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Diterpenoid and norditerpenoid alkaloids from *Delphinium carduchorum*

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Abstract

From the aerial parts of *Delphinium carduchorum*, we have isolated three known norditerpenoid alkaloids (delcaroline, deltatsine, 18-hydroxy-14-*O*-methyl-gadesine) and two new diterpenoid alkaloids, carduchoron and delcarduchol. The structures of the newly isolated alkaloids were established from spectroscopic data. © 1999 Elsevier Science Ltd. All rights reserved.

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1. Introduction

In continuation of our investigations of Turkish *Delphinium* species (Ulubelen, Meriçli, Meriçli, & Ilarslan, 1992, 1993; Ulubelen, Meriçli, Meriçli, Ilarslan, & Matlin, 1992; Ulubelen, Meriçli, Meriçli, Ilarslan, & Voelter, 1993; Ulubelen, Meriçli, & Meriçli, 1993), we have now studied the aerial parts of *D. carduchorum*. We have isolated two new diterpenoid and three known norditerpenoid alkaloids. The known compounds were established as delcaroline (Pelletier, Mody, & Desai, 1981), deltatsine (Joshi et al., 1984) and 18-hydroxy-14-*O*-methylgadesine (Gonzalez, de la Fuente, Mungia, & Henrick, 1981) by comparison of their NMR data with those of literature values. The structures of the new compounds carduchoron (**1**) and delcarduchol (**2**) were derived from 1-D and 2-D NMR techniques.

2. Results and discussion

The HR mass spectrum (*m*/*z* 339.1827, calc. 339.1834) indicated the molecular formula $C_{21}H_{25}NO_3$ for carduchoron (**1**). The NMR spectra indicated the presence of an *exo*-methylene group [δ_H 4.97 (1H, brs, H-17) and 4.78 (1H, brs, H-17′); δ_C 110.1 t, C-17 and 146.8 s, C-16]. The IR and ^{13}C NMR spectra showed the presence of three carbonyl groups at 1710, 1690 cm^{-1} and δ_C 207.6, 209.0 and 177.5, respectively. The presence of an *N*-methyl group was observed in the NMR spectra [δ_H 2.50, (3H, s); δ_C 42.6 q] and in the IR spectrum, a band 2780 cm^{-1} correlated with the presence of this group. The absence of methoxyl groups in the NMR spectra together with the presence of the *exo*-methylene group indicated that carduchoron (**1**) is a diterpenoid alkaloid with three carbonyl groups. The location of these groups was accomplished by ^1H and ^{13}C NMR, ^1H–^1H COSY, ^1H–^{13}C HETCOR and by COLOC spectra. The chemical shift of C-18 methyl group (δ_H 1.50 (3H, s); δ_C 23.8q) is

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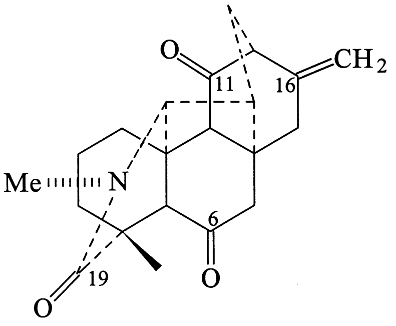
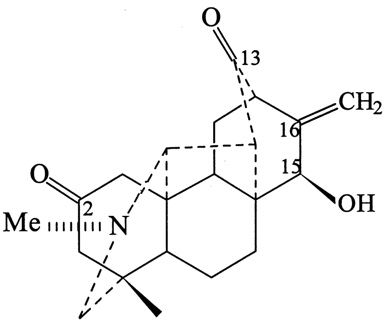
only possible when there is a carbonyl group at C-6, as also observed in spirasine II (Farg, Xiao-tian, & De quan, 1986; Wu, Wu, Niwa, Lu, & Hirata, 1988) hetidine (Pelletier, Aneja, & Gopinath, 1968; Jiang & Pelletier, 1988), thalicsessine (Wu, Wu, Niwa, Lu, & Hirata, 1987). The oxo group at C-6 also caused the chemical shift at C-5 (δ_C 58.9) and C-7 (δ_C 50.9) to move towards higher fields, as also observed in the above three compounds. Twenty-one carbons were observed in the 1-D, ^{1}H-coupled ^{13}C (APT) spectrum and the chemical shift patterns indicated two methyl, seven methylene, five methine and seven quaternary carbons. The two other carbonyl groups could be placed at one of the following positions: C-1-C-3, C-7, C-11, C-13, C-15, and C-19. The chemical shifts (Table 1) clearly indicated that no carbonyl group is present at C-1 to C-3, C-7 is seen to be an isolated methylene, with AB doublets at δ_H 2.25 and 2.75 ($J = 18$Hz) and with δ_C 50.9 t. Since the chemical shift of C-16 is at δ_C 144.5, there should not be a carbonyl group at C-15; also, the C-15 protons were observed at δ 2.26 and 2.38 as doublets (J = 14 Hz). This leaves only three positions C-11, C-13, and C-19 for the placement of the two carbonyl groups. One of the carbonyl signals is at δ 177.5, indicating that the carbonyl should be attached to the nitrogen and, therefore, should be placed at C-19. Due to chemical shifts induced on C-9 (δ_C 74.1) and C-12 (δ_C 61.1), the last carbonyl should be placed at C-11 instead of C-13; COLOC experiments correlated this decision. A survey in the literature showed the presence of a compound thalicsessine (**3**) (Wu et al., 1987) with an N-CH_2CH_2OH group and three carbonyl groups at C-6, C-11 and C-19. The ^{13}C NMR shifts of compound **1** Table 1 are quite similar to those. Thus, carduchoron was assigned the structure (**1**).



1



2

The second new compound delcarduchol (**2**) had the molecular formula $C_{21}H_{27}NO_3$ (m/z 341.1984, calc. 341.1991) as indicated by its HR mass spectrum. The NMR spectra indicated a diterpenoid alkaloid instead of a norditerpene. The *exo*-methylene group was observed at δ_H 5.01 (1H, t, $J = 1.5$ Hz), and 4.97 (1H, t, $J = 1.5$ Hz); δ_C 155.1 s, C-16 and 110.0 t C-17. The chemical shift of C-16 indicated the presence of a hydroxyl group at C-15 [δ_H 3.95 brs; δ_C 75.0 d H-15 α]. Twenty-one carbons were observed in the ^{1}H-coupled ^{13}C (APT) spectrum of **2**, and indicated two methyl, seven methylene, six methine and six quaternary carbons. Two of the quaternary carbons were keto groups as indicated in the IR (1710 and 1700 cm^{-1}) and in the ^{13}C NMR spectra (δ_C 210.5 and 213.0). Since the location of the hydroxyl group was evident, the two keto groups should be placed at one of the following positions: C-1-C-3, C-6, C-7, C-11, C-13 or C-19. The chemical shift of Me-18 being at δ_H 1.00 (3H, s) and δ_C 27.3 clearly showed that there was no carbonyl group at C-6. The presence of an N-methyl group at δ_H 2.37 s, δ_C 41.8 q instead of δ_H 2.50, as in compound **1**, ruled out the presence of a keto group at C-19; also the lack of a carbonyl group signal around δ_C 170–180 correlated with the absence of a carbonyl group at this position. The chemical shift of C-1 to δ_C 48.2 t and C-3 to δ_C 52.0 t, and the lack of a triplet signal around δ_C 20.0 for C-2, indicated the presence of a carbonyl group at C-2. The second carbonyl was placed at C-13 due to the chemical shifts of C-12 (δ_C 53.4 d) and C-14 (δ_C 56.6 d). Both positions were also correlated by COLOC experiments. Table 2 shows the ^{1}H–^{1}H COSY, HETCOR and COLOC results of delcarduchol (**2**).

3. Experimental

3.1. General

IR spectra were recorded in $CHCl_3$. ^{1}H NMR spectra were measured at 200 MHz, ^{13}C NMR at 50 MHz

Table 1
NMR data of carduchorone (**1**) and ^{13}C NMR of thalicsessine (**3**)

Position	^{13}C	^{1}H	COSY ^{1}H–^{1}H	COLOC ^{13}C–^{1}H	**3**
1	38.1t	α 2.01 dd (5,12)	1β, 2α, 2β	C-5, C-9, C-20	39.8
		β 1.60 brd (12)	1α, 2α		
2	23.0t	α 1.75m	1α, 2β		20.6
		β 1.40m	1α, 1β, 2α		
3	35.2t	α 1.85m	2α, 2β, 3β		34.2
		β 1.40m	2β, 3α		
4	46.9s				46.5
5	58.9s	2.50s		C-6, C-19, C-20	60.0
6	207.6s				207.6
7	50.9t	α 2.75d (18)	7β		51.5
		β 2.25d (18)	7α		
8	44.5s				43.9
9	74.1d	1.66s		C-6, C-11	75.6
10	43.5s				42.9
11	209.0s				208.9
12	61.1d	2.30brs		C-11, C-17	63.7
13	29.7t	α 1.90m	13β, 14		33.3
		β 1.40m	13α, 14		
14	47.4d	1.80m	13α, 13β		47.0
15	48.5t	α 2.26d (14)	15β	C-12, C-16, C-17	51.5
		β 2.38d (14)	15α		
16	144.5s				141.6
17	110.1t	4.97brs		C-12, C-15	111.1
17′		4.78brs			
18	23.8q	1.50s		C-6, C-10	25.5
19	177.5s				177.1
20	53.2d	2.02d (3)		C-5, C-12, C-13	53.9
21	42.6q	2.50s			49.7
22					60.9

in $CDCl_3$. HR-MS were measured at 70 eV. Chromatographic separations were carried out on a Chromatotron instrument using rotors coated with 1-mm thick layers of neutral Al_2O_3.

3.2. Plant material

Aerial parts of *D. carduchorum* Chowdhuri and Davis were collected in eastern Turkey from the Van-Gevas Mountain at an altitude of 2500 m in August 1993. A voucher specimen is deposited at the University of Süleyman Demirel (Isparta), Faculty of Sciences, under H.Ö. 6326.

3.3. Extraction of alkaloids

Dried and powdered aerial parts were extracted by percolation at room temp., using MeOH. After evap. in vacuo, a residue (7g) was obtained. This was dissolved in EtOH and adjusted to pH 1.5 (5% H_2SO_4) and extracted with CH_2Cl_2 (20 × 100ml) to give a neutral fr. (5.5g). The aq. soln was basified (pH 8–10) and extracted with CH_2Cl_2 (25 × 100ml) to yield 200 mg of a crude alkaloid mixt. This was separated on a neutral Al_2O_3 rotor of a Chromatotron with petrol–EtOAc–MeOH systems to yield the alkaloids in the following order: delcaroline (12 mg), deltatsine (8 mg), **1** (22 mg), **2** (15 mg) and 18-hydroxy-14-*O*-methylgadenine (6 mg).

3.4. Carduchoron (*1*)

IR ν^{CHCl_3} cm^{-1}: 3050, 2980, 2860, 2780, 1710, 1690, 1645, 1370, 1250, 1050, 980, 890. ^{1}H and ^{13}C NMR ($CDCl_3$) in Table 1. HRMS *m*/*z* (rel. int.): 339.1827 $[M]^+$ (78), 324 $[M\text{-}15]^+$ (14), 310 $[M\text{-}29]^+$ (100), 296 (15), 279 (20), 178 (12), 124 (60), 113 (26), 97 (16), 83 (20), 71 (33), 57 (42).

3.5. Delcarduchol (*2*)

IR ν^{CHCl_3} cm^{-1}: 3480, 3040, 2960, 2840, 2778, 1710, 1700, 1650, 1420, 1370, 1268, 1150, 1050, 960, 890. ^{1}H and ^{13}C NMR ($CDCl_3$) in Table 2. HRMS *m*/*z* (rel. int.): 341.1984 $[M]^+$ (76), 326 $[M\text{-}15]^+$ (62), 313 $[M\text{-}28]^+$ (22), 298 (14), 282 (18), 254 (15), 192 (23), 176 (15), 136 (12), 98 (12), 84 (100), 83 (97), 70 (17).

Table 2
NMR data of delcarduchol (**2**)

Position	^{13}C	^{1}H	COSY ^{1}H–^{1}H	COLOC ^{13}C–^{1}H
1	48.2t	α 3.26 d (13)	1β	C-2, C-5, C-20
		β 1.30 d (13)	1α	
2	213.0s			
3	52.0t	α 2.90d (12)	3β	C-2, C-5, C-10
		β 1.90d (12)	3α	
4	41.0s			
5	59.9d	1.86brs		
6	29.3^{a}t	α 2.85m	6β, 7α, 7β	C-4, C-10, C-20
		β 1.60m	6α, 7α, 7β	
7	36.2t	α 2.75m	6α, 6β, 7β	C-15
		β 1.65m	6α, 6β, 7α	
8	40.6s			
9	46.6d	2.04dd (4,7)	11α, 11β	
10	50.4s			
11	23.4^{a}t	α 1.80m	9, 11 β	C-13, C-16, C-17
		β 2.35m	9, 11 α	
12	53.4d	2.60brd (3Hz)		C-13, C-16, C-17
13	210.5s			
14	56.6d	1.65m		
15	75.0d	α 3.95brs		
16	155.1s			
17	110.0t	5.01t (1.5)	17′	
17′		4.97t (1.5)	17	
18	27.3q	1.00s		
19	57.9t	α 2.16d (13)	19β	
		β 1.98d (13)	19α	
20	67.3d	2.97brs		
21	41.8q	2.37s		

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