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A BERBINE ALKALOID, LIENKONINE FROM *CORYDALIS OCHOTENSIS**

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Key Word Index—*Corydalis ochotensis*; Fumariaceae; alkaloid; berbine-type; lienkonine.

Abstract—Lienkonine, a further alkaloid from *Corydalis ochotensis*, has been isolated and elucidated as (−)-2,3,10-trimethoxy-8α-methyl-13aαH-berbine-9-ol by the spectral data and chemical properties.

INTRODUCTION

Besides protopine, an ordinary alkaloid of *Corydalis* spp., several alkaloids from *Corydalis ochotensis* Turcz (Fumariaceae) have been isolated previously[1]. There are yenhusomine, yenhusomidine and ochotensimine which belong to the spirobenzylisoquinoline type; corytenchine (**1**), corytenchirine (**2**) and didehydrocheilantifoline which belong to the berbine type and adlumidine which belongs to the phthalideisoquinoline type. Here we report a further new berbine alkaloid, lienkonine, isolated from this plant.

RESULTS AND DISCUSSION

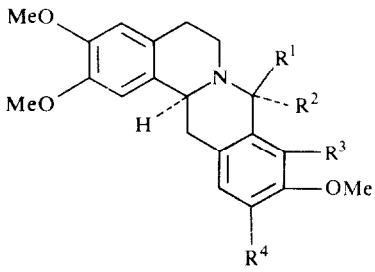
The base D, a molecular compound of corytenchine (**1**) and corytenchirine (**2**) formerly separated from part A shown in the scheme of the previous paper [1] was also found in part B. After separating base D from part B, the HCl salt was obtained while the mother liquid was acidified with HCl. When this salt was converted into free base, lienkonine was produced.

Owing to the positive Gibbs test and the information from IR and UV spectra, lienkonine was indicated as a phenolic berbine derivative. The ^{1}H NMR (60 MHz, $CDCl_3$) spectrum shows the presence of three methoxyl groups at δ3.85 (6H, *s*, 2×OMe) and 3.88 (3H, *s*, 1×OMe), four aromatic protons at δ6.65 (1H, *d*, J = 6 Hz), 6.62 (1H, *s*), 6.69 (1H, *s*) and 6.77 (1H, *d*, J = 6.5 Hz), one methyl group centred at δ1.43 (3H, *d*, J = 6.5 Hz) and one hydroxyl group at δ5.75 (1H, *br s*); thus lienkonine is of the 2,3,9,10-oxygenated berbine type. Methylation of lienkonine with diazomethane produced a colourless, oily base whose ^{1}H NMR spectrum shows four methoxyl groups which progressively supported one phenolic group in the lienkonine molecule. The mass spectrum (70 eV) exhibited a molecular ion at *m/z* 355 and fragment ions at *m/z* 340, 192 [ion (**6**)], 190 [ion (**7**)] and 164 [ion (**8**)] which indicated that one hydroxyl group must be attached to ring D [2]. On the other hand, the signals for methyl groups centred at δ1.43 in the ^{1}H NMR spectrum and the fragment at *m/z* 164 [ion (**8**)] in the mass spectrum of lienkonine suggested that a methyl group may be located at C-8 or C-13.

The stereochemistry of the structures of 2,3,9,10-tetramethoxyberbine and 13-methylberbine (corydaline and mesocorydaline) have already been studied extensively. The spectral data of these diastereomers have been reported [3–7] but the IR ($CHCl_3$) and ^{1}H NMR spectra of *O*-methyllienkonine are different from those of (±)-corydaline and (±)-mesocorydaline which have been synthesized by the methods reported in the literature [8, 9].

In order to determine the stereochemistry of *O*-methyllienkonine, the IR and ^{1}H NMR spectra were compared with *O*-methylcorytenchirine whose steric structure has already been decided [1]. Signals due to the 8-methyl group of *O*-methyllienkonine appeared at δ1.43 (3H, *d*, J = 6.5 Hz) and are similar to those of *O*-methylcorytenchirine (δ1.40, 3H, *d*, J = 6.5 Hz), but are different from the chemical shifts of aromatic protons. In the IR spectra, both *O*-methylcorytenchirine and *O*-methyllienkonine show no Bohlmann band absorption in the 2800–2700 cm^{-1} regions. In accordance with these facts, the B/C ring junction of *O*-methyllienkonine must be a *cis*-fused system similar to *O*-methylcorytenchirine. Therefore, the steric relationship of hydrogens at the C-8 and C-13a

*Part VII in the series "Studies on the Alkaloids of Formosan *Corydalis* Species". For Part VI see ref. [1].



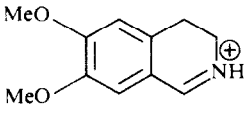
1 $R^1 = R^2 = R^3 = H$, $R^4 = OH$

2 $R^1 = R^3 = H$, $R^2 = Me$, $R^4 = OH$

3 $R^1 = Me$, $R^2 = R^3 = H$, $R^4 = OH$

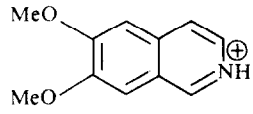
4 $R^1 = R^4 = H$, $R^2 = Me$, $R^3 = OH$

5 $R^1 = Me$, $R^2 = R^4 = H$, $R^3 = OH$



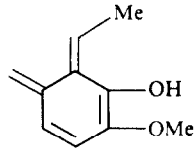
m/z 192

6



m/z 190

7



m/z 164

8

positions in *O*-methyllienkonine are *trans*, as in *O*-methylcorytenchirine. However, both the chiral centres at the 13a position of *O*-methyllienkonine and lienkonine are assigned to the *S*-configuration because of their levorotations [10].

Kametani *et al.* [11] have obtained four products, (±)-corytenchirine [rac-(**2**)], (±) - 2,3,10 - trimethoxy - 8β - methylberbine - 11 - ol [rac-(**3**)], (±) - 2,3,10 - trimethoxy - 8α - methylberbine - 9 - ol [rac-(**4**)], (±) - 2,3,10 - trimethoxy - 8β - methyl - 9 - ol [rac-(**5**)], by a Mannich reaction of 1,2,3,4-tetrahydro - 1 - (3 - hydroxy - 4 - methoxybenzyl) - 6,7 - dimethoxyisoquinoline. Because of the similarity in properties, the ^{1}H NMR spectrum of lienkonine was compared with that of (±) - 2,3,10 - trimethoxy - 8α - methylberbine - 9 - ol [rac-(**4**)]. Both absorption patterns and chemical shifts are identical. Therefore, the structure of lienkonine can be assigned to (−)-2,3,10-trimethoxy - 8α - methyl - 13aαH - berbine - 9 - ol (**4**) which has not been isolated previously from natural sources. In our studies on Formosan *Corydalis ochotensis*, we found (−)-corytenchirine (**2**) [1] and (−)-lienkonine(**4**) which is of biosynthetic significance.

EXPERIMENTAL

Mps are uncorr.

Isolation of lienkonine (**4**). The phenolic base, part B, shown in the scheme of the previous paper [1], deposited base D as crystals with mp 247–248° (decomp.). After separating base D, 10% HCl was added drop-by-drop to the Me_2CO soln of the residue until the Congo red paper changed from red to blue. The acidic Me_2CO soln was evapd to dryness, and then the residue was contacted with a small amount of MeOH to afford fine needles of the HCl salt. When the HCl salt was recrystallized (×3) from MeOH, colourless prisms with mp 257–258° (decomp.) were obtained. In order to obtain lienkonine (**4**), the H_2O suspension of the HCl crystals was basified with NH_3 and the base generated was extracted with $CHCl_3$. The $CHCl_3$ soln was dried and evapd to a light yellow-brown viscous residue which was crystallizable. By recrystallizing from EtOH, 719 mg lienkonine were obtained as colourless columns with mp 166–167°, $[\alpha]_D^{29}$ − 180° (EtOH; *c* 1.0), $C_{21}H_{25}NO_4$ (Found: C, 70.97; H, 7.11; N, 3.89. Requires: C, 70.97; H, 7.09; N, 3.95.) $\nu_{max}^{CHCl_3}$ cm^{-1}: 3540 (–OH). There is no Bohlmann band in the 2800–2700 cm^{-1} regions. UV λ_{max}^{EtOH} nm (log ϵ): 283 (3.770), λ_{min}^{EtOH} nm (log ϵ): 253 (2.737). MS 70 eV, *m/z* (rel. int.): 355 $[M]^+$ (2.2), 340 (49), 192 (100), 190 (16), and 164 (60); ^{1}H NMR (60 MHz, $CDCl_3$): δ1.43 (3H, *d*, *J* = 6.5 Hz, Me-8α), 3.85 (6H), and 3.88 (3H) (each *s*, 3 × OMe), 4.23 (1H, *dd*, *J* = 6 and 10 Hz, H-13aα), 4.37 (1H, *q*, *J* = 6.5 Hz, H-8β), 6.56 (1H, *d*, *J* = 6.5 Hz), 6.62 (1H, *s*), 6.69 (1H, *s*) and 6.77 (1H, *d*, *J* = 6.5 Hz) (4 × Ar H), 5.75 (1H, *br s*, –OH).

Methylation of lienkonine (**4**). An Et_2O soln of CH_2N_2 prepared from nitrosomethylurea (5 g) was added to 50 mg lienkonine (**4**). The mixture was allowed to stand for 3 days at room temp. and then excess CH_2N_2 was destroyed by adding HOAc. The Et_2O soln was shaken with 2% NaOH in order to remove the unreacted phenolic base. The non-phenolic base was then extracted with 2% H_2SO_4 and the acid soln was filtered. The filtrate was basified with 10% NaOH. The generated free non-phenolic base was extracted with Et_2O. The Et_2O soln was dried and evapd giving an almost colourless, viscous residue (50 mg), which was hardly crystallizable, with $[\alpha]_D^{20}$ − 188° ($CHCl_3$; *c* 0.5). The IR spectrum ($CHCl_3$) had no Bohlmann band in the 2800–2700 cm^{-1} regions. In the ^{1}H NMR (60 MHz, $CDCl_3$) spectrum, four methoxyl groups were shown at δ3.85 (6H), 3.88 (3H), and 3.90 (3H) (each *s*).

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