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Chiral Synthesis of Polyketide-derived Natural Products. Part 3.[1] Stereocontrolled Synthesis of a Chiral Fragment Corresponding to Both the C-1—C-4 and C-9—C-12 Units of Erythromycin A from D-Glucose

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A chiral synthon, 3,6-dideoxy-1,2-*O*-isopropylidene-3-*C*-methyl-β-L-*lyxo*-hexofuranos-5-ulose (**7**), for the total synthesis of erythromycin A (**1**) corresponding to both the C-1—C-4 and C-9—C-12 fragments was synthesized highly stereoselectively from D-glucose (**2**) *via* stereoselective hydrogenation of 3,6-dideoxy-1,2-*O*-isopropylidene-3-*C*-methyl-α-D-*glycero*-hex-3-enofuranos-5-ulose (**12**).

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Polyketide-derived natural products such as macrolide and polyether ionophore antibiotics have recently attracted particular attention as synthetic targets not only because of their complex chemical structures but also because of significant biological and pharmacological properties. For the total synthesis of such complex compounds having many chiral centres in macrocyclic or acyclic systems,[2] it is very important to develop new methodologies other than those for the synthesis of polycyclic natural products mainly consisting of rings with fewer than six members.

Stereochemical control in cyclic systems has resulted in a number of elegant syntheses of polycyclic compounds such as steroids, alkaloids, and terpenes, *etc.* In addition, stereochemical control in acyclic systems is essential for the total synthesis of macrolides as well as polyether ionophores. In fact, it has become feasible to synthesize such complex natural products as a result of significant progress recently with stereoselective reactions in open-chain systems,[3] *e.g.* the asymmetrical aldol reaction,[4] asymmetric epoxidation,[5] stereocontrolled hydroboration,[2c,6] and stereoselective reduction,[7] *etc.*

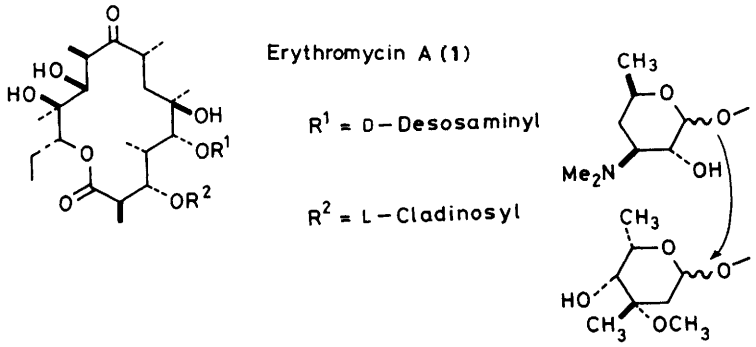
Selection of the most suitable protecting groups is also important, especially where there are many hydroxy groups which must be protected so as to be differentiated from each other. Recently we reported a benzyl-type protecting group for a hydroxy function, MPM (*p*-methoxyphenylmethyl), which can be selectively removed by DDQ (2,3-dichloro-5,6-dicyano-1,4-benzoquinone) oxidation under neutral conditions,[8] and its variations, MP (*p*-methoxyphenyl) acetals, and MP esters, *etc.*[9] This MPM protection method will hopefully be useful in a wide range of organic syntheses, especially in sugar chemistry.

As part of the investigation of the chiral synthesis of polyketide-derived natural products with complex structures, we planned recently to synthesize the well known macrolide antibiotic erythromycin A (**1**) from D-glucose (**2**) using MPM protection and stereocontrolled reactions in acyclic systems. D-Glucose (**2**) is, of course, one of the most readily available and inexpensive chiral starting materials. In 1979, Corey *et al.* reported the first total synthesis of the aglycone erythronolide A,[10] and Woodward *et al.* achieved the total synthesis of (**1**) itself.[11] Both methods provided excellent examples of stereocontrol basically in cyclic systems rather than in acyclic systems. Stork *et al.* recently reported a simpler synthesis of the non-cyclic chiral sequence of erythronolide A.[12] Our retrosynthetic analysis of (**1**) is shown in Scheme 1, and compound (**7**) was expected to be the common key chiral intermediate for both segments i (**4**) and ii (**5**). In the present paper, we report several syntheses of (**7**) from (**2**) as a chiral starting material.

Results and Discussion

Synthesis of (**7**) via anti-*Elimination and Stereoselective Hydrogenation.*—The conversion of the diol (**8**), readily derived from D-glucose (**2**), into the alcohol (**10**) *via* a tosylate and an epoxide has already been reported though the yield was unsatisfactory.[13] An improved and more convenient method was provided as follows. When the diol (**8**) was treated with lead tetra-acetate in benzene, the aldehyde (**9**) was easily isolated in excellent yield. The conventional Grignard reaction of (**9**) gave the alcohol (**10**), which was a diastereoisomeric mixture with respect to the carbinol carbon, but which, without further purification, was converted into the oily ketone (**11**) by oxidation with pyridinium chlorochromate (PCC).

anti-Elimination of methanol from (**11**) was expected to give the enone (**12**), but all attempts were unsuccessful. No reaction occurred even by treatment with strong acids such as camphor-



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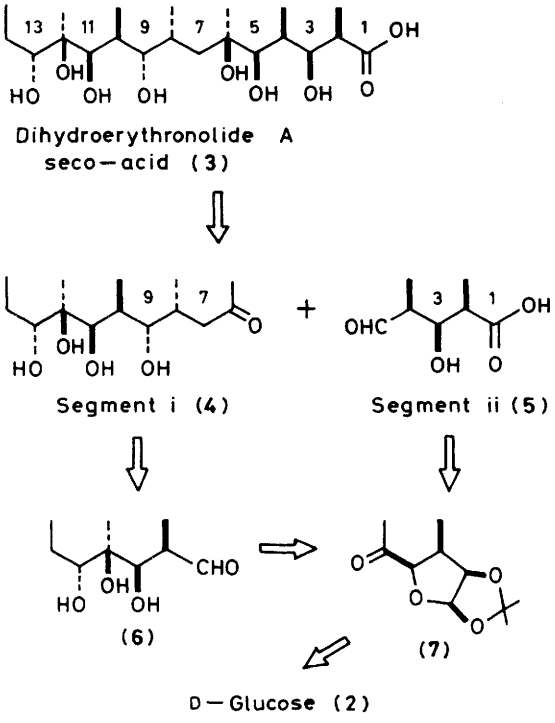


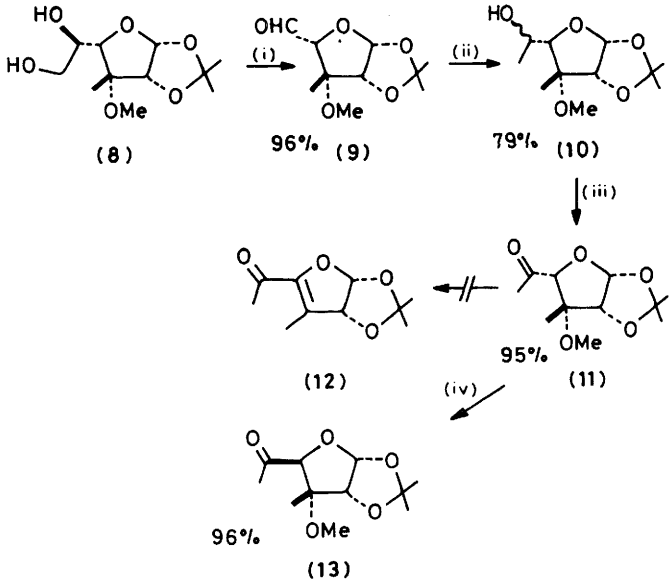
Scheme 1.

10-sulphonic acid at room temperature, and at 80 °C only an intractable mixture was obtained. Although no reaction occurred under weakly basic conditions with triethylamine, sodium acetate, or sodium hydrogen carbonate, treatment with potassium carbonate in methanol at room temperature readily gave the isomeric ketone (**13**) in excellent yield; the expected enone (**12**) was not obtained, because the α-side* of (**11**) is so crowded as to cause it to isomerize to the thermodynamically more stable isomer (**13**). Treatment with 1,5-diazabicyclo-[5.4.0]undec-5-ene (DBU) in dichloromethane gave the same result (Scheme 2A).

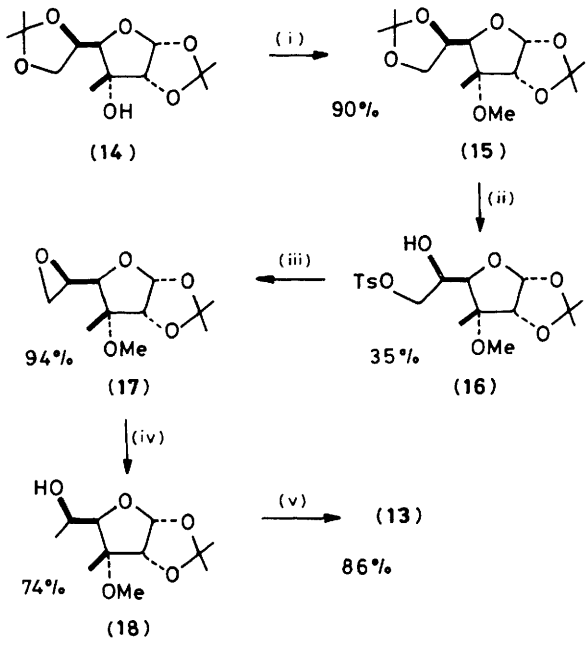
The structure of (**13**) was confirmed by an alternative synthesis from (**14**)[14] *via* an epoxide (**17**) in a manner basically similar to the published method.[14] Compound (**14**), derived readily from (**2**), was methylated in the usual way, and the 5,6-isopropylidene protection was selectively removed by treatment with 1.9% sulphuric acid followed by tosylation of the primary alcohol to give the monotosylate (**16**), which was converted into the epoxide (**17**); this was in turn reduced with lithium aluminium hydride. PCC oxidation of the resultant alcohol (**18**) readily gave ketone (**13**) (Scheme 2B).

Since the attempts to convert (**11**) into (**12**) were unsuccessful, the reactivity of another ketone (**22**), isomeric with (**11**) at both C-3 and C-4, was next examined. The synthesis of (**22**) is shown in Scheme 3. Compound (**19**),[15] also derived from (**2**), was similarly methylated to give (**20**) in high yield, followed by selective hydrolysis to the 5,6-diol, which was converted into (**22**) *via* the aldehyde (**21**) in the same way as in the synthesis of (**11**).

When the ketone (**22**) was treated with potassium carbonate in methanol at room temperature, in contrast to (**11**), *anti*-elimination of methanol occurred smoothly to give the expected enone (**12**) as an oil in high yield. DBU was also a catalyst for the



Scheme 2A. *Reagents:* (i) $Pb(OAc)_4$, PhH; (ii) MeMgI, Et_2O; (iii) PCC, molecular sieves, CH_2Cl_2; (iv) K_2CO_3, MeOH. Wavy bond indicates mixture of diastereoisomers



Scheme 2B. *Reagents:* (i) MeI, NaH, DMSO; (ii) dil. H_2SO_4, then TsCl, Py; (iii) K_2CO_3, MeOH; (iv) $LiAlH_4$, Et_2O; (v) PCC, molecular sieves, CH_2Cl_2

elimination, though too slowly to use practically. Hydrogenation of (**12**) over 10% palladium–charcoal in ethyl acetate at ordinary pressure and temperature gave the required compound (**7**), as an oil, completely stereoselectively in quantitative yield, because of steric hindrance of the α-side[16] of (**12**) due to the isopropylidene group. Thus (**7**) was synthesized from (**19**) in the sequence of conventional reactions in 34.5% overall yield. Although rather stable under neutral conditions, the 4-α-keto compound (**7**) was unstable and isomerized to the more stable 4-β-keto compound (**24**), which was also prepared from (**23**),[17] under alkaline conditions.[18]

* The terms α and β are used with reference to each atom or group which lies behind the plane of the molecule and in front of it, respectively, as for steroids, as well as to denote anomeric configurations.

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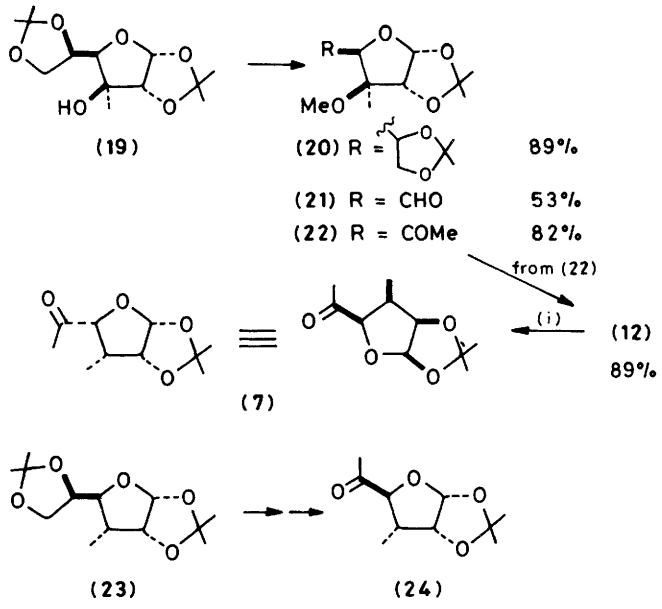
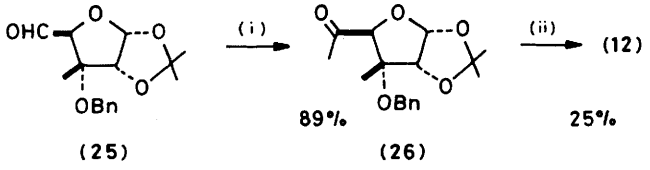


Scheme 3. *Reagents:* (i) H_2/Pd–c, EtOAc

These two compounds were clearly differentiated from each other by their n.m.r. spectra, in which the signals of the β-hydrogen of (**7**) and the α-hydrogen of (**24**) at their respective C-4 positions were observed at δ 4.30 (d, *J* 9.5 Hz) and 4.08 (d, *J* 10.5 Hz), respectively.[19]

Synthesis via syn-*Elimination*.—If *syn*-elimination of methanol from compound (**13**), isomeric with (**22**) at the C-3, occurs smoothly, this method *via* (**13**) must be more convenient than that *via* (**22**), because (**13**)-type compounds are more easily derived from (**2**). However, all attempts to obtain (**12**) from (**13**) with potassium carbonate, DBU, 2% sodium hydroxide, or potassium t-butoxide were unsuccessful. On the other hand, the benzyl ether (**26**) gave (**12**) though in very poor yield.

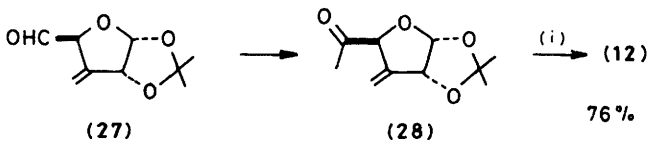
Compound (**26**) was synthesized similarly and more easily from (**2**) *via* the known aldehyde (**25**).[20] Although ketone (**26**) was stable to potassium carbonate, treatment with a stronger base, potassium t-butoxide, in dimethyl sulphoxide (DMSO) at room temperature for 10 min gave the enone (**12**) (Scheme 4).



Scheme 4. *Reagents:* (i) MeMgI, then PCC; (ii) Bu^{t}OK, DMSO

However, the yield was less than 25%, and prolonged treatment with the same base caused considerable decomposition of the product (**12**), and hence this method is not of practical use.

Synthesis via *Isomerization*.—The following method *via* the olefinic aldehyde (**27**) is more convenient for the synthesis of (**7**), though the overall yield from (**2**) was inferior to that of the first method. The aldehyde (**27**)[21] was similarly converted into the β,γ-unsaturated ketone (**28**), and when the latter was treated with potassium carbonate in methanol at room temperature for only 10 min, base-catalysed isomerization occurred quite smoothly to give the conjugated enone (**12**) (Scheme 5); this was then converted into (**7**) as described above. Thus we have established a practical method for the synthesis of the first key chiral intermediate to erythromycin A.



Scheme 5. *Reagents:* (i) K_2CO_3, MeOH

Experimental

M.p.s were measured on a Yamato MP-1 micro melting point apparatus and are uncorrected. Optical rotations were measured with a JASCO DIP-4 digital polarimeter. I.r. spectra were recorded on a JASCO IRA-2 spectrophotometer. Low- and high-resolution mass spectra were taken on a JEOL JMS D-300 or JEOL JMS-01 SG spectrometer. ^{1}H N.m.r. spectra were recorded on a JEOL JNM FX-100 or JEOL JNM FX-200 instrument.

1,2-O-*Isopropylidene*-3-C-*methyl*-3-O-*methyl*-β-L-lyxo-*pentodialdo*-1,4-*furanose* (**9**).—$Pb(OAc)_4$ (600 mg, 1.35 mmol) was added to a stirred solution of 1,2-*O*-isopropylidene-3-*C*-methyl-3-*O*-methyl-α-D-gulofuranose (**8**) (200 mg, 0.81 mmol) in benzene (6 ml) at room temperature. After 10 min, the supernatant of the reaction mixture was applied to a silica gel column and elution with CH_2Cl_2–MeOH (24:1) gave a solid (168 mg, 96%) which was recrystallized from ether–*light* petroleum to afford the *title compound* as needles, m.p. 80—81.5 °C (Found: C, 55.4; H, 7.5. $C_{10}H_{16}O_5$ requires C, 55.54; H, 7.46%); $[\alpha]_D^{14}$ −47° (*c* 1.24 in $CHCl_3$); $\nu_{max.}$(Nujol) 1 720 cm^{-1} (CHO); $\delta_H(CDCl_3)$ 1.35 (3 H, s), 1.47 (3 H, s), 1.61 (3 H, s), 3.41 (3 H, s), 4.15 (1 H, d, *J* 2.5 Hz), 4.35 (1 H, d, *J* 3.0 Hz), 5.87 (1 H, d, *J* 3.0 Hz), and 9.87 (1 H, d, *J* 2.5 Hz).

6-*Deoxy*-1,2,-O-*isopropylidene*-3-C-*methyl*-3-O-*methyl*-β-L-lyxo-*hexofuranos*-5-*ulose* (**11**).—To a stirred solution of MeMgI prepared from MeI (355 mg, 2.5 mmol) and Mg (60 mg, 2.5 mg-atom) in ether (8 ml) was added dropwise a solution of compound (**9**) (180 mg, 0.83 mmol) in ether (2 ml) at 0 °C under argon. After 30 min, aqueous NH_4Cl was added and the mixture was extracted with ether. The extract was washed with brine, dried ($MgSO_4$), and evaporated to give solid (**10**) (153 mg, 79.1%), which was used without purification in the next reaction; *m*/*z* 217 (M^+ − 15, 5.8%), 187 (7.2), 156 (34.7), and 127 (100).

Pyridinium chlorochromate (PCC) (668 mg, 3.1 mmol) and powdered molecular sieves 3A (360 mg) were added to a stirred solution of compound (**10**) (120 mg, 0.52 mmol) in CH_2Cl_2 (10 ml), and the mixture was heated under reflux for 3 h. Insoluble materials were filtered off and the filtrate was evaporated and chromatographed on a silica gel column with ether as eluant to give the title compound as an oil (113 mg, 95%), $[\alpha]_D^{14}$ +14° (*c* 1.16 in $CHCl_3$); $\nu_{max.}$ 1 710 cm^{-1} (CO); $\delta_H(CDCl_3)$ 1.38 (3 H, s), 1.49 (3 H, s), 1.67 (3 H, s), 2.24 (3 H, s), 3.37 (3 H, s), 4.04 (1 H, s), 4.33 (1 H, d, *J* 4.0 Hz), and 5.77 (1 H, d, *J* 4.0 Hz); *m*/*z* 215 (M^+ − 15, 3.5%), 187 (72), and 99 (100).

6-*Deoxy*-1,2-O-*isopropylidene*-3-C-*methyl*-3-O-*methyl*-α-D-ribo-*hexofuranos*-5-*ulose* (**13**).—(*a*) K_2CO_3 (75 mg, 0.54 mmol) was added to a stirred solution of compound (**11**) (25 mg, 0.11

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mmol) in MeOH (2.5 ml) at room temperature. After 1.5 h, the reaction mixture was neutralized with saturated aqueous NH_4Cl, the solvent was evaporated under reduced pressure, and the residue was extracted with CH_2Cl_2. The extract was washed with water, dried (Na_2SO_4), and evaporated under reduced pressure to afford the *title compound* (**13**) as a solid (24 mg, 96%), m.p. 82.5—84.5 °C (from ether–hexane) (Found: $M^+ - CH_3$, 215.0916. $C_{10}H_{15}O_5$ requires *m/z* 215.0915); $[\alpha]_D^{18}$ +104° (*c* 1.0 in $CHCl_3$); $\nu_{max.}$(Nujol) 1 725 cm^{-1}; δ_H 1.13 (3 H, s), 1.37 (3 H, s), 1.60 (3 H, s), 2.21 (3 H, s), 3.44 (3 H, s), 4.35 (1 H, d, *J* 3.5 Hz), 4.62 (1 H, s), and 5.83 (1 H, d, *J* 3.5 Hz); *m/z* 215 (M^+ − 15, 4.8%), 187 (60), 157 (42), and 99 (100).

(*b*) The alcohol (**18**) (60 mg) in CH_2Cl_2 (2 ml) was oxidized with PCC (111 mg) in the presence of molecular sieves 3A (180 mg) as described for the preparation of (**11**) to give (**13**) (51 mg, 86%).

1,2:5,6-*Di*-O-*isopropylidene*-3-C-*methyl*-3-O-*methyl*-α-D-*allofuranose* (**15**).—A solution of compound (**14**) (1.83 g, 6.7 mmol) in tetrahydrofuran (THF) (5 ml) was added to a stirred solution of dimsylsodium, prepared from 50% NaH dispersion (384 mg, 8 mmol) in dimethyl sulphoxide (DMSO) (30 ml), at room temperature under argon. After 30 min, MeI (623 mg, 10 mmol) was added. The mixture was stirred for an additional 1 h, then poured into ice–aqueous NH_4Cl, and extracted with CH_2Cl_2. The extract was washed with water, dried, and evaporated under reduced pressure. The residue was purified on a silica gel column with n-hexane–EtOAc (4:1) as eluant to afford compound (**15**) as an oil (1.73 g, 90%), δ_H($CDCl_3$) 1.24 (3 H, s), 1.35 (3 H, s), 1.36 (3 H, s), 1.56 (3 H, s), 1.44 (3 H, s), 3.42 (3 H, s), 3.90—4.15 (4 H, m), 4.28 (1 H, d, *J* 3.5 Hz), and 5.65 (1 H, d, *J* 3.5 Hz).

1,2-O-*Isopropylidene*-3-C-*methyl*-3-O-*methyl*-6-O-(p-*tolylsulphonyl*)-α-D-*allofuranose* (**16**).—To a stirred solution of compound (**15**) (1.73 g) in methanol (25 ml) was added 1.9% aqueous H_2SO_4 (8 ml) at room temperature. After 18 h, the solution was neutralized with $NaHCO_3$ (solid) and evaporated under reduced pressure. The residue was taken up in CH_2Cl_2, and the extract was washed with water, dried (Na_2SO_4), and evaporated to give crude oily 1,2-*O*-isopropylidene-3-*C*-methyl-3-*O*-methyl-α-D-allofuranose (1.06 g, 71.1%), which was subjected to the next reaction without further purification; δ_H($CDCl_3$) 1.31 (3 H, s), 1.35 (3 H, s), 1.60 (3 H, s), 2.33 (1 H, t, *J* 5 Hz), 2.78 (1 H, s), 3.43 (3 H, s), 3.60—4.00 (4 H, m), 4.31 (1 H, d, *J* 3.5 Hz), and 5.69 (1 H, d, *J* 3.5 Hz).

A stirred pyridine (1 ml) solution of the above oil (182 mg) was treated with toluene-*p*-sulphonyl chloride (147 mg) at room temperature. After 5 h, the solution was poured into ice–brine and extracted with CH_2Cl_2. The extract was washed successively with saturated aqueous $KHCO_3$ and brine, dried (Na_2SO_4), and evaporated under reduced pressure. Chromatography on silica gel with n-hexane–EtOAc (1:1) as eluant gave the tosylate (**16**) (134 mg, 49.1%) as a viscous oil, δ_H($CDCl_3$) 1.24 (3 H, s), 1.33 (3 H, s), 1.55 (3 H, s), 2.43 (3 H, s), 2.75 (1 H, s), 3.38 (3 H, s), 3.80—4.20 (4 H, m), 4.30 (1 H, d, *J* 3.5 Hz), 5.63 (1 H, d, *J* 3.5 Hz), 7.32 (2 H, d, *J* 8.5 Hz), and 7.80 (2 H, d, *J* 8.5 Hz).

5,6-*Anhydro*-1,2-O-*isopropylidene*-3-C-*methyl*-3-O-*methyl*-α-D-*allofuranose* (**17**).—A MeOH solution (4 ml) of the tosylate (**16**) (134 mg) was stirred with K_2CO_3 (60 mg) at room temperature for 1 h. After removal of the solvent under reduced pressure, the residue was extracted with CH_2Cl_2 and the extract was washed with water, dried (Na_2SO_4), and evaporated to leave oily anhydride (**17**) (78 mg, 94%), δ_H($CDCl_3$) 1.31 (3 H, s), 1.35 (3 H, s), 1.57 (3 H, s), 2.70—2.95 (2 H, m), 2.96—3.10 (1 H, m), 3.42 (3 H, s), 3.87 (1 H, d, *J* 5.0 Hz), 4.31 (1 H, d, *J* 3.5 Hz), and 5.70 (1 H, d, *J* 3.5 Hz).

6-*Deoxy*-1,2-O-*isopropylidene*-3-C-*methyl*-3-O-*methyl*-α-D-*allofuranose* (**18**).—The epoxide (**17**) (87 mg) and $LiAlH_4$ (16 mg) were stirred in ether (3 ml) at 0 °C under argon for 0.5 h. Work-up gave the oily product (**18**) (60 mg, 74%), δ_H($CDCl_3$) 1.27 (3 H, d, *J* 6 .0 Hz), 1.27 (3 H, s), 1.37 (3 H, s), 1.60 (3 H, s), 2.61 (1 H , s), 3.42 (3 H, s), 3.67 (1 H, d, *J* 9.0 Hz), 3.70—3.95 (1 H, m), 4.30 (1 H, d, *J* 3.5 Hz), and 5.67 (1 H, d, *J* 3.5 Hz).

1,2:5,6-*Di*-O-*isopropylidene*-3-C-*methyl*-3-O-*methyl*-α-D-*glucofuranose* (**20**).—A solution of compound (**19**) (20 g, 72.9 mmol) in THF (50 ml) was added to a stirred solution of dimsylsodium, prepared from 50% NaH dispersion (5.2 g, 108 mmol) in DMSO (300 ml), at room temperature under argon. After 30 min, MeI (15.3 g, 108 mmol) was added. The mixture was stirred for an additional 1 h. Work-up gave the oily *product* (**20**) (18.68 g, 88.9%), b.p. 70 °C/0.1 mmHg (Kugelrohr) (Found: C, 58.1; H, 8.4. $C_{14}H_{24}O_6$ requires C, 58.31; H, 8.39%); $[\alpha]_D^{25}$ +1.3° (*c* 2.44 in $CHCl_3$); δ_H 1.33 (3 H, s), 1.36 (3 H, s), 1.40 (3 H, s), 1.42 (3 H, s), 1.51 (3 H, s), 3.32 (3 H, s), 3.88 (1 H, d, *J* 7.0 Hz), 4.02 (1 H, d, *J* 6.5 Hz), 4.03 (1 H, d, *J* 3.0 Hz), 4.01—4.16 (1 H, m), 4.40 (1 H, d, *J* 3.5 Hz), and 5.81 (1 H, d, *J* 3.5 Hz); *m/z* 273 (M^+ − 15, 45%), 215 (9.7), and 101 (100).

1,2-O-*Isopropylidene*-3-C-*methyl*-3-O-*methyl*-α-D-xylo-*pentodialdo*-1,4-*furanose* (**21**).—2% H_2SO_4 (80 ml) was added to a stirred solution of compound (**20**) (16.5 g) in MeOH (250 ml) at room temperature. After 10 h, the solution was neutralized with $NaHCO_3$ (solid) concentrated under reduced pressure to remove the MeOH, and extracted with CH_2Cl_2. The extract was washed with brine, dried (Na_2SO_4), and evaporated under reduced pressure to leave the oily diol (12.4 g, 87.3%), which was used without purification in the next reaction; δ_H($CDCl_3$) 1.33 (3 H, s), 1.44 (3 H, s), 1.51 (3 H, s), 2.37 (1 H, t, *J* 6.0 Hz), 2.71 (1 H, d, *J* 5.5 Hz), 3.33 (3 H, s), 3.72—4.10 (4 H, m), 4.43 (1 H, d, *J* 4.0 Hz), and 5.83 (1 H, d, *J* 4.0 Hz); *m/z* 233 (M^+ − 15, 3.1%), 187 (14), and 101 (100).

$Pb(OAc)_4$ (25.3 g, 57 mmol) was added to a stirred solution of the diol (11.5 g, 47.5 mmol) in benzene (150 ml) at room temperature. After 15 min, precipitates were filtered off, and the filtrate was washed with aqueous $NaHCO_3$, dried (Na_2SO_4), and evaporated to leave a solid residue of compound (**21**) (6.1 g, 60.9%). Recrystallization from ether–light petroleum gave the *aldehyde* (**21**) as needles, m.p. 72—72.5 °C (Found: C, 55.5; H, 7.5. $C_{10}H_{16}O_5$ requires C, 55.54; H, 7.46%); $\nu_{max.}$($CHCl_3$) 1 730 cm^{-1} (CHO); δ_H($CDCl_3$) 1.36 (3 H, s), 1.48 (3 H, s), 1.50 (3 H, s), 3.23 (3 H, s), 4.16 (1 H, d, *J* 2 Hz), 4.47 (1 H, d, *J* 3.5 Hz), 6.07 (1 H, d, *J* 3.5 Hz), and 9.63 (1 H, d, *J* 2 Hz); *m/z* 201 (M^+ − 15, 12%), 187 (58), 157 (87), and 99 (100).

6-*Deoxy*-1,2-O-*isopropylidene*-3-C-*methyl*-3-O-*methyl*-α-D-xylo-*hexofuranos*-5-*ulose* (**22**).—A solution of compound (**21**) (216 mg, 1.0 mmol) in THF (2 ml) was added to a stirred solution of MeMgI, prepared from MeI (354 mg, 2.5 mmol) and Mg (60 mg, 2.5 mg-atom) in ether (10 ml), at 0 °C under argon. After 15 min, saturated aqueous NH_4Cl was added to the solution, and the organic layer was evaporated. The residue was passed through a short silica gel column with n-hexane–EtOAc (3:2) as eluant to afford an oily 4:1 mixture of alcohols (210 mg, 90.4%), *m/z* 217 (M^+ − 15, 4.7%), 187 (12), 156 (25), 101 (95), and 100 (100).

PCC (21.5 g, 99.8 mmol) and powdered molecular sieves 3A (10 g) were added to a stirred solution of the mixture of alcohols (5.8 g, 24.9 mmol) in CH_2Cl_2 (200 ml) at room temperature. After 4 h, the insoluble materials were filtered off, and the filtrate was evaporated to *ca.* 20 ml and passed through a short

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silica gel column with ether as eluant to afford a solid residue of compound (**22**) (5.2 g, 90.6%). Recrystallization from light petroleum gave the *title compound* as needles, m.p. 53—53.5 °C (Found: C, 57.3; H, 7.85. $C_{11}H_{18}O_5$ requires C, 57.38; H, 7.88%); $[\alpha]_D^{18}$ −107° (*c* 2.15 in $CHCl_3$); $\nu_{max.}$(Nujol) 1 710 cm^{-1} (CO); $\delta_H(CDCl_3)$ 1.35 (3 H, s), 1.45 (3 H, s), 1.49 (3 H, s), 2.23 (3 H, s), 3.21 (3 H, s), 4.19 (1 H, s), 4.42 (1 H, d, *J* 3.5 Hz), and 6.02 (1 H, d, *J* 3.5 Hz); *m/z* 215 (M^+ − 15, 4.8%), 187 (69), 157 (49), 101 (80), and 99 (100).

3,6-*Dideoxy*-1,2-O-*isopropylidene*-3-C-*methyl*-α-D-glycero-*hex*-3-*enofuranos*-5-*ulose* (**12**).—(*a*) K_2CO_3 (20 g, 145 mmol) was added to a stirred solution of compound (**22**) (6.6 g, 28.7 mmol) in MeOH (650 ml) at room temperature. After 24 h, saturated aqueous NH_4Cl was added, the solvent was removed under reduced pressure, and then the residue was extracted with CH_2Cl_2. The extract was washed with water, dried (Na_2SO_4), and evaporated under reduced pressure to leave a pale yellow oil which was purified on a short silica gel column with n-hexane–EtOAc (4:1) as eluant to afford the title compound as an oil (5.05 g, 89.1%), $\nu_{max.}$(neat) 1 700 cm^{-1} (CO); $\delta_H(CDCl_3)$ 1.41 (3 H, s), 1.46 (3 H, s), 2.09 (3 H, d, *J* 1.0 Hz), 2.30 (3 H, s), 5.14 (1 H, dq, *J* 5.5, 1.0 Hz), and 5.99 (1 H, d, *J* 5.5 Hz); *m/z* 198 (M^+, 3%), 169 (45), 98 (100), 97 (95), 69 (40), 59 (65), and 43 (100).

(*b*) Bu^{t}OK (35 mg, 0.31 mmol) was added to a stirred solution of compound (**26**) (100 mg, 0.326 mmol) in DMSO (3 ml) at room temperature. After 10 min, the reaction mixture was poured into ice–aqueous NH_4Cl and extracted with CH_2Cl_2. The extract was washed with water, dried (Na_2SO_4), and evaporated under reduced pressure, and the residue was chromatographed on a silica gel column with n-hexane–EtOAc (3:1) as eluant to afford compound (**12**) as an oil (16 mg, 25%).

(*c*) K_2CO_3 (60 mg, 0.43 mmol) was added to a stirred solution of compound (**28**) (1.06 g, 5.35 mmol) in MeOH (30 ml) at room temperature. After 10 min, NH_4Cl (23 mg, 0.43 mmol) was added, and then the solvent was evaporated to dryness under reduced pressure. The residue was extracted with CH_2Cl_2. The extract was washed with water, dried (Na_2SO_4), and chromatographed on a silica gel column with n-hexane–EtOAc (3:1) as eluant to afford oily (**12**) (0.805 g, 75.9%).

3,6-*Dideoxy*-1,2-O-*isopropylidene*-3-C-*methyl*-β-L-lyxo-*hexofuranos*-5-*ulose* (**7**).—A solution of compound (**12**) (3.56 g) in EtOAc (150 ml) was hydrogenated in the presence of 10% Pd–C (0.36 g) at ordinary temperature and pressure for 2 h. After removal of the catalyst by filtration, the filtrate was evaporated under reduced pressure to leave oily (**7**) (3.56 g, 99%), b.p. 60 °C/0.08 mmHg (Kugelrohr) (Found: C, 59.0; H, 8.15. $C_{10}H_{16}O_4 \cdot 0.25H_2O$ requires C, 58.68; H, 7.82%); $[\alpha]_D^{17}$ +4.2° (*c* 1.12 in $CHCl_3$); $\nu_{max.}$(neat) 1 710 cm^{-1}; $\delta_H(CDCl_3)$ 1.22 (3 H, d, *J* 7.5 Hz), 1.33 (3 H, s), 1.54 (3 H, s), 2.33 (3 H, s), 2.44—2.80 (1 H, m), 4.30 (1 H, d, *J* 9.5 Hz), 4.58 (1 H, dd, *J* 5.0, 4.0 Hz), and 5.87 (1 H, d, *J* 4.0 Hz); *m/z* 200 (M^+, 0.76%), 185 (11), 157 (43), 99 (42), 71 (38), 59 (84), and 43 (100).

3-O-*Benzyl*-6-*deoxy*-1,2-O-*isopropylidene*-3-C-*methyl*-α-D-ribo-*hexafuranos*-5-*ulose* (**26**).—The aldehyde (**25**) (1.0 g, 3.42 mmol) was treated with MeMgI (64 mmol) in ether, as indicated for the preparation of compound (**10**), to afford an oil (1.01 g, 95.7%) which was a mixture of alcohols, and which was used without purification in the next reaction; *m/z* 293 (M^+ − 15, 0.64%), 250 (0.68), 205 (1.9), 143 (6.2), and 91 (100).

The mixture of alcohols (1.0 g, 3.24 mmol) in CH_2Cl_2 (60 ml) was oxidized with PCC (4.27 g, 19.8 mmol) as indicated for the preparation of compound (**11**) to give compound (**26**) as a solid (0.92 g, 92.6%). Recrystallization from n-hexane–ether gave *needles*, m.p. 78.5—80 °C (Found: C, 66.6; H, 7.25. $C_{17}H_{22}O_5$ requires C, 66.65; H, 7.24%); $[\alpha]_D^{16}$ +113° (*c* 1.0 in $CHCl_3$); $\nu_{max.}$(Nujol) 1 725 cm^{-1} (CO); $\delta_H(CDCl_3)$ 1.21 (3 H, s), 1.38 (3 H, s), 1.61 (3 H, s), 2.22 (3 H, s), 4.42 (1 H, d, *J* 3.5 Hz), 4.66 (2 H, s), 4.73 (1 H, s), 5.87 (1 H, d, *J* 3.5 Hz), and 7.18—7.50 (5 H, m).

3,6-*Dideoxy*-1,2-O-*isopropylidene*-3-C-*methylene*-α-D-erythro-*hexofuranos*-5-*ulose* (**28**).—Compound (**27**) (2.0 g, 10.9 mmol) was treated with MeMgI (27.4 mmol) in ether as indicated for the preparation of compound (**10**) to afford an oily 1:1 mixture of alcohols (1.51 g, 69.5%), $\nu_{max.}$(neat) 3 400 cm^{-1}.

The mixture of alcohols (1.5 g, 7.5 mmol) was oxidized with PCC (4.04 g, 18.7 mmol) as described for the preparation of compound (**11**) to afford compound (**28**) as an oil (1.06 g, 71.6%), $\nu_{max.}$(neat) 1 735 cm^{-1}; $\delta_H(CDCl_3)$ 1.40 (3 H, s), 1.51 (3 H, s), 2.18 (3 H, s), 4.9—5.0 (2 H, m), 5.30 (1 H, dd, *J* 1.0, 2.0 Hz), 5.48 (1 H, dd, *J* 0.5, 2.5 Hz), and 6.01 (1 H, d, *J* 3.5 Hz).

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