NMR (90 MHz) δ 5.1-4.6 (m, 4 H), 4.02 (s, 3 H), 3.83, 3.72 (2 s, 3 H), 3.54 (m, 1 H), 3.43 (s, 3 H), 2.91-2.48 (m, 2 H), 1.49 (d, 3 H); IR ($CHCl_3$) 1810, 1760 cm^{-1}; MS, *m/e* 411 (4%, M^+), 396 (35%), 380 (10%), 336 (10%), 120 (100%); HRMS calcd for $C_{14}H_{22}NPO_{11}$ 411.0930, found 411.0942.

Acetolysis of Phosphorylaziridine 27. Preparation of Racemic Triacetate 5. A solution of the dicarbonate aziridine **27** (41 mg, 0.1 mmol) in acetic acid (1 mL) was heated at 50 °C for 12 h then 90 °C for an additional 4 h, cooled, and evaporated. The residue presumed to contain compound **28** (vide infra) was dissolved in MeOH (2 mL), K_2CO_3 (100 mg) was added, and the mixture was heated to 60 °C for 12 h, cooled, and evaporated. The residue, presumed to contain (±)-**4**, was suspended in pyridine (1 mL), and acetic anhydride (1 mL) was added; then the mixture was stirred for 12 h at 25 °C, evaporated, and partitioned between EtOAc (20 mL) and 1 N HCl solution (5 mL). The layers were separated, the aqueous layer was back extracted with EtOAc (10 mL), and the organic layers were combined, washed with saturated $NaHCO_3$ solution (2 mL) and brine, dried (Na_2SO_4), filtered, and evaporated. The residue was chromatographed (100% EtOAc) to give the fully synthetic pentaacetate **15** (20 mg, 45%): mp 243-245 °C (EtOAc/hexane); ^1H NMR (500 MHz) δ 5.56 (d, *J* = 10 Hz, 1 H), 5.37 (d, *J* = 3 Hz, 1 H), 5.22 (dd, *J* = 8.5, 10 Hz, 1 H), 5.10 (dq, *J* = 3, 7 Hz, 1 H), 4.98 (dd, *J* = 3, 10 Hz, 1 H), 4.57 (d"t", *J* = 3, 10 Hz, 1 H), 4.37 (d, *J* = 8 Hz, 1 H), 3.65 d, *J* = 9.5 Hz, 1 H), 3.53 (s, 3 H), 2.15, 2.08, 2.07, 1.98, 1.93 (5 s, 5 × 3 H), 1.33 (d, *J* = 7 Hz, 3 H); IR ($CHCl_3$) 3400, 2950, 1740, 1710 sh, 1680, 1360, 1240, 1060 cm^{-1}. Anal. Calcd for $C_{19}H_{29}NO_{11}$: C, 51.00; H, 6.53; N, 3.13. Found: C, 51.28; H, 6.66; N, 2.97. HRMS calcd for $M^+ - CH_3CO_2(CH_3)CH\cdot$ 360.1294, found 360.1293.

Flash chromatography (2.5% MeOH/$CHCl_3$) of the crude product from the acetic acid solvolysis above gave the phosphoramide **28** as the major mobile component: ^1H NMR (500 MHz) δ 5.27 (qd, *J* = 7, 3.5 Hz, 1 H), 5.13 (dd, *J* = 8, 1 Hz, 1 H), 4.89 ("t", *J* = 3.5 Hz, 1 H), 4.82 (dd, *J* = 8, 3.5 Hz, 1 H), 4.77 (d, *J* = 3.5 Hz, 1 H), 3.87 (s, 3 H), 3.77 (d, *J* = 15 Hz, 6 H), 2.09 (s, 3 H), 1.32 (d, *J* = 7 Hz, 3 H); IR ($CHCl_3$) 1810, 1755, 1735 cm^{-1}.

Conversion of Methyl Thiolincosaminide Pentaacetate (2) to Authentic D-Triacetate (+)-5. To a cold (0 °C) solution of pentacetyl MTL (230 mg, 0.50 mmol) in MeOH (3 mL) was added *N*-bromosuccinimide (90 mg, 0.50 mmol) in MeOH (2 mL) dropwise. After 1 h, the mixture was concentrated and the residue chromatographed to give the β-methyl glycoside **5** (105 mg, 47%): mp 255-257 °C (EtOAC/hexane); $[\alpha]^{20}_D$ +41° (c 1.03, $CHCl_3$); ^1H NMR (500 MHz) δ 5.61 (br d, *J* = 9 Hz, 1 H), 5.37 (d, *J* = 3 Hz, 1 H), 5.22 (dd, *J* = 8.5, 10 Hz, 1 H), 5.10 (dq, *J* = 3, 7.5 Hz, 1 H), 4.98 (dd, *J* = 3, 10 Hz, 1 H), 4.57 (d"t", *J* = 3, 9 Hz, 1 H), 4.37 (d, *J* = 8 Hz, 1 H), 3.65 (d, *J* = 9 Hz, 1 H), 3.53 (s, 3 H), 2.15, 2.08, 2.06, 1.99, 1.93 (5s, 5 × 3 H), 1.33 (d, *J* = 7.5 Hz, 3 H); IR ($CHCl_3$) 3410, 3350, 2950, 1740, 1675, 1360, 1240, 1060 cm^{-1}. Anal. Calcd for $C_{19}H_{29}NO_{11}$: C, 51.00; H, 6.53; N, 3.13. Found: C, 50.99; H, 6.55; N, 3.10. HRMS calcd for $M^+ - CH_3CO_2(CH_3)CH\cdot$ 360.1294, found 360.1307.

Acknowledgment. This work was supported by PHS Grant AI 16943. An Americal Cancer Society Postdoctoral Fellowship (PF2020) to Eric R. Larson is gratefully acknowledged. We thank Clarence Maring for helpful discussions regarding the chemistry of the trioxygenated dienes **7**. NMR spectra were obtained through the auspices of the Northeast Regional NSF/NMR Facility at Yale University, which was supported by NSF Chemistry Division Grant CHE 7916210.

Registry No. (±)-**2**, 13038-00-1; **4**, 87462-03-1; (±)-**4**, 92077-23-1; **5**, 87462-04-2; (±)-**5**, 92077-21-9; (*Z,E*)-**7**, 92054-25-6; (*E,E*)-**7**, 92011-04-6; **8**, 87461-95-8; **9**, 87461-96-9; **10a**, 92011-05-7; **10b**, 87461-97-0; **15**, 87461-98-1; **16**, 92011-06-8; **17**, 87461-99-2; **19**, 87462-00-8; **20**, 92011-11-5; **21**, 92011-07-9; **22**, 92011-08-0; **23**, 92011-09-1; **24**, 87462-01-9; **25**, 92054-26-7; **26**, 92011-12-6; **27**, 87462-02-0; **28**, 92011-10-4; lincosamine, 92077-22-0; (*E*)-1-methoxy-4-(benzyloxy)but-1-en-3-one, 92011-03-5; 2-butenal, 4170-30-3; boron trifluoride etherate, 109-63-7; trimethyl phosphite, 121-45-9.

Supplementary Material Available: Table I (fractional coordinates and temperature factors), Table II (bond distances in angstroms), Table III (bond angles in degrees), and ORTEP drawing for **16** and crystal data for (7 pages). Ordering information is given on any current masthead page.

Total Synthesis of (±)-3-Deoxy-D-*manno*-2-octulopyranosate (KDO)

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Contribution from the Department of Chemistry, Yale University, New Haven, Connecticut 06511. *Received May 29, 1984*

Abstract: Cyclocondensation of 2-(phenylseleno)propionaldehyde with 1-(α-furyl)-1-methoxy-3-[(trimethylsilyl)oxy]-4-(benzoyloxy)-1,3-butadiene under the influence of boron trifluoride produces a predominance (2.4:1) of *cis-/trans*-3-(benzoyloxy)-6-(α-furyl)-2-[(1-phenylseleno)ethyl]-2,3-dihydro-4*H*-pyran-4-one (**13**). This is converted to (±)-3-deoxy-D-*manno*-2-octulopyranosonate ((±)-KDO) in nine steps.

Unique polysaccharides have been uncovered during studies of the biochemistry of microorganisms. These polysaccharides are characteristic of the classification of the microbe.[1,2] For instance, the teichoic acids (polymers of glycerol or ribotol phosphate) are isolated from the cell walls and membranes of Gram-positive bacteria. While the analogy is far from exact, the lipopolysaccharides (LPS), also known as endotoxins, play a similar role in Gram-negative bacteria. The external section is responsible for the antigenic specificity of the LPS. The interior carbohydrate section, known as the core region, is comprised of galactose, glucose, glucosamine, *N*-acetylglucosamine, and L-glycero-D-*manno*-heptose residues. The lipid section, known as lipid A, is joined to the core region through ketosidic bonds to an eight-carbon sugar residue which has been identified as 3-deoxy-D-*manno*-2-octulopyranosate (KDO).[3,4] The KDO "section" of LPS ap-

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(1) Sharon, N. "Complex Carbohydrates; Their Chemistry, Biosynthesis and Functions"; Addison-Wesley: Reading, MA 1975.

(2) Kennedy, J. F.; White C. A. "Bioactive Carbohydrates: In Chemistry, Biochemistry and Biology"; Ellis Horward Limited: West Sussex, England (distributed by Wiley: New York), 1983.

(3) Unger, F. M. *Adv. Carbohydr. Chem. Biochem.* **1981**, *38*, 323-388.

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0002-7863/85/1507-1280$01.50/0

parently involves a network of three such monomers joined to one another and to the core and lipid A sections.[4] Thusfar, it seems that KDO is unique to Gram-negative bacteria and, conversely, all Gram-negative bacteria contain KDO.

Following the identification of this important and unique function of KDO and the determination of its structure, several partial syntheses from simpler sugars were accomplished.[3,5] The basic strategy involved coupling of a suitable arabinose derivative with either a pyruvate or an oxaloacetate to complete the octose chain.

Of course, there is a great deal of interest in finding compounds that would inhibit the biosynthesis of LPS.[3,6] Success along these lines could allow for the development of a new strategy for antibiotic therapy against Gram-negative microbes. Since KDO plays such a central structural role in cementing the crucial sections of LPS, it has been argued that inhibition of the biosynthesis or metabolism of KDO could accomplish the desirable goal of discouraging the buildup of LPS.

One of the concerns of our laboratory involves the total synthesis of the higher saccharides from noncarbohydrate sources. Such structures fall within the scope of chemistry involving the cyclocondensation of oxygenated dienes with aldehydes.[7a,b] The advantages of total synthesis in the KDO area are obvious. In principle, a much greater degree of structural and stereochemical latitude in analogue synthesis in the search for LPS inhibitors is possible through a de novo capability. The only disadvantage of our approach, i.e., that racemic rather than optically active materials are being produced, is one that we view as a temporary inconvenience while a parallel quest for chiral induction in the cyclocondensation reaction goes forward on several fronts.[8] This paper describes the first total synthesis of (±)-KDO.

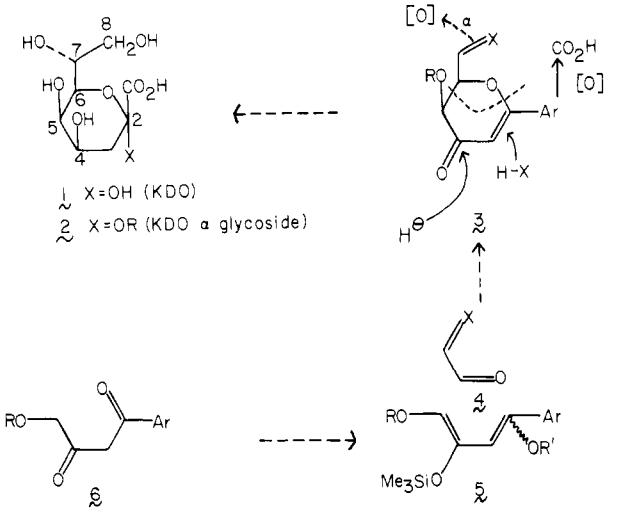
Synthetic Plan

The overall plan is summarized below wherein a diene **5** bearing an aryl group and an alkoxy group at its 1-position is to condense with aldehyde **4**. The dihydropyrone **3**, anticipated from such a now-familiar process, would provide a framework for the installation of oxygen functions at carbons 2, 4, 5, 7, and 8 in the required relative configurations. Coordinated with these operations, in a fashion whose optimal sequence remained to be established, would be the oxidative transformation of the aryl function to a carboxylic acid.

An important feature of this plan would lie in its provision for the alcoholysis of the enol ether of compound **3**. Such a process would lead directly to the potentially important KDO glycosides. While glycosylations by suitably protected and activated "intact" KDO substrates have been reported, such processes are by no means simple.[9,10] The possibility of generating KDO glycosides of the type **2** by alcoholysis of a "glycal-like" double bond, to be derived from **3**, presented itself.

Thus, the aryl group at the 1-position of diene **5** would serve several functions. First, it should help to confer nucleophilic character on the diene for the cyclocondensation reaction. Second, it should foster alcoholysis of the double bond of **3** or a derivative thereof. Finally, it should be amenable to smooth oxidative conversion to a carboxylic acid.

It was assumed that the hydroxyl groups at C_7 and C_8 could be introduced by oxidation of a vinyl group (X in structure **3** = CH_2). Our experiences in the lincosamine series[7b] suggested that

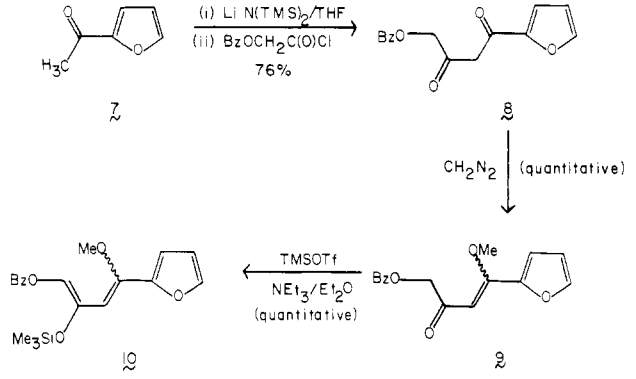


the required 7*R* stereochemistry[12] would be available through such a route. However, the prospect of starting with acrolein (**11**) was abandoned when this aldehyde did not perform well in the cyclocondensation reaction with dienes related to the projected **5**. Accordingly, α-(phenylseleno)propionaldehyde (**12**) was chosen an acrolein equivalent. A corollary advantage in the use of **12** was that the unsaturation in the pyran ring and on the side chain could be generated in sequence, rather than in tandem, thus allowing for greater latitude in the functionalization reactions.

Discussion of Results

On the basis of the considerations detailed above, diene **10** emerged as a possibility to fill the role hypothesized for the generalized system **5**. It was hoped, without the benefit of any particularly convincing analogies,[13] that the unsymmetrical β-diketone **8** would function as an effective precursor toward diene **10**.

Acylation of the enolate obtained from the action of lithium hexamethyldisilazide on 2-acetylfuran with (benzoyloxy)acetyl chloride afforded a 76% yield of **8**, mp 81.5–82.5 °C. Indeed, it was found that reaction of **8** with diazomethane in ether afforded a quantitative yield of enol ether **9** as a mixture of *E*,*Z* isomers. Enol silylation of **9** according to Simchen[14] gave a quantitative yield of **10**. That the enol ethers and the dienes are accurately



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(8) Bednarski, M.; Danishefsky, S. *J. Am. Chem. Soc.* **1983**, *105*, 6968. Bednarski, M.; Maring, C.; Danishefsky, S. *Tetrahedron Lett.* **1983**, *24*, 3451.

(9) See ref 3, pp 373–378.

(10) Waldstätten, P.; Christian, R.; Schulz, G.; Unger, F. M. in ref 4, Chapter 6, pp 121–140.

(11) For the preparation of 2,3-unsaturated derivatives of KDO, see ref 9 and Claesson et al.: Claesson, A.; Luthman, K. *Acta Chem. Scand. Ser. B* **1982**, *36*, 719. The utility of these carboxy-substituted "glycals" for the introduction of alcohols was not addressed.

(12) Although the present work involves racemic materials, one enantiomer is drawn for convenience. The 7*R* stereochemistry refers to the enantiomer shown (D-sugar). The ORTEP drawing of compound **18** is shown as the L-antipode (7*S*).

(13) For example, see: Gompper, R.; Vogt, H.-H. *Chem. Ber.* **1981**, *114*, 2866.

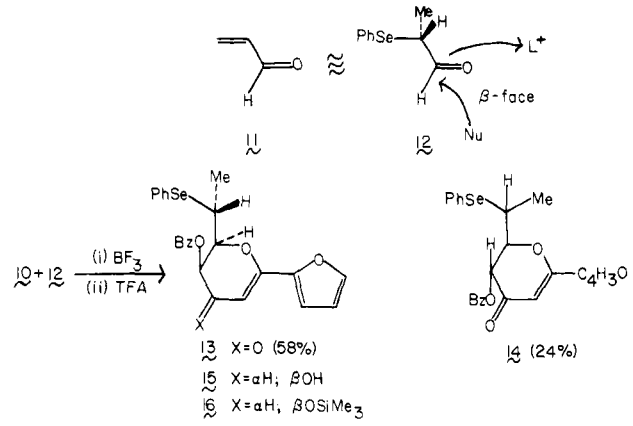
represented by structures **9** and **10** was only established by future events (vide infra).[15]

The reaction of phenylseleno aldehyde **12** with diene **10** was carried out in ether at −78 °C under BF_3 catalysis. Treatment of the product thus obtained with trifluoroacetic acid (TFA) afforded a 58% isolated yield of the crystalline cis dihydropyone derivative **13**, mp 107–108.5 °C. Unfortunately, this process also gave rise to a 24% yield of the easily separable trans isomer **14**. This 2.4:1 ratio of cis/trans dihydropyrones is regrettably lower than that obtained from the reaction of various aldehydes with the "parent" 1-(benzoyloxy)-2-[(trimethylsilyl)oxy]-4-methoxy-1,3-butadiene.[7b] However, in terms of overall synthetic conciseness, a workable route to an advanced intermediate of the type **3** had been achieved in a straightforward fashion.

In this connection, it is important to emphasize the facial specificity in the cyclocondensations of the α-phenylseleno aldehyde **12**. While the relative relationship of side chain and ring asymmetries is not known at this stage, the production of a single facial isomer was most helpful in a practical sense. The erythro stereochemistry which is in fact shown for compounds **13**, **15**, and **16**, anticipates the findings for compound **18**. The diastereofacial sense of the cyclocondensation reaction can be rationalized in terms of conformer **12** with the phenylseleno function "anti" to the carbonyl group. Nucleophilic attack occurs syn to the hydrogen.[16] Alternatively the result can be rationalized utilizing an orthogonal PhSeCC=O conformer.[17] While we cannot distinguish between these formulations, we note that very high selectivity has already been encountered in several instances in the Lewis acid catalyzed cyclocondensation chemistry.[18] Presumably, the minor trans compound **14** is also in the erythro series though we have no experimental evidence that bears on this matter.

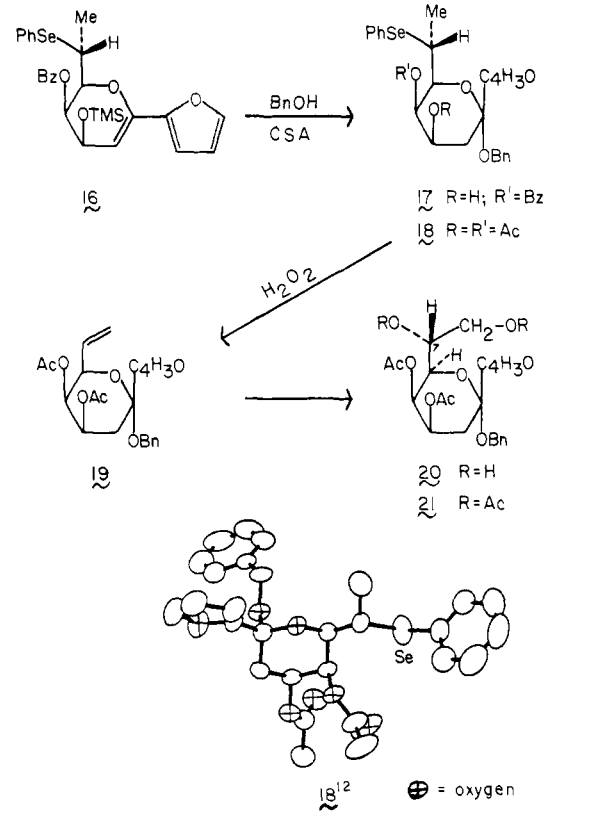
Reduction of the pyrone with sodium borohydride in the presence of ceric chloride according to Luche[19] provided the glycal **15**, which was protected as its trimethylsilyl ether **16**, in 92% overall yield.

Reaction of **16** with benzyl alcohol in the presence of camphorsulfonic acid (CSA) produced a single glycoside **17** in which the silyl ether group had been removed.[20] The benzoyl group was cleaved (K_2CO_3) to afford a diol which on acetylation (DMAP/Ac_2O) gave rise to a diacetate, mp 94–95 °C, in 69% overall yield from **16**. *Presumably, the vinylogous ketene-acetal-like character conferred on the double bond by the α-furyl residue rendered the olefin particularly susceptible to acid-catalyzed alcoholysis.* We theorized on the basis of the chemical shift of the C_4 proton (see Experimental Section) that the benzyl glycoside is in fact α.[21] This result would arise from axial addition of the benzyl alcohol to the cationoid center at C_2 (KDO numbering). An X-ray crystallographic determination of the diacetate served to verify this assignment. At the same time, it revealed the configuration at C_7 to be "*R*". An ORTEP drawing[12,22] of this structure is provided.



In addition to providing rigorous answers to all of the configurational questions at issue, the crystallographic data provide some fascinating insights into the conformation of this novel type of glycoside. The angle of the Se–C–C–O bonds is 179.8°. Similarly, the pyransidic oxygen is essentially trans periplanar to the furyl oxygen of the C-glycoside (O–C–C–O angle = 175.9°). These antiperiplanar arrangements could well arise from their ability to minimize dipole–dipole repulsions of the electron-withdrawing heteroatoms. This conformational tendency might also be applicable to aldehyde **12** as it undergoes bonding to the Lewis acid. A high conformational specificity would be required to account for the remarkably high diastereofacial specificity exhibited by compound **12** in these reactions.

Oxidative deselenation of **18** with aqueous hydrogen peroxide gave rise to the side chain vinyl compound **19**, mp 103.5–104 °C, in 96% yield. The latter underwent smooth hydroxylation through



(14) Emde, H.; Domsch, D.; Feger, H.; Frick, U.; Götz, A.; Hergott, H. H.; Hofmann, K.; Kober, W.; Krägeloh, K.; Oesterle, J.; Steppan, W.; West, W.; Simchen, G. *Synthesis* **1982**, 1.

(15) Model studies with 1-(α-furyl)-1,3-butanedione showed that normal conditions for methylation of β-dicarbonyl compounds (MeOH/$(MeO)_3CH$/*p*-TsOH or K_2CO_3/Me_2SO_4) provided only 3-methoxy-1-(α-furyl)-2-buten-1-one as a single isomer. Evidence for this regioisomer was gained by conversion to 1-(α-furyl)-3-methoxy-1-[(trimethylsilyl)oxy]-1,3-butadiene, which failed to undergo cyclocondensation with aldehydes under a variety of Lewis acid-catalyzed conditions and failed to react with electrophiles such as *m*-chloroperbenzoic acid. A similar sequence with diene **8** led to a diene which also did not undergo the cyclocondensation chemistry. Conversely, diazomethane treatment of 1-(α-furyl)-1,3-butanedione provided debenzoyl-**9** and hence debenzoyl-**10**. The latter underwent cyclocondensation reactions, thereby indicating that it has the silyloxy group at the 3-position and the methoxy group at the 1-position. This analogy was used in charting the route from **8** to **10**.

(16) Cram, D. J.; Abd Elhafez, F. A. *J. Am. Chem. Soc.* **1952**, *74*, 5828.

(17) Chefest, M.; Felkin, H.; Prudent, N. *Tetrahedron Lett.* **1968**, 2199.

(18) Danishefsky, S. J.; Pearson, W. H.; Harvey, D. F. *J. Am. Chem. Soc.* **1984**, *106*, 2455, 2456.

(19) Luche, J.-L.; Gemal, A. L. *J. Am. Chem. Soc.* **1979**, *101*, 5848.

(20) Attempted reaction of the unprotected glycal **15** under these and related conditions led to its decomposition.

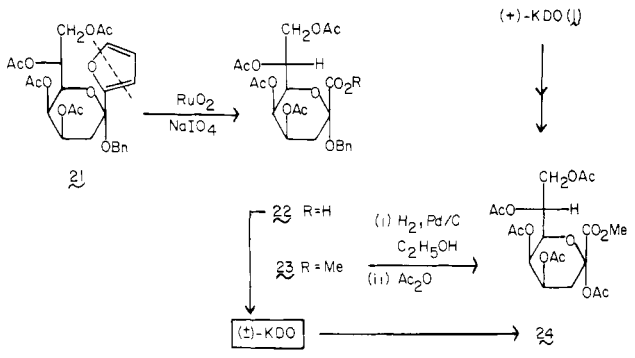
(21) The anomeric configuration of derivatives of KDO have been assigned by the chemical shift of the C-4 hydrogen. In α-ketosidic derivatives, this hydrogen is deshielded by ca. 0.5 ppm (ca. δ 5.4) relative to β-ketosides (ca. δ 4.9). The chemical shift of this proton is ca. 5.4 ppm in compounds **17–19** and **21–24**. See ref 10, pp 126–127; ref 3, pp 359–365.

(22) See supplementary material for the fractional coordinates, temperature parameters, bond distances, and bond angles for **18**.

the action of osmium tetroxide under the Van Rheenen conditions.[23] Acetylation of the crude diol **20** gave a 77% overall yield of the tetraacetate **21**, mp 122.5–123.5 °C, from **19**. The stereochemistry at C_7 in this compound was not known with certainty at this stage. The C_6–C_7 erythro arrangement was proposed by analogy with the result of osmylation of a related alkenylpyranoside during the course of our total synthesis of lincosamine.[7b] The correctness of this analogy was demonstrated by the conversion of compound **21** to KDO.

Cleavage of the furan ring by the action of ruthenium tetraoxide[24] produced the acid **22** (86%). The latter was converted (diazomethane) to the ester **23** (95%). Hydrogenolysis of the "anomeric" benzyl ether followed by acetylation of the C_2 hydroxyl group afforded the racemic pentaacetic methyl ester **24** in 93% yield, mp 129–129.5 °C. The infared, NMR (250 MHz), and mass spectra as well as the TLC behavior of the racemate thus obtained were identical with those of the optically active compound prepared from (±)-KDO as previously described.[25] The stereochemical assignments are thus confirmed.

Finally, methanolysis of the acetates and hydrogenolysis of the benzyl ether of **22** produced fully synthetic (±)-KDO, best isolated as its ammonium salt, mp 122.5–124.0 °C. The NMR spectrum and the TLC behavior of the fully synthetic KDO ammonium salt were identical with that of an authentic sample. The NMR spectrum of KDO ammonium salt is not readily interpretable due to furanose and pyranose equilibria.[26] For completeness, the fully synthetic KDO was converted to racemic **24** by the same method used with (+) KDO.[25] The NMR spectrum of **24** produced in this way was identical with that produced from **23** and from **1**. The total synthesis of KDO and a stereoselective route to KDO glycosides had been achieved.



Experimental Section

(Benzoyloxy)acetyl Chloride. A mixture of (benzoyloxy)acetic acid[27] (34.0 g, 0.189 mmol) and thionyl chloride (67.4 g, 0.567 mmol) was heated at reflux for 3 h. The excess thionyl chloride was removed in vacuo and the residue was distilled (short path) to give 34.0 g (91%) of the title compound as a clear, low-melting solid: mp ca. 22 °C; bp 60–70 °C (0.5 mmHg); IR ($CHCl_3$) 1810, 1734, 1595, 1450, 1400, 1270 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 8.2–7.3 (m, 5 H), 5.12 (s, 2 H); MS, *m/e* (%) 198 (M^+, 7), 161 (3), 135 (5), 106 (7), 105 (100), 77 (26).

4-(Benzoyloxy)-1-(α-furyl)-1,3-butanedione (8). Hexamethyldisilazane (15.4 g, 95.3 mmol) in 45 mL of THF was cooled to 0 °C and treated with *n*-butyllithium (45.4 mL of a 2.1 M solution in hexane, 95.3 mmol) in a dropwise fashion. After 30 min, 2-acetylfuran (10.0 g, 90.8 mmol) in 11 mL of THF was added over 30 min. The solution was cooled to −78 °C and diluted with toluene (180 mL). a solution of (benzoyloxy)acetyl chloride (9.02 g, 45.4 mmol) in toluene (15 mL) was added over 5 min, and the orange mixture was stirred 0.5 h then poured into 75 mL of 2 N HCl. The pH was adjusted to ca. 4 with 2 N HCl, and the organic layer was separated, washed with brine, dried ($MgSO_4$), and concentrated in vacuo to give a semicrystalline material. Crystallization from ether/hexane gave 6.20 g of product. Flash chromatography of the mother liquor (25% ethyl acetate/hexane, R_f 0.3) afforded 3.20 g more product for a total of 9.40 g (76%) of the title compound, which is almost totally enolized by ^1H NMR. Another recrystallization (ether/hexane) afforded analytically pure sample: mp 81.5–82.5 °C; IR ($CDCl_3$) 3000 (br, w), 1725, 1620, 1600, 1540, 1460, 1445, 1425, 1265, 1110 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 15–11 (br, 1 H), 8.15 (m, 2 H), 7.65–7.30 (m, 4 H), 7.20 (d, *J* = 3 Hz, 1 H), 6.55 (dd, *J* = 3, 2 Hz, 1 H), 6.28 (s, 1 H), 5.00 (s, 2 H). In addition, ca. 12% of the nonenolized β-diketone was present: ^1H NMR δ 5.05 (s, 2 H), 4.05 (s, 2 H). MS, *m/e* (%) 273 (M + 1, 3), 272 (M^+, 16), 137 (100), 105 (43), 95 (13). Anal. ($C_{15}H_{12}O_5$) C, H.

4-(Benzoyloxy)-1-(α-furyl)-1-methoxy-1-buten-3-one (9). Ethereal diazomethane (ca. 45 mmol in 80 mL of ether) was added to a mixture of the diketone **8** (3.53 g, 13.0 mmol) in 20 mL of ether at 0 °C. After 40 min, the solution was concentrated in vacuo to provide 3.72 g (100%) of the title compound as a pale yellow oil: IR ($CDCl_3$) 1735, 1665, 1612, 1460, 1275, 1118 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 8.1 (m, 2 H), 7.6–7.3 (m, 4 H), 7.10 (d, *J* = 3.5 Hz, 0.5 H),* 6.80 (d, *J* = 3.5 Hz, 0.5 H),* 6.45 (m, 1 H), 6.20 (s, 0.5 H),* 6.02 (s, 0.5 H),* 5.10 (s, 1 H),* 4.88 (s, 1 H),* 4.00 (s, 3 H) (* indicates one of the duplicated signals arising from the 1:1 mixture of olefin isomers); MS, *m/e* (%) 287 (M + 1, 1), 286 (M^+, 5), 181 (26), 164 (9), 152 (9), 151 (100), 105 (65), 77 (17).

(3*Z*)-4-(Benzoyloxy)-1-(α-furyl)-1-methoxy-3-[(trimethylsilyl)oxy]-1,3-butadiene (10). (Trimethylsilyl)trifluoromethane sulfonate (3.09 g, 13.7 mmol) was added dropwise to a solution of the enone **9** (3.72 g, 13.0 mmol) and triethylamine (1.97 g, 19.5 mmol) in ether (150 mL) at −78 °C. After 10 min, the mixture was stirred at room temperature for 0.5 h. The ether layer was decanted from the viscous residue, washed with saturated aqueous sodium bicarbonate, dried (K_2CO_3), and concentrated in vacuo to provide 4.65 g (100%) of the title compound as a clear, pale yellow oil after subjection to ca. 0.2 mmHg for several hours. This material was pure by ^1H NMR and was not purified further. Furthermore, ^1H NMR analysis showed a mixture of two isomers in a ca. 1:1 ratio, presumably a mixture of *E* and *Z* olefin isomers at C_1. IR ($CHCl_3$) 1725, 1640, 1600, 1450, 1260, 1130 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 8.19 (m, 2 H), 7.61–7.36 (m, 3.5 H),* 7.24 (s, 0.5 H),* 6.54–6.41 (m, 2 H), 6.33 (s, 0.5 H),* 5.79 (s, 0.5 H),* 3.83 (s, 1.5 H),* 3.74 (s, 1.5 H),* 0.33 (s, 4.5 H),* 0.28 (s, 4.5 H)* (* indicates one of the duplicated signals arising from the ca. 1:1 mixture of olefin isomers); MS, *m/e* (%) 359 (M + 1, 1), 358 (M^+, 4), 253 (20), 225 (10), 151 (19), 149 (21), 121 (15), 105 (100), 73 (53).

2-(Phenylseleno)propionaldehyde (12).[28] A solution of diphenyl diselenide (10.0 g, 32.0 mmol) in 75 mL of THF was added slowly to bromine in THF (35 mL) at room temperature. After 10 min, the dark solution was cooled to 0 °C and treated with ethyl propenyl ether (11.0 g, 128 mmol). After 0.5 h, the ice bath was removed, and the mixture was stirred with 5% HCl (30 mL) for 0.5 h, poured into water, and extracted twice with ether. The combined organics were washed with brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was distilled through a 10-cm Vigreux column to afford 8.25 g (61%) of the title compound as a very pale yellow oil: bp 78–80 °C (0.2 mmHg); IR ($CDCl_3$) 2820, 2720, 1720, 1578, 1475, 1438 cm^{-1}; ^1H NMR ($CDCl_3$, 90 MHz) δ 9.48 (d, *J* = 3 Hz, 1 H), 7.6–7.2 (m, 5 H), 3.7 (qd, *J* = 7, 3 Hz, 1 H), 1.44 (d, *J* = 7 Hz, 3 H); MS, *m/e* (%) 214 (M^+, 10), 185 (11), 157 (20), 155 (11), 105 (24), 85 (64), 83 (100).

***cis*- and *trans*-3-(Benzoyloxy)-6-(α-furyl)-2-[(1-phenylseleno)ethyl]-2,3-dihydro-4*H*-pyran-4-one (13 and 14).** Boron trifluoride etherate (1.84 g, 13.0 mmol) was added dropwise to a solution of the diene **10** (4.65 g, 13.0 mmol) and the aldehyde **12** (3.05 g, 14.3 mmol) in dichloromethane (175 mL) at −78 °C. After 20 min, the solution was poured into saturated aqueous sodium bicarbonate and extracted with methylene chloride (2 × 30 mL). The combined organic layers were dried ($MgSO_4$) and stirred with trifluoroacetic acid (0.7 mL) for 1 h, then washed with water and saturated aqueous sodium bicarbonate, dried ($MgSO_4$), and concentrated in vacuo to give the crude product. Flash chromatography (23% ethyl acetate/hexane) gave 1.46 g (24%) of the *trans*-dihydropyrone **14** (R_f 0.38) as a pale yellow oil and 3.54 g (58%)

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of the *cis*-dihydropyrone **13** (R_f 0.25) as colorless needles from ether/hexane, mp 107–108.5 °C. Spectral data for *trans*-**14**: IR ($CHCl_3$) 1738, 1685, 1630, 1550, 1479, 1458, 1420, 1348, 1273 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 8.05 (m, 2 H), 7.65–7.25 (m, 9 H), 7.03 (d, J = 4 Hz, 1 H), 6.55 (dd, J = 4, 2 Hz, 1 H), 6.00 (s, 1 H), 5.80 (d, J = 13 Hz, 1 H), 4.88 (dd, J = 13, 2 Hz, 1 H), 3.62 (qd, J = 7.5, 2 Hz, 1 H), 1.62 (d, J = 7.5 Hz, 3 H); MS, m/e (%) 468 (M^+, 2), 346 (1), 311 (4), 241 (1), 190 (1), 189 (10), 175 (2), 161 (4), 106 (7), 105 (100). Spectral data for *cis*-**13**: IR ($CHCl_3$) 1733, 1664, 1620, 1539, 1470, 1445, 1412, 1257 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 8.00 (dd, J = 8.3, 1.2 Hz, 2 H), 7.61–7.17 (m, 9 H), 6.97 (d, J = 3.5 Hz, 1 H), 6.56 (dd, J = 3.5, 1.8 Hz, 1 H), 6.04 (s overlapping narrow m, 2 H), 4.56 (dd, J = 8.9, 2.0 Hz, 1 H), 3.50 (qd, J = 8.9, 7.1 Hz, 1 H), 1.67 (d, J = 7.1 Hz, 3 H); MS, m/e (%) 468 (M^+, 1), 311 (2), 206 (1), 189 (5), 175 (2), 161 (3), 106 (7), 105 (100). Anal. ($C_{24}H_{20}O_5Se$) C, H.

(2*S,3*S**,4*R**)-3-(Benzoyloxy)-6-(α-furyl)-4-hydroxy-2-[(1-phenylseleno)ethyl]-2,3-dihydro-4*H*-pyran (15).** Ceric chloride heptahydrate (1.75 g, 4.71 mmol) was added to a solution of the cis dihydropyrone **13** (2.20 g, 4.71 mmol) in methylene chloride (25 mL) and absolute ethanol (25 mL) at −78 °C. Sodium borohydride (4.71 mL of a 1 M solution in ethanol) was added over 1 h via a syringe pump. The mixture was warmed to −20 °C over 1 h and quenched by careful addition of 45 mL of phosphate buffer (pH 7.0). The mixture was extracted with ether (2x), ethyl acetate, and dichloromethane. The combined organics were washed with brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was purified rapidly by flash chromatography (50% ethyl acetate/hexane, R_f 0.6; 100 g of silica gel) to provide 2.17 g (98%) of the title compound as a colorless foam: IR ($CHCl_3$) 3570, 1720, 1660, 1594, 1558, 1484, 1445, 1270 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 8.0 (m, 2 H), 7.65–7.10 (m, 9 H), 6.4 (m, 2 H), 6.07 (bd, J = 5 Hz, 1 H), 5.28 (t, J = 2 Hz, 1 H), 4.8 (m, 1 H), 4.6 (brs, 1 H), 4.05 (bd, J = 9 Hz, 1 H), 4.3 (qd, J = 9, 7 Hz, 1 H), 1.6 (d, J = 7 Hz, 3 H); MS, m/e (%) 470 (M^+, 0.2), 243 (2), 192 (2), 191 (14), 158 (7), 139 (40), 122 (17), 105 (100), 95 (19), 77 (12), 71 (43).

(2*S,3*S**,4*R**)-3-(Benzoyloxy)-6-(α-furyl)-2-[(1-phenylseleno)ethyl]-4-[(trimethylsilyl)oxy]-2,3-dihydro-4*H*-pyran (16).** Trimethylsilyl trifluoromethanesulfonate (1.25 g, 5.54 mmol) was added in a dropwise fashion to a solution of the alcohol **15** (2.17 g, 4.61 mmol) and 2,6-lutidine (0.74 g, 6.9 mmol) in dichloromethane (100 mL) at −78 °C. After 0.5 h, the solution was added to saturated aqueous sodium bicarbonate containing 1 mL of triethylamine. The mixture was extracted with dichloromethane (2x) and the organic layers were washed with saturated aqueous ammonium chloride, dried ($MgSO_4$), and concentrated in vacuo. The resultant oil was purified by flash chromatography (4% ethyl acetate/hexane, R_f 0.3) to give 2.35 g (94%) of a colorless foam: IR ($CHCl_3$) 1721, 1662, 1560, 1485, 1445, 1270 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 8.00 (dd, J = 8.3, 1.2 Hz, 2 H), 7.60–7.20 (m, 9 H), 6.47 (bd, J = 3.2 Hz, 1 H), 6.39 (dd, J = 3.2, 1.8 Hz, 1 H), 6.09 (brd, J = 5.0 Hz, 1 H), 5.20 (t, J = 2.0 Hz, 1 H), 4.76 (dd, J = 5.0, 2.0 Hz, 1 H), 4.03 (d, J = 9.2 Hz, 1 H), 3.42 (qd, J = 9.2, 7.0 Hz, 1 H), 2.62 (d, J = 7.0 Hz, 3 H), 0.13 (s, 9 H); MS, m/e (%) 542 (M^+, 2), 316 (4), 315 (13), 263 (9), 175 (9), 106 (7), 105 (100). Anal. ($C_{27}H_{30}O_5SeSi$) C, H.

(2*R,4*R**,5*S**,6*S**)-4,5-Bis(acetyloxy)-2-(benzyloxy)-2-(α-furyl)-6-[(phenylseleno)ethyl]tetrahydropyran (18).** Camphorsulfonic acid (50 mg, 0.22 mmol) was added to a solution of the silyl glycal **16** (2.35 g, 4.34 mmol) and benzyl alcohol (1.03 g, 9.55 mmol) in toluene (45 mL) at 0 °C. After 3 h, the solution was washed with saturated aqueous sodium bicarbonate, dried ($MgSO_4$), and concentrated in vacuo, and the residue was subjected to ca. 0.22 mmHg for several hours to afford the crude alcohol **17**, which was not purified further: ^1H NMR (250 MHz, $CDCl_3$) δ 8.0 (dd, J = 8, 1 Hz, 2 H), 7.60–7.0 (m, 14 H), 6.55 (m, 1 H), 6.40 (dd, J = 3, 2 Hz, 1 H), 5.98 (brd, J = 3 Hz, 1 H), 4.73 (brd, J = 6 Hz, 1 H, exchange), 4.65 (m, $w_{1/2}$ = 23 Hz, 1 H), 4.32, 4.10 (AB, J = 12 Hz, 2 H), 3.95 (bd, J = 9 Hz, 1 H), 3.45 (qd, J = 9, 7 Hz, 1H), 2.55 (dd, J = 12.3, 4.2 Hz, 1 H), 2.00 (apparent t, J = 12.3 Hz, 1 H), 1.63 (d, J = 7 Hz, 3 H). The crude product was stirred with potassium carbonate (0.92 g, 6.7 mmol) and methanol (20 mL) for 30 min at room temperature, then the mixture was added to water and extracted with ether (4x). The combined organic layers were washed with brine, dried ($MgSO_4$), and concentrated in vacuo, and the residue was subjected to ca. 0.2 mmHg to remove the last traces of solvent. The resultant diol was dissolved in dichloromethane (50 mL) and stirred with acetic anhydride (1.6 mL), pyridine (1.5 mL), and 4-(dimethylamino)pyridine (10 mg) for 18 h. The solution was washed with 5% aqueous hydrochloric acid (2x) and saturated aqueous sodium bicarbonate, then dried ($MgSO_4$), and concentrated in vacuo. Flash chromatography of the residue (18% ethyl acetate/hexane, R_f 0.25) gave 1.68 g (69%) of the title compound as a colorless solid. Crystalization from ether/pentane provided analytically pure needles, mp 94.0–95.0 °C. Crystals suitable for X-ray diffraction could be obtained by slow evaporation of an ether/pentane solution: IR ($CDCl_3$) 1744, 1568, 1427, 1242 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.57 (dd, J = 8, 3 Hz, 2 H), 7.40 (m, 1 H), 7.35–7.23 (m, 6 H), 7.10 (m, 2 H), 6.50 (dd, J = 3, 0.8 Hz, 1 H), 6.38 (dd, J = 3, 1.7 Hz, 1 H), 5.93 (bd, J = 3 Hz, 1 H), 5.42 (ddd, J = 12.2, 4.9, 3.0 Hz, 1 H), 4.22, 4.07 (AB, J = 11.5 Hz, 2 H), 3.86 (dd, J = 9.2, 1.1 Hz, 1 H), 3.32 (qd, J = 9.2, 7.0 Hz, 1 H), 2.42 (dd, J = 12.2, 4.9 Hz, 1 H), 2.13 (apparent t, J = 12.2 Hz, 1 H), 2.00 (s, 3 H), 1.98 (s, 3 H), 1.62 (d, J = 7.0 Hz, 3 H); MS, m/e (%) 560 (M + 2, 2), 559 (M + 1, 2), 558 (M^+, 7), 233 (9), 191 (16), 175 (13), 174 (20), 92 (9), 91 (100). Anal. ($C_{28}H_{30}O_7Se$) C, H. See supplementary material for X-ray data.

(2*R,4*R**,5*S**,6*R**)-4,5-Bis(acetyloxy)-2-(benzyloxy)-2-(α-furyl)-6-vinyltetrahydropyran (19).** Hydrogen peroxide (5.5 mL of a 30% aqueous solution) was added dropwise to an ice-cold solution of the selenide **18** (1.59 g, 2.85 mmol) and pyridine (1.8 mL) in THF (25 mL), which was then stirred 1 h at room temperature and poured into refluxing carbon tetrachloride (270 mL). After 5 min the mixture was cooled and the organic layer was washed with saturated aqueous sodium bicarbonate and 5% aqueous hydrochloric acid, then dried ($MgSO_4$), and concentrated in vacuo. Flash chromatography (20% ethyl acetate/hexane, 100 g of silica gel, R_f 0.6) provided 1.10 g (96%) of the title compound as colorless needles, mp 103.5–104.0 °C (ether/pentane): IR ($CHCl_3$) 1745, 1595, 1375, 1359, 1245 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.42 (dd, J = 1.8, 0.8 Hz, 1 H), 7.37–7.22 (m, 5 H), 6.56 (dd, J = 3.2, 0.8 Hz, 1 H), 6.40 (dd, J = 3.2, 1.8 Hz, 1 H), 5.90–5.75 (m, 1 H), 5.53–5.36 (m, 3 H), 5.25 (apparent dt, J = 10.8, 1.5 Hz, 1 H), 4.45 (apparent dq, J = 5.5, 1.5 Hz, 1 H), 4.36, 4.21 (AB, J = 11.5 Hz, 2 H), 2.50 (ddd, J = 12.5, 5.0, 1.0 Hz, 1 H), 2.14 (apparent t, J = 12.5 Hz, 1 H), 2.08 (s, 3 H), 1.98 (s, 3 H); MS, m/e (%) 400 (M^+, 0.4), 292 (19), 174 (14), 172 (69), 150 (16), 123 (15), 95 (25), 92 (11), 91 (100).

(2*R,4*R**,5*S**,6*R**,1*R**)-4,5-Bis(acetyloxy)-2-(benzyloxy)-2-(α-furyl)-6-(1,2-diacetoxyethyl)tetrahydropyran (21).** Osmium tetraoxide (0.35 mL of a 0.39 M solution in THF, 0.14 mmol) was added to a solution of *N*-methylmorpholine *N*-oxide (0.45 g, 3.3 mmol), *tert*-butyl alcohol (3 mL), and water (0.75 mL) in THF (15 mL). After 10 min, the olefin **19** (1.10 g, 2.75 mmol) in THF (1 mL) was added dropwise. After 4 h, Florisil (4 g), dichloromethane (5 mL), and water (0.5 mL) were added, followed by sodium bisulfite (1.0 g). After 15 min, the mixture was filtered, washing with ethyl acetate and dichloromethane. The filtrate was concentrated in vacuo to give the crude diol **20** as a colorless foam. The material was dissolved in dichloromethane (15 mL) and treated with acetic anhydride (0.84 g, 8.3 mmol), pyridine (0.65 g, 8.3 mmol), and 4-(dimethylamino)pyridine (20 mg). After 2 h, the solution was washed with 5% aqueous hydrochloric acid (2x) and saturated aqueous sodium bicarbonate, and the organic layer was dried ($MgSO_4$) and concentrated in vacuo. Crystallization from ether/pentane gave 842 mg of colorless needles. Flash chromatography of the mother liquor (28% ethyl acetate/hexane, R_f 0.30) followed by crystallization from ether/pentane afforded 250 mg of additional product, thus providing a total of 1.09 g (77%) of the title compound: mp 122.5–123.5 °C; IR ($CHCl_3$) 1748, 1360, 1220 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.42 (dd, J = 1.8, 0.75 Hz, 1 H), 7.38–7.23 (m, 5 H), 6.50 (dd, J = 3.3, 0.75 Hz, 1 H), 6.40 (dd, J = 3.3, 1.8 Hz, 1 H), 5.49 (ddd, J = 12.2, 5.0, 3.2 Hz, 1 H), 5.45 (brs, 1 H), 5.25 (ddd, J = 9.8, 3.8, 2.2 Hz, 1 H), 4.62 (dd, J = 12.3, 2.3 Hz, 1 H), 4.38, 4.15 (AB, J = 12.0 Hz, 2 H), 4.32 (dd, J = 9.8, 1.2 Hz, 1 H), 4.21 (dd, J = 12.3, 3.8 Hz, 1 H), 2.49 (ddd, J = 13.0, 5.0, 1.3 Hz, 1 H), 2.15 (dd, J = 13.0, 12.2 Hz, 1 H), 2.07 (s, 3 H), 2.01 (s, 3 H), 1.98 (s, 3 H), 1.9 (s, 3 H); MS, m/e (%) 518 (M^+, 0.1), 411 (13), 351 (11), 291 (18), 232 (18), 231 (40), 205 (12), 190 (18), 189 (100), 91 (13). Anal. ($C_{26}H_{30}O_{11}$) C, H.

(±)-4,5,7,8-Tetra-*O*-acetyl-2-*O*-benzyl-3-deoxy-D-*manno*-2-octulopyranosonate (22). Ruthenium dioxide monohydrate (6.5 mg, 0.049 mmol)[24] was added to a stirred mixture of sodium periodate (5.2 g, 24 mmol), water (20 mL), carbon tetrachloride (20mL), and acetonitrile (30 mL). After 0.5 h, the furan **21** (0.842 g, 1.63 mmol) in 2 mL of acetonitrile was added dropwise, followed by 5 mL more of water. After 2 h, more water was added, and the mixture was extracted with dichloromethane (2x), ether (2x), and ethyl acetate. The organics were combined, washed with saturated aqueous sodium bisulfite and brine, then dried ($MgSO_4$), concentrated in vacuo, and passed through a short plug of Celite/decolorizing carbon/$MgSO_4$. Concentration gave 0.770 g of a colorless oil, which solidified upon trituration with ether. This material was dissolved in ether and washed with saturated aqueous sodium bicarbonate (3x). The aqueous layers were combined and carefully acidified to pH 4 at 0 °C with concentrated hydrochloric acid then extracted with ether (3x). The combined ether layers were dried ($MgSo_4$) and concentrated in vacuo to provide 0.695 g (86%) of the title compound as a colorless foam, which was pure by ^1H NMR: IR ($CHCl_3$) 3200–2600, 1742, 1360, 1220 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 9.50 (brs, 1 H), 7.35 (m, 5 H), 5.43 (brs, 1 H), 5.45–5.37 (m, 1 H),

5.27 (dt, J = 9.5, 2.5 Hz, 1 H), 4.64 (dd, J = 12.3, 2.21 Hz, 1 H), 4.56 (s, 2 H), 4.28–4.17 (m, 2 H), 2.35 (m, 1 H), 2.20 (t, J = 12.3 Hz, 1 H), 2.10 (s, 3 H), 2.00 (s, 3 H), 1.98 (s, 3 H), 1.91 (s, 3 H); MS, m/e (%) 451 (M – CO_2H, 2), 390 (12), 141 (24), 112 (12), 91 (100).

(±)-Methyl 4,5,7,8-Tetra-*O*-acetyl-2-*O*-benzyl-3-deoxy-D-*manno*-2-octulopyranosonate (23). A solution of the acid **22** (127 mg, 0.254 mmol) in ether (5 mL) was treated with an excess of etheral diazomethane. After 10 min, the solution was concentrated in vacuo. Flash chromatography (35% ethyl acetate/hexane, R_f 0.35) provided 124 mg (95%) of the title compound as a colorless glass: IR ($CHCl_3$) 1755, 1738, 1438, 1369, 1230 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.35 (m, 5 H), 5.42 (brs, 1 H), 5.40 (ddd, J = 12.3, 4.9, 2.5 Hz, 1 H), 5.27 (ddd, J = 9.8, 3.2, 2.3 Hz, 1 H), 4.63 (dd, J = 12.3, 2.3 Hz, 1 H), 4.58, 4.47 (AB, J = 12.2 Hz, 2 H), 4.23 (dd, J = 9.8, 1.2 Hz, 1 H), 4.21 (dd, J = 12.3, 3.2 Hz, 1 H), 3.79 (s, 3 H), 2.30 (ddd, J = 12.3, 4.9, 1.2 Hz, 1 H), 2.15 (t, J = 12.3 Hz, 1 H), 2.10 (s, 3 H), 2.00 (s, 3 H), 1.98 (s, 3 H), 1.92 (s, 3 H); MS, m/e (%) no M^+, 452 (2), 451 (7), 405 (9), 404 (45), 301 (18), 224 (10), 182 (18), 181 (21), 145 (12), 121 (12), 112 (12), 92 (10), 91 (100).

(±)-Methyl 2,4,5,7,8-Penta-*O*-acetyl-3-deoxy-D-*manno*-2-octulopyranosonate (24). A mixture of the benzyl ether **23** (111 mg, 0.217 mmol), 10% palladium on carbon (20 mg), and ethanol (3 mL) was stirred under a balloon of hydrogen for 20 h then filtered through Celite, washing with dichloromethane. The filtrate was concentrated in vacuo to give the crude alcohol, which was dissolved in dichloromethane (2 mL) and treated with acetic anhydride (44 mg, 0.43 mmol), pyridine (34 mg, 0.43 mmol) and 4-(dimethylamino)pyridine (2 mg). After 3 h, the solution was washed with 10% aqueous hydrochloric acid and saturated aqueous sodium bicarbonate, then dried ($MgSO_4$), and concentrated in vacuo to provide 93.1 mg (93%) of the title compound as a colorless solid, mp 129.0–129.5 °C (ethyl acetate/hexane) lit. mp[25] for (+)-**24** 155–158 °C, which was identical with material prepared from (+)-NH_4 KDO (Sigma) according to Unger[25] with regard to its TLC behavior (R_f 0.25, 40% ethyl acetate/hexane) and its IR, ^1H NMR (250 MHz), and mass spectra: IR ($CHCl_3$) 1748, 1429, 1363, 1220 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 5.38 (m, 1 H), 5.32 (ddd, J = 10.7, 6.5, 3.0 Hz, 1 H), 5.22 (ddd, J = 9.9, 3.9, 2.2 Hz, 1 H), 4.47 (dd, J = 12.3, 2.2 Hz, 1 H), 4.17 (dd, J = 9.9, 1.3 Hz, 1 H), 4.09 (dd, J = 12.3, 3.9 Hz, 1 H), 3.81 (s, 3 H), 2.23 (m, 2 H), 2.14 (s, 3 H), 2.08 (s, 3 H), 2.05 (s, 3 H), 2.002 (s, 3 H), 1.997 (s, 3 H); MS, m/e (%) no M^+, 431 (1), 405 (2), 404 (8), 403 (39), 361 (48), 301 (100), 300 (47), 282 (49), 259 (31), 241 (34), 240 (62), 227 (20), 217 (37), 199 (39), 198 (35), 185 (20), 181 (100), 180 (20), 168 (26), 167 (74), 157 (34), 155 (56), 145 (40), 143 (24), 139 (70), 128 (20), 127 (20), 126 (65), 115 (51), 103 (26).

(±)-Ammonium 3-Deoxy-D-*manno*-2-octulopyranosonate ((±)-NH_4 KDO) (1). A solution of the acid **22** (203 mg, 0.409 mmol) in methanol (4 mL) was stirred with sodium methoxide (111 mg, 2.05 mmol) for 6 h, then neutralized with methanol-washed Dowex 50-8x (20–50 mesh) ion-exchange resin. The mixture was filtered, washing the resin with small portions of methanol. Palladium (10% on charcoal, 50 mg) was added to the filtrate and the mixture was stirred under a balloon of hydrogen for 16 h then filtered through Celite, washing with methanol. The filtrate was treated with excess anhydrous methanolic ammonia, and the solution was concentrated in vacuo to provide 96.0 mg (92%) of the title compound as a colorless, amophous solid (mp 119–122 °C) whose 250-MHz ^1H NMR spectrum in D_2O was essentially identical with that of an authentic sample of (+)-NH_4 KDO (Sigma, mp 122–124 °C) with the exception of a few very minor impurities, which were absent after recrystallization. Mobility by TLC was identical with that of an authentic sample, R_f 0.58 (10:10:3 methanol/chloroform/water, p-anisaldehyde/sulfuric acid visualization). Slow crystallization from aqueous ethanol provided pure (±)-NH_4 KDO (**1**) as colorless plates, mp 122.5–124.0 °C (lit. mp[25a] of (+)-**1** 122–125 °C); ^1H NMR (250 MHz, D_2O, Me_4Si reference) δ 4.47–4.37 (m), 4.10 (m), 4.03–3.92 (m), 3.88–3.49 (m), 2.50 (dd, J = 14, 7 Hz), 2.25 (m), 2.03–1.76 (m).

Peracetylation and diazomethane esterification of 7.1 mg (0.028 mmol) of the crude product according to the literature procedure[25] afforded 10.4 mg (81%) of (±)-**24** as a colorless solid (mp 128–129 °C) after flash chromatography (40% ethyl acetate/hexane, R_f 0.31), which was identical in all respects with that prepared above from **23**.

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Registry No. 1, 92693-58-8; **8**, 92641-45-7; *E*-**9**, 92622-29-2; *Z*-**9**, 92622-30-5; *E*-**10**, 92622-31-6; *Z*-**10**, 92622-32-7; **12**, 92622-33-8; **13**, 92641-46-8; **14**, 92622-34-9; **15**, 92641-47-9; **16**, 92622-35-0; **17**, 92622-36-1; **18**, 92622-37-2; **19**, 92622-38-3; **20**, 92622-39-4; **21**, 92622-40-7; **22**, 92622-41-8; **23**, 92622-42-9; **24**, 92693-59-9; 2-acetylfuran, 1192-62-7; (benzoyloxy)acetyl chloride, 54150-57-1; (benzoyloxy)acetic acid, 614-44-8; diphenyl diselenide, 1666-13-3; ethyl propenyl ether, 928-55-2.

Supplementary Material Available: Tables containing fractional coordinates, temperature factors, bond distances, and bond angles for compound **18** (5 pages). Ordering information is given on any current masthead page.

Total Synthesis of Vineomycinone B_2 Methyl Ester

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Abstract: Two homo-Diels–Alder reactions and a hetero-Diels–Alder reaction, each using siloxydienes, were used in a total synthesis of the title compound.

Background

The anthracycline antibiotics such as adriamycin are among the most important of the natural products in antitumor chemotherapy.[1] These compounds characteristically contain an anthraquinone chromophore within a hydrotetracene ring system. The tetracene moiety is linked to a "carbohydrate region" through a glycosidic bond.

An interesting subgroup of anthracycline antibiotics are those in which an anthracene or a tetracene derivative is joined to a carbohydrate residue through a C-glycosidic bond.[2] In some instances there are two such C-glycosidic bonds. Combinations of C- and O-glycosidic attachments of sugars to an anthracycline system are also known. Finally, and most relevant to the inves-

(1) Cf. Inter. Alia: (a) "The Chemistry of Antitumor Antibiotics"; Remers, W. A., Ed.; Wiley: New York, 1978. (b) "Anticancer Agents Based on Natural Product Models"; Cassady, J. M.; Douros, J. D., Eds.; Academic Press: New York, 1980. (c) "Antineoplastic Agents"; Remers, W. A., Ed.; Wiley: New York, 1984.

(2) Cf. Inter. Alia. (a) nogalamycin: Hauser, F. M., Adams, T. C. *J. Org. Chem.* **1984**, *49*, 2296 and references therein. (b) Pluramycin A: Kondo, S.; Muyamoto, M.; Naganawa, H.; Takeuchi, T.; Umezawa, H. *J. Antibiot.* **1977**, *12*, 1143. (c) Granaticin: Chang, C. J.; Floss, H. G.; Soong, P.; Chan, C. T. *Ibid.* **1975**, *28*, 156. (d) Griseusin: Kometani, T.; Takeuchi, Y.; Yoshi, E. *J. Org. Chem.* **1983**, *48*, 2311. (e) Aquayamycin: Sezaki, M.; Kondo, S.; Maeda, K.; Umezawa, H.; Ohno, M. *Tetrahedron* **1970**, *26*, 5171.

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