HOMOLOGATION OF *O*-ACETYLATED METHYL HEXOPYRANOSIDES WITH A GRIGNARD C_1 REAGENT

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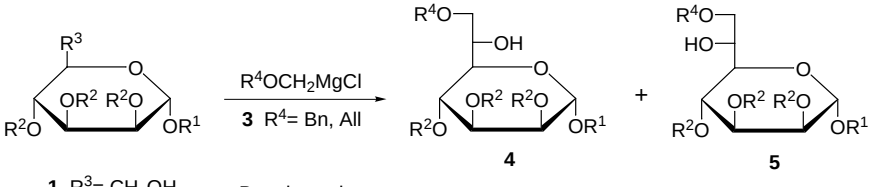
Dedicated to Professor Otakar Červinka on the occasion of his 75th birthday in appreciation of his contribution to organic stereochemistry.

Three methyl 2,3,4-tri-*O*-acetyl-α-D-hexopyranosides of the *manno*, *gluco*, and *galacto* configuration were oxidized to the corresponding methyl hexodialdo-1,5-pyranosides and then reacted with allyloxymethylmagnesium chloride. Methyl heptopyranosides of the D- and L-*glycero*-α-D-*manno*-, -α-D-*gluco*, and -α-D-*galacto* configuration were obtained in moderate yields. Migration of the 4-*O*-acetyl group in the products was observed. An interpretation of the results was proposed.

Key words: Homologation reactions; Carbohydrates; Heptoses; Heptopyranosides; Grignard reagents; Aldehydes; Additions; Allyloxymethylmagnesium chloride.

Homologation of an alkyl α-D-mannopyranoside **1** to L- and D-*glycero*-α-D-*manno*-heptopyranosides **4** and **5** can be best performed by a Grignard reaction of alkyl α-D-*manno*-hexodialdo-1,5-pyranoside (**2**) and (allyloxy)methyl- or (benzyloxy)methylmagnesium chlorides[1–4] (**3**) (Scheme 1). Both heptopyranosides are obtained in a good to very good overall yield and their separation can be readily performed by column chromatography.

This homologation method has obviously a larger potential and recently we have shown that all pentoses can be readily converted to hexoses fol-

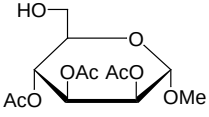


SCHEME 1

lowing essentially the same pathway[5]. Grignard methodology requires suitable protection of the hydroxy groups and, consequently, ether- or acetal-type blocking groups have been invariably used in all the reactions performed so far.

The ester-type protection is employed very often in carbohydrate chemistry. Therefore we became interested in examining the chain-elongation reaction with a Grignard C_1 reagent on methyl hexodialdo-1,5-pyranosides having OH groups at positions 2, 3, and 4 blocked with acetyl groups. We reasoned that in Grignard reactions, performed at low temperature, the aldehyde group should be distinctly more reactive than the ester groupings. There is a precedent in monosaccharide chemistry, although not connected with the aldehyde reactivity, namely, high-yield thioglycoside formation from peracetylated glycosyl thiocyanates and various Grignard reagents when the reaction was conducted at –40 °C (see ref.[6]).

For the present studies, we selected methyl α-D-*manno*- (**6**), α-D-*gluco*- (**7**), and α-D-*galacto*-pyranosides (**8**). Preparation of 2,3,4-tri-*O*-acetyl derivatives of **6**–**8** followed the conventional route (tritylation, acetylation, detritylation). Swern oxidation of **6** was accompanied by elimination reaction and led the unsaturated aldehyde[7] **9**. Dess–Martin[8] and chromium trioxide–dipyridine complex oxidations[9] proved to be practical. Particularly the Dess–Martin procedure was efficient and yielded over 70% of the desired aldehydes **10**–**12**. The reaction of aldehydes with preformed (allyloxy)methylmagnesium reagent (THF, –30 °C, 1.5 h) afforded the desired methyl heptosides in moderate yields.



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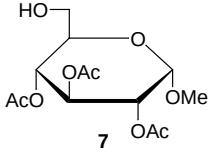

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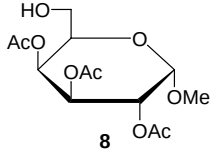

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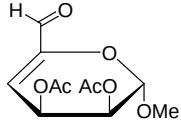

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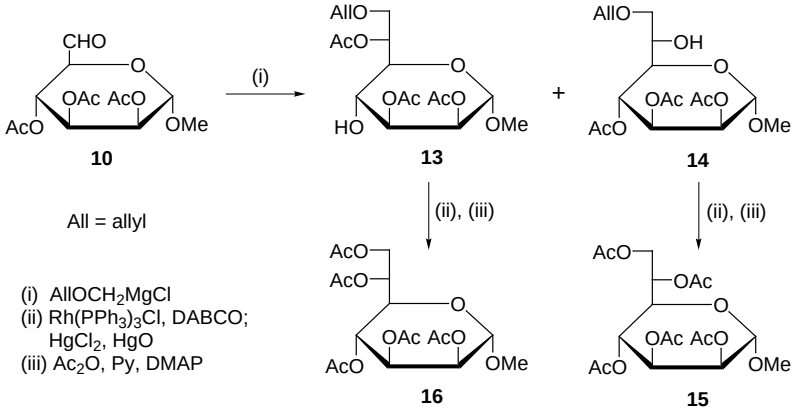
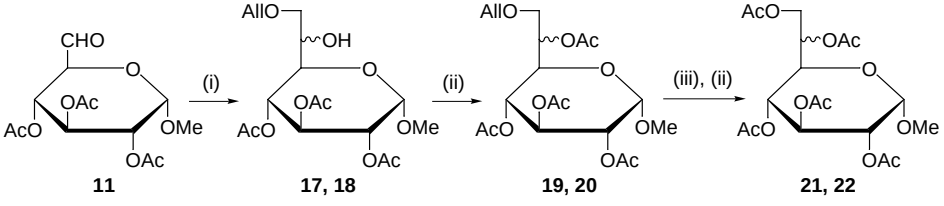
The reaction with the *manno*-aldehyde **10** yielded two readily separable products, methyl 2,3,6-tri-*O*-acetyl-7-*O*-allyl-D-*glycero*-α-D-*manno*-heptopyranoside (**13**,21%) and methyl 2,3,4-tri-*O*-acetyl-7-*O*-allyl-L-*glycero*-α-D-*manno*-heptopyranoside (**14**, 17%) (Scheme 2). The structure of **14** could be ascertained by conversion to the known methyl 2,3,4,6,7-penta-*O*-acetyl-L-*glycero*-α-D-*manno*-heptopyranoside[10] (**15**). For **13** the D-*glycero*-α-D-*manno* configuration (as well as the location of the acetyl groups) could

be derived from its ^{1}H NMR data[4] and from the spectrum of the corresponding penta-*O*-acetyl derivative **16**.



SCHEME 2

The *gluco*-aldehyde **11** yielded under similar reaction conditions (Scheme 3) an unseparable mixture of methyl tri-*O*-acetyl D- and L-*glycero*-α-D-*gluco*-heptopyranosides (**17** and **18**, 35%, 1 : 1.4). In the 500 MHz ^{1}H NMR spectrum of the mixture, the signals of **17** could be discerned, which, similarly to the case of the D-*glycero*-D-*manno* stereoisomer **13**, pointed to the migration of the 4-*O*-acetyl group to 6-OH position (for discussion *vide infra*). Acetylation of the mixture of **17** and **18** led to a new mixture, **19** and **20**, which again could not be separated. Deallylation of the latter mixture and acetylation furnished methyl 2,3,4,6,7-penta-*O*-acetyl-D- and L-*glycero*-α-D-*gluco*-heptopyranosides (**21** and **22**) whose ^{1}H NMR spectral data were very well in accord with the literature values[11].



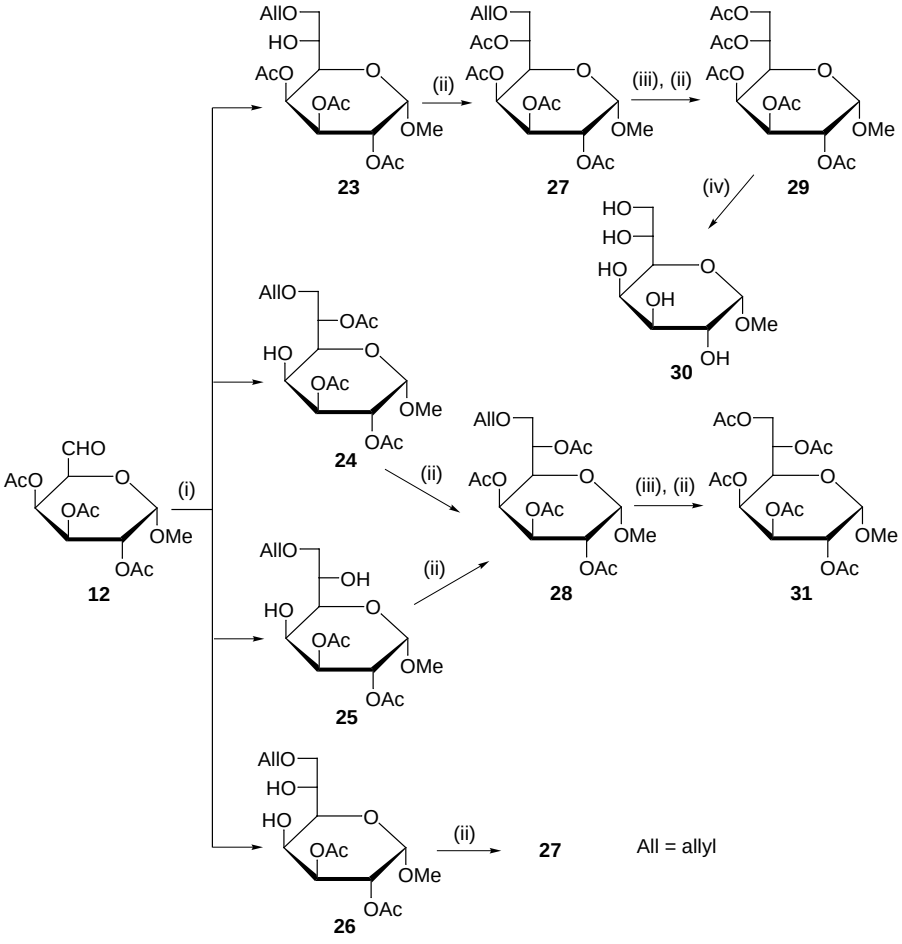
All = allyl (i) $AllOCH_2MgCl$; (ii) Ac_2O, Py, DMAP; (iii) $Rh(PPh_3)_3Cl$, DABCO; $HgCl_2$, HgO

SCHEME 3

Identification of **19** and **20** (as well as **17** and **18**) was based on ^{1}H NMR data obtained after deallylation at C-7 and subsequent acetylation at this position. Chemical shifts and coupling constants in the well separated (500 MHz)

spectra were in full accord with the data reported by Aspinall[11] for methyl 2,3,4,6,7-penta-*O*-acetyl-D- and L-*glycero*-α-D-*gluco*-heptopyranosides.

The reaction of the *galacto*-aldehyde **12** with the Grignard reagent was most complicated (Scheme 4) and furnished four products (**23**–**26**) which could be separated by column chromatography. From the analytical and spectral data, the following structures could be deduced for the products : methyl 2,3,4-tri-*O*-acetyl-7-*O*-allyl-D-*glycero*-α-D-*galacto*-heptopyranoside (**23**, 19%), methyl 2,3,6-tri-*O*-acetyl-7-*O*-allyl-L-*glycero*-α-D-*galacto*-heptopyranoside (**24**, 15%) and two C-4 deacetylated products, methyl



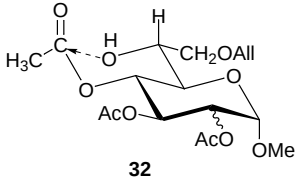
(i) $AllOCH_2MgCl$; (ii) Ac_2O, Py, DMAP; (iii) $Rh(PPh_3)_3Cl$, DABCO; $HgCl_2$, HgO; (iv) MeONa, MeOH

SCHEME 4

2,3-di-*O*-acetyl-7-*O*-allyl-L- and D-*glycero*-α-D-*galacto*-heptopyranosides (**25**, 10% and **26**, 9%). Acetylation of **23** and **26** led to the same tetraacetate **27**. And, similarly, acetylation of **24** and **25** gave the same tetraacetate **28**. Deallylation of **23** and acetylation furnished the known methyl 2,3,4,6,7-penta-*O*-acetyl-D-*glycero*-α-D-*galacto*-heptopyranoside[12] (**29**). Full deacetylation of **29** led to free methyl D-*glycero*-α-D-*galacto*-heptopyranoside[12] (**30**). Therefore, for **24**, **25**, tetraacetate **28**, and pentaacetate **31** (prepared as above) results the alternative configuration, *i.e.* L-*glycero*-α-D-*galacto*.

The experiments described above clearly demonstrated that Grignard-type elongation of the carbon atom chain in acetylated methyl hexodialdo-1,5-pyranosides is feasible. Although the yields of the chain-elongated products are moderate, the method retains its value as the substrates are cheap and can readily be obtained in any desired quantity.

The migration of the acetyl group from 4-O position to 6-O in D-*glycero*-α-D-*manno*- (**13**), D-*glycero*-α-D-*gluco*- (**17**), and L-*glycero*-α-D-*galacto*-heptopyranoside (**24**) in the presence of an excess of Grignard reagent deserves attention. The six-membered, chair-like transition states (**32**, **33**) clearly demonstrate that only for D-*glycero* stereoisomers **13** and **17** and for L-*glycero* compound **24**, the bulky allyloxymethyl group can adopt the unhindered equatorial position thus facilitating migration of the acetyl group from 4-O to 6-O position. For the other stereoisomeric forms no migration of the 4-*O*-acetyl was observed, except the deacetylation of the axial *O*-acetyl group in the *galacto* compounds.



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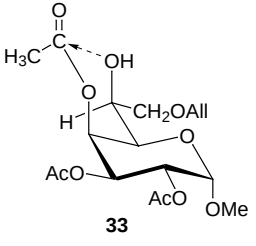

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EXPERIMENTAL

Optical rotations were measured with a Jasco DIP 360 automatic polarimeter at 20 ± 2 °C and are given in 10^{-1} deg cm^2 g^{-1}. NMR spectra were recorded with a Varian Gemini AC-200 (200 MHz) or Bruker AM-500 (500 MHz) spectrometer in $CDCl_3$ solutions with Me_4Si as internal standard unless otherwise noted. ^{13}C NMR spectra were recorded in the DEPT mode. TLC was performed on Silica Gel HF-254 ready plates and column chromatography on Silica

Gel 230–400 or 70–230 mesh (Merck). Mass spectra (LSI MS, positive mode) were recorded on an AMD-604 mass spectrometer.

Methyl 2,3,4-tri-*O*-acetyl-6-*O*-trityl-α-D-mannopyranoside[13] was detritylated with formic acid in ethyl acetate (1 : 1.5 v/v) to give[14] **6** in 76% yield. Analogously were prepared methyl 2,3,4-tri-*O*-acetyl-α-D-glucopyranoside[15] (**7**, 56%) and methyl 2,3,4-tri-*O*-acetyl-α-D-galactopyranoside[16] (**8**, 49%) from the corresponding 6-*O*-trityl derivatives[7,15].

Swern oxidation product **9** displayed analogous m.p., optical rotation, and ^{1}H NMR data as Perlin's aldehyde[7]; ^{13}C NMR 184.8 (CHO); 116.7 (C-4); 99.2 (C-1); 64.8, 63.8 (C-2, C-3); 56.1 (OMe); 20.2, 20.1 (2 × $COCH_3$).

Oxidation with Dess–Martin Periodinane Reagent – General Procedure

To a solution of alcohol (2.9 mmol) in dichloromethane (40 ml) the Dess–Martin periodinane reagent[8] (1,1,1-triacetoxy-1,1-dihydro-1,2-benziodoxol-3(1*H*)-one, 1.48 g, 3.5 mmol) was added and the solution was stirred 15 min at room temperature. The reaction mixture was diluted with dichloromethane (40 ml), and saturated aqueous solutions of $Na_2S_2O_3$ (80 ml) and $NaHCO_3$ (80 ml) were added. After the mixture was stirred for 15 min, the organic layer was separated, dried ($MgSO_4$), and concentrated to dryness. The residue was purified by chromatography in hexane–EtOAc, 1:1–1:2.

Methyl 2,3,4-tri-*O*-acetyl-α-D-mannopyranoside (**6**, 0.93 g, 2.9 mmol) was converted to methyl 2,3,4-tri-*O*-acetyl-α-D-*manno*-hexodialdo-1,5-pyranoside (**10**, 0.740 g, 80%; ^{1}H NMR: 9.63 s, 1 H, (CHO)). Methyl 2,3,4-tri-*O*-acetyl-α-D-glucopyranoside (**7**, 1.52 g, 4.75 mmol) afforded methyl 2,3,4-tri-*O*-acetyl-α-D-*gluco*-hexodialdo-1,5-pyranoside (**11**, 1.12 g, 73 %). Methyl 2,3,4-tri-*O*-acetyl-α-D-galactopyranoside (**8**, 1.14 g, 3.6 mmol) afforded methyl 2,3,4-tri-*O*-acetyl-α-D-*galacto*-hexodialdo-1,5-pyranoside (**12**, 0.91g, 80%; ^{1}H NMR: 9.55 s, 1 H (CHO)).

Oxidation with Chromium Trioxide–Dipyridine Complex – General Procedure

Chromium trioxide (3.745 g, 37.5 mmol) was addded to a solution of dry pyridine (5.8 ml) in dichloromethane (95.5 ml) to give a 10% solution of CrO_3 × 2 C_6H_5N complex[9]. The mixture was stirred with exclusion of moisture for 15–20 min at 25 °C to afford a deep-red solution. A solution of the alcohol (1.0 g, 3.1 mmol) in dichloromethane (7 ml) was added in one portion. The mixture was stirred for another 15–20 min. The solution was decanted into a separatory funnel containing an equal volume of ice-cold saturated aqueous sodium hydrogen carbonate. The combined organic layers were dried and concentrated. Toluene was added to the residue and the solution was several times evaporated under reduced pressure to remove traces of pyridine. Obtained aldehyde was used in the next step without any additional purification.

From methyl 2,3,4-tri-*O*-acetyl-α-D-mannopyranoside (**6**, 1.0 g, 3.1 mmol) was obtained methyl 2,3,4-tri-*O*-acetyl-α-D-*manno*-hexodialdo-1,5-pyranoside (**10**, 0.53 g, 53%). Methyl 2,3,4-tri-*O*-acetyl-α-D-glucopyranoside (**7**, 1.0 g, 3.1 mmol) afforded methyl 2,3,4-tri-*O*-acetyl-α-D-*gluco*-hexodialdo-1,5-pyranoside (**11**, 0.51 g, 51%) and methyl 2,3,4-tri-*O*-acetyl-α-D-galactopyranoside (**8**, 1.0 g, 3.1 mmol) gave methyl 2,3,4-tri-*O*-acetyl-α-D-*galacto*-hexodialdo-1,5-pyranoside (**12**, 0.53 g, 53%).

Methyl 2,3,6-Tri-*O*-acetyl-7-*O*-allyl-D-*glycero*-α-D-*manno*-heptopyranoside (**13**) and
Methyl 2,3,4-Tri-*O*-acetyl-7-*O*-allyl-L-*glycero*-α-D-*manno*-heptopyranoside (**14**)

To dry magnesium turnings (304 mg, 12.5 mmol) under freshly distilled THF (0.5 ml) sublimed $HgCl_2$ (50 mg) was added and a few drops of freshly distilled (allyloxy)methyl chloride[17], were added while lowering the temperature –10 to –15 °C. When the formation of the Grignard reagent started, the rest of (allyloxy)methyl chloride (1.278 g, 12 mmol) in THF (2 ml) was added at –18 to –20 °C and stirring was continued for 2 h. The temperature was then lowered to –30 °C and a solution of aldehyde **10** (0.661 g, 2.08 mmol) in absolute THF (9 ml) was added dropwise. The mixture was stirred at –20 °C for 1.5 h. A cold (0 °C) aqueous saturated solution of NH_4Cl (50 ml) was added and the products were extracted with ether. The ether extract was dried ($MgSO_4$), concentrated to dryness and the residue was chromatographed with hexane–ethyl acetate (3 : 2) to give **13** (0.174 g, 21%), m.p. 100–102 °C, $[\alpha]_D$ +37 (*c* 0.9, $CHCl_3$). ^{1}H NMR (C_6D_6): 5.77–5.69 m, 1 H (C**H**=CH_2); 5.68 ddd, 1 H, *J*(6,7A) = 4.9, *J*(6,7B) = 5.1, *J*(6,5) = 3.0 (H-6); 5.50–5.45 m, 2 H (H-2, H-3); 5.19–4.96 m, 2 H (CH=C**H**$_2$); 4.50 bs, 1 H (H-1); 4.27 t, 1 H, *J*(4,3) = 9.6, *J*(4,5) = 9.7 (H-4); 3.87 dd, 1 H (H-5); 3.81–3.71 m, 2 H (CH_2=CHC**H**$_2$O); 3.76 dd, 1 H, *J*(7A,7B) = 10.6 (H-7A); 3.63 dd, 1 H (H-7B); 2.98 s, 3 H (OCH_3); 1.75, 1.73, 1.70 3 s, 9 H (3 × $COCH_3$). ^{13}C NMR: 134.92 (CH_2=CH); 117.67 (CH_2=CH); 98.43 (C-1); 72.32 (CH_2=CHCH_2O); 67.98 (C-7); 72.11, 72.05, 71.68, 69.57, 65.95 (C-2, C-3, C-4, C-5, C-6); 55.1 (OCH_3); 21.02, 20.85, 20.75 (3 × $COCH_3$). HR MS (LSI MS), for $C_{17}H_{26}NaO_{10}$ $[M + Na]^+$ calculated: 413.14236; found: 413.14409.

The next eluted compound was **14** (0.139 g, 17.2%), oil, $[\alpha]_D$ +51 (*c* 1.01, $CHCl_3$). ^{1}H NMR: 5.94–5.85 m, 1 H (C**H**=CH_2); 5.39 dd, 1 H, *J*(3,4) = 9.7, *J*(3,2) = 3.3 (H-3); 5.36 t, 1 H (H-4); 5.30–5.17 m, 3 H (CH=C**H**$_2$, H-2); 4.74 d, 1 H, *J*(1.2) = 1.7 (H-1); 4.08–3.97 m, 2 H (CH=CHC**H**$_2$O); 3.86 dd, 1 H, *J*(5,6) < 1, *J*(5,4) = 9.0 (H-5); 3.78 ddd, 1 H, *J*(6,7B) = 7.1, *J*(6,7A) = 6.2 (H-6); 3.62 dd, 1 H, *J*(7A,7B) = 9.2 (H-7A); 3.59 dd, 1 H (H-7B); 3.38 s, 3 H (OCH_3); 2.81 d, 1 H, *J*(H,OH) = 6.1 (OH); 2.14, 2.08, 2.00 3 s, 9 H (3 × $COCH_3$). ^{13}C NMR: 134.30 (CH_2=CH); 117.26 (CH_2=CH); 98.71 (C-1); 72.35 (CH_2=CH**C**H_2O); 69.90 (C-7); 69.52, 69.07, 68.97, 67.16, 66.44 (C-2, C-3, C-4, C-5, C-6); 55.1 (OCH_3); 20.87, 20.74, 20.65 (3 × $COCH_3$). HR MS (LSI MS), for $C_{17}H_{26}NaO_{10}$ $[M + Na]^+$ calculated: 413.14236; found: 413.14344.

Methyl 2,3,6-Tri-*O*-acetyl-7-*O*-allyl-D-*glycero*-α-D-*gluco*-heptopyranoside (**17**) and
Methyl 2,3,4-Tri-*O*-acetyl-7-*O*-allyl-L-*glycero*-α-D-*gluco*-heptopyranoside (**18**)

Starting from the aldehyde **11** (0.76 g, 2.3 mmol), (allyloxy)methyl chloride (250 mg, 2.3 mmol, in 1 ml THF), and magnesium (60 mg, 25 mmol) an inseparable diastereomeric mixture of **17** and **18** (0.329 g, 35%) was obtained. Proportion of diastereomers **17** and **18** was determined to be 1 : 1.4 on the basis of ^{1}H NMR spectral signals for both H-7B and for *O*-acetyl groups.

Compound **17**. ^{1}H NMR: 5.92–5.80 m, 1 H (C**H**=CH_2); 5.32 dt, 1 H, *J*(6,5) = 2.8, *J*(6,7A) ≈ *J*(6,7B) = 4.9 (H-6); 5.29 dd, 1 H, *J*(3,4) = 9.0, *J*(3,2) = 10.1 (H-3); 5.27–5.17 m, 2 H (CH=C**H**$_2$); 4.85 d, 1 H, *J*(1.2) = 3.7 (H-1); 4.78 dd, 1 H (H-2); 4.04–3.95 m, 2 H (CH_2=CHC**H**$_2$O); 3.85 dd, 1 H, *J*(5,4) = 9.9 (H-5); 3.74 dd, 1 H, *J*(7A,7B) = 10.8 (H-7A); 3.63 dd, 1 H (H-7B); 3.36 s, 3 H (OCH_3); 2.69 bs, 1 H (OH); 2.09, 2.07, 2.06 3 s, 9 H (3 × $COCH_3$). ^{13}C NMR: 133.80 (CH=CH_2); 117.78 (CH=CH_2); 96.63 (C-1); 72.75, 71.69, 71.04, 70.65, 69.54 (C-2, C-3, C-4, C-5, C-6); 72.29 (CH_2=CHCH_2O); 67.82 (C-7).

Compound **18**. ^{1}H NMR: 5.92–5.80 m, 1 H (C**H**=CH_2); 5.52 t, 1 H, *J*(3,4) = 9.8, *J*(3,2) = 9.9 (H-3); 5.27–5.17 m, 2 H (CH=C**H**$_2$); 5.14 t, 1 H, *J*(4,5) = 9.8 (H-4); 4.96 d, 1 H, *J*(1.2) = 3.6

(H-1); 4.85 dd, 1 H (H-2); 4.04–3.95 m, 2 H (CH_2=CHC**H**$_2$O); 3.87 dd, 1 H, *J*(5,6) = 1.2 (H-5); 3.57 dd, 1 H, *J*(7A,6) = 6.6, *J*(7A,7B) = 9.2 (H-7A); 3.53 dd, 1 H, *J*(7B,6) = 7.0 (H-7B); 3.36 s, 3 H (OCH_3); 1.78 bs, 1 H (OH); 2.05, 2.04, 2.00 3 s, 9 H (3 × $COCH_3$); signals of H-4 from **17** and H-6 from **18** overlapped giving a multiplet at 3.74–3.80. ^{13}C NMR 134.24 (CH=CH_2); 117.25 (CH=CH_2); 96.73 (C-1); 72.29 (CH_2=$CHCH_2O$); 70.93, 69.98, 68.92, 67.71, 67.01 (C-2, C-3, C-4, C-5, C-6); 69.94 (C-7).

The mixture of **17** and **18** (0.1 g) was acetylated in the conventional manner (acetic anhydride (0.25 ml), pyridine (0.25 ml), and a crystal of 4-dimethylaminopyridine (DMAP), room temperature), to give an inseparable mixture of 6-*O*-acetyl derivatives **19** and **20** in a quantitative yield (0.11 g).

*Methyl 2,3,4,6-tetra-O-acetyl-7-O-allyl-*D*-glycero-*α*-*D*-gluco-heptopyranoside* (**19**). ^{1}H NMR: 5.91–5.82 m, 1 H (C**H**=CH_2); 5.44 t, 1 H, *J*(3,4) = 9.4, *J*(3,2) = 10.0 (H-3); 5.30–5.13 m, 3 H (CH=C**H**$_2$, H-6); 5.09 dd, 1 H, *J*(4,5) = 10.3 (H-4); 4.92 d, 1 H, *J*(1.2) = 3.7 (H-1); 4.83 dd, 1 H (H-2); 4.04 dd, 1 H, *J*(5,6) = 2.8 (H-5); 4.02–3.93 m, 2 H (CH_2=CHC**H**$_2$O); 3.67 dd, 1 H, *J*(7A,6) = 4.6, *J*(7A,7B) = 10.7 (H-7A); 3.60 dd, 1 H, *J*(7B,6) = 7.0 (H-7B); 3.39 s, 3 H (OCH_3); 2.08, 2.07, 2.05, 2.00 4 s, 12 H (4 × $COCH_3$).

*Methyl 2,3,4,6-tetra-O-acetyl-7-O-allyl-*L*-glycero-*α*-*D*-gluco-heptopyranoside* (**20**). ^{1}H NMR: 5.91–5.82 m, 1 H (C**H**=CH_2); 5.47 t, 1 H, *J*(3,4) = 9.8 (H-3); 5.30–5.13 m, 3 H (CH=C**H**$_2$, H-6); 5.05 t, 1 H, *J*(4,5) = 10.1 (H-4); 4.99 d, 1 H, *J*(1.2) = 3.7 (H-1); 4.90 dd, 1 H, *J*(2,3) = 10.2 (H-2); 4.15 dd, 1 H, *J*(5,6) = 1.9 (H-5); 4.02–3.93 m, 2 H (CH_2=CHC**H**$_2$O); 3.63 dd, 1 H (H-7A); 3.54 dd, 1 H, *J*(7B,6) = 6.2, *J*(7A,7B) = 9.2 (H-7B); 3.40 s, 3 H (OCH_3); 2.10, 2.07, 2.01, 2.00 4 s, 12 H (4 × $COCH_3$).

Methyl 2,3,4-Tri-*O*-acetyl-7-*O*-allyl-D-*glycero*-α-D-*galacto*-heptopyranoside (**23**),
Methyl 2,3,6-Tri-*O*-acetyl-7-*O*-allyl-L-*glycero*-α-D-*galacto*-heptopyranoside (**24**), and
Methyl 2,3-Di-*O*-acetyl-7-*O*-allyl-L- and D-*glycero*-α-D-*galacto*-heptopyranosides (**25** and **26**)

Starting from aldehyde **12** (0.963 g, 3 mmol), (allyloxy)methyl choride (335 mg, 3.13 mmol in 1 ml THF), and magnesium (77 mg, 3.2 mmol) **23** (0.225 g, 19%), **24** (0.173 g, 15%), **25** (0.119 g, 10%), and **26** (0.104 g, 8.8%) were obtained and then separated by column chromatography (hexane–ethyl acetate, 7 : 3).

Compound **23**, oil, $[\alpha]_D$ +106 (*c* 0.96, $CHCl_3$). ^{1}H NMR: 5.94–5.85 m, 1 H (CH_2=C**H**); 5.63 dd, 1 H, *J*(4,5) = 1.2, *J*(4,3) = 3.3 (H-4); 5.38 dd, 1 H, *J*(3,2) = 10.9 (H-3); 5.30–5.18 m, 2 H (C**H**$_2$=CH); 5.15 dd, 1 H, *J*(2,1) = 3.6 (H-2); 4.96 d, 1 H (H-1); 4.07–3.98 m, 2 H (C**H**$_2$-CH=CH_2); 3.97 dd, 1 H, *J*(5,6) = 9.2, *J*(5,4) = 0.9 (H-5); 3.70 dddd, 1 H, *J*(6,7A) = 2.7, *J*(6,7B) = 4.5, *J*(6,OH) = 6.8 (H-6); 3.64 dd, 1 H, *J*(7A,7B) = 9.6 (H-7A); 3.60 dd, 1 H (H-7B); 3.37 s, 3 H (OCH_3,) 2.61 d, 1H (OH); 2.16, 2.08, 1.99 3 s, 15 H (3 × $COCH_3$). ^{13}C NMR: 134.21 (CH_2=CH); 117.38 (CH_2=CH); 97.15 (C-1); 72.38 (CH_2=$CHCH_2O$); 70.22 (C-7); 68.62, 68.47, 67.87, 67.83, 67.72 (C-2, C-3, C-4, C-5, C-6); 55.24 (OCH_3); 20.81, 20.72, 20.65 (3 × $COCH_3$). HR MS, for $C_{17}H_{26}NaO_{10}$ $[M + Na]^+$ calculated: 413.14236; found: 413.13893.

Compound **24**, $[\alpha]_D$ +126 (*c* 1.1, $CHCl_3$). ^{1}H NMR: 5.93–5.82, m, 1 H (C**H**=CH_2); 5.30–5.20 m, 5 H (H-2, H-3, H-6, C**H**$_2$=CH); 4.98 d, 1 H, *J*(1,2) = 3.4 (H-1); 4.19 bs, 1 H (H-4); 4.06 bd, 1 H, *J*(5,6) = 7.3 (H-5); 4.05–3.97 m, 2 H (CH_2=CHC**H**$_2$O); 3.66 dd, 1 H, *J*(7A,6) = 3.7 (H-7A); 3.63 dd, 1 H, *J*(7B,6) = 4.7, *J*(7B,7A) = 10.8 (H-7B); 3.38 s, 3 H (OCH_3); 2.10, 2.10, 2.07 9 H (3 × $COCH_3$). ^{13}C NMR (50 MHz): 133.63 (CH_2=CH); 118.23 (CH_2=CH); 97.05 (C-1); 72.48 (CH_2=$CHCH_2O$); 71.51, 70.02, 68.60, 68.18, 67.68 (C-2, C-3, C-4, C-5, C-6); 67.62 (C-7);

55.18 (OCH_3); 21.08, 20.94, 20.83 (3 × $COCH_3$). HR MS, for $C_{17}H_{26}NaO_{10}$ $[M + Na]^+$ calculated: 413.14237; found: 413.14098.

Compound **25** was isolated as a diacetate (^{1}H NMR signals of the OAc groups at δ 2.13 and 2.09) and was characterized after additional acetylation to **28**.

Compound **26**, $[\alpha]_D$ +120 (*c* 0.94, $CHCl_3$). ^{1}H NMR: 5.95–5.85 m, 1 H (CH_2=C**H**); 5.33–5.19 m, 2 H (C**H**$_2$=CH); 5.29 dd, 1 H, *J*(3,4) = 2.9, *J*(3,2) = 10.7 (H-3); 5.26 dd, 1 H, *J*(2,1) = 3.4 (H-2); 4.97 d, 1 H (H-1); 4.38 bs, 1 H (H-4); 4.10–3.99 m, 3 H (H-6, CH_2=CHC**H**$_2$O); 3.84 bd, 1 H, *J*(5,6) = 7.7 (H-5); 3.65 dd, 1 H, *J*(6,7A) = 3.6, *J*(7A,7B) = 9.6 (H-7A); 3.61 dd, 1 H, *J*(6,7B) = 5.0 (H-7B); 3.37 s, 3 H (OCH_3); 2.60 d, *J*(OH,4) = 2.8 (OH); 2.25 d, *J*(OH,6) = 6.3 (OH); 2.10, 2.08 2 s, 6 H (2 × $COCH_3$). ^{13}C NMR (50 MHz): 134.14 (CH_2=CH); 117.57 (CH_2=CH); 97.28 (C-1); 72.34 (CH_2=$CHCH_2O$); 70.46, 70.16, 68.73, 68.52, 68.41 (C-2, C-3, C-4, C-5, C-6); 67.37 (C-7); 55.19 (OCH_3); 20.94, 20.87 (2 × $COCH_3$).

Methyl 2,3,4,6,-Tetra-*O*-acetyl-7-*O*-allyl-D-*glycero*-α-D-*galacto*-heptopyranoside (**27**)

Compound **23** (0.1 g, 0.26 mmol) was acetylated with acetic anhydride (0.25 ml, 27 mmol), pyridine (0.25 ml, 24 mmol), and a small crystal of DMAP to give 0.1 g (90%) of **27**. Acetylation of **26** (50 mg, 0.14 mmol) as above gave **27** (60 mg, 96%).

Compound **27**, $[\alpha]_D$ +87 (*c* 0.4, $CHCl_3$). ^{1}H NMR (C_6D_6): 5.79 dd, 1 H, *J*(3,4) = 3.5, *J*(3,2) = 10.5 (H-3); 5.77 dd, 1 H, *J*(4,5) = 1.1 (H-4); 5.76–5.68 m, 1 H (C**H**=CH_2); 5.51 dd, 1 H, *J*(2,1) = 3.5 (H-2); 5.41 ddd, 1 H, *J*(6,7A) = 4.1, *J*(6,7B) = 2.1, *J*(6,5) = 9.9 (H-6); 5.17–4.97 m, 2 H (C**H**$_2$=CH); 5.11 d, 1 H (H-1); 4.28 dd, 1 H (H-5); 3.80–3.64 m, 2 H (CH_2=CHC**H**$_2$O); 3.62 dd, 1 H, *J*(7A,7B) = 11.1 (H-7A); 3.53 dd, 1 H (H-7B); 3.08 s, 3 H (OCH_3); 1.84, 1.75, 1.73, 1.67 4 s, 12 H (4 × $COCH_3$). ^{13}C NMR (C_6D_6): 134.89 (CH_2=CH); 116.5 (CH_2=CH); 97.69 (C-1); 72.18 (CH_2=$CHCH_2O$); 68.99, 68.97, 68.10, 67.69, 66.09 (C-2, C-3, C-4, C-5, C-6); 68.87 (C-7); 55.08 (OCH_3); 20.49, 20.34, 2 × 20.30 (4 × $COCH_3$).

Methyl 2,3,4,6,-Tetra-*O*-acetyl-7-*O*-allyl-L-*glycero*-α-D-*galacto*-heptopyranoside (**28**)

Compound **24** (0.1 g, 0.26 mmol) was acetylated with acetic anhydride (0.25 ml, 27 mmol), pyridine (0.25 ml, 24 mmol), and a small crystal of DMAP to give 0.1 g (90%) of **28**. Acetylation of **25** (45 mg, 0.13 mmol) as above gave **28** (45 mg, 81%).

Compound **28**, $[\alpha]_D$ +127 (*c* 1.69, $CHCl_3$). ^{1}H NMR (C_6D_6): 5.84 dd, 1 H, *J*(4,5) = 1.0, *J*(4,3) = 3.3 (H-4); 5.80–5.72 m, 1 H (CH_2=C**H**); 5.77 dd, 1 H, *J*(3,2) = 10.9 (H-3); 5.56 dd, 1 H, *J*(2,1) = 3.6 (H-2); 5.53 ddd, 1 H (H-6); 5.13–4.99 m, 2 H (C**H**$_2$=CH); 5.11 d, 1 H (H-1); 4.33 dd, 1 H, *J*(5,4) = 0.7, *J*(5,6) = 8.3 (H-5); 3.75–3.64 m, 2 H (CH_2=CHC**H**$_2$O); 3.45 dd, 1 H, *J*(7A,6) = 3.4, *J*(7A,7B) = 11.0 (H-7A); 3.40 dd, 1 H, *J*(7B,6) = 4.3 (H-7B); 3.05 s, 3 H (OCH_3); 1.74, 1.73, 1.65, 1.60 4 s, 12 H (4 × $COCH_3$). ^{13}C NMR (C_6D_6): 134.51 (CH_2=CH); 117.46 (CH_2=CH); 97.43 (C-1); 72.35 (CH_2=$CHCH_2O$); 71.50, 68.78, 68.73, 68.61, 68.14 (C-2, C-3, C-4, C-5, C-6); 68.48 (C-7); 54.74 (OCH_3); 20.55, 20.35, 20.27, 20.09 4 s (4 × $COCH_3$).

Cleavage of Allyl Protecting Group – General Procedure

To a solution of the heptopyranoside derivative (20 mg, 0.05 mmol) in a mixture of ethanol (1.8 ml), benzene (0.3 ml) and water (0.1 ml) 1,4-diazabicyclo[2.2.2]octane (DABCO, 1.2 mg, 0.01 mmol) was added and the solution was heated to 80 °C. Wilkinson's catalyst (3.2 mg) was added, the mixture was refluxed for 3 h and left at room temperature overnight. The mixture was filtered and the filtrate was concentrated under lowered pressure. The re-

maining oil was dissolved in acetone–water (15 : 1), and to this solution HgO (12 mg, 0.06 mmol) and $HgCl_2$ (15 mg, 0.06 mmol) were added. The suspension was stirred for 30 min at room temperature, filtered and the filtrate was concentrated. The products were chromatographed with light petroleum–ethyl acetate (7 : 3).

Heptoside derivative **14** (20 mg, 0.05 mmol) yield a product (16 mg, 88%) which was acetylated under standard conditions to give methyl 2,3,4,6,7-penta-*O*-acetyl-L-*glycero*-α-D-*manno*-heptopyranoside (**15**, 11 mg, 59%), $[\alpha]_D$ +20 (*c* 1.08, $CHCl_3$); ref[10] $[\alpha]_D$ +20 (*c* 1.0, $CHCl_3$).

Methyl 2,3,4,6,7-penta-O-acetyl-D-glycero-α-D-manno-heptopyranoside (**16**). Heptoside derivative **13** (20 mg, 0.05 mmol) was converted to **16** (18 mg, 95%), $[\alpha]_D$ + 54 (*c* 0.79, $CHCl_3$). ^{1}H NMR: 5.30 dd, 1 H, *J*(3,2) = 3.2, *J*(3,4) = 9.7 (H-3); 5.26 t, 1 H, *J*(4,5) = 9.5 (H-4); 5.22–5.17 m, 2 H (H-2, H-6); 4.68 d, 1 H, *J*(1,2) = 1.5 (H-1); 4.44 dd, 1 H, *J*(7A,6) = 3.6, *J*(7A,7B) = 12.0 (H-7A); 4.27 dd, 1 H, *J*(7B,6) = 7.4 (H-7B); 3.97 dd, 1 H *J*(5,6) = 2.9, (H-5); 3.39 s, 3 H (OCH_3); 2.14, 2 × 2.08, 2.07, 1.99 5 s, 15 H (5 × $COCH_3$). ^{13}C NMR: 98.33 (C-1); 70.28, 69.76, 69.36, 69.14, 66.73 (C-2, C-3, C-4, C-5, C-6); 61.70 (C-7); 55.19 (OCH_3); 2 × 20.82, 2 × 20.72. 20.63 (5 × $COCH_3$). HR MS (LSI MS), for $C_{18}H_{26}NaO_{12}$ $[M + Na]^+$ calculated: 457.13220; found: 457.13226.

Methyl 2,3,4,6,7-penta-O-acetyl-D- and L-glycero-α-D-gluco-heptopyranosides (**21** and **22**). A mixture of the heptoside derivatives **17** and **18** (40 mg) was converted to the mixture (1 : 1) of peracetylated products **21** and **22** (32 mg, 82%), $[\alpha]_D$ +101 (*c* 0.9, $CHCl_3$).

Methyl 2,3,4,6,7-penta-O-acetyl-D-glycero-α-D-galacto-heptopyranoside (**29**). The heptoside derivative **23** (145 mg, 0.37 mmol) was converted to **29** (160 mg, 99%), m.p. 145–148 °C, $[\alpha]_D$ +139 (*c* 1.15, $CHCl_3$); ref[12] m.p. 156 °C, $[\alpha]_D$ +138 ($CHCl_3$). ^{1}H NMR: 5.48 dd, 1 H, *J*(4,3) = 3.4, *J*(4,5) = 1.3 (H-4); 5.39 dd, 1 H, *J*(3,2) = 10.9 (H-3); 5.15 dd, 1 H, *J*(2,1) = 3.6 (H-2); 5.16 ddd, 1 H, *J*(6,5) = 9.9, *J*(6,7A) = 2.1, *J*(6,7B) = 4.1 (H-6); 5.03 d, 1 H (H-1); 4.54 dd, 1 H, *J*(7A,7B) = 12.3 (H-7A); 4.21 dd, 1 H (H-5); 4.15 dd, 1 H (H-7B); 3.42 s, 3 H (OCH_3); 2.12, 2.11, 2.10, 2.02, 2.00 5 s, 15 H (5 × $COCH_3$). ^{13}C NMR: 97.38 (C-1); 68.06, 67.55, 67.40, 66.94, 65.68 (C-2, C-3, C-4, C-5, C-6); 62.26 (C-7); 55.49 (OCH_3); 20.79, 20.69, 20.63, 20.60, 20.59 (5 × $COCH_3$). HR MS (LSI MS), for $C_{18}H_{26}NaO_{12}$ $[M + Na]^+$ calculated: 457.13220; found: 457.13457.

Methyl 2,3,4,6,7-penta-O-acetyl-L-glycero-α-D-galacto-heptopyranoside (**31**). Heptoside derivative **24** (33 mg, 0.08 mmol) was converted to **31** (19 mg, 53%), $[\alpha]_D$ +87 (*c* 0.44, $CHCl_3$). ^{1}H NMR: 5.47 dd, 1 H, *J*(4,3) = 3.3, *J*(4,5) = 1.1 (H-4); 5.33 dd, 1 H, *J*(3,2) = 10.9 (H-3); 5.25 ddd, 1 H, *J*(6,5) = 7.8, *J*(6,7A) = 3.4, *J*(6,7B) = 5.9 (H-6); 5.15 dd, 1 H, *J*(2,1) = 3.7 (H-2); 5.01 d, 1 H (H-1); 4.38 dd, 1 H, *J*(7A,7B) = 12.3 (H-7A); 4.11 dd, 1 H (H-5); 3.90 dd, 1 H (H-7B); 3.40 s, 3 H (OCH_3); 2.18, 2 × 2.08, 2.06, 1.98 4 s, 15 H (5 × $COCH_3$). ^{13}C NMR: 97.05 (C-1); 69.87, 67.98, 67.97, 67.71, 67.10 (C-2, C-3, C-4, C-5, C-6); 62.05 (C-7); 55.37 (OCH_3); 20.81, 20.77, 20.64, 20.60, 20.59 (5 × $COCH_3$). HR MS (LSI MS), for $C_{18}H_{26}NaO_{12}$ $[M + Na]^+$ calculated: 457.13220; found: 457.13152.

Methyl D-*glycero*-α-D-*galacto*-Heptopyranoside (**30**)

To a solution of compound **29** (121 mg, 0.28 mmol) in MeOH (3 ml) 1 M methanolic NaOMe (0.3 ml) was added and the mixture was stirred at room temperature overnight. The mixture was neutralized with cation-exchange resin (H^+), filtered, and concentrated to give the deacetylated product **30** in a quantitative yield (62 mg), $[\alpha]_D$ +165 (*c* 0.9, H_2O); ref.[12] $[\alpha]_D$ +178 (*c* 1.0, H_2O). ^{13}C NMR (D_2O): 99.54 (C-1); 69.73, 69.05, 68.21, 68.17 (C-2, C-3, C-4, C-5, C-6); 63.05 (C-7).

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