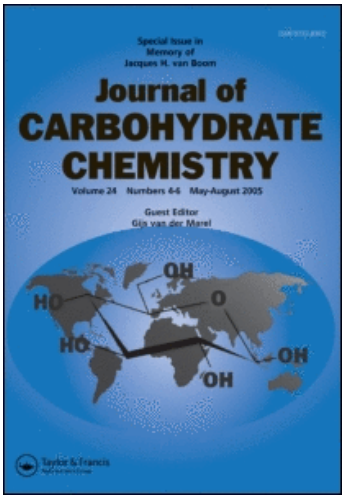

Journal of Carbohydrate Chemistry

Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713617200

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To cite this Article Li, Lian-Sheng , Wu, Yikang and Wu, Yu-Lin(1999) 'An Efficient Approach to the Synthesis of Ethyl Esters of 2,6-Anhydro-3-Deoxy-D-*Gluco* And D-*Allo*-Heptanoates', Journal of Carbohydrate Chemistry, 18: 9, 1067 — 1077

To link to this Article: DOI: 10.1080/07328309908544055

URL: http://dx.doi.org/10.1080/07328309908544055

J. CARBOHYDRATE CHEMISTRY, 18(9), 1067–1077 (1999)

AN EFFICIENT APPROACH TO THE SYNTHESIS OF ETHYL ESTERS OF 2,6-ANHYDRO-3-DEOXY-D-*GLUCO* AND D-*ALLO*-HEPTANOATES

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Received April 9, 1999 - Final Form September 2, 1999

ABSTRACT

An efficient synthesis of analogues of DAH (3-deoxy-D-*arabino*-hept-2-ulosonic acid) and DRH (3-deoxy-D-*ribo*-hept-2-ulosonic acid) is described. The route exploits a previously published highly double-stereoselective hetero Diels-Alder reaction catalyzed by a chiral salenCo(II) complex. Asymmetric dihydroxylation followed by selective reduction leads to stereoselective introduction of hydroxy groups at C-4 and C-5. Oxidative cleavage of the C-6 side-chain, *in situ* reduction of the resulting aldehyde and deprotection afford the desired targets, which may be useful precursors to the simple analogues of the anti-influenza agent GG167.

INTRODUCTION

Ulosonic acids are a group of naturally occurring carbohydrates that are involved in many biologically important processes and have attracted considerable attention in the last few years.[1] The seven carbon-atom analogue in this series, 3-deoxy-D-*arabino*-hept-2-ulosonic acid[2] (DAH), is formed in plants by stereoselective condensation of phosphoenolpyruvate with D-erythrose 4-phosphate mediated by DAHP synthase and it has been shown[3] that DAH is a key intermediate in the biosynthesis of aromatic amino

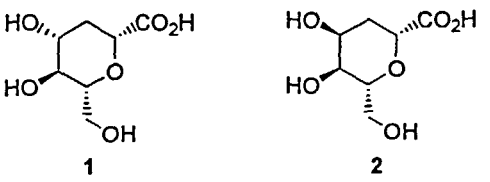


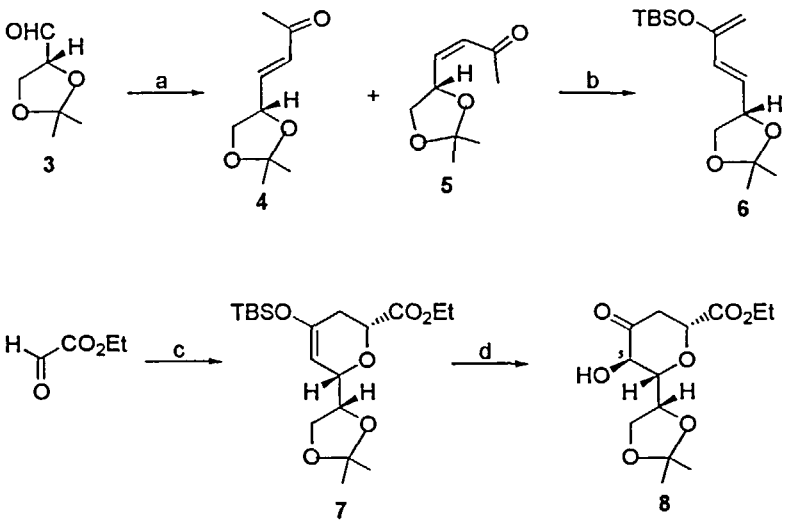
Figure 1

acids from glucose (Shikimate pathway). It is therefore not surprising that compounds of this type have become targets of many synthetic endeavors.

The vast majority[4-6] of the work reported on the syntheses of such compounds adopted synthetic strategies based on aldol condensation, except for the work of Lubineau[7] et al., where a more straightforward approach to the methyl ester of DRH relying on a hetero Diels-Alder reaction of conjugated diene and sodium glyoxylate was chosen. However, the selectivity (*endo/exo* = 1.5:1) of the cycloaddition step was rather poor and the products were racemic. Using the chiral catalyst salenCo(II)[8-10] complex in the hetero Diels-Alder reaction led to significant improvement in both the yield and the selectivities, which allowed us to effect a formal synthesis of 3-deoxy-D-*manno*-2-octulosonic acid (Kdo) and a synthesis of Kdn skeleton.[8-10] Below we wish to report an application of this efficient methodology to the synthesis of the ethyl esters of 2,6-anhydro-3-deoxy-D-*gluco*-heptanoic acid (**1**), and 2,6-anhydro-3-deoxy-D-*allo*-heptanoic acid (**2**) (Figure 1).

RESULT AND DISCUSSION

A key step in our synthesis involved the efficient elaboration of the silyl enol ether **7**, which was prepared from D-glyceraldehyde acetonide **3** according to our published[8] procedure (Scheme 1). Attempts to oxidize the silyl enol ether with *m*-chloroperbenzoic acid (MCPBA) gave the TBDMS protected α-hydroxy ketone in poor yield (8%), along with a number of complex byproducts. Hydroxylation of **7** with a catalytic amount of OsO_4 (10 mol%) and 2 equiv of NMO in acetone-water (3:1) at room temperature for 9 h provided a 4:1 mixture of **8** and presumably its C-5 isomer (the ratio based on GC analysis of product mixture) in 90% yield. The diastereoselectivity was, however, unacceptably

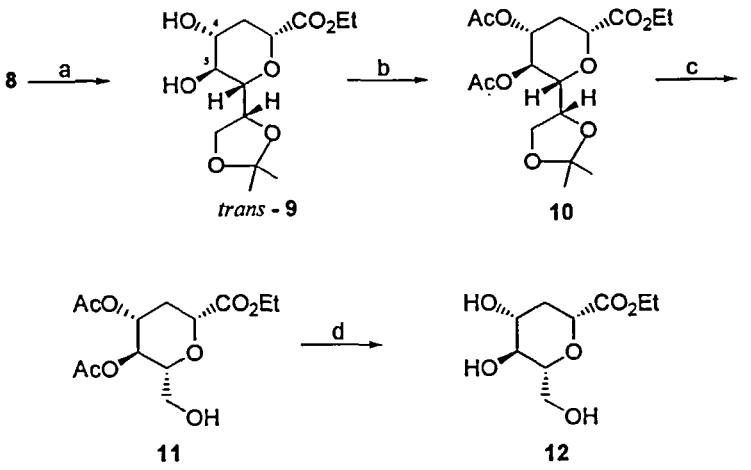


Reagents and conditions: (a) $Ph_3P{=}CHCOCH_3$, THF, 90 °C, 90%; (b) TBDMSOTf, Et_3N, dry ether, 0 °C, 96%; (c) cat. (R,R)-salenCo(II) (10 mol%), **6**, CH_2Cl_2, rt, 65%; (d) $K_3Fe(CN)_6$ (3 eq), K_2CO_3 (3 eq), $NaHCO_3$ (3 eq), $K_2OsO_2(OH)_4$ (5 mol%), $(DHQD)_2$-PHAL (5 mol%), *t*-BuOH-H_2O (1:1), 0 °C, 84%.

Scheme 1

low and separation of the products was very difficult. We next tested the asymmetric dihydroxylation on **7**. In the beginning, this was also troublesome; treatment of **7** with AD-mix-β[11] at 0 °C or room temperature led to only 10% conversion of the starting material, even after prolonged reaction time (7 days). Better conversion was later achieved by employing larger amounts of $K_2OsO_2(OH)_4$. With as much as 5 mol% of $K_2OsO_2(OH)_4$, a single diastereoisomer **8** could be obtained in 84% yield. The excellent diastereoselectivity was attributed to the matched interactions between the substrate chirality and that of the chiral ligand. The β-orientation of the hydroxy group at C-5 in **8** was confirmed by ^1H NMR and ^1H-^1H COSY analyses. The H-5 of **8** appears as a doublet at δ 4.18 with a large coupling constant of 10.0 Hz, which is consistent with the known rule that in cyclohexane systems $^3J_{a,a}$ is normally 8-12 Hz.

Reduction of α-hydroxy ketone **8** with $NaBH_4$ at 0 °C in ethanol (Scheme 2) provided product *trans*-**9** in 94 % yield. Neither *cis*-diol nor the triol (with the ester



Reagents and conditions: (a) $NaBH_4$, EtOH, 0 °C, 94%; (b) Ac_2O, Pyridine, DMAP, CH_2Cl_2, rt, 97%; (c) H_5IO_6, EtOAc, 0 °C to rt; $NaBH_4$, EtOH, 0 °C, 85% (two steps); (d) K_2CO_3, EtOH, 87%.

Scheme 2

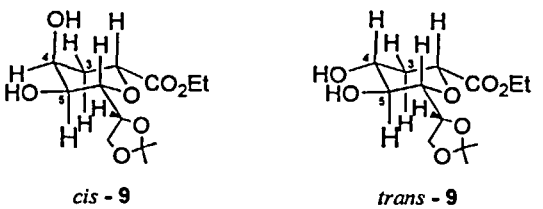
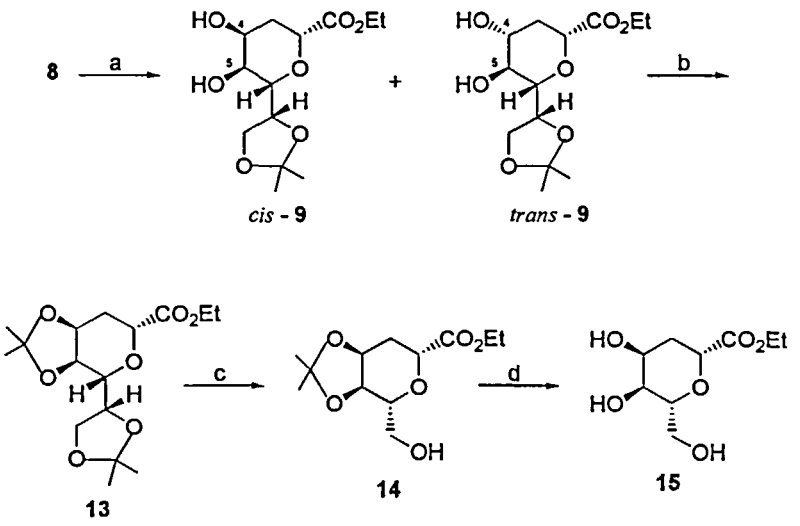


Figure 2

functionality being reduced) was detected. The stereochemistry of the newly formed hydroxy at C-4 was assigned to an α-configuration on the basis of the ^1H NMR and ^1H-^1H COSY experiments, in which the H-5 appeared as a triplet at δ 3.59 with J = 8.9 Hz, whereas the H-3ax was a quartet at δ 1.67 with J = 12.4 Hz (Figure 1). The hydroxy groups were then protected as acetates to give **10** in 97% isolated yield. The following selective hydrolysis of terminal *O*-isopropylidene acetals and the oxidative cleavage[12] of the exposed glycol with periodic acid followed by reduction of the resulting terminal aldehyde with $NaBH_4$ gave compound **11** in 85 % (two steps) isolated yield. Finally,



Reagents and conditions: (a) $LiAl[OC(CH_3)_3]H$, THF, 0 °C, 90%; (b) DMOP, CSA, CH_2Cl_2, rt, 91%; (c) H_5IO_6, EtOAc, 0 °C to rt; $NaBH_4$, EtOH, 0 °C, 82% (two steps); (d) Dowex 50W (H^+), EtOH/H_2O (9:1), 50 °C, 98%.

Scheme 3

deprotection of **11** with K_2CO_3/EtOH afforded ethyl 2,6-anhydro-3-deoxy-D-*gluco*-heptanoate (**12**).

Treatment of **8** with hindered lithium tri-*tert*-butoxy aluminium hydride in THF at 0 °C for 10 h (Scheme 3) gave a 2:1 mixture of *cis*- and *trans*-isomers in 80% yield. But the desired *cis*-**9** could be easily chromatographically separated from the mixture. Both the selectivity and the yield were improved (*cis*/*trans* = 3:1, 90% yield) when the reaction temperature was lowered to -15 °C. Reducing the reaction temperature to -30 °C, however, did not result in any further improvement as the reduction did not occur at all.

The structure for *cis*-**9** was established also on the basis of its ^1H NMR spectrum, in which H-5 appeared as doublet-doublet at δ 3.68 with J = 9.3, 3.1 Hz while H-3ax appeared as doublet-doublet-doublet at δ 1.79 with J = 14.3, 12.0, 2.6 Hz (Figure 2). After protecting the 4,5-dihydroxy as an isopropylidene acetal (**13**, 91% isolated yield), compound **14** was obtained in 82% yield by the same method described above for the conversion of **10** to **11**. The isopropylidene was then removed by reaction with Dowex

50W (H^+) in ethanol-water (9:1) at 50 °C to afford the ethyl 2,6-anhydro-3-deoxy-D-*allo*-heptanoate (**15**) quantitatively.

In brief, we have developed an efficient approach to the ethyl esters of 2-deoxy-DAH and 2-deoxy-DRH (i.e., **12** and **15**). These esters may be useful precursors to the simple analogues[13] of the anti-influenza agent GG167. The method[14] for the stereoselective introduction of hydroxy groups at C-4 and C-5 illustrated in this work may be also applicable to syntheses of other members in this series of compounds. Some further applications of this strategy in the syntheses of Kdn, Neu5Ac, GG167 and their analogues are also under investigation in this laboratory and will be reported in due time.

EXPERIMENTAL

General methods

IR spectra were recorded on a Shimadzu IR-440 spectrometer. ^1H and ^{13}C NMR were recorded on an EM-360A, an FX 90q, or an AMX-300 spectrometers with TMS as the internal standard. Mass spectra were taken on a VG Quattro MS/MS or an HP5989A instrument. HRMS (EI) spectra were obtained on a Finnigan Mat 8430 mass spectrometer. Optical rotations were measured on a Perkin-Elmer 241 MC polarimeter. Flash column chromatography was performed on silica gel H (10-40 μm) with petrol ether-ethyl acetate or ethyl acetate-ethanol system as eluant.

Ethyl 2,6-anhydro-3-deoxy-7,8-*O*-isopropylidene-D-*allo*-oct-4-ulosonate (8). To a solution of $K_3[Fe(CN)_6]$ (494 mg, 1.5 mmol), K_2CO_3 (207 mg, 1.5 mmol), and $NaHCO_3$ (126 mg, 1.5 mmol) in a 1:1(vol.) *t*-BuOH-H_2O mixture (8 mL) at 0 °C, was added $(DHQD)_2$-PHAL (9.4 mg, 5 mol%) and $K_2OsO_2(OH)_4$ (18 mg, 5 mol%). After stirring for 10 min compound **7** (193 mg, 0.5 mmol) was added. The reaction mixture was stirred at 0 ° C for 10 h. Solid sodium sulfite (500 mg) was added, and the mixture was stirred for an additional hour. After separation of the layers, the aqueous layer was extracted with ethyl acetate (25 mL × 2). The combined organic extracts were dried over anhydrous magnesium sulfate and concentrated *in vacuo* to give a yellow solid, which was purified by flash chromatography on a silica gel column (petroleum ether/ethyl acetate, 2:1) to afford pure compound **8** (127 mg, 84 %) as a white solid. mp 133-134 °C; $[\alpha]_D$ +47.6 (*c* 0.34, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 4.50 (1 H, dt, J = 6.6, 3.9 Hz, H-

7), 4.25 (2 H, q, J = 7.1 Hz, O$\underline{CH_2}CH_3$), 4.24 (1 H, dd, J = 12.0, 3.0 Hz, H-2), 4.21 (1 H, dd, J = 8.5, 6.4 Hz, H-8), 4.18 (1 H, d, J = 10.0 Hz, H-5), 4.13 (1 H, dd, J = 8.4, 6.9 Hz, H-8), 3.52 (1 H, dd, J = 9.6, 4.2 Hz, H-6), 2.88 (1 H, dd, J = 14.4, 3.0 Hz, H-3eq), 2.82 (1 H, ddd, J = 14.4, 12.0, 1.2 Hz, H-3ax), 1.48 (3 H, s), 1.41 (3 H, s), 1.30 (3 H, t, J = 7.1 Hz, OCH$_2\underline{CH_3}$); EIMS *m/z* (%) 289 (M^+ + 1, 5.5), 273 (100.0), 101 (75.6), 43 (70.9); IR (KBr) 3501, 2985, 1749, 1721, 1259, 1085, 855 cm^{-1}; HR EIMS Calcd for $C_{12}H_{17}O_7$ (M^+ - CH_3) 273.0969, found 273.0971.

Ethyl 2,6-anhydro-3-deoxy-7,8-*O*-isopropylidene-D-*gluco*-D-*glycero*-octanoate (*trans*-9). To a solution of compound **8** (80 mg, 0.28 mmol) in 5 mL of abs EtOH at 0 °C, was added $NaBH_4$ (10.64 mg, 1 eq). The reaction mixture was stirred for 30 min, then neutralized with 1 N aqueous HCl (2 drops). The mixture was diluted with 20 mL of EtOAc, washed with water and brine. The organic layer was dried over magnesium sulfate, filtered and concentrated in *vacuo*. The residue was purified by flash chromatography on a silica gel column (petroleum ether/ethyl acetate, 1:2) to afford the product **9** as a colorless oil (72 mg, 90%). $[\alpha]_D$ +18.9 (*c* 0.68, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.21-4.18 (1 H, m, H-7), 4.20 (2 H, qd, J = 7.1, 1.6 Hz, O$\underline{CH_2}CH_3$), 4.03 (1 H, dd, J = 12.0, 2.2 Hz, H-2), 4.01 (1 H, dd, J = 8.9, 4.4 Hz, H-8), 4.05 (1 H, dd, J = 8.9, 6.2 Hz, H-8), 4.06-3.99 (1 H, m, H-4), 3.59 (1 H, t, J = 8.9 Hz, H-5), 3.27 (1 H, dd, J = 9.0, 8.3 Hz, H-6), 2.29 (1 H, ddd, J = 12.9, 5.0, 2.2 Hz, H-3 eq), 1.67 (1 H, q, J = 12.4 Hz, H-3ax), 1.44 (3 H, s), 1.34 (3 H, s), 1.26 (3 H, t, J = 7.1 Hz, OCH$_2\underline{CH_3}$); IR (neat): 3446, 2983, 1734, 1376, 1216, 1062, 920, 850 cm^{-1}; EIMS *m/z* (%) 291 (M^+ + 1, 34.3), 275 (M^+ - CH_3, 58.4), 101 (100.0), 43 (27.2); HR EIMS Calcd for $C_{13}H_{22}O_7$(M^+) 290.1359, found 290.1386.

Ethyl 2,6-anhydro-3-deoxy-4,5-*O*-diacetyl-7,8-*O*-isopropylidene-D-*gluco*-D-*glycero*-octanoate (10). To a solution of compound **9** (44 mg, 0.15 mmol) in 5 mL of CH_2Cl_2, was added DMAP (1 mg) and a 1:1 (vol) mixture of pyridine and acetic anhydride (200 μL). The reaction mixture was stirred at room temperature for 2 h. After TLC showed the completion of the reaction, the mixture was diluted with 20 mL of ethyl acetate, washed with water and brine . The organic layer was then dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo, the residue was purified by flash chromatography on a silica gel column (petroleum ether/ethyl acetate, 2:1) to afford

product **10** (55 mg, 97 %). mp 83-84 °C; $[\alpha]_D$ +5.72 (*c* 0.82, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 5.03 (1 H, m, H-4), 4.94 (1 H, t, *J* = 9.4 Hz, H-5), 4.19 (2 H, q, *J* = 7.1 Hz, $O\underline{CH_2}CH_3$), 4.20-3.98 (4 H, m, H-2, H-7, H-8, H-8), 3.46 (1 H, dd, *J* = 9.4, 5.4 Hz, H-6), 2.46 (1 H, ddd, *J* = 12.8, 5.0, 2.1 Hz, H-3eq), 2.02 (3 H, s, OAc), 2.01 (3 H, s, OAc), 1.75 (1 H, q, *J* = 12.8 Hz, H-3ax), 1.40 (3 H, s), 1.30 (3 H, s), 1.25 (3 H, t, *J* = 7.1 Hz); IR (KBr) 3466, 2985, 2937, 1747, 1371, 1248, 1058, 942, 853 cm^{-1}; EIMS *m/z* (%) 374 (M^+, 8.8), 358 (80.6), 316 (100.0), 197 (35.5), 101 (47.1), 43(56.8); HR EIMS Calcd for $C_{16}H_{23}O_9$ (M^+ - CH_3) 359.1335, found 359.1339.

Ethyl 2,6-anhydro-3-deoxy-4,5-*O*-diacetyl-D-*gluco*-heptanoate (11). To a solution of compound **10** (65 mg, 0.17 mmol) in 10 mL of EtOAc stirred at 0 °C under nitrogen, was added H_5IO_6 (46.5 mg, 1.2 eq). The reaction mixture was stirred for 1 h at room temperature, then filtered. The filtrate was concentrated and the residue was dissolved in 10 mL of abs EtOH. To the solution $NaBH_4$ (6.5 mg, 0.17 mmol) was then added with vigorous stirring at 0 °C. The stirring was continued for 1.5 h before the reaction was quenched with 5% aqueous HCl (2 drops). The solvent was evaporated and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate, 2:1) to give product **11** (43 mg, 82 %, two steps) as a white solid. mp 93-94 °C; $[\alpha]_D$ -19.5 (*c* 0.8, CH_2Cl_2); ^1H NMR (300 MHz, $CDCl_3$) δ 4.88 (1 H, m), 4.46 (1 H, dd, *J* = 12.4, 4.3 Hz), 4.36 (1 H, dd, *J* = 12.0, 1.1 Hz), 4.20 (2 H, q, *J* = 7.1 Hz), 4.09 (1 H, dd, *J* = 12.2, 2.2 Hz), 3.48 (2 H, d, *J* = 5.3 Hz), 2.43 (1 H, ddd, *J* = 12.8, 5.2, 2.2 Hz), 2.11 (3 H, s), 2.10 (3 H, s), 1.72 (1 H, q, *J* = 12.4 Hz), 1.27 (3 H, t, *J* = 7.1 Hz); IR (neat) 3486, 2941, 1743, 1724, 1262, 1243, 1058 cm^{-1}; EIMS *m/z* (%) 305 (M^+ + 1, 18.2), 111 (81.2), 43 (100.0); HR EIMS Cacld for $C_{13}H_{21}O_8$ (M^+ + H) 305.1230, found 305.1240.

Ethyl 2,6-anhydro-3-deoxy-D-*gluco*-heptanoate (12). To a solution of the compound **11** (25 mg, 0.08 mmol) in 5 mL of ethanol (95%), was added solid K_2CO_3 (23 mg, 2 eq). The suspension was stirred at room temperature for 30 min. TLC showed the reaction was completed. The reaction mixture was filtered and concentrated, and the residue was purified by flash chromatography on a silica gel column (ethyl acetate/ethanol, 15:1) to give compound **12** as white crystals (18 mg, 87%). mp 118-119 °C; $[\alpha]_D$ +20 (*c* 0.07, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 4.18 (2 H, dq, *J* = 7.2, 2.4 Hz), 4.13 (1 H, dd, *J* = 12.0, 2.4 Hz), 3.82 (1 H, dd, *J* = 12.6, 1.2 Hz), 3.68-3.64 (2 H, m), 3.25 (2 H, d, *J*

= 4.8 Hz), 2.22 (1 H, ddd, J = 13.2, 5.4, 2.4 Hz), 1.53 (1 H, q, J = 12.0 Hz), 1.25 (3 H, t, J = 7.2 Hz); EIMS *m/z* (%) 221 (M^+ + 1), 203 (1.2), 147 (29.7), 129 (100.0), 101 (27.5), 73 (47.2), 43 (23.9); IR (KBr) 3459, 3351, 2932, 1743, 1260, 1105, 1072, 586 cm^{-1}; HR EIMS Calcd for $C_9H_{16}O_6$ (M^+) 220.0942, found 220.0917.

Ethyl 2,6-anhydro-3-deoxy-7,8-*O*-isopropylidene-D-*allo*-D-*glycero*-octanoate (*cis*-9). To a solution of compound **8** (110 mg, 0.38 mmol) in abs THF (10 mL) at -15 °C under nitrogen was slowly added a suspension of $LiAl[OC(CH_3)_3]_3H$ (119.3 mg, 1.2 eq) in abs. THF (5 mL) over a 30 min period. Stirring was continued for 8 h at -15 °C, then the reaction was destroyed by addition of water (2 mL). The aqueous layer was extracted with EtOAc (10 mL × 2) and the combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated. The residue was purified by flash chromatography (petroleum ether/ethyl acetate, 2:1) on silica gel to afford the products (83 mg, 80%), (*cis*/*trans* = 3:1). $[\alpha]^{20}_D$ +27.2 (*c* 0.42, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 4.39 (1 H, dd, J = 8.1, 2.2 Hz), 4.18 (2 H, dq, J = 7.1, 2.2 Hz), 4.22-4.13 (2 H, m), 4.05-4.00 (2 H, m), 3.68 (1 H, dd, J = 9.34, 3.1 Hz, H-5), 3.48 (1 H, t, J = 9.0 Hz, H-6), 2.23 (1 H, ddd, J = 14.3, 3.4, 2.4 Hz), 1.79 (1 H, ddd, J = 14.3, 12.0, 2.6 Hz), 1.45 (3 H, s), 1.35 (3 H, s), 1.25 (3 H, t, J = 7.1 Hz); IR (neat) 3467, 2964, 1739, 1261, 1216, 1094, 1064, 1036, 799 cm^{-1}; EIMS *m/z* (%) 291 (M^+ + 1), 275 (67.3), 233 (88.4), 197 (21.2), 101 (100.0), 43 (77.7); HR EIMS Calcd for $C_{12}H_{19}O_7$ (M^+ - CH_3) 275.1125, found 275.1140.

Ethyl 2,6-anhydro-3-deoxy-4,5:7,8-di-*O*-isopropylidene-D-*allo*-D-*glycero*-octanoate (13). To a solution of compound *cis*-**9** (52 mg, 0.18 mmol) in 10 mL of dry CH_2Cl_2, was added 2,2-dimethoxypropane (100 μL) and 10-camphorsulfonic acid (2 mg). The reaction mixture was stirred at room temperature for 2 h, then neutralized with triethylamine, and concentrated in *vacuo*. The residue was eluted from a column of silica gel with petrol ether-ethyl acetate (3:1) to give product **13** (53 mg, 91%) as a colorless oil. $[\alpha]_D$ +51.7 (*c* 0.20, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 4.43 (1 H, m), 4.30-4.23 (2 H, m), 4.20 (2 H, q, J = 7.1 Hz), 4.12-3.98 (3 H, m), 3.49 (1 H, dd, J = 9.0, 4.2 Hz), 2.38 (1 H, dt, J = 14.8, 2.4 Hz), 2.03 (1 H, ddd, J = 15.0, 12.1, 3.3 Hz), 1.50 (3 H, s), 1.46 (3 H, s), 1.38 (3 H, s), 1.37 (3 H,s), 1.26 (3 H, t, J = 7.1 Hz); IR (neat) 2987, 1759, 1218, 1072, 1052, 848 cm^{-1}; EIMS *m/z* (%) 330 (M^+, 2.6), 315 (M^+ - CH_3, 7.7), 273 (3.4), 101 (100.0), 43 (51.4); HR EIMS Calcd for $C_{16}H_{26}O_7$ (M^+) 330.1671, found 330.1703.

Ethyl 2,6-anhydro-3-deoxy-4,5-*O*-isopropylidene-D-*allo*-heptanoate (14). Using the same procedure as for the synthesis of compound **12**, **14** was obtained as a colorless oil. Yield: 82%. $[\alpha]^{20}_D$ +73.4 (*c* 0.91, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 4.40 (1 H, m), 4.28 (1 H, dd, *J* = 12.0, 2.7 Hz), 4.20 (2 H, q, *J* = 7.1 Hz , 3.87 (1 H, dd, *J* = 9.3, 4.9 Hz), 3.84 (1 H, dd, *J* = 12.1, 4.8 Hz), 3.65 (1 H, dd, *J* = 12.1, 6.3 Hz), 3.44 (1 H, ddd, *J* = 9.3, 6.3, 4.9 Hz), 2.41 (1 H, br, -OH), 2.39 (1 H, dt, *J* = 14.9, 2.7 Hz), 1.99 (1 H, ddd, *J* = 15.0, 12.0, 4.1Hz), 1.48 (3 H, s), 1.34 (3 H, s), 1.26 (3 H, t, *J* = 7.1 Hz); IR (film) 3490, 1743, 1258, 1115, 911 cm^{-1}; EIMS *m/z* (%) 261 (M^+ + 1), 245 (79.0), 203 (49.2), 185 (100.0), 171 (38.4), 111 (58.3), 85 (37.0), 43 (59.9); HR EIMS Calcd for $C_{12}H_{20}O_6$ (M^+) 260.1254, found 260.1250.

Ethyl 2,6-anhydro-3-deoxy-D-*allo*-heptanoate (15). To a solution of **14** (20 mg, 0.08 mmol) in a 9:1 (vol) EtOH/H_2O mixture (10 mL), was added Dowex 50W (H^+) (30 mg). The mixture of the reaction was stirred at 50 °C for 5 h, then filtered and the filtrate was concentrated in *vacuo*. The residue was purified by flash chromatography on a column of silica gel (ethyl acetate/ethanol, 15:1) to give compound **15** as white crystals (17 mg, 98%). mp: 107-108 °C; $[\alpha]_D$ +43.9 (*c* 0.27, $CHCl_3$); ^1H NMR (300 MHz, CD_3COCD_3) δ 4.18 (1 H, dd, *J* = 12.1, 2.5 Hz), 4.17 (2 H, q, *J* = 7.1 Hz), 4.10 (1 H, m), 3.78 (1 H, m), 3.68-3.58 (2 H, m), 3.50 (1 H, dd, J = 9.7, 3.3 Hz), 2.10 (1 H, ddd, *J* = 15.6, 3.8, 2.5 Hz), 1.76 (1 H, ddd, *J* = 15.6, 12.1, 2.5 Hz), 1.25 (3 H, t, *J* = 7.1 Hz); IR (KBr) 3446 (broad), 2926, 1730,1633, 1236, 1141, 1075, 600 cm^{-1}; EIMS *m/z* (%) 221 (M^+ + 1), 203 (11.6), 185 (10.5), 147 (84.5), 129 (76.1), 101 (48.2), 73 (100.0), 43 (71.3); HR EIMS Calcd for $C_9H_{14}O_5$ (M^+ - H_2O) 202.0837, found 202.0827.

ACKNOWLEDGMENTS

We thank the Chinese Academy of Sciences (KJ952-S1-503, KJ-95-A1-504), the National Natural Science Foundation of China (29790126, 29872049), and the Ministry of Science and Technology (970211006-6) for financial support.

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