Alkaloids from *Delphinium staphisagria*

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Three new diterpenoid alkaloids, isoazitine (**1**), 19-oxodihydroatisine (**2**), and 22-*O*-acetyl-19-oxodihydroatisine (**3**), and eight known alkaloids—azitine (**4**), dihydroatisine (**5**), delphinine, neoline, bullatine C (14-acetylneoline), chasmanine, 14-acetylchasmanine, and the quaternary base atisinium chloride (**7**)—were isolated from the aerial parts of *Delphinium staphisagria*. Structures of the new alkaloids were established mainly by 1D and 2D NMR spectroscopy, including ^{1}H COSY, HMQC, HMBC, and ROESY. The ^{1}H and ^{13}C NMR data for alkaloids **4** and **5** are also reported.

The majority of the phytochemical studies of the *Aconitum*, *Delphinium*, and *Consolida* genera, the main sources of biologically active diterpenoid alkaloids,[1] have been carried out with species from Asia, Europe, and North America.[2] While searching for new diterpenoid alkaloids, we have investigated *Delphinium staphisagria* L. (Ranunculaceae), gathered in Morocco. The isolation and structure elucidation of several diterpenoid alkaloids from *D. staphisagria* were reported in previous papers.[3] Further study of the constituents of this species has now resulted in the isolation of three additional new diterpenoid alkaloids, isoazitine (**1**), 19-oxodihydroatisine (**2**), and 22-*O*-acetyl-19-oxodihydroatisine (**3**), together with eight known alkaloids. Structures of the new alkaloids were elucidated on the basis of spectral evidence; the known alkaloids were identified by comparison of their spectral data with those in the literature.

Results and Discussion

Isoazitine (**1**) was isolated as a resin, and the molecular formula, $C_{20}H_{29}NO$, was deduced from HRMS. The ^{1}H and ^{13}C NMR spectra (Tables 1 and 2) were very similar to those of atisine azomethine (azitine) (**4**),[4] indicating the structural similarity of the two alkaloids. The ^{1}H NMR spectrum showed signals characteristic for a tertiary methyl group (δ 1.07), an exocyclic double bond (δ 5.10 and 5.04), an imine proton at δ 7.43, and one secondary hydroxyl group (δ 3.61). This last should be located next to the exocyclic methylene group to account for the downfield shift of C-16 and C-17 (δ 156.6 s and 109.7 t) compared to that of azitine (**4**) (δ 156.6 s and 109.1 t) and other related compounds.[4] Three-bond correlations obtained from the HMBC experiment (Table 3) showed coupling between protons of the tertiary methyl group (δ 1.07) and the imine carbon (at δ 169.0 d), and between the imine proton and the methyl carbon (at δ 23.7 q) and the methylene carbon (at δ 55.5 t). Two-bond correlation was also observed between the imine proton and one quaternary carbon (δ 38.9 s). The downfield shift of this signal was attributed to C-4 adjacent to a double bond in the form N=C(19).[5] In the HMBC experiment, methylene double bond signals at δ 5.10 and 5.04 were correlated with the methine carbon resonances at δ 36.3 and 77.0 (HMQC δ 2.34 br s and 3.61 br t) and were therefore assigned to C-12 and C-15, respectively, which corroborated the presence of the secondary hydroxyl group on C-15. Inasmuch as the H-15 signal (δ 3.61) showed an NOE, with H-17 z and H-14 β in the ROESY spectrum, H-15 must be equatorial and α, with the OH β on C-15. Thus, the structure of isoazitine was assigned as **1**.

Compound **2** was obtained as colorless crystals, mp 221−223 °C. Its molecular formula $C_{22}H_{33}NO_3$ was deduced from the mass spectrum [*m*/*z* 359 (M^+)] and ^{1}H and ^{13}C NMR. The ^{1}H and ^{13}C NMR spectra revealed the presence of a hydroxyethyl group attached to nitrogen [^{1}H NMR δ 3.58 (H_{21}a), 3.51 (H_{21}b), 3.83 (H_{22}a), 3.79 (H_{22}b) and ^{13}C NMR δ 50.8 and 61.7], one lactam keto group [IR $\nu^{NaCl}{}_{max}$ cm^{-1} 1619 and ^{13}C NMR δ 176.8(s)], an exocyclic methylene group [^{1}H NMR δ 5.10 and 5.04, each (1H, br t, J = 1.5 Hz) and ^{13}C NMR δ 110.1 and 155.8], an angular methyl, and a secondary hydroxyl group. There was a close resemblance between compound **2** and the known diol dihydroatisine (**5**) in terms of ^{13}C NMR spectra (Table 2), indicating that **2** has a similar C_{20}-atisane skeleton.[4] The three-bond correlation observed in HMBC (Table 4) between the tertiary methyl group at δ 1.15 and the keto-group at δ 176.8 placed the carbonyl group at C-19. Acetylation of **2** with Ac_2O/C_5H_5N at room temperature followed by chromatographic purification afforded the diacetate **6** and the monoacetyl derivative **3**, the latter being identical with the new alkaloid discussed in the next paragraph. The ^{1}H NMR of **6** (Table 1) contained signals at δ 2.13 and 2.02 and the ^{13}C NMR at δ 21.3(q), 171.2(s), 20.8 (q), and 170.7(s). The three-proton signal in **2** at δ 3.83 and 3.79 (HMQC δ 61.7 t) and the 3.63 br t, (HMQC δ 76.7 d), which moved downfield after acetylation (δ 4.34 and 4.23 and 5.13 br t, J = 2 Hz), were assigned to H_2-C_{22} and H-15, respectively. The existence of a secondary hydroxyl group at C-15β was deduced as in **1**. 19-Oxodihydroatisine (**2**) was prepared earlier by mild permanganate oxidation of isoatisine;[6] this is the first report of the natural occurrence of this alkaloid.

Comparison of the mass and ^{1}H NMR spectra of **3** with the spectra of the synthetic diacetate **6** indicated that **3** had a hydroxyl group on C-15 and an acetyl group on C-22 (Table 1). The presence of the acetyl group at C-22 in **3** was corroborated by the long-range correlation observed in the HMBC between the protons attached to C-22 and the carbonyl carbon of the acetyl group.

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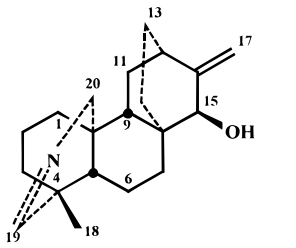

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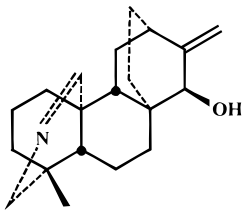

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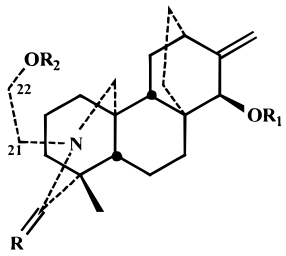

2 R = O, R_1 = R_2 = H
3 R = O, R_1 = H, R_2 = Ac
5 R = H_2, R_1 = R_2 = H
6 R = O, R_1 = R_2 = Ac

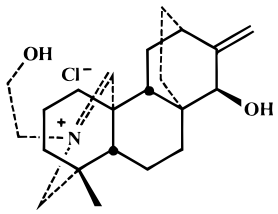

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Table 2. ^{13}C NMR Chemical Shift Assignments for Compound **1**−**6**[a]

carbon	1	2	3	4	5	6
1	41.4 t	41.3 t	41.4 t	34.2 t[b]	40.2 t[b]	41.4 t
2	20.2 t	20.1 t	20.1 t	20.0 t	23.3 t	20.0 t
3	37.6 t	39.6 t	39.6 t	42.4 t[b]	41.3 t	39.6 t
4	38.9 s	41.8 s	41.8 s	32.9 s	33.6 s	41.7 s
5	47.6 d	50.1 d	50.2 d	46.9 d	49.6 d	50.3 d
6	19.6 t	19.5 t	19.6 t	19.5 t	17.3 t	19.4 t
7	31.0 t	30.9 t	31.0 t	30.9 t[b]	31.4 t[b]	31.4 t
8	36.4 s	37.5 s	37.6 s	37.3 s	37.4 s	36.9 s
9	38.4 d	37.9 d	38.0 d	38.0 d	39.5 d	39.1 d
10	37.6 s	36.0 s	36.0 s	42.5 s	38.0 s	36.0 s
11	28.4 t	28.9 t	28.9 t	28.0 t[b]	28.1 t[b]	28.8 t
12	36.3 d	35.9 d	36.0 d	35.9 d	36.3 d	35.9 d
13	26.3 t	26.4 t	26.4 t	26.0 t	26.3 t	26.2 t
14	27.0 t	27.2 t	27.2 t	25.1 t[b]	27.6 t	26.9 t
15	77.0 d	76.7 d	76.7 d	75.8 d	77.0 d	76.7 d
16	156.6 s	155.8 s	155.8 s	156.6 s	156.7 s	150.4 s
17	109.1 t	110.1 t	110.2 t	109.1 t	109.8 t	111.1 t
18	23.7 q	23.0 q	23.2 q	25.9 q	26.5 q	23.1 q
19	169.0 d	176.8 s	174.6 s	60.7 t	60.7 t	174.5 s
20	55.5 t	54.4 t	54.5 t	165.8 d	53.9 t[b]	54.3 t
21		50.8 t	46.4 t		60.2 t[b]	46.4 t
22		61.7 t	62.4 t		57.9 t[b]	62.4 t

[a] Resonances for the acetate group in **3** and **6**: 170.7 s, 20.8 q (C_{22}Ac) and 171.2 s, 21.2 q (C_{15}Ac). Chemical shifts in ppm (δ) relative to TMS. Carbon multiplicities were determined by DEPT experiments. [b] Indicates values that are revised from those reported earlier.[4]

Experimental Section

General Experimental Procedures. Melting points, uncorrected, were taken on a Reichert Thermovar apparatus. IR spectrum: Bruker-IFS-55 spectrometer. Optical rotation: Perkin-Elmer-241 polarimeter, 1-dm cell. EIMS and exact mass measurements: Micromass Autospec spectrometer at 70 eV. NMR spectra: Bruker-AMX-400 or Bruker-AMX-500 spectrometers; $CDCl_3$; δ values in parts per million relative to internal TMS; J values in Hz. Al_2O_3 Merck (neutral, 200−300 mesh) and Schleicher and Schuell 394 732 was used for column chromatography (CC) and TLC, respectively. Sephadex LH-20, Pharmacia. Spots on chromatograms were detected with Dragendorff's reagent.

Table 1. ^{1}H NMR Data for Compounds **1**−**6**[a,b]

H	1	2	3	4	5	6
1a	1.70 m	1.81 m	1.79 m	1.69 br dt (13.2, 2)	1.90 br dd (13.5, 6.3)	1.79 m
1b	1.00 m	1.19 m	1.12 m	1.09 dd (15.7, 3)	1.14 m	1.15 m
2a	1.50 m	1.57 m	1.56 m	1.49 dd (13.3, 2.3)	2.40 m	1.57 m
2b	1.27 m	1.51 m	1.41 tt (13.5, 4.5)	1.32 dt (13.5, 4.5)	1.50 m	1.44 tt (13.5, 4.5)
3a	1.49 m	1.80 m	1.78 m	1.45 ddd (14, 4.5, 2.3)	1.70 td (13.5, 5)	1.78 td (12, 7)
3b	1.28 m	1.36 td (13.5, 4.5)	1.33 td (13.5, 4.5)	1.22 br td (13.5, 4.5)	1.40 m	1.39 td (13.5, 4.5)
5	0.98 m	1.69 m	1.15 m	1.01 dt (12.5, 2.2)	0.99 br dd (11.6, 4.5)	1.11 m
6a	1.56 m	1.68 m	1.68 m	1.60 m	1.52 m	1.66 m
6b	0.99 m	1.14 m	1.14 m	1.07 br dd (12.2, 3)	1.52 m	1.13 m
7a	1.68 m	1.71 m	1.72 m	1.80 m	1.70 m	1.23 m
7b	1.12 br dt (13.5, 3)	1.47 m	1.16 m	1.13 dt (13.5, 3)	1.16 m	1.23 m
9	1.58 m	1.74 m	1.73 m	1.81 dd (9, 2)	1.63 m	1.76 m
11a	1.72 m	1.73 m	1.74 m	1.75 m	1.60 m	1.82 m
11b	1.36 ddd (12.5, 7.7, 2)	1.12 m	1.19 m	1.75 m	1.40 m	1.19 m
12	2.34 br s	2.32 br s	2.32 m	2.39 quint (3)	2.31 quint (2)	2.39 br s
13a	1.57 m	1.62 m	1.62 br t(13)	1.60 m	1.60 m	1.68 m
13b	1.57 m	1.46 m	1.48 m	1.60 m	1.39 m	1.52 m
14α	2.14 ddd (15, 11, 4.5)	2.13 ddd (15, 11.5, 3)	2.15 ddd (15, 11.5, 3)	1.93 ddd (15, 11, 4.5)	2.06 ddd (15, 11.5, 3)	2.23 ddd (15, 11.5, 3)
14β	0.92 dddd (15, 11, 7, 2)	0.97 ddd (15, 12, 7)	0.97 ddd (15, 12, 7)	0.88 dddd (15, 11, 7, 2)	0.86 br ddd (15, 12, 7)	1.12 m
15α	3.61 br t (2)	3.63 br t (2)	3.63 br t (2)	3.70 br t (2)	3.58 br t (2)	5.13 br t(2)
17z	5.10 t (1.5)	5.10 t (1.5)	5.10 t (1.5)	5.10 t (1.5)	5.07 t (1.5)	5.04 t (1.5)
17e	5.04 t (1.5)	5.04 t (1.5)	5.04 t (1.5)	5.04 t (1.5)	5.01 t (1.5)	4.91 t (1.5)
18	1.07 s	1.15 s	1.11 s	0.84 s	0.78 s	1.14 s
19a	7.43 br s			3.82 d (2.5)	2.45 br d (11)	
19b				3.82 d (2.5)	2.20 dd (11, 2.5)	
20a	3.92 dt (19, 2)	3.72 dd (13, 1.5)	3.76 dd (13, 1.5)	7.88 dd (4.5, 2.5)	2.77 br d (11)	3.77 d (14)
20b	3.42 dd (19, 3)	3.12 br d (13)	3.09 d (13)		2.57 dd (11, 2.5)	3.13 d (14)
21a		3.58 ddd (14.5, 6, 4.5, 3.6)	3.76 ddd (14.5, 6, 4.5)		2.45 m	3.78 ddd (14.5, 6, 4.5)
21b		3.51 ddd (14.5, 7, 4.5, 3.7)	3.44 ddd (14.5, 7, 4.5)		2, 45 m	3.46 ddd (14.5, 7, 4.5)
22a		3.83 ddd (11.5, 6, 4.5, 3.6)	4.31 ddd (11.5, 6, 4.5)		3.62 t (5.5)	4.34 ddd (11.5, 6, 4.5)
22b		3.79 ddd (11.5, 7, 4.5)	4.20 ddd (11.5, 7, 4.5)		3.62 t (5.5)	4.23 ddd (11.5, 7, 4.5)
Ac			2.02 s			2.02 s
Ac						2.13 s

[a] 500 MHz, $CDCl_3$; assignments based on COSY and HMQC. [b] Chemical shifts in ppm relative to TMS; coupling constants (J) in Hz.

Table 3. HMQC and HMBC NMR Data for Compounds **1**, **4**, and **5**[a]

	1		**4**		**5**	
H	HMQC	HMBC	HMQC	HMBC	HMQC	HMBC
1a	41.5 t	3, 5	34.2 t	5, 9, 3	40.2 t	2, 3, 5, 10
1b	41.5 t		34.2 t	5, 9, 3	40.2 t	2, 3, 20
2a	20.2 t		20.0 t	1, 3, 5	23.3 t	
2b	20.2 t		20.0 t	10	23.3 t	
3a	37.6 t	5	42.4 t	1, 2, 5	41.3 t	
3b	37.6 t	2, 19	42.4 t	2, 4, 5, 18, 19	41.3 t	1, 2, 4, 19
5	47.7 d	6, 7	46.9 d	4, 6, 20	49.6 d	4, 10, 6
6a	19.7 t		19.5 t		17.3 t	
6b	19.7 t	7, 10	19.5 t	7, 10	17.3 t	
7a	31.1 t	6, 8	30.9 t		31.4 t	
7b	31.1 t	5, 6	30.9 t	5, 6, 9, 14	31.4 t	6
9	38.4 d	1, 8, 14, 15, 20	38.0 d	1, 8, 10, 11, 14, 20	39.5 d	11, 20
11a	28.5 t	13	28.0 t		28.1 t	
11b	28.5 t	8, 12, 13, 16	28.0 t		28.1 t	10
12	36.3 d	9, 14, 15	35.9 d	9, 14, 15, 16, 17	36.3 d	
13a	26.3 t		26.0 t		26.2 t	
13b	26.3 t		26.0 t		26.3 t	
14α	27.2 t	7, 8, 13, 15	25.1 t	8, 13, 15	27.6 t	
14*β*	27.2 t	9, 13, 15	25.1 t	9, 13, 15	27.6 t	9
15α	77.0 d	7, 9, 14, 16, 17	75.8 d	7, 9, 12, 14, 16, 17	77.0 d	8, 9, 14, 16, 17
17z	109.7 d	12, 15, 16	109.1 d	12, 15, 16	109.8 t	12, 15, 16
17e	109.7 d	12, 15, 16	109.1 d	12, 15, 16	109.8 t	12, 15, 16
18	23.7 q	5, 3, 19	25.9 q	5, 3, 19	26.5 q	3, 4, 5, 19
19a	169.0 d	4, 18, 20	60.7 t	3, 4, 5, 18, 20	60.7 t	4, 5, 20
19b			60.7 t	3, 4, 5, 18, 20	60.7 t	3, 10, 19
20a	55.5 t	1, 9, 19	165.8 d	5, 9, 10, 19	53.9 t	5, 10, 19
20b	55.5 t	1, 5, 9, 19			53.9 t	1, 19
21a					60.2 t	
21b					60.2 t	
22a					57.9 t	21
22b					57.9 t	21

[a] Chemical shifts in ppm relative to TMS. C-multiplicities were established by DEPT experiment.

Table 4. HMQC and HMBC NMR Data for the Compounds **2**, **3**, and **6**[a]

	2		**3**		**6**	
H	HMQC	HMBC	HMQC	HMBC	HMQC	HMBC
1a	41.3 t	9	41.4 t	5, 9	41.4 t	5, 9
1b	41.3 t	5, 10	41.4 t	20	41.4 t	20
2a	20.1 t	3	20.1 t	3	20.0 t	3
2b	20.1 t		20.1 t	3	20.0 t	3
3a	39.6 t	1, 5	39.6 t	2, 4, 5	39.6 t	5
3b	39.6 t	2, 4, 19	39.6 t	2, 4, 5, 18, 19	39.6 t	2, 4, 19
5	50.1 d	20	50.2 d	6, 20	50.3 d	6, 20
6a	19.5 t	8	19.6 t	5	19.4 t	5
6b	19.5 t		19.6 t		19.4 t	
7a	30.9 t		31.0 t	6, 17	31.4 t	6, 17
7b	30.9 t	14	31.0 t	5, 6, 15	31.4 t	5, 6, 15
9	37.8 d	1, 12, 14, 15, 20	38.0 d	11, 15, 20	39.1 d	1, 14, 15, 20
11a	28.9 t		28.9 t		28.8 t	
11b	28.9 t	16	28.9 t	3, 8, 16	28.8 t	16
12	35.9 d	15, 14	36.0 d	14, 15	35.9 d	9, 15, 14
13a	26.4 t	8	26.4 t	11	26.2 t	
13b	26.4 t	16	26.4 t	11, 16	26.2 t	16
14α	27.2 t		27.2 t	15	26.9 t	15
14*β*	27.2 t	9, 13, 15	27.2 t	9, 13, 15	26.9 t	9, 13, 15
15α	76.7 d	7, 9, 14, 16, 17	76.7 d	16, 17	76.7 d	7, 9, 14, 16, 17,CO (171.1)
17z	110.1 t	12, 15, 16	111.0 t	15, 16	111.1 t	12, 15
17e	110.1 t	12, 15, 16	111.0 t	15	111.1 t	2, 15, 16
18	23.0 q	4, 5, 19	23.1 q	4, 5, 19	23.1 q	4, 5, 19
20a	54.4 t	1, 10, 19	54.3 t	19	54.3 t	1, 10, 19
20b	54.4 t	1, 5, 10, 19	54.3 t	19	54.3 t	1, 5, 10, 19, 21
21a	50.8 t		46.4 t	19	46.4 t	19, 20, 22
21b	50.8 t		46.4 t	19	46.4 t	19, 20, 22
22a	61.7 t		62.4 t	CO (170.7)	62.4 t	21, CO (170.7)
22b	61.7 t		62.4 t	CO (170.7)	62.4 t	21, CO (170.7)
Ac			20.8 q		20.8 q	
Ac					21.2 q	

[a] Chemical shifts in ppm relative to TMS. C-multiplicities were established by DEPT experiment.

Plant Material. *Delphinium staphysagria* L. was collected in the spring (1985) outside Tetuán City, Morocco, by Dr. Julián Molero Briones, Botany Department, Faculty of Pharmacy, Universidad de Barcelona, where a voucher specimen (BC 808403) has been deposited.

Extraction and Isolation. Air-dried and powdered plant

material (aerial parts, 2.9 kg) were extracted with 80% EtOH in a Soxhlet. After removing the solvent under vacuum, the ethanolic extract was treated with 0.5 M H_2SO_4 and filtered. The acidic solution was extracted with $CHCl_3$ to give a crude material (7.5 g). This was adsorbed on 12 g of neutral alumina and subjected to flash chromatography over 110 g of the same adsorbent. Elution with hexane (3 L), hexane−EtOAc (1:1) (3 L), and MeOH (2 L) gave 1.2, 3.5, and 1.95 g in the respective eluates. The material eluted with hexane gave a gummy residue, which contained no alkaloid. Crystallization of the material eluted with hexane−EtOAc (1:1) gave pure delphinine[7] (2.6 g), which was the major alkaloid isolated. The fraction eluted with MeOH (1.95 g) afforded atisonium chloride **7**[8] (1.3 g) after crystallization from EtOAc−MeOH (9:1). The acid aqueous phase was neutralized to pH 7 and extracted with $CHCl_3$ to give a crude material (9.5 g). Chromatography of this residue on alumina, using gradient elution with hexane−EtOAc, followed by further purification over Sephadex LH-20 (hexane−$CHCl_3$−MeOH, 2:1:1) when necessary, allowed the isolation, in order of increasing polarity, of delphinine (17 mg), bullatine C (14-acetylneoline)[7] (1.3 g), chasmanine[9] (300 mg), 14-acetylchasmanine[9] (450 mg), and neoline[7] (525 mg). The neutral aqueous phase was basified with 20% NaOH to pH 12 and extracted with $CHCl_3$ to give a crude alkaloidal material (6.4 g). This residue was chromatographed over Al_2O_3 and eluted with hexane−EtOAc (1:1) (3 L), EtOAc (2.5 L), and MeOH (2 L) to give three fractions: F_1 (2.3 g), F_2 (1.8 g), and F_3 (2.2 g). Repeated chromatography of the residue (2.3 g) obtained from hexane−EtOAc (1:1) over Sephadex LH-20 (hexane−MeOH−$CHCl_3$, 2:1:1) furnished 93 mg of 19-oxodihydroatisine (**2**), 5 mg of 22-*O*-acetyl-19-oxodihydroatisine (**3**), and 76 mg of **5**.[4] Fraction F_2, after crystallization (EtOAc−MeOH, 9:1) yielded 0.8 g of pure **4**.[4] The mother liquors, after separation of azitine, were rechromatographed on alumina preparative plates (hexane−EtOAc, 2:1, twice). Two bands were cut. The lower zone was extracted with EtOAc to give 7 mg of isoazitine (**1**). The upper band gave 40 mg of **4**.[4] Fraction F_3 was a very polar mixture that was not investigated further. Known alkaloids were identified by comparison of mp and spectral data (IR, MS, ^{1}H and ^{13}C NMR) with literature values.

Isoazitine (1): resin; $[\alpha]^{25}_D$ −6.7° (*c* 0.63, $CHCl_3$); IR ν^{NaCl}_{max} 3376, 2931, 2866, 1711, 1650, 1459, 1447, 1076, 1057, 910, 731 cm^{-1}; ^{1}H and ^{13}C NMR (Tables 1 and 2); EIMS *m*/*z* 299 $[M]^+$ (100), 284 (18), 272 (6), 256 (14), 242 (8); HREIMS *m*/*z* 299.2257 (calcd for $C_{20}H_{29}NO$, 299.2249).

19-Oxodihydroatisine (2): crystalline, mp 221−223° from $CHCl_3$; $[\alpha]^{25}_D$ −31.2° (*c* 0.57, $CHCl_3$); IR ν^{NaCl}_{max} 3373, 2931, 2865, 1619, 1445, 1054, 900, 752 cm^{-1}; ^{1}H and ^{13}C NMR (Tables 1 and 2); EIMS *m*/*z* 394 $[M]^+$ (52), 344 (18), 322 (100), 315 (78), 300 (15); HREIMS *m*/*z* 359.2463 (calcd for $C_{22}H_{33}NO_3$, 359.2460).

Acetylation of 2. Compound **2** (22 mg) was acetylated using 0.5 mL of Ac_2O and 3 drops of pyridine and stirring the solution at room temperature for 6 h. Workup by pouring into cold H_2O, extraction with $CHCl_3$, drying ($MgSO_4$), and removal of solvent gave 19 mg of acetylated product. Column chromatography (neutral Al_2O_3) using hexane−EtOAc (6:2) as eluent led to the isolation of 9 mg of **6** and 2.5 mg of **3**. Compound **3** was identical (TLC, EIMS, ^{1}H, and ^{13}C NMR) with 22-*O*-acetyl-19-oxodihydroatisine also isolated from this plant.

22-*O*-Acetyl-19-oxodihydroatisine (3): gum; $[\alpha]^{25}_D$ −35.18° (*c* 0.54, $CHCl_3$); IR ν^{NaCl}_{max} 3421, 2931, 2866, 2360, 1740, 1625, 1230, 1050 753 cm^{-1}; ^{1}H and ^{13}C NMR (Tables 1 and 2); EIMS *m*/*z* 401 $[M]^+$ (37), 359 (9), 358 (24), 341 (100), 328 (47), 315 (21); HREIMS *m*/*z* 401.2572 (calcd for $C_{24}H_{35}NO_4$, 401.2566).

15,22-*O*-Diacetyl-19-oxodihydroatisine (6): gum; $[\alpha]^{25}_D$ −68.75° (c 0.40, $CHCl_3$); IR ν^{NaCl}_{max} 2932, 2868, 1739, 1638, 1234, 1045, 754 cm^{-1}; ^{1}H and ^{13}C NMR (Tables 1 and 2); EIMS *m*/*z* 443 $[M]^+$ (46), 401 (16), 400 (28), 383 (100), 370 (45), 357 (20), 340 (25); HREIMS *m*/*z* 443. 2646 (calcd for $C_{26}H_{37}NO_5$, 443.2671).

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