Pyrrolizidine Alkaloids from *Senecio roseus* and *Senecio helodes*†

Ana-L. Pérez-Castorena,‡ Amira Arciniegas,‡ Agustín Castro,‡ José L. Villaseñor,§ Rubén A. Toscano,‡ and Alfonso Romo de Vivar*,‡

Instituto de Química, Universidad Nacional Autónoma de México, Circuito Exterior, Ciudad Universitaria, Coyoacán 04510, México D.F., Mexico, and Instituto de Biología, Universidad Nacional Autónoma de México, Circuito Exterior, Ciudad Universitaria, Coyoacán 04510, México D.F., Mexico

Received May 2, 1997⊗

Two new 13-membered macrocyclic pyrrolizidine alkaloids, (13*R*)-13-hydroxyretroisosenine (**2b**) and (12*S*)-12-hydroxyretroisosenine (**2c**), have been isolated from *Senecio roseus* and *Senecio helodes*. Their structures were established from spectral and chemical studies including 2D NMR. The hydrochloride of retroisosenine (**2a**·HCl) was also isolated, and its absolute configuration was determined by X-ray diffraction analysis.

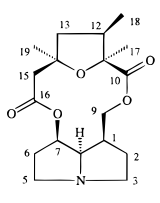
Previous work on *Senecio* species (Asteraceae) has shown the presence of pyrrolizidine alkaloids (PAs),[1,2] which exhibit hepatotoxic activity and a broad range of other pharmacological actions.[3,4] Plants containing hepatotoxic PAs are considered a health hazard for both humans and livestock. This induced us to undertake a systematic study of *Senecio* species from the section *Mulgediifolii*, which are rich in PAs.[5,6] In this paper we report the results obtained from the chemical studies on *S. roseus* Sch. Bip. and *S. helodes* Benth.

Two collections of *S. roseus* were studied. The first afforded mulgediifoline (**1**),[6] retroisosenine (**2a**),[6] and the new compounds (13*R*)-13-hydroxyretroisosenine (**2b**) and (12*S*)-12-hydroxyretroisosenine (**2c**). The second collection gave **2a**, **2b**, and **2c**, and, in addition, the hydrochloride of retroisosenine (**2a**·HCl) was obtained. The known compounds **1** and **2a** were identified by comparison with authentic samples.[6]

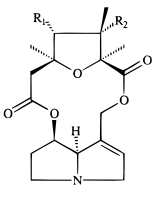
Compound **2b**, $[\alpha]^{25}_{D}$ +116.4°, exhibited in its IR spectrum bands for hydroxyl and ester groups (3495 and 1732 cm^{-1}). The HRFABMS gave a protonated molecular ion peak at *m/z* 352.1779 corresponding to the molecular formula $C_{18}H_{26}NO_6$ $[M + 1]^+$. The ^{1}H-NMR spectrum (Table 1) of **2b** was almost superimposable with that of retroisosenine (**2a**),[6] differing only in the H-12, H-13, and CH_3-19 signals. The H-13 signal was observed as a doublet at δ 4.15 indicating its *gem* relationship to one hydroxyl group. The chemical shifts of CH_3-19 and H-12 signals (δ 1.28 s and 2.08 dq), as well as the multiplicity of the latter, suggested that these groups were in vicinal positions to the alcohol function. In the ^{13}C-NMR spectrum (Table 2), the C-12 and C-13 signals showed downfield shifts ($\Delta\delta$ +5.0 and +35.9, respectively), and those of C-11, C-15, C-18, and C-19 presented upfield shifts ($\Delta\delta$ −2.8, −1.6, −2.5, and −5.8, respectively), when compared with the analogous signals of **2a**. The acetyl derivative **2d** confirmed the presence of the OH group and the saponification products of **2b** (retronecine and **3a**) corroborated its relationship with **2a**. The structure of the new acid **3a** was deduced from its spectral data (Tables 1 and 2) and a NOESY experiment, which showed the following correlations: CH_3-9 with H-4; H-3 with Me-8 and Me-10; H-4 with CH_3-9 and C-6 methylene; and CH_3-8 with Me-10.

The results of a NOESY experiment of **2b** (Figure 1), indicated a "sandwich" conformation, similar to that described for retroisosenine (**2a**).[6] The absolute configuration of C-13 was inferred from the NOE effects between CH_3-18 and H-13, and those of H-12 with CH_3-17 and CH_3-19. Therefore, the new PA **2b** corresponds to (13*R*)-13-hydroxyretroisosenine.

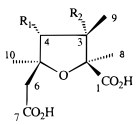
Compound **2c**, $[\alpha]^{25}_{D}$ +88°, differs from **2b** in having the alcohol function at C-12. This was apparent from the ^{1}H-NMR spectrum (Table 1), which showed the CH_3-18 and C-13 methylene signals as singlets at δ 1.44 and 2.21, respectively. The proposed position of the hydroxyl group was in agreement with the ^{13}C-NMR spectrum (Table 2), in which the C-12 and CH_3-18 resonances had shifted significantly downfield from δ 49.4 and 11.9 to 81.4 and 25.3, respectively. The saponification of **2c** gave retronecine[6] and the new necic acid **3b**, whose NOESY spectrum indicated an anti relationship between CH_3-9 and CH_3-10. Similar results were obtained from a NOESY experiment on **2c**. The C-13 methylene signal correlated with the CH_3-17 and CH_3-19 signals, and the H-15a signal with the CH_3-18 signal, and therefore the alcohol function, CH_3-17, and CH_3-19 are in the same side of the molecule of **2c**. If we suppose that C-11 and C-14 have the same configuration as those of **2a** and **2b**, then C-12 should have a *S* configuration. Because no NOE effect was observed between the hydrogens of the basic and acidic moieties of the molecule, the new alkaloid **2c**, should possess an unfolded conformation, which is different from those of **2a** and **2b**.



1



2a R_1=H R_2=H
2b R_1=OH R_2=H
2c R_1=H R_2=OH
2d R_1=OAc R_2=H



3a R_1=OH R_2=H
3b R_1=H R_2=OH

† Contribution No. 1592 of the Instituto de Química, UNAM.
‡ Instituto de Química.
§ Instituto de Biología.
* To whom correspondence should be addressed. Phone: (525) 6224412. FAX: (525) 6-162217. E-mail: iqunam@servidor.unam.mx.
⊗ Abstract published in *Advance ACS Abstracts,* November 15, 1997.

S0163-3864(97)00228-0 CCC: $14.00

Table 1. ^{1}H-NMR Spectral Data of Compounds **2a**·HCl, **2b**−**2d**, and **3a** and **3b** (500 MHz, $CDCl_3$)[a]

proton	**2a**·HCl	**2b**[b]	**2c**	**2d**[b,c]	**3a**[b,d]	**3b**[d]
2	5.93 br s	5.86 br s	5.88 s	5.93 br s		
3a	4.57 d (15.5)	3.94 dddd (15.9, 3.5, 1.9, 1.6)	4.07 br d (16.8)	4.22 m		
3b	3.75 dt (15.5, 2.0)	3.45 ddd (15.9, 6.1, 1.7)	3.48 dd (16.8, 5.3)	3.64 m		
5a	4.08 m	3.29 m	3.46 m	3.64 m		
5b	3.03 dt (11.0, 9.3)	2.65 ddd (10.2, 8.4, 8.1)	2.69 m	2.88 ddd (12.0, 9.6, 6.5)		
6	2.42 m	2.07 m	2.18 m	2.22 m		
7	5.55 ddd (5.0, 2.5, 2.5)	5.45 ddd (4.6, 3.2, 2.1)	5.34 br t (4.5)	5.54 br td (4.2, 1.4)		
8	5.09 br s	4.36 br s	4.51 br s	4.74 m		
9a	5.06 d (13.0)	4.93 *d* (11.7)	5.27 *d* (12.0)	5.15 d (12.2)		
9b	4.23 ddd (12.5, 2.5, 1.0)	4.18 br d (11.7)	4.16 dd (12.0, 1.3)	4.19 d (12.2)		
12/3[e]	2.34 dquint (11.0, 7.0)	2.08 dq (9.9, 6.9)		2.34 dq (9.6, 7.2)	2.18 dq (10.4, 6.9)	
13a/4[e]	2.06 dd (12.5, 7.0)	4.15 d (9.9)	2.21 s	5.36 d (9.7)	3.95 d (10.4)	2.25 d (13.5)
13b/4[e]	1.94 dd (12.5, 11.0)					2.09 d (13.5)
15a/6a[e]	2.65 d (13.0)	2.69 d (12.7)	2.66 d (12.5)	2.72 d (13.1)	2.90 d (16.3)	3.05 d (15.0)
15b/6b[e]	2.59 d (13.0)	2.54 d (12.7)	2.45 d (12.5)	2.59 d (13.1)	2.74 d (16.3)	2.69 d (15.0)
17/8[e]	1.44 s	1.44 s	1.46 s	1.31 s	1.44 s	1.38 s
18/9[e]	1.05 d (7.0)	1.01 d (7.0)	1.44 s	1.04 d (7.1)	1.04 *d* (7.0)	1.18 *s*
19/10[e]	1.42 *s*	1.28 *s*	1.60 s	1.49 s	1.23 s	1.46 s

[a] Assignments are based on COSY, long-range HETCOR, COLOC, HMQC, and HMBC experiments. [b] **2a** was run at 200 MHz, and **2d** and **3a** were run at 300 MHz. [c] Ac signal at δ 2.11, s. [d] **3a** in $(CH_3)_2CO$-d_6 and **3b** in CH_3OH-d_4. [e] Numbering of **3a** and **3b**.

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

carbon	**2a**·HCl	**2b**	**2c**[b]	**2d**	**3a**[c]	**3b**[c]
1	132.2 s	133.2 s	133.1 s	132.1 s		
2	128.1 d	132.7 d	131.3 d	131.4 d		
3	59.6 t	62.0 t	61.6 t	60.6 t		
5	53.8 t	53.9 t	53.7 t	53.4 t		
6	34.2 t	34.9 t	34.5 t	34.5 t		
7	72.2 d	74.0 d	74.1 d	73.2 d		
8	77.9 d	77.7 d	77.3 d	77.1 d		
9	58.7 t	59.9 t	60.1 t	59.5 t		
10/1[d]	172.3 s	172.5 s	173.4 s	171.7 s	174.9 s	177.6 s
11/2[d]	86.9 s	84.2 s	89.2 s	84.1 s	84.7 s	91.7 s
12/3[d]	44.4 d	49.4 d	81.4 s	47.7 d	49.3 d	81.5 s
13/4[d]	46.7 t	81.5 d	52.3 t	81.7 d	81.2 d	51.6 t
14/5[d]	81.7 s	81.6 s	80.2 s	81.3 s	82.2 s	82.7 s
15/6[d]	47.0 t	45.5 t	46.9 t	45.6 t	44.0 t	47.9 t
16/7[d]	168.7 s	169.2 s	169.6 s	168.8 s	174.5 s	173.4 s
17/8[d]	24.9 q	24.7 q	20.8 q	24.4 q	25.9 q	20.1 q
18/9[d]	14.4 q	11.9 q	25.3 q	11.9 q	13.2 q	24.9 q
19/10[d]	30.3 q	24.9 q	30.5 q	25.0 q	22.8 q	28.1 q
Ac				170.4 s		
				20.8 q		

[a] Assignments are based on DEPT, long-range HETCOR, COLOC, HMQC, and HMBC experiments. [b] Run at 125 MHz. [c] **3a** in $(CH_3)_2CO$-d_6 and **3b** in CH_3OH-d_4. [d] Numbering of **3a** and **3b**.

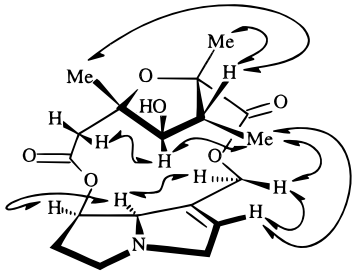


Figure 1. Results of NOESY experiment of **2b**.

The hydrochloride of retroisosenine (**2a**·HCl), $[\alpha]^{25}_D$ +46°, exhibited ^{1}H- and ^{13}C-NMR spectra (Tables 1 and 2) very similar to those of **2a**, except in the signals of H-3, H-5, H-8, C-1, C-2, and C-7, whose chemical shifts resembled those of oxyretroisosenine.[6] The absolute configuration of this hydrochloride was determined by X-ray analysis (Figure 2). The presence of **2a**·HCl might have arisen because of the use of $CHCl_3$ and CH_2Cl_2 during extraction, since these solvents produce HCl as a product of decomposition.[7]

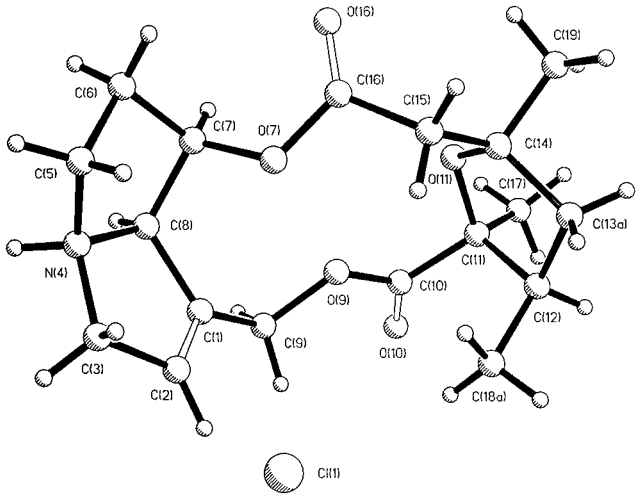


Figure 2. ORTEP projection of **2a**·HCl (crystallographic numbering).

The present study on *S. helodes* has afforded retroisosenine (**2a**), (12*S*)-12-hydroxyretroisosenine (**2c**), and retroisosenine hydrochloride (**2a**·HCl). The similarity in alkaloidal content of *S. roseus*, *S. helodes*, and *S. mulgediifolius*,[6] is consistent with their inclusion in the same section (*Mulgediifolii*) of the genus *Senecio*.

Compounds **1**, **2a**·HCl, **2a**, and **2b** showed to be inactive against the Gram-negative bacteria *Escherichia coli* ATCC 10536, and the fungi *Trichoderma viride* and *Aspergillus niger*. The toxicity of these compounds in the brine shrimp (*Artemia salina*) assay was very modest (LC_{50} > 300 μg/mL).

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. EIMS data were determined on a JEOL JMS-AX505HA mass spectrometer at 70 eV. FABMS were obtained on a JEOL, JMS-SX102A mass spectrometer operated with an acceleration voltage of 10 kV, and samples were desorbed from a nitrobenzyl alcohol matrix using 6 keV Xenon atoms. HRMS measurements in the FAB mode were performed at 10 000

resolution using electric field scans and poly(ethylene glycol) ions (Fluka 200 and 300) as the reference material. ^{1}H-NMR and ^{13}C-NMR data were obtained on a Varian Unity Plus 500, Varian Unity 300, and/or Varian Gemini 200 instruments. Chemical shifts were referred to TMS (δ 0). Standard Varian programs were used for COSY and NOESY spectra at 300 or 500 MHz. HETCOR and HMQC experiments were obtained for $^1J_{CH}$ =140 Hz at 75 and 500 MHz, respectively. Long-range HETCOR and HMBC experiments were obtained for $^nJ_{CH}$ = 9 Hz at 75 and 500 MHz, respectively. Column chromatographies were carried out on Kieselgel G (Merck, Darmstadt, Germany). TLC was performed on Si gel 60 F_{254} (Merck).

Plant Material. *S. roseus* Sch. Bip. was collected in Cofre de Perote, Veracruz, México, in December 1994 (MEXU 620273) and December 1995 (MEXU 722087). *S. helodes* Benth. was collected in the vicinity of Angangueo, Michoacán, México, in October 1995 (MEXU 528643). Voucher specimens are deposited at the Herbario del Instituto de Biología, UNAM, Coyoacán, México D. F., México.

Extraction and Isolation. Dried roots of *S. roseus* (343.1 g), collected in 1994, were extracted with MeOH. The extract was concentrated and stirred overnight at room temperature with aqueous 1 N HCl (200 mL) and Zn powder (34 g). The mixture was filtered; the solution, basified (NH_4OH to pH 10) and extracted with $CHCl_3$. Elimination of the solvent afforded 4.19 g of a residue that was purified by column chromatography using as eluent mixtures of Me_2CO−MeOH (7:3, 3:2, and 1:1). Fractions eluted with Me_2CO−MeOH (3:2 and 1:1) afforded 169.2 mg of **1**.[6] Fractions eluted with Me_2CO−MeOH (7:3) were combined to give 1.91 g of a gum (fraction A). The dried and ground aerial parts (660 g) of *S. roseus* were extracted with MeOH. The extract was worked up in a manner similar to that described for the roots, affording 2.96 g of a residue that was purified by column chromatography using as eluent Me_2CO−MeOH (7:3). As a result, 13.5 mg of **1** and 1.94 g of a gum (fraction B) were obtained. Fractions A and B were combined and purified by several column chromatographic separations using different mixtures of $CHCl_3$−MeOH as eluents to give 1.01 g of **2a**,[6] 199 mg of **2b**, and 19.2 mg of **2c**. Compounds **1** and **2a** were identified by comparison with authentic samples of mulgediifoline and retroisosenine, respectively.[6]

Dried roots of *S. roseus* (750 g), collected in 1995, were extracted with MeOH. The solvent was evaporated and the residue stirred overnight with 2.5% aqueous H_2SO_4 (400 mL) and Zn powder (75 g). The mixture was filtered, and the filtrate was washed with CH_2Cl_2, basified (NH_4OH to pH 10), and extracted several times with CH_2Cl_2 until it became Dragendorff negative. The first 10 extracts were combined and yielded 12 g of an alkaloidal mixture, as pale yellow crystals. The remaining extracts gave **2b** (300 mg). The alkaloidal mixture was purified by consecutive column chromatographic separations using as eluent $CHCl_3$−MeOH (19:1) and Me_2CO−MeOH (7:3), affording **2a** (3.85 g), **2b** (1.25 g), **2c** (60 mg), and **2a**·HCl (165 mg). The extraction of dried and ground leaves (1.198 kg) from the same collection, was carried out as previously described above for the roots. The alkaloidal extract (2.7 g) was purified by repeated column chromatography yielding **2a** (300 mg), **2b** (730 mg), and **2c** (48 mg).

The leaves and roots of *S. helodes* (115 g) were extracted with MeOH. The extract was purified as described above for *S. roseus*. The alkaloidal residue (800 mg) was purified by repeated column chromatography using as eluent CH_2Cl_2−MeOH (19:1), affording **2a** (261 mg), **2c** (12 mg), and **2a**·HCl (18 mg).

(13*R*)-13-Hydroxyretroisosenine (2b): white crystals from hexane−Me_2CO; mp 187−190 °C; $[\alpha]^{25}_D$ +116.4° (*c* 2.01, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3495, 1732, 1452 cm^{-1}; ^{1}H-NMR data, see Table 1; ^{13}C-NMR data, see Table 2; EIMS *m/z* 351 $[M]^+$ (2), 336 (1), 307 (8), 236 (21), 136 (36), 120 (69), 119 (100), 93 (37); HR-FABMS *m/z* found $[M + 1]^+$ 352.1779 ($C_{18}H_{26}NO_6$ requires 352.1760).

(12*S*)-12-Hydroxyretroisosenine (2c): white crystals from hexanes−EtOAc; mp 167−170 °C; $[\alpha]^{25}_D$ +88° (*c* 2.0, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3600, 1726, 1460 cm^{-1}; ^{1}H-NMR data, see Table 1; ^{13}C-NMR data, see Table 2; EIMS *m/z* 351 $[M]^+$ (0.5), 307 (4), 264 (8), 220 (37), 138 (36), 136 (41), 120 (56), 119 (100), 93 (33); HRFABMS *m/z* found $[M]^+$ 351.1672 ($C_{18}H_{25}NO_6$ requires 351.1682).

Retroisosenine Hydrochloride (2a·HCl). Those fractions containing **2a** were combined and washed with hot hexane, the insoluble part was dissolved in Me_2CO and crystallized on addition of EtOAc to give **2a**·HCl: mp 215−220 °C; $[\alpha]^{25}_D$ +46° (*c* 2.0, $CHCl_3$); IR ($CHCl_3$) ν_{max} 2291, 2229, 1739, 1460, 859 cm^{-1}; ^{1}H-NMR data, see Table 1; ^{13}C-NMR data, see Table 2. A solution of **2a**·HCl (20 mg) in CH_2Cl_2 (5 mL, previously washed with base) was washed with aqueous NaOH (0.5 N, 3 × 2 mL), dried with Na_2SO_4, and concentrated to yield 17 mg of **2a**, mp 118−120 °C.

Acetylation of (13*R*)-13-Hydroxyretroisosenine (2b). Compound **2b** (20 mg) was acetylated in the usual manner with 1 mL of pyridine and 1 mL of Ac_2O. After 1 h, the reaction mixture was dried under an air stream. The residue was dissolved in CH_2Cl_2, washed with saturated $NaHCO_3$, and then with H_2O, dried, and concentrated, yielding 18.2 mg of **2d** as a yellow oil: IR ($CHCl_3$) ν_{max} 1735, 1456 cm^{-1}; ^{1}H-NMR data, see Table 1; ^{13}C-NMR data, see Table 2; EIMS *m/z* 393 $[M]^+$ (2), 346 (2), 290 (13), 289 (13), 179 (13), 169 (32), 136 (54), 120 (78), 119 (100), 93 (48), 43 (44).

Saponification of (13*R*)-13-Hydroxyretroisosenine (2b). Compound **2b** (100 mg) and KOH (100 mg) in MeOH (10 mL) were refluxed for 3.5 h. The solvent was evaporated and the residue extracted with hot $CHCl_3$ (10 × 10 mL). Elimination of the solvent gave a brown oil (40 mg) that by sublimation at 3 mm Hg and 100 °C yielded 7 mg of retronecine: mp 113−115 °C; $[\alpha]^{25}_D$ +45.4° (*c* 2.2, MeOH).[10] The basic residue was dissolved in H_2O, acidified with 2% aqueous H_2SO_4, extracted with Et_2O, dried, and concentrated to give 22 mg of (4*R*)-4-hydroxy-*cis*-nemorensic acid (**3a**) from EtOAc: mp 172−174 °C; $[\alpha]^{25}_D$ +34° (*c* 2.06, MeOH); IR (KBr) ν_{max} 3218, 1725, 1698 cm^{-1}; ^{1}H-NMR data, see Table 1; ^{13}C-NMR data, see Table 2; EIMS *m/z* 232 $[M]^+$ (0.4), 215 (1), 187 (100), 169 (4), 127 (30), 115 (16), 109 (13), 85 (18) 83 (14), 73 (13), 43 (48); HRFABMS *m/z* found $[M + 1]^+$ 233.1030 ($C_{10}H_{17}O_6$ requires 233.1025).

Saponification of (12*S*)-12-Hydroxyretroisosenine (2c). Compound **2c** (20 mg) and KOH (20 mg) in MeOH (5 mL) were refluxed for 3.5 h. The reaction

Table 3. Atomic Coordinates [× 10^4] and Equivalent Isotropic Displacement Parameters [Å^2 × 10^3] for **2a**·HCl (U(eq) is Defined as One Third of the Trace of the Orthogonalized U_{ij} Tensor)

	x	y	z	U(eq)
Cl (1)	−4726 (3)	7568 (3)	2242 (1)	83 (1)
C (1)	460 (16)	4855 (9)	1897 (2)	59 (3)
C (2)	−1010 (15)	4260 (10)	2102 (2)	70 (3)
C (3)	−402 (13)	2676 (10)	2262 (2)	75 (2)
N (4)	1814 (10)	2409 (9)	2125 (2)	58 (2)
C (5)	2130 (16)	901 (9)	1913 (2)	73 (3)
C (6)	3724 (15)	1369 (10)	1618 (2)	85 (3)
C (7)	2949 (13)	3003 (9)	1512 (2)	60 (2)
O (7)	987 (8)	2895 (5)	1299 (1)	59 (2)
C (8)	2436 (15)	3772 (9)	1871 (2)	60 (2)
C (9)	392 (15)	6442 (8)	1723 (2)	72 (3)
O (9)	222 (10)	6203 (5)	1333 (1)	64 (2)
C (10)	−93 (13)	7468 (11)	1127 (2)	66 (2)
O (10)	−75 (14)	8805 (7)	1241 (2)	117 (3)
C (11)	−581 (17)	7059 (9)	743 (2)	64 (2)
O (11)	465 (9)	5600 (7)	654 (1)	67 (2)
C (12)	−3030 (22)	6754 (15)	697 (3)	112 (4)
C (13A)	−3048 (24)	5311 (22)	458 (5)	108 (7)
C (13B)	−2932 (61)	5044 (40)	739 (11)	103 (14)
C (14)	−1015 (20)	4433 (12)	526 (2)	95 (3)
C (15)	−857 (17)	2964 (12)	750 (2)	107 (4)
C (16)	1250 (21)	2701 (12)	939 (2)	80 (3)
O (16)	2901 (13)	2453 (9)	797 (2)	110 (10)
C (17)	267 (20)	8328 (10)	492 (2)	128 (4)
C (18A)	−4257 (23)	6435 (26)	1054 (4)	126 (9)
C (18B)	−4144 (71)	8123 (49)	904 (9)	146 (18)
C (19)	−377 (26)	4109 (13)	148 (2)	227 (9)

mixture was worked up as described for the saponification of **2b**, and afforded 8 mg of retronecine as brown oil, $[\alpha]^{25}_D$ +44° (*c* 1.96, EtOH)[10] and 9 mg of (3*S*)-3-hydroxy-*cis*-nemorensic acid (**3b**) as a yellow oil. The later compound exhibited $[\alpha]^{25}_D$ +24.2° (*c* 3.6, MeOH); IR (film) ν_{max} 3196, 1728, 1713 cm^{-1}; ^{1}H-NMR data, see Table 1; ^{13}C-NMR data, see Table 2; HRFABMS *m*/*z* found $[M + 1]^+$ 233.1035 ($C_{10}H_{17}O_6$ requires 233.1025).

X-ray Diffraction Structure Determination for 2a·HCl.[8] Crystal data: $C_{18}H_{26}ClNO_5$; crystal size (mm), 0.20 × 0.16 × 0.08; crystal system, orthorhombic; space group, $P2_12_12_1$; unit cell dimensions, a = 6.230 (1) Å, b = 8.391 (2) Å, c = 36.869 (7) Å; volume, 1927.4 (7) Å; Z = 4; formula weight, 371.85; density (calcd), 1.281 mg/m^3; absorption coefficient, 1.968 mm^{-1}; F(000), 792.

Data Collection. Diffractometer used, Nicolet P3P; radiation, Cu Kα (λ = 1.54178 Å); temperature (K), 293 (2); monochromator, Ni-filter crystal; 2θ range, 3.0 to 115°; scan type, ω; scan range (ω), 1.4°; background measurement, stationary counter at beginning and end of scan, each for 50.0% of total scan time; standard reflections, three measured every 97 reflections; index range, $0 \le h \le 4$, $0 \le k \le 9$, $0 \le l \le 40$ plus Friedel pairs; independent reflections, 2233; empirical absorption corrections (XABS 2).[9]

Solution Refinement. System used, SHELXL-93; solution, direct methods SIR92; refinement method, full-matrix least-squares on F^2; quantity minimized, $\sum\omega(F_0^2\text{-}F_c^2)^2$; absolute structure parameter, −0.03 (5); extinction correction, 0.0019 (3); hydrogen atoms, riding model, fixed isotropic U = 0.08 Å^{-2}; weighting scheme, $\omega^{-1} = \sigma^2(F_0^2) + (0.0638P)^2$ where $P = (F_0^2 - 2F_c^2)/3$; number of parameters refined, 239; final R indices (observed data), R_1 = 6.71%, ωR^2 = 13.10%; R indices (all data), R = 11.76%, ωR^2 = 15.31%; goodness-of-fit on F^2, 0.979; largest and mean Δ/σ, 0.004, 0.001; data-to-parameter ratio, 9.343; largest difference peak, 0.19 eÅ^{-3}; largest difference hole, −0.16 eÅ^{-3}. See Table 3.

Acknowledgment. We are indebted to Carmen Gutiérrez Coutiño, Rubén Gaviño, Isabel Chávez, Beatriz Quiroz, Hector Ríos, Rocío Patiño, Claudia Contreras, Luis Velasco, and Javier Pérez for technical assistance.

References and Notes

(1) Robins, D. J. *Nat. Prod. Rep.* **1994**, *11*, 613−619.
(2) Robins, D. J. *Nat. Prod. Rep.* **1995**, *12*, 413−418.
(3) Hartmann, T.; Witte, L. In *Alkaloids: Chemical and Biological Perspectives*; Pelletier, S. W., Ed.; Pergamon: Oxford, UK, 1995; Vol. 9, Chapter 4, pp 155−233.
(4) Roeder, E. *Pharmazie* **1995**, *50*, 83−98.
(5) Romo de Vivar, A.; Pérez, A.-L.; Vidales, P.; Nieto, D. A.; Villaseñor, J. L. *Biochem. System. Ecol.* **1996**, *24*, 175−176.
(6) Romo de Vivar, A.; Pérez, A.-L.; Arciniegas, A.; Vidales, P.; Gaviño, R.; Villaseñor, J. L. *Tetrahedron*, **1995**, *51*, 12521−12528.
(7) Miall, S. *Diccionario de Química*; Editorial Atlante: México D.F., México, 1943.
(8) X-ray data for compound **2a**·HCl have been deposited in the Cambridge Crystallographic Data Centre and are available on request from Dr. Olga Kennard, University Chemical Laboratory, 12 Union Road, Cambridge CB2 1EZ, UK.
(9) Parkin, S.; Moezzi, B.; Hope, H. *J. Appl. Crystallogr.* **1995**, *28*, 53−56.
(10) Culvenor, C. C. J.; Heffernan, M. L.; Woods, W. G. *Aust. J. Chem.* **1965**, *18*, 1605−1624.

NP9702289