Iodanthine, a Pyrrolizidine Alkaloid from *Senecio iodanthus* and *Senecio bracteatus*§

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A phytochemical study of *Senecio iodanthus* and *Senecio bracteatus* afforded the new pyrrolizidine alkaloid iodanthine (**3**) in addition to the four known alkaloids retroisosenine (**1**), bulgarsenine (**2**), mulgediifoliine (**4**), and (12*S*)-12-hydroxyretroisosenine (**6**). The structure and absolute stereochemistry of the new compound (**3**) were determined by its spectral properties and confirmed by an X-ray diffraction analysis.

It is well documented that plants containing pyrrolizidine alkaloids (PAs) are toxic to humans and livestock.[1,2] Many of these compounds are mutagenic, cytotoxic, and genotoxic.[3,4] Inasmuch as Mexico is a diversification center of the genus *Senecio* (Asteraceae) whose main secondary metabolites are PAs, we started, in 1995, a systematic search for PAs in the section *Mulgediifolii*, constituted by 15 species, most of which are indigenous to Mexico.[5] As a result of these studies, five new 13-membered macrocyclic PAs[6−8] can be added to the original group of four of these alkaloids. Now, in continuation of these studies, we report the structure elucidation of a new 13-membered macrocyclic PA (**3**) isolated from *Senecio iodanthus* Greenm. and *Senecio bracteatus* Klatt, in addition to four known alkaloids.

The aerial parts of *S. iodanthus* afforded the known PAs retroisosenine and its hydrochloride (**1** and **1**·HCl),[7] bulgarsenine hydrochloride (**2**·HCl),[8] mulgediifoline hydrochloride (**4**·HCl), and the new PA iodanthine as its hydrochloride (**3**·HCl). Compounds **1**, **1**·HCl, and **2**·HCl were identified by comparison with authentic samples. The downfield chemical shifts for H-3, H-5, and H-8 of **4**·HCl (Table 1) suggested it was present as a hydrochloride; this was confirmed by its conversion into mulgediifoline (**4**)[6] after a treatment with aqueous NaOH. The fact that some of the PAs were isolated as hydrochlorides could be explained by use of CH_2Cl_2 and $CHCl_3$, which are known to produce these artifacts.[8]

Compound **3**·HCl had a MS very similar to that of **2**·HCl.[8] Its IR spectrum showed bands of alcohol and ester functions (3502 and 1728 cm^{-1}), as well as characteristic bands for a hydrochloride at 2291 and 850 cm^{-1}. The ^1H NMR spectrum of **3**·HCl (Table 1) resembles that of **2**·HCl,[8] with different chemical shifts for the H-7, H-9a, H-9b, H-14a, and H-14b signals. The last two hydrogens were significantly affected by their proximity to the alcohol function. Similar variations were observed in its ^{13}C NMR spectrum (Table 2), and therefore it was inferred that iodanthine (**3**) is a stereoisomer of bulgarsenine (**2**).

Saponification of **3**·HCl afforded a necine and a mixture of two necic acids. The ^1H NMR spectrum of the mixture showed that the acids were tetrahydrofuran derivatives that did not correspond either to nemorensic or to *cis*-nemorensic acid.[6] The necine was platynecine, identified as its hydrochloride, because its ^1H NMR spectrum showed the signals of H-3, H-5, and H-8 shifted to downfield.[6] Therefore, iodanthine (**3**) differs from bulgarsenine (**2**) in the acid moiety.

NOESY experiments of iodanthine (**3**) and iodanthine hydrochloride (**3**·HCl) showed a NOE effect between H-16 and Me-24, indicating a *Z* configuration of the double bond, as found in bulgarsenine (**2**).[9] This led us to suppose that the difference between **2** and **3** was the stereochemistry at C-12 and/or C-13. The absolute configuration of **3**·HCl was determined by X-ray diffraction analysis (Figure 1). The configurations of C-12 and C-13 (*S*, *S*) were opposite those of bulgarsenine (**2**, 12*R*, 13*R*).

A comparison between the X-ray analysis of iodanthine hydrochloride (**3**·HCl) and that reported in the literature[9] for bulgarsenine bitartrate shows, besides the differences in the bond distances for C-2, C-3, and C-11, C-12, an overall similarity of their bond lengths and angles. Figure 1 shows the opposite stereochemistry at the asymmetric centers C-12 and C-13 relative to bulgarsenine, and the antiparallel disposition of the ester carbonyl groups. The Cremer and Pople parameters[10] for the five-membered rings C-1, C-2, C-3, N-4, C-8 (Q = 0.402 Å, φ = 62.9°) and N-4, C-5, C-6, C-7, C-8 (Q = 0.423 Å, φ = 274.2°) of the pyrrolizidine nucleus indicate an intermediate conformation between the envelope ^3E and twisted $^2T_3$ for the first ring and a twisted $^4T_3$ conformation for the second ring, contrary to the observed envelope E_1 (Q = 0.4147 Å, φ = 176.7°) and twisted $^4T_3$ (Q = 0.4723 Å, φ = 278.6°) conformations in bulgarsenine. The most striking difference between iodanthine hydrochloride (**3**·HCl) and bulgarsenine bitartrate was found in the conformation of the 13-membered macrocycle. While in bulgarsenine the macroring adopted a conformation rather wide and open (C-8 ... C-14, 5.041 Å), in iodanthine the conformation of this macro-ring was tight and completely extended (C-8 ... C-14, 6.060 Å) (Figure 2). The "side chains," joined at C-1 (C-9, O-10, C-11, O-19, C-12) and C-7 (O-18, C-17, O-20, C-16, C-15, C-14), are almost planar and run nearly parallel to each other (angle between planes 8.7°), causing the appearance of several short transannular contacts not observed in the structure of bulgarsenine.

Based on NOESY experiments, the conformations of **2**·HCl, **3**, and **3**·HCl in solution, can be similar to those shown in Figures 1 and 2. Thus, if we consider the X-ray structure of **3**·HCl, the NOE effect observed between H-16 and H-9a

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Table 1. ^{1}H-NMR Spectral Data of Compounds **3**, **3**·HCl, **4**·HCl, and **5**·Cl (300 MHz, $CDCl_3$)[a]

position	**3**[b]	**3**·HCl	**4**·HCl	**5**·Cl[c]
1	2.66 m	3.02 m	2.95 m	
2a	2.35 m	2.64 m	2.54 m	6.06 br s
2b	1.76 br ddd (13.5, 9.5, 5.5)	1.95 m	2.10 m	
3a	2.76 m	3.79 m	3.95 ddd (11.7, 10.5, 7.8)	4.99 br d (17.1)
3b	2.76 m	2.92 td (11.0, 5.7)	3.22 ddd (11.7, 9.3, 2.7)	4.67 br d (17.1)
5a	2.87 m	3.88 br t (7.7)	4.10 ddd (11.4, 8.7, 1.5)	4.60 ddd (12.3, 7.2, 5.1)
5b	2.87 m	3.07 m	3.12 ddd (11.7, 11.7, 6.6)	4.1 ddd (12.3, 9.3, 6)
6a	2.35 m	2.53 m	2.3 m	2.99 m
6b	2.79 dddd (14.0, 6.0, 4.0, 1.5)	2.22 dd (14.1, 5.7)	2.3 m	2.45 br ddt (15.6, 5.1, 4.5)
7	5.79 ddd (4.5, 4.0, 1.5)	5.98 br s	5.62 br t (3.0)	5.68 m
8	3.36 dd (7.5, 4.0)	4.48 dd (8.6, 4.7)	4.29 dd (8.1, 3.6)	5.67 m
9a	4.01 dd (11.5, 5.0)	4.13 dd (11.7, 5.4)	4.57 dd (12.9, 4.5)	5.6 d (12.6)
9b	3.95 t (11.5)	3.97 t (11.7)	4.13 br d (13.5)	4.35 d (12.6)
13	2.46 dqd (12.5, 7.0, 2.0)	2.44 dqd (11.8, 6.8, 2.5)	2.44 m	2.29 m
14a	3.89 br t (13.0)	3.77 dd (13.4, 12.2)	2.17 m	2.02 d (9.3)
14b	1.70 dd (13.0, 2.0)	1.72 br d (13.8)	2.17 m	2.02 d (9.3)
16a	5.67 br s	5.60 s	2.76 d (12.9)	2.66 d (12.9)
16b			2.69 d (12.6)	2.57 d (12.9)
21	1.31 s	1.29 s	1.47 s	1.40 s
23	1.09 d (7.0)	1.06 d (6.9)	0.98 d (7.2)	1.04 d (6.9)
24	1.89 d (1.0)	1.88 s	1.41 s	1.37 s

[a] Assignments are based on COSY, long-range HETCOR, COLOC, HMQC and HMBC experiments. [b] Run at 500 MHz. [c] CH_2Cl AB system δ: 6.19 d and 6.03, J = 9.6 Hz.

Table 2. ^{13}C NMR Spectral Data of Compounds **3**, **3**·HCl, **4**·HCl, and **5**·Cl (75 MHz, $CDCl_3$)[a]

carbon	**3**[b]	**3**·HCl	**4**·HCl	**5**·Cl[c]
1	36.1 d	36.6 d	38.5 d	132.3 s
2	32.9 t	31.9 t	27.0 t	128.1 d
3	52.2 t	53.1 t	54.9 t	62.8 t
5	49.9 t	51.0 t	53.6 t	69.8 t
6	37.0 t	36.0 t	34.9 t	32.5 t
7	71.7 d	71.1 d	72.2 d	73.0 d
8	70.3 d	69.8 d	71.2 d	86.1 d
9	66.6 t	64.8 t	59.9 t	58.9 t
11	176.7 s	176.3 s	173.0 s	169.0 s
12	75.8 s	75.8 s	87.5 s	86.8 s
13	39.3 d	39.6 d	43.9 d	44.5 d
14	36.0 t	36.2 t	46.2 t	46.3 t
15	160.0 s	162.4 s	81.2 s	81.7 s
16	117.5 d	115.9 d	47.0 t	47.0 t
17	168.2 s	166.8 s	168.0 s	172.2 s
21	26.2 q	26.2 q	25.3 q	24.7 q
23	16.4 q	16.3 q	14.4 q	14.2 q
24	25.3 q	25.4 q	30.8 q	30.4 q

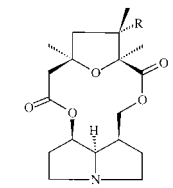
[a] Assignments are based on DEPT, long-range HETCOR, COLOC, HMQC and HMBC experiments. [b] Run at 125 MHz. [c] CH_2Cl δ: 70.30 t.

for **3** and **3**·HCl could be explained assuming that C-16 and C-9 are directed inward toward the macro-ring. This NOE effect was not observed for **2**·HCl, because its C-9 is directed downward from the macro-ring and very distant from C-16, as shown in Figure 2.

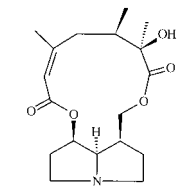
Bulgarsenine bitartrate has the macro-ring semi-folded toward the pyrrolizidine nucleus (Figure 2). A similar conformation should be adopted by **2**·HCl, because NOE effects between H-14b and H-2b and between Me-23 and Me-24 were observed. These NOE effects were not observed for the new alkaloid (**3**·HCl), because the macro-ring is unfolded; the C-13 configuration is opposite to that of bulgarsenine, and the Me-23 and Me-24 have an anti orientation.

The H-8α signal exhibited a NOE effect with H-2a and H-6a, and a weak effect with H-3 and H-5, suggesting an equilibrium between the twisted $^2T_3$–$^4T_3$ and $^3T_2$–$^2T_4$ conformations of the pyrrolizidine nucleus of free iodanthine (**3**).

A phytochemical study of *S. bracteatus* collected in 1995, afforded the new alkaloid iodanthine as hydrochloride (**3**·HCl) and the known compounds retroisosenine (**1**), its hydrochloride (**1**·HCl), and mulgediifoline as hydrochloride (**4**·HCl). The alkaloids **1**, **1**·HCl, **2**, **3**, **4**, *N*-chloromethyl-retroisosenine chloride (**5**·Cl), and (12*S*)-12-hydroxyretro-isosenine (**6**)[7] were isolated from collection from 1997, of the same species. The structure of **5**·Cl was established by an analysis of the spectral data (Tables 1 and 2), including 2D NMR techniques. The presence of a Cl^- ion was supported by the *m*/*z* 35 and 37 fragments observed in negative ion FABMS of **5**·Cl. A similar artifact was described from *Senecio callosus*.[8]



1 R= H Δ1,2
4 R=H
6 R=OH Δ1,2



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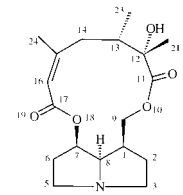
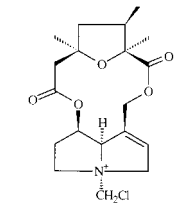


3



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Experimental Section

General Experimental Procedures. Melting points were determined on a Fisher–Johns melting point apparatus and are uncorrected. Optical rotations were determined on a JASCO DIP-360 digital polarimeter. IR spectra were recorded on a Nicolet Magna-IR 750 spectrometer. ^{1}H NMR and ^{13}C NMR data were obtained on Varian Unity Plus 500 and Varian Unity 300 instruments. Chemical shifts were referred to TMS (δ 0). Standard Varian programs were used for COSY and NOESY spectra at 300 and 500 MHz. HETCOR and HMQC experiments were obtained for $^1J_{CH}$ = 140 Hz at 75 and 500 MHz, respectively. LR–HETCOR and HMBC experiments were obtained for $^nJ_{CH}$ = 9 Hz at 75 and 500 MHz, respectively. EIMS data were determined on a JEOL JMS-AX505HA mass

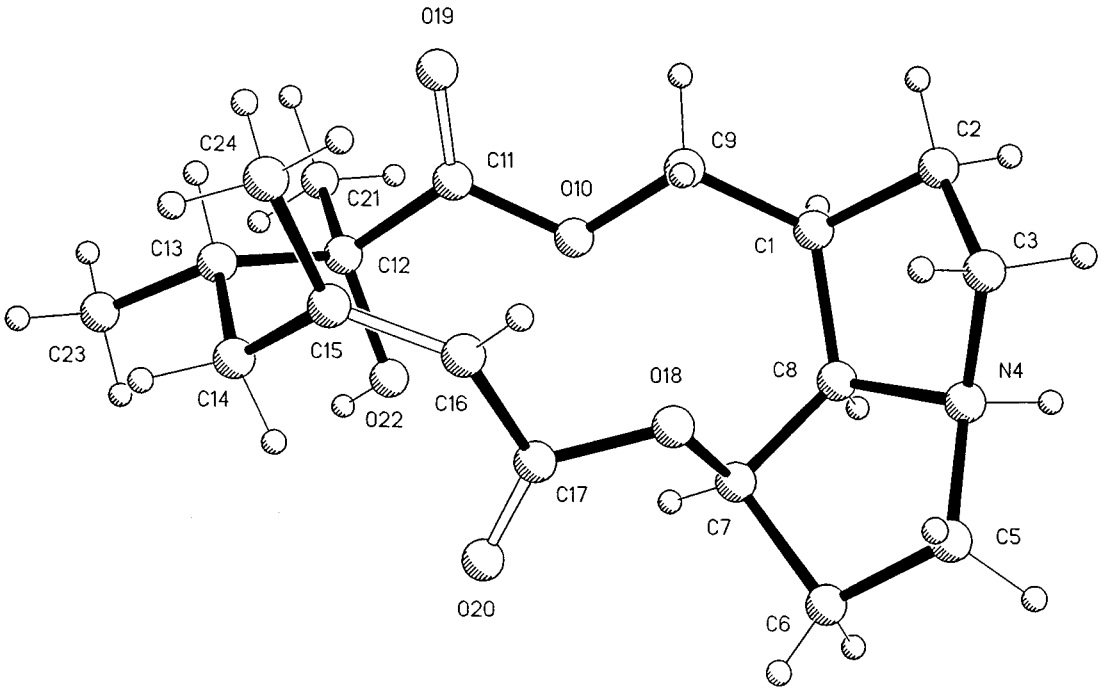

Figure 1. ORTEP projection of **3**·HCl (crystallographic numbering).

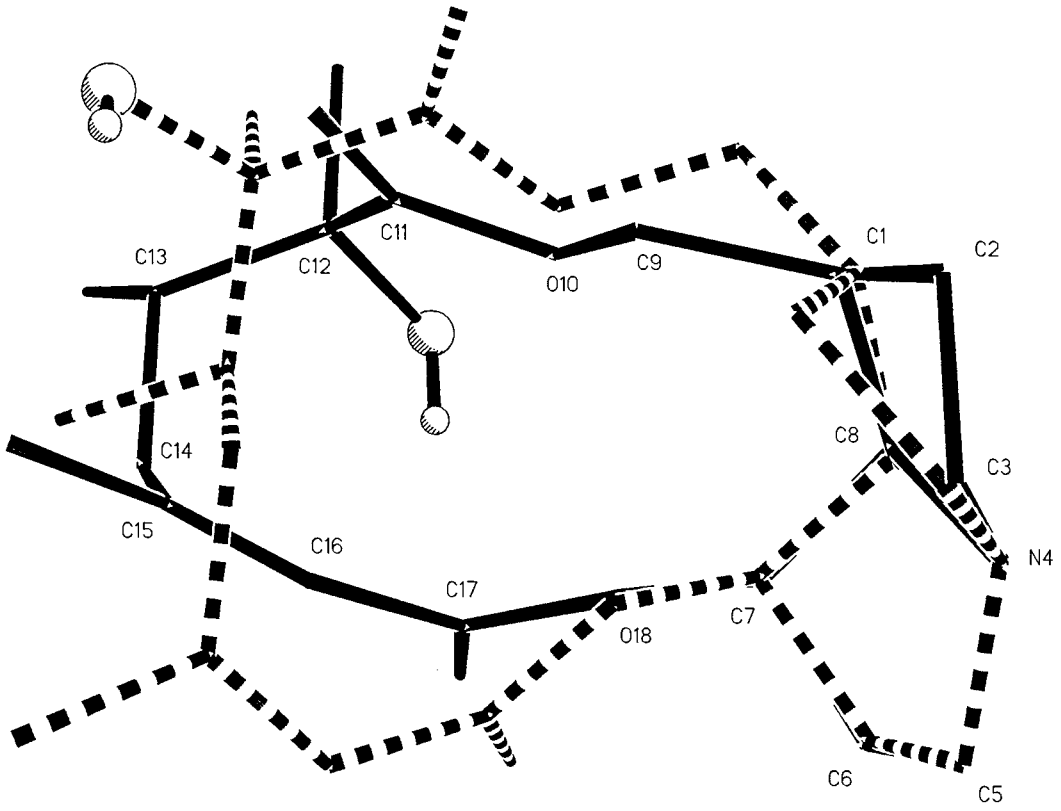

Figure 2. Dashed line corresponds to bulgarsenine bitartrate.[9] Straight line corresponds to **3**·HCl.

spectrometer at 70 eV. FABMS were obtained on a JEOL JMS−SX102A mass spectrometer operated with an acceleration voltage of 10 kV. Samples were desorbed from a nitrobenzyl alcohol matrix using 6 keV xenon atoms. HRFABMS measurements were performed at 10 000 resolution using electric field scans and poly(ethylene glycol) ion (Fluka 200 and 300), as the reference material. Column chromatography was carried out on Kieselgel G (Merck, Darmstadt, Germany). TLC was performed on Si gel 60 F_{254} plates (Merck).

Plant Material. *S. iodanthus* Greenm. was collected in Nevado de Toluca, State of Mexico, Mexico, in October 1995 (MEXU 525953). *S. bracteatus* Klatt was collected in Santiago de Juxtlahuaca, Oaxaca, Mexico, in November 1995 (MEXU 860891), and in Miahuatlan, Oaxaca, Mexico, in June 1997 (MEXU 861025). Voucher specimens are deposited at the Herbarium del Instituto de Biología, UNAM.

Extraction and Isolation. Dried and ground aerial parts (403 g) of *S. iodanthus* were extracted with MeOH. The extract was concentrated, acidified with 2.5% aqueous H_2SO_4 (to pH 1), stirred overnight with Zn powder (40.3 g), and filtered. The filtrate was washed with CH_2Cl_2, basified with NH_4OH (to pH 10), and extracted with CH_2Cl_2 until negative to Dragendorff

solution. Elimination of the solvent afforded 5.14 g of alkaloidal extract that, after repeated column chromatographies using CH_2Cl_2−MeOH (19:1) as eluent, gave 212 mg of retroisosenine (**1**), 15 mg of retroisosenine hydrochloride (**1**·HCl), 237 mg of bulgarsenine hydrochloride (**2**·HCl), 34.4 mg of iodanthine hydrochloride (**3**·HCl), and 48.8 mg of mulgediifoline hydrochloride (**4**·HCl).

Dried and ground roots of *S. bracteatus* (179 g), collected in 1995, were extracted with MeOH. The extract, when worked up as described above for *S. iodanthus*, afforded 5.03 g of alkaloidal residue, which, after purification by column chromatography using CH_2Cl_2−MeOH (19:1) as eluent, yielded 1.32 g of **1** and 22.3 mg of **3**·HCl.

Dried and ground aerial parts of *S. bracteatus* (270 g) collected in 1995, were extracted with MeOH. The extract worked up as described above, afforded 3.85 g of alkaloidal residue, which, after purification by consecutive column chromatographies using CH_2Cl_2−MeOH mixtures as eluent, gave 314.4 mg of **1**, 41.5 mg of **1**·HCl, and 22.2 mg of **4**·HCl.

Dried and ground roots of *S. bracteatus* (200 g), collected in 1997, were extracted with MeOH. The extract was worked up as described above for *S. iodanthus*, except for the use of a $CHCl_3$−hexane (1:1) mixture instead of CH_2Cl_2 and afforded 5.2 g of alkaloidal residue. This was purified by column chromatography using $CHCl_3$−hexane−MeOH (9:9:2 and 2:2:1) as eluent. Fractions eluted with $CHCl_3$−hexane−MeOH (9:9:2) gave 1.23 g of **1**. Fractions eluted with $CHCl_3$−hexane−MeOH (2:2:1) were submitted to successive column chromatographies using Me_2CO−MeOH (9:1) and $CHCl_3$−MeOH (9:1) as eluents, to yield a 1:6 mixture (90 mg) of **2** and **3**, 250 mg of **4**, and 205 mg of (12*S*)-12-hydroxyretroisosenine (**6**).

Dried and ground aerial parts of *S. bracteatus* (525 g), collected in 1997, were treated as described above to yield 16.8 g of alkaloidal extract. Purification by column chromatography using CH_2Cl_2−MeOH gradients as eluent, afforded 9.6 g of **1**, 170 mg of **1**·HCl, and 930 mg of *N*-chloromethylretroisosenine chloride (**5**·Cl) from the fractions eluted with CH_2Cl_2−MeOH (19:1). Fractions eluted with CH_2Cl_2−MeOH (9:1) were combined and purified by column chromatography eluted with $CHCl_3$−MeOH (9:1) to give 490 mg of **4** and 170 mg of **6**. Compounds **1**, **1**·HCl, **2**·HCl, and **6** were identified by comparison with authentic samples.[6−8]

Iodanthine hydrochloride (3·HCl): white crystals from hexane−EtOAc; mp 217−220 °C; $[\alpha]^{25}_D$ −103.33° (*c* 2.1, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3502, 2291, 1728, 1639, 1139, 850 cm^{-1}; ^1H NMR data, see Table 1; ^{13}C NMR data, see Table 2; EIMS *m/z* 337 $[M]^+$ (30), 211 (50), 140 (100), 138 (55), 122 (75), 96 (82), 55 (23), 43 (22); HRFABMS *m/z* found $[M + 1]^+$ 338.1976 ($C_{18}H_{28}O_5N$ requires 338.1967).

A solution of **3**·HCl (20 mg) in CH_2Cl_2 (5 mL) was washed with aqueous NaOH (0.5 N, 3 × 2 mL), dried over Na_2SO_4, and concentrated to yield **3** (17 mg) as an oil; $[\alpha]^{25}_D$ −64.8° (*c* 2.5, $CHCl_3$); UV (EtOH) λ_{max} (log ϵ) 221 (4.07) nm; IR (KBr) ν_{max} 3428, 1728, 1643, 1254, 1143 cm^{-1}; ^1H NMR data, see Table 1; ^{13}C NMR data, see Table 2.

Mulgediifoline hydrochloride (4·HCl): white crystals from EtOAc; mp 227−231 °C; $[\alpha]^{25}_D$ −26.19° (*c* 2.1, $CHCl_3$); IR ($CHCl_3$) ν_{max} 2316, 1739, 1602, 1139, 859 cm^{-1}; ^1H NMR data, see Table 1; ^{13}C NMR data, see Table 2.

A solution of **4**·HCl (18 mg) in CH_2Cl_2 (5 mL) was treated in a manner similar to that described for **3**·HCl, yielding free mulgediifoline (**4**), which was identified by comparison with an authentic sample.[6]

***N*-Chloromethylretroisosenine chloride (5·Cl):** white powder from EtOAc; mp 138−140 °C dec; $[\alpha]^{25}_D$ +51.43° (*c* 0.21, MeOH); IR ($CHCl_3$) ν_{max} 3347, 1741, 1602 cm^{-1}; ^1H NMR data, see Table 1; ^{13}C NMR data, see Table 2; HRFABMS *m/z* found $[M]^+$ 384.1581 ($C_{19}H_{27}O_5NCl$ requires 384.1578).

Saponification of Iodanthine Hydrochloride (3·HCl). A mixture of **3**·HCl (27.8 mg) and KOH (66.1 mg) in MeOH (4 mL) was refluxed for 3 h. The solvent was evaporated to dryness under reduced pressure, and the residue was extracted with hot $CHCl_3$ (5 × 3 mL). Evaporation of the solvent gave 14.2 mg of platynecine hydrochloride[6] as a brown oil: ^1H NMR (MeOH-d_4, 300 MHz) δ 2.52 (1H, ddt, J = 19.5, 7.2, 5.7 Hz, H-1), 2.11 (1H, tdd, J = 12, 10.2, 9 Hz, H-2a), 1.87 (1H, dtd, J = 11.7, 7.2, 2.4 Hz, H-2b), 3.33 (1H, m, H-3a), 3.06 (1H, ddd, J = 12.9, 2.4 Hz, H-3b), 3.52 (1H, ddd, J = 10.2, 5.4, 2.7 Hz, H-5a), 3.09 (1H, td, J = 10.4, 8.5 Hz, H-5b), 1.97 (2H, m, H-6a, H-6b), 4.39 (1H, m, H-7), 3.62 (1H, dd, J = 8.1, 3.2 Hz, H-8), 3.98 (1H, dd, J = 10.8, 6.3 Hz, H-9a), 3.93 (1H, dd, J = 10.8, 5.4 Hz, H-9b); ^{13}C NMR (MeOH-d_4, 75 MHz) δ 44.73 (d, C-1), 28.85 (t, C-2), 56.58 (t, C-3), 55.12 (t, C-5), 37.20 (t, C-6), 72.63 (d, C-7), 73.63 (d, C-8), 61.20 (t, C-9).

The basic residue was dissolved in 2.5% aqueous H_2SO_4 and extracted with ether (10 × 5 mL). The solution was dried with Na_2SO_4 and evaporated to give a 2:1 mixture of two tetrahydrofuran diacid derivatives (11 mg): IR (film) ν_{max} 3188, 1713, 1380, 1123 cm^{-1}; ^1H NMR (MeOH-d_4, 300 MHz) δ 2.68 (1H, dquint, J = 12.3, 6.6 Hz, H-3), 2.66 (1H, m, H-3′), 2.07 (1H, dd, J = 12.3, 6.9 Hz, H-4a), 2.25 (1H, dd, J = 12.3, 6.9 Hz, H-4′a), 1.92 (1H, t, J = 12.3 Hz, H-4b), 1.68 (1H, t, J = 12.3 Hz, H-4′b), 2.62 (1H, d, J = 14.6 Hz, H-6a), 2.60 (1H, d, J = 14 Hz, H-6′a), 2.54 (1H, d, J = 14.6 Hz, H-6b), 2.47 (1H, d, J = 14 Hz, H-6′b), 1.33 (3H, s, H-8), 1.40 (3H, s, H-8′), 1.11 (3H, d, J = 7.2 Hz, H-9), 1.12 (3H, d, J = 6.9 Hz, H-9′), 1.24 (3H, s, H-10), 1.28 (3H, s, H-10′); EIMS *m/z* 217 $[M + 1]^+$ (0.7), 171 (100), 157 (36), 125 (47), 111 (21), 107 (10), 83 (14), 72 (20), 69 (21), 55 (10), 43 (95), 41 (16).

X-ray Diffraction Structure Determination for 3·HCl.[11] Crystal data: $C_{18}H_{28}ClNO_5$; crystal size (mm), 0.48 × 0.10 × 0.08; crystal system, orthorhombic; space group, $P2_12_12_1$; unit cell dimensions, a = 7.281(1) Å, b = 13.608(1) Å, c = 19.550(1) Å; volume, 1937.0(3) Å; Z = 4; formula weight, 373.86; density (calcd), 1.282 Mg/m^3; absorption coefficient, 1.976 mm^{-1}; F(000), 800.

Data Collection. Diffractometer used, Siemens P4/PC; radiation, Cu Kα (λ = 1.54178 Å, temperature (K), 293(2); monochromator, graphite crystal; θ range, 1.54 to 56.74°; scan type, θ: 2θ; scan range (ω), 1.4°; background measurement, stationary counter at beginning and end of scan, scan for 50.0% of total scan time; standard reflections; index range, $0 \le h \le 7$, $0 \le k \le 14$, $0 \le l \le 21$ plus Friedel pairs; independent reflections, 2581; empirical absorption corrections (PSI−SCAN).

Solution Refinement. System used, SHELXL-97; solution, direct methods SIR92; refinement method, full-matrix least-squares on F^2; quantity minimized, $\sum\omega(F_o^2 - F_c^2)^2$; absolute structure parameter, −0.04(4); extinction correction, 0.0098(7); hydrogen atoms, riding model, fixed isotropic $U = 1.2U_{eq}$ parent atom; weighting scheme, $\omega^{-1} = \sigma^2(F_o^2) + (0.0603P)^2 + 0.2099P$ where $P = (F_o^2 - 2F_c^2)/3$; number of parameters refined 233; final R indices (observed data), R_1 = 5.13%, ωR_2 = 12.45%; R indices (all data), R_1 = 6.30%, ωR_2 = 13.25%; goodness-of-fit on F^2, 1.042; largest and mean Δ/σ, 0.004, 0.001; data-to-parameter ratio, 11.07; largest difference peak, 0.16 e $Å^{-3}$; largest difference hole, 0.21 e $Å^{-3}$.

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Supporting Information Available: Tables of atomic coordinates, bond lengths, bond angles for **3**·HCl and torsion angles in the 13-membered macrocycle for bulgarsenine bitartrate and **3**·HCl and short transannular distances for **3**·HCl. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Glowaz, S. L.; Michnika, M.; Huxtable, R. J. *Toxicol. Appl. Pharmcol.* **1992**, *115*, 168−173.
(2) Noble, J. W.; Crossley, J. B.; Hill, B. D.; Pierce, R. J.; McKenzie, R. A.; Debritz, M.; Morley, A. A. *Aust. Vet. J.* **1994**, *71*, 196−200
(3) Roeder, E. *Pharmazie* **1995**, *50*, 83−98.
(4) Mattocks, A. R. *Chemistry and Toxicology of Pyrrolizidine Alkaloids*; Academic: London, 1986.
(5) Villaseñor, J. L. The Systematics of Senecio Section *Mulgediifolii* (Asteraceae: Senecioneae). Ph.D. Dissertation, The Claremont Graduate School, Claremont, CA, 1991.

(6) Romo de Vivar, A.; Pérez, A.-L.; Arciniegas, A.; Vidales, P.; Gaviño, R.; Villaseñor, J. L. *Tetrahedron* **1995**, *51*, 12521−12528.
(7) Pérez-Castorena, A.-L.; Arciniegas A.; Castro, A.; Villaseñor, J. L.; Toscano, R. A.; Romo de Vivar, A. *J. Nat. Prod*. **1997**, *60*, 1322−1325.
(8) Pérez-Castorena, A.-L.; Arciniegas A.; Pérez, A. R.; Villaseñor, J. L.; Romo de Vivar, A. *J. Nat. Prod*. **1998**, *61*, 1288−1291.
(9) Stoeckli-Evans, H. *Acta Cryst*. **1980**, *B36*, 3150−3153.
(10) Cremer, D.; Pople, J. A. *J. Am. Chem. Soc.* **1975**, *97*, 1354−1358.
(11) X-ray data for compound have been deposited in the Cambridge Crystallographic Data Centre (No. CCDC 119740). Copies of the data can be obtained free of charge on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-(0)1223-336033; E-mail: deposit@ccdc.cam.ac.uk).

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