at isolating these compounds were unsuccessful. Without further characterization, this mixture was used in the following step.

(12*S*)-15,16-Epoxy-19-norneoclerodane-4,13(16),14-triene-18,6α;20,12-diolide (12, Teucvin[6a,10]) from Compounds 11a and 11b. The mixture of compounds **11a** and **11b** (26 mg) was oxidized with the CrO_3-pyridine complex (50 mg of CrO_3 in 0.5 mL of pyridine) in pyridine (0.5 mL) solution at rt for 2 h. The reaction was worked up as usual to provide a crude product that was purified by chromatography (silica gel column, $CHCl_3$-MeOH (19:1) as eluent) yielding 16 mg of a substance (48% yield from **4**, mp 206-208 °C (EtOAc-*n*-hexane); $[\alpha]_D^{21}$ +185.3° (*c* 0.413, $CHCl_3$)) identical in all respects (mp, $[\alpha]_D$, IR, ^1H NMR, MS) with teucvin (**12**, lit.[6a,10] mp 205-208 °C; $[\alpha]_D^{28}$ +186.1° (*c* 0.59, $CHCl_3$)). Comparison (mmp, TLC) with an authentic sample[6a] proved the identity of the products.

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Registry No. 1, 71774-90-8; **2**, 136176-59-5; **3**, 136176-60-8; **4**, 136176-61-9; **5**, 136176-62-0; **6**, 92632-30-9; **7**, 136176-63-1; **8**, 136176-64-2; **9**, 41759-79-9; **10**, 136176-65-3; **11a**, 136176-66-4; **11b**, 136235-35-3; **12**, 51918-98-0.

Supplementary Material Available: Table II containing ^{13}C NMR spectra (50.3 MHz) of **2-5**, **8**, and **10** (1 page). Ordering information is given on any current masthead page.

The Furan Approach to Oxygenated Natural Products. Total Synthesis of (+)-KDO

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A de novo asymmetric synthesis of the higher monosaccharide 3-deoxy-D-*manno*-2-octulosonic acid, (+)-KDO (**1**), was completed in 12 steps starting from furan and isopropylidene-D-glyceraldehyde. The synthesis commenced with the conversion of furan (**4**) into the protected furfuryl carbinol **5** by the highly stereoselective addition of 2-lithiofuran to isopropylidene-D-glyceraldehyde and subsequent trapping of the intermediate alkoxide. Metalation of **5** followed by alkylation with benzyl chloromethyl ether and hydroxyl deprotection then provided **9** in a single operation. The key transformation of the synthesis entailed sequential oxidative processing of **9** with *t*-BuOOH in the presence of a catalytic amount of $VO(acac)_2$ and O-methylation of the intermediate hemiacetal moiety to furnish the α-methyl glycoside **12** as the major product. Stereoselective 1,2-reduction of **12** using K-Selectride (Aldrich) gave the allylic alcohol **15**, which was elaborated to **20** by electrophile-induced cyclization of the allylic carbamate **19**. Refunctionalization of **20** proceeded in a straightforward fashion by a process involving reductive removal of iodide at C(3) and the benzyl protecting group at C(1) to furnish **23**. Oxidation of the intermediate primary alcohol moiety at C(1) of **23** and deprotection of the remaining hydroxyl functions delivered (+)-KDO (**1**).

Introduction

3-Deoxy-D-*manno*-2-octulosonic acid, (+)-KDO (**1**),[2] is a higher monosaccharide that forms a vital and unique link between the hydrophobic lipid A and the hydrophilic polysaccharide subunits in the outer membrane lipopolysaccharides (LPS) of Gram-negative bacteria.[3] The rate-limiting enzyme for the incorporation of KDO into these LPS is CMP-KDO synthetase (3-deoxy-D-*manno*-octulosonate cytidylyl transferase),[4] and the preparation of analogues of **1** as potential inhibitors of this enzyme emerged as an attractive strategy for the discovery of novel antibiotics.[5] These investigations lead to the development of several effective antibacterial agents derived from 2-deoxy-KDO that specifically inhibit LPS biosynthesis.

The biological importance of (+)-KDO (**1**) has also served as the impetus for a number of efforts directed toward its total synthesis.[6] Inasmuch as (+)-KDO is a higher monosaccharide, it follows that simple carbohydrates, which could provide all of the requisite stereogenic centers present in **1**, would be attractive starting materials. Indeed, with only two exceptions,[6c,l] the common strategic device employed in previous approaches to **1** has involved extension of the carbohydrate backbone of D-mannose or D-arabinose by two or three carbon atoms, respectively. A number of useful chemical and enzymatic methods were developed and implemented to effect this key construction. It was against this backdrop that we were attracted to the challenge of developing a concise and efficient strategy for

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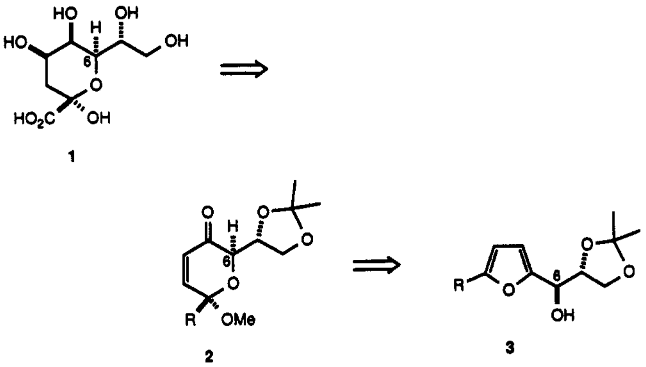
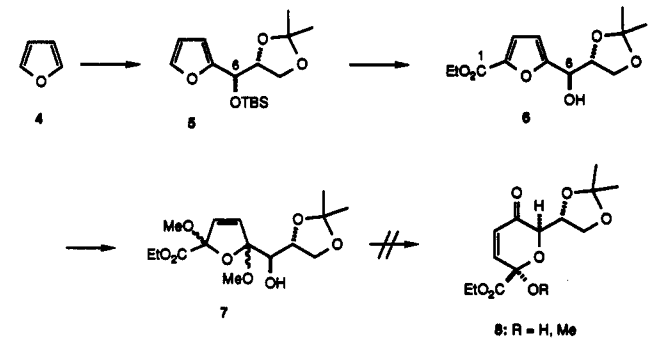
Scheme I



Scheme II



the asymmetric synthesis of (+)-KDO from noncarbohydrate starting materials. Of obvious appeal was the possibility that discoveries leading to the successful realization of this goal might be extended to the de novo syntheses of other higher monosaccharides.

We have been interested in exploiting furans and hydropyranones derived therefrom as key intermediates in the asymmetric syntheses of highly oxygenated natural products. Recent applications of this strategy from our laboratories have resulted in short syntheses of a number of interesting targets including Prelog–Djerassi lactone, tirandamycin, and the seco acid of erythronolide B.[7] Consideration of this prior art led to the formulation of an approach to (+)-KDO that involved the oxidative conversion of a suitably functionalized furfuryl carbinol as **3** into the derived dihydro-3-pyranone **2** (Scheme I). According to this plan, the critical stereogenic center at C(6) of **1** would be established with the correct absolute configuration in the first stage of the endeavor by preparation of **3**. The absolute stereochemistry at this center would then be exploited in **2** and subsequent hydropyranoid intermediates to introduce the remaining stereocenters in the target with the proper relative orientations. Indeed, in our earlier work,[7] we demonstrated that hydropyranones provide excellent templates for efficient, stereoselective introduction of new functional groups and substituents onto the hydropyran ring.[8] Herein we report the details of our investigations that culminated in the successful total synthesis of (+)-KDO (**1**).[9]

Results and Discussion

From the outset of these investigations, we held the development and execution of a concise approach to (+)-KDO as one of the primary goals. Toward this end, we sought to minimize the number of unproductive steps that involved protective maneuvers and simple refunctionalizations. Such an objective could be achieved by incorporating the C(1) carbon in the proper state of oxidation at the inception of the sequence, and our initial efforts were thus directed toward the preparation and subsequent oxidative transformation of the 2-alkyl-5-furoate ester **6** into the corresponding 6-carboalkoxy-3-(2*H*)-pyranone **8** (Scheme II). The critical stereogenic center at C(6) (KDO numbering) was created in the first step of the synthesis by the highly stereoselective[10] addition of 2-furyllithium to isopropylidene-D-glyceraldehyde[11] in the presence of $ZnBr_2$ under strictly controlled conditions. The intermediate alkoxide was trapped in situ by the addition of *tert*-butyldimethylsilyl chloride (1 equiv) to furnish the anti adduct **5** in 53% overall yield ($J_{5,6}$ = 6.1 Hz). We were unable to detect any of the isomeric syn silyl ether either by ^1H NMR or by GLC. Metalation of the furan ring of **5** (*tert*-BuLi (1 equiv); THF, −78 → 0 °C, 4 h) and sequential addition of ethyl chloroformate (0 → 25 °C, 12 h) and $(n\text{-Bu})_4NF$ (1 M aqueous THF, 25 °C, 12 h) then provided **6** (56%), which contains the full complement of carbon atoms present in **1**.

Despite the well-established nature of such processes, we encountered insurmountable difficulties in the next phase of the operation, which required the oxidative transformation of the 5-carboethoxyfurfuryl carbinol **6** into the dihydropyranone **8**. Although treatment of **6** with bromine in methanol at −78 °C followed by neutralization with ammonia smoothly furnished the dimethoxy dihydrofuran **7**, all attempts to effect the selective transformation of **7** into **8** through the agency of either Lewis (e.g., $BF_3 \cdot Et_2O$) or Bronsted (e.g., *p*-toluenesulfonic or camphorsulfonic acid, PhH; or AcOH, H_2O) acids furnished products with loss of the acetonide protecting group. Alternative conditions for oxidative processing of the furan ring under conditions that would not be expected to induce concomitant removal of the acid labile acetonide protecting group were also examined. However, **6** proved to be unreactive toward the following: (1) bromine in aqueous acetonitrile in the presence of pyridine;[8e] (2) singlet oxygen generated either photochemically ($^3O_2$, $h\nu$, methylene blue, CH_2Cl_2, −78 °C) or chemically (ceric ammonium nitrate, KOCl);[12] (3) peracids (MCPBA);[7b] and (4) peroxides [*t*-BuOOH, $VO(acac)_2$ (cat.), CH_2Cl_2].[13] We ultimately concluded that the presence of the electron-withdrawing carboethoxyl group deactivated the furan ring of **6** and the dimethoxy dihydrofuran array in **7** to the extent that mild conditions compatible with the labile acetonide moiety could not be employed to effect oxidation

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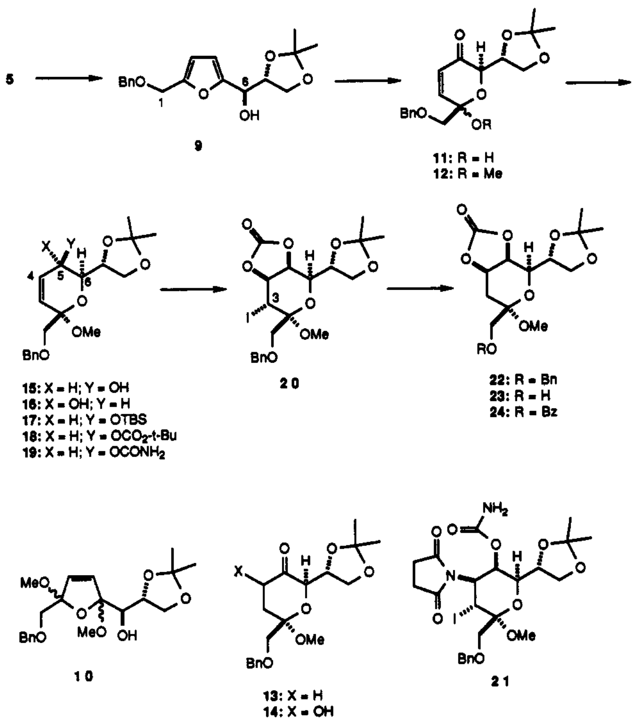
(13) (a) Ho, T.-L.; Sapp, S. G. *Synth. Commun.* **1983**, *13*, 207. For extensions to kinetic resolution of racemic furfuryl carbinols, see: (b) Kusakabe, M.; Kitano, Y.; Kobayashi, Y.; Sato, F. *J. Org. Chem.* **1989**, *54*, 2085. (c) Kametani, T.; Tsubuki, M.; Tatsuzaki, Y.; Honda, T. *J. Chem. Soc., Perkin Trans. 1* **1990**, 639.

Scheme III



of the furan ring of 6 or to induce selective hydrolysis of 7 to give 8.

At this juncture two modifications of the basic plan were considered. Since the acetonide in intermediates 6 and 7 was a source of difficulty, one possibility was to change the nature of the protecting group for the hydroxyl groups at C(7) and C(8). However, there were obvious disadvantages to engaging this tactic. Other hydroxyl-protected derivatives of D-glyceraldehyde are not as readily available. Moreover, the levels of stereochemical control that might be achieved in nucleophilic additions to such derivatives to secure the key stereocenter at C(6) were not as well defined and appeared somewhat more problematic.[14] The other option involved altering the oxidation state of the functionality at C(1) from that of a carboxyl function as in 6 to that of a protected primary alcohol as in 9. Untoward deactivation of the furan ring during oxidative processing would thereby be obviated, and selective deprotection and subsequent oxidation of C(1) at a later stage of the synthesis would be expected to be straightforward.

In the event, metalation of the furan ring of 5 [*t*-BuLi (1 equiv); THF, $-78 \rightarrow 0$ °C, 4 h] followed by sequential addition of benzyl chloromethyl ether ($0 \rightarrow 25$ °C, 12 h) and *n*-Bu_4NF (1 M aqueous THF, 25 °C, 12 h) furnished 9 in 92% yield (Scheme III). Treatment of 9 with Br_2 (MeOH, -78 °C; NH_3) smoothly afforded the dimethoxydihydrofuran 10. However, we were still unable to induce selectively acid-catalyzed hydrolysis of the dimethoxy dihydrofuran moiety in 10 and the subsequent transformation into the desired hydropyranone 11 while maintaining the integrity of the acetonide protecting group; an alternative protocol for oxidative processing of the furan ring was obviously required. Although singlet oxygen *m*-CPBA and *t*-BuOOH/cat. $VO(acac)_2$ effected the transformation of 9 into 11, superior yields of 11 were obtained using the latter oxidant, which provided 11 as a mixture (4.5:1) of α- and β-anomers in 91% yield. Subsequent treatment of the anomeric mixture of 11 with excess methyl iodide in the presence of silver(I) oxide furnished a readily separable mixture (ca. 4.5:1) of the α-methyl glycoside 12 together with the corresponding β-anomer in 82% combined yield.

In the initial attempts to introduce the requisite hydroxyl group at C(4), we focused upon methods for effecting α-hydroxylation of the ketone 13, which was prepared by reduction of 12 (H_2/10% Pd–C, EtOH, 1 h; 67%). However, conversion of 13 to its enolate (LDA, THF, -78 °C) followed by reaction with MoOPH[15] and other oxidants returned only starting material and unidentified products. When the trimethylsilyl enol ether derived from 13 was treated with MCPBA, a mixture of epimeric α-hydroxy ketones 14 were isolated, albeit in only modest yield. It thus appeared that a plan to refunctionalize at C(4) of 13 would not lead to a satisfactory solution to the problem of elaborating the *vic*-dihydroxy array at C(4) and C(5).

We then turned to an examination of those techniques that might be employed to install a hydroxyl group at C(4) of the allylic alcohol 15. Reduction of 12 with $NaBH_4$ and DIBALH furnished separable mixtures in which the equatorial allylic alcohol 16 ($J_{5,6} = 8.7$ Hz) predominated (2–3:1) over the desired axial epimer 15 ($J_{5,6} = 1.8$ Hz); however, treatment of 12 with K-Selectride (THF, -78 °C, 30 min) cleanly delivered 15 as the major product (15:16 = 9.8:1) in 88% isolated yield. Presumably, 1,4-reduction of 12, which is commonly observed in reductions of β-unsubstituted enones using K-Selectride,[16] does not occur owing to the steric hindrance imposed by the adjacent, fully substituted anomeric center.

In an initial attempt to functionalize 15 at C(4), we briefly explored the feasibility of effecting stereoselective hydroboration–oxidation (BH_3–THF, 0 °C, 2 h; NaOH, H_2O_2, H_2O) of the double bond in the corresponding protected allylic alcohol 17 (15, TBDMSCl, imidazole, DMF, RT, 12 h; 77%). Unfortunately, this reaction afforded a mixture of at least three products, the major of which appeared to be the undesired α-alcohol. Preliminary attempts to invert the configuration of this alcohol according to the standard Mitsunobu[17] protocol were unavailing and provided only traces of the desired product. This approach was then abandoned in favor of a more productive avenue.

Procedures for introducing the requisite C(4) hydroxyl group via electrophile-induced cyclization[18] of derivatives of the allylic alcohol 15 were then considered. Toward this end, the *tert*-butyl carbonate 18 was readily prepared (BOC-ON, *n*-BuLi, Et_2O; 99%), but it was completely unreactive toward various electrophilic species including I_2, PhSeBr, and PhSeOTf. The failure of 18 to form the desired C(4)–C(5) cyclic carbonate can be attributed to a combination of unfavorable steric interactions that occur in the transition state for cyclization. The hydropyran ring must assume a boat conformation in which there is buttressing between the C(1) methylene and the incoming oxygen at C(4), and the approach of the iodonium ion from the opposite face of the double bond is impeded by the anomeric methoxyl group. The cyclofunctionalizations of mixed carbonates of axially-oriented, allylic alcohols in simple carbohydrate systems had been previously observed to be problematic;[19,20] however, cyclic carbonates of cis diols

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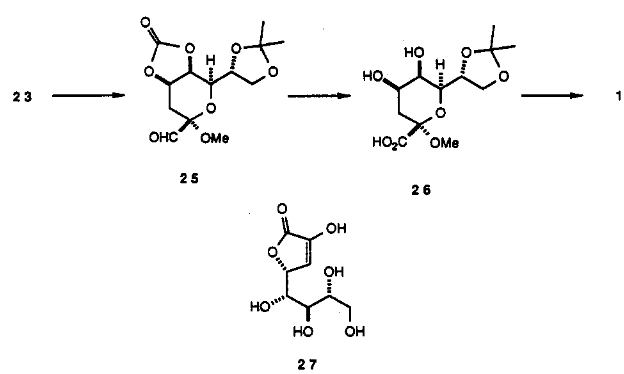
may be prepared in such circumstances by the iodonium ion induced cyclization of the corresponding primary allylic carbamates.[20] To evaluate the suitability of this tactic in the present situation, the primary urethane **19** was prepared in 95% yield from the alcohol **15** by the action of trichloroacetyl isocyanate.[21] Unfortunately, the electrophile-induced cyclization of **19** using $I(Collidine)_2ClO_4$[22] (3 equiv) under a variety of conditions proved to be extraordinarily sluggish. The optimized procedure provided the iodocarbonate **20** in only 31% yield together with considerable quantities of starting material (91% yield based upon recovered **19**). Although the action of *N*-iodosuccinimide on **19** provided **20** in slightly higher yield (35%), the remaining starting material was consumed by formation of an addition product that was tentatively identified as **21** based upon its ^1H NMR spectrum. Other electrophiles including I_2, PhSeBr, and PhSeOTf were even less suited to the task. The difficulty encountered in achieving the efficient transformation **19** → **20** underscores the need to invent improved tactics for inducing electrophilic cyclizations of allylic alcohol derivatives in sterically demanding situations.

It was our original intention to effect the simultaneous, reductive cleavage of the iodide function from C(3) and the benzyl protecting group from the C(1) hydroxyl at this stage. However, all attempts to achieve this seemingly simple objective by catalytic hydrogenation using palladium catalysts or Raney nickel were unsuccessful. One side product commonly encountered during these efforts was the allylic alcohol **15** arising from an unexpected β-elimination. It was then necessary to examine several stepwise alternatives, and an optimized solution to this vexing problem emerged after only some effort. Thus, removal of the iodide from **20** by free-radical reduction[23] ($HSn(n\text{-}Bu)_3$, AIBN, $PhCH_3$, reflux, 3 h) gave **22**, and subsequent hydrogenolysis of the *O*-benzyl group (H_2 (60 psi), Raney Ni, EtOH, 25 °C, 48 h) furnished the primary alcohol **23** in 79% overall yield from **20**. The relative stereochemical relationships in **22** were confirmed by single crystal X-ray analysis.[24] Noteworthy of the structure of **22** is that the cyclic carbonate bridging C(4) and C(5) appears to force the hydropyran ring into a boatlike conformation. Based upon the observed ^1H NMR coupling constants ($J_{3ax,4}$ = 3.5 Hz; $J_{3eq,4}$ = 3.9 Hz; $J_{4,5}$ = 8.4 Hz, $J_{5,6}$ =1.7 Hz; $J_{6,7}$ = 8.2 Hz), the conformation of **22** in solution is similar to that found in the solid state. Interestingly, during our first experiments to effect radical deiodination of **20**, variable amounts of the benzoate **24** and the alcohol **23** were formed. Although the origin of these compounds was not unequivocally established, it seems likely that the initially formed radical isomerized via hydrogen atom transfer through a six-membered transition state to generate a benzyl radical. This intermediate radical then either suffered homolysis to provide **23** or was quenched by adventitious oxygen to give **24**. We were unable to optimize these side reactions to return the desired alcohol **23**.

Elaboration of **23** into (+)-KDO (**1**) now required selective oxidation of the primary alcohol to a carboxyl group and deprotection of the various hydroxyl functions (Scheme IV). Numerous known methods for oxidizing primary alcohols directly to carboxylic acids using ruthenium- or chromium-based oxidants were evaluated for converting **23** to the corresponding carboxylic acid derivative, but none proved efficacious. Presumably, these techniques failed because of the neopentyl nature of the primary hydroxyl group at C(1). Nevertheless, a convenient stepwise procedure was devised that commenced with a Swern oxidation of **23** to afford **25**, which was then simply treated with silver(I) oxide in aqueous NaOH to effect simultaneous oxidation of the formyl group and hydrolysis of the carbonate moiety to furnish **26** in 80% overall yield from **23**. Examination of the ^1H NMR spectrum revealed that the hydropyran ring of **26**, which lacks the cyclic carbonate moiety at C(4)–C(5), existed preferentially in the chair conformation ($J_{3ax,4}$ = 12.8 Hz; $J_{3eq,4}$ = 5.1 Hz).

Scheme IV



It then remained to hydrolyze the methyl glycoside and the acetonide protecting group on **26** to complete the asymmetric synthesis of (+)-KDO (**1**). While this represents a superficially straightforward operation, cognizance of the known instability of **1** to strong acid and base was imperative to its successful execution.[25,26] Under mildly acidic conditions, **1** exhibits a strong propensity to form the ene lactone **27**, which can be opened by treatment with aqueous ammonia to give the ammonium salt of (+)-KDO.[27] Unfortunately, the methyl glycoside moiety of **26** was rather stable, and somewhat forcing acidic conditions that frequently led to considerable decomposition were required for its hydrolysis. After extensive experimentation, we discovered that hydrolysis of **26** under carefully defined conditions ((a) DOWEX 50W(H^+), H_2O, 80 °C, 1 h; (b) 5% NH_4OH, 0 °C, 24 h) followed by sequential chromatography on cellulose and Sephadex G-10 delivered the ammonium salt of (+)-KDO (**1**) in 44% yield. In control experiments, we determined that (+)-KDO and the derived ene lactone **27** were only modestly stable to these hydrolytic conditions and suffered approximately 50% degradation after only 2 h.

A facile total synthesis if (+)-KDO (**1**) has thus been completed in 12 steps from furan and isopropylidene-D-glyceraldehyde. The key stereochemistry at C(6) was established in the first step of the synthesis by the preparation of **5**, which was readily transformed in three operations into the optically active hydro-3-pyranone **12**. The subsequent conversion of **12** into **22** exploited conformational biases inherent in hydropyran rings, and the synthesis of **1** was then consumated by refunctionalization of **22**. This account of the preparation of **1** serves to further establish our general strategy for the asymmetric syntheses

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of highly oxygenated natural products via furans and hydro-3-pyranones derived therefrom, and further applications will be reported in due course.

Experimental Section

General. Unless otherwise noted, all starting materials were obtained from commercial suppliers and were used without further purification. Melting points were determined using a capillary melting point apparatus and are uncorrected. Ether, THF, and toluene were distilled from either sodium or potassium/benzophenone ketyl immediately prior to use, whereas triethylamine and DMSO were distilled from calcium hydride. Benzyl chloromethyl ether was purified by passing through a column of basic alumina gel immediately prior to use. All reactions involving oxygen- or water-sensitive reagents or intermediates were conducted under N_2 in oven-dried glassware cooled under a stream of nitrogen. Unless otherwise indicated IR spectra were determined in $CHCl_3$. The ^1H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ unless noted otherwise. Mass spectra are reported as a combination of high- and low-resolution data. Flash chromatography was performed on silica gel according to the Still protocol.[28]

[*R*-(*R,*R**)]-(2,2-Dimethyl-α-(2-furanyl)-1,3-dioxolan-4-yl)methyl *tert*-Butyldimethylsilyl Ether (5).** To a solution of furan (16.34 g, 240 mmol) in THF (240 mL) cooled to −78 °C was slowly added with stirring *n*-BuLi (92 mL, 2.6 N, 240 mmol). The solution was allowed to warm to 0 °C and stirred for 4 h, whereupon $ZnBr_2$ (54.0 g, 240 mmol) was slowly added. A solution of isopropylidene D-glyceraldehyde (31.20 g, 240 mmol)[29] in THF (50 mL) cooled to 0 °C was then added. The temperature was maintained at 0 °C for 8 h and then allowed to warm to rt. A solution of *tert*-butyldimethylsilyl chloride (36.1 g, 240 mmol) dissolved in THF (50 mL) was added and the resulting solution stirred for 8 h at rt. The reaction was quenched by the addition of saturated $NaHCO_3$ (ca. 100 mL), and the resulting mixture was extracted with ether (3 × 100 mL). The combined extracts were washed with water (2 × 100 mL), dried ($MgSO_4$), and concentrated under reduced pressure. Crude 5 was purified by flash chromatography (4:1 hexanes/EtOAc) and then distilled bp = 94 °C (0.1 mm) to provide 19.80 g (53%) of 5 as a clear colorless liquid: $[\alpha]^{23}_D$ = +41.4° (*c* = 1.0, $CHCl_3$); ^1H NMR (500 MHz) δ 7.35 (br s, 1 H), 6.31 (m, 1 H), 6.24 (d, *J* = 3.2 Hz, 1 H), 4.69 (d, *J* = 6.1 Hz, 1 H), 4.31 (dd, *J* = 6.2, 6.1 Hz, 1 H), 4.05 (m, 1 H), 1.41 (s, 3 H), 1.33 (s, 3 H), 0.86 (s, 9 H), 0.05 (s, 3 H), −0.12 (s, 3 H); ^{13}C NMR (125 MHz) δ 154.4, 141.9, 110.2, 109.4, 107.6, 77.9, 69.0, 66.2, 26.7, 25.7, 25.4, 18.1, −5.1, −5.1; mass spectrum *m/z* 312.1763 ($C_{16}H_{28}SiO_4$ requires 312.1757), 211, 197, 167, 101, 81, 73, 43.

[*R*-(*R,*R**)]-2,2-Dimethyl-α-[5-(carbethoxy)-2-furanyl]-1,3-dioxolane-4-methanol (6).** To a stirred solution of the silyl ether 5 (0.823 g, 2.64 mmol) in THF (10 mL) at −78 °C was added dropwise *t*-BuLi (18.8 mL, 30.0 mmol). Stirring was continued for an additional 4 h at 0 °C, whereupon ethyl chloroformate (0.543 g, 5.0 mmol) was added and the reaction allowed to warm to rt and stirred for 10 h. A solution of *n*-Bu_4NF (5 mL, 1 N in THF, 5 mmol) was added and stirring continued for 8 h, whereupon the solution was decanted into saturated $NaHCO_3$ (20 mL) and extracted with ether (3 × 20 mL). The combined ether extracts were washed with brine (2 × 10 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The crude 6 was purified by flash chromatography (3:2 hexanes/EtOAc) to provide 0.404 g (56%) of 6 as a yellow oil: $[\alpha]^{23}_D$ = +25.3° (*c* = 0.1, $CHCl_3$); ^1H NMR (300 MHz) δ 7.13 (d, *J* = 3.5 Hz, 1 H), 6.47 (d, *J* = 3.5 Hz, 1 H), 4.88 (d, *J* = 5.0 Hz, 1 H), 4.47 (m, 1 H), 4.35 (q, *J* = 7.1 Hz, 2 H), 4.06 (m, 2 H), 2.60 (br s, 1 H), 1.45 (s, 3 H), 1.37 (s, 3 H), 1.37 (t, *J* = 7.1 Hz, 3 H); ^{13}C NMR (75 MHz) δ 158.6, 158.0, 144.3, 118.5, 109.7, 109.2, 77.0, 68.0, 65.5, 60.8, 26.4, 25.0, 14.2; IR ν 3600, 1705, 1645 cm^{-1}; mass spectrum *m/z* 270.1108 ($C_{13}H_{18}O_6$ requires 270.1103), 254, 224, 212, 194, 169, 166, 149, 141, 123, 101.

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[*R*-(*R,*R**)]-2,2-Dimethyl-α-[5-[(phenylmethoxy)methyl]-2-furanyl]-1,3-dioxolane-4-methanol (9).** To a solution of silyl ether 5 (9.36 g, 30.0 mmol) in THF (30 mL) cooled to −78 °C was added dropwise with stirring *t*-BuLi (18.8 mL, 30.0 mmol), and stirring was continued for 4 h at 0 °C. A solution of benzyl chloromethyl ether (5.46 g, 35 mmol) dissolved in THF (35 mL) was added, and the reaction was stirred at rt for 10 h. *n*-Bu_4NF (30 mL, 1 N in aqueous THF, 30 mmol) was added, the solution was stirred for 8 h, then the reaction was quenched by addition to saturated $NaHCO_3$ (50 mL). The resulting mixture was extracted with ether (3 × 50 mL), and the combined extracts were washed with brine (2 × 20 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The crude product was purified by distillation, bp = 158 °C (0.1 mm) to provide 8.80 g (92%) of 9 as a yellow oil: $[\alpha]^{23}_D$ = +22.1° (*c* = 1.0, $CHCl_3$); ^1H NMR (500 MHz) δ 7.34 (br s, 5 H), 6.29 (s, 1 H), 4.82 (d, *J* = 5.1 Hz, 1 H), 4.54 (s, 2 H), 4.45 (s, 2 H), 4.38 (ddd, *J* = 6.6, 6.1, 5.1 Hz, 1 H), 4.09 (dd, *J* = 8.8, 6.1 Hz, 1 H), 4.02 (dd, *J* = 8.8, 6.6 Hz, 1 H), 2.43 (br s, 1 H), 1.45 (s, 3 H), 1.37 (s, 3 H); ^{13}C NMR (125 MHz) δ 153.3, 151.5, 137.7, 128.1, 127.5, 127.4, 109.3, 107.9, 76.3, 71.7, 67.6, 65.1, 63.7, 26.2, 24.9; IR ν 3400 cm^{-1}; mass spectrum *m/z* 318.1477 ($C_{18}H_{22}O_5$ requires 318.1467), 217, 142, 135, 109, 101, 91, 43.

[2*R*-[2α(*R),6β]]-2-(2,2-Dimethyl-1,3-dioxolan-4-yl)-6-hydroxy-6-[(phenylmethoxy)methyl]-2*H*-pyran-3(6*H*)-one (11).** A mixture of 9 (8.80 g, 27.7 mmol), vanadyl acetylacetone (0.01 g, 0.03 mmol), and *t*-BuOOH (10 mL of 3 N in trimethylpentane, 30 mmol) in CH_2Cl_2 (30 mL) was stirred 3 h at rt at which time a further portion (0.5 equiv) of *t*-BuOOH was added and stirring continued for 3 h. The solution was poured into saturated $NaHCO_3$ (25 mL), and the mixture was extracted with CH_2Cl_2 (3 × 25 mL). The combined organic extracts were washed with saturated brine (2 × 20 mL), decolorized by treatment with activated charcoal, dried ($MgSO_4$), filtered through Celite, and concentrated under reduced pressure. The residue was purified by flash chromatography (3:2, hexanes/ EtOAc) to provide 8.25 g (91%) of 11 as a mixture (4.5:1) of α/β anomers as a clear colorless coil: $[\alpha]^{23}_D$ = +31.0° (*c* = 1.0, $CHCl_3$); ^1H NMR (300 MHz) δ 7.35 (br s, 5 H), 6.82 (d, *J* = 10.2 Hz, 1 H), 6.10 (d, *J* = 10.2 Hz, 1 H), 4.85 (d, *J* = 3.5 Hz, 1 H), 4.74 (d, *J* = 12.0 Hz, 1 H), 4.66 (d, *J* = 12.0 Hz, 1 H), 4.64 (m, 1 H), 4.02 (dd, *J* = 8.8, 6.8 Hz, 1 H), 3.97 (dd, *J* = 8.8, 7.1 Hz, 1 H), 3.66 (d, *J* = 10.3 Hz, 1 H), 3.61 (d, *J* = 10.3 Hz, 1 H), 1.67 (br s, 1 H), 1.44 (s, 3 H), 1.39 (s, 3 H); ^{13}C NMR (75 MHz) δ 194.5, 145.9, 137.2, 128.2, 127.7, 127.6, 127.5, 109.4, 93.1, 74.4, 74.0, 73.6, 73.0, 64.2, 25.9, 25.3. IR ν 3410, 1700 cm^{-1}; mass spectrum *m/z* 334.1408 ($C_{18}H_{22}O_6$ requires 334.1416), 101, 91.

[2*R*-[2α(*R),6β]]-2-(2,2-Dimethyl-1,3-dioxolan-4-yl)-6-methoxy-6-[(phenylmethoxy)methyl]-2*H*-pyran-3(6*H*)-one (12).** A suspension containing the anomeric mixture of 11 (6.10 g, 18.3 mmol) obtained as above, iodomethane (10.0 g, 142 mmol), and Ag_2O (2.12 g, 9.15 mmol) was stirred for 12 h at rt with the exclusion of light. The mixture was passed through a pad of Celite and poured into saturated $NaHCO_3$ (50 mL), and the mixture was extracted with ether (3 × 20 mL). The combined organic extracts were washed with saturated brine (2 × 20 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by flash chromatography (4:1 hexanes/EtOAc) to provide 4.27 g (67%) of 12 as a clear colorless oil together with 0.95 g (15%) of the corresponding C(2) epimer. For 12: $[\alpha]^{23}_D$ = +82.6° (*c* = 1.0, $CHCl_3$); ^1H NMR (300 MHz) δ 7.34 (br s, 5 H), 7.04 (d, *J* = 10.3 Hz, 1 H), 6.06 (d, *J* = 10.3 Hz, 1 H), 4.71 (ddd, *J* = 7.2, 6.6, 3.5 Hz, 1 H), 4.61 (s, 2 H), 4.60 (d, *J* = 3.3 Hz, 1 H), 4.00 (dd, *J* = 8.8, 7.2 Hz, 1 H), 3.94 (dd, *J* = 8.8, 6.6 Hz, 1 H), 3.80 (d, *J* = 10.7 Hz, 1 H), 3.46 (d, *J* = 10.7 Hz, 1 H), 3.37 (s, 3 H), 1.42 (s, 3 H), 1.37 (s, 3 H); ^{13}C NMR (75 MHz) δ 194.0, 146.1, 137.5, 128.4, 127.9, 127.7, 127.0, 109.5, 95.8, 74.6, 73.7, 73.6, 69.9, 64.4, 50.0, 26.0, 25.4; IR ν 1685 cm^{-1}; mass spectrum *m/z* 333.1349 [$C_{18}H_{21}O_6$ ($M^+ - CH_3$) requires 333.1338], 258, 227, 169, 152, 137, 127, 101, 91, 43.

[2*R*-[2α(*R*),6β]]-2-(2,2-Dimethyl-1,3-dioxolan-4-yl)-6-methoxy-6-[(phenylmethoxy)methyl]-2,4-dihydro-5*H*-pyran-3(6*H*)-one (13). A solution of 12 (0.182 g, 0.523 mmol) in absolute ethanol (2 mL) containing Pd/C (5%, 0.01 g) was placed under a balloon of H_2 for 1 h. The mixture was filtered through Celite and the filtrate concentrated under reduced pressure. The residue was purified by flash chromatography (4:1 hexanes/EtOAc) to furnish 0.123 g (67%) of **13** as a clear colorless liquid: $[\alpha]^{23}_D = +120.8°$ (c = 0.07, $CHCl_3$); ^1H NMR (200 MHz) δ 7.34 (m, 5 H), 4.61 (s, 2 H), 4.53 (ddd, J = 6.8, 5.4, 3.5 Hz, 1 H), 4.26 (d, J = 3.5 Hz, 1 H), 3.96 (dd, J = 10.3, 6.8 Hz, 1 H), 3.67 (dd, J = 10.3, 5.4 Hz, 1 H), 3.43 (d, J = 10.4 Hz, 1 H), 3.37 (d, J = 10.4 Hz, 1 H), 2.45 (m, 2 H), 1.45 (m, 2 H), 1.39 (s, 3 H), 1.37 (s, 3 H); ^{13}C NMR (50 MHz) δ 208.8, 137.5, 130.0, 128.4, 127.6, 109.5, 98.8, 74.5, 74.4, 73.4, 69.2, 64.6, 49.0, 34.5, 30.7, 26.0, 25.4; IR (film) ν 1725 cm^{-1}; mass spectrum m/z 319.1539 [$C_{18}H_{23}O_5$ ($M^+ - OCH_3$) requires 319.1545], 261, 237, 229, 203, 171, 147, 123.

Hydride Reduction of Compound 12. To a solution of **12** (2.65 g, 7.62 mmol) in THF (10 mL) at −78 °C was added a solution of K-Selectride (7.7 mL, 1 N in THF, 7.7 mmol), and the mixture was stirred for 30 min and then allowed to warm to 0 °C. The reaction was quenched by the addition of saturated $NaHCO_3$ (20 mL), and the mixture was then extracted with ether/EtOAc (1:1, 3 × 20 mL). The combined organic extracts were washed with saturated brine (2 × 20 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The resulting mixture (9.8:1) of **15** and **16** was separated by flash chromatography (3:2 hexanes/EtOAc) to provide 2.34 g (88%) of **15** and 0.24 g (9%) of **16**, each as clear colorless oils.

For methyl 3,4-dideoxy-7,8-*O*-(1-methylethylidene)-1-*O*-(phenylmethyl)-α-D-*arabino*-oct-3-en-2-ulopyranoside (15): $[\alpha]^{23}_D = -68°$ (c = 2.0, $CHCl_3$); ^1H NMR (300 MHz) δ 7.34 (br s, 5 H), 6.36 (dd, J = 10.2, 6.1 Hz, 1 H), 5.89 (d, J = 10.2 Hz, 1 H), 4.58 (d, J = 12.1 Hz, 1 H), 4.53 (d, J = 12.1 Hz, 1 H), 4.32 (ddd, J = 8.1, 6.3, 5.0 Hz, 1 H), 4.17 (dd, J = 8.6, 6.3 Hz, 1 H), 4.01 (dd, J = 8.6, 5.0 Hz, 1 H), 3.96 (ddd, J = 9.8, 6.1, 1.8 Hz, 1 H), 3.78 (dd, J = 8.1, 1.8 Hz, 1 H), 3.50 (d, J = 9.7 Hz, 1 H), 3.47 (d, J = 9.7 Hz, 1 H), 3.29 (s, 3 H), 2.52 (d, J = 9.8 Hz, 1 H), 1.41 (s, 3 H), 1.37 (s, 3 H); ^{13}C NMR (75 MHz) δ 137.2, 130.8, 129.9, 128.4, 127.9, 127.8, 109.1, 96.7, 74.5, 73.9, 73.5, 71.3, 67.1, 60.6, 49.7, 26.7, 25.2; IR ν 3440 cm^{-1}; mass spectrum m/z 319.1553 [$C_{18}H_{23}O_5$ ($M^+ - CH_3O$) requires 319.1546], 303, 229, 220, 112, 111, 101, 91, 43.

For methyl 3,4-dideoxy-7,8-*O*-(1-methylethylidene)-1-*O*-(phenylmethyl)-α-D-*ribo*-oct-3-en-2-ulopyranoside (16): $[\alpha]^{23}_D = +65°$ (c = 2.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.33 (br s, 5 H), 5.94 (d, J = 10.5 Hz, 1 H), 5.93 (d, J = 10.5 Hz, 1 H), 4.59 (d, J = 12.3 Hz, 1 H), 4.54 (d, J = 12.3 Hz, 1 H), 4.22 (d, J = 8.7 Hz, 1 H), 4.17 (m, 2 H), 3.98 (m, 1 H), 3.60 (d, J = 10.4 Hz, 1 H), 3.58 (t, J = 8.3 Hz, 1 H), 3.28 (s, 3 H), 3.25 (d, J = 10.4 Hz, 1 H), 1.63 (br s, 1 H), 1.46 (s, 3 H), 1.38 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.0, 131.6, 128.4, 127.7, 127.4, 110.1, 96.4, 78.3, 73.7, 73.1, 71.3, 71.2, 67.9, 67.4, 49.8, 26.5, 25.2; IR ($CDCl_3$) ν 3480 cm^{-1}; HRMS m/z 319.1537 [$C_{18}H_{23}O_5$ ($M^+ - CH_3O$) requires 319.1546].

Methyl 3,4-Dideoxy-5-(*tert*-Butylcarboxy)-7,8-*O*-(1-methylethylidene)-1-*O*-(phenylmethyl)-α-D-*arabino*-oct-3-en-2-ulopyranoside (18). To a solution of **15** (0.413 g, 0.409 mmol) in Et_2O (10 mL) was added n-BuLi (0.14 mL of a 2.9 M solution in hexane, 0.41 mmol), and the solution was stirred at rt for 0.5 h. A solution of BOC-ON (1.0 mmol) in THF (10 mL) was then added, and stirring was continued for 4 h. The solution was decanted into saturated $NaHCO_3$ (20 mL) and the mixture extracted with ether (3 × 20 mL). The combined ether extracts were washed with saturated brine (2 × 10 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The crude carbonate was purified by flash chromatography (9:1 hexanes/EtOAc) to provide 0.167 g (99%) of **18** as a clear oil: $[\alpha]^{23}_D = -30.2°$ (c = 0.5, $CHCl_3$); ^1H NMR (300 MHz) δ 7.34 (m, 5 H), 6.25 (d, J = 10.1 Hz, 1 H), 6.15 (dd, J = 10.1, 5.3 Hz, 1 H), 4.93 (dd, J = 5.3, 2.5 Hz, 1 H), 4.61 (d, J = 8.1 Hz, 1 H), 4.54 (d, J = 8.1 Hz), 4.25 (q, J = 6.0 Hz, 1 H), 4.06 (m, 2 H), 3.97 (dd, J = 8.5, 5.6 Hz, 1 H), 3.71 (d, J = 10.5 Hz, 1 H), 3.33 (d, J = 10.5 Hz, 1 H), 3.28 (s, 3 H), 1.47 (s, 9 H), 1.40 (s, 3 H), 1.34 (s, 3 H); ^{13}C NMR (75 MHz) δ 153.1, 137.9, 132.8, 128.4, 127.9, 127.8, 124.1, 109.1, 96.2, 82.2, 74.0, 73.6, 71.1, 70.4, 66.9, 65.5, 49.2, 27.8, 26.7, 25.5; IR ν 1740 cm^{-1}; HRMS m/z 435.2027 [$C_{23}H_{31}O_8$ ($M^+ - CH_3$) requires 435.2019].

Methyl 3,4-Dideoxy-7,8-*O*-(1-methylethylidene)-1-*O*-(phenylmethyl)-α-D-*arabino*-oct-3-en-2-ulopyranoside, Carbamate (19). A solution of **15** (0.131 g, 0.375 mmol) and trichloroacetyl isocyanate (0.075 g, 0.40 mmol) in CH_2Cl_2 (10 mL) was stirred at 0 °C for 30 min and then at rt, whereupon a saturated solution of Na_2CO_3 in H_2O/MeOH (1:1) was added. After being stirred for 2 h, the mixture was poured into saturated $NaHCO_3$ (10 mL), and the mixture was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic extracts were washed with saturated brine (2 × 5 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by flash chromatography (1:1 hexanes/EtOAc) to provide 0.139 g (95%) of **19** as a clear colorless oil: $[\alpha]^{23}_D = -25.1°$ (c = 1.0, $CHCl_3$); ^1H NMR (300 MHz) δ 7.34 (br s, 5 H), 6.21 (d, J = 10.3 Hz, 1 H), 6.19 (d, J = 10.3 Hz, 1 H), 4.99 (dd, J = 4.1, 2.5 Hz, 1 H), 4.62 (d, J = 12.1, 1 H), 4.62 (br s, 2 H), 4.53 (d, J = 12.1 Hz, 1 H), 4.23 (dd, J = 8.8, 6.2 Hz, 1 H), 4.04 (m, 2 H), 3.71 (d, J = 10.5 Hz, 1 H), 3.34 (d, J = 10.5 Hz, 1 H), 3.30 (s, 3 H), 1.40 (s, 3 H), 1.34 (s, 3 H); ^{13}C NMR (75 MHz) δ 157.7, 156.2, 137.4, 131.9, 128.2, 127.6, 124.7, 108.9, 96.0, 73.6, 73.3, 70.6, 69.8, 63.2, 49.0, 26.5, 25.1. IR ν 3510, 3400, 1730 cm^{-1}; mass spectrum m/z 378.1540 [$C_{19}H_{24}NO_7$ ($M^+ - CH_3$) requires 378.1553], 303, 272, 229, 211, 153, 121, 112, 111, 101, 91, 43.

Methyl 3-Deoxy-3-iodo-7,8-*O*-(1-methylethylidene)-1-*O*-(phenylmethyl)-D-*glycero*-α-D-*galacto*-2-octulopyranoside, Cyclic Carbonate (20). A solution of **19** (0.410 g, 1.05 mmol) and iodonium collidine perchlorate (ICP)[22] (0.53 g, 1.1 mmol) in acetonitrile (10 mL) was stirred with exclusion of light for 24 h, whereupon a second equivalent if ICP was added; after an additional 24 h, a third equivalent of ICP was added. After another 24 h (72 h total), water (1 mL) was added and the solution stirred 10 h. The reaction mixture was poured into saturated $NaHCO_3$ (10 mL), and the mixture was extracted with ether (3 × 10 mL). The combined organic extracts were washed with a mixture (1:1) of saturated $Na_2S_2O_3$ and saturated $NaHCO_3$ (2 × 5 mL), saturated NH_4Cl (3 × 10 mL), saturated $CuSO_4$ (3 × 10 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by flash chromatography (3:2 hexanes/EtOAc) to provide 0.171 g (31%) of **20** as a clear colorless oil; starting carbamate **19** could be recovered (0.24 g, 60%) by subsequent elution of the column with hexanes/EtOAc (1:2): $[\alpha]^{23}_D = +43.7°$ (c = 2.0, $CHCl_3$); ^1H NMR (300 MHz) δ 7.34 (br s, 5 H), 5.19 (dd, J = 7.8, 6.6 Hz, 1 H), 4.72 (dd, J = 6.6, 2.4 Hz, 1 H), 4.62 (d, J = 12.0 Hz, 1 H), 4.54 (d, J = 12.0 Hz, 1 H), 4.45 (d, J = 7.8 Hz, 1 H), 4.38 (ddd, J = 8.5, 6.2, 4.5 Hz, 1 H), 4.17 (dd, J = 8.8, 6.2 Hz, 1 H), 3.96 (dd, J = 8.8, 4.5 Hz, 1 H), 3.92 (dd, J = 8.5, 2.4 Hz, 1 H), 3.78 (d, J = 10.2 Hz, 1 H), 3.64 (d, J = 10.2 Hz, 1 H), 3.27 (s, 3 H), 1.44 (s, 3 H), 1.37 (s, 3 H); ^{13}C NMR (75 MHz) δ 153.0, 137.0, 128.4, 127.9, 127.9, 109.7, 98.8, 80.0, 74.2, 73.7, 73.2, 70.2, 68.3, 66.7, 49.8, 26.8, 25.0, 24.5; IR ν 1815 cm^{-1}; mass spectrum m/z 520.0542 ($C_{20}H_{25}IO_8$ requires 520.0594), 505, 399, 287, 211, 105, 91, 43.

Methyl 3-Deoxy-7,8-*O*-(1-methylethylidene)-1-*O*-(phenylmethyl)-α-D-*manno*-2-octulopyranoside, Cyclic Carbonate (22). A solution of iodide **20** (0.201 g, 0.386 mmol), tributyltin hydride (0.22 g, 0.77 mmol), and AIBN (0.001 g) in toluene (4 mL) was heated under reflux for 3 h, whereupon the toluene was removed under reduced pressure. Hexanes (10 mL) were added to the residue, and this mixture extracted with acetonitrile (3 × 10 mL). The combined acetonitrile extracts were washed with hexanes (2 × 10 mL) and concentrated under reduced pressure. The residue was purified by flash chromatography (3:1 hexanes/EtOAc) to provide 0.120 g (79%) of **22** as a crystalline solid: mp = 92–93 °C (from hexane); $[\alpha]^{23}_D = +13.8°$ (c = 0.6, $CHCl_3$); ^1H NMR (300 MHz) δ 7.34 (br s, 5 H), 5.01 (ddd, J = 8.4, 3.9, 3.5 Hz, 1 H), 4.83 (dd, J = 8.4, 1.7 Hz, 1 H), 4.65 (d, J = 12.0 Hz, 1 H), 4.58 (d, J = 12.0 Hz, 1 H), 4.24 (ddd, J = 8.2, 6.1, 4.8 Hz, 1 H), 4.11 (dd, J = 8.5, 6.1 Hz, 1 H), 3.85 (dd, J = 8.5, 4.8 Hz, 1 H), 3.71 (dd, J = 8.2, 1.7 Hz, 1 H), 3.62 (d, J = 10.5 Hz, 1 H), 3.32 (d, J = 10.5 Hz, 1 H), 3.12 (s, 1 H), 2.65 (dd, J = 16.0, 3.9 Hz, 1 H), 1.83 (dd, J = 16.0, 3.5 Hz, 1 H), 1.41 (s, 3 H), 1.35 (s, 3 H); ^{13}C NMR (75 MHz) δ 153.9, 137.2, 128.4, 127.9, 109.6, 98.5, 73.5, 73.3, 72.7, 72.2, 69.4, 69.0, 67.0, 48.3, 30.9, 26.7, 24.9; IR ν 1815 cm^{-1}; mass spectrum m/z 379.1385 [$C_{19}H_{23}O_8$ ($M^+ - CH_3$) requires 379.1373], 274, 273, 215, 171, 153, 111, 101, 91, 43. Anal. Calcd for $C_{20}H_{26}O_8$: C, 60.90; H, 6.64. Found: C, 60.76; H, 6.60.

Methyl 3-Deoxy-7,8-*O*-(1-methylethylidene)-α-D-*manno*-2-octulopyranoside, Cyclic Carbonate (23). A solution of **22** (0.120 g, 305 mmol) in absolute ethanol (2 mL) containing freshly prepared W-2 Raney nickel (ca. 0.1 g) was shaken under an atmosphere of H_2 (65 psi) in a Parr hydrogenator apparatus for 48 h. The catalyst was removed by suction filtration and the filtrate concentrated under reduced pressure. The residue was purified by flash chromatography (1:3 hexanes/EtOAc) to provide 0.091 g (99%) of **23** as a clear colorless oil: $[\alpha]^{23}{}_D = 25.5°$ (c = 1.0, $CHCl_3$); ^1H NMR (300 MHz) δ 5.05 (ddd, J = 8.5, 3.9, 3.3 Hz, 1 H), 4.86 (dd, J = 8.5, 1.7 Hz, 1 H), 4.29 (ddd, J = 8.1, 6.3, 4.8 Hz, 1 H), 4.16 (dd, J = 8.6, 6.3 Hz, 1 H), 3.90 (dd, J = 8.6, 4.8 Hz, 1 H), 3.79 (d, J = 11.8 Hz, 1 H), 3.73 (J = 8.1, 1.7 Hz, 1 H), 3.52 (d, J = 11.8 Hz, 1 H), 3.29 (s, 3 H), 2.62 (dd, J = 16.0, 3.9 Hz, 1 H), 1.80 (br s, 1 H), 1.78 (dd, J = 16.0, 3.3 Hz, 1 H), 1.42 (s, 3 H), 1.36 (s, 3 H); ^{13}C NMR (75 MHz) δ 154.0, 109.7, 99.1, 73.3, 72.9, 72.3, 68.7, 67.5, 48.5, 30.4, 26.7, 25.0; IR ν 1805 cm^{-1}; mass spectrum m/z 304.1165 ($C_{13}H_{20}O_8$ requires 304.1158), 289, 273, 257, 153, 11, 101, 95, 43.

Methyl 3-Deoxy-7,8-*O*-(1-methylethylidene)-α-D-*manno*-octos-2-ulo-2,6-pyranoside, Cyclic Carbonate (25). To a solution of DMSO (0.086 g, 1.1 mmol) in CH_2Cl_2 (4 mL) at -78 °C was added oxalyl chloride (0.070 g, 0.55 mmol). The solution was stirred for 15 min, and alcohol **23** (0.0834 g, 0.274 mmol) dissolved in CH_2Cl_2 (5 mL) was added dropwise. After 15 min at -78 °C, triethylamine (0.17 g, 2.2 mmol) was added, and the solution was stirred for 0.5 h while warming to rt. The reaction mixture was poured into saturated $NaHCO_3$ (5 mL), and the mixture was extracted with ether (3 × 10 mL). The combined organic extracts were washed with saturated $NaHCO_3$ (5 mL), dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by flash chromatography (3:2 hexanes/EtOAc) to furnish 0.067 g (80%) of **25** as a clear colorless oil; $[\alpha]^{23}{}_D$ +40.3° (c = 1.0, $CHCl_3$); ^1H NMR (300 MHz) δ 9.48 (s, 1 H), 5.04 (ddd, J = 8.5, 3.6, 2.9 Hz, 1 H), 4.91 (dd, J = 8.5, 1.7 Hz, 1 H), 4.41 (ddd, J = 8.1, 6.2, 4.6 Hz, 1 H), 4.23 (dd, J = 8.6, 6.2 Hz, 1 H), 3.98 (dd, J = 8.6, 4.6 Hz, 1 H), 3.82 (dd, J = 8.1, 1.7 Hz, 1 H), 3.32 (s, 3 H), 2.60 (dd, J = 16.2, 3.6 Hz, 1 H), 1.95 (dd, J = 16.2, 2.9 Hz, 1 H), 1.45 (s, 3 H), 1.39 (s, 3 H); ^{13}C NMR (75 MHz) δ 197.4, 153.3, 109.9, 98.6, 72.8, 72.5, 71.2, 70.5, 67.0, 51.1, 30.9, 26.8, 24.9; IR ν 1805 cm^{-1}; mass spectrum m/z 287.0759 [$C_{12}H_{15}O_8$ ($M^+ - CH_3$) requires 287.0767], 273, 111, 101, 95, 43.

Methyl 3-Deoxy-7,8-*O*-(1-methylethylidene)-α-D-*manno*-octos-2-ulo-2,6-pyranosonic Acid (26). A mixture of **25** (0.014 g, 0.045 mmol) and Ag_2O (0.011 g, 0.045 mmol) in 2 N NaOH (0.11 mL) and 50% aqueous EtOH (0.4 mL) was stirred for 24 h at rt with the exclusion of light. The solids were removed by filtration through a pad of Celite, and the filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography on purified cellulose (1:1 $CHCl_3$/MeOH) to deliver 0.13 g (96%) of **26** as a white solid: $[\alpha]^{23}{}_D$ = +43.4° (c = 0.3, H_2O); ^1H NMR (300 MHz, D_2O) δ 4.41 (m, 1 H), 4.24 (dd, J = 9.0, 6.1 Hz, 1 H), 4.08 (dd, J = 9.0, 4.6 Hz, 1 H), 4.02 (m, 1 H), 3.91 (d, J = 2.2 Hz, 1 H), 3.56 (d, J = 8.2 Hz, 1 H), 3.15 (s, 3 H), 2.00 (dd, J = 13.4, 5.1 Hz, 1 H), 1.76 (dd, J = 13.4, 12.8 Hz, 1 H), 1.44 (s, 3 H), 1.39 (s, 3 H); ^{13}C NMR (75 MHz, D_2O) δ 175.3, 109.6, 100.7, 73.4, 72.7, 67.4, 66.5, 65.4, 50.5, 34.8, 25.7, 24.2; IR (film) ν 1690 cm^{-1}; mass spectrum 277.0929 [$C_{11}H_{17}O_8$ ($M^+ - CH_3$) requires 277.0923], 262, 201, 44.

3-Deoxy-α-D-*manno*-2-octulopyranosonic Acid, Ammonium Salt [(+)-KDO] (1). The pH of a solution of **26** (0.139 g, 0.52 mmol) in water (2 mL) was adjusted to <2 with Dowex 50 W (H^+), and the mixture was heated with stirring at 80–85 °C for 1.5 h. The pH was adjusted to 10 with NH_4OH (5%) and the solution stored at 0 °C for 24 h. The pH of the solution was then adjusted to 7 with Dowex 50 W (H^+), and the water was removed by lyophilization. The crude (+)-KDO was then purified by sequential chromatography on cellulose (MeOH/$CHCl_3$/H_2O (10:10:1)) followed by passage of the resulting solution through Sephadex G-10. The combined filtrates were concentrated in vacuo to afford 0.059 g (44%) of the ammonium salt of **1** as a white solid that was identical (mp, mixed mp, ^1H and ^{13}C NMR, $[\alpha]_D$, and TLC) with a commerical sample purchased from Sigma Chemical Co: mp = 121.5–123 °C (lit.[25] mp = 121.5–123 °C); $[\alpha]^{23}{}_D$ = +42.4° [c = 1.7, H_2O (lit.[25] $[\alpha]^{23}{}_D$ = +41.5°, c = 1.7, H_2O)]; ^1H NMR (500 MHz, D_2O) δ 4.5 (m, 0.5 H), 4.3 (m, 0.2 H), 4.1–3.9 (m, 1.3 H), 3.8–3.6 (m, 2.1 H), 3.7–3.5 (m, 1.9 H), 2.6 (m, 0.3 H), 2.1 (m, 0.3 H), 2.0–1.8 (m, 1.4 H); ^{13}C NMR (125 MHz, D_2O) δ 177.5, 176.9, 176.7, 175.4, 104.2, 103.0, 97.3, 96.4, 85.5, 85.0, 73.5, 72.5, 71.5, 71.4, 71.1, 70.9, 70.7, 69.7, 69.3, 69.2, 69.0, 67.6, 67.4, 66.5, 66.5, 66.3, 66.3, 66.2, 65.7, 65.3, 63.8, 63.1, 62.9, 62.8, 44.6, 43.5, 35.0, 33.7, 33.6.

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Supplementary Material Available: ^1H and/or ^{13}C NMR spectra for all new compounds described in the Experimental Section for which there is no combustion analysis (26 pages). Ordering information is given on any current masthead page.

Total Synthesis of (−)-Colletol

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The first total synthesis of the unsymmetrical bis-macrolide (−)-colletol is described. The synthesis involves a Lewis acid mediated addition of triphenylallylstannane to aldehyde 14 to set the C_{12} stereochemistry. The penultimate step utilized macrolactonization to assemble the 14-membered ring. The natural product was prepared in 12 linear steps and 12% overall yield.

Colletol (1) was first isolated from the fermentation broth of *Colletotrichum capsici* in 1973 along with three other related metabolites, colletodiol (2), colletoketol (3) and colletallol (4).[1] Although no biological activity was

