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A synthetic route to 3-*C*-alkyl (or 3-*C*-phenyl-) 2,3-dideoxy-D-*erythro*-pentono-1,4-lactones: intermediates in the synthesis of 2(3*H*)-furanones *,†

Panolil C. Raveendranath, Vincent J. Blazis, Kwasi Agyei-Aye, Anna K. Hebbler, Lisa N. Gentile ‡, Elma S. Hawkins, Stephen C. Johnson and David C. Baker **

Department of Chemistry, The University of Tennessee, Knoxville, TN 37996-1600 (USA)

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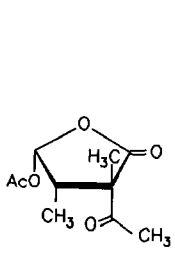
ABSTRACT

A series of 3-*C*-alkyl- (and 3-*C*-phenyl-) 2,3-dideoxy-D-*erythro*-pentono-1,4-lactones, compounds which are important in the synthesis of modified nucleosides and antibiotic sugars, were synthesized from D-ribonolactone. By a route that proceeded via 5-*O*-protected D-ribonolactone, 5-*O*-protected 2,3-dideoxy-D-*glycero*-pent-2-enono-1,4-lactones were synthesized and reacted with R_2CuLi or a complex $PhSCu(RMgBr)_n$ to give respectively the 3-*C*-alkyl or 3-*C*-phenyl compounds. Details of the preparation of the *O*-protected intermediates, as well as the selection of the organometallic reagents, are provided.

INTRODUCTION

One approach to the synthesis of certain modified 2(3*H*)-furanone antibiotics [e.g., acetomycin (**1**)[3]],



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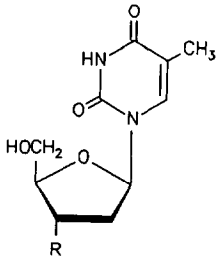

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* For preliminary reports, see refs 1 and 2.

† This work was carried out in The Department of Chemistry, The University of Alabama, Tuscaloosa, AL 35487, USA.

‡ NSF Summer Undergraduate Research Participant, 1986.

** Corresponding author.

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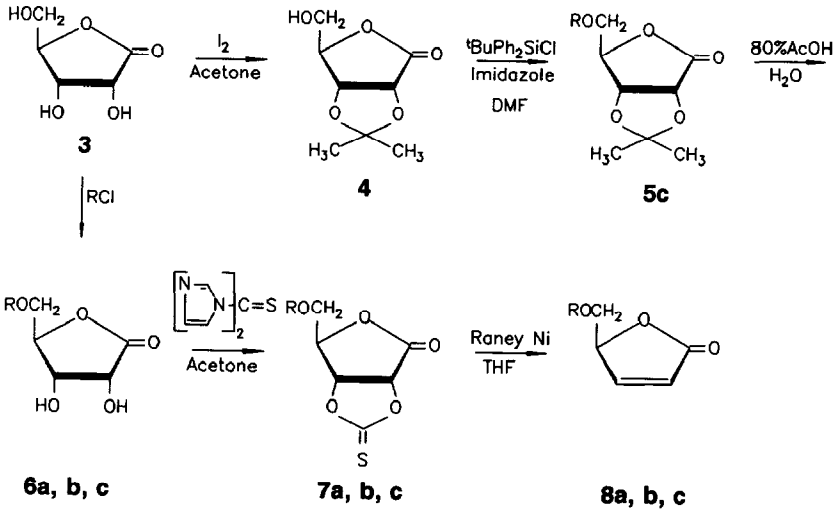
as well as certain 3′-*C*-alkyl-2′,3′-dideoxynucleosides[4] (**2**) requires that one have ready access to 2,3-dideoxy-5-*O*-protected-D-*glycero*-pent-2-enono-1,4-lactones [i.e., *O*-protected *S*-hydroxymethyl-2(5*H*)-furanones or (4*S*)-hydroxymethyl-2-buten-4-olides such as **8a–8c**, Scheme 1]. These versatile intermediates[5–10] serve as chiral substrates for the stereospecific 1,4-addition of organometallic reagents to give 3-*C*-alkyl- (or 3-*C*-phenyl-) 2,3-dideoxy-D-*erythro*-pentono-1,4-lactones (**9–21**, Scheme 2), which are direct precursors for 2(3*H*)-furanone antibiotics[13,14] and 3-*C*-alkyl-3-deoxy nucleosides[4], among other important classes of compounds including ionophores[7,11] and α-methylene lactones[12]. In this paper are presented detailed, workable, preparative procedures by which D-ribono-1,4-lactone[15] (**3**), a commercially available compound, is converted by way of butenolides **8a–8c** to the 5-*O*-protected 3-*C*-alkyl- (or 3-*C*-phenyl-) pentono-1,4-lactones **9–21**.

RESULTS AND DISCUSSION

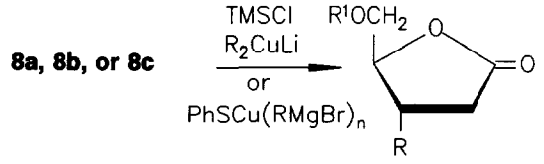
Butenolide synthesis (compounds **8a–8c**).—While numerous methods have been reported for the synthesis of 5-*O*-protected (4*S*)-hydroxymethyl-2-buten-4-olides, very few of the methods were found in our hands to be directly amenable to modest sized preparations of intermediates (e.g., 10–100 mmol reactions) required for a serious synthetic program.

For the preparation of the 5-*O*-triphenylmethyl- (trityl-) protected butenolide **8a** (Scheme 1), D-ribono-1,4-lactone (**3**) could be directly tritylated at elevated tem-



Series a. R = Ph_3C—
b. R = *tert*-$BuMe_2Si$—
c. R = *tert*-$BuPh_2Si$—

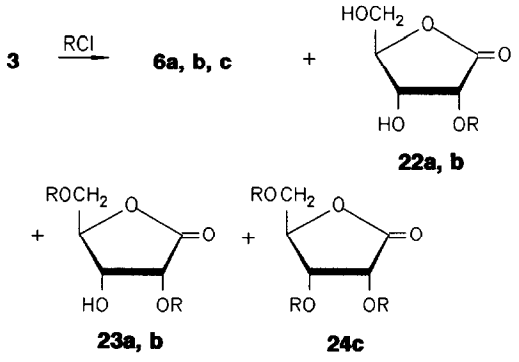
Scheme 1.



No.	R =	R¹ =
9	Me—	*tert*-BuPh$_2$Si—
10	Et—	*tert*-BuPh$_2$Si—
11	Pr—	*tert*-BuPh$_2$Si—
12	Bu—	*tert*-BuPh$_2$Si—
13	Me—	Ph$_3$C—
14	Et—	Ph$_3$C—
15	Pr—	Ph$_3$C—
16	2-Pr—	Ph$_3$C—
17	Bu—	Ph$_3$C—
18	*sec*-Bu—	Ph$_3$C—
19	Ph—	Ph$_3$C—
20	Me—	*tert*-BuMe$_2$Si—
21	Bu—	*tert*-BuMe$_2$Si—

Scheme 2.

peratures in pyridine using a procedure based on one that was originally reported by Ireland and co-workers[7]. While the process is shown in our work to also produce a 2-*O*-trityl derivative **22a** (Scheme 3), isolated in one experiment in 3.2% yield, and 14.2% of a 2,5-di-*O*-trityl compound **23a**, the original procedure was modified to allow for the direct crystallization of 5-*O*-triphenylmethyl-D-ribono-1,4-lactone (**6a**). Crystallization, together with recovery of additional product from the mother liquors by chromatography, consistently afforded **6a** directly from **3** in yields of ca. 70% on a 110-mmol scale. The structures for byproducts **22a** and **23a**,



Series a. R = Ph$_3$C—
b. R = *tert*-BuMe$_2$Si—
c. R = *tert*-BuPh$_2$Si—

Scheme 3.

which may prove to be useful as selectively protected D-ribonolactones, were established by ^1H NMR spectral studies. The ^{13}C NMR assignments are unambiguous. For example, in **22a** the resonances for C-2 and C-3 appear respectively at δ 71.9 and 69.3. ^{13}C–^1H Heteronuclear coordination (XHCOR) experiments unequivocally allowed the assignments of the H-2 and H-3 signals at δ 4.67 and 2.47, respectively. For the bis-tritylated product **23a**, similar techniques allowed for the assignment of the structure as the 2,5-di-*O*-trityl compound. Note that H-2 (δ 4.01) resonates at higher field than H-3 (δ 4.86). Such a shift undoubtedly arises via anisotropic effects from the 5′-*O*-trityl group. A loss of the C*H*–O*H* coupling, upon exchange with D_2O further served to establish the assignment of the H-3 resonance. Both compounds were characterized by elemental analysis. The enhanced reactivity of the 2-OH group in D-ribonolactone over the 3-OH group is noteworthy.

Using a similar approach for the preparation of 5-*O*-*tert*-butyldimethylsilyl-D-ribono-1,4-lactone (**6b**), problems were encountered in that greater amounts of byproducts, including the 2-*O*- and 2,5-di-*O*-silyl derivatives **22b** and **23b**, respectively, were encountered, resulting in lowered yields of **6b** and attendant difficulties in its purification. By reacting *tert*-butylchlorodimethylsilane (Bu^tMe_2SiCl) in DMF–imidazole at room temperature using Corey and Venkateswarlu's original procedure[16], **6b** could be isolated in a yield of 54% by column chromatography, along with 1.7% of the 2-*O*-Bu^tMe_2Si (**22b**) and 11.8% of the 2,5-di-*O*-Bu^tMe_2Si (**23b**) derivatives. XHCOR studies allowed definitive assignments for both **22b** and **23b** by procedures analogous to those used for **22a** and **23a** (see previous paragraph). Lowering the reaction temperature to −20°C resulted in little change in the overall spectrum of products. Given the fact that yields of **6b** could routinely be obtained in ca. 50% yield, no further attempts to improve the procedure were made.

The situation with the *tert*-butyldiphenylsilyl (Bu^tPh_2Si) analogue **6c**, however, was even more problematic. Despite a report to the contrary[17], reaction of *tert*-butylchlorodiphenylsilane (Bu^tPh_2SiCl) with **3** gave, in our hands, only a 5% yield of the desired **6c**, with a large proportion (26%) of the product being the tris-silylated **24c**, along with numerous byproducts as shown by TLC. While these products were not isolated and identified, their TLC behavior was similar to that for **22b** and **23b**, leading one to speculate that similar 2-*O*- and 2,5-di-*O*-silyl derivatives were formed. Numerous alterations in reaction conditions failed to produce an acceptable direct synthesis of **6c**. [Note: While this work was in progress, Hanessian and Murray reported[11] a procedure to directly silylate **3** at low temperature to give **5c**; however, the procedure requires a 2:1 ratio of **3**:Bu^tPh_2SiCl, which is wasteful of **3**, as the latter compound is not easily recovered from the reaction mixture.]

A workable process to produce **6c** is shown in Scheme 1. D-Ribono-1,4-lactone (**3**) is first converted by means of a high-yielding iodine-catalyzed acetonation procedure[18] to 2,3-*O*-isopropylidene-D-ribono-1,4-lactone (**4**), which is then sily-

lated at 60°C with Bu^tPh_2SiCl–DMF–imidazole to give **5c**. The latter compound is subsequently deacetonated in 80% acetic acid to furnish **6c** in 54% yield over the three steps on a ca. 15–75-mmol scale.

Consideration was given to several methodologies for the conversion of the protected lactones **6a–6c** to their respective 5-*O*-protected 2,3-dideoxy-D-*glycero*-pent-2-enono-1,4-lactones **8a–8c**. Camps and co-workers used pyrolysis of the 2,3-orthoester of **6a** to give **8a** in respectable yield[6,19]; however, attempts to scale up the process led to diminishing yields for any preparation of greater than ca. 5-mmol scale, even when using a Kugelrohr apparatus as has been advocated[17] for the preparation on a 10-g scale. Other methods, e.g., use of the 2,3-dimethylaminomethylene acetal[20,21] or the classical Corey–Winter procedure[22], were evaluated and found unsatisfactory for the preparation of **8a** (experimental data not provided). A reliable process for all three butenolides proved to be the conversion of 5-*O*-protected D-ribono-1,4-lactones (**6a–6c**) to their 2,3-thionocarbonates **7a–7c**, with subsequent treatment with deactivated Raney nickel[7] to give the butenolides **8a–8c** (Scheme 1). By means of this two-step process, **8a**, **8b**, and **8c** could be produced in yields of 74, 84, and 96%, respectively. The butenolide synthesis was found to proceed with minimal difficulties (e.g., formation of the 2,3-saturated compound from over-reduction) if precautions were taken to properly deactivate the Raney nickel in refluxing acetone. The products, in general, were identical in physical constants and in spectroscopic data with the compounds previously reported. One notable exception was the ^1H NMR spectrum of **8a** where the chemical shifts were erroneously assigned for H-2 and H-3 in the original report[7], a fact which has been confirmed by others[10]. Optical rotation data for **8a–8c** were found to differ among reports in the literature, due no doubt, in part, to the method of synthesis for the given example. Racemization under some reaction conditions undoubtedly occurs (e.g., the reaction of either Bu^tMe_2SiCl or Bu^tPh_2SiCl with (4*S*)-hydroxymethyl-2-buten-4-olide[9,10] in base) giving rise to smaller absolute values being observed for specific rotations. The wide divergence in optical rotation noted for **8b** prepared in this study from the values reported[9,10] is unexplained. The product reported herein contained no saturated isomer as observed by ^1H NMR spectroscopy at 200 MHz.

*Synthesis of 3-C-alkyl-(or 3-C-phenyl-) 2,3-dideoxy-*D-erythro-*pentono-1,4-lactones* (**9–21**).—Addition of organocopper reagents was shown, both in the present study and in an earlier report[4], to be an effective means of introducting an alkyl or aryl substituent at the C-3 position of butenolides **8a–8c** to stereoselectively give the 3-*C*-substituted D-*erythro*-pentono-1,4-lactones **9–21** (Scheme 2). However, the procedures were not straightforward. Owing to differences in reactivities among organocuprate reagents, as well as the availability of suitable organometallic precursors for their preparation, the procedures were varied as shown by the examples listed in Table I.

For examples where the required organolithium reagents were either commercially available (or could be conveniently prepared in the laboratory), either of two

TABLE I

Physicochemical data for compounds **9–21**

Compound no.	Method [a]	Yield (%)	TLC [b] (R_f)	Physical state	mp (°C)	Optical Rotation [c] $[\alpha]_D$ (c, $CHCl_3$)	Formula	Elemental Analyses			
								Calculated		Found	
								C	H	C	H
9 [d]	A	42									
9 [d]	B	87									
9 [d]	C	95									
10 [d]	A	67									
11 [d]	A	77									
12 [d]	A	76									
13 [e]	B	86	0.29	crystal	107–109	+27.6 (1.13)	$C_{25}H_{24}O_3$	80.62	6.49	80.53	6.55
14	A	76	0.34	syrup		+16.3 (0.89)	$C_{26}H_{26}O_3$	80.80	6.78	80.68	6.81
15	A	67	0.39	syrup		+24.2 (2.40)	$C_{27}H_{28}O_3$	80.97	7.05	80.90	7.08
16	A	76	0.38	syrup		+27.6 (1.14)	$C_{27}H_{28}O_3$	80.97	7.05	80.74	7.13
17	B	73	0.43	crystal	118–119	+35.3 (2.60)	$C_{28}H_{30}O_3$	81.13	7.29	81.24	7.33
18	B	68	0.43	syrup		[f]	$C_{28}H_{30}O_3$	81.13	7.29	81.02	7.32
19	B	52	0.38	crystal	138–139	+19.8 (1.13)	$C_{30}H_{26}O_3$	82.92	6.03	82.83	6.07
20	C	93		syrup		+4.9 (3.0)	$C_{12}H_{24}O_3Si$	58.97	9.90	59.21	9.98
21	C	37	0.47	syrup		+14.3 (7.00)	$C_{15}H_{30}O_3Si$	62.89	10.55	62.81	10.60

[a] A, using $PhSCu(RMgX)_n$ reagent of ref 27; B, using the R_2CuLi reagent from CuI of ref 23; C, using the Me_2CuLi reagent from $CuBr \cdot Me_2S$ of refs 24 and 25. [b] Solvent: 8:2 hexanes–EtOAc; [c] t, 22±1°C; [d] See ref 4 for data. [e] See ref 7. [f] Mixture of diastereomers.

organocopper reagents were found to be generally useful for preparation of the 3-substituted butanolides (Methods B or C, Table I). Conversion of **8c** to **9** in previous studies[4,24] had shown that an effective reagent (Method B, Table I) was the Me_2CuLi complex formed from MeLi, and CuI, and chlorotrimethylsilane (Me_3SiCl)[23]. Equally effective, or slightly better, was the Me_2CuLi complex (Method C, Table I) formed from $CuBr \cdot Me_2S$ (refs 24 and 25); however, the latter reagent was problematic in its use as the complex was most effective only when the $CuBr \cdot Me_2S$ was freshly prepared for immediate use. Thus, for the preparation of **13** and **17–19**, the RLi–CuI–Me_3SiCl methodology was successfully employed (Table I), with good results for both the *n*-butyl and *sec*-butyl examples cited. Earlier work[24] had used R_2CuLi prepared from $CuBr \cdot Me_2S$, which was found to be quite workable, but its preparation rendered the process a more labor-intensive procedure. Under no circumstances was any racemization observed with these reagents as has been reported in the case of a 2-phenylthio-substituted butenolide[26].

In examples where the alkyl lithium reagents were either commercially unavailable and/or difficult to prepare and manipulate (e.g., the ethyl-, propyl-, or 2-propyl-lithium reagents), an alternate methodology using the appropriate Grignard reagent complexed with phenylthiocopper[27] proved most effective. This was initially reported[4] for examples **9–12**, and in the present study the truly versatile nature of the reagent was clearly demonstrated in the preparation of the 5-*O*-trityl compounds **14–16**, where yields of 67–76% were consistently observed for the reaction of $PhSCu(RMgX)_n$ with **8a**. In examples from the earlier study[4], the method favorably compared with either of the methods using R_2CuLi reagents. This magnesium-based reagent is to be recommended on account of its ease of preparation and moderate to high yields of adducts as attested by the examples given in Table I. Products **13–19** have been used to prepare analogues of acetomycin (**1**) reported in the accompanying paper[14].

EXPERIMENTAL

General procedures.—Melting points were determined on a Thomas–Hoover capillary melting point apparatus equipped with a Cole–Parmer model 8520-50 Digi-Sense digital thermometer that was calibrated with known standards. Solvents were evaporated at aspirator vacuum at ca. 40°C. ^1H NMR spectra were determined at 200 MHz on ca. 0.1% solutions using a Nicolet NT-200 or at 360 MHz using a Bruker AM 360 instrument as indicated. Chemical shifts are reported as δ (ppm) downfield from an internal standard of tetramethylsilane. Multiplicities are first-order values (in Hz) and are indicated as: d, doublet; dd, doublet of doublets; m, multiplet; q, quartet; s, singlet; and t, triplet. ^{13}C NMR spectra were determined at 100 MHz on ca. 1–2% solutions in $CDCl_3$ using a Bruker AMX 400 instrument. Chemical shifts are reported as δ (ppm) with respect to the solvent. Low-resolution mass spectrometry (MS) was carried out at 70 eV on a Hewlett–

Packard 5985 MS system. Optical rotations at the sodium D-line were determined at 22 ± 1°C in $CHCl_3$ on a Perkin–Elmer model 241 spectropolarimeter using 1-dm cells. Infrared (IR) spectra were recorded on a Perkin–Elmer 728B instrument. Thin-layer (TLC) and column chromatography were carried out using E. Merck silica gel products [aluminum-backed TLC plates with a 0.2-mm coating (cat. no 5554) and bulk silica gel of either (A) 63–200 or (B) 40–63 μm particle size (cat. nos. 7734 and 9385, respectively)]. TLC visualization was by either 245-nm UV light or by spray–heat development using an anisaldehyde–H_2SO_4 reagent[28]. Chemicals were of reagent grade and were used directly. Anhydrous solvents were prepared as follows: acetone, dried over anhyd Na_2SO_4 and distilled after refluxing with $KMnO_4$; tetrahydrofuran (THF) and diethyl ether, distilled from K–benzophenone ketyl. *N,N'*-Thiocarbonyldiimidazole was either prepared[29,30] or purchased from Fluka Chemical Co. Active Raney nickel was purchased from Aldrich Chemical Co. or W.R. Grace and Co. D-Ribono-1,4-lactone was purchased from Sigma Chemical Co.; a current supplier is Pfanstiehl Laboratories, Waukegan, IL (USA). Elemental analyses were carried out by Atlantic Microlab, Inc., Norcross, GA (USA). In cases where the compounds retained solvent of crystallization, the solvent was confirmed by ^1H NMR spectroscopy on the analytical sample.

Preparation of 2,3-O-isopropylidene-D-ribono-1,4-lactone (**4**).—To a solution of iodine (3.6 g, 14 mmol) in 360 mL of acetone was added D-ribono-1,4-lactone (**3**, 15.0 g, 101 mmol), and the mixture was stirred for 12 h at room temperature. The mixture was then diluted with $CHCl_3$ (1 L) and washed with 0.2 M aq $Na_2O_3S_2$ (2 × 500 mL). The combined aqueous layer was extracted with $CHCl_3$ (2 × 150 mL), and the dried ($MgSO_4$) extracts were evaporated to give pure **4** (17.5 g, 92%) as a white solid: mp 134–136°C; $[\alpha]_D^{23}$ −70.5° (*c* 1.2, pyridine). [lit.[31] mp 138–139°C; $[\alpha]_D^{24}$ −65.7° (*c* 2.13, pyridine).]

5-O-tert-Butyldiphenylsilyl-2,3-O-isopropylidene-D-ribono-1,4-lactone (**5c**).—To a solution of **4** (15.0 g, 78.8 mmol) and imidazole (7.8 g, 115 mmol) in DMF (30 mL) was added Bu^tPh_2SiCl (22.2 g, 80.7 mmol). The mixture was stirred for 2.5 h at 60°C under an atmosphere of dry N_2, at then end of which time diethyl ether (1 L) was added, and the solution was extracted with water (3 × 250 mL). The organic layer was dried ($MgSO_4$) and evaporated to give a pale-yellow syrup which was chromatographed ($CHCl_3$ eluent) to give **5c** (27.9 g, 82%) as a white solid: mp 92–94°C; $[\alpha]_D^{23}$ −10.9° (*c* 2.0, $CHCl_3$); ^1H NMR data ($CDCl_3$): δ 7.43–7.62 (m, 10 H, aryl), 4.89 (m, 1 H, H-2), 4.72 (m, 1 H, H-3), 4.57 (m, 1 H, H-4), 3.78, 3.94 (AB of ABX, J_{AB} 11.6, $J_{AX} = J_{BX} = 2.3$ Hz, H-5a,5b), 1.47, 1.49 (2s, 6 H, CMe_2). Anal. Calcd for $C_{24}H_{30}O_5 \cdot 0.1\ CHCl_3$: C, 66.01; H, 6.92. Found: C, 66.03; H, 7.02.

Preparation of 5-O-tert-butyldiphenylsilyl-D-ribono-1,4-lactone (**6c**).—A suspension of **5c** (25.0 g, 57.0 mmol) in 80% (v/v) aq AcOH (1500 mL) was heated under reflux for 1.5 h, at the end of which time a colorless solution had formed. The solvent was evaporated to dryness, and the residual syrup was dissolved in EtOAc (500 mL), dried ($MgSO_4$), and the solvent was evaporated to afford a pale-yellow

syrup. The syrup was purified by column chromatography (98:2 $CHCl_3$–MeOH eluent) to give pure **6c** (15.98 g, 72%) as a white amorphous solid: mp 80–82°C; $[\alpha]_D$ +44.2° (*c* 5.2, $CHCl_3$). [lit.[11] mp 83°C; $[\alpha]_D$ +46.5° (*c* 1.1, $CHCl_3$.] Anal. Calcd for $C_{21}H_{26}O_5Si$: C, 65.25; H, 6.78. Found: C, 65.25; H, 6.83.

Preparation of 5-O-tert-*butyldiphenylsilyl-2,3-O-thiocarbonyl-*D-*ribono-1,4-lactone* (**7c**).—To a solution of **6c** (12.0 g, 31.0 mmol) in dry acetone (1200 mL) was added *N,N'*-thiocarbonyldiimidazole (12.0 g, 67.3 mmol), and the resulting solution was heated for 2.5 h, under reflux in an atmosphere of dry N_2. At the end of this time, the mixture was cooled to room temperature, concentrated to half the original volume, and then poured into water (400 mL). The resulting mixture was extracted with CH_2Cl_2 (3 × 300 mL), and the combined organic layers were successively washed with satd aq $NaHCO_3$ (2 × 200 mL) and water (200 mL), dried ($MgSO_4$), and the solvent was evaporated to give a syrup. The syrup was dissolved in CH_2Cl_2 and percolated through a short column of silica gel (7 × 19 cm) and eluted with $CHCl_2$ to give **7c** (12.8 g, 96%) as a yellow solid: mp 116–118°C; $[\alpha]_D$ −18.1° (*c* 1.5, $CHCl_3$). [lit.[17] mp 116.5–117°C; $[\alpha]_D^{24}$ −21° (*c* 10.9, ether).]

Preparation of 5-O-tert-*butyldiphenylsilyl-2,3-dideoxy-*D-glycero-*pent-2-enono-1,4-lactone* (**8c**).—A suspension of Raney nickel (80 g wet weight) in acetone (350 mL) was heated under reflux overnight, at the end of which time the solvent was carefully decanted, and the catalyst was resuspended in THF (400 mL). (Caution: fire hazard!) To the stirred suspension was added **7c** (10.5 g, 24.5 mmol), and the mixture was heated to reflux for 2.5 h, after which time it was cooled to room temperature and filtered. The catalyst was washed with THF (2 × 100 mL), and the combined filtrates were evaporated to give **8c** (8.3 g, 96%) as a pale-yellow solid: mp 78–80°C; $[\alpha]_D$ −71.5° (*c* 29.2, $CHCl_3$). [lit.[17] mp 79–80°C; $[\alpha]_D$ −76.6° (*c* 10.5, $CHCl_3$); lit.[11] mp 83–84°C; $[\alpha]_D$ −85.2° (*c* 1.2, $CHCl_3$).]

5-O-tert-*Butyldimethylsilyl-*D-*ribono-1,4-lactone* (**6b**).—*Method A (at room temperature).* To a solution of D-ribono-1,4-lactone (**3**, 7.41 g, 50 mmol) and imidazole (6.81 g, 100 mmol) in 300 mL of dry DMF was added Bu^tMe_2SiCl (8.29 g, 55 mmol) in two equal portions, 24 h apart. The mixture was stirred for a total of 72 h at room temperature, then the excess reagent was decomposed with 10 mL of MeOH. The solvent was evaporated, and the resulting syrup was partitioned between EtOAc (200 mL) and water (100 mL). The aqueous layer was extracted with additional EtOAc (2 × 120 mL), and the combined organic layers were washed with water (100 mL), dried ($MgSO_4$), and the solvent was evaporated. The residue was purified by column chromatography (A), eluting with an 8:2 → 6.5:3.5 CH_2Cl_2–EtOAc gradient, to sequentially give, after combining the appropriate fractions and evaporating the solvent, **23b**, **22b**, and **6b**. These compounds were characterized as follows:

Compound **23b** (2.22 g, 11.8%): mp 80–81°C; R_f 0.55 (6:4 hexanes–EtOAc); $[\alpha]_D^{22}$ +42.0° (*c* 2.75, $CHCl_3$); ^1H NMR data ($CDCl_3$) δ 4.70 (d, 1 H, $J_{2,3}$ 5.5 Hz, H-2), 4.48 (m, 1 H, H-4), 4.29 (d, 1 H, $J_{2,3}$ 5.6 Hz, H-3), 3.90 and 3.84 (A and B of ABX, 2 H, J_{AX} 1.9, J_{BX} 1.51 Hz, H-5a,5b), 0.96 (s, 9 H, *tert*-Bu), 0.90 (s, 9 H,

tert-Bu), 0.25 (s, 3 H, $SiCH_3$), 0.21 (s, 3 H, $SiCH_3$), 0.08 and 0.07 (2 s, 6 H, $SiCH_3$). Compound **23b** has been reported, albeit without full characterization[32]. Partial ^{13}C NMR data: δ 84.2 (C-4), 70.4 (C-2), 70.0 (C-3), 63.0 (C-5).

Compound **22b** (0.22 g, 1.7%): noncrystalline solid; R_f 0.21 (as for **23b**); $[\alpha]_D^{22}$ +53.0° (*c* 3.35, $CHCl_3$); ^1H NMR data (Me_2SO-d_6): δ 5.30 (d, 1 H, *J* 4.6 Hz, OH-3), 5.23 (t, 1 H, *J* 5.4 Hz, OH-5), 4.63 (d, 1 H, $J_{2,3}$ 5.4 Hz, H-2), 4.27 (m, 1 H, H-4), 4.15 (t, 1 H, *J* 4.8 Hz, H-3), 3.62 (dd, 2 H, J_1 3.7, J_2 4.8 Hz, H-5a,5b), 0.92 (s, 9 H, *tert*-Bu), 0.14 and 0.13 (2 s, 6 H, CH_3Si). The resonances at δ 5.30 and 5.23 disappeared upon addition of D_2O, and the δ 4.15 resonance collapsed to a d. The AB pattern of the δ 3.62 resonance simplified. Partial ^{13}C NMR data: δ 84.8 (C-4), 70.2 (C-2), 70.0 (C-3), 61.9 (C-5). Anal. Calcd for $C_{11}H_{22}O_5Si$: C, 50.36; H, 8.45. Found: C, 50.34; H, 8.46.

Compound **6b** (6.9 g, 52%): white solid, crystallized from ethyl ether–hexanes: mp 104–105°C; R_f 0.29 (8:2 CH_2Cl_2–EtOAc); $[\alpha]_D^{22}$ +15.7° (*c* 4.3, $CHCl_3$); ^1H NMR data ($CDCl_3$): δ 4.67 (d, 1 H, $J_{2,3}$ 5.5 Hz, H-2), 4.53 (m, 1 H, H-4), 4.52 (d, 1 H, *J* 5.4 Hz, H-3), 3.87 (AB of ABX, 2 H, $J_{4,5a}$ 2.2, $J_{4,5b}$ 1.8, $J_{5a,5b}$ 11.8 Hz, H-5a,5b), 0.87 (s, 9 H, Me_3C), 0.07 and 0.05 (2 s, 6 H, Me_2Si). Anal. Calcd for $C_{11}H_{22}O_5Si$: C, 50.36; H, 8.45. Found: C, 50.31; H, 8.48.

*Preparation of 5-*O*-*tert*-butyldimethylsilyl-*D*-ribono-1,4-lactone* (**6b**).—*Method B (at low temperature).* To a mixture of D-ribono-1,4-lactone (**3**, 7.47 g, 50.0 mmol) and imidazole (3.74 g, 55.0 mmol) in DMF (40 mL) cooled to −20°C was added dropwise Bu^tMe_2SiCl (7.54 g, 50.0 mmol) in DMF (40 mL) over a period of 30 min. The mixture was stirred for 2 h at −20° to −1°C, then poured into a mixture of EtOAc (200 mL) and water (100 mL). The aqueous layer was extracted with additional EtOAc (2 × 100 mL), and the combined organic layers were washed with water (100 mL), dried ($MgSO_4$), filtered, and evaporated to give a syrupy residue. The crude product was chromatographed over silica gel as in the preceding example to give 6.26 g (47.8%) of **6b**, identical in all respects to the product obtained under Method A.

*5-*O*-tert-Butyldimethylsilyl-2,3-*O*-thiocarbonyl-*D*-ribono-1,4-lactone* (**7b**).—To a solution of **6b** (2.62 g, 10.0 mmol) in dry acetone (500 mL) was added *N,N'*-thiocarbonyldiimidazole (2.74 g, 15.4 mmol), and the resulting solution was heated to reflux in a dry N_2 atmosphere for 3.5 h. The cooled mixture was concentrated to one-third the original volume and poured into water (400 mL). The mixture was extracted with CH_2Cl_2 (3 × 175 mL), and the combined organic extracts were sequentially washed with satd aq $NaHCO_3$ (150 mL) and water (150 mL), dried ($MgSO_4$), and evaporated to give a syrup. The residue was purified by column chromatography (A), eluting with 8:2 hexanes–EtOAc to give **7b** (2.6 g, 7.6 mmol, 76%) which was crystallized from EtOAc–hexanes: mp 166–167°C; R_f 0.49 (8:2 hexanes–EtOAc); $[\alpha]_D^{23}$ −66.0° (*c* 3.6, $CHCl_3$); ^1H NMR data ($CDCl_3$): δ 5.41 (d, 1 H, *J* 6.9 Hz, H-2), 5.28 (d, 1 H, *J* 6.6 Hz, H-3), 4.95 (m, 1 H, H-4), 3.93 (AB of ABX, 2 H, J_{AB} 11.6, J_{AX} 1.5, J_{BX}, 1.0 Hz, H-5a,5b), 0.88 (s, 9 H, Me_3C), 0.09 and

0.08 (2 s, 6 H, Me_2Si). Anal. Calcd for $C_{12}H_{20}O_5SSi$: C, 47.34; H, 6.62; S, 10.53. Found: C, 47.42; H, 6.64; S, 10.50.

Preparation of 5-O-tert-*butyldimethylsilyl-2,3-dideoxy*-D-glycero-*pent-2-enono-1,4-lactone* (**8b**).—A suspension of Raney nickel (25 g wet weight) was washed with acetone and resuspended in dry acetone (125 mL), then heated to reflux overnight. (Caution: fire hazard!) The solvent was carefully decanted from the cooled mixture, and the catalyst was resuspended in distilled THF (300 mL). To the vigorously stirred solution was added **7b** (2.4 g, 8.0 mmol), and the mixture was heated to reflux for 24 h. The cooled mixture was filtered, and the catalyst was washed with THF (2 × 50 mL). The solvent was evaporated from the combined filtrates, and the residue was purified by column chromatography (A), eluting with 7:3 hexanes–EtOAc, to yield **8b** (1.53 g, 6.60 mmol, 84%): mp 30–31°C; $[\alpha]_D^{22}$ −122.0° (*c* 4.4, $CHCl_3$). [lit.[10] mp 32°C; $[\alpha]_D^{20}$ −136.2° (*c* 1.13, $CHCl_3$); lit.[9] mp 31–32°C; $[\alpha]_D^{25}$ −141° (c 0.937, $CHCl_3$).]

Preparation of 5-O-*(triphenylmethyl)*-D-*ribono-1,4-lactone* (**6a**).—In a 1-L round-bottom flask equipped with reflux condenser and maintained under a dry N_2 atmosphere, chlorotriphenylmethane (37.2 g, 133 mmol) was added to a stirred solution of D-ribono-1,4-lactone (**3**, 16.3 g, 110 mmol) in pyridine (800 mL), and the mixture was heated for 20 h at 60–65°C. The mixture was quenched with MeOH (10 mL), evaporated to approximately one-third the original volume, then diluted with CH_2Cl_2 (900 mL), and washed sequentially with water (2 × 400 mL), satd aq $NaHCO_3$ (400 mL), and water (400 mL). The organic extract was dried ($MgSO_4$), and the solvent was evaporated.

The residue was dissolved in warm (40°C) EtOAc (275 mL), and the insoluble material was filtered. The volume of solvent was then reduced to ~ 125 mL, and hexanes (75 mL) was added. The solution was seeded and kept at 5°C overnight to give crystals of pure **6a** (21.7 g). The mother liquor was chromatographed (B, 500 g) with 1:1 hexanes–EtOAc to give additional product (7.9 g), bringing the total yield to 69%. The product was recrystallized from EtOAc–hexanes: mp 172–173°C; $[\alpha]_D$ +51.3° (*c* 2.1, $CHCl_3$). [lit.[7] mp 170–172°C; $[\alpha]_D^{20}$ +50° (*c* 3.8, CH_2Cl_2)]; ^1H NMR data ($CDCl_3$): δ 7.20–7.38 (m, 15 H, Ph_3C), 4.88 (d, 1 H, $J_{2,3}$ 5.4 Hz, H-2), 4.52 (m, 1 H, H-4), 4.5 (d, 1 H, $J_{2,3}$ 5.4 Hz, H-3), 3.19 and 3.68 (A and B of ABX, 2 H, J_{AB} 10.97, J_{AX} 3.0, J_{BX} 2.2 Hz, H-5a,5b), 4.5 (d, 1 H, $J_{2,3}$ 5.4 Hz, H-3), 4.52 (m, 1 H, H-4), 4.88 (d, 1 H, $J_{2,3}$ 5.4 Hz, H-2), 7.20–7.38 (m, 15 H, Ph_3C).

Isolation of 2-O-*(triphenylmethyl)*-(**22a**) *and* 2,5-*di*-O-*(triphenylmethyl)*-D-*ribono-1,4-lactone* (**23a**) *from a preparation of* **6a**.—In a separate experiment, **3** (3.7 g, 25 mmol) was reacted with chlorotriphenylmethane (8.1 g, 29 mmol), and the crude product was purified by column chromatography as in the preceding section, collecting **22a** and **23a** in appropriate fractions. The products isolated after evaporation of the solvent were characterized as follows:

Compound **22a** (0.68 g, 3.2%): mp 169–172°C; R_f 0.39 (6:4 hexanes–EtOAc); $[\alpha]_D^{27}$ +48.2°C (*c* 1.09, $CHCl_3$); ^1H NMR data ($CDCl_3$): δ 7.26–7.69 (m, 15 H, Ph_3C), 4.67 (d, 1 H, $J_{2,3}$ 4.9 Hz, H-2), 4.23 (m, 1 H, H-4), 3.73 and 3.44 (A and B of

ABX, 2 H, J_{AX} 2.1, J_{BX} 2.2, J_{AB} 12.3 Hz, H-5a,5b), and 2.47 (d, 1 H, $J_{2,3}$ 4.9 Hz, H-3). Partial ^{13}C NMR data: δ 84.0 (C-4), 71.9 (C-2), 69.3 (C-3), 61.6 (C-5). Anal. Calcd for $C_{24}H_{22}O_5$: C, 73.83; H, 5.68. Found: C, 73.81; H, 5.71.

Compound **23a** (2.34 g, 14.2%): mp 215–217°C; R_f 0.56 (6:4 hexanes–EtOAc); $[\alpha]_D^{20}$ +54.2° (*c* 8.5, $CHCl_3$); ^1H NMR data ($CDCl_3$): δ 7.17–7.30 (m, 30 H, 2 Ph_3C), 4.86 (dd, 1 H, $J_{2,3}$ 6.4, $J_{3,OH}$ 9.8 Hz, H-3), 4.01 (d, 1 H, *J* 6.4 Hz, H-2), 3.30 and 2.43 (A and B of ABX, 2 H, J_{AX} 2.1, J_{BX} 1.3, J_{AB} 11.2 Hz, H-5a,5b), 3.02 (d, 1 H, J_{OH} 9.8 Hz, OH), 2.96 (m, 1 H, H-4); with addition of D_2O: δ 4.83 (d, 1 H, $J_{2,3}$ 6.5 Hz, H-3) and 4.70 (s, 1 H, HOD). Partial ^{13}C NMR data: δ 82.9 (C-4), 72.1 (C-2), 68.7 (C-3), 61.7 (C-5). Anal. Calcd for $C_{43}H_{36}O_5$: C, 81.62; H, 5.73. Found: C, 81.58; H, 5.80.

Compound **6a** (5.63 g, 58%) was also isolated and found to be identical with the product described in the preceding section.

Preparation of 2,3-O-(thiocarbonyl)-5-O-(triphenylmethyl)-D-ribono-1,4-lactone (**7a**).—To a stirred solution of 5-*O*-(triphenylmethyl)-D-ribono-1,4-lactone (**6a**, 20.5 g, 52.5 mmol) in dry acetone (1 L) was added a solution of freshly prepared *N,N'*-thiocarbonyldiimidazole. The mixture was heated to gentle reflux for 2 h, at the end of which time examination of a sample by TLC (6:4 hexanes–EtOAc) indicated complete reaction of the starting material. The mixture was cooled, concentrated under reduced pressure to one-half the original volume, then poured into satd aq NaCl (350 mL) and ice (500 g). The product was extracted with CH_2Cl_2 (4 × 250 mL), and the combined organic phases were washed with satd aq $NaHCO_3$ (100 mL), dried ($MgSO_4$), filtered, and evaporated. Compound **7a** was easily separated from a slow-running byproduct by short-column chromatography (A, 100 g) using CH_2Cl_2 (1 L) as eluent. The solvent was evaporated, and the product so obtained was used without further purification. ^1H NMR ($CDCl_3$): δ 5.50 (d, 1 H, $J_{2,3}$ 6.9 Hz, H-2), 5.05 (d, 1 H, $J_{3,2}$ 6.8 Hz, H-3), 4.90 (m, 1 H, H-4), 3.15 and 3.86 (A and B of ABX, 2 H, J_{AB} 10.9, J_{AX} 2.0, J_{BX} 1.25 Hz, H-5a,5b). An analytical sample was crystallized from EtOAc–hexanes; mp 191–193°C [lit.[7] mp 189–190°C].

Preparation of 2,3-dideoxy-5-O-(triphenylmethyl)-D-glycero-pent-2-enono-1,4-lactone (**8a**).—In a 500-mL round-bottom flask, W-2 (ref 33) (or W.R. Grace No. 28) Raney nickel (120 g wet weight) was washed sequentially with the following solvents, then decanted: distilled water (2 × 200 mL), acetone (2 × 150 mL), and dry acetone (2 × 150 mL). (Caution: fire hazard!) Dry acetone was then added to the catalyst, and the mixture was refluxed overnight. After cooling the mixture, the acetone was decanted, and the Raney nickel was washed with dry THF (2 × 75 mL). 2,3-*O*-Thiocarbonyl-5-*O*-(triphenylmethyl)-D-ribono-1,4-lactone (**7a**, 14 g, 81 mmol) was added in dry THF (350 mL), and the mixture was vigorously stirred with a mechanical stirrer and heated to a gentle reflux. The reaction was monitored by TLC (6:4 hexanes–EtOAc) until the starting material was shown to have completely reacted (~ 3 h). The cooled mixture was then filtered through a bed of Celite and activated carbon, and the filtered product was washed with THF (200

mL). The solvent was evaporated, and the residue was crystallized from EtOAc–hexanes to give **8a** (14 g, 39 mmol, 74% based on **6a**): mp 153–154°C; $[\alpha]_D^{23}$ −89.5° (*c* 3.65, $CHCl_3$); [lit.[10] mp 152–154°C; $[\alpha]_D^{20}$ −97.1° (*c* 1.10, $CHCl_3$); lit.[6] mp 152–154°C; $[\alpha]_D^{20}$ −95.1° (*c* 3.42, $CHCl_3$).] ^{1}H NMR data (acetone-d_6): δ 7.23–7.47 (m, 15 H, Ph_3),and 7.23 (dd, 1 H, $J_{3,4}$ 1.3, $J_{2,3}$ 5.7, H-3), 6.24 (dd, 1 H, $J_{2,4}$ 2.0, $J_{2,3}$ 5.7 Hz, H-2), 5.29 (m, 1 H, H-4), 3.31 and 3.50 (A and B of ABX, 2 H, J_{AB} 10.2, J_{AX} 4.9, J_{BX} 3.8 Hz, H-5a,5b).

Reaction of D-*ribono-1,4-lactone* (**3**) *with* tert-*butylchlorodiphenylsilane to give 2,3,5-tri-*O-tert-*butyldiphenylsilyl-*D-*ribono-1,4-lactone* (**24c**) *and* 5-O-tert-*butyldiphenylsilyl-*D-*ribono-1,4-lactone* (**6c**).—To a solution of D-ribono-1,4-lactone (**3**, 1.0 g, 6.7 mmol) in dry DMF (10 mL) was added Bu^tPh_2SiCl (0.80 g, 2.9 mmol) and imidazole (0.4 g, 5.8 mmol). The mixture was kept for 30 min at room temperature, after which time MeOH (10 mL) was added. The MeOH was evaporated in vacuo, and the remaining solution was partitioned between $CHCl_3$ (150 mL) and water (100 mL). The aqueous layer was extracted with $CHCl_3$ (2 × 50 mL). The combined organic layers were dried ($MgSO_4$), and the solvent was evaporated. The residue was separated by column chromatography, eluting successively with 95:5 $CHCl_3$–hexanes (250 mL) and 98:2 $CHCl_3$–MeOH to give 1.5 g (26%) of the tris(silyl) derivative **24c**: mp 50–56°C; R_f 0.85 ($CHCl_3$); $[\alpha]_D$ −1.0° (*c* 4.4, $CHCl_3$); ^{1}H NMR data ($CDCl_3$): δ 7.39–7.62 (m, 10 H, Ar), 4.83 (d, 1 H, $J_{2,3}$ 5.4 Hz, H-2), 4.50 (m, 2 H, H-3,4), 3.75–3.92 (m, 2 H, H-5a,5b), 1.02 (s, 9 H, *tert*-Bu). Anal. Calcd for $C_{53}H_{62}O_5Si \cdot 0.3CHCl_3$: C, 75.94; H, 7.45. Found: C, 75.67; H, 7.42.

Later fractions gave 0.13 g (5%) of 5-*O*-silylated **6c**, identical with the product isolated from the hydrolysis of **5c**.

Reaction of $PhSCu(RMgX)_n$ *with butenolides* **8a–8c** *to give* **14–16**.—*General procedure*. To a yellow slurry of phenylthiocopper (0.87 g, 5.0 mmol) in dry THF (10 mL) at −45 to −40°C under N_2 was added a solution of the appropriate Grignard reagent (15 mmol) in THF. The mixture was warmed to −15°C and stirred for 30 min, by which time the color changed to tan. A solution of butenolide **8a**, **8b**, or **8c** (5 mmol) in THF (10 mL) was added dropwise at −15°C. After addition of the appropriate butenolide, the solution darkened, and a sample indicated by TLC complete reaction of the starting material. The reaction was quenched by addition of satd aq NH_4Cl (60 mL), and the mixture was then stirred until the copper salts completely precipitated. The mixture was then filtered, and the product was isolated from the filtrate by extraction with EtOAc (3 × 50 mL). The combined organic extracts were washed with 2% aq $Na_2O_3S_2$ (30 mL), dried ($MgSO_4$), filtered, and the solvent was evaporated. The residual syrup was purified by column chromatography (A) using 2:8 EtOAc–hexanes as eluent to give **14**, **15**, or **16**. For yields and physical constants, see Table I; for ^{1}H NMR data, see Table II.

Reaction of butenolides **8a–8c** *with* R_2CuLi *to give* **13**, **17**, **18**, *and* **19**.—*General procedure for the RLi–CuI–*Me_3SiCl *method*. To a stirred suspension of copper(I)

TABLE II. ^{1}H NMR (200 MHz) spectral data [a] for compounds 13–21

Compound no.	Chemical shifts (δ) and apparent first-order couplings (Hz)									
	H-2a	H-2b	H-3	H-4	H-5a	H-5b	C_nH_{2n}	$-CH_3$	Ar	Others
13	2.13dd [b] (J_{AX} 7.6, J_{AB} 17.1)	2.78dd [c] (J_{BX} 8.4)	2.38m	4.11m	3.16dd [c] (J_{AX} 4.4, J_{AB} 10.7)	3.41dd [c] (J_{BX} 3.3)		1.01d (J 6.7)	7.17–7.46m	
14	2.22 [c,d] (J_{AX} 6.4, J_{AB} 19.7	2.80dd [c] (J_{BX} 10.9)	2.27m	4.23m	3.14dd [c] (J_{AX} 4.3, J_{AB} 10.6)	3.44dd [c] (J_{BX} 3.3)	1.32–1.44m [n = 1]	0.85t (J 7.2)	7.15–7.46m	
15	2.20dd [c,d] (J_{AX} 7.0, J_{AB} 16.7)	2.80dd [c] (J_{BX} 8.2)	2.32m	4.22m	3.08dd [c] (J_{AX} 4.1, J_{AB} 10.5)	3.48dd [c] (J_{BX} 3.1)	1.18–1.38m [n = 2]	0.85t (J 6.8)	7.16–7.46m	
16	2.30dd [c,d] (J_{AX} 5.6, J_{AB} 17.9)	2.76dd [c] (J_{BX} 9.7)	2.15m	4.38m	3.08dd [c] (J_{AX} 4.1, J_{AB} 10.5)	3.48 [c] (J_{BX1} 3.1)		0.84d [e] (J 6.6) 0.78d (J 6.7)	7.16–7.46m	1.57–1.67m, $CHMe_2$
17	2.20dd [c,d] (J_{AX} 7.0, J_{AB} 16.6)	2.80dd [c] (J_{BX} 7.9)	2.30m	4.22m	3.14dd [c] (J_{AX} 4.2, J_{AB} 10.5)	3.44dd [c] (J_{BX} 3.2)	1.12–1.43m [n = 3]	0.85t (J 6.6)	7.18–7.46m	
18 [f]	2.29m [d]	2.71m	2.29m	4.24m	3.08m	3.48m		0.82m	7.20–7.46m	1.21m, CH_2–CH
19	3.03–3.19m [g]	2.72dd (J_{BX} 8.6, (J_{AB} 17.8)	3.03–3.19m [g]	4.52m	3.40–3.67m [h]				7.06–7.44m [i] (20 H)	
19 [j]	2.90d (J 9.9)		3.64dd (J_1 9.5, J_2 18.9)	4.61m	3.04dd (J_{AX} 4.5, J_{AB} 10.8)	3.30dd (J_{BX} 1.9)			7.26–7.30m [i] (20 H)	
20	2.13dd [c] (J_{AX} 6.6, J_{AB} 17.1)	2.77dd [c] (J_{BX} 8.8)	2.54m	4.10m	3.72dd [c] (J_{AX} 3.4, J_{AB} 11.4)	3.85dd [c] (J_{BX} 3.3)		1.17d (J 6.7)		0.07s, Me_2Si; 0.89s, *tert*-Bu
21	2.17dd [c] (J_{AX} 6.1, J_{AB} 17.3)	2.75dd [c] (J_{BX} 8.9)	2.42m	4.18m	3.69dd [c] (J_{AX} 3.3, J_{AB} 11.4)	3.86dd [c] (J_{BX} 3.2)	1.20–1.75m [n = 3]	0.89t (J 5.8)		0.07s Me_2Si; 0.89s, *tert*-Bu

[a] Spectra were obtained in $CDCl_3$ with Me_4Si as internal standard, except where noted otherwise. δ-Values are downfield (ppm) from Me_4Si. Spin–spin splittings are apparent, first-order values reported in Hz: d, doublet; dd, doublet of doublets; m, multiplet; s, singlet; and t, triplet. [b] Data for compounds **9–12** are in the previous paper[4]. [c] AB of an ABX system. [d] Partially obscured by H-3. [e] CH_3– of 2-Pr group. [f] Mixture of isomers. [g] H-2a and H-3 overlap. [h] H-5a and H-5b overlap. [i] Ph and Tr overlap. [j] Me_2SO-d_6.

iodide (1.19 g, 6.25 mmol) in anhyd diethyl ether (5 mL) at −20°C was added slowly, under N_2, the appropriate alkyllithium reagent (12.5 mmol). After 30 min the solution was cooled to −78°C, and Me_3SiCl (0.65 g, 6.0 mmol) was added, followed by the appropriate butenolide **8a–8c** (5 mmol) in dry THF (10 mL). The reaction was monitored by TLC, and after 1 h no butenolide was detected. The reaction was then quenched with satd aq NH_4Cl (60 mL), the mixture was filtered, and the product was extracted with EtOAc (3 × 50 mL). The combined extracts were washed with 2% $Na_2O_3S_2$ (30 mL), dried ($MgSO_4$), filtered, and the solvent was evaporated. Chromatography (A, 80 g) of the residue with 2:8 EtOAc–hexanes gave the desired products **13**, **17**, **18**, and **19**. For yields and physicochemical data, see Table I. For ^1H NMR data, see Table II.

5-O-tert-*Butyldimethylsilyl-2,3-dideoxy-3*-C-*methyl*-D-erythro-*pentono-1,4-lactone* (**20**).—A suspension of the copper(I) bromide–Me_2S complex (0.70 g, 3.4 mmol, freshly recrystallized from Me_2S and hexanes) in anhyd diethyl ether (100 mL) and Me_2S (20 mL) was cooled to −78°C under an atmosphere of N_2. To this mixture was added dropwise, over a period of 10 min, methyllithium (4 mL of a 1.4 M solution in diethyl ether, 5.6 mmol). The colorless solution was allowed to stir at −78°C for an additional 10 min, after which time a solution of **8b** (0.78 g, 3.4 mmol) in anhyd diethyl ether (10 mL) was added dropwise. The solution was allowed to stir for 30 min at −78°C and then for 5 min at ambient temperature. The reaction was quenched by the addition of NH_4Cl (5 g), followed by satd aq NH_4Cl (100 mL). The aqueous phase was extracted with EtOAc (3 × 150 mL), and the combined organic solutions were washed once with 2% aq $Na_2O_3S_2$ (150 mL). The solvent was dried ($MgSO_4$) and evaporated, yielding analytically pure **20**: GLC–MS {$k' = 7.0$; m/z (%) 229 (1, $[M - CH_3]^+$), 187 (100, $[M - Me_3C]^+$), 143 (95, $[M - Me_3C - CO_2]^+$), 75 (63)}; ^{13}C NMR ($CDCl_3$): δ 176.9 (C-2), 86.9 (C-5), 63.7 (C-6), 37.0 (C-3), 31.5 (C-4), 25.8 (Me_3C), 19.0 (CH_3), 18.3 (Me_3C), −5.5 (Me_2Si). For yields and physical constants, see Table I; for ^1H NMR data, see Table II.

5-O-(tert-*Butyldiphenylsilyl)-2,3-dideoxy-3*-C-*methyl*-D-erythro-*pentono-1,4-lactone* (**9**).—Following the experimental procedure described for **20**, **8c** (5.77 g, 16.4 mmol) was methylated at −78°C with lithium dimethylcuprate (32.8 mmol) in anhyd diethyl ether (100 mL) and anhyd Me_2S (20 mL) to yield analytically pure **9** (5.48 g, 95%): R_f 0.28 (1:1 $CHCl_3$–hexanes); GLC–MS {$k' = 12.9$; m/z (%) 311 (100, $[M - Me_3C]^+$), 267 (37, $[M - Me_3C - CO_2]^+$), 199 (53), 167 (22)}. The compound was identical by ^1H NMR and optical rotation with the sample previously reported[4] using Method B.

3-C-*Butyl-5*-O-(tert-*butyldimethylsilyl)-2,3-dideoxy*-D-erythro-*pentono-1,4-lactone* (**21**).—A suspension of the copper(I) bromide–Me_2S complex (0.387 g, 1.60 mmol) in anhyd diethyl ether (50 mL) and Me_2S (10 mL) was cooled to −78°C under N_2. To this mixture was added dropwise over a period of 10 min a solution of butyllithium in hexanes (4.0 mL, 3.2 mmol). The resulting tan solution was allowed to stir at −78°C for an additional 10 min, after which time a solution of butenolide

8b (0.393 g, 1.70 mmol) in anhyd diethyl ether (10 mL) was added dropwise. The solution was allowed to stir for 30 min at −78°C, then for 5 min at ambient temperature. The reaction was quenched by addition of NH_4Cl (5 g), followed by satd aq NH_4Cl (100 mL). The aqueous phase was extracted with EtOAc (3 × 150 mL), and the organic extract was washed with 2% aq $Na_2O_3S_2$ (150 mL), dried over $MgSO_4$, and evaporated. The resulting syrup was chromatographed (A, 60 g), eluting with 7:3 hexanes–EtOAc to yield pure **21** (0.081 g, 37%). For physicochemical data, see Table I; for ^1H NMR data, see Table II.

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