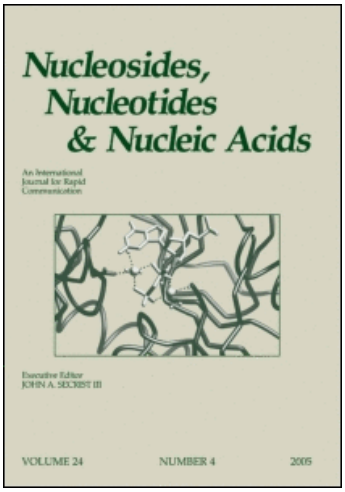

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Oxetanocin—Oxetanose Chemistry: Lewis Acid Promoted Glycosidations of the D-Erythrooxetanose Derivatives

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OXETANOCIN - OXETANOSE CHEMISTRY: LEWIS ACID PROMOTED GLYCOSIDATIONS OF THE D-ERYTHROOXETANOSE DERIVATIVES

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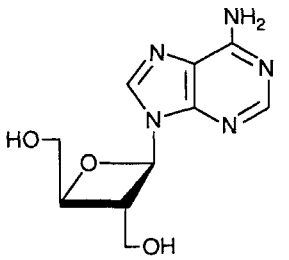
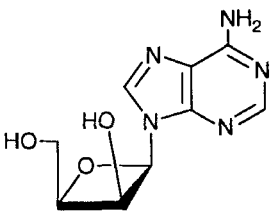
Abstract: Upon treatment of 1-O-acetyl-D-erythrooxetanoses (**17a,b** and **26**) with trimethylsilyl N-benzoyladenine or allyltrimethylsilane in the presence of $SnCl_4$, the ring expanded products (**18**, **19** and **29**) or the acyclic compounds (**27** and **28**) were obtained. The reaction mechanism involving a novel ring opening process is discussed.

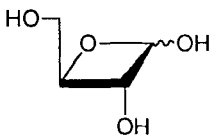
The antibiotic oxetanocin-A (**1**)[1] exhibits potent antiviral activities derived from the novel nucleoside structure containing a four-membered ring sugar (oxetanose) moiety. A number of synthetic studies on derivatives of **1**[2] have shown great promise as antiviral agents, and indeed some are already at the clinical stage. Amongst these derivatives, epinor-oxetanocin-A (**2**) which carries D-threooxetanose synthesized by chemical modification of **1** by the Nippon Kayaku group[3] exhibits much more potent antiviral activities than the parent antibiotic (**1**). This observation prompted us to initiate synthetic studies of a



OXETANOCIN-A (**1**)



EPINOR-OXETANOCIN-A (**2**)



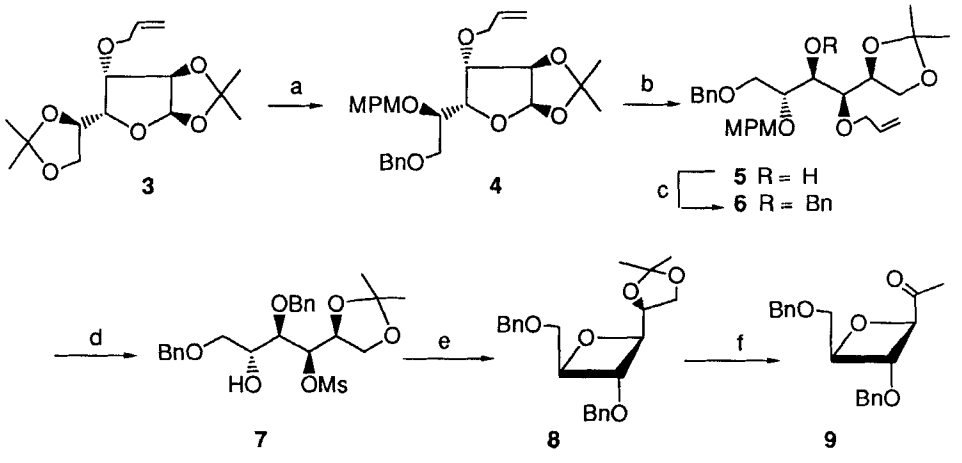
D-ERYTHROOXETANOSE

Dedicated to the memory of the late Professor Tohru Ueda.

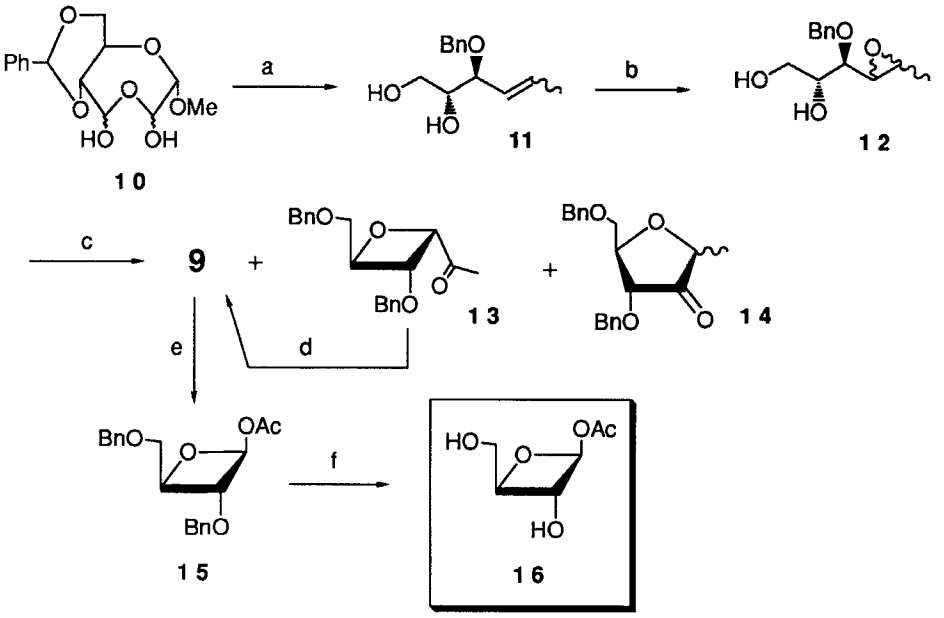
representative D-erythrooxetanose and its glycosidation reactions. Until now, with the exception of our investigations[2] only a few reports have appeared concerning chemical features of oxetanoses. For instance, during the course of our total synthesis of **1**,[4] the oxetanoses were found to be stable as 1-O-acyl derivatives, which could then be coupled to adenine aided by the seven-membered ring participation of the neighboring group, which is different from those of the well-known five or six-membered rings. With these prospects in mind we believe it would be interesting to develop the chemistry of the new oxetanose group.[5]

Synthesis of 1-O-acetyl-β-D-erythrooxetanose (16).

The title compound **16** was synthesized *via* the key intermediate (**9**), which could be obtained by two different paths. In the first method, diacetone glucose derivative **3**[6] was chosen as the starting material. Selective hydrolysis of **3**, followed by stepwise etherification provided **4** in good yield. Conversion of **4** to the corresponding glucitol derivative (**6**) *via* **5** was undertaken to distinguish the OH group at the C_4 position from the others. Removal of the allyl group of **6** under neutral conditions, followed by mesylation and DDQ oxidation afforded mesylate **7**. Treatment of **7** with NaH effected the intramolecular S_N2 reaction to the desired **8**. However, contrary to the case of the naturally occurring branched chain oxetanose,[4] formation of **8** was rather troublesome, probably due to the instability of **7**. Removal of the isopropylidene group of **8**, followed by chlorination using Ph_3P - CCl_4 gave rise to the regioselective introduction of a chlorine atom at the terminal carbon.



a. i) 2% H_2SO_4, room temp. (65%); ii) nBu_2SnO, then BnCl, nBu_4NBr / PhH (85%); iii) MPMCl, NaH / DMF (96%). b. i) 4M HCl - THF, room temp. (53%); ii) $NaBH_4$ / aq.dioxane (75%); iii) 2,2-dimethoxypropane, cat. TsOH / acetone (80%). c. BnBr, NaH / PhH, reflux temp. (98%). d. i) $(Ph_3P)_3RhCl$, DABCO / aq.EtOH, then $HgCl_2$, HgO / aq.acetone (98%); ii) MsCl, pyr. (97%); iii) DDQ / CH_2Cl_2 - H_2O (91%). e. NaH / PhMe, reflux temp. (38%). f. i) 2% H_2SO_4 (96%); ii) Ph_3P / CCl_4 - pyr. (83%); iii) $LiAlH_4$ / Et_2O (80%); iv) Swern oxid. (97%).



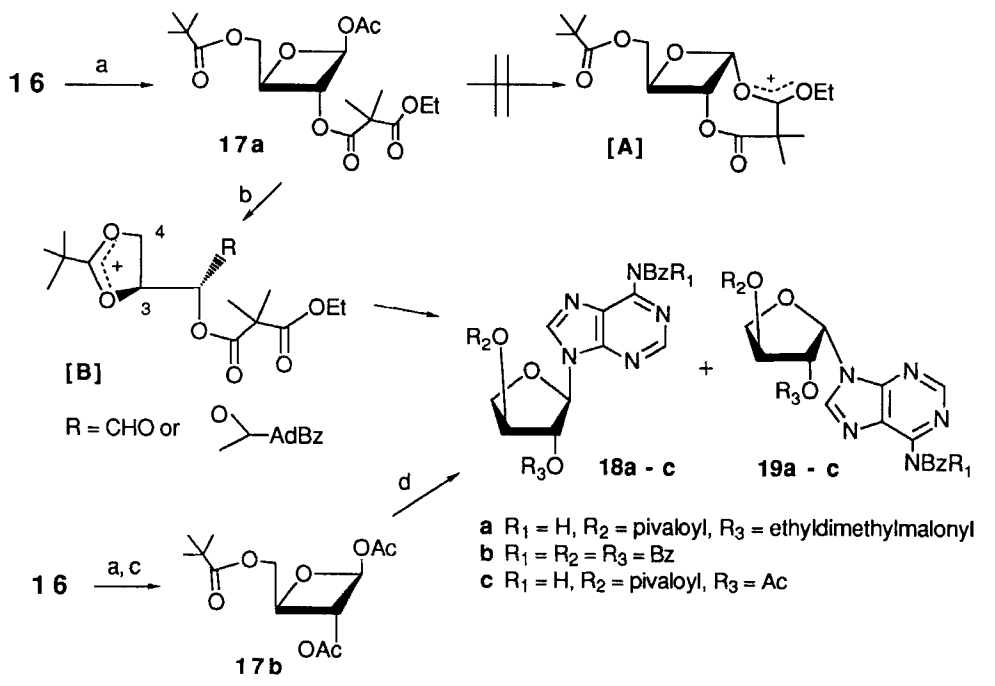
a. i) Ph_3PEtBr, nBuLi / THF; ii) DIBAL / PhMe (37% in 2 steps). b i) nBu_2SnO, then BnBr, nBu_4NBr / PhMe (100%); ii) mCPBA (100%). c. i) aq.KOH / DMSO, 165°C; ii) DMSO-DCC, pyr., TFA (**9**: 18%, **13**: 14%, **14**: 25% in 2 steps). d. NaOMe / MeOH (**9**: 62%, **13**: 22%). e. mCPBA / CH_2Cl_2 (97%). f. H_2, Pd-black / MeOH (97%).

Standard hydride reduction of the chlorinated compound, and Swern oxidation provided the expected methyl ketone (**9**) in high overall yield. This compound was also accessible by the following process involving the cyclization of **12**.[7]

The known dial hydrate[8] (**10**) was used as a starting material in which the two chiralities of **9** are already set up. Direct Wittig reaction of **10**, following DIBAL reduction afforded a mixture of geometrical isomers (**11**, Z : E = 3 : 1). The ratio of the isomers was determined by the ^1H NMR spectrum. Compound **11** was successively submitted to selective benzylation of the primary alcohol and epoxidation to give **12**. The key cyclization of **12** was effected under the KOH / aq. DMSO condition,[9] to yield **9**, **13**, and **14** in 18, 14, and 25% yields, respectively. Fortunately, treatment of **13** with NaOMe gave rise to isomerization of the methyl ketone group to furnish a ca. 3 : 1 mixture of **9** and **13**. Baeyer - Villiger oxidation of methyl ketone **9** smoothly provided the 1-O-acetyl-oxetanose (**15**) without formation of possible isomers. Upon catalytic hydrogenation, **15** was converted to the stable 1-O-acetyl-β-D-erythrooxetanose (**16**).

Glycosidation of the D-erythrooxetanose derivative (17a,b) with silylated adenine.

1-O-Acetyl-β-D-erythrooxetanose (**16**) was fully acylated to **17a**, which offers the possibility for glycosidation reactions *via* the seven-membered ring participation as in **[A]**. Actually, this participation was the crucial factor in the Lewis acid promoted glycosidation in our total synthesis of **1**.[4] However, upon treatment of **17a** with bistrimethylsilyl N-benzoyladenine, the reaction proceeded in an entirely different way to produce a mixture of L-threofuranosyl adenine derivatives (**18a** + **19a**, 71%), which were characterized as their tetrabenzoate (**18b** and **19b**). These structures were unambiguously established by comparisons of their spectral data and optical rotations with the authentic 9-(D-threofuranosyl) adenine tetrabenzoates, synthesized by the known procedure.[9] Inversion of configuration at the C_3 position suggested that the ring expansion reaction might pass through the acyclic

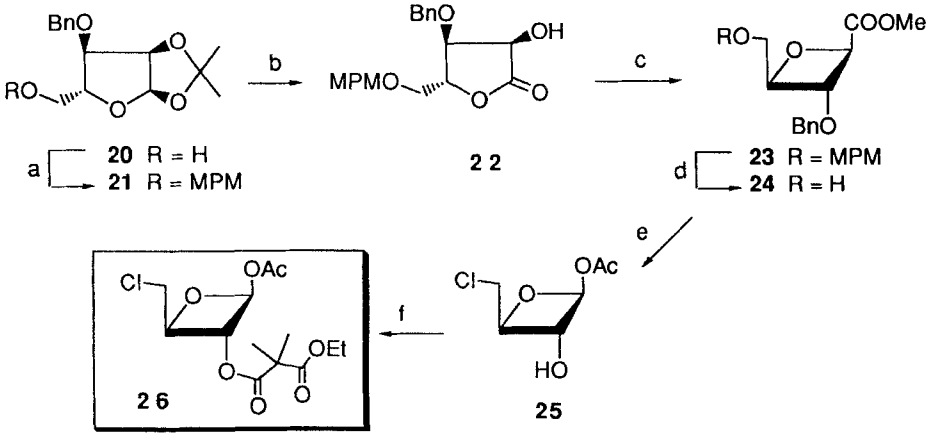


a. i) pivaloyl chloride / pyr. (58%); ii) ethyldimethylmalonyl chloride / pyr. (73%). b. i) $SnCl_4$, bistrimethylsilyl N-benzoyladenine / $(CH_2Cl)_2$ (**18a+19a**, 71%); ii) NaOMe / MeOH; iii) BzCl, pyr. (**18**: 75%, **19**: 17% in 2 steps). c. Ac_2O, pyr. (91%). d. $SnCl_4$, bistrimethylsilyl N-benzoyladenine / $(CH_2Cl)_2$ (**18c**: 33%, **19c**: 21%).

intermediate [B] generated by pivaloyl group participation from the C_4 position, followed by recyclization to preferentially yield the less strained furanose derivatives over the corresponding oxetanose, although it was not clear whether this process took place before or after the N-glycosidation. Additionally, glycosidation of **17b** bearing the acetyl group at the C_2 position was also attempted under the same conditions as in the case of **17a**. As expected, the ring expanded products (**18c** and **19c**) were obtained, the structures of which were confirmed by transformation into the tetrabenzoates (**18b** and **19b**). From this result, the glycosidation of **17b** might include a similar acyclic intermediate to [B], which led to **18c** and **19c** without the necessity of seven-membered ring participation. In any case, acyl group participation might initiate this unusual ring expansion reaction. Consequently, our attention turned to intercept the participation of the C_4 substituent of the oxetanose. In an evaluation of suitable functional groups we selected the 4-chloro-4-deoxy compound (**26**) which does not participate as the acyl group and can be easily transformed into the corresponding alcohols.

Synthesis of the 4-chloro-4-deoxy-D-erythrooxetanose derivative (26).

Protection of the OH group at the C_5 position of **20**[11] with the MPM group led to **21**, and the following two step rearrangement provided the ribonolactone (**22**). Compound **22** was successively submitted to Fleet's ring contraction[12] where the triflate derivative was



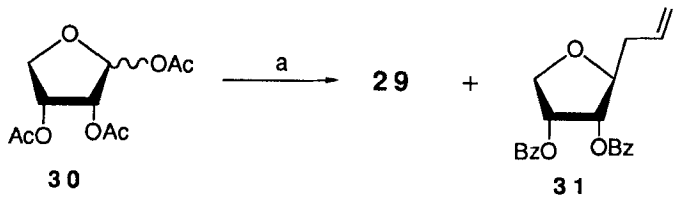
a. MPMCl, NaH / DMF (89%). b. i) 4M HCl - THF (76%); ii) Br_2, NaOAc / DMF (89%). c. $(CF_3SO_2)_2O$, pyr., then K_2CO_3 / MeOH (39%). d. DDQ / CH_2Cl_2 - H_2O (72%). e. i) $LiOH{\cdot}H_2O$ / dioxane; ii) MeLi / THF (47% in 2 steps); iii) Ph_3P / CCl_4, reflux. (86%); iv) mCPBA / CH_2Cl_2 (94%); v) H_2, Pd-black (97%). f. ethyldimethylmalonyl chloride, pyr. (94%).

treated with K_2CO_3 in MeOH to yield the corresponding oxetane (**23**). The MPM group of **23** was oxidatively removed to give **24**. Conversion of the methoxycarbonyl group of **24** to the methyl ketone was effected by hydrolysis and methylation with MeLi. An alternative route involving $Pb(OAc)_4$ oxidation of the corresponding carboxylic acid to the acetoxy group was also attempted, although a lower yield was obtained. The OH group at the C_4 position was exchanged with a chlorine atom under the Ph_3P - CCl_4 conditions. Baeyer - Villiger oxidation, followed by catalytic hydrogenation provided **25**. Consequently, **25** was transformed into the ethyldimethylmalonyl derivative (**26**) using the same method as in the case of **17a**.

Lewis acid-promoted glycosidation of 26 with allyltrimethylsilane.

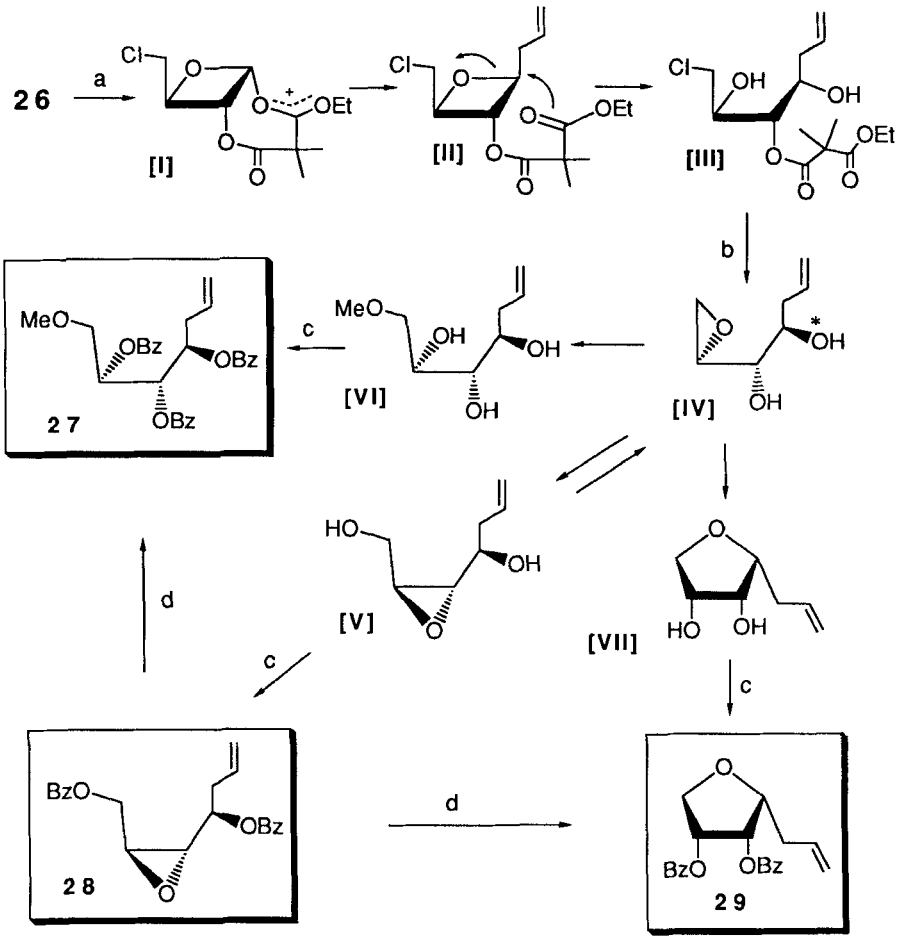
Reaction of the functionalized erythrooxetanose (**26**) with allyltrimethylsilane was performed to give a crude product, which was derivatized *via* basic treatment and benzoylation to afford **27**, **28** and **29**. In addition, exposure of epoxide **28** to NaOMe followed by benzoylation furnished a mixture of **27** and **29**. The structure of **29** was directly compared with an authentic sample which was independently synthesized from **30**+, and those of **27** and **28** were established by their ^1H NMR spectra and correlation of their chemical transformations. Based on these results, one plausible reaction mechanism can be considered: the reaction is initiated by abstraction of the acetoxy group leading to the seven-membered oxonium ion **[I]**. The following attack by allyltrimethylsilane, mainly from the β-side, gives the expected allyloxetane **[II]**, however, further reaction of **[II]** with the Lewis acid can cause ring opening, which on aqueous quenching provides the acyclic

+ As seen in the following Scheme, **29** and its isomer (**31**) were synthesized by glycosidation of **30** with allyltrimethylsilane, followed by the two steps manipulation of the protective groups under the same conditions as the cases of **17a,b** and **26**.



30 **31**

a. i) $SnCl_4$, allyltrimethylsilane / $(CH_2Cl)_2$ (57%); ii) NaOMe / MeOH; III) BzCl, pyr. (**29**: 9.4%, **31**: 53% in 2 steps).



a. $SnCl_4$, allyltrimethylsilane / $(CH_2Cl)_2$. b. NaOMe / MeOH. c. BzCl, pyr. (**27**: 29%, **28**: 14%, **29**: 11% in 3 steps). d. i) NaOMe / MeOH; ii) BzCl, pyr. (**27**: 22%, **29**: 50% in 2 steps).

product **[III]**. Exposure of **[III]** to NaOMe in the next step gives rise to the oxirane ring formation to **[IV]**, which can isomerize under this condition to **[V]**. Consequently, the reactive terminal epoxide of **[IV]** suffers a nucleophilic attack from either the methoxy anion leading to **[VI]**, or the alkoxide (*) to make the furanoside **[VII]**. Upon benzoylation, **[VI]**, **[V]** and **[VII]** are converted to **27**, **28** and **29**, respectively.

Contrary to furanose and pyranose sugars, the erythrooxetanoses have their chemical potentials at the C_3 position, which disturb the normal acyloxy group assisted glycosidation. This novel ring opening may be similar to those of β-lactones.[13] Further

synthetic studies and evaluations of the biological activities of oxetanosyl nucleosides are still in progress.

EXPERIMENTAL

IR spectra were recorded on a JASCO Model A-202 spectrophotometer. ^1H NMR spectra were obtained on a JEOL FX-90 A (90 MHz) or JEOL JNM GX-400 (400 MHz) NMR spectrometers in deuteriochloroform ($CDCl_3$) solution using tetramethylsilane as an internal standard. High resolution mass spectra were obtained on a Hitachi M-80 GC-MS spectrometer operating with an ionization energy (70 eV). Optical rotations were measured on a JASCO DIP-360 polarimeter in chloroform, unless otherwise stated. Preparative and analytical TLC were carried out on silica-gel plates (Kieselgel 60 F254, E. Merck A. G., Germany) using UV light and/or 5% molybdophosphoric acid in ethanol for detection. Katayama silica-gel (K 070) was used for column chromatography.

3-O-Allyl-6-O-benzyl-1,2-O-isopropylidene-5-O-*p*-methoxybenzyl-α-D-glucofuranose (4). A solution of 3-O-allyl-1,2:5,6-di-O-isopropylidene-α-D-glucofuranose (**3**)[6] (212 mg) in 2% H_2SO_4 (1 ml) - dioxane (4 ml) was stirred at room temperature for 12 h. The reaction mixture was neutralized with sat. aq. $NaHCO_3$, and filtered. The filtrate was evaporated to dryness, and the residue was chromatographed on a silica gel column (5 g, hexane - EtOAc = 1 : 1) to give 3-O-allyl-1,2-O-isopropylidene-α-D-glucofuranose (119 mg, 65%) and the unreacted starting material (71 mg).

A mixture of the monoisopropylidene (1.50 g, 5.8 mmol) and nBu_2SnO (1.45 g, 5.8 mmol) in benzene (25 ml) equipped with Dean-Stark trap was heated at refluxing temperature for 23 h. To the resulting mixture benzyl chloride (0.9 ml, 7.8 mmol) and nBu_4NBr (0.4 g, 1.24 mmol) were added, and the reaction mixture was further heated at the same temperature for 4 h. The mixture was partitioned between EtOAc and 2M HCl, and the organic layer was washed with brine, dried over anhydrous Na_2SO_4, then evaporated. The residue was purified on a silica gel column (100 g, hexane - EtOAc = 2 : 1) to give 3-O-allyl-6-O-benzyl-1,2-O-isopropylidene-α-D-glucofuranose (1.72 g, 85%).

To a solution of the benzyl ether (5.50 g, 15.7 mmol) in DMF (30 ml) was added NaH (0.66 g, 16.5 mmol, 60% dispersion in mineral oil) at 0 °C, and the mixture was stirred at room temperature for 30 h. After addition of *p*-methoxybenzyl chloride (4 ml, 29.5 mmol), the reaction suspension was further stirred at the same temperature for 27 h. The reaction was quenched by addition of methanol (5 ml) and the resulting mixture was partitioned between EtOAc and H_2O. The EtOAc layer was washed with brine, dried over anhydrous Na_2SO_4, then evaporated to give a residue, which on purification on a silica gel

column (150 g, hexane - EtOAc = 4 : 1) afforded **4** (7.07 g, 96%). $[\alpha]_D^{28}$ -20.3° (*c* 0.73); IR (film): 1650, 1610, and 1515 cm^{-1}; ^1H NMR: δ 1.30 (3H, s), 1.45 (3H, s), 3.63 (1H, dd, J= 6, 10.5 Hz), 3.77 (3H, s), 3.5 - 4.3 (5H, complex), 4.45 (1H, d, J= 10.5 Hz), 4.57 (4H, br. signal), 4.75 (1H, d, J= 10.5 Hz), 5.05 - 5.39 (2H, complex), 5.85 (1H, d, J= 3 Hz, overlapped with 1H signal), 6.83 (2H, d, J= 9 Hz), and 7.3 (7H, complex). Found: m/z 470.2273. Calcd for $C_{27}H_{34}O_7$: M, 470.2302.

3-O-Allyl-6-O-benzyl-1,2-O-isopropylidene-5-O-*p*-methoxybenzyl-D-glucitol (5). A solution of **4** (7.07 g) in 4M HCl (50 ml) and THF (100 ml) was stirred at room temperature for 2 days. After neutralization with $NaHCO_3$, the reaction mixture was partitioned between EtOAc and H_2O. The organic layer was washed with brine, dried over anhydrous Na_2SO_4, then evaporated to dryness. The residue was chromatographed on silica gel (150 g, hexane - EtOAc = 1 : 1) to give 3-O-allyl-6-O-benzyl-5-O-*p*-methoxybenzyl-D-glucofuranose (3.42 g, 53%) and the unreacted **4** (2.38 g). The hemiacetal was dissolved in dioxane (120 ml) - H_2O (40 ml). To this solution was added $NaBH_4$ (0.18 g, 4.8 mmol) at 0 °C, and the mixture was stirred at room temperature for 15 h. The reaction mixture was concentrated *in vacuo* to yield a crude mixture, which on a silica gel column purification (100 g, hexane - EtOAc = 1 : 2) provided 3-O-allyl-6-O-benzyl-5-O-*p*-methoxybenzyl-D-glucitol (2.79 g, 75%) and the starting material (0.55 g).

A mixture of the triol (3.85 g) and 2,2-dimethoxypropane (0.2 ml) in acetone (150 ml) containing catalytic amounts of TsOH and Molecular Sieves 4A (0.5 g) was kept at room temperature for 13 h. After neutralization with $NaHCO_3$, the resulting mixture was filtered, and the filtrate was evaporated. The residue obtained was chromatographed on a silica gel column (100 g, hexane - EtOAc = 4 : 1) to give **5** (3.37 g, 80%). $[\alpha]_D^{28}$ -33.9° (*c* 0.43); IR (film): 3500, 1650, 1610, and 1510 cm^{-1}; ^1H NMR: δ 1.36 (3H, s), 1.41 (3H, s), 2.67 (1H, d, J= 8 Hz), 3.48 (1H, m), 3.62 (2H, complex), 3.72 (2H, complex), 3.79 (3H, s), 3.84 (1H, dd, J= 3, 10 Hz), 3.91 (1H, m), 4.03 (1H, dd, J= 6.8, 8.3 Hz), 4.33 (2H, complex), 4.75 (1H, d, J= 12 Hz), 4.59 (1H, d, J= 12 Hz), 4.68 (1H, d, J= 11 Hz), 5.11 (1H, dd, J= 1.5, 10.7 Hz), 5.20 (1H, m), 5.87 (1H, m), 6.86 (2H, d, J= 8.3 Hz), and 7.3 (7H, complex). Found: m/z 472.2459. Calcd for $C_{27}H_{36}O_7$: M, 472.2459.

3-O-Allyl-4,6-di-O-benzyl-1,2-O-isopropylidene-5-O-*p*-methoxybenzyl-D-glucitol (6). A mixture of **5** (3.84 g, 8.1 mmol) and NaH (0.49 g, 60% dispersion in mineral oil) in benzene (100 ml) was heated at refluxing temperature for 1 h. To this mixture was added benzyl bromide (2 ml, 16.8 ml) at room temperature and the resulting mixture was further heated at refluxing temperature for 13 h. The reaction was quenched and purified as described in the case of **4** to provide **6** (4.49 g, 98%). $[\alpha]_D^{28}$ -18.6° (*c*

0.53); IR (film): 1650, 1610, 1585, and 1510 cm^{-1}; ^1H NMR: δ 1.30 (3H, s), 1.39 (3H, s), 3.51 (1H, dd, J= 3.4, 6.8 Hz), 3.58 (2H, dd, J= 2, 6.8 Hz), 3.63 (1H, dd, J= 3.9, 6 Hz), 3.68 (1H, dd, J= 5, 11.3 Hz), 3.79 (3H, s), 3.83 (1H, dd, J= 3.4, 10.7 Hz), 3.90 (1H, m), 4.07 (1H, dd, J= 6, 10.7 Hz), 4.26 (2H, complex), 4.48 (2H, complex), 4.51 (1H, d, J= 11.2 Hz), 4.57 (1H, d, J= 11.7 Hz), 4.63 (1H, d, J= 11.2 Hz), 4.69 (1H, d, J= 11.7 Hz), 5.10 (1H, m), 5.21 (1H, dd, J= 2, 5.6 Hz), 5.90 (1H, m), 6.83 (2H, d, J= 8.8 Hz), and 7.29 (12H, complex). Found: m/z 471.2382. Calcd for $C_{27}H_{35}O_7$: M-C_7H_7, 471.2380.

4,6-Di-O-benzyl-1,2-O-isopropylidene-3-O-mesyl-D-glucitol (7). A mixture of **6** (4.49 g, 8.0 mmol), $(Ph_3P)_3RhCl$ (0.15 g, 0.16 mmol) and DBU (0.26 g, 2.3 mmol) in EtOH (100 ml) - H_2O (5 ml) was refluxed for 1.5 h. The reaction mixture was evaporated, and partitioned between ether and brine. The organic layer was dried over anhydrous Na_2SO_4 and evaporated. The residue was dissolved in acetone (90 ml) and H_2O (30 ml). To this solution was added HgO (3.36 g, 15.5 mmol) and $HgCl_2$ (3.37 g, 12.4 mmol), and the suspension was stirred at room temperature for 20 min. The reaction mixture was filtered using a Celite pad, and the filtrate was concentrated *in vacuo*. The residue was diluted with H_2O, and extracted with $CHCl_3$. The $CHCl_3$ extract was successively washed with aq. KI, H_2O and brine, then dried over anhydrous Na_2SO_4. After evaporation, the resulting crude product was purified on a silica gel column (100 g, benzene - EtOAc = 10 : 1) to afford 4,6-di-O-benzyl-1,2-O-isopropylidene-5-O-*p*-methoxybenzyl-D-glucitol (4.07 g, 98%).

A mixture of the alcohol (4.07 g, 7.8 mmol) and mesyl chloride (4 ml, 52 mmol) in pyridine (4 ml) and CH_2Cl_2 (50 ml) was kept at room temperature overnight. The reaction mixture was partitioned between $CHCl_3$ and H_2O, and the $CHCl_3$ layer was washed with sat. aq. $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4, then evaporated. The residue was purified by silica gel column chromatography (50 g, hexane - EtOAc = 10 : 1) to give 4,6-di-O-benzyl-1,2-O-isopropylidene-3-O-mesyl-5-O-*p*-methoxybenzyl-D-glucitol (4.51 g, 97%). $[\alpha]_D^{27}$ -12.5° (*c* 0.36); IR (film): 1610, 1580, 1510, 1350, and 1170 cm^{-1}; ^1H NMR: δ 1.29 (3H, s), 1.42 (3H, s), 3.04 (3H, s), 3.59 (1H, dd, J= 6.8, 8.8 Hz), 3.67 (2H, complex), 3.80 (3H, s), 3.83 (3H, complex), 4.21 (1H, dd, J= 6.8, 13.7 Hz), 4.47 - 4.55 (4H, complex), 4.61 (1H, d, J= 11.2 Hz), 4.74 (1H, d, J= 11.2 Hz), 4.91 (1H, dd, J= 3.9, 7.3 Hz), 6.85 (2H, d, J= 8.3 Hz), and 7.33 (12H, complex). Found: m/z 509.1834. Calcd for $C_{25}H_{33}O_9S$: M-C_7H_7, 509.1842.

A mixture of the mesylate (536 mg, 0.89 mmol) and DDQ (450 mg, 2.0 mmol) in CH_2Cl_2 (20 ml) containing H_2O (1 ml) was stirred at room temperature for 2 h. The reaction mixture was filtered , and the filtrate was evaporated. The residue was partitioned

between EtOAc and H_2O, and the organic layer was washed with brine, dried over anhydrous Na_2SO_4, then evaporated. The residue was successively purified by silica gel column chromatography (20 g, hexane - EtOAc = 3 : 1) and preparative TLC (hexane - EtOAc = 2 : 1) to give **7** (391 mg, 91%). $[\alpha]_D^{27}$ +7.13° (*c* 0.35); IR (film): 3550, 1500, 1350, and 1170 cm^{-1}; ^1H NMR: δ 1.30 (3H, s), 1.43 (3H, s), 2.86 (1H, d, J= 6 Hz), 3.12 (3H, s), 3.58 (1H, dd, J= 7, 8.8 Hz), 3.64 (1H, dd, J= 2.4, 8 Hz), 3.66 - 3.75 (3H, complex), 3.96 (1H, m), 4.38 (1H, dd, J= 7, 13.7 Hz), 4.50 (1H, d, J= 11.2 Hz), and 7.35 (10H, complex). Found: m/z 480.1814. Calcd for $C_{24}H_{32}O_8S$: M, 480.1815.

3,5-Anhydro-4,6-di-O-benzyl-1,2-O-isopropylidene-D-allitol (8). A mixture of **7** (1.34 g, 2.8 mmol) and NaH (0.36 g, 60% dispersion in mineral oil) in toluene (60 ml) was refluxed for 15 min. The reaction mixture was quenched by addition of methanol (5 ml), and partitioned between EtOAc and H_2O. The organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was separated on a silica gel column (50 g, benzene - EtOAc = 8 : 1) to provide **8** as an oil (410 mg, 38%). $[\alpha]_D^{24}$ +26.0° (*c* 0.70); IR (film): 1605 and 1500 cm^{-1}; ^1H NMR: δ 1.35 (3H, s), 1.40 (3H, s), 3.49 (1H, dd, J= 4.4, 11.2 Hz), 3.54 (1H, dd, J= 4, 11.2 Hz), 3.81 (1H, dd, J= 5.4, 8.8 Hz), 4.05 (1H, dd, J= 6.8, 8.8 Hz), 4.23 (1H, q, J= 6.4 Hz), 4.32 (1H, t, J= 5 Hz), 4.55 (1H, d, J= 11.7 Hz), 4.49 (1H, dd, J= 5.4, 6.8 Hz), 4.55 (2H, d, J= 6.8 Hz), 4.57 (1H, d, J= 12.2 Hz), 4.70 (1H, q, J= 3.3 Hz), and 7.32 (10H, complex). Found: m/z 384.1936. Calcd for $C_{23}H_{28}O_5$: M, 384.1935.

3,5-Anhydro-4,6-di-O-benzyl-1-deoxy-2-oxo-D-ribohexitol (9). A solution of **8** (390 mg) in 2% H_2SO_4 (6 ml) and dioxane (24 ml) was stirred at 50 °C for 3 h. After cooling to room temperature, the reaction mixture was neutralized with $NaHCO_3$, and filtered. The filtrate was evaporated to dryness, and the residue was purified by silica gel column chromatography (5 g, hexane - EtOAc = 1 : 2) to give 3,5-anhydro-4,6-di-O-benzyl-D-allitol (335 mg, 96%).

A solution of the diol (354 mg) and Ph_3P (560 mg) in pyridine (12.5 ml) and CCl_4 (2 ml) was heated at 55 °C for 75 min. To this mixture was added MeOH (8 ml), and the resulting reaction solution was further heated at the same temperature for 1 h, cooled to room temperature, and evaporated. Separation of the residue by silica gel column chromatography (5 g, hexane - EtOAc = 1 : 1) provided 3,5-anhydro-4,6-di-O-benzyl-1-chloro-1-deoxy-D-allitol (308 mg, 83%). Found: m/z 362.1277. Calcd for $C_{20}H_{23}O_4Cl$: M, 362.1283.

To an ice-cooled solution of the chloride (308 mg, 0.85 mmol) in ether (15 ml) was added $LiAlH_4$ (80 mg, 2.1 mmol), and the resulting suspension was stirred at 8 °C for 2

days. The reaction mixture was partitioned between EtOAc and 1M HCl, and the organic layer was washed with sat. aq. $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4, then evaporated. The residue was purified by silica gel column chromatography (5 g, hexane - EtOAc = 2 : 1) to give 3,5-anhydro-4,6-di-O-benzyl-1-deoxy-D-allitol (223 mg, 80%). $[\alpha]_D^{26}$ +35.7° (*c* 1.15); IR (film): 3470 and 1500 cm^{-1}; ^1H NMR: δ 1.08 (3H, d, J= 6 Hz), 3.15 - 3.35 (2H, complex), 3.52 (1H, dd, J= 2, 12 Hz), 4.40 - 4.65 (6H, complex), 7.27 ((5H, complex), and 7.30 (5H, complex). Found: m/z 328.1680. Calcd for $C_{20}H_{24}O_4$: M, 328.1673.

To a solution of oxalyl chloride (0.25 ml, 2.9 mmol) and DMSO ((0.4 ml, 5.6 mmol) in CH_2Cl_2 (2 ml) at -20 °C was added the alcohol (223 mg, 0.68 mmol) in CH_2Cl_2 (8 ml), and the resulting mixture was stirred at the same temperature for 45 min. After addition of Et_3N (1 ml, 7.2 mmol), the reaction mixture was further stirred for 30 min, and partitioned between EtOAc and H_2O. The EtOAc layer was washed with brine, dried over anhydrous Na_2SO_4, and evaporated. The residue obtained was purified by silica gel column chromatography (5 g, hexane - EtOAc = 3 : 1) to yield **9** (214 mg, 97%). $[\alpha]_D^{26}$ +69.0° (*c* 1.29); IR (film): 1715, 1600, and 1500 cm^{-1}; ^1H NMR: δ 2.25 (3H, s), 3.42 (1H, dd, J= 3.4, 11.7 Hz), 3.57 (1H, dd, J= 3, 11.7 Hz), 4.41 (1H, br. t, J= 5 Hz), 4.45 (1H, d, J= 11.7 Hz), 4.50 (1H, d, J= 12 Hz), 4.57 (1H, d, J= 12 Hz), 4.64 (1H, d, J= 11.7 Hz), 4.73 (1H, m), 4.85 (1H, d, J= 5 Hz), and 7.32 (10H, complex). Found: m/z 326.1518. Calcd for $C_{20}H_{22}O_4$: M, 326.1517.

Alternative Synthesis of the Methyl Ketone (9). To a suspension of Ph_3PEtBr (7.5 g, 20 mmol) in THF (50 ml) was added 1.57M nBuLi (12.6 ml, 20 mmol), and the mixture was stirred at room temperature for 0.5 h. After addition of 7,9-dihydroxy-6α-methoxy-2-phenyl-*trans-m*-dioxano[5,4-e][1,4]-dioxepan hydrate[8] (**10**, 1.2 g, 3.8 mmol) at -30 °C, the reaction mixture was refluxed for 24 h, and partitioned between $CHCl_3$ and H_2O. The $CHCl_3$ extracts were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was partially separated on a silica gel column (100 g, hexane - EtOAc = 3 : 1) to give a crude product, which was dissolved in toluene (15 ml). To this solution cooled to -30 °C was added 1.5M DIBAL (8.5 ml, 12.8 mmol), and the mixture was stirred at room temperature for 10 h. The reaction was quenched in the usual manner. Purification of the crude product by silica gel column chromatography (40 g, hexane - EtOAc = 1 : 1) afforded a mixture (Z : E = 3 : 1) of **11** (308 mg, 37%).

A mixture of **11** (77 mg, 0.35 mmol) and nBu_2SnO (99 mg, 0.4 mmol) in toluene (5 ml) was heated at refluxing temperature for 23 h. The resulting product was treated with the same procedure as the synthesis of **4** to give the dibenzyl derivative (109 mg, 100%, Z : E = 3 : 1).

A 35 mg portion of the dibenzyl ether was dissolved in CH_2Cl_2 (2 ml). After addition of mCPBA (66 mg, 0.38 mmol), the reaction mixture was kept at 4 °C for 2 days to yield epoxide **12** (36 mg, 100%), which was used for the next cyclization reaction without further separation of the corresponding geometrical isomers.

To a solution of **12** (39 mg, 0.12 mmol) in DMSO (4 ml) was added 2.5M aq. KOH (1 ml), and the mixture was stirred at 165 °C for 50 min. The reaction mixture was diluted with H_2O and extracted with EtOAc. The EtOAc layer was washed with brine, dried over anhydrous Na_2SO_4, and evaporated. The residue was dissolved in benzene (1.5 ml). To the solution was added, successively, DMSO (0.15 ml, 2.1 mmol), DCC (300 mg, 1.5 mmol), pyridine (0.03 ml, 0.4 mmol) and TFA (0.03 ml, 0.4 mmol), and the mixture was stirred at room temperature. After 21 h, the reaction was quenched by addition of sat. aq. oxalic acid in MeOH (2 ml), and then filtered. The filtrate was evaporated, and the residue was partitioned between EtOAc and H_2O. The organic layer was washed with brine, dried over anhydrous Na_2SO_4, then evaporated. The crude product was submitted to preparative TLC (hexane - EtOAc = 3 : 1) to give **9** (7.1 mg, 18%), the α-methyl ketone (**13**, 5.3 mg, 14%), and a mixture of the tetrahhydrofurans (**14**, 9.6 mg, 25%, α / β = 1). **13**: ^{1}H NMR: δ 2.36 (3H, s), 3.49 (1H, dd, J= 4, 11.2 Hz), 3.59 (1H, dd, J= 3.4, 11.2 Hz), 4.38 (1H, d, J= 11.7 Hz), 4.54 (2H, d, J= 11.2 Hz), 4.68 (1H, dd, J= 4.9, 7.3 Hz), 4.83 (1H, br. q, J= 4 Hz), 5.04 (1H, dd, J= 1, 7.3 Hz), and 7.22 - 7.38 (10H, complex). Found: m/z 326.1554. Calcd for $C_{20}H_{22}O_4$: M, 326.1517.

Isomerization of the α-Methyl Ketone (13) to β-Derivative (9). A solution of **13** (7.5 mg) in 0.05M NaOMe / MeOH (2 ml) was kept at room temperature for 10 h. The mixture was evaporated, and the residue was separated by preparative TLC (hexane - EtOAc = 3 : 1) to give **9** (4.6 mg, 62%) and **13** (1.6 mg, 22%).

1-O-Acetyl-2,4-di-O-benzyl-β-D-erythrooxetanose (15). A mixture of **9** (108 mg, 0.33 mmol) and mCPBA (133 mg, 0.77 mmol) in CH_2Cl_2 (2 ml) was kept at 8 °C for 2 days. The reaction mixture was partitioned between EtOAc and 1M aq. Na_2SO_3, and the EtOAc layer was washed with sat. aq. $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4, and then evaporated. The residue was chromatographed on a silica gel column (5 g, hexane - EtOAc = 4 : 1) to give **15** (110 mg, 97%). $[\alpha]_D^{25}$ -2.7° (*c* 0.75); IR (film): 1750 and 1500 cm^{-1}; ^{1}H NMR: δ 2.03 (3H, s), 3.54 (2H, br. d, J= 4 Hz), 4.25 - 4.75 (6H, complex), 6.21 (1H, d, J= 3 Hz), and 7.31 (10H, complex). Found: m/z 299.1285. Calcd for $C_{18}H_{19}O_4$: M-C_2H_3O, 299.1282.

1-O-Acetyl-β-D-erythrooxetanose (16). A solution of **15** (108 mg) in MeOH (2 ml) was stirred at room temperature in the presence of a catalytic amount of Pd-black under an atmosphere of hydrogen. After 5 h, the catalyst was filtered, and the filtrate was evaporated. The residue was chromatographed on a silica gel column (2 g, $CHCl_3$ - MeOH = 10 : 1) to yield **16** (50 mg, 97%). $[\alpha]_D^{28}$ +13.6° (*c* 0.44); IR (film): 3400 and 1740 cm^{-1}; ^1H NMR: δ 2.12 (3H, s), 3.70 - 3.85 (2H, complex), 4.43 (1H, m), 4.60 (1H, m), and 6.12 (1H, d, J= 3 Hz).

1-O-Acetyl-2-O-ethyl(dimethylmalonyl)-4-O-pivaloyl-β-D-erythrooxetanose (17a). A mixture of **16** (18 mg, 0.11 mmol), pivaloyl chloride (0.03 ml, 0.24 mmol) and pyridine (0.05 ml) in CH_2Cl_2 (1 ml) was kept at 8 °C for 20 h. The reaction mixture was diluted with H_2O, and extracted with EtOAc. The organic layer was successively washed with 1M HCl, H_2O, and sat. aq. $NaHCO_3$, then dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography (5 g, hexane - EtOAc = 4 : 1) to give 1-O-acetyl-4-O-pivaloyl-β-D-erythrooxetanose (16 mg, 58%). $[\alpha]_D^{27}$ -1.4° (*c* 0.34); IR (film): 3450 and 1730 cm^{-1}; ^1H NMR: δ 1.23 (9H, s), 2.09 (3H, s), 2.95 (1H, m), 4.20 - 4.30 (2H, complex), 4.40 - 4.45 (2H, complex), and 6.12 (1H, d, J= 3 Hz).

The 4-O-pivaloyl derivative (7.2 mg, 0.03 mmol) was treated with ethyldimethylmalonyl chloride (0.2 ml) and pyridine (0.2 ml) in CH_2Cl_2 (1 ml) at room temperature for 18 h. The reaction mixture was treated with the same procedure as described above to yield **17a** (8.3 mg, 73%). $[\alpha]_D^{24}$ -20.4° (*c* 0.51); IR (film): 1735 cm^{-1}; ^1H NMR: δ 1.27 (9H, s, overlapped with 3H, t, J= 7 Hz), 1.47 (6H, s), 2.13 (3H, s), 4.19 (2H, q, J= 7 Hz), 4.28 (1H, m), 4.35 (1H, m), 4.51 (1H, m), 5.19 (1H, dd, J= 3, 4.5 Hz), and 6.30 (1H, d, J= 3 Hz). Found: m/z 329.1570. Calcd for $C_{16}H_{25}O_7$: M-$C_2H_3O_2$, 329.1598.

Reaction of 17a with the Silylated Adenine. A mixture of **17a** (39 mg, 0.10 mmol) and powdered Molecular Sieves 4A (50 mg) in 1,2-dichloroethane (3 ml) was stirred at room temperature for 1 h under Ar. To this ice-cooled mixture was added bistrimethylsilyl N-benzoyladenine (130 mg, 0.34 mmol) and $SnCl_4$ (0.08 ml, 0.68 mmol). After 40 min, the reaction was quenched by addition of sat. aq. $NaHCO_3$, and then filtered. The filtrate was concentrated *in vacuo* to give a residue which on purification by preparative TLC (hexane - EtOAc = 1 : 4) afforded a white solid (**18a** + **19a**, 41 mg, 71%). The crude product was dissolved in 0.05M NaOMe / MeOH (3 ml), and the mixture was stirred at room temperature for 15 h, and then evaporated. The residue was treated with benzoyl chloride (1.5 ml) and pyridine (1.5 ml) at room temperature for 20 h. The reaction was worked up in the usual manner and the crude product was repeatedly separated by column

chromatography (benzene and $CHCl_3$ - MeOH = 4 : 1) and preparative TLC (benzene - EtOAc = 4 : 1) to give **18b** (35 mg, 75%) and **19b** (8.2 mg, 17%). **18b**: $[\alpha]_D^{27}$ -2.49° (*c* 0.52); IR (film): 1725, 1700, 1600, 1580, and 1490 cm^{-1}; ^1H NMR: δ 4.55 (1H, dd, J= 2.4, 11.2 Hz), 4.57 (1H, dd, J= 4.9, 11.2 Hz), 5.77 (1H, m), 6.26 (1H, br. s), 6.47 (1H, d, J= 1.5 Hz), 7.33 - 7.37 (4H, complex), 7.45 - 7.52 (5H, complex), 7.59 - 7.67 (3H, complex), 7.84 - 7.88 (4H, complex), 8.08 - 8.12 (4H, complex), 8.40 (1H, s), and 8.62 (1H, s). **19b**: $[\alpha]_D^{22}$ +304.9° (*c* 0.40); IR (film): 1720, 1700, 1600, 1585, and 1490 cm^{-1}; ^1H NMR: δ 4.02 (1H, dd, J= 3.4, 11.2 Hz), 4.12 (1H, dd, J= 1.5, 11.2 Hz), 4.80 (1H, d, J= 4.4 Hz), 5.48 (1H, br. d, J= 3 Hz), 6.34 (1H, s), 6.41 (1H, d, J= 4.9 Hz), 7.44 - 7.78 (12H, complex), 7.94 - 7.97 (2H, complex), 8.01 - 8.06 (3H, complex), 8.09 - 8.13 (3H, complex), and 8.71 (1H, s).

Reaction of 1,2-Di-O-acetyl-4-O-pivaloyl-β-D-erythrooxetanose (17b) with the Silylated Adenine. 1-O-Acetyl-4-O-pivaloyl-β-D-erythrooxetanose (5.5 mg) which was the synthetic intermediate of **17a**, was dissolved in CH_2Cl_2 (1 ml). To this solution was added Ac_2O (0.2 ml) and pyridine (0.2 ml), and the reaction mixture was kept at 8 °C for 18 h, then worked up by the same procedure as the case of **17a**. The crude product was purified on a silica gel column (2 g, hexane - EtOAc = 5 : 1) to give **17b** (5.9 mg, 91%) as an oil. IR (film): 1745 cm^{-1}; ^1H NMR: δ 1.27 (9H, s), 2.13 (6H, br.s), 4.22 (1H, dd, J= 3.5, 11.5 Hz), 4.42 (1H, dd, J= 2.5, 11.5 Hz), 4.54 (1H, m), 5.20 (1H, dd, J= 3.5, 4 Hz), and 6.35 (1H, d, J= 3.5 Hz).

To a mixture of **17b** (5.8 mg, 0.02 mmol) and powdered Molecular Sieves 4A (50 mg) in 1,2-dichloroethane (1 ml) was added bistrimethylsilyl N-benzoyladenine (44 mg, 0.12 mmol) and $SnCl_4$ (0.04 ml, 0.34 mmol). The reaction mixture was stirred at 0 °C for 40 min, and worked up by the same procedure as the case of **17a**. The crude product was separated by preparative TLC ($CHCl_3$ - MeOH = 20 : 1) to yield **18c** (3.1 mg, 33%) and **19c** (2.0 mg, 21%). **18c**: $[\alpha]_D^{27}$ -10.7° (*c* 0.1); IR (film): 1740, 1605, and 1580 cm^{-1}; ^1H NMR: δ 1.13 (9H, s), 2.20 (3H, s), 4.28 (1H, dd, J= 2, 11 Hz), 4.49 (1H, dd, J= 4, 11 Hz), 5.37 (1H, m), 5.80 (1H, m), 6.27 (1H, d, J= 2 Hz), 7.52 - 7.60 (3H, complex), 8.01 - 8.27 (2H, complex), 8.31 (1H, s), and 8.82 (1H, s). **19c**: $[\alpha]_D^{27}$ +38.7° (*c* 0.05); IR (film): 1740, 1610, and 1580 cm^{-1}; ^1H NMR: δ 1.29 (9H, s), 1.87 (3H, s), 4.00 (1H, dd, J= 2.5, 12 Hz), 4.72 (1H, dd, J= 6, 12 Hz), 5.45 - 5.60 (2H, complex), 6.61 (1H, d, J= 4.5 Hz), 7.50 - 7.68 (3H, complex), 8.16 - 8.42 (2H, complex), 8.21 (1H, s), and 8.88 (1H, s).

Small portions of **18c** and **19c** were treated with NaOMe / MeOH, followed by benzoyl chloride and pyridine by the same procedure as the syntheses of **18b** and **19b**, and formations of **18b** and **19b** were monitored by TLC.

3-O-Benzyl-1,2-O-isopropylidene-5-O-*p*-methoxybenzyl-α-D-ribofuranose (21). To an ice-cooled solution of 3-O-benzyl-1,2-O-isopropylidene-α-D-ribofuranose (**20**)[13] (17 g, 0.06 mol) in DMF (50 ml) was added NaH (5 g, 0.13 mol, 60% dispersion in mineral oil), and the mixture was stirred at room temperature for 20 h. After addition of *p*-methoxybenzyl chloride (12 ml, 0.09 mol), the reaction mixture was further stirred at room temperature for 13 h. The reaction was quenched and the mixture was purified in the usual manner to give **21** (21.7 g, 89%). $[\alpha]_D^{26}$ +76.7° (*c* 0.83); IR (film): 1610, 1585, and 1515 cm^{-1}; ^1H NMR: δ 1.34 (3H, s), 1.62 (3H, s), 3.61 (1H, dd, J= 4, 12 Hz), 3.68 (1H, m), 3.80 (3H, s), 3.86 (1H, m), 4.12 (1H, m), 4.40 - 4.65 (4H, complex), 4.72 (1H, d, J= 12 Hz), 5.77 (1H, d, J= 5 Hz), 6.85 (2H, d, J= 10 Hz), 7.22 (2H, d, J= 10 Hz), and 7.35 (5H, complex). Found: m/z 400.1900. Calcd for $C_{23}H_{28}O_6$: M, 400.1884.

3-O-Benzyl-5-O-*p*-methoxybenzyl-D-ribono-1→4-lactone (22). A solution of **21** (666 mg, 1.67 mmol) in 4M HCl (7.5 ml) - THF (15 ml) was kept at room temperature for 17 h. After neutralization with $NaHCO_3$, the mixture was partitioned between $CHCl_3$ and H_2O. The organic layer was washed with brine, dried over anhydrous Na_2SO_4, and evaporated. Preparative TLC purification (hexane - EtOAc = 1 : 1) of the residue afforded 3-O-benzyl-5-O-*p*-methoxybenzyl-D-ribofuranose (458 mg, 76%).

To an ice-cooled mixture of the diol (13.5 g, 0.38 mol), NaOAc (12 g, 0.15 mol) and AcOH (1 ml) in DMF (60 ml) was added, dropwise, bromine (12 ml, 0.13 mol) during 40 min, and then the resulting mixture was stirred at 0 °C for 9 h. After quenching with sat. aq. Na_2CO_3, the reaction mixture was partitioned between EtOAc and H_2O. The organic layer was washed with brine, dried over anhydrous Na_2SO_4, and evaporated. The crude product obtained was purified on a silica gel column (500 g, hexane - EtOAc = 2 : 1) to yield **22** (11.9 g, 89%). $[\alpha]_D^{24}$ +42.4° (*c* 2.97); IR (film): 3460, 1780, 1605, and 1500 cm^{-1}; ^1H NMR: δ 2.90 (1H, br. d, J= 9 Hz), 3.49 (1H, dd, J= 3, 10 Hz), 3.64 (1H, dd, J= 3, 10 Hz), 3.88 (3H, s), 4.07 - 4.24 (2H, complex), 4.38 (2H, br. s), 4.49 (1H, m), 4.68 (2H, s), 6.84 (2H, d, J= 9 Hz), and 7.32 (7H, complex). Found: m/z 313.1419. Calcd for $C_{19}H_{21}O_4$: M-CHO_2, 313.1438.

2,4-Anhydro-3-O-benzyl-5-O-*p*-methoxybenzyl-D-ribonic Acid Methyl Ester (23). To a solution of **22** (10.9 g, 30.4 mmol) in CH_2Cl_2 (200 ml) was added successively $(CF_3SO_2)_2O$ (15.5 ml, 92 mmol) and pyridine (5.2 ml, 64 mmol) at -60 °C, and the mixture was stirred at -40 °C for 5 h. The reaction mixture was diluted with H_2O and extracted with CH_2Cl_2. The organic layer was washed with brine, dried over anhydrous Na_2SO_4, and evaporated. The residue was dissolved in MeOH (50 ml) and then K_2CO_3 (4.2 g, 30 mmol) was added. After 15 min, the reaction mixture was partitioned between

$CHCl_3$ and H_2O. The organic layer was washed with brine, dried over anhydrous Na_2SO_4, and evaporated to dryness. The residue was chromatographed on a silica gel column (350 g, hexane - EtOAc = 3 : 1) to give **23** (4.37 g, 39%). IR (film): 1769, 1605, and 1500 cm^{-1}; ^1H NMR: δ 3.54 (2H, d, J= 5 Hz), 3.77 (3H, s), 3.88 (3H, s), 4.41 - 4.65 ((5H, complex), 4.74 (1H, m), 5.00 (1H, d, J= 5 Hz), 6.83 (2H, d, J= 9 Hz), and 7.33 (7H, complex).

2,4-Anhydro-3-O-benzyl-D-ribonic Acid Methyl Ester (24). A mixture of **23** (2.33 g, 6.3 mmol) and DDQ (1.5 g, 6.3 mmol) in CH_2Cl_2 (20 ml) containing H_2O (1 ml) was stirred at room temperature for 24 h. The reaction mixture was filtered, and the filtrate was concentrated *in vacuo*. The residue was repeatedly purified by silica gel column chromatography (gradient elution from benzene to EtOAc, hexane - EtOAc = 1 : 1, and hexane - EtOAc = 2 : 1) to give **24** (1.14 g, 72%). IR (film): 3500, 1740, and 1500 cm^{-1}; ^1H NMR: δ 3.44 (1H, dd, J= 2.5, 13 Hz), 3.70 (3H, s), 3.71 (1H, dd, J= 3, 13 Hz), 4.46 (1H, d, J= 12 Hz), 4.60 (1H, m), 4.64 (1H, d, J= 12 Hz), 4.72 (1H, m), 5.03 (1H, d, J= 6 Hz), and 7.45 (5H, complex). Found: m/z 235.0943. Calcd for $C_{13}H_{15}O_4$: M-OH, 235.0986.

1-O-Acetyl-4-chloro-4-deoxy-β-D-erythrooxetanose. (25). To a stirred solution of **24** (191 mg, 0.76 mmol) in dioxane (5 ml) was added $LiOH{\cdot}H_2O$ (80 mg, 1.63 mmol). After 20 min at room temperature, the reaction mixture was partitioned between EtOAc and H_2O. The aqueous layer was acidified with conc. HCl until pH 4, and extracted with EtOAc, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was dissolved in THF (2 ml). To the stirred solution cooled at -70 °C was added 1.08M MeLi (5 ml, 5.4 mmol), and stirring was continued at the same temperature for 1 h, and then at 0 °C for 0.5 h. The reaction mixture was partitioned between EtOAc and H_2O, and the organic layer was washed with brine, dried over anhydrous Na_2SO_4, then evaporated. The residue was purified by preparative TLC (hexane - EtOAc = 1 : 2) to give 85 mg (47%) of 3,5-anhydro-4-O-benzyl-1-deoxy-2-oxo-D-ribohexitol. IR (film): 3470, 1715, and 1500 cm^{-1}; ^1H NMR: δ 2.58 (3H, s), 3.37 (1H, dd, J= 2, 13 Hz), 3.75 (1H, dd, J= 2, 13 Hz), 4.40 - 4.80 (4H, complex), 4.98 (1H, d, J= 5 Hz), and 7.34 (5H, complex).

A mixture of the methyl ketone (471 mg, 2.0 mmol) and Ph_3P (1.10 g, 4.2 mmol) in THF (5 ml) - CCl_4 (2 ml) was refluxed for 1 h. The reaction mixture was evaporated and purified by preparative TLC (hexane - EtOAc = 3 : 1) to provide 3,5-anhydro-4-O-benzyl-6-chloro-1,6-dideoxy-2-oxo-D-ribohexitol (437 mg, 86%). IR (film): 1715 and 1500 cm^{-1}; ^1H NMR: δ 2.24 (3H, s), 3.40 (1H, dd, J= 5, 12 Hz), 3.57 (1H, dd, J= 6, 12 Hz), 4.31

(1H, t, J= 5 Hz), 4.49 (1H, d, J= 12 Hz), 4.68 (1H, d, J= 12 Hz), 4.77 (1H, m), 4.86 (1H, d, J= 5 Hz), and 7.34 (5H, complex).

The chloride (17 mg, 0.07 mmol) was oxidized with mCPBA (45 mg, 0.21 mmol) in CH_2Cl_2 (1 ml) as described in the case of **15** to yield 1-O-acetyl-2-O-benzyl-4-chloro-4-deoxy-β-D-erythrooxetanose (17 mg, 94%).

A solution of the acetate (16 mg) in MeOH (1.5 ml) was stirred at room temperature in the presence of Pd-black under an atmosphere of hydrogen. After 3 h, the catalyst was filtered, and the filtrate was evaporated to dryness. The residue was chromatographed on a silica gel column (1 g, hexane - EtOAc = 2 : 1) to give **25** (11 mg, 97%). $[\alpha]_D^{25}$ -42.5° (*c* 3.35); IR (film): 3450 and 1745 cm^{-1}; ^1H NMR: δ 2.14 (3H, s), 2.50 (1H, br.s), 3.73 (2H, br.d, J= 5 Hz), 4.40 - 4.55 (2H, complex), and 6.15 (1H, d, J= 3 Hz). Found: m/z 121.0053. Calcd for $C_4H_6O_2Cl$: M-$C_2H_3O_2$, 121.0055.

1-O-Acetyl-4-chloro-4-deoxy-2-O-ethyl(dimethylmalonyl)-β-D-erythro-oxetanose (26). To a solution of **25** (36 mg, 0.2 mmol) in CH_2Cl_2 (1 ml) was added, successively, pyridine (0.5 ml) and ethyldimethylmalonyl chloride (0.3 ml), and the mixture was kept at room temperature for 2 days, and then partitioned between EtOAc and H_2O. The EtOAc layer was washed with 1M HCl, H_2O, sat. aq. $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4, then evaporated to dryness. The residue was purified on a silica gel column (2 g, hexane - EtOAc = 4 : 1) to give **26** (61 mg, 94%). IR (film): 1720 cm^{-1}; ^1H NMR: δ 1.27 (3H, t, J= 7 Hz), 1.46 (6H, s), 2.16 (3H, s), 3.81 (2H, br. d, J= 6 Hz), 4.21 (2H, q, J= 7 Hz), 4.53 (1H, q, J= 5 Hz), 5.17 (1H, dd, J= 3, 5 Hz), and 6.32 (1H, d, J= 3 Hz). Found: m/z 263.0674. Calcd for $C_{11}H_{16}O_5Cl$: M-$C_2H_3O_2$, 263.0684.

Reaction of 26 with Allyltrimethylsilane. A mixture of **26** (44 mg, 0.14 mmol) and Molecular Sieves 4A (50 mg) in 1,2-dichloroethane (2 ml) was stirred under Ar at room temperature for 1 h. To the stirred mixture was added allyltrimethylsilane (0.2 ml, 1.23 mmol) and $SnCl_4$ ((0.03 ml, 0.26 mmol). After 15 min, the reaction was quenched with sat. aq. $NaHCO_3$ and filtered. The filtrate was evaporated and the residue was partially separated by preparative TLC (hexane - EtOAc = 1 : 1) to give an oil (28 mg). The oil was treated with 0.05M NaOMe / MeOH (2 ml) for 3 h. The mixture was evaporated and the residue was benzoylated as described in the syntheses of **18b** and **19b** to give **27** (19 mg, 29%), **28** (6.8 mg, 14%) and **29** (5 mg, 11%). **27**: IR (film): 1720, 1640, 1600, 1580, and 1495 cm^{-1}; ^1H NMR: δ 2.58 (2H, complex), 3.32 (3H, s), 3.67 (1H, dd, J= 5.8, 11.2 Hz), 3.81 (1H, dd, J= 3.9, 11.2 Hz), 5.07 (1H, dd, J= 1.4, 10.2 Hz), 5.12 (1H, dd, J= 1.4, 17 Hz), 5.60 (1H, m), 5.65 (1H, m), 5.83 (2H, complex), 7.34 - 7.41 (3H, complex), 7.42 - 7.62 (6H, complex), 7.93 - 8.02 (3H, complex), and 8.03 - 8.10 (3H,

complex). Found: m/z 368.1271. Calcd for $C_{21}H_{20}O_6$: M-Bz-Me, 368.1259. **28**: IR (film): 1720, 1640, 1600, 1580, and 1495 cm^{-1}; ^1H NMR: δ 2.61 (2H, complex), 3.29 (1H, dd, J= 2, 5.4 Hz), 3.33 (1H, ddd, J= 2, 3.4, 5.9 Hz), 4.26 (1H, dd, J= 5.9, 12.2 Hz), 4.60 (1H, dd, J= 3.4, 12.2 Hz), 5.10 - 5.14 (2H, complex), 5.19 (1H, dd, J= 1.5, 17 Hz), 5.85 (1H, m), 7.43 - 7.47 (4H, complex), 7.56 - 7.60 (2H, complex), and 8.03 - 8.07 (4H, complex).

Conversion of 28 into 27 and 29. A solution of **28** (2 mg) in 0.05M NaOMe / MeOH (1 ml) was kept at room temperature for 3 h. The reaction mixture was evaporated and benzoylated to give a crude product, which on repeated chromatographic purification (gradient elution from benzene to EtOAc and hexane - EtOAc = 3 : 1) yielded **27** (0.5 mg, 22%) and **29** (1.5 mg, 50%).

3-(2,3-Di-O-benzoyl-α- and β-D-erythrofuranosyl)-1-propene (29, 31). 1,2,3-Tri-O-acetyl-D-erythrofuranose (**30**, 206 mg, 0.84 mmol) was subjected to the same reaction as described in the case of **26** to give an anomeric mixture of the corresponding C-glycosides (109 mg, 57%). The product (79 mg) was successively deacylated, followed by benzoylation as described in the syntheses of **18b** and **19b** to give **29** (11 mg, 9.4%) and **31** (65 mg, 53%). **29**: $[\alpha]_D^{25}$ -83.7° (*c* 0.57); IR (film); 1735, 1645, 1600, 1585, and 1495 cm^{-1}; ^1H NMR: δ 2.47 (1H, m), 2.56 (1H, m), 4.02 (1H, dd, J= 4.4, 10.3 Hz), 4.27 (1H, q, J= 5 Hz), 4.45 (1H, dd, J= 5.9, 10.3 Hz), 5.15 (1H, dd, J= 1, 10.3 Hz), 5.21 (1H, dd, J= 1, 17 Hz), 5.32 (1H, t, J= 5 Hz), 5.66 (1H, q, J= 5 Hz), 5.90 (1H, m), 7.30 - 7.47 (4H, complex), 7.51 - 7.56 (2H, complex), and 7.91 - 8.05 (4H, complex). Found: m/z 311.0917. Calcd for $C_{18}H_{15}O_5$: M-C_3H_5, 311.0918. **31**: $[\alpha]_D^{27}$ -18.3° (*c* 3.2); IR (film): 1725, 1645, 1600, 1585, and 1500 cm^{-1}; ^1H NMR: δ 2.48 - 2.63 (2H, complex), 4.09 (1H, dd, J= 5.4, 10 Hz), 4.22 (1H, m), 4.27 (1H, dd, J= 6.6, 10 Hz), 5.09 (1H, ddd, J= 1.5, 3.2, 10.5 Hz), 5.13 (1H, ddd, J= 1.5, 3.2, 10.5 Hz), 5.72 (1H, q, J= 5.4 Hz), 5.79 (1H, dd, J= 4.4, 5 Hz), 5.85 (1H, m), 7.28 (2H, complex), 7.41 (2H, complex), 7.48 (1H, m), 7.56 (1H, m), 7.85 (2H, complex), and 8.04 (2H, complex). Found: m/z 352.1317. Calcd for $C_{21}H_{20}O_5$: M, 352.1310.

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