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NEW SYNTHESES OF D- AND L-*glycero*-D-*manno*-HEPTOSES*

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ABSTRACT

Three methods for the synthesis of the title compounds starting from benzyl 2,3,4-tri-*O*-benzyl-α-D-*manno*-hexodialdo-1,5-pyranoside (**7**) have been elaborated. Conversion of **7** into the cyanohydrin followed by reduction to give the amine and then deamination gave a derivative of L-*glycero*-D-*manno*-heptose in low yield. Condensation of **7** with 2-methylfuran gave two stereoisomeric 6-*C*-(2-methyl-5-furyl) derivatives. The preponderant stereoisomer was ozonised and then reduced to give a derivative of D-*glycero*-D-*manno*-heptose. Condensation of **7** with allyloxymethylmagnesium chloride gave derivatives of both heptoses in good yield and with an L-*glycero*–D-*glycero* ratio of 3.2:1. Deprotection of these derivatives gave the heptoses in high yield.

INTRODUCTION

D- (**1**) and L-*glycero*-D-*manno*-Heptose (**2**) are components of many bacterial polysaccharides[1]. Although their biological function is not fully clear[2], there are indications that the "core" region (where they usually occur) can induce immunological reactions[3]. In order to examine the biological properties in more detail, it is necessary to have both heptoses in sufficient amounts. Since their isolation from natural sources is laborious and yields only small amounts, convenient syntheses have been developed.

Two syntheses of **1** have been described starting from D-altrose[4,5] and a synthesis from D-glyceraldehyde and furan has been reported[6]. A synthesis of **2** from L-galactose has been proposed[7] and a second method has been presented recently by Paulsen *et al.*[8]. All of these methods are tedious or require substrates that are not easily available. We have explored new routes to **1** and **2** starting from D-mannose. C_1-Homologation of monosaccharides from C-1 is a well-established procedure and such methods have been employed[4,5,7,8] for the synthesis of **1** and **2**. We have used a C_1-extension from C-6 of D-mannose.

*Dedicated to Professor N. K. Kochetkov.

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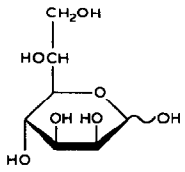
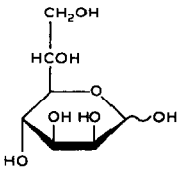
RESULTS AND DISCUSSION

The three methods developed started from benzyl 2,3,4-tri-*O*-benzyl-α-D-*manno*-hexodialdo-1,5-pyranoside (**7**). Conversion of benzyl α-D-mannopyranoside (**3**) into the 6-*O*-trityl derivative **4** (85%) followed by benzylation (→**5**) and removal of the trityl group afforded **6**[9] (61%), Swern oxidation of which furnished **7**.



1



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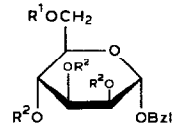
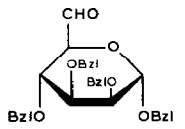


3 $R^1 = R^2 = H$
4 $R^1 = Tr, R^2 = H$
5 $R^1 = Tr, R^2 = Bzl$
6 $R^1 = H, R^2 = Bzl$



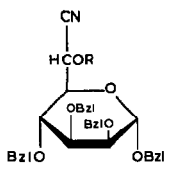
7

Treatment of **7** with hydrogen cyanide and pyridine afforded the stereoisomeric cyanohydrins **8** (34%) and **9** (19%), which were readily separated by flash chromatography and characterised as the acetates **10** and **11**, respectively. It was shown subsequently that **8** had the L-*glycero*-D-*manno* configuration. However, **9** was not the D-*glycero*-D-*manno* isomer, but a structure with inverted configuration at C-5. This conclusion was based on the 500-MHz ^{1}H-n.m.r. spectrum of the acetate **11**, which displayed coupling constants ($J_{1,2}$ 8.2, $J_{2,3}$ 2.0, $J_{3,4} \approx J_{4,5}$ = 3.0 Hz) compatible with a $^1C_4$ chair form. This product was not examined further and its configuration at C-6 remains unknown. Moreover, the D-*glycero*-D-*manno* isomer of **8** was not detected among the products of reaction.

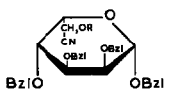
Reduction of the cyano group in **8** gave the amine **12** (characterised as the di-*N*,*O*-acetyl derivative **13**), deamination of which with nitrous acid gave **14** (36%) and **16** (18%). Compound **14**, which was characterised as diacetate **15**, was hydrogenolysed (H_2, Pd/C) to give L-*glycero*-D-*manno*-heptose which was identified by conversion into the diethyl dithioacetal **17**.

The structure of **16** was assigned, on the basis of i.r. and ^{1}H-n.m.r. data, as benzyl 2,3,4-tri-*O*-benzyl-7-deoxy-α-D-*manno*-heptopyranosid-6-ulose; the formation of a methyl ketone on deamination of an ethanolamine system was not unexpected[10].

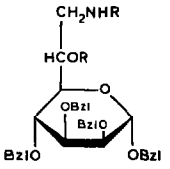
Acid-catalysed reaction of **7** with 2-methylfuran[6,11] afforded a mixture of stereoisomeric 6-*C*-(2-methyl-5-furyl) derivatives isolated as the 6-acetates **18** (4.1%) and **19** (25.7%). The furan ring in **19** was degraded by ozonolysis[12] and decomposition of the ozonide with triphenylphosphine. The resulting aldehyde was reduced *in situ* to give a primary alcohol which was acetylated and isolated (11%) by chromatography. This product (**20**) was identical with benzyl 6,7-di-*O*-acetyl-



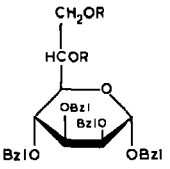
8 R = H
10 R = Ac



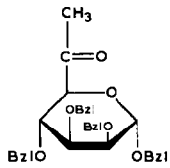
9 R = H
11 R = Ac



12 R = H
13 R = Ac



14 R = H
15 R = Ac



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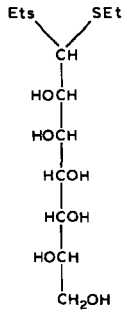

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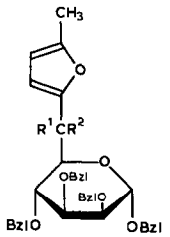
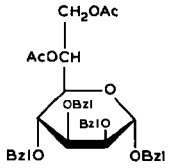


18 R^1 = OAc, R^2 = H
19 R^1 = H, R^2 = OAc



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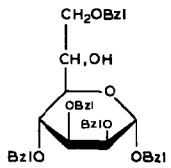

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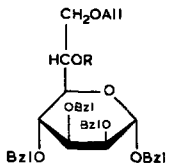
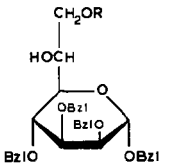


22 R = H
24 R = Ac



23 R = Allyl
25 R = H

2,3,4-tri-*O*-benzyl-α-D-*glycero*-D-*manno*-heptopyranoside described below. The low yield of **18** did not allow its conversion into L-*glycero*-D-*manno*-heptose.

The third approach involved the direct conversion CHO→CHOH-CH_2OH, which was effected by reaction of **7** with an alkoxymethyl Grignard reagent[13,14], a procedure not applied hitherto in carbohydrate synthesis.

Condensation of **7** with benzyloxymethylmagnesium chloride gave 65% of a mixture (**21**) of stereoisomeric benzyl 2,3,4,7-tetra-*O*-benzyl-α-D- and -β-L-*glycero*-D-*manno*-heptopyranosides in the proportions 1:3 (determined by h.p.l.c.), but a suitable preparative scale fractionation of this mixture was not found. However, condensation of **7** with allyloxymethylmagnesium chloride gave 67.5% of a mixture of benzyl 7-*O*-allyl-2,3,4-tri-*O*-benzyl- β-L- (**22**) and -α-D-*glycero*-D-*manno*-heptopyranoside (**23**) in the proportions 3.2:1, which could be fractionated readily by flash chromatography. Compound **22** was converted into the 6-acetate **24**.

Deallylation of **22** and **23** gave the respective diols **14** and **25** which were

acetylated to give **15** and **20**, respectively. Hydrogenolysis of **14** and **25** then afforded the parent heptoses in quantitative yields, each of which was identified as the diethyl dithioacetal.

The above three methods for the synthesis of **1** and/or **2** are simple and can be performed on a relatively large scale, although the yields of the first two syntheses are rather low. The preponderant product of the third method, namely, L-*glycero*-D-*manno*-heptose, was that predicted on the basis of Cram's cyclic model of 1,2-asymmetric induction[15].

EXPERIMENTAL

General methods. — T.l.c. was performed on silica gel G (Merck) and column chromatography on silica gel (40–63 μm, Merck). ^{1}H-N.m.r. spectra were recorded with Jeol JNM-4H-100 (100 MHz), Varian XL-200 (200 MHz), Bruker WH-400 (400 MHz), and WM-500 (500 MHz) spectrometers for solutions in $CDCl_3$ (internal Me_4Si). I.r. spectra were recorded with a Beckman IR 4240 spectrophotometer. Optical rotations were measured with a Perkin–Elmer 141 automatic polarimeter. Acetylations were performed conventionally with acetic anhydride and pyridine. For hydrogenolysis, 10% Pd/C (Degussa) was used.

*Benzyl α-*D*-mannopyranoside* (**3**). — An improved procedure was used which increased the yield from 42[16,17] to 66%. To a stirred suspension of dry D-mannose (200 g) in benzyl alcohol (850 mL) at 0° was added, dropwise, acetyl chloride (50 mL). The mixture was stirred at room temperature for 4 days and then poured into ether (10 L), the precipitate was collected, the ethereal solution was concentrated to dryness, and the excess of benzyl alcohol was evaporated under vacuum. Ether (~3 L) was added to the residue, and the precipitate was collected. A solution of the combined precipitates (~270 g) in hot water (200 mL) was cooled to room temperature and extracted with ether in order to remove benzyl acetate and benzyl alcohol. The aqueous solution was then extracted continuously with ethyl acetate to afford **3** (198 g, 66%), m.p. 128–129° (from ethyl acetate), $[\alpha]_D^{18}$ +73° (*c* 1.4, water); lit.[17] m.p. 130–131; lit.[16] $[\alpha]_D$ +74° (*c* 1.3, water).

*Benzyl 6-*O*-trityl-α-*D*-mannopyranoside* (**4**). — To a solution of **3** (55 g) in pyridine (150 mL) were added trityl chloride (63 g) and a few crystals of 4-dimethylaminopyridine. The mixture was kept at 40° until t.l.c. (ethyl acetate–methanol, 9:1) showed the disappearance of **3** (3 days). The solution was then poured into ice–water (2 L) and extracted four times with toluene. The combined extracts were washed with aqueous cupric sulfate and water, dried ($MgSO_4$), and concentrated under vacuum. The resulting amorphous solid was washed with light petroleum (b.p. 60–80°) and dried *in vacuo* to give **4** (89 g, 85%), $[\alpha]_D^{16}$ +26° (*c* 2.8, chloroform).

Anal. Calc. for $C_{32}H_{32}O_6$: C, 75.0; H, 6.3. Found: C, 75.6; H, 6.3.

*Benzyl 2,3,4-tri-*O*-benzyl-α-*D*-mannopyranoside* (**6**). — To a stirred suspension of sodium hydroxide (120 g) in methyl sulfoxide (300 mL) kept in an ice–water

bath was gradually added a solution of **4** (89 g) in methyl sulfoxide (120 mL). After a few minutes of stirring, benzyl chloride (90 mL) was added, and, after storage for 1.5 h at room temperature, the mixture was poured into ice–water and extracted with ether. The combined extracts were washed with water, dried, and concentrated to yield crude, syrupy **5** (148 g) slightly contaminated with dibenzyl ether. To a solution of this product (148 g) in 1,4-dioxane (200 mL) and methanol (400 mL) was added trifluoroacetic acid (18 mL), and the mixture was boiled under reflux until t.l.c. (light petroleum–ether–methanol, 60:40:3) showed the disappearance of **5**. The solution was then neutralised (K_2CO_3), filtered, and concentrated to dryness. Column chromatography of the residue on silica gel (Macherey–Nagel, 35–70 mesh), using a gradient light petroleum→light petroleum–ethyl acetate (1:1), gave **6** (57.5 g, 61% from **4**), isolated as a syrup, $[\alpha]_D^{17}$ +46° (*c* 1.8, chloroform); lit.[9] $[\alpha]_D^{20}$ +55° (*c* 1.5, chloroform).

Anal. Calc. for $C_{34}H_{36}O_6$: C, 75.5; H, 6.7. Found: C, 75.0; H, 6.9.

*Benzyl 2,3,4-tri-*O*-benzyl-β-*L-glycero-D-manno-*heptopyranurononitrile* (**8**) *and its* D(L)-glycero-L-gulo *stereoisomer* (**9**). — To a solution of oxalyl chloride (4.1 mL) in dry dichloromethane (100 mL) at −60° was added a mixture of methyl sulfoxide (6.9 mL) and dichloromethane (50 mL), followed after a few minutes by dropwise addition of a solution of **6** (22 g) in dichloromethane (50 mL). The mixture was stirred for 30 min, triethylamine (28.5 mL) was added, stirring at −60° was continued for 15 min, and the mixture was then allowed to attain room temperature. The mixture was diluted with water (100 mL), and the dichloromethane layer was washed twice with water, dried, and concentrated to give syrupy benzyl 2,3,4-tri-*O*-benzyl-α-D-*manno*-hexodialdo-1,5-pyranoside (**7**; 22 g, 100%), which contained no trace of **6** (t.l.c.; light petroleum–ether–methanol, 60:40:3), $[\alpha]_D^{16}$ +47° (*c* 6.5, chloroform); ν_{max} 1750 cm^{-1}. ^{1}H-N.m.r. data: δ 10.1 (bs, 1 H, CHO), 7.3 (m, 20 H, 4 Ph), 4.4–5.2 (m, 9 H, H-1 and 4 PhCH_2), 3.6–4.1 (m, 4 H, H-2,3,4,5).

A solution of **7** (8.14 g) in pyridine (13 mL) at 0° was treated with hydrogen cyanide (1.5 mL). After storage for 2 h at 0°, the mixture was allowed to attain room temperature. T.l.c. (light petroleum–ether–methanol, 60:40:3) after 24 h revealed the absence of **7**. The mixture was poured into ice–water and extracted with chloroform, and the extract was washed with water, dried, and concentrated to dryness. Flash chromatography (light petroleum–ether–methanol, 80:20:3) of the residue (8.2 g) gave, first, **9** (1.6 g, 18.7%). The 6-acetate (**11**) of **9** had m.p. 101–102° (from light petroleum–ethyl acetate), $[\alpha]_D^{11}$ −21° (*c* 1, chloroform). ^{1}H-N.m.r. (500 MHz) data: δ 5.63 (d, 1 H, $J_{5,6}$ 8.4 Hz, H-6), 4.96 (d, 1 H, $J_{1,2}$ 8.2 Hz, H-1), 4.2–4.9 (s and ABq, 8 H, 4 PhCH_2), 4.23 (dd, 1 H, $J_{2,3}$ 2.0 Hz, H-2), 3.79 (t, 1 H, $J_{3,4} \approx J_{4,5} \approx$ 3.0 Hz, H-4), 3.67 (dd, 1 H, H-3), 3.64 (dd, 1 H, H-5), 2.1 (s, 3 H, OAc).

Anal. Calc. for $C_{37}H_{37}NO_7$: C, 73.1; H, 6.1; N, 2.3. Found: C, 72.6; H, 6.2; N, 2.3.

Eluted second was **8** (2.9 g, 34%), $[\alpha]_D^{11}$ +59° (*c* 1.1, chloroform); ν_{max} 2240 cm^{-1} (CN).

Anal. Calc. for $C_{35}H_{35}NO_6$: C, 74.3; H, 6.2; N, 2.5. Found: C, 74.0; H, 6.2; N, 2.4.

The 6-acetate (**10**) of **8** had m.p. 107–108° (from light petroleum–ethyl acetate), $[\alpha]_D^{11}$ +82° (*c* 1.2, chloroform). ^{1}H-N.m.r. (400 MHz) data: δ 5.74 (d, 1 H, $J_{6,5}$ 1.5 Hz, H-6), 5.03 (d, 1 H, $J_{1,2}$ 1.6 Hz, H-1), 4.4–4.9 (s and ABq, 8 H, 4 PhCH_2), 3.99 (dd, 1 H, $J_{3,2}$ 2.7 Hz, $J_{3,4}$ 9.1 Hz, H-3), 3.97 (dd, 1 H, $J_{5,4}$ 9.1 Hz, H-5), 3.93 (dd, 1 H, H-4), 3.82 (dd, 1 H, H-2), and 2.1 (s, 3 H, OAc).

Anal. Calc. for $C_{37}H_{37}NO_7$: C, 73.1; H, 6.1; N, 2.3. Found: C, 73.3; H, 6.1; N, 2.1.

*Benzyl 2,3,4-tri-*O*-benzyl-β-*L-glycero-D-manno-*heptopyranoside* (**14**). — To a filtered solution of lithium aluminum hydride (0.25 g) in oxolane (5 mL) at 0° was added, dropwise, a solution of **8** (0.82 g) in oxolane (8 mL). After ~10 min, the reaction was complete (t.l.c.; light petroleum–ether–methanol, 50:50:5). Water (0.8 mL) and aqueous 15% sodium hydroxide (0.2 mL) were then added, and the mixture was filtered, dried, and concentrated to yield crude **12** (0.8 g) which gave an oily diacetyl derivative **13**. ^{1}H-N.m.r. (100 MHz) data: *inter alia,* δ 1.92 and 2.18 (2 s, 6 H, NAc and OAc).

To a solution of crude **12** (0.82 g) in 1,4-dioxane (22 mL) at 0° was added a solution of sodium nitrite (2 g) in an acetate buffer (pH 4.6; 16.4 mL of 0.2M acetic acid and 3.4 mL of 0.2M sodium acetate). The mixture was stirred at room temperature for 5 h, aqueous 10% sodium carbonate (10 mL) was added, the mixture was extracted with chloroform, and the extract was dried and concentrated. Flash chromatography (light petroleum–ether–methanol, 60:40:2) of the residue gave, first, **16** (0.15 g, 18.3%), isolated as a thick syrup, $[\alpha]_D^{27}$ +86.5° (*c* 1, chloroform); ν_{max} 1750 cm^{-1}. ^{1}H-N.m.r. (500 MHz) data: δ 4.98 (d, 1 H, $J_{1,2}$ 2.4 Hz, H-1), 4.49–4.8 (s and ABq, 8 H, 4 PhCH_2), 4.09 (m, 2 H, H-4,5), 3.96 (dd, 1 H, $J_{2,3}$ 2.7, $J_{3,4}$ 7.7 Hz, H-3), 3.79 (t, 1 H, H-2), 2.17 (s, 3 H, H-7).

Anal. Calc. for $C_{35}H_{36}O_6$: C, 76.0; H, 6.6. Found: C, 75.6; H, 6.7.

Eluted second was **14** (0.29 g, 35.6%), isolated as a syrup, $[\alpha]_D^{27}$ +17° (*c* 0.9, chloroform). The diacetate (**15**) of **14** had $[\alpha]_D^{27}$ +20° (*c* 1, chloroform). ^{1}H-N.m.r. (100 MHz) data: δ 5.8 (bt, 1 H, H-6), 4.5–5.2 (m, 11 H, H-1,6,6′, 4 PhCH_2), 3.9–4.2 (m, 4 H, H-2,3,4,5), 2.0, 2.2 (2 s, 6 H, 2 OAc).

Anal. Calc. for $C_{39}H_{42}O_9$: C, 71.5; H, 6.5. Found: C, 71.4; H, 6.5.

Debenzylation of **14** and reaction of the product with ethanethiol in conc. hydrochloric acid gave L-*glycero*-D-*manno*-heptose diethyl dithioacetal (**17**), m.p. 201–202°, $[\alpha]_D^{18}$ +11° (*c* 1, pyridine); lit.[7] m.p. 202–203°, $[\alpha]_D^{26}$ +10.2° (*c* 1.2, pyridine).

Anal. Calc. for $C_{11}H_{24}O_6S_2$: C, 41.8; H, 7.6; S, 20.3. Found: C, 41.7; H, 7.7; S, 20.3.

*Benzyl 6-*O*-acetyl-2,3,4-tri-*O*-benzyl-6-*C*-(2-methyl-5-furyl)-α-*D-glycero-D-manno-*hexopyranoside* (**18**) *and its* L-glycero-D-manno *stereoisomer* (**19**). — To a solution of **7** (1.73 g, prepared as described above) in 2-methylfuran (6 mL) was added a solution of chloroacetic acid (0.83 g) in 2-methylfuran (4 mL). After 12 h,

the mixture was diluted with ether and neutralised with aqueous 10% sodium hydrogencarbonate, and the organic phase was dried and concentrated. The oily residue (1.75 g) was treated with acetic anhydride and pyridine to give a mixture of **18** and **19**. ^{1}H-N.m.r. (200 MHz) data: *inter alia*, δ 6.52 and 6.41 (d and s, 0.75 and 0.25 H, H-6 of **18** and **19**), 6.35 and 6.28 (2 d, 1 H, H-4 of 2-methylfuryl residue), 5.9 (m, 1 H, H-3 of 2-methylfuryl residue), 5.04 (s, 1 H, H-1), 2.24 and 2.21 (2 s, 3 H, Me of 2-methylfuryl residue), 2.07 and 2.18 (2 s, 3 H, OAc). Integration of the signals of the methyl group (or H-3 or H-4) of the 2-methylfuryl residue indicated a 3:1 ratio of **18** and **19**. Flash chromatography (light petroleum–ether–methanol, 80:20:2) of this mixture gave **18** (0.55 g, 25.7%), **19** (0.09 g, 4.1%), and a mixture (0.11 g) containing mostly **19**. Compound **18**, isolated as a syrup, had $[\alpha]_D^{18}$ +38° (*c* 1, chloroform).

Anal. Calc. for $C_{41}H_{42}O_8$: C, 74.3; H, 6.4. Found: C, 74.8; H, 6.2.

*Benzyl 6,7-di-*O*-acetyl-2,3,4-tri-*O*-benzyl-α-*D-glycero-D-manno-*heptopyranoside* (**20**). — A solution of **18** (0.55 g) in dichloromethane (30 mL) was ozonised at −78° for 3.5 min (disappearance of **18**) and then poured into dichloromethane (10 mL) containing triphenylphosphine (0.5 g). After 2 h, the solution was concentrated to dryness and to a solution of the residue in a few mL of benzene was added ether (~10 mL); the mixture was then filtered and concentrated. To a solution of the residual oil in dry ether was gradually added an ethereal solution of lithium aluminum hydride (0.47 g). The mixture was stirred at room temperature for 2 h, and water (0.47 mL) and aqueous 15% sodium hydroxide (0.47 mL) were then added. The ethereal solution was decanted, dried, and concentrated. The residual oil was acetylated. Column chromatography (benzene–ether, 98:2) of the product gave **20** (0.06 g, 11%), $[\alpha]_D^{23}$ +27° (*c* 1, chloroform), which was identical (t.l.c., i.r. data) with the product obtained from **25**.

Anal. Calc. for $C_{39}H_{42}O_9$: C, 71.5; H, 6.5. Found: C, 71.5; H, 6.5.

*Benzyl 2,3,4,7-tetra-*O*-benzyl-α-*D- *and -β-*L-glycero-D-manno-*heptopyranoside* (**21**). — To a stirred suspension of dry magnesium turnings (0.7 g) and mercuric chloride (3–4 mg) in oxolane (3 mL) under dry argon were added a few drops of benzyloxymethyl chloride. After the formation of the Grignard reagent had started, a solution of benzyloxymethyl chloride (3.34 mL) in oxolane (10 mL) was added dropwise at 0°. After stirring for ~30 min, the Grignard reagent was cooled to −30° and a solution of dry **7** (8.6 g) in oxolane (20 mL) was added slowly. After 2 h, the mixture was allowed to attain room temperature and stirring was continued for 12 h. The solution was then shaken with saturated aqueous ammonium chloride and extracted with ether, and the extract was dried and concentrated. Flash chromatography (light petroleum–ether–methanol, 70:30:3) of the oily residue (10.6 g) gave **21** (6.8 g, 65%), $[\alpha]_D^{27}$ +33° (*c* 0.9, chloroform).

Anal. Calc. for $C_{42}H_{44}O_7$: C, 76.3; H, 6.7. Found: C, 75.8; H, 6.9.

Debenzylation of **21** and treatment of the product with ethanethiol in conc. hydrochloric acid gave a diethyl dithioacetal, m.p. 180–183°, $[\alpha]_D^{16}$ +9° (*c* 0.8, pyridine). This $[\alpha]_D$ value indicated a 4:1 mixture of the diethyl dithioacetals of

L-*glycero*-D-*manno*-heptose, $[\alpha]_D^{16}$ +10° (*c* 0.9, pyridine), and of D-*glycero*-D-*manno*-heptose, $[\alpha]_D^{16}$ +5° (*c* 1.1 pyridine).

*Benzyl 7-O-allyl-2,3,4-tri-O-benzyl-β-*L- (**22**) *and -α-*D-glycero-D-manno-*heptopyranoside* (**23**). — To the Grignard reagent prepared from magnesium turnings (1.76 g) and allyloxymethyl chloride (5.9 g) as described above was added a solution of **7** (13 g) in dry oxolane (15 mL) dropwise at −30°. Stirring was continued for 2 h at −20° and the mixture was allowed to attain room temperature. After 18 h, the solution was washed with cold aqueous ammonium chloride and extracted with ether, and the extracts were washed with water, dried, and concentrated. Column chromatography (light petroleum–ethyl acetate, 95:5) of the residue gave, first, **22** (7.53 g, 51.5%), isolated as a syrup, $[\alpha]_D^{27}$ +35° (*c* 1.1, chloroform). ^{1}H-N.m.r. data: *inter alia,* δ 7.3 (m, 20 H, 4 Ph), 5.9 (m, 1 H, allyl -CH=), 5.06 (s, 1 H, H-1).

Anal. Calc. for $C_{38}H_{42}O_7$: C, 74.7; H, 6.9. Found: C, 74.5; H, 7.1.

The 6-acetate (**24**) of **22** had m.p. 86–87° (from hexane–ethyl acetate), $[\alpha]_D^{16}$ +18° (*c* 1.5, chloroform). ^{1}H-N.m.r. (400 MHz) data: *inter alia,* δ 5.73 (bt, 1 H, Σ*J* 14 Hz, H-6), 5.9 (m, 1 H, allyl -CH=), 5.30 and 5.19 (2 d, 2 H, allyl CH_2=), 5.09 (s, 1 H, H-1), 4.05 (m, 4 H, H-3,5, allyl CH_2O), 3.94 (t, 1 H, Σ*J* 18 Hz, H-4), 3.87 (bd, 1 H, H-2), 3.72 (m, 2 H, H-7,7′), 2.16 (s, 3 H, OAc).

Anal. Calc. for $C_{40}H_{44}O_8$: C, 73.6; H, 6.8. Found: C, 73.4; H, 6.7.

Eluted second was **23** (2.26 g, 16%), isolated as a syrup, $[\alpha]_D^{27}$ +16° (*c* 0.7, chloroform). ^{1}H-N.m.r. (500 MHz) data: δ 5.85 (m, 1 H, allyl -CH=), 5.23 and 5.12 (d and dd, 2 H, allyl CH_2=), 4.89 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1), 4.18 (t, 1 H, $J_{3,4} \approx J_{4,5} \approx$ 9.6 Hz, H-4), 3.99 (bt, 1 H, Σ*J* 11 Hz, H-6), 3.94 (dd, 1 H, $J_{3,2}$ 3.0 Hz, H-3), 3.79 (dd, 1 H, H-2), 3.75 (bd, 1 H, Σ*J* 9 Hz, H-5), 3.55 (m, 2 H, H-7,7′).

Anal. Calc. for $C_{38}H_{42}O_7$: C, 74.7; H, 6.9. Found: C, 74.1; H, 6.9.

L-glycero-D-manno-*Heptose* (**2**). — To a solution of **22** (0.65 g) in methanol (12 mL) and water (0.5 mL) were added 10% Pd/C (0.52 g) and a crystal of toluene-*p*-sulfonic acid, and the mixture was boiled under reflux for 20 min, then filtered, and concentrated. Flash chromatography (light petroleum–ether–methanol, 60:40:2) of the residue gave a product (0.42 g, 69%) which was identical (t.l.c., i.r. and ^{1}H-n.m.r. spectra) with **14**. Also, its 6,7-diacetate, $[\alpha]_D^{21}$ +22° (*c* 1, chloroform), was identical with **15**.

Catalytic hydrogenation of benzyl 2,3,4-tri-*O*-benzyl-*β*-L-*glycero*-D-*manno*-heptopyranoside (0.33 g) yielded **2** (0.12 g, ~100%) as a colorless oil. Reaction of **2** with ethanethiol and conc. hydrochloric acid gave a diethyl dithioacetal, m.p. 202.5–203° (from ethanol), $[\alpha]_D^{24}$ +12° (*c* 1.2, pyridine), which was identical with **17**.

D-glycero-D-manno-*Heptose* (**1**). — Deallylation of **23** (0.76 g), as decribed for **22**, yielded benzyl 2,3,4-tri-*O*-benzyl-*α*-D-*glycero*-D-*manno*-heptopyranoside (**25**; 0.49 g, 69%), $[\alpha]_D^{23}$ +30° (*c* 0.8, chloroform). The 6,7-diacetate, $[\alpha]_D^{25}$ +28° (*c* 2.1, chloroform), was identical with **20**.

Catalytic hydrogenation of **25** (0.49 g) yielded D-*glycero*-D-*manno*-heptose

(**1**; 0.18 g, 100%), isolated as a colorless oil. The diethyl dithioacetal had m.p. 155–156° (from ethanol), $[\alpha]_D^{24}$ +29° (*c* 2.1, water); lit.[4] m.p. 155–156°, $[\alpha]_D^{25}$ +29.6° (*c* 2.1, water).

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