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Synthesis of carbocyclic analogues of 3-deoxy-D-*manno*-2-octulosonic acid and *N*-acetylneuraminic acid ☆

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Abstract

A carbocyclic analogue of *N*-acetylneuraminic acid was synthesised from the Diels–Alder *endo*-adduct of furan and acrylic acid, and its ammonium salt was subjected to bioassay. In addition, carbocyclic analogues of 3-deoxy-D-*manno*-2-octulosonic acid were synthesised in racemic form from the same synthetic intermediate.

Keywords: Carba-sugars; Cyclitols; Carbocyclic Neu5Ac-analogues; Carbocyclic Kdo-analogues; Sialidase inhibitors

1. Introduction

Extensive synthetic studies of many kinds of analogues [2,3] and derivatives [4] of *N*-acetylneuraminic acid (Neu5Ac, **1**), both as potential inhibitors of sialidases and as probes for the elucidation of sialic acid metabolism, have been carried out. Since the analogues which contain a nitrogen or sulfur atom instead of the pyranoid oxygen atom showed some activity [5], we were interested in a synthesis [6] of the carba-sugar analogue *N*-acetyl-6a-carbaneuraminic acid (**2**). Starting from the *endo*-adduct [7] **5** of furan and acrylic acid, the penta-*O*-acetyl derivative (+)-**64** of the methyl ester was

☆ Pseudo-sugars, Part 36. For Part 35, see ref. [1]

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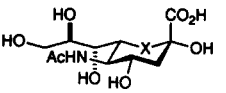
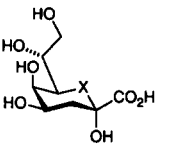
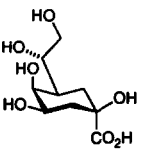


1 X = O [*N*-Acetylneuraminic acid (Neu-5Ac)]
2 X = CH_2 [6a-Carba-Neu-5Ac]





3 X = O [3-Deoxy-D-*manno*-2-octulosonic acid (Kdo)]
4α X = CH_2 [6a-Carba-Kdo]

4β

Scheme 1.

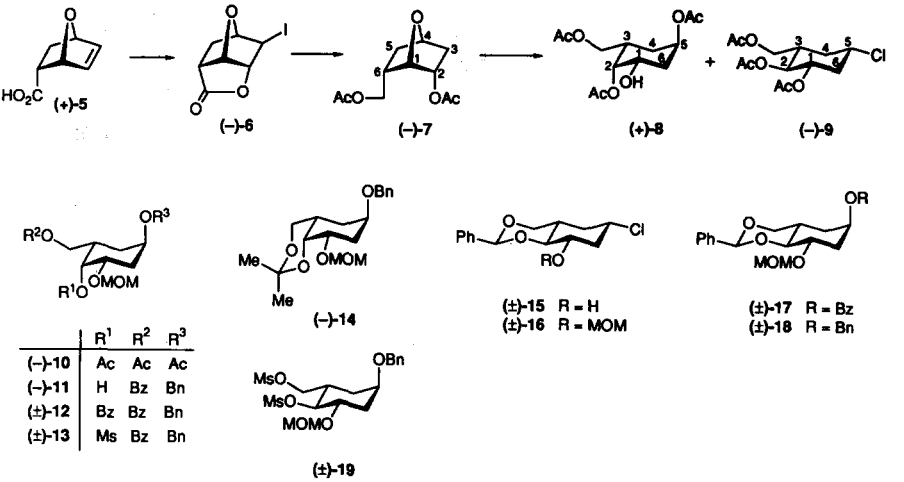
obtained in 30 reaction steps, and the ammonium salt of **2** was assayed for neuraminidases. In the course of this synthesis, some potential intermediates for preparation of 5a-carba-2-deoxyhexopyranose derivatives were obtained, from one of which the carbocyclic analogues **4α** and **4β** of 3-deoxy-D-*manno*-2-octulosonic acid (Kdo, **3**) were synthesised in racemic form (Scheme 1).

2. Results and discussion

Preparation of 5a-carba-2-deoxyhexopyranose derivatives.—The construction of 5a-carbahexopyranose structures by cleavage of the 1,4-anhydro ring of 2,3-dihydroxy-6-hydroxymethyl-7-oxabicyclo[2.2.1]heptane derivatives has been thoroughly demonstrated [8–11]. Thus two 5a-carba-2-deoxyhexopyranoses have so far been synthesised by acetolysis of 2-acetoxy-6-acetoxymethyl-7-oxabicyclo[2.2.1]heptane [(±)-**7**] [10]. In this paper, Lewis acid catalysed cleavage of the anhydro ring of **7** was attempted in order to prepare partially protected 5a-carba-2-deoxyhexopyranoses mainly through a neighbouring assistance by the 2-acetoxyl function.

Thus, treatment of (−)-**7** with excess of titanium tetrachloride in dichloromethane containing acetic acid at room temperature produced non-selectively the triacetate (+)-**8** (37%) and the chloride (−)-**9** (19%), the structures of which were deduced on the basis of their ^{1}H NMR spectra. The former seemed to be obtained as expected via an intramolecular attack of the 2-acetoxy group at C-1 and the latter through a preferential displacement by chloride ion at C-4. The following transformations using compounds **8** and **9** were then carried out in order to prepare the intermediates useful for synthesis of the carba-sugar analogues of biological interest (Scheme 2).

The hydroxyl group of (+)-**8** was first protected as the methoxymethyl (MOM) group by treatment with chloromethyl methyl ether and *N*,*N*-diisopropylethylamine in CH_2Cl_2 to give the triacetate (−)-**10** (93%). Similar protection using diisopropylamine



	R^1	R^2	R^3
(−)-10	Ac	Ac	Ac
(−)-11	H	Bz	Bn
(±)-12	Bz	Bz	Bn
(±)-13	Ms	Bz	Bn

Scheme 2. For convenience, the structures of the racemic compounds depict only one of the respective enantiomers.

as a base produced two products resulting from an acetyl group migration. Zemplén *O*-deacetylation of (−)-**10**, followed by successive *O*-isopropylidenation with 2,2-dimethoxypropane–*p*-toluenesulfonic acid (PTSA) in *N*,*N*-dimethylformamide (DMF) and *O*-benzylation with benzyl bromide–sodium hydride in DMF, gave the benzyl ether (−)-**14** in 55% overall yield. *O*-Deisopropylidenation of (±)-**14** [1] followed by selective benzoylation of the primary hydroxyl group gave the benzoate (±)-**11** (85%). On the other hand, *O*-deacetylation of the chloride (±)-**9** and successive benzylidenation with α,α-dimethoxytoluene–PTSA in DMF gave the alcohol (±)-**15** (95%), which was converted into the methoxymethyl ether (±)-**16** (97%). Treatment of (±)-**16** with excess of sodium benzoate in dimethyl sulfoxide at 130°C gave, through an S_N2 reaction, the benzoate (±)-**17** (60%). *O*-Deacylation of (±)-**17** followed by benzylation gave the benzyl ether (±)-**18** (80%), the benzylidene group of which was removed by treatment with aqueous acetic acid followed by conventional mesylation, affording the dimesylate (±)-**19** (70%). Reaction of (±)-**19** with excess of sodium benzoate in Me_2SO readily proceeded to give the dibenzoate (±)-**12** (80%), which was identical with material prepared (82%) by benzoylation of (±)-**11**. The above transformations also verified the assigned structures of **8** and **9**.

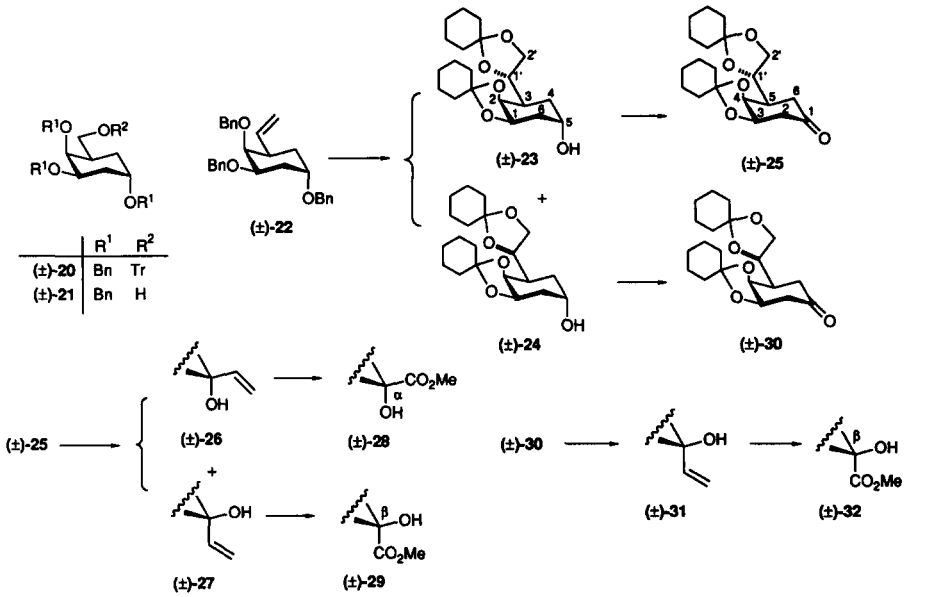
Synthesis of carbocyclic analogue of Kdo.—Molin and Pring [12] described the first synthesis of the carbocyclic analogue of β-Kdo from (−)-quinic acid and showed the ester of Kdo to be a moderate inhibitor of LPS-biosynthesis. Therefore, a synthesis of racemic carba-α- (**4α**) and -β-analogues (**4β**) of Kdo has been carried out to demonstrate the versatility of the intermediates and, in addition, to elaborate a possible synthetic route to a new carbocyclic analogue **2** of Neu5Ac.

[1] The racemates (±)-**9** and (±)-**14** were used for the following transformations.

O-Deacetylation of (±)-**8** gave the tetraol, the 7-OH group of which was selectively tritylated and then benzylated to afford the tribenzyl ether (±)-**20** (70%). Removal of the trityl group of (±)-**20** with aqueous sulfuric acid gave the alcohol (±)-**21** (87%), oxidation of which with pyridinium chlorochromate (PCC)–alumina in dichloromethane gave the aldehyde. Wittig reaction of the aldehyde with methyltriphenylphosphonium bromide and butyllithium in hexane gave the vinylcyclohexane compound (±)-**22** (77%). Osmylation of the alkene (±)-**22** in 1-butanol and THF at room temperature, subsequent hydrogenolysis using palladium hydroxide in ethanol containing acetic acid, and *O*-cyclohexylidenation with α,α-dimethoxycyclohexane–PTSA in DMF produced two isomeric di-*O*-cyclohexylidene derivatives (±)-**23** and (±)-**24** in 75 and 18% overall yields, respectively. The stereochemistry of the two hydroxyl groups newly introduced were assigned later by transforming (±)-**23** into the known derivative (±)-**36** [12] of the carba-β-Kdo. The major product of the osmylation had the relative C-1′ configuration corresponding to that of natural Kdo, in contrast to the stereochemistry to be expected from the pyranoid models [13], owing possibly to lack of the ring-oxygen atom. The alcohols (±)-**23** and (±)-**24** were oxidised with PCC to give the respective ketones (±)-**25** and (±)-**30** in quantitative yields. Grignard reaction of (±)-**25** with 1 M vinylmagnesium bromide in hexane at 0°C followed by standard processing gave, after silica gel column chromatography, two vinylcyclohexane derivatives (±)-**26** (12%) and (±)-**27** (72%). The preferential axial attack from the less-hindered α-face led to compound (±)-**27**. Ozonolysis of (±)-**26** in methanol at −78°C gave the aldehyde which was treated with sodium perchlorate, sulfamic acid, and sodium phosphate in acetone–water at room temperature, followed by esterification with diazomethane, to afford the methyl ester (±)-**28** (80%). *O*-Decyclohexylidenation of (±)-**28** with 1 M hydrochloric acid in 1:1 methanol–THF gave, after acetylation and silica gel column chromatography, the pentaacetate (±)-**33** (33%), together with the lactone (±)-**35** and a mono-*O*-cyclohexylidene derivative. Formation of (±)-**35** verified the 1,3-*cis* relationship between the stereochemistry of the carboxylate and 3-hydroxyl group in (±)-**28**. On the other hand, (±)-**27** likewise gave the methyl ester (±)-**29** (93%), which was readily deprotected to give, after acetylation, the penta-*O*-acetyl derivative (±)-**36** in good yield (82%). The ^{1}H NMR (400 MHz, CD_3OD) data of the methyl ester (±)-**37** obtained from (±)-**36** were very similar to those described [12] for the optically active methyl carba-β-Kdo. The ammonium salts (±)-**34** and (±)-**38** were obtained by treatment of (±)-**33** and (±)-**37**, respectively, with 0.5 M sodium hydroxide at room temperature followed by neutralisation and acidification with Amberlite IR-120 (H^+) resin and treatment with 1 M aqueous ammonia (Schemes 3 and 4).

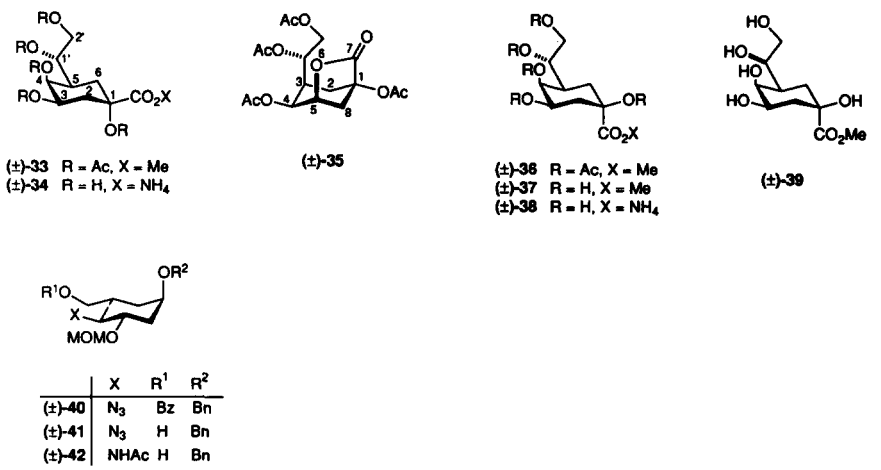
Similarly, the 7-epimer (±)-**39** of carba-β-Kdo was prepared via (±)-**31** and (±)-**32** from (±)-**30**. Its ^{1}H NMR spectrum was clearly different from that of (±)-**37**, thereby firmly supporting the assigned configuration of C-1′ of (±)-**23** and (±)-**24**.

Synthesis of carbocyclic analogue of Neu5Ac.—Introduction of a nitrogen function at C-2 of **8** with inversion of the configuration was carried out through direct substitution with an azide ion, for the stereochemistry of the product would match that assigned to carbocyclic analogue **2**. Thus, the benzoate (±)-**11** was converted into the mesylate (±)-**13**, treatment of which with sodium azide in DMF at 90°C gave the azide (±)-**40** (78%) via direct S_N2 mechanism. *O*-Deacylation of (±)-**40** gave the alcohol (±)-**41**



Scheme 3. For convenience, the structures of the racemic compounds depict only one of the respective enantiomers.

(97%), which was hydrogenated in methanol containing acetic anhydride in the presence of Raney nickel at room temperature, to afford the *N*-acetyl derivative (±)-**42** (65%). Attempted oxidation of the hydroxymethyl function of (±)-**41** with PCC or CrO_3 cleanly gave the aldehyde, but it readily underwent elimination during the purification



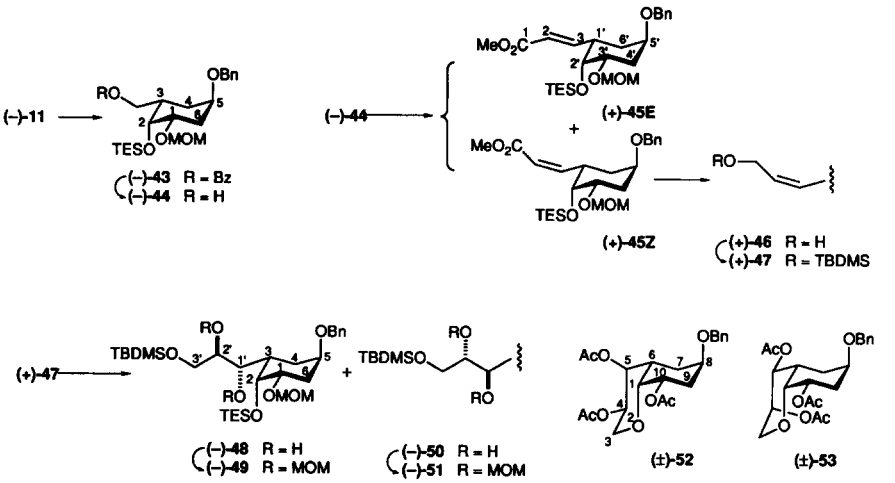
Scheme 4. For convenience, the structures of the racemic compounds depict only one of the respective enantiomers.

process to give the 2-cyclohexenone derivative. Similar oxidation of (±)-**42** produced a complex mixture of products. Accordingly, these results suggested that the acetamido group should be introduced at C-2 after extension of the branched chain – construction of the 1,2,3-trihydroxypropyl function being performed.

1,4,6-Tri-*O*-acetyl-2-deoxy-5a-carba-L-*arabino*-hexopyranose [(−)-**8**] was then chosen for the starting compound, because the absolute configurations at C-1 and C-3 originally matched those at C-4 and C-6 of **2**, except for that of C-5, which could be later generated via Walden inversion involving introduction of a nitrogen nucleophile. Compound (+)-**8** was obtained from the (+)-*endo*-adduct [6] [(+)-**5**] by iodolactonisation [→ (+)-**6**], reduction with LAH [→ (−)-**7**], and oxygen bridge cleavage [→ (−)-**8**], and the following sequence was elaborated on the basis of the preliminary experiments.

Compound (−)-**11** was first protected with the triethylsilyl (TES) group [→ (−)-**43**] and then *O*-debenzoylated to give the alcohol (−)-**44**. Oxidation of (−)-**44** with CrO_3 gave the aldehyde which without purification was directly subjected to Horner–Emmons reaction. Thus, treatment of the aldehyde with trimethyl phosophonoacetate and 0.5 M potassium hexamethyldisilazide–toluene in THF in the presence of 18-crown-6-ether at −78°C gave, after silica gel column chromatography, the alkenes (+)-**45E** (18%) and (+)-**45Z** (68%). The *Z* isomer was as expected the major product. The structures were assigned mainly on the basis of the coupling constants of the alkenic protons in the ^{1}H NMR spectra. Thus, in the ^{1}H NMR spectrum of (+)-**45E** the signals due to H-3 and H-2 appeared at δ 7.00 (dd, *J* 7.7, *J* 15.8 Hz) and 5.80 (dd, *J* 1.1, *J* 15.8 Hz), respectively. By contrast, in (+)-**45Z** the corresponding signals were observed at δ 6.29 (dd, *J* 10.3, *J* 11.4 Hz) and 5.78 (dd, *J* 1.0, *J* 11.4 Hz). Compound **45Z** was reduced with diisobutylaluminium hydride (DIBAL-H) to give the alcohol [→ (+)-**46** (86%)], which was conventionally protected with the *tert*-butyldimethylsilyl (TBDMS) group [→ (+)-**47** (97%)]. *cis*-Hydroxylation of (+)-**47** with osmium tetraoxide in the presence of *N*-methylmorpholine *N*-oxide in aqueous acetone smoothly yielded, after chromatography, two diols (−)-**48** (44%) and (−)-**50** (48%) in good yields but non-selectively. Brimacombe et al. [14] reported the diastereoselectivity of the dihydroxylation of *Z*-enoates of two hexopyranose derivatives. However, several attempts to improve the diastereoselectivity, as had been observed in the carba-Kdo synthesis, failed.

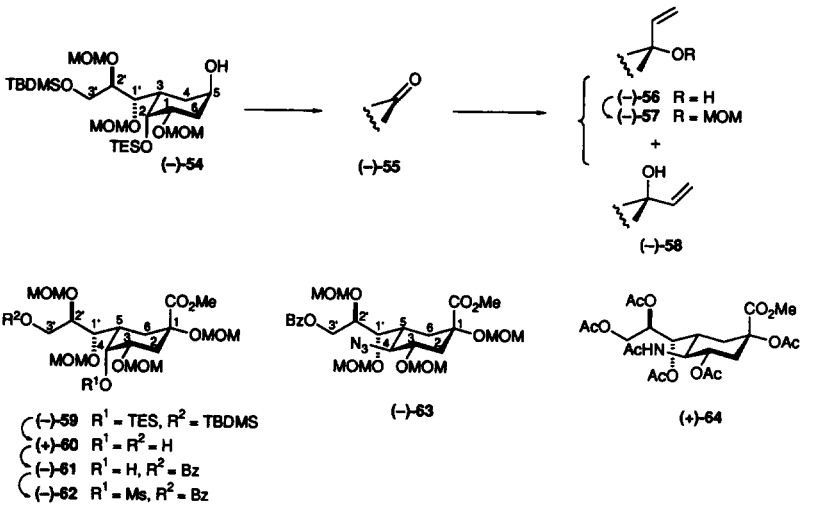
The structures of (−)-**48** and (−)-**50** were determined by converting the corresponding racemic modifications into the respective bicyclic compounds, 2-oxabicyclo[4.4.0]decane derivatives (±)-**52** and (±)-**53**, whose ^{1}H NMR spectra permitted assignment of the stereochemistry of the two hydroxyl groups newly introduced. Thus, after protection of two hydroxyl groups of (±)-**48** obtained from (±)-**11** with MOM groups [→ (±)-**49**], two silyl groups were then deprotected with 1 M tetrabutylammonium fluoride–THF, and the primary hydroxyl group was selectively tosylated. Treatment of the tosylate with methanolic 1 M sodium methoxide in methanol at 50°C resulted in intramolecular attack of the 2-OH at C-3′ to give rise to the bicyclic compound, which was isolated and characterised as the triacetate (±)-**52** (42% overall yield). Likewise, the isomeric (±)-**53** was obtained from (±)-**50** through the tris(methoxymethyl) ether (±)-**51**. The stereochemistry of C-4 and C-5 of (±)-**52** and (±)-**53** was unambiguously established on the basis of the ^{1}H NMR data, thereby



Scheme 5.

establishing the configurations at C-2′ and C-1′ of (−)-**48** and (−)-**50** as shown in Scheme 5.

The benzyl ether group of the tris(methoxymethyl) ether (−)-**49** was hydrogenolysed in the presence of Pd–C in ethanol [→ (−)-**54**], the alcohol was oxidised with PCC and 4A molecular sieves in dichloromethane [→ (−)-**55**], and the resulting ketone was then treated with vinylmagnesium bromide in THF to give after chromatography two vinylcyclohexanes, as expected, the axial-attack (−)-**56** and equatorial-attack products (−)-**58** in 54 and 8% overall yields, respectively. The structure of (−)-**56** was assigned by analogy with the similar Grignard reaction of (±)-**25**, and by the ^{1}H NMR spectra of (−)-**56** and (−)-**58** in which the H-4 signal was more deshielded by the axial 1-OH in (−)-**56** compared to (−)-**58**. Ozonolysis of (−)-**56** gave a complex mixture of products contrary to our expectation. The tertiary hydroxyl group was then first protected with the methoxymethyl group [→ (−)-**57** (93%)], and, on successive ozonolysis, oxidation, and esterification, **57** could be converted into the methyl ester (−)-**59** (93%). Both silyl groups of (−)-**59** were removed with 1 M tetrabutylammonium fluoride–THF [→ (−)-**60** (79%)], the primary hydroxyl group was selectively benzoylated [→ (−)-**61** (88%)], and the 4-hydroxyl was mesylated to give the mesylate (−)-**62** (88%). Treatment of (−)-**62** with sodium azide in DMF at 90°C gave a single azide (−)-**63** (78%). The azido group of (−)-**63** was hydrogenated in the presence of Raney nickel in ethanol containing acetic anhydride, the protecting groups were removed by treatment with 2 M hydrochloric acid at 60°C, the hydroxyl groups were acetylated, and the free acid, some of which was formed partially during hydrolysis, was esterified with diazomethane to give the penta-*O*-acetyl derivative (+)-**64** of the carbocyclic α-Neu5Ac methyl ester in 80% overall yield (Scheme 6). The ^{1}H NMR spectrum supported the structure proposed. *O*-Deacetylation was achieved by treatment with 0.5 M sodium hydroxide at room temperature and, after neutralisation with Amberlite IR-120B (H^+) resin, the free acid **2**



Scheme 6.

was converted into the ammonium salt which was isolated and directly subjected to bioassay. It showed about 30% inhibition against sialidase from *Streptococcus* sp. at a final concentration of 0.1 mmol dm^{-1}, and almost no inhibitory activity against that from *Arthrobacter ureafaciens*.

3. Experimental

General methods.—Mp's were determined on a MEL-TEMP capillary melting-point apparatus and are uncorrected. Optical rotations were measured with a Jasco DIP-370 polarimeter. ^1H NMR spectra were recorded for solutions in $CDCl_3$ (standard: Me_4Si), or CD_3OD, or D_2O with a Jeol JNM-EX 90 (90 MHz), GSX-270 (270 MHz), or JNM-GX 400 FT (400 MHz) instrument, and *J*-values are given in Hz. IR spectra were measured with a Jasco IR-810 or Hitachi FTS-65 spectrometer. High-resolution mass spectra were measured with a Jeol JMS-DX-302 (EI method at 70 eV). TLC was performed on Silica Gel 60 F-254 (E. Merck, Darmstadt). The silica gel used for column chromatography was Wakogel C-300 (Wako Junyaku Kogyo Co., Osaka, Japan; 300 mesh) or Silica Gel 60 KO 70 (Katayama Kagaku Kogyo Co., Osaka, Japan). Organic solutions were dried over anhyd Na_2SO_4 or $MgSO_4$, and concentrated at $< 45°C$ under diminished pressure. Unless otherwise reported, the racemic compounds used in this paper were prepared and characterised according to the procedures described for synthesis of the corresponding optically active compounds.

(1R,2R,4S)-7-Oxabicyclo[2.2.1]hept-5-ene-2-carboxylic acid [7] [(+)-**5**].—The racemic *endo*-adduct [15] of furan and acrylic acid was conventionally converted into a mixture of (*S*)-(−)-α-methylbenzylamine salts, which was recrystallised from EtOH

repeatedly, giving the pure salt of (+)-**5**: $[\alpha]_D^{25}$ +70° (*c* 1.0, MeOH). The free acid was obtained by treatment of aqueous solution of the amine salt with Dowex 50W-X2 (H^+) resin: $[\alpha]_D^{25}$ +117° (*c* 1.0, H_2O).

(1R,4R,5R,6R,8S)-5-Iodo-3,7-dioxatricyclo[4.2.1.0^{4,8}]nonan-2-one [(−)-**6**].—To a solution of (+)-**5** (45.0 g, 0.32 mol) in satd aq $NaHCO_3$ (1.1 L, 0.35 mol/L) was added dropwise a THF solution of I_2 (0.22 L, 1.6 mol/L) under ice-cooling, and the mixture was stirred for 2 h at room temperature. The precipitates were collected by filtration and then dissolved in CH_2Cl_2. The solution was washed with satd aq Na_2SO_3 and H_2O, dried, and evaporated to give the iodolactone (−)-**6** (73.4 g, 86%) as crystals; mp 117–119°C (from EtOH); $[\alpha]_D^{25}$ −113° (*c* 1.04, $CHCl_3$); ^{1}H NMR data (90 MHz, $CDCl_3$): δ 5.62 (t, 1 H, $J_{1,8} = J_{4,8} = 5.0$ Hz, H-8), 5.19 (d, 1 H, H-1), 4.87 (d, 1 H, $J_{5exo,6}$ 5.0 Hz, H-6), 4.35 (s, 1 H, H-9), 2.75 (ddd, 1 H, $J_{4,5exo}$ 6.0, J_{gem} 10.0 Hz, H-5exo), 2.30–1.83 (m, 2 H, H-4,5endo). Anal. Calcd for $C_7H_7IO_3$: C, 31.60; H, 2.65. Found: C, 31.77; H, 2.87.

The racemic (±)-**6** (100.6 g, 88%) was obtained similarly from racemic (±)-**5** (60.0 g); mp 151–152°C (from EtOH) [lit. [16] mp 157–157.5°C (from EtOAc)].

(1S,2S,4R,6S)-2-Acetoxy-6-acetoxymethyl-7-oxabicyclo[2.2.1]heptane [(−)-**7**].—To an ice-cooled solution of the iodolactone (−)-**6** (72.8 g, 0.27 mol) in THF (300 mL) was added a suspension of $LiAlH_4$ (20.5 g, 0.54 mol) in THF (180 mL), and then the mixture was stirred for 3 days at 60°C. To the mixture were added in turn carefully H_2O (25 mL), aq 15% NaOH (30 mL), H_2O (50 mL), and acetone–H_2O (300 mL), and an insoluble material was removed by filtration through a Celite bed. After neutralisation with 4 M HCl, the filtrate was evaporated and the residue was treated with Ac_2O (100 mL) and pyridine (200 mL) overnight at room temperature. After treatment with MeOH (10 mL), the mixture was evaporated, the residue was dissolved in EtOAc (400 mL), and the solution was washed successively with 1 M HCl, H_2O, and saline, dried, and concentrated. The residue was crystallised from EtOAc–hexane to give (−)-**7** (38.0 g, 61%) as crystals; mp 49–51°C; $[\alpha]_D^{25}$ −6.2° (*c* 1.0, $CHCl_3$); ^{1}H NMR data (90 MHz, $CDCl_3$): δ 5.23 (ddt, 1 H, $J_{1,2} = J_{2,3endo} = 4.5$, $J_{2,3exo}$ 11.3 Hz, H-2), 4.82–4.63 (m, 2 H, H-1,4), 4.48 (d, 2 H, $J_{6,8}$ 8.8 Hz, H-8,8), 2.9–1.8 (m, 3 H, H-3exo,5exo,6), 2.10 (s, 6 H, 2 Ac) and 1.51–1.18 (m, 2 H, H-3endo,5endo). Anal. Calcd for $C_{11}H_{16}O_5$: C, 57.88; H, 7.07. Found: C, 58.00; H, 6.93.

The racemic (±)-**7** (0.74 g, 86%) was obtained similarly from the racemic (±)-**6** (1.0 g); mp 45–46°C (from EtOAc–hexane) (lit. [9] mp 48–49°C).

*(1S,2R,3S,5R)-2,5-Diacetoxy-3-acetoxymethylcyclohexan-1-ol (1,4,6-tri-O-acetyl-2-deoxy-5a-carba-α-*L*-lyxo-hexopyranose)* [(+)-(**8**)] *and (1S,2S,3S,5S)-1,2-diacetoxy-3-acetoxymethyl-5-chlorocyclohexane (3,4,6-tri-O-acetyl-2-deoxy-5a-carba-β-*L*-xylo-hexopyranosyl chloride)* [(−)-**9**].—To a solution of the acetate (−)-**7** (28.7 g, 0.13 mol) in CH_2Cl_2 (550 mL) were added AcOH (72 mL) and titanium tetrachloride (174 mL) at 0°C, and the mixture was stirred overnight at room temperature. The mixture was poured into ice–H_2O and the solution was extracted with CH_2Cl_2. The extracts were washed with satd aq $NaHCO_3$ and H_2O, dried, and evaporated. The residue was chromatographed on a column of silica gel (300 g) with 1:3 butanone–toluene as eluent to give, first, the triacetate (+)-**8** (13.3 g, 37%); mp 83–84°C; $[\alpha]_D^{25}$ +5.5° (*c* 1.0, $CHCl_3$); selected ^{1}H NMR data (90 MHz; $CDCl_3$): δ 5.49 (t, 1 H, $J_{1,2} = J_{2,3} = 3.0$ Hz,

H-2), 5.37 (m, 1 H, H-5), 4.12 (dd, 1 H, $J_{3,4ax}$ 9.0, J_{gem} 12.0 Hz, H-4*ax*), 3.98 (dd, 1 H, $J_{3,4eq}$ 6.8 Hz, H-4*eq*), 2.45 (d, 1 H, $J_{1,OH}$ 6.0 Hz, OH), 2.18, 2.12 (2 s, 3 and 6 H, 3 Ac). Anal. Calcd for $C_{13}H_{20}O_7$: C, 54.16; H, 6.99. Found: C, 54.00; H, 6.87.

The second fraction gave the chloride (−)-**9** (7.18 g, 19%); mp 66–67°C (from diethyl ether–petroleum ether); $[\alpha]_D^{25}$ −6.2° (*c* 1.2, $CHCl_3$); ^{1}H NMR data (400 MHz; $CDCl_3$): δ 4.96 (dd, 1 H, $J_{1,2}$ 9.8, $J_{2,3}$ 10.8 Hz, H-2), 4.83 (ddd, 1 H, $J_{1,6ax}$ 11.7, $J_{1,6eq}$ 4.4 Hz, H-1), 4.08 (dd, 1 H, $J_{3,7a}$ 5.4, J_{gem} 11.2 Hz, H-7a), 3.94 (dd, 1 H, $J_{3,7b}$ 3.4 Hz, H-7b), 3.91 (tt, 1 H, $J_{4ax,5} = J_{5,6ax} = 12.2$, $J_{4eq,5} = J_{5,6eq} = 4.4$ Hz, H-5), 2.57 (ddt, $J_{4eq,6eq}$ 2.9, J_{gem} 12.2 Hz, H-6*eq*), 2.31 (ddt, 1 H, $J_{3,4eq}$ 4.4, J_{gem} 13.2 Hz, H-4*eq*), 2.07, 2.04, 2.02 (3 s, each 3 H, 3 Ac), 1.94 (m, 1 H, H-3), 1.81 (dt, 1 H, H-6*ax*), 1.74 (dt, 1 H, H-4*ax*). Anal. Calcd for $C_{13}H_{19}ClO_6$: C, 50.90; H, 6.24. Found: C, 50.70; H, 6.20.

The racemic (±)-**7** (20.0 g, 87.6 mmol) was similarly converted into (±)-**8** (9.74 g, 39%), mp 83–84°C (from EtOH), and (±)-**9** (9.75 g, 39%), mp 65.5–67°C (from diethyl ether–petroleum ether).

*(1*S*,2*R*,3*S*,5*R*)-2,5-Diacetoxy-3-acetoxymethyl-1-(methoxymethoxy)cyclohexane (1,4,6-tri-*O*-acetyl-2-deoxy-3-*O*-methoxymethyl-5a-carba-α-*L*-lyxo-hexopyranose)* [(−)-**10**].—A mixture of (+)-**8** (2.00 g, 6.94 mmol), *N*,*N*-diisopropylethylamine (1.81 mL, 10.4 mmol), chloromethyl methyl ether (0.69 mL, 9.08 mmol), and CH_2Cl_2 (30 mL) was refluxed for 2 days. After cooling, the mixture was poured into 1 M HCl and the organic layer was washed with satd aq $NaHCO_3$ and H_2O, dried, and evaporated. The residue was chromatographed (60 g, 1:7 butanone–toluene) to give (−)-**10** (2.14 g, 93%) as a syrup; $[\alpha]_D^{25}$ −64.4° (*c* 1.00, $CHCl_3$); selected ^{1}H NMR data (90 MHz, $CDCl_3$): δ 5.68 (bt, $J_{1,2} = J_{2,3} = 3.0$ Hz, H-2), 5.43 (quintet, 1 H, *J* 3.0 Hz, H-5), 4.90 and 4.64 (ABq, each 1 H, J_{gem} 7.5 Hz, CH_2OCH_3), 3.48 (s, 3 H, CH_2OCH_3), 2.17, 2.13, and 2.12 (3 s, each 3 H, 3 Ac). Anal. Calcd for $C_{15}H_{24}O_8$: C, 54.21; H, 7.28. Found: C, 54.19; H, 7.21.

*(1*R*,6*S*,8*R*,10*S*)-8-Benzyloxy-10-methoxymethoxy-3,3-dimethyl-2,4-dioxabicyclo[4.4.0]decane (1-*O*-benzyl-2-deoxy-4,6-*O*-isopropylidene-3-*O*-methoxymethyl-5a-carba-*L*-lyxo-hexopyranose)* [(−)-**14**].—Compound (−)-**10** (3.52 g, 10.6 mmol) was treated with 1 M methanolic NaOMe (10.6 mL) in MeOH (70 mL) for 8 h at room temperature. After neutralisation with Amberlite IR-120B (H^+) resin, the mixture was evaporated to give a crude triol (2.51 g), which, without purification, was treated with 2,2-dimethoxypropane (13.0 mL, 0.10 mmol) and *p*-toluenesulfonic acid monohydrate (PTSA) (150 mg) in dry DMF (50 mL) for 2 h at room temperature. Excess of $NaHCO_3$ was added, and the mixture was evaporated. The residue was partitioned between EtOAc and H_2O, and the organic layer was washed with H_2O, dried, and evaporated. The product was treated with 60% NaH (0.85 g, ca. 2 equiv) in dry DMF (50 mL) for 30 min at 0°C, and then benzyl bromide (1.9 mL, 1.5 equiv) was added to the mixture, which was further stirred overnight at room temperature. After addition of MeOH, the mixture was evaporated and the residue was taken up in EtOAc, which was washed with H_2O, dried, and evaporated. The product was chromatographed (1:15 butanone–toluene) to give (−)-**14** (3.21 g, 90%) as a syrup; $[\alpha]_D^{25}$ −12.9° (*c* 1.95, $CHCl_3$); selected ^{1}H NMR (90 MHz, $CDCl_3$): δ 7.61 (s, 5 H, Ph), 4.85 and 4.67 (2 s, each 2 H, CH_2OCH_3 and CH_2Ph), 4.47 (bs, 1 H, H-1), 4.25 (dd, 1 H, $J_{5a,6}$ 3.0, J_{gem}

12.0 Hz, H-5a), 3.63 (d, 1 H, H-5b), 1.53 and 1.48 (2 s, each 3 H, CMe_2). Anal. Calcd for $C_{19}H_{28}O_5$: C, 67.83; H, 8.39. Found: C, 67.71; H, 8.27.

*(1S,2R,3S,5R)-3-Benzoyloxymethyl-5-benzyloxy-1-(methoxymethoxy)cyclohexan-2-ol (6-O-benzoyl-1-O-benzyl-3-O-methoxymethyl-5a-carba-α-*L*-lyxo-hexopyranose)* [(−)-**11**].—Compound (−)-**14** (3.50 g, 10.4 mmol) was treated with aq 80% AcOH (80 mL) for 1 h at room temperature and then evaporated. The crude diol (3.03 g) was dissolved in dry pyridine (60 mL) and treated with benzoyl chloride (1.45 mL, 12.5 mmol) for 30 min at 0°C. After addition of MeOH, the mixture was evaporated and the residue was chromatographed (1:10 butanone–toluene) to give (−)-**11** (4.00 g, 96%) as a syrup; $[\alpha]_D^{25}$ −5.9 (*c* 1.48, $CHCl_3$); selected ^{1}H NMR (90 MHz, $CDCl_3$): δ 4.64 and 4.45 (2 s, each 2 H, CH_2OCH_3 and CH_2Ph), 3.34 (s, 3 H, CH_2OCH_3). Anal. Calcd for $C_{23}H_{28}O_6$: C, 68.98; H, 7.05. Found: C, 68.97; H, 6.98.

(1S,2R*,3S*,5R*)-3-Benzoyloxymethyl-5-benzyloxy-2-mesyloxy-1-(methoxymethoxy)cyclohexane (6-O-benzoyl-1-O-benzyl-2-deoxy-4-O-mesyl-3-O-methoxymethyl-5a-carba-α-*DL*-lyxo-heptopyranose)* [(±)-**13**].—Compound (±)-**11** (28 mg, 0.07 mmol) was treated with mesyl chloride (10 mL, 0.13 mmol) in dry pyridine (1 mL) for 30 h at room temperature. After addition of MeOH at 0°C, the mixture was evaporated and the residue was extracted with EtOAc. The solution was washed with H_2O, dried, and evaporated. The product was purified by preparative TLC (1:4 butanone–hexane) to give (±)-**13** (27 mg, 82%) as a syrup; selected ^{1}H NMR data (90 MHz, $CDCl_3$): δ 5.45 (bs, 1 H, H-2), 3.52 (s, 3 H, CH_2OCH_3), 3.23 (s, 3 H, Ms). Anal. Calcd for $C_{24}H_{30}O_8S$: C, 60.23; H, 6.32. Found: C, 60.24; H, 6.27.

(1S,3S*,6S*,8S*,10S*)-8-Chloro-3-phenyl-2,4-dioxabicyclo[4.4.0]decan-10-ol (4,6-O-benzylidene-1-chloro-1,2-dideoxy-5a-carba-β-*DL*-xylo-hexopyranose)* [(±)-**15**].—Compound (±)-**9** (500 mg, 1.63 mmol) was *O*-deacetylated with methanolic NaOMe conventionally and the crude triol formed was treated with α,α-dimethoxytoluene (3.0 mL, 4.4 mmol) and PTSA (10 mg) in DMF (7 mL) for 4 h at 50°C under diminished pressure (aspirator). After neutralisation with $NaHCO_3$, the mixture was poured into ice–H_2O and extracted with EtOAc. The extract was washed with H_2O thoroughly, dried, and evaporated. The residue was chromatographed (15 g, 1:25 butanone–toluene) to give (±)-**15** (393 mg, 95%) as crystals; mp 140–142°C (from diethyl ether); selected ^{1}H NMR data (90 MHz, 1:1 $CDCl_3$–CD_3OD): δ 5.90 (s, 1 H, C*H*Ph), 2.33 (m, 1 H, H-6). Anal. Calcd for $C_{14}H_{17}ClO_3$: C, 62.57; H, 6.38. Found: C, 62.86; H, 6.44.

(1S,3S*,6S*,8S*,10S*)-8-Chloro-10-methoxymethoxy-3-phenyl-2,4-dioxabicyclo[4.4.0]decane (4,6-O-benzylidene-1-chloro-1,2-dideoxy-3-O-methoxymethyl-5a-carba-β-*DL*-xylo-hexopyranose)* [(±)-**16**].—Compound (±)-**15** (620 mg, 2.31 mmol) was treated with *N*,*N*-diisopropylethylamine (0.60 mL, 3.44 mmol) and chloromethyl methyl ether (0.25 mL, 3.29 mmol) in CH_2Cl_2 (15 mL) for 16 h at reflux temperature. After the usual processing, the product was chromatographed (10 g, 1:10 butanone–toluene) to give (±)-**16** (700 mg, 97%) as crystals; mp 88–89°C (from diethyl ether); selected ^{1}H NMR data (90 MHz, $CDCl_3$): δ 5.55 (s, 1 H, C*H*Ph), 4.84 and 4.68 (ABq, each 1 H, J_{gem} 6.8 Hz, CH_2OCH_3), 4.12 (dd, 1 H, $J_{5a,6}$ 4.1, J_{gem} 11.0 Hz, H-5a), 3.56 (d, 1 H, H-5b), 3.40 (s, 3 H, CH_2OCH_3), 2.59 (m, 1 H, H-6). Anal. Calcd for $C_{16}H_{20}ClO_4$: C, 61.64; H, 6.47. Found: C, 61.83; H, 6.79.

(1S,3S*,6S*,8R*,10S*)-8-Benzoyloxy-10-methoxymethoxy-3-phenyl-2,4-di-*

*oxabicyclo[4.4.0]decane (1-O-benzoyl-4,6-O-benzylidene-2-deoxy-3-O-methoxymethyl-5a-carba-α-*DL-xylo-*hexopyranose)* [(±)-**17**].—A mixture of (±)-**16** (1.00 g, 3.21 mmol) and NaOBz (3.60 g, 25 mmol) in dry DMF (20 mL) was stirred for 20 h at 130°C. After cooling, the mixture was poured into ice–H_2O and extracted with CH_2Cl_2. The product was chromatographed (40 g, 1:20 butanone–toluene) to give (±)-**17** (0.76 g, 60%) as a syrup; selected ^{1}H NMR data (90 MHz, $CDCl_3$): δ 5.65 (s, 1 H, C*H*Ph), 5.48 (quintet, *J* 3 Hz, H-8), 4.89 and 4.72 (ABq, each 1 H, J_{gem} 6.7 Hz, CH_2OCH_3), 4.18 (dd, 1 H, $J_{5a,6}$ 4.7, J_{gem} 10.8 Hz, H-5a), 3.60 (d, 1 H, H-5b), 3.35 (s, 3 H, CH_2OCH_3). Anal. Calcd for $C_{23}H_{26}O_6$: C, 69.33; H, 6.58. Found: C, 68.98; H, 6.33.

(1S,3S*,6S*,8R*,10S*)-8-Benzyloxy-10-methoxymethoxy-3-phenyl-2,4-dioxabicyclo[4.4.0]decane (1-O-benzyl-4,6-O-benzylidene-2-deoxy-3-O-methoxymethyl-5a-carba-α-*DL-xylo-*hexopyranose)* [(±)-**18**].—Compound (±)-**17** (620 mg, 1.56 mmol) was *O*-deacylated with 1 M methanolic NaOMe (10 mL) conventionally. The product was chromatographed (10 g, 1:10 butanone–toluene) to give the alcohol, which was treated with 60% NaH (95 mg, 2.4 mmol) in dry DMF (6 mL) at 0°C and then with benzyl bromide (0.28 mL, 2.4 mmol) for 2 h at room temperature. After the usual processing, the product was chromatographed (24 g, 1:15 butanone–toluene) to give (±)-**18** (480 mg, 80%) as a syrup; selected ^{1}H NMR data (90 MHz, $CDCl_3$): δ 5.80 (s, 1 H, C*H*Ph), 5.08 and 4.94 (ABq, each 1 H, J_{gem} 6.0 Hz, CH_2OCH_3), 4.72 (s, 2 H, CH_2Ph), 3.50 (s, 3 H, CH_2OCH_3). Anal. Calcd for $C_{23}H_{28}O_5$: C, 71.85; H, 7.34. Found: C, 71.90; H, 7.37.

(1S,2S*,3S*,5R*)-5-Benzyloxy-2-mesyloxy-3-mesyloxymethyl-1-(methoxymethoxy)cyclohexane (1-O-benzyl-2-deoxy-4,6-di-O-mesyl-3-O-methoxymethyl-5a-carba-α-*DL-xylo-*hexopyranose)* [(±)-**19**].—Compound (±)-**18** (350 mg, 0.91 mmol) was treated with aq 80% AcOH (10 mL) overnight at room temperature. After the usual processing, the diol obtained was dissolved in dry pyridine (8 mL) and treated with mesyl chloride (0.28 mL, 3.6 mmol) for 2 days at room temperature. After addition of MeOH, the mixture was evaporated and the residue was chromatographed (15 g, 1:15 butanone–toluene) to give (±)-**19** (287 mg, 70%) as crystals; mp 82–85°C (from EtOH); selected ^{1}H NMR data (90 MHz, $CDCl_3$): δ 4.83 and 4.63 (2 s, each 2 H, CH_2OCH_3 and CH_2Ph), 3.50 (s, 3 H, CH_2OCH_3), 3.18 and 3.12 (2 s, each 3 H, 2 OMs). Anal. Calcd for $C_{18}H_{28}O_9S_2$: C, 47.77; H, 6.24. Found: C, 47.56; H, 6.00.

(1S,2R*,3S*,5R*)-2-Benzoyloxy-3-benzoyloxymethyl-5-benzyloxy-1-(methoxymethoxy)cyclohexane (4,6-di-O-benzoyl-1-O-benzyl-2-deoxy-3-O-methoxymethyl-5a-carba-α-*DL-lyxo-*hexopyranose)* [(±)-**12**].—(*a*) A mixture of (±)-**19** (160 mg, 0.35 mmol), NaOBz (510 mg, 3.54 mmol), and DMF (10 mL) was stirred for 2 days at 120°C. After cooling, the mixture was poured onto ice–H_2O and extracted with EtOAc, and the extracts were dried and evaporated. The residue was chromatographed on a column of silica gel (6 g, 1:5 butanone–toluene) to give (+)-**12** (143 mg, 80%); mp 121–123°C (from EtOH); selected ^{1}H NMR data (90 MHz, $CDCl_3$): δ 5.90 (bs, 1 H, H-2), 4.67 (ABq, 2 H, J_{gem} 7.0 Hz, CH_2OCH_3), 4.56 (s, 2 H, PhCH_2), 3.35 (s, 3 H, CH_2OCH_3), 2.64 (m, 1 H, H-3). Anal. Calcd for $C_{30}H_{32}O_7$: C, 71.41; H, 6.39. Found: C, 71.22; H, 6.36.

(*b*) Compound (±)-**11** (73 mg, 0.18 mmol) was treated with benzoyl chloride (42 mL, 0.36 mmol) in dry pyridine (2 mL) for 3 days at 50°C. After cooling, MeOH (3 mL)

was added and the mixture was evaporated. The residue was similarly chromatographed on silica gel to give (±)-**12** (78 mg, 85%), identical with the compound obtained from (±)-**19** in all respects.

(1R,2S*,3R*,5S*)-1,2,5-Tribenzyloxy-3-(triphenyloxymethyl)cyclohexane (1,3,4-tri-O-benzyl-2-deoxy-6-O-trityl-5a-carba-α-*DL-lyxo-*hexopyranose)* [(±)-**20**].—Compound (±)-**8** (3.00 g, 10.4 mmol) was *O*-deacetylated with methanolic NaOMe conventionally, and the tetraol (1.83 g) formed was dissolved in dry pyridine (30 mL) and treated with triphenylmethyl chloride (3.78 g, 13.6 mmol) overnight at room temperature. After addition of MeOH, the mixture was evaporated and the product was chromatographed (1:10 EtOH–toluene) to give the triphenylmethyl ether (3.55 g). It was benzylated with 60% NaH (1.5 g, 38 mmol) and benzyl bromide (4.0 mL, 34 mmol) in dry DMF (60 mL) for 33 h at room temperature. After the usual processing, the product was chromatographed (1:20 EtOAc–hexane) to give (±)-**20** (4.9 g, 70%) as a syrup; selected ^{1}H NMR data (90 MHz, $CDCl_3$): δ 5.08 and 4.57 (ABq, each 1 H, J_{gem} 12.0 Hz, CH_2Ph), 4.80 and 4.60 (s, each 2 H, 2 CH_2Ph), 4.35 (bs, 1 H, H-2), 3.33 (dd, 1 H, $J_{3,7a} = J_{gem} = 9.0$ Hz, H-7a), 3.20 (dd, 1 H, $J_{3,7b}$ 6.0 Hz, H-7b). Anal. Calcd for $C_{47}H_{46}O_4$: C, 83.65; H, 6.87. Found: C, 83.24; H, 6.93.

(1R,2S*,3R*,5S*)-1,2,5-Tribenzyloxy-3-(hydroxymethyl)cyclohexane (1,3,4-tri-O-benzyl-2-deoxy-5a-carba-α-*DL-lyxo-*hexopyranose)* [(±)-**21**].—A mixture of (±)-**20** (4.90 g, 7.26 mmol), EtOH (20 mL), THF (60 mL), and 1 M H_2SO_4 (30 mL) was refluxed for 3.5 h. After cooling, the mixture was neutralised with aq $NaHCO_3$ and then concentrated to one-third volume. The mixture was extracted with CH_2Cl_2 and the extract was dried and evaporated. The residue was chromatographed (1:4 EtOAc–hexane) to give (±)-**21** (2.74 g, 87%) as a syrup; selected ^{1}H NMR data (90 MHz, $CDCl_3$): δ 5.18 and 4.78 (ABq, each 1 H, J_{gem} 12.0 Hz, CH_2Ph), 4.75 and 4.60 (2 s, each 2 H, 2 CH_2Ph), 4.23 (bs, 1 H, H-2), 3.70 (d, 2 H, $J_{3,7}$ 5.6 Hz, H-7,7), 2.03 (bs, 1 H, OH). Anal. Calcd for $C_{28}H_{32}O_4$: C, 77.75; H, 7.46. Found: C, 77.37; H, 7.43.

(1R,2S*,3R*,5S*)-1,2,5-Tribenzyloxy-3-vinylcyclohexane (1,3,4-tri-*O*-benzyl-2,6,7-trideoxy-5a-carba-α-*DL-lyxo-*hept-6-enopyranose)* [(±)-**22**].—To a solution of (±)-**21** (1.13 g, 2.61 mmol) in dry CH_2Cl_2 (20 mL) was added pyridinium chlorochromate (PCC)–alumina (7.8 g), and the mixture was stirred for 2 h at room temperature. An insoluble material was immediately removed by filtration, the filtrate was evaporated, and the residue was passed through a short column of silica gel with excess of diethyl ether as eluent to give after evaporation the crude aldehyde. To a suspension of methyltriphenylphosphonium bromide (2.35 g, 6.48 mmol) in dry THF (15 mL) was added 1.62 M butyllithium–hexane (4.00 mL, 6.5 mmol), and the mixture was stirred for 20 min at room temperature. To the mixture was added dropwise a solution of the aldehyde in THF (14 mL), and it was stirred vigorously for 40 min at room temperature. The mixture was diluted with EtOAc, washed with H_2O, and evaporated. The residue was chromatographed (1:30 EtOAc–hexane) to give (±)-**22** (826 mg, 74%) as a syrup; selected ^{1}H NMR data (90 MHz, $CDCl_3$): δ 6.19 (ddd, 1 H, J_{cis} 11.0, J_{trans} 18.0, $J_{3,1'}$ 8.0 Hz, H-1′), 5.13 and 4.75 (ABq, each 1 H, CH_2Ph), 4.73 and 4.60 (s, each 2 H, 2 CH_2Ph). Anal. Calcd for $C_{29}H_{32}O_3$: C, 81.27; H, 7.53. Found: C, 81.21; H, 7.52.

*Di-*O*-cyclohexylidene derivative* [(±)-**23**] *of (1R*,2S*,3R*,5S*)-1,2,5-trihydroxy-3-[(1S*)-1,2-dihydroxyethyl]cyclohexane and that* [(±)-**24**] *of (1R*,2S*,3R*,5S*)-*

1,2,5-trihydroxy-3-[(1R)-1,2-dihydroxyethyl]cyclohexane (3,4:6,7-di-O-cyclohexylidene-2-deoxy-5a-carba-α-*DL*-manno- and -gulo-heptopyranoses).*—To a stirred mixture of osmium tetraoxide–1-butanol (19 mL, 0.02 mmol L^{-1}), *tert*-butyl alcohol (8 mL), THF (42 mL), and H_2O (2 mL) was added dropwise a solution of (±)-**22** (3.3 g, 7.7 mmol) in THF (10 mL), and the mixture was stirred for 4.5 h at room temperature. Silica gel (20 g), H_2O (1.5 mL), EtOAc (15 mL), and $NaHSO_4$ (2.8 g) were added in turn, and the mixture was passed through a silica gel bed. The filtrate was evaporated, the residue was dissolved in EtOH (40 mL) containing AcOH (4 mL), and the solution was hydrogenated in the presence of palladium hydroxide overnight at room temperature under atmospheric pressure of H_2. The catalyst was removed by filtration and the filtrate was evaporated. The residue was then treated with α,α-dimethoxycyclohexane (4.2 mL) and PTSA (100 mg) in dry DMF (40 mL) for 1 h at 50°C under diminished pressure (aspirator). TLC (1:1 EtOAc–hexane) indicated the formation of two di-*O*-cyclohexylidene compounds (R_f 0.46 and 0.50) together with mono-*O*-cyclohexylidene compound (R_f 0.06). After neutralisation with solid Na_2CO_3, the mixture was diluted with EtOAc, and the solution was washed with H_2O, dried, and evaporated. The residual products were roughly fractionated by chromatography (1:3 EtOAc–hexane) to give the slower-moving component, which was *O*-decyclohexylidenated with 1 M HCl and again subjected to the above reaction conditons. After this recycling process had been repeated three times, the products were combined and chromatographed (1:3 EtOAc–hexane) to give (±)-**23** (2.0 g, 75%) and (±)-**24** (0.49 g, 18%). Anal. Calcd for $C_{20}H_{32}O_5$: C, 68.15; H, 9.22. Found: for (±)-**23**, C, 68.15; H, 8.98; for (±)-**24**, C, 68.35; H, 8.79.

*Di-*O*-cyclohexylidene derivative* [(±)-**25**] *of (3R*,4S*,5R*)-3,4-dihydroxy-5-[(1S*)-1,2-dihydroxyethyl]cyclohexan-1-one (3,4:6,7-di-*O*-cyclohexylidene-2-deoxy-5a-carba-*DL*-manno-heptopyranolactone).*—To a solution of (±)-**23** (323 mg, 0.92 mmol) in CH_2Cl_2 (7 mL) was added PCC–alumina (2.8 g), and the mixture was stirred for 1 h at room temperature. An insoluble material was removed by filtration through a silica gel column with EtOAc. The filtrate was evaporated and the residue was chromatographed (diethyl ether) to give (±)-**25** (321 mg, 100%) as crystals; mp 86.5–87°C (from petroleum ether); ^1H NMR data (400 MHz, $CDCl_3$): δ 4.68 (ddd, 1 H, $J_{2a,3}$ 2.4, $J_{2b,3}$ 3.4, $J_{3,4}$ 7.3 Hz, H-3), 4.62 (ddd, 1 H, $J_{4,5}$ 2.4, $J_{4,6a}$ 1.5 Hz, H-4), 4.23 (m, 1 H, H-1′), 4.03 (dd, 1 H, $J_{1',2'a}$ 6.0, J_{gem} 8.5 Hz, H-2′a), 3.67 (dd, 1 H, $J_{1',2'b}$ 7.0 Hz, H-2′b), 2.69 (dd, 1 H, J_{gem} 16.6 Hz, H-2a), 2.44 (dd, 1 H, H-2b), 2.29 (dd, 1 H, $J_{5,6b}$ 14.0, J_{gem} 18.0 Hz, H-6b), 2.14 (dd, 1 H, $J_{5,6a}$ 3.0 Hz, H-6a), 2.14 (m, 1 H, H-5), 1.64–1.34 (m, 20 H, 2 CMe_2). Anal. Calcd for $C_{20}H_{30}O_5$: C, 68.55; H, 8.63. Found: C, 68.49; H, 8.67.

*Di-*O*-cyclohexylidene derivative* [(±)-**30**] *of (3R*,4S*,5R*)-3,4-dihydroxy-5-[(1R*)-1,2-dihydroxyethyl]cyclohexan-1-one (3,4:6,7-di-*O*-cyclohexylidene-2-deoxy-5a-carba-*DL*-gulo-heptopyranolactone).*—Compound (±)-**24** (0.732 g, 2.08 mmol) was oxidised as described for preparation of (±)-**25**, to give (±)-**30** (726 mg, 100%) as crystals; mp 94–95°C (from petroleum ether–hexane). Anal. Calcd for $C_{20}H_{30}O_5$: C, 68.55; H, 8.63. Found: C, 68.14; H, 8.55.

*Di-*O*-cyclohexylidene derivative* [(±)-**26**] *of (1R*,2S*,3R*,5S*)-1,2,5-trihydroxy-3-[(1S*)-1,2-dihydroxyethyl]-5-vinylcyclohexane and that* [(±)-**27**] *of the (1R*,2S*,3R*,5R*)-isomer (5,6:8,9-di-*O*-cyclohexylidene-1,2,4-trideoxy-7a-carba-α-*

*and -β-*DL-manno-*non-1-en-3-ulopyranose).*—To a stirred suspension of 1 M vinylmagnesium bromide–hexane (8 mL, 8.00 mmol) was added dropwise a solution of (±)-**25** (0.929 g, 2.65 mmol) in dry THF (10 mL) at 0°C. After 10 min, aq satd NH_4Cl was added and the mixture was extracted with EtOAc. The extract was washed with H_2O, dried, and evaporated. The residue was chromatographed (1:5 EtOAc–hexane) to give (±)-**26** (0.118 g, 12%) and (±)-**27** (0.717 g, 72%), together with the unidentified substitution product (0.10 g).

For (±)-**26**: selected ^{1}H NMR data (90 MHz, $CDCl_3$): δ 6.17 (dd, 1 H, C*H* = CH_2), 5.39 (dd, 1 H, J_{trans} 18.0, J_{gem} 2.0 Hz, CH = C*H*$_{trans}$), 5.21 (dd, 1 H, J_{cis} 11.0 Hz, CH = C*H*$_{cis}$). Anal. Calcd for $(C_{22}H_{34}O_5)^+$: 378.2405. Found: *m/z* 378.2418 $(M)^+$.

For (±)-**27**: selected ^{1}H NMR data (90 MHz, $CDCl_3$): δ 6.08 (dd, 1 H, C*H* = CH_2), 5.44 (dd, 1 H, J_{trans} 18.0, J_{gem} 2.0 Hz, CH = C*H*$_{trans}$), 5.26 (dd, 1 H, J_{cis} 11.0 Hz, CH = C*H*$_{cis}$), 2.85 (s, 1 H, Ph). Anal. Found: *m/z* 378.2421 $(M)^+$.

*Di-*O*-cyclohexylidene derivative* [(±)-**28**] *of methyl (1*S*,*3*R*,*4*S*,*5*R*)*-1,3,4-trihydroxy-5-[(1*S*)*-1,2-dihydroxyethyl]cyclohexane-1-carboxylate (methyl 4,5:7,8-di-*O*-cyclohexylidene-3-deoxy-6a-carba-α-*DL-manno-*2-octulopyranosonate).*—Into a solution of (±)-**26** (196 mg, 0.52 mmol) in MeOH (8 mL) was bubbled O_3 for 7 min at −78°C and then dry air was introduced for 30 min. An aqueous solution (8 mL) containing Na_2HPO_4 (0.88 g), $NaClO_2$ (0.93 g, 10.3 mmol), and NH_2SO_2OH (1.25 g, 12.9 mmol) was added at this temperature, and the mixture was stirred for 1 h at room temperature and then evaporated. The residue was extracted with CH_2Cl_2 and the extracts were evaporated. The product was dissolved in diethyl ether (5 mL) and treated with diazomethane at 0°C. The product was chromatographed (1:8 butanone–toluene) to give (±)-**28** (171 mg, 80%) as a syrup; selected ^{1}H NMR data (400 MHz, $CDCl_3$): δ 4.03 (dd, 1 H, $J_{1',2'a}$ 6.6, J_{gem} 8.4 Hz, H-2′a), 3.80 (s, 3 H, CO_2Me), 3.73 (dd, 1 H, $J_{1',2'b}$ 7.4 Hz, H-2′b), 2.92 (s, 1 H, OH), 2.54 (ddt, 1 H, $J_{4,5}$ 3.4, $J_{5,6ax}$ 13.2, $J_{5,1'}$ 6.8 Hz, H-5), 1.95 [ddd, 1 H, $J_{2eq,3}$ 6.8, J_{gem} 13.2, $J_{2eq,4}$ ($J_{2eq,6eq}$) 2.0 Hz, H-2*eq*], 1.84 (t, 1 H, J_{gem} 13.2 Hz, H-6*ax*), 1.80 (dd, 1 H, $J_{2ax,3}$ 9.0 Hz, H-2*ax*), 1.70–1.30 (20 H, 2 cyclohexylidene). Anal. Calcd for $(C_{22}H_{34}O_7)^+$: 410.2302. Found: *m/z* 410.2283 $(M)^+$.

*Di-*O*-cyclohexylidene derivative* [(±)-**29**] *of methyl (1*R*,*3*R*,*4*S*,*5*R*)*-1,3,4-trihydroxy-5-[(1*S*)*-1,2-dihydroxyethyl]cyclohexane-1-carboxylate (methyl 4,5:7,8-di-*O*-cyclohexylidene-3-deoxy-6a-carba-β-*DL-manno-*2-octulopyranosonate).*—Compound (±)-**27** (0.424 mg, 1.12 mmol) was treated with ozone as described for preparation of (±)-**28** and the product was likewise oxidised and esterified to give (±)-**29** (0.427 g, 93%) as a syrup; ^{1}H NMR data (400 MHz, $CDCl_3$): δ 4.53 (dt, 1 H, $J_{2ax,3}$ 6.3, $J_{2eq,3}$ 4.6 Hz, H-3), 4.39 (dd, 1 H, $J_{4,5}$ 2.4 Hz, H-4), 4.17 (dt, 1 H, $J_{1',2'a}$ 5.9, $J_{1',2'b} = J_{1',5}$ = 7.3 Hz, H-1′), 4.02 (dd, 1 H, J_{gem} 8.3 Hz, H-2′a), 3.79 (s, 3 H, CO_2Me), 3.67 (bdd, 1 H, H-2′b), 3.38 (s, 1 H, OH), 2.14 (dd, 1 H, J_{gem} 14.7 Hz, H-2*eq*), 1.95 (dd, 1 H, H-2*ax*), 1.92 (m, 1 H, H-5), 1.83 (dd, 1 H, $J_{5,6eq}$ 3.4, J_{gem} 13.7 Hz, H-6*eq*), 1.73 (t, 1 H, $J_{5,6ax}$ 13.7 Hz, H-6*ax*), 1.58 (m, 20 H, 2 cyclohexylidene). Anal. Calcd for $(C_{22}H_{34}O_7)^+$: 410.2302. Found: *m/z* 410.2327 $(M)^+$.

*Di-*O*-cyclohexylidene derivative* [(±)-**31**] *of (1*R*,*2*S*,*3*R*,*5*R*)*-1,2,5-trihydroxy-3-[(1*R*)*-1,2-dihydroxyethyl]-5-vinylcyclohexane (5,6:8,9-di-*O*-cyclohexylidene-1,2,4-trideoxy-7a-carba-β-*DL-gulo-*1-non-en-3-ulopyranose).*—Compound (±)-**30** (0.921 g,

2.62 mmol) was treated with vinylmagnesium bromide–hexane (7.9 mL, 7.9 mmol), as described for the preparation of (±)-**26** and (±)-**27**, to give (±)-**31** (0.475 g, 48%) as a syrup; selected ^{1}H NMR data (90 MHz, $CDCl_3$): δ 6.09 (dd, 1 H, $CH=CH_2$), 5.41 (dd, 1 H, J_{trans} 17.0, J_{gem} 2.0 Hz, $CH=CH_{trans}$), 5.25 (dd, 1 H, J_{cis} 10.0 Hz, $CH=CH_{cis}$). Anal. Calcd for $C_{22}H_{34}O_5$: 378.2405. Found: *m/z* 378.2423.

Di-O-cyclohexylidene derivative [(±)-**32**] *of methyl (1R*,3R*,4S*,5R*)-1,3,4-trihydroxy-5-[(1R*)-1,2-dihydroxyethyl]cyclohexane-1-carboxylate (methyl 4,5:7,8-di-O-cyclohexylidene-3-deoxy-6a-carba-β-*DL-gulo-*octulopyranosonate).*—Compound (±)-**31** (135 mg, 0.36 mmol) was treated with ozone as described for the preparation of (±)-**28**, and likewise oxidised and esterified to give (±)-**32** (0.141 g, 96%) as a syrup; ^{1}H NMR data (400 MHz, $CDCl_3$): δ 4.50 (dt, 1 H, $J_{2eq,3}$ 4.9, $J_{2ax,3}=J_{3,4}=6.4$ Hz, H-3), 3.83 (dd, 1 H, $J_{1',2'a}$ 9.0, J_{gem} 10.0 Hz, H-2'a), 3.24 (s, 1 H, OH), 2.27 (d, 1 H, J_{gem} 10.5 Hz, H-6*ax*), 2.18 (dd, 1 H, J_{gem} 14.2 Hz, H-2*eq*), 1.90 (dd, 1 H, H-2*ax*), 1.79 (d, 1 H, H-6*ax*), 1.75–1.35 (20 H, 2 cyclohexylidene). Anal. Calcd for $(C_{22}H_{34}O_7+H)^+$ 410.2302. Found: *m/z* 410.2309 $(M+H)^+$.

Methyl (1S,3R*,4S*,5R*)-1,3,4-triacetoxy-5-[(1S*)-1,2-diacetoxyethyl]cyclohexane-1-carboxylate (methyl 2,4,5,7,8-penta-*O*-acetyl-3-deoxy-6a-carba-α-*DL-manno-*2-octulopyranosonate)* [(±)-**33**] *and (1S*,3R*,4S*,5R*)-1,4-diacetoxy-3-[(1S*)-1,2-diacetoxyethyl]-6-oxabicyclo[3.2.1]octan-7-one* [(±)-**35**].—To a solution of (±)-**28** (171 mg, 0.42 mmol) in 1:1 MeOH–THF (7.0 mL) was added 1 M HCl (0.9 mL), and it was stirred overnight at room temperature. The mixture was evaporated and the residue was treated with Ac_2O (3 mL) and pyridine (6 mL) for 2 days at room temperature. Evaporation of the excess reagent gave the products which were chromatographed (1:2 EtOAc–hexane) to give (±)-**33** (64 mg, 33%) and (±)-**35** (11 mg) contaminated with the 4,5,7,8-tetra-*O*-acetyl derivative, together with the 7,8-*O*-cyclohexylidene derivative (42 mg, 24%).

For (±)-**33**: ^{1}H NMR data (400 MHz, $CDCl_3$): δ 5.47 (bs, 1 H, H-4), 5.05 (ddd, 1 H, $J_{2ax,3}$ 12.7, $J_{2eq,3}$ 4.9, $J_{3,4}$ 2.7 Hz, H-3), 4.94 (ddd, 1 H, $J_{1',2'a}$ 2.0, $J_{1',2'b}$ 4.9, $J_{1',5}$ 10.3 Hz, H-1'), 4.36 (dd, 1 H, J_{gem} 12.7 Hz, H-2'a), 3.99 (dd, 1 H, H-2'b), 3.77 (s, 3 H, CO_2Me), 2.34–2.29 (m, 2 H, H-2*eq*,5), 2.19 (t, 1 H, H-2*ax*), 2.12, 2.07, 2.06, 2.03 (4 s, each 3 H, 4 Ac), 1.90 (t, 1 H, $J_{5,6ax}=J_{gem}=13.8$ Hz, H-6*ax*), 1.98 (s, 3 H, Ac). Anal. Calcd for $(C_{20}H_{29}O_{12}+H)^+$ 461.1657. Found: *m/z* 461.1657 $(M+H)^+$.

For (±)-**35**: ^{1}H NMR data (400 MHz, $CDCl_3$): δ 5.06 (dt, 1 H, $J_{4,5}$ 2.0, $J_{5,8ax}$ 2.4, $J_{5,8eq}$ 9.3 Hz, H-5), 4.97 (dt, 1 H, $J_{3,1'}$ 10.3, $J_{1',2'a}$ 2.9, $J_{1',2'b}$ 3.9 Hz, H-1'), 4.71 (bs, 1 H, H-4), 4.47 (dd, 1 H, J_{gem} 12.7 Hz, H-2'a), 4.07 (dd, 1 H, H-2'b), 2.69 (dd, 1 H, J_{gem} 14.4 Hz, H-8*eq*), 2.45 (dt, 1 H, $J_{long\text{-}range}$ 2.4 Hz, H-8*ax*), 2.39 (dt, 1 H, $J_{2a,3}$ 10.3, $J_{2b,3}$ 5.4 Hz, H-3), 2.14, 2.10, 2.097, 2.09 (4 s, each 3 H, 4 Ac). Anal. Calcd for $(C_{17}H_{23}O_{10}+H)^+$ 387.1289. Found: *m/z* 387.1288 $(M+H)^+$.

(1S,3R*,4S*,5R*)-1,3,4-Trihydroxy-5-[(1S*)-1,2-dihydroxyethyl]cyclohexane-1-carboxylic acid ammonium salt (ammonium 3-deoxy-6a-carba-α-*DL-manno-*2-octulopyranosonate)* [(±)-**34**].—A solution of (±)-**33** (64 mg, 0.14 mmol) in THF (2.5 mL) was treated with aq 0.5 M NaOH (4.5 mL) for 3 h at room temperature. After neutralisation with Amberlite IR-120 (H^+) resin, the solution was evaporated, and the residue was again evaporated with aq 1 M ammonia to give (±)-**34** (100%); ^{1}H NMR data [400 MHz, D_2O (*p*-dioxane)]: δ 3.97 (bs, 1 H, H-4), 3.66 (ddd, 1 H, *J* 4.6, *J* 2.7

Hz, H-3), 3.33 (m, 1 H, H-1'), 1.85 (dt, 1 H, J 12.7 Hz, $J_{\text{long-range}}$ 4.4 Hz, H-2*ax* or 6*ax*), 1.67 (m, 1 H, H-5), 1.60 (dt, 1 H, J 12.9 Hz, H-6*ax* or 2*ax*), 1.48 (bdd, 1 H, J 13.2, J 3.4 Hz, H-2*eq* or 6*eq*), 1.17 (bdd, 1 H, J 12.7, J 2.0 Hz, H-6*eq* or 2*eq*). ^{13}C NMR data (100 MHz, D_2O): δ 182.20, 75.70, 71.56, 68.65, 68.13, 63.69, 37.92, 35.33, 30.26.

Methyl (1R,3R*,4S*,5R*)-1,3,4-triacetoxy-5-[(1S*)-1,2-diacetoxyethyl]cyclohexane-1-carboxylate (methyl 2,4,5,7,8-penta-O-acetyl-3-deoxy-6a-carba-β-*DL-manno-*2-octulopyranosonate)* [(±)-**36**].—Compound (±)-**29** (414 mg, 1.01 mmol) was treated with 1 M HCl (4 mL) in 1:1 MeOH–THF (32 mL) overnight at room temperature, and then evaporated. The residue was treated with Ac_2O (7 mL) in pyridine (14 mL) for 2 days at room temperature. The product was chromatographed (1:2 EtOAc–hexane) to give (±)-**36** (381 mg, 82%) as a syrup; ^{1}H NMR data (400 MHz, $CDCl_3$): δ 5.45 (bs, 1 H, H-4), 5.14 (ddd, 1 H, $J_{2ax,3}$ 12.7, $J_{2eq,3}$ 4.9, $J_{3,4}$ 2.9 Hz, H-3), 4.91 (ddd, 1 H, $J_{1',2'a}$ 2.2, $J_{1',2'b}$ 5.1, $J_{1',5}$ 10.3 Hz, H-1'), 4.33 (dd, 1 H, J_{gem} 12.5 Hz, H-2'a), 4.05 (dd, 1 H, H-2'b), 3.77 (s, 3 H, CO_2Me), 2.51 (bdd, 1 H, J_{gem} 12.7 Hz, H-2*eq*), 2.41 (dddd, 1 H, $J_{4,5}$ 2.4, $J_{5,6ax}$ 13.2, $J_{5,6eq}$ 3.9 Hz, H-5), 2.31 (ddd, $J_{2eq,6eq}$ 1.0, J_{gem} 13.2 Hz, H-6*eq*), 2.08, 2.07, 2.03 (3 s, 3, 6, 3 H, 4 Ac), 1.98 (t, 1 H, H-2*ax*), 1.97 (s, 3 H, Ac), 1.70 (t, 1 H, H-6*ax*) 1.97 (s, 3 H, Ac). Anal. Calcd for $(C_{20}H_{29}O_{12} + H)^+$ 461.1657. Found: *m/z* 461.1658 $(M + H)^+$.

Methyl (1R,3R*,4S*,5R*)-1,3,4-trihydroxy-5-[(1S*)-1,2-dihydroxyethyl]cyclohexane-1-carboxylate (methyl 3-deoxy-6a-carba-β-*DL-manno-*2-octulopyranosonate)* [(±)-**37**].—Compound (±)-**29** (194 mg, 0.47 mmol) was treated with 1 M HCl (2 mL) in 1:1 MeOH–THF (16 mL) overnight at room temperature. The mixture was evaporated and the residue was chromatographed (4:1 $CHCl_3$–MeOH) to give (±)-**37** (63 mg, 58%) as a syrup; ^{1}H NMR data (400 MHz, CD_3OD): δ 4.06 (bs, 1 H, H-4), 3.72 (s, 3 H, CO_2Me), 3.51 (ddd, 1 H, J 3.4, J 4.9 Hz, H-1'), 2.16 (ddd, 1 H, $J_{2eq,3}$ 4.4, J_{gem} 12.2, $J_{\text{long-range}}$ 1.5 Hz, H-2*eq*), 1.84 (t, 1 H, $J_{2ax,3}$ 12.2 Hz, H-2*ax*), 1.88–1.80 (m, 1 H, H-6*eq*), 1.72 (t, 1 H, J 12.9 Hz, H-6*ax*), 1.63–1.57 (m, 1 H, H-5). ^{13}C NMR (100 MHz, CD_3OD): δ 175.94, 75.73, 74.21, 70.75, 69.31, 65.56, 52.94, 40.16, 38.51, 33.06.

(1R,3R*,4S*,5R*)-1,3,4-Trihydroxy-5-[(1S*)-1,2-dihydroxyethyl]cyclohexane-1-carboxylic acid ammonium salt (ammonium 3-deoxy-6a-carba-β-*DL-manno-*2-octulopyranosnate)* [(±)-**38**].—A solution of (±)-**36** (22 mg, 0.047 mmol) in THF (1.0 mL) was treated with 0.5 M NaOH (1.5 mL) for 3 h at room temperature. After neutralisation with Amberlite IR-120 (H^+) resin, the product was treated with ammonia to give (±)-**38** quantitatively; ^{1}H NMR data (400 MHz, D_2O): δ 3.91 (bs, 1 H, H-4), 3.70 (ddd, 1 H, $J_{2ax,3}$ 12.2, $J_{2eq,3}$ 4.4, $J_{3,4}$ 2.9 Hz, H-3), 3.55 (dd, 1 H, $J_{1',2'a}$ 2.9, J_{gem} 11.7 Hz, H-2'a), 3.47 (ddd, 1 H, $J_{1',2'b}$ 6.8, $J_{1',5}$ 8.8 Hz, H-1'), 3.34 (dd, 1 H, H-2'b), 1.90 (bdd, 1 H, J_{gem} 12.2 Hz, H-2*eq*), 1.60–1.57 (m, 2 H, H-6*eq*), 1.52 (t, 1 H, H-2*ax*), 1.26 (t, 1 H, $J_{5,6ax} = J_{\text{gem}} = 13.7$ Hz, H-6*ax*). ^{13}C NMR data (100 MHz, D_2O): δ 179.75, 75.01, 71.73, 69.28, 67.49, 63.78, 38.88, 36.75, 31.54.

Methyl (1R,3R*,4S*,5R*)-1,3,4-trihydroxy-5-[(1R*)-1,2-dihydroxyethyl]cyclohexane-1-carboxylate (methyl 3-deoxy-6a-carba-β-*DL-gulo-*2-octulosonate)* [(±)-**39**].—Compound (±)-**32** (141 mg, 0.34 mmol) was treated with 1 M HCl (0.8 mL) in 1:1 MeOH–THF (6 mL) overnight at room temperature. The product was chromatographed

(4:1 $CHCl_3$–MeOH) to give (±)-**39** (40 mg, 46%) as a syrup; ^{1}H NMR data (400 MHz, CD_3OD): δ 3.85 (bs, 1 H, H-4), 3.72 (s, 3 H, CO_2Me), 3.71–3.65 (m, 2 H, H-3,1′), 3.54 (dd, 1 H, $J_{1',2'a}$ 3.9, J_{gem} 11.2 Hz, H-2′a), 3.58 (dd, 1 H, $J_{1',2'b}$ 5.9 Hz, H-2′b), 2.18–2.11 (m, 2 H, H-2*eq*,6*eq*), 1.82 (t, 1 H, *J* 12.2 Hz, H-2*ax* or 6*ax*), 1.68 (dd, 1 H, *J* 11.2, *J* 13.7 Hz, H-2*ax* or 6*ax*), 1.63 (m, 1 H, H-5); ^{13}C NMR data (100 MHz, CD_3OD): δ 175.76, 75.39, 74.76, 70.89, 70.41, 64.56, 52.54, 40.02, 38.26, 31.71.

(1S,2S*,3R*,5R*)-2-Azido-1-benzoyloxymethyl-5-benzyloxy-3-(methoxymethoxy)cyclohexane (4-azido-6-*O*-benzoyl-1-*O*-benzyl-2,4-dideoxy-3-*O*-methoxymethyl-5a-carba-α-*DL*-xylo-hexopyranose)* [(±)-**40**].—A mixture of (±)-**13** (25 mg, 0.05 mmol), NaN_3 (20 mg, 0.31 mmol), and dry DMF (2 mL) was stirred for 15 h at 90°C. After cooling, the mixture was poured onto ice–H_2O and extracted with EtOAc. The extracts were washed with H_2O, dried, and evaporated. The residue was chromatographed on silica gel (1:5 butanone–hexane) to give (±)-**40** (17 mg, 78%) as a syrup; ν_{max} 2100 (N_3) and 1720 (C = O ester) cm^{-1}; selected ^{1}H NMR data (90 MHz, $CDCl_3$): δ 4.95 and 4.68 (2 s, each 2 H, CH_2OCH_3 and $PhCH_2$), 3.58 (s, 3 H, CH_2OCH_3). Anal. Calcd for $C_{23}H_{27}N_3O_5$: C, 64.93; H, 6.40; N, 9.88. Found: C, 64.83; H, 6.45; N, 9.54.

(1S,2S*,3R*,5R*)-2-Azido-5-benzyloxy-1-hydroxymethyl-3-(methoxymethoxy)cyclohexane (4-azido-1-*O*-benzyl-2,4-dideoxy-3-*O*-methoxymethyl-5a-carba-α-*DL*-xylo-hexopyranose)* [(±)-**41**].—Compound (±)-**40** (673 mg, 1.58 mmol) was treated with 1 M methanolic NaOMe (15 mL) for 3 h at room temperature. After neutralisation with Amberlite IR-120 (H^+) resin, the mixture was evaporated and the residue was subjected to chromatography (1:3 butanone–hexane) to give (±)-**41** (493 mg, 97%) as a syrup; ν_{max} 3450 (OH) and 2100 cm^{-1} (N_3); selected ^{1}H NMR data (90 MHz, $CDCl_3$): δ 4.93 and 4.63 (2 s, each 2 H, CH_2OCH_3 and $PhCH_2$), 3.51 (s, 3 H, CH_2OCH_3), 2.40 (bs, 1 H, OH). Anal. Calcd for $C_{16}H_{23}N_3O_4$: C, 59.80; H, 7.21; N, 13.07. Found: C, 59.60; H, 7.13; N, 13.00.

(1S,2S*,3R*,5R*)-2-Acetamido-5-benzyloxy-1-hydroxymethyl-3-(methoxymethoxy)cyclohexane (4-acetamido-1-*O*-benzyl-2,4-dideoxy-3-*O*-methoxymethyl-5a-carba-α-*DL*-xylo-hexopyranose)* [(±)-**42**].—A solution of (±)-**41** (50 mg, 0.16 mmol) in EtOH (1.5 mL) containing Ac_2O (18 mL, 0.19 mmol) was hydrogenated in the presence of a catalytic amount of Raney nickel T-4 for 3 h at room temperature under atmospheric pressure of H_2. The mixture was filtered through a Celite bed and the filtrate was evaporated. The residue was chromatographed (1:6 butanone–toluene) to give (±)-**42** (34 mg, 65%) as a syrup; ν_{max} 3600–3150 (NH, OH) and 1650 cm^{-1} (C = O amide); selected ^{1}H NMR data (90 MHz, $CDCl_3$): δ 7.63 (bs, 5 H, Ph), 6.43–6.07 (m, 1 H, NH), 4.75 and 4.63 (2 s, each 2 H, CH_2OCH_3 and $PhCH_2$), 3.50 (s, 3 H, CH_2OCH_3), 2.10 (s, 3 H, Ac). Anal. Calcd for $C_{18}H_{27}NO_5$: C, 64.06; H, 8.06; N, 4.15. Found: C, 63.98; H, 7.97, N, 4.10.

(1S,2R,3S,5R)-3-Benzoyloxymethyl-5-benzyloxy-1-methoxymethoxy-2-(triethylsilyloxy)cyclohexane [(-)-**43**].—To a solution of (−)-**11** (1.48 g, 3.7 mmol) in dry pyridine (30 mL) was added triethylsilyl chloride (1.20 mL, 7.20 mmol), and it was stirred at 60°C for 2 days. After addition of MeOH, the mixture was evaporated and the residue was diluted with $CHCl_3$. The solution was washed with H_2O, dried, and evaporated. The residue was chromatographed (1:5 EtOAc–hexane) to give (−)-**43**

(1.85 g, 97%) as a syrup; $[\alpha]_D^{25}$ −9.5° (*c* 0.71, $CHCl_3$); ^1H NMR data (270 MHz; $CDCl_3$): δ 8.04 (2 d, 2 H, Ph), 7.56 (m, 1 H, Ph), 7.45 (m, 2 H, Ph), 7.32 (m, 5 H, PhCH_2), 4.68 and 4.64 (ABq, each 1 H, J_{gem} 6.6 Hz, PhCH_2 or CH_2OCH$_3$), 4.51 (s, 2 H, PhCH_2 or CH_2OCH$_3$), 4.24 (dd, 2 H, J_{gem} 8.8, $J_{3,7}$ 1.5 Hz, H-7,7), 4.22 (bs, 1 H, H-2), 3.87 (ddd, 1 H, $J_{1,2}$ 2.2, $J_{1,6ax}$ 11.3, $J_{1,6eq}$ 4.4 Hz, H-1), 3.84 (m, 1 H, H-5), 3.37 (s, 3 H, OMe), 2.33 (m, 1 H, H-3), 2.04 (bdt, 1 H, J_{gem} 11.3 Hz, H-6*eq*), 1.87 (dt, 1 H, $J_{5,6ax}$ 2.9 Hz, H-6*ax*), 1.75–1.55 (m, 2 H, H-4), 0.93 [t, 9 H, (CH_3CH$_2$)$_3$Si], 0.62 [m, 6 H, (CH$_3$CH_2)$_3$Si]. Anal. Calcd for $C_{23}H_{28}O_6Si$: C, 67.67; H, 8.22. Found: C, 67.67; H, 7.98.

(1S,3R,4S,5R)-5-Benzyloxy-3-hydroxymethyl-1-methoxymethoxy-2-(triethylsilyloxy)cyclohexane [(−)-**44**].—A solution of (−)-**43** (1.83 g, 3.56 mmol) in MeOH (40 mL) was treated with 1 M methanolic NaOMe (5.0 mL) at 0°C for 6 h. After neutralisation with AcOH, the mixture was evaporated. The residue was dissolved in EtOAc and the solution was washed with H_2O, dried, and evaporated. The residue was chromatographed (1:10 butanone–toluene) to give (−)-**44** (1.27 g, 87%) as a syrup; $[\alpha]_D^{25}$ −14.5° (*c* 1.0, $CHCl_3$); selected ^1H NMR data (270 MHz; $CDCl_3$): δ 7.32 (m, 5 H, Ph), 4.66 and 4.63 (ABq, each 1 H, J_{gem} 6.6 Hz, PhCH_2 or CH_2OCH$_3$), 4.53 and 4.48 (ABq, each 1 H, J_{gem} 12.1 Hz, PhCH_2 or CH_2OCH$_3$), 4.18 (bs, 1 H, H-2), 3.88–3.80 (m, 2 H, H-1,5), 3.68–3.56 (m, 2 H, H-7,7), 3.36 (s, 3 H, OMe), 0.96 [t, 9 H, (CH_3CH$_2$)$_3$Si], 0.64 [m, 6 H, (CH$_3$CH_2)$_3$Si]. Anal. Calcd for $C_{22}H_{38}O_5Si$: C, 64,35; H, 9.3. Found: C, 64.5; H, 9.1.

Methyl (E)- *and* (Z)-*3-[(1′S,2′R,3′S,5′R)-5′-benzyloxy-3′-methoxymethoxy-2′-(triethylsilyloxy)cyclohexyl]propenoate* [(+)-**45E** *and* (+)-**45Z**].—A suspension of dry CrO_3 (4.04 g, 40.5 mmol) in a mixture of CH_2Cl_2 (35 mL) and dry pyridine (6.55 mL, 81 mmol) was stirred at 0°C for 30 min under Ar, and to it was added a solution of (−)-**44** (1.67 g, 4.10 mmol) in CH_2Cl_2 (7 mL) at 0°C. The mixture was stirred for 30 min at room temperature and then transferred with an excess of Celite to the top of a short column of silica gel. The column was thoroughly eluted with diethyl ether and the eluate was evaporated to give crude syrupy aldehyde (1.53 g). To a two-necked flask containing 18-crown-6-ether (4.90 g, 17.2 mmol) were added in turn THF (30 mL), trimethyl phosphonoacetate (0.61 mL, 3.70 mmol), and 0.5 M potassium hexamethyldisilazane–toluene (7.5 mL, 3.70 mmol) at −78°C under Ar, and the mixture was stirred for 15 min. To it was added a solution of the aldehyde in THF (11 mL), and it was stirred for 30 min at −78°C. After addition of aq NH_4Cl the mixture was vigorously agitated with diethyl ether (150 mL) and H_2O (100 mL). The organic layer was dried and evaporated. The residue (1.82 g) was chromatographed (180 g, 1:23 EtOAc–hexane) to give (+)-**45Z** (1.28 g, 68%) and (+)-**45E** (332 mg, 18%).

For (+)-**45E**: colourless syrup; $[\alpha]_D^{25}$ +7.6° (*c* 0.58, $CHCl_3$); selected ^1H NMR data (270 MHz; $CDCl_3$): δ 7.32 (m, 5 H, Ph), 7.00 (dd, 1 H, $J_{2,3}$ 15.8, $J_{3,1'}$ 7.7 Hz, H-3), 5.80 (dd, 1 H, $J_{2,1'}$ 1.1 Hz, H-2), 4.63 and 4.50 (ABq, each 1 H, J_{gem} 6.6 Hz, PhCH_2 or CH_2OCH$_3$), 4.47 and 4.60 (ABq, each 1 H, J_{gem} 2.1 Hz, PhCH_2 or CH_2OCH$_3$), 4.02 (bs, 1 H, H-2′), 3.73 (s, 3 H, CO_2Me), 3.36 (s, 3 H, OMe), 2.66 (m, 1 H, H-1′), 2.00 (bd, 1 H, H-4′*eq*), 1.66 (bd, 1 H, H-6′*eq*), 0.95 [t, 9 H, (CH_3CH$_2$)$_3$Si], 0.60 [q, 6 H, (CH$_3$CH_2)$_3$Si]. Anal. Calcd for $C_{25}H_{40}O_6Si$: C, 64.62; H, 8.68. Found: C, 64.72; H, 8.45.

For (+)-**45Z**: colourless syrup; $[\alpha]_D^{25}$ +28.9° (*c* 0.405, $CHCl_3$); selected ^1H NMR data (270 MHz; $CDCl_3$): 7.34 (m, 5 H, Ph), 6.29 (dd, 1 H, $J_{2,3}$ 11.4, $J_{3,1'}$ 10.3 Hz, H-3), 5.78 (dd, 1 H, $J_{2,1'}$ 1.0 Hz, H-2), 4.65 and 4.62 (ABq, each 1 H, J_{gem} 6.6 Hz, PhCH_2 or CH_2OCH$_3$), 4.60 and 4.47 (ABq, each 1 H, J_{gem} 2.1 Hz, PhCH_2 or CH_2OCH$_3$), 4.03 (bs, 1 H, H-2′), 3.89 (ddd, 1 H, J_{gem} 11.4, $J_{2',3'}$ 2.2, $J_{3',4'eq}$ 4.4 Hz, H-3′), 3.79 (quintet, 1 H, $J_{4'ax,5'} = J_{4'eq,5'} = J_{5',6'}$ = 3.0 Hz, H-5′), 3.76 (m, 1 H, H-1′), 3.69 (s, 3 H, CO_2Me), 3.35 (s, 3 H, OMe), 0.90 [t, 9 H, (CH_3CH$_2$)$_3$Si], 0.60 [q, 6 H, (CH$_3$CH_2)$_3$Si]. Anal. Found: C, 64.93; H, 8.43.

(1S,2R,3S,5R)-5-Benzyloxy-3-[(Z)-3-hydroxyprop-1-enyl]-1-methoxymethoxy-2-(triethylsilyloxy)cyclohexane [(+)-**46**].—To a solution of (+)-**45Z** (232 mg, 0.50 mmol) in CH_2Cl_2 (5.0 mL) was added 1.5 M diisopropylaluminium hydride–toluene (0.85 mL, 1.25 mmol) at −78°C under Ar atmosphere and the mixture was stirred for 30 min at the same temperature. After addition of a small amount of H_2O, an insoluble material was removed by filtration through a Celite bed and the filtrate was evaporated. The residue was dissolved in $CHCl_3$ and the solution was washed with H_2O and saline, dried, and evaporated. The residue (219 mg) was chromatographed (6 g, 1:10 butanone–toluene) to give (+)-**46** (188 mg, 86%) as a colourless syrup; $[\alpha]_D^{25}$ +15.8° (*c* 1.40, $CHCl_3$); ^1H NMR data (270 MHz; $CDCl_3$): δ 7.32 (m, 5 H, Ph), 4.64 and 4.61 (ABq, each 1 H, J_{gem} 8.3 Hz, PhCH_2 or CH_2OCH$_3$), 4.53 and 4.48 (ABq, each 1 H, J_{gem} 12.6 Hz, PhCH_2 or CH_2OCH$_3$), 4.17 (d, 2 H, $J_{2',3'}$ 5.5 Hz, H-3′,3′), 3.87 (bs, 1 H, H-2), 3.36 (s, 3 H, OMe), 2.79 (m, 1 H, H-3), 1.96 (bd, 1 H, H-6*eq*), 1.83 (ddd, 1 H, $J_{1,6ax}$ 11.7, J_{gem} 11.7, $J_{5,6ax}$ 2.9 Hz, H-6*ax*), 1.74 (ddd, 1 H, $J_{3,4ax}$ 11.0, J_{gem} 11.0, $J_{4ax,5}$ 2.6 Hz, H-4*ax*), 0.95 [t, 9 H, (CH_3CH$_2$)$_3$Si], 0.60 [q, 6 H, (CH$_3$CH_2)$_3$Si]. Anal. Calcd for $C_{24}H_{40}O_5Si$: C, 66.01; H, 9.23. Found: C, 65.78; H, 8.90.

*(1S,2R,3S,5R)-5-Benzyloxy-3-[(Z)-3-(*tert*-butyldimethylsilyloxy)prop-1-enyl]-1-methoxymethoxy-2-(triethylsilyloxy)cyclohexane* [(+)-**47**].—To a solution of (+)-**46** (430 mg, 0.98 mmol) in CH_2Cl_2 (10 mL) were added 4,4-dimethylaminopyridine (120 mg, 0.98 mmol), Et_3N (0.82 mL, 5.72 mmol), and *tert*-butyldimethylsilyl chloride (550 mg, 4.10 mmol), and the mixture was stirred for 5 h at room temperature. The mixture was diluted with CH_2Cl_2 and the solution was washed with H_2O and saline, dried, and evaporated. The residue was chromatographed (30 g, toluene) to give (+)-**47** (527 mg, 97%) as a colourless syrup; $[\alpha]_D^{25}$ +10.7° (*c* 1.15, $CHCl_3$); ^1H NMR data (270 MHz; $CDCl_3$): δ 7.32 (m, 5 H, Ph), 4.63 (t, 2 H, J_{gem} 7.0 Hz, PhCH_2 or CH_2OCH$_3$), 4.50 (s, 2 H, PhCH_2 or CH_2OCH$_3$), 4.22 (d, 2 H, $J_{2',3'}$ 4.8 Hz, H-3′,3′), 3.87 (bs, 1 H, H-2), 3.35 (s, 3 H, OMe), 2.76 (m, 1 H, H-3), 1.95 (bd, 1 H, H-6*eq*), 1.84 (ddd, 1 H, $J_{1,6ax} = J_{gem}$ = 11.7, $J_{5,6ax}$ 2.9 Hz, H-6*ax*), 1.72 (ddd, 1 H, $J_{3,4ax} = J_{gem}$ = 11.0, $J_{4ax,5}$ 2.6 Hz, H-4*ax*), 1.52 (bd, 1 H, H-4*eq*), 0.95 [t, 9 H, (CH_3CH$_2$)$_3$Si], 0.89 (s, 9 H, *tert*-Bu), 0.60 [q, 6 H, (CH$_3$CH_2)$_3$Si], 0.060 (s, 6 H, $SiMe_2$). Anal. Calcd for $C_{30}H_{54}O_5Si_2$: C, 65.40; H, 9.88. Found: C, 65.52; H, 9.59.

*(1S,2R,3R,5R)-5-Benzyloxy-3-[(1S,2R)- and (1R,2S)-3-(*tert*-butyldimethylsilyloxy)-1,2-dihydroxypropyl]-1-(methoxymethoxy)-2-(triethylsilyloxy)cycohexane* [(−)-**48** *and* (−)-**50**].—A solution of (+)-**47** (512 mg, 0.93 mmol) in aq 60% acetone (12 mL) was treated with *N*-methylmorpholine *N*-oxide (327 mg, 2.79 mmol) and 0.05 M osmium tetraoxide–*tert*-butyl alcohol (2.8 mL, 0.14 mmol) for 3 h at room temperature. Sodium hydrogensulfate (300 mg) was then added to the mixture, and it was stirred for 2

h and evaporated. The residue was dissolved in EtOAc and the solution was washed with H_2O, dried, and evaporated. The residue was chromatographed (60 g, 1:25 EtOAc–hexane) to give (−)-**48** (240 mg, 44%) and (−)-**50** (259 mg, 48%) as colourless syrups.

For (−)-**48**: $[\alpha]_D^{25}$ −3.1° (*c* 0.41, $CHCl_3$); selected ^{1}H NMR data (270 MHz; $CDCl_3$): δ 7.32 (m, 5 H, Ph), 4.64 and 4.62 (ABq, each 1 H, J_{gem} 8.1 Hz, PhCH_2 or CH_2OCH$_3$), 4.57 and 4.45 (ABq, each 1 H, J_{gem} 11.6 Hz, PhCH_2 or CH_2OCH$_3$), 4.18 (bs, 1 H, H-2), 3.53 (m, 1 H, H-1), 3.35 (s, 3 H, OMe), 0.96 [t, 9 H, (CH_3CH$_2$)$_3$Si], 0.90 (s, 9 H, *tert*-Bu), 0.60 [q, 6 H, (CH$_3$CH_2)$_3$Si], 0.060 (s, 6 H, SiMe$_2$). Anal. Calcd for $C_{30}H_{56}O_7Si_2$: C, 61.60; H, 9.65. Found: C, 61.48; H, 9.31.

For (−)-**50**: $[\alpha]_D^{25}$ −20° (*c* 0.53, $CHCl_3$); selected ^{1}H NMR data (270 MHz; $CDCl_3$): δ 7.32 (m, 5 H, Ph), 4.66 and 4.63 (ABq, each 1 H, J_{gem} 6.6 Hz, PhCH_2 or CH_2OCH$_3$), 4.53 and 4.46 (ABq, each 1 H, J_{gem} 12.1 Hz, PhCH_2 or CH_2OCH$_3$), 4.46 (bs, 1 H, H-2), 3.36 (s, 3 H, OMe), 3.16 (d, 1 H, *J* 6.6 Hz, OH), 2.80 (d, 1 H, *J* 5.8 Hz, OH), 0.96 [t, 9 H, (CH_3CH$_2$)$_3$Si], 0.89 (s, 9 H, *tert*-Bu), 0.63 [q, 6 H, (CH$_3$CH_2)$_3$Si], 0.061 (s, 6 H, SiMe$_2$). Anal. Found: C, 61.38; H, 9.31.

*(1*S*,2*R*,3*R*,5*R*)-5-Benzyloxy-3-[(1*S*,2*R*)-3-(*tert*-butyldimethylsilyloxy)-1,2-bis(methoxymethoxy)propyl]-1-(methoxymethoxy)-2-(triethylsilyloxy)cyclohexane* [(−)-**49**].—A mixture of (−)-**48** (27 mg, 0.047 mmol), *N,N*-diisopropylethylamine (25 mL, 1.4 mmol), chloromethyl methyl ether (54 μL, 0.69 mmol), and CH_2Cl_2 (1.0 mL) was refluxed for 2 days. The mixture was diluted with $CHCl_3$ and the solution was washed with H_2O, dried, and evaporated. The residue was chromatographed (2 g, 1:20 EtOAc–hexane) to give (−)-**49** (27 mg, 83%) as a syrup; $[\alpha]_D^{25}$ −15.3° (*c* 1.98, $CHCl_3$); selected ^{1}H NMR data (270 MHz, $CDCl_3$): δ 7.32 (m, 5 H, Ph), 4.74 (s, 2 H, PhCH_2 or CH_2OCH$_3$), 4.78 and 4.65 (ABq, each 1 H, J_{gem} 6.6 Hz, PhCH_2 or CH_2OCH$_3$), 4.64 and 4.61 (ABq, each 1 H, J_{gem} 6.6 Hz, PhCH_2 or CH_2OCH3), 4.53 and4.45 (ABq, each 1 H, J_{gem} 12.1 Hz, PhCH_2 or CH_2OCH$_3$), 4.04 (bs, 1 H, H-2), 3.40, 3.38, and 3.35 (3 s, each 3 H, 3 OMe), 0.94 [t, 9 H, (CH_3CH$_2$)$_3$Si], 0.88 (s, 9 H, *tert*-Bu), 0.67 [q, 6 H, (CH$_3$CH_2)$_3$Si], 0.052 and 0.046 (2 s, each 3 H, SiMe$_2$). Anal. Calcd for $C_{34}H_{64}O_9Si$: C, 60.67; H, 9.58. Found: C, 60.66; H, 9.20.

*(1*S*,2*R*,3*R*,5*R*)-5-Benzyloxy-3-[(1*R*,2*S*)-3-(*tert*-butyldimethylsilyloxy)-1,2-bis(methoxymethoxy)propyl]-1-(methoxymethoxy)-2-(triethylsilyloxy)cyclohexane* [(−)-**51**].—Compound (−)-**50** (28 mg, 0.048 mmol) was similarly converted into (−)-**51** (28 mg, 86%) as a syrup; $[\alpha]_D^{25}$ −12.0° (*c* 0.845, $CHCl_3$); selected ^{1}H NMR data (270 MHz, $CDCl_3$): δ 7.30 (m, 5 H, Ph), 4.80 and 4.77 (ABq, each 1 H, J_{gem} 5.9 Hz, PhCH_2 or CH_2OCH$_3$), 4.79 and 4.77 (ABq, each 1 H, J_{gem} 6.6 Hz, PhCH_2 or CH_2OCH$_3$), 4.51 and 4.45 (ABq, each 1 H, J_{gem} 12.1 Hz, PhCH_2 or CH_2OCH$_3$), 4.26 (bs, 1 H, H-2), 3.41, 3.38, and 3.35 (3 s, each 3 H, 3 OMe), 1.78 (ddd, 1 H, $J_{5,6ax}$ 2.9, $J_{1,6ax} = J_{6gem} = 12.8$ Hz, H-6*ax*), 1.72–1.54 (m, 2 H, H-4,4), 0.95 [m, 9 H, (CH_3CH$_2$)$_3$Si], 0.87 (s, 9 H, *tert*-Bu), 0.71–0.61 [m, 6 H, (CH$_3$CH_2)$_3$Si], 0.030 and 0.023 (2 s, each 3 H, SiMe$_2$). Anal. Calcd for $C_{34}H_{64}O_9Si$: C, 60.67; H, 9.58. Found: C, 60.44; H, 9.36.

*(1*R**,4*R**,5*S**,6*S**,8*R**,10*S**)-4,5,10-Triacetoxy-8-benzyloxy-2-oxabicyclo[4.4.0]decane* [(±)-**52**].—Compound (±)-**49** (27 mg, 41 mmol) was treated with 1 M tetrabutylammonium fluoride–THF (163 mL, 0.16 mmol) in THF (1 mL) for 3

h at room temperature. After the usual processing, the product was chromatographed (1.2 g, 1:1.4 butanone–toluene) to give the diol (17 mg, 96%), which was treated with *p*-toluenesulfonyl chloride (23 mg, 0.12 mmol) in dry pyridine (1.0 mL) overnight at 5°C. The crude product was chromatographed (1 g, 1:4 butanone–toluene) to give the monotosylate (20 mg, 87%), the structure of which was supported by the ^{1}H NMR spectrum. The tosylate was treated with 1 M methanolic NaOMe (0.1 mL, 0.1 mmol) in MeOH (0.5 mL) overnight at 50°C, and the product was purified by silica gel column chromatography (1 g, 1:3 acetone–hexane) to give the bicyclic compound (13 mg, 96%). Removal of the protecting groups was effected by hydrolysis with 2 M HCl overnight at 60°C, and then the triol formed was acetylated conventionally to give, after preparative TLC (1:2 acetone–hexane), the tri-*O*-acetyl derivative (±)-**52** (5.5 mg, 53% overall yield) as a syrup; selected ^{1}H NMR data (270 MHz, $CDCl_3$): 7.33 (m, 5 H, Ph), 4.55 and 4.46 (ABq, each 1 H, J_{gem} 11.7 Hz, PhCH_2), 4.08 (bs, 1 H, H-1), 3.93 (dd, 1 H, $J_{3eq,4}$ 5.9, J_{gem} 11.0 Hz, H-3*eq*), 3.90 (bt, 1 H, H-8), 3.64 (t, 1 H, $J_{3ax,4}$ 11.0 Hz, H-3*ax*), 2.26 (bd, 1 H, H-6), 2.12, 2.11, and 1.99 (3 s, each 3 H, 3 Ac). Anal. Calcd for $C_{22}H_{28}O_8$: C, 62.85; H, 6.71. Found: C, 62.72; H, 6.74.

*(1*R**,4*S**,5*R**,6*S**,8*R**,10*S**)-4,5,10-Triacetoxy-8-benzyloxy-2-oxabicyclo[4.4.0]decane* [(±)-**53**].—Compound (±)-**51** (28 mg, 41 mmol) was similarly converted by the successive 5-step sequence into the bicyclic compound (±)-**53** (4.0 mg, 37% overall yield); selected ^{1}H NMR data (270 MHz, $CDCl_3$): δ 7.33 (m, 5 H, Ph), 5.06 (dd, 1 H, $J_{4,5}$ 5.1, $J_{5,6}$ 4.0 Hz, H-5), 4.52 and 4.45 (ABq, each 1 H, J_{gem} 11.7 Hz, PhCH_2), 4.12 (dd, 1 H, $J_{3eq,4}$ 1.5, J_{gem} 13.2 Hz, H-3*eq*), 3.91 (bt, 1 H, H-8), 3.79 (bs, 1 H, H-1), 3.68 (dd, 1 H, J_{gem} 13.2, $J_{3ax,4}$ 1.5 Hz, H-3*ax*), 2.40 (m, 1 H, H-6), 2.10, 2.03, and 2.01 (3 s, each 3 H, 3 Ac). Anal. Calcd for $C_{22}H_{28}O_8$: C, 62.85; H, 6.71. Found: C, 63.09; H, 6.86.

*(1*S*,2*R*,3*R*,5*R*)-3-[(1*S*,2*R*)-3-(*tert*-Butyldimethylsilyloxy)-1,2-bis(methoxymethoxy)propyl]-1-(methoxymethoxy)-2-(triethylsilyloxy)cyclohexan-5-ol* [(−)-**54**].—A solution of (−)-**49** (85 mg, 0.13 mmol) in EtOH (2.0 mL) was hydrogenated in the presence of 10% Pd–C (40 mg) for 3 h at 5°C under atmospheric pressure of H_2. The mixture was filtered through a Celite bed and the filtrate was evaporated to give crude (−)-**54** (ca. 80 mg), a small portion of which was purified by chromatography to give the analytical sample as a syrup; $[\alpha]_D^{25}$ −23.7° (*c* 1.57, $CHCl_3$); selected ^{1}H NMR data (270 MHz, $CDCl_3$): δ 4.79 and 4.64 (ABq, each 1 H, J_{gem} 5.9 Hz, CH_2OCH$_3$), 4.74 (s, 2 H, CH_2OCH$_3$), 4.66 and 4.62 (ABq, each 1 H, J_{gem} 5.0 Hz, CH_2OCH$_3$), 4.23 (bt, 1 H, H-5), 4.04 (bs, 1 H, H-2), 3.393, 3.39, and 3.35 (3 s, each 3 H, 3 OMe), 0.98 [t, 9 H, (CH_3CH$_2$)$_3$Si], 0.90 (s, 9 H, *tert*-Bu), 0.68 [q, 6 H, (CH$_3$CH_2)$_3$Si], 0.066 (2 s, each 3 H, SiMe$_2$). Anal. Calcd for $C_{27}H_{58}O_9Si_2$: C, 55.63; H, 10.03. Found: C, 55.66; H, 9.72.

*(3*S*,4*R*,5*R*)-5-[(1*S*,2*R*)-3-(*tert*-Butyldimethylsilyloxy)-1,2-bis(methoxymethoxy)propyl]-3-methoxymethoxy-4-triethylsilyloxy-1-cyclohexanone* [(−)-**55**].—The crude (−)-**54** (74 mg) was treated with powdered 4A molecular sieves (100 mg) and PCC (109 mg, 0.50 mmol) in CH_2Cl_2 (1.5 mL) for 40 min at room temperature. The mixture was taken up on a short column of silica gel and eluted thoroughly with diethyl ether to give crude ketone (−)-**55** (ca. 70 mg). A small portion of the product was purified by chromatography to give the analytical sample; $[\alpha]_D^{25}$

−34.8° (*c* 0.57, $CHCl_3$); selected ^1H NMR data (270 MHz, $CDCl_3$): δ 4.78 and 4.60 (ABq, each 1 H, J_{gem} 6.6 Hz, CH_2OCH_3), 4.72 (s, 2 H, CH_2OCH_3), 4.64 and 4.61 (ABq, each 1 H, J_{gem} 7.0 Hz, CH_2OCH_3), 4.25 (bs, 1 H, H-4), 3.38 and 3.34 (2 s, 6 and 3 H, OMe), 2.76 (dd, 1 H, $J_{2ax,3} = J_{gem} = 12.1$ Hz, H-2*ax*), 2.01 (m, 1 H, H-5), 1.00 [t, 9 H, $(CH_3CH_2)_3Si$], 0.88 (s, 9 H, *tert*-Bu), 0.71 [q, 6 H, $(CH_3CH_2)_3Si$], 0.061 and 0.054 (2 s, each 3 H, $SiMe_2$). Anal. Calcd for $C_{27}H_{58}O_9Si_2$: C, 55.83; H, 9.72. Found: C, 55.94; H, 9.31.

(1S,2R,3R,5S)- [(−)-**56**] *and (1S,2R,3R,5R)-3-[(1S,2R)-3-(*tert*-Butyldimethylsilyloxy)-1,2-bis(methoxymethoxy)propyl]-1-methoxymethoxy-2-triethylsilyloxy-5-vinylcyclohexan-5-ol* [(−)-**58**].—A solution of the crude ketone (−)-**55** (65 mg) in THF (1.5 mL) was treated with 1 M vinylmagnesium chloride–THF (0.63 mL, 0.63 mmol) for 15 min at room temperature under Ar atmosphere. After addition of a small amount of satd aq NH_4Cl, the mixture was evaporated and the residue was dissolved in EtOAc. The solution was washed with H_2O and saline, dried, and evaporated. The residue was chromatographed (3 g, 1:20 acetone–hexane) and the fractions were further purified by preparative TLC (2:5 EtOAc–hexane) to give (−)-**56** [42 mg, ca. 54% based on (−)-**49** used] and (−)-**58** (6.5 mg, 8%).

For (−)-**56**: $[\alpha]_D^{25}$ −11.7° (*c* 0.425, $CHCl_3$); selected ^1H NMR data (270 MHz, $CDCl_3$): δ 5.94 (dd, 1 H, J_{cis} 11.0, J_{trans} 17.4 Hz, $CH=CH_2$), 5.37 (dd, 1 H, J_{gem} 1.1 Hz, $CH=CH_{cis}$), 5.19 (dd, 1 H, $CH=CH_{trans}$), 4.73 and 4.61 (ABq, each 1 H, J_{gem} 6.3 Hz, CH_2OCH_3), 4.68 (s, 2 H, CH_2OCH_3), 4.61 and 4.55 (ABq, each 1 H, J_{gem} 7.0 Hz, CH_2OCH_3), 3.94 (bs, 1 H, H-2), 3.36 (m, 1 H, H-1), 3.40, 3.37, and 3.35 (3 s, each 3 H, 3 OMe), 0.98 [t, 9 H, $(CH_3CH_2)_3Si$], 0.88 (s, 9 H, *tert*-Bu), 0.67 [q, 6 H, $(CH_3CH_2)_3Si$], 0.052 and 0.045 (2 s, each 3 H, $SiMe_2$). Anal. Calcd for $C_{29}H_{60}O_9Si_2$: C, 57.20; H, 9.93. Found: C, 57.58; H, 9.48.

For (−)-**58**: $[\alpha]_D^{25}$ −10.1° (*c* 0.105, $CHCl_3$); selected ^1H NMR data (270 MHz, $CDCl_3$): δ 5.97 (dd, 1 H, J_{cis} 10.6, J_{trans} 17.2 Hz, $CH=CH_2$), 5.24 (dd, 1 H, J_{gem} 1.1 Hz, $CH=CH_{trans}$), 5.03 (dd, 1 H, $CH=CH_{cis}$), 4.79 and 4.62 (ABq, each 1 H, J_{gem} 6.6 Hz, CH_2OCH_3), 4.74 (s, 2 H, CH_2OCH_3), 4.65 and 4.62 (ABq, each 1 H, J_{gem} 7.0 Hz, CH_2OCH_3), 4.05 (bs, 1 H, H-2), 3.39, 3.38, and 3.35 (3 s, each 3 H, 3 OMe), 2.13 (m, 1 H, H-3), 0.97 [t, 9 H, $(CH_3CH_2)_3Si$], 0.90 (s, 9 H, *tert*-Bu), 0.68 [q, 6 H, $(CH_3CH_2)_3Si$], 0.069 (2 s, each 3 H, $SiMe_2$). Anal. Found: C, 57.35; H, 9.99.

*(1S,2R,3R,5S)-3-[(1S,2R)-3-(*tert*-Butyldimethylsilyloxy)-1,2-bis(methoxymethoxy)propyl]-1,5-bis(methoxymethoxy)-2-triethylsilyloxy-5-vinylcyclohexane* [(−)-**57**].—Compound (−)-**56** (39 mg, 0.064 mmol) was treated with *N,N*-diisopropylethylamine (0.33 mL, 1.9 mmol) and chloromethyl methyl ether (97 mL, 1.3 mmol) overnight at 60°C. After the usual processing, the product was chromatographed (1.5 g, 1:10 EtOAc–hexane) to give (−)-**57** (38 mg, 93%); $[\alpha]_D^{25}$ −5.9° (*c* 0.68, $CHCl_3$); selected ^1H NMR data (270 MHz, $CDCl_3$): δ 5.68 (dd, 1 H, J_{cis} 11.0, J_{trans} 17.6 Hz, $CH=CH_2$), 5.38 (dd, 1 H, J_{gem} 0.7 Hz, $CH=CH_{cis}$), 5.35 (dd, 1 H, $CH=CH_{trans}$), 4.74 and 4.54 (ABq, each 1 H, J_{gem} 6.6 Hz, CH_2OCH_3), 4.67 (s, 2 H, CH_2OCH_3), 4.65 and 4.61 (ABq, each 1 H, J_{gem} 7.3 Hz, CH_2OCH_3), 4.61 and 4.59 (ABq, each 1 H, J_{gem} 6.6 Hz, CH_2OCH_3), 3.94 (bs, 1 H, H-2), 3.37 (m, 1 H, H-1), 3.41, 3.37, 3.35, and 3.34 (4 s, each 3 H, 4 OMe), 0.99 [t, 9 H, $(CH_3CH_2)_3Si$], 0.88 (s, 9 H, *tert*-Bu), 0.68 [q, 6 H, $(CH_3CH_2)_3Si$], 0.045 and 0.037 (2 s, each 3 H, $SiMe_2$). Anal. Calcd for $C_{31}H_{64}O_{10}Si_2$: C, 57.02; H, 9.88. Found: C, 57.07; H, 9.51.

Methyl (1S,3S,4R,5R)-5-[(1S,2R)-3-(tert-butyldimethylsilyloxy)-1,2-bis(methoxymethoxy)propyl]-1,3-bis(methoxymethoxy)-4-triethylsilyloxycyclohexane-1-carboxylate [(−)-**59**].—Into a solution of (−)-**57** (38 mg, 0.059 mmol) in MeOH (3.0 mL) was bubbled O_3 for 15 min at −75°C. To the mixture was then added immediately a mixture of Na_2HPO_4 (172 mg, 1.2 mmol), $NaClO_4$ (181 mg, 2 mmol) and sulfamic acid (245 mg, 2.5 mmol) in 1:1 acetone–H_2O (5 mL), and it was stirred vigorously for 30 min at the same temperature. After standing at room temperature, the mixture was evaporated and the residue was digested thoroughly with CH_2Cl_2 and washed with H_2O. The organic solution was evaporated and the residue (ca. 40 mg) was dissolved in diethyl ether (2 mL), and treated with ethereal CH_2N_2. The product was chromatographed (1.2 g, 1:5 EtOAc–hexane) to give (−)-**59** (39 mg, 93%) as a syrup; $[\alpha]_D^{25}$ −9.1° (*c* 1.4, $CHCl_3$); selected ^{1}H NMR data (270 MHz, $CDCl_3$): δ 4.80–4.60 (m, 8 H, 4 CH_2OCH$_3$), 3.96 (bs, 1 H, H-4), 3.73 (s, 3 H, CO_2Me), 3.53 (m, 1 H, H-3), 3.41, 3.373, 3.366, and 3.34 (4 s, each 3 H, 4 OMe), 1.90 and 1.75 (2 t, each 1 H, H-2*ax*,6*ax*), 1.58 (bt, 1 H, H-6*eq*), 0.98 [t, 9 H, (CH_3CH$_2$)$_3$Si], 0.89 (s, 9 H, *tert*-Bu), 0.68 [q, 6 H, (CH$_3$CH_2)$_3$Si], 0.054 and 0.048 (2 s, each 3 H, SiMe$_2$). Anal. Calcd for $C_{31}H_{64}O_{12}Si_2$: C, 54.35; H, 9.42. Found: C, 54.49; H, 9.17.

Methyl (1S,3S,4R,5R)-4-hydroxy-5-[(1S,2R)-3-hydroxy-1,2-bis(methoxymethoxy)propyl]-1,3-bis(methoxymethoxy)cyclohexane-1-carboxylate [(+)-**60**].—Compound (−)-**59** (36 mg, 0.053 mmol) was treated with 1 M tetrabutylammonium fluoride–THF (0.26 mL, 0.26 mmol) in THF (1.0 mL) for 1 h at room temperature. The product was chromatographed (1 g, 1:2 acetone–hexane) to give (+)-**60** (19 mg, 79%) as a syrup; $[\alpha]_D^{25}$ +27.5° (*c* 1.43, $CHCl_3$); selected ^{1}H NMR data (270 MHz, $CDCl_3$): δ 4.85–4.68 (m, 8 H, 4 CH_2OCH$_3$), 4.21 (bs, 1 H, H-4), 3.85 (dd, 1 H, $J_{1',2'}$ 8.1 Hz, $J_{5,1'}$ 1.1 Hz, H-1'), 3.75 (s, 3 H, CO_2Me), 3.61 (ddd, 1 H, $J_{2ax,3}$ 12.1, $J_{2eq,3}$ 4.0, $J_{3,4}$ 2.6 Hz, H-3), 3.44, 3.43, 3.40, and 3.34 (4 s, each 3 H, 4 OMe), 2.95–2.88 (m, 2 H, 2 OH), 2.50 (ddd, 1 H, $J_{2eq,6eq}$ 1.5, J_{gem} 11.7 Hz, H-2*eq*), 2.05 (dt, 1 H, $J_{5,6eq}$ 1.5, J_{gem} 13.2 Hz, H-6*eq*), 1.97 (t, 1 H, H-2*ax*), 1.83 (t, 1 H, H-6*ax*), 1.60 (m, 1 H, H-5). Anal. Calcd for $C_{19}H_{36}O_{12}$: C, 49.99; H, 7.95. Found: C, 49.95; H, 7.73.

Methyl (1S,3S,4R,5R)-5-[(1S,2R)-3-benzoyloxy-1,2-bis(methoxymethoxy)propyl]-4-hydroxy-1,3-bis(methoxymethoxy)cyclohexane-1-carboxylate [(−)-**61**].—A mixture of (+)-**60** (19 mg, 0.041 mmol) and benzoyl chloride (12 μL, 0.10 mmol) in pyridine (0.5 mL) was stirred for 2 h at room temperature. The product was chromatographed (1 g, 1:4.5 acetone–hexane) to give (−)-**61** (20 mg, 88%) as a syrup; $[\alpha]_D^{25}$ −5.7° (*c* 0.91, $CHCl_3$); selected ^{1}H NMR data (270 MHz, $CDCl_3$): δ 8.04 (d, 2 H, Ph), 7.56 (m, 1 H, Ph), 7.45 (m, 2 H, Ph), 4.88–4.69 (m, 8 H, 4 CH_2OCH$_3$), 4.61 (dd, 1 H, $J_{2',3'a}$ 3.7, J_{gem} 12.1 Hz, H-3'a), 4.42 (dd, 1 H, $J_{2',3'b}$ 6.6 Hz, H-3'b), 4.20 (dt, 1 H, $J_{1',2'}$ 6.6 Hz, H-2'), 4.05 (bs, 1 H, H-4), 3.96 (dd, 1 H, $J_{5,1'}$ 2.6 Hz, H-1'), 3.73 (s, 3 H, CO_2Me), 3.70 (m, 1 H, H-3), 3.43, 3.38, 3.355, and 3.352 (4 s, each 3 H, 4 OMe). Anal. Calcd for $C_{26}H_{40}O_{13}$: C, 55.71; H, 7.19. Found: C, 56.07; H, 6.88.

Methyl (1S,3S,4R,5R)-5-[(1S,2R)-3-benzoyloxy-1,2-bis(methoxymethoxy)propyl]-4-mesyloxy-1,3-bis(methoxymethoxy)cyclohexane-1-carboxylate [(−)-**62**].—To a solution of (−)-**61** (28 mg, 0.050 mmol) in dry pyridine (0.5 mL) was added mesyl chloride (80 mL, 1.0 mmol) and it was stirred for 3 h at room temperature. The product was chromatographed (2 g, 2:3 EtOAc–hexane) to give (−)-**62** (28 mg, 88%); $[\alpha]_D^{25}$ −10.2°

(*c* 0.625, $CHCl_3$); ν_{max} 1720 (C = O ester) and 1180 cm^{-1} (Ms); selected ^1H NMR data (270 MHz, $CDCl_3$): δ 8.00 (d, 2 H, Ph), 7.55 (m, 1 H, Ph), 7.45 (m, 2 H, Ph), 5.11 (bs, 1 H, H-4), 4.88–4.64 (m, 8 H, 4 CH_2OCH_3), 4.64 (dd, 1 H, $J_{2',3'a}$ 3.7, J_{gem} 12.1 Hz, H-3'a), 4.35 (dd, 1 H, $J_{2',3'b}$ 6.2 Hz, H-3'b), 4.19 (dt, 1 H, $J_{1',2'}$ 6.6 Hz, H-2'), 3.70 (s, 3 H, CO_2Me), 3.40, 3.363, and 3.356 (3 s, 6, 3, and 3 H, 4 OMe), 3.19 (s, 3 H, $MeSO_2$), 2.00 (m, 1 H, H-6*eq*), 1.87 and 1.70 (2 t, each 1 H, H-2*ax*,6*ax*). Anal. Calcd for $C_{27}H_{42}O_{15}S$: C, 50.77; H, 6.63. Found: C, 51.03; H, 6.50.

Methyl (1S,3S,4S,5R)-4-azido-5-[(1S,2R)-3-benzoyloxy-1,2-bis(methoxymethoxy)propyl]-1,3-bis(methoxymethoxy)cyclohexane-1-carboxylate [(−)-**63**].—A mixture of (−)-**62** (28 mg, 0.044 mmol) and NaN_3 (26 mg, 0.39 mmol) in dry DMF (0.5 mL) was stirred overnight at 90°C. The product was chromatographed (3.5 g, 2:3 EtOAc–hexane) to give (−)-**63** (20 mg, 78%) as a syrup; $[\alpha]_D^{25}$ −23.5° (*c* 0.073, $CHCl_3$); ν_{max} 2100 (N_3) and 1720 cm^{-1} (C = O ester); selected ^1H NMR data (270 MHz, $CDCl_3$): δ 8.08 (2 d, 2 H, Ph), 7.57 (m, 1 H, Ph), 7.48 (m, 2 H, Ph), 4.83–4.65 (m, 8 H, 4 CH_2OCH_3), 4.62 (dd, 1 H, $J_{2',3'a}$ 3.3, J_{gem} 12.1 Hz, H-3'a), 4.40 (dd, 1 H, $J_{2',3'b}$ 4.4 Hz, H-3'b), 4.16 (d, 1 H, $J_{1',2'}$ 7.3 Hz, H-1'), 3.91 (ddd, 1 H, H-2'), 3.75 (s, 3 H, CO_2Me), 3.65 (ddd, 1 H, $J_{2eq,3}$ 4.4, $J_{2ax,3}$ 11.7, $J_{3,4}$ 9.5 Hz, H-3), 3.46, 3.43, 3.35, and 3.34 (4 s, each 3 H, 4 OMe), 3.43 (t, 1 H, $J_{3,4} = J_{4,5}$ = 9.5 Hz, H-4), 2.88 (m, 1 H, H-2*eq*), 2.50 (dd, 1 H, $J_{5,6eq}$ 2.9, J_{gem} 9.5 Hz, H-6*eq*). Anal. Calcd for $C_{26}H_{39}N_3O_{12}$: C, 53.33; H, 6.71; N, 7.18. Found: C, 53.40; H, 6.35; N, 6.95.

Methyl (1S,3S,4S,5R)-4-acetamido-1,3-diacetoxy-5-[(1S,2R)-1,2,3-triacetoxypropyl]cyclohexane-1-carboxylate (2,4,5,8,9-penta-O-acetyl-6a-carba-α-N-acetylneuraminic acid) [(+)-**64**].—A solution of (−)-**63** (10 mg, 17 mmol) in EtOH (0.2 mL) containing a trace of Ac_2O was hydrogenated in the presence of a catalytic amount of Raney nickel T-4 for 1 h at room temperature under atmospheric pressure of H_2. The mixture was filtered through a Celite bed and the filtrate was evaporated. The residue (11 mg) was treated with 1 M methanolic NaOMe (35 mL) in MeOH (0.3 mL) for 5 h at room temperature. After neutralisation with Amberlite IR-120B (H^+) resin, the mixture was evaporated and the residue was hydrolysed with 2 M HCl (0.2 mL) overnight at 60°C. The product was acetylated conventionally, and the free acid formed by partial hydrolysis was converted into the ester by treatment with CH_2N_2 in its diethyl ether solution (1 mL). The residual product (11 mg) was chromatographed (1 g, 1:3 acetone–toluene) to give (+)-**64** (7.4 mg, 80% overall yield) as a syrup; $[\alpha]_D^{25}$ +10.2° (*c* 0.375, $CHCl_3$); ν_{max} 3370, 3300 (NH), 1750 (C = O ester), 1670 and 1540 cm^{-1} (C = O amide); selected ^1H NMR data (270 MHz, $CDCl_3$): δ 5.24 (dd, 1 H, $J_{5,1'}$ 2.6, $J_{1',2'}$ 8.4 Hz, H-1'), 4.23 (dd, 1 H, $J_{2',3'a}$ 2.9, J_{gem} 12.5 Hz, H-3'a), 3.98 (ddd, 1 H, $J_{4,5} = J_{3,4} = J_{4,NH}$ = 10.3 Hz, H-4), 3.74 (s, 3 H, CO_2Me), 2.77 (ddd, 1 H, $J_{2eq,3}$ 2.2, $J_{2eq,6eq}$ 2.6, J_{2gem} 12.5 Hz, H-2*eq*), 2.54 (ddd, 1 H, $J_{5,6eq}$ 2.6, J_{gem} 13.2 Hz, H-6*eq*), 2.11 (m, 1 H, H-5), 2.11, 2.10, 2.06, 2.04, 2.01, and 1.91 (6 s, each 3 H, 6 Ac), 1.79 (t, 1 H, $J_{2ax,3} = J_{gem}$ = 12.5 Hz, H-2*ax*), 1.71 (t, 1 H, $J_{5,6ax}$ 13.2 Hz, H-6*ax*). Anal. Calcd for $C_{23}H_{33}NO_{13}$: C, 51.97; H, 6.26; N, 2.64. Found: C, 51.65; H, 6.26; N, 2.34.

(1S,3S,4S,5R)-4-Acetamido-1,3-dihydroxy-5-[(1S,2R)-1,2,3-trihydroxypropyl]cyclohexane-1-carboxylic acid (**2**) *ammonium salt (ammonium 6a-carba-α-N-acetylneuraminate).*—A solution of (+)-**64** (9.5 mg, 18 mmol) in THF (0.5 mL) was treated with aq 0.5 M NaOH (0.5 mL) for 2 h at room temperature. After

neutralisation with Amberlite IR-120B (H^+) resin, the solution was evaporated with 1 M ammonia (0.5 mL) to give the ammonium salt of **2** (6.0 mg, 100%) as a pale-yellow syrup; $[\alpha]_D^{25}$ −19° (*c* 0.20, H_2O). This compound was directly subjected to bioassay.

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