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FIVE DITERPENOID ALKALOIDS FROM *CONSOLIDA GLANDULOSA*

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Key Word Index—*Consolida glandulosa*; Ranunculaceae; diterpenoid alkaloids; 11,13-*O*-diacetyl-9-deoxyglanduline; 13-*O*-acetyl-9-deoxyglanduline; 14-*O*-acetyl-9-deoxyglanduline; 13-*O*-acetylglanduline; glanduline.

Abstract—Five new hetisine-type diterpenoid alkaloids, 11,13-*O*-diacetyl-9-deoxyglanduline, 13-*O*-acetyl-9-deoxyglanduline, 14-*O*-acetyl-9-deoxyglanduline, 13-*O*-acetyl-glanduline and glanduline, were isolated from *Consolida glandulosa*. The structures of the new alkaloids were determined mainly by NMR spectroscopy, ^{1}H COSY, HMQC, HMBC and ROESY. Copyright © 1997 Elsevier Science Ltd

INTRODUCTION

In continuation of our studies on Turkish *Consolida* species [1], we report on the isolation and structure determination of five new hetisine-type diterpenoid alkaloids, 11,13-*O*-diacetyl-9-deoxyglanduline (**1**), 13-*O*-acetyl-9-deoxyglanduline (**2**), 14-*O*-acetyl-9-deoxyglanduline (**3**), 13-*O*-acetylglanduline (**4**) and glanduline (**5**), isolated from *Consolida glandulosa* (Boiss. et Huet) Bornm., syn. *Delphinium glandulosum* Boiss. et Huet, a common annual species growing in central and east Anatolia [2].

RESULTS AND DISCUSSION

The NMR spectra of the new compounds showed the characteristic signals of the highly functionalized hetisine-type diterpenoid alkaloids [3]. Glanduline (**5**), $C_{27}H_{37}NO_8$, and the other alkaloids have an exocyclic double bond, δ_H 4.73–4.83 (1H, *s*) and 4.91–5.02 (1H, *s*), δ_C 108.7–110.6 *t* and 141.8–143.6 *s*; an angular methyl group, δ_H 1.02–1.12 (3H, *s*) and δ_C 25.4–25.8 *q*; at least one acetate group, δ_H 2.00–2.02 (3H, *s*), δ_C 20.7 *q* and 170.0–170.6 *s*; and a 2-methylbutyrate group, δ_H 0.89–0.97 (3H, *t*), 1.18–1.25 (3H, *d*) 1.48–1.50 and 1.68–1.70 (1H each, *ddq*), 2.36–2.46 (1H, *sext*), δ_C 11.5–11.6 *q*, 17.0–17.2 *q*, 26.1–26.6 *t*, 41.3–41.6 *d*, and 175.6–175.9 *s*. The 2-methylbutyrate group was also evident from the fragmentation ions at *m/z* $[M-85]^+$, $[M-101]^+$, 85 and 57 in their mass spectra. The alkaloid 13-*O*-acetyl-9-deoxyglanduline (**2**), $C_{29}H_{39}NO_8$, 14-*O*-acetyl-9-deoxyglanduline (**3**), $C_{29}H_{39}NO_8$, and 13-*O*-acetyl-glanduline (**4**), $C_{29}H_{39}NO_9$, have an additional acetate group, δ_H 1.99 (3H, *s*) and δ_C 169.6–177.6 *s* and 20.6–21.4 *q*; and the alkaloid 11,13-*O*-diacetyl-9-deoxyglanduline (**1**), $C_{31}H_{41}NO_9$, has two more acetate groups, δ_H 1.99–2.00 (3H, *s*), δ_C 169.3–170.4 *s* and 21.2–21.4 *q*.

The one-proton signals at δ_H 2.50–2.73 and 3.34–3.65 (each *d*, AB-system) for compounds **1**–**5**, which showed a one-bond correlation with the methylene carbon resonance at δ_C 58.6–59.9 *t* in their HMQC spectra [4] (Tables 1, 3, 5, 7 and 9), were assigned to the non-equivalent C-19 methylene protons because of the three-bond connectivity with the C-18 resonance observed in the HMBC spectra [5] (Tables 1, 3, 5, 7 and 9). In those spectra, three-bond correlations were also observed between the H-18 signal and δ_C 55.0–61.6 *d* (δ_H 1.79–2.71 *s*, from HMQC), and between the H-19α signal and δ_C 67.7–69.5 *d* (δ_H 3.54–4.21 *s*), 61.8–63.2 *d* (δ_H 3.10–3.51 *br s*) and 73.1–74.2 *d* (δ_H 4.90–4.98 *d*), and between the signal at δ_H 1.79–2.72 *s* and δ_C 67.7–69.5 *d*. Furthermore, the one-proton *br s* at δ_H 3.10–3.51 showed scalar coupling to the methylene protons at δ_H 1.41–1.85 *d* and 1.70–2.16 *d* (δ_C 26.1–31.6 *t* from HMQC) in the ^{1}H COSY spectra (Tables 2, 4, 6, 8 and 10). These findings allowed us to assign the one-proton signals at δ_H 4.90–4.98 *d*, 1.79–2.72 *s*, 3.1–3.51 *br s*, 3.54–4.21 *s*, 1.41–1.85 *d* and 1.70–2.16 *d*, to H-3, H-5, H-6, H-20, H-7β and H-7α, respectively, and the carbon resonances at δ_C 73.1–74.2 *d*, 55.0–61.6 *d*, 61.8–63.2 *d*, 67.7–69.5 *d*, and 26.1–31.6 *t*, were assigned to C-3, C-5, C-6, C-20, and C-7,

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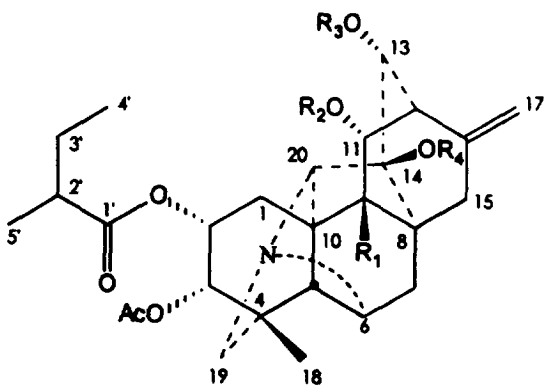
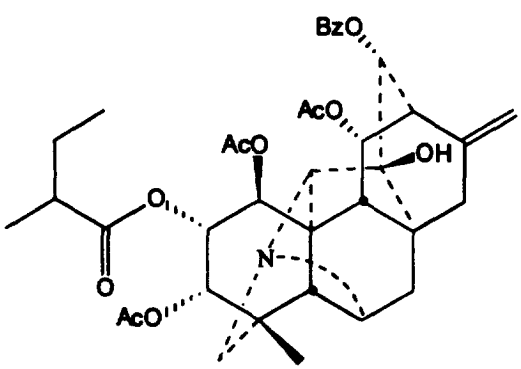
respectively, in compounds **1–5**. The one-proton signal at δ_H 4.90–4.98 *d* and its correlated methine carbon resonance at δ_C 73.1–74.2 *d* in the HMQC spectra were assigned to H-C(3), and since that proton signal gave a three-bond connectivity with a carbonyl acetate at δ_C 170.0–170.6 in the HMBC spectra, a secondary acetate group was situated at C-3 in compounds **1–5**. Because the H-3 signal gave a spatial correlation with the H-5 signal in the ROESY spectra (Tables 2, 4, 6, 8 and 10) [6], the secondary acetate group at C-3 must be in the equatorial α configuration (Ring A chair). Most of the proton signals of the 2-methylbutyrate group gave a long-range correlation with the carbonyl carbon resonance at δ_C 175.6–175.9 *q* in the HMBC spectra of alkaloids **1–5**. These data, together with those from the ^{1}H COSY and HMQC spectra led us to assign the proton and carbon resonances for the 2-methylbutyrate group in compounds **1–5**. The H-3β signal at δ_H 4.90–4.98 *d* showed a typical axial–equatorial coupling (J = 4.4–4.7 Hz) with the one-proton signal at δ_H 5.45–5.50 *m* (δ_C 67.2–68.1 *d* from HMQC)



1 R_1= R_4 = H; R_2= R_3= Ac
2 R_1= R_2 = R_4= H; R_3= Ac
3 R_1= R_2 = R_3= H; R_4= Ac
4 R_1= OH; R_2 = R_4= H; R_3= Ac
5 R_1= OH; R_2 = R_3= R_4= H



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in the ^{1}H COSY spectra, indicating that an ester group in the axial α configuration is situated at C-2. In addition, the observation that the secondary methyl group of the 2-methylbutyrate ester at δ_H 1.18–1.25 *d* gave a NOE with the H-19α in the ROESY spectra, permitted that ester group to be placed at C-2 in alkaloids **1–5**. Also a three-bond connectivity was observed between the H-2β signal and the carbonyl carbon resonance for the 2-methylbutyrate group in the HMBC spectra, in the case of compounds **1**, **2** and **4**.

The quaternary carbon resonances at δ_C 44.0–50.7 and 45.6–47.3 in compounds **1–5** were assigned to C-8 and C-10, respectively, because they showed, among others, three-bond connectivities with the H-6 and H-20 signals, in the HMBC spectra. A three-bond correlation was also noted between the H-2β and the quaternary carbon resonance at δ_C 45.6–45.9 (C-10), in compounds **1** and **2**. The similarity between the NMR spectra of cardiodine (**6**) [3] and those of compounds **1–3** suggested that oxygen functions are located at C-11α, C-13α and C-14, in those compounds. Indeed, an acetate group was placed at C-11 in alkaloid **1** as the one-proton signal at δ_H 5.11 (*d*, J = 9.0 Hz) (δ_C 75.1 from HMQC) gave three-bond connectivities with the carbon signals at δ_C 170.4 *s*, 45.6 *s* (C-10), and 141.8 *s* (C-16); and a secondary hydroxyl was positioned at C-11 in alkaloids **2–5**, since the one-proton signal at δ_H 4.10–4.28 (δ_C 74.7–85.3 *d* from HMQC) displayed three-bond correlations with the C-10 and C-16 resonances. In compounds **1–3**, the one-proton signal at δ_H 2.04–2.23 (*d*, J = 8.7–9.0 Hz) was assigned to H-9 in agreement with the three-bond connectivities between the said proton signal and the C-5 and C-20 carbon resonances shown in the HMBC spectra, and its spatial correlation observed with the H-5 and H-7β signals, in the ROESY spectra. Consequently, as the aforementioned H-11 signal was coupled to the H-9 signal, the H-11 must be in the β configuration, α for an acetate group in compound **1** and for a hydroxyl group in compounds **2–3**. The H-11 signal gave a three-bond connectivity with the methine carbon resonance at δ_C 79.7–81.1 (δ_H 4.09–5.06 from HMQC) in the HMBC spectra of alkaloids **1–5**, indicating that an oxygen function is loaded at C-13. The W coupling observed between the H-11 and H-13 signals in the ^{1}H COSY spectra of the said compounds, characteristic of this family of alkaloids having the same set of functions [7–9], pointed to the fact that both protons are in a ψ-axial (β) configuration. Thus, the secondary hydroxyl group at C-11 must be in the α configuration in alkaloids **4** and **5**, and considering the chemical shift of the H-13 protons, a secondary acetate group in alkaloids **1**, **2** and **4**, and a secondary hydroxyl group in alkaloids **3** and **5** must be located at C-13, also in the α configuration.

The one-proton signal at δ_H 2.51–2.68 (δ_C 46.1–51.6 *d* from HMQC) in compounds **1–5**, which in turn showed a small coupling to H-13β in the ^{1}H COSY

Table 1. ^{1}H, HMQC and HMBC NMR data of compound **1***

H		Correlated C-atom	
		HMQC	HMBC
1α	2.85 *dd* (15.3, 1.8)	29.9 *t*	C-2, C-3, C-5, C-10
1β	1.83 *dd* (15.3, 4.5)	29.9 *t*	C-10, C-20
2β	5.47 *m* ($W_{1/2}$ = 14.0)	67.9 *d*	C-4, C-10, 175.7
3β	4.92 *d* (4.7)	73.9 *d*	C-2, C-4, C-18, C-19, 170.2
5	1.80 *s*	61.1 *d*	C-9, C-18, C-19, C-20
6	3.14 *br s* ($W_{1/2}$ = 6.2)	62.5 *d*	C-8, C-10, C-20
7α	1.91 *dd* (14.0, 3.3)	31.3 *t*	C-5, C-14
7β	1.44 *dd* (14.0, 2.0)	31.3 *t*	C-8, C-14
9	2.23 *d* (9)	51.3 *d*	C-5, C-8, C-11, C-12, C-14, C-20
11β	5.11 *d* (9)	75.1 *d*	C-10, C-13, C-16, 170.4
12	2.68 *d* (2.4)	46.1 *d*	C-9, C-11, C-13, C-14, C-15, C-16, C-17
13β	5.02 *br s*	80.5 *d*	C-11, C12, C-14
15α	2.20 *d* (14.0)	30.6 *t*	C-8, C-9, C-16
15β	2.12 *d* (14.0)	30.6 *t*	C-14, C-16
17e	4.83 *br s*	110.6 *t*	C-12, C15
17z	5.02 *br s*	110.6 *t*	C-12
18	1.02 *s*	25.4 *q*	C-3, C-4, C-5, C-19
19α	3.34 *d* (12.5)	59.6 *t*	C-3, C-6, C-18, C-20
19β	2.50 *d* (12.5)	59.6 *t*	C-4, C-18, C-20
20	3.57 *s*	69.3 *d*	C-1, C-3, C-6, C-8, C-14, C-19
2′	2.38 *sext* (7.4)	41.4 *d*	C-3′, C-4′, C-5′, 175.7
3′A	1.70 *ddq* (14.8, 7.4, 7.4)	26.2 *t*	C-2′, C-4′, C-5′, 175.7
3′B	1.50 *ddq* (14.8, 7.4, 7.4)	26.2 *t*	C-2′, C-4′, C-5′, 175.7
4′	0.92 *t* (7.4)	11.6 *q*	C-2′, C-3′
5′	1.24 *d* (7.0)	17.1 *q*	C-2′, C-3′, 175.7
3α-OAc	2.02 *s*	20.7 *q*	170.2
11α-OAc	2.00 *s*	21.2 *q*	170.4
13α-OAc	1.99 *s*	21.4 *q*	169.3

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

Table 2. Scalar and spatial correlation of the protons of compound **1**

H	COSY	ROESY
1α	H-1β, H-2β	H-1β, H-2β, H-20
1β	H-1α, H-2β	H-1α, H-2β, H-3β, H-9
2β	H-1α, H-1β, H-3β	H-1α, H-1β, H-3β
3β	H-2β	H-1β, H-2β, H-5, H-3β
5		H-3β, H-6, H-9, H-18
6	H-7α, H-7β	H-5, H-7α, H-7β, H-18, H-19β
7α	H-6, H-7β	H-6, H-7β
7β	H-6, H-7α	H-6, H-7α, H-9
9	H-11β	H-1β, H-5, H-7β, H-11β
11β	H-9, H-13β (W)	H-9, H-12, H-15β
12	H-13β	H-11β, H-13β, H-17e, H-17z
13β	H-11β (W), H-12	H-12
15α	H-15β, H-17z	H-15β, H-17z
15β	H-15α, H-17z	H-11β, H-15α, H-17z
17e	H-17z	H-12, H-17z
17z	H-15α, H-15β, H-17e	H-12, H-15α, H-15β, H-17e
18		H-3β, H-5, H-6, H-19β
19α	H-19β	H-19β, H-20, H-5′
19β	H-19α	H-6, H-18, H-19α
20		H-1α, H-19α, H-5′
2′	H-5′	H-4′, H-5′
3′A	H-3′B, H-4′	H-3′B, H-4′
3′B	H-3′A, H-4′	H-3′A, H-4′, H-5′
4′	H-3′A, H-3′B	H-2′, H-3′A, H-3′B
5′	H-2′	H-2′, H-3′B, H-19α, H-20

Table 3. ^{1}H, HMQC and HMBC NMR data of compound **2***

H		Correlated C-atom	
		HMQC	HMBC
1α	3.07 *dd* (16.2, 2.2)	29.7 *t*	C-2, C-3, C-5, C-10
1β	2.07 *dd* (16.2, 4.4)	29.7 *t*	C-10, C-20
2β	5.50 *m* ($W_{1/2}$ = 14.0)	68.0 *d*	C-4, C-10, 175.7
3β	4.98 *d* (4.4)	74.1 *d*	C-2, C-4, C-18, C-19, 170.3
5	1.79 *s*	61.6 *d*	C-9, C-18, C-19, C-20
6	3.13 *br s* ($W_{1/2}$ = 6.4)	62.6 *d*	C-8, C-10, C-20
7α	1.89 *dd* (14.0, 3.4)	31.6 *t*	
7β	1.41 *dd* (14.0, 2.5)	31.6 *t*	C-8, C-14, C-15
9	2.04 *d* (8.9)	53.2 *d*	C-5, C-11, C-12, C-14, C-20
11β	4.28 *d* (8.9)	74.7 *d*	C-10, C-13, C-16
12	2.64 *d* (2.5)	49.7 *d*	C-9, C-11, C-13, C-14, C-15, C-16, C-17
13β	5.06 *t* (2.2)	81.1 *d*	C-11, C-14
15α	2.17 *d* (17.9)	30.7 *t*	C-8, C-9, C-16, C-17
15β	2.02 *m*	30.7 *t*	C-14, C-16
17e	4.77 *s*	109.5 *t*	C-12, C15
17z	4.97 *s*	109.5 *t*	C-12, C-15
18	1.02 *s*	25.4 *q*	C-3, C-4, C-5, C-19
19α	3.35 *d* (12.5)	59.6 *t*	C-3, C-6, C-18, C-20
19β	2.50 *d* (12.5)	59.6 *t*	C-4, C-18, C-20
20	3.54 *s*	69.5 *d*	C-6, C-8, C-13, C-14, C-19
2′	2.35 *sext* (7.0)	41.4 *d*	C-3′, C-4′, C-5′, 175.7
3′A	1.69 *ddq* (14.0, 7.0, 7.0)	26.1 *t*	C-2′, C-4′, C-5′, 175.7
3′B	1.48 *ddq* (14.0, 7.0, 7.0)	26.1 *t*	C-2′, C-4′, C-5′, 175.7
4′	0.89 *t* (7.4)	11.6 *q*	C-2′, C-3′
5′	1.25 *d* (7.0)	17.2 *q*	C-2′, C-3′, 175.7
3α-OAc	2.01 *s*	20.7 *q*	170.3
13α-OAc	1.99 *s*	21.4 *q*	169.6

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

Table 4. Scalar and spatial correlation of the protons of compound **2**

H	COSY	ROESY
1α	H-1β, H2β	H-1β, H-2β, H-20
1β	H-1α, H-2β	H-1α, H-2β
2β	H-1α, H-1β, H-3β	H-1α, H-1β, H-3β
3β	H-2β	H-2β, H-5, H-9, H-18
5		H-3β, H-6, H-7β, H-9, H-18
6	H-7α, H-7β, H-20 (W)	H-5, H-7α, H-7β, H-18, H-19β
7α	H-6, H-7β	H-6, H-7β, H-15α
7β	H-6, H-7α	H-5, H-6, H-7α, H-9, H-15β
9	H-11β	H-3β, H-5, H-7β, H-11β
11β	H-9, H-13β (W)	H-9, H-12, H-15β
12	H-13β	H-11β, H-13β, H-17z
13β	H-11β (W), H-12	H-12
15α	H-15β, H-17e, H-17z	H-7α, H-15β, H-17e
15β	H-15α, H-17e, H-17z	H-7β, H-11β, H-15α
17e	H-15α, H-15β, H-17z	H-15α, H-17z
17z	H-15α, H-15β, H-17e	H-12, H-17e
18		H-3β, H-5, H-6, H-19β
19α	H-19β	H-19β, H-20, H-5′
19β	H-19α	H-6, H-18, H-19α
20	H-6 (W)	H-1α, H-19α
2′	H-5′	H-4′, H-5′
3′A	H-3′B, H-4′	H-3′B, H-4′, H-5′
3′B	H-3′A, H-4′	H-3′A, H-4′
4′	H-3′A, H-3′B	H-2′, H-3′A, H-3′B, H-5′
5′	H-2′	H-2′, H-3′A, H-4′, H-19a

Table 5. ^{1}H, HMQC and HMBC NMR data of compound **3***

H		Correlated C-atom	
		HMQC	HMBC
1α	3.03 *brd* (15.5)	31.1 *t*	C-2, C-3, C-5, C-10
1β	2.11 *dd* (14.5, 5.5)	31.1 *t*	C-10, C-20
2β	5.46 *m* ($W_{1/2}$ = 14.0)	67.2 *d*	
3β	4.95 *d* (4.6)	73.1 *d*	C-2, C-4, C-18, C-19, 170.0
5	1.98 *s*	60.4 *d*	C-1, C-18, C-19, C-20
6	3.51 *br s* ($W_{1/2}$ = 6.3)	63.2 *d*	C-8, C-10, C-20
7α	2.16 *dd* (14.0, 3.5)	31.3 *t*	C-5, C-14
7β	1.50 *br d* (14.0)	31.3 *t*	C-8, C-14
9	2.08 *d* (8.7)	53.3 *d*	C-5, C-11, C-12, C-14, C-20
11β	4.24 *d* (8.8)	75.6 *d*	C-10, C-13, C-16
12	2.56 *s*	51.6 *d*	C-9, C-11, C-13, C-14, C-15, C-16, C-17
13β	4.14 *s*	80.8 *d*	C-11, C12, C-14
15α	2.15 *d* (17.7)	30.5 *t*	C-8, C-9, C-16, C-17
15β	2.04 *d* (17.7)	30.5 *t*	C-14, C-16
17e	4.73 *s*	108.7 *t*	C-12, C15
17z	4.93 *s*	108.7 *t*	C-12, C-15
18	1.12 *s*	25.5 *q*	C-3, C-4, C-5, C-19
19α	3.65 *d* (12.5)	58.6 *t*	C-3, C-6, C-18, C-20
19β	2.73 *d* (12.5)	58.6 *t*	C-3, C-4, C-18, C-20
20	4.21 *s*	69.2 *d*	C-1, C-6, C-8, C-13, C-14, C-19
2′	2.46 *sext* (7.0)	41.5 *d*	C-3′, C-4′, C-5′, 175.6
3′A	1.70 *ddq* (14.0, 7.0, 7.0)	26.6 *t*	C-2′, C-4′, C-5′, 175.6
3′B	1.49 *m* (14.0, 7.0, 7.0)	26.6 *t*	C-2′, C-4′, C-5′, 175.6
4′	0.94 *t* (7.4)	11.5 *q*	C-2′, C-3′
5′	1.21 *d* (7.0)	17.0 *q*	C-2′, C-3′, 175.6
3α-OAc	2.00 *s*	20.7 *q*	170.0
14α-OAc	1.99 *s*	20.6 *q*	177.6

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

Table 6. Scalar and spatial correlation of the protons of compound **3**

H	COSY	ROESY
1α	H-1β, H-2β	H-1β, H-2β, H-20
1β	H-1α, H-2β	H-1α, H-2β, H-3β, H-5
2β	H-1α, H-1β, H-3β	H-1α, H-1β, H-3β
3β	H-2β	H-1β, H-2β, H-5, H-18
5		H-1β, H-3β, H-6, H-7β, H-9, H-18
6	H-7α, H-7β, H-20 (W)	H-5, H-7α, H-7β, H-18, H-19α
7α	H-6, H-7β	H-6, H-7β, H-15α
7β	H-6, H-7α	H-5, H-6, H-7α, H-9, H-15β
9	H-11β	H-5, H-7β, H-11β
11β	H-9, H-13β (W)	H-9, H-12
12	H-13β	H-11β, H-13β, H-17z
13β	H-11β (W), H-12	H-12, H-15β
15α	H-15β, H-17e, H-17z	H-7α, H-15β
15β	H-15α, H-17e, H-17z	H-7β, H-13β, H-15α, H-17e
17e	H-15α, H-15β, H-17z	H-15β, H-17z
17z	H-15α, H-15β, H-17e	H-12, H-17e
18		H-3β, H-5, H-6, H-19α, H-19β, H-20
19α	H-19β	H-6, H-18, H-19β, H-20, H-5′
19β	H-19α	H-18, H-19α, H-20
20	H-6 (W)	H-1α, H-18, H-19α, H-19β, H-2′, H-5′
2′	H-5′	H-3′A, H-3′B, H-4′, H-5′, H-20
3′A	H-3′B, H-4′	H-2′, H-3′B, H-4′, H-5′
3′B	H-3′A, H-4′	H-2′, H-3′A, H-4′, H-5′
4′	H-3′A, H-3′B	H-2′, H-3′A, H-3′B, H-5′
5′	H-2′	H-2′, H-3′A, H-3′B, H-4′, H-19α, H-20

Table 7. ^{1}H, HMQC and HMBC NMR data of compound **4***

H		Correlated C-atom	
		HMQC	HMBC
1α	3.13 *dd* (16.6, 2.0)	28.8 *t*	C-3, C-5, C-8, C-10, C-20
1β	2.09 *dd* (16.6, 4.7)	28.8 *t*	C-10
2β	5.50 *m* ($W_{1/2}$ = 14.0)	68.1 *d*	C-3, C-4, 175.9
3β	4.90 *d* (4.7)	74.2 *d*	C-2, C-4, C-18, C-19, 170.6
5	2.59 *s*	55.7 *d*	C-19, C-20
6	3.10 *br s* ($W_{1/2}$ = 6.1)	61.8 *d*	C-5, C-8, C-10, C-20
7α	1.70 *dd* (13.4, 3.0)	26.4 *t*	C-14
7β	1.75 *dd* (13.8, 2.2)	26.4 *t*	C-6, C-8
11β	4.10 *s*	84.0 *d*	C-9, C-10, C-12, C-13, C-14, C-16
12	2.65 *d* (2.2)	48.4 *d*	C-9, C-11, C-14, C-15, C-16, C-17
13β	4.96 *d* (2.2)	80.4 *d*	C-11, C-14
15α	2.04 *d* (18.0)	27.9 *t*	C-9, C-14
15β	1.99 *d* (18.0)	27.9 *t*	C-9, C-14
17e	4.78 *s*	109.5 *t*	C-12, C15
17z	4.97 *s*	109.5 *t*	C-12, C-15
18	1.03 *s*	25.7 *q*	C-3, C-4, C-5, C-19
19α	3.38 *d* (12.5)	59.9 *t*	C-3, C-6, C-18, C-20
19β	2.54 *d* (12.5)	59.9 *t*	C-4, C-18, C-20
20	3.62 *s*	68.0 *d*	C-1, C-6, C-8, C-9, C-14, C-19
2′	2.36 *sext* (7.0)	41.3 *d*	C-3′, C-4′, C-5′, 175.9
3′A	1.68 *ddq* (14.6, 7.3, 7.3)	26.1 *t*	C-2′, C-4′, C-5′, 175.9
3′B	1.48 *ddq* (14.6, 7.3, 7.3)	26.1 *t*	C-2′, C-4′, C-5′, 175.9
4′	0.89 *t* (7.4)	11.5 *q*	C-2′, C-3′
5′	1.23 *d* (7.0)	17.1 *q*	C-2′, C-3′, 175.9
3α-OAc	2.02 *s*	20.7 *q*	170.6
13α-OAc	1.99 *s*	21.4 *q*	169.8

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

Table 8. Scalar and spatial correlation of the protons of compound **4**

H	COSY	ROESY
1α	H-1β, H-2β	H-1β, H-2β, H-20
1β	H-1α, H-2β	H-1α, H-2β, H-3β, H-5, H-11β
2β	H-1α, H-1β, H-3β	H-1α, H-1β, H-3β
3β	H-2β	H-1β, H-2β, H-5, H-18
5		H-1β, H-3β, H-6, H-7β, H-18
6	H-7α, H-7β, H-20 (W)	H-5, H-7α, H-7β, H-18, H-19β
7α	H-6, H-7β	H-6, H-7β, H-15α
7β	H-6, H-7α	H-5, H-6, H-7α, H-15β
11β	H-13β (W)	H-1β, H-12, H-15α
12	H-13β, H-17z	H-11β, H-13β, H-17z
13β	H-11β (W), H-12	H-12
15α	H-15β, H-17e, H-17z	H-7α, H-11β, H-15β, H-17e
15β	H-15α, H-17e, H-17z	H-7β, H-15α
17e	H-15α, H-15β, H-17z	H-15α, H-17z
17z	H-12, H-15α, H-15β, H-17e	H-12, H-17e
18		H-3β, H-5, H-6, H-19β
19α	H-19β	H-19β, H-20, H-5′
19β	H-19α	H-6, H-18, H-19α
20	H-6 (W)	H-1α, H-19α, H-5′
2′	H-5′	H-4′, H-5′
3′A	H-3′B, H-4′	H-3′B, H-4′, H-5′
3′B	H-3′A, H-4′	H-3′A, H-4′, H-5′
4′	H-3′A, H-3′B	H-2′, H-3′A, H-3′B, H-5′
5′	H-2′	H-2′, H-3′A, H-3′B, H-4′, H-19α, H-20

Table 9. ^{1}H, HMQC and HMBC NMR data of compound **5***

H		Correlated C-atom	
		HMQC	HMBC
1α	3.04 *br d* (16.0)	29.7 *t*	C-3, C-5, C-10
1β	2.15 *dd* (16.0, 3.7)	29.7 *t*	C-10, C-20
2β	5.45 *m* ($W_{1/2}$ = 14.0)	67.9 *d*	
3β	4.90 *d* (4.7)	73.5 *d*	C-2, C-4, C-18, C-19, 170.2
5	2.72 *br s*	55.0 *d*	C-18, C-19, C-20
6	3.34 *br s* ($W_{1/2}$ = 6.4)	62.6 *d*	C-8, C-10, C-20
7α	1.80 *d* (18.0)	26.1 *t*	C-5, C-6, C-8, C-9, C-14
7β	1.85 *d* (18.0)	26.1 *t*	C-5, C-6, C-8, C-9, C-14
11β	4.12 *s*	85.3 *d*	C-9, C-10, C-12, C-13, C-16
12	2.51 *d* (1.8)	51.0 *d*	C-9, C-11, C-13, C-14, C-15, C-16, C-17
13β	4.09 *br s*	79.7 *d*	C-11
15α	2.10 *d* (16.0)	28.0 *t*	C-14, C-16
15β	2.00 *d* (16.0)	28.0 *t*	C-8, C-9, C-16
17e	4.74 *s*	108.8 *t*	C-12, C15
17z	4.91 *s*	108.8 *t*	C-12, C-15
18	1.10 *s*	25.8 *q*	*C*-3, *C*-4, *C*-5, *C*-19
19α	3.59 *d* (12.5)	59.4 *t*	C-3, C-6, C-18, C-20
19β	2.70 *d* (12.5)	59.4 *t*	C-4, C-18, C-20
20	4.06 *s*	61.7 *d*	C-6, C-8, C-9, C-14, C-19
2′	2.45 *sext* (7.0)	41.6 *d*	C-3′, C-4′, C-5′, 175.9
3′A	1.70 *ddq* (14.0, 7.0, 7.0)	26.6 *t*	C-2′, C-4′, C-5′, 175.9
3′B	1.49 *ddq* (14.0, 7.0, 7.0)	26.6 *t*	C-2′, C-4′, C-5′, 175.9
4′	0.92 *t* (7.4)	11.6 *q*	C-2′, C-3′
5′	1.18 *d* (17.0)	17.0 *q*	C-2′, C-3′, 175.9
3α-OAc	2.01 *s*	20.7 *q*	170.2

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

Table 10. Scalar and spatial correlation of the protons of compound **5**

H	COSY	ROESY
1α	H-1β, H-2β	H-1β, H-2β
1β	H-1α, H-2β	H-1α, H-2β, H-3β
2β	H-1α, H-1β, H-3β	H-1α, H-1β, H-3β, 3α-OAc
3β	H-2β	H-1β, H-2β, H-5, H-18, 3α-OAc
5		H-3β, H-6, H-18
6	H-7α, H-7β	H-5, H-7α, H-7β, H-18, H-19β
7α	H-6, H-7β	H-6, H-7β, H-15α
7β	H-6, H-7α	H-6, H-7α, H-15β
11β	H-13β (W)	H-12
12	H-13β	H-11β, H-13β, H-17z
13β	H-11β (W), H-12	H-12
15α	H-15β, H-17e, H-17z	H-7α, H-15β
15β	H-15α, H-17e, H-17z	H-7β, H-15α, H-17e
17z	H-15α, H-15β, H-17e	H-12, H-17e
17e	H-15α, H-15β, H-17z	H-15β, H-17z
18		H-3β, H-5, H-6, H-19β
19α	H-19β	H-19β, H-20, H-5′
19β	H-19α	H-6, H-18, H-19α
20		H-19α
2′	H-5′	H-3′A, H-4′, H-5′
3′A	H-3′B, H-4′	H-2′, H-3′B, H-4′, H-5′
3′B	H-3′A, H-4′	H-3′A, H-4′, H-5′
4′	H-3′A, H-3′B	H-2′, H-3′A, H-3′B, H-5′
5′	H-2′	H-2′, H-3′A, H-3′B, H-4′, H-19α
3α-OAc		H-2β, H-3β

Table 11. ^{13}C NMR chemical shifts assignments for compounds **1–6**

Carbon	1	2	3	4	5	6
1	29.9 *t*	29.7 *t*	31.1 *t*	28.8 *t*	29.7 *t*	72.4 *d*
2	67.9 *d*	68.0 *d*	67.2 *d*	68.1 *d*	67.9 *d*	65.8 *d*
3	73.9 *d*	74.1 *d*	73.1 *d*	74.2 *d*	73.5 *d*	70.9 *d*
4	42.2 *s*	42.2 *s*	41.1 *s*	41.8 *s*	41.2 *s*	42.5 *s*
5	61.1 *d*	61.6 *d*	60.4 *d*	55.7 *d*	55.0 *d*	58.0 *d*
6	62.5 *d*	62.6 *d*	63.2 *d*	61.8 *d*	62.6 *d*	62.5 *d*
7	31.3 *t*	31.6 *t*	31.3 *t*	26.4 *t*	26.1 *t*	31.3 *t*
8	44.9 *s*	44.7 *s*	44.0 *s*	50.6 *s*	50.7 *s*	44.9 *s*
9	51.3 *d*	53.2 *d*	53.3 *d*	80.9 *s*	81.0 *s*	49.7 *d*
10	45.6 *s*	45.9 *s*	46.1 *s*	47.3 *s*	46.7 *s*	49.5 *s*
11	75.1 *d*	74.7 *d*	75.6 *d*	84.0 *d*	85.3 *s*	74.9 *s*
12	46.1 *d*	49.7 *d*	51.6 *d*	48.4 *d*	51.0 *d*	47.9 *d*
13	80.5 *d*	81.1 *d*	80.8 *d*	80.4 *d*	79.7 *d*	80.4 *d*
14	78.6 *s*	78.8 *s*	80.2 *s*	77.3 *s*	78.5 *s*	78.6 *s*
15	30.6 *t*	30.7 *t*	30.5 *t*	27.9 *t*	28.0 *t*	30.7 *s*
16	141.8 *s*	143.3 *s*	143.0 *s*	143.1 *s*	143.6 *s*	141.5 *s*
17	110.6 *t*	109.5 *t*	108.7 *t*	109.5 *t*	108.8 *t*	110.6 *t*
18	25.4 *q*	25.4 *q*	22.5 *q*	25.7 *q*	25.8 *q*	25.3 *q*
19	59.6 *t*	59.6 *t*	58.6 *t*	59.9 *t*	59.4 *t*	59.1 *t*
20	69.3 *d*	69.5 *d*	69.2 *d*	68.0 *d*	67.7 *d*	67.0 *d*
1′	175.7 *s*	175.7 *s*	175.6 *s*	175.9 *s*	175.9 *s*	174.5 *s*
2′	41.4 *d*	41.4 *d*	41.5 *d*	41.3 *d*	41.6 *d*	39.6 *d*
3′	26.2 *t*	26.1 *t*	26.6 *t*	26.1 *t*	26.6 *t*	24.9 *t*
4′	11.6 *q*	11.6 *q*	11.5 *q*	11.5 *q*	11.6 *q*	10.7 *q*
5′	17.1 *q*	17.2 *q*	17.0 *q*	17.1 *q*	17.0 *q*	15.8 *q*
3αOAc	170.2 *s*	170.3 *s*	170.0 *s*	170.6 *s*	170.2 *s*	169.9 *s*
	20.7 *q*	20.7 *q*	20.7 *q*	20.7 *q*	20.7 *q*	20.6 *q*
11α-OAc	170.4 *s*					171.0 *s*
	21.2 *q*					21.4 *q*
13α-OAc	169.3 *s*	169.6 *s*		169.8 *s*		
	21.4 w	21.4 *q*		21.4 *q*		
14-OAc			177.6 *s*			
			20.6 *q*			

Chemical shifts in ppm relative to TMS. Carbon multiplicities were established by DEPT data.

spectra, was ascribed to H-12 because of its three-bond correlation with the C-17 carbon resonance in the HMBC spectra. Further, in those spectra the H-12 signal gave a long-range correlation with the quaternary carbon resonance at δ_C 77.3–80.2, revealing that a tertiary oxygen function should be placed at C-14 in compounds **1–5**. The fact that the H-13β signal is not at least a broad double of $J \sim 10$ Hz, as it should be if there was a proton at C-14 [3], led to the conclusion that there is a tertiary hydroxyl group at C-14 in compounds **1**, **2**, **4** and **5**, and the remaining acetate group in alkaloid **3** is located also at C-14. For similar reasons, the remaining hydroxyl group was placed at C-9 in the molecule of **4** and **5**, the H-12 signal showed a long-range correlation with the quaternary carbon resonance at δ_C 80.9–81.0 in the HMBC spectra, and in these cases the H-11β proton appeared as a singlet rather than a doublet of $J \sim 9$ Hz [3]. The location of a tertiary hydroxyl group at C-9 in **4** and **5** was also coherent with the α (28 ppm), β (2–10 ppm), and γ (-1–6 ppm) effects observed in the corresponding carbon resonances. The remaining correlations between proton and carbon resonances displayed in the 2D spectra of **1–5** are consistent with the proposed structures.

EXPERIMENTAL

General. Mps: uncorr.; mixt. of hexane–AcOEt were used as crystallization solvent; OR: MeOH, 1 dm cell; EI-MS and exact mass measurements: Hewlett Packard 5989A and VG-Micromass-ZAB-2F instruments, respectively, 70 eV; NMR: 400 (^1H) and 100 (^{13}C) MHz, $CDCl_3$ with TMS as int. standard; DEPT and 2D NMR experiments were carried out with the standard pulse sequences given in the Bruker manual. CC and TLC: Al_2O_3 Merck Art. 1077 and 5581, respectively. Visualization was with Dragendorff's reagent.

Plant material. Plants were collected 20 km beyond Malatya, towards Gaziantep, Turkey, at an altitude of 1000 m at the edges of fields, and authenticated by Professors J. Molero and C. Blanché, Botany Laboratory, Faculty of Pharmacy, University of Barce-

lona, where a voucher specimen, BCF 37805, has been deposited.

Extraction and isolation. Aerial parts of plants were air-dried (1.72 kg) and extracted with 70% EtOH by percolation at room temp. The solvent was removed under vacuum and the EtOH extract partitioned between 1% H_2SO_4 and EtOAc. The acid soln was then made alkaline with Na_2CO_3 to pH 8 and extracted with EtOAc to give a crude alkaloid material B (5.0 g). The resulting aq. phase was raised to Ph 12 with Na_2CO_3 and extracted with EtOAc to yield additional crude alkaloid material C (3.6 g). CC of fr. B using a hexane–EtOAc step gradient, EtOAc and an EtOAc–MeOH step gradient led to the isolation of individual alkaloids, purified by further CC, in the following elution order: **1** (7 mg), **3** (10 mg) and **4** (6 mg). CC of fr. C using EtOAc and an EtOAc–MeOH step gradient yielded, after further CC, the alkaloids **2** (5 mg) and **5** (16 mg).

11,13-O-*Diacetyl-9-deoxyglanduline* (**1**). Crystalline, mp 195–198°, $[\alpha]_D+36°$ (*c* 0.50). $[M]^+$ *m/z* 571.2797 for $C_{31}H_{41}NO_9$ (calc. 571.2781). IR ν_{max}^{NaCl} cm^{-1}: 3205, 3089, 2925, 2845, 1737, 1652, 1459, 1369, 1229, 1145, 1045, 951, 884, 847; EI-MS *m/z* (rel. int.): 571 (4) $[M]^+$, 556 (1), 528 (10), 513 (20), 512 (59), 498 (3), 486 (2), 470 (2), 468 (2), 452 (3), 428 (4), 410 (3), 368 (5), 340 (3), 326 (4), 324 (3), 308 (7), 280 (5), 174 (4), 144 (24), 105 (29), 92 (24), 85 (31), 57 (100); ^1H NMR and ^{13}C NMR: Tables 1 and 11.

13-O-*Acetyl-9-deoxyglanduline* (**2**). Crystalline, mp 154–156°, $[\alpha]_D+46.6°$ (*c* 0.39). $[M]^+$ *m/z* 592.2706 for $C_{29}H_{39}NO_8$ (calc. 529.2675). IR ν_{max}^{NaCl} cm^{-1}: 3406, 2919, 2840, 1736, 1636, 1549, 1573, 1512, 1436, 1369, 1236, 1179, 1142, 1092, 1062, 1029, 975, 925, 883; EI-MS *m/z* (rel. int.): 529 (7) $[M]^+$, 512 (7), 498 (6), 486 (24), 471 (30), 470 (100), 456 (12), 446 (18), 444 (1), 440 (2), 428 (3), 410 (7), 386 (17), 368 (9), 342 (5), 326 (13), 308 (28), 298 (22), 174 (15), 144 (10), 105 (9), 91 (8), 85 (9), 69 (10), 57 (52), 55 (15); ^1H NMR and ^{13}C NMR: Tables 3 and 11.

14-O-*Acetyl-9-deoxyglanduline* (**3**). Crystalline, mp 145–148°, $[\alpha]_D+20°$ (*c* 0.2). $[M]^+$ *m/z* 529.2692 for $C_{29}H_{39}NO_8$ (calc. 529.2675). IR ν_{max}^{NaCl} cm^{-1}: 3409, 2951, 2929, 1735, 1652, 1567, 1457, 1237, 1183, 1148, 1091, 1061, 1040, 975, 872, 896; EI-MS (15 eV) *m/z* (rel. int.): 529 (0.1) $[M]^+$, 503 (1), 487 (18), 473 (9), 470 (10), 459 (10), 458 (7), 456 (5), 445 (6), 444 (8), 442 (10), 431 (8), 431 (8), 430 (9), 429 (29), 428 (100), 415 (11), 414 (42), 410 (8), 396 (3), 386 (6), 344 (9), 326 (9), 308 (4), 174 (5), 146 (2), 144 (2), 105 (2), 94 (2), 85 (2), 60 (8), 57 (14), 45 (8), 43 (11); ^1H NMR and ^{13}C NMR: Tables 5 and 11.

13-O-*Acetylglanduline* (**4**). Crystalline, mp 110–115° $[\alpha]_D+15.2°$ (*c* 0.46). $[M]^+$ *m/z* 545.2640 for $C_{28}H_{39}NO_9$ (calc. 545.2624). IR ν_{max}^{NaCl} cm^{-1}: 3393, 2930, 1731, 1657, 1578, 1460, 1368, 1233, 1184, 1147, 1098, 1936, 1024, 975, 883; EI-MS *m/z* (rel. int.): 545 (3) $[M]^+$, 528 (2), 503 (10), 502 (15), 487 (30), 486 (100), 475 (5), 474 (6), 472 (12), 458 (5), 445 (9), 444 (33), 430 (5), 426 (5), 402 (21), 384 (13), 360 (15), 342 (21), 324 (31), 314 (10), 312 (7), 297 (10), 296 (7), 174 (10), 144 (12), 131 (9), 105 (11), 91 (10), 85 (11), 83 (10), 81 (10), 71 (11), 57 (69); ^1H NMR and ^{13}C NMR ($CDCl_3$–CD_3OD 9:1): Tables 7 and 11.

Glanduline (**5**). Crystalline, mp 134–137°, $[\alpha]_D+24°$ (*c* 0.5). $[M]^+$ *m/z* 503.2517 for $C_{27}H_{37}NO_8$ (calc. 503.2519). IR ν_{max}^{NaCl} cm^{-1}: 3351, 2938, 2924, 2853, 1736, 1720 (sh), 1657, 1461, 1373, 1258, 1231, 1176, 1139, 1113, 1088, 1075, 1031, 968; EI-MS *m/z* (rel. int.): 503 (17) $[M]^+$, 487 (11), 486 (30), 475 (14), 474 (15), 472 (18), 470 (9), 459 (8), 458 (14), 445 (27), 444 (94), 430 (15), 428 (18), 426 (5), 418 (2), 414 (5), 402 (11), 386 (5), 360 (41), 342 (27), 324 (24), 296 (9), 174 (9), 144 (17), 105 (16), 95 (13), 94 (14), 91 (18), 85 (18), 71 (17), 69 (18), 57 (100), 55 (27); ^1H NMR and ^{13}C NMR: Tables 9 and 11.

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