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THE STRUCTURE AND CONFIGURATION OF CASEAMINE AND CASEADINE TWO NOVEL TETRAHYDROPROTOBERBERINES FROM CORYDALIS CASEANA A. GRAY

C.-Y. Chen*, D. B. MacLean*, and R. H. F. Manske**

*Department of Chemistry, McMaster University, Hamilton, Ontario

**Research Laboratories, Uni-Royal Limited, Guelph, Ontario

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Some years ago, one of us (R.H.F.M.) (1) isolated two phenolic alkaloids, F-33(I) and F-35(II), from Corydalis caseana A. Gray for which we propose the names of caseamine and caseadine, respectively. We now present evidence that these alkaloids are tetrahydroprotoberberines with an unusual 1,2, - dioxygenation pattern.

Caseamine (I), $C_{19}H_{21}NO_4$, melted at 257° and had the following physical constants: $[\alpha_D]$ - 406° (C = 0.12 in $CHCl_3$), $\lambda_{max}^{EtOH\dagger}$ 206, 228 (sh), and 286 mμ(log ε 4.85, 4.07, and 3.71).

Caseadine (II), $C_{20}H_{23}NO_4$, melted at 145° and had the following physical constants: $[\alpha_D]$ - 393° (C = 1.12 in $CHCl_3$), λ_{max}^{EtOH} 206, 228 (sh), and 286 mμ(log ε 4.82, 4.08, and 3.74), $\nu_{max}^{CHCl_3}$ 3530 cm^{-1} (s) (ortho-OH weakly bonded to a methoxy group), 2745 cm^{-1} (w) (Bohlmann band). Upon methylation with diazomethane, both caseamine (I) and caseadine (II) gave the same tetramethoxy derivative (III) which melted at 186° and had the following physical constants: $[\alpha_D]$ - 360° (C = 0.4 in $CHCl_3$), λ_{max}^{EtOH} 206, 228 (sh), and 286 mμ(log ε 4.81, 4.11, and 3.72), $\nu_{max}^{CHCl_3}$ 2740 cm^{-1} (w), Bohlmann bands. The U. V. spectrum of III suggested (2) a tetrahydroprotoberberine skeleton. Further evidence for this skeleton came from the mass spectrum of III (FIG. 1,) which is typical (3) of that of tetrahydroprotoberberine alkaloids. The fact that III is not identical with any of the known tetramethoxy tetrahydroprotoberberines recorded in the literature (4) indicated that we had a tetrahydroprotoberberine with a novel substitution pattern.

The p.m.r. spectrum of caseadine (II) was most informative. The spectrum after exchange with D_2O is represented in FIG. 2. The aromatic region, reproduced in the inset, suggests that of the four aromatic protons, two are ortho to each other (τ_{HA} 3.10, τ_{HB} 3.16, and J_{AB} =

[†] The spectrometers used in this study were: i) p.m.r.: Varian A-60, ii) Infra-red: Perkin-Elmer 521 and iii) Ultraviolet: Cary Model 14-R.

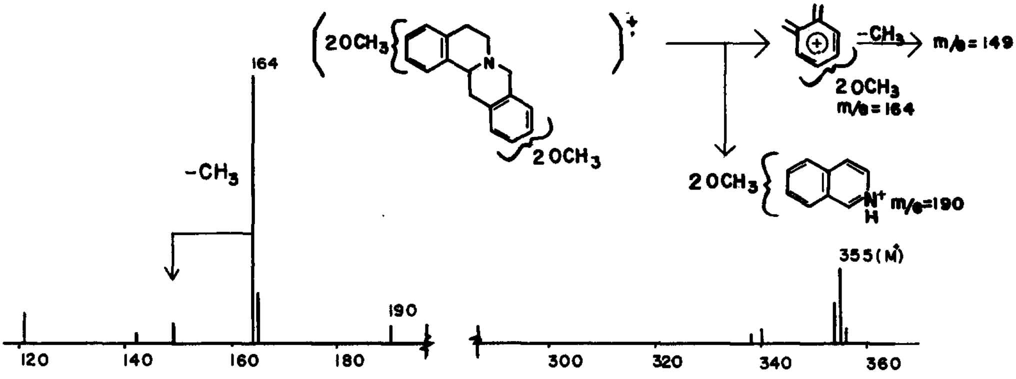


FIG. 1

The mass spectrum of caseadine O-Me ether (III)

8.4 Hz) and two are para to each other (τ_{HC} 3.21, τ_{HD} 3.24 and $J_{CD} \cong 0$ Hz). It is of interest to note that protons H_B, H_C, and H_D were all long-range coupled (5) to neighbouring benzylic protons resulting in relatively broad signals compared with that of H_A, a phenomenon

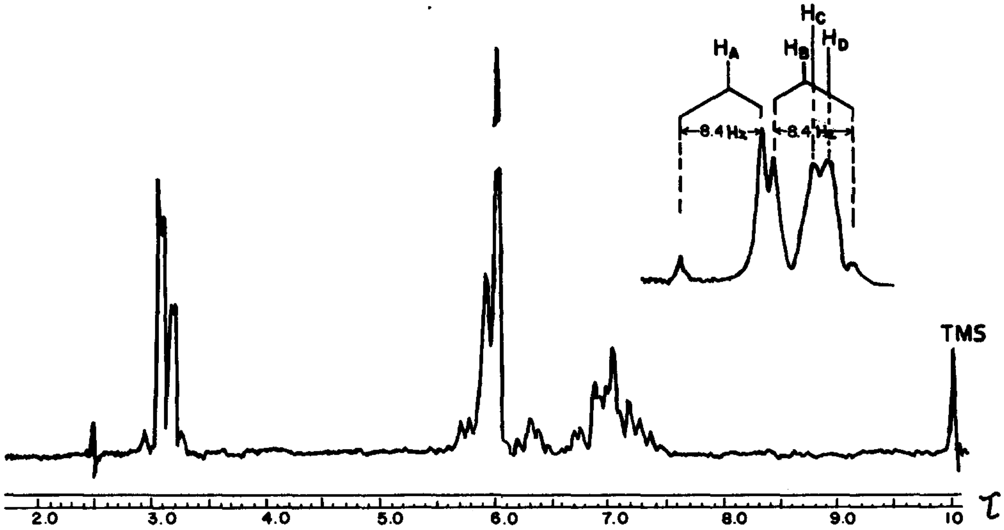
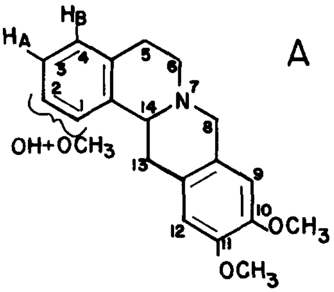
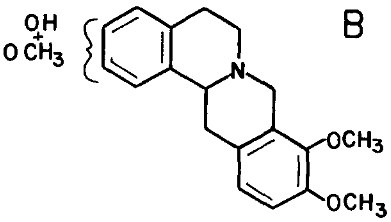


FIG. 2

The p.m.r. spectrum of caseadine in $CDCl_3$ after D_2O exchange


A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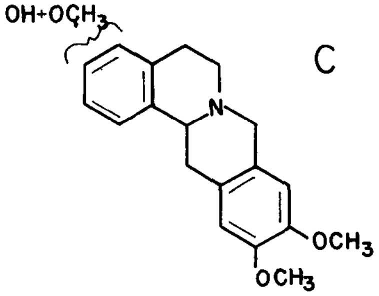
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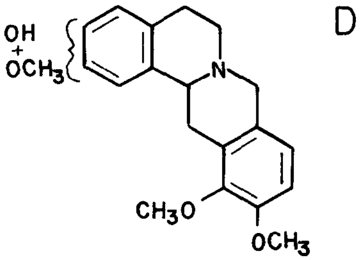

D

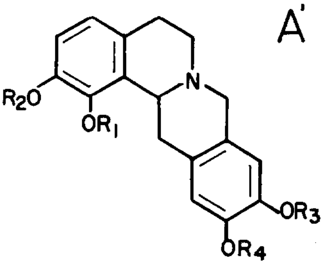
which was helpful in the determination of the orientation of the hydroxyl group in caseadine.

The n.m.r. data and the observation that the mass spectrum of caseadine showed prominent peaks at m/e 341, 176, and 164 requires that it should have one of the above substitution patterns.

Structure B is dismissed because caseadine O-Me ether (III) is not identical with (-) tetrahydropalmatine. Structure C is unlikely on biogenetic grounds (6) since protoberberines are generally regarded as derived from benzylisoquinoline precursors and, so far, only the precursors with either 6,7 or 7,8 oxygenation pattern are known. When caseadine was dissolved in ca. 12 N DCl and heated briefly, one of the aromatic protons was exchanged. The p.m.r. spectrum of monodeuterated caseadine (IV) showed that the signal due to H_B had disappeared and that the doublet from H_A had collapsed into a broad singlet. Since it has been established (7) that, under these conditions, only the hydrogens ortho and/or para to a phenolic hydroxyl group will exchange, the p.m.r. data definitely rule out the possibility that caseadine might have the structure B or D. Therefore, it should have structure A and the hydroxyl group in caseadine must be at C_1. The insolubility and the paucity of caseamine

(I) did not permit a detailed p.m.r. study to define the orientation of the substituents. Nevertheless, the mass spectrum of I exhibited prominent peaks at m/e 327, 178, and 150 indicating that the two hydroxyl groups were not on the same ring. We thus concluded that caseamine (I) and caseadine (II) have the novel structure A' as illustrated.

A'



CASEAMINE (I)

$R_1 + R_2 = R_3 + R_4 = H + CH_3$

CASEADINE (II)

$R_1 = H$

$R_2 = R_3 = R_4 = CH_3$

The presence of a "trans" quinolizidine nucleus in caseadine is revealed by the presence of Bohlmann bands (8) in its i.r. spectrum. The large negative optical rotation in $CHCl_3$ of caseadine indicates that the hydrogen at C_{14} should have an α-orientation as indicated (9). Accordingly, the relative and absolute configuration of caseadine (II) and therefore, of caseamine (I) and the compound III should be that given in FIG. 3.

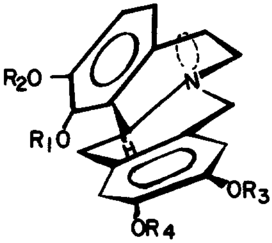


FIG. 3

The relative and absolute configuration of caseamine (I) and caseadine (II)

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