.40 in 3 and 5 and in each the coupling is

stronger to H_{B} . (See Fig. 1a and 1b.) H_{B} is ortho to the methylene group in 3 and para in 5 whereas H_A is meta in both. The coupling of the methylene to H_B in 3 (J = 1.2 Hz) is stronger than with H_B in 5 (J < 1.0 Hz). This difference is in the order expected for ortho and para benzylic coupling (6). $H_{A'}$ in 3 and 5 is broader than $H_{B'}$, because of *o*-benzylic coupling to one or both of the protons at C-5 and is, therefore, assigned to C-4. The assignment of the same substitution pattern to 1 as to 3 rests on a study of nuclear Overhauser effects discussed in an accompanying communication (7). These alkaloids have the same basic skeleton as ochotensimine (8). Whether they are precursors or oxidation products of the latter skeleton is an interesting biogenetic puzzle.

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- 1. R. H. F. MANSKE. Can. J. Research, 16B, 438 (1938).
- R. H. F. MANSKE. To be published.
 H. BUDZIEKIEWICZ, C. DJERASSI, and D. H. WILLIAMS. Structure elucidation of natural products by mass spectrometry. Vol. I. Holden-Day Inc., San Francisco.
- spectrometry. Vol. I. Holden-Day Inc., San Francisco. 1964. p. 19.
 S. McLEAN, M.-S. LIN, and J. WHELAN. Tetrahedron Letters, No. 20, 2425 (1968).
 J. W. EMSLEY, J. FEENEY, and L. H. SUTCLIFFE. High resolution nuclear resonance spectroscopy. Vol. 11. Pergamon Press Ltd., Oxford. 1966. p. 750.
 D. T. WITTIAK, D. B. PATEL, and Y. LIN. J. Am. Chem. Soc. 89, 1908 (1967).
 J. K. SAUNDERS, R. A. BELL, C.-Y. CHEN, D. B. MACLEAN, and R. H. MANSKE. Can. J. Chem. This issue.
- issue.
- MCLEAN and M.-S. LIN. Tetrahedron Letters, 8. 3819 (1964). S. McLean, M.-S. LIN, A. C. Mac-DONALD, and J. TROTTER. Tetrahedron Letters, 185 (1966). S. McLean, M.-S. LIN, and R. H. F. MANSKE. Can. J. Chem. 44, 2449 (1966).

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