Controlled Access to Furanose Precursors Related to Sesquiterpene Lactones.† 1

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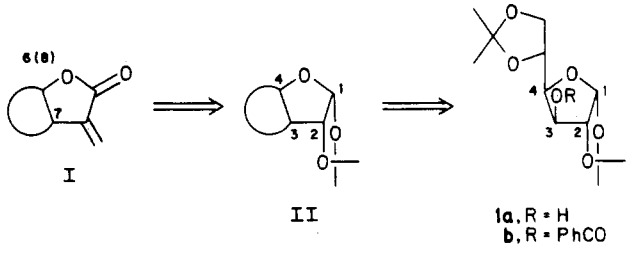
The diester **4a** which is readily obtained from "diacetone glucose" (**1**) undergoes Dieckmann cyclization to give the two possible β-keto esters, **5** and **6**, in a ratio of 8:1. The carbonyl and ester groups on the cyclohexane ring of the major isomer are processed to give a dienol, **10**, which undergoes the anionic oxy-Cope rearrangement to afford the cyclodecenofuranose **11**. This ring-expansion rearrangement reaction is specifically mediated by the presence of tetra-*n*-butylammonium iodide. Attempts to bias regioselectivity in the Dieckmann cyclization of **4a** in favor of **6** were not promising, and hence the lactonic ester **14** was conceived, since it was capable of only one mode of cyclization. Conditions were found to control the C-5 off template stereocenter so that **17** was obtained stereochemically pure. Dieckmann cyclization did afford the β-keto-γ-butyrolactone **26a** exclusively, which was then α-methylated to **26b**. X-ray analysis of the latter confirmed its structure.

The use of 1,2-*O*-isopropylidenefuranose derivatives (for example, II) as precursors for syntheses of sesquiterpene lactones (e.g., I) has been an area of interest in this laboratory, the general plan for which is summarized in Scheme I.[1,2] It was our hope that the cis-fused trioxa[3.3.0]bicyclooctyl moiety of the ultimate precursor, diacetone glucose (**1a**), would provide (a) a reliable template for stereocontrolled annulation leading to II and, thereafter, (b) a convenient synthon for the lactone moiety of I. One avenue for the latter objective (b) has already been explored.[1b] With respect to the former, it is instructive to note that the C-4 oxygen of **1** has the same absolute configuration as does the C-6 oxygen in cis-fused sesquiterpene lactones and as the C-8 oxygen in the corresponding trans-fused counterparts.[2] Thus, **1a** could be a precursor for either the cis- or trans-fused forms of I. Recent publications from our laboratory have focused on Diels–Alder routes to cis-fused systems,[2] and in this manuscript we outlined some of our studies relating to the trans-fused analogues.

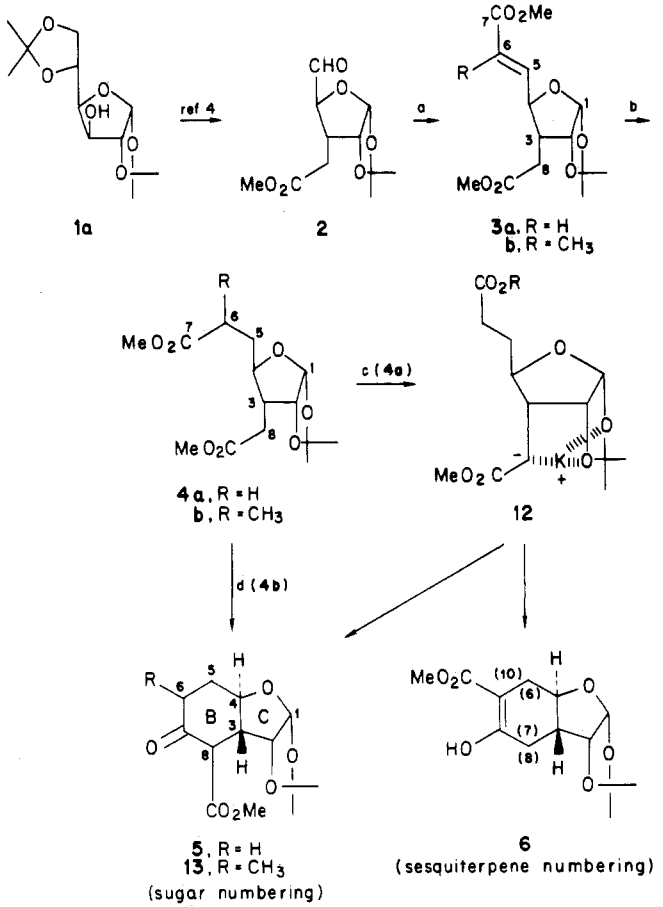
In our initial approach to the trans relationship at C-3/C-4 of II[1c] (Scheme II) we sought to take advantage of the known aldehydic ester, **2**.[4] Accordingly the diester **4a**, obtained by routine procedures, was treated with 1 equiv of potassium *tert*-butoxide in benzene to afford an 8:1 mixture of **5** and **6** as separable, crystalline compounds in a combined yield of 89%. The configuration at C-8 of **5** was defined on the basis of the value $J_{3,8}$ = 13.5 Hz observed in the 220-MHz NMR spectrum. Isomer **6** existed in the enolic form only, judging from the intensity of the enolic proton at 12.84 ppm. The expected infrared bands for the α,β-unsaturated moiety (1610, 1650 cm^{-1}) and enol (2500–3000 cm^{-1}) were clearly observable.

Encouraged by the ready accessibility of **5**, we decided to test the viability of the system for elaboration into a ten-membered ring,[5,6] as a model study for possible germacranolide syntheses (Scheme III). Reduction with lithium aluminum hydride led to the diol **7a** which was subjected to a sequence of protecting group manipulations so as to allow for oxidation of the primary alcohol (in **7d**) to the aldehyde **8a**. After a Wittig reaction, the resulting olefin **8b** was deprotected, and alcohol **8c** was oxidized to the crystalline ketone **9**, which underwent additional of

Scheme I



Scheme II[a]



[a] (a) **3a**, Ph_3PCHCO_2Me, **3b**, $Ph_3PC(CH_3)CO_2Me$; (b) H_2, 5% Pd/C; (c) *t*-BuOK, C_6H_6, reflux 7 days, 90% (**5** + **6**); *t*-BuOK, C_6H_6, reflux 11 days, 60% (**13**).

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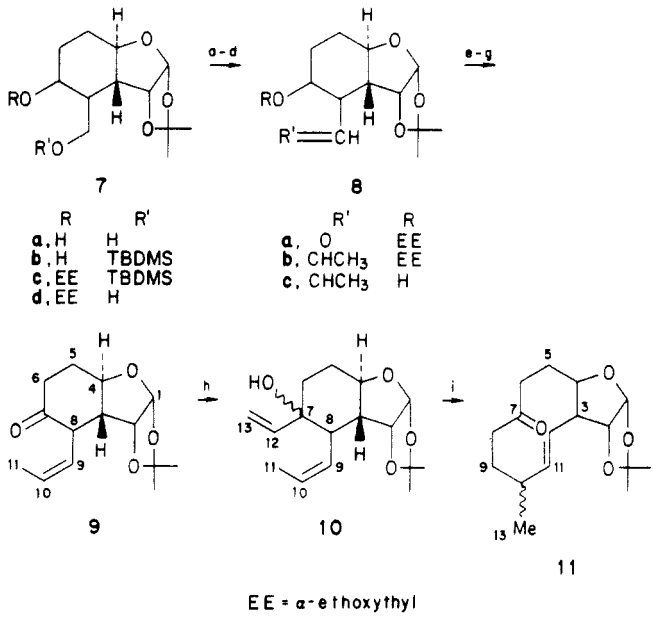
Scheme III[a]



[a] (a) TBDMSCl, DMF, IMD; (b) EVE, PPTS, CH_2Cl_2; (c) n-Bu_4NF, THF; (d) CrO_3, pyridine; (e) Ph_3PCHCH_3, DMF; (f) PPTS, MeOH; (g) CrO_3, pyridine; (h) vinyllithium, THF; (i) KH, n-Bu_4NI, THF.

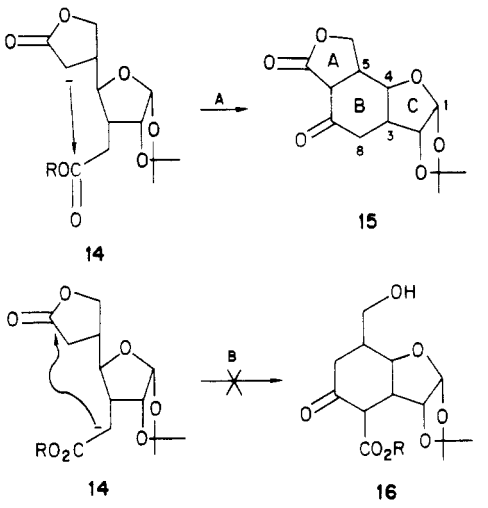
vinyllithium to give a mixture of allylic alcohols **10** in near quantitiative yield.

In order to effect the oxy-Cope rearrangement for ring expansion of **10**, we examined the standard Evans' conditions, viz potassium hydride in tetrahydrofuran, with and without added crown ether.[5] However, the substrate was decomposed, and the same fate was experienced when the palladium-catalyzed procedure of Overman[7] was attempted.

Noting (1) that the success of the Evans' oxy-Cope rearrangement depends, apparently, on the quality of the oxyanion and (2) that Czernecki and co-workers[8] had shown the alkylation of oxyanions was dramatically potentiated by the presence of tetra-*n*-butylammonium iodide, we decided to add a catalytic amount of this salt to the standard Evans' mixture.[5] Gratifyingly, the rearrangement **10** to **11** occurred in 12 h with a yield of 74%.

The studies outlined in Scheme III were based on the major product, **5**, of the Dieckmann cyclization of **4a**; however, it is obvious from the sesquiterpene numbering in parentheses shown in Scheme II, that **6** would be the more appropriate isomer for further elaboration. Thus, the activated center in **6** coincides with C-10, a sesquiterpene site which normally carries an angular methyl group. The methoxycarbonyl group could serve for purposes of activation for formation of ring A and then subsequently be converted into the ubiquitous C-10 methyl residue. By contrast, the activated center in **5** corresponds to C-8 which, at best, may carry a hydroxyl group.

Scheme IV



We suspected that chelation depicted in **12** was largely responsible for the observed regioselectivity, and credence to this notion came from the observation that use of 4 equiv of potassium tertiary butoxide (instead of one) improved the relative amount of **6** from 11% to 40%. The hindered kinetic base lithium tetramethylpiperidine did lead to a preponderance of **6** (See Scheme II), but we still desired better.

The procedure in Scheme II allowed for the ubiquitous C-10 methyl group to be put into place much earlier. Accordingly, aldehyde **2** was reacted with methyl (triphenylphosphoranyl)propionate, and the resulting product, **3b**, was hydrogenated to give **4b**. However, under the conditions that had succeeded so well for **4a** (89%), the Dieckmann cyclization of **4b** proved to be much slower and gave evidence of decomposition. After 11 days, an optimum situation existed, but there was only 60% conversion, and the yield of **13** based on recovered starting materials was only 32%.

It was, therefore, apparent that a synthetic precursor would have to be devised that would negate the propitious chelation suggested in **12**. The lactonic ester **14** surfaced as an ideal candidate. Thus, Dieckmann cyclization to **15** via path A is the only option available, since the alternative (path B) leading to **16** would require a tetrahedral intermediate containing an impossible trans-fused [3.2.1]bicyclooctyl system (Scheme IV). In refining the new strategy further, it was apparent that the cis A/B ring junction would be thermodynamically favored over the trans alternative.[9] There are two cis A/B relationships, and the choice between the two possibilities depended, ultimately, on the configuration at C-5 of the precursor. *The task, therefore, was to ensure that the C-5 center in the precursor* **17** *(Scheme V) was created with high stereoselectivity.*

We were influenced by the work of Redlich[10] who had shown that bulky protecting groups on O-3 dramatically affected the selectivity in furanose derivatives. Thus, it was our hope that the course of hydrogenation of a double bond in **18** would be controllable by the bulk of the protecting group at O-3.

The synthetic route to **17**, outlined in Scheme V, began with the known benzoate **19a**[11] and led routinely to ketone

(1) (a) Fraser-Reid, B.; Tam, T. F.; Sun, K. J. In "Organic Synthesis Today and Tomorrow"; Trost, B. M. Hutchinson, C. R., Eds.; Pergamon Press: New York, 1981. (b) Tam, T. F.; Fraser-Reid, B. *J. Chem. Soc., Chem. Commun.* **1980**, 556. (c) Sun, K. M.; Fraser-Reid, B.; Tam, T. F. *J. Am. Chem. Soc.* **1982**, *104*, 367.

(2) (a) Sun, K. M.; Fraser-Reid, B. *Synthesis* **1982**, *28*. (b) Fraser-Reid, B.; Benko, Z.; Giuliano, R.; Sun, K. M.; Taylor, N. *J. Chem. Soc., Chem. Commun.* **1984**, 1029.

(3) Fischer, N. H.; Olivier, E. J.; Fischer, D. *Fortschr. Chem. Org. Naturst.* **1979**, *38*, 47 and references therein.

(4) Rosenthal, A.; Nguyen, L. *J. Org. Chem.* **1969**, *34*, 1029.

(5) Evans, D. A.; Goleb, A. M.; *J. Am. Chem. Soc.* **1975**, *97*, 4765.

(6) Still, W. C. *J. Am. Chem. Soc.* **1977**, *99*, 4186; **1979**, *101*, 2493.

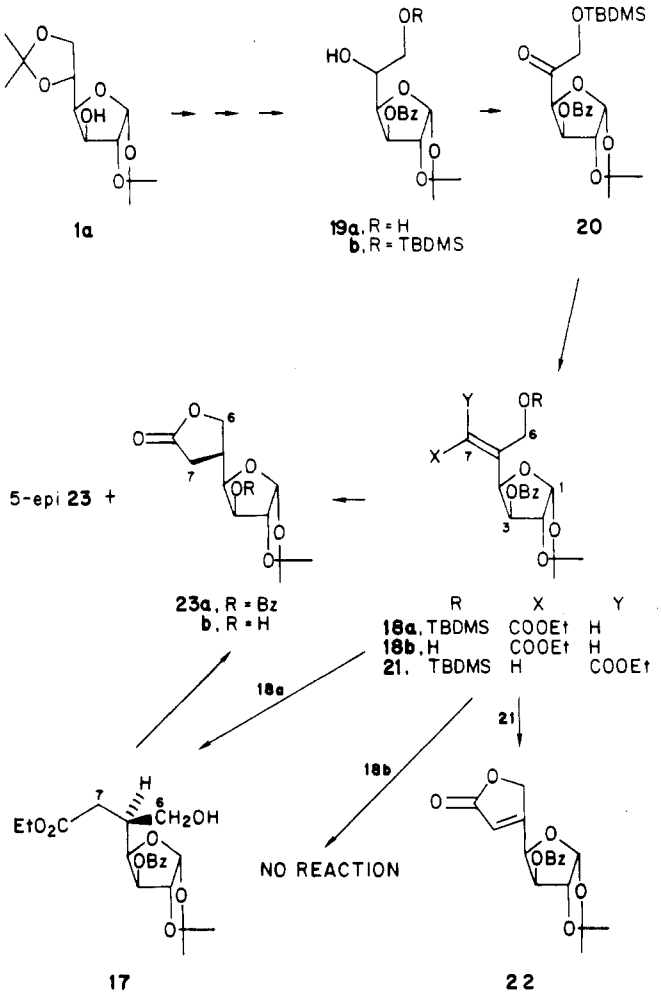
(7) Overman, L. E.; Knoll, F. M. *J. Am. Chem. Soc.* **1980**, *102*, 867.

(8) Ozernecki, C.; Georgoulis, C.; Provenlenghium, C. *Tetrahedron Lett.* **1976**, 3535.

(9) Eliel, E. L. "Stereochemistry of Carbon Compounds"; McGraw Hill: New York, 1962; Chapter 10.

(10) Redlich, H.; Neumann, H.-J. *Chem. Ber.* **1981**, *114*, 2020.

Scheme V[a]



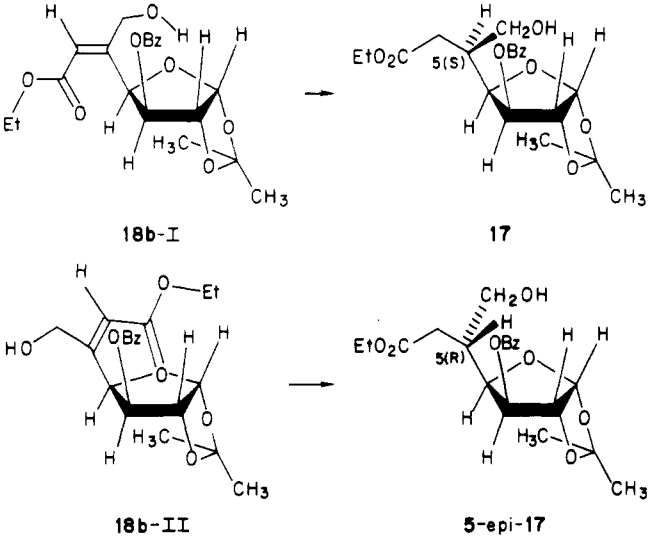
[a] (a) CrO_3, pyridine; (b) Ph_3PCHCO_2Et, CH_3CN; (c) NH_4F, MeOH, H_2O; (d) H_2, 5% Pd/C; (e) TsOH, MeOH.

20, from which the alkenes **18a** and **21** were obtained in 4.7:1 ratio. Assignment of configurations as *Z* and *E*, respectively, rested on the fact that upon treatment with ammonium fluoride, in refluxing aqueous methanol, the minor isomer afforded the butenolide **22** spontaneously (1780, 1750 cm^{-1}), whereas the major isomer existed as a hydroxy ester and hence was judged to be the desired geometric isomer **18b**. Extensive experimentation showed that the relative amount of **18a** could be increased by carrying out the Wittig reaction of **20** in dimethyl sulfoxide. In this solvent, only a trace of **21** was detectable by ^1H NMR, and so the product was ready for use after one recrystallization.

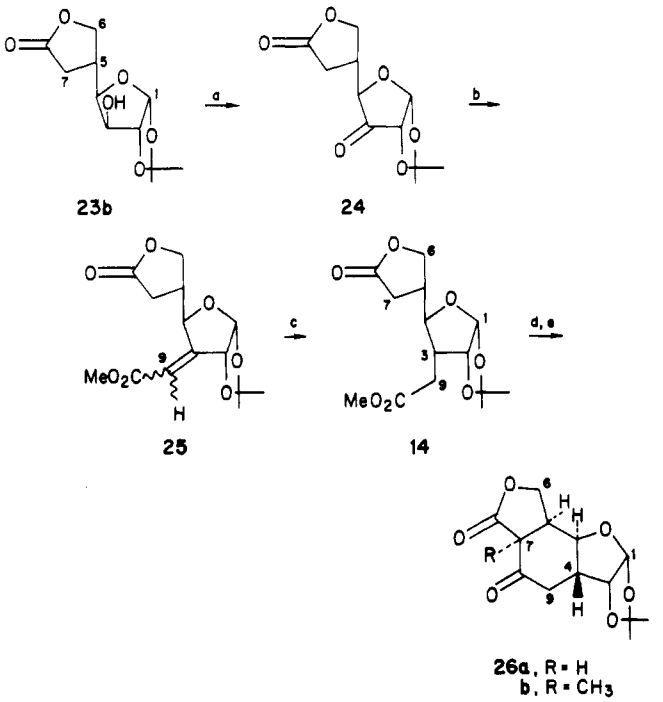
The double bond of **18a** was now to be hydrogenated; but this process proved to be surprisingly difficult. That the silyl ether played a role in this problem was evident since the corresponding alcohol **18b** was reduced smoothly.[12] With 5% palladium on carbon as catalyst, a mixture of epimers was formed (Scheme V) whose relative amounts could not be determined because they had undergone partial lactonization. Consequently, this process was driven to completion by treatment with *p*-toluenesulfonic acid, and the resulting lactone mixture was debenzoylated. The 400-MHz ^1H NMR spectrum of the resulting alcohol, **23b** and its 5-epimer, showed two sets of signals for H-4,

(11) Compound **19a** was prepared from "diacetone glucose" by benzoylation followed by selective hydrolysis in the usual way. See, for example: Anderson, R. C.; Fraser-Reid, B. J. *Org. Chem.*, in press.
(12) Private communication from Professor P. Wuts.

Scheme VI



Scheme VII[a]



[a] (a) P_2O_5, Me_2SO; (b) Ph_3PCHCO_2Me, CH_3CN; (c) H_2, 5% Pd/C; (d) *t*-BuOK, C_6H_6; (e) (i) *t*-BuOK, Me_2SO, (ii) MeI.

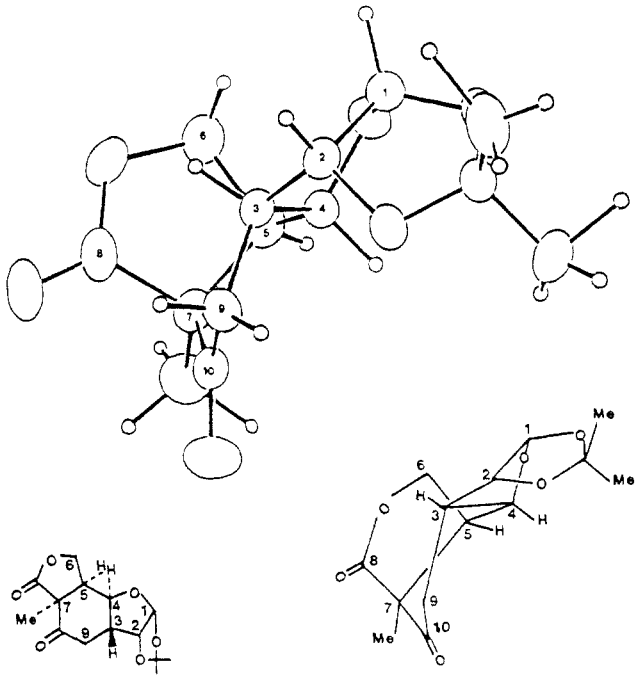
integration of which showed that the C-5 epimers were present in 9:1 ratio.

The major isomer **23a** could be obtained pure after two recrystallizations; nevertheless, we were gratified to find that upon changing the hydrogenation catalyst to 5% *platinum* on carbon, **17** (and thence **23a**) was obtained without any trace of unwanted 5-epimer.

[At this juncture, assignment of the C-5 configuration, as depicted in **17**, rested upon our assumption that of the two extreme rotamers of the olefinic precursor shown in Scheme VI, (**18b**-I would be preferred to **18b**-II). On the basis of Redlich's observation,[10] the bulky C-3 benzoate should force hydrogenation to occur from "behind", therefore, leading to **17**. However, final proof of the C-5 configuration had to be awaited, (vide infra).]

With the lactone **23b** in hand, it was necessary to develop the C-3 appendage (Scheme VII). However, when the well-established protocol[4] was followed, oxidation of

Scheme VIII



23b with Collins' reagent,[13] or ruthenium tetraoxide under conditions which had given only one isomer with 1, led to mixtures of 24 and its C-4 epimer. Fortunately, this problem was overcome by oxidation with phosphorus pentoxide/dimethyl sulfoxide, and the esters 25 and 14 were then obtained in the usual way.

In keeping with the analysis outlined in Scheme IV, the Dieckmann cyclization of 14, induced by the use of potassium *tert*-butoxide in benzene, proceeded smoothly to give a single crystalline product in 91% yield. Since the product had been formed under thermodynamic conditions, structure **26a** was assumed.[9] However, it was now necessary to determine the fact of cis fusion, as well as to finally establish, inter alia, that the orientation at C-5 was indeed as we had been assuming in 17. The crucial information came from the coupling constants $J_{7a,7}$ and $J_{6,7}$ in the 400-MHz NMR spectrum which were found to be 6.8 and 6.4 Hz, respectively. These values show that all three hydrogens, H-7a, H-7 (≡ H-5), and H-6, were syn related and hence that the H-5 configuration was indeed as shown in 17.

Alkylation of **26a** with potassium *tert*-butoxide and methyl iodide gave a single product in 84% yield whose structure was established to be **26b** by an X-ray analysis, Scheme VIII. The C-7 (≡ C-5) orientation was given final confirmation, and it was found that the cyclohexane ring existed in a twist-boat rather than a pseudo-chair conformation.

Experimental Section

General Methods. Melting points were determined in capillary tubes in a Buchi Model 510 spectrometer and are uncorrected. ^{1}H NMR spectra were determined in deuteriochloroform with internal tetramethylsilane as the standard. Coupling constants were measured directly from the spectra or calculated from the peak listings. The numbering sequences used for the NMR data are shown in the schemes in the text. For IR spectra, neat samples were smeared on sodium chloride plates, and solutions were placed in sodium chloride cells. TLC was performed with aluminum plates precoated with silica gel containing a fluorescent indicator. The chromatograms were viewed under a UV light (254 nm), sprayed with concentrated sulfuric acid, and heated until charring occurred. Medium-pressure chromatography refers to column chromatography on silica gel performed under a pressure of air adjusted such that the flow rate of the solvent through the column is approximately 2–4 mL/min for small to medium size columns (50–300 mL) and 10 mL/min for large size columns (300–900 mL).

Methyl 3-*C*-[(Carbomethoxy)methyl]-1,2-*O*-isopropylidene-3,5,6-trideoxy-α-D-*ribo*-hept-5-enofuranuronate (3a). A solution of aldehyde **2**[4] (1.70 g, 7.0 mmol) and methyl (triphenylphosphoranylidene)acetate (2.8 g, 8.4 mmol) in acetonitrile was stirred at room temperature for 2 h. The solution was concentrated to a yellow solid residue which was extracted repeatedly with diethyl ether until the ether extract showed the absence of product **3a** on TLC. the combined organic extracts were concentrated to a syrup. Column chromatography over silica gel (5% ethyl acetate in petroleum ether) gave **3a** (1.71 g, 82%): R_f 0.64 (50% ethyl acetate in petroleum ether); mp 97–98 °C; $[\alpha]^{20}_D$ +18.90° (*c* 3.1, $CHCl_3$); IR 2970, 1730, 1650 cm^{-1}; ^{1}H NMR (80 MHz) δ 1.39 (s, 3 H, CCH_3), 1.55 (s, 3 H, CCH_3), 2.1–2.4 (m, 1 H, H3), 2.4–2.8 (m, 2 H, H8a, H8b), 3.7 (s, 1 H, OCH_3), 3.75 (s, 1 H, OCH_3), 4.15–4.50 (m, 1 H, H4), 4.76–4.90 (m, $J_{1,2}$ = 4.0 Hz, 1 H, H2), 5.90 (d, 1 H, H1), 6.10 (d, $J_{5,6}$ = 15.0 Hz, 1 H, H6), 6.7–7.0 (dd, $J_{4,5}$ = 8.0 Hz, 1 H, H5). Anal. Calcd for $C_{17}H_{20}O_7$: C, 55.99; H, 6.71. Found: C, 55.77; H, 6.77.

Methyl 3-*C*-[(Carbomethoxy)methyl]-1,2-*O*-isopropylidene-3,5,6-trideoxy-α-D-*ribo*-heptofuranuronate (4a). A solution of **3a** (1.7 g, 5.67 mmol) in ethanol (40 mL) was hydrogenated over 5% palladium on charcoal at ambient conditions for 30 min. The mixture was filtered through Celite, and the filtrate was evaporated to solid residue **4a** (1.71 g, quantitative yield): R_f 0.45 (40% ether in petroleum ether); mp 48–49 °C; $[\alpha]^{20}_D$ 88.9° (*c* 0.8, $CHCl_3$); IR 2960, 2940, 1730 cm^{-1}; ^{1}H NMR (220 MHz) δ 1.29 (s, 3 H, CCH_3), 1.44 (s, 3 H, CCH_3), 1.53–1.76 (m, 1 H, H5), 1.88–2.11 (m, 2 H, H3, H5′), 2.27–2.42 (dd, $J_{3,8}$ = 4.0 Hz, 1 H, H8), 2.42–2.57 (m, 2 H, H6), 2.57–2.73 (dd, $J_{3,8'}$ = 10.0 Hz, 1 H, H8′), 3.73 (s, 3 H, OMe), 3.76 (s, 3 H, OMe), 3.71–3.83 (m, 1 H, H4), 4.68 (t, $J_{1,2}$ = 4.0 Hz, 1 H, H2), 5.72 (d, 1 H, H1). Anal. Calcd for $C_{14}H_{22}O_7$: C, 55.62; H, 7.33. Found: C, 55.79; H, 7.43.

2(*R*)-(Methoxycarbonyl)(3,5-dideoxy-1,2-*O*-isopropylene-α-D-*ribo*-furano)[3,4-*c*]cyclohexanone (5) and 1-Hydroxy-2-(methoxycarbonyl)(3,5-dideoxy-1,2-*O*-isopropylidene-α-D-*ribo*-furano)[4,5-*d*]cyclohexene (6). A solution of **4a** (0.324 g, 1.07 mmol) in dry benzene (100 mL) was refluxed with potassium *tert*-butoxide (0.12 mg, 1.70 mmol) for 7 days. The solution was then cooled, diluted with ether, and washed with 5% hydrochloric acid solution (30 mL), saturated sodium bicarbonate solution (30 mL), and water 30 mL). The organic extract was dried (Na_2SO_4) and concentrated to give a yellow residue under reduced pressure. Column chromatography over silica gel (30% ethyl acetate in petroleum ether) yielded **5** (231 mg, 80%) and **6** (26 mg, 9%). For **5**: R_f 0.27 (30% ethyl acetate in petroleum ether); mp 165–166 °C (recrystallized from ether); $[\alpha]^{20}_D$ +52.96° (*c* 0.33, $CHCl_3$); IR 2940–2980, 1740 cm^{-1}; ^{1}H NMR (220 MHz) δ 1.14 (s, 3 H, CCH_3), 1.40 (s, 3 H, CCH_3), 1.56–1.78 (m, 1 H, $H5_{ax}$), 1.92–2.08 (m, $J_{3,8ax}$ = 13.5 Hz, $J_{2,3}$ = 4.0 Hz, $J_{3,4}$ = 11.0 Hz, 1 H, H3), 2.34–2.50 (m, $J_{4,5eq}$ = 4.0 Hz, 2 H, $H5_{eq}$ and $H6_{eq}$), 3.44 (d, 1 H, H8), 3.66 (s, 3 H, OMe), 3.94–4.04 (m, $J_{4,5ax}$ = 11.0 Hz, 1 H, H4), 4.42 (t, 1 H, H2), 5.74 (d, 1 H, H1). Anal. Calcd for $C_{13}H_{18}O_6$: C, 57.77; H, 6.71. Found: C, 57.66; H, 6.81. For **6**: R_f 0.45 (30% ethyl acetate in petroleum ether); mp 129–130 °C (recrystallized from ether); $[\alpha]^{20}_D$ −12.35° (*c* 2.93, $CHCl_3$); IR 1650 (conjugated C=O), 1610 (C=C), 2500–3000 (enolic OH) cm^{-1}; ^{1}H NMR (200 MHz) δ 1.24 (s, 3 H, CCH_3), 1.44 (s, 3 H, CCH_3), 1.56–1.73 (m, $J_{3,8eq}$ = 6.0 Hz, $J_{3,8ax}$ = 11.0 Hz, $J_{3,4}$ = 11.0 Hz, 1 H, H3), 1.88–2.18 (m, $J_{4,5ax}$ = 14.5 Hz, J_{5ax5eq} = 15.0 Hz, 1 H, $H5_{ax}$), 2.32–2.70 (m, 2 H, H8), 2.77–2.89 (dd, $J_{4,5eq}$ = 5.5 Hz, 1 H, $H5_{eq}$), 3.68 (s, 3 H, OMe), 3.76–3.86 (m, 1 H, H4), 4.56 (t, 1 H, H2), 5.84 (d, 1 H, H1), 12.84 (s, 1 H, enolic OH). Anal. Calcd for $C_{13}H_{18}O_6$: C, 57.77; H, 6.71. Found: C, 57.73; H, 6.81.

2(*S*)-(Hydroxymethyl)(3,5-dideoxy-1,2-*O*-isopropylidene-α-D-*ribo*-furano)[3,4-*c*]-1(*S*)-cyclohexanol (7a). Lithium aluminum hydride (14 mg, 0.368 mmol) was added slowly to a solution of **5** (66 mg, 0.244 mmol) in tetrahydrofuran cooled in an ice bath. TLC indicated reaction completion after 0.5 h. The solution was diluted with ether (40 mL) and quenched with sodium sulfate tetrahydrate crystals (1 g). A greyish white pre-

(13) Collins, J. C.; Hess, W. W.; Frank, F. *Tetrahedron Lett.* **1968**, 3363.

cipitate was formed after 15 min. The solution was filtered through a pad of Celite, and the organic filtrate was dried over anhydrous sodium sulfate. Solvent evaporation gave **7a** (65 mg, 90%): mp 131–132 °C (recrystallized from ether); $[\alpha]^{20}_D$ +85.8° (*c* 0.46, $CHCl_3$); IR 3200–3600 (OH) 2940, 2980 cm^{-1}; ^1H NMR (80 MHz) δ 1.30 (s, 3 H, CCH_3), 1.51 (s, 3 H, CCH_3), 1.0–2.25 (overlapping peaks, 6 H, H3, H5, H6, H8), 3.5–4.15 (overlapping peaks, 4 H, H4, H7, H9), 4.60 (t, $J_{1,2} = J_{2,3}$ = 3.7 Hz, 1 H, H2), 5.84 (d, 1 H, H1). Anal. Calcd for $C_{12}O_5H_{20}$: C, 59.00; H, 8.25. Found: C, 58.91; H, 8.29.

1(*S*)-(Ethoxyethoxy)-2(*R*)-(hydroxymethyl)(3,5-dideoxy-1,2-*O*-isopropylidene-α-D-*ribo*-furano)[3,4-*c*]cyclohexane (7d). *tert*-Butyldiphenylsilyl chloride (0.716 mL, 98% solution) was added to **7a** (0.689 g, 2.83 mmol), and imidazole (0.422 g, 6.19 mmol) was dissolved in dry dimethylformamide (18 mL). The solution was stirred for 30 h at which time TLC (30% ethyl acetate in petroleum ether) indicated completion. The solution was diluted with ether (40 mL) and extracted with water (3 × 10 mL). The organic extract, dried over anhydrous sodium sulfate, was evaporated to a thick syrup. Column chromatography over silica gel (30% ethyl acetate in petroleum ether) yielded **7b** (85 mg, 63%): R_f 0.36 (30% ethyl acetate in petroleum ether), *m/e* 468 (M^+), 426, 367, 349, 289. A solution of **7b** (0.85 g, 1.82 mmol), pyridinium *p*-toluenesulfonate[14] (0.22 g, 0.87 mmol), and ethyl vinyl ether (4 mL) in dry methylene chloride (20 mL) was stirred at room temperature for 4 h. The solution was diluted with methylene chloride and extracted with water (2 × 100 mL). The organic extract, dried over anhydrous sodium sulfate, was evaporated to a thick syrup. Column chromatography over silica gel with 10% ether in petroleum ether as an eluent removed all the polymeric impurities. Further elution with 40% ether in petroleum ether yielded **7c** (0.88 g, 91%): R_f 0.63 (30% ethyl acetate in petroleum ether); MS, *m/e* 540 (M^+), 400. A solution of **7c** (0.884 g, 1.60 mmol) and tetra-*n*-butylammonium fluoride (3.19 mL, 1 M solution) in dry tetrahydrofuran (20 mL) was refluxed overnight. Solvent evaporation, followed by column chromatography on silica gel (ether), yielded **7d** (0.348 g, 69%): R_f 0.27 (ether); IR 3300–3600 (OH stretch), 2900–3000 cm^{-1}; ^1H NMR (60 MHz) δ 1.0–2.4 (overlapping peaks, 15 H, H3, H5, H6, H8, CH_3CCH_3, $CH_3CH_2OCH(CH_3)O$), 3.36–4.0 (overlapping peaks, 9 H, H4, H7, H9, CH_3CH_2O), 4.5–4.8 (m, 2 H, H2, $OCHOCH_3O$), 5.78 (d, 1 H, H1); MS, *m/e* 301 ($M^+ - CH_3$), 271 ($M^+ - CH_3CH_2O$), 255 ($M^+ - CH_3 - CH_3CH_2OH$).

2(*R*)-(*Z*)-Propenyl-(3,5-dideoxy-1,2-*O*-isopropylidene-α-D-*ribo*-furano)[3,4-*c*]cyclohexanol (8c). By use of the standard procedure for Collin's oxidation, **7d** (0.348 g, 1.1 mmol) was oxidized to the aldehyde **8a** in 40 min. Workup and column chromatography over silica gel (ether) yielded **8a** (0.315 g, 91%): R_f 0.67 (ether); IR 2900–3000, 1720 cm^{-1}; MS, *m/e* 299 ($M^+ - CH_3 - CH_3CH_2OH$). By use of the standard Wittig reaction procedure,[13] aldehyde **8a** (0.31 g, 0.987 mmol) was treated with ethylidenetriphenylphosphorane (3 equiv) at −20 °C. The reaction was left at room temperature for 4 h at which time TLC (30% ethyl acetate in petroleum ether) indicated that the reaction was complete. After workup, the crude product was purified by flash column chromatography on silica gel with 20% methylene chloride in petroleum ether as an eluent to remove impurities. Further elution with 60% ether in petroleum ether gave the product **8b** (0.293 g, 91%): R_f 0.80 (30% ethyl acetate in petroleum ether); MS, *m/e* 326 (M^+), 311 ($M^+ - CH_3$), 281 ($M^+ - CH_3CH_2O$), 254 ($M^+ - CH_3CH_2OCH{=}CH_2$). A solution of **8b** (0.28 g, 0.85 mmol) and pyridinium *p*-toluenesulfonate[12] (53 mg, 0.20 mmol) in absolute ethanol (15 mL) was stirred at room temperature for 3.5 h. TLC (40% ethyl acetate in petroleum ether) indicated that the reaction was complete. Solvent evaporation, followed by column chromatography over silica gel (40% ethyl acetate in petroleum ether), yielded **8c** (0.19 g, 87%): R_f 0.36 (40% ethyl acetate in petroleum ether); IR 3300–3600 (OH stretch), 2850–2900 cm^{-1}; ^1H NMR (80 MHz) δ 1.30 (s, 3 H, CCH_3), 1.53 (s, 3 H, CCH_3), 1.72 (dd, 3 H, H11), 2.0–2.22 (m, 1 H, H3), 2.15–2.8 (m, 1 H, H8), 3.2–3.4 (m, 2 H, H4, H7), 5.0–5.56 (m, $J_{9,10}$ = 1.5 Hz, 1 H, H9), 5.6–6.0 (m, $J_{10,11}$ = 6.5 Hz, 1 H, H10); MS, *m/e* 254 (M^+), 239 ($M^+ - CH_3$), 196 ($M^+ - CH_3COCH_3$).

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2(*R*)-(*Z*)-Propenyl-(3,5-dideoxy-1,2-*O*-isopropylidene-α-D-*ribo*-furano)[3,4-*c*]cyclohexanone (9). By use of the standard procedure for Collin's oxidation,[13] the alcohol **8c** (0.185 g, 0.734 mmol) was oxidized to the ketone **9**. The reaction was completed in 30 min. Workup and column chromatography over silica gel (35% ethyl acetate in petroleum ether) gave **9** (0.15 g, 82%): R_f 0.54 (30% ethyl acetate in petroleum ether); mp 97–98 °C (recrystallized from ether–petroleum ether); $[\alpha]^{20}_D$ −8.68° (*c* 0.87, $CHCl_3$); IR 2850–2900, 1715 cm^{-1}; ^1H NMR (360 MHz) δ 1.33, 1.58 (s, 3 H, CCH_3), 1.58 (s, 3 H, CCH_3), 1.62–1.65 (dd, 3 H, $CH_3C{=}C$), 1.65–1.73 (m, $J_{2,3}$ = 3.6 Hz, $J_{3,8}$ = 9.0 Hz, 1 H, H3), 1.75–1.87 (m, $J_{4,5eq}$ = 4.5 Hz, 1 H, $H5_{eq}$), 2.35–2.47 (m, 2 H, $H6_{eq}$, $H5_{ax}$), 2.55–2.63 (m, 1 H, $H6_{ax}$), 3.53 (dd, $J_{8,10}$ = 3.6 Hz, 1 H, H8), 4.24 (ddd, $J_{4,5ax}$ = 11.0 Hz, 1 H, H4), 4.47 (m, 1 H, H2), 5.34 (m, $J_{9,11}$ = 1.8 Hz, $J_{9,10}$ = 10.8 Hz, 1 H, H9), 5.75–5.85 (m, $J_{10,11}$ = 7.2 Hz, 1 H, H10), 5.87 (d, $J_{1,2}$ = 3.7 Hz, 1 H, H1). Anal. Calcd for $C_{14}H_{20}O_4$: C, 66.65; H, 8.00. Found: C, 66.90; H, 8.04.

2(*R*)-(*Z*)-Propenyl-1-vinyl-(3,5-dideoxy-1,2-*O*-isopropylidene-α-D-*ribo*-furano)[3,4-*c*]cyclohexanol (10). A three-necked flask equipped with a stopper, a vacuum adaptor, a balloon, and a syringe cap was flushed with argon 3 times. A solution of ketone **9** (0.15 g, 0.595 mmol) in dry tetrahydrofuran (10 mL) under argon was cooled to −78 °C in a dry ice–acetone bath. Vinyllithium (0.77 mL, 2.3 M solution was added via a syringe over a period of 2 min. The solution was allowed to warm to room temperature slowly and then quenched by adding ether (2 × 20 mL) and water (5 mL). The solution was extracted with ether (3 × 10 mL), and the combined organic extracts washed with water (15 mL) and dried. Solvent evaporation afforded **10** (0.158 g, 95%) as an inseparable mixture of isomers: R_f 0.36 (20% ethyl acetate in petroleum ether); IR 3300–3600 (OH stretch), 2850–3000 cm^{-1}; ^1H NMR (80 Mhz) δ 1.30 (s, 3 H, CCH_3), 1.52 (s, 3 H, CCH_3), 1.75 (dd, 3 H, $CH_3CH{=}C$), 1.8–2.4 (overlapping peaks, 5 H, H3, H5, H6), 2.4–3.0 (m, 1 H, H8), 3.7–4.0 (m, 1 H, H4), 4.35–4.60 (m, 1 H, H2), 5.0–5.6 (overlapping peaks, 3 H, H9, H13), 5.80 (d, 1 H, H1), 5.6–6.0 (overlapping peaks, 1 H, H10), 6.0–6.4 (m, 1 H, H12); HRMS, $C_{16}H_{24}O_4$ calcd for ($M^+ - CH_3$) 265.1440, found 265.1438.

4-Methyl-(3,5-dideoxy-1,2-*O*-isopropylidene-α-D-*ribo*-furano)[7,8-*f*]cyclodec-5-enone (11). To a solution of **10** (55 mg, 0.207 mmol) in a dry tetrahydrofuran (10 mL) was added potassium hydride (3 mg, 0.075 mmol) and tetra-*n*-butylammonium iodide (10 mg). The solution was refluxed overnight at which time TLC (20% ethyl acetate in petroleum ether) indicated reaction completion. The solution was diluted with ether (20 mL) and quenched by slow addition of water (5 mL) and then partitioned between ether and water. The combined ethereal extract, dried over sodium sulfate, was evaporated to a yellow syrup. Column chromatography over silica gel (20% ethyl acetate in petroleum ether) gave **11** (40 mg, 74%): R_f 0.30 (20% ethyl acetate in petroleum ether); IR 2900–3000, 1700 cm^{-1}; ^1H NMR (360 MHz) δ 1.30 (s, 3 H, CCH_3), 1.58 (s, 3 H, CCH_3), 1.08 (d, 3 H, CH_3(H13)), 1.9–2.6 (overlapping peaks, 10 H, H3, H5, H6, H8, H9, H10), 3.7–3.85 (m, 1 H, H;), 4.55 (t, 1 H, H2), 5.25–5.60 (overlapping peaks, 2 H, H11, H12), 5.78 (d, 1 H, H1); HRMS, $C_{16}H_{24}O_4$ calcd for ($M^+ - CH_3$) 265.1440, found 265.1447.

Methyl 3-*C*-[(Carbomethoxy)methyl]-1,2-*O*-isopropylidene-6-*C*-methyl-3,5,6-trideoxy-α-D-*ribo*-hept-5-enofuranuronate (3b). A solution of aldehyde **2** (5 g, 20.5 mmol) and methyl triphenylphoranylidenepropionate (7.54 g, 21.7 mmol) in acetonitrile was stirred at room temperature for 2 h. The solution was concentrated under vacuum to a yellow syrup, and the residue was extracted repeatedly with diethyl ether until the ether extract showed the absence of product **3b** on TLC (40% ether in petroleum ether). The combined ethereal extract was concentrated to a syrup. Column chromatography on silica gel (40% ether in petroleum ether) gave **3b** which was purified by recrystallization from ether:hexane (5.19 g, 80.7%); R_f 0.4 (40% ether in petroleum ether); mp 160–162 °C; $[\alpha]^{20}_D$ +57.1° (*c* 0.9, $CHCl_3$); IR 2980, 2960, 1730 cm^{-1}; ^1H NMR (60 MHz) δ 1.33 (s, 3 H, CCH_3), 1.50 (s, 3 H, CCH_3) 1.9 (d, $J_{5,7}$ = 1.5 Hz, 3 H, H7), 2.0–2.5 (m, 2 H, H3, H8a), 2.6–3.0 (m, 1 H, H8b), 4.5 (t, $J_{3,4} = J_{4,5}$ = 8 Hz, 1 H, H4), 4.6–4.7 (2s, 6 H, 20Me)8 4.75 (t, $J_{2,3}$ = 4 Hz, 1 H, H2), 5.89 (d, $J_{1,2}$ = 4 Hz, 1 H, H1), 6.3–6.66 (m, 1 H, H5). Anal. Calcd for $C_{15}H_{22}O_7$: C, 57.32; H, 7.05. Found: C, 57.18; H, 7.03.

Methyl 3-*C*-[(Carbomethoxy)methyl]-1,2-*O*-isopropylidene-6-*C*-methyl-3,5,6-trideoxy-α-D-*ribo*-heptofuranuronate (4b). A solution of **3b** (5.19 g, 16.52 mmol) in ethanol (100 mL) was hydrogenated over 5% palladium on charcoal at ambient conditions for 30 min. The mixture was filtered through Celite, and the filtrate was evaporated to give a solid residue **4b** (5.18 g, 99.2%): IR 2920–2980, 1740 cm^{-1}; ^1H NMR (60 MHz) δ 1.15 (s, 3 H, H7), 1.3, (s, 3 H, CCH_3), 1.49 (s, 3 H, CCH_3), 1.6–2.3 (overlapping peaks, 3 H, H3, H5), 2.3–2.8 (overlapping peaks, 3 H, H6, H8), 3.72, 3.78 (2s, 6 H, 20Me), 4.7 (t, 1 H, H2), 5.7 (d, 1 H, H1); MS, *m/e* 316 (M^+), 301 ($M^+ - CH_3$).

2(*R*)-(Methoxycarbonyl)-6(*S*)-methyl-(3,5-dideoxy-1,2-*O*-isopropylidene-α-D-*ribo*-furano)[3,4-*c*]cyclohexanone (13). A solution of **4b** (5.8 g, 18.35 mmol) in dry benzene (100 mL) was refluxed with potassium *tert*-butoxide (2.36 g, 21.03 mmol) for 11 days. It was then cooled, diluted with ether (100 mL), and washed with 5% hydrochloric acid solution (30 mL), sodium bicarbonate solution (30 mL), and water (30 mL). The organic extract, dried over sodium sulfate, was concentrated to a yellow residue. Column chromatography on silica gel (35% ethyl acetate in petroleum ether) yielded a purified mixture of **4b** and **13**. When this mixture was kept overnight under high vacuum, a semicrystalline syrup was formed. Recrystallization of this material from hexane gave **13** (0.46 g, 8.8%). When the mother liquor was evaporated to dryness, **13** (2.319 g) was recovered: R_f 0.5 (30% ethyl acetate in petroleum ether); mp 161–162 °C; $[\alpha]^{20}_D$ +35.83° (*c* 1.73, $CHCl_3$); IR 2960, 1755 (ester), 1725 (ketone) cm^{-1}; ^1H NMR (80 MHz) δ 1.05 (d, 3 H, CH_3), 1.28 (s, 3 H, CCH_3), 1.5 (s, 3 H, CCH_3), 1.4–1.7 (m, $J_{4,5eq}$ = 3.75 Hz, 1 H, $H5_{eq}$), 1.75–2.2 (dddd, $J_{3,4}$ = 11.5 Hz, 1 H, H3), 2.25–2.65 (m, $J_{4,5ax}$ = 11.5 Hz, 2 H, $H5_{ax}$, H6), 3.5, 3.78 (2d, $J_{3,8}$ = 3.5 Hz, $J_{6,8}$ = 1 Hz, 1 H, H8), 5.15 (ddd, $J_{2,3}$ = 3.8 Hz, 1 H, H2), 6.85 (d, $J_{1,2}$ = 3.5 Hz, 1 H, H1); ^{13}C NMR δ 14.69 (Me), 26.19, 26.38 (CH_3CCH_3), 36.81 (C5), 42.89 (C3), 51.08 (C6), 52.48 (OMe), 54.87 (C8), 75.0, 75.6 (C2/C4), 107.8 (CH_3C-CH_3), 112.32 (C1), 168.85 (C9), 177.35 (C7). Anal. Calcd for $C_{14}H_{20}O_6$: C, 59.14; H, 7.09. Found: C, 59.26; H, 7.18.

3-*O*-Benzoyl-1,2-*O*-isopropylidene-6-*O*-(*tert*-butyldimethylsilyl)-α-D-*xylo*-hexofuran-5-ulose (20). To a solution of 3-*O*-benzoyl-1,2-*O*-isopropylidene-α-D-glucofuranose (**19a**)[11] (324 mg, 1 mmol) in dry pyridine (3 mL) at 23 °C under argon was added *tert*-butyldimethylsilyl chloride (165 mg, 1.1 mmol). The reaction mixture was stirred for 1 h, diluted with methylene chloride (30 mL), washed with ice-cold 0.5 N hydrochloric acid and brine, dried (Na_2SO_4), and concentrated in vacuo to yield an oil. Purification by medium-pressure chromatography on silica gel (27:75 diethyl ether–petroleum ether (30–60 °C), R_f 0.76) afforded 365 mg (80%) of pure **19b** as a colorless oil. An oxidizing medium was prepared as follows: to a solution of dry pyridine (0.55 mL) in dry methylene chloride (5 mL) at 23 °C under argon was added chromium trioxide (340 mg, 3.4 mmol). The reaction mixture was stirred for 30 min, and Celite (350 mg) was added followed immediately by the addition of **19b** (300 mg, 0.7 mmol) in dry methylene chloride (2 mL). After 5 min, acetic anhydride (0.13 mL8 1.4 mmol) was added. The reaction mixture was stirred for an additional 1 h, poured into 10 mL of diethyl ether, and filtered through a bed of Fluorisil covered by a layer of Celite. The clear filtrate was concentrated in vacuo. Residual pyridine was removed via its azeotrope with toluene to afford 245 mg (80%) of **20** as a colorless oil: R_f 0.33 (15:85 diethyl ether–petroleum ether (30–60 °C); $[\alpha]^{23}_D$ +45.8° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 2925, 2885, 2855, 1730 (ketone, benzoate), 1600 (C=C) cm^{-1}; ^1H NMR (80 MHz) δ 0.10 (s, 6 H, $Si(CH_3)_2$), 0.91 (s, 9 H, $SC(CH_3)_3$), 1.35 (s, 3 H, CCH_3), 1.55 (s, 3 H, CCH_3), 4.42 (s, 2 H, H6, H6), 4.68 (d, $J_{3,4}$ = 3.3 Hz, 1 H, H4), 5.24 (d, $J_{1,2}$ = 3.5 Hz, 1 H, H2), 5.80 (d, $J_{3,4}$ = 3.3 Hz, 1 H, H3), 6.10 (d, $J_{1,2}$ = 3.5 Hz, 1 H, H1), 7.33–7.65 (m, 3 H, aromatic)8 7.82–8.07 (m, 3 H, aromatic); MS, *m/e* 423 ($[M^+ + 2] - CH_3$), 422 ($[M^+ + 1] - CH_3$), 421 ($M^+ - CH_3$), 321 ($M^+ - Si(CH_3)_2C(CH_3)_2$).

Ethyl 3-*O*-Benzoyl-5-*C*-[[(*tert*-butyldimethylsilyl)oxy]-methyl]-5-deoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hept-5(*Z*,-*E*)-enofuranuronate (18a and 21). A solution of **20** (1.8 g, 4.1 mmol) and [(carbethoxy)methylene]triphenylphosphorane (1.175 g, 5 mmol) in dry acetonitrile (30 mL), under argon, was refluxed for 2 h. The solvent was removed in vacuo to yield a dark oil that crystallized upon standing. The crystals were washed with 50 mL of diethyl ether–petroleum ether (30–60 °C (1:1), and the undissolved triphenylphosphine oxide was removed by filtration. The filtrate was concentrated in vacuo to yield a dark oil that was purified by medium-pressure chromatography on silica gel (30:70 diethyl ether–petroleum ether (30–60 °C) to afford 187 mg (9%) of **21** and 850 mg (41%) of **18a** as colorless oils. For 21: R_f 0.65 (30:70 diethyl ether–petroleum ether (30–60 °C); IR 3560, 2945, 1723, 1650 (C=C α,β-unsaturated ester)8 1600 (C=C benzoate), cm^{-1}; ^1H NMR (80 MHz) δ 0.00 (s, 6 H, $Si(CH_3)_2$), 0.89 (s, 9 H, $Si(CH_3)_2$), 1.20–1.59 (m, 9 H, $C(CH_3)_2$, $CO_2CH_2CH_3$), 4.18 (q, 2 H, $CO_2CH_2CH_3$), 4.55 (brs, 2 H, H6, H6), 4.65 (d, $J_{1,2}$ = 3.9 Hz, 1 H, H2), 5.85–6.20 (m, 4 H, H1, H3, H4, C=CH), 7.30–7.62 (m, 3 H aromatic), 7.84–8.03 (m, 2 H, aromatic). For 18a: R_f 0.57 (30:70 diethyl ether–petroleum ether (30–60 °C); IR 3563, 2945, 1720, 1650 (C=C α,β-unsaturated ester), 1605 (C=C benzoate) cm^{-1}; ^1H NMR (80 MHZ) δ 0.00 (s, 6 H, $Si(CH_3)_2$), 0.91 (s, 9 H, $Si(CH_3)_2$), 1.01–1.63 (m, 6 H, $C(CH_3)_2$, $CO_2CH_2CH_3$), 4.12 (q, 2 H, $CO_2CH_2CH_3$), 4.71 (brd, 2 H, H6, H6), 5.00 (brs, 1 H, H2), 5.40 (brs, 1 H, H1), 5.68 (d, *J* = 2.0 Hz, 1 H, H3), 5.98–6.07 (m, 2 H, H4, C=CH).

The above reaction was repeated with dimethyl sulfoxide (15 mL) as the solvent. After 48 h at 23 °C under argon, the reaction mixture was diluted with water (15 mL) and extracted with petroleum ether. The organic fractions were combined, washed with brine, dried (Na_2SO_4), and concentrated in vacuo to yield an oil. Purification by chromatography on silica gel (30:70 diethyl ether–petroleum ether) afforded 1.84 g (88%) of **18a** contaminated with only a trace amount of **21**: MS, *m/e* 492 ($[M^+ + 1] - CH_3$), 491 ($M^+ - CH_3$), 391 ($M^+ - Si[CH_3]_2C[CH_3]_3$).

Ethyl 3-*O*-Benzoyl-5-deoxy-5-*C*-(hydroxymethyl)-1,2-*O*-isopropylidene-α-D-*xylo*-hept-5(*Z*)-enofuranuronate (18b). To a solution of **18a** (20.0 g, 40 mmol) in methanol (200 mL) was added ammonium fluoride (2.9 g, 80 mmol) in water (40 mL). The reaction mixture was refluxed for 3 h and cooled, and the methanol was removed. The resulting aqueous mixture was extracted with methylene chloride which was washed with brine, dried (Na_2SO_4), and concentrated to give an oil. Further purification by medium-pressure chromatography on silica gel (12:88 diethyl ether–methylene chloride, R_f 0.38) afforded 12.6 g (81%) of pure **18b** as a colorless oil: IR 3670, 3560 (OH), 2930, 1720 (ester and benzoate), 1653 (C=C α,β-unsaturated ester), 1600 (C=C benzoate) cm^{-1}; ^1H NMR (80 MHz) δ 1.18–1.33 (m, 6 H, CCH_3, OCH_2CH_3), 1.60 (s, 3 H, CCH_3), 2.08 (brs, 1 H, OH), 4.19 (q, 2 H, OCH_2CH_3), 4.44 (brd, 2 H, H6, H6), 4.66 (d, $J_{1,2}$ = 3.9 Hz, 1 H, H2), 5.92–6.18 (m, 4 H, H1, H3, H4, H7), 7.38–7.66 (m, 3 H, aromatic), 7.85–8.09 (m, 2 H, aromatic); *m/e* 377 ($M^+ - CH_3$), 374 ($M^+ - H_2O$), 331 ($M^+ - C_2H_5O_2$).

3-*O*-Benzoyl-5-(carboxymethyl)-5-deoxy-8-hydroxy-1,2-*O*-isopropylidene-α-D-*xylo*-hept-5-enofuranose 5,8-Lactone (22). Desilylation of **21** (506 mg, 1 mmol) as described for **18a** afforded 220 mg (76%) of **22** as a pale yellow oil: IR 2960, 1780, 1750 (α,β-unsaturated lactone—two bands due to Fermi resonance), 1725 (benzoate), 1655 (C=C α,β-unsaturated lactone), 1610 (C=C benzoate) cm^{-1}; ^1H NMR (80 MHz) δ 1.36 (s, 3 H, CCH_3), 1.58 (s, 3 H, CCH_3), 4.75 (d, $J_{1,2}$ = 3.8 Hz, 1 H, H2), 4.89 (2s, 2 H, H6, H6), 5.29 (brs, 1 H, H4) , 5.65 (d, $J_{3,4}$ = 3.2 Hz, 1 H, H3), 6.00–6.22 (m, 2 H, H1, H7), 7.32–7.66 (m, 3 H, aromatic), 7.80–8.03 (m, 2 H, aromatic); MS, *m/e* 347 ($M^+ + 1$), 346 (M^+), 332 ($M^+ - CH_3$).

5-(Carboxymethyl)-5-deoxy-8-hydroxy-1,2-*O*-isopropylidene-3-oxo-α-L-*ido*-heptofuranose 5,8-Lactone (23b). A solution of **18b** (4.0 g, 10 mmol) in benzene (100 mL) was hydrogenated over 5% platinum on carbon at 500 psi. After 45 min, the catalyst was removed by filtration, and the filtrate was concentrated to yield an oil that gave two "spots" on TLC (3:97 methanol–methylene chloride, R_f 0.46, 0.81). (It was assumed that the less polar product was **23a** and the more polar one **17**.) To a solution of the oil in diethyl (100 mL) was added *p*-toluenesulfonic acid (120 mg, 0.6 mmol). After 6 h at 23 °C, the reaction mixtur was quenched with triethylamine, washed with brine, dried (Na_2SO_4), and concentrated in vacuo to afford 3.4 g (96%) of **23a** as a colorless oil. To a solution of **23a** (1.10 g, 3.2 mmol) in methanol (7 mL) was added sodium methoxide (24 mg, 0.44 mmol). After 3 h at 23 °C, the reaction mixture was concentrated in vacuo. The residue was diluted with brine, and the aqueous mixture was extracted with hexane followed by methylene chloride. The methylene chloride fractions were combined, dried (Na_2SO_4), and concentrated in vacuo to yield a crystalline material.

Recrystallization from methylene chloride–hexane afforded 0.61 g (79%) of **23b**: R_f 0.44 (4:96 methanol–methylene chloride); mp 138–139 °C; $[\alpha]^{23}_D$ −47.9° (*c* 0.4, $CHCl_3$); IR 3400 (hydrogen-bonded OH), 2910, 1775 (lactone) cm^{-1}; ^1H NMR (400 MHz) δ 1.31 (s, 3 H, CCH_3), 1.49 (s, 3 H, CCH_3), 1.5 (s, 1 H, OH), 2.70 (ddd, 2 H, H7, H7), 3.00 (q, 1 H, H5), 4.09–4.17 (m, 3 H, H3, H6, H6), 4.46 (dd, 1 H, H4), 4.50 (d, $J_{1,2}$ = 3.7 Hz, 1 H, H2), 5.91 d, $J_{1,2}$ = 3.7 Hz, 1 H, H1). Anal. Calcd for $C_{11}H_{16}O_6$: C, 54.09; H, 6.60. Found: C, 54.15; H, 6.76.

5-(Carboxymethyl)-5-deoxy-8-hydroxy-1,2-*O*-isopropylidene-α-L-*lyxo*-heptofuran-3-ulose 5,8-Lactone (24). To a solution of **23b** (1.2 g, 5 mmol) and dimethyl sulfoxide (1.4 mL, 20 mmol) in dimethylformamide (35 mL) under argon phosphorus pentoxide (2.56 g, 18 mmol) was added. The reaction mixture was heated at 65–75 °C for 2 h, then cooled, and poured into water. The resulting aqueous solution was extracted with methylene chloride which was washed with brine, dried (Na_2SO_4), and concentrated in vacuo. Residual dimethylformamide was removed by chromatography on silica gel (15:85 diethyl ether–methylene chloride, R_f 0.43) to afford 994 mg (83%) of **24** as an oil: IR 2900, 1774 (lactone, ketone) cm^{-1}; ^1H NMR (80 MHz), δ 1.40 (s, 3 H, CCH_3), 1.53 (s, 3 H, CCH_3), 1.82–2.16 (m, 3 H, H5, H7, H7), 4.15–4.62 (m, 4 H, H2, H4, H6, H6), 6.07 (d, $J_{1,2}$ = 4.3 Hz, 1 H, H1); MS, *m/e* 242 (M^+).

Methyl 5-(Carboxymethyl)-3,5-dideoxy-8-hydroxy-1,2-*O*-isopropylidene-α-L-*lyxo*-hept-3(*Z*,*E*)-enofuranuronate 5,8-Lactone (25). To a solution of **24** (3.1 g, 13 mmol) in dry acetonitrile (50 mL) under argon (carbomethoxymethylene)triphenylphosphorane (5.0 g, 15 mmol) was added. The reaction mixture was refluxed for 2 h, cooled, and concentrated. The oily residue was dissolved in diethyl ether (50 mL) and cooled to 0 °C. Triphenylphosphine oxide crystallized out and was removed by filtration. The filtrate was concentrated in vacuo to give a dark oil that was further purified by medium-pressure chromatography on silica gel (4:96 methanol–methylene chloride, R_f 0.76, 0.81) to afford 2.98 g (78%) of **25** as a mixture of geometric isomers: IR (2978, 2938, 1778 (C=C), 178 (lactone), 1723 (α,β-unsaturated ester) cm^{-1}; ^1H NMR (80 MHz) δ 1.50 (s, 3 H, CCH_3), 1.66 (s, 3 H, CCH_3), 2.27 (d, 1 H, H7), 2.39 (d, 1 H, H7), 2.64–3.21 (m, 1 H, H5), 3.78 (2s, 3 H, CO_2CH_3), 4.41–4.51 (m, 2 H, H6, H6), 4.90 (brs, 1 H, H4), 5.58–6.21 (m, 3 H, H1, H2, H9); MS, *m/e* 285 ($[M^+ + 2] - CH_3$), 284 ($[M^+ + 1] - CH_3$), 283 ($M^+ - CH_3$).

Methyl 5-(Carboxymethyl)-3,5-dideoxy-8-hydroxyl-1,2-*O*-isopropylidene-α-L-*talo*-heptofuranosyluronate 5,8-Lactone (14). A solution of **25** (5.0 g, 17 mmol) in benzene (100 mL) was hydrogenated over 5% palladium on carbon (300 mg) at 200 psi. After 30 min, uptake of hydrogen had ceased. The reaction mixture was diluted with methylene chloride (100 mL), and the catalyst was removed by filtration through a bed of Celite. The filtrate was concentrated in vacuo to yield a white crystalline product. Recrystallization from ethanol afforded 4.7 g (94%) of 14 as granular crystals: R_f 0.47 (15:85 diethyl ether–methylene chloride); mp 152–153.5 °C; $[\alpha]^{23}_D$ + 62.5° (*c* 1.3 $CHCl_3$); IR 2930, 1772 (lactone), 1730 (ester) cm^{-1}; ^1H NMR (400 MHz) δ 1.32 (s, 3 H, CCH_3), 1.48 (s, 3 H, CCH_3, 2.09–2.16 (m, 1 H, H5), 2.34 (dd, $J_{5,7}$ = 4.2, $J_{7,7}$ = 15.2 Hz, 1 H, H7), 2.47 (dd, $J_{5,7}$ = 9.0 Hz, $J_{7,7}$ = 15.2 Hz, 1 H, H7), 2.57 (dd, $J_{3,9}$ = 9.0 Hz, $J_{9,9}$ = 15.2 Hz, 1 H, H9), 2.69–2.79 (m, 2 H, H3, H9), 3.73 (s, 3 H, CO_2CH_3), 3.88 (dd, $J_{3,4}$ = 2.7 Hz, $J_{4,5}$ = 9.0 Hz, 1 H, H4), 4.29 (t, $J_{5,6}$ = $J_{6,6}$ = 9.0 Hz, 1 H, H6), 4.41 (t, $J_{6,6}$ = $J_{5,6}$ = 9.0 Hz, 1 H, H6), 4.79 (t, $J_{1,2}$ = $J_{2,3}$ = 4.0 Hz, 1 H, H2), 5.85 (d, $J_{1,2}$ = 4.0 Hz, 1 H, H1). Anal. Calcd for $C_{14}H_{20}O_7$: C, 55.99; H, 6.71. Found: C, 56.15; H, 6.84.

(2*R*,3*R*,3a*R*,6*S*,7*S*,7a*R*)-6-Carboxy-7-(hydroxymethyl)-2,3-(isopropylidenedioxy)-5-oxooctahydrobenzo[4,3-*b*]furan 6,7-Lactone (26a). To a solution of **14** (10.2 g, 34 mmol) in freshly distilled benzene (250 mL) at 23 °C under argon was added potassium *tert*-butoxide (4.5 g, 40 mmol). The reaction mixture was refluxed for 15 min, cooled, and washed with ice-cold 0.25 N hydrochloric acid. The aqueous layer was washed with ethyl acetate (1 × 100, 1 × 50 mL). The benzene and ethyl acetate fractions were combined, washed with brine, dried (Na_2SO_4), and concentrated in vacuo to afford 8.2 g (91%) of a crystalline product. Recrystallization from methanol afforded **26a**: R_f 0.48 (50:50 ethyl acetate–benzene); mp 199–201 °C; $[\alpha]^{23}_D$ −23.1° (*c* 0.3, $CHCl_3$); IR 2927, 1770 (lactone), 1725 (ketone) cm^{-1}; ^1H NMR (400 MHz) δ 1.35 (s, 3 H, CCH_3), 1.51 (s, 3 H, CCH_3), 2.22 (m, 1 H, H3), 2.61 (dd, $J_{3,9ax}$ = 11.0, $J_{9,9}$ = 12.0 Hz, 1 H, H9), 2.75 (dd, $J_{3,9eq}$ = 6.3 Hz, $J_{9,9}$ = 12.0 Hz, 1 H, H9), 3.47 (m, 1 H, H5), 3.65 (d, 1 H, H7), 4.08 (dd, $J_{4,5}$ = 6.8 Hz, $J_{3,4}$ = 11.6 Hz, 1 H, H4), 4.39 (t, $J_{5,6}$ = $J_{6,6}$ = 8.2 Hz, 1 H, H6), 4.63–4.71 (m, 2 H, H2, H6), 5.98 (d, $J_{1,2}$ = 3.0 Hz, 1 H, H1). Anal. Calcd for $C_{13}H_{16}O_6$: C, 58.20; H, 6.01. Found: C, 58.13, H, 6.05.

(2*R*,3*R*,3a*R*,6*S*,7*S*,7a*R*)-6-Carboxy-7-(hydroxymethyl)-2,3-(isopropylidenedioxy)-6-methyl-5-oxooctahydrobenzo-[4,3-*b*]furan 6,7-Lactone (26b). To a solution of **26a** (5.50 g, 22 mmol) in dry dimethyl sulfoxide (50 mL) at 25 °C under an atmosphere of argon was added potassium *tert*-butoxide (2.46 g, 22 mmol). After 15 min, the reaction was quenched with methyl iodide (2.2 mL, 35 mmol), and the mixture was poured into ice water and extracted 3 times with ethyl acetate. The ethyl acetate fractions were combined, washed with brine, dried, and evaporated in vacuo to yield a pale yellow oil. Medium-pressure chromatography on silica gel (50:50 ethyl acetate–benzene), followed by recrystallization (methylene chloride–hexane), afforded 5.2 g (84%) of **26b**: mp 119–121 °C; $[\alpha]^{20}_D$ −72.3° (*c* 1.2, $CHCl_3$) IR 3450, 3405, 3350, 1763 (lactone), 1718 (ketone) cm^{-1}; ^1H NMR (80 MHz) δ 1.21–1.65 (m, 9 H, $C[CH_3]_2$, CH_3), 2.11–2.48 (m, 1 H, H3), 2.69 (2d, 2 H, H9, H9), 2.95 (dt, $J_{5,6}$ = 3.0 Hz, $J_{4,5}$ = $J_{5,5}$ = 7.5 Hz, 1 H, H5), 3.97 (dd, $J_{4,5}$ = 7.5 Hz, $J_{3,4}$ = 11.0 Hz, 1 H, H4), 4.23–4.86 (m, 3 H, H2, H6, H6), 5.95 (d, $J_{1,2}$ = 4.0 Hz, 1 H, H1). Anal. Calcd for $C_{14}H_{18}O_6$: C, 59.56; H, 6.42. Found: C, 59.80; H, 6.43.

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