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MINOR ALKALOID FROM *COSCINIUM FENESTRATUM**

S. Malhotra, S. C. Taneja and K. L. Dhar

Natural Products Chemistry Division, Regional Research Laboratory, Canal Road, Jammu-Tawi 180001, India

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Key Word Index—*Coscinium fenestratum*; Menispermeaceae; stem; 12,13-dihydro-8-oxo-berberine; ^{13}C NMR.

Abstract—*Coscinium fenestratum* furnished a new minor alkaloid, 12,13-dihydro-8-oxo-berberine, [5,6,13,13a-tetrahydro-9,10-dimethoxydibenzo(*a,g*)1,3-benzodioxolo(5,6a)quinalizine-8-one], as well as berberine, oxyberberine, tetrahydroberberine (canadine), sitosterol and stigmasterol.

INTRODUCTION

Coscinium fenestratum (N. O. Menispermeaceae) is well known for its medicinal properties [1–4]. Recent studies in our laboratory showed that it possesses marked anti-hypertensive activity. Recently its activity against tetanus has also been investigated [5].

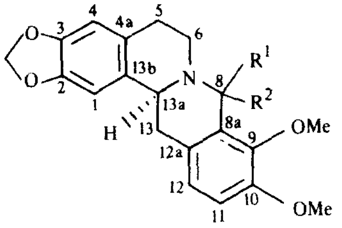
RESULTS AND DISCUSSION

A literature review indicated the presence of several alkaloids in sister species of *C. fenestratum* [6, 7]. Our studies established that the stem of the plant is rich in berberine (5%). Apart from 12,13-dihydro-8-oxo-berberine five other compounds have also been isolated and identified as berberine, oxyberberine, tetrahydroberberine (canadine), sitosterol and stigmasterol.

Compound **1**, mp 218°, analysed for $C_{20}H_{19}NO_5$ ($[M]^+ m/z$ 353) and has been characterized as 5,6,13,13a-tetrahydro-9,10-dimethoxy dibenzo(*a,g*)1,3-benzodioxolo(5,6a)quinalizine-8-one (12,13-dihydro-8-oxo-berberine) from the following studies.

In its ^1H NMR characteristic protoberberine signals for methoxyl, methylene dioxy and four aromatic protons were observed. The signals for the H-6a proton appeared at $\delta 3.79$ as a singlet and H-6e as doublet at $\delta 4.95$. The benzylic protons appeared at $\delta 2.82$ and 2.98, respectively. The position of H-13a was located at $\delta 4.61$–4.78 as a double doublet. The relationship between H-13a and the benzylic proton was established by double irradiation experiments, where on irradiating the latter signal a singlet for H-13a and H-6a was produced. Similarly irradiation of signals for H-6a and H-6e resulted in the simplification of the benzylic proton signals.

When **1** was treated with alkaline potassium permanganate it formed noroxyhydrostane (**3**) (identified by lit. comparison [8,9]) thus establishing the presence of a methylenedioxy group in ring A. The structure of **1** was further confirmed by its partial transformation from tetrahydroberberine [10,11]. Controlled oxidation of tetrahydroberberine (**2**) with potassium permanganate in acetone resulted in the formation of several oxidation products. Purification by CC gave **1** as one of the minor



1 $R^1, R^2 = {=}O$

2 $R^1, R^2 = H$

Table 1. ^{13}C NMR spectra of compounds **1** and **2**

	Chemical shift ($CDCl_3$)	
C	**1**	**2**
1	106.0 *d*	104.0 *d*
2	147.0 *s*	145.2 *s*
3	147.0 *s*	145.4 *s*
4	108.5 *d*	107.0 *d*
4a	129.0 *s*	127.7 *s*
5	39.1 *t*	35.0 *t*
6	39.1 *t*	51.0 *t*
8	163.0 *s*	53.4 *t*
8a	122.8 *s*	126.2 *s*
9	152.2 *s*	144.1 *s*·
10	149.5 *s*	149.4 *s*
11	115.5 *d*	110.0 *d*
12	121.4 *d*	123.0 *d*
12a	131.0 *s*	126.2 *s*
13	38.0 *t*	28.1 *t*
13a	61.2 *d*	55.2 *d*
13b	129.0 *s*	129.0 *s*
$\begin{matrix}-O\\-O\end{matrix}\rangle CH_2$	101.0 *t*	100.9 *t*
–OMe	55.0 *q*	59.0 *q*
–OMe	56.1 *q*	59.2 *q*

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products (5%) together with noroxyhydrostane (**3**) as the major oxidation product. ^{13}C NMR signal assignments for structure (**1**) were also made by comparison with data for tetrahydroberberine (**2**) (Table 1). Recently ^{13}C NMR data for berberine and sanguinarine has been recorded by C. Blaskó *et al.* [12]. The mass spectral fragmentation of the compound also supported the proposed structure.

Recently a compound namely lemiocranine [13] with the same molecular formula and related features has been isolated from *B. darwinii*. However, comparison of the spectral data of **1** and lemiocranine, showed that they possess different structures.

EXPERIMENTAL

General. Mps: uncorr. ^1H NMR were recorded at 60 and 90 MHz.

Plant material. Stems of *C. fenestratum* Colebr. were collected from the Attapadi forest in Western Ghats, Kerala, India and identified by AICRPE Division, RRL, Jammu. The $CHCl_3$ extract of the dried and powdered plant material was subjected to CC on silica gel G.

Compound (**1**). Mp 218 °C, $[\alpha]_D^{28^\circ}$(MeOH) -40, analysed for $C_{20}H_{19}NO_5$ (observed C 67.8, H 5.2, N 3.8, required C 67.98, H 5.38 and N 3.96%). λ_{max}^{MeOH} 277 nm, −ve Cotton effect; ν_{max}^{KBr} cm^{-1}, 2945, 1645, (C=O), 1540, 1500, 1388, 1240, 1160 (OMe), 1020, 930, $\left(\begin{matrix}-\mathrm{O}\\-\mathrm{O}\end{matrix}\!>\mathrm{CH_2}\right)$ and 910. ^1H NMR ($CDCl_3$) δ: 6.95 (*s*, 2H, H-11 and H-12), 6.70 (*s*, 2H, H-1 and H-4), 5.90 $\left(s,\ 2\mathrm{H},\ \begin{matrix}-\mathrm{O}\\-\mathrm{O}\end{matrix}\!>\mathrm{CH_2}\right)$ 4.95 (*d*, 1H, $J = 5$ Hz, H-6e), 4.61–4.78 (*dd*, 1H, $J = 5$ and 11 Hz, H-13a), 4.0 (*s*, 3H, –OMe), 3.84 (*s*, 3H, –OMe), 3.79 (*s*, 1H, H-6a), 2.98 (*d*, 2H, $J = 5$ Hz, H-13), 2.82 (*s*, 2H, H-5). MS *m/z* 353 $[M]^+$ 338, 310, 296, 281, 267, 178 (66%), 176, 148, 144.

Alkaline oxidation. To a soln of **1** (25 mg) in dry Me_2CO (3 ml) and 10% NaOH (1 ml), $KMnO_4$ (40 mg) in Me_2CO was added with continuous stirring at room temp. After one hr of stirring, the reaction mixt. was worked-up to afford compound **3**, identified as nor-oxyhydrostane, mp 188° (lit. 188) $[M]^+$ *m/z* 191, ^1H NMR CCl_4 δ: 7.4 (*br s*, 1H, H-1), 6.6 (*br s*, 1H, H-4), 6.0 $\left(s,\ 2\mathrm{H},\ \begin{matrix}-\mathrm{O}\\-\mathrm{O}\end{matrix}\!>\mathrm{CH_2}\right)$, 3.98 (*br s*, 2H, H-6), 3.0–2.9 (*br s*, 2H, H-5).

Partial oxidation of tetrahydroberberine. THB (250 mg), in Me_2CO (50 ml) was refluxed with $KMnO_4$ for 45 min and then worked-up as usual. Sepn by CC afforded different products and one of them was identified as **1** by direct comparison with the isolated natural compound (co-TLC, mmp and spectral studies); yield 5%.

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