Journal of Natural Products
Vol. 46, No. 6, pp. 934-935, Nov-Dec 1983

IZMIRINE: A NEW PROTOPINE ALKALOID

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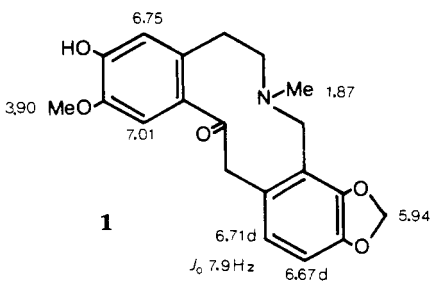
Several chemical studies of the creeper *Fumaria parviflora* Lam. (Fumariaceae) have been reported (1), as a result of which it is known that this plant produces a variety of protoberberine, phthalideisoquinoline, benzophenanthridine, spirobenzylisoquinoline, aporphine, and protopine alkaloids. Even so, *F. parviflora* of Turkish origin had never been investigated. Because this plant grows profusely on and near the campus of Ege University (University of the Aegean), in Bornova, Izmir, we decided to carry out a rapid screening of its alkaloidal content in a specific search for new alkaloids.

Column chromatography of the basic alkaloidal fraction from *F. parviflora*, followed by tlc, thus provided a sample of the new, amorphous and optically inactive, phenolic alkaloid izmirine (**1**), $C_{20}H_{21}O_5N$, whose ir spectrum, ν max ($CHCl_3$) 1665 and 3540 cm^{-1}, indicated the presence of a conjugated carbonyl function, as well as of a hydroxyl.

Mass spectroscopy can furnish useful data towards the structural elucidation of protopines. For cryptopine (**2**), it is known that the base peak, *m/z* 148, is due to the quinoidal ion **4**. In the case of the phenolic hunnemanine (**3**), however, the base peak is *m/z* 206, representing lactam fragment **5**. The mass spectrum of izmirine shows molecular ion *m/z* 355. Significantly, the base peak is *m/z* 148, denoting ion **4**. The phenolic function of izmirine is thus located on ring A, while the methylenedioxy substituent is attached to the bottom ring. As expected, diazomethane *O*-methylation of izmirine (**1**) provided cryptopine (**2**), so that izmirine is an *O*-demethylcryptopine (2).

Comparison of the ^{1}H-nmr chemical



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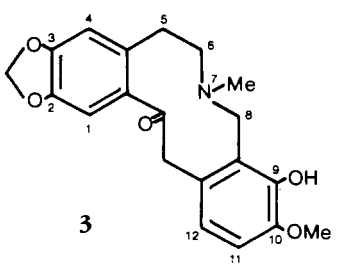

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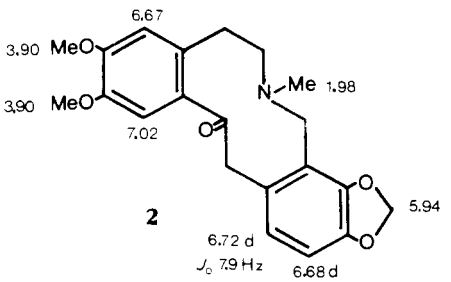

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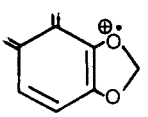

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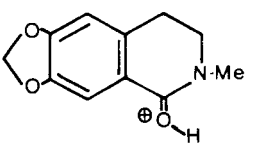

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shifts for the aromatic protons of izmirine (**1**) and cryptopine (**2**) shows that it is only H-4 that is appreciably affected by the *O*-methylation, moving upfield from δ 6.75 to 6.67. Such a specific shift reflects the fact that the phenolic function in izmirine is located at C-3, *ortho* to H-4, rather than at C-2.[2]

The uv spectrum of izmirine (**1**) shows λ max (EtOH) 238 sh, 285 nm (log ε 3.81, 3.66), λ max (EtOH-OH^-) 241 sh, 293, 312 nm (log ε 3.98, 3.81, 3.83). It is known that the uv spectra of *o*-hydroxyketones and *m*-hydroxyketones undergo bathochromic shifts of about 4 and 13 nm, respectively, upon addition of base, and that only *p*-hydroxyketones suffer larger bathochromic shifts (3). In the case of izmirine (**1**), the bathochromic shift of the $A \rightarrow L_b$ band from 285 nm to 312 nm upon basification is consonant with a *p*-hydroxyketone system, so that the phenolic function of this alkaloid is indeed located at C-3.

Izmirine (**1**) is the first protopine-type alkaloid to possess a phenolic function at C-3 (4).[3]

Several known alkaloids were also obtained as part of the present effort and will be reported in a brief, separate paper.

EXPERIMENTAL

ISOLATION OF IZMIRINE (**1**).—Powdered, dried plant (2 kg) was extracted with ethanol at room temperature. After solvent evaporation, the residue was washed with petroleum ether to remove neutral compounds. The material that did not dissolve in the petroleum ether was triturated with 0.5 N hydrochloric acid. The aqueous acid layer was basified with ammonium hydroxide and and extracted with chloroform. The solution was dried, and the solvent was evaporated to furnish 7 g of crude alkaloids. This material was placed on a chromatographic column of silica gel (350 g). Elution was with chloroform and increasing amounts of methanol. Izmirine was eluted with 10% methanol in chloroform, and was further purified by tlc on silica gel using benzene-ethyl acetate-acetone (40:20:40) in an atmosphere saturated with ammonia. A total of 2.4 mg of amorphous **1** was thus obtained.

O-METHYLATION OF **1**.—Izmirine (1½ mg) was dissolved in methanol; the solution was treated with ethereal diazomethane for 72 h. Work-up provided 1 mg of cryptopine (**2**), identical with an authentic sample.

ACKNOWLEDGMENTS

This research was supported by grant CHE-8210699 from the National Science Foundation.

LITERATURE CITED

1. For a lead reference, see S.F. Hussain, R.D. Minard, A.J. Freyer, and M. Shamma, *J. Nat. Prod.*, **44**, 169 (1981).
2. For a discussion of the mass spectra of protopines, see M. Shamma, "The Isoquinoline Alkaloids, Chemistry and Pharmacology," Academic Press, New York, 1972, pp 352-353.
3. A.I. Scott, "Interpretation of the Ultraviolet Spectra of Natural Products," Macmillan Company, New York, 1964, p 109.
4. For a listing of the protopine alkaloids, together with their physical and spectral properties, see H. Guinaudeau and M. Shamma, *J. Nat. Prod.*, **45**, 237 (1982).

Received 16 February 1983

[2]The NMR spectra were obtained in $CDCl_3$ solution at 200 MHz (FT).

[3]The poorly characterized alkaloid vaillantine may or may not possess a phenolic group at C-3; see reference (4).