Journal of Natural Products
Vol. 52, No. 2, pp. 389-390, Mar-Apr 1989

(−)-ANTOFINE: A PHENANTHROINDOLIZIDINE FROM *VINCETOXICUM NIGRUM*

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ABSTRACT.—The phenanthroindolizidine alkaloid (−)-antofine has been isolated from *Vincetoxicum nigrum*.

A small sample of the aerial parts of *Vincetoxicum nigrum* L. Moench (Asclepiadaceae) growing in localized areas of the Balearic Islands (Spain) has been studied in a search for new phenanthroindolizidine alkaloids (1). Only the well known tylophorine and a second closely related, though not properly identified, alkaloid had been isolated previously from a *Vincetoxicum* species (*Vincetoxicum officinale*) (2). In folk medicine, phenanthroindolizidine alkaloids have been used as emetic, expectorant, and antidysenteric agents (3). Some of these alkaloids have been reported to possess significant activity against L-1210 leukemia cells (4).

This note reports the isolation of (−)-antofine, which possesses pronounced antifungal and antibacterial activity (5). Two other minor alkaloids were also present in the crude alkaloid extract from *V. nigrum*, as evidenced by hplc analysis [C_{18} μ-Bondapack, MeOH-H_2O (1:1), 1 ml/min, uv detector 280 nm], though they were not isolated due to the scarcity of plant material.

The structure of (−)-antofine was unambiguously determined on the basis of its spectroscopic data (uv, ir, nmr, ms). In particular, the analysis of its nOe difference spectrum as well as selective decoupling experiments left no doubt of its being (−)-antofine (6,7) and not the isomeric 3,6,7-phenanthroindolizidine. (−)-Antofine has been isolated previously from *Cynanchum vincetoxicum* (6) and *Antitoxicum funebre* (7).

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Uv and ir spectra were determined using Perkin-Elmer 550S and Hitachi 260-10 spectrometers. Mass spectra were carried out with a Hewlett Packard 5985A apparatus. ^{1}H-nmr spectra were recorded on Varian CTF-80A and Bruker WM-250 spectrometers.

PLANT MATERIAL.—Stems and leaves of *V. nigrum* were collected near Çap Pinar, Mallorca, and identified by Dr. Ll. Llorenç, University of the Balearic Islands; a voucher specimen has been deposited at the herbarium of the Department of Biology.

ISOLATION PROCEDURES.—Coarsely ground, dried plant material (140 g) was thoroughly extracted with boiling MeOH (4 × 500 ml). The crude extracts were partially evaporated under vacuo (250 ml), treated with aqueous 1% H_2SO_4 (750 ml), filtered, and washed with Et_2O (5 × 50 ml). The aqueous solution was then made alkaline with 37% NH_3 and thoroughly extracted with $CHCl_3$. Removal of the solvent yielded a crude residue (140 mg) which was chromatographed on a Si gel column ($CHCl_3$/MeOH) thus yielding 60 mg of slightly impure (−)-antofine. Rechromatography on Si gel with $CHCl_3$-MeOH (9:1) provided 40 mg of pure antofine which crystallized as a white solid: mp 210–212° [lit. (2) 208–217°], $[\alpha]_D$ −159° (c = 0.192, $CHCl_3$) [lit. (6) $[\alpha]_D$ −165° (c = 1.92, $CHCl_3$)].

IDENTIFICATION.—Unambiguous identification was based on the analysis of its spectral data (uv, ir, ms, nmr) and especially nOe difference and selective decoupling spectra. Full details of the isolation and identification data are available on request to the senior author.

ACKNOWLEDGMENTS

We thank Dr. D. Dominguez and Dr. G. Togo (U. Santiago de Compostela) for determining our 250 MHz nmr spectra.

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Received 28 July 1988