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MORPHINANDIENONE ALKALOIDS FROM *CORYDALIS INCISA*

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Abstract—Separation of the alkaloids from *Corydalis incisa* (Pers) collected in Sendai in May gave the two morphinandienone alkaloids, sinoacutine and pallidine, together with corynoline, acetylcorynoline, isocorynoline, corynoloxine, protopine and corycavine.

WE RECENTLY isolated the morphinandienone alkaloids, sinoacutine (I) and pallidine (II), from *Corydalis pallida* var. *tenuis* (Yatabe).[1] Therefore, in the hope of finding alkaloids of this type elsewhere, the basic fractions from other *Corydalis* species have been examined. The alkaloids of *C. incisa* (Pers) have been already well studied[2–5] and it was found that they varied with the environment and the age of the plant. We have investigated the alkaloids from *C. incisa*, which was collected in Sendai in May, and isolated sinoacutine (I) and pallidine (II) together with corynoline (III), acetylcorynoline (VI), corynoloxine (V), isocorynoline, protopine (VI) and corycavine (VII).

The basic extract from *C. incisa* was separated by the usual method into phenolic and non-phenolic bases, which were characterized after separation by silica gel column chromatography. The phenolic bases, present in very small amounts, gave sinoacutine (I) and pallidine (II), identical with authentic samples[1] in their IR and NMR spectra.

From the non-phenolic bases, six alkaloids, *A*, m.p. 217–218°; *B*, m.p. 159–160°, *C*, m.p. 209–210°; *D*, m.p. 234–235° [$[\alpha]_D^{25}$ +125° (in MeOH)]; *E*, m.p. 207–208°; and *F*, m.p. 221–222°, were isolated. Alkaloid *A*, which was a main alkaloid of this plant, was identical with corynoline (III)[6] by its m.p., NMR[4] and mass spectra. Acetylation of corynoline afforded the alkaloid *B*, whose IR, NMR[4] and mass spectra were compatible with those of acetylcorynoline (IV). Hydrogenation of alkaloid *C*, whose IR, NMR[4] and mass spectra suggested the structure of corynoloxine (V),[4] in the presence of 30% palladium-charcoal gave corynoline (III). The NMR and mass spectra of alkaloid *D* were similar with those of corynoline and its IR spectrum was superimposable on that of isocorynoline (donated by Prof. Nishioka). No depression was observed on a mixed m.p. test with the authentic sample, which is a stereoisomer of corynoline (III). Acetylation of isocorynoline gave acetylisocorynoline, m.p. 210–211°, $[\alpha]_D^{28}$ + 62·8° (in $CHCl_3$), whose IR and NMR spectra were superimposable on those of an authentic sample. The properties of alkaloid *E* were identical with those of protopine (VI)[1] in all respects. The IR spectrum of alkaloid *F*

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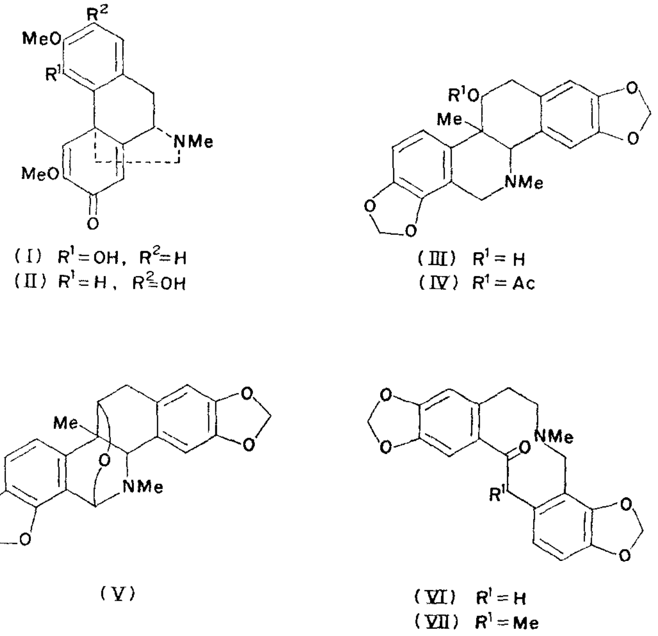

Scheme 1.

showed a carbonyl absorption of 1655 cm^{-1} like protopine and NMR spectrum (in $CDCl_3$) showed a methyl group at 1·33 ppm as doublet with *J* 7·5 Hz. Furthermore, the mass spectrum, by reference to the fragmentation pattern of protopine alkaloids,[7] confirmed the alkaloid *F* to be corycavine (VII).[8]

It is of interest that the morphinandienone alkaloids, sinoacutine and pallidine, have been isolated only from plants grown in Sendai in the northern part of Japan and were not found in the same plant grown in the southern part of Japan.

EXPERIMENTAL

M.ps are uncorrected. The IR spectra were taken in $CHCl_3$ to remove with a Hitachi EPI-3 spectrophotometer and NMR spectra were measured on a Hitachi R-20 in $CDCl_3$ using TMS as an internal standard. Mass spectra were measured on a Hitachi RMU-7. Optical rotations were measured with JASCO-PIP-SL automatic polarimeter.

Preliminary Separation of the Alkaloids

Dried material (1·39 kg) from *Corydalis incisa* (Pers), was finely cut and extracted 3 × hot MeOH. The extract was concentrated to give a dark brown gum (240 g), to which was added 3% HCl (1·5 l); the resulting mixture was heated at 70° for 15 min, cooled and well extracted with Et_2O. The acidic layer was basified (conc. NH_4OH) and well extracted with $CHCl_3$. The $CHCl_3$ extract was washed (H_2O), dried (Na_2SO_4), and evaporated to afford a dark brown residue (12·5 g) which was dissolved in 3% HCl (200 ml) The solution was washed with Et_2O, and the acidic layer basified with 10% NaOH and well extracted with Et_2O. The Et_2O extract was washed (H_2O), dried (Na_2SO_4), and evaporated to give a dark brown gum (6·9 g) (non-phenolic fraction). The alkaline layer was adjusted to about pH 6·0 with solid NH_4Cl and extracted with $CHCl_3$. The extract was washed (H_2O), dried (Na_2SO_4), and evaporated to afford a dark brown gum (1·1 g) as a phenolic fraction.

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Phenolic Fraction

The above phenolic fraction (1·1 g) was chromatographed on silica gel (60 g) with $CHCl_3$ [fractions (100 ml each) 1–14], $CHCl_3$–MeOH (99:1, v/v; fractions 15–26), $CHCl_3$–MeOH (98:2, v/v; fractions 27–49) and $CHCl_3$–MeOH (95:5, v/v; fractions 50–61).

Fractions 27–31 gave a brown gum (180 mg), whose IR spectrum showed a dienone absorption. This fraction was rechromatographed on alumina (20 g) with $CHCl_3$–benzene (1:1, v/v) as eluant to give a yellowish powder. Recrystallization from MeOH–Et_2O gave sinoacutine (45 mg) (I) as colourless prisms, m.p. 198–199°, $[\alpha]_D^{25}$ $-114°$ (c = 0·5 in methanol), with IR, NMR spectra and TLC behaviour which were identical with those of an authentic sample.[1]

Fractions 37–44 gave a brown gum (250 mg), which was rechromatographed on alumina (20 g) with $CHCl_3$ as eluant to give pallidine (II) (52 mg) as a pale yellowish syrup, whose IR and NMR spectra and TLC behaviour were identical with those of an authentic sample.[1] A mixture of pallidine (30 mg), Ac_2O (1 ml), and dry pyridine (2 ml) was set aside at room temp. for 2 days. A usual work-up gave a yellowish powder, whose recrystallization from MeOH–Et_2O afforded *O*-acetylpallidine (20 mg) as colourless needles, m.p. 186–187°, $[\alpha]_D^{25}$ $-73°$ (c = 0·11 in $CHCl_3$), whose IR and NMR spectra were superimposable on those of an authentic sample and no depression was shown on mixed m.p.

Non-phenolic Fraction

The non-phenolic fraction mentioned above was chromatographed on silica gel with $CHCl_3$ [fractions (300 ml each) 1–18], $CHCl_3$–MeOH, 99:1, v/v (fractions 19–25) and 98:2, (fractions 26–33) as eluants.

Fraction 4 gave a yellowish powder, which was recrystallized from MeOH to give acetylcorynoline (IV) as colourless plates, m.p. 159–160° (lit.,[3] m.p. 159–160°) (Found: C, 67·60; H, 5·77; N, 3·23. Calc. for $C_{23}H_{23}NO_6$: C, 67·46; H, 5·66; N, 3·42%), *m/e* 409 (M^+), 366, 349, 334, 318, 202, 190, 176 and 162.

Fractions 5–7 gave a yellowish powder, which was recrystallized from MeOH to give corynoline (III) (1·32 g) as colourless plates, m.p. 217–218° (lit.,[3] m.p. 216–217°) (Found: C, 68·70; H, 5·92; N, 3·74. Calc. for $C_{21}H_{21}NO_5$: C, 68·65; H, 5·76; N, 3·81%), *m/e* 367 (M^+), 349, 334, 318, 202, 190, 176 and 162. Acetylation of corynoline with Ac_2O–pyridine gave acetylcorynoline, m.p. 159–160°, whose IR and NMR spectra and TLC behaviour were identical with those of the sample prepared as above.

Fraction 8 gave a powder, which was recrystallized from MeOH to give isocorynoline (15 mg) as colourless needles, m.p. 234–235°, $[\alpha]_D^{25}$ $+125°$ (c = 0·12 in MeOH) [lit.,[3] m.p. 235–236°, $[\alpha]_D^{25}$ $+112·02°$ (in $CHCl_3$)], δ 1·10 (3H, s, 12a-Me), 2·49 (3H, s, NMe), 5·88 and 5·94 (each 2H, each s, 2 × $O\cdot CH_2\cdot O$), 6·88 and 7·15 (each 1H, each s, 7- and 12-H), 6·70 and 6·88 ppm (each 1H, each d, *J* 8 Hz, 1- and 2-H) *m/e* 367 (M^+), 349, 334, 318, 307, 202, 190, 176 and 162, whose IR spectrum was identical with that of an authentic sample[5] donated by Prof. Nishioka and no depression was observed on mixed m.p. Acetylation of isocorynoline gave acetylisocorynoline, m.p. 210–211°, $[\alpha]_D^{28}$ $+62·8°$ (c = 0·33 in $CHCl_3$), with IR and NMR [δ 1·17 (3H, s, 12a-Me), 1·75 (3H, s, COMe), 2·50 (3H, s, NMe), 5·90 and 5·93 (each 2H, each s, 2 × $O\cdot CH_2\cdot O$), 6·55 and 7·19 (each 1H, each s, 7- and 10-H), 6·71 ppm (2H, s, 1- and 2-H)] spectra which were identical with those of an authentic sample.[5]

Fractions 10–20 gave a brown powder, which was recrystallized from MeOH to afford corynoloxine (V) (55 mg) as colourless pillars, m.p. 209–210° (lit.,[3] 209–210°) (Found: C, 69·17; H, 5·39; N, 4·03. Calc. for $C_{21}H_{19}NO_5$: C, 69·05; H, 5·24; N, 3·83%), *m/e* 365 (M^+), 336, 306, 280, 202, 189, 188 and 175.

Fractions 23–28 gave a brown syrup (120 mg), which was rechromatographed on alumina (10 g) with $CHCl_3$ as eluant to give a yellowish powder. Recrystallization from MeOH gave corycavine (VII) (90 mg) as a colourless powder, m.p. 221–222° (Found: C, 67·95; H, 5·88; N, 3·80. Calc. for $C_{20}H_{19}NO_5$: C, 67·98; H, 5·42; N, 3·96%), with IR [ν_{max} ($CHCl_3$) 1655 cm^{-1} (C=O)], NMR [δ 1·34 (3H, d, *J* 7·5 Hz, 13-Me), 1·81 (3H, s, NMe), 5·88 (4H, s, 2 × $O\cdot CH_2\cdot O$), 6·60 and 6·91 (each 1H, each s, 1- and 4-H), 6·73 ppm (2H, s, 11- and 12-H)] and mass (*m/e* 367, 206, 204, 163 and 162) spectra, which were identical with those of an authentic sample.[5] No depression was observed on mixed m.p.

Fractions 30–33 gave a yellowish powder, whose recrystallization from MeOH gave protopine (VI) as colourless prisms, m.p. 207–208°, with IR and NMR spectra identical with those of an authentic sample.[1]

Hydrogenation of Corynoloxine

A solution of corynoloxine (V) (50 mg) in MeOH (20 ml) was shaken in the presence of 30% Pd-C (50 mg) under H_2. After filtration, removal of the solvent gave a yellowish powder, whose recrystallization from MeOH gave corynoline (III) (42 mg) as colourless plates, m.p. 217–218°, with IR and NMR spectra and TLC, which were identical with those of the above authentic sample.

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