

(-)-CORYDALISOL: A NEW SECOBERBINE ALKALOID

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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).

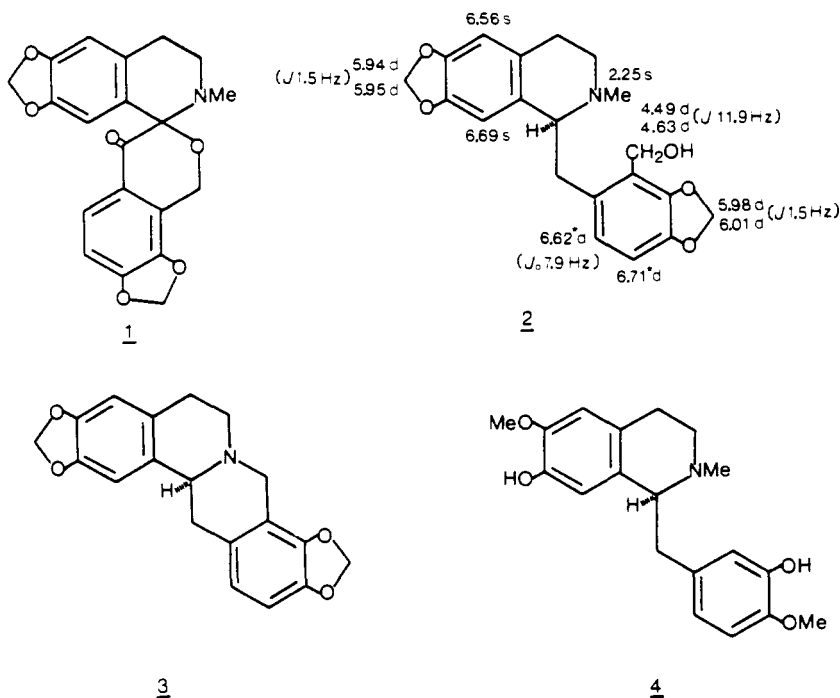
Immediately following (±)-hypercorinine (**1**), 6 mg of a colorless, non-phenolic compound were obtained, which corresponds to the new secoberbine, (-)-corydalisol (**2**), C₂₀H₂₁O₅N. The 360 MHz (FT) deuteriochloroform nmr spectrum of this base has been summarized around expression **2**. The uv spectrum, 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).

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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 berbine 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 *Hypecoum*.



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 (+)-canadoline 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); $[\alpha]^{23D} - 18^\circ$ (c 0.11, MeOH); cd $\Delta\epsilon$ (nm) +1.55(2.88), -0.26(261), -0.29(256), +3.17(235).

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