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Construction of a branched chain at C-3 of a hexopyranoside. Synthesis of miharamycin sugar moiety analogs

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Dedicated to the memory of Professor Stanislas Czernecki

Abstract

Synthesis of the conveniently protected epimer at C-3′ of the miharamycin sugar moiety was accomplished starting from the corresponding 3,3′-spiroepoxide. Reaction of the epoxide with lithium cyanide, followed by hydrolysis and spontaneous cyclization, afforded the intermediate deoxylactone methyl 4,6-*O*-benzylidene-3-*C*-(carboxymethyl)-α-D-glucopyranoside-3′,2-lactone (**8**). Stereoselective hydroxylation with MoO_5·py·HMPA, reduction with lithium aluminum hydride and cyclization with diethyl azodicarboxylate–triphenylphosphine gave the target molecule methyl 2,3″-anhydro-4,6-*O*-benzylidene-3-*C*-[(*R*)-1,2-dihydroxyethyl]-α-D-glucopyranoside (**5**). Direct reduction of **8** gave other analogs having no C-3′ hydroxyl group together with having a C-3″ hydroxyl group (hemiacetal). In addition, C-3′ epimers were also synthesized through C-3′, C-3″ dihydroxy analogs. Wittig reaction of an appropriate ketosugar with [(ethoxycarbonyl)methylene]triphenylphosphorane leading to a 7:3 Z/E mixture, followed by hydroxylation with osmium tetroxide, reduction and cyclization afforded the target molecule **5** and the miharamycin sugar moiety methyl 2,3″-anhydro-4,6-*O*-benzylidene-3-*C*-[(*S*)-1,2-dihydroxyethyl]-α-D-glucopyranoside. Examination of X-ray data for **5** and its NMR spectroscopy data allowed us to explain a contradiction reported in the literature.

Keywords: Miharamycin sugar moiety analogues; Stereoselective synthesis; Branched-chain sugars

1. Introduction

Amipurimycin and miharamycin A (**1**) and B (**2**) are nucleoside antibiotics that act as potent inhibitors of *Pyricularia oryzae*, known to cause the rice blast disease [1]. In a previous work, we have described the synthesis of the amipurimycin sugar moiety [2]. Miharamycin A (**1**) and B (**2**) are produced by *Streptomyces miharaensis* SF-489 [1] and the structural studies of these two antibiotics were reported based on ^{1}H and ^{13}C NMR spectral analysis [3].

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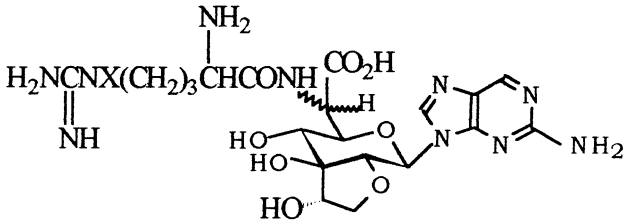


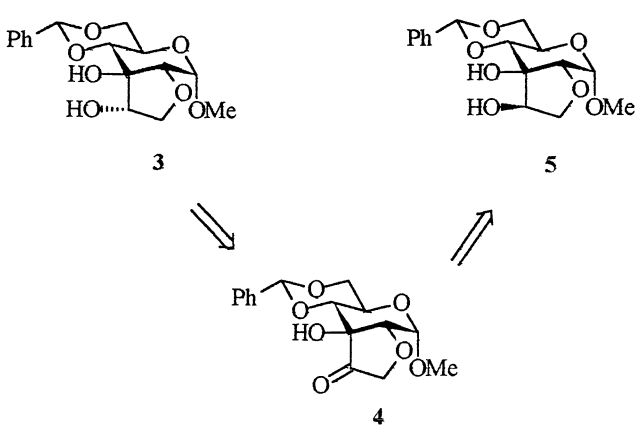
1 X = OH

2 X = H

Synthesis of the hexopyranosidic carbohydrate moiety **3** has been described in the literature by Sinaÿ and Fairbanks [4] by stereoselective reduction with $NaBH_4$ of the ketosugar **4**. In this work, we report a highly stereoselective branched-chain construction at C-3 of a hexopyranosidic unit **5**, which is an epimeric analog of the miharamycin sugar moiety **3** and may be considered as a precursor for its synthesis as depicted in Scheme 1, as well as other analogues containing the tetrahydrofuran ring or this ring hydroxylated at C-3″.

2. Results and discussion

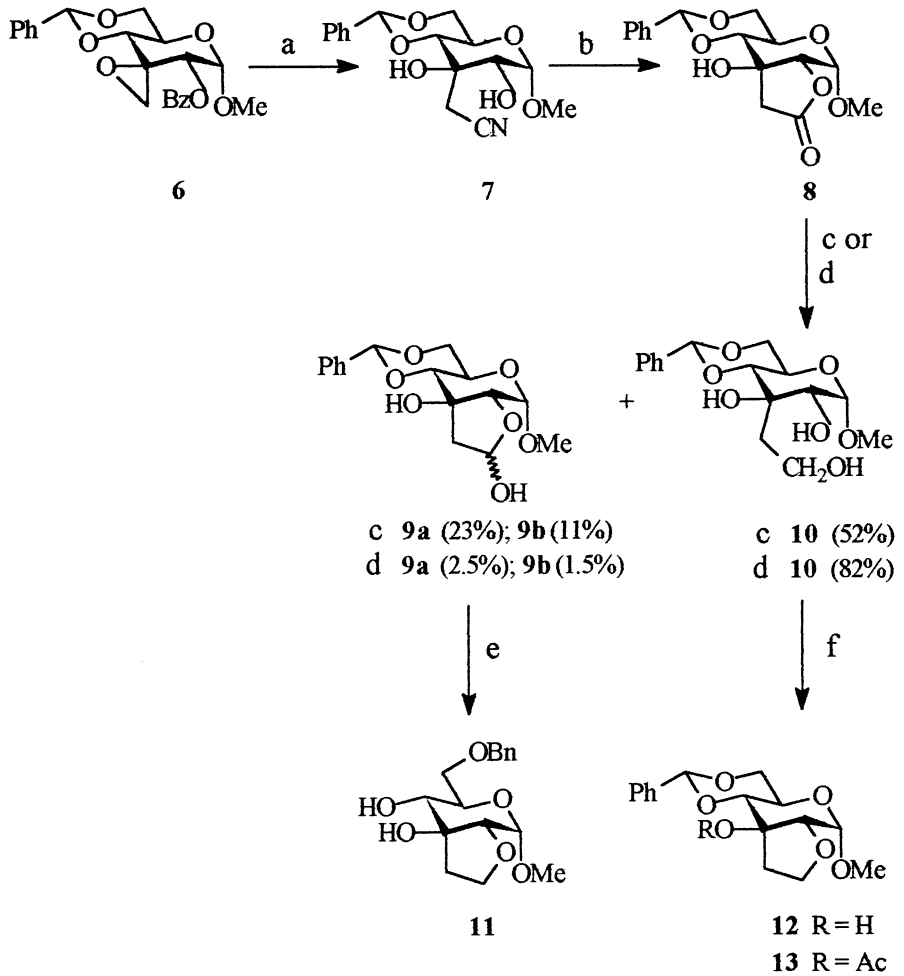
The new highly stereoselective synthesis of **5** was accomplished using as starting material the epoxide **6** [5] (Scheme 2), which possesses the appropriate configuration at C-3. Spectroscopic data of **6** were in agreement with those reported for it by Yoshimura et al. [5], with the exception of the chemical shifts given for H-1 and H-2 by those authors, values of which should be interchanged as confirmed by us by $^{1}H-^{13}C$ heteronuclear multiple quantum correlation. Reaction of **6** with lithium cyanide in anhydrous tetrahydrofuran for 12 h under reflux and argon atmosphere, followed by removal of the benzoyl group, afforded the nitrile **7** isolated by column chromatography with silica gel in 78% yield. Compound **7** is very unstable and hydrolyses spontaneously in the presence of traces of silica gel, leading to the formation of the lactone **8** in 82% yield. Attempts to hydrolyse **7** under mild acidic conditions such as ammonium chloride in methanol under reflux for 24 h left the starting material unchanged. When sodium cyanide in dimethylformamide or potassium cyanide in methanol were used under reflux, followed by addition of ammonium chloride, a complex mixture of products was obtained, also containing traces of the lactone **8** as detected by thin-layer chromatography (TLC).



Scheme 1.

Hydrolysis and esterification of **7** was tried by treatment with sodium methoxide in methanol at room temperature for 1 week and no reaction occurred. Alkylation of **7** to an *N*-alkylnitrilium ion with the system 2-chloropropane–$FeCl_3$, followed by addition of triethylsilane and hydrolysis [6], did not give the expected aldehyde, but led to the complete decomposition of the substrate. All these attempts made it clear that the described conditions for the formation of **8** are so far the most suitable ones.

Further modifications of **8** were performed to provide analogues of the hexopyranosidic sugar moiety of miharamycin in order to allow structure–activity relationship studies. Reduction of the lactone **8** with diisobutylaluminum hydride [7] in toluene at −40 °C for 1 h gave the lactols **9a**,**b** in 34% yield and ratio 2:1, together with the primary alcohol **10** in 52% yield. Treatment of **9** with boron trifluoride diethyl etherate–triethylsilane [8] in acetonitrile at −30 °C afforded **11** (36% yield). The opening of the 4,6-*O*-benzylidene residue was highly regioselective, and this result is in good agreement with a previous observation given by Garegg et al. [9] for the reductive opening of benzylidene dioxane rings using electrophiles with a small steric requirement. The low yield for the cyclic ether **11** from the lactone **8** resulting from this pathway encouraged us to examine the reduction of **8** with lithium aluminum hydride in tetrahydrofuran. In this case, **10** was obtained



Scheme 2. (a) LiCN 0.5 M in DMF, THF, Δ, 12 h (78%); (b) H_2O, silica gel (82%); (c) DIBAHL, toluene–THF, 3 h, −78 °C and 1 h, −40 °C; (d) $LiAlH_4$, THF, 5 h, 40 °C and 1 h, Δ; (e) $BF_3{\cdot}Et_2O$, Et_3SiH, CH_3CN, −30 °C, 1.5 h (36%); (f) Ph_3P–DEAD, $CHCl_3$, 4 Å powdered molecular sieves, 2.5 h, 5 °C (82%) for **12** and Ac_2O, DMAP, py, room temperature, 3 h (94%) for **13**.

in 82% yield. Cyclization with diethyl azodicarboxylate–triphenylphosphine [10,11] allowed the preparation of **12** in 82% yield. Since, H-3″a, H-3″b, H-3′a and H-3′b of **12** consist of an ABCD spin system and the AB part is overlapped with H-6e, we have synthesized its 3-*O*-acetyl derivative **13** by reaction with acetic anhydride, 4-dimethylaminopyridine and pyridine at room temperature for 3 h in 94% yield. This derivative presents the H-3″a (A), H-3″b (B), H-3′a (C) and H-3′b (D) protons each as a multiplet at δ 4.21, 4.04, 2.53 and 2.20, respectively. The coupling constants $J_{AB} = -7.33$, $J_{AC} = 9.74$, $J_{AD} = 1.88$, $J_{BC} = 9.88$, $J_{BD} = 7.00$ and $J_{CD} = -13.63$ Hz were determined by computational simulation using the iterative program LAOCOON (Fig. 1).

Hydroxylation of **8** (Scheme 3) was accomplished using lithium diisopropylamide in tetrahydrofuran at −78 °C to obtain the corresponding enolate, which then reacted with the molybdenum pentoxide–pyridine–hexamethylphosphoramide complex (MoOs·py·HMPA) [12–14] for 3 h at −78 °C affording the 3′-hydroxylactone **14** in 50% yield, based on the reacted starting material, which was recovered in 48% yield. Reduction of **14** with lithium aluminum hydride in tetrahydrofuran, followed by reaction with diethyl azodicarboxylate–triphenylphosphine in chloroform at 5 °C [10,11] led to the synthesis of the desired cyclic ether **5** in 23% overall yield from **14**.

The confirmation of the expected S configuration of the new stereogenic center [15] in **14**

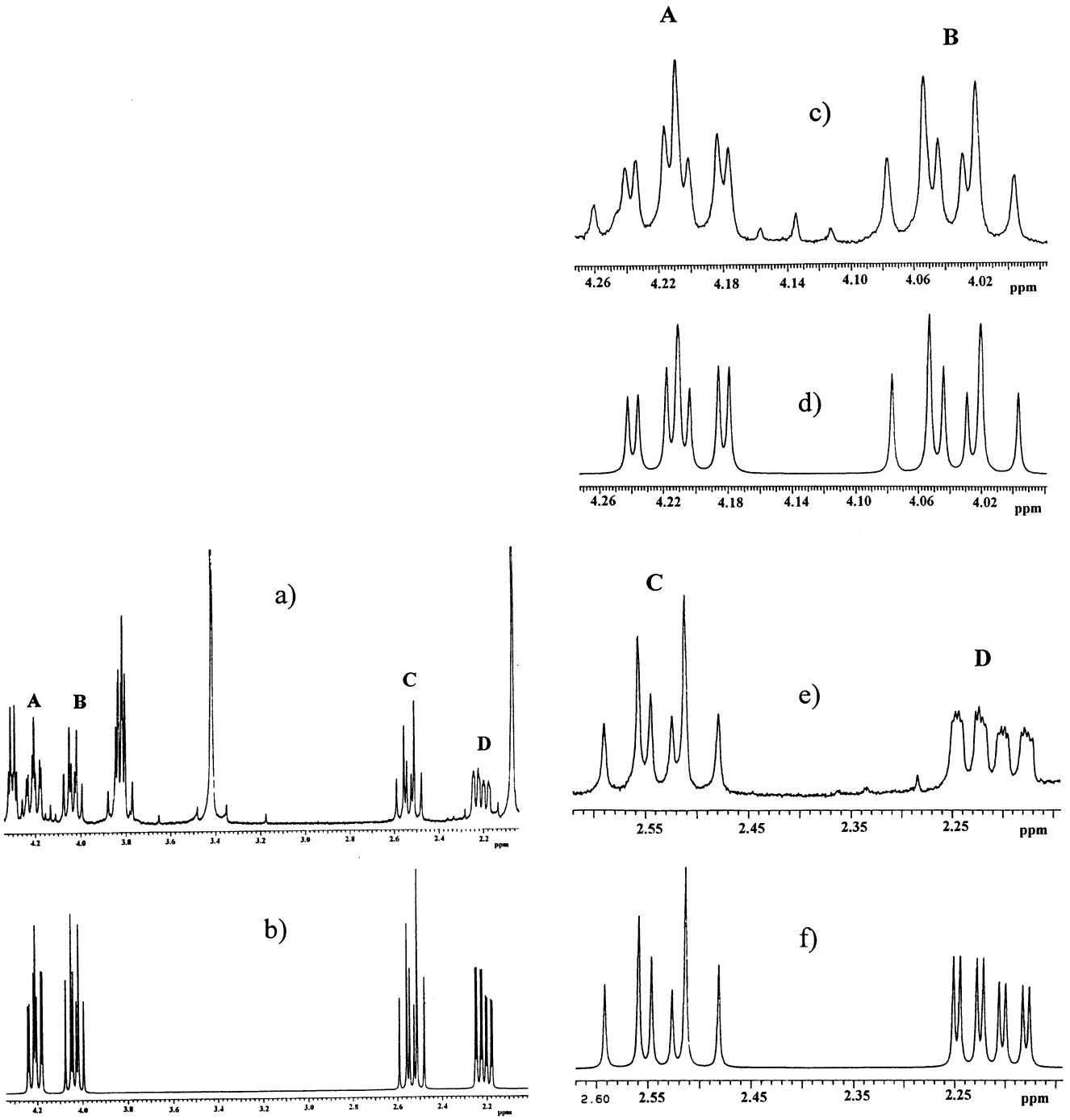
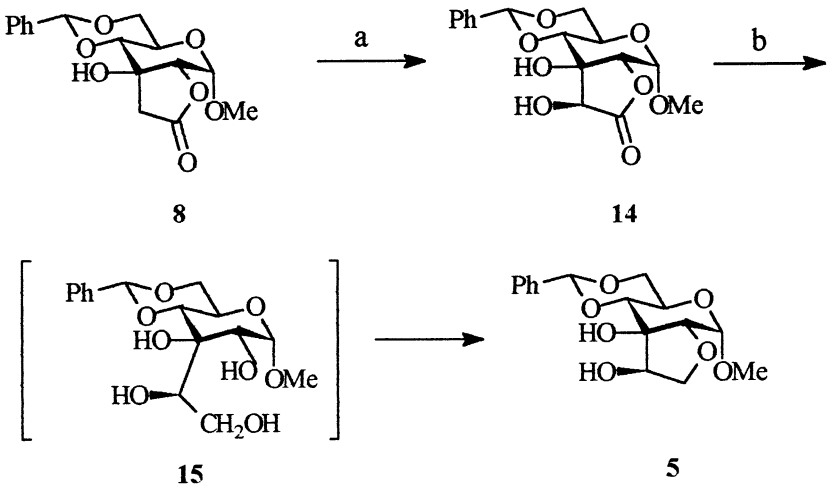


Fig. 1. (a) Experimental and (b) theoretical ^{1}H NMR spectra of **13** (chemical shifts between δ 4.32 and 2.02) analysed as an ABCD spin system; (c) ^{1}H NMR spectrum of **13** (chemical shifts between δ 4.27 and 4.00); (d) simulated spectrum of the nucleus AB; (e) ^{1}H NMR spectrum of **13** (chemical shifts between δ 2.62 and 2.10); (f) simulated spectrum of the nucleus CD.

was effected by nuclear Overhauser effect spectroscopy (NOESY) by detection of the interaction between OH-3–OH-3′ and H-3′–H-5 (Fig. 2). Since the spectroscopic data of **5** were not in agreement with the corresponding data reported by Hara et al. [16], we have investigated a reaction pathway similar to the one described by those authors, who used as starting material the ketosugar **16** [17], and its Wittig reaction with ethyl diethylphosphonoacetate, followed by reduction with lithium aluminum hydride, acetylation of the hydroxyl groups formed, addition of osmium tetroxide, deprotection and cyclization with camphorsul-

fonyl chloride–pyridine. The branched-chain construction of the miharamycin hexopyranosidic sugar moiety was accomplished by a four-step sequence. Olefination of the ketosugar **16** was performed with [(ethoxycarbonyl)methylene]triphenylphosphorane affording a 7:3 mixture of the Z/E isomers **17** and **18**, respectively, in 88% yield (Scheme 4). Oxidation of the mixture **17**/**18** with osmium tetroxide in pyridine [18] led to the synthesis of a mixture of stereoisomers in quantitative yield, whereas when osmium tetroxide was used in catalytic amount in the presence of 4-methylmorpholine *N*-oxide in acetone–water, [19] the mixture **19a**,**b** was isolated in 66% yield. Reduction of **19a**,**b** with lithium aluminum hydride in tetrahydrofuran under reflux for 24 h led to a 3:1 mixture of tetrols **20a**,**b** in 48% yield and to secondary products, i.e., the lactols **21a**,**b** in a 1:1 ratio and **22**, obtained in 14 and 9% yield, respectively. When the reaction was conducted at 25 °C for



Scheme 3. (a) LDA, THF, −78 °C, 50 min; MoO_5·py·HMPA, −78 °C, 3 h (50%); (b) $LiAlH_4$, THF, Δ, 96 h; DEAD–Ph_3P, $CHCl_3$, 5 °C, 4 Å powdered molecular sieves (23%).

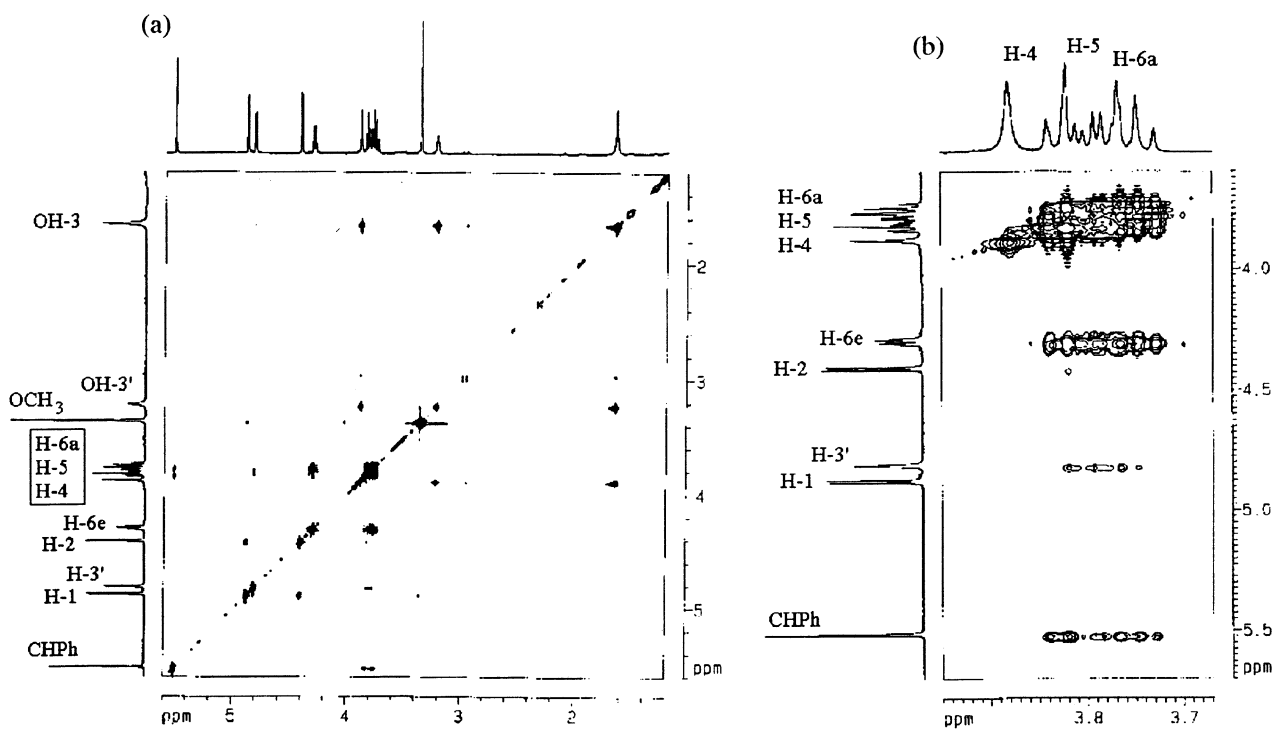
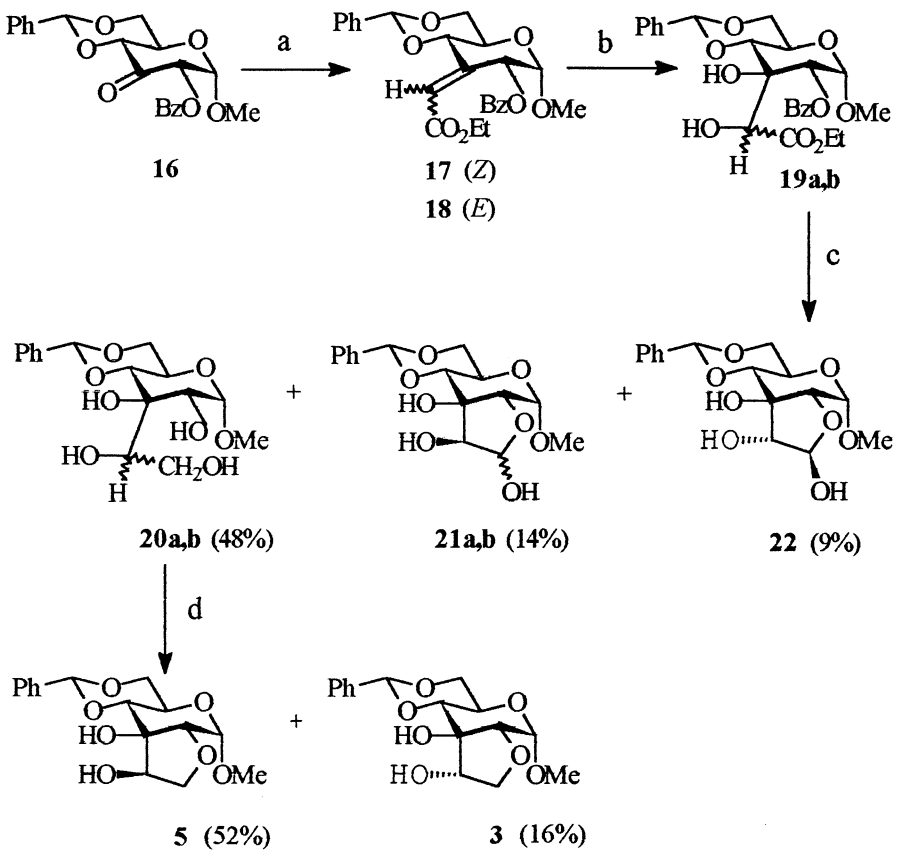


Fig. 2. (a) NOESY spectrum of **14**; (b) amplified spectrum of **14** between δ 3.95 and 3.67.



Scheme 4. (a) $Ph_3P{=}CHCO_2Et$, $CHCl_3$, Δ, 5.5 h (88%); (b) OsO_4, py., room temperature, 2.5 h (100%); (c) $LiAlH_4$, THF, Δ, 24 h; (d) Ph_3P–DEAD, $CHCl_3$, 4 Å powdered molecular sieves, 5 °C, 2.5 h.

3.5 h, **20a**,**b** was isolated only in 36% yield but the lactols **21a**,**b** and **22** were obtained in 18 and 27% yield, respectively. The ^1H NMR spectrum of **21a**,**b** was identical to the one of the lactols obtained by reduction of the lactone **14**. The configuration of C-3″ in **22** was inferred by the analysis of its ^1H NMR spectrum since H-3″ appears as a doublet coupling only with OH-3″ with $J_{3'',OH\text{-}3''} = 7.59$ Hz, confirmed by addition of deuterium oxide. The absence of coupling with H-3′ is only possible if both protons are trans to each other. Cyclization of **20a**,**b** with diethyl azodicarboxylate–triphenylphosphine in chloroform at 5 °C for 2.5 h [10,11] afforded the isomers **5** and **3** in 52 and 16% yields, respectively. Attempts to use diisopropyl azodicarboxylate–triphenylphosphine as cyclization system did not improve the yields of **5** and **3** nor simplify their chromatographic purification, since the starting material was also present under the same experimental conditions used with the system diethyl azodicarboxylate–triphenylphosphine. Compound **3** was compared with a sample kindly sent by Professor P. Sinaÿ and exhibited spectroscopic data which are in full agreement with those reported for it by Sinaÿ and Fairbanks [4]. These authors have unambiguously elucidated the structure of **3** by X-ray crystallography. Since spectroscopic and physical data of compound **5** were in complete accordance with the data reported by Hara et al. [16] for 'their' compound **3**, we assume that they had assigned an erroneous structure. Single-crystal X-ray crystallographic analysis of **5** confirmed the proposed structure and established the C-3′ configuration to be R (Fig. 3). The most noticeable differences between our molecule and the one reported by Sinaÿ and Fairbanks [4] are the C-phenyl distance, 1.506(11) Å and all the torsion angles around atoms C-3, C-3′and C-3″, particularly O-3′–C-3′–C-3–O-3 whose value 38.7(8)°, compared with the corresponding angle of 160.67°, is determinant in the assignment of the correct configuration (see Tables 2 and 3).

This synthetic pathway afforded complex mixtures but allowed the inconsistencies reported in the literature for the synthesis of the miharamycin sugar moiety to be explained.

3. Experimental

General methods.—Melting points were determined with a melting point apparatus (Tottoli) and are uncorrected. ^{1}H NMR spectra were recorded in $CDCl_3$ at 250, 300 and 500 MHz and ^{13}C NMR spectra recorded in $CDCl_3$ at 62.9 MHz. Chemical shifts are expressed in ppm downfield from Me_4Si. NOESY spectra were recorded in $CDCl_3$ at 500 MHz at 290 K. The ^{1}H and ^{13}C HMQC spectra was recorded in $CDCl_3$ at 125.77 MHz (^{13}C) and 500.13 MHz (^{1}H). The simulation of ^{1}H NMR spectra was performed using the iterative spin simulation computer program LAOCOON with a Varian Unity 300. HRMS mass spectra were recorded with a Finnigan FT/MS 2001-DT FTICR mass spectrometer equipped with a 3 T superconducting magnet and interfaced with a Spectra-Physics Quants-Ray GCR-11 Nd:YAG laser operated at the fundamental wavelength (1064 nm). Electron impact mass spectra were obtained with a Jeol JMS-DX300 (70 eV). The LSIMS mass spectra were recorded with a VG-ZAB-T four-sector mass spectrometer equipped with an inhomogeneous field, plane parallel electrostatic analyzer and a 2048 microchannel photodiode (MCP) array detector and using glycerol as matrix. Analytical TLC was performed on E. Merck aluminum pre-coated plates of Silica Gel 60 F254 (thickness of 0.2 mm) with detection by spraying with a 2.5% vanillin–sulfuric acid soln. Column chromatography was performed using Silica Gel 60 G (0.040–0.063 mm, E. Merck) and elution under reduced pressure. Evaporation of solvents was carried out under reduced pressure under 40 °C. Elemental analysis was conducted at the Service of Microanalyses of Instituto Superior Técnico da Universidade Técnica de Lisboa.

*Methyl 2,3″-anhydro-4,6-*O*-benzylidene-3-C-[(*S*)-1,2-dihydroxyethyl]-α-*D*-glucopyranoside* (**3**).—Triphenylphosphine (210 mg, 0.81 mmol) and 4 Å powdered molecular sieves (30 mg) were added to a soln of **20a**,**b** (100 mg, 0.29 mmol) in dry $CHCl_3$ (8 mL) at room temperature (rt) under argon. After cooling to 5 °C, diethyl azodicarboxylate (DEAD) (0.15 mL, 0.95 mmol) was added and the reaction mixture was stirred at 5 °C for 2.5 h. Filtration and evaporation gave a residue which was purified by column chromatography with 2:1 EtOAc–toluene giving **3** as a solid (15 mg, 16%); mp 188–191 °C; $[\alpha]_D^{20} + 94.4°$ (*c* 0.93,

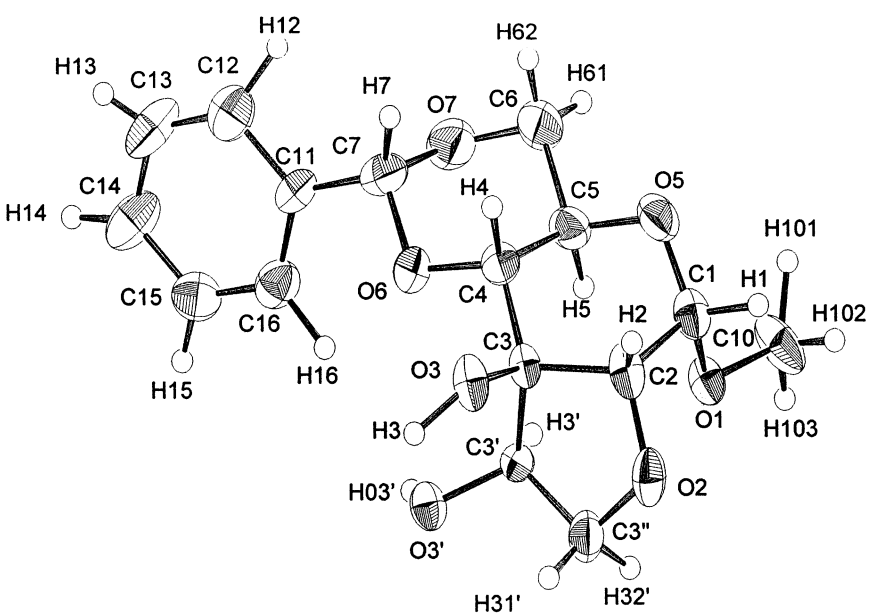


Fig. 3. Molecular drawing of diol **5** showing the crystallographic numbering scheme (ORTEP II, ellipsoids with 40% probability).

Table 1
Crystal data and structure refinement for **5**

Empirical formula	$C_{16}H_{20}O_7$
Formula weight	324.36
Temperature (K)	293(2)
Wavelength (Å)	0.71069
Crystal system	orthorhombic
Space group	$P2_12_12_1$
Unit cell dimensions	
a (Å)	5.433(8)
b (Å)	10.672(1)
c (Å)	26.903(4)
Volume (Å^3)	1559.7(7)
Z	4
D_{calcd} (Mg m^{-3})	1.381
Absorption coefficient (mm^{-1})	0.067
F(000)	688
θ Range for data collection (°)	1.51–24.96
Index ranges	$0\leq h\leq 6$; $0\leq k\leq 12$; $0\leq l\leq 31$
Reflections collected/unique	1626/1626 [$R_{int}=0.0000$]
Completeness to $2\theta=24.96$ (%)	99.9
Refinement method	full-matrix least-squares on F^2
Data/restraints/parameters	1626/0/288
Goodness-of-fit on F^2	1.210
Final *R* indices [$I>2\sigma(I)$]	$R_1=0.0601$, $wR_2=0.0940$
R indices (all data)	$R_1=0.1245$ $wR_2=0.1252$
Absolute structure parameter	0(5)
Largest difference peak and hole (e Å^{-3})	0.233 and −0.196

$CHCl_3$); IR (KBr): ν 3387 cm^{-1} (OH); ^{1}H NMR (300 MHz): δ 7.60–7.43 (m, 5 H, Ph), 5.63 (s, 1 H, CHPh), 4.89 (d, 1 H, $J_{1,2}$ 5.43 Hz, H-1), 4.44 (dd 1 H, $J_{3',3''a}$ 4.38, $J_{3''a,3''b}$ 9.48 Hz, H-3″a), 4.35 (dd, 1 H, $J_{5,6e}$ 4.59, $J_{6a,6e}$ 9.72 Hz, H-6e), 4.27–4.17 (m, 2 H, H-3′, H-5), 4.08 (d, 1 H, H-2), 3.98 (d, 1 H, H-3″b), 3.93 (d, 1 H, $J_{4,5}$ 9.72 Hz, H-4), 3.66 (t, 1 H, H-6a), 3.54 (s, 3 H, OCH_3), 2.63 (s, OH); ^{13}C NMR: δ 137.0, 129.4, 128.4, 126.5 (Ph), 103.0 (*C*HPh), 99.3 (C-1), 83.4, 82.0 (C-4, C-2), 78.6 (C-3″), 77.5 (C-3), 77.0 (C-3′), 70.0 (C-6), 60.5 (C-5), 55.9 (OCH_3); HRMS: calcd for $C_{16}H_{20}O_7$ 324.348, found: 324.121.

*Methyl 2,3″-anhydro-4,6-*O*-benzylidene-3-*C*-[(*R*)-1,2-dihydroxyethyl]-α-*D*-glucopyranoside* (**5**)

Method A. The same procedure described above for **3** was used, giving **5** as a solid (49.3 mg, 52%).

Method B. A soln of **14** (50 mg, 0.15 mmol) in dry THF (0.5 mL) was added to a suspension of $LiAlH_4$ (28 mg) in dry THF (3.5 mL) at 0 °C under argon. After heating the reaction mixture under reflux for 96 h, the workup was the same as described for **20a**,**b**. The residue (44 mg) was dissolved in dry $CHCl_3$ (2.5 mL) and triphenylphosphine (55 mg, 0.21 mmol) and 4 Å powdered molecular sieves (6 mg) were added to the soln, under argon. DEAD (0.05 mL, 0.3 mmol) was added to the reaction mixture, previously cooled to 5 °C. Stirring at 5 °C for 3 h, filtration and evaporation afforded a mixture separated by preparative TLC with 1:1 EtOAc–toluene giving **5** (11 mg, 23% global yield): mp 124–126 °C (CH_2Cl_2–cyclohexane); $[\alpha]_D^{20}+75.1°$ (*c* 1.1, $CHCl_3$); IR (KBr): ν 3396 cm^{-1} (OH); ^{1}H NMR (500 MHz): δ 7.56–7.50 (m, 2 H, Ph), 7.24–7.22 (m, 3 H, Ph), 5.57 (s, 1 H, CHPh), 4.93 (dt, 1 H, $J_{3',OH}$ 3.21, $J_{3',3''a}$ 7.8 Hz, H-3′), 4.75 (d, 1 H, $J_{1,2}$ 5.05 Hz, H-1), 4.32 (dd, 1 H, $J_{6a,6e}$ 10.08, $J_{5,6e}$ 4.6 Hz, H-6e), 4.29 (t, 1 H, $J_{3''a,3''b}$ 7.8 Hz, H-3″a), 4.11 (d, 1 H, H-2), 3.93 (d, 1 H, $J_{4,5}$ 10.08 Hz, H-4), 3.83 (dt, 1 H, $J_{5,6a}$ 10.08 Hz, H-5), 3.76 (t, 1 H, H-6a), 3.71 (t, 1 H, $J_{3',3''b}$ 7.8 Hz, H-3″b), 3.40 (s, 3 H, OCH_3); ^{13}C NMR: δ 137.1, 129.4, 128.5, 126.1 (Ph), 102.3 (*C*HPh), 99.7 (C-1), 83.3 (C-4), 82.3 (C-2), 76.3 (C-3), 72.6 (C-3″), 71.6 (C-3′), 69.3 (C-6), 59.7 (C-5), 55.7 (OCH_3); EIMS: *m*/*z* 292 (95, $[M-CH_3OH]^+$), 149 (23, $[C_6H_5CHOCH_2CHO]^+$), 105 (49, $[C_6H_5CO]^+$), 107 (100, $[C_6H_5CHOH]^+$); LSIMS: *m*/*z* 325 (100; $[M+H]^+$), 293 (92; $[M+H-CH_3OH]^+$), 107 (40; $[C_6H_5CHOH]^+$); HRMS: calcd for $C_{16}H_{20}O_7$ 324.348, found: 324.121; Crystal data for **5**, crystallized from CH_2Cl_2–cyclohexane: data were collected in a CAD4 diffractometer using graphite monochromated Mo K_α radiation. Details of data collection and refinement are presented in Table 1. 1626 reflections were measured and used in the soln and refinement of the crystal structure by direct methods. Remaining non-hydrogen and hydrogen atoms were located in successive difference Fourier syntheses. The structure was refined by least-squares methods until convergence, allowing the refinement of Flack's parameter with all the other parameters in the same full matrix. All calculations required to solve and refine the molecular

Table 2
Bond lengths (Å) and angles (°) for **5**

Bond lengths	
O-1–C-1	1.398(8)
O-1–C-10	1.431(9)
O-3′–C-3′	1.413(8)
C-3′–C-3	1.515(8)
C-3′–C-3″	1.534(9)
O-6–C-4	1.429(7)
O-6–C-7	1.430(8)
O-3–C-3	1.423(7)
C-1–O-5	1.398(9)
C-1–C-2	1.534(10)
C-4–C-3	1.497(9)
C-4–C-5	1.518(9)
C-3–C-2	1.551(8)
O-2–C-2	1.401(9)
O-2–C-3″	1.433(10)
O-7–C-7	1.423(9)
O-7–C-6	1.457(13)
O-5–C-5	1.442(9)
C-7–C-11	1.506(11)
C-16–C-11	1.367(11)
C-16–C-15	1.382(12)
C-5–C-6	1.509(11)
C-15–C-14	1.365(11)
C-11–C-12	1.362(10)
C-12–C-13	1.389(14)
C-13–C-14	1.349(15)
Bond angles	
C-1–O-1–C-10	113.2(6)
O-3′–C-3′–C-3	112.7(6)
O-3′–C-3′–C-3″	109.5(6)
C-3–C-3′–C-3″	103.3(6)
C-4–O-6–C-7	111.8(6)
O-1–C-1–O-5	112.6(7)
O-1–C-1–C-2	107.4(6)
O-5–C-1–C-2	112.7(6)
O-6–C-4–C-3	108.5(5)
O-6–C-4–C-5	107.7(6)
C-3–C-4–C-5	113.2(6)
O-3–C-3–C-4	110.9(6)
O-3–C-3–C-3′	109.9(6)
C-4–C-3–C-3′	117.0(6)
O-3–C-3–C-2	107.1(5)
C-4–C-3–C-2	110.6(6)
C-3′–C-3–C-2	100.5(5)
C-2–O-2–C-3″	109.7(6)
C-7–O-7–C-6	110.0(8)
C-1–O-5–C-5	110.7(6)
O-2–C-2–C-1	112.4(6)
O-2–C-2–C-3	105.8(6)
C-1–C-2–C-3	114.4(6)
O-7–C-7–O-6	110.0(6)
O-7–C-7–C-11	106.6(7)
O-6–C-7–C-11	108.4(7)
C-11–C-16–C-15	121.2(9)
O-5–C-5–C-6	110.1(8)
O-5–C-5–C-4	107.2(7)

Table 2

C-6–C-5–C-4	108.8(8)
C-14–C-15–C-16	119.1(10)
O-7–C-6–C-5	105.2(8)
C-16–C-11–C-12	118.2(9)
C-16–C-11–C-7	120.6(7)
C-12–C-11–C-7	121.2(9)
O-2–C-3″–C-3′	106.9(6)
C-11–C-12–C-13	121.4(10)
C-14–C-13–C-12	119.1(10)
C-13–C-14–C-15	121.0(11)

structure were performed with SHELX-86 [20] and SHELX-97 [21]. The molecular diagram was drawn with ORTEP II [22]. Selected bond lengths and angles are presented in Table 2. Table 3 contains the torsion angles relevant to the configuration of the molecule.

*Methyl3,3′-anhydro-2-*O*-benzoyl-4,6-*O*-benzylidene-3-*C*-hydroxymethyl-α-*D*-glucopyranoside* (**6**).—The experimental procedure is the same as described by Yoshimura et al. [5], giving **6** as a syrup in 80% yield. $[\alpha]_D^{23} + 113°$ (*c* 1.06, $CHCl_3$); IR ($CHCl_3$): *ν* 1724 cm^{-1} (C=O), 1602 cm^{-1} (Ph); ^1H NMR (300 MHz): *δ* 7.95–7.26 (m, 10 H, Ph), 5.49 (s, 1 H, CHPh), 5.37 (d, 1 H, $J_{1,2}$ 3.66 Hz, H-2), 5.05 (d, 1 H, H-1), 4.28 (dd, 1 H, $J_{6a,6e}$ 10.17, $J_{5,6e}$ 4.35 Hz, H-6e), 3.99–3.89 (ddd, 1 H, H-5), 3.91 (d, 1 H, $J_{4,5}$ 9.45 Hz, H-4), 3.78 (t, 1 H, $J_{5,6a}$ 9.9 Hz, H-6a), 3.35 (s, 3 H, OCH_3), 3.12 (m, 2 H, H-3′a, H-3′b); ^{13}C NMR: *δ* 165.3 (C(=O)O), 136.8, 133.4, 129.8, 129.1, 128.3, 128.1, 126.4 (Ph), 101.4 (*C*HPh), 98.3 (C-1), 75.6 (C-4), 69.0 (C-6), 68.0 (C-2), 63.4 (C-5), 57.3 (C-3), 55.5 (OCH_3), 46.9 (C-3′).

*Methyl 4,6-*O*-benzylidene-3-*C*-(carboxymethyl)-α-*D*-glucopyranoside-3′,2-lactone* (**8**).—Lithium cyanide in DMF (0.5 M, 10.5 mL, 5.30 mmol) was added to a soln of **6** (527 mg, 1.32 mmol) in dry THF (2 mL) under argon at rt. After heating under reflux for 12 h, the reaction mixture was cooled to rt, hydrolyzed with water (15 mL) and extracted with $CHCl_3$ (3×15 mL). The organic phase was dried (Na_2SO_4) and evaporated to dryness. Column chromatography with 2:1 EtOAc–toluene gave methyl 4,6-*O*-benzylidene-3-*C*-cyanomethyl-α-*D*-glucopyranoside (**7**) as a syrup (331 mg, 78%), which suffered hydrolysis and spontaneous cyclization at rt to give **8**, isolated by column chromatography

Table 3
Torsion angles (°) for **5**

C-10–O-1–C-1–O-5	68.2(9)
C-10–O-1–C-1–C-2	−167.2(8)
C-7–O-6–C-4–C-3	179.1(6)
C-7–O-6–C-4–C-5	−58.0(8)
O-6–C-4–C-3–O-3	−76.1(7)
C-5–C-4–C-3–O-3	164.4(6)
O-6–C-4–C-3–C-3′	51.0(7)
C-5–C-4–C-3–C-3′	−68.4(8)
O-6–C-4–C-3–C-2	165.3(5)
C-5–C-4–C-3–C-2	45.8(8)
O-3′–C-3′–C-3–O-3	38.7(8)
C-3″–C-3′–C-3–O-3	−79.4(7)
O-3′–C-3′–C-3–C-4	−88.9(7)
C-3″–C-3′–C-3–C-4	153.0(6)
O-3′–C-3′–C-3–C-2	151.3(6)
C-3″–C-3′–C-3–C-2	33.3(7)
O-1–C-1–O-5–C-5	61.0(7)
C-2–C-1–O-5–C-5	−60.7(8)
C-3″–O-2–C-2–C-1	−100.7(7)
C-3″–O-2–C-2–C-3	24.8(8)
O-1–C-1–C-2–O-2	40.3(8)
O-5–C-1–C-2–O-2	164.9(6)
O-1–C-1–C-2–C-3	−80.4(8)
O-5–C-1–C-2–C-3	44.2(9)
O-3–C-3–C-2–O-2	78.4(7)
C-4–C-3–C-2–O-2	−160.7(6)
C-3′–C-3–C-2–O-2	−36.4(7)
O-3–C-3–C-2–C-1	−157.3(6)
C-4–C-3–C-2–C-1	−36.4(8)
C-3′–C-3–C-2–C-1	87.9(7)
C-6–O-7–C-7–O-6	−63.8(10)
C-6–O-7–C-7–C-11	178.9(7)
C-4–O-6–C-7–O-7	60.7(9)
C-4–O-6–C-7–C-11	176.9(6)
C-1–O-5–C-5–C-6	−173.4(9)
C-1–O-5–C-5–C-4	68.4(7)
O-6–C-4–C-5–O-5	178.5(5)
C-3–C-4–C-5–O-5	−61.5(8)
O-6–C-4–C-5–C-6	59.5(10)
C-3–C-4–C-5–C-6	179.4(9)
C-11–C-16–C-15–C-14	−2.3(14)
C-7–O-7–C-6–C-5	64.1(12)
O-5–C-5–C-6–O-7	−179.1(8)
C-4–C-5–C-6–O-7	−61.9(13)
C-15–C-16–C-11–C-12	2.6(13)
C-15–C-16–C-11–C-7	−177.0(8)
O-7–C-7–C-11–C-16	85.8(9)
O-6–C-7–C-11–C-16	−32.5(10)
O-7–C-7–C-11–C-12	−93.8(9)
O-6–C-7–C-11–C-12	147.9(8)
C-2–O-2–C-3″–C-3′	−2.8(8)
O-3′–C-3′–C-3″–O-2	−140.9(6)
C-3–C-3′–C-3″–O-2	−20.6(8)
C-16–C-11–C-12–C-13	−0.5(14)
C-7–C-11–C-12–C-13	179.1(8)
C-11–C-12–C-13–C-14	−1.8(16)
C-12–C-13–C-14–C-15	2.1(16)
C-16–C-15–C-14–C-13	−0.1(15)

with 1:2 EtOAc–toluene as a solid (272 mg, 82%). mp 175–177 °C; $[\alpha]_D^{20} + 124.7°$ (*c* 1, $CHCl_3$); IR ($CHCl_3$): *v* 3568 cm^{-1} (OH), 1785 cm^{-1} (C(=O)O) and 1602 cm^{-1} (Ph); ^1H NMR (250 MHz): δ 7.44–7.40 (m, 5 H, Ph), 5.58 (s, 1 H, CHPh), 4.92 (d, 1 H, $J_{1,2}$ 5.06 Hz, H-1), 4.46 (d, 1 H, H-2), 4.35 (br d, 1 H, $J_{6a,6e}$ 5.58 Hz, H-6e), 3.82 (br s, 3 H, H-4, H-5, H-6a), 3.42 (s, 3 H, OCH_3), 3.09, 3.02 (1 H, part A of AB system, J_{AB} 17.63 Hz, H-3′a), 2.42, 2.35 (1 H, part B of AB system, H-3′b), 2.81 (s, 1 H, OH); ^{13}C NMR: δ 175.0 (C-3″), 136.7, 129.6, 128.4, 126.2 (Ph), 102.6 (*C*HPh), 97.3 (C-1), 82.0 (C-4), 80.6 (C-2), 76.3 (C-3), 68.9 (C-6), 59.7 (C-5), 56.0 (OCH_3), 38.1 (C-3′); EIMS: *m*/*z* 322 (15, $[M]^{+\bullet}$), 321 (5.7, $[M-H]^+$), 173 (30, $[M-C_6H_5CHOCH_2CHO]^+$), 149 (30, $[C_6H_5CHOCH_2CHO]^+$), 105 (100, $[C_6H_5CO]^+$), 91 (45, $[C_6H_5CH_2]^+$), 77 (40, $[C_6H_5]^+$), 51 (15, $[C_4H_3]^+$); Anal. Calcd for $C_{16}H_{18}O_7$: C, 59.62; H, 5.63. Found: C, 59.90; H, 5.75.

*Methyl 2,3″-anhydro-4,6-*O*-benzylidene-3-*C*-[(2*R*)-/(2*S*)-2,2-dihydroxyethyl]-α-*D*-glucopyranoside* (**9a**,**b**) *and methyl 4,6-*O*-benzylidene-3-*C*-(2-hydroxyethyl)-α-*D*-glucopyranoside* (**10**)

Method A. Diisobutylaluminum hydride (DIBALH) in toluene (1 M, 1.7 mL, 1.7 mmol) was added dropwise to a soln of **8** (91 mg, 0.28 mmol) in 2:1 anhyd THF–toluene (1.5 mL) at −78 °C under argon. After stirring for 3 h at −78 °C and 1 h at −40 °C, the reaction mixture was poured into a biphasic system containing sodium potassium tartrate satd soln (1.5 mL) in $CHCl_3$ (5 mL) and stirred for 10 min. Chloroform (10 mL) was then added and stirring was kept up for 2 h at rt. Extraction with $CHCl_3$ (3 × 15 mL), dryness (Na_2SO_4) and evaporation afforded **10** as a solid (48 mg, 52%) and **9a**,**b** as a syrup (31 mg, 34%).

Method B. A soln of **8** (85 mg, 0.26 mmol) in dry THF (4 mL) was added to a suspension of $LiAlH_4$ (30 mg, 0.79 mmol) in dry THF (1.5 mL) at 0 °C under argon. The reaction mixture was heated at 40 °C for 5 h and under reflux for 1 h. The workup in method B was followed affording **10** (71 mg, 82%) and **9a**,**b** (3.5 mg, 4%).

Data for **9a**,**b**: IR (KBr): *v* 3380 cm^{-1} (OH); ^1H NMR (300 MHz): δ 7.48–7.34 (m,

10 H, Ph, Ph*), 5.78–5.64 (m, 2 H, H-3″, H*-3″), 5.59 (s, 1 H, CHPh), 5.57 (s, 1 H, CH*Ph), 4.83 (d, 1 H, $J_{1,2}$ 5.16 Hz, H*-1), 4.73 (d, 1 H, $J_{1,2}$ 5.19 Hz, H-1), 4.34–4.29 (m, 3 H, H-6e, H*6-e, H-2), 4.09 (d, 1 H, H*-2) 3.90–3.71 (m, 6 H, H-4, H-5, H-6a, H*-4, H*-5, H*-6a), 3.50 (s, 3 H, OCH_3^*), 3.38 (s, 3 H, OCH_3), 2.58 (dd, 1 H, $J_{3'a,3''}$ 5.76, $J_{3'a,3'b}$ 13.90 Hz, H-3′a), 2.44 (d, 1 H, $J_{3'',OH}$ 4.47 Hz, OH-3″), 2.38 (dd, 1 H, $J^*_{3'a,3''}$ 5.88, $J_{3'a,3'b}$ 14.82 Hz, H*-3′a), 2.14 (dd, 1 H, $J^*_{3'b,3''}$ 5.82 Hz, H*-3′b), 2.01 (d, 1 H, $J_{3'a,3'b}$ 13.90 Hz, H-3′b); ^{13}C NMR: δ 139.2, 136.9, 129.6, 129.3, 129.2, 128.5, 128.3, 126.2 (Ph, Ph*), 102.2 (*C*HPh, *C*HPh), 101.7 (C*-3″), 100.9 (C-3″), 98.5 (C*-1), 98.0 (C-1), 84.0 (C-2), 82.6 (C*-4), 82.1 (C*-2, C-4), 80.2 (C*-3), 78.8 (C-3), 69.1 (C-6, C*-6), 59.9 (C-5), 59.4 (C*-5), 55.6 (OCH_3), 55.5 (OCH_3^*), 43.1 (C*-3′), 40.3 (C-3′); Anal. Calcd for $C_{16}H_{20}O_7$: C, 59.26; H, 6.21. Found: C, 59.49; H, 6.50.

Data for **10**: mp 124–125 °C; $[\alpha]_D^{20}$ + 48.4° (*c* 1.0, $CHCl_3$); IR (KBr): *v* 3328 cm^{-1} (OH); ^{1}H NMR (300 MHz): δ 7.48–7.34 (m, 5 H, Ph), 5.53 (s, 1 H, CHPh), 4.77 (d, 1 H, $J_{1,2}$ 3.81 Hz, H-1); 4.32 (dd, 1 H, $J_{5,6e}$ 4.11, $J_{6a,6b}$ 9.61 Hz, H-6e), 4.03–3.84 (m, 2 H, H-3″a, H-3″b), 3.81–3.60 (m, 4 H, H-2, H-4, H-5, H-6a), 3.42 (s, 3 H, OCH_3), 2.29–2.35 (m, 2 H, H-3′a, H-3′b); ^{13}C NMR: δ 137.1, 129.2, 126.3, 126.2 (Ph), 101.9 (*C*HPh), 100.8 (C-1), 84.4 (C-4), 75.0 (C-2), 74.6 (C-3), 69.2 (C-6), 61.5 (C-5), 58.6 (C-3″), 56.0 (OCH_3), 32.8 (C-3′); EIMS: *m*/*z* 326 (0.3, $[M]^{+\bullet}$), 307 (2.2, $[M-H-H_2O]^+$), 294 (4.4; $[M-CH_3OH]^{+\bullet}$), 281 (3.3, $[M-CH_2CH_2OH]^+$), 188 (13.2, $[M-H-C_6H_5CHO-CH_2OH]^+$), 179 (21; $[C_{10}H_{11}O_3]^+$), 149 (26, $[C_6H_5CHOCH_2CHO]^+$), 107 (97, $[C_6H_5CHOH]^+$), 106 (47, $[C_6H_5CHO]^{+\bullet}$), 105 (100, $[C_6H_5CO]^+$), 45 (32, $[CH_2CH_2OH]^+$), 31 (16, $[CH_2OH]^+$); Anal. Calcd for $C_{16}H_{22}O_7$: C, 58.88; H, 6.79. Found: C, 58.72; H, 6.79.

*Methyl 2,3″-anhydro-6-*O*-benzyl-3-*C*-(2-hydroxyethyl)-α-*D*-glucopyranoside* (**11**).—Triethylsilane (0.1 mL, 0.63 mmol) was added to a soln of **9a**,**b** (35 mg, 0.11 mmol) in MeCN (1 mL) under argon at −30 °C followed by addition of $BF_3{\cdot}Et_2O$ (0.1 mL, 0.81 mmol). After 90 min at −30 °C, a satd soln of potassium carbonate (1 mL) was poured into the reaction mixture, which was then stirred for 30 min at rt. The aq phase was extracted with $CHCl_3$ (3 × 10 mL), dried (Na_2SO_4) and evaporated. The residue was purified by preparative TLC with 12:1 EtOAc–toluene to give **11** as a syrup (12 mg, 36%); $[\alpha]_D^{20}$ + 67° (*c* 0.7, $CHCl_3$); ^{1}H NMR (300 MHz): δ 7.39–7.30 (m, 5 H, Ph), 4.71 (d, 1 H, $J_{1,2}$ 5.16 Hz, H-1), 4.66, 4.62 (1 H, part A of AB system, $J_{A,B}$ 11.88 Hz, CH_2Ph), 4.58, 4.54 (1 H, part B of AB system, CH_2Ph), 4.15–4.07 (m, 2 H, H-3″a, H-3″b), 3.99 (dd, 1 H, $J_{4,5}$ 9.24, $J_{4,OH}$ 2.88 Hz, H-4), 3.89 (d, 1 H, H-2), 3.79–3.35 (m, 3 H, H-5, H-6e, H-6a), 3.43 (s, 3 H, OCH_3), 2.96 (d, 1 H, OH-4), 2.44–2.34 (m, 1 H, H-3′a), 1.86–1.82 (m, 1 H, H-3′b); ^{13}C NMR: δ 137.5, 128.5, 127.9, 127.6 (Ph), 99.0 (C-1), 81.8 (C-2), 81.0 (C-3), 73.8 (*C*H_2Ph), 73.7 (C-4), 70.4 (C-6), 68.4 (C-3″), 67.0 (C-5), 55.5 (OCH_3), 33.7 (C-3′); HRMS: calcd for $C_{16}H_{22}O_6$ 310.348, found: 310.142.

*Methyl 2,3″-anhydro-4,6-*O*-benzylidene-3-*C*-(2-hydroxyethyl)-α-*D*-glucopyranoside* (**12**).—Triphenylphosphine (73 mg, 0.28 mmol) and powdered 4 Å molecular sieves (100 mg) were added to the soln of **10** (91 mg, 0.28 mmol) in dry $CHCl_3$ (5 mL) under argon. After cooling at 5 °C, DEAD (0.15 mL, 0.92 mmol) was added dropwise and the reaction mixture was stirred at 5 °C for 2.5 h. Filtration, evaporation and column chromatography with 2:1 EtOAc–toluene afforded **12** as a solid (70 mg, 82%); mp 133–135 °C; $[\alpha]_D^{20}$ + 96.5° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$): *v* 3320 cm^{-1} (OH); ^{1}H NMR (300 MHz): δ 7.49–7.37 (m, 5 H, Ph), 5.58 (s, 1 H, CHPh), 4.75 (d, 1 H, $J_{1,2}$ 4.17 Hz, H-1), 4.36–4.15 (m, 3 H, H-6e, H-3″a, H-3″b), 4.01 (d, 1 H, H-2), 3.91 (d, 1 H, $J_{4,5}$ 8.88 Hz, H-4), 3.83–3.72 (m, 2 H, H-5, H-6a), 3.40 (s, 3 H, OCH_3), 2.54–2.42 (m, 1 H, H-3′a), 1.94–1.88 (m, 1 H, H-3′b); ^{13}C NMR: δ 137.1, 129.2, 128.3, 126.2 (Ph), 102.3 (*C*HPh), 99.3 (C-1), 83.0 (C-4), 82.6 (C-2), 79.8 (C-3), 69.3 (C-6), 69.1 (C-3″), 59.6 (C-5), 55.5 (OCH_3), 33.6 (C-3′); EIMS: *m*/*z* 308 (14.3, $[M]^{+\bullet}$); 307 (43, $[M-H]^+$), 280 (79, $[M-C_2H_4]^{+\bullet}$), 277 (21, $[M-OCH_3]^+$), 276 (54, $[M-CH_3OH]^{+\bullet}$); 229 (36, $[M-C_6H_7]^+$), 205 (15, $[M-C_4H_7O_3]^+$), 149 (15, $[C_6H_5CHOCH_2CHO]^+$), 107 (100, $[C_6H_5CHOH]^+$), 106 (20, $[C_6H_5CHO]^{+\bullet}$), 105 (65, $[C_6H_5CO]^+$), 91 (55, $[C_6H_5CH_2]^+$), 79 (30, $[C_6H_7]^+$), 77 (40,

$[C_6H_5]^+$); Anal. Calcd for $C_{16}H_{20}O_6$: C, 62.33; H, 6.54. Found: C, 62.60; H 6.83.

Methyl 2,3″-anhydro-4,6-O-benzylidene-3-O-acetyl-3-C-(2-hydroxyethyl)-α-D-glucopyranoside (**13**).—Acetic anhydride (26 μL) and 4-dimethyl aminopyridine (DMAP) (catalytic amount) were added to a soln of **12** (36 mg, 0.12 mmol) in pyridine (0.5 mL) and the reaction mixture was stirred at rt for 3 h. Column chromatography eluted with 1:5 EtOAc–toluene gave **13** as a syrup (38.6 mg, 94%); $[\alpha]_D^{20}$ + 37.6° (*c* 0.9, $CHCl_3$); IR (KBr): *ν* 1724 cm^{-1} (C=O); ^1H NMR (300 MHz):*δ* 7.50–7.26 (m, 5 H, Ph), 5.57 (s, 1 H, CHPh), 4.90–4.86 (m, 3 H, H-1, H-2, H-4), 4.29 (dd, 1 H, $J_{6a,6e}$ 8.07 Hz, $J_{5,6e}$ 5.13 Hz, H-6e), 4.21 (m, 1 H, J_{AB} − 7.33, J_{AC} 9.74, J_{AD} 1.88 Hz, A), 4.04 (m, 1 H, J_{BC} 9.88, J_{BD} 7.00 Hz, B), 3.88–3.82 (m, 2 H, H-5, H-6a), 3.42 (s, 3 H, OCH_3), 2.53 (m, 1 H, J_{CD} − 13.63 Hz, C), 2.20 (m, 1 H, D), 2.07 (s, 3 H, CH_3); ^{13}C NMR: *δ* 171.2 (C=O), 137.2, 129.1, 128.3, 126.2 (Ph), 101.8 (*C*HPh), 96.6 (C-1), 88.9 (C-3), 78.8, 76.5 (C-2, C-4), 69.2 (C-6), 68.4 (C-3″), 60.4 (C-5), 55.6 (OCH_3), 32.3 (C-3′), 22.5 (CH_3); HRMS: calcd for $C_{18}H_{22}O_7$ 350.365, found: 350.136.

Methyl 4,6-O-benzylidene-3-C-[(R)-(carboxy)hydroxymethyl]-α-D-glucopyranoside-3′,2-lactone (**14**).—A soln of **8** (80 mg, 0.25 mmol) in dry THF (2 mL) was added dropwise to a soln of lithium diisopropyl amine (LDA) [14] (0.6 M, 3 mL) at − 78 °C under argon and the mixture was stirred for 50 min. The complex MoO_5·py·HMPA [14] (650 mg, 1.49 mmol) was then added and the reaction mixture was stirred for 3 h at − 78 °C. When the temperature reached 25 °C, a satd aq $NaHSO_3$ soln (3 mL) was poured into the reaction mixture, which was stirred for 20 min. After extraction with $CHCl_3$ (3 × 25 mL), the organic layers were dried (Na_2SO_4) and evaporated. Column chromatography eluted with 1:2 EtOAc–toluene followed by preparative TLC with the same solvent system afforded **14** as a syrup (22 mg, 0.06 mmol, 50% on the basis of the reacted deoxylactone **8**, recovered in 47.5% yield); $[\alpha]_D^{20}$ + 114.6° (*c* 0.5, $CHCl_3$); IR ($CHCl_3$): *ν* 3440 (OH) and 1798 cm^{-1} (C=O); ^1H NMR (300 MHz): *δ* 7.42–7.30 (m, 5 H, Ph), 5.52 (s, 1 H, CHPh), 4.88 (d, 1 H, $J_{1,2}$ 5.01 Hz, H-1), 4.84 (br s, 1 H, H-3′), 4.41 (d, 1 H, H-2), 4.31 (dd, 1 H, $J_{5,6e}$ 3.30, $J_{6a,6e}$ 10.59 Hz, H-6e), 3.87–3.74 (m, 3 H, H-4, H-5, H-6a), 3.37 (s, 3 H, OCH_3), 3.20 (br s, 1 H, OH-3′), 1.80 (s, 1 H, OH-3); ^{13}C NMR: *δ* 174.7 (C-3″), 136.5, 129.3, 128.4, 126.1 (Ph), 102.3 (*C*HPh), 96.8 (C-1), 81.9 (C-4), 77.8 (C-2), 75.2 (C-3), 68.9 (C-6), 68.6 (C-3′), 59.7 (C-5), 55.9 (OCH_3); EIMS: *m/z* 338 (40, $[M]^{+\bullet}$), 337 (27, $[M-H]^+$), 189 (25, $[M-C_6H_5CHOCH_2CHO]^+$), 149 (36, $[C_6H_5CHOCH_2CHO]^+$), 107 (86, $[C_6H_5CHOH]^+$), 106 (29, $[C_6H_5CHO]^{+\bullet}$), 105 (100, $[C_6H_5CO]^+$), 91 (43, $[C_6H_5CH_2]^+$), 77 (36, $[C_6H_5]^+$); LSIMS: *m/z* 339 (100; $[M+H]^+$) 233 (31, $[M+H-C_6H_5CHO]^+$) 107 (22, $[C_6H_5CHOH]^+$); HRMS: calcd for $C_{16}H_{18}O_8$ 338.311, found: 338.100.

Methyl 2-O-benzoyl-4,6-O-benzylidene-α-D-ribo-hexopyranosid-3-ulose (**16**).—A soln of methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-α-D-glucopyranoside [23] (1.58 g, 4.1 mmol) in dry CH_2Cl_2 (12 mL) was added dropwise at rt to the suspension of PCC (2.02 g, 9.4 mmol) and powdered 3 Å molecular sieves (3.65 g) in dry CH_2Cl_2 (18 mL). The mixture was stirred for 15 h at rt. Celite (2.0 g) was added to the reaction mixture, which was then stirred for 20 min. The solids were filtered off and the filtrate evaporated to dryness. The residue was dissolved in EtOAc (200 mL) and the soln was filtered through Florisil (15 g). Evaporation of the solvent gave **16** (1.46 g, 93%) as a solid; mp 210–213 °C, lit. 211–213 °C [18]; $[\alpha]_D^{20}$ + 69.6° (*c* 1.02, $CHCl_3$); IR ($CHCl_3$): *ν* 1764 (C=O) and 1726 (C=O); ^1H NMR (300 MHz): *δ* 8.07–7.27 (m, 10 H, Ph), 5.56 (d, 1 H, $J_{1,2}$ 4.68 Hz, H-2), 5.53 (s, 1 H, CHPh), 5.27 (d, 1 H, H-1), 4.41–4.34 (m, 2 H, H-4, H-6e), 4.16–4.08 (ddd, 1 H, $J_{5,6e}$ 4.56, $J_{5,6a}$ 10.23, $J_{4,5}$ 10.08 Hz, H-5), 3.92 (t, 1 H, $J_{6a,6e}$ 10.26 Hz, H-6a), 3.41 (s, 3 H, OCH_3); ^{13}C NMR: *δ* 191.9 (C=O), 165.6 (C=O), 136.3, 133.6, 130.1, 129.2, 128.3, 128.2, 126.3 (Ph), 101.8 (*C*HPh), 101.3 (C-1), 82.0 (C-4), 74.8 (C-2), 69.3 (C-6), 65.4 (C-5); 55.6 (OCH_3).

Methyl 2-O-benzoyl-4,6-O-benzylidene-3-C-[(Z)-(ethoxycarbonyl)methylene]-α-D-ribo-hexopyranoside (**17**) *and methyl 2-O-benzoyl-4,6-O-benzylidene-3-C-[(E)-(ethoxycarbonyl)-methylene]-α-D-ribo-hexopyranoside* (**18**).—A soln of [(ethoxycarbonyl)methylene]triphenyl-

phosphorane (3.60 g, 10.4 mmol) in dry $CHCl_3$ (40 mL) was added at rt to a soln of **16** (1.0 g, 2.6 mmol) in dry $CHCl_3$ (8 mL). The mixture was stirred under reflux for 5.5 h. Evaporation of the solvent and purification by column chromatography eluted with 1:5 EtOAc–hexane afforded **17** and **18** in a 7:3 ratio as a syrup (1.07 g, 88%); IR ($CHCl_3$): ν 1718 (C=O), 1606 (C=C); 1590 cm^{-1} (Ph); ^1H NMR (300 MHz) data for **17**: δ 8.09–7.36 (m, 10 H, Ph), 6.18 (t, 1 H, $J_{3',4}$ 1.47 Hz, H-3′), 5.92 (t, 1 H, $J_{2,3'}$ 2.94 Hz, H-2), 5.64 (s, 1 H, CHPh), 4.93 (d, 1 H, $J_{1,2}$ 4.41 Hz, H-1), 4.36–4.31 (m, 1 H, H-6e), 4.11 (dd, 1 H, $J_{4,5}$ 8.82 Hz, H-4), 4.01–3.97 (m, 1 H, H-5), 3.88 (m, 1 H, H-6a), 3.80–3.73 (m, 2 H, CH_2–Et), 3.44 (s, 3 H, OCH_3) 0.98 (t, 3 H, CH_3–Et); ^1H NMR (300 MHz) data for **18**: δ 8.09–7.36 (m, 10 H, Ph), 6.09 (t, 1 H, $J_{3',4}$ 1.45 Hz, H-3′), 5.92 (t, 1 H, $J_{2,3'}$ 2.94 Hz, H-2), 5.59 (s, 1 H, CHPh), 5.06 (d, 1 H, $J_{1,2}$ 3.66 Hz, H-1), 4.36–4.31 (m, 1 H, H-6e), 4.11 (dd, 1 H, $J_{4,5}$ 8.82 Hz, H-4), 4.01–3.97 (m, 1 H, H-5), 3.88 (m, 1 H, H-6a), 3.80–3.73 (m, 2 H, CH_2–Et), 3.44 (s, 3 H, OCH_3) 0.98 (t, 3 H, CH_3–Et); ^{13}C NMR data for **17**: δ 167.5 (C=O), 165.3 (C=O), 136.5 (Ph), 135.3 (C-3), 133.7, 130.2, 129.4, 129.1, 128.4, 126.4 (Ph), 114.5 (C-3′), 101.9 (*C*HPh), 98.7 (C-1), 77.5 (C-4), 70.6 (C-2), 69.9 (C-6), 64.8 (C-5); 60.9 (CH_2–Et), 55.8 (OCH_3), 13.9 (CH_3–Et); ^{13}C NMR data for **18**: δ 167.9 (C=O), 165.0 (C=O), 137.1 (Ph), 135.3 (C-3), 133.8, 130.1, 129.2, 128.7, 128.2, 126.5 (Ph), 114.2 (C-3′), 101.8 (*C*HPh), 98.5 (C-1), 78.8 (C-4), 70.2 (C-2), 69.3 (C-6), 64.8 (C-5); 60.8 (CH_2–Et), 55.7 (OCH_3), 13.8 (CH_3–Et); EIMS: m/z 454 (0.4, $[M]^{+\bullet}$), 394 (36, $[M-OCHOCH_3]^{+\bullet}$); 289 (23, $[M-OCHOCH_3-COC_6H_5]^+$); 183 (27, $[M-OCHOCH_3-COC_6H_5-C_6H_5CHO]^+$); 149 (19, $[C_6H_5CHOCH_2CHO]^+$); 91 (100, $[C_6H_5CH_2]^+$).

*Methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-3-*C*-[*(R)- *and* (S)-(ethoxycarbonyl)hydroxymethyl]-α-*D*-glucopyranoside* (**19a**,**b**)

Method A. Osmium tetraoxide (250 mg, 0.98 mmol) was added to a soln of **17**,**18** (446 mg, 0.98 mmol) in dry pyridine (4 mL), and the mixture was stirred at rt for 2.5 h. A satd aq soln of $NaHSO_3$ (10 mL) and pyridine (4 mL) were added, and within 30 min the complex was cleaved to give an orange soln. The mixture was extracted with $CHCl_3$ (3 × 25 mL), dried (Na_2SO_4) and evaporated to give **19a**,**b** as a syrup (479 mg, 100%).

Method B. Compounds **17**,**18** (152 mg, 0.33 mmol) and 4-methylmorpholine-*N*-oxide (94 mg, 0.8 mmol) were dissolved in 8:1 acetone–water (3.04 mL). A catalytic amount of osmium tetraoxide was added, and the reaction mixture was stirred overnight at rt. The soln was filtered and extracted with $CHCl_3$ (3 × 15 mL). The organic phase was dried (Na_2SO_4), filtered and evaporated to give **19a**,**b** as a syrup (109 mg, 66%).

*Methyl 4,6-*O*-benzylidene-3-*C*-[(R)-/(S)-1,2-dihydroxyethyl]-α-*D*-glucopyranoside* (**20a**,**b**), *methyl 2,3″-anhydro-4,6-*O*-benzylidene-3-*C*-[(1*S*,2*R*)-/(1*S*,2*S*)-1,2,2-trihydroxyethyl]-α-*D*-glucopyranoside* (**21a**,**b**) *and methyl 2,3″-anhydro-4,6-*O*-benzylidene-3-*C*-[(1*R*,2*R*)-1,2,2-trihydroxyethyl]-α-*D*-glucopyranoside* (**22**)

Method A. A soln of **19a**,**b** (250 mg, 0.51 mmol) in dry THF (9 mL) was added dropwise to a suspension of $LiAlH_4$ (40.6 mg, 1.07 mmol) in dry THF (2 mL), at 0 °C under argon. The temperature was raised to rt and the mixture was then stirred for 3 h 30 min. The reaction mixture was poured into a biphasic system of sodium potassium tartrate aq satd soln (15 mL) and $CHCl_3$ (15 mL) at 0 °C and the mixture was stirred vigorously for 2 h at rt. After extraction with 5:1 $CHCl_3$–THF (3 × 30 mL), the organic phase was dried (Na_2SO_4) and evaporated. Column chromatography with 2:1 AcOEt–toluene afforded **20a**,**b** (63.8 mg, 36%) and the secondary products methyl 2,3″-anhydro-4,6-*O*-benzylidene-3-*C*-[(1*S*,2*R*)-/(1*S*,2*S*)-1,2,2-trihydroxyethyl]-α-D-glucopyranoside (**21a**,**b**) (29.4 mg, 18%) and methyl 2,3″-anhydro-4,6-*O*-benzylidene-3-*C*-[(1*R*,2*R*)-1,2,2-trihydroxyethyl]-α-D-glucopyranoside (**22**) (46 mg, 27%).

Method B. A soln of **19a**,**b** (250 mg, 0.51 mmol) in dry THF (9 mL) was added dropwise to a suspension of $LiAlH_4$ (116 mg, 3.06 mmol) in dry THF (2 mL) at 0 °C under argon. The mixture was stirred under reflux for 24 h. After the workup described above, column chromatography with 2:1 EtOAc–toluene afforded **20a**,**b** (84 mg, 48%), **21a**,**b** (24 mg, 14%) and **22** (15 mg, 9%).

Data for **20a**,**b**: IR (KBr): ν 3456 cm^{-1} (OH); ^1H NMR ($CDCl_3/D_2O$) (300 MHz) of **20a**: δ 7.46–7.34 (m, 5 H, Ph), 5.46 (s, 1 H, CHPh), 4.79 (d, 1 H, $J_{1,2}$ 3.63 Hz, H-1), 4.58 (br s, 1 H, H-3′), 4.33 (dd, 1 H, $J_{5,6e}$ 5.01, $J_{6a,6e}$ 10.47 Hz, H-6e), 4.24 (dd, 1 H, $J_{3''a,3''b}$ 11.97, $J_{3'a,3''a}$ 3.3 Hz, H-3″a); 3.92–3.84 (m, 2 H, H-3″b, H-5), 3.69 (d, 1 H, H-2), 3.66–3.52 (m, 2 H, H-4, H-6a), 3.49 (s, 3 H, OCH_3); ^{13}C NMR of **20a**: δ 135.5, 128.1, 127.3, 124.3 (Ph), 101.3 (*C*HPh), 99.9 (C-1), 85.6 (C-4), 74.3 (C-3), 73.1 (C-2), 71.0 (C-3′), 68.2 (C-6), 62.7 (C-3″), 60.7 (C-5), 54.8 (OCH_3); EIMS: m/z 342 (0.2, $[M]^{+\bullet}$), 311 (7.3, $[M-CH_2OH]^+$); 282 (5.9, $[M-CHOHCH_2OH]^+$); 281 (8.8, $[M-H-CHOHCH_2OH]^{+\bullet}$); 263 (5.9, $[M-CHOHCH_2OH-H_2O]^+$); 179 (8.8, $[C_{10}H_{11}O_3]^+$); 149 (30, $[C_6H_5CHOCH_2CHO]^+$), 107 (71, $[C_6H_5CHOH]^+$), 106 (38, $[C_6H_5CHO]^{+\bullet}$); 105 (43, $[C_6H_5CO]^+$), 87 (75, $[C_4H_7O_2]^+$), 31 (100, $[OCH_3]^+$); HRMS: calcd for $C_{16}H_{22}O_8$ 342.348, found: 342.131.

Data for **21a**,**b**: IR (KBr): ν 3396 cm^{-1} (OH); ^1H NMR (300 MHz) of **21a**: δ 7.48–7.45 (m, 5 H, Ph), 5.56 (s, 1 H, CHPh), 5.41 (d, 1 H, $J_{3',3''}$ 5.55 Hz, H-3″), 4.85 (d, 1 H, $J_{1,2}$ 5.13 Hz, H-1), 4.66 (d, 1 H, H-3′), 4.34 (m, 1 H, H-6e), 4.22 (d, 1 H, H-2), 3.84–3.74 (m, 3 H, H-4, H-5, H-6a), 3.44 (s, 3 H, OCH_3); **21b**: δ 7.48–7.35 (m, 5 H, Ph), 5.56 (s, 1 H, CHPh), 5.26 (d, 1 H, $J_{3',3''}$ 4.19 Hz, H-3″); 4.77 (d, 1 H, $J_{1,2}$ 5.13 Hz, H-1), 4.44 (d, 1 H, H-3′), 4.34 (m, 1 H, H-6e), 4.29 (d, 1 H, H-2), 3.84–3.74 (m, 3 H, H-4, H-5, H-6a), 3.42 (s, 3 H, OCH_3); ^{13}C NMR of **21a**: δ 136.9, 129.3, 128.4, 126.0 (Ph), 105.1 (C-3″), 102.2 (*C*HPh), 98.3 (C-1), 82.7 (C-4), 81.7 (C-2), 78.6 (C-3′), 77.2 (C-3), 69.1 (C-6), 59.8 (C-5), 55.6 (OCH_3); **21b**: δ 136.7, 129.3, 128.4, 126.0 (Ph), 102.2 (*C*HPh), 98.0 (C-1), 97.7 (C-3″), 80.2 (C-2), 70.5 (C-3′), 69.0 (C-6), 59.3 (C-5), 82.7 (C-4), 77.2 (C-3), 55.6 (OCH_3); HRMS: calcd for $C_{16}H_{20}O_8$ 340.327, found: 340.116.

Data for **22**: $[\alpha]_D^{20} + 48.5°$ (*c* 1.1, $CHCl_3$); IR (KBr): ν 3369 cm^{-1} (OH); ^1H NMR (300 MHz): δ 7.53–7.34 (m, 5 H, Ph), 5.47 (s, 1 H, CHPh), 5.33 (d, 1 H, $J_{3'',OH}$ 7.59 Hz, H-3″), 4.76 (d, 1 H, $J_{1,2}$ 5.5 Hz, H-1), 4.39 (d, 1 H, H-2), 4.31 (dd, 1 H, $J_{5,6e}$ 5.21, $J_{6a,6e}$ 10.2 Hz, H-6e), 4.18–4.09 (m, 2 H, H-3′, H-5), 3.65 (d, 1 H, $J_{4,5}$ 10.35 Hz, H-4), 3.64 (t, 1 H, $J_{5,6a}$ 9.84 Hz, H-6a); 3.51 (s, 3 H, OCH_3), ^{13}C NMR: δ 136.9, 129.5, 128.3, 126.4 (Ph), 106.8 (C-3″), 102.9 (*C*HPh), 97.8 (C-1), 83.4 (C-2), 82.7 (C-4), 79.2 (C-3′), 78.9 (C-3), 69.7 (C-6), 60.3 (C-5), 55.7 (OCH_3); HRMS: calcd for $C_{16}H_{20}O_8$ 340.327, found: 340.116.

4. Supplementary material

Tables of atomic coordinates, bond lengths, bond angles, isotropic and anisotropic displacement parameters have been deposited with the Cambridge Crystallographic Data Centre. These tables may be obtained on request from The Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

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