

THE STRUCTURE AND PARTIAL SYNTHESIS OF DELELATINE, AN ALKALOID FROM *DELPHINIUM* SPECIES

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Key Word Index—*Delphinium elatum*; *D. tatsienense*; Ranunculaceae; delelatine; C₁₉-diterpenoid alkaloid.

Abstract—A new C-19-diterpenoid alkaloid designated as delelatine has been isolated from *Delphinium elatum* L. and *D. tatsienense* Franch. and its structure has been elucidated by spectroanalytical methods. Delelatine has been correlated with 14-acetyl-10-deoxydictyocarpine and synthesized from dictyocarpine, thus confirming its structure and stereochemistry.

INTRODUCTION

The roots of *Delphinium tatsienense* native to Yunnan, China are used in Chinese medicine. Previous work from our laboratory on the constituents of this plant included the isolation of tatsiensine [1], tatsinine [2, 3] and deltatine [4]. The roots of *D. tatsienense* also contain the C₁₉-diterpenoid alkaloids browniine, deacetylbambiguine, delcosine, lycocotinine [1] and the C₂₀-diterpenoid alkaloids ajaconine, dictyzine [5-7], hetisine, and hetisinone [1]. *Delphinium elatum* L. is known to contain delpheline, deltaline, elatine and methyllycaconitine [8].

RESULTS AND DISCUSSION

We wish to report in this paper, the isolation of a polar alkaloid designated as delelatine (1) from the seeds of *D. elatum* as well as from *D. tatsienense*. Delelatine was obtained as colourless crystals, mp 84.5-86.5°; C₂₄H₃₇NO₆: M⁺ m/z 435; IR (nujol) 3360 (OH) cm⁻¹; ¹H NMR (CDCl₃): δ 0.95 (3H, s, *tert*-methyl), 1.05 (3H, t, J = 7 Hz, NCH₂Me), 3.30, 3.40 (each 3H, s, OMe), 4.15 [1H, t, J = 4.5 Hz, C(14)-β-H], 4.22 [1H, s, C(6)-α-H], 5.10, 5.20 [each 1H, s, O-CH₂-O]. The presence of two methoxyls, an ethyl and a methylenedioxy group in the molecule suggests that delelatine is a new C₁₉-diterpenoid alkaloid. The proton noise-decoupled ¹³C NMR spectrum showed 22 lines for 24 carbon atoms of the molecule. The SFORD spectrum indicated four quaternary carbons appearing at δ 94.0, 81.8, 49.7 and 34.2 that can be readily assigned to C(7), C(8), C(11) and C(4), respectively. The presence of a methylenedioxy grouping at C(7), C(8) was evident from the above data and the methylene carbon signal at δ 93.3. As delelatine is a lycocotinine-type alkaloid, the normal oxygen functions at C(1), C(6), C(14) and a methoxyl group at C(16) can be assumed to be present. On the basis of these data and comparison of the ¹³C NMR spectral assignments of related compounds [8], delelatine probably possesses the partial structure of delpheline in which two of the hydroxyl groups and the remaining methoxyl group should be placed at C(1), C(6) or C(14). Location of

the methoxyl group at C(1) was deduced from the mass spectrum, which showed the loss of 31 mass units from the molecular ion [9]. The tentative structure 1 can thus be derived for the new alkaloid.

The structure of delelatine was established by treatment with acetylchloride to afford 14-acetyl-10-deoxydictyocarpine (2), a compound previously prepared by deoxygenation of 14-acetyldictyocarpine (4) [10]. The structure was confirmed by synthesis from dictyocarpine (3), whose structure has been established by an X-ray crystal study [11]. Dictyocarpine was converted to 14-acetyldictyocarpine (4) [12]. Treatment of 4 with SOCl₂ afforded the corresponding 10-chloro-10-deoxy-derivative (5) [10]. Treatment of 5 with tributyltin hydride [13] furnished 14-acetyl-10-deoxydictyocarpine which was identical with delelatine 6,14-diacetate (2). Also hydrolysis of 2, prepared from dictyocarpine via 4 and 5, in methanolic Sodium hydroxide furnished delelatine (1), identical by comparison of mp, TLC, CO-TLC, IR and mass spectrum with natural delelatine. In summary, the structure of delelatine was established by two correlation sequences: 1 → 2; and 3 → 4 → 5 → 2 → 1.

EXPERIMENTAL

Mps: corr. ¹H NMR spectra were recorded at 90 MHz using TMS as int. standard, ¹³C NMR spectra were recorded in CDCl₃ soln. Mass spectra were determined on a Finnegan Quadrupole 4023 instrument.

Isolation of delelatine (1). (a) from *D. elatum*. Seeds of *D. elatum* (450 g) from Harris Moran Seeds were ground, suspended in a mixture of 95% EtOH (1.7 l), H₂O (0.42 l) and hexane (0.52 l), heated under reflux for 2 hr and then vigorously stirred at room temp. for 48 hr. The mixture was filtered and the filtrate allowed to stand till the layers separated. Evapn of the hexane extract gave an oil (73.1 g).

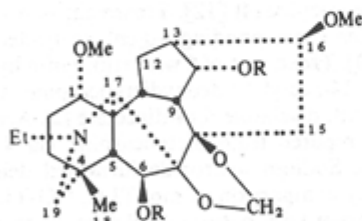
The aq. ethanolic extract was evapd to give a yellow solid which was partitioned between CH₂Cl₂ (2 × 2.1 l) and 0.75 M H₂SO₄ (2.1 l). Evaporation of the CH₂Cl₂ extract gave a neutral fraction (4.6 g). Basification of the acidic layer (Na₂CO₃; pH 10) and extraction with Et₂O (3 × 2 l) gave a crude alkaloidal fraction (9.6 g). Chromatographic separation (VLC) [14] (9.1 g)

on silica gel by elution with hexane and increasing amounts (1–10%) of hexane–EtOH, subsequent purification on a rotor of a Chromatotron (silica gel 60 PF; 2 mm) and finally sepn on a prep. TLC plate (silica gel) afforded delelatine (**1**; 104 mg), mp 84.5–86.5°, $[\alpha]_D^{23.5} -27.7^\circ$ (CHCl₃; c 1.05).

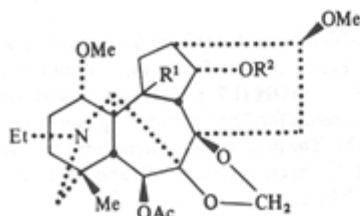
(b) from *D. tatsienense* Franch. The mixture of alkaloids obtained during the isolation of lycocotinine [**1**] (2.02 g) was chromatographed on 35 g of Al₂O₃ (neutral, grade III) and eluted with toluene with increasing amount of Et₂O. The fraction which moved close to lycocotinine was collected (50 mg) and chromatographed twice on prep. TLC plates (Al₂O₃) and eluted with toluene: 10% MeOH. Delelatine (24 mg) was isolated as a gum which crystallized from ether, mp 74°; recrystallization from ether gave material melting at 83.5–84.5°. MS, *m/z* (rel. int.) 435 [M]⁺ (2), 404 (25), 403 (100), IR (nujol), 3360, 1160, 1130, 1050, 930 cm⁻¹.

¹H NMR (90 MHz, CDCl₃): δ 0.95 [3H, s, C(4)–Me], 1.05 (3H, *t*, *J* = 7 Hz, N–CH₂–Me), 3.30, 3.40 (each 3H, s, OMe) 4.15 [1H, *t*, *J* = 4.5 Hz, C(14)–β-H], 4.22 [1H, *br s*, C(6)–α-H], 5.10, 5.20 (each 1H, s, O–CH₂–O); ¹³C NMR: ppm 83.9 C(1), 26.3* C(2), 36.8 C(3), 34.2 C(4), 55.9 C(5), 78.8 C(6), 94.0 C(7), 81.8 C(8), 47.8 C(9), 42.6 C(10), 49.7 C(11), 27.0* C(12), 36.5 C(13), 73.9 C(14), 32.2 C(15), 81.8 C(16), 63.9 C(17), 25.3 C(18), 57.5 C(19), 50.6 N–CH₂–Me, 14.0 N–CH₂–Me, 56.4 C(1) OMe, 56.4 C(16) OMe, 93.2 O–CH₂–O (*these assignments may be interchanged).

Conversion of delelatine (**1**) to delelatine 6,14-diacetate (**2**). Delelatine (30 mg) was stirred with MeCOCl (1 ml) at 25° for 24 hr. Evapn *in vacuo* gave a residue that was chromatographed on neutral Al₂O₃ (Act III) to afford **2** (32 mg), $[\alpha]_D^{23} -62.4^\circ$ (CHCl₃; c 0.62) EIMS: *m/z* 519 (M⁺, C₂₈H₄₁NO₈). The ¹H and ¹³C NMR spectra were identical with those of an authentic sample [10].



1 R = H Delelatine
2 R = Ac



3 R¹ = OH, R² = H
4 R¹ = OH, R² = Ac
5 R¹ = Cl, R² = Ac

14-Acetyldictyocarpine (**4**). Dictyocarpine (**3**) was acetylated in the usual manner to afford **4**, identical with an authentic sample by comparison of the ¹H and ¹³C NMR spectra [8, 12].

14-Acetyl-10-chloro-10-dehydroxydictyocarpine (**5**). 14-Acetyldictyocarpine (**4**, 110 mg) was dissolved in dry benzene (7 ml), treated with freshly dist. SOCl₂ (1.5 ml) and stirred at room temp. for 24 hr. The solvent was removed *in vacuo* and the residue purified on a Chromatotron (Al₂O₃) to afford **5** (110 mg). The properties agreed with those of an authentic sample [10].

14-Acetyl-10-deoxydictyocarpine (**2**) from **5**. A soln of the chloro compound (**5**, 101 mg) in dry C₆H₆ (25 ml) was heated under reflux in a N₂ atm with a soln of tributyltin hydride (250 mg in 2 ml C₆H₆) for 16 hr. An additional quantity of tributyltin hydride (110 mg in 2 ml C₆H₆) was added and the heating continued for 4 hr. The solvents were removed under red. pres. and the oily residue purified with a Chromatotron successively on Al₂O₃ and silica gel plates. The first band that eluted with hexane: 25% Et₂O (silica gel rotor) gave the starting material **5**, 37 mg. The major band that eluted with hexane: Et₂O (1:1) afforded (**2**) as an amorphous compound (61 mg). The ¹³C NMR spectrum (CDCl₃) was identical with that of an authentic sample [10].

Hydrolysis of 14-acetyl-10-deoxydictyocarpine (**2**) to delelatine (**1**). A solution of (60 mg) of **2**, prepared from dictyocarpine via **4** and **5**, in MeOH (13 ml) was stirred with 10% NaOH (1 ml) at room temp. for 50 hr. The progress of the hydrolysis was monitored by TLC. Usual work-up and extraction with CHCl₃ (30 ml × 5) gave a residue (45.5 mg) that was purified on a silica gel rotor of a Chromatotron by elution with Et₂O: 0.1% MeOH to give colourless crystals of **1**, mp 75–77° (25 mg); recrystallization gave a sample with mp of 84–86° (17 mg). Identity with authentic delelatine was confirmed by comparison of its TLC, co-TLC, IR and ¹³C NMR spectral properties.

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