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(±)-8-OXOHYPECORININE FROM *HYPECOUM PROCUMBENS* VAR. *GLAUCESCENS*

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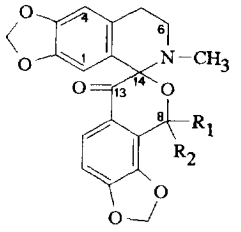
Key Word Index—*Hypecoum procumbens* var. *glaucescens*; Hypecoaceae; isoquinoline alkaloids; secoberbines; (±)-8-oxohypecorinine; (±)-hypercorinine; aporphines; isocorydine; protopines; allocryptopine; cryptopine; protopine.

Abstract—A new secoberbine alkaloid, (±)-8-oxohypecorinine, together with (±)-hypecorinine, isocorydine, allocryptopine, cryptopine and protopine were isolated from *Hypecoum procumbens* var. *glaucescens* and spectroscopically characterized.

INTRODUCTION

The genus *Hypecoum* [1] comprises *ca* 15 species growing in the Mediterranean region, central Asia, Pakistan and northern China [2]. It is represented in Egypt by nine species [1]. Although nothing could be traced in the current literature about the phytochemical study of *H. procumbens* var. *glaucescens* native to Egypt, the alkaloids of *H. procumbens* growing in different localities has been the subject of several investigations [3–10]. Protopines, berbines, secoberbines, benzophenanthridines and aporphines were reported as major groups [4]. In continuation of our work on *Hypecoum* species of Egypt [11], the alkaloids of *H. procumbens* var. *glaucescens* were investigated. It afforded, in addition to (±)-hypecorinine (**1**), isocorydine, allocryptopine, cryptopine and protopine, the new secoberbine alkaloid (±)-8-oxohypecorinine (**2**), whose structure elucidation is described herein.



$R_1 + R_2 = H_2$ **1**

$R_1 + R_2 = O$ **2**

RESULTS AND DISCUSSION

From whole plants of *H. procumbens* var. *glaucescens*, the new optically inactive secoberbine alkaloid, (±)-8-oxohypercorinine (**2**), and five known tertiary bases belonging to the secoberbine ((±)-hypercorinine **1** [11, 12]) aporphine (isocorydine [13]) and protopine (allocryptopine [14], cryptopine [14], protopine [14]) groups were isolated.

(±)-8-Oxohypecorinine (**2**), was obtained as an amorphous orange powder from the chloroform–isopropanol extract by column chromatography and preparative TLC. It showed UV maxima of a secoberbine alkaloid of the hypercorinine type, but with a strong bathochromic shift for the band at longer wavelength. The IR spectrum demonstrated two carbonyl adsorption bands at 1665 and 1645 cm^{-1} of a six-membered lactone and a conjugated ketone [10]. The EI-mass spectrum displayed a weak $[M]^+$ at *m/z* 381 consistent with the molecular formula $C_{20}H_{15}NO_7$ (calcd 381.08484) with an unsaturation number of 14. The ^1H NMR (Table 1) showed close resemblance with (±)-hypecorinine (**1**) by signals for four aromatic protons at δ6.61 (H-1), 6.73 (H-4), 7.01 (H-11) and 7.90 (H-12) of two tetrasubstituted benzene rings and two methylenedioxy protons at δ5.99 and 6.11. However, it was significantly different from **1** by the absence of the CH_2-8 proton resonances of δ4.79 (1H, *d*, J = 15.9 Hz) and 5.14 (1H, *d*, J = 15.9 Hz), the strong downfield shift of N-Me protons to δ2.71 and the resonance of the other protons at lower fields by *ca* 0.1–0.2 ppm. These features together with an extra oxygen atom in the molecular formula of **2** indicate that the two methylene hydrogens in (±)-hypecorinine **1** were replaced by an oxygen atom as part of a lactone fragment in **2**.

Structure **2** was finally established by detailed analysis of its ^{13}C NMR and DEPT spectra (Table 1). It revealed

Table 1. ^1H and ^{13}C NMR spectral data (360, 90 MHz, $CDCl_3$) of **1** and **2**

Atom	δ_H		δ_C^*	
	1	**2**	**1**	**2**
1	6.52 *s*	6.61 *s*	107.9 *d*	107.7 *d*
2	—	—	147.6 *s*	147.1 *s*
3	—	—	151.9 *s*	151.0 *s*
4	6.62 *s*	6.73 *s*	108.7 *d*	108.3 *d*
4a	—	—	125.6 *s*	126.4 *s*
5	3.39 *m* 3.05 *m*	3.1–4.0 *m*	24.7 *t*	28.1 *t*
6	2.60 *m* 2.93 *m*	3.1–4.0 *m*	45.6 *t*	46.2 *t*
8	4.79 *d* (15.9) 5.14 *d* (15.9)	—	57.4 *t*	170.1 *s*
8a	—	—	125.2 *s*	135.0 *s*
9	—	—	145.7 *s*	152.8 *s*
10	—	—	145.7 *s*	154.3 *s*
11	6.88 *d* (8.3)	7.01 *d* (8.5)	107.9 *d*	114.5 *d*
12	7.79 *d* (8.3)	7.90 *d* (8.5)	124.1 *d*	121.0 *d*
12a	—	—	129.5 *s*	126.0 *s*
13	—	—	192.2 *s*	191.1 *s*
14	—	—	91.4 *s*	110.6 *s*
14a	—	—	123.0 *s*	125.1 *s*
N-Me	2.37 *s*	2.71 *s*	37.5 *q*	39.8 *q*
O-CH_2-O	5.88 *s*	5.99 *s*	100.9 *t*	101.0 *t*
	6.09 *s*	6.11 *s*	102.5 *t*	102.3 *t*

*^{13}C multiplicities were determined by DEPT pulse sequence.

the presence of 20 carbon signals and proved the presence of a lactonic carbonyl at δ170.1, instead of the CH_2-8 carbon resonance at δ57.4 in **1**, the strong downfield shift of the C-14 spirocarbon to δ110.6 and the resonance of the N-Me carbon at a lower field by *ca* 2.5 ppm. The above results, together with the fragment ions at *m/z* 194 $[C_9H_6O_5]^+$, 188 $[C_{11}H_{10}NO_2]^+$, 176 $[C_9H_4O_4]^+$ and 148 $[C_8H_4O_3]^+$ are consistent with the proposed structure **2** for (±)-8-oxohypecorinine.

It should be pointed out that the secoberbine alkaloid, (±)-8-oxohypecorinine, is the sixth alkaloid of this structural type isolated from the genus *Hypecoum*. It is closely related to procumbine isolated from *H. procumbens* and *H. leptocarpum* [9, 10]. It is quite likely that **2** results from the *in vivo* enzymatic oxidation of (±)-hypecorinine (**1**) and represents another intermediate stage in the biogenetic transformations of protoberberines into other structural types of isoquinoline alkaloids. The present isolation of (±)-oxohypecorinine from *H. procumbens* var. *glaucescens* is a further indication that secoberbines may be considered as a characteristic chemotaxonomical feature of the genus *Hypecoum*. Accordingly, it substantiates the taxonomical separation of this genus from the Papaveraceae and treating it as a distinct family, the Hypecoaceae [1].

EXPERIMENTAL

General. Mps: uncorr. $[\alpha]_D^{22}$ and UV spectra were measured in MeOH. IR spectra were recorded in CCl_4. EIMS were obtained at 70 eV. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ with TMS as an int. standard. ^{13}C-multiplicites were determined by the DEPT pulse sequence [15]. Analytical and prep. TLC were performed on precoated silica gel GF_{254} plates (0.25 and 1 mm) using $CHCl_3$–MeOH (9:1) and MeOH–Et_2NH (4:1), respectively, and spots were detected under UV light at 254 nm and/or by spraying with Dragendorff's or potassium iodoplatinate reagents. CC was done on silica gel, 70–230 mesh.

Plant material. Flowering and fruiting plants of *H. procumbens* L. var. *glaucescens* (Guss.) Moris were collected, in March 1991, from irrigated gardens near to El-Arish, Sinai Peninsula. Identification was kindly verified by Dr I. Mashaly, Department of Botany, Faculty of Science, University of Mansoura.

Extraction and isolation. Air-dried, powdered whole plants (1.115 kg) were exhaustively extracted with 95% EtOH. The alcoholic extract was concd to a syrupy consistency, dissolved in H_2SO_4 (2%, 900 ml), filtered and then defatted with petrol. The acidic filtrate was brought to pH 7.5 with a satd soln of Na_2CO_3 and extracted with Et_2O. The mother liquor was brought to pH 10 with NH_4OH 25% and extracted with $CHCl_3$–15% isoPrOH. Evapn of solvents left the crude extracts A (1.3 g) and B (6.8 g), respectively. CC of the Et_2O extract on a silica gel column (2.5 cm i.d, 30 g) eluted with $CHCl_3$–MeOH (99:1) afforded (±)-hypecorinine (**1**) (13 mg) and isocorydine (4 mg). CC of the $CHCl_3$–15% isoPrOH extract on a silica gel column (2.5 cm i.d, 150 g) eluted with a C_6H_6–$CHCl_3$–MeOH gradient followed by repeated prep. TLC on silica gel F_{254} plates in MeOH–Et_2NH (4:1) afforded protopine (2.1 g), cryptopine (5 mg), allocryptopine (18 mg) and (±)-8-oxohypecorinine (**2**) (8 mg).

(±)-*8-Oxohypecorinine* (**2**). Amorphous orange powder. UV λ_{max}^{MeOH} nm (log ε) 224 (4.46), 245sh (4.11), 308 (3.82), 362 (3.80). IR ν^{CCl_4} cm^{-1}: 3090, 2990, 2845, 1665, 1645, 1595, 1490, 1040, 1020, 750. ^1H and ^{13}C NMR (360, 90 MHz, $CDCl_3$): see Table 1. ^{13}C DEPT (90 MHz, $CDCl_3$, 135°): 1 CH_3, 4 CH_2, 4 CH, 11 C. EIMS (70 eV) *m/z* (rel. int.): 381 $[M]^+$ (2.8), (calcd for $C_{20}H_{15}NO_7$, 381.08484), 204 (11), 194 (25), 188 (100), 187 (10), 186 (19), 176 (12), 148 (30).

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