Seven New Norditerpenoid Alkaloids from Spanish *Consolida orientalis*

by **Alenguer Alva**[a]), **Maritza Grandez**[a]), **Alberto Madinaveitia**[a]), **Gabriel de la Fuente**[b])[1]), and **José A. Gavín***[a])

[a]) Instituto Universitario de Bio-Orgánica 'Antonio González', Universidad de La Laguna, Avenida Astrofísico Francisco Sánchez 2, E-38206 La Laguna, Tenerife
(phone: +34 922 318598; fax: +34 922 318571; e-mail: jgavin@ull.es)
[b]) Instituto de Productos Naturales y Agrobiología, Consejo Superior de Investigaciones Científicas, Avenida Astrofísico Francisco Sánchez 3, E-38206 La Laguna, Tenerife

Dedicated to Professor *Raffaele Tabacchi* on the occasion of his 64th birthday

Seven new norditerpenoid alkaloids named 1-*O*-demethyltricornine (**1**), 14-*O*-benzoyltakaosamine (**2**), 1-*O*,19-didehydrotakaosamine (**3**), 14-*O*-demethyldelboxine (**4**), all belonging to the lycoctonine-type alkaloids, and 8-*O*-methylconsolarine (**5**), 14-*O*-deacetylpubescenine (**6**), and 18-*O*-benzoyl-14-*O*-deacetyl-18-*O*-demethylpubescenine (**7**), these belonging to the rare group of the 6-epilycoctonine-type alkaloids, were isolated from the aerial parts of *Consolida orientalis* (GAY) SCHRÖD. The structures of the new compounds were elucidated by 1D- and 2D-NMR and HR-EI-MS. Moreover, 37 known norditerpenoid alkaloids (lycoctonine-type) were isolated and identified by comparing their spectral data with those reported in the literature.

Introduction. – Plants species of the genera *Aconitum* and *Delphinium* are known sources for diterpenoid alkaloids with pharmacological and economic significance due to cattle poisoning [1][2]. The insecticidal and antifeedant activity in some diterpene alkaloids [3a][4] and the presence of highly toxic alkaloid levels in the *Delphinium barbeyi* leaves and stems early in the growing season suggest that these compounds played a defensive role in young plant tissues [5a,b], though only a few structures have been investigated for their antifeedant effects.

Following our research on the diterpenoid alkaloids in the Spanish *Aconitum*, *Delphinium*, and *Consolida* species, we have restudied the *Consolida orientalis* (GAY) SCHRÖDINGER subs. *orientalis* (Ranunculaceae) collected in Molina de Aragón (Guadalajara) and Alfambra (Teruel), located in the Spanish mainland. In a previous research on this plant's diterpenoid alkaloids collected by our group [6][7], the occurrence of delcosine, delsoline, gigactonine, 18-methoxygadesine, and 18-hydroxy-14-*O*-methylgadesine was reported. Research on this species collected in Turkey led to the isolation of a new C_{20} diterpene alkaloid, consorientaline, along with takaosamine, gigactonine, delcosine, and delsoline [8]. More recently, a new norditerpenoid alkaloid has been reported, 18-*O*-demethylpubescenine [9], along with four other known compounds: 14-*O*-demethyltuguaconitine, takaosamine, gigactonine, and delcosine, obtained from a Hungarian population of *C. orientalis.*

[1]) Deceased in 1999.

This paper reports on the isolation and structure elucidation of seven new norditerpenoid alkaloids: 1-*O*-demethyltricornine (**1**), 14-*O*-benzoyltakaosamine (**2**), 1-*O*,19-didehydrotakaosamine (**3**), 14-*O*-demethyldelboxine (**4**), all belonging to the lycoctonine-type alkaloids, and 8-*O*-methylconsolarine (**5**), 14-*O*-deacetylpubescenine (**6**), and 18-*O*-benzoyl-14-*O*-deacetyl-18-*O*-methylpubescenine (**7**), these latter belonging to the rare group of the 6-epilycoctonine-type alkaloids[2]). Compounds **1**, **3**, **4**, and **6** were isolated from the plant collected in Alfambra (Teruel, Spain) and **2** and **4**–**7** from that collected in Molina de Aragón (Guadalajara, Spain). The 14-*O*-deacetylpubescenine (**6**) was previously described by our group as a synthetic derivative of pubescenine, obtained earlier from *Consolida pubescens* [10]. In connection with *Gonzalez-Coloma*'s group [3a], we have tested the insect-antifeedant and toxic activity of 43 norditerpenoid alkaloids from *Spodoptera littoralis* and *Leptinotarsa decemlineata* [3b]. Thus, 8-*O*-methylconsolarine (**5**) showed antifeedant activity towards *L. decemlineata* ($EC_{50} < 1$), 14-*O*-deacetylpubescenine (**6**) and 18-*O*-benzoyl-14-*O*-deacetyl-18-*O*-methylpubescenine (**7**) were toxic to *L. decemlineata* (% mortality > 45), and 14-*O*-demethyldelboxine (**4**) had selective toxicity effects against insect-derived Sf 9 cells. Recently, we have reported on three new norditerpenoid alkaloids obtained from a Turkish population of *C. orientalis:* dehydrodeltatsine, 14-*O*-acetyltakaosamine, and 18-demethoxypubescenine [3c]. The known compounds are: ajadine, 18-demethoxypubescenine, 14-*O*-acetyltakaosamine, and 14-*O*-deacetylajadine, which were isolated in the *C. orientalis* extract collected in Guadalajara; deltatsine, didehydrodelsoline, 18-methoxygadesine, 18-*O*-demethylpubescenine, tuguacoinitina, potanine, and browniine, which were isolated in the *C. orientalis* extract collected in Teruel; and delsoline, pubescenine, 14-*O*-acetyldelcosine, 18-hydroxy-14-*O*-methylgadesine (dehydrogigactonine), gigactonine, delbonine, delcosine, takaosamine, ajacine, 14-*O*-demethyltuguaconitine, 14-*O*-acetyldelectinine, lycoctonine, and ajadelphinine, which were collected in both places. Extensive NMR studies, including COSY, ROESY, HSQC, and HMBC experiments, resulted in complete and unambiguous ^{1}H-NMR and ^{13}C-NMR chemical-shift assignments for **1**–**7**, whose structures were also supported by HR-EI-MS data.

Results and Discussion. – The new bases **1**–**7**, whose elementary compositions were determined by HR-MS and ^{13}C-NMR, showed characteristic signals of norditerpenoid alkaloids in their NMR spectra [11][12] and characteristic fragmentation of such compounds in their mass spectra [13]. The multiplicity of the C-signals was deduced from DEPT135 and DEPT90 experiments.

The $C_{26}H_{41}NO_8$ molecular formula of 1-*O*-demethyltricornine (**1**) was derived from the HR-EI-MS spectrum (M^+ *m*/*z* at 495.2803, calc. 495.2832) and from ^{13}C-NMR data. Furthermore the structure, of **1** was substantiated by comparison of its ^{1}H- and ^{13}C-NMR data with those of related compounds such as tricornine [14][15] and gigactonine [16].

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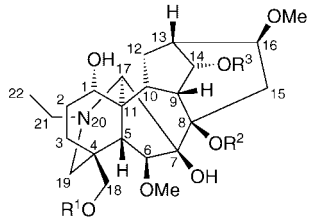
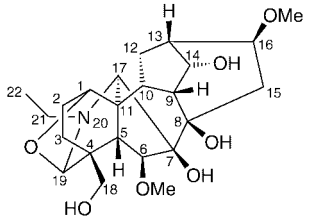
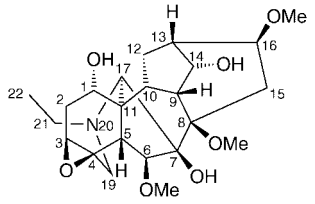
[2]) Numbering of the aconitane parent; lycoctonine = (1α,6β,14α,16β)-20-ethyl-4-(hydroxymethyl)-1,6,14,16-tetramethoxyaconitane-7,8-diol; for systematic names of **1**–**7**, see *Exper. Part*.



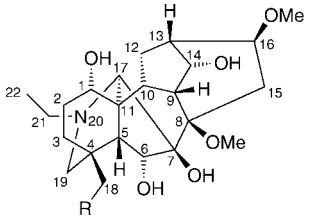
1 R^1 = Ac, R^2 = H, R^3 = Me
2 R^1 = H, R^2 = H, R^3 = Bz



3 (1-*O*,19-Didehydrotakaosamine)



4 (14-*O*-Demethyldelboxine)



5 R = H
6 R = MeO
7 R = BzO

The NMR spectra of **1** (see *Tables 1* and *2*) did not show signals for any angular Me group, though they showed resonances for an EtN group at δ(H) 1.12 (*t*, *J* = 7.2 Hz, 3 H) (δ,C) 13.5 (*q*) and at δ(H) 2.86 and 2.99 (*dq*, *J* = 7.2, 12.8 H, 1 H each) (δ(C) 50.3 (*t*)), as well as for three secondary MeO groups at δ(H) 3.32, 3.37, 3.42 (3*s*, 3 H each), and for two quaternary oxygenated C-atoms at δ(C) 78.5 and 87.8, which could be attributed to the characteristic tertiary vicinal-diol system of a lycoctonine-type alkaloid [11]. Moreover, compound **1** gave signals for a primary acetyloxy group at δ(H) 2.11 (*s*, 3 H), (δ(C) 20.8 (*q*), 171.0(*s*)), which was located at C(18) following the usual substitution pattern in norditerpenoid alkaloids [11][12]. One-proton signals at δ(H) 3.97 and 4.00 (each *d*, *J* = 11.0) (δ(C) 68.8 (*t*)) were assigned to the nonequivalent CH_2(18) protons on the basis of three-bond connectivities in the HMBC experiment with a CH_2, *i.e.*, C(19), at δ(C) 56.9 and a two-bond connectivity with a quaternary C-atom, *i.e.*, C(4), at δ(C) 36.4. Signals at δ(H) 3.97 and 4.00 are downfield shifted compared with a typical 4-(hydroxymethyl) group (see δ(H) 3.40 and 3.66 in **2**) due to the presence of the acetyloxy group. The remaining secondary OH group was placed in α-position at C(1), based on the δ(C) value of the *d* at δ(C) 72.4 (δ(H) 3.68 (br. *t*; ring-A boat)). The one-proton signal at δ(H) 2.84 (*d*, *J* = 1.7 Hz) (δ(C) 65.8 (*d*)) gave three-bond connectivities in the HMBC experiment with two CH_2 groups at δ(C) 50.3 and 56.9, attributed to C(21) and C(19) (in α to N(20)), respectively, and was assigned to H–C(17). Further correlations were observed in the same experiment with three *C*H at δ(C) 72.4, 45.2, and 90.9 and with a quaternary C at δ(C) 78.5, which were, thus, assigned to C(1), C(5), C(6), and C(8), respectively. The one-proton signal of H–C(5) at δ(H) 1.82 (*d*, *J* = 1.8 Hz) (δ(C) 45.2)) showed a typical scalar correlation with the H–C(17) signal (W coupling) in the COSY experiment. Secondary MeO groups were located at C(6), C(14), and C(16), based on their ^{1}H- and ^{13}C-NMR data and were corroborated by the analysis of the 2D-NMR spectra. Thus, the *t* at δ(H) 3.64 (*t*, *J* = 4.5 Hz), (δ(C) 84.5 (*d*)), which is characteristic of H_β–C(14), showed heteronuclear long-range correlation with the resonances at δ(C) 78.5 (*s*) and 82.9 (*d*), in accordance with the presence of OH–C(8) and MeO_β–C(16).

The 14-*O*-benzoyltakaosamine (**2**) was isolated as an amorphous powder, and its $C_{30}H_{41}NO_8$ molecular formula was deduced from the HR-EI-MS (M^+ at *m*/*z* 543.2835, calc. 543.2832). The IR spectrum (KBr) showed the presence of OH (3448 cm^{-1}),

Table 1. *^{1}H-NMR* (500 MHz) *Data for Compounds* **1**–**7**[a])

	1	**2**	**3**	**4**	**5**	**6**	**7**
H_β–C(1)	3.71 (br. *s*, $w_{1/2}$ = 6.0)	3.74 (br. *s*, $w_{1/2}$ = 8.3)	3.70 (*d*, *J* = 5.1)	3.93 (br. *s*, $w_{1/2}$ = 7.0)	3.66 (br. *s*, $w_{1/2}$ = 7.4)	3.66 (br. *s*, $w_{1/2}$ = 8.7)	3.71 (*m*)
H_α–C(2)	1.67 (*m*)	1.67 (*m*)	1.80 (*ddd*, *J* = 12.6, 9.2, 5.1)	2.22 (*ddd*, *J* = 14.0, 5.5, 2.4)	1.54 (*m*)	1.67 (*m*)	1.71 (*m*)
H_β–C(2)	1.49 (*dddd*, *J* = 13.8, 13.8, 4.3, 2.5)	1.53 (*dddd*, *J* = 13.9, 13.9, 6.2, 3.2)	1.51 (*ddd*, *J* = 12.6, 9.2, 9.2)	1.26 (*ddd*, *J* = 14.0, 7.1, 2.4)	1.52 (*m*)	1.51 (*dddd*, *J* = 13.8, 13.8, 6.2, 3.4)	1.54 (*dddd*, *J* = 14.6, 14.6, 6.1, 3.1)
H_α–C(3)	1.73 (*m*)	1.70 (*m*)	1.60 (*dd*, *J* = 12.0, 9.2)	3.11 (*dd*, *J* = 7.1, 5.5)	1.75 (*m*)	1.70 (*m*)	1.67 (*m*)
H_β–C(3)	1.83 (*m*)	1.96 (*m*)	1.68 (*ddd*, *J* = 12.0, 9.2, 9.2)	–	1.46 (*ddd*, *J* = 13.2, 3.6, 3.6)	1.96 (*m*)	1.78 (*m*)
H–C(5)	1.82 (*d*, *J* = 1.8)	1.91 (*d*, *J* = 1.8)	1.58 (br. *s*, $w_{1/2}$ = 4.1)	1.42 (*d*, *J* = 2.9)	1.91 (*d*, *J* = 6.8)	2.17 (*d*, *J* = 7.3)	2.1 (*d*, *J* = 6.1)
H_α–C(6)	3.96 (*s*)	4.00 (*s*)	3.97 (*d*, *J* = 1.4)	4.24 (*s*)	–	–	–
H_β–C(6)	–	–	–	–	4.53 (*d*, *J* = 6.8)	4.51 (*t*, *J* = 6.0)	4.56 (*m*)
H–C(9)	2.96 (*dd*, *J* = 6.8, 4.5)	3.21 (*dd*, *J* = 7.0, 4.7)	2.73 (*dd*, *J* = 4.8, 6.9)	3.32 (*t*, *J* = 5.9)	2.16 (*dd*, *J* = 6.9, 4.5)	2.18 (*dd*, *J* = 6.9, 5.9)	2.11 (*m*)
H–C(10)	1.98 (*ddd*, *J* = 11.7, 6.8, 4.5)	2.10 (*ddd*, *J* = 11.8, 7.0, 4.7)	1.96 (*ddd*, *J* = 11.2, 6.9, 6.9)	2.10 (*m*)	1.87 (*ddd*, *J* = 11.9, 6.9, 5.1)	1.90 (*ddd*, *J* = 11.5, 7.0, 5.0)	1.89 (*ddd*, *J* = 11.6, 6.8, 5.1)
H_α–C(12)	1.74 (*dd*, *J* = 13.1, 4.5)	1.80 (*dd*, *J* = 14.2, 4.7)	1.08 (*dd*, *J* = 14.0, 6.9)	1.58 (*t*, *J* = 8.9)	1.75 (*dd*, *J* = 14.4, 5.2)	1.77 (*dd*, *J* = 14.3, 4.9)	1.76 (*dd*, *J* = 14.4, 5.0)
H_β–C(12)	2.07 (*ddd*, *J* = 13.1, 11.7, 7.4)	2.21 (*ddd*, *J* = 14.2, 11.8, 7.5)	1.85 (*ddd*, *J* = 14.0, 11.2, 6.9)	2.09 (*m*)	2.04 (*ddd*, *J* = 14.4, 11.0, 7.3)	2.07 (*ddd*, *J* = 14.2, 11.2, 7.3)	2.05 (*m*)
H–C(13)	2.41 (*dd*, *J* = 7.4, 4.5)	2.63 (*dd*, *J* = 7.5, 4.7)	2.46 (*m*)	2.32 (*t*, *J* = 6.1)	2.31 (*dd*, *J* = 7.6, 4.5)	2.35 (*dd*, *J* = 7.6, 4.7)	2.34 (*dd*, *J* = 7.3, 4.7)
H_β–C(14)	3.64 (*t*, *J* = 4.5)	5.09 (*t*, *J* = 4.7)	4.10 (*t*, *J* = 4.8)	4.05 (*ddd*, *J* = 4.6, 4.6, 3.4)	4.05 (*t*, *J* = 4.5)	4.09 (*t*, *J* = 4.7)	4.07 (*t*, *J* = 4.7)
H_α–C(15)	2.63 (*dd*, *J* = 14.6, 8.3)	2.78 (*dd*, *J* = 15.1, 8.9)	2.68 (*dd*, *J* = 17.1, 8.8)	2.70 (*dd*, *J* = 16.2, 8.9)	2.68 (*dd*, *J* = 15.3, 8.9)	2.74 (*dd*, *J* = 15.1, 8.9)	2.76 (*dd*, *J* = 15.1, 8.8)
H_β–C(15)	1.77 (*dd*, *J* = 14.6, 8.3)	1.77 (*dd*, *J* = 15.1, 7.7)	1.81 (*dd*, *J* = 17.1, 8.1)	1.84 (*dd*, *J* = 16.2, 6.0)	1.77 (*dd*, *J* = 15.3, 6.7)	1.77 (*dd*, *J* = 15.1, 7.7)	2.05 (*dd*, *J* = 15.1, 6.9)
H_α–C(16)	3.30 (*t*, *J* = 8.3)	3.41 (*m*)	3.39 (*m*)	3.42 (*m*)	3.48 (*t*, *J* = 5.5)	3.49 (*m*)	3.48 (*t*, *J* = 6.0)
H–C(17)	2.84 (*d*, *J* = 1.8)	2.87 (*d*, *J* = 1.8)	2.60 (*d*, *J* = 2.7)	2.93 (*d*, *J* = 2.9)	2.79 (*s*)	2.77 (*s*)	2.81 (*s*)
H_a–C(18)/(Me(18))	4.00 (*d*, *J* = 11.0)	3.66 (*d*, *J* = 10.4)	3.69 (*d*, *J* = 10.6)	–	1.29 (*s*)	3.62 (*d*, *J* = 8.9)	5.10 (*d*, (*d*, *J* = 10.5)
H_b–C(18)	3.97 (*d*, *J* = 11.0)	3.40 (*d*, *J* = 10.4)	3.62 (*d*, *J* = 10.6)	–	–	3.42 (*d*, *J* = 8.9)	4.21 (*d*, *J* = 10.5)
H_α–C(19)	2.53 (*d*, *J* = 11.5)	2.46 (*d*, *J* = 11.6)	–	2.53 (*d*, *J* = 9.6)	2.39 (*d*, *J* = 11.0)	2.40 (*d*, *J* = 10.9)	2.50 (*d*, *J* = 10.3)
H_β–C(19)	2.50 (*d*, *J* = 11.5)	2.44 (*d*, *J* = 11.6)	4.07 (*s*)	3.46 (*d*, *J* = 9.6)	2.78 (*d*, *J* = 11.0)	2.84 (*d*, *J* = 10.9)	3.01 (*d*, *J* = 10.3)
H_a–C(21)	2.99 (*dq*, *J* = 12.8, 7.2)	2.99 (*dq*, *J* = 12.8, 7.2)	2.96 (*dq*, *J* = 12.3, 7.0)	3.03 (*dq*, *J* = 13.8, 7.4)	3.04 (*dq*, *J* = 14.0, 7.0)	303 (*dq*, *J* = 13.9, 7.2)	3.07 (*dq*, *J* = 13.9, 7.3)
H_b–C(21)	2.86 (*dq*, *J* = 12.8, 7.2)	2.85 (*dq*, *J* = 12.8, 7.2)	2.71 (*dq*, *J* = 12.3, 7.0)	3.02 (*dq*, *J* = 13.8, 7.4)	2.91 (*dq*, *J* = 14.0, 7.0)	2.93 (*dq*, *J* = 13.9, 7.2)	2.97 (*dq*, *J* = 13.9, 7.3)
Me(22)	1.12 (*t*, *J* = 7.2)	1.12 (*t*, *J* = 7.2)	1.10 (*t*, *J* = 7.0)	1.10 (*t*, *J* = 7.4)	1.14 (*t*, *J* = 7.2)	1.15 (*t*, *J* = 7.2)	1.18 (*t*, *J* = 7.2)
MeO–C(6)	3.32 (*s*)	3.39 (*s*)	3.41 (*s*)	3.48 (*s*)	–	–	–
MeO–C(8)	–	–	–	3.50 (*s*)	3.45 (*s*)	3.49 (*s*)	3.49 (*s*)
MeO–C(14)	3.42 (*s*)	–	–	–	–	–	–
MeO–C(16)	3.37 (*s*)	3.34 (*s*)	3.37 (*s*)	3.42 (*s*)	3.41 (*s*)	3.45 (*s*)	3.45 (*s*)
MeO–C(18)	–	–	–	–	–	3.42 (*s*)	–
MeCOO–C(18)	2.11 (*s*)	–	–	–	–	–	–
PhCO: H_o	–	8.11 (*d*, *J* = 7.5)	–	–	–	–	8.09 (*d*, *J* = 7.6)
H_p	–	7.53 (*t*, *J* = 7.5)	–	–	–	–	7.62 (*t*, *J* = 7.3)
H_m	–	7.43 (*t*, *J* = 7.5)	–	–	–	–	7.50 (*t*, *J* = 7.7)

[a]) Assignments confirmed by COSY, ROESY, HMQC, HMBC, and DEPT spectra. Chemical shifts δ in ppm relative to $SiMe_4$; coupling constants *J* and $w_{1/2}$ in Hz.

Table 2. *^{13}C-NMR Data for Compounds* **1**–**7**[a])

	1[b])	**2**[c])	**3**[c])	**4**[c])	**5**[b])	**6**[c])	**7**[c])
C(1)	72.4	72.4	68.6	77.6	72.3	72.3	72.1
C(2)	26.9	29.3	21.8	31.8	28.9	29.4	29.7
C(3)	30.4	26.7	24.8	58.1	34.8	29.6	29.5
C(4)	36.4	38.1	43.5	58.8	33.7	38.3	38.1
C(5)	45.2	44.5	49.8	52.4	50.3	46.0	46.0
C(6)	90.9	90.3	90.0	90.0	71.2	70.5	70.8
C(7)	87.8	87.5	85.1	92.7	85.1	85.2	85.4
C(8)	78.5	78.2	76.0	81.3	80.7	80.6	80.6
C(9)	44.0	43.0	45.2	39.7	45.3	44.0	45.0
C(10)	43.4	43.6	36.7	44.0	44.2	47.4	43.9
C(11)	49.5	49.3	46.4	53.6	47.5	47.3	47.2
C(12)	29.1	29.8	27.5	28.8	29.1	29.2	29.5
C(13)	37.7	37.8	37.9	40.1	40.4	40.4	40.4
C(14)	84.5	76.5	75.2	74.6	75.0	75.1	75.1
C(15)	33.5	34.1	33.7	31.1	29.2	29.8	29.0
C(16)	82.9	82.5	81.5	82.1	82.2	82.4	82.4
C(17)	65.8	66.2	64.2	67.5	63.4	63.8	63.8
C(18)	68.8	66.8	63.9	–	30.1	80.7	72.2
C(19)	56.9	57.1	84.9	54.3	60.5	56.6	56.3
C(21)	50.3	50.3	47.3	50.0	50.5	50.6	50.6
C(22)	13.5	13.6	13.6	14.1	13.8	13.8	13.7
*Me*O–C(6)	–	57.7	58.0	60.3	–	–	–
*Me*O–C(8)	–	–	–	51.4	52.8	53.0	53.0
*Me*O–C(16)	–	56.1	56.5	56.4	56.6	56.5	56.6
*Me*O–C(18)	–	–	–	–	–	80.7	–
BzO–C(14)	–	[d])	–	–	–	–	–
BzO–C(18)	–	–	–	–	–	–	[d])

[a]) Chemical shifts in ppm relative to $CDCl_3$. [b]) 75 MHz. [c]) 50 MHz. [d]) Data in the text.

carbonyl (1716, 1278 cm^{-1}), and aromatic groups (1451, 753, 714 cm^{-1}). The ^{1}H- and ^{13}C-NMR spectra (see *Tables 1* and *2*) closely resembled those of **1** and 14-*O*-acetyltakaosamine ([3c]). The structure of **2** was confirmed by comparison of its NMR data with those of takaosamine [17]. Treatment of **2** with KOH/MeOH gave takaosamine in 64.6% yield.

The NMR spectra of **2** showed signals for an EtN group (δ(H) 1.12 (*t*, *J* = 7.2 Hz, 3 H) and 2.85 and 2.99 (2*dq*, 1 H each) (δ(C) 13.6 (*q*) and 50.3 (*t*)), 2 MeO groups (δ(H) 3.34 and 3.39 (2*s*, 3 H each); δ(C) 56.1 and 57.7 (2*q*)), a benzoate group (δ(H) 7.43 (*t*, *J* = 7.8 Hz, 2 H), 7.53 (*t*, *J* = 7.4 Hz, 1 H), and 8.11 (*t*, *J* = 7.8 Hz, 2 H); δ(C) 128.3 (*d*, 2C), 129.8 (*d*, 2C), 130.1 (*s*), 132.7 (*d*), and 166.5 (*s*)), and 2 quaternary oxygenated C-atoms at δ(C), 78.2 and 87.5, which are characteristic of a tertiary vicinal diol moiety in a lycoctonine-type alkaloid [11][12]. The benzoate group was tentatively in located in α-position at C(14) because of the δ(H) value of its geminal proton (δ(H) 5.09 (*t*, *J* = 4.7 Hz); δ(C) 76.5 (*d*)) and compared with the corresponding signal in **1** (δ(H)3.64 (*t*, *J* = 4.5 Hz); δ(C) 84.5 (*d*)) and in 14-*O*-acetyltakaosamine (δ(H)4.77 (*t*, *J* = 4.7 Hz); δ(C) 76.3 (*d*).

The HR-EI-MS data of 1-*O*,19-didehydrotakaosamine (**3**) suggested the molecular formula $C_{23}H_{35}NO_7$ (M^+ at *m*/*z* 437.2393, calc. 437.2413). The structure of **3** was substantiated by chemical correlations with takaosamine [17]. Treatment of takaosamine with I_2 in benzene gave **3** in 35% yield.

The NMR spectra of **3** (see *Tables 1* and *2*) gave signals for an EtN group, 2 MeO groups at δ(H) 3.37 and 3.41 (2*s*, 3 H each) (δ(C) 56.5 and 58.0 (2*q*)), and two oxygenated C-atoms at δ(C) 76.0 and 85.1, which are characteristic of a tertiary vicinal diol moiety in a lycoctonine-type alkaloid [11]. The presence of two diastereotopic CH_2 protons at δ(H) 3.62 and 3.69 (each *d*, $J = 10.6$ Hz) (δ(C), 63.9 (*d*)) are typical of a hydroxymethylene group at C(4) in norditerpenoid alkaloids [11][12]. The loss of an acrylaldehyde molecule from the ions at *m*/*z* 437 (M^+), 381 (3, $[M-56]^+$) in the MS [13], the presence of the strong absorption bands at 891 and 996 cm^{-1} in the IR, and one-proton signals at δ(H) 3.70 (*d*, $J = 5.1$ Hz) (δ(C) 68.6 (*d*)) and δ(H) 4.07 (*s*) (δ(*C*) 84.9 (*d*)) indicated the presence of a C(1)–O–C(19) ether bridge in **3** [18]. Moreover, correlations observed in the HMBC experiment between the signal at δ(H) 4.07 (*s*) with C(18) (δ(C) 63.9 (*t*)), C(21) (δ(C) 47.3 (*t*)), C(17) (δ(C) 64.2 (*d*)), C(5) (δ(C) 49.8 (*d*)), and C(1) (δ(C) 68.6 (*d*)) confirmed the C(1)–O–C(19) ether linkage. The one-proton signal at δ(H) 4.10 (*t*, $J = 4.8$ Hz) (δ(C) 75.2 (*d*)) was typical for a proton H_β–C(14) geminal to a secondary OH group [11][12].

The NMR spectra of 14-*O*-demethyldelboxine (**4**) did not show signals of any angular Me group at C(4) or a C(19) functionality (see *Tables 1* and *2*). In accordance with its molecular formula $C_{23}H_{35}NO_7$, derived from HR-EI-MS (M^+ at *m*/*z* 437.2418, calc. 437.2413) and ^{13}C-NMR data, **4** must be a bis-norditerpenoid alkaloid having an epoxy moiety in the molecule. A comparison of its ^{13}C-NMR spectra with those of the related alkaloids 14-*O*-demethyltuguaconitine [9][16], tuguaconitine [19], and delboxine [20] suggested that this epoxy moiety is located at C(3)/C(4) in β position.

In the HMBC spectrum of **4**, the one-proton signal at δ(H) 3.11 (*dd*, $J = 7.1$, 5.5 Hz) (δ(C) 58.1 (*d*)) was assigned to H–C(3) since it gave three-bond correlations with the C(19) (δ(C) 54.3 (*t*)), and two-bond correlations with C(2) (δ(C) 31.8 (*t*)) and C(4) (δ(C) 58.8 (*s*)). Moreover, the COSY cross-peak between the signal at δ(H) 3.11 and H_α–C(2) at δ(H) 2.22 (*ddd*, $J = 14.0$, 5.5, 2.4 Hz) and H_β–C(2) at δ(H) 1.26 (*ddd*, $J =$ 14.0, 7.1, 2.4 Hz), and the ROESY cross-peak with H_α–C(2) and H_α–C(19) at δ(H) 2.53 (*d*, $J = 9.6$ Hz) (δ(C) 54.3 (*t*)), confirmed that H–C(3) is in α position and the epoxy moiety in β position. Moreover, the boat conformation of ring A, which generally occurs in 3,4-epoxy-substituted bisnorditerpenoid alkaloids [20], was also present in **4** as established by the spatial correlations observed between the equatorial H_β–C(1) at δ(H) 3.93 (br. *s*, $w_{1/2} = 7.0$ Hz) (δ(C) 77.6 (*d*)), and both equatorial and axial H–C(2). The *d* at δ(C) 77.6 corroborated the presence of a 3,4-epoxy group, because the δ(C) range of an OH_α–*C*(1) in the presence of a 3,4-epoxy group is reported to be 77.0–77.5 [11].

HR-EI-MS Data suggested the molecular formula $C_{23}H_{37}NO_6$ for 8-*O*-methylconsolarine (**5**) (M^+ at *m*/*z* 423.2606, calc. 423.2621). Its structure was confirmed by comparison of their ^{1}H- and ^{13}C-NMR data with those of 18-demethoxypubescenine ([3c]). Basic hydrolysis of this latter compound with KOH/MeOH gave **5** in 78% yield. Compound **5** is a new natural product belonging to the unusual group of the 6-epilycoctonine-type alkaloids: pubescenine [10], 18-*O*-demethylpubescenine [9], consolidine [17], and 18-demethoxypubescenine. All these compounds showed a typical feature in their ^{13}C-NMR spectra, *i.e.*, C(6) is much more shielded than C(6) of the lycoctonine-type alkaloids (δ(C) 70.3–71.3 *vs. ca.* 90, resp.).

The ^{1}H- and ^{13}C-NMR spectra of **5** (see *Tables 1* and *2*) gave characteristic signals for an EtN group at δ(H) 1.14 (*t*, $J = 7.2$ Hz, 3 H) (δ(C) 13.8 (*q*)) and at δ(H) 2.91 and 3.04 (*dq*, $J = 14.0$, 7.0 Hz, 1 H each) (δ(C) 50.5 (*t*)), one angular Me at δ(H) 1.29 (*s*) (δ(C) 30.1 (*q*)), and 2 MeO groups at δ(H) 3.41 and 3.45 (2*s*, (δ(C) 3 H each) 56.6 and 52.8 (2*q*)). The ^{13}C-NMR spectrum displayed 23 C-signals. The DEPT spectrum showed 9 CH, 6 CH_2, and 4 Me groups. Oxygenated quaternary C-atoms at δ(C) 85.1 and 80.7 were assigned to C(7) and C(8), respectively. Signals at δ(C) 33.7 and 47.5 were attributed to the non-oxygenated C(4) and C(11), respectively. The positions of the MeO groups were evident from the three-bond correlations between the MeO protons and the skeletal C-atoms at δ(C) 80.7 (C(8)) and 82.2 (C(16)). Four of the nine CH were oxygenated (δ(C) 72.3, 71.2, 75.0, and 82.2). The signal at δ(H) 4.05 (*t*, $J = 4.5$ Hz (δ(C) 75.0) was characteristic of H_β–C(14) geminal to

an OH group in this type of compounds [11][12]. The broad *s* at δ(H) 3.66 ($w_{1/2}$ = 7.4) (δ(C) 72.3) was attributed to H–C(1). Their position and multiplicity suggested that ring A possesses a boat conformation, which is confirmed by the ROE correlation between the β-oriented axial H–C(2) (δ(H) 1.52 (*m*)) and H_β–C(5) (δ(H) 1.91 (*d*)). This assignment was confirmed by the long-range ^{1}H,^{13}C correlations in the HMBC experiment with C(18) (δ(C) 30.1 (*q*)), C(4) (δ(C) 33.7 (*s*)), C(10) (δ(C) 44.2 (*d*)), C(19) (δ(C) 60.5 (*t*)), C(17) (δ(C) 63.4 (*d*)), C(6) (δ(C) 71.2 (*d*)), C(7) (δ(C) 85.1 (*s*)). We observed a ^{1}H,^{1}H correlation in the COSY experiment between H_β–C(5) and the signal at δ(H) 4.53 (*d*, *J* = 6.8 Hz) (δ(C) 71.2 (*d*)) of H–C(6). Several important NOE interactions were observed between H_β–C(5) and H–C(6), H–C(6) and H–C(9), H–C(9) and H–C(10), establishing their β configuration. Moreover, the coupling between H_β–C(5) and H–C(6) (*J* = 6.8 Hz) was consistent with a β-oriented H–C(6).

The 14-*O*-deacetylpubescenine (**6**) was previously described by our group as a synthetic derivative of pubescenine, the first lycoctonine-type C_{19} diterpenoid alkaloid with an α-positioned O-function at C(6), obtained earlier from *Consolida pubescens* [10]. The molecular formula $C_{24}H_{39}NO_7$ was assigned to **6** by HR-EI-MS (M^+ at *m*/*z* 453.2731, calc. 453.2726) and ^{13}C-NMR data. The ^{1}H- and ^{13}C-NMR spectra showed close similarities with those of pubescenine (see *Tables 1* and *2*), except for the lack of the AcO group at C(14) and the position of H_β–C(14) (δ(H) 4.09 instead of 4.78 in pubescenine), and with those of 8-*O*-methylconsolarine (**5**), except for the presence of a $MeOCH_2$(18) group (δ(H) 3.42 and 3.62 (each *d*); δ(C) 80.7) instead of one angular Me group (δ(H) 1.29; δ(C) 30.1). Moreover, the ^{13}C-NMR assignments initially proposed [10] for pubescenine and 14-*O*-deacetylpubescenine (**6**), as regards the C(5) and C(10) positions, should be interchanged.

The amorphous compound 18-*O*-benzoyl-14-*O*-deacetyl-18-*O*-demethylpubescenine (**7**) was homogeneous on TLC. Its structure was deduced from the analysis of its spectroscopic data. The HR-EI-MS of **7** (M^+ at *m*/*z* 543.2848, calc. 543.2832) suggested the molecular formula $C_{30}H_{41}NO_8$. Comparison of the ^{1}H- and ^{13}C-NMR data with those of pubescenine [9], 18-*O*-demethylpubescenine [10], 8-*O*-methylconsolarine (**5**), and 14-*O*-deacetylpubescenine (**6**), showed great similarity and allowed us to assign the structure of **7**.

The ^{1}H- and ^{13}C-NMR spectra of **7** (see *Tables 1* and *2*) gave characteristic signals for one EtN group at δ(H) 1.18 (*t*, *J* = 7.2 Hz, 3 H) (δ(C) 13.7 (*q*)) and δ(H) 2.97 and 3.07 (*dq*, *J* = 13.9, 7.3 Hz, 1 H each) (δ(C) 50.6 (*t*)), and for 2 MeO groups at δ(H) 3.45 and 3.49 (2*s*, 3 H each) (δ(C) 56.6 and 53.0 (2*q*)). Moreover, the signals at δ(H) 7.50 (*t*, *J* = 7.7 Hz, 2 H), 7.62 (*t*, *J* = 7.3 Hz, 1 H), and 8.09 (*d*, *J* = 7.6 Hz, 2 H) and δ(C) 128.5 (*d*, 2 C), 129.6 (*d*, 2 C), 130.1 (*s*), 133.1 (*d*), and 167.2 (*s*) were characteristic of a benzoate group. ^{1}H,^{1}H Connectivities in the COSY spectrum indicated two isolated CH_2 groups (δ(H) 4.21 and 5.10 (each *d*), δ(C) 72.2); δ(H) 2.50 and 3.01 (each *d*), δ(C) 56.3). Long-range ^{1}H,^{13}C correlations in the HMBC spectrum between the signal of H_b–C(18) at δ(H) 4.21 and C(3) at δ(C) 29.5 (*t*), C(4) at δ(C) 38.1 (*s*), C(5) at δ(C) 46.0 (*d*), and C=O at δ(C) 167.2 (*s*), and those between H_a–C(18) at δ(H) 5.10 and the C-atoms at δ(C) 29.5 (*t*), 38.1 (*s*), 46.0 (*d*), 167.2 (*s*, C=O), and 56.3 (C(19)), indicated the presence of the benzoate group at C(18).

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Experimental Part

1. *General*. Column chromatography (CC): Alumina *Merck* Art. 1077. Prep. TLC: Alumina *Merck 1101* visualization with a *Dragendorff* reagent. $[\alpha]_D$: *Perkin-Elmer 241* polarimeter; 1-dm cell. IR Spectra: *Perkin-Elmer 1600* spectrophotometer; $\tilde{\nu}$ in cm^{-1}. 1D- and 2D-NMR Spectra: *Bruker AMX-500* and *WP-200-SY*

spectrometers; δ values in ppm rel. to the solvent ($CDCl_3$) signal; DEPT, ^1H,^1H COSY, HSQC, 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*. Mass spectra: *Micromass-Autospec* instrument.

2. *Plant Material. Consolida orientalis* (GAY) SCHRÖDINGER subs. *Orientalis*, taken in Molina de Aragón, Guadalajara, Spain, was collected in June 1995 after the flowering period, and the samples taken in Alfambra, Teruel, Spain were collected in June 1997 during the flowering period. In both cases, the plant was identified by Professors *C. Blanché* and *J. Molero*, Botany Department of the School of Pharmacy at the University of Barcelona, where voucher specimens (BCF-46982 and BCF-42607) have been deposited.

3. *Extraction and Isolation*. 3.1. *Plants Collected at Molina de Aragón*. Seventeen known compounds were isolated: ajadine (8.0 mg), 14-*O*-acetyl-8-*O*-methylconsolarine (5.5 mg), 14-*O*-acetyldelcosine (3.6 mg), pubescenine (3.0 mg), ajacine (6.4 mg), delcosine (12.5 mg), delsoline (7.1 mg), 14-*O*-deacetylajadine (5.0 mg), 14-*O*-demethyltuguaconitine (3.2 mg), gigactonine (54.0 mg), 14-*O*-acetyltakaosamine (5.0 mg), 18-hydroxy-14-*O*-methylgadesine (3.3 mg), delbonine (2.5 mg), lycoctonine (4.1 mg), ajadelphinine (5.1 mg), takaosamine (17.3 mg). Five new compounds were obtained: 14-*O*-deacetylpubescenine (**6**; 3.2 mg), 18-*O*-benzoyl-14-*O*-deacetyl-18-*O*-demethylpubescenine (**7**; 3.0 mg), 14-*O*-benzoyltakaosamine (**2**; 2.1 mg), 14-*O*-demethyldelboxine (**4**; 3.5 mg), and 8-*O*-methylconsolarine (**5**, 2.1 mg).

Dried powdered aerial parts of the plant (6.0 kg) were defatted with hexane (5 l) for one week and extracted repeatedly by maceration with 80% EtOH (2×5 l) at r.t. for another week. After evaporation, the EtOH extract (3.94 g) was treated with 0.1M H_2SO_4 and filtered. The acidic soln. was extracted with CH_2Cl_2 to give an acidic residue (1.28 g). The aq. soln. was subjected to a pH-gradient extraction with 10% NaOH, soln. and the aq. phases were extracted with CH_2Cl_2 to give a neutral residue at pH 7 (1.07 g) and a basic residue at pH 12 (0.23 g). TLC (alumina) showed that the neutral residue was the richest in variety and quantity of the alkaloids. This residue was subjected to CC (*Sephadex LH-20*, hexane/CH_2Cl_2/MeOH 1:1:8): *Fr. A* (272.5 mg) and *B* (637.7 mg). *Fr. A* was subjected to CC (*Sephadex LH-20*, $CHCl_3$/MeOH 9:1) and analyzed by TLC: seven main fractions. The combined *Fr. A4* and *A5* were separated by prep. TLC alumina, hexane/AcOEt 1:1, 3 times): *ajadine* (8.0 mg) and *rhoeagenine* (3.1 mg). The combined *Fr. A6* and *A7* were subjected to prep. TLC (alumina, hexane/AcOEt 2:3, 3 times): *14*-O-*acetyl-8*-O-*methylconsolarine* (5.5 mg) and *14*-O-*acetyldelcosine* (3.6 mg). *Fr. A8* was subjected to prep. TLC (alumina, hexane/AcOEt 3:7, 3 times): *pubescenine* (3.0 mg) and *ajacine* (3.4 mg). *Fr. A9* was subjected to prep. TLC (alumina, hexane/AcOEt 1:4, 3 times): *ajacine* (3 mg) and delcosine (12.5 mg). The combined *Fr. A10* and *A11* were subjected to prep. TLC (alumina, hexane/AcOEt 1:4, 3 times): *delsoline* (7.1 mg). The combined *Fr. A12 – A24* were subjected to prep. TLC (alumina, AcOEt/MeOH 49:1): *14*-O-*deacetylajadine* (5.0 mg). Finally, *Fr. A25* afforded, after prep. TLC (alumina, AcOEt/MeOH 95:5, 3 times) *14*-O-*demethyltuguaconitine* (2.0 mg) and *gigactonine* (54.0 mg). *Fr. B* was subjected to CC (*Sephadex LH-20*, CH_2Cl_2/MeOH 4:1) and analyzed by TLC: *Fr. B1* (120.4 mg), *B2* (287.7 mg), and *B3* (74.7 mg). *Fr. B1* was subjected to CC (neutral alumina, gradient AcOEt/MeOH starting with AcOEt). *Fr. B1.14* and *B1.15* (41.4 mg) were combined and rechromatographed by prep. TLC (alumina, AcOEt, 3 times): *gigactonine* (9 mg) and *14*-O-*acetyltakaosamine* (3.0 mg). *Fr. B1.16 – B1.18* (15.6 mg) were combined and subjected to prep. TLC (alumina, AcOEt/MeOH 19:1, 2 times): *gigactonine* (5.0 mg) and *18-hydroxy-14*-O-*methylgadesine* (3.3 mg). The combined *Fr. B1.19 – B1.29* (29.6 mg) were subjected to prep. TLC (alumina, AcOEt/MeOH 19:1, 3 times): *14*-O-*demethyltuguaconitine* (1.2 mg), *14*-O-*deacetylpubescenine* (**6**; 3.2 mg), and *18*-O-*benzoyl-14*-O-*deacetyl-18*-O-*demethylpubescenine* (**7**; 3.0 mg). *Fr. B2* (272.5 mg) was subjected to CC (basic alumina, similar conditions as for *Fr. B1*) and further analyzed by TLC: five main fractions. The combined *Fr. B2.3 – B2.6* (20.8 mg) were subjected to prep. TLC (alumina, hexane/AcOEt 7:3): *delbonine* (2.5 mg). The combined *Fr. B2.7 – B2.15* (26.4 mg) were subjected to prep. TLC (alumina, hexane/AcOEt 3:7, 2 times): *14*-O-*acetyl-8*-O-*methylconsolarine* (5.5 mg). *Fr. B2.16 – B2.20* (27.7 mg) were subjected to prep. TLC (alumina, hexane/AcOEt 3:7, 3 times): *delsoline* (2.1 mg), *14*-O-*benzoyltakaosamine* (**2**; 2.8 mg), *14*-O-*acetyltakaosamine* (2.0 mg), *14*-O-*acetyldelectinine* (2.8 mg), and *14*-O-*demethyldelboxine* (**4**; 3.5 mg). The combined *Fr. B2.21 – B2.26* (67.9 mg) were subjected to prep. TLC (AcOEt/MeOH 95:5, 3 times): *gigactonine* (20 mg) and *lycoctonine* (4.1 mg). Finally, *Fr. B2.27 – B2.39* (34.6 mg) were subjected to prep. TLC (silica gel, AcOEt/MeOH 95:5, 2 times): *ajadelphinine* (5.1 mg), *takaosamine* (17.3 mg), and *8*-O-*methylconsolarine* (**5**; 2.1 mg).

3.2. *Plants Collected at Alfambra*. Twenty known compounds were isolated: delsoline (6.4 mg), didehydrodelsoline (10.8 mg), lycoctonine (8.4 mg), 14-*O*-acetyldelectinine (7.7 mg), gigactonine (435.4 mg), pubescenine (3.1 mg), delbonine (8.5 mg), 14-*O*-acetyldelcosine (15.3 mg), deltatsine (5.0 mg), ajacine (1.5 mg), 18-hydroxy-14-*O*-methylgadesine (didehydrogigactonine) (19.8 mg), delcosine (107.2 mg), 18-methoxygadesine (3.7 mg), takaosamine (63.2 mg), ajadelphinine (1.3 mg), tuguaconitine (14.7 mg), potanine (1.8 mg), browniine (5.6 mg), 14-*O*-demethyltuguaconitine (9.0 mg) and 18-*O*-demethylpubescenine

(16.3 mg). Four new compounds were obtained: 1-*O*-demethyltricornine (**1**; 1.8 mg), 1-*O*,19-didehydrotakaosamine (**3**; 7.8 mg), 14-*O*-demethyldelboxine (**4**; 25.3 mg), and 14-*O*-deacetylpubescenine (**6**; 3.0 mg).

Dried powdered aerial parts of the plant (1.2 kg) were defatted with hexane (5 l) for one week and repeatedly extracted by maceration with 80% EtOH (4 × 4 l) at r.t. for two other weeks. After evaporation, the EtOH extract (150 ml) was treated with 0.1M H_2SO_4 and filtered. The acidic soln. was extracted with CH_2Cl_2 to give an acidic residue (0.32 g). The aq. soln. was subjected to a pH-gradient extraction with 10% NaOH soln., and the aq. phases were extracted with CH_2Cl_2 to give a neutral residue at pH 7 (2.15 g) and a basic residue at pH 12 (0.62 g). TLC (alumina) showed that the acidic and neutral residues were the richest in variety and quantity of alkaloids. The acidic residue (*Fr. C*) was subjected to CC (*Sephadex LH-20*, hexane/CH_2Cl_2/MeOH 2:2:1) and analyzed by TLC. The combined *Fr. C4–C10* were subjected to prep. TLC (alumina, hexane/AcOEt 3:7, 2 times): didehydrodeslsoline, and delsoline. The combined *Fr. C11–C15* were subjected to prep. TLC (alumina, AcOEt, 2 times): *14*-O-*acetyldelectinine* and *lycoctonine*. The neutral residue (2.15 g; *Fr. D*) was subjected to CC (neutral alumina, gradient AcOEt/MeOH starting with AcOEt) and analyzed by TLC: *Fr. D1* (49.8 mg), *D2* (106.5 mg), *D3* (183 mg), *D4* (510.6 mg), *D5* (71 mg), *D6* (106.1 mg), and *D7* (207.3 mg). *Fr. D1* was subjected to CC (*Sephadex LH-20*, hexane/CH_2Cl_2/MeOH 7:2:1): *delbonine* and *14*-O-*acetyldelcosine*. *Fr. D2* was subjected to CC (*Sephadex LH-20*, hexane/CH_2Cl_2/MeOH 7:2:1): *Fr. D2.1–D2.3*. *Fr. D2.1* was subjected to prep. TLC (alumina, AcOEt, 2 times): *ajacine*. *Fr. D2.2* was subjected to prep. TLC (alumina, AcOEt, 2 times): *deltatsine* and *14*-O-*acetyldelcosine*. *Fr. D2.3* was subjected to prep. TLC (alumina AcOEt/MeOH 19:1, 2 times): *14*-O-*demethyldelboxine* (**4**). The combined *Fr. D3* was subjected to CC (*Sephadex LH-20*, hexane/CH_2Cl_2/MeOH 5:2:1): *delsoline tuguaconitine*, *pubescenine*, and *14*-O-*demethyldelboxine* (**4**). The combined *Fr. D4* was subjected to CC (*Sephadex LH-20*, hexane/CH_2Cl_2/MeOH 5:2:1): *gigactonine*, *1*-O-*demethyltricornine* (**1**; 1.8 mg) and *potanine*. The combined *Fr. D5* was subjected to CC (*Sephadex LH-20*, hexane/CH_2Cl_2/MeOH 1:2:1): *browniine*, *gigactonine*, *lycoctonine*, and *18-hydroxy-14*-O-*methylgadesine*. *Fr. D6* was subjected to CC (*Sephadex LH-20*, hexane/CH_2Cl_2/MeOH 1:2:1). *Fr. D6.1–D6.5*. *Fr. D6.1* was subjected to prep. TLC (silica gel, $CHCl_3$/MeOH 99:1, 3 times): *delcosine* and *18*-O-*methoxygadesine*. *Fr. D6.2* was subjected to prep. TLC (silica gel, $CHCl_3$/MeOH 99:1, 3 times): *delcosine*. *Fr. D6.3* was subjected to prep. TLC (silica gel, AcOEt/MeOH 95:5, 2 times): *14*-O-*demethyltuguaconitine*. *Fr. D6.4* was subjected to prep. TLC (silica gel, AcOEt/MeOH/ammonia 93:4.5:2.5): *14*-O-*demethyltuguaconitine*. *Fr. D6.5* was separated by prep. TLC (silica gel AcOEt/MeOH/amoniaque 93:4.5:2.5, 2 times): *18*-O-*demethylpubescenine*. Finally, *Fr. D7* was subjected to CC (*Sephadex LH-20*, hexane/CH_2Cl_2/MeOH 1:2:1) and analyzed by TLC to give seven main fractions. These fractions were separated by prep. TLC (alumina or silica gel, AcOEt/MeOH 95:5 or AcOEt/MeOH/ammonia, resp.): *delcosine*, *gigactonine*, *14*-O-*deacetylpubescenine*, *14*-O-*demethyltuguaconitine*, *18*-O-*demethylpubescenine*, *ajadelphinine*, *takaosamine*, and *1*-O,*19-didehydrotakaosamine* (**3**; 7.8 mg; eluted with AcOEt/MeOH 95:5).

4. *New Compounds. 1*-O-*Demethyltricornine* (=*(1α,6β,14α,16β)-4-[(Acetyloxy)methyl]-20-ethyl-6,14,16-trimethoxyaconitane-1,7,8-triol*; **1**). Amorphous solid. $[\alpha]_D^{25} = +18.7$ ($c = 0.16$, $CHCl_3$). IR ($CHCl_3$): 3463, 2930, 2853, 2822, 1740, 1461, 1385, 1363, 1300, 1238, 1227, 1123, 1119, 1091, 1036, 755. ^{1}H-NMR ($CDCl_3$, 500 MHz): *Table 1*. ^{13}C-NMR ($CDCl_3$, 75 MHz): *Table 2*. EI-MS 495 (1, M^+), 481 (28), 480 (100), 479 (27), 478 (96), 477 (7), 465 (15), 464 (55), 463 (19), 462 (67), 460 (30), 434 (12), 418 (10), 380 (18), 75 (13), 71 (15).

14-O-*Benzoyltakaosamine* (=*(1α,6β,14α,16β)-20-Ethyl-4-(hydroxymethyl)-6,16-dimethoxyaconitane-1,7,8,14-tetrol 14-Benzoate*; **2**). Amorphous solid. $[\alpha]_D^{25} = +34$ ($c = 0.12$, $CHCl_3$). IR ($CHCl_3$): 3448, 2933, 2868, 1716, 1451, 1397, 1349, 1319, 1279, 1221, 1178, 1123, 1083, 1030, 1015, 753, 714. ^{1}H-NMR ($CDCl_3$, 500 MHz): *Table 1*. ^{13}C-NMR ($CDCl_3$, 50 MHz): *Table 2*. EI-MS 543 (24, M^+), 529 (33), 528 (100), 527 (14), 526 (44), 513 (15), 512 (47), 511 (18), 510 (53), 368 (13), 105 (43), 77 (10), 58 (16).

1-O,*19-Didehydrotakaosamine* (=*(1α,6β,14α,16β)-1,19-Epoxy-20-ethyl-4-(hydroxymethyl)-6,16-dimethoxyaconitane-7,8,14-triol*; **3**). Amorphous solid. $[\alpha]_D^{25} = +55.2$ ($c = 0.65$, $CHCl_3$). IR ($CHCl_3$): 3440, 2939, 2872, 2832, 1459, 1397, 1220, 1197, 1174, 1123, 1092, 1029, 996, 891, 750. ^{1}H-NMR ($CDCl_3$, 500 MHz): *Table 1*. ^{13}C-NMR ($CDCl_3$, 50 MHz): *Table 2*. EI-MS 437 (1, M^+), 423 (24), 422 (100), 405 (18), 404 (68), 381 (3), 374 (25), 330 (38), 105 (12).

14-O-*Demethyldelboxine* (=*(1α,3β,6β,14α,16β)-3,4-epoxy-20-ethyl-6,8,16-trimethoxyaconitane-1,7,14-triol*; **4**). Amorphous solid. $[\alpha]_D^{25} = +43.3$ ($c = 0.50$, $CHCl_3$). IR ($CHCl_3$): 3422, 2932, 2889, 2862, 1458, 1394, 1265, 1191, 1142, 1078, 1034, 964, 929, 872, 752. ^{1}H-NMR ($CDCl_3$, 500 MHz): *Table 1*. ^{13}C-NMR ($CDCl_3$, 50 MHz): *Table 2*. EI-MS 437 (42, M^+), 422 (16), 420 (19), 407 (26), 406 (100), 405 (35), 394 (22), 390 (14), 268 (21).

8-O-*Methylconsolarine* (=*(1α,6α,14α,16β)-20-Ethyl-8,16-dimethoxy-4-methylaconitane-1,6,7,14-tetrol*; **5**). Light yellowish oil. $[\alpha]_D^{25} = +15.0$ ($c = 0.30$, $CHCl_3$). IR ($CHCl_3$): 3404, 2933, 2877, 1456, 1377, 1215, 1167, 1095, 1042, 994, 965, 935, 870, 753. ^{1}H-NMR ($CDCl_3$, 500 MHz): *Table 2*. ^{13}C-NMR ($CDCl_3$, 75 MHz): *Table 2*. EI-MS

423 (20, M^+), 408 (32), 407 (15), 406 (84), 393 (27), 392 (100), 391 (69), 390 (22), 376 (24), 374 (25), 367 (14), 363 (17), 362 (20), 361 (18), 360 (17), 358 (14), 348 (43), 346 (14), 335 (32), 334 (18), 333 (17), 332 (20), 320 (24), 306 (12), 305 (12), 304 (819), 207 (23), 194 (21), 162 (11), 148 (18).

14-O-*Deacetylpubescenine* (=*(1α,6α,14α,16β)-20-Ethyl-8,16-dimethoxy-4-(methoxymethyl)aconitane-1,6,7,14-tetrol*; **6**). Light yellowish oil. $[\alpha]_D^{25} = +17.6$ ($c = 1.00$, $CHCl_3$). IR ($CHCl_3$): 3409, 2933, 2876, 2830, 1461, 1380, 1296, 1213, 1168, 1096, 1040, 994, 942, 928, 872, 852, 754. ^{1}H-NMR ($CDCl_3$, 500 MHz): *Table 2*. ^{13}C-NMR ($CDCl_3$, 50 MHz): *Table 2*. EI-MS: 453 (20, M^+), 438 (24), 437 (16), 436 (60), 423 (25), 422 (100), 421 (42), 420 (21), 406 (18), 404 (15), 390 (12), 366 (10), 237 (10).

18-O-*Benzoyl-14*-O-*deacetyl-18*-O-*demethylpubescenine* (=*(1α,6α,14α,16β)-4-(Benzoyloxy)-20-ethyl-8,16-dimethoxyaconitane-1,6,7,14-tetrol*; **7**). Amorphous solid. $[\alpha]_D^{25} = +23.3$ ($c = 0.15$, $CHCl_3$). IR ($CHCl_3$): 3430, 2933, 2874, 1717, 1452, 1376, 1276, 1169, 1096, 1037, 1023, 980, 944, 754, 713. ^{1}H-NMR ($CDCl_3$, 500 MHz): *Table 2*. ^{13}C-NMR ($CDCl_3$, 50 MHz): *Table 2*. EI-MS 543 (12, M^+), 526 (30), 513 (10), 512 (29), 511 (30), 510 (13), 468 (13), 422 (12), 421 (15), 406 (12), 391 (28), 390 (75), 389 (38), 388 (17), 376 (10), 374 (14), 362 (14), 358 (10), 264 (72), 233 (67), 231 (18), 177 (19), 133 (29), 122 (28), 121 (10), 117 (10), 105 (100), 89 (42), 77 (53).

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