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ALKALOIDS OF *FUMARIA VAILLANTII*

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Key Word Index—*Fumaria vaillantii*; Fumariaceae; isoquinoline alkaloids; (+)-juziphine; isoquinolones; N-methylcorydaldine; secophthalideisoquinolines; E-fumaramine.

Abstract—The aerial parts of Turkish *Fumaria vaillantii* yielded 26 isoquinoline alkaloids. Of these, oxysanguinarine, (±)-8-acetonyldihydrosanguinarine, (±)-8-methoxydihydrosanguinarine and fumaramidine are reported for the first time from this plant. New alkaloids for the genus *Fumaria* are dihydrosanguinarine, norsanguinarine, (+)-isocorydine, (−)-corledine and (+)-juziphine. This is the first occurrence of the isoquinolone *N*-methylcorydaldine in a member of the Fumariaceae. Spectral data are given for the new compound, *E*-fumaramine.

INTRODUCTION

Previous studies on the chemistry of *Fumaria vaillantii* have shown this plant to be a generous source of isoquinolines [1–15].‡ These alkaloids include the phthalideisoquinolines adlumine [14], (−)-adlumine [7], adlumidine [14], (−)-capnoidine [7], bicuculline [14], (+)-bicuculline [7, 15], α-hydrastine [15], (+)-α-hydrastine [4, 7, 14], (−)-*N*-methyladlumine [14], *N*-methylhydrastine [8, 15], *N*-methylhydrasteine [8, 9, 15], fumaramine [4, 7], fumaridine [1, 3, 4, 7] and adlumidiceine [14]; the spirobenzylisoquinolines (+)-fumariline [14], fumaritine [3], parfumine [5, 13, 14], (+)-parfumine [15] and parfumidine [5]; the protopines protopine [1, 3, 4, 6, 7, 10–12, 14, 15], cryptopine [12] and vaillantine [7]; the protoberberines stylopine [12], (+)-stylopine [13, 14], (−)-stylopine [15], (−)-stylopine methohydroxide [13, 14], cheilanthifoline [13, 14], scoulerine [14], (−)-scoulerine [15] and sinactine [12]; the benzophenanthridine sanguinarine [2, 15]; the benzylisoquinolines (−)-norjuziphine [13, 14], ledecorine [14], reticuline [14] and coclaurine [14]; and the aporphine isoboldine [14].

Recently, we became interested in reinvestigating *F. vaillantii* of Turkish origin in conjunction with the use of a 360 MHz (FT) NMR spectrometer which allowed us to study even the minor alkaloids of the plant.

RESULTS AND DISCUSSION

Twenty-six alkaloids were isolated from the aerial parts of *F. vaillantii* by CC and subsequent prep. TLC. Of these alkaloids, 15 had been isolated previously from the same plant by other workers. These are the phthalideisoquinolines (+)-bicuculline, (−)capnoidine, (−)-adlumine, *N*-methylhydrasteine, *Z*-fumaramine and adlumidiceine; the spirobenzylisoquinolines (+)-fumariline, (+)-parfumine and (+)-parfumidine; the protopine alkaloid protopine; the protoberberines (+)-stylopine, (−)-cheilanthifoline and (−)-scoulerine; the benzylisoquinoline (−)-norjuziphine; and the aporphine (+)-isoboldine.

We now extend the list of alkaloids present in *F. vaillantii* by including the benzophenanthridines oxysanguinarine, (±)-8-acetonyldihydrosanguinarine, (±)-8-methoxydihydrosanguinarine, and the phthalideisoquinoline fumaramidine [16]. Although no acetone was used in the present work-up of the plant, there is still a possibility that (±)-8-acetonyldihydrosanguinarine could be an artifact. It is also likely that (±)-8-methoxydihydrosanguinarine was formed during the isolation sequence since the compound is a racemate, and 8-alkoxydihydrosanguinarines are known to be formed during recrystallization of sanguinarine salts from alcohols [17].

Five alkaloids previously found in other genera of the Fumariaceae were obtained for the first time from the genus *Fumaria*. These are the benzophenanthridines dihydrosanguinarine and norsanguinarine, the aporphine (+)-isocorydine [18], the phthalideisoquinoline (−)-corledine [16] and the benzylisoquinoline (+)-juziphine. We report the CD curve of juziphine in an effort to complete the spectral data on this alkaloid. The negative tail beyond 217 nm is diagnostic of the *R*-configuration as assigned by Ziyaev *et al.* [19]. It is interesting to note that the positive sign of the specific rotation we found, $[\alpha]_D^{25}$ +14° (MeOH; *c* 0.17), is usually characteristic of the *S*-configuration in an *N*-methyltetrahydrobenzylisoquinoline. In the present case, however, the lower pendant aromatic ring C is forced away from ring A due to substitution at C-8 and lies on the same side as the *N*-methyl group. It is this conformational alteration which explains the change in the sign of the specific rotation.

New for the Fumariaceae is *N*-methylcorydaldine, a member of the isoquinolone group of alkaloids [20]. It

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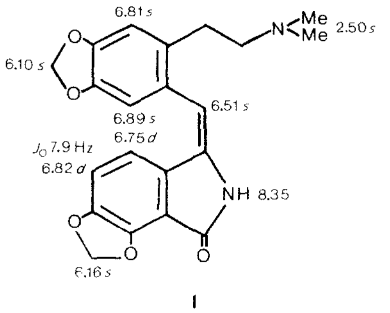
‡ Since the present paper deals primarily with the alkaloids of *F. vaillantii*, the bases present in *F. vaillantii* var. *schrammii*, which is identical with *F. schrammii*, are not included in our listing [see *Index Kewensis* (1959) Suppl. VI, p. 88. Oxford University Press, Oxford].



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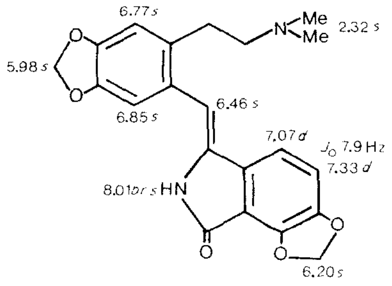

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should be pointed out here that isoquinolones are end products of the catabolism of isoquinoline alkaloids and will be found wherever isoquinoline alkaloids are present.

The secophthalideisoquinoline keto acids and secophthalideisoquinoline enelactams may exist as *Z* or *E* geometric isomers, and these differ significantly in their UV and NMR spectra [21]. The secophthalide enelactam fumaramine has been reported so far only in the *Z* form [16]. We have now characterized *E*-fumaramine. The NMR spectrum of this compound is outlined in formula **1**. The aromatic doublet of doublets for H-2′ and H-3′ appears at higher field than for the corresponding *Z*-isomer, **2**. The UV spectral data of **1** is also in keeping with the expected values for an *E*-isomer. There are maxima at 264 and 357 nm, whereas the Z analogue exhibits maxima at 275 and 369 nm. It is known that photoirradiation of either the Z- or the E-isomers of a secophthalideisoquinoline enelactam provides the alternate isomer [21]. Additionally, secophthalideisoquinoline enelactams could very well be artifacts of isolation [21]. It follows that **1** is most probably not a natural product.

EXPERIMENTAL

General. ^{1}H NMR spectra were recorded at 360 MHz using $CDCl_3$ as solvent and TMS as int. standard. MS were obtained using a direct inlet system. Elemental analyses were confirmed by high resolution mass spectrometry.

Plant material. The aerial parts of *F. vaillantii* Loisel. were collected near Simav, Kütahya, Turkey, and the plant was identified by Professor Dr. Asuman Baytop (Istanbul University). A voucher specimen No. 514 is deposited in the Herbarium of Pharmacognosy, Faculty of Pharmacy, Ege University, Izmir, Turkey.

Extraction and fractionation. Coarsely powdered aerial parts (650 g) were extracted exhaustively with EtOH at room temp. The EtOH extract was concd *in vacuo*, acidified with 1 % HCl and washed with petrol. The aq. layer was made alkaline with NH_4OH and the alkaloids extracted with $CHCl_3$. Evaporation of solvent yielded a crude extract (5.65 g). This extract was placed on a Si gel (0.023–0.6 mesh) column which was eluted first with $CHCl_3$ and then with $CHCl_3$ containing increasing amounts of MeOH. The eluates were monitored by TLC, fractions of similar compositions combined, and then further separated and purified by prep. TLC on Si gel G. Bands were visualized under short-wave UV and by spraying with Dragendorff's reagent. The bands were eluted from the layer using CH_2Cl_2–MeOH (4:1).

Identification of alkaloids. All known alkaloids were identified on the basis of their physical and spectral data (UV, IR, NMR, MS, CD). Whenever available, authentic samples were used for confirmation. Amounts isolated were as follows: (+)-bicuculline (16 mg), (−)-capnoidine (30 mg), (−)-adlumine (110 mg), (−)-corledine (2 mg), *N*-methylhydrasteine (3 mg), *Z*-fumaramine (18 mg), fumaramidine (3 mg), adlumidiceine (5 mg), (+)-fumariline (35 mg), (+)-parfumine (220 mg), (+)-parfumidine (6 mg), protopine (183 mg), (−)-norjuziphine (7 mg), (+)-stylopine (5 mg), (−)-cheilanthifoline (4 mg) (−)-scoulerine (5 mg), oxysanguinarine (1 mg), (±)-8-acetonyldihydrosanguinarine (2 mg), (±)-8-methoxydihydrosanguinarine (3 mg), dihydrosanguinarine (5 mg), norsanguinarine (2 mg), (+)-isocorydine (4 mg), (+)-isoboldine (4 mg), *N*-methylcorydaldine (1 mg). (+)-Juziphine (22 mg), CD $\Delta\varepsilon$ (nm) MeOH −1.5 (274), −0.3 (254), −5.2 (237), −3.5 (231), −3.6 (228), −2.3 (224), and *E*-fumaramine (4 mg), UV λ_{max}^{MeOH} nm (log ε): 205 (4.59), 219 sh (4.42), 238 sh (4.21), 264 (3.99), 357 (4.04); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1705; MS *m/z* 380 (1), 378 (1), 335 (2), 334 (2), 333 (3), 320 (1), 281 (1), 219 (1), 207 (3), 204 (8), 149 (5), 58 (100) were also isolated.

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