Pergamon

PII: S0031-9422(97)01075-3

Phytochemistry, Vol. 48, No. 4, pp. 651–656, 1998

Printed in Great Britain
0031-9422/98 $19.00+0.00

5,6-DIHYDRO-α-PYRONES FROM *SYNCOLOSTEMON ARGENTEUS*

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(*Received* 7 *October* 1997)

Key Word Index—*Syncolostemon argenteus*; Lamiaceae; 5,6-dihydro-α-pyrones; synargentolides A–E.

Abstract—The chemical structures of five new α-pyrones, synargentolides A–E, isolated from *Syncolostemon argenteus*, have been established as 6*R*-[4*R*,5*R*,6*S*-triacetyloxy-1*E*-heptenyl]-5,6-dihydro-2H-pyran-2-one, 6*R*-[5,6*S*-diacetyloxy-1,2-dihydroxy-3*E*-heptenyl]-5,6-dihydro-2H-pyran-2-one, 6*R*-[5,6*S*-diacetyloxy-1,2-dihydroxy-3*E*-heptenyl]-5*S*-acetyloxy-5,6-dihydro-2H-pyran-2-one, 6*R*-[5,6*S*-diacetyloxy-1,2-dihydroxy-3*E*-heptenyl]-5-hydroxy-5,6-dihydro-2H-pyran-2-one and 6*S*-[4,6*S*-diacetyloxy-1,5-dihydroxy-2*E*-heptenyl]-5*S*-acetyloxy-5,6-dihydro-2H-pyran-2-one, respectively, based on spectral chiroptical and chemical evidence.

INTRODUCTION

In continuation of our search for new 6-substituted 5,6-dihydro-α-pyrones from the Southern African genus *Syncolostemon* [1], we have examined *S. argenteus* from the Ongoya forest in the Kwazulu-Natal midlands of South Africa.

RESULTS AND DISCUSSION

Column chromatography of an acetone extract of the dried aerial parts of *S. argenteus* gave oleanolic acid as the major constituent, as has been observed for *S. parviflorus* [1], *S. rotundifolius* [2] and *S. densiflorus* [3]. A fraction eluted by hexane–EtOAc (1:1) was further purified by flash chromatography and HPLC to afford the α-pyrone, synargentolide A (**1**). Similar purification of a more polar (EtOAc) fraction provided synargentolides B–E (**2**–**5**).

The molecular formula of **1**, the major compound, was established as $C_{18}H_{24}O_8$ by HREI mass spectrometry and its IR spectrum is consistent with the presence of an α,β-unsaturated δ-lactone (ν_{max} 1735 cm^{-1}) and a *trans*-disubstituted double bond (ν_{max} 940 cm^{-1}). Although ^{13}C NMR spectroscopy (Table 1) only accounted for 17 of the 18 carbon atoms, it was clear from an HMQC experiment that an oxymethine carbon signal was concealed beneath the $CDCl_3$ solvent peak. From the chemical shifts of the ^{13}C signals, it was apparent that **1** contained four carbonyl carbons (δ 163.8, 170.0, 170.1 and 170.2), arising from three acetate moieties and the carbonyl carbon of the 5,6-dihydro-α-pyrone ring, and four vinylic carbons (δ 121.6, 128.3, 130.9 and 144.5) from an endocyclic and an exocyclic double bond. These data were supported by the ^1H NMR spectrum (Table 2), which revealed signals for the α- and β-protons of the α-pyrone ring (δ 6.01 and 6.84), two further vinylic protons (δ 5.64 and 5.71), four oxymethine protons (δ 4.86, 4.96, 5.08 and 5.15) and three acetate methyl singlets (δ 1.99, 2.02 and 2.12). All seven degrees of unsaturation implied by the molecular formula are thus accounted for.

The *E*-configuration of the exocyclic double bond in **1**, suggested from the IR data, was established using spin-decoupling NMR experiments. Irradiation of the 3′-methylene protons reduced the signal for H-2′ from a double triplet, which overlapped with the H-1′ resonance, to a doublet with $J_{1',2'} = 15.7$ Hz, indicative of a *trans*-disubstituted double bond (J = 9–11 Hz for a *cis*-olefin [4]).

Synargentolide A has four chiral centres. A positive $n \rightarrow \pi^*$ Cotton effect in the CD spectrum (λ_{max} = 265 nm, $\Delta\varepsilon = +3.5$) confirmed the expected (6*R*)-stereochemistry observed in all the 6-substituted 5,6-dihydro-α-pyrones thus far isolated from the Lamiaceae [1]. The configurations of the remaining 4′,5′ and 6′ asymmetric carbons were established as follows. Synargentolide A (**1**) was saponified and the acetonides prepared by filtering an acetone solution of saponified **1** through a column of Amberlyst 15 resin [5]. The acetonides, obtained in poor yield, were separated by HPLC to afford compounds **6** and **7** as the major and minor products, respectively. Although the chemical shift of the C-8′ quaternary carbon (δ 108.6) in the

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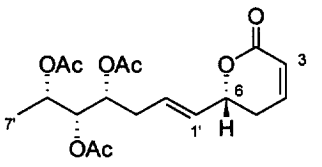

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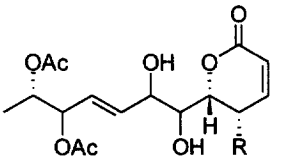

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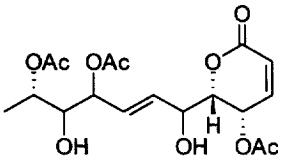

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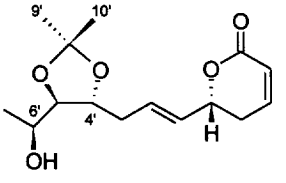

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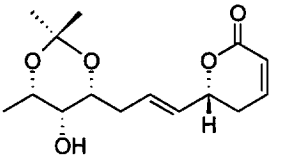

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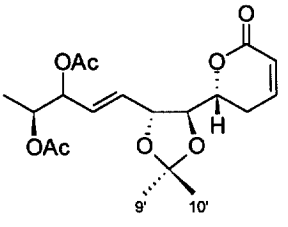

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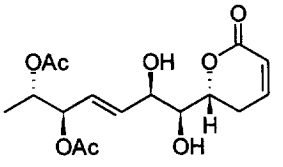

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acetonide **6** demonstrated the presence of a five-membered acetonide ring [6], neither HMBC two or three bond H–C correlations nor recourse to the chemical shifts of the oxymethine protons could define the position of this ring. However, the downfield shift of the H-6′ multiplet in the MTPA esters of **6** clearly showed that the C-6′ hydroxyl group had been esterified and the acetonide ring thus bridged C-4′ and C-5′. Furthermore, careful examination of the ROESY NMR spectrum of the (*S*)-MTPA ester of **6** revealed NOE correlations between H-4′ and one of the acetonide methyl groups and between H-5′ and the other acetonide methyl group, suggesting an *anti*-stereochemistry for the acetonide ring. Having positioned the acetonide ring, the absolute stereochemistry of the C-6′ secondary hydroxyl group in **6** was determined by application of the MTPA determination rule to the (*S*)- and (*R*)-MTPA esters [7]. The positive and negative $\Delta\delta_H$-values observed for the signals of the protons in the left and right segments (Fig. 1), respectively, indicated a 6′(*S*)-stereochemistry, consistent with the observation that all such 6-substituted 5,6-dihydro-α-pyrones isolated thus far from the Lamiaceae possess this stereochemistry [1]. In order to assign the absolute stereochemistry of C-4′ and C-5′, it was necessary to relate their stereochemistry to that of C-6′. The *syn*-stereochemistry at C-4′ and C-6′ in **1** could be inferred from the ^{13}C chemical shifts of the two acetonide methyls (δ 19.5 and 29.5) in **7**, which revealed that the six-membered 1,3-dioxolane ring possessed a chair conformation, with one of the methyl groups axial, the other equatorial [8]. Syn-

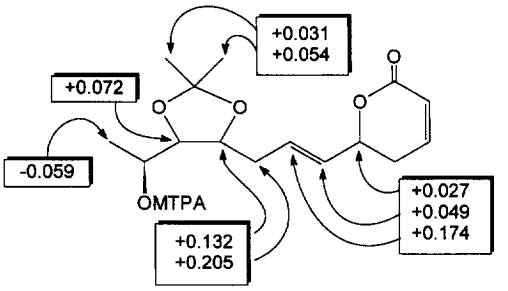

Fig. 1. MTPA ester of compound **6** ($\Delta\delta_H$ values in ppm).

argentolide A is therefore 6*R*-[4*R*,5*R*,6*S*-triacetyloxy-1*E*-heptenyl]-5,6-dihydro-2H-pyran-2-one.

HREI mass spectrometry suggested a molecular formula $C_{16}H_{22}O_8$ for synargentolide B (**2**), the second most abundant compound. IR data clearly showed the presence of hydroxyl groups (ν_{max} 3450 cm^{-1}), a *trans*-double bond (ν_{max} 950 cm^{-1}) and the carbonyl of an α-pyrone ring (ν_{max} 1735 cm^{-1}). ^{13}C NMR (Table 1) accounted for all 16 carbons, with resonances consistent with three carbonyls, two pairs of vinylic carbons and five oxymethine carbons. The ^1H NMR (Table 2) data also indicated two pairs of vinylic protons, with the H-3 and H-3′ signals (δ 5.97 and 5.94) overlapping, and five oxymethine protons (δ 3.65, 4.31, 4.53, 5.04 and 5.40). In addition, two methyl singlets (δ 2.01 and 2.05) indicated that two acetate moieties were present, which accounted for two of the carbonyl carbons (δ 171.8 and 172.2) and two of the oxymethine protons (δ 5.04 and 5.40). The α-pyrone ring accommodated the third carbonyl carbon (δ 166.3), one of the pairs of double bond protons (δ 5.97 and 7.06) and a third oxymethine proton (δ 4.53). It was thus concluded that the remaining two oxymethine protons were indicative of two hydroxyl substituents at these positions, although no hydroxyl protons were observed in the ^1H NMR spectrum, presumably due to deuterium exchange with the methanol-d_4 solvent.

The *E*-stereochemistry of the exocyclic double bond could be deduced from the $J_{3',4'}$ = 15.7 Hz, obtained directly from the H-4′ signal, which was a well resolved double doublet with coupling constants of 15.7 and 6.8 Hz. Measurement of the coupling constants of H-5′ ($J_{4',5'}$ = 6.8; $J_{5',6'}$ = 3.5 Hz) confirmed that the large H-4′ coupling was due to H-3′.

Synargentolide B possesses five asymmetric carbons. Once again a (6*R*)-configuration was assigned from the positive n → π* Cotton effect in the CD spectrum. The absolute stereochemistry at C-6′ was tentatively assigned as (*S*) from biosynthetic arguments, since the stereochemistry at this centre in **1** and other α-pyrones from the Lamiaceae has consistently been shown to have this stereochemistry [1]. The relative stereochemistry of the C-1′, C-2′ diol was investigated after the preparation of the five-membered acetonide derivative **8**. The $J_{1',2'}$ coupling constant (7.4 Hz) obtained from ^1H spin-decoupling experiments, suggested that H-1′ and H-2′ formed a dihedral angle of ca 18° or 154°, calculated from the Karplus equation. The former small angle is unlikely since it requires the bulky alkyl substituents to adopt a highly strained, nearly eclipsed diaxial conformation. The angle of 154°, however, implies that H-1′ and H-2′ are *trans*-diaxial, with the alkyl substituents in pseudo-equatorial orientations. This *trans*-diaxial orientation was confirmed by NOE difference experiments. Although the H-2′ and H-6 signals were too close for meaningful irradiation of H-2′, irradiation of H-1′ did not produce any enhancement of the H-2′ signal, confirming that H-1′ and H-2′ are *anti* to each other. The ROESY spectrum confirmed this arrangement. The absolute configurations at C-1′ and C-2′, however, remain undetermined.

The C-5′ stereochemistry of **2** was unassigned. A diastereomer of synargentolide B, compound (**9**) $[\alpha]_D$ +28.8° ($CHCl_3$), has been isolated from another member of the Lamiaceae, *Hyptis oblongfolia* [9]. Surprisingly, while synargentolide B is totally insoluble in $CDCl_3$ (no NMR spectrum could be obtained in this solvent), **9** is soluble. The structure 6*R*-[5,6*S*-diacetyloxy-1,2-dihydroxy-3*E*-heptenyl]-5,6-dihydro-2H-pyran-2-one is tentatively proposed for synargentolide B.

The NMR (Tables 1 and 2) and IR spectra of synargentolides B and C, $C_{18}H_{24}O_{10}$, (**3**) were very similar. It was apparent from the additional methyl singlet and lack of the characteristic endocyclic methylene proton signals that the α-pyrone ring in **3** contained a C-5 acetate substituent shown to be (*S*) from NOE experiments. A paucity of synargentolides C–E pre-

Table 1. ^{13}C NMR spectral data of compounds **1–5***

C	1†	2‡	3‡	4‡	5§
2	163.8	166.3	164.5	164.0	162.1
3	121.6	121.2	125.5	121.8	124.3
4	144.5	148.6	142.9	144.1	141.1
5	29.4	26.4	62.9	68.5	60.7
6	77.2	79.0	78.5	81.1	79.9
1′	130.9	75.8	71.5	74.6	66.9
2′	128.3	71.5	70.5	80.2	133.0
3′	34.0	136.6	136.8	131.9	127.2
4′	69.7	126.7	126.6	128.9	72.9
5′	73.8	76.3	76.3	76.0	73.1
6′	67.4	72.2	72.3	72.0	69.3
7′	16.0	15.2	15.1	15.1	15.8
Ac-CO	170.2[a]	172.2	172.2[c]	172.2[e]	169.4[g]
Ac-CO	170.1[a]	171.8	172.0[c]	171.8[e]	169.3[g]
Ac-CO	170.0[a]		171.5[c]		169.3[g]
Ac-Me	21.0[b]	21.0	21.1[d]	21.0[f]	20.8[h]
Ac-Me	20.9[b]	21.1	21.0[d]	20.9[f]	20.7[h]
Ac-Me	20.8[b]		20.5[d]		20.3[h]

† $CDCl_3$; ‡ CD_3OD; § DMSO-d_6.

* 100 MHz; δ; resonances with identical superscripts may be interchanged.

Table 2. ^{1}H NMR spectral data of compounds **1–5***

H	1†	2‡	3‡	4‡	5§
3	6.01 *dt* (9.8, 1.7)	5.97 *m* (9.7)	6.21 *d* (9.7)	5.98 *d* (10.5)	6.20 *d* (9.6)
4	6.84 *m*	7.06 *m*	7.17 *dd* (9.7, 6.0)	6.76 *dd* (10.1, 3.5)	7.09 *dd* (9.6, 6.0)
5	2.39 *m*	2.56 *m*	5.39 *dd* (6.0, 2.4)	4.68 *dd* (3.5, 8.0)	5.31 *m*
6	4.86 *m*	4.53 *td* (3.2, 6.5)	4.64 *dd* (2.4, 9.6)	5.14 *dd* (8.1, 4.8)	4.31 *dd* (2.4, 9.2)
1′	5.64 *dd* (5.6, 15.7)	3.65 *m*	3.78 *d* (9.5)	4.32 *dd* (4.8, 3.9)	4.22 *m*
2′	5.71 *m*	4.31 *m*	4.45 *d* (5.4)	4.40 *dd* (3.8, 6.5)	5.87 *m*
3′	2.28 *m*	5.94 *ddd* (5.8, 15.7, 0.9)	5.99 *dd* (5.5, 15.7)	5.87 *dd* (6.5, 15.9)	5.87 *m*
4′	5.15 *m*	5.79 *ddd* (15.7, 6.8, 1.2)	5.87 *ddd* (15.7, 6.8, 1.0)	5.76 *dd* (15.9, 6.4)	5.30 *m*
5′	5.08 *dd* (7.2, 4.0)	5.40 *dd* (6.8, 3.5)	5.45 *dd* (6.7, 3.4)	5.40 *dd* (6.4, 3.5)	3.58 *m*
6′	4.96 *m*	5.04 *m*	5.06 *dq* (3.5, 6.5)	5.03 *dq* (3.5, 6.6)	4.71 *m*
7′	1.18 *d* (6.4)	1.20 *d* (6.6)	1.22 *d* (6.5)	1.19 *d* (6.6)	1.17 *d* (6.3)
Ac-Me	1.99 *s*	2.05 *s*	2.01 *s*	2.05 *s*	2.04 *s*
Ac-Me	2.02 *s*	2.01 *s*	2.05 *s*	2.00 *s*	2.00 *s*
Ac-Me	2.12 *s*	—	2.06 *s*	—	1.95 *s*
1′-OH	—	—	—	—	5.56 *s*
5′-OH	—	—	—	—	5.30 *s*

† $CDCl_3$; ‡ CD_3OD; § DMSO-d_6.

* 400 MHz; δ; *J*-values in parentheses in Hz; assignments were confirmed by decoupling and 2D NMR experiments (COSY, HMQC, HMBC).

vented unequivocal assignment of the absolute stereochemistry at all the acyclic chiral centres in these minor compounds. Therefore, only the same 6′(*S*)-stereochemistry, suggested for **2**, and a 6(*R*)-configuration established from standard CD measurements are proposed for synargentolide C.

Synargentolide D (**4**) was unstable and decomposed before accurate mass, optical rotation and IR data could be obtained. However, the structure was established from one and two dimensional NMR studies. Acetylation of synargentolides C and D would have established if they had the same configurations but decomposition of the latter compound prevented further stereochemical studies. Comparison of the coupling constants of the C-5′ and C-6′ protons in **3** and **4** suggested a similar C-5′, C-6′ configuration, while the stereochemistry at C-5, C-1′, C-2′ and C-5′ remains unassigned.

The stereochemistry of the exocyclic double bond in synargentolide E, $C_{18}H_{24}O_{10}$ (**5**) could not be determined by measurement of the vicinal coupling constant because the chemical shifts of H-2′ and H-3′ were identical. However, examination of the IR spectrum revealed the absence of strong absorption between 730 and 675 cm^{-1}, characteristic of a *cis*-disubstituted double bond, and the presence of peaks at 995 and 927 cm^{-1} suggestive of a *trans*-double bond [10]. The 6(*S*)-stereochemistry (a Cahn-Ingold-Prelog priority order reversal has occurred) followed as usual from the CD data. A NOE correlation between H-6 and H-5 indicated a *syn*-stereochemistry here, while biosynthetic arguments suggested a 6′(*S*)-configuration. The stereochemistry of the other three chiral centres were not assigned.

EXPERIMENTAL

NMR were run on a Bruker 400 Mz instrument and IR run neat on either NaCl or AgCl discs. A Whatman Magnum 9-Partisil 10 column was used for semi-prep. HPLC. *Syncolostemon argenteus* was collected from the Ongoya forest in Kwazulu-Natal by Dr T. J. Edwards, Botany Department, University of Natal, Pietermaritzburg, in August, 1995. No voucher specimens could be taken because of the lack of flowers but a specimen had been collected previously from the same population (Hilliard and Burtt 5638, December 1968).

Isolation

Air-dried leaves (44.8 g) and stems (46.5 g) were separately extracted in a Soxhlet apparatus (Me_2CO)

for 3 days. The solns were decolourized with activated charcoal, filtered through a Celite pad and evapd *in vacuo* to give a light yellow solid (5.08 g and 0.77 g). The combined solids (5.85 g) were boiled with EtOAc, cooled, the insol. material consisting largely of oleanolic acid filtered off, and the filtrate evapd. The residue (4.58 g) was chromatographed on silica gel (Merck No. 7734, 50 g) and eluted with hexane–EtOAc. The frs eluted with hexane–EtOAc (2:1) gave crude oleanolic acid (1.40 g) as the major component. The frs eluted with hexane–EtOAc (1:1) (0.27 g) and EtOAc (0.47 g) were further separately purified by flash CC on silica gel (Merck No. 9385) and on normal phase HPLC in hexane–EtOAc (2:3) or (1:4) or EtOAc to afford synargentolide A (148.3 mg), synargentolide B (47.6 mg), synargentolide C (7.1 mg), synargentolide D (2.4 mg) and synargentolide E (9.5 mg), all as colourless oils.

Synargentolide A (**1**). $[\alpha]_D^{23} = +40°$ ($CHCl_3$; *c* 1.1). CD (MeOH) $\lambda_{max} = 265$ nm ($\Delta\varepsilon = +3.5$). IR ν_{max}^{NaCl} cm^{-1}: 1735, 1360, 1215, 1055, 1020, 940, 800. EIMS (70 eV) *m/z* (rel. int.): No $[M]^+$, 248 (3), 231 (2), 206 (15), 204 (11), 188 (15), 162 (17), 149 (15), 129 (25), 120 (26), 81 (28), 69 (24), 68 (80), 43 (100). HREIMS: $[M]^+$ 368.1464, $C_{18}H_{24}O_8$ requires 368.1469.

Synargentolide B (**2**). $[\alpha]_D^{25} = +45.6°$ (MeOH; *c* 1.2). CD (MeOH) $\lambda_{max} = 258$ nm ($\Delta\varepsilon = +3.2$). IR ν_{max}^{AgCl} cm^{-1}: 3450, 1735, 1370, 1240, 1060, 1025, 950, 800. EIMS (70 eV) *m/z* (rel. int.): No $[M]^+$, 206 (3), 167 (5), 149 (100), 141 (13), 128 (17), 113 (18), 97 (37), 85 (47), 81 (34), 71 (59), 69 (39), 57 (67), 43 (33). HREIMS: $[M]^+$ 342.1498, $C_{16}H_{22}O_8$ requires 342.1298.

Synargentolide C (**3**). $[\alpha]_D^{25} = +140°$ (MeOH; *c* 0.72). CD (MeOH) $\lambda_{max} = 266$ nm ($\Delta\varepsilon = +2.0$). IR ν_{max}^{AgCl} cm^{-1}: 3450, 1735, 1370, 1230, 1090, 1020, 945, 920, 805. EIMS (70 eV) *m/z* (rel. int.): No $[M]^+$, 198 (3), 194 (4), 193 (3), 185 (4), 155 (18), 149 (14), 143 (15), 126 (34), 125 (23), 113 (32), 99 (35), 97 (93), 96 (73), 95 (82), 86 (32), 81 (100), 71 (19), 69 (19), 57 (23), 43 (86). HREIMS: $[M]^+$ 400.1356, $C_{18}H_{24}O_{10}$ requires 400.1369.

Synargentolide E (**5**). $[\alpha]_D^{25} = +53°$ (MeOH; *c* 0.61). CD (MeOH) $\lambda_{max} = 265$ nm ($\Delta\varepsilon = +1.1$). IR ν_{max}^{AgCl} cm^{-1}: 3450 (OH), 1735, 1725 (sh), 1370, 1235, 1095, 1050, 1020, 995, 927, 805. EIMS (70 eV) *m/z* (rel. int.): No $[M]^+$, 224 (2), 181 (5), 164 (5), 153 (13), 148 (13), 125 (15), 117 (23), 99 (51), 97 (78), 96 (33), 85 (30), 83 (26), 81 (54), 69 (17), 68 (22), 57 (30), 43 (100); HREIMS: $[M]^+$ 400.1353, $C_{18}H_{24}O_{10}$ requires 400.1369.

Acetonides **6** *and* **7**

A soln of **1** (118.4 mg) in 2 ml MeOH and 2 ml 1 M NaOH was left for 2.5 days at 5°. The soln was acidified with 1 M HCl and heated for 2 min at 100°. The cooled soln was satd with NaCl (1 g) and the product extracted with Et_2O for 24 h. A soln of the product (69 mg) in 5 ml dry Me_2CO was left on a column (33 × 1 cm) of Amberlyst-15 resin [previously left to equilibrate for 1.5 h in dry Me_2CO (60 ml)] for 25 min and then slowly eluted with 90 ml Me_2CO and concd *in vacuo*. The product was chromatographed on Merck neutral alumina (20 g) in EtOAc and further purified by semiprep. HPLC on a normal phase column (EtOAc) to give acetonides **6** and **7** as oils (24.1 and 2.9 mg, respectively).

Acetonide **6**. ^1H NMR ($CDCl_3$): δ 1.20 (3H, *d*, $J_{6',7'} = 5.9$ Hz, H-7′), 1.36 (3H, *s*, H-10′), 1.37 (3H, *s*, H-9′), 2.00 (1H, *s*, OH), 2.34 (1H, *m*, H-3′), 2.43 (2H, *m*, H-5), 2.45 (1H, *m*, H-3′), 3.56 (1H, *m*, H-5′), 3.87 (1H, *m*, H-6′), 4.02 (1H, *m*, H-4′), 4.88 (1H, *m*, H-6), 5.68 (1H, *dd*, $J_{6,1'} = 6.7$ Hz, $J_{1',2'} = 15.5$ Hz, H-1′), 5.90 (1H, *m*, H-2′), 6.01 (1H, *dd*, $J_{3,4} = 9.8$ Hz, $J_{3,5} = 1.8$ Hz, H-3), 6.86 (1H, *m*, H-4). ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.3 (C-7′), 27.0 (C-10′), 27.3 (C-9′), 29.6 (C-5), 36.9 (C-3′), 67.5 (C-6′), 76.6 (C-4′), 77.8 (C-6), 83.6 (C-5′), 108.6 (C-8′), 121.5 (C-3), 129.4 (C-1′), 130.8 (C-2′), 144.7 (C-4), 164.0 (C-2). EIMS (70 eV) *m/z* (rel. int.): No $[M]^+$, 267 (20), 167 (3), 149 (9), 145 (17), 138 (34), 133 (8), 101 (16), 68 (63), 59 (85), 55 (23), 45 (32), 43 (100).

Acetonide **7**. ^1H NMR ($CDCl_3$): δ 1.25 (3H, *d*, $J_{6',7'} = 5.9$ Hz, H-7′), 1.38 (3H, *s*, H-9′), 1.47 (3H, *s*, H-10′), 1.53 (1H, *s*, OH), 2.32 (1H, *m*, H-3′), 2.43 (2H, *m*, H-5), 2.50 (1H, *m*, H-3′), 3.00 (1H, *m*, H-5′), 3.65 (1H, *m*, H-4′), 3.70 (1H, *m*, H-6′), 4.90 (1H, *m*, H-6), 5.69 (1H, *dd*, $J_{6,1'} = 6.7$ Hz, $J_{1',2'} = 15.5$ Hz, H-1′), 5.93 (1H, *m*, H-2′), 6.04 (1H, *dd*, $J_{3,4} = 9.8$ Hz, $J_{3,5} = 1.8$ Hz, H-3), 6.86 (1H, *m*, H-4). ^{13}C NMR (100 MHz, $CDCl_3$): δ 18.4 (C-7′), 19.5 (C-9′), 29.5 (C-10′), 29.8 (C-5), 34.9 (C-3′), 69.8 (C-6′), 72.7 (C-4′), 72.8 (C-5′), 78.0 (C-6), 98.5 (C-8′), 121.7 (C-3), 129.3 (C-1′), 131.0 (C-2′), 144.6 (C-4).

Preparation of (R)- *and* (S)-*MTPA esters of acetonide* **6**.

The following preparation is representative. A soln of **6** (4.4 mg) and DMAP (5.2 mg) in CH_2Cl_2 (1 ml) was added to a soln of (*R*)-MTPA (16 mg) and DCC (33 mg) in CH_2Cl_2 (0.2 ml). The mixt. was shaken periodically and after 90 min was dild with a few drops of H_2O and EtOAc (10 ml). The EtOAc layer was filtered to remove the dicyclohexylurea ppt., worked up as usual and chromatographed on silica gel (benzene–hexane–EtOAc). The fr. eluted with EtOAc–hexane (1:2) afforded the (*R*)-MTPA ester (7.6 mg).

R-MTPA ester of **6**. ^1H NMR ($CDCl_3$): δ 1.29 (3H, *s*, H-9′ or 10′), 1.34 (3H, *s*, H-9′ or 10′), 1.42 (3H, *d*, $J_{6',7'} = 6.3$ Hz, H-7′), 2.04 (1H, *m*, H-3′), 2.15 (1H, *m*, H-3′), 2.40 (2H, *m*, H-5), 3.57 (3H, *s*, OMe), 3.64 (1H, *dd*, $J_{4',5'} = 7.0$ Hz, $J_{5',6'} = 7.0$ Hz, H-5′), 3.74 (1H, *m*, H-4′), 4.83 (1H, *m*, H-6), 5.05 (1H, *m*, H-6′), 5.51 (1H, *dd*, $J_{6,1'} = 6.2$ Hz, $J_{1',2'} = 15.6$ Hz, H-1′), 5.64 (1H, *m*, H-2′), 6.04 (1H, *d*, $J_{3,4} = 9.8$ Hz, H-3), 6.87 (1H, *m*, H-4), 7.38 (2H, *m*, Ph), 7.51 (2H, *m*, Ph).

S-MTPA ester of **6**. ^1H NMR ($CDCl_3$): δ 1.34 (3H, *s*, H-9′ or 10′), 1.36 (3H, *d*, $J_{6',7'} = 6.8$ Hz, H-7′), 1.37 (3H, *s*, H-9′ or 10′), 2.24 (1H, *m*, H-3′), 2.35 (1H, *m*, H-3′), 2.39 (2H, *m*, H-5), 3.48 (3h, *s*, OMe), 3.71 (1H,

dd, H-5′), 3.87 (1H, *m*, H-4′), 4.86 (1H, *m*, H-6), 5.10 (1H, *m*, H-6′), 5.60 (1H, *dd*, $J_{6,1'} = 6.3$ Hz, $J_{1',2'} = 15.6$ Hz, H-1′), 5.81 (1H, *m*, H-2′), 6.03 (1H, *dd*, $J_{3,4} = 9.8$ Hz, $J_{3,5} = 1.6$ Hz, H-3), 6.85 (1H, *m*, H-4), 7.41 (2H, *m*, Ph), 7.50 (2H, *m*, Ph).

Acetonide **8**. Acetonide **8** was prepd from **2** (9.0 mg) as described above. It was evident from TLC on silica gel in EtOAc–hexane (3:2) that the product from the alumina column consisted of a single compound, acetonide **8** (7.2 mg); no further purification was required. ^{1}H NMR ($CDCl_3$): δ 1.20 (3H, *d*, $J_{6,7} = 6.5$ Hz, H-7′), 1.41 (3H, *s*, H-10′), 1.42 (3H, *s*, H-9′), 2.03 (3H, *s*, Ac-Me), 2.07 (3H, *s*, Ac-Me), 2.52 (2H, *m*, H-5), 3.87 (1H, *dd*, $J_{6,1'} = 7.0$ Hz, $J_{1',2'} = 7.4$ Hz, H-1′), 4.43 (1H, *td*, $J_{5,6} = 7.6$ Hz, $J_{6,1'} = 6.9$ Hz, H-6), 4.48 (1H, *dd*, $J_{1',2'} = 7.4$ Hz, $J_{2',3'} = 4.3$ Hz, H-2′), 5.06 (1H, *dq*, $J_{5',6'} = 3.5$ Hz, $J_{6',7'} = 6.6$ Hz, H-6′), 5.39 (1H, *dd*, $J_{4',5'} = 5.0$ Hz, $J_{5',6'} = 3.4$ Hz, H-5′), 5.86 (1H, *m*, H-3′), 5.86 (1H, *m*, H-4′), 6.02 (1H, *dt*, $J_{3,4} = 9.9$ Hz, $J_{3,5} = 1.6$ Hz, H-3), 6.89 (1H, *dt*, $J_{3,4} = 9.9$ Hz, $J_{4,5} = 4.4$ Hz, H-4). ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.0 (C-7′), 21.0 (Ac-Me), 21.1 (Ac-Me), 26.3 (C-5), 26.9 (C-9′), 26.9 (C-10′), 70.6 (C-6′), 74.5 (C-5′), 78.0 (C-6), 79.1 (C-2′), 80.9 (C-1′), 110.4 (C-8′), 121.5 (C-3), 127.3 (C-4′), 132.4 (C-3′), 144.5 (C-4), 162.6 (C-2), 169.9 (Ac-CO), 170.3 (Ac-CO).

Acknowledgements—We thank Dr T. J. Edwards of the Botany Department, University of Natal, Pietermaritzburg, for the collection and identification of plant material, Prof. Ferreira of the University of the Orange Free State for CD measurements and Rhodes University and the Foundation for Research Development for financial assistance.

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