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CLERODANES FROM *SOLIDAGO VIRGAUREA*

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Key Word Index—*Solidago virgaurea*; Compositae; Astereae; *cis*-clerodane lactones.

Abstract—The isolation and structure determination of four known and eight new *cis*-clerodane lactones from the aerial parts of *Solidago virgaurea* are described.

INTRODUCTION

The chemistry of *Solidago* species has been reviewed [1–3]. Characteristic constituents, primarily of the roots, are diterpenoids of various types, especially clerodanes [2–7]. In the present article we describe the isolation of four known and eight previously unknown *cis*-clerodane lactones from the aerial parts of *S. virgaurea* L. collected in Northeast India. Previous reports on the phytochemistry of this taxon dealt with acetylenes, cinnamates, hydroxybenzoates and their glycosides, flavonoids, steroids, saponins and polysaccharides [1–3, 8–15] and one article [16] contains the statement that *S. virgaurea* (presumably the roots) contains no diterpenes.

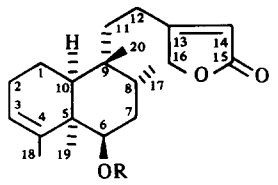
RESULTS AND DISCUSSION

Eight of the clerodanes were isolated in the form of four isomer pairs **1a**/**1b**; **4a**/**4c**; **6a**/**6c** and **7a**/**7b** from which **4c**, **6a**, **6c** and **7b** were separated in pure form after extensive chromatography. Clerodane **5** was also isolated from one of these fractions. Lactones **2a** and **3** remained as a mixture after separation of **2b**. Compounds **1a** (elongatolide C, solidagolactone II), **1b** (solidagolactone III), **2a** (elongatolide E, solidagolactone VII) and **3** (solidagolactone V) have been obtained previously, together with related clerodanes, from the roots of *S. elongata* [17] and/or *S. altissima* [18]; **2a** was also found in very small quantity in the roots of *S. nemoralis* [3]. Structures of these substances, originally thought to be *trans*-type clerodanes with H-10β, C-5 methyl α and C-9 methyl α [17, 18], have recently been revised [7] to those shown in the formulae; our ^{1}H NMR data (see Experimental) corresponded to those reported by the Japanese authors. The ^{1}H NMR spectrum of the previously undescribed **2b** differed from that of **2a** only in the signals of the ester side chain on C-6.

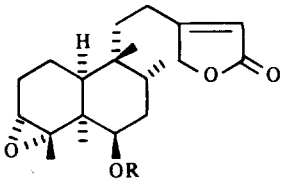
The ^{1}H NMR spectrum of ester pair **4a**/**4c** (or the pure isomer **4c**), like that of **1a**/**1b**, exhibited the triplet (J = 3 Hz) of the equatorial H-6 under the ester function near δ5. In addition a multiplet at δ4.16 which was coupled to the vinylic proton at C-3 ($J_{2,3}$ = 6 Hz) and moved downfield on acetylation to **4b**/**4d** indicated the presence of an α-orientated hydroxyl group at C-2. This was confirmed by oxidation (CrO_3–pyridine) to an α,β-unsaturated ketone pair **10a**/**10b**. The same **10a**/**10b** pair was also obtained by CrO_3–pyridine oxidation of **1a**/**1b**, a correlation which established the remaining stereochemistry of **4a**/**4c** whereas oxidation of **1a**/**1b** with SeO_2 gave the α,β-unsaturated aldehyde pair **9a**/**9b**. Oxidation of **1a**/**1b** with *m*-chloroperbenzoic acid gave as major product an ester pair **8a**/**8b** isomeric with **2a**/**2b** as evidenced by the chemical shift and coupling of H-3 which was a doublet at δ3.04, J = 4 Hz, in contrast with the broadened singlet of H-3 in **2a**/**2b** at δ2.74. More significant was the diamagnetic shift of H-6 relative to that of H-6 in **2a**/**2b**, δ4.89 in **8a**/**8b** vs. δ5.42 in **2a**/**2b** due to the deshielding effect of the α-orientated epoxide in the naturally-occurring ester pair.

Clerodane **5** was isolated in very small quantity only after extensive chromatography. Attachment of a hydroxyl group at C-2 was apparent from the presence of a broad multiplet at δ4.40 and the simplification of the H-3 signal to a somewhat broadened singlet. The half-height widths of these signals ($W_{1/2}$ = 16 Hz for H-2, $W_{1/2}$ = 5 Hz for H-3) indicated that the orientation of the hydroxyl group differed from that in **4a**/**4b** and was β. Absence of the C-6 ester function was made evident by the ^{1}H NMR spectrum; the presence of a keto group could be deduced from the molecular formula and it was logical to assume that it was located at C-6. This assumption was confirmed by the ^{1}H NMR spectrum which exhibited a sharp *dd* at δ2.52 (J = 15, 5 Hz). As this is also found in the ^{1}H NMR spectrum of **3**, it can be attributed to H-7a as the A part of an ABX system, the B part (H-7b) being somewhat farther upfield and obscured by other signals. Location of the carbonyl group of **5** at C-7, C-11 or C-12 is thus excluded.

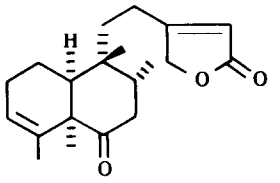
That **6a** and **6c** were glycols derived from **1a**/**1b** was indicated by the molecular formula and the spectroscopic evidence which included hydroxyl absorption in the IR, the presence of one C–O singlet and one C–O doublet in the ^{13}C NMR spectrum and the presence of a one proton multiplet at δ3.38 characteristic of hydrogen under hydroxyl in the ^{1}H NMR spectrum as well as the chemical shift of the C-4 methyl (δ1.24) comparable to that in **2a**/**2b**. Conversion to a monoacetate pair **6b**/**6d** produced the expected paramagnetic shift of the signal at δ3.38 to



R
1a Ang
1b Tig



R
2a Ang
2b Tig



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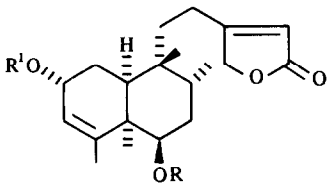
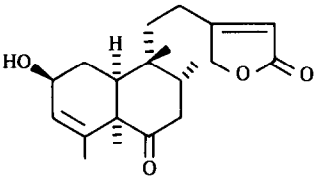
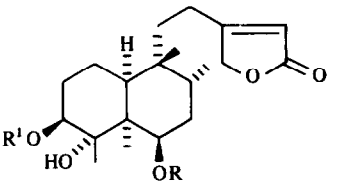


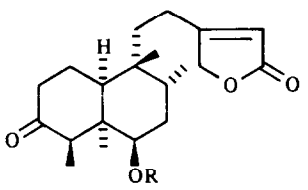
4a R = Ang, R^1 = H
4b R = Ang, R^1 = Ac
4c R = Tig, R^1 = H
4d R = Tig, R^1 = Ac



5

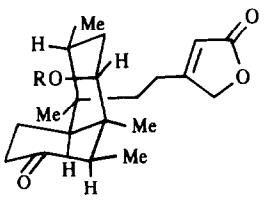


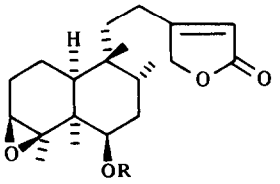
6a R = Ang, R^1 = H
6b R = Ang, R^1 = Ac
6c R = Tig, R^1 = H
6d R = Tig, R^1 = Ac



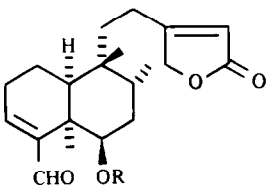
R
7a Ang
7b Tig

≡

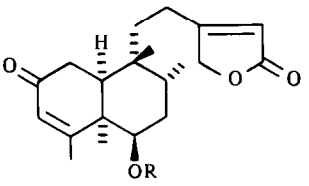




R
8a Ang
8b Tig



R
9a Ang
9b Tig



R
10a Ang
10b Tig

δ4.83; further reaction of **6b/6d** with trichloroacetylisocyanate (TAI) [19] resulted in a monocarbamate whose ^{1}H NMR spectrum exhibited significant downfield shifts of H-19 (Δδ0.45) and H-18 (Δδ0.20) and a further downfield shift of the δ4.83 multiplet to δ5.66. Consequently the tertiary hydroxyl group of **6a/6b** was located at C-4, *cis* to the α-orientated C-5 methyl group, and the secondary hydroxyl group was at C-3, *cis* to the tertiary hydroxyl group and α.

As for the remaining previously unknown ester pair **7a/7b**, its ^{1}H NMR spectrum exhibited two methyl singlets and two methyl doublets, but had no low field signals other than those of H-6, H-13 and H-16a,b common to other compounds of the series. Since the ^{13}C NMR spectrum of **7b** (Table 1) contained a new frequency at δ209.76, the presence of a carbonyl group at

Table 1. ^{13}C NMR Spectra of compounds **6a**, **6c** and **7b** (67.89 MHz, $CDCl_3$)*

C	6a	6c	7b
1	19.31 *t*	19.71 *t*	26.56 *t*
2	29.97 *t*	29.97 *t*	40.81 *d*
3	75.38 *d*†	75.42 *d*†	209.76
4	77.87	77.87	53.04 *d*
5	46.50	46.42	47.19
6	75.21 *d*†	75.24 *d*†	73.38 *d*
7	32.13 *t*‡	32.13 *t*‡	31.70 *t*
8	32.03 *d*	32.03 *d*	31.62 *d*
9	38.75	38.72	39.39
10	42.35 *d*	42.35 *d*	45.04 *d*
11	33.21 *t*‡	33.21 *t*‡	33.53 *t*
12	23.41 *t*	23.41 *t*	23.44 *t*
13	173.81	173.81	173.63
14	115.28 *d*	115.28 *d*	115.54 *d*
15	170.68	170.68	170.21
16	73.00 *t*	73.00 *t*	72.94 *t*
17	15.27 *q*	15.27 *q*	15.23 *q*
18	28.41 *q*	28.41 *q*	7.37 *q*
19	23.67 *q*	23.67 *q*	28.46 *q*
20	21.76 *q*	21.76 *q*	26.66 *q*
1′	166.94	166.94	166.99
2′	127.88	129.34	128.13
3′	136.67 *d*	137.75 *d*	138.10 *d*
4′	15.62 *q*	14.70 *q*	14.48 *q*
5′	20.40 *q*	12.44 *q*	12.01 *q*

*Unmarked signals are singlets.

†‡Assignments with the same sign in each column may be interchanged.

C-3 was suspected. This was confirmed by the following fortuitous result. In an attempt to correlate **6a**/**6c** with **1a**/**1b**, the **6a**/**6c** mixture in methyl cyanide was exposed to NAI-trimethylsilyl chloride [20]. The product, formed as the result of a pinacol rearrangement, was **7a**/**7b**. The C-4 methyl group of **7a**/**7b** is therefore assigned the stable equatorial and β configuration.

As mentioned earlier, *cis*-clerodanes of the backbone type described here have been isolated also from the roots of *S. elongata* [17], *S. altissima* [18] and *S. nemoralis* [3]; similar compounds have been isolated from *S. rugosa* [3] and *S. gigantea* var *serotina* [21, 22] and it has been suggested [22] that two clerodanes from the roots of *S. shortii* [16] also belong to this class. *Cis*-clerodanes of a different backbone type and one *trans*-clerodane have been isolated from the roots of *S. arguta* [22] whereas roots of *S. missouriensis* [23, 24] *S. juncea* [21] and *S. serotina* [25] only yielded *trans*-clerodanes.

EXPERIMENTAL

Extraction of Solidago virgaurea *and isolation of constituents.* Above ground parts of *S. virgaurea* L. (1.5 kg) collected in the Khasi Hills, Meghalaya, India, were extracted with $CHCl_3$ in a Soxhlet apparatus until the extract was colorless. After removal of $CHCl_3$ at red. pres. the residue was allowed to stand overnight with 200 ml of MeOH containing 10% H_2O and filtered. After having been washed with petrol (60–80°, 5 × 250 ml) the MeOH fraction was concd at red. pres. and the residue was thoroughly extracted with $CHCl_3$ (6 × 200 ml). The washed and dried extract was evaporated at red. pres. and the residue (12 g) chromatographed over 500 g silica gel (60–120 mesh, BDH, India), 200 ml fractions being collected as follows. Fr. 1–9 (C_6H_6), 10–33 (C_6H_6–EtOAc, 9:1), 34–44 (C_6H_6–EtOAc, 5:1), 45–50 (C_6H_6–EtOAc, 3:1), 51–62 (C_6H_6–EtOAc, 2:1), 63–72 (C_6H_6–EtOAc, 1:1), 73–78 (EtOAc), 79–82 (EtOAc–MeOH, 19:1) 83–85 (EtOAc–MeOH, 9:1), 86–87 (EtOAc–MeOH, 4:1), 88–89 (EtOAc–MeOH, 1:1), 90 (MeOH).

Fr. 12–15 (300 mg) were combined and purified by prep. TLC (C_6H_6–EtOAc, 9:1, two developments, plate thickness 0.5 mm) to give 0.15 g of **1a**/**1b** mixture (ratio of **1a** to **1b** approx 1:2 by ^1H NMR analysis), IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1775, 1745, 1690, 1650, 1440, 1350, 960, 875 and 84; ^1H NMR (270 MHz, $CDCl_3$): δ5.52 (*m*, H-3), 5.05 and 5.03 (*t*, *J* = 3 Hz, H-6 of **1a** and **1b**), 5.87 (*t*, *J* = 2 Hz, H-14), 4.78 (*d*, *J* = 2 Hz, H-16a,b), 1.57 and 1.54 (*br*, H-18 of **1a** and **1b**), 1.22 and 1.21 (H-19), 1.07 (H-20), 0.87 (*d*, *J* = 6 Hz, H-17), 6.79 and 6.01 (*br q*, *J* = 7 Hz, H-3 of **1b** and **1a**), 1.98 and 1.78 (*br d*, *J* = 7 Hz, H-4′ of **1a** and **1b**), 1.82 and 1.80 (*br*, H-5′ of H-**1a** and **1b**).

Combination of fr. 20–25 (350 mg) and separation of the two main spots by prep. TLC (C_6H_6–EtOAc, two developments) gave as the less polar material a 1:2 mixture of **2a** and **3** (0.15 g); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1780, 1750, 1700, 1640, 1450, 1385 and 885; ^1H NMR (270 MHz, $CDCl_3$) of **2a**: δ5.83 (*t*, *J* = 2 Hz, H-14), 5.42 (*t*, *J* = 3 Hz, H-6), 4.75 (*d*, *J* = 2 Hz, H-16a, b), 2.74 (*br*, H-3), 1.31 (H-18), 1.22 (H-19), 1.03 (H-20), 0.89 (*d*, *J* = 7 Hz, H-17), 6.05 (*br q*, H-3′), 2.03 (*br d*, H-4′), 1.97 (*br*, H-5′); ^1H NMR of **3**: δ5.83 (*t*, *J* = 2 Hz, H-14), 5.62 (*m*, H-3), 4.72 (*d*, *J* = 2 Hz, H-16a,b), 2.60 (*dd*, *J* = 15, 6 Hz, H-7a), 1.51 (*d*, *J* = 1 Hz, H-18), 1.22 (H-19 and H-20), 0.83 (*d*, *J* = 7 Hz, H-17).

The more polar material (20 mg) was **2b** (gum), IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1780, 1750, 1700, 1650, 900, 825, 785 and 720; ^1H NMR (270 MHz, $CDCl_3$); δ6.92 (*br q*, *J* = 7 Hz, H-3′), 5.85 (*t*, *J* = 1.5 Hz, H-14), 5.41 (*dd*, *J* = 4, 3 Hz, H-6), 4.75 (*d*, *J* = 2 Hz, H-6a, b), 2.75 (*br*, H-3), 2.04 (*br*, H-5′), 1.81 (*br d*, *J* = 7 Hz, H-4′), 1.30 (H-18), 1.22 (H-19), 1.04 (H-20), 0.88 (*d*, *J* = 7 Hz, H-20).

Combination of fr. 41–53 (400 mg) and separation of the two main spots by prep. TLC (C_6H_6–EtOAc, 2:1) gave a complex mixture as the less polar material. The more polar material (100 mg) was a 1:2 mixture of **7a**/**7b**; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1775, 1750, 1710, 1700, 1650, 1450, 1375, 1250, 1065, 1025, 965 and 875; ^1H NMR (270 MHz, $CDCl_3$) of **7a**: δ5.88 and 5.86 (*quint*, *J* = 2 Hz, H-14 of **7b** and **7a**), 4.87 (*br t*, *J* = 3 Hz, H-6), 4.78 and 4.76 (*d*, *J* = 2 Hz, H-16a, b of **7b** and **7a**), 2.16 (*q*, *J* = 7 Hz, H-4), 1.33 (*br*, H-19), 1.10 (*br*, H-20), 0.98 (*d*, *J* = 7 Hz, H-18), 0.86 (*d*, *J* = 7 Hz, H-17), 6.69 and 6.05 (*br q*, *J* = 7 Hz, H-3′ of **7b** and **7a**), 2.01 and 1.81 (*br d*, *J* = 7 Hz, H-4′ of **7a** and **7b**), 1.88 and 1.76 (*br*, H-5′ of **7a** and **7b**). Prep. TLC of this mixture (C_6H_6–EtOAc, 9:1, two developments) gave an essentially pure sample of **7b** (gum) whose ^{13}C NMR spectrum is listed in Table 1, ^1H NMR (C_6D_6): δ6.89 (*br q*, H-3′), 5.48 (*quint*, H-14), 4.98 (*br t*), 3.97 (*d*, H-16a,b) 1.84 (*br*, H-5′), 1.49 (*br d*, H-4′), 1.09 (*d*, H-18), 0.74 (*br*, H-19), 0.62 (*br*, H-20), 0.57 (*d*, H-17). The MS did not exhibit the molecular ion; significant peaks were at *m/z* (rel. int.) 387 $[M-CHO]^+$ (2.0), 316 $[M-C_5H_8O_2]^+$ (2), 288 (5.4), 287 (6.4), 273 (3.6), 231 (1.7), 217 (1.9), 206 (4.1), 194 (2.8), 189 (2.6), 187 (3.5), 177 (16.2), 175 (11.6), 173 (4.2), 163 (4.0), 161 (2.3), 136 (9.9), 121 (11.9), 111 (11.4), 107 (10.3), 95 (12.4), 83 (100).

Combination of fr. 59–76 (400 mg) and prep. TLC ($CHCl_3$–MeOH, 49:1, two developments) furnished 200 mg of a 1:2 mixture of **4a**/**4c**, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450, 1775, 1700, 1600, 1459, 1375, 1070, 1025, 960 and 850; ^1H NMR (270 MHz, $CDCl_3$): δ5.82 (*quint*, *J* = 2 Hz, H-14), 5.67 (*br d*, *J* = 6 Hz, H-3), 5.07 and 4.99 (*br t*, *J* = 3 Hz, H-6 of **4a** and **4c**), 4.73 (*d*, *J* = 2 Hz, H-16a, b), 4.16 (*m*, $W_{1/2}$ = 12 Hz, H-2), 1.64 and 1.62 (*br*, H-18 of

4b and **4a**), 1.26 (*br*, H-19), 1.08 (*br*, H-20), 0.89 and 0.88 (*d*, J = 7 Hz, H-17 of **4a** and **4c**); 6.69 and 6.01 (*br q*, H-3′ of **4c** and **4a**), 1.98 and 1.78 (*br d*, H-4′ of **4a** and **4c**), 1.76 (*br*, H-5′). The separation of pure **4c** is described below.

Combination of fr. 79–83 (500 mg) and prep. TLC ($CHCl_3$–MeOH, 19:1) gave 300 mg of a 1:3 mixture of **6a**/**6c**; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3540, 1775, 1750, 1700, 1635, 1520, 1415 and 1375; ^1H NMR spectra of the pure components are given below; ^{13}C NMR spectra are listed in Table 1.

For isolation of pure **4c**, **5**, **6a** and **6c**, 80 mg of material from the spot corresponding to **4a**/**4c** and 100 mg of material from the spot corresponding to **6a**/**6c** were combined, chromatographed over 100 g silica gel and eluted in 200 ml fractions as follows: fr. 1–3 (C_6H_6), 4–6 (C_6H_6–EtOAc, 9:1), 7–9 (C_6H_6–EtOAc, 4:1), 10–13 (C_6H_6–EtOAc, 2:1), 14–35 (C_6H_6–EtOAc, 1:1), 36–48 (1:2, C_6H_6–EtOAc), 49–54 (EtOAc). Fr. 29 contained 7 mg pure **4c** and fr. 30 contained 35 mg pure **6a**. The other fractions were rechromatographed over 100 g silica gel (100–120 mesh, Acme, India), 100 ml fractions being collected as follows: fr. 1–3 (C_6H_6), 4–6 (C_6H_6–EtOAc, 9:1), 7.12 (C_6H_6–EtOAc, 4:1), 13–40 (C_6H_6–EtOAc, 2:1), 41–58 (C_6H_6–EtOAc, 1:1), 59–62 (C_6H_6–EtOAc, 1:2), 63–64 (EtOAc). Fr. 34 afforded 10 mg of pure **4c** (gum), fr. 39–40 gave 4 mg of **5**, fr. 42 gave 12 mg of pure **6a** and fr. 50 gave 8 mg of pure **6c**.

Compound **4c** (*gum*). ^1H NMR as described above for **4c** component of **4a**/**4c** mixture. MS m/z (rel. int.): 416, $[M]^+$ (0.2), 399 (0.7), 333 (6.5), 316 (8.0), 301 (3.7), 299 (3.3), 219 (4.4), 217 (1.6), 215 (1.4), 206 (6.3), 205 (5.3), 203 (6.0), 191 (2.3), 189 (2.4), 187 (8.3), 177 (3.4), 175 (3.2), 173 (2.5), 167 (2.9), 165 (2.9), 163 (4.2), 161 (3.5), 159 (3.9), 150 (6.0), 149 (8.7), 137 (21.7), 135 (37.8), 123 (15.6), 123 (15.6), 121 (13.2), 119 (12.8), 111 (15.6), 110 (13.2), 109 (12.5), 107 (18.6), 97 (43.4), 95 (12.8), 83 (100).

Compound **5** (*gum*). ^1H NMR: δ5.82 (*quint*, J = 2 Hz, H-14), 5.64 (*m*, $W_{1/2}$ = 5 Hz, H-3), 4.71 (*d*, J = 2 Hz, H-16a,b), 4.40 (*m*, $W_{1/2}$ = 16 Hz, H-2), 2.52 (*dd*, J = 15, 5 Hz, H-7a), 1.57 (*br*, H-18), 1.30 (*br*, H-19), 1.17 (*br*, H-20), 0.84 (*d*, J = 7 Hz, H-17); MS m/z (rel. int.): 332 $[M]^+$ (6.0), 317 (6.0), 314 (7.8), 299 (14.5), 285 (5.8), 271 (13.9), 221 (43.8), 207 (7.9), 203 (23.0), 201 (12.1), 189 (8.2), 175 (16.9), 173 (11.5), 161 (15.7), 159 (16.0), 151 (13.6), 149 (21.8), 147 (12.7), 137 (91.5), 135 (26.6), 133 (29.0), 123 (67.7), 122 (67.7), 121 (33.5), 111 (69.2), 107 (61.3), 98 (65.0), 69 (100). [Calc. for $C_{20}H_{28}O_4$: MW, 332.1986. Found: MW (MS), 332.1973.]

Compound **6a** (*gum*). ^1H NMR: δ6.02 (*br q*, J = 7 Hz, H-3′), 5.86 (*quint*, J = 2 Hz, H-14), 4.90 (*br t*, J = 3 Hz, H-6), 4.76 (*d*, J = 2 Hz, H-16a, b), 3.36 (*br t*, J = 2 Hz, H-3), 1.93 (*br d*, J = 7 Hz, H-4′), 1.96 (*br*, H-5′), 1.26 (*br*, H-18), 1.23 (*br*, H-19), 1.06 (*br*, H-20), 0.88 (*d*, J = 7 Hz, H-7). The MS did not exhibit the molecular ion; significant peaks were at m/z (rel. int.) 334 $[M-C_5H_8O_2]^+$ (3.3), 317 (7.4), 316 (3.4), 299 (2.4), 291 (21.6), 273 (5.9), 233 (3.4), 224 (59), 206 (9.1), 167 (22.6), 163 (11.9), 151 (25.8), 150 (21.2), 149 (20.8), 137 (11.3), 136 (17.2), 135 (12.6), 133 (12.5), 123 (23.0), 121 (18.2), 119 (12.6), 111 (60.6), 109 (22.2), 107 (22.8), 105 (12.3), 95 (68.1), 83 (100).

Compound **6c** (*gum*). ^1H NMR: δ6.81 (*br q*, J = 7 Hz, H-3′), 5.86 (*quint*, J = 2 Hz, H-14), 4.92 (*br t*, J = 3 Hz, H-6), 4.77 (*d*, J = 2 Hz, H-16a, b), 3.37 (*br t*, J = 2 Hz, H-3), 1.91 (*br*, H-5′), 1.88 (*br d*, H-4′), 1.27 (*br*, H-18), 1.24 (*br*, H-19), 1.09 (*br*, H-20), 0.88 (*d*, J = 7 Hz, H-17). MS m/z (rel. int.): 334 $[M-C_5H_8O_2]^+$ (2.8), 317 (4.0), 316 (3.3), 300 (3.3), 291 (20.3), 273 (5.4), 258 (4.9), 247 (6.4), 223 (2.9), 224 (52.5), 205 (100), 175 (11.2), 167 (20.3), 163 (11.4), 151(23.4), 150 (18.9), 149 (10.5), 137 (9.4), 136 (15.0), 135 (11.8), 133 (10.6), 123 (22.4), 121 (16.5), 119 (10.7), 111 (53.8), 109 (18.2), 107 (18.5), 98 (20.6), 95 (57.8), 83 (67.7).

Oxidations of **1a**/**1b**. (a) A soln of 25 mg of **1a**/**1b** and 48 mg of CrO_3 in 1 ml pyridine was kept at room temp. for 2 days. After addition of 1 ml MeOH and dilution with H_2O, the mixture was extracted with EtOAc. The residue from the washed and dried extract was purified by prep. TLC (C_6H_6–EtOAc, 2:1). The gummy material from the major spot corresponded to **10a**/**10b**; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1780, 1750, 1700, 1650, 1250, 1125, 1060, 1025, 880 and 850; ^1H NMR: δ5.95 (*br*, H-3), 5.87 (*br*, H-14), 5.16 (*m*, H-6), 4.76 (*d*, J = 1 Hz, H-16a, b), 2.87 (*m*, H-2a), 1.78 (*br*, H-18), 1.37 (*br*, H-19), 1.04 (*br*, H-20), 0.97 (two closely spaced *d*, J = 7 Hz, H-17), 6.73 and 6.05 (*br q*, J = 7 Hz, H-3′ of **10b** and **10a**), 1.99 and 1.78 (*br d*, H-4′ of **10a** and **10b**), 1.96 and 1.78 (*br*, H-5′ of **10a** and **10b**; MS m/z (rel. int.): 414 $[M]^+$ (2.1), 331 (0.5), 315 (6.1), 305 (31.6), 203 (1.7), 180 (3.8), 175 (1.4), 161 (1.1), 149 (1.5), 147 (1.1), 135 (4.2), 123 (9.7), 122 (3.3), 121 (2.3), 111 (1.5), 109 (1.6), 107 (2.3), 98 (13.2), 95 (3.3), 83 (100). [Calc. for $C_{25}H_{34}O_5$: MW, 414.2406. Found: MW (MS), 414.2395.]

(b) A soln of 20 mg of **1a**/**1b** in 2 ml dioxane was refluxed with 20 mg of SeO_2 for 1 hr when reaction was complete. The usual work-up followed by prep. TLC (C_6H_6–EtOAc, 4:1) gave 10 mg of **9a**/**9b** as a gum; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1780, 1750, 1700, 1685, 1640, 1500, 1475, 1375, 1150, 1070, 1025 and 880 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): δ9.32 and 9.30 (H-18 of **9a** and **9b**), 6.87 (*dd*, J = 6, 5 Hz, H-3), 5.87 (*t*, J = 1 Hz, H-14), 5.33 (*m*, H-6), 4.76 (*d*, J = 1 Hz, H-16a, b), 1.48 (*br*, H-19), 1.08 (*br*, H-20), 0.86 (two closely spaced *d*, J = 7 Hz, H-17), 6.67 and 6.07 (*br q*, H-3′ of **9b** and **9a**), 1.94 and 1.75 (*br d*, H-4′ of **9a** and **9b**), 1.94 and 1.75 (*br*, H-5′ of **9a** and **9b**); MS m/z (rel. int.): 414 $[M]^+$ (0.1), 399 (0.2), 331 (20.2), 315 (3.5), 314 (4.9), 204 (3.3), 203 (3.1), 189 (1.8), 175 (2.7), 173 (2.2), 161 (2.0), 149 (2.9), 148 (3.5), 147 (2.6), 135 (3.1), 133 (3.5), 121 (3.1), 119 (3.3), 111 (4.0), 109 (2.2), 105 (4.5), 98 (4.4), 83 (100). [Calc. for $C_{25}H_{34}O_5$: MW, 414.2404. Found: MW (MS), 414.2395.]

(c) A soln of 20 mg of **1a**/**1b** and 10 mg *m*-chloroperbenzoic acid in 2 ml $CHCl_3$ was kept at 0° for 48 hr, diluted with 100 ml EtOAc, washed repeatedly with H_2O and $NaHSO_3$, dried and evaporated at red. pres. The residue was purified by prep. TLC (C_6H_6–EtOAc, 5:1) to give 10 mg **8a**/**8b** as a gum, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1780, 1750, 1700, 1640, 1450, 1385 and 885; ^1H NMR (270 MHz, $CDCl_3$): δ5.84 (*t*, J = 2 Hz, H-14), 4.89 (*br t*, J = 3 Hz, H-6), 4.74 (*d*, J = 2 Hz, H-16a, b), 3.04 (*d*, J = 4 Hz, H-3), 1.27 and 1.26 (H-18 of **8b** and **8a**), 1.16 and 1.14 (H-19 of **8b** and **8a**), 0.99 (H-20), 0.85 and 0.84 (*d*, J = 7 Hz, H-17 of **8a** and **8b**), 6.83 and 6.11 (*br q*, H-3′ of **8b** and **8a**), H-4′ and H-5′ signals in region δ1.75–2; MS m/z (rel. int.): 416 $[M]^+$ (0.2), 401 (0.2), 333 (23.6), 317 (3.6), 316 (4.6), 301 (1.4), 297 (1.1), 291 (1.8), 287 (3.8), 273 (3.2), 231 (1.1), 213 (1.0), 205 (10.2), 203 (1.7), 187 (3.3), 177 (3.6), 163 (4.0), 149 (4.8), 147 (4.0), 135 (5.2), 133 (5.4), 125 (7.5), 123 (4.4), 121 (8.6), 119 (6.0), 111 (9.0), 109 (7.6), 107 (10.4), 95 (9.2), 83 (100). [Calc. for $C_{25}H_{36}O_5$: MW, 416.2560. Found: MW (MS), 416.2547.]

Reactions of **4a**/**4c**. (a) Acetylation of 35 mg of **4a**/**4c** in 1 ml pyridine and 2 ml of Ac_2O at room temp. for 24 hr followed by the usual work-up and prep. TLC (C_6H_6–EtOAc, 1:1) of the crude product afforded 35 mg of **4b**/**4d** as a gum, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1775, 1750, 1725, 1700, 1650, 1450, 1375, 1250 and 1020; ^1H NMR (270 MHz, $CDCl_3$): δ5.87 (*quint*, J = 2 Hz, H-14), 5.67 (*br d*, J = 6 Hz, H-3), 5.21 (*m*, H-2), 5.07 and 5.02 (*br t*, J = 3 Hz, H-6 of **4d** and **4b**), 4.78 (*d*, J = 2 Hz, H-16a, b), 1.67 and 1.64 (*br*, H-18 of **4d** and **4b**), 1.28 (*br*, H-19), 1.05 (*br*, H-20), 0.89 and 0.88 (*d*, J = 7 Hz, H-17 of **4d** and **4b**), 6.72 and 6.02 (*br q*, J = 7 Hz, H-3′ of **4d** and **4b**), 2.07 and 2.06 (Ac of **4b** and **4d**), 1.97 and 1.80 (*br d*, J = 7 Hz, H-4′ of **4d** and **4b**, 1.78 (*br*, H-5′ of **4d**).

(b) Oxidation of 15 mg of **4a**/**4c** with 10 mg of CrO_3 in 1 ml pyridine at 0° for 24 hr, work-up as described for the oxidation of **1a**/**1b** and prep. TLC (C_6H_6–EtOAc, 5:1) gave 8 mg of **10a**/**10b** identical with material from oxidation of **1a**/**1b**, although the proportions of the two esters differed somewhat.

Reactions of **6a**/**6c**. (a) Acetylation of 25 mg of **6a**/**6c** in the

manner described for **4a**/**4c** and prep. TLC of the crude product ($CHCl_3$–MeOH, 49:1) afforded 25 mg of **6b**/**6d** (1:1 mixture) as a gum, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3530, 1780, 1725, 1700, 1645, 1450, 1375, 1250, 1175, 1065 and 1065; ^1H NMR (270 MHz, $CDCl_3$): δ5.84 (*quint*, J = 2 Hz, H-14), 5.00 (*m*, H-6), 4.83 (*m*, H-3), 4.75 (*d*, J = 2 Hz, H-16a, b), 1.24 (*br*, H-18), 1.17 and 1.15 (*br*, H-19 of **6b** and **6d**), 1.06 and 1.04 (*br*, H-20 of **6d** and **6b**), 0.87 and 0.85 (*d*, J = 7 Hz, H-17 of **6b** and **6d**), 6.91 and 6.13 (*br q*, J = 7 Hz, H-3′ of **6d** and **6b**), 2.08 and 1.82 (*br d*, H-4′ of **6b** and **6d**), 2.00 and 1.90 (*br*, H-5′ of **6b** and **6d**), 1.93 and 1.85 (Ac of **6b** and **6d**). On addition of TAI, a new signal appeared at δ8.24 (NH) and the following shifts were observed: H-3 to 5.66 (*m*), H-6 to 5.11 (*m*), H-16 to 4.80 and 4.79 (*d*), H-18 to 1.69 (*br*), H-19 to 1.35 (*br*), H-20 to 1.08 and 1.09 (*br*), H-17 to 0.90 (*d*). Signals of H-14, H-3′, H-4′ and H-5′ were not affected significantly.

(b) To a soln of 100 mg of **6a**/**6c** in 5 ml MeCN was added 180 mg NaI and 6 drops of trimethylsilyl chloride with stirring. After 10 min the reaction was complete (TLC). Dilution with 100 ml of H_2O, extraction with $CHCl_3$ and evaporation of the washed ($Na_2S_2O_3$) and dried extract gave a residue which exhibited two spots on TLC. The less polar material (35 mg) obtained by preparative TLC (C_6H_6–EtOAc, 4:1) was a mixture whose composition was not investigated further; the more polar material (55 mg) was a 5:1 mixture of **7a** and **7b**.

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