(−)-CORLUMINE, A NEW PHTHALIDEISOQUINOLINE ALKALOID FROM *FUMARIA PARVIFLORA*

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ABSTRACT.—*Fumaria parviflora* Lam. (Fumariaceae) has yielded the new phthalideisoquinoline alkaloid (−)-corlumine (**2**) previously known only in its dextrorotatory form. Two known alkaloids not previously detected in *F. parviflora* are (+)-adlumidine (**1**) and (−)-cheilanthifoline (**3**). Phthalideisoquinoline alkaloids as isolated from plants show no pronounced stereochemical preference either at C-1 or at C-9. Most protoberberine alkaloids, however, possess the S- chirality at C-14.

As part of a program of studying the flora of Pakistan for its alkaloidal content, we had occasion recently to investigate the creeper *Fumaria parviflora* Lam., which is identical with *F. indica* Pugsley (Fumariaceae), of widespread distribution in that country (1). Three new alkaloids were isolated and characterized as a result of that investigation, namely the substituted *o*-(β-dimethylaminoethyl) benzoic acid fumariflorine obtained as its ethyl ester, the glycosidic spirobenzylisoquinoline parviflorine, and the ring B opened phthalideisoquinoline fumaramidine. In addition, *F. parviflora* is also a rich source of previously known spirobenzylisoquinolines and phthalideisoquinolines (1).

Since a supply of the spirobenzylisoquinolines fumariline, parfumidine, and parfumine was required for a projected study of the chemistry of spirobenzylisoquinolines, and since *F. parviflora* was known to be a satisfactory source for these bases, it was decided to repeat our procedure for the isolation of alkaloids from this plant (1). For this purpose, the dried ethanol extracts (46 g) corresponding to extract A from 12 kg of dried whole plant material were chromatographed on a silica gel column as previously described. Eight major fractions were collected.

In our initial isolation, 35 g of extract A had been chromatographed. In our second and present study, when 46 g were placed on the column, unexpectedly we obtained not only the spirobenzylisoquinolines we desired, but also other isoquinoline alkaloids which had eluded us in our initial study. Specifically, (+)-adlumidine (**1**) (35 mg), and (−)-corlumine (**2**) (4 mg) were obtained. The former is a known phthalideisoquinoline which had not been previously found in *F. parviflora*; (−)-corlumine is a new phthalideisoquinoline previously recognized only in its dextrorotatory form in several members of the Fumariaceae (3). Our corlumine possessed a circular dichroism (cd) curve opposite to that of the fully characterized (+)-corlumine (2), yet corresponded to that alkaloid in all of its spectral properties.

Another alkaloid not previously detected in *F. parviflora* is the protoberberine (−)-cheilanthifoline (**3**) (20 mg). This phenolic base had been initially found in *Cordydalis platycarpa* Makino (Fumariaceae) (4, 5) and possesses the S- chirality because of its negative specific rotation and the shape of its cd curve.[3]

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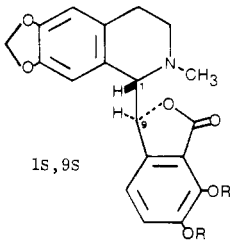
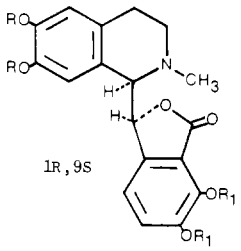
[3]We have found the cd curve of (−)-cheilanthifoline to be similar to that of (−)-canadine and (−)-stylopine; see G. Snatzke, J. Hrbek, Jr., L. Hruban, A. Horeau and F. Šantavy, *Tetrahedron*, **26**, 5013 (1970).

Some interesting stereochemical conclusions can be drawn when the above results are added to the already large body of optical data available for the protoberberines and phthalideisoquinolines. Most protoberberine alkaloids are derived biogenetically from the tetrahydrobenzylisoquinoline (+)-reticuline (**6**) which incorporates the S- configuration (6, 7), so most, but not all, protoberberine bases possess the S- configuration. As for the phthalideisoquinolines, it has been shown that they are derived in plants from protoberberines in a complex series of transformations whose intimate details are still not completely understood, but in which the integrity of the hydrogen at the asymmetric center is maintained (8–10). In spite of this retention of the asymmetric hydrogen, however, phthalideisoquinolines as found in nature show no pronounced stereochemical preference either at C–1 or at C–9. In the present case, for example, of the four classical type phthalideisoquinolines found in *F. parviflora*, (+)-bicuculline (**7**) possesses the 1S,9R configuration, while (+)-α-hydrastine (**8**) and (+)-adlumidine (**1**) have the 1S,9S arrangement, and (−)-corlumine (**2**) is 1R,9S.

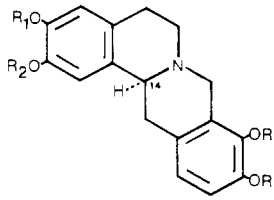


1, R + R = CH_2

8, R = CH_3



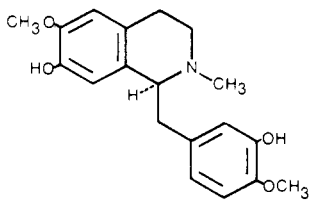
2, R = CH_3, R_1 + R_1 = CH_2



3, R_1 = CH_3, R_2 = H, R + R = CH_2

4, R_1 + R_2 = CH_2, R = CH_3

5, R_1 + R_2 = R + R = CH_2



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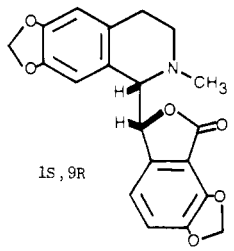

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EXPERIMENTAL

GENERAL PROCEDURES.—Melting points are uncorrected. All nmr data were collected on a Bruker 200 MHz Supercon (FT) spectrometer in $CDCl_3$ solution with TMS as internal standard. Mass spectra were taken with an AEI MS-902 instrument. The circular dichroism measurements were done on a JASCO-20 spectropolarimeter, and the ultraviolet spectra were recorded on a Hewlett-Packard 8450A UV/VIS spectrophotometer. All uv and cd curves are in methanol. Tlc was performed on silica gel F–254 plates in benzene-methanol 100:12 v/v (System A) or in ether-methanol 100:5 v/v (System B). The plant material was collected in the vicinity of Peshawar, Pakistan. Dr. S. M. A. Kazmi, Plant Taxonomist at the PCSIR Laboratories, Peshawar, assisted in the plant identification.

COLUMN CHROMATOGRAPHY.—Extract A (46 g) from *F. parviflora* Lam. (1) was chromatographed on Silica Gel 60 (2.5 kg) (70–230 mesh ASTM). The column was eluted first with chloroform and then with 1% methanol in chloroform. A total of 75 liters of solvent was

passed. The different fractions were collected into eight groups, AI and AVIII, based on their tlc characteristics.

Fraction AI.—Fraction AI (1.22 g) was fractionated by tlc (benzene-methanol 100:20). (+)-Adlumidine (**1**) (35 mg) and (−)-corlumine (**2**) (4 mg) were found close to the previously reported (1) stylopine (**5**) (44 mg), mp 205–207° (EtOH) (lit. mp 204–208°) (11), R_f 0.64 (System A), 0.68 (System B), and (+)-α-hydrastine (**8**) (20 mg), mp 159–161° (EtOH) (lit. mp 160–161°) (12), R_f 0.51 (System A), 0.51 (System B).

(+)-Adlumidine (**1**) (oil), R_f 0.57 (System A), 0.61 (System B), $C_{20}H_{17}O_6N$, *m/e* 336 (0.1, M^-), 328 (0.3), 190 (100); λ max 221, 235 sh, 295, 324 nm (log ε 4.42, 4.15, 3.77, 3.70), λ min 215, 264, 307 nm (log ε 4.40, 3.22, 3.61); nmr δ2.55 (s, 3H, NCH_3), 5.86 (s, 2H, OCH_2O), 6.11 (s, 2H, OCH_2O), 4.04 (d, 1H, *J* 3.3 Hz, H-1), 5.63 (d, 1H, *J* 3.3 Hz, H-9), 6.41 (s, 1H, H-8), 6.67 (s, 1H, H-5), 6.94 (d, 1H, *J* 8 Hz, H-2'), 7.13 (d, 1H, *J* 8 Hz, H-3'); cd $\Delta\epsilon_{nm}$ -0.6_{330}, -2.0_{297}, -2.44_{250}, $+8.80_{232}$.

(−)-Corlumine (**2**) (oil), R_f 0.51 (System A), 0.48 (System B), $C_{21}H_{21}O_6N$, *m/e* 382 (0.2, M^-), 351 (0.3), 333 (0.6), 332 (1.6), 207 (42), 206 (100), 191 (7.4), 190 (31.5), 177 (9.2), 176 (1.4), 162 (6.8), 161 (5.1), 148 (3.6); λ max 220, 235 sh, 293, 323 nm (log ε 4.49, 4.21, 3.67, 3.71), λ min 215, 263, 303 nm (log ε 4.46, 3.28, 3.57); nmr δ2.59 (s, 3H, NCH_3), 3.71 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 6.16 (s, 2H, OCH_2O), 4.10 (d, 1H, *J* 3.5 Hz, H-1), 5.67 (d, 1H, *J* 3.5 Hz, H-9), 6.37 (s, 1H, H-8), 6.61 (s, 1H, H-5), 6.24 (d, 1H, *J* 8 Hz, H-2'), 6.94 (d, 1H, *J* 8 Hz, H-3'); $\Delta\epsilon_{nm}$ -2.46_{325}, $+0.43_{280}$, -1.45_{270}, $+16.3_{255}$, $+23.2_{226}$.

Fractions AII to AVI.—These contained fumariline, parfumidine and parfumine (1).

Fraction AVII.—Fraction AVII (0.83 g) was fractionated by tlc to furnish (+)-bicuculline (**7**) (170 mg), mp 195–196° ($CHCl_3$-MeOH) (lit. mp 196°) (13), R_f 0.43 (System A), 0.32 (System B); and (−)-cheilanthifoline (**3**) (20 mg).

(−)-Cheilanthifoline (**3**), mp 198–199° ($CHCl_3$) (lit. mp 200–201°) (4) (lit. $[\alpha]^{20}D$ −331±15°) (14), R_f 0.37 (System A), 0.46 (System B), $C_{19}H_{15}O_4N$, *m/e* 325 (38, M^+), 324 (23), 178 (1.2), 177 (1.6), 176 (10), 149 (15), 148 (100); λ max 236 sh, 286 nm (log ε 3.90, 3.79); nmr δ3.87 (s, 3H, OCH_3), 5.93 and 5.97 (q, 2H, J_{gem} 1.3 Hz, OCH_2O), 6.60 (s, 1H, H-1), 6.82 (s, 1H, H-4), 6.65 (d, 1H, *J* 8 Hz, H-12), 6.71 (d, 1H, *J* 8 Hz, H-11); cd $\Delta\epsilon_{nm}$ $+0.19_{285}$, -6.16_{235}.

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