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FUMADENSINE, A PHTHALIDEISOQUINOLINE FROM *FUMARIA DENSIFLORA*

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Key Word Index—*Fumaria densiflora*; Fumariaceae; phthalideisoquinoline alkaloid; fumadensine.

Abstract—The new phthalideisoquinoline, fumadensine, has been isolated from extracts of *Fumaria densiflora*.

INTRODUCTION

Fumaria densiflora is an annual herb common in western Jordan, especially in the Jordan Valley and surrounding hills. Previous studies on this plant had resulted in the isolation of the isoquinoline alkaloids fumaramine [1, 2], adlumidiceine, coptisine, palmatine, sinactine, protopine, cryptopine and densiflorine [3]. As part of a research programme involving the study of the chemical constituents of the Jordanian flora, the alkaloidal fraction of *F. densiflora* was reinvestigated.

RESULTS AND DISCUSSION

The plant was collected in the Jordan Valley, near Al-Ram, *ca* 15 km to the north-east of the Dead Sea. The whole dried plant was powdered and extracted following established procedure. Alumina chromatography of the extracts furnished the new racemic base fumadensine (**1**), $C_{30}H_{34}N_2O_6$, ν_{max} ($CHCl_3$) 1680 cm^{-1}. Fumadensine is the first phthalideisoquinoline to incorporate a simple, unsubstituted, phenethylamine side chain [4].

The ^1H NMR spectrum of fumadensine in $CDCl_3$ solution (360 MHz) is summarized around expression **1**. Notable features of this spectrum are the five-proton multiplet between δ7.19 and 7.35 due to the phenyl ring, and four multiplets between δ3.05 and 3.92 representing the four protons of the two-carbon bridge connecting the phenyl ring to the phthalimido moiety. More specifically, irradiation of either of the two downfield multiplets (δ3.52–3.60 and 3.83–3.92) due to this bridge affected only the two upfield multiplets (δ3.05–3.12 and 3.14–3.19) also representing the bridge.

The ^{13}C NMR spectrum of the alkaloid in $CDCl_3$ displayed a lactam carbonyl resonance at δ165.0, while the fully substituted carbinol carbon of the five-membered ring absorbed at δ89.7. The methylene carbon adjacent to the carbinol group appeared at δ39.4. The two methylene carbons forming the bridge connecting the phenyl ring to the phthalimido nitrogen atom absorbed at δ35.1 and 41.2, with the signal further downfield assigned to the carbon adjacent to nitrogen.

The mass spectrum of fumadensine includes a small $[M]^+$ *m/z* 518 (0.1%), and a slightly more intense *m/z* 500 (0.9%) peak due to loss of water. The base peak *m/z* 58 is assigned to the *N,N*-dimethyliminium cation.

Treatment of fumadensine with TFA led to a 3:5 mixture of stilbenes **2** and **3**, $C_{30}H_{32}N_2O_5$, which could not be readily separated by TLC. Nevertheless, the NMR spectrum of this mixture at 360 MHz in $CDCl_3$ could be clearly identified as being due to its two components as indicated in the Experimental.

Final confirmation of structure of the alkaloid was achieved by synthesis. Treatment of the known stilbene *N*-methylhydrastine (**4**) [5–7] with β-phenethylamine afforded fumadensine (**1**) in high yield.

It is conceivable that *N*-methylhydrastine (**4**) and β-phenethylamine exist in the plant independently of each other, and that fumadensine (**1**) is formed from these two components during the isolation process.

EXPERIMENTAL

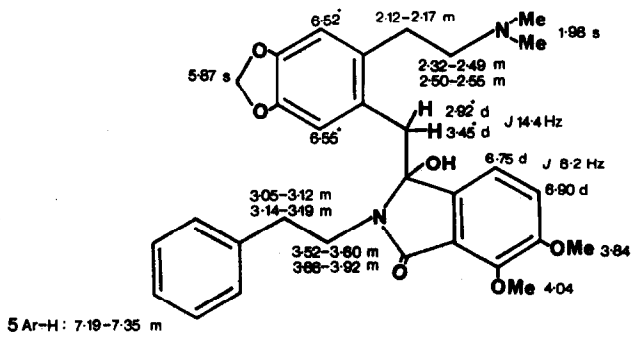
Plant material. F. densiflora DC. (*F. micrantha* LAG.) was collected in April, 1982. The plant was identified by Professor Dawud M. Al-Eisawi of the Department of Biological Sciences, University of Jordan, Amman. A voucher specimen is deposited in the herbarium of this Department.

Extraction and chromatography. Powdered dried plant (12 kg) was extracted with cold EtOH. The dried extract was treated with 5% HCl and the acidic soln basified with NH_4OH. $CHCl_3$ extraction and evapn of the organic solvent furnished the crude alkaloids (30 g). This material was placed on an alumina chromatographic column (1.7 kg, Fluka 507 C) packed in $CHCl_3$. Elution was with $CHCl_3$ containing increasing amounts of MeOH. Six major fractions (I–VI) were collected. Fumadensine (120 mg) was obtained from further CC of fraction III (4 g).

Fumadensine (**1**). Colourless crystals, mp 168–170° (MEOH); λ_{max} (MeOH) 292 nm (log ε 3.85); *m/z* 518 ($[M]^+$, $C_{30}H_{34}N_2O_6$) (0.1), 500 (0.9), 398 (0.1), 397 (0.2), 350 (0.5), 336 (1), 323 (0.4), 312 (1.3), 296 (1), 204 (33), 105 (5), 58 (100).

Dehydration of **1**. Fumadensine (1 mg) in TFA was refluxed gently for 10 min. Work-up, including TLC, provided a mixture of stilbenes **2** and **3** which were not sepd; *m/z* 500 ($[M]^+$, $C_{30}H_{32}N_2O_5$) (0.4), 204 (20), 58 (100). Compound **3**, NMR δ2.18 (*s*, 6H, NMe), 3.86 and 4.08 (2*s*, 2 × 3H, OCH_3), 6.00 (*s*, 2H, OCH_2O); compound **2**, 2.23 (*s*, 6H, NMe), 3.95 and 4.11 (2*s*, 2 × 3H, OCH_3), 5.97 (*s*, 2H, OCH_2O).

Synthesis of **1**. *N*-Methylhydrastine (**4**) (180 mg) in dry C_6H_6 (20 ml) was treated with excess phenethylamine (0.2 ml). The mixture was heated for 6 hr at 60–70°; work-up gave an oil which



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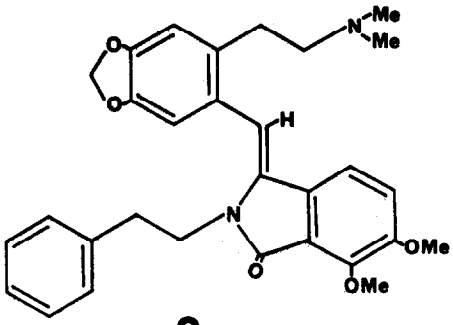

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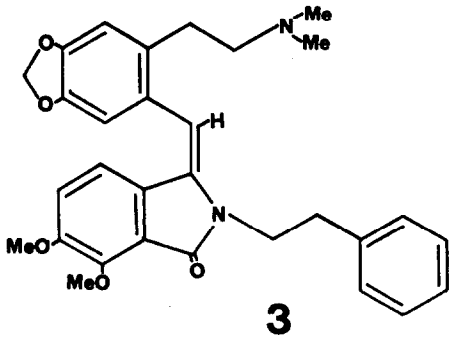

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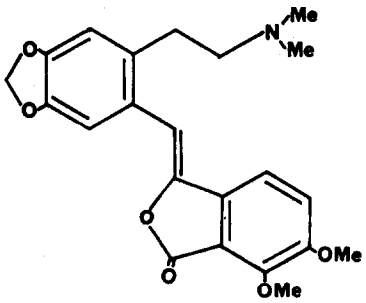

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crystallized from MeOH. Recrystallization from the same solvent yielded **1** (198 mg, 84%).

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