ALKALOIDS OF Fumaria vaillantii

STRUCTURE OF VAILLANTINE

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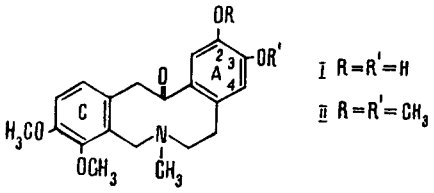
Protopine, cryptopine, d-α-hydrastine, parfumine, parfumidine, fumaridine, fumaramine, and fumvailline have previously been isolated from Fumaria vaillantii Loisl. [1-3].

In the present paper we give the results of an investigation of F. vaillantii collected in the environs of the village of Aktash (Karzhantau range, Western Tien-Shan) in the period of flowering and the beginning of fruit bearing. Chloroform extraction yielded 0.62% of combined alkaloids (ether fraction 0.4% and chloroform fraction 0.22%). When the ether fraction was concentrated, the alkaloids crystallized out. Fractional recrystallization from a mixture of chloroform and methanol of the precipitated crystals led to the isolation of protopine and fumaridine [2, 4]. When the mother liquor from the ethereal fraction was treated with methanol, d-α-hydrastine separated out, after which the residue was chromatographed on a column of alumina. In addition to the three alkaloids mentioned above, fumaramine, d-bicuculline, *l*-adlumine, *l*-adlumidine, and a base with mp 165-167°C (decomp.) were obtained. All the alkaloids were identified by direct comparison with authentic samples [2, 5]. It must be noted that the alkaloid fumvailline isolated previously [1] has physicochemical properties very close to those of *l*-adlumine, and it is possible that they are identical.

The base with mp 165-167°C is sparingly soluble in ether, benzene, chloroform, acetone, and ethanol, and readily soluble in alkaloids. Its UV spectrum has an absorption maximum at 292 nm (log ε 3.92). Molecular weight 357 (mass spectrometrically). The base is a new one, and we have called it vaillantine (I). The production of a O,O-dimethyl ether (II) with mp 174-175°C (M^+ 385) on methylation with diazomethane shows the presence of two phenolic hydroxy groups in the base. In the IR spectrum of (II), as in that of the base itself, there are absorption bands at 1650 cm^{-1} (C=O) and 1600 cm^{-1} (aromatic ring), and in its NMR spectrum there are signals in the form of a three-proton singlet at 1.80 ppm due to an $N-CH_3$ group, the signals from four methoxy groups at 3.80 ppm (3H) and 3.84 ppm (9H), two one-proton singlets at 6.60 and 6.97 ppm (para-aromatic protons), and two one-proton doublets at 6.74 and 6.88 ppm (J=8 Hz) (ortho-aromatic protons). The UV, IR, NMR, and mass spectra of (I) and (II) are characteristic for protopine alkaloids.

The spectral characteristics given, and also the melting point of (II), coincide with the characteristics of muramine [6]. The mass spectrum of (II), the main peaks of which are due to ions with m/e 121, 149, 164 (100%), 179, 206, and 385, coincides with that of muramine [7]. The results of a direct comparison of (II) and an authentic sample of muramine, kindly provided by Prof. F. Shantavy, showed their identity. The peak of an ion with m/e 164 is the maximum peak in the mass spectra of vaillantine and its methyl ether (II). Since this ion is formed from ring C, hydroxy groups must be present in ring A at C_2 and C_3. On the basis of the facts given, structure (I) follows for vaillantine.



I R=R'=H

II R=R'=CH_3

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EXPERIMENTAL

The UV spectra were taken on a Hitachi spectrophotometer, the IR spectra on a UR-10 instrument (tablets with KBr), the mass spectra on an MKh-1303 mass spectrometer fitted with a system for direct introduction into the ion source, and the NMR spectra on a JNM-4H 100/100 MHz spectrometer.

The air-dry plant material (13 kg) was moistened with 7% ammonia and extracted with chloroform. The alkaloids were re-extracted from the chloroform solution with 10% sulfuric acid. The acid solution was made alkaline with 25% ammonia and the alkaloids were extracted with ether and then with chloroform. This gave 52.97 g (0.4%) of combined ether-soluble and 27.74 g (0.22%) of combined chloroform-soluble alkaloids. When the ether-soluble fraction was treated with a mixture of chloroform and methanol, 7.0 g of protopine separated out with mp 204-205°C. On standing, the mother liquor deposited 4.1 g of fumaridine with mp 189-190°C. After the separation of the protopine and fumaridine, retreatment of the mother liquor with methanol gave 0.96 g of d-α-hydrastine. The remainder of the ether-soluble fraction (40.0 g) was chromatographed on a column of alumina with elution by chloroform, chloroform–methanol, and methanol. The eluate was collected in 50-ml fractions. The first-third chloroform fractions yielded an additional 5.6 g of protopine and 3.7 g of fumaridine, and the fourth and fifth gave 0.4 g of fumaramine. On elution with chloroform–methanol (98 : 2), the second-fourth fractions yielded 2.5 g of d-α-hydrastine and 0.7 g of d-bicuculline, the seventh and eighth gave 0.25 g of *l*-adlumine, and the tenth and eleventh fractions, 0.21 g of *l*-adlumidine. Elution with chloroform–methanol (1 : 1) led to the isolation of 0.11 g of vaillantine with mp 165-167°C (decomp., acetone–methanol).

O,O-Dimethyl Ether of (I)(II). The methylation of (I) (27 mg) with diazomethane gave a crystalline substance with mp 174-175°C (from methanol).

SUMMARY

The plant Fumaria vaillantii Loisl. has yielded protopine, fumaridine, fumaramine, d-α-hydrastine, *l*-adlumine, d-bicuculline, and *l*-adlumidine (this being the first time that *l*-adlumidine has been isolated from the genus Fumaria), and the new base vaillantine. On the basis of UV, IR, NMR, and mass spectra, and also the identity of O,O-dimethylvaillantine with muramine, the structure of vaillantine has been established as 2,3-didemethylmuramine.

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