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NORDITERPENOID ALKALOIDS OF *DELPHINIUM MUNZIANUM*

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Key Word Index—*Delphinium munzianum*; Ranunculaceae; norditerpenoid alkaloids; 14-*O*-benzoylperegrine; 14-*O*-acetylperegrine; 14-*O*-methylperegrine; peregrine; munzianone; munzianine; 10-hydroxyperegrine.

Abstract—Five new norditerpenoid alkaloids, 14-*O*-benzoylperegrine, 14-*O*-acetylperegrine, munzinanone, munzianine and 10-hydroxyperegrine, together with peregrine and 14-*O*-methylperegrine, were isolated from *Delphinium munzianum*. The structures of the new alkaloids were elucidated mainly by NMR spectroscopy, including 2-D techniques, and partial synthesis starting from peregrine.

INTRODUCTION

Delphinium munzianum P. H. Davis & Kit Tan is an endemic perennial species found in north-east Anatolia [1]. As a part of our work on Turkish *Delphinium* species [2–7], we report herein on the isolation of five new aconitine-type norditerpenoid alkaloids from the title species, 14-*O*-benzoylperegrine (**1**), 14-*O*-acetylperegrine (**2**), munzianone (**5**), munzianine (**6**) and 10-hydroxyperegrine (**7**), besides the known norditerpenoid alkaloids, peregrine (**4**) and 14-*O*-methylperegrine (**3**).

RESULTS AND DISCUSSION

The new compounds, the empirical formulae of which were obtained from HR mass and ^{13}C NMR spectra, presented characteristic features of aconitine-type norditerpenoid alkaloids in their NMR and mass spectra [8–10]. The alkaloids, 14-*O*-benzoylperegrine (**1**), $C_{33}H_{45}NO_7$, and 14-*O*-acetylperegrine (**2**), $C_{28}H_{43}NO_7$, showed NMR spectra similar to those of peregrine (**4**) [11, 12], with signals at δ_H0.81–0.82 (3H, *s*) and δ_c25.9–26.1 *q* for the angular methyl group, and δ_H1.02–1.04 (3H, *t*, $J \approx 7$ Hz), δ_C48.5–49.1 *t* and 13.6–13.5 *q* for an *N*-ethyl group. Compound **1** also gave signals for three methoxyl groups at δ_H2.67, 3.28 and 3.38 (3H each, *s*) and δ_C47.5 and 55.9 (*q* each), an acetate group at δ_H1.93 (3H, *s*) and δ_c171.4 *s* and 21.5 *q*, and a benzoate group at δ_H7.43 (3H, *m*), 8.04 (2H, *m*) and δ_C128.1 *d*, 129.5 *d*, 131.2 *s*, 132.2 *d* and 166.6 *s*. Two one-proton *dd* signals at δ_H3.11 (J = 9.9 and 7.2 Hz) and δ_H3.46 (J = 12.5 and 7.2 Hz), and carbon resonances at δ_C84.3 and 83.3 (*d* each) and 78.3 *s* allowed us to place the three methoxyl groups at C-1α, C-16β and C-8. The similarity between the NMR spectra of **1** and those of peregrine (**4**) [11, 12] indicated the close relationship of the two alkaloids, while the one-proton doublet at δ_H 5.17 (J = 7.4 Hz), the one-proton triplet at δ_H4.96 (J = 4.9 Hz) and the upfield methoxyl group signal at δ_H2.67 revealed that the acetate and benzoate groups are at C-6β and C-14α in the molecule, respectively.

From the NMR spectra, the structure of alkaloid **2** was also recognized to be very similar to that of peregrine (**4**). But **2** has two acetate groups [δ_H1.97 (6H, *s*), δ_C171.4 *s* and 21.3 and 21.6 (*q* each)]. A new one-proton triplet at δ_H4.68 (J = 4.8 Hz) in the spectrum of alkaloid **2** as compared with the spectrum of peregrine, indicated that the extra acetate group in **2** is placed at C-14α.

The structures of the new alkaloids **1** and **2** were confirmed by partial synthesis. Treatment of peregrine (**4**) with PhCOCl-pyridine and Ac_2O-pyridine, yielded 14-*O*-benzoylperegrine (**1**) and 14-*O*-acetylperegrine (**2**), respectively, identical with the natural alkaloids.

The IR spectrum of munzianone (**5**), $C_{24}H_{37}NO_5$, showed a ketone group absorption at 1730 cm^{-1}, and the NMR spectra exhibited signals at δ_H0.93 (3H, *s*) and δ_C25.3 *q* for a tertiary methyl group, δ_H1.08 (3H, *t*, J = 7.1 Hz), δ_C49.4 *t* and 13.7 *q* for an *N*-ethyl group, δ_H3.30, 3.33 and 3.37 (3H each, *s*), and δ_C49.4, 56.6 and 56.8 (*q* each) for three methoxyl groups, and δ_C214.6 *s* for a ketonic carbonyl group. In addition, the carbonyl carbon resonance in the ^{13}C NMR spectrum had three singlets at δ_C34.5 (C-4), 47.3 (C-11) and 78.6 (C-8), which together with the tertiary methoxyl carbon resonance at δ_C49.4 showed that munzianone (**5**) is an aconitine-type norditerpenoid alkaloid having a methoxyl group at C-8 [8, 9]. The one-proton signals at δ_H3.19 (*dd*, J = 10.5 and 6.7 Hz), 3.47 *m* and 3.96 (*dt*, J = 6.9 and 5.1 Hz, becoming

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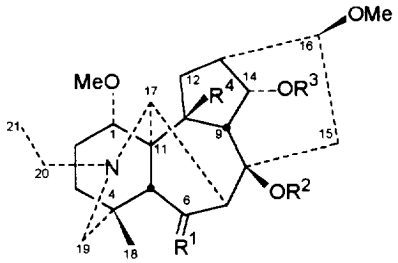

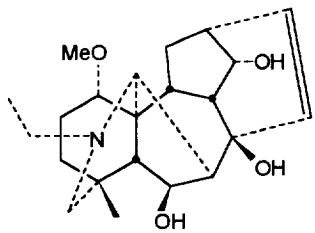

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1 R^1 = αH, βOAc; R^2 = Me; R^3 = Bz; R^4 = H

2 R^1 = αH, βOAc; R^2 = Me; R^3 = Ac; R^4 = H

3 R^1 = αH, βOAc; R^2 = Me; R^3 = Me; R^4 = H

4 R^1 = αH, βOAc; R^2 = Me; R^3 = R^4 = H

5 R^1 = O; R^2 = Me; R^3 = R^4 = H

6 R^1 = αH, βOH; R^2 = R^3 = R^4 = H

7 R^1 = αH, βOAc; R^2 = Me; R^3 = H; R^4 = OH

8 R^1 = αH, βOH; R^2 = Me; R^3 = R^4 = H

9 R^1 = αH, βOH; R^2 = Me; R^3 = Ac; R^4 = H

10 R^1 = O; R^2 = Me; R^3 = Ac; R^4 = H

a *t*, $J = 4.9$ Hz when D_2O was added) and their correlated methine carbon resonances at δ_C 84.8, 82.1 and 74.9, respectively, in the HMQC [14] spectrum (see Table 2), revealed that the two methoxyl groups and a hydroxyl group are situated at C-1α, C-16β and C-14α, respectively, in the molecule of munzianone (**5**) [8, 9]. Since the one-proton broad singlet at δ_H 3.48, attributed to H-17 (HMQC δ62.5 *d*), gave a three-bond connectivity with the carbonyl carbon resonance at δ_C 214.6, this functional group was placed at C-6. The ^{13}C assignments of munzianone (**5**) (Table 1), in accord with the proposed structure, have been made by correlation with the spectra of peregrine (**4**) and its derivatives [12], and the heteronuclear connectivities observed in the HMQC and HMBC [15] spectra (Table 2).

The structure of munzianone (**5**) was corroborated by partial synthesis starting from peregrine (**4**). Smooth acetylation of peregrine alcohol (**8**), obtained by basic hydrolysis of peregrine, with Ac_2O in pyridine at 0° gave the 14-*O*-acetyl derivative **9** in 61% yield. Its ^1H NMR spectrum displayed signals at δ_H 2.03 (3H, *s*) and one-proton signals at δ_H 4.27 (*d*, $J = 7.4$ Hz) and 4.79 (*t*, $J = 4.5$ Hz) for H-6α and H-14β, respectively, pointing to the introduction of only one acetate group, at C-14α. The CrO_3 oxidation of 9 in HOAc-H_2O gave the 6-keto compound **10** in 91% yield. Its $[M]^+$ at *m/z* 461 was two mu less than that of **9** and the NMR spectra did not show signals for carbinyl C-6 but contained a new singlet at δ_C 213.4 with respect to the spectrum of **9**. Basic hydrolysis of **9** with methanolic KOH at room temperature yielded munzianone (**5**) (93%), identical with the natural alkaloid.

The structure of munzianine (**6**), $C_{23}H_{37}NO_5$, was deduced from NMR spectra which almost matched those of peregrine alcohol (**8**) [11, 12], indicating the great structural similarity between both alkaloids. The NMR spectra of munzianine gave signals of an *N*-ethyl group at δ_H 1.04 (3H, *t*, $J = 7.2$ Hz), δ_C 49.5 *t* and 13.6 *q*, a tertiary methyl group at δ_H 0.95 (3H, *s* and δ_C 25.8 *q*), and two methoxyl groups at δ_H 3.26 and 3.36 (3H each, *s*), and δ_C 56.3 and 56.5 (each *q*). From the signals at δ_H 3.07 (1H, *dd*, $J = 10.5$ and 6.9 Hz, H-1β), 4.16 (1H, *t*, $J = 4.8$ Hz, H-14α), 4.32 (1H, *d*, $J = 7.2$ Hz, H-6α), δ_C 72.7 *d* (C-6), 75.3 *s* (C-8), 75.5 *d* (C-14), 82.2 (C-16) and 85.9 *d* (C-1) it was clear that munzianine (**6**) had two methoxyl groups, located at C-1α and C-16β, and three hydroxyl groups at C-6β, C-14α and C-8, in an aconitine-type skeleton [8, 9].

The structure of munzianine (**6**) was also confirmed by synthesis from peregrine (**4**). Thus, heating peregrine with 15% H_2SO_4 at 100° gave munzianine (**6**) in 23% yield, identical with the natural alkaloid. After CC of the solvolysis product the *iso*pyro derivative (**11**) was isolated in 14% yield, as a less polar compound. Its ^1H NMR spectrum displayed signals at δ_H 3.25 (3H, *s*) for a sole methoxyl group, and the mass spectrum gave the $[M]^+$ at 32 mu less than that of munzianine (**6**). The base peak at *m/z* 344 $[M-31]^+$ indicated that the methoxyl group was at C-1 [10]. The one-proton signals at δ_H 3.12 (*dd*, $J = 10.4$ and 7 Hz, H-1β), 4.05 (*t*, $J = 4.5$ Hz, H-14β) and 4.48 (*d*, $J = 7.3$ Hz, H-6α) proved that the methoxyl group is at C-1α and that the two secondary hydroxyl groups are at C-14α and C-6β. The vinylic protons at δ_H 5.56 (*dd*, $J = 10.6$ and 1.8 Hz) and 5.97 (*dd*, $J = 9.4$ and 6.9 Hz) were ascribed to H-15 and H-16, respectively. The formation of *iso*pyro compounds, such as **11**, during pyrolysis and solvolysis is characteristic of aconitine-type norditerpenoid alkaloids [16, 17].

The alkaloid 10-hydroxyperegrine (**7**), $C_{26}H_{41}NO_7$, was also recognized to be structurally related to peregrine (**4**) on the basis of the similarities of their NMR spectra,

Table 1. ^{13}C NMR assignments for compounds **1–10**

C	1	2	3	4	5	6	7	8	9	10
1	84.2	84.2	84.3	84.7	84.8	85.9	77.8	85.6	84.9	83.9
2	26.8	27.1	26.8	26.5	26.8	26.0	26.4	26.5	26.7	26.7
3	37.1	37.2	36.9	37.1	38.5	37.3	36.6	37.5	35.8	37.9
4	34.1	34.2	34.1	34.5	34.6	34.7	34.1	34.6	34.1	34.1
5	56.2	56.5	56.2	56.4	63.1	58.1	52.1	58.9	58.5	60.7
6	72.9	73.1	73.2	73.4	214.6	72.7	73.4	73.0	72.5	213.4
7	42.0	42.0	42.1	42.4	49.5	45.9	41.8	45.9	43.4	48.8
8	78.3	78.5	78.1	79.1	78.6	75.3	77.9	80.9	80.8	77.5
9	41.4	41.2	41.3	44.6	46.7	49.5	54.4	43.8	42.9	43.3
10	45.8	46.0	46.4	46.2	46.2	46.0	81.4	46.3	45.4	45.3
11	48.4	48.5	48.4	48.2	47.3	48.4	53.7	48.3	48.4	46.6
12	28.3	28.6	28.6	28.6	28.2	28.1	39.5	28.5	28.7	28.5
13	38.3	39.1	39.3	38.6	37.7	37.5	39.1	37.7	37.2	37.7
14	76.4	76.3	84.1	75.5	74.4	75.5	73.5	75.2	75.7	74.7
15	35.3	35.8	35.6	33.0	32.3	39.3	35.4	33.1	35.8	35.1
16	83.3	83.6	83.6	82.5	82.1	82.2	81.9	82.4	82.9	82.7
17	63.9	64.0	63.6	64.7	62.5	64.2	64.4	64.3	63.4	61.9
18	25.9	26.1	25.9	25.9	25.3	25.8	25.9	26.0	25.9	24.9
19	57.3	57.5	57.4	57.6	57.6	58.1	57.3	58.1	57.8	57.0
20	49.1	48.5	49.0	49.3	49.4	49.5	49.2	49.6	49.3	48.9
21	13.5	13.6	13.4	13.6	13.7	13.6	13.4	13.8	13.5	13.2
1′	55.9	56.0	55.9	56.0	56.6	56.3	55.7	56.3	56.1	56.1
8′	47.5	48.0	47.7	48.3	49.4		48.2	48.6	47.8	48.7
14′			57.5							
16′	55.9	56.5	56.2	56.4	56.8	56.5	56.4	56.5	56.2	56.3
Ac	171.4	171.5	170.9	170.2			170.9		171.1	171.3
	21.5	21.7	21.7	21.7			21.7		21.3	21.2

Chemical shifts in ppm down-field from TMS.
Carbon multiplicities were determined by DEPT pulse sequence.
Data for Bz in **1**: 166.6 *s*, 131.2 *s*, 128.1 *d*, 129.5 *d* and 132.2 *d*; for the second Ac in **2**: 171.5 *s* and 21.4 *q*.

Table 2. Heteronuclear correlations of munzianone (**5**)

	Correlated carbon	
Proton	HMQC	HMBC
H-1β	84.8 *d*	C-10, C-11, C-17, C-1′
H-5	63.1 *d*	C-4, C-6, C-10, C-17, C-18, C-19
H-7	49.5 *d*	C-5, C-6, C-8, C-9, C-11, C-15, C-17
H-9	46.7 *d*	C-10, C-12, C-14, C-16
H-14β	74.9 *d*	C-8, C-6
H-16α	82.1 *d*	C-8, C-14
H-17	62.5 *d*	C-5, C-6, C-7, C-10, C-11, C-19
H-18	25.3 *q*	C-3, C-4, C-5, C-19
H-19α	57.6 *t*	C-3, C-4, C-17
H-20A	49.4 *t*	C-17, C-19, C-21
H-21	13.7 *q*	C-20
H-1′	56.6 *q*	C-1
H-8′	49.4 *q*	C-8
H-16′	56.8 *q*	C-16

which afforded signals at δ_H 0.86 (3H, *s*) and δ_C 25.9 3*q* for an angular methyl group, δ_H 1.06 (3H, *t*, J = 7.1 Hz), δ_C 49.2 *t* and 13.4 *q* for an *N*-ethyl group δ_H 3.08, 3.26, 3.53 (3H each, *s*) and δ_C 48.2, 55.7 and 56.4 (each *q*) for three methoxyl groups, one of them tertiary (δ48.2 *q*), and δ_H 2.05 (3H, *s*), δ_C 21.7 *q* and 170.9 *s* for an acetate group. The one-proton signals at δ_H 3.31 (*m*, H-16α), 3.71 (*dd*, J = 9.6 and 7.4 Hz, H-1β), 4.55 (*t*, J = 4.8 Hz, H-14β) and 5.31 (*d*, J = 7.3 Hz, H-6α), together with their correlated methine carbon resonances at δ_C 81.9, 77.8, 73.5 and 73.4, respectively, in the HMQC spectrum (Table 3), were in agreement with the presence of two methoxyl groups at C-1α and C-16β, a hydroxyl group at C-14α and an acetate group at C-6β, in an aconitine skeleton. On the other hand, the carbon singlets at δ_C 34.1, 53.7 and 77.9 were assigned to C-4, C-11 and C-8 and indicated that the tertiary methoxy group (δ_C 48.2 *q*) is at C-8. The existence of a tertiary hydroxyl group at C-10 was deduced from the three-bond connectivities between the carbon singlet at δ81.4 and the H-1β, in the HMBC experiment (Table 3). With respect to the ^{13}C NMR spectrum of peregrine (**4**), the introduction of the hydroxyl group at C-10 in **7** produced an α-effect with a downfield shift of 35.4 ppm, β effects on C-11, C-9 and C-12 of 5.7, 10.1 and 11.1 ppm, respectively, and upfield γ-effects on C-1, C-5 and C-14 of -6.6, -3.9 and -1.7 ppm, respectively. Furthermore, in the ^{1}H NMR spectrum of peregrine (**4**) [12] the signals for H-1β, H-4 and H-14β appeared at δ_H 3.10 (partially obliterated by the methoxyl

Table 3. Heteronuclear correlations of 10-hydroxyperegrine (7)

Proton	Correlated carbon	
	HMQC	HMBC
H-1β	77.8 *d*	C-2, C-10, C-1, C-17, C-1′
H-5	52.1 *d*	C-4, C-6, C-11, C-17, C-18, C-19
H-6α	73.4 *d*	C-4, C-5, C-7, C-8, C-11
H-7	41.8 *d*	C-5, C-8, C-9, C-11, C-15, C-17
H-9	54.4 *d*	C-8, C-10, C-13, C-14, C-15
H-12α	39.5 *t*	C-11, C-13, C-14, C-16
H-12β	39.5 *t*	C-10, C-13, C-16
H-14β	73.5 *d*	C-8, C-9, C-16
H-16α	81.9 *d*	C-8, C-13, C-14, C-16′
H-17	64.4 *d*	C-1, C-5, C-6, C-8, C-11, C-19, C-20
H-18	25.9 *q*	C-3, C-4, C-5, C-19
H-19α	57.3 *t*	C-3, C-4, C-5, C-17
H-21	13.4 *q*	C-20
Ac	21.7 *q*	
H-1′	57.7 *q*	C-1
H-8′	48.2 *q*	C-8
H-16′	56.4 *q*	C-16

Table 4. Spatial correlations of 10-hydroxyperegrine

Proton	ROESY
H-1β	H-5, H-1′
H-5	H-1β, H-6α, H-9, H-18
H-6α	H-5, H-7, H-18
H-7	H-6α, H-17, H-8′
H-9	H-5, H-14β, H-8′
H-12α	H-12β, H-16α, H-1′
H-12β	H-12α, H-14β, H-1′
H-14β	H-9, H-12β
H-16α	H-12α, H-17
H-17	H-7, H-21, H-16α, H-1′
H-18	H-6α, H-5
H-21	H-17
H-1′	H-1β, H-12α, H-12β, H-17
H-8′	H-7, H-9

group signal at 3.08), 1.46 and 4.0, respectively, while in **7** they appeared at 0.61, 0.23 and 0.55 ppm lower field, respectively, owing to the 1,3-diaxial configuration between the said protons and the hydroxyl group at C-10. The one-proton doublet at δ_H 5.31 (J = 7.3 Hz) showed three-bond connectivities with the carbon singlets at δ_C 34.1 (C-4) and 77.9 (C-8), in the HMBC experiment, and a NOE with the C-4 methyl group at δ0.86 *s*, in the ROESY spectrum [18] (Table 4), only possible if the acetate group in **7** is at C-6 and in the β-configuration.

The norditerpenoid alkaloids isolated from *D. munzianum* could be biogenetically derived from munzianine (**6**), which by methylation at *O*-8 gives peregrine alcohol (**8**), which however was not isolated from the plant. Oxidation and acetylation of **8** at C-6 will lead to munzianone (**5**) and peregrine (**4**), respectively. Peregrine (**4**) will provide the 14-*O*-derivatives by acylation and methylation, and 10-hydroxyperegrine (**7**) by hydroxylation at C-10. Like *D. peregrinum* [4, 11], *D. bicolor* [19], *D. speciosum* [20] and *D. caeruleum* [21], *D. munzianum* afforded aconitine-type norditerpenoid alkaloids with an oxygen function at C-6β, but not lycoctonine-type alkaloids, as did the other species mentioned.

EXPERIMENTAL

General. Mps: uncorr. IR: $CHCl_3$. OR: $CHCl_3$ 1 dm cell. EIMS: 70 eV. NMR spectra were recorded in $CDCl_3$ on Bruker WP-200 SY and AMX spectrometers, using TMS and solvent as int. standards; chemical shifts δ in ppm down-field from TMS. DEPT, ^{1}H COSY, HMQC, HMBC (J = 7 Hz) and ROESY (spin lock 700 msec) experiments were carried out with the standard pulse sequences given in the Bruker manual. Alumina Merck Art. 1077 and 5581 were used for CC and TLC, respectively. Visualization was made with Dragendorff's reagent.

Plant material. Plants growing on rocky limestone slopes were collected during the flowering period near Oltu, Erzurum, Turkey, and authenticated by Dr Resit Ilarsland. Voucher Specimen Ilarslan 1663 has been deposited at the Herbarium of the Faculty of Science, University of Ankara.

Extraction and isolation. Aerial parts were air-dried (1 kg) and extracted with EtOH by percolation for 7 days at room temp. After solvent removal under vaccum, the EtOH extract (150 g) was partitioned between 0.5 M H_2SO_4 and $CHCl_3$. The acid soln was basified with 20% NaOH to pH 10 and extracted with $CHCl_3$ to give crude alkaloid material (4.17 g). CC using a hexane-EtOAc step gradient, EtOAc and a EtOAc-MeOH step gradient led to the isolation of individual alkaloids, purified by further CC, in the following elution order: 14-*O*-benzoylperegrine (**1**) (7 mg), 14-*O*-acetylperegrine (**2**) (71 mg), 14-*O*-methylperegrine (**3**) (35 mg), peregrine (**4**) (1.27 g), munzianone (**5**) (21 mg), munzianine (**6**) (24 mg) and 10-hydroxyperegrine (**7**) (23 mg).

14-O-Benzoylperegrine (**1**). Crystalline, mp 112–114°, from hexane-EtOAc. $[\alpha]_D$ − 21° (*c* 0.1). $[M]^+$ *m/z* 567.3212 for $C_{33}H_{45}NO_7$ (Calc. 567.3196). IR ν_{max} cm^{-1}: 2950, 2800, 1720, 1600, 1580, 1450, 1360, 1310, 1270, 1250, 1170, 1160, 1115, 1070, 1040, 990, 940, 870, 710. ^{1}H NMR (200 MHz) δ0.82 (3H, *s*, H-18), 1.04 (3H, *t*, J = 7 Hz, H-21), 1.44 (1H, *br s*, H-5), 1.93 (3H, *s* OAc), 2.62 (1H, *d*, J = 7.4 Hz, H-7), 3.11, 3.28 and 3.38 (3H each, *s*, 3xOMe), 2.97 (1H, *d*, J = 2 Hz, H-17), 3.11 (1H, *dd*, J = 9.9 and7.2 Hz, H-1β), 3.46 (1H, *dd*, J = 12.5 and 7.2 Hz, H-16α), 4.96 (1H, *t*, J = 4.9 Hz, H-14β), 5.17 (1H, *d*, J = 7.4 Hz, H-6α), 7.43 (3H, *m*) and 8.04 (2H, *m*) for the aromatic protons. EIMS *m/z* (rel. int.), 567 (3) $[M]^+$, 552 (1), 537 (39), 536 (100), 524 (4), 508 (2), 506 (3), 504 (3), 492 (2), 476 (5), 462 (2), 430 (2), 404 (2), 372 (2), 342 (3), 323 (2), 282 (3), 267 (5), 225 (2), 213 (2), 199 (2), 187 (5), 178 (2), 167 (3), 157 (2), 145 (2), 136 (3), 129 (3), 122 (4), 110 (3), 105 (52), 96 (3), 91 (4), 81 (3), 77 (14), 58 (5). For ^{13}C NMR (50 MHz) see Table 1.

14-O-*Benzoylperegrine from peregrine.* A mixt. of peregrine (**4**) (30 mg), pyridine (1 ml) and PhCOCl (1 ml) was stirred at room temp. for 18 hr. The reaction product (29.5 mg), obtained by solvent elimination under vacuum, was chromatographed over alumina with hexane-EtOAc (3:2) to yield 14-*O*-benzoylperegrine (**1**) (18 mg, 50%), identical with the natural alkaloid (TLC, IR, MS and ^{1}H NMR).

14-O-*Acetylperegrine* (**2**). Resin. $[\alpha]_D$ − 49.6° (*c* 0.24). $[M]^+$ *m/z* 505.3046 for $C_{28}H_{43}NO_7$ (Calc. 505.3039). IR ν_{max} cm^{-1}: 2950, 2840, 1730, 1455, 1365, 1260, 1162, 1115, 1080, 990, 980, 940, 872. ^{1}H NMR (200 MHz) δ0.81 (3H, *s*, H-18), 1.02 (3H, *t*, *J* = 7 Hz, H-21), 1.39 (1H, *br s*, H-5), 1.52 (1H, *dm*, *J* = 16.9 Hz, H-3α), 1.97 (6H, *s*,2xOAc), 2.40 (2H, *m*, H-20), 2.59 (1H, *d*, *J* = 12.9 Hz, H-19α), 2.69 (1H, *d*, *J* = 7.2 Hz, H-7), 2.89 (1H, *d*, *J* = 2 Hz, H-17), 2.98, 3.24 and 3.36 (3H each, *s*, 3xOMe), 3.07 (1H, *dd*, *J* = 9.8 and 7.3 Hz, H-1β), 4.68 (1H, *t*, *J* = 4.8 Hz, H-14β), 5.16 (1H, *d*, *J* = 7.3 Hz, H-6α), EIMS *m/z* (rel. int.), 505 (1) $[M]^+$, 490 (3), 474 (100), 462 (6), 445 (3), 444 (1), 430 (3), 414 (5), 400 (2), 341 (2), 339 (1), 146 (1), 119 (1), 91 (1), 58 (3), 43 (3). For ^{13}C NMR (50 MHz) see Table 1.

14-O-*Acetylperegrine from peregrine.* Peregrine (**4**) (50 mg) was treated with pyridine (1 ml) and Ac_2O (1 ml) for 10 hr at 70°. After solvent removal, the reaction product was purified on an alumina column using hexane-EtOAc (1:1) to give 14-*O*-acetylperegrine (**2**) (52.1 mg, 95%), identical with the natural compound by TLC, IR, MS and ^{1}H NMR.

14-O-*Methylperegrine* (**3**). Resin $[\alpha]_D$ − 19° (*c* 0.26). $[M]^+$ *m/z* 477.3061 for $C_{27}H_{43}NO_6$ (Calc. 447.3090). IR ν_{max} cm^{-1}: 2950, 2845, 1725, 1460, 1383, 1315, 1298, 1260, 1163, 1117, 1085, 1007, 993, 871. ^{1}H NMR (200 MHz) δ0.84 (3H, *s*, H-18), 1.05 (3H, *t*, *J* = 7.1 Hz, H-21), 1.39 (1H, *bs*, H-5), 2.08 (3H, *s*, OAc), 2.72 (1H, *d*, *J* = 7.3 Hz, H-7), 2.92 (1H, *d*, *J* = 1.7 Hz, H-17), 3.04, 3.27, 3.35 and 3.37 (3H each, *s*, 4xOMe), 3.56 (1H, *t*, *J* = 4.6 Hz, H-14β), 5.24 (1H, *d*, *J* = 7.4 Hz, H-6α). EIMS *m/z* (rel. int.), 477 (4) $[M]^+$, 462 (1), 446 (100), 434 (3), 418 (2), 414 (4), 402 (3), 386 (5), 372 (3), 370 (3), 354 (4), 340 (2), 314 (2), 296 (2), 280 (2), 246 (3), 222 (6), 206 (5), 195 (5), 172 (8), 165 (16), 160 (12), 151 (19), 139 (18), 129 (20), 122 (32), 121 (34), 109 (29), 96 (45), 91 (29), 83 (23). For ^{13}C NMR (50 MHz) see Table 1. Identical with an authentic sample isolated from *D. gueneri* [13] (TLC, IR, MS, ^{1}H and ^{13}C NMR).

14-O-*Methylperegrine from peregrine.* To peregrine (**4**) (7 mg) dissolved in CH_2Cl_2 (2.5 ml) *N,N,N',N'*-tetramethyl-1,8-naphthalenediamine (8 mg) and trimethyloxonium tetrafluoroborate (14 mg) was added, The reaction mixt. was stirred at room temp. for 18 hr, basified with NH_4OH and extracted with $CHCl_3$. The solvent was removed *in vacuo* and the product chromatographed over alumina with hexane-EtOAc (19:1) to give 14-*O*-methylperegrine (**3**) (3.8 mg, 53%), identical with the natural alkaloid (TLC, IR, MS and ^{1}H NMR).

Peregrine (**4**). Crystalline, mp 120–122° from hexane-EtOAc $[\alpha]_D$ + 20° (*c* = 0.2) [11]. IR ν_{max} cm^{-1} 3500, 2950, 1725, 1460, 1365, 1250, 1160, 1090, 990, 975, 945, 910, 880. EIMS *m/z* (rel. int.) 463 (2) $[M]^+$, 448 (2), 434 (6), 433 (31), 432 (100), 430 (3), 420 (7), 404 (5), 402 (3), 401 (3), 400 (9), 388 (3), 372 (11), 370 (10), 358 (3), 356 (3), 340 (6), 148 (4), 122 (5), 96 (6), 91 (9), 71 (12), 58 (19), 43 (46). For ^{1}H and ^{13}C NMR see ref. [12]. Identified by comparison with an authentic sample (TLC, mp, IR, MS, ^{1}H and ^{13}C NMR).

Munzianone (**5**). Crystalline, mp 117–118° from hexane-EtOAc $[\alpha]_D$ − 25° (*c* 0.17). $[M]^+$ *m/z* 419.2663 for $C_{24}H_{37}NO_5$ (Calc. 419.2672). IR ν_{max} cm^{-1}: 3450, 2900, 2800, 1730, 1455, 1360, 1280, 1085, 990, 970, 865. ^{1}H NMR (400 MHz) δ0.93 (3H, *s*, H-18), 1.08 (3H, *t*, *J* = 7.1 Hz, H-21), 1.72 (1H, *s*, H-5), 2.09 (1H, *t*, *J* = 4.7 Hz, H-9), 2.34 (1H, *dq*, *J* = 12.1 and 7 Hz, H-20A), 2.58 (1H, *d*, *J* = 12.1 Hz, H-19β), 2.67 (1H, *s*, H-7), 3.19 (1H, *dd*, *J* = 10.5 and 6.7 Hz, H-1β), 3.30, 3.33 and 3.37 (3H each, *s*, 3xOMe), 3.47 (1H, *m*, H-16α), 3.48 (1H, *br s*, H-17), 3.74 (1H, *d*, *J* = 7.7 Hz, disappearing when D_2O added, 14α-OH), 3.96 (1H, *dt* *J* = 6.9 and 5.1 Hz, becoming a *t*, *J* = 4.9 Hz when D_2O added, H-14β). EIMS *m/z* (rel. int.), 419 (10) $[M]^+$, 404 (4), 402 (1), 389 (24), 388 (100), 386 (1), 370 (1), 358 (1), 356 (4), 322 (2), 230 (2), 206 (2), 111 (3), 96 (20). For ^{13}C NMR (100 MHz) see Table 1.

Peregrine alcohol from peregrine. Peregrine (**4**) (58.2 mg) was refluxed in 5% KOH in MeOH (5 ml) for 6 hr, after which the reaction mixt. was poured into H_2O and extracted with $CHCl_3$. The solvent was removed and the reaction product chromatographed over alumina with EtOAC to yield peregrine alcohol (**8**) (49.8 mg, 94%), identified by TLC, mp, IR, MS and ^{1}H NMR [11, 12].

Acetylation of peregrine alcohol. To compound **8** (49.8 mg) dissolved in pyridine (1 ml), Ac_2O (1.9 ml) was added dropwise with stirring at 0° for 7 days. Water was then added and the reaction mixt. basified with 10% KOH and extracted with $CHCl_3$. After solvent removal, the reaction product (58 mg) was chromatographed on alumina with hexane-EtOAc (9:1) to give 14-*O*-acetylperegrine (**2**) (10.8 mg, 18%), identified by comparison with the natural alkaloid (TLC, IR, MS and ^{1}H NMR), and the 14-*O*-acetyl derivative **9** (33.4 mg, 61%), mp 107–110°, recrystallized from hexane-EtOAc. IR ν_{max} cm^{-1}: 3500, 2900, 1730, 1450, 1360, 1245, 1155, 1075, 900. ^{1}H NMR (200 MHz) δ0.95 (3H, *s*, H-18), 1.06 (3H, *t*, *J* = 7.2 Hz, H-21), 1.40 (1H, *s*, H-5), 2.03 (3H, *s*, OAc), 2.42 (2H, *m*, H-20), 2.56 (1H, *d*, *J* = 13.4 Hz, H-19α), 2.61 (1H, *d*, *J* = 7.6 Hz, H-7), 2.93 (1H, *d*, *J* = 2.1 Hz, H-17), 3.08 (1H, *dd*, *J* = 10.2 and 7.2 Hz, H-1β), 3.22 (1H, *dd*, *J* = 9.4 and 4.4 Hz, H-16α), 3.28, 3.29 and 3.33 (3H, each, *s*, 3xOMe), 4.27 (1H, *d*, *J* = 7.4 Hz, H-6α), 4.79 (1H, *t*, *J* = 4.5 Hz, H-14β), 5.08 (1H, *s*, disappearing when D_2O added). EIMS *m/z* (rel. int.), 463 (7) $[M]^+$, 448 (3), 433 (39), 432 (100), 430 (4), 416 (3), 414 (3), 402 (4), 400 (3), 388 (5), 372 (6), 358 (4), 346 (3), 298 (71), 279 (8), 265 (4), 247 (4), 238 (7), 223 (7), 210 (9), 206 (9), 189 (8), 172 (10), 167 (24), 124 (15), 97 (15), 82 (15), 71 (9). For ^{13}C NMR (50 MHz) see Table 1.

6-*Keto derivative* **10** *from compound* **9**. To the 14-*O*-acetyl derivative **9** (25 mg) dissolved in HOAc–H_2O (17:3) (2 ml) was added to reagent (0.5 ml) formed by dissolving CrO_3 (100 mg) in HOAc–H_2O (17:3) (2 ml).

The reaction mixt. was stirred at room temp. for 1.5 hr. Then excess reagent was destroyed with EtOH, the mixt. treated with 10% KOH to pH 12 in an ice-bath and extracted with $CHCl_3$. Solvent evapn afforded the reaction product which was chromatographed over alumina with hexane-EtOAc (7:3) to give the 6-keto derivative **10** (22.7 mg, 91%), mp 157–160°, recrystallized from hexane-EtOAc. IR ν_{max} cm^{-1}: 3000, 2930, 2815, 1733, 1460, 1363, 1325, 1200, 1255, 1170, 1090, 1020, 1000, 970, 950, 910. ^1H NMR (200 MHz) δ0.88 (3H, *s*, H-18), 1.06 (3H, *t*, J = 7.2 Hz, H-21), 1.65 (1H, *s*, H-5), 1.98 (3H, *s*, OAc), 2.55 (1H, *d*, J = 12.4 Hz, H-19α), 2.63 (1H, *s*, H-7), 3.16 (1H, *dd*, J = 10.4 and 6.8 Hz, H-1β), 3.23 (1H, *d*, J = 1.9 Hz, H-17), 3.28, 3.29 and 3.31 (3H, each, *s*, 3xOMe), 4.74 (1H, *t*, J = 4.8 Hz, H-14β). EIMS *m/z* (rel. int.), 461 (4) $[M]^+$, 446 (1), 431 (31), 430 (100), 416 (2), 402 (2), 401 (3), 390 (4), 385 (3), 372 (7), 339 (5), 299 (3), 268 (4), 224 (4), 218 (7), 167 (32), 141 (10), 137 (7), 127 (16), 122 (17), 111 (25), 109 (22), 96 (23), 83 (41), 81 (23), 91 (18), 71 (52), 57 (66). For ^{13}C NMR (50 MHz) see Table 1.

Munzianone from compound **10**. The 6-keto compound **10** (18 mg) was treated with 5% KOH in MeOH–H_2O (9:1) (3 ml) for 30 min at room temp. The reaction mixt. was worked up in the usual way and the product chromatographed on alumina with EtOAc to give munzianone (**5**) (15.2 mg, 93%), identical with the natural alkaloid (TLC, IR, MS and ^1H NMR).

Munzianine (**6**). Crystalline, mp 154–157° from hexane-EtOAc. $[\alpha]_D$ + 3.8° (*c* 0.2). $[M]^+$ *m/z* 407.2654 for $C_{23}H_{37}NO_5$ (Calc. 407.2672). IR ν_{max} cm^{-1}: 3495, 2950, 2825, 1460, 1375, 1320, 1295, 1283, 1162, 1087, 1015, 997, 975, 935. ^1H NMR (200 MHz) δ0.95 (3H, *s*, H-18), 1.04 (3H, *t*, J = 7.1 Hz, H-21), 1.42 (1H, *br*, *s*, H-5), 1.56 (1H, *dm*, J = 12.9 Hz, H-3α), 2.56 (1H, *d*, J = 11.6 Hz, H-19α), 3.07 (1H, *dd*, J = 10.5 and 6.91 Hz, H-14β), 3.26 and 3.35 (3H each, *s*, 2xOMe), 4.16 (1H, *t*, J = 4.8 Hz, H-14β), 4.32 (1H, *d*, J = 7.2 Hz, H-6α), 4.67 (1H, *s*, disappearing when D_2O added). EIMS *m/z* (rel. int.), 407 (7) $[M]^+$, 392 (18), 390 (4), 389 (4), 377 (100), 378 (100), 374 (29), 358 (33), 345 (10), 344 (41), 342 (19), 328 (11), 326 (11), 208 (6), 205 (5), 166 (6), 198 (9), 177 (8), 91 (100), 71 (10). For ^{13}C NMR (50 MHz) see Table 1.

Munzianine from peregrine. Peregrine (**4**) (53 mg) was treated with 15% H_2SO_4 (10 ml) at 100° for 27 hr, after which the reaction mixt. was basified with 10% KOH to pH 12 and extracted with $CHCl_3$. Solvent was removed and the product (45 mg) chromatographed over alumina with EtOAc–MeOH–NH_4OH (19:1:0.1) to give, as the more polar compound, munzianine (**6**) (10.9 mg, 23%), identical with the natural alkaloid (TLC, IR, MS and ^1H NMR). The less polar compound, the *iso*pyro derivative (**11**) (5.8 mg, 14%), mp 139–142°, recrystallized from hexane-EtOAc. IR ν_{max} cm^{-1}: 3400, 2925, 2855, 1650, 1430, 1385, 1340, 1320, 1160, 1080, 915, 875, 795, 775, 690, 670. ^1H NMR (200 MHz) δ0.96 (3H, *s*, H-18), 1.01 (3H, *t*, J = 7.2 Hz, H-21), 1.42 (1H, *brs*, H-5), 1.57 (1H, *dm*, J = 16.1 Hz, H-3α), 2.55 (1H, *dd*, J = 11.9 Hz, H-19α), 3.06 (1H, *d*, J = 2.2 Hz, H-17), 3.12 (1H, *dd*, J = 10.4 and 7Hz, H-1β), 3.25 (3H, *s*, OMe), 4.05 (1H, *t*, J = 4.5 Hz, H-14β), 4.48 (1H, *d*, J = 7.3 Hz, H-6α), 5.56 (1H, *dd*, J = 10.6 and 1.8 Hz, H-15), 5.97 (1H, *dd*, J = 9.4 and 4.9 Hz, H-16). EIMS *m/z* (rel. int.), 375 (3) $[M]^+$, 360 (3), 358 (3), 357 (9), 345 (26), 344 (100), 343 (5), 342 (17), 328 (14), 326 (19), 298 (3), 284 (4), 256 (3), 220 (4), 206 (4), 178 (7), 122 (4), 91 (5), 71 (4).

10-*Hydroxyperegrine* (**7**). Amorphous. $[\alpha]_D$ + 15° (*c* 0, 18). $[M]^+$ *m/z* 479.2898 for $C_{26}H_{41}NO_7$ (Calc. 479.2883). IR ν_{max} cm^{-1}: 3450, 2920, 2800, 1725, 1450, 1360, 1250, 1230, 1116, 1085, 1045, 965, 932, 908, 865. ^1H NMR (400 MHz) δ0.86 (3H, *s*, H-18), 1.06 (3H, *t*, J = 7.1 Hz, H-21), 1.69 (1H, *br*, *s*, H-5), 1.74 (1H, *dd*, J = 15.7 and 7.4 Hz, H-12β), 2.05 (3H, *s*, OAc), 2.62 (1H, *d*, J = 11.8 Hz, H-19α), 2.72 (1H, *d*, J = 7.4 Hz, H-7), 2.82 (1H, *d*, J = 5 Hz, H-9), 2.96 (1H, *d*, J = 15.8 Hz, H-12α), 3.01 (1H, *s*, H-17) 3.08, 3.26 and 3.35 (3H each, *s*, 3xOMe), 3.31 (1H, *m*, H-16α), 3.71 (1H, *d*, J = 9.6 and 7.4 Hz, H-1β), 4.55 (1H, *t*, J = 4.8 Hz, H-14β), 5.31 (1H, *d*, J = 7.3 Hz, H-6α). EIMS *m/z* (rel. int.), 479 (1) $[M]^+$, 464 (2), 450 (6), 449 (30), 448 (100), 446 (1), 436 (5), 420 (2), 418 (3), 416 (2), 390 (7), 388 (11), 372 (3), 370 (3), 358 (3), 328 (2), 281 (2), 167 (2), 122 (3), 98 (2), 91 (3), 71 (3), 58 (6). For ^{13}C NMR (100 MHz) see Table 1.

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