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PROCUMBINE, A NEW SECOBERBINE ALKALOID ≠

Eva Táborská[a], František Věžník[a], Jiří Slavík[a], Petr Sedmera[b],
and Vilím Šimánek[c+]

a. Department of Medical Chemistry and Biochemistry, Purkyně
University, 662 43 Brno, Czechoslovakia

b. Institute of Microbiology, Czechoslovak Academy of Sciences,
142 20 Prague, Czechoslovakia

c. Institute of Medical Chemistry, Palacký University,
775 15 Olomouc, Czechoslovakia

Abstract —— The structure determination of the secoberbine alkaloid procumbine (2) isolated from Hypecoum procumbens and H. leptocarpum is reported.

The alkaloids from Hypecoum procumbens L. and H. leptocarpum Hook f. et Thoms (Papaveraceae) have been the subject of several investigations[1-6]. Recently, we have reported on the isolation of alkaloids from the whole plants of both species[7]. In addition, we have isolated, in low yield, an orange-red base to which we have assigned the trivial name procumbine. The structure of procumbine is described in the present communication.

Procumbine, an optically inactive compound, mp 191-192°C (MeOH), was obtained by repeated crystallization of the quaternary alkaloids fraction[7]. It gave a positive $FeCl_3$ test for phenols. Its uv spectrum is characteristic of cyclic secoberbines of the hypecorinine type (1) and is pH-dependent (Fig. 1)[8,9]. The ^1H nmr spectrum of procumbine in $CDCl_3$ (Table 1) showed the presence of two tetrasubstituted benzene rings (one of them with two para protons and the other with two ortho protons), one methoxyl, one methylenedioxy group, one $-NCH_3$ group, and one phenolic group. The aliphatic part of the spectrum also

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≠ Dedicated to Professor Tetsuji Kametani on the occassion of his 70th birthday

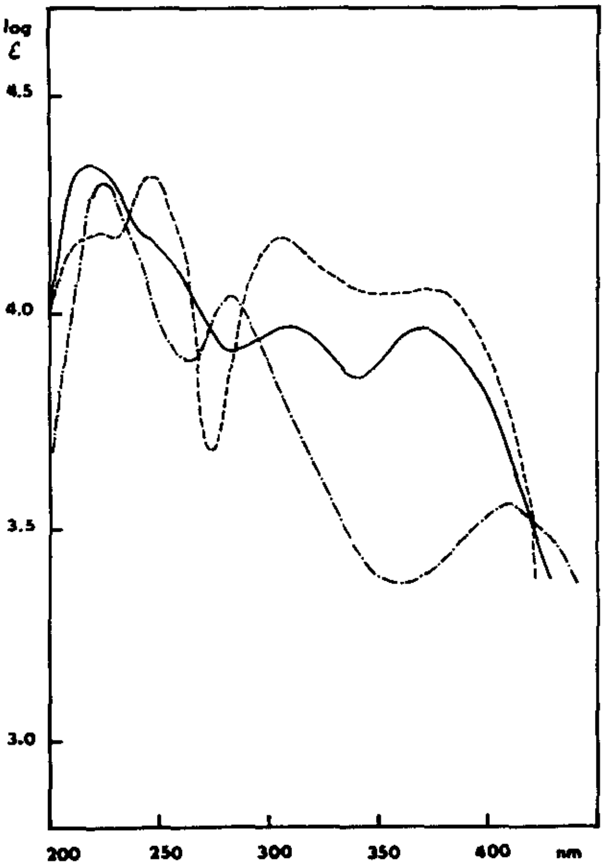
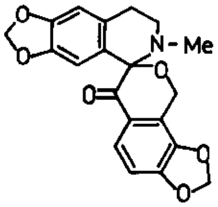


Fig. 1. Uv spectra of procumbine (2) in methanol (——), in 0.01 M methanolic NaOH (-.-.) and in 0.01 M methanolic HCl (---).

exhibited one four-protons multiplet. In CD_3OD, the $-NCH_3$ singlet is shifted downfield by 0.94 ppm and aliphatic part of the spectrum displays two two-protons triplets (Table 1). The ^{13}C nmr spectrum showed 20 lines corresponding to the 20 carbon atoms of the molecule (Table 1). This spectrum revealed the presence of four methine sp^2 carbons, one methoxyl, one $-NCH_3$ group, one methylenedioxy group, and two methylene groups. Chemical shifts of both methylene carbons correspond to the moiety $Ar-CH_2-CH_2-N$. The molecule also contains two carbonyl groups. One of these resonates at 189.6 ppm, typical for a conjugated carbonyl group, the other, at 169.1 ppm, belongs to the carboxyl carbon of the corresponding lactone fragment. Of nine quaternary carbons, four singlets correspond to sp^2 carbons bound to oxygen, four sp^2 carbons bound to carbon, and the singlet at 111.6 ppm is due to sp^3 carbon bound to oxygen with the vicinal electron-negative substituent. The ir spectrum (KBr) exhibited strong absorptions at 1655 and 1638 cm^{-1} due to a six-membered lactone and conjugated carbonyl groups.

Spectral data indicate that procumbine belongs to the secoberbine type structurally related to hypecorinine (1)[10]. It differs from 1 by substitution on ring A and by the oxo group at the C-8 position. The position of the methoxyl on ring A can be deduced from its chemical shift (Table 1). In the tetramethoxy analog of hypecorinine, the methoxyl singlet at 3.66 ppm is characteristic of the C-2 substituent[9]. The methoxyl resonating at 4.04 ppm (Table 1) must be attached to C-3 position of ring A.

The spectral data support the proposed cyclic secoberbine structure (2) for procumbine. Further proof was obtained from the mass spectrum[11]; in addition to the molecular ion at m/z 383 which confirmed the molecular formula $C_{20}H_{17}NO_7$ deduced by elemental analysis[7], the position of substituents on both aromatic nuclei is determined by fragments a at m/z 190 ($C_{11}H_{12}NO_2$) and b at m/z 194 ($C_9H_6O_5$). The ion b loses water and yields the fragment c at m/z 176 ($C_9H_4O_4$).



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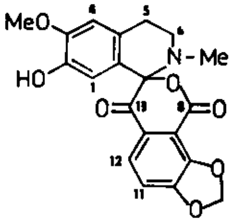

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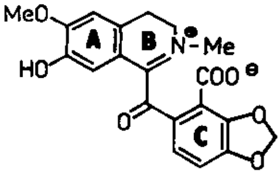

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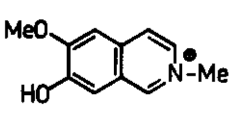
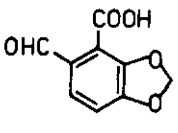


a



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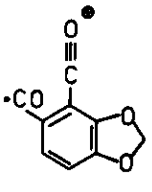

c

Shamma et al.[12] suppose that *secoberbines are biogenetically derived from* protoberberines. Except hypecorinine (13-oxohypecorine, 1) and hypecorine, all known secoberbine alkaloids possess a 1-benzyltetrahydroisoquinoline skeleton with hydroxymethyl, formyl or carboxyl group on the ring C at position 2'[13]. The pH-dependent changes in uv spectra of procumbine (2) indicate an equilibrium between the cyclic form 2 and the open form of quaternary iminium salt of the secoberbine carboxylic acid 3. Procumbine (2) represents another intermediate stage in biogenetic transformations of *protoberberines into other structural* types of isoquinoline alkaloids.

Table 1. ^{1}H (59.80 MHz) and ^{13}C (15.04 MHz) nmr data of procumbine (2)

Proton	$CDCl_3$	CD_3OD	Carbon[a]	$CDCl_3$
1-H	6.64s	6.91s	1	106.3
4-H	6.33s	6.51s	2	146.6
5-H_2	3.12m	3.16t (J 6.1)	3	149.4
6-H_2		4.00t (J 6.1)	4	108.4
11-H	7.20d (J 8.5)	7.19d (J 8.5)	4a	135.0
12-H	7.80d (J 8.5)	7.53d (J 8.5)	5	28.3
N-CH_3	2.69s		6	46.7
N^+-CH_3		3.63s	8	169.1
O-CH_3	4.04s	3.96s	8a	135.0
OH	12.68bs		9	152.3
OCH_2O	5.90s	6.02s	10	155.2
			11	115.3
			12	121.0
			12a	125.0
			13	189.6
			14	111.6
			14a	124.8
			OCH_3	56.5
			N-CH_3	39.6
			OCH_2O	101.6

[a] tentative assignment

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7. E. Táborská, M. Mikešová, F. Věžník, and J. Slavík, Coll. Czech. Chem. Commun., 1987, **52**, 508. We isolated 23.0 mg of procumbine from H. procumbens (6.11 kg of dry plant) and 3.3 mg of that from H. leptocarpum (3.90 kg of dry plant). Anal. Found: C, 62.66; H, 4.31, M, 3.61. $C_{20}H_{17}NO_7$ requires: C, 62.66; H, 4.43; N, 3.65%.
8. Uv spectra of procumbine: λ_{max} (MeOH) 222, 247sh, 310, and 370 nm (log ε 4.35, 4.19, 3.96, and 3.96); λ_{max} (0.01 M NaOH) 224, 285, and 408 nm (log ε 4.30, 4.04, and 3.57); λ_{max} (0.01 M HCl) 247, 304, and 370 nm (log ε 4.34, 4.18, and 4.05).
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11. Ms (m/z, rel. intensity, %) 383 (M^+, 3.8), 339 (1.1), 338 ($C_{19}H_{16}NO_5$, 1.6), 324 (1.1), 310 ($C_{18}H_{16}NO_4$, 3.2), 206 ($C_{11}H_{12}NO_3$, 9.7), 194 ($C_9H_6O_5$, 23), 191 (8), 190 ($C_{11}H_{12}NO_2$, 100), 189 (12), 188 ($C_{11}H_{10}NO_2$, 17), 176 ($C_9H_4O_4$, 10), 165 ($C_8H_5O_4$, 10), 150 (6.5), 148 ($C_8H_4O_3$, 27), 147 (C_8H_9NO, 13.5), 122 ($C_7H_6O_2$, 16).
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