Three New Norditerpenoid Alkaloids from *Consolida orientalis*

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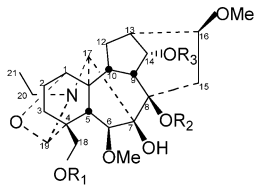
The structures of three new norditerpenoid alkaloids named dehydrodeltatsine (1), 14-*O*-acetyltakaosamine (2), 18-demethoxypubescenine (3) isolated from the aerial parts of *Consolida orientalis* (GAY) SCHRÖD., were elucidated by 1D and 2D NMR spectroscopy and HR-EIMS. Twelve known norditerpenoid alkaloids (type lycoctonine) and the diterpenoid alkaloid ajaconine have been isolated. Several assignments of ^{13}C-NMR data for delbonine (4) were revised and the complete assignment for 18-hydroxy-14-*O*-methylgadesine (5) was realized.

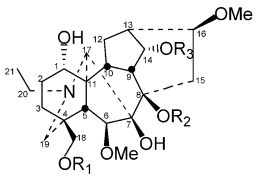
Key words *Consolida orientalis*; Ranunculaceae; norditerpenoid alkaloid

The genera *Consolida* is, like the genera *Aconitum* and *Delphinium*, a rich source of diterpenoid alkaloids. This kind of compounds have attracted considerable interest because of their complex structure, and noteworthy physiological effects. Norditerpenoid alkaloids have been found to exert anti-inflammatory, analgesics, and various cardiovascular effects.[2,3)] In connection with our studies of the genera *Delphinium*, *Aconitum* and *Consolida* which possess diverse biological activities,[4)] we have isolated from the aerial parts of *Consolida orientalis* (GAY) SCHRÖD. (Ranunculaceae) the new alkaloids dehydrodeltatsine (**1**), 14-*O*-acetyltakaosamine (**2**), and 18-demethoxypubescenine (**3**), together with the known norditerpenoid alkaloids delbonine (**4**), 18-hydroxy-14-*O*-methylgadesine (**5**), deltatsine (**6**), dehydrodelsoline, 14-*O*-acetyldelcosine, delsoline, pubescenine, gigactonine, delcosine, 18-methoxygadesine, 18-*O*-demethyl-14-*O*-deacetylpubescenine, 18-demethylpubescenine, takaosamine and the diterpene alkaloid ajaconine. The known alkaloids were identified by analysis of their ^{1}H- and ^{13}C-NMR spectra, and comparison with published data.

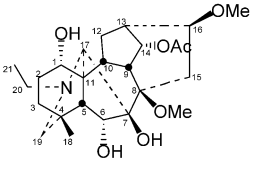
Previous phytochemical studies realized in our group demonstrated the occurrence of gigactonine, delcosine, delsoline, 18-methoxygadesine and 18-hydroxy-14-*O*-methylgadesine in *C. orientalis* collected in Spain.[5,6)] Recently, the investigation of this species collected in Turkey led to isolation of a new C_{20} diterpenoid alkaloid, consorientaline, together with takaosamine, gigactonine, delcosine, and delsoline.[7)]



(**1**) R_1 = Me R_2 = Me R_3 = H
(**5**) R_1 = H R_2 = H R_3 = Me



(**2**) R_1 = H R_2 = H R_3 = Ac
(**4**) R_1 = Me R_2 = Me R_3 = Ac
(**6**) R_1 = Me R_2 = Me R_3 = H



(**3**) 18-demethoxypubescenine

Extensive NMR studies, including COSY, ROESY, HSQC and HMBC experiments, resulted in complete and unambiguous assignments of the NMR data for **1**—**3** and revision of some assignments of ^{13}C-NMR data for **4** and **5**.

Dried and powdered plants of *C. orientalis*, collected in the flowering stage, were extracted at room temperature with EtOH. The extract was subjected to solvent partitioning and then to multiple chromatographic separations, affording compounds **1**—**5** together with twelve others alkaloids.

The HR-EI-MS spectrum (*m*/*z* 465.2748, Calcd 465.2726) indicated the molecular formula $C_{25}H_{39}NO_7$ for dehydrodeltatsine (**1**). Analysis of the NMR spectra revealed that it belongs to the lycoctonine type norditerpenoid alkaloids.[8,9)] The NMR spectra of **1** (see Tables 1, 2) did not show signals of an angular methyl group, though they showed resonances for an *N*-ethyl group [δ_H 1.10 (3H, t, J=7.2 Hz), 2.56 and 3.00 (1H each, dq, J=7.2, 12.3 Hz); δ_C 13.8 (q), 47.9 (t)], two 3H singlets [δ_H 3.40, 3.45 (3H each, s); δ_C 56.5, 59.4 (each q)], corresponding to two secondary methoxyl groups, and to two quaternary oxygenated carbons [δ_C 79.6, 87.3] that could be attributed to the tertiary α-glycolic system characteristic of a lycoctonine-type alkaloid.[8,9)] Moreover, compound **1** gave signals for a primary methoxyl group [δ_H 3.36 (3H, s); δ_C 59.7 (q)], which was located at C-18 following the usual substitution pattern in norditerpenoid alkaloids.

The proton signals at δ_H 3.24 and 3.37 (1H each, d, J=9.1 Hz), assigned to the non-equivalent C-18 methylene protons, gave the correlations for three-bond connectivities in the HMBC experiment with a methoxyl [δ_C 59.7], a methylene [δ_C 25.7], and two methines [85.2, 52.1] carbons signals that have consequently been assigned to CH_3O-18, C-3, C-19, and C-5 respectively. The loss of 56 mass unit of acrolein (2%) from the molecular ion peak at *m*/*z* 465 in the mass spectrum,[10)] the strong absorption bands at 998 and 895 cm^{-1} in the IR spectrum, and the proton signals at δ_H 3.71 (1H, d, J=5.2 Hz) and δ_H 3.98 (1H, s) suggested the existence of a C_1–O–C_{19} ether in the compound.[9)] Besides, further correlations were observed in the HMBC experiment between the signals at δ_H 3.98 with C-5 (δ_C 52.1), C-17 (δ_C

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Table 1. ^{1}H- and ^{13}C-NMR Data for Compounds **1**—**3** in $CDCl_3$[a)]

Proton	**1**		**2**		**3**	
	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C
1β	3.71 d (5.2)	68.7 d	3.68 br s ($w_{1/2}$=10.2)	72.5 d	3.63 br s ($w_{1/2}$=6.9)	72.2 d
2α	1.75 m	22.0 t	1.66 m	29.3 t	1.55 m	29.2 t
2β	1.47 m		1.48 dddd (13.9, 13.9, 6.6, 3.2)		1.52 m	
3α	1.66 m	25.7 t	1.63 m	26.7 t	1.72 ddd (12.7, 12.7, 5.0)	34.7 t
3β	1.68 m		1.93 m		1.44 m	
4		30.3 s		38.1 s		33.6 s
5	1.56 br s ($w_{1/2}$=5.3)	52.1 d	1.85 d (1.9)	44.4 d	1.92 d (6.4)	50.1 d
6α	3.57 d (1.9)	90.2 d	3.96 s	90.3 d		
6β					4.50 dd (6.4, 6.4)	71.3 d
7		87.3		87.7 s		85.0 s
8		79.6		78.3 s		80.6 s
9	2.91 dd (4.8, 7.0)	42.9 d	3.09 dd (7.1, 4.7)	42.6 d	2.28 dd (7.0, 5.1)	43.4 d
10	2.02 ddd (11.5, 7.0, 7.0)	37.2 d	2.01 ddd (11.9, 7.1, 4.9)	43.5 d	1.92 m	43.2 d
11		45.5 s		49.3 s		47.7 s
12α	1.09 dd (14.0, 7.0)	28.9 t	1.71 dd (14.2, 4.7)	29.8 t	1.81 dd (14.2, 4.6)	29.4 t
12β	1.84 ddd (14.0, 11.5, 7.8)		2.09 ddd (14.2, 11.9, 7.6)		2.07 ddd (14.2, 11.4, 7.3)	
13	2.43 ddd (7.8, 4.8, 1.7)	39.1 d	2.45 dd (7.6, 4.7)	37.9 d	2.48 dd (7.3, 4.6)	37.8 d
14β	4.08 dt (4.8, 5.5)	75.1 d	4.77 t (4.7)	76.3 d	4.77 t (4.6)	75.5 d
14αOH	3.73 d (5.5)					
15α	2.66 dd (16.4, 8.7)	29.1 t	2.67 dd (15.0, 8.8)	33.8 t	2.62 dd (14.5, 8.6)	28.4 t
15β	2.14 dd (16.4, 4.7)		1.60 dd (15.0, 8.4)		1.96 dd (14.5, 8.6)	
16α	3.34 dd (4.7, 8.7)	82.8 d	3.31 m	82.6 d	3.43 t (8.6)	82.6 d
17	2.40 d (2.9)	66.3 d	2.79 d (1.9)	66.1 d	2.72 s	63.1 d
18a	3.37 d (9.1)	73.6 t	3.64 d (10.5)	67.0 t	1.27 s	30.1 q
18b	3.24 d (9.1)		3.37 d (10.5)			
9a		85.2 d	2.40 d (11.8)	57.1 t	2.71 d (11.0)	60.3 t
19b	3.98 s		2.43 d (11.8)		2.34 d (11.0)	
20a	3.00 dq (12.3, 7.2)	47.9 t	2.95 dq (12.8, 7.2)	50.3 t	2.98 dq (14.2, 7.2)	50.6 t
20b	2.56 dq (12.3, 7.2)		2.81 dq (12.8, 7.2)		2.88 dq (14.2, 7.2)	
21	1.10 t (7.2)	13.8 q	1.08 t (7.2)	13.6 q	1.12 t (7.2)	13.8 q
MeO-6	3.45 s	59.4 q	3.37 s	57.7 q		
MeO-8	3.59 s	53.1 q			3.41 s	52.6 q
MeO-16	3.40 s	56.5 q	3.32 s	56.3 q	3.38 s	56.6 q
MeO-18	3.36 s	59.7 q				
AcO-14α			2.04 s	21.5 q	2.05 s	21.2 q
CO				171.4 s		171.4 s

a) Chemical shifts in ppm relative to TMS; coupling constants (*J*) in Hz. ^{13}C-NMR multiplicities were established by DEPT data.

66.3), C-18 (δ_C 73.6), C-1 (δ_C 68.7) and δ_H 3.71 with C-5, C-3 (δ_C 25.7), C-19 (δ_C 85.2), C-10 (δ_C 37.2), and C-11 (δ_C 45.5) in accordance with a C_1–O–C_{19} bond. The proton signal at δ_H 4.08 (1H, dt, J=4.8, 5.5 Hz), which becomes a triplet of J=4.8 Hz and the disappearance of the doublet at δ_H 3.73, when D_2O was added, suggested the presence of a secondary hydroxyl group at C-14 α-OH. The signals at δ_H 3.40, 3.45 and 3.59 (3H each, s) corresponding to methoxyl groups, were showing correlations in the HMBC experiment with the carbons at δ_C 82.8, 90.2 and 79.6 respectively. Those values are typical of the positions 16, 6, and 8 in lycoctonine-type norditerpenoid alkaloids.[8,9)] The stereochemistry of **1** was confirmed by analyzing a Dreiding model with respect to Overhauser effects detected in a ROESY spectrum. Starting from the β position of the proton at the ring junction (H-5), it was found that the β-oriented H-1, H-9, H-10, H-14 and the CH_2-18 protons were present from the spatial correlations found between H-5 and H-9, H-10; H-9 and H-1, H-10, H-5 and H-14; H-14 and H-9, H-13. The structure of **1** was verified from the fact that **1** was converted from deltatsine (**6**) by treatment with iodine in benzene in 83% yield.[11)]

Compound **2** was isolated as an amorphous solid. Its HR-EI-MS showed the molecular ion peak at *m/z* 481.2681 corresponding to the molecular formula, $C_{25}H_{39}NO_8$, (Calcd 481.2675). The ^{1}H- and ^{13}C-NMR spectra of **2** were similar to those of **1** and gave signals of a *N*-ethyl group [δ_H 1.08 (3H, t, J=7.2 Hz), 2.81 and 2.95 (1H each, dq, J=7.2, 12.8 Hz); δ_C 13.6 (q), 50.3 (t), two methoxyl groups [δ_H 3.32, 3.37 (3H each, s); δ_C 56.3, 57.7 (each q)], an acetate group [δ_H 2.04 (3H, s); δ_C 21.5(q), 171.4 (s)], two quaternary oxygenated carbons [δ_C 78.3, 87.7 (each s)], characteristic of a tertiary α-glycolic system in a lycoctonine-type alkaloid.[8,9)] (see Tables 1, 2). Furthermore, **2** was lacking the typical signals of C_1–O–C_{19} bond.[9)] The acetoxy group was located at C-14α in view of the multiplicity and chemical shift of its geminal proton δ_H 4.77 (1H, t, J=4.7 Hz) while the corresponding signal in **1** is at δ_H 4.08 (1H, dt, J=4.8, 5.5 Hz). The positions of the methoxyl groups were evident from the three-bond correlations between the methoxy protons and the skeletal carbons (C-6 and C-16, 90.3 and 82.6, each d). Moreover, the signal at δ_C 67.0 was typical of the C-18 hydroxymethylene group, because it is δ_C 77—79 in the case of the methoxymethylene group.[8,9)] The structure of **2** was confirmed by comparison of their ^{1}H- and ^{13}C-NMR data with those of takaosamine.[12)] Basic hydrolysis of **2** with methanolic KOH gave takaosamine in 74.6% yield. Thus, it

Table 2. HMBC Data of **1**—**5** in $CDCl_3$

Proton	**1**	**2**	**3**	**4**	**5**
1β	C-3, 5, 10, 11, 19	C-3, 5	C-3, 10	C-3, 5, 10	C-3, 5, 10, 19
2α	C-4	C-4		C-1, 3, 4	C-1, 4, 11
2β	C-1, 3, 11		C-4	C-1, 3	C-3
3α	C-1, 2, 5, 19	C-2, 5, 19		C-1, 2, 4, 5, 18, 19	C-2, 4, 5, 19
3β	C-1, 19	C-1, 2, 4, 18, 19	C-4, 19	C-1, 2, 4, 18, 19	C-2, 4, 5, 18, 19
5	C-3, 6, 10, 17, 19	C-4, 6, 7, 10, 11, 17, 19	C-1, 4, 7, 10, 11, 17, 19	C-1, 4, 6, 7, 10, 11, 17, 19	C-1, 3, 4, 6, 7, 10, 11, 17, 18, 19
6α	C-4, 5, 6′, 7, 8, 11	C-4, 6′, 7, 8, 11		C-4, 5, 6′, 7, 8, 11	C-4, 5, 7, 8, 11
6β			C-4, 7, 8, 17		
9	C-8, 12, 13, 14	C-8, 10, 12, 13, 15	C-8, 12, 13, 14	C-7, 8, 10, 12, 13, 14, 15	C-7, 8, 12, 13, 15
10	C-8, 9, 11, 17	C-8, 9, 11, 12, 17	C-11, 12, 17	C-5, 8, 12, 13, 17	C-8, 9, 11, 17
12α	C-10, 11, 13, 14, 16	C-9, 10, 11, 13, 14, 16	C-13, 16	C-10, 11, 13, 14, 16	C-11, 13, 14
12β	C-10, 16	C-10, 11, 13, 16	C-13	C-10, 13, 16	C-9, 10, 11, 13, 16
13	C-9, 12, 16	C-10, 14, 16	C-9, 10, 14, 16	C-9, 10, 12, 14, 16	C-9, 10, 12, 15, 16
14β	C-8, 16	C-8, 16, 171.4	C-8, 171.4	C-8, 13, 16, 170.6	C-8, C-9
15α	C-7, 8, 9, 13, 16	C-7, 8, 9, 13, 16	C-7, 8, 9, 13	C-7, 8, 13, 16	C-7, 8, 9, 13
15β	C-7, 8, 13, 16	C-7, 8, 16	C-8, 16	C-7, 8, 13, 16	C-8, 16
16α	C-8, 14, 16′	C-12, 14, 15, 16′	C-14, 15, 16′	C-8, 12, 13, 14, 16′	C-12, 14, 15, 16′
17	C-5, 6, 10, 11, 19, 20	C-5, 6, 8, 10, 11, 19, 20	C-1, 5, 8, 10, 11, 19	C-5, 6, 7, 8, 10, 11, 19	C-5, 6, 8, 11
18a	C-3, 18′, 19	C-3, 4, 5, 19	C-3, 4, 5, 19	C-3, 4, 5, 19	C-3, 4, 5, 19
18b	C-3, 5, 18′, 19	C-3, 5		C-3, 4, 5, 19	C-3, 4, 5, 19
19a		C-3, 4, 5, 17, 20	C-4, 17, 20	C-3, 4, 17, 18	C-1, 4, 5, 17, 18, 20
19b	C-1, 5, 17, 18, 20	C-3, 4, 5, 17, 20	C-3, 18, 20	C-3, 4, 5, 17	
20a	C-17, 19	C-17, 19, 21	C-17, 19, 21	C-17, 19, 21	C-17, 19, 21
20b	C-17, 19, 21	C-17, 19, 21	C-17, 19, 21	C-17, 19, 21	C-17, 21
21	C-20	C-20	C-20	C-20	C-20
MeO-6	C-6	C-6		C-6	C-6
MeO-8	C-8		C-8	C-8	
MeO-16	C-16	C-16	C-16	C-16	C-16
MeO-18	C-18			C-18	
AcO-14α		171.4	171.4	170.6	

was confirmed that **2** is 14-*O*-acetyltakaosamine.

Compound **3** was isolated as an amorphous solid. The molecular formula, $C_{25}H_{39}NO_7$, was deduced from HR-EI-MS (M^+ *m/z* 465.2746, Calcd 465.2726). The ^{1}H- and ^{13}C-NMR spectra of **3** gave characteristic signals for a *N*-ethyl group [δ_H 1.12 (3H, t, J=7.2 Hz), 2.88 and 2.98 (1H each, dq, J=7.2, 14.2 Hz); δ_C 13.8 (q), 50.6 (t)], one angular methyl [δ_H 1.27 (3H, s); δ_C 30.1 (q)], one acetoxy group [δ_H 2.05 (3H, s); δ_C 21.2 (q), 171.4 (s)] and two methoxyl groups [δ_H 3.38, 3.41 (3H each, s); δ_C 56.6 (q), 52.6 (q)]. The ^{13}C-NMR spectrum displayed 25 carbon signals. The DEPT spectrum showed nine methine, six methylene and five methyl carbons. The location of the acetoxy group at C-14 was concluded from the correlation, in the HMBC experiment, of the carboxyl carbon and the skeletal proton at δ_H 4.77 (1H, t, J=4.6 Hz) assigned to H-14. The oxygenated quaternary carbons at δ_C 85.0 and 80.6 were assigned to C-7 and C-8, respectively. The signals at δ_C 33.6 and 47.7 were attributed to the non-oxygenated quaternary carbons C-4 and C-11, respectively. Four of the nine methine carbons were oxygenated (δ_C 72.2, 71.3, 75.5, 82.6). Comparison of the ^{13}C-NMR spectral data of **3** with those of the known alkaloids pubescenine[13] and 18-demethylpubescenine[14] suggested that the two methoxyl signals at δ_C 52.6 (q) and 56.6 (q) can be assigned to methoxyl groups at C-8 and C-16, respectively. Those assignments were confirmed by HMBC correlations of the methoxyl protons at δ_H 3.41 (s) and 3.38 (s) to the skeletal carbons at δ_C 80.6 (s) and 82.6 (d), respectively. The signals at δ_H 1.92 (1H, d, J=6.4 Hz) which gave long-range ^{1}H–^{13}C correlations with the carbons at δ_C 72.2, 33.6 (C-4), 85.0 (C-7), 43.2 (C-10), 47.7 (C-11), 63.1, 60.3, was assigned to H-5β. Consequently, the signals at δ_C 72.2, 63.1 and 60.3 were attributed to C-1, C-17, and C-19. The broad singlet at δ_H 3.63 ($w_{1/2}$=6.9 Hz) correspond to H-1. Their position and multiplicity suggested that ring A possessed a boat conformation, which is best manifested by the ROE correlation between the β-configurative axial H-2 (δ_H 1.52 m) and H-5 (δ_H 1.92, d, J=6.4 Hz) protons. We observed a proton–proton correlation in the COSY experiment between H-5 and the signal at δ_H 4.50 (1H, dd, J=6.4, 6.4 Hz) corresponding to H-6 which became a doublet of J=6.4 Hz when D_2O was added, confirming the presence of a hydroxyl group at this position. The stereochemistry of H-6 was concluded to be β from its ROESY cross-peak with H-5 and the 6.4 Hz coupling constant between H-5 and H-6. This compound is a new natural product belonging to the unusual group of 6-*epi*-lycoctonine-type alkaloids: pubescenine,[13] 18-demethylpubescenine,[14] and consolidine.[15]

Delbonine (**4**) was isolated for the first time from *Delphinium bonvalotti* in 1984[16] and the complete assignments of ^{13}C-NMR data were realized in 2000 by Shrestha and Katz.[17] We found identical ^{13}C-NMR chemical shifts, but our two-dimensional NMR investigations, including ^{1}H–^{1}H COSY, HSQC and HMBC experiments, permitted some revised assignments (C-2, C-3, C-5, C-9).

The signal at δ_H 2.80 (1H, d, J=1.9 Hz) was characteristical for H-17 in this type of compounds and correlated, W coupling, with H-5 at δ_H 1.71 (1H, d, J=1.9 Hz) in the ^{1}H–^{1}H COSY. The long-range correlations between H-5 and C-1, C-4, C-6, C-11, C-7, C-10, C-17, C-19 observed in the

Table 3. ^{1}H- and ^{13}C-NMR Data for Compounds **4**—**5** in $CDCl_3$[a)]

Proton	**4**		**5**	
	δ_H	δ_C	δ_H	δ_C
1β	3.66 br s ($w_{1/2}$=5.8)	72.2 d	3.76 d (5.2)	68.9 d
2α	1.52 m	29.3 t	1.78 ddd (13.7, 9.1, 5.4)	21.8 t
2β	1.45 dddd (13.9, 13.9, 6.1, 3.1)		1.46 ddd (12.5, 9.0, 9.0)	
3α	1.63 m	26.9 t	1.63 ddd (12.3, 8.5, 8.5)	25.1 t
3β	1.91 dd (13.8, 6.6)		1.57 dd (12.3, 9.1)	
4		37.0 s		43.4 s
5	1.71 d (1.9)	48.5 d	1.55 s	49.8 d
6α	3.83 s	90.7 d	3.96 s	90.5 d
7		90.8 s		84.5 s
8		81.6 s		76.9 s
9	3.32 m	38.1 d	2.68 dd (6.5, 4.5)	43.2 d
10	2.10 m	44.4 d	2.01 ddd (12.0, 6.5, 5.6)	37.1 d
11		49.1 s		47.2 s
12α	1.73 t (9.3)	29.3 t	1.20 dd (13.9, 5.6)	30.6 t
12β	1.83 m		1.87 ddd (13.9, 12.0, 7.8)	
13	2.52 br t ($w_{1/2}$=9.2)	36.6 d	2.39 dd (7.8, 4.5)	38.6 d
14β	4.80 dt (5.3, 0.9)	75.3 d	3.65 t (4.5)	84.1 d
15α	2.56 dd (15.4, 8.7)	30.2 t	2.70 dd (15.0, 8.4)	33.3 t
15β	1.74 dd (15.4, 7.8)		1.74 dd (15.0, 8.4)	
16α	3.34 m	82.2 d	3.13 t (8.4)	82.9 d
17	2.80 d (1.9)	66.2 d	2.36 s	63.7 d
18a	3.31 d (8.9)	78.6 t	3.67 d (10.5)	64.0 t
18b	3.15 d (8.9)	78.6 t	3.60 d (10.5)	
19a	2.51 d (11.5)	57.2 t		
19b	2.46 d (11.5)	57.2 t	4.06 s	85.1 d
20a	2.93 dq (14.0, 7.2)	50.3 t	2.94 dq (14.0, 7.2)	47.4 t
20b	2.82 dq (14.0, 7.2)	50.3 t	2.69 dq (14.0, 7.2)	
21	1.09 t (7.2)	13.7 q	1.08 t (7.2)	13.6 q
MeO-6	3.37 s	59.2 q	3.40 s	58.9 q
MeO-8	3.31 s	50.6 q		
MeO-14			3.41 s	57.8 q
MeO-16	3.36 s	56.1 q	3.33 s	56.3 q
MeO-18	3.38 s	59.3 q		
AcO-14α	2.05 s	21.4 q		
CO		170.6		

a) Chemical shifts in ppm relative to TMS; coupling constants (*J*) in Hz. ^{13}C-NMR multiplicities were established by DEPT data.

HMBC spectrum, confirmed this assignment. Moreover, the signal at δ_H 4.80 (1H, dt, *J*=5.3, 0.9 Hz) corresponding to H-14β, that is geminal to an acetate group, showed correlations in the COSY experiment with H-9 δ_H 3.32 (1H, m) and H-13 δ_H 2.52 (1H, br t, $w_{1/2}$=9.2 Hz). The signal at δ_H 1.91 (1H, dd, *J*=13.8, 6.6 Hz) showed long-range correlations with C-4, C-18 and C-19, between others, and was assigned to H-3β. Its diastereotopic proton H-3α at δ_H 1.63 m gave spatial correlations with H-19α in the ROESY spectrum. In the COSY experiment H-1β geminal to a hydroxyl group (δ_H 3.66 br s) showed correlations with two protons H-2 at δ_H 1.45 (1H, dddd) and 1.52 (1H, m). Consequently, the correct assignments for C-2, C-3, C-5 and C-9 are δ_C 29.3, 26.9, 48.5 and 38.1, respectively (see Table 3).

18-Hydroxy-14-*O*-methylgadesine (**5**) has been previously reported,[5,18)] but in our knowledge the complete assignment was lack. The values given in Table 3 were based on NMR and mass spectra, and by comparison with the spectral data of 18-methoxygadesine,[6)] gigactonine,[14)] and other reported spectral values for related alkaloids.[8,9)]

Experimental

General Experimental Procedures The optical rotations were obtained on a Perkin-Elmer 241 polarimeter, 1 dm cell. IR spectra were recorded with a Perkin-Elmer 1600 spectrophotometer. Mass spectra were measured with a Micromass Autospec instrument. 1D and 2D NMR spectra were recorded using a Bruker AMX-500 and Bruker WP-200 SY spectrometers; δ values in parts per million relative to solvent ($CDCl_3$) signal. DEPT, ^{1}H–^{1}H COSY, HMQC, HMBC (optimized for *J*=7.7 Hz, *J*=3.3 Hz), and ROESY (spin lock 500 ms) experiments were carried out with the pulse sequences given by Bruker. Alumina Merck Art. 1077 and silica gel Merck Art. 7734 were used for column chromatography and Alumina Merck Art. 1101 for preparative TLC. Zones on TLC plates were visualized with Dragendorff's reagent.

Plant Material *Consolida orientalis* (Gay) Schrödinger ssp. *orientalis* was collected in June (1989) near Bolu in eastern Turkey, during the flowering period, and identified by Prof. C. Blanché and J. Molero, Botany Departament, Faculty of Pharmacy, University of Barcelona, where a voucher specimen BCF-37799 has been deposited.

Extraction and Isolation Dried powdered aerial parts of the plant (2.0 kg) were defatted with *n*-hexane (5 l) over one week and extracted repeatedly by maceration with 80% ethanol (2×5 l) at room temperature during one week. After removing the solvent under-vacuum, the EtOH extract (73.8 g) was brought to pH 1.5 with 0.1 M H_2SO_4 and filtered. The acidic solution was extracted with CH_2Cl_2 to give an acidic residue (3.1 g). The aqueous solution was subjected to a pH gradient extraction using 10% NaOH. The aqueous phases were extracted with CH_2Cl_2 to obtain a neutral residue at pH 7 (2.2 g), and a basic residue at pH 12 (0.4 g). The acidic residue was subjected to chromatography over Sephadex LH-20 (*n*-hexane–dichloromethane–methanol, 7 : 2 : 1). Fifty-one fractions (5 ml each) were collected and pooled according to their TLC pattern to give four main fractions. Combined fractions 2—10 were chromatographed on alumina preparative plates (*n*-hexane–EtOAc, 1 : 1, 3 times) to afford dehydrodelsoline (6.8 mg), 14-*O*-acetyldelcosine (3.5 mg), delsoline (80.0 mg), deltatsine (3.0 mg), and dehydrodeltatsine (**1**, 2.8 mg). Combined fractions 11—16 were

chromatographed on alumina preparative plates (*n*-hexane–EtOAc, 3 : 7) to give pubescenine (3.8 mg) and 18-demethoxypubescenine (**3**, 3.2 mg). Combined fractions 17—33 were chromatographed on alumina preparative plates (EtOAc, 3 times) to give 18-hydroxy-14-*O*-methylgadesine (**5**, 20.0 mg) and finally combined fractions 34—45 (EtOAc, 4 times), two alkaloids: 14-*O*-acetyltakaosamine (**2**, 5.3 mg) and gigactonine (3.2 mg). The neutral residue was subjected to column chromatography over neutral alumina, eluting with a gradient system of *n*-hexane, ethyl acetate and methanol starting with hexane–EtOAc (4 : 1) to afford 173 fractions of 200 ml each. Fractions 10—14 (67.0 mg), eluted with *n*-hexane–EtOAc (4 : 1), were combined for chromatography on an alumina column to yield delbonine (5.0 mg); fractions 15—28 (32.3 mg) yield delsoline (17.0 mg) after recrystallization in *n*-hexane–EtOAc; fractions 36—59 (532.4 mg) were combined and chromatographed over silica gel to afford gigactonine (215.0 mg); fractions 70—128 (91.4 mg) eluted with *n*-hexane–EtOAc (1 : 1, 1 : 4) were assembled and chromatographed over another alumina column to yield delcosine (17.2 mg), gigactonine (25.1 mg) and 18-methoxygadesine (38.2 mg); fractions 147—173 (300.5 mg) eluted with EtOAc–MeOH (19 : 1) gave after chromatography over neutral alumina three alkaloids: gigactonine (4.1 mg), takaosamine (93.2 mg), 18-demethylpubescenine (11.0 mg). The basic residue (380.0 mg) was chromatographed over a neutral alumina column using similar conditions as for the neutral residue and further purified by preparative TLC over alumina plates to afford takaosamine (40.5 mg), 18-*O*-demethyl-14-*O*-deacetylpubescenine (3.5 mg) and ajaconine (15.3 mg, diterpenoid alkaloid).

Dehydrodeltatsine (**1**): Amorphous solid; $[\alpha]_D^{25}$ +20° (c=0.1, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3423, 2926, 2871, 1459, 1386, 1272, 1174, 1119, 1094, 1024, 998, 895 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz), see Table 1; ^{13}C-NMR ($CDCl_3$, 50 MHz), see Table 1; EI-MS *m*/*z* 465 $[M]^+$ (1), 451 (24), 450 (89), 434 $[M-OCH_3]^+$ (8), 433 (10), 419 (26), 418 $[M-CH_3-CH_3OH]^+$ (100), 409 $[M-C_3H_4O]^+$ (2), 390 (20).

Oxidation of Deltatsine to Dehydrodeltatsine (1) To a mixture of deltatsine (**6**) (3.0 mg), sodium bicarbonate (35.0 mg) and benzene (1 ml), I_2 (3.3 mg) in benzene (0.2 ml) was gradually added during 4 h at room temperature. Then, the excess reagent was destroyed with $NaHSO_3$. After solvent removal, the reaction product was chromatographed on neutral alumine to give dehydrodeltatsine (**1**) (2.5 mg, 83% yield) identical with the natural alkaloid (TLC, EI-MS and ^{1}H-NMR).

14-*O*-Acetyltakaosamine (**2**): Amorphous solid; $[\alpha]_D^{25}$ +25.3° (c=0.4, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3436, 2931, 2868, 1735, 1459, 1380, 1365, 1311, 1249, 1218, 1150, 1084, 1022, 958, 911, 864, 755 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz), see Table 1; ^{13}C-NMR ($CDCl_3$, 50 MHz), see Table 1; EI-MS *m*/*z* 481 $[M]^+$ (18), 467 (27), 466 $[M-CH_3]^+$ (100), 465 (14), 464 $[M-OH]^+$ (50), 451 (17), 450 $[M-OCH_3]^+$ (66), 449 (15), 448 $[M-Me-H_2O]^+$ (50).

Hydrolysis of 14-*O*-Acetyltakaosamine (2) to Takaosamine A solution of **2** (3.3 mg) in 5 % MeOH–KOH (1 ml) was stirred at room temperature for 6 h. The reaction mixture was poured into H_2O and extracted with $CHCl_3$. The $CHCl_3$ extract was dried (Na_2SO_4), and evaporated *in vacuo* to give takaosamine (2.7 mg, 74.6%), identical with the natural alkaloid (TLC, EI-MS and ^{1}H-NMR).

18-Demethoxypubescenine (**3**): Amorphous solid; $[\alpha]_D^{25}$ +1.1° (c=0.4, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3404, 2927, 2871, 1739, 1365, 1245, 1164, 1115, 1096, 1040, 937, 868, 757 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz), see Table 1; ^{13}C-NMR ($CDCl_3$, 50 MHz), see Table 1; EI-MS *m*/*z* 465 $[M]^+$ (18), 451 $[M+H-Me]^+$ (16), 450 $[M-Me]^+$ (30), 449 (43), 448 $[M-OH]^+$ (64), 436 (34), 435 $[M+H-OMe]^+$ (87), 434 $[M-OMe]^+$ (100), 433 $[M-MeOH]^+$ (19), 432 $[M-Me-H_2O]^+$ (10).

Delbonine (**4**): Amorphous solid; $[\alpha]_D^{25}$ +35.3° (c=0.8, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3504, 2931, 2869, 2826, 1737, 1459, 1365, 1246, 1197, 1170, 1117, 1095, 999, 943, 812, 753 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz), see Table 1; ^{13}C-NMR ($CDCl_3$, 50 MHz), see Table 1; EI-MS *m*/*z* 509 $[M]^+$ (11), 494 $[M-Me]^+$ (33), 493 (27), 492 $[M-OH]^+$ (100), 479 $[M+H-OMe]^+$ (19), 478 $[M-OMe]^+$ (62), 477 $[M-MeOH]^+$ (18), 476 $[M-Me-H_2O]^+$ (14), 462 $[M-Me-MeOH]^+$ (50), 460 $[M-H_2O-OMe]^+$ (93), 444 $[M-Me-H_2O-AcOH]^+$ (23), 432 $[M-OH-AcOH]^+$ (32).

18-Hydroxy-14-*O*-methylgadesine (**5**): Colorless needles (*n*-hexane–ethyl acetate), mp 108—110 °C; $[\alpha]_D^{25}$ +50.0° (c=0.8, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3431, 2928, 2869, 2825, 1458, 1381, 1319, 1226, 1168, 1120, 1093, 1031, 994, 891, 811, 752 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz), see Table 1; ^{13}C-NMR ($CDCl_3$, 100 MHz), see Table 1; EI-MS *m*/*z* 451 $[M]^+$ (3), 437 $[M+H-Me]^+$ (24), 436 $[M-Me]^+$ (100), 434 (5), 433 $[M-H_2O]^+$ (3), 419 $[M-MeOH]^+$ (8), 418 $[M-Me-H_2O]^+$ (14).

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