A straightforward synthesis of DAH (3-deoxy-D-*arabino*-hept-2-ulosonic acid) and DRH (3-deoxy-D-*ribo*-hept-2-ulosonic acid)

Ke-Gang Liu, Shou-Gang Hu, Yikang Wu, Zhu-Jun Yao and Yu-Lin Wu*

State Key Laboratory of Bio-organic and Natural Products Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Road, Shanghai, 200032, China. E-mail: ylwu@pub.sioc.ac.cn

Received (in Cambridge, UK) 24th May 2002, Accepted 21st June 2002
First published as an Advance Article on the web 19th July 2002

Based on the oxidation of corresponding terminal alkynes to α-keto esters, DAH (3-deoxy-D-*arabino*-hept-2-ulosonic acid) in its pyranose form and DRH (3-deoxy-D-*ribo*-hept-2-ulosonic acid) in its protected pyranose–furanose mixture form were efficiently synthesized. These terminal alkynes were in turn obtained by C_1- or C_3-homologation of corresponding protected sugars, respectively. Along with the application of this strategy, the syntheses of two C_6-ulosonic acids, 3-deoxy-D-*erythro*-hex-2-ulosonic acid and 3-deoxy-L-*erythro*-hex-2-ulosonic acid in their protected pyranose form, were also described.

Introduction

3-Deoxy-2-ulosonic acids are a family of naturally occurring carbohydrates, among which 3-deoxy-D-*arabino*-hept-2-ulosonic acid (DAH, **1**), 3-deoxy-D-*manno*-oct-2-ulosonic acid (KDO, **2**), 3-deoxy-D-*glycero*-D-*galacto*-non-2-ulosonic acid (KDN, **3**) and 5-acetamido-3,5-dideoxy-D-*glycero*-D-*galacto*-non-2-ulosonic acid (*N*-acetylneuraminic acid or sialic acid **4**) are the most common members (Fig. 1). These carbohydrates

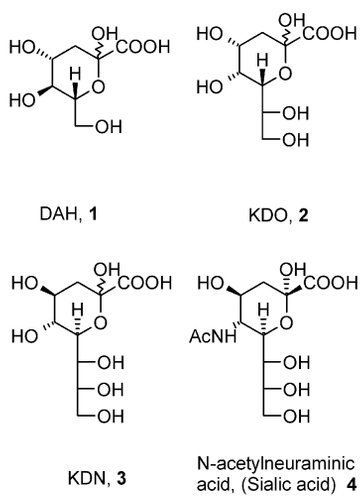


Fig. 1

are involved in many biologically important processes and recently have attracted considerable attention from both chemists and biologists. The seven-carbon-atom analogue of this family, 3-deoxy-D-*arabino*-hept-2-ulosonic acid (DAH),[1] is formed in plants by stereoselective condensation of phosphoenolpyruvate with D-erythrose 4-phosphate mediated by 3-deoxy-D-arabino-hept-2-ulopyranosonate 7-phosphate (DAHP) synthase [EC 4.1.2.15] and it has been shown[2] that DAH is a key intermediate in the biosynthesis of aromatic amino acids from glucose (shikimate pathway). Therefore, a number of publications have appeared devoted to finding an efficient synthesis of DAH and its derivatives or analogues.[3]

In most cases[3a–i,3m–p] carbohydrates are utilized as the chiral starting material for the synthesis of DAH, except for a few asymmetric or racemic syntheses.[3j,k] Along with our interesting in the general synthetic methodology of 3-deoxy-2-ulosonic acids, we have reported the synthesis[3l] of 2-deoxy-DAH and 2-deoxy-DRH based on the salen-Co(II)-catalyzed asymmetric hetero-Diels–Alder reaction.[4] Recently we developed an efficient method for synthesis of α-keto acid esters from terminal alkynes and also successfully applied this method to the synthesis of KDO and 4-*epi*-KDN.[5] Herein we report another successful application of this method, to the synthesis of DAH (**1**), DRH (**5**), 3-deoxy-D-*erythro*-hex-2-ulosonic acid (**6**) and 3-deoxy-L-*erythro*-hex-2-ulosonic acid (**7**) (Fig. 2).

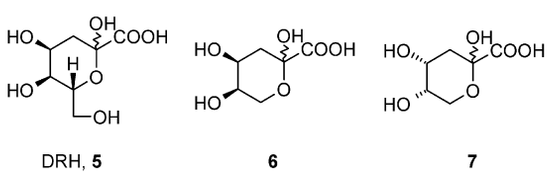


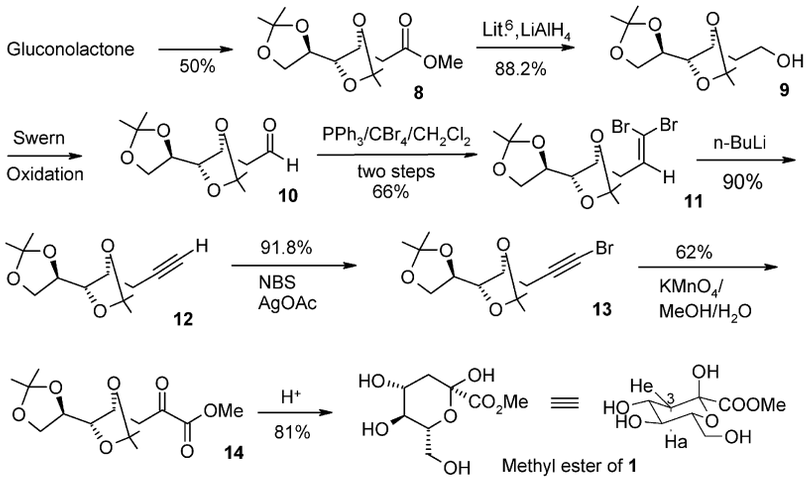
Fig. 2

Results and discussion

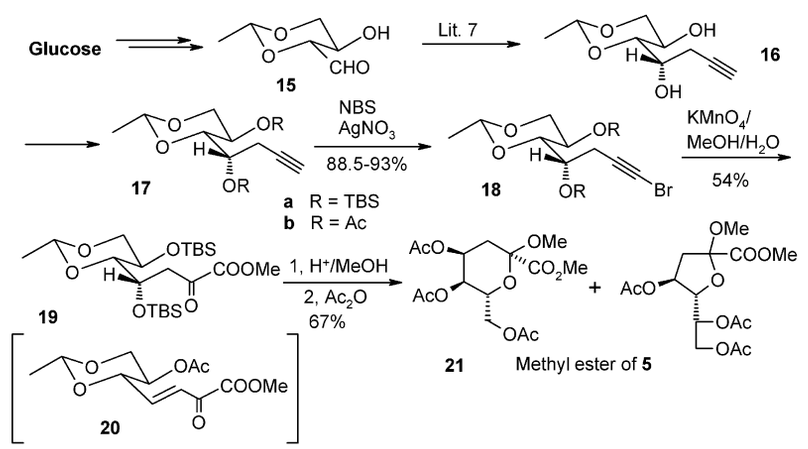
Synthesis of DAH (3-Deoxy-D-*arabino*-hept-2-ulosonic acid, 1)

Starting from D-glucono-δ-lactone, methyl 2-deoxy-D-gluconate bisacetonide **8** was prepared according to the literature method.[6] Reduction of the ester **8** and subsequent re-oxidation of the obtained alcohol **9** with Swern's reagents gave the aldehyde **10**. Treatment of **10** with PPh_3 and CBr_4 and debromination of **11** with 2 M *n*-BuLi at 0 °C afforded the seven-carbon terminal alkyne **12** in 48% yield for these four steps. According to our protocol[5] compound **12** was first converted to the corresponding bromoalkyne **13** (91.8%) by stirring it with *N*-bromosuccinimide and silver acetate at room temperature, and subsequent oxidation of the bromoalkyne with $KMnO_4$ in aqueous methanol afforded the key intermediate α-keto methyl ester (**14**) in 62% yield. The linear compound **14** was treated with 40% aqueous HF at room temperature for 2 h to give the methyl ester of target compound **1** (DAH). All the physical data, except the sign of optical rotation, were in accordance with those reported in the literature[3c] for L-DAH methyl ester. The chemical shifts and coupling constants of C3–H^aH^e, 2.14 (dd, J = 12.9, 5.0 Hz, H^e) and 1.81 (dd, J = 12.9, 11.7 Hz, H^a),

 DOI: 10.1039/b205047a



Scheme 1



Scheme 2

showed that the obtained DAH ester was almost exclusively in its pyranose form. Thus, the methyl ester of DAH was simply synthesized from easily available gluconolactone using a [6 + 1] strategy and oxidation of a terminal alkyne as the key step in an unoptimized 11% overall yield (Scheme 1).

Synthesis of DRH (3-deoxy-D-*ribo*-hept-2-ulosonic acid, 5)

DRH is the C^4-epimer of DAH (**1**) and shows an *erythro* configuration of the hydroxy groups at C3 and C4. Therefore, the [4 + 3] strategy with diastereoselective propargylation and oxidation of a terminal alkyne as the key steps now could be applied in its synthesis. Thus, aldehyde **15**, easily obtained from D-glucose, was treated with propargyl (prop-2-ynyl) bromide and zinc dust in a solvent mixture of DMF and diethyl ether as reported before.[7] It was a little unsatisfactory that the *erythro*/*threo* selectivity was only 2.5–3.5 when aldehyde **15** was taken as the substrate. Both hydroxy groups of the *erythro* compound **16** were protected with *tert*-butyldimethylsilyl (TBS) groups to give the desired protected alkyne **17a** in 90% yield. Bromination of **17a** and subsequence oxidation of alkyne **18a** with $KMnO_4$ in aqueous methanol gave the α-keto ester **19** in 42% yield. For these conversions we also used an acetyl group to protect both hydroxy groups, but unfortunately an α,β-unsaturated keto ester **20** was obtained from the last oxidation reaction in this case. Treatment of **19** with TsOH–MeOH removed all the protecting groups from the hydroxy groups (two silyl ethers and an acetal), and then reprotection of these free hydroxy groups by acetylation gave the methyl ester triacetate **21** of DRH. ^1H NMR showed that the cyclized product was a mixture of pyranose and furanose forms in a ratio of about 45 : 55 (Scheme 2).

Synthesis of 3-deoxy-D-*erythro*-hex-2-ulosonic acid (6) and 3-deoxy-L-*erythro*-hex-2-ulosonic acid (7)

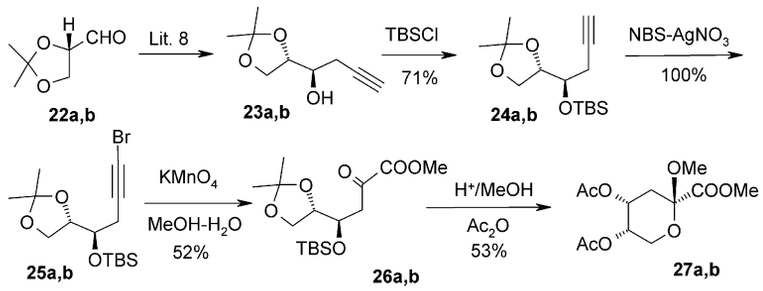
For the further exploration of this propargylation–oxidation protocol a pair of six-carbon ulosonic acids, 3-deoxy-D-*erythro*-hex-2-ulosonic acid (**6**) and 3-deoxy-L-*erythro*-hex-2-ulosonic acid (**7**), were also synthesized. Starting from both protected glyceraldehydes (**22a**,**b**), diastereoselective propargylation and then protection of the hydroxy group gave the terminal alkyne **24a**,**b**. Bromination and oxidation with potassium permanganate smoothly yielded the α-keto ester **26a**,**b**. Removal of protecting groups with hydrochloric acid in methanol and then acetylation afforded the fully protected target molecules **6** and **7** in their pyranose form (Scheme 3).

In summary, DAH, DRH and a pair of six-carbon ulosonic acids were synthesized with the bromination and oxidation of a terminal alkyne as the key step. These syntheses showed that this protocol was convenient and effective. Its further application will be reported in due course.

Experimental

General methods

IR spectra were recorded on Bio-Rad FTS-185 spectrometers. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ or CD_3OD on a Mercury-300 or Gemini-2000 spectrometer with TMS as internal standard. Mass spectra were taken on a HP5973N or HP5989A instrument. HRMS (EI and ESI) spectra were obtained on an APEXIII 7.0 Tesla FTMS mass spectrometer. Optical rotations were measured on a Perkin-Elmer 241 MC polarimeter; $[\alpha]_D$-values are given in units of 10^{-1} deg cm^2 g^{-1}.



Scheme 3

Elemental analyses were carried out at the Microanalytic Laboratory of Shanghai Institute of Organic Chemistry. Flash column chromatography was performed on silica gel H (10–40 μm). Petroleum ether refers to the fraction with distillation range 60–90 °C.

2-Deoxy-3,4:5,6-di-*O*-isopropylidene-D-*arabino*-hexose (10). Dimethyl sulfoxide (1.2 mL, 15 mmol) was added dropwise to a solution of oxalyl dichloride (0.71 mL, 7.5 mmol) in anhydrous dichloromethane (20 mL) at −78 °C under nitrogen. The mixture was stirred for 30 min and then a solution of the alcohol **9** (1.23 g, 5 mmol) in anhydrous dichloromethane (10 mL) was added. The mixture was stirred for 2 h at −78 °C and then triethylamine (2.1 mL) was added. The mixture was stirred for a further 10 min at −78 °C, and then raised to room temperature over a 1 h period. Water (2 mL) was added and the mixture was extracted with diethyl ether (100 mL × 3). The combined extracts were washed with brine (20 mL × 2), dried over Na_2SO_4 and evaporated under reduced pressure to afford crude aldehyde **10** (1.20 g).

1,1-Dibromo-1,2,3-trideoxy-4,5:6,7-di-*O*-isopropylidene-D-*arabino*-hept-1-enitol (11). To a solution of PPh_3 (5.0 g, 9.9 mmol) in CH_2Cl_2 (13 mL) was added a solution of CBr_4 (3.29 g, 9.96 mmol) in CH_2Cl_2 (13 mL) at 0 °C. After the reaction mixture had been stirred for 10 min a solution of the crude aldehyde **10** (5 mmol) in CH_2Cl_2 (8 mL) was added and then stirring was continued for 3 h at room temperature. The reaction mixture was quenched by addition of saturated aqueous $NaHCO_3$ and was extracted with Et_2O (50 mL × 3). The combined extracts were washed successively with water and brine, dried over Na_2SO_4 and concentrated to give a solid, which was washed with Et_2O several times and the filtrate was concentrated to leave an oil, which was chromatographed with hexane–Et_2O (20 : 1) as eluent to give compound **11** (1.32 g, two steps in 66% yield) as a pale yellow oil, IR (film) 2988, 2935, 2883, 1456, 1381, 1372, 1068 cm^{-1}; ^1H NMR (300 MHz; $CDCl_3$) 6.57 (t, J = 7.0 Hz, 1H, H-2), 4.14 (dd, J = 8.1, 5.9 Hz, 1H, H-7), 4.03 (m, 2H, H-4, H-6), 3.94 (dd, J = 8.1, 4.8 Hz, 1H, H-7), 3.55 (dd, J = 8.1, 7.7 Hz, 1H, H-5), 2.60 (ddd, J = 15.8, 7.0, 4.4 Hz, 1H, H-3), 2.42 (dt, J = 15.8, 7.0 Hz, 1H, H-3), 1.43 (s, 3H, CH_3), 1.36 (s, 3H, CH_3), 1.40 (s, 3H, CH_3), 1.34 (s, 3H, CH_3); CI-MS (*m*/*z*, %) 399 (M^+ + 1, 1), 398 (M^+, 1), 306 (100). This compound was used for the next step without further purification or characterization.

1,2,3-Trideoxy-4,5:6,7-di-*O*-isopropylidene-D-*arabino*-hept-1-ynitol (12). To a solution of **11** (1.1 g, 2.75 mmol) in dry THF (26 mL) was added *n*-BuLi (3.45 mL; 2 M) in an ice–brine bath, and the reaction mixture was stirred for 20 min. It was then quenched with saturated aqueous NH_4Cl and extracted with diethyl ether (50 mL × 2). The organic phases were washed successively with water and brine, dried over anhydrous sodium sulfate and then evaporated under reduced pressure to afford a crude product. The residue was purified by flash chromatography with hexane–Et_2O (15 : 1) as eluent to give alkyne **12** (0.594 g, 90%) as a pale yellow oil, $[\alpha]_D^{20}$ +24.0 (*c* 0.25, $CHCl_3$); IR (film) 2989, 2937, 2882, 2119, 1382, 1373, 1218, 1071 cm^{-1}; ^1H NMR (300 MHz; $CDCl_3$) 4.13 (dd, J = 7.7, 5.9 Hz, 1H, H-7), 4.05 (m, 2H, H-4, H-6), 3.98 (dd, J = 8.1, 4.4 Hz, 1H, H-7), 3.77 (t, J = 7.7 Hz, 1H, H-5), 2.75 (dt, J = 17.4, 3.6 Hz, 1H, H-3), 2.53 (ddd, J = 17.4, 6.3, 3.0 Hz, 1H, H-3), 2.05 (t, J = 2.6 Hz, 1H, H-1), 1.41 (s, 3H, CH_3), 1.39 (s, 3H, CH_3), 1.36 (s, 3H, CH_3), 1.34 (s, 3H, CH_3). EI-MS (*m*/*z*, %) 225 (M^+ − Me, 76.21), 185 (34.36), 81 (31.48), 59 (50.35), 43 (100). Calc. for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39. Found: C, 64.69; H, 8.23%.

1-Bromo-1,2,3-trideoxy-4,5:6,7-di-*O*-isopropylidene-D-*arabino*-hept-1-ynitol (13). To a solution of **12** (0.514 g, 2.14 mmol) in acetone (12 mL) were added NBS (0.533 g, 3.0 mmol) and silver acetate (143 mg, 0.856 mmol). The mixture was stirred for 4 h in darkness at room temperature. The salts were removed by filtration through a Celite pad and were washed with diethyl ether. The combined organic layers were washed successively with water and brine, dried over Na_2SO_4, concentrated *in vacuo* and chromatographed (hexane–diethyl ether, 15 : 1) to afford bromide **13** (0.627 g, 91.8%) as a yellowish solid, mp 41–42 °C; $[\alpha]_D^{20}$ +23.0 (*c* 0.8, $CHCl_3$); IR (KBr) 2989, 2940, 2873, 2238, 1382, 1218, 1071 cm^{-1}; ^1H NMR (300 MHz; $CDCl_3$) 4.14 (dd, J = 5.4, 2.4 Hz, 1H, H-7), 4.03 (m, 3H, H-4, H-6, H-7), 3.75 (t, J = 7.5, 1H, H-5), 2.80 (dd, J = 16.8, 4.8 Hz, 1H, H-3), 2.55 (dd, J = 16.8, 5.1 Hz, 1H, H-3), 1.43 (s, 6H, 2 × CH_3), 1.39 (s, 3H, CH_3), 1.34 (s, 3H, CH_3); EI-MS (*m*/*z*, %) 319 (M^+, 20.74), 149 (5.82), 109 (22.70), 91 (15.49), 59 (25.77), 43 (100). Calc. for $C_{13}H_{19}O_4Br$: C, 48.92; H, 6.00. Found: C, 49.09; H, 6.08%.

Methyl 3-deoxy-4,5:6,7-di-*O*-isopropylidene-D-*arabino*-hept-2-ulosonate (14). To a solution of **13** (0.57 g, 1.79 mmol) in MeOH (27 mL) was added a solution of $NaHCO_3$ (89.5 mg, 1.074 mmol) and $MgSO_4$ (0.420 g, 3.58 mmol) in water (27 mL) at 0 °C. After the reaction mixture had been stirred for 10 min, $KMnO_4$ (0.730 g, 4.48 mmol) was added in portions. The reaction mixture was stirred at 0 °C for 30 min and was then poured into ice–water. The solids were removed by filtration through a Celite pad and washed with ethyl acetate. The aqueous phase was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4, concentrated *in vacuo* and chromatographed (hexane–diethyl ether, 8 : 3) to afford *keto ester* **14** (0.335 g, 62%) as a pale oil, $[\alpha]_D^{20}$ +22.8 (*c* 1.4, $CHCl_3$); IR (KBr) 2989, 2938, 2891, 1750, 1734, 1437, 1382, 1373, 1068 cm^{-1}; ^1H NMR (300 MHz; $CDCl_3$) 4.44 (td, J = 7.7, 4.6 Hz, 1H, H-4), 4.15 (dd, J = 8.4, 5.9, 1H, H-7), 4.02 (dt, J = 8.4, 5.9 Hz, 1H, H-6), 3.93 (dd, J = 8.4, 5.9 Hz, 1H, H-7), 3.88 (s, 3H, OCH_3), 3.59 (dd, J = 8.4, 7.7, 1H, H-5), 3.26 (dd, J = 16.8, 4.60 Hz, 1H, H-3), 3.19 (dd, J = 16.8, 7.7 Hz, 1H, H-3), 1.39 (s, 3H, CH_3), 1.38 (s, 6H, 2 × CH_3), 1.32 (s, 3H, CH_3); EI-MS (*m*/*z*, %) 287 (M^+ − Me, 24.27), 143 (49.64), 101 (70.15), 59 (42.81), 43 (100); ^{13}C NMR (75 MHz; $CDCl_3$) 190.8, 160.9, 109.8, 109.7, 80.6, 76.6, 75.5, 67.8, 53.0, 42.8, 26.9, 26.8, 26.5, 25.1. Calc. for $C_{14}H_{22}O_7$: C, 55.62; H, 7.33. Found: C, 55.58; H, 7.14%.

DAH methyl ester (methyl 3-deoxy-D-*arabino*-hept-2-ulopyranosonate). To a solution of **14** (0.15 g, 0.5 mmol) in MeCN (20 mL) in a plastic bottle at room temperature was added aq. HF (40%; 4 mL). The reaction mixture was stirred for 2 h and was then neutralized by saturated aq. $NaHCO_3$. The solvent was removed *in vacuo*. The residue was chromatographed (dichloromethane–methanol, 4 : 1) to give the methyl ester of **1** (90 mg, 81%) as white solid, mp 108–110 °C; $[a]_D^{20}$ +47.5 (*c* 0.40, MeOH) (lit.,[3c] for L-DAH methyl ester $[a]_D$ −41.7 (*c* 0.86, MeOH)), $[a]_D^{20}$ +43.7 (*c* 0.48, H_2O) (lit.,[3d] for D-DAH ethyl ester $[a]_D^{26}$ +37.0 (*c* 0.62, H_2O)); IR (KBr) 3480, 3149, 2995, 2918, 1747, 1437, 1316, 1152, 1077 cm^{-1}; ^1H NMR (300 MHz; CD_3OD) 3.92–3.82 (m, 2H, H-5, H-7), 3.78–3.68 (m, 3H, H-4, H-6, H-7), 3.77 (s, 3H, OCH_3), 2.14 (dd, *J* = 12.9, 5.0 Hz, 1H, H-3e), 1.81 (dd, *J* = 12.9, 11.7 Hz, 1H, H-3a); ESI-MS 245 (M^+ + Na, 100).

1,2,3-Trideoxy-4,6-bis-*O*-(*tert*-butyldimethylsilyl)-5,7-*O*-ethylidene-D-*ribo*-hept-1-ynitol (17a). To a solution of **16**[7] (290 mg, 1.56 mmol) in DMF (5 mL) were added imidazole (648 mg, 9.59 mmol) and TBSCl (1.0 g, 6.63 mmol) and the reaction mixture was kept for 24 h at room temperature. The solution was diluted with diethyl ether (30 mL) and washed successively by water and brine. The organic layer was dried over anhydrous Na_2SO_4 and evaporated to dryness. The residue was chromatographed on silica gel, using petroleum ether–AcOEt (40 : 1) as eluent to yield compound **17a** (572 mg, 90%) as a clear liquid, $[a]_D^{20}$ −31.3 (*c* 0.86, $CHCl_3$); ^1H NMR (300 MHz; $CDCl_3$) 0.09 (s, 3H, $SiCH_3$), 0.12 (s, 3H, $SiCH_3$), 0.13 (s, 3H, $SiCH_3$), 0.15 (s, 3H, $SiCH_3$), 0.87, 0.90, 0.93 (s, 18H, 2 × $SiC(CH_3)_3$), 1.33 (d, *J* = 5.0 Hz, 3H, CH_3CH), 2.01 (t, *J* = 2.7 Hz, 1H, H-1), 2.45 (ddd, *J* = 2.8, 7.5, 16.8 Hz, 1H, H-3), 2.60 (ddd, *J* = 2.6, 6.9, 16.7 Hz, 1H, H-3), 3.34 (m, 1H), 3.55 (dd, *J* = 0.9, 8.8 Hz, 1H), 3.85 (m, 1H), 4.01 (m, 2H), 4.65 (q, *J* = 5.0 Hz, 1H, CH_3CH); IR (film) 3317, 2958, 2931, 2889, 2860, 1473, 1465, 1410 cm^{-1}; EIMS *m*/*z* (%) 415 (M^+ + H, 4.87), 414 (M^+, 4.89), 413 (M^+ − H, 7.33), 398 (7.27), 356 (15.93), 338 (23.82), 282 (38.51), 73 (100); HRMS (ESI) *m*/*z* Calc. for $C_{21}H_{42}O_4Si_2Na$ (M^+ + Na): 437.2514. Found: 437.2533.

1,2,3-Trideoxy-4,6-di-*O*-acetyl-5,7-*O*-ethylidene-D-*ribo*-hept-1-ynitol (17b). To a solution of **16** (351 mg, 1.89 mmol) in anhydrous CH_2Cl_2 (15 mL) were added pyridine (3.5 mL, 43.0 mmol), 4-(dimethylamino)pyridine (DMAP) (30 mg) and acetic anhydride (3.0 mL, 29.4 mmol) under nitrogen. The reaction mixture was stirred for 24 h at room temperature and then ethyl acetate (40 mL) and water (5 mL) were added. The separated organic phase was washed successively with water and brine, dried over anhydrous Na_2SO_4 and evaporated to dryness. Chromatography of the residue was carried out on silica gel, using petroleum ether–AcOEt (6 : 1) as eluent to yield compound **17b** (482 mg, 95%) as a clear liquid, $[a]_D^{20}$ −31.8 (*c* 1.0, CH_2Cl_2); ^1H NMR (300 MHz; $CDCl_3$) 1.31 (d, *J* = 5.2 Hz, 3H, CH_3CH), 1.98 (t, *J* = 2.7 Hz, 1H, H-1), 2.07 (s, 3H, acetyl), 2.10 (s, 3H, acetyl), 2.60 (dd, *J* = 6.5, 2.8 Hz, 2H, H_2-3), 3.38 (t, *J* = 10.3 Hz, 1H, H-7), 3.82 (dd, *J* = 3.2, 9.9 Hz, 1H, H-5), 4.21 (dd, *J* = 5.5, 10.5 Hz, 1H, H-7), 4.68 (q, *J* = 4.9 Hz, 1H, CH_3CH), 4.88 (ddd, *J* = 5.4, 9.9, 14.3 Hz, 1H, H-6), 5.10 (ddd, *J* = 3.3, 6.6, 9.9 Hz, 1H, H-4); IR (film) 3286, 2996, 2473, 1749, 1415 cm^{-1}; EIMS *m*/*z* (%) 271 (M^+ + H, 16.34), 270 (M^+, 4.89), 269 (M^+ − H, 18.37), 227 (16.34), 183 (10.57), 115 (28.00), 43 (100); HRMS *m*/*z* Calc. for $C_{13}H_{17}O_6$ (M^+ − H): 269.1020. Found: 269.1022.

1-Bromo-1,2,3-trideoxy-4,6-bis-*O*-(*tert*-butyldimethylsilyl)-5,7-*O*-ethylidene-D-*ribo*-hept-1-ynitol (18a). To a solution of **17a** (102 mg, 0.25 mmol) in acetone (12.5 mL) were added NBS (52.5 mg, 0.465 mmol) and silver nitrate (22.5 mg, 0.135 mmol). The mixture was stirred for 10 h in darkness at room temperature. The salts were removed by filtration through a Celite pad and washed with diethyl ether. The organic layer was washed successively with water and brine, dried over Na_2SO_4 and evaporated to dryness. Chromatography of the residue on silica gel, using petroleum ether–AcOEt (30 : 1) as eluent, yielded bromide **18a** (115 mg, 93%) as a clear liquid, $[a]_D^{20}$ −30.7 (*c* 1.01, CH_2Cl_2); ^1H NMR (300 MHz; $CDCl_3$) 0.08 (s, 3H, $SiCH_3$), 0.11 (s, 3H, $SiCH_3$), 0.13 (s, 3H, $SiCH_3$), 0.14 (s, 12H, 4 × $SiCH_3$), 0.88 (s, 9H, $SiC(CH_3)_3$), 0.93 (s, 9H, $SiC(CH_3)_3$), 1.32 (d, *J* = 5.1 Hz, 3H, CH_3CH), 2.55 (t, *J* = 7.3 Hz, 2H, H_2-3), 3.33 (m, 1H, H-4), 3.49 (dd, *J* = 1.2, 9.2 Hz, 1H, H-5), 3.80 (ddd, *J* = 5.5, 10.7, 14.5 Hz, 1H, H-6), 4.02 (m, 2H, H_2-7), 4.65 (q, *J* = 5.0 Hz, 1H, CH_3CH); IR (film) 2957, 2931, 2889, 2859, 1473, 1464, 1410 cm^{-1}; EIMS *m*/*z* (%) 435 (M^+ − C_4H_9, 2.47), 393 (2.65), 355 (3.81), 327 (3.35), 261 (5.29), 245 (12.10), 189 (7.45), 147 (20.21), 73 (100). This compound was used for the next step without further purification or characterization.

1-Bromo-1,2,3-trideoxy-4,6-di-*O*-acetyl-5,7-*O*-ethylidene-D-*ribo*-hept-1-ynitol (18b). Transformation of **17b** (135 mg, 0.5 mmol) according to the same preparation procedure for **18a** gave bromide **18b** (154 mg, 88.5%) as a clear liquid, $[a]_D^{20}$ −25.3 (*c* 0.25, CH_2Cl_2); ^1H NMR (300 MHz; $CDCl_3$) 1.35 (d, 3H, *J* = 4.8 Hz, CH_3CH), 2.10 (s, 3H, acetyl), 2.08 (s, 3H, acetyl), 2.65 (m, 2H, H_2-3), 3.60 (t, *J* = 10.3 Hz, 1H, H-7), 3.80 (dd, *J* = 3.3, 9.9 Hz, 1H, H-5), 4.20 (dd, *J* = 5.5, 10.7 Hz, 1H, H-7), 4.70 (q, *J* = 5.0 Hz, 1H, CH_3CH), 4.82 (ddd, *J* = 5.4, 9.8, 15.3 Hz, 1H, H-6), 5.10 (ddd, *J* = 3.3, 6.3, 9.6 Hz, 1H, H-4); IR (film) 2998, 2945, 1745, 1726 cm^{-1}; EIMS *m*/*z* (%) 349 (M^+ + H, 0.88), 348 (M^+, 0.13), 292 (2.53), 263 (2.95), 221 (8.31), 188 (14.59), 159 (12.24), 115 (66.65), 43 (100). This compound was used for the next step without further purification or characterization.

Methyl 3-deoxy-4,6-bis-*O*-(*tert*-butyldimethylsilyl)-5,7-*O*-ethylidene-D-*ribo*-hept-2-ulosonate (19). To a solution of **18a** (87 mg, 0.18 mmol) in MeOH (12 mL) was slowly added a solution of $NaHCO_3$ (13 mg, 0.15 mmol) and $MgSO_4$ (57 mg, 0.48 mmol) in water (7 mL) at 0 °C. After being stirred for 15 min, the reaction mixture was slowly treated with $KMnO_4$ (130 mg, 0.81 mmol) added in portions at 0 °C. The system was stirred for another 6 h at 0 °C and then poured into ice–water (30 mL). The solid was removed by filtration through a Celite pad and washed with ethyl acetate. The filtrate's aqueous phase was extracted with ethyl acetate. The combined organic layers were washed with brine and then dried over Na_2SO_4. Flash chromatography (petroleum ether–AcOEt, 30 : 1) gave *keto ester* **19** (45 mg, 54%) as a clear liquid, $[a]_D^{20}$ −28.7 (*c* 0.8, CH_2Cl_2); ^1H NMR (300 MHz; $CDCl_3$) 0.04 (s, 3H, $SiCH_3$), 0.06 (s, 3H, $SiCH_3$), 0.07 (s, 3H, $SiCH_3$), 0.12 (s, 3H, $SiCH_3$), 0.85 (s, 9H, $SiC(CH_3)_3$), 0.89 (s, 9H, $SiC(CH_3)_3$), 1.32 (d, *J* = 5.0 Hz, 3H, CH_3CH), 2.92 (dd, *J* = 3.8, 7.7 Hz, 1H, H-3), 3.32 (dd, *J* = 3.7, 9.3 Hz, 1H, H-3), 3.36 (m, 2H), 3.70 (m, 1H), 3.88 (s, 3H, OCH_3), 4.00 (dd, *J* = 5.2, 10.5 Hz, 1H, H-7), 4.52 (ddd, *J* = 1.2, 3.9, 5.0 Hz, 1H, H-5), 4.65 (q, *J* = 5.0 Hz, 1H, CH_3CH); ^{13}C NMR (75 MHz; $CDCl_3$) −5.12, −4.59, −4.28, −1.00, 17.77, 18.10, 20.41, 25.82 (×6), 42.91, 52.90, 62.48, 68.42, 71.51, 84.20, 98.66, 161.16, 192.43; IR (film) 2958, 2859, 1736, 1465, 1411, 1256 cm^{-1}; EIMS *m*/*z* (%) 476 (M^+, 1.03), 460 (16.10), 459 (17.02), 283 (16.34), 246 (17.02), 241 (39.77), 159 (100); HRMS (ESI) *m*/*z* Calc. for $C_{22}H_{44}O_7Si_2Na$ (M^+ + Na): 499.2518. Found: 499.2537.

Methyl 3,4-dideoxy-6-*O*-acetyl-5,7-*O*-ethylidene-D-*erythro*-hept-3-en-2-ulosonate (20). To a solution of **18b** (144 mg, 0.414 mmol) in MeOH (15 mL) was slowly added a solution of $NaHCO_3$ (22 mg, 0.26 mmol) and $MgSO_4$ (107 mg, 0.89 mmol) in water (15 mL) at 0 °C. The reaction mixture was stirred for 15 min and then $KMnO_4$ (130 mg, 0.81 mmol) was slowly added in

portions at 0 °C. The system was stirred for another 4 h at 0 °C, and poured into ice–water (30 mL). The solid was removed by filtration through a Celite pad, and washed with ethyl acetate. The filtrate's aqueous phase was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4 and evaporated to dryness. Flash chromatography of the residue (petroleum ether–AcOEt, 3 : 1) gave keto ester **20** (52 mg, 40%) as a clear liquid, $[\alpha]_D^{20}$ −30.9 (*c* 0.7, CH_2Cl_2); ^{1}H NMR (300 MHz; $CDCl_3$) 1.40 (d, *J* = 5.0 Hz, 3H, C*H*$_3$CH), 2.08 (s, 3H, acetyl), 3.45 (m, 1H), 3.90 (s, 3H, OCH_3), 4.30 (m, 2H), 4.65 (m, 1H), 4.78 (q, *J* = 5.0 Hz, 1H, C*H*CH$_3$), 7.01 (d, *J* = 16.0 Hz, 1H, H-3), 7.10 (dd, *J* = 3.9, 15.9 Hz, 1H, H-4); IR (film) 3463, 2997, 2959, 2870, 1749, 1709, 1635 cm^{-1}; EIMS *m*/*z* (%) 271 (M^+ − H, 2.01), 230 (2.82), 229 (5.87), 217 (2.23), 169 (31.46); HRMS *m*/*z* Calc. for $C_{12}H_{15}O_7$ (M^+ − H): 271.0812. Found: 271.0811.

Methyl 2-*O*-methyl-3-deoxy-4,6,7-tri-*O*-acetyl-D-*ribo*-hept-2-ulofuranosonate and methyl 2-*O*-methyl-3-deoxy-4,5,7-tri-*O*-acetyl-D-*ribo*-hept-2-ulopyranosonate (21). To a stirred solution of **19** (110 mg, 0.23 mmol) in anhydrous MeOH (20 mL) was added toluene-*p*-sulfonic acid monohydrate (100 mg, 0.53 mmol). After being refluxed for 10 h, the reaction mixture was carefully neutralized by saturated aqueous $NaHCO_3$ and then was concentrated *in vacuo*. The residue was purified by flash chromatography (CH_2Cl_2–MeOH, 6 : 1) to give a crude product (41 mg).

To the above crude product (41 mg) were added pyridine (2.2 mL, 27.0 mmol), DMAP (10 mg) and acetic anhydride (1.6 mL, 15.68 mmol) under nitrogen at room temperature. After 24 h the solvent was removed *in vacuo*. The residue was purified by flash chromatography over silica gel (petroleum ether–AcOEt (2 : 1) to give title compounds **21** (54 mg, two steps 67%), $[\alpha]_D^{20}$ +20.1 (*c* 1.1, $CHCl_3$); ^{1}H NMR (300 MHz; $CDCl_3$) 2.04 (s, 1.35H, acetyl), 2.06 (s, 1.65H, acetyl), 2.07 (s, 1.65H, acetyl), 2.08 (s, 1.35H, acetyl), 2.09 (s, 1.65 H, acetyl), 2.11 (s, 1.35 H, acetyl), 2.25 (dd, *J* = 14.9, 1.8 Hz, 0.45H, H-3), 2.41 (dd, *J* = 14.8, 3.6 Hz, 0.55H, H-3), 2.52 (dd, *J* = 7.7, 14.6 Hz, 0.45H, H-3), 2.65 (dd, *J* = 14.8, 7.0 Hz, 0.55H, H-3), 3.31 (s, 1.35H, OCH_3), 3.38 (s, 1.65H, OCH_3), 3.81 (s, 1.65H, OCH_3), 3.86 (s, 1.35H, OCH_3), 4.10–4.25 (m, 1H), 4.30–4.47 (m, 2H), 5.25 (m, 2H); IR (film) 2961, 2843, 1747, 1678, 1438, 1373 cm^{-1}; EIMS *m*/*z* (%) 303 (M^+ − CO_2CH_3, 20.41), 217 (7.29), 183 (15.64), 157 (16.43), 109 (8.23), 141 (20.66), 43 (100). Calc. for $C_{15}H_{22}O_{10}$: C, 49.72; H, 6.12. Found: C, 49.55; H, 6.31%.

1,2,3-Trideoxy-4-*O*-(*tert*-butyldimethylsilyl)-5,6-*O*-isopropylidene-L-*erythro*-hex-1-ynitol (24a). To a solution of **23a**[8] (2.88 g, 16.9 mmol) in DMF (6 mL) were added imidazole (3.00 g, 44.4 mmol) and TBSCl (3.19 g, 20.9 mmol) and the reaction mixture was kept for 24 h at room temperature before being diluted with 40 mL of diethyl ether and washed successively with water and brine. The organic layer was dried over anhydrous $NaSO_4$. Removal of solvent and then flash chromatography (petroleum ether–ethyl acetate, 40 : 1) gave the product **24a** (3.36 g, 71%) as a clear liquid, ^{1}H NMR (300 MHz; $CDCl_3$) 0.10 (s, 3H, $SiCH_3$), 0.13 (s, 3H, $SiCH_3$), 0.84 (s, 9H, $SiC(CH_3)_3$), 1.27 (s, 3H, CH_3C), 1.35 (s, 3H, C*H*$_3$C), 1.94 (dd, *J* = 2.3, 5.5 Hz, 1H, H-1), 2.37–2.41 (m, 2H, H_2-3), 3.62–3.78 (m, 2H), 3.82–3.94 (m, 1H), 3.98–4.08 (m, 1H); IR (film) 3315, 2988, 2932, 1462 cm^{-1}; EIMS *m*/*z* (%) 269 (M^+ − CH_3, 13.27), 227 (M^+ − C_4H_9, 6.54), 209 (13.88), 183 (25.04), 169 (96), 73 (100); HRMS *m*/*z* Calc. for $C_{14}H_{25}O_3Si$ (M^+ − CH_3): 269.1567. Found: 269.1570.

1,2,3-Trideoxy-4-*O*-(*tert*-butyldimethylsilyl)-5,6-*O*-isopropylidene-D-*erythro*-hex-1-ynitol 24b. Transformation of **23b**[8] (1.13 g, 6.6 mmol) according to the same preparation procedure for **24a** gave compound **24b** (1.37 g, 73%) as a clear liquid, ^{1}H NMR (300 MHz; $CDCl_3$) 0.11 (s, 3H, $SiCH_3$), 0.14 (s, 3H, $SiCH_3$), 0.85 (s, 9H, $SiC(CH_3)_3$), 1.30 (s, 3H, CH_3C), 1.36 (s, 3H, CH_3C), 1.97 (dd, *J* = 2.17, 5.22 Hz, 1H, H-1), 2.42–2.48 (m, 2H, H_2-3), 3.72–3.80 (m, 1H), 3.80–3.87 (m, 1H), 3.96–4.04 (m, 1H), 4.10–4.18 (m, 1H).

1-Bromo-1,2,3-trideoxy-4-*O*-(*tert*-butyldimethylsilyl)-5,6-*O*-isopropylidene-L-*erythro*-hex-1-ynitol 25a. To a solution of **24a** (466 mg, 1.64 mmol) in acetone (20 mL) were added NBS (440 mg, 2.47 mmol) and silver nitrate (112 mg, 0.66 mmol). The reaction mixture was stirred for 9 h in darkness at room temperature. The salts were removed by filtration through a Celite pad and washed with diethyl ether. The organic layer was washed successively with water and brine, dried over Na_2SO_4 and evaporated to dryness. Chromatography of the residue on silica gel, using petroleum ether–AcOEt (30 : 1) as eluent, gave bromide **25a** (596 mg, 100%) as a clear liquid, $[\alpha]_D^{20}$ −11.4 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (300 MHz; $CDCl_3$) 0.10 (s, 3H, $SiCH_3$), 0.13 (s, 3H, $SiCH_3$), 0.90 (s, 9H, $SiC(CH_3)_3$), 1.36 (s, 3H, CH_3C), 1.41 (s, 3H, CH_3C), 2.41 (d, 1H, *J* = 4.9 Hz, H-3), 2.44 (d, 1H, *J* = 4.8 Hz, H-3), 3.70–3.80 (m, 1H), 3.80–3.90 (m, 1H), 3.90–4.10 (m, 2H); IR (film) 2989, 2957, 2932, 2860, 1733, 1473, 1438 cm^{-1}; EIMS *m*/*z* (%) 362 (M^+, 2.08), 364 (1.10), 347 (M^+ − CH_3, 3.60), 349 (8.79), 329 (2.46), 331 (12.85), 290 (5.55), 247 (37.73), 168 (31.51), 73 (100). Calc. for $C_{15}H_{27}O_3SiBr$: C, 49.58; H, 7.49. Found: C, 49.44; H, 7.55%.

1-Bromo-1,2,3-trideoxy-4-*O*-(*tert*-butyldimethylsilyl)-5,6-*O*-isopropylidene-D-*erythro*-hex-1-ynitol 25b. Transformation of **24b** (461 mg, 1.62 mmol) according to the same preparation procedure for **25a** gave bromide **25b** (546 mg, 93 %) as a clear liquid, ^{1}H NMR (300 MHz; $CDCl_3$) 0.09 (s, 3H, $SiCH_3$), 0.13 (s, 3H, $SiCH_3$), 0.89 (s, 9H, $SiC(CH_3)_3$), 1.35 (s, 3H, CH_3C), 1.39 (s, 3H, CH_3C), 2.41 (d, 1H, *J* = 4.8 Hz, H-3), 2.45 (d, 1H, *J* = 5.1 Hz, H-3), 3.73–3.81 (m, 1H), 3.82–3.90 (m, 1H), 3.95–4.10 (m, 2H); IR (film) 2988, 2932, 2859, 2223, 1473, 1464, 1381 cm^{-1}; EIMS *m*/*z* (%) 347 (M^+ − CH_3, 4.36), 349 (4.52), 289 (3.37), 287 (2.91), 167 (27.07), 102 (56.53), 73 (100). This compound was used for the next step without further purification or characterization.

Methyl 3-deoxy-4-*O*-(*tert*-butyldimethylsilyl)-5,6-*O*-isopropylidene-L-*erythro*-hex-2-ulosonate (26a). To a solution of **25a** (213 mg, 0.587 mmol) in MeOH (15 mL) was slowly added a solution of $NaHCO_3$ (30 mg, 0.357 mmol) and $MgSO_4$ (140 mg, 1.17 mmol) in water (15 mL) at 0 °C. After being stirred for 15 min, the reaction mixture was slowly treated with $KMnO_4$ (185 mg, 1.17 mmol) added in portions at 0 °C. The system was stirred for another 4 h at 0 °C and was then poured into ice–water (30 mL). The solid was removed by filtration through a Celite pad and was washed with ethyl acetate. The aqueous phase was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4 and evaporated to dryness. Flash chromatography of the residue (petroleum ether–AcOEt, 3 : 1) gave keto ester **26a** (105 mg, 52%) as a clear, colorless liquid, $[\alpha]_D^{20}$ +3.4 (*c* 0.8, $CHCl_3$); ^{1}H NMR (300 MHz; $CDCl_3$) 0.07 (s, 3H, $SiCH_3$), 0.11 (s, 3H, $SiCH_3$), 0.85 (s, 9H, $SiC(CH_3)_3$), 1.27 (s, 3H, CH_3C), 1.30 (s, 3H, CH_3C), 2.90 (dd, *J* = 5.2, 14.7 Hz, 1H, H-3), 3.20 (dd, *J* = 7.4, 14.7 Hz, 1H, H-3), 3.83 (dd, *J* = 5.0, 8.2 Hz, 1H, H-6), 3.87 (s, 3H, OCH_3), 3.93 (m, 1H), 4.05 (dd, *J* = 6.4, 8.3 Hz, 1H, H-6), 4.14 (m, 1H); ^{13}C NMR (75 MHz; $CDCl_3$) −4.3, −4.1, 18.2, 25.1, 25.9 (×3), 26.2, 45.6, 52.8, 67.0, 71.8, 79.0, 109.9, 161.6, 191.0; IR (film) 2989, 2937, 2860, 1733, 1473, 1438, 1372 cm^{-1}; EIMS *m*/*z* (%) 346 (M^+, 1.28), 272 (14.25), 246 (26.46), 231 (15.50), 213 (22.47), 202 (21.85), 73 (100); HRMS (ESI) *m*/*z* Calc. for $C_{16}H_{30}O_6SiNa$ (M^+ + Na): 369.1704. Found: 369.1708.

Methyl 3-deoxy-4-*O*-(*tert*-butyldimethylsilyl)-5,6-*O*-isopropylidene-D-*erythro*-hex-2-ulosonate (26b). Transformation of **25b** (320 mg, 0.88 mmol) according to the same preparation procedure for **26a** gave keto ester **26b** (183 mg, 59%) as a clear, colorless liquid, ^{1}H NMR (300 MHz; $CDCl_3$) 0.08 (s, 3H, $SiCH_3$), 0.11 (s, 3H, $SiCH_3$), 0.82 (s, 9H, $SiC(CH_3)_3$), 1.26 (s, 3H, CH_3C), 1.30 (s, 3H, CH_3C), 2.92 (dd, J = 5.5, 14.9 Hz, 1H, H-3), 3.22 (dd, J = 7.1, 14.8 Hz, 1H, H-3), 3.82 (dd, J = 5.3, 7.4 Hz, 1H, H-6), 3.86 (s, 3H, OCH_3), 3.96 (m, 1H), 4.04 (m, 1H), 4.14 (m, 1H); ^{13}C NMR (75 MHz; $CDCl_3$) −4.6, −4.0, 17.9, 25.1, 25.9 (×3), 26.2, 45.2, 53.0, 67.1, 71.6, 78.8, 109.8, 161.8, 191.2; IR (film) 2989, 2932, 2860, 1733, 1473, 1438, 1373 cm^{-1}; EIMS *m*/*z* (%) 347 (M^+ + H, 3.60), 346 (M^+, 5.66), 345 (M^+ − H, 5.76), 331 (M^+ − CH_3, 12.85), 289 (30.57), 271 (62.94), 159 (74.09), 129 (81.89), 187 (100); HRMS (ESI) *m*/*z* Calc. for $C_{16}H_{30}O_6SiNa$ (M^+ + Na): 369.1704. Found: 369.1714.

Methyl 2-*O*-methyl-3-deoxy-4,5-di-*O*-acetyl-L-*erythro*-hex-2-ulopyranosonate (27a). To a well-stirred solution of **26a** (38 mg, 0.11 mmol) were slowly added anhydrous MeOH (7 mL) and concentrated hydrochloric acid (0.2 mL) at 0 °C. After 15 min the reaction mixture was warmed to room temperature and stirred for 4 days. The mixture was carefully neutralized with saturated aqueous $NaHCO_3$ at 0 °C and then concentrated *in vacuo*. The residue was purified by flash chromatography (CH_2Cl_2–MeOH, 10 : 1) to give a crude product (17 mg).

To a solution of the above crude product (17 mg) in anhydrous CH_2Cl_2 (5 mL) were added pyridine (3 mL, 36.8 mmol), DMAP (10 mg) and acetic anhydride (2 mL, 19.6 mmol) under nitrogen at room temperature. The reaction mixture was stirred for 24 h at room temperature and then ethyl acetate (20 mL) and water (2 mL) were added. The separated organic phase was washed successively with water and brine and was then dried over anhydrous Na_2SO_4. Chromatographic separation was carried out on silica gel, using petroleum ether–AcOEt (6 : 1) as eluent, to give compound **27a** (17 mg, 53%) as an oil, $[a]_D^{20}$ +18.5 (*c* 0.3, $CHCl_3$); ^{1}H NMR (300 MHz; $CDCl_3$) 2.07 (s, 3H, acetyl), 2.11 (s, 3H, acetyl), 2.40 (dd, J = 14.3, 5.3 Hz, 1H, H-3), 2.70 (dd, J = 14.3, 7.1 Hz, 1H, H-3), 3.31 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 4.15 (dd, J = 11.7, 5.4 Hz, 1H, H-6), 4.38 (dd, J = 11.7, 4.8 Hz, 1H, H-6), 4.47 (dd, J = 4.4, 10.0 Hz, 1H, H-5), 5.25 (m, 1H, H-4); ^{13}C NMR (75 MHz; $CDCl_3$) 20.85, 20.78, 42.5, 52.0, 52.8, 63.8, 74.1, 83.8, 106.3, 168.3, 170.2, 171.1; IR (film) 2961, 2850, 1747, 1439, 1372 cm^{-1}; EIMS *m*/*z* (%) 231 (M^+ − CO_2CH_3, 17.31), 217 (2.57), 171 (3.77), 157 (11.25), 146 (4.01), 111 (56.59), 43 (100); HRMS *m*/*z* Calc. for $C_{11}H_{15}O_7$ (M^+ − OCH_3): 259.0818. Found: 259.0791.

Methyl 2-*O*-methyl-3-deoxy-4,5-di-*O*-acetyl-D-*erythro*-hex-2-ulopyranosonate (27b). Transformation of **26b** (166 mg, 0.48 mmol) according to the same preparation procedure for **27a** gave compound **27b** (67 mg, 48%) as an oil, $[a]_D^{20}$ −16.3 (*c* 1.2, $CHCl_3$); ^{1}H NMR (300 MHz; $CDCl_3$) 2.07 (s, 3H, acetyl), 2.11 (s, 3H, acetyl), 2.40 (dd, J = 14.3, 5.2 Hz, 1H, H-3), 2.70 (dd, J = 14.2, 7.2 Hz, 1H, H-3), 3.31 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 4.18 (dd, J = 11.7, 6.3 Hz, 1H, H-6), 4.40 (dd, J = 11.7, 4.8 Hz, 1H, H-6), 4.48 (m, 1H), 5.25 (ddd, J = 4.9, 3.7, 7.2 Hz, 1H, H-4); ^{13}C NMR (75 MHz; $CDCl_3$) 20.79, 20.83, 42.2, 51.8, 53.0, 74.0, 82.8, 106.3, 169.0, 170.8, 171.0; IR (film) 2960, 2850, 1745, 1439, 1370 cm^{-1}; EIMS *m*/*z* (%) 231 (M^+ − CO_2CH_3, 5.98), 157 (4.28), 139 (3.74), 129 (4.71), 111 (28.15), 57 (6.89), 43 (100); HRMS *m*/*z* Calc. for $C_{11}H_{15}O_7$ (M^+ − OCH_3): 259.0818. Found: 259.0823.

Acknowledgements

This work was supported by the National Natural Science Foundation of China (No. 29790126), the Chinese Academy of Sciences (KJ 95–A1–504), and the State Ministry of Science and Technology (G2000077502).

References

1 (*a*) E. Haslam, *The Shikimate Pathway*, Wiley, New York, 1974; (*b*) B. Ganem, *Tetrahedron*, 1978, **34**, 3353; (*c*) P. M. Dewick, *Nat. Prod. Rep.*, 1988, **5**, 73; (*d*) E. Haslam, *Shikimic Acid Metabolism and Metabolites*, Wiley, New York, 1993.

2 (*a*) P. R. Srinivasan, M. Katagiri and D. B. Sprinson, *J. Biol. Chem.*, 1959, **234**, 713; (*b*) F. Unger, *Adv. Carbohydr. Chem. Biochem.*, 1981, **38**, 323; (*c*) J. W. Frost and J. R. Knowles, *Biochemistry*, 1984, **23**, 4465.

3 (*a*) R. Ramage, A. M. MacLeod and G. W. Rose, *Tetrahedron*, 1991, **47**, 5625; (*b*) A. Dondoni, A. Marra and P. Merino, *J. Am. Chem. Soc.*, 1994, **116**, 3324; (*c*) P.-A. Driguez, B. Barrere, G. Quash and A. Doutheau, *Carbohydr. Res.*, 1994, **262**, 297; (*d*) D. H. R. Barton and W. Liu, *Tetrahedron Lett.*, 1997, **38**, 367; D. H. R. Barton and W. Liu, *Tetrahedron*, 1997, **53**, 12067; (*e*) J. Mlynarski and A. Banaszek, *Tetrahedron Lett.*, 1998, **39**, 5425; (*f*) J. Mlynarski and A. Banaszek, *Tetrahedron*, 1999, **55**, 2785; (*g*) F. S. García, G. M. P. Cebrián, A. H. López and F. J. López Herrera, *Tetrahedron*, 1998, **54**, 6867; (*h*) F. Sarabia, S. Chammaa and F. J. López Herrera, *Tetrahedron*, 2001, **57**, 10271; (*i*) M. Reiner, F. Stolz and R. R. Schmidt, *Eur. J. Org. Chem.*, 2002, 57; (*j*) C. R. Johnson and J. Kozak, *J. Org. Chem.*, 1994, **59**, 2910; (*k*) A. Lubineau and Y. Queneau, *J. Carbohydr. Chem.*, 1995, **14**, 1295; (*l*) L.-S. Li, Y. Wu and Y.-L. Wu, *J. Carbohydr. Chem.*, 1999, **18**, 1067; earlier syntheses (*m*) D. B. Sprinson, J. Rothschild and M. Sprecher, *J. Biol. Chem.*, 1963, **238**, 3170; (*n*) K. M. Herrmann and M. D. Poling, *J. Biol. Chem.*, 1975, **250**, 6817; (*o*) V. Trigalo, M. Level and L. Szabo, *J. Chem. Soc., Perkin Trans. 1*, 1975, 600; (*p*) D. Charon and L. Szabo, *J. Chem. Soc., Perkin Trans. 1*, 1973, 1175.

4 (*a*) Y.-J. Hu, X.-D. Huang, Z.-J. Yao and Y.-L. Wu, *J. Org. Chem.*, 1998, **63**, 2456; (*b*) L.-S. Li, Y.-K. Wu, Y.-J. Hu and Y.-L. Wu, *Tetrahedron: Asymmetry*, 1998, **9**, 2271; (*c*) Y.-J. Hu, X.-D. Huang and Y.-L. Wu, *J. Carbohydr. Chem.*, 1998, **17**, 1095.

5 L.-S. Li and Y.-L. Wu, *Tetrahedron Lett.*, 2002, **43**, 2427.

6 T.-S. Hu, Q. Yu, Y.-L. Wu and Y.-K. Wu, *J. Org. Chem.*, 2001, **66**, 853.

7 W.-L. Wu, Z.-J. Yao, Y.-L. Li, J.-C. Li, Y. Xia and Y.-L. Wu, *J. Org. Chem.*, 1995, **60**, 3257.

8 Y.-F. Wang, J.-C. Li and Y.-L. Wu, *Chim. J. Chem.*, 1993, **51**, 409.