Alkaloids of fumariaceous plants. LVII. Miscellaneous observations

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The isolation of a number of new alkaloids from plants previously investigated is reported. Several known alkaloids have been encountered for the first time in plants also previously examined.

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A further investigation of plants already reported upon has disclosed a number of new alkaloids and a number of new sources of known alkaloids. These were recovered from new lots of plant material and from a further study of some mother liquors. Several alkaloids which had been given F-numbers have been shown to be mixtures or have been identified with known bases.

Fumaria officinalis L.

This much investigated plant has been subjected to further study in that a new lot of plant material had become available. The alkaloids already reported (1) were again obtained but the combined mother liquors gave the known scoulerine and two new alkaloids, fumariline, $C_{20}H_{17}O_5N$ and F63, $C_{20}H_{21}O_5N$ which may be identical with fumaritine isolated from *F. schleicheri* Soyer-Willem (2). A request to the senior author (P. S. Massagetov) for a specimen for direct comparison remains unanswered. The structures and properties of F37 (fumaricine), fumaritine, and fumariline have been reported (4).

Corydalis ochroleuca Koch (3)

Five alkaloids, none new but, not previously isolated, isocorydine, 1-sinactine, *d*-glaucine, 1-scoulerine, and adlumidine were obtained.

Corydalis tuberosa DC. (5)

In addition to the alkaloids which had been shown to be elaborated by this plant there were obtained, capnoidine, domestine, and narcotine. There were also obtained a number of fractions of alkaloids of doubtful homogeneity which are currently under study.

Corydalis pallida (Thunb.) Pers. (6)

Corydaline, cryptopine, and *dl*-stylopine were obtained.

Corydalis sibirica (L.) Pers. (7)

The alkaloid F16 proved to be not quite pure adlumidine. After another recrystallization from chloroform it melted sharply at 237° either alone or in admixture with authentic adlumidine.

Experimental

The mother liquors from previous examinations, together with fresh alkaloids from additional plant material, were reworked by the procedure (8) which has been generally satisfactory. The fractions BS and BSE refer respectively to non-phenolic and phenolic bases whose hydrochlorides are *not* extractable from aqueous solution by chloroform. The fractions BC and BCE are respectively non-phenolic and phenolic bases whose hydrochlorides are extractable from aqueous solution by chloroform. All melting points are corrected.

Fumana officinalis

The bases in the filtrate from which alkaloid F37 (fumaricine) had been crystallized were redissolved in dry chloroform and passed through a long column of ca. 250 g neutral alumina. Four eluates of approximately 200 ml each were obtained, pale-yellow, colorless, pale-orange, and colorless. The two last fractions yielded some more F37. The first two fractions were converted to hydrochlorides and yielded a salt from which the free base was regenerated. When recrystallized from methanol, fumariline (F64), obtained in stout prisms, melted at 138°.

Anal. Calcd. for $C_{20}H_{17}O_5N$: C, 68.37; H, 4.84; N, 3.99; NMe, 4.27. Found: C, 68.29; H, 4.93; N, 3.88; NMe, 4.74.

When this alkaloid was treated with carbon disulfide in concentrated ether solution, there was rapid separation of pale-yellow stout prisms which melted at 92° with gas evolution. A test for carbon disulfide was strongly positive (9) and when this compound was admixed with that melting at 138°, the mixture m.p. was 138°, when slowly heated. The infrared (i.r.) and nuclear magnetic resonance (n.m.r.) spectra of the two compounds were superimposable. The yield of this alkaloid was about 0.3 g from 110 kg of dried plant material, and the yields of scoulerine and fumaritine were about 0.1 and 0.5 g respectively.

The total phenolic base fraction from the above amount of plant material weighed only several grams. It was converted to hydrochloride in methanol and then precipitated with excess dry ether with which the pasty residue was repeatedly triturated. When in contact with acetone containing a trace of methanol it became crystalline and was recrystallized from methanol–acetone and then consisted of a mixture of two hydrochlorides.

The portion very sparingly soluble in water proved to be the hydrochloride of 1-scoulerine (free base, m.p. and mixture m.p. 205°). The very soluble hydrochloride (m.p. 248°) was converted to free base and this crystallized readily from dry ether in fine colorless needles melting at 157°. Fumaritine, so obtained, gave a nondescript dirty green color with concentrated sulfuric acid.

Anal. Calcd. for $C_{20}H_{21}O_5N$: C, 67.60; H, 5.92; N, 3.94; 1 OMe, 8.73. Found: C, 67.87, 68.00; H, 5.32, 5.56; N, 3.83, 4.13; OMe, 9.00, 9.60.

When a solution of fumaritine in methanol was treated with diazomethane there was rapid evolution of nitrogen and the non-phenolic base isolated from the reaction mixture was identical with fumaricine.

Corydalis ochroleuca

The more soluble fraction from which 1-isocorypalmine had been separated was converted to hydrobromide and the base was then regenerated from the sparingly soluble salt. The free base was recrystallized from methanol–ether and then consisted of colorless plates, m.p. 184°, either alone or mixed with *d*-isocorydine.

The fraction from which the 1-tetrahydropalmatine had been separated was dissolved in dry chloroform and passed through a long column of (ca. 250 g) neutral alumina. The base from the front zone of ca. 100 ml solvent was converted to hydrobromide (m.p. 248° decomp.) and the base regenerated again. When recrystallized from methanol it melted at 175–176°. The m.p. was unchanged when admixed with a specimen of 1-sinactine.

The subsequent eluates gave a fraction which yielded a mixture of perchlorates, pale-yellow needles and stout dark polyhedra. The former, more soluble in acetone, proved to be 1-tetrahydropalmatine perchlorate. The less soluble salt was recrystallized from methanol–acetone (m.p. 233°) and the m.p. was not lowered when the salt was admixed with *d*-glaucine perchlorate. The free base, prepared from the perchlorate, was recrystallized from dry ether and then melted at 120° either alone or mixed with *d*-glaucine.

The combined mother liquors from which the protopine and ochroberine had been separated were dissolved in dilute hydrochloric acid and the bases regenerated and dissolved in dry ether. The solution was filtered through a short column of alumina and then deposited a sparingly soluble base which, when recrystallized from chloroform–methanol, melted at 237° either alone or mixed with adlumidine.

The phenolic fraction BSE in contact with methanol yielded some isocorydine. The bases in the soluble fraction were dissolved in dry chloroform and passed through a column of ca. 250 g neutral alumina. When continued percolation with chloroform removed nothing further, the column was eluted with 4% methanol in chloroform. The residue from the eluate crystallized readily when dissolved in hot methanol. It melted at 208° (*in vacuo*) and the m.p. was unchanged when mixed with 1-scoulerine.

Corydalis tuberosa

The somewhat less basic fraction (BC) from which thalictricavine had been separated was converted to perchlorate in methanol. The sparingly soluble salt which separated proved to be the perchlorate of corycavine. The base in the soluble portion was converted to l-tartrate and the sparingly soluble salt thus obtained was recrystallized first from hot methanol (sparingly soluble) and then from water–methanol. The *l*-tartrate then melted at 223° and the base regenerated from it melted at 140° when recrystallized from dry ether in which it was sparingly soluble.

Anal. Calcd. for $C_{20}H_{21}O_4N$: C, 70.80; H, 6.20; 2 OMe, 18.30. Found: C, 71.32, 71.03; H, 6.05, 5.99; OMe, 18.64, 18.39.

The tartrate analyzed satisfactorily for $C_{20}H_{21}O_4N{\cdot}C_4H_6O_4{\cdot}1/2\ MeOH$. The methine, prepared in the usual way from the methiodide, melted at 130° (lit. (10), m.p. 133°) when recrystallized from ether. A specimen of domestine received from Professor Tatsuo Ohta (Tokyo College of Pharmacy, Shinjuku-ku, Japan) melted at 139° and a mixture of it with the above base melted at the same temperature.

The mother liquors from the crystallization of the corydaline were also divided into a number of fractions of progressively weaker bases by successive elution with hydrochloric acid from ether solution. The middle fractions were converted to nitrates in methanol and the salt, which separated and proved to consist largely of corydaline nitrate, was removed. The bases in the soluble portion were regenerated and the portion which then crystallized from ether was recrystallized from chloroform–methanol.

Anal. Calcd. for $C_{22}H_{23}O_7N$: C, 63.91; H, 5.61. Found: C, 64.20, 64.40; H, 5.82, 5.82.

Infrared and n.m.r. spectra showed the presence of a lactone carbonyl, three methoxyls, one *N*-methyl, and one methylenedioxy group. Its m.p. (176°) and the above properties suggest that this alkaloid is narcotine and a mixture m.p. confirmed its identity.

The mother liquors from the separation of the corycavine were converted to oxalates a second time in methanol. The mixture of salts thus obtained consisted largely of the sparingly soluble corycavine oxalate and a second minor component which was removed by warming with water. The base, regenerated from the soluble portion, was recrystallized from chloroform–methanol and then melted at 238°, either alone or mixed with capnoidine. When some of this and an equal weight of adlumidine were recrystallized from chloroform–methanol there was formed *dl*-capnoidine which melted at 206°, either alone or mixed with an authentic specimen.

Corydalis pallida

The mother liquors from which *d*-tetrahydropalmatine had crystallized were converted to hydrochloride and another crop separated. The soluble portion was converted to free base and its solution in ether was dried over potassium hydroxide. Removal of the ether and contact of the residue with methanol yielded a crop of *d*-corydaline which, alone or mixed with an authentic specimen, melted at 135°.

The filtrate from the corydaline was converted to acid oxalate in methanol–acetone. The sparingly soluble salt which slowly separated was washed with acetone and the base regenerated from it crystallized in contact with methanol and proved to be cryptopine (m.p. and mixture m.p., 223°).

The oxalates which remained in solution from the above experiment were reconverted to the free base mixture. A methanol solution of these yielded a mixture of crystalline bases. The portion sparingly soluble in warm methanol was recrystallized from chloroform–methanol and the resultant *dl*-stylopine (m.p. 220°) was identified by a mixture m.p. determination.

1. R. H. F. Manske. Can. J. Res. **B16**, 438 (1938).
2. T. F. Platonova, P. S. Massagetov, A. D. Kuzovkov, and L. M. Utkin. Zh. Obshch. Khim. **26**, 173 (1956).
3. R. H. F. Manske. Can. J. Res. **B17**, 95 (1939); Can. J. Chem. **46**, 2873 (1968).
4. J. K. Saunders, R. A. Bell, C.-Y. Chen, D. B. MacLean, and R. H. F. Manske. Can. J. Chem. **46**, 2873, 2876 (1968).
5. R. H. F. Manske. J. Am. Chem. Soc. **75**, 4928 (1953).
6. R. H. F. Manske. Can. J. Res. **B18**, 80 (1940).
7. R. H. F. Manske. Can. J. Res. **B14**, 354 (1936).
8. R. H. F. Manske. Can. J. Res. **8**, 210 (1933).
9. F. Feigl and K. Weisselberg. Z. anal. Chem. **83**, 101 (1931).
10. H. Shishido. Bull. Chem. Soc. Japan, **13**, 247 (1938).