Notes

New Annulated Furanoses: A New Free-Radical Isomerization of an *S*-Methyl Hex-5-enylxanthate to an *S*-(Cyclopentylmethyl) *S*-Methyl Dithiocarbonate

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In recent years, free-radical chemistry has emerged as a powerful method for the synthesis of carbocycles.[1] In their seminal studies, Wilcox,[2] RajanBabu,[3] and Bartlett[4] established useful routes for the preparation of enantiomerically pure polyoxygenated cyclopentanoid compounds. We have also developed new, chiral, free-radical-based strategies for the synthesis of polyfunctionalized cyclohexane rings,[5] and more recently we have designed simple and efficient approaches to complex cyclopentane molecules.[6,7]

In our current work on iridoids[8,9] (**A**) a projected key intermediate is the annulated furanose[10,11] (**B**), the critical step being the unprecedented cyclization of an endocyclic carbon centered radical[12] at C3 over an acceptor located at C7 of a furanose chiron (**C**) (Scheme I).

In this work we report the successful accomplishment of this objective, the synthesis of the annulated furanoses **5**, **6**, **9**, **11**, **13**, and **14**, and the new, free-radical isomerization of dithiocarbonate **4** to the dithiolcarbonate **6**.

In our approach the obvious starting material is the readily available diacetone glucose **1**[13] (Scheme I). Standard manipulations allowed us to synthesize diol **2**;[14] sodium periodate cleavage[15] followed by Lewis acid catalyzed (BF_3·Et_2O) allyltrimethylsilane addition to the resulting aldehyde[16] gave compound **3** (Scheme II) in good chemical yield (73%) and as the only detected isomer (^{1}H NMR). In accordance with the results described by Danishefsky[17] in a study involving related *xylose* derivatives, the absolute configuration at C5 in compound **3** has been assigned as *R*. Finally, acetylation gave the radical precursor acetate **4** in fair yield. With this compound in hand we attempted the desired free-radical cyclization. Under the initial conditions [slow addition (8 h) of tributyltin hydride (2 equiv) and AIBN (cat.) to substrate **4** (0.03 M) in toluene] and after careful flash chromatography,[18] we isolated product **5** in good yield (74%) as well as the carbocycle **6** (10%) and traces of a mixture of isomeric acetates (ratio 1:3.6) **7**, which we could not separate (Scheme II). Compound **7** is the result of oxygen–carbon (thioxo group) cleavage; this process gives a hydroxyacetate that partially rearranges to its isomer by acetyl migration. Compound **5** is the expected 5-exo cyclization carbocycle obtained in a large diastereomeric excess (91%; ^{1}H NMR analysis); the analytical and spectroscopic data (see Tables I and II) are consistent with this structure. Note the chemical shifts of H3 (δ 2.68, dd, $J_{3,4}$ = 4.7 Hz, $J_{3,7}$ = 9.3 Hz) and C(8)H_3 (δ 1.04, d, J = 6.8 Hz) in the ^{1}H NMR spectrum. In the ^{13}C NMR analysis we observed C3, C7, and C(8)H_3 at 49.51, 28.68, and 16.69 ppm, respectively; these values are in good agreement with the recorded data for compound **12** (see Scheme II and Tables I and II), whose absolute configuration at the newly formed stereocenter C7 has been shown to be *S*.[7] Additional evidence was obtained after NOE experiments between H3/H7 (8.8%) in the ^{1}H NMR spectrum. The obtention of a major cis isomer in this process is to be expected, according to general trends in the cyclization of 1-alkylhex-5-enyl-substituted radicals.[19] On the other hand, the formation of furanose **6** was totally unexpected. The elemental analysis and the mass spectrum suggest a molecular formula $C_{15}H_{22}S_2O_6$. Careful analysis of the spectroscopic values (see Tables I and II) firmly established the structure. Particularly, in the ^{1}H NMR spectrum we observed H8 as the AB part (δ 3.14, dd; 3.00, dd, $J_{8,8'}$ = 7.2 Hz, $J_{8,7}$ = 7.0 Hz, $J_{8',7}$ = 8.3 Hz) of an ABX system; H3 at 2.80 ppm, d, $J_{3,4}$ = 4.4 Hz, $J_{3,7}$ = 10.2 Hz, and a singlet integrating for three protons at 2.43 ppm corresponding to –SC(O)SCH_3. This carbonyl group appeared in the ^{13}C NMR spectrum at 189.00 ppm

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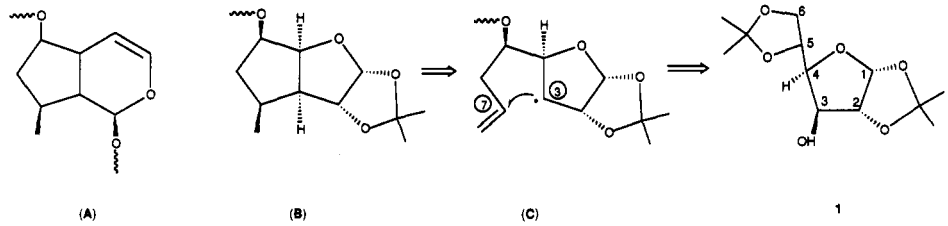
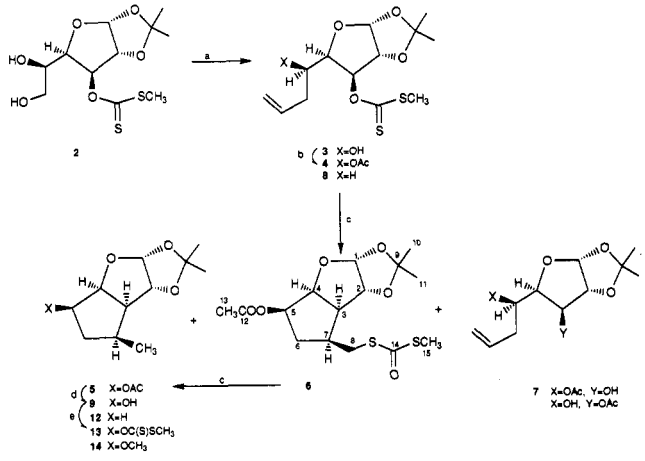
Scheme I



Scheme II[a]

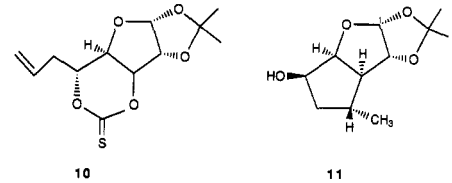


[a] Reagents: (a) (i) $NaIO_4$, SiO_2, CH_2Cl_2 (100%); (ii) $(CH_3)_3SiCH_2CH{=}CH_2$, $BF_3{\cdot}Et_2O$ (73%); (b) (i) Ac_2O, pyridine (90%); (c) Bu_3SnH, AIBN, toluene, reflux; (d) MeOH, Et_3N, H_2O (81%); (e) NaH, S_2C, ICH_3 (89%).

and in the IR spectrum as a strong band[20] at 1650 cm^{-1}. Compound **6** was also obtained with very good diastereoselectivity (88%). As expected,[21] when this compound was treated with tributyltin hydride (5 equiv) plus AIBN, at reflux overnight, the furanose **5** was obtained in good yield (71%); this result clearly establishes that the absolute configuration at C7 in **6** is *S* and that the formation of compound **6** from **5** requires stronger conditions than those initially used by us. It is likely that the reactions leading to **5** and **6** are competitive processes with different rate constants (see below). A possible mechanism which accounts for these observations is shown in Scheme III. Radical **A** fragments to **B** and, after 5-exo cyclization, isomerizes to radical **C**; final hydrogen transfer provides product **5**, but radical **C** *also attacks the sulfur of the thioxo group in the radical precursor* **4**, giving rise to **6** and the radical **B**, which then propagates the free-radical chain reaction. The overall result is a remarkable new isomerization of a hex-5-enyl xanthate to a cyclopentanemethyl methyl dithiolcarbonate.

It is important to note that, as several authors have observed, one of the limitations of synthetic sequences based on free radical carbon–carbon forming reactions is that they are generally terminated by hydrogen atom transfer.[22] Alternative radicals capable of attacking at other elements are desirable.[23] Zard and co-workers have recently reported novel radical-chain reactions based on O-alkyltin dithiocarbonates as reagents which eliminate these problems.[24] The present example is also one of these cases and features the new and unprecedented behavior of a xanthate in a 5-exo free-radical ring closure; previous cyclizations of this type[4,9,25] gave the corresponding carbocycles free of products similar to **6** (Scheme II). In view of this fact, several experiments were carried out in order to gain more insight into this process: First, compound **4**, warmed to 120 °C in toluene over 20 h, was recovered unchanged; this result excludes any type of thermal isomerization[20] and indicates a free-radical mechanism. Second, AIBN alone does not initiate the radical chain reaction, either thermally or photolytically. Third, using the initial conditions (see above), but allowing the reaction to run overnight, after slow addition, the previously observed ratio **5**/**6** (80/20) remained unchanged (84/16). Fourth, at low conversion (45%), using tributyltin hydride (0.17 equiv), the ratio **5**/**6** was 88/12, showing that the hydrogen atom transfer from tributyltin hydride is more rapid than the attack of radical (**C**) to compound **4** (Scheme III). Fifth, slow addition of the organostannane is not critical: under the initial conditions, but mixing substrates and reagents at the same time, compounds **7** and **5** (accompanied by 6% of the trans isomer) were obtained in 11 and 72% yields, respectively. Product **6** was not detected. Sixth, using UV photolysis, always under the same conditions, but at 5 °C, compound **5** (57%) was the only isolated product. Finally, suppressing the source of hydrogen, and using hexabutylditin as initiator, under UV irradiation, and after 14 h at room temperature, compound **4** was partially recovered (52% of conversion), yielding a mixture of **5**/**6** (1:1); in this case, probably, toluene was the source of hydrogen. Using benzene as solvent and after 7 h of irradiation under the same conditions, precursor **4** was recovered (47% conversion) and **6** (19%) plus **7** (10%) were isolated.

The results obtained in the free-radical cyclization of compound **4** prompted us to analyze the carbocyclization of compound **3** (Scheme II). In this process, after chromatography, we isolated the carbocycle **9** (22% yield; diastereomeric excess 90%, Scheme II), product **10** (15%),



and a complex mixture of more polar compounds, probably arising from the nonselective tributyltin hydride reduction of the 1,3-diol thiocarbonyl[26] moiety present in compound **10**. This product is the result of intramolecular attack by

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Table I. ^{1}H NMR ($CDCl_3$; ppm) data for the annulated furanoses 5, 6, 9, 11 and 12

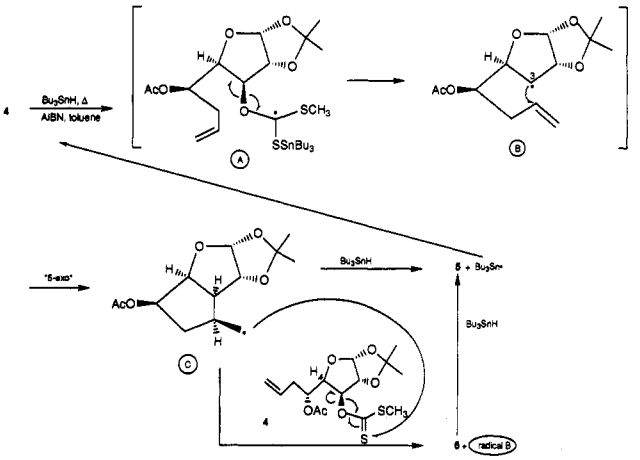
	5		6		9		11		12	
H1	5.78, d	$J_{1,2}$ = 3.4 Hz	5.84, d	$J_{1,2}$ = 3.4 Hz	5.75, d	$J_{1,2}$ = 3.5 Hz	5.87, d	$J_{1,2}$ = 3.5 Hz	5.70, d	$J_{1,2}$ = 3.9 Hz
H2	4.67, d		4.67, d		4.71–4.60, m		4.51, d		4.66, d	
H3	2.68, dd	$J_{3,4}$ = 4.7 Hz	2.80, dd	$J_{3,4}$ = 4.4 Hz	2.72, dd	$J_{3,4}$ = 5.1 Hz	2.26, t	$J_{3,4}$ = $J_{3,7}$ = 6.6 Hz	2.66, dd	$J_{3,4}$ = 5.2 Hz
		$J_{3,7}$ = 9.3 Hz		$J_{3,7}$ = 10.2 Hz		$J_{3,7}$ = 10 Hz				$J_{3,7}$ = 10.5 Hz
H4	4.90–4.74, m		4.88–4.76, m		4.71–4.60, m		4.75, t		4.84, t	$J_{4,5}$ = 4.6 Hz
H5					3.91, m		4.16, m		1.87, m	
									1.45, m	
H6					1.65, m		1.45, m		1.78, m	
									1.25, m	
H7	2.30–2.00, m		2.40–2.32, m		2.15–2.00		1.90–1.80, m		2.10, m	
H8	1.04, d	J = 6.8 Hz	3.14, dd	$J_{8,8'}$ = 7.2 Hz	1.05, d	J = 6.9 Hz	1.06, d	J = 6.6 Hz	1.02, d	J = 7.2 Hz
			3.00, dd	$J_{8,7}$ = 7.0 Hz						
				$J_{8',7}$ = 8.3 Hz						
H9										
H10,11	1.48, 1.30; s, s		1.49, 1.32; s, s		1.52, 1.32; s, s		1.52, 1.34; s, s		1.51, 1.32; s, s	
H12										
H13	2.07, s		2.43, s							
H14										
H15			2.08, s							

Table II. ^{13}C NMR ($CDCl_3$; ppm) Data for the Annulated Furanoses 5, 6, 9, 11, and 12[a]

	5	6	9	11	12
C1	106.86	106.60	106.51	107.13	106.70
C2	83.06*	82.84*	85.30*	85.98*	86.35*
C3	49.51	49.23	49.64	56.01	52.33
C4	82.57*	82.34*	85.23*	85.48*	83.10*
C5	74.24	73.62	73.79	72.49	33.92**
C6	35.97	33.73**	40.33	41.40	32.36**
C7	28.68	34.79	29.45	33.29	33.30
C8	16.69	32.08**	16.38	20.10	16.93
C9	111.53	111.95	111.88	112.36	110.82
C10	27.34	27.31	27.62	27.56	27.55
11	26.58	26.63	26.87	26.86	26.77
C11	170.68	189.20			
C13	20.85	13.07			
C14		170.56			
C15		20.86			

[a] The values with an asterisk can be interchanged.

Scheme III



the free hydroxyl group in C5 on the thiocarbonyl of the xanthate at C3. Compound **9** is the expected cis cyclized product, also obtained with high stereoselectivity (90%); the ^{1}H and ^{13}C NMR spectroscopic data are in good accordance with the values described for **5** or **6** (see Tables I and II). In addition, basic hydrolysis of substrate **5** gave a compound in 76% yield similar in its analytical and spectroscopic values and behavior in TLC with product **9** (Scheme II). Apart from this, minor amounts of the trans carbocycle **11** were isolated; the spectroscopic data (see Tables I and II) strongly support the assigned configuration at C7. Particularly significant are the shifts to higher field of the resonances for carbons C3, C7, C8 ($\Delta\delta$ +6.37, +3.84, +3.72, respectively); this is in good accordance with the observed patterns for cis- and trans-substituted cyclopentanes.[27] In no case in the cyclization of precursor **3** could we detect products related to **6**. Note also that in the ring closure of compounds **3** or **4** no products arising from 6-endo cyclization were observed.

In fact, in the cyclization of compound **8**, only compound **12** (Scheme II) was obtained in low yield (35%), but no product related to **6** was detected.[7] The structure and stereochemistry of the annulated furanose **9** was correlated with **12** by treating the derived xanthate **13** with tributyltin hydride under typical reduction conditions.[28] In addition

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to other complex products whose structure could not be determined, we isolated **12** (9%), the product of OC(S) cleavage **9** (33%), and the unexpected methyl ether **14** (15%).

Thus, we can conclude that the formation of compound **6** is probably structure dependent and that in the formation of this compound the mode of addition of the reagents is critical, a phenomenon that is well known in reactions under kinetic control.[29]

In summary, a series of new annulated furanoses have been synthesized in good yields and excellent diastereoselectivities. The transformation of compound **4** to **6** represents the only known case of the isomerization of an *S*-methyl hex-5-enylxanthate to an *S*-(cyclopentylmethyl) *S*-methyl dithiocarbonate via a new free-radical chain reaction.

Experimental Section

General Procedures. Melting points were determined in a Kofler apparatus and are uncorrected. The ^{1}H NMR coupling constants were verified by homonuclear decoupling experiments. The progress of all reactions was monitored by thin-layer chromatography (TLC) performed on aluminum plates precoated with silica gel HF-254 (0.2-mm layers) containing a fluorescent indicator (Merck, 5539). Detection was by UV (254 nm), followed by charring with sulfuric acid spray, or with a solution of ammonium molybdate(VI) tetrahydrate (12.5 g) and cerium sulfate hydrate (5.0 g) in 10% aqueous sulfuric acid (500 mL). Flash chromatography was performed using Kiesegel 60 (230–400 mesh, Merck) silica gel and hexane/ethyl acetate mixtures as eluent.

Free-Radical Cyclization. Standard Procedure. To a solution of the radical precursor in toluene (0.03 M), treated with argon for 1 h, was added a solution of tributyltin hydride (2 equiv) plus AIBN (cat.) in toluene (0.8 M) over a period of 8 h via syringe pump at reflux and under argon. The solvent was removed and the residue dissolved in ether and stirred with an equal volume of 20% aqueous potassium fluoride solution overnight. The organic phase was separated, dried, and concentrated. The residue was submitted to flash chromatography.

Radical Precursor 3. To a mixture of silica gel (20 g) in methylene chloride (30 mL) and an aqueous solution of sodium periodate (14.7 mL, 9.65 mmol; 0.65 M), was added the diol **2**[14] (2.28 g, 7.37 mmol) dissolved in methylene chloride (15 mL). After 40 min at room temperature the reaction was filtered over Celite and the cake washed with methylene chloride. The organic phase was dried and evaporated and the residue submitted to chromatography (hexane/EtOAc (9/1)) giving an aldehyde (1.90 g, 6.83 mmol), which, without further analysis, was immediately submitted to reaction. After the mixture was cooled at −78 °C, boron trifluoride etherate (2.57 mL, 20.49 mmol) was added to the solution of the aldehyde in dry methylene chloride (20 mL) followed by dropwise addition of allyltrimethylsilane (2.71 mL, 17.07 mmol). After 3 h the mixture was warmed to room temperature and stirred (1 h 30 min). The reaction mixture was added to a saturated solution of aqueous sodium bicarbonate, extracted with ethyl acetate, washed with brine, and dried. Flash chromatography (hexane/EtOAc (9/1)) gave alcohol **3** (1.6 g, 73%): oil; $[\alpha]^{25}_D$ +21 (*c* 3.7, $CHCl_3$); IR (film) ν 3500, 3080, 1645, 1220 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.07 (d, $J_{3,4}$ = 2.8 Hz, 1 H, H3), 5.95 (d, $J_{1,2}$ = 3.8 Hz, 1 H, H1), 5.90 (m, 1 H, H7), 5.20 (m, 2 H, 2 H8), 4.66 (d, $J_{1,2}$ = 3.8 Hz, 1 H, H2), 4.18 (dd, $J_{4,3}$ = 2.8 Hz, $J_{4,5}$ = 8.7 Hz, 1 H, H4), 2.60 (s, 3 H, −OC(S)SCH_3), 2.70–2.50 (m, 1 H, H5), 2.30–2.20 (m, 1 H, H5′), 2.07 (d, *J* = 4.3 Hz, 1 H, O*H*), 1.53, 1.32 (s, s; 3 H, 3 H); MS (70 eV) *m*/*z* 321 (M^+ + 1, 1). Anal. Calcd for $C_{13}H_{20}SO_5$: C, 48.73; H, 6.29; S, 20.01. Found: C, 49.02; H, 6.44; S, 19.81.

Radical Precursor 4. The alcohol **3** (1.9 g, 5.93 mmol) dissolved in pyridine (10 mL) was treated with acetic anhydride (10 mL) at room temperature overnight, the solvents were evaporated, and the residue was submitted to chromatography (hexane/EtOAc (9/1)) giving **4** (2.1 g, 98%): oil; $[\alpha]^{25}_D$ −29 (*c* 3.0, $CHCl_3$); IR (film) ν 3080, 1750, 1645, 1235, 1075 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.01 (d, $J_{3,4}$ = 2.9 Hz, 1 H, H3), 5.94 (d, $J_{1,2}$ = 3.9 Hz, 1 H, H1), 5.79 (m, 1 H, H7), 5.20–5.08 (m, 2 H, 2 H8), 4.60 (d, $J_{1,2}$ = 3.9 Hz, 1 H, H2), 4.40 (dd, $J_{4,3}$ = 2.9 Hz, $J_{4,5}$ = 9.0 Hz, 1 H, H4), 2.74–2.64 (m, 1 H, H5), 2.57 (s, 3 H, OC(S)SCH_3), 2.45–2.33 (m, 1 H, H5′), 1.95 (s, 3 H, $OCOCH_3$), 1.53, 1.32 (s, s; 3 H, 3 H). Anal. Calcd for $C_{15}H_{22}S_2O_6$: C, 49.70; H, 6.11; S, 17.69. Found: C, 49.65; H, 6.00; S, 17.31.

Free-Radical Cyclization of Compound 4. Under the typical conditions, precursor **4** (1.64 g, 4.5 mmol) gave, after flash chromatography (hexane/EtOAc (9/1)), products **5** (854 mg, 74%), **6** (174 mg, 10%), and **7** (10 mg). **5**: oil; $[\alpha]^{25}_D$ +51 (*c* 0.14, $CHCl_3$); IR (film) ν 1740, 1385, 1250, 1165 cm^{-1}; ^{1}H and ^{13}C NMR (see Tables I and II); MS (70 eV) *m*/*z* 257 (M^+ + 1, 9). Anal. Calcd for $C_{13}H_{20}O_5$: C, 60.92; H, 7.87. Found: C, 61.21; H, 8.15. **6**: oil; $[\alpha]^{25}_D$ +31 (*c* 0.27, $CHCl_3$); IR (film) ν 1740, 1650, 1245, 1075, 1020 cm^{-1}; ^{1}H and ^{13}C NMR (see Tables I and II); MS (70 eV) *m*/*z* 347 (M^+ − 15, 16). Anal. Calcd for $C_{15}H_{22}S_2O_6$: C, 49.70; H, 6.11. Found: C, 50.05; H, 6.40. **7** (mixture of isomers): oil; IR (film) ν 3480, 1740, 1645, 1245 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) (major isomer) δ 5.90 (d, $J_{1,2}$ = 3.5 Hz, 1 H, H1), 5.89–5.70 (m, 1 H, H7), 5.25–5.05 (m, 2 H, 2 H8), 4.98 (dt, $J_{5,4}$ = 3.2 Hz, $J_{5,6}$ = 6.7 Hz, 1 H, H5), 4.55 (d, $J_{1,2}$ = 3.5 Hz, 1 H, H2), 3.98 (m, 1 H, H4), 2.70–2.30 (m, 4 H, 2 H6, 2 H3), 2.11 (s, 3 H, $OCOCH_3$), 1.49, 1.31 (s, s; 3 H, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) (major isomer) δ 172.47 ($OCOCH_3$), 132.86 (C7), 118.26 (C8), 111.73 (C9), 104.73 (C1), 84.50 (C5), 80.72, 73.63, 70.49 (C2, C3, C4), 35.83 (C6), 26.59, 26.21 [$(CH_3)_2C$], 20.86 ($OCOCH_3$); MS (70 eV) *m*/*z* 257 (M^+ − 15, 100). Anal. Calcd for $C_{13}H_{20}O_6$: C, 57.34; H, 7.40. Found: C, 57.11; H, 7.84.

Free-Radical Cyclization of Compound 3. Following the standard procedure radical precursor **3** (258 mg, 0.8 mmol) gave, after flash chromatography (hexane/EtOAc (9/1)), alcohols **9** (38 mg, 32%) and **10** (33 mg, 15%) and a mixture of very polar products (55 mg), whose structures could not be absolutely determined. **9**: oil; $[\alpha]^{25}_D$ +40 (*c* 3.9, $CHCl_3$); IR (film) ν 3460, 1455, 1380, 1375, 1220 cm^{-1}; ^{1}H and ^{13}C NMR (see Tables I and II); MS (70 eV) *m*/*z* 214 (M^+, 26), 199 (100), 185 (3), 157 (7), 139 (4). Anal. Calcd for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47. Found: C, 61.36; H, 8.81. **10**: oil; $[\alpha]^{25}_D$ +38 (*c* 0.4, $CHCl_3$); IR (film) ν 3080, 1755, 1400, 1190 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.97 (d, $J_{1,2}$ = 3.7 Hz, 1 H, H1), 5.80 (dt, $J_{7,6}$ = 7.4 Hz, $J_{7,8}$ = 10 Hz, $J_{7,8'}$ = 17 Hz, 1 H, H7), 5.30–5.20 (m, 2 H, 2 H8), 4.81 (d, $J_{3,4}$ = 3.0 Hz, 1 H, H3), 4.74 (d, $J_{1,2}$ = 3.7 Hz, 1 H, H2), 4.69 (dt, $J_{5,6}$ = 7 Hz, $J_{5,4}$ = 1.6 Hz, 1 H, H5), 4.36 (dd, $J_{5,4}$ = 1.6 Hz, $J_{4,3}$ = 3.0 Hz, 1 H, H4), 2.65–2.40 (m, 2 H, 2 H6), 1.49, 1.33 (s, s; 3 H, 3 H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 187.07 (C12), 130.44 (C7), 120.40 (C8), 112.93 (C9), 104.66 (C1), 83.56 (C2, C4), 77.98, 72.15, (C3, C5), 37.20 (C6), 26.59, 26.16 (C10,11). Anal. Calcd for $C_{12}H_{16}SO_5$: C, 52.99; H, 5.92; S, 11.77. Found: C, 52.74; H, 5.68; S, 11.60.

Hydrolysis of Compound 5. Acetate **5** (294 mg, 1.15 mmol) was dissolved at 0 °C in a mixture of methanol (5 mL), water (4 mL), and triethylamine (1 mL). After 2 h 20 min, the reaction was warmed to room temperature and stirred for 4 h 30 min. The solvent was removed and the residue submitted to flash chromatography (hexane/EtOAc (75/25)), giving **9** (187 mg, 76%), **9** + **11** (9 mg, 3%), and **11** (6 mg, 2%). **11**: oil; $[\alpha]^{25}_D$ +12 (*c* 0.27, $CHCl_3$); IR (film) ν 3480, 1380, 1375, 1240, 1170 cm^{-1}; ^{1}H and ^{13}C NMR (see Tables I and II); MS (70 eV) *m*/*z* 214 (M^+, 2). Anal. Calcd for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47. Found: C, 61.47; H, 8.68.

Xanthate 13. To a suspension of sodium hydride (95%, 50 mg, 2.0 mmol, 1.5 equiv) in dry tetrahydrofuran (15 mL) were added carbon disulfide (0.12 mL, 2.0 mmol) and methyl iodide (0.25 mL, 4.0 mmol). Then, the alcohol **9** (286 mg, 1.33 mmol) was added dropwise, at room temperature. After being stirred for 2 h, the mixture was quenched with acetic acid, the solvent evaporated, and the residue diluted with ethyl acetate and washed with a saturated aqueous solution of sodium bicarbonate and brine. The organic phase was dried and evaporated and the residue submitted to flash chromatography (hexane/EtOAc (9/1)) giving **13** (362 mg, 89%): oil; $[\alpha]^{25}_D$ +42 (*c* 1.1, $CHCl_3$); IR (film) ν 2975, 1380, 1375, 1220, 1165 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.84 (d, $J_{1,2}$ = 3.5 Hz, 1 H, H1), 5.60 (m, 1 H, H5), 4.93

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(t, $J_{4,5} = J_{3,4} = 4.4$ Hz, 1 H, H4), 4.71 (d, $J_{1,2} = 3.5$ Hz, 1 H, H2), 2.75 (dd, $J_{3,4} = 4.4$ Hz, $J_{3,7} = 10.3$ Hz, 1 H, H3), 2.56 (s, 3 H, $OCOCH_3$), 2.32–2.15 (m, 2 H, H6, H7), 1.70–1.50 (m, 1 H, H6'), 1.50, 1.33 (s, s; 3 H, 3 H), 1.09 (d, $J = 6.7$ Hz, 3 H, CH_3 (8)); MS (70 eV) m/z 289 ($M^+ - 15$, 10). Anal. Calcd for $C_{13}H_{20}S_2O_4$: C, 51.29; H, 6.62; S, 21.06. Found: C, 51.42; H, 6.90; S, 20.79.

Reduction of Xanthate 13. Xanthate 13 (342 mg, 1.12 mmol) was dissolved in toluene (10 mL). AIBN (cat.) and tributyltin hydride (0.44 mL, 1.68 mmol, 1.5 equiv) were added. The mixture was heated at reflux, overnight, and then the same quantity of AIBN and Bu_3SnH was added and heating continued for 1 h more. The solvent was evaporated and the residue submitted to chromatography (hexane/EtOAc (9/1)) giving **12** (20 mg, 9%), similar in its spectroscopic data and behavior in TLC to the compound obtained in the cyclization of precursor 8,[7] **14** (38 mg, 15%), and **9** (79 mg, 33%). **12**: oil; $[\alpha]^{25}_D$ +15 (c 0.4, $CHCl_3$); IR (film) $\bar{\nu}$ 2978, 1420, 1380, 1375, 1020 cm^{-1}; ^1H and ^{13}C NMR (see Tables I and II); MS (70 eV) m/z 199 ($M^+ + 1$, 14). Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.90; H, 9.31. **14**: oil; $[\alpha]^{25}_D$ +32 (c 2.4, $CHCl_3$); IR (film) $\bar{\nu}$ 2970, 1380, 1375, 1250, 1165 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.80 (d, $J_{1,2} = 3.6$ Hz, 1 H, H1), 4.77 (t, $J = 4.3$ Hz, 1 H, H4), 4.68 (d, $J_{1,2} = 3.6$ Hz, 1 H, H2), 3.53 (ddd, $J_{4,5} = 3.6$ Hz, $J_{5,6} = 6.0$ Hz, $J_{5,6'} = 9.1$ Hz, 1 H, H5), 3.42 (s, 3 H, OCH_3), 2.66 (dd, $J_{3,4} = 4.9$ Hz, $J_{3,7} = 10.2$ Hz, 1 H, H3), 2.20–1.97 (m, 2 H, H6, H7), 1.50 (s, 3 H), 1.35 (m, 1 H, H6'), 1.32 (s, 3 H), 1.03 (d, $J = 7.1$ Hz, 3 H, CH_3 (8)); MS (70 eV) m/z 227 ($M^+ - 1$, 20). Anal. Calcd for $C_{12}H_{20}O_4$: C, 63.13; H, 8.83. Found: C, 63.53; H, 8.77.

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