

(-)-CORYDALISOL: A NEW SECOBERBINE ALKALOID

TEKANT GÖZLER,¹ MUSTAFA ALI ÖNÜR,¹ ROBERT D. MINARD, and MAURICE SHAMMA*

*Department of Chemistry, The Pennsylvania State University,
University Park, PA 16802*

ABSTRACT.—(-)-Corydalisol (**2**), which possesses the S absolute configuration, has been found in Turkish *Hypecoum procumbens* L. (Papaveraceae).

The genus *Hypecoum* is usually classified within the plant family Papaveraceae, although it also stands botanically close to the Fumariaceae (1). It is known that *Hypecoum* species are rich in isoquinolines, and table 1 summarizes past findings regarding the alkaloidal content of the genus. We are presently attempting a complete screening of the alkaloids of Turkish *Hypecoum* species.

TABLE 1. Alkaloids previously found in the genus *Hypecoum*.

Berbines: Coptisine (2)
Protopines: Allocryptopine (2-4), cryptopine (4), protopine (2-9)
Benzophenanthridines: Chelerythrine (2,3,9), chelirubine (2), sanguinarine (2-4,9), dihydrosanguinarine (4)
Secoberbines: (±)-Hypecorine (8), (±)-hypecorinine (8), (-)-peshawarine (7)

Hypecoum procumbens L. is a small annual herb found alongside the beaches of southwestern Turkey. The known alkaloids that previously had been reported in this plant are few and include the berbinium salt, coptisine; the protopines, protopine and allocryptopine; and the benzophenanthridines, chelerythrine, chelirubine, and sanguinarine (2).

Presently, work-up of 1.35 kg of dried plant, followed by column and then thin layer chromatography supplied a variety of known alkaloids, which are listed in table 2.

TABLE 2. Known alkaloids presently found in *H. procumbens* L.

Berbines: (-)-Scoulerine (2 mg)
Protopines: Protopine (5 g)
Benzophenanthridines: 8-Acetyldihydrosanguinarine (6 mg) (could be an artifact), 8-methoxydihydrosanguinarine (2 mg) (could be an artifact), norsanguinarine (12 mg), oxysanguinarine (29 mg)
Secoberbines; (±)-Hypecorinine (3 mg)
Aporphines: (+)-Glaucine (4 mg) (+)-Isocorydine (3 mg)
Additionally, 82 mg of the known amide feruloyl-tyramine were obtained (10).

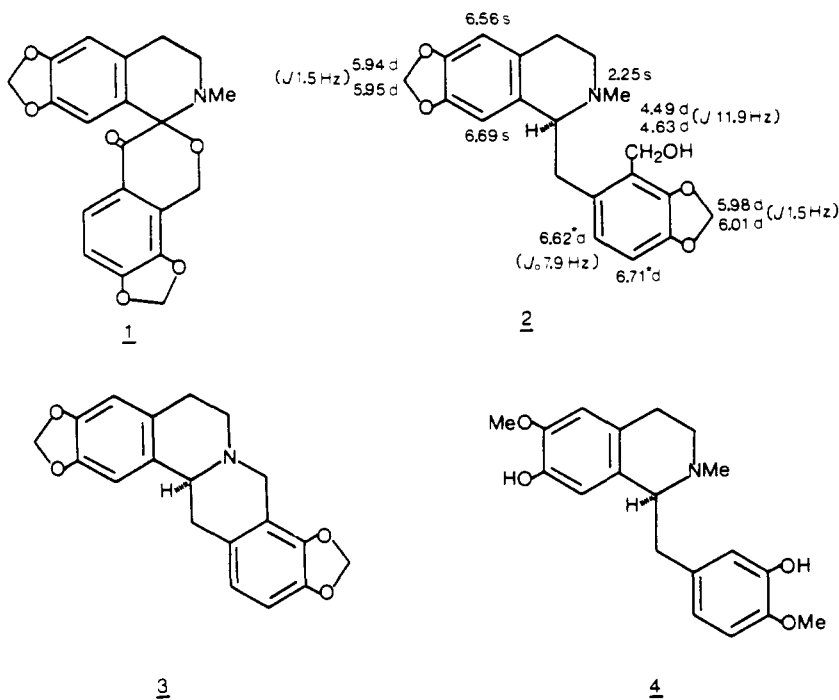
Immediately following (±)-hypercorinine (**1**), 6 mg of a colorless, non-phenolic compound were obtained, which corresponds to the new secoberbine, (-)-corydalisol (**2**), C₂₀H₂₁O₅N. The 360 MHz (FT) deuteriochloroform nmr spectrum of this base has been summarized around expression **2**. The uv spectrum, with a maximum at 293 nm shows no change either in acid or in basic solution. Previously, corydalisol had been isolated from *Corydalis incisa* (Thunb.) Pers. (Fumariaceae), and was known as a natural product solely in the R-(+) configuration (11). The nmr and uv spectra of our alkaloid correspond in their general characteristics to those recorded for (+)-corydalisol (11).

¹Permanent address: Department of Pharmacognosy, Faculty of Pharmacy, Ege University, Izmir, Turkey.

Nevertheless, the cd curve of our levorotatory alkaloid shows a positive maximum at 235 nm, indicating the S absolute configuration. The S chirality among *N*-methyl-tetrahydrobenzylisoquinolines is usually associated with a positive specific rotation (12). In the present instance, however, the extra hydroxymethyl substituent at C-10 forces the lower aromatic ring to lie *syn* to the *N*-methyl group, as shown in expression **2**, rather than in the more common *anti* relationship. It is this change in conformation that causes a reversal of the sign of the specific rotation. In like fashion, the previously known R-corydalisol is dextrorotatory (11).

The isolation of (-)-corydalisol (**2**) is of biogenetic importance, inasmuch as it may be considered to be a natural derivative of the levorotatory berberine scoulerine (**3**). The latter alkaloid is derived from S-(+)-reticuline (**4**), which is the main building block for a large number of isoquinolines. It has so far been one of the anomalies of the optically active secoberbines that they belong to the unusual R configuration.² The present characterization of (-)-corydalisol (**2**) indicates that S-secoberbines also are to be found in nature.

It should also be pointed out that the present isolation of S-(+)-glaucine and S-(+)-isocorydine (table 2) represents the first detection of aporphines in the genus *Hypocoum*.



EXPERIMENTAL

ISOLATION.—Powdered plant material (1.35 kg) was extracted exhaustively with ethanol at room temperature. The extract was concentrated *in vacuo* and acidified with 2% hydrochloric acid. The aqueous solution was then made alkaline with ammonium hydroxide, and the alkaloids were extracted with chloroform. Evaporation of the organic layer left a crude extract weighing 7.5 g. This material was placed on a silica gel (70-230 mesh) column, which was eluted first with chloroform, and then with chloroform containing increasing amounts of methanol. The eluates were monitored by tlc, and fractions of similar

²The secoberbine (-)-peshawarine has an absolute configuration opposite to that of (+)-canadalinine and (+)-corydalisol. This is because an S_N2 inversion probably occurred during formation of the δ -lactone ring. For a discussion of the secoberbines, see M. Shamma and J. L. Moniot, "Isoquinoline Alkaloids Research, 1972-1977," Plenum Press, NY (1978), pp. 261-270.

composition were combined. These were further separated and purified by tlc on Merck Silica Gel G glass plates. Bands were differentiated under short-wave uv light, and by spraying with the Dragendorff reagent. The bands were eluted from the silica gel layer using methylene chloride-methanol (8:2 v/v).

(-)-CORYDALISOL (2).— λ max (MeOH) 210, 235 sh, 293 nm (log ϵ 4.45, 3.83, 387); ν max (CHCl₃) 3100, 2920, 2865, 1600, 1475, 1450, 1380, 1370, 1340, 1250-1190, 1050, 1020, 985, 840 cm⁻¹; ms: m/z 354 (M-1)⁺ (0.2), 337 (0.2), 323 (0.3), 322 (0.3), 320 (0.2), 293 (0.1), 191 (33), 190 (100), 175 (3), 160 (3), 148 (2); [α]^{23D} -18° (c 0.11, MeOH); cd $\Delta\epsilon$ (nm) +1.55(2.88), -0.26(261), -0.29(256), +3.17(235).

ACKNOWLEDGMENT

This research was supported by grants CHE-8210699 from the National Science Foundation and INT-8216876 from the National Science Foundation international program.

Received 20 September 1982

LITERATURE CITED

1. J. C. Willis (revised by H. K. A. Shaw), "A Dictionary of the Flowering Plants and Ferns," 8th ed., Cambridge University Press, Cambridge (1980), pp. 584-584.
2. J. Slavík and L. Slavíkova, *Coll. Czech. Chem. Commun.*, **26**, 1472 (1961).
3. K. G. Kiryakov and P. Panov, *Med. Probl.*, **21**, 91 (1969); see also F. Šantavý in "The Alkaloids," Vol. 17, R. H. F. Manske and R. G. A. Rodrigo, eds., Academic Press, NY 1979), p. 394.
4. H. Kiryakov, Z. Mardirossian, P. Panov, and D. Barov, *Folia Med. (Plovdiv)*, **22**, 17 (1980); *Chem. Abstr.*, **94**, 80256s (1981).
5. M. N. Komarova and K. F. Blinova, *Tr. Leningrad Khim. Farm. Inst.*, **26**, 163 (1968); *Chem. Abstr.*, **73**, 32350n (1970).
6. T. F. Platonova, P. S. Massagetov, A. D. Kuzuvkov, and L. M. Utkin, *Zh. Obshch. Khim.*, **26**, 173 (1956); and *J. Gen. Chem.*, **26**, 181 (1956).
7. M. Shamma, A. S. Rothenberg, G. S. Jayatilake, and S. F. Hussain, *Heterocycles*, **5**, 41 (1976).
8. L. D. Yakhontova, M. N. Komarova, M. E. Perel'son, K. F. Blinova, and O. N. Tolkachev, *Khim. Prirodn. Soedin.*, 624 (1972); *Chem. Nat. Comp.*, 592 (1974).
9. S. Yu. Yunusov, S. T. Akramov, and G. P. Sidiyakin, *Doklady Akad. Nauk Uzbek. S.S.R.*, 23 (1957); *Chem. Abstr.*, **53**, 3606f (1959).
10. S. F. Hussain, B. Gözler, M. Shamma, and T. Gözler, *Phytochemistry*, **21**, 2979 (1982).
11. G. Nonaka and I. Nishioka, *Chem. Pharm. Bull.*, **23**, 294 (1975); G. Nonaka, H. Okabe, I. Nishioka, and N. Takao, *J. Pharm. Soc. Jap.*, **93**, 87 (1973).
12. For a discussion of the absolute configuration of the tetrahydrobenzylisoquinolines, see M. Shamma, "The Isoquinoline Alkaloids," Academic Press, NY (1973), p. 75.