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Norditerpene and diterpene alkaloids from *Consolida hohenackeri*

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Abstract

Four diterpenoid alkaloids, two of them being the known compounds lycoctonine and ajaconine, were isolated from the aerial parts of *Consolida hohenackeri*. The two new compounds were C_{19} alkaloids, hoheconsoline and consolinine. The structures of the compounds were elucidated by 1-D and 2-D NMR techniques.

Keywords: Consolida hohenackeri; Ranunculaceae; Diterpenoid alkaloids; Hoheconsoline; Consolinine; Lycoctonine; Ajaconine

1. Introduction

Consolida hohenackeri (Boiss.) Grossh. (Syn. *Aconitella hohenackeri*, *Delphinium hohenackeri*) is a native plant of Turkey, abundantly present in eastern Turkey. In the two previous studies with this species the plants were collected from eastern Turkey. In the first study seven norditerpene alkaloids, lycoctonine, delcorine, dehydrodelcorine, delectinine, bicolorine, hohenackerine and tortumine, the last two being new compounds, were isolated. In addition an aporphine type alkaloid isoboldine was also obtained (Şener, Bingöl, & Baykal, 1989).

In the second study, the same plant (*A. hohenackeri*) yielded two norditerpenoid alkaloids, 1-demethylwinkleridine and 18-demethyl-14-deacetylpubescenine, and a bisnorditerpene alkaloid, hohenackeridine, all three compounds being new (Almanza, Bastida, Codina, & de la Fuente, 1997).

In the present study, the plant material was also collected from eastern Turkey, almost from the same district as in the first studies. Four diterpenoid alkaloids hoheconsoline (**1**), consolinine (**2**), ajaconine (**3**) (Pelletier et al., 1986) and lycoctonine (**4**) (Pelletier, Panu, Kulanthaivel, & Olsen, 1988) were isolated, the first two compounds being new. Lycoctonine was found in the first on this plant study (Şener et al., 1989), but no other common compound was obtained in this study.

2. Results and discussion

The molecular formula of hoheconsoline (**1**), $C_{26}H_{43}O_6N$ (*m*/*z* 465.3107, calc. 465.3091), indicated six degrees of unsaturation as double bond equivalents. Since no ketone or acetyl groups were present and no double bonds were observed in the IR and the NMR spectra, all six, were accounted for by six rings. The ^{13}C NMR (APT) spectrum showed the presence of six methyl, seven methylene, ten methine and three quaternary carbons for 26 C atoms. The presence of the methoxyl groups at δ 3.25, 3.33, 3.35, 3.40 and 3.45, as well as the *N*-ethyl group (δ_H 1.1 t, $J=7$ Hz; δ_C 11.2 q and δ_H 3.1 m, δ_C 50.3 t) indicated a norditerpene alkaloid. The ^1H spectrum showed a triplet signal at δ 3.60 ($J=4.5$ Hz) indicating the presence of one of the methoxyl groups at C-14, a doublet signal ($J=6$ Hz) at δ 4.52 showed another methoxyl group at C-6, biogenetically the third methoxyl group should be placed at C-16. The lack of a signal at around δ 70–72 indicated that there should be a methoxyl group at C-1 instead of a hydroxyl group. The chemical shifts in the NMR (δ_H 3.62 (1H, $J=5$ Hz, H-1β) and δ_C 86.6 d) correlated with the presence of a methoxyl group at C-1. The last methoxyl had to be placed at either C-8 or C-18. In the case of a methoxyl group at C-18 a triplet signal

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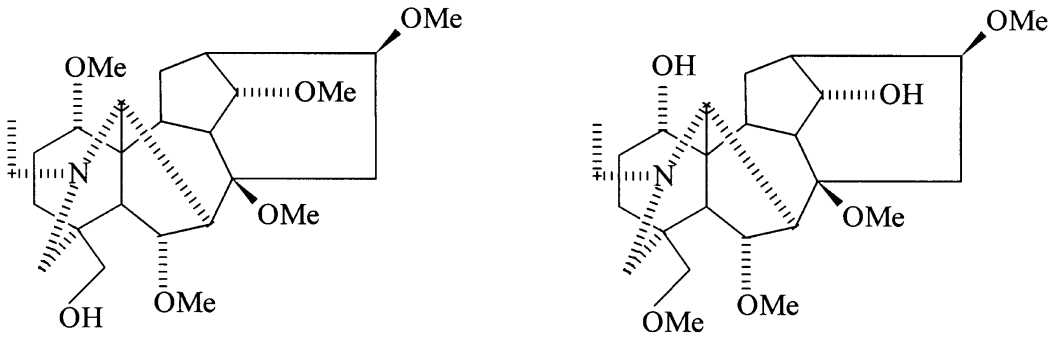

1 **2**

Structure

Table 1
NMR data of hoheconsoline (**1**)

	^{1}H	^{13}C	COSY	HMBC
1β	3.67 d (4.5)	86.6 d	H-2α, H-2β	C-10, C-17
2α	1.95 dd (5, 12)	27.7 t	H-1β, H-2β, H-3α, H-3β	C-1
2β	1.28 m		H-1β, H-2α, H-3α, H-3β	
3α	1.30 m	29.8 t	H-2α, H-2β, H-3β	C-1, C-19
3β	2.20 m		H-2α, H-2β, H-3α	C-1, C-4, C-18, C-19
4	–	38.0 s		
5	1.72 d (6)	46.8 d	H-6	C-7, C-10, C-17
6	4.52 d (6)	82.6 d	H-5, H-7β	C-4, C-7, C-11, C-17
7β	2.90 s	52.8 d	H-6	C-5, C-11
8	–	77.6 s		
9	2.70 dd (5,7)	56.1 d	H-10, H-14β	C-11, C-14
10	2.30 ddd (5,7,11)	39.6 d	H-9, H-12α, H-12β	C-9, C-13, C-14
11	–	50.3 s		
12α	1.20 ddd (8,11,14)	31.6 t	H-10, H-12β	C-11, C-14, C-17
12β	1.90 dd (7,14)		H-10, H-12α	
13	2.45 dd (5,7)	46.4 d	H-12β, H-14β	C-10, C-14
14β	3.60 t (4,5)	85.6 d	H-9, H-13	C-8, C-12
15α	2.95 m	42.0 t	H-15β, H-16α	C-9, C-13, C-14, C-16
15β	3.05 m		H-15α, H-16α	
16α	3.50 m	82.0 d	H-15α, H-15β	C-14, C-15
17	3.25 s	67.7 d		C-1, C-5, C-10
18α	2.85 d (10)	70.4 t	H-18β	C-5, C-19
18β	3.00 d (10)		H-18α	C-5, C-19
19α	2.40 d (11.5)	54.2 t	H-19β	C-4, C-5, C-18
19β	2.00 m		H-19α	C-4, C-5, C-18
N–CH_2	3.10 dt (7,14)	50.3 t		
CH_3	1.10 t (7)	11.2 q		
1-OMe	3.22 s	56.4 q		
6-OMe	3.35 s	58.9 q		
8-OMe	3.45 s	48.7 q		
14-OMe	3.33 s	58.2 q		
16-OMe	3.40 s	56.1 q		

should be observed at around δ_C 78–81, whereas in compound **1** it was situated at δ_C 70.4 (t) indicating a hydroxyl group at C-18, instead of a methoxyl, therefore the last methoxyl was placed at C-8. The HMQC and HMBC (Table 1) spectral data showed that hoheconsoline (**1**) was a 1,6,8,14,16-pentamethoxyaconitine type compound. Since there is no functional group at C-7 both C-6 α- and β-hydroxyl groups should give the same splitting pattern at δ 4.52, therefore the stereochemistry at C-6 was left unknown.

The second norditerpenoid alkaloid consolinine (**2**) had the molecular formula $C_{25}H_{41}NO_6$ (m/z 451.4922,

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

	^{1}H	^{13}C	COSY	HMBC	NOESY
1β	3.65 m	71.3	H-2α, H-2β	C-3, C-10	H-2α, H-2β, H-10
2α	1.95 dd (7,12)	29.7 t	H-1β, H-2β	C-4	
2β	1.30 ddd (3,6,12)		H-1β, H-2α		
3α	1.50 m	31.4 t	H-2α, H-2β, H-3β		
3β	1.80 m		H-2α, H-2β, H-3α		
4	–	39.2 s			
5	2.07 d (6,5)	45.0 d	H-6β	C-7, C-10	H-6β
6β	3.54 d (6,5)	83.7 d	H-5	C-4, C-7, C-17	H-5
7β	3.20 brs	48.8			
8	–	78.3 s			
9	2.65 dd (5,7)	46.7 d	H-10, H-14β	C-11, C-14	H-12β
10	2.30 dd (5,11)	40.1 d	H-9, H-12	C-9, C-14	H-14β
11	–	51.5 s			
12α	1.40 ddd (7,11,14)	29.9 t	H-10, H-12β	C-11, C-17	H-1β, H-12β, H-17
12β	2.00 dd (7,14)		H-10, H-12α		
13	2.20 t (6,5)	38.6 d	H-12, H-14	C-10, C-14	
14β	4.20 t (4,5)	75.7 d	H-9, H-13	C-8, C-16	H-9, H-10, H-12β
15α	2.25 dd (7,14)	37.0 t	H-15β, H-16	C-8, C-9	H-16α
15β	2.00 m		H-15α		
16α	3.47 d (7)	83.6 d	H-15α, H-15β	C-8, C-14	
17	3.20 s	61.9 d		C-1, C-5, C-6	H-12α, H-15α, H-16α
18α	3.75 m	79.0 t	H-18β		
18β	3.60 m		H-18α		
19α	3.25 d (12)	53.6 t	H-19β		
19β	3.00 d (12)		H-19α		
N–CH_2	2.90 m	49.0 t			
CH_3	0.97 t (7)	13.0 q			
6-OMe	3.35 s	56.5 q			
8-OMe	3.34 s	48.3 q			
16-OMe	3.42 s	56.6 q			
18-OMe	3.40s	59.3 q			

calc. 451.4934), indicating six degrees of unsaturation which were accounted for the hexacyclic skeleton of **2**. The NMR data showed the presence of an aconitine type alkaloid with four methoxyl groups and an *N*-ethyl group. The other two oxygen functions were hydroxyls which were assigned to C-1 and C-14 due to their ^{1}H and ^{13}C NMR signals. The signal at δ_H 3.65 (1H, m, H-1β) and δ_C 71.3 (d) and clearly showed that there was a hydroxyl group at C-1 and the triplet signal at δ_H 4.2 ($J=4.5$ Hz) and δ_C 75.7 (d) indicated that the second hydroxyl group was placed at C-14. One of the four methoxyl groups was assigned to C-16 on biogenetic considerations and because of the signals at δ_H 3.47 (1H, d, $J=6$ Hz) and δ_C 83.6 (d). The second methoxyl was placed at C-6 based and the NMR shifts at δ_H 3.54 (1H, d, $J=5.8$ Hz) and δ_C 83.7 (d), which was observed as α from the NOESY experiment. The other two methoxyl groups were placed at C-18 (δ_H 3.75 m; δ_C 79.0 t) and C-8 (δ_C 78.3). The HMQC, COSY, HMBC and NOESY spectra (Table 2) were in agreement with the suggested structure of a 6,8,16,18-tetramethoxy-1,14-dihydroxy-aconitine type compound for consolinine (**2**). Although this is the first isolation of this compound from nature, Pelletier, Desai, Jiang and Ross (1990) obtained the 1-*epi*-isomer of this compound namely 8-*O*-methyl-1-*epi*-neoline from its 14-*O*-acetyl derivative by solvolysis. The ^{13}C NMR values were comparable; in the present study, however, the C-1 hydroxyl is α as indicated by the NOESY experiment.

3. Experimental

3.1. General

Optical rotations: $CHCl_3$ for **1** and in MeOH for **2**; IR: $CHCl_3$; HRMS: 70 eV; ^{1}H NMR: 500 MHz; ^{13}C NMR: 125 MHz using $CDCl_3$. Chromatographic separation of the alkaloids was carried out on a chromatotron using rotors coated with a 1 mm thick layer of neutral Al_2O_3.

3.2. Plant material

Aerial parts of *C. hohenackeri* (Boiss.) Grossh. were collected in eastern Turkey from Erzurum, near Tortum

waterfall, Yamaçlar village at an altitude of 1050 m. The plant was identified by one of us (H.Ö.). A voucher specimen H.Ö. 6405 is deposited in the Herbarium of Faculty Science and Literature, University of Süleyman Demirel (Isparta, Turkey).

3.3. Extraction of crude alkaloids

Dried and powdered plant material (2400 g) was macerated (six times) with 95% EtOH at room temperature. After removal of the solvent in vacuo, 50 g of the extract was dissolved in aq EtOH, was acidified with 2% H_2SO_4 (pH 1.5) and extracted with CH_2Cl_2 (20×250 ml) in order to separate the nonalkaloidal part. The remaining aq soln was basified (pH 9–10) with cold 10% NaOH and extracted with CH_2Cl_2 (25×250 ml). The alkaloidal mixture (1.1 g) was directly separated on a neutral Al_2O_3 rotor on a chromatotron eluting with hexane followed by gradients of CH_2Cl_2 and MeOH. The compounds obtained were **1** (25 mg), **2** (17 mg), ajaconine (20 mg), lycoctonine (40 mg) and mixtures of alkaloids.

3.4. Hoheconsoline (*1*)

$[\alpha]_D$ $+27^\circ$ ($CHCl_3$ c, 1.2); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3400, 2940, 2830, 1650, 1480, 1440, 1150, 1110, 1020, 950, 750; ^1H and ^{13}C NMR: Table 1; HRMS *m/z* (rel.int.): 465.3107 $[M]^+$ (24), 450 $[M–Me]^+$ (28), 434 $[M–OMe]^+$ (95), 390 (100), 348 (32), 328 (25), 180 (35), 71 (33), 57 (68).

3.5. Consolinine (*2*)

$[\alpha]_D$ $+184^\circ$ (MeOH c, 2.0); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3454, 2950, 2850, 1645, 1480, 1420, 1145, 1100, 1080, 1050, 1020, 950, 730; ^1H and ^{13}C NMR: Table 2; HRMS *m/z* (rel. int.): 451.4922 $[M]^+$ (5), 436 $[M–OMe]^+$ (100), 418 $[436–H_2O]^+$ (20), 404 (38), 392 (28), 342 (40), 330 (58), 300 (10), 109 (5), 83 (95), 71 (12).

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