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# ALKALOIDS OF *PAPAVERACEAE* (XIX)[1]. ALKALOIDS OF *GLAUCIUM PAUCILOBUM* POPULATION GOLESTAN FOREST

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**Abstract**

The *Glaucium paucilobum* Freyn population of the Golestan forest contained three major alkaloids; protopine (0.5%), α-allocryptopine (0.2%), corydine (0.1%), and six minor alkaloids; *N*-methyllind carpine (0.006), bulbocapnine (0.04%), 4-hydroxy bulbocapnine (0.001%), Isocorydine (0.04%), arosine (0.002%) and corydine-β-*N*-oxide (0.003%). *N*-methyllindcrapine, 4-hydroxybulbocapnine and corydine--β-*N*-oxide were detected for the first time in *Glaucium paucilobum* Freyn. The stereochemistry at the *N*-oxide center was determined by NOE difference measurement.

## Introduction

In continuation of phytochemical studies of Iranian wild species of the *Papaveraceae* family [1, 2], the alkaloids of *G. paucilobum* of the Golestan forest were studied. *G.paucilobum* is a biennial plant scattered near the Goletan forest in the north of Iran. The plant blooms from May until the end of July. The height of the plant is 40-60cm.

## Results and Discussion

The following alkaloids were isolated from the G. paucilobum Freyn population of the Golestan forest through column chromatography and preparative TLC (Table1, Figure 1).

The mp and spectral data of the above alkaloids were identical with those reported [6-9]. *N*-Methyllindcarpine, 4-hydroxybulbocarpnine and corydine-β-*N*-oxide were detected for the first time in *G.paucilobum* Freyn. The structure of the corydine-*N*-oxide was confirmed by synthesis of the latter through the oxidation of (+)-corydine with m-chloroperbenzoic acid. The stereochemistry of the *N*-oxide center was determined by NOE difference.

It is noteworthy that stylopine and crabbine which existed in the *G.paucilobum* population of the Bujnurd could not be detected in the *G.paucilobum* population of the Golestan forest. In addition, compounds 1, 5, and 9 existing in the Golestan population could not be detected in the Bujnurd population. This demonstrated that similar species from different regions may have different alkaloids.

## Experimental Section

Melting pxoints were taken on a Kofler hot stage apparatus and are uncorrected. The $[\alpha]_D$ was obtained using a polarimeter Perkin-Elmer Model 241. The UV spectra were recorded using a Perking-Elmer Model 550 SE. The IR spectra were obtained using a Perkin-Elmer Model 781 spectrograph (potassium bromide disks).HNMR spectra were recorded on a Bruker FT-80

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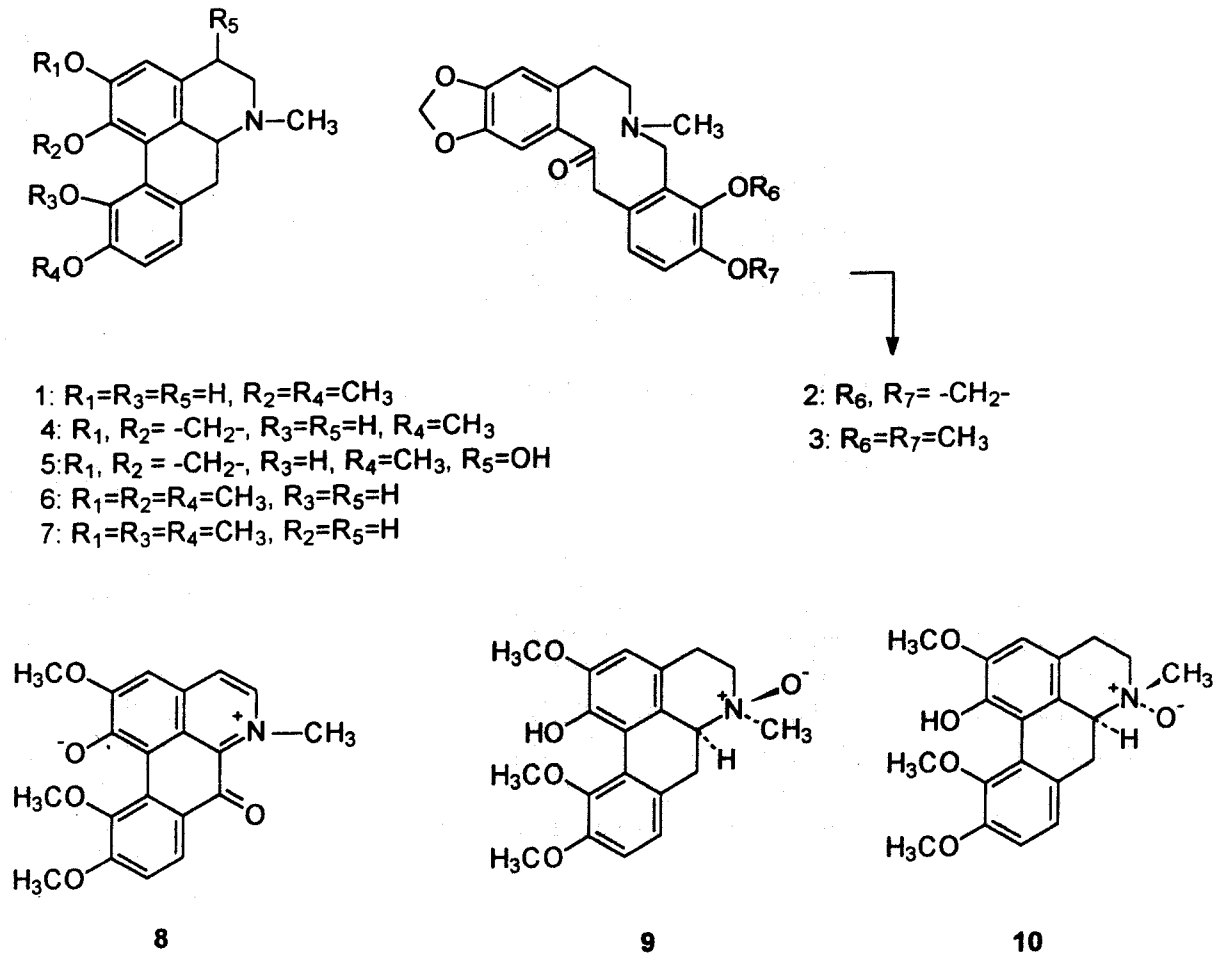


**Figure 1**

or Varian FT-400 unity plus spectrometers and chemical shifts (δ) are in ppm relative to internal tetramethyl silane. The mass spectra were run on Finnigan TSQ-70 spectrometer at 70 eV.

**Plant Material**

The aerial parts of the *Glaucium paucilobum* Freyn population in the Golestan forest were collected in May 1996, air dried in the shade and then at 60° to a constant weight and powdered so that all the material could be passed through a mesh not larger than 0.5 mm.

**Extraction Procedure**

Starting from 1500 g powdered plant material, the alkaloids were extracted as reported [5] to give 14g (0.93%) of a crude mixture of alkaloids.

**Column Chromatography**

The crude extract (14g) was dissolved in chloroform (35ml) and placed on a chromatographic column (4.5 cm diameter, 500 g) with silica gel (mesh 230-400) as the absorbent. The column was eluted as reported [5].

**Preparative TLC**

Similar fractions obtained from column chromatography were combined. After evaporation of the solvent under reduced pressure, the residue was purified by preparative TLC using silica gel and solvent system ethyl acetate-methanol-ammonia (85:10:5).

***N*-Methyllindcarpine (1)**

Combined fractions which were eluted with 40% chloroform-petroleum ether contained mainly one alkaloid and were crystallized from ethanol: m.p. 198-200° [lit 7, m.p. 198-200°], m.m.p. with an authentic sample at 198-200°.

**Protopine (2) and α-Allocryptopine (3)**

Combined fractions which were eluted with 70% chloroform-petroleum ether contained two alkaloids.

They were separated by preparative TLC (silica gel, solvent system ethyl acetate-methanol-ammonia 85:10:5).

The fast moving fraction (Rf=0.77) was crystallized from methanol to give protopine: m.p. 207-208° [lit. 6, m.p. 207-208°], m.m.p. with an authentic sample at 207-208°. The slow moving graction (Rf=0.58) was crystallized from ethanol to give α-allocryptopine: m.p. 160-161° [lit.6, m.p. 160-161°], m.m.p. with an authentic sample at 160-161°.

**Bulbocapnine (4) and 4-Hydroxybulbocapnine (5)**

Combined fractions which were eluted with 90% chloroform-petroleum ether contained two alkaloids. They were separated by preparative TLC (silica gel, solvent system ethyl acetate-methanol-ammonia 85:10:5).

The fast moving fraction ($R_f$=0.65) was crystallized from ethanol to give bulbocapnine: m.p. 202-203° [lit. 7, m.p. 201-203°], m.m.p. with an authentic sample at 201-203°.

The slow moving fraction (Rf=0.55) was crystallized from methanol to five 4-hydroxybulbocapnine: m.p. 231-233° [lit 8, m.p. 231-233°], m.m.p. with an authentic sample at 231-233°.

**Isocorydine (6) and Corydine (7)**

Combined fractions which were eluted with 10% methanol-chloroform contained two alkaloids. They were separated by preparative TLC (silica gel, solvent system ethyl acetate-methanol-ammonia 85:10:5).

The fast moving fraction ($R_f$=0.73) was crystallized from methanol to give isocorydine: m.p. 183-185° [lit. 7, m.p. 185°], m.m.p. with an authentic sample at 183-185°.

The slow moving fraction (Rf=0.68) was crystallized from ethanol to give corydine: m.p. 147-148° (lit. 7, m.p. 148°], m.m.p. with an authentic sample at 147-148°.

**Arosine (8)**

Combined fractions which were eluted with 30% methanol-chloroform contained mainly one alkaloid, which was purified by preparative TLC and crystallized from ethanol to give arosine: m.p. 246-248° (dec.) [lit.9, m.p. 245-248°(dec.)], m.m.p. with an authentic sample at 246-248°.

**Corydine -β-*N*-oxide (9)**

Combined fractions which were eluted with 40% methanol-chloroform contained mainly one alkaloid which was purified by preparative TLC. It was crystallized from acetone: m.p. 162-164° (dec.):$[\alpha]_D^{20}$ = +130° (c 0.2, MeOH); UV (EtOH): $\lambda_{max}$ (logε) 235 (4.43), 265 (3.89), 305 (3.70) nm; $^1$H-NMR ($CDCl_3$): 3.39 (s, 3H, $NCH_3$), 3.74 (s, 3H, $OCH_3$), 3.88 (s, 6H, 2×$OCH_3$), 6.72 (s, 1H, H3), 6.88, 7.12ppm (2d, each 1H, $H_{8,9}$, J=8Hz); ms: m/z (%) 357 ($M^+$, 29), 341 (73), 340 (34), 310 (100), 298 (89), 282 (42), 267 (25); $^{13}$NMR ($CDCl_3$): 24.4 (C-4), 30.8 (C-7), 55.9 ($NCH_3$), 58.2 (C-5), 61.9 ($OCH_3$), 62.2 ($OCH_3$), 64.0 ($OCH_3$), 71.9 (C-6a), 110.9 (C-3), 111.3 (C-9), 119.2 (C-1a)*, 121.5 (C-3a)*, 121.8 (C-1b)*, 124.9 (C-8), 125.5 (C-11a), 128.0 (C-12a), 143.0 (C-1), 143.6 (s, C-11), 150.1(C-2), 152.1 (C-10).

The C-13 data were similar to N-methyl corydine [10,11].

The 400 MHz $^1$H-NMR spectrum of 9 in $CDCl_3$ exhibited the *N*-methyl signal at δ 3.39, while H-6a appeared as a doublet of doublets at δ 4.08. Different NOE experiments were used to settle the stereochemistry at the *N*-oxide center. Irradiation of the δ 3.39 *N*-methyl singlet led to a 11.3% enhancement of the signal at δ 4.08 (H-6a). Conversely, irradiation at δ 4.08 produced a 6.7% enhancement of the δ 3.39 singlet ($N-CH_3$). Therefore, the *N*-methyl group and H-6a must be syn to each other. Because the (+)-corydine has the S configuration, the (+)-corydine -β-*N*-oxide belongs to the C-6a S absoulte configuration as indicated in structure 9 [12]. This alkaloid was identical in all respects with the sample of corydine-β-*N*-oxide prepared by treatment of corydine with m-chloroperbenzoic acid.

**Preparation of Corpydine *N*-oxide**

(+) - Corydine (200mg) was dissolved in $CHCl_3$ (5ml) and m-chloroperbenzoic acid (200 mg) in $CHCl_3$ (5ml) was added slowly. The ice-cold mixture was stirred for 1 hour brought to room temperature, diluted with $CHCl_3$ and washed with 10% aqueous $NaHCO_3$ to remove excess acid. The $CHCl_3$ solution was washed with a little $H_2O$, dried, filtered and concentrated under vacuum to an amorphous solid.

TLC (slovent system: $CCl_4$-n-BuOH-MeOH-Conc.$NH_4OH$, 40: 30: 30: 3) showed the presence of two *N*-oxides, one major ($R_f$=0.38), the other minor ($R_f$=0.44) which were separated.

The major isomer crystallized from $Me_2CO$ as white needles, m.p. 162 - 164° (dec.), yield 145 mg (69%). It was identical with corydine-β-*N*-oxide (9) in terms of MS, 13C-, $^1$H-NMR spectra, TLC, $R_f$ value, mp and speciffic rotation.

The minor isomer was obtained as an amorphous solid, 15mg (7%), $[\alpha]_D^{20}$ = +70° (c 0.1, MeOH), UV (EtOH):$\lambda_{max}$ 234 (4.42), 266 (3.90), 305 (3.69)nm; $^1$H-

* Signals may be reversed.

NMR ($CDC_3$): 3.06 (s, 3H, $NCH_3$), 3.73 (s, 3H, $OCH_3$), 3.93 (s, 6H, 2x OCH3), 6.71 (s, 1H, $H_3$), 6.92, 7.20 ppm (2d, each 1H, $H_{8,9}$, J = 8Hz); ms: m/z (%) 357 ($M^+$ 3), 341 (100), 340 (33), 310 (85), 298 (16), 289 (16), 282 (16), 267 (22), 252 (66), No NOE's were observed between the *N*-methyl (δ 3.06) and H-6a (δ 4.32). Therefore, an anti arrangement must exist between H-6a and the *N*-methyl group and the minor isomer is corydine-α-*N*-oxide (**10**).

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