Diastereoselectivity in the synthesis of D-glycero-D-aldoheptoses by 2-trimethylsilylthiazole homologation from hexodialdo-1,5-pyranose derivatives

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This paper is dedicated to Professors David B. MacLean and Ian D. Spenser

NAVEEN K. KHARE, RAMESH K. SOOD, and GERALD O. ASPINALL. Can. J. Chem. **72**, 237 (1994).

An exploration of the synthesis of D-*glycero*-D-*altro*-heptose, a constitutent of O antigen chains in lipopolysaccharides from *Campylobacter jejuni* serotypes O:23 and O:36 led to a study of the 2-trimethylsilylthiazole homologation procedure for heptose synthesis. In contrast to the diastereoselective formation of a 1,2:3,4-di-*O*-isopropylidene-D-*glycero*-α-D-*galacto*-heptopyranose derivative from 1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose, methyl 2,3,4-tri-*O*-benzyl-D-hexodialdo-1,5-pyranosides with the *gluco* and *manno* configurations showed no preference for the formation of compounds with the D-*glycero* configuration. Attempts to achieve high diastereoselectivity in the conversion of L-*glycero* into the D-*glycero* isomers by oxidation at C-6 followed by reduction with L-selectride were unsuccessful with the thiazole adducts, but the desired products were formed in similar reactions of methyl 2,3,4-tri-*O*-benzyl-7-*O*-*tert*-butyldimethylsilyl-D-heptopyranosides. The approach to homologation in the *altro* series was thwarted by epimerization at C-5 in the attempted formation of methyl 2,3,4-tri-*O*-benzyl-α-D-*altro*-hexodialdo-1,5-pyranoside. The successful synthesis of methyl D-*glycero*-α-D-*altro*-heptopyranoside from methyl α-D-glucopyranoside was achieved by homologation followed by configurational alteration from the D-*gluco* to the D-*altro* series.

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Une exploration de la synthèse du D-*glycéro*-D-*altro*-heptose, un constituant des chaînes O antigéniques des lipopolysaccharides des sérotypes O:23 et O:36 du *Campylobacter jejuni* a conduit à étudier la possibilité d'utiliser la procédure d'homologation du 2-triméthylsilylthiazole pour réaliser la synthèse d'heptoses. Par opposition à la formation diastéréosélective d'un dérivé 1,2:3,4-di-*O*-isopropylidène-D-*glycéro*-α-D-*galacto*-heptopyranose à partir 1,2:3,4-di-*O*-isopropylidène-α-D-*galacto*-hexodialdo-1,5-pyranose, les 2,3,4-tri-*O*-benzyl-D-hexodialdo-1,5-pyranosides de méthyles avec des configurations *gluco* et *manno* ne présentent aucune préférence pour la formation de composés avec la configuration D-*glycéro*. Les essais effectués sur des adduits thiazoles dans le but d'obtenir une grande diastéréosélectivité lors de la conversion des isomères L-*glycéro* en D-*glycéro* par le biais d'une oxydation en C-6 suivie par une réduction à l'aide de L-sélectride se sont avérés vains; toutefois, les produits désirés se forment lors de réactions semblables avec des 2,3,4-tri-*O*-benzyl-7-*O*-*tert*-butyldiméthylsilyl-D-heptopyranosides de méthyle. L'approche à l'homologation dans la série *altro* ne peut être réalisée à cause d'une épimérisation en C-5 lorsqu'on essaie de former le 2,3,4-tri-*O*-benzyl-α-D-*altro*-hexodialdo-1,5-pyranoside de méthyle. On a réalisé la synthèse du D-*glycéro*-α-D-*altro*-heptopyranoside de méthyle à partir de l'α-D-glucopyranoside de méthyle en procédant à une homologation suivie d'une modification de configuration de la série D-*gluco* à D-*altro*.

[Traduit par la rédaction]

Introduction

L-*glycero*-D-*manno*-Heptose is a commonly encountered component of the core region of lipopolysaccharides (LPS) on Gram-negative bacteria (1). In view of the immunological importance of this region of LPS structure considerable attention has been directed to efficient methods for the preparation of derivatives of the sugar for incorporation into synthetic oligosaccharides (2–6). Methods of choice have been those involving a one-carbon extension from benzyl (**1**) or methyl (**2**) 2,3,4-tri-*O*-benzyl-α-D-*manno*-hexodialdo-1,5-pyranoside of which that involving reaction with (phenyldimethylsilyl)magnesium chloride (**4**) proceeds with high diastereoselectivity to give derivatives of L-*glycero*-D-*manno*-heptose from which glycosides of the parent sugar may be readily obtained. In a recent study of the O antigen chains of LPSs of *Campylobacter jejuni* serotypes O:23 and O:36 unusual heptose sugars were found as four variants with the same configurationally unusual *altro* ring configuration (7). LPS preparations all contained trisaccharide, -3-β-D-GlcNAc-(1→3)-α-D-Gal-(1→2)-α-Hep 1-, repeating units with the same linkages and anomeric configurations, but with the heptose residue present in varying proportions as 6-deoxy-D-*altro*-heptose (8) and 6-deoxy-3-*O*-methyl-D-*altro*-heptose (unpublished synthesis with G.V. Reddy), for which enantiomeric configurations have been confirmed, and D-*glycero*-D-*altro*-heptose and 3-*O*-methyl-D-*glycero*-D-*altro*-heptose or their respective enantiomers. In view of the close structural, and presumably also biosynthetic, relationship between the four variants it was highly probable that all had the α-D-*altro* ring configuration. It was still necessary to confirm the absolute configurations of the two latter sugars through the synthesis of defined reference compounds before making preparative quantities for oligosaccharide assembly. The only reported C-6 homologation of a D-hexodialdo-1,5-pyranose derivative proceeding with high diastereoselectivity for the formation of the D-*glycero* product is that reported by Dondoni et al. (5, 6) using 2-(trimethylsilyl)thiazole (TMSthiazole) as a one-carbon synthon in reaction with 1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose (**3**). This procedure therefore seemed worthy of exploration for the synthesis of D-*glycero*-D-*altro*-heptose derivatives. Two alternative overall strategies seemed possible starting from D-glucopyranose derivatives: (A) 2,3-inversion to gain entry into the D-altropyranose series, followed by C-6 homologation; and (B)

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TABLE 1. Gas chromatographic analysis of heptitol acetates

Parent sugar	Relative retention times[a] of heptitol acetates with respect to Glucitol hexaacetate	Galactitol hexaacetate
L-*glycero*-D-*manno*-Heptose	1.90	2.08
D-*glycero*-D-*manno*-Heptose	1.65	1.80
L-*glycero*-D-*gluco*-Heptose	2.07	2.26
D-*glycero*-D-*gluco*-Heptose	1.75	1.90
L-*glycero*-D-*galacto*-Heptose	2.06	2.28
D-*glycero*-D-*galacto*-Heptose	1.90	2.08
D-*glycero*-D-*altro*-Heptose	1.47	1.61
3-*O*-Methyl-D-*glycero*-D-*altro*-heptose	1.52	1.66

[a]Gas chromatography using program A.

C-6 homologation in the D-glucopyranose series, followed by 2,3-inversion of the D-*glycero*-D-*gluco*-heptopyranose product. In the event unexpected problems were encountered in both proposed routes. Route A was rejected at an early stage when it was observed that oxidation of methyl 2,3,4-tri-*O*-benzyl-α-D-altropyranoside to give the dialdohexo-1,5-pyranoside was accompanied by substantial epimerization at C-5 with formation of the corresponding β-L-*galacto* derivative. Route B ultimately proved successful for the preparation of the desired heptoses but no diastereoselectivity was observed in the C-6 homologation reaction. We report herein syntheses of these heptoses in confirmation of their absolute configurations, but discuss first diastereoselectivity in the TMSthiazole homologation together with experiments related to the C-5 epimerization accompanying oxidation at C-6 of both altrose and galactose derivatives.

Results and discussion

Configurational assignments for heptose derivatives epimeric at C-6

All homologations were performed and the thiazole adducts were converted into heptose derivatives as described by Dondoni et al. (5, 6) and *O*-debenzylated. Since all 10 diastereomeric heptitol heptaacetates are separable by gas–liquid chromatography (glc) (9) (see Table 1 for examples now reported), formation of these derivatives by hydrolysis of glycosides, reduction, and acetylation was the simplest method for distinguishing the pairs of D-*glycero*/L-*glycero* epimers that may result from C-6 homologations. Other, sometimes quantitatively dominant, compounds are produced in varying amounts due to accompanying 1,6- and (or) 1,7-anhydroheptose formation under hydrolysis conditions, as in the case of D-*glycero*-D-*altro*-heptose (7). In the example reported by Dondoni et al. (5, 6), the absolute configuration at C-6 of the thiazole adduct, (6*S*)-1,2:3,4-di-*O*-isopropylidene-6-(2-thiazolyl)-α-D-*galacto*-hexo-1,5-pyranose (**4**), formed as the sole product from 1,2:3,4-di-*O*-isopropylidene-D-*galacto*-hexodialdo-1,5-pyranose (**3**), was established by conversion into a previously characterized D-*glycero*-α-D-*galacto*-heptose derivative (10). However, derivatives of defined configuration from rarely encountered heptoses are unlikely to be available for comparison. Furthermore for the compounds of present interest, we have found that the differences in nmr parameters for C-6 and H-6 in epimeric heptose derivatives are insufficiently consistent to provide a basis for configurational assignments.

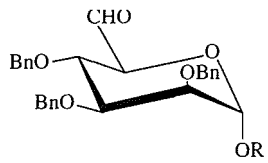
Diastereoselectivity in C-6 homologation of mannose and glucose derivatives

With access to heptitol heptaacetates derived from L-*glycero*- and D-*glycero*-D-*manno*-heptoses for comparison, the TMSthiazole homologation reaction was examined as an alternative to the above-mentioned homologation of **1** with (phenyldimethyl)silylmethylmagnesium chloride, which had been used in the preparation of derivatives of L-*glycero*-D-*manno*-heptose with high diastereoselectivity (3, 4). Diastereoselectivity in homologation was first examined for methyl 2,3,4-tri-*O*-benzyl-α-D-*manno*-hexodialdo-1,5-pyranoside (**2**), prepared as required on Swern oxidation (11) of methyl 2,3,4-tri-*O*-benzyl-α-D-mannopyranoside with oxalyl chloride and methyl sulfoxide. Reaction of **2** with TMSthiazole gave the chromatographically separable 6-(2-thiazolyl)-derivatives (**5** and **6**) in respective yields of 55 and 37%. Conversion of **5** and **6** into the respective methyl 2,3,4-tri-*O*-benzylheptopyranosides (**7** and **8**), in four steps with overall yields of 60–70%, by successive *N*-methylation, reduction with $NaBH_4$, hydrolysis in the presence of $HgCl_2$, and reduction again with $NaBH_4$. Since this research was completed Dondoni et al. (12) have reported an improved procedure for the thiazole to formyl deblocking protocol. Configurational assignments for **7** and **8** were made by conversion into L-*glycero*- and D-*glycero*-D-*manno*-heptitol heptaacetates.

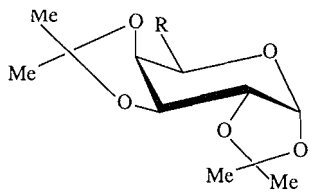
TMSthiazole homologation of the hexodialdo-1,5-pyranoside (**9**) formed on oxidation of methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside was next explored with very similar results to those in the mannose series. Reaction of **9** with TMSthiazole furnished a mixture of 6-(2-thiazolyl) derivatives from which **10** and **11** were obtained in chromatographically pure form in yields of 54 and 18%. These compounds were converted into the corresponding methyl 2,3,4-tri-*O*-benzylheptopyranosides **12** and **13**, as described above, and thence after *O*-debenzylations into the respective methyl glycosides **14** and **15**. Compounds **14** and **15** (and similarly others elsewhere) were converted into their acetylated derivatives **16** and **17** to provide satisfactory elemental analyses and to give well-dispersed one-dimensional ^1H nmr spectra for structural assignments. Relative configurations were assigned after conversion of **14** and **15** into heptitol heptaacetates that were indistinguishable on glc from those derived respectively from L-*glycero*- and D-*glycero*-D-*gluco*-heptitols.

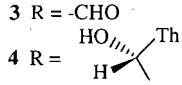
Configurational inversions at C-6 of heptose derivatives

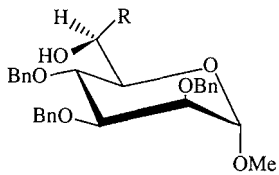
In the light of the preceding results attention was turned to the



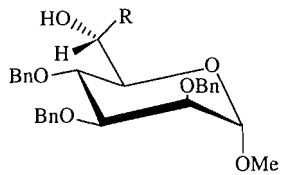
1 R = Bn
2 R = Me



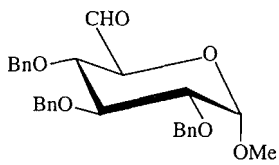
3 R = -CHO
4 R = 



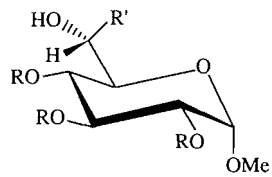
5 R = Th
7 R = CH_2OH
21 R = $CH_2OTBDMS$



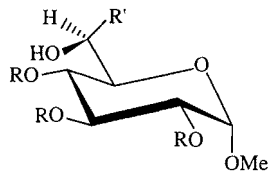
6 R = Th
8 R = CH_2OH



9



11 R = Bn; R' = Th
13 R = Bn; R' = CH_2OH
15 R = H; R' = CH_2OH
17 R = Ac; R' = CH_2OAc
20 R = Bn; R' = $CH_2OTBDMS$
30 R = Bn; R' = $CH_2OTBDPS$
31 R = H; R' = $CH_2OTBDPS$



10 R = Bn; R' = Th
12 R = Bn; R' = CH_2OH
14 R = H; R' = CH_2OH
16 R = Ac; R' = CH_2OAc
19 R = Bn; R' = $CH_2OTBDMS$

Th = Thiazolyl = 

TBDMS = *tert*-butyldimethylsilyl
TBDPS = *tert*-butyldiphenylsilyl

possibility of achieving a high-yield conversion of L-*glycero* into the epimeric D-*glycero* compounds. Dondoni et al. (13) have described inversion of configuration at C-6 of the (2-thiazolyl) derivative **4** by oxidation to the 6-ulose followed by stereoselective reduction with L- or K-selectride to give the (6*R*) epimer (**18**).

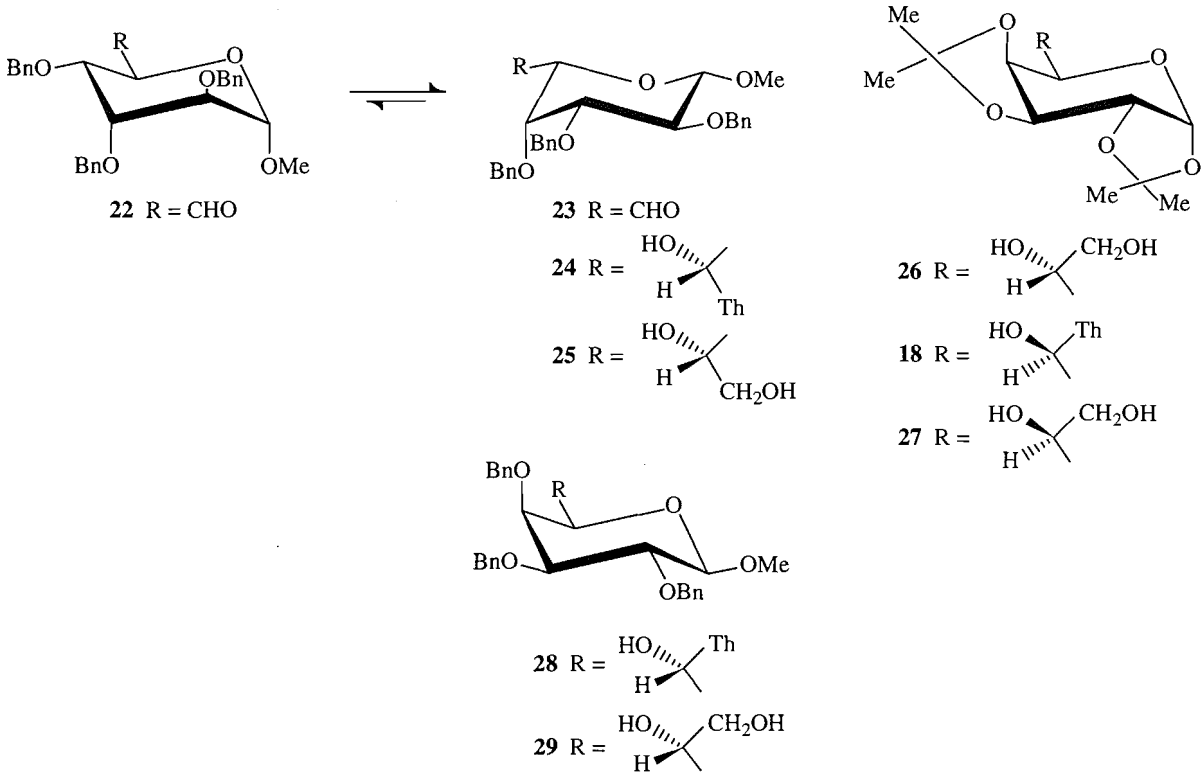
With formation of the L-*glycero* compound **7** as the major product of TMSthiazole homologation in the *gluco series* the possibility of achieving improved overall yields of D-*glycero*-D-*gluco*-heptose derivatives by configurational inversions at C-6 was examined for three derivatives. The 6-(2-thiazolyl) derivative **10** was oxidized with periodinane (14) and the resulting 6-ulose, without purification, was treated with L-selectride to regenerate a mixture of thiazolyl derivatives **10** and **11**, now in the proportions of 2:3. Alternative methods for the configurational inversion were explored for 7-*tert*-butyldiphenylsilyl (TBDPS) and 7-*tert*-butyldimethylsilyl (TBDMS) derivatives of **12** and **13**. In the case of a preliminary experiment performed on TBDPS derivatives from an unresolved mixture of **12** and **13**, Swern oxidation (11) to give the 6-ulose followed by reduction with L-selectride gave back derivatives of **12** and **13** in the same proportions. Samples of the respective TBDMS derivatives (**19** and **20**) of **12** and **13** were prepared so that the reduction of the 6-ulose could be monitored, and complete conversion of **19** to **20** was achieved when **19** was submitted to the oxidation–reduction sequence. A single product was detected by tlc as reduction of the 6-ulose with L-selectride proceeded, but when the reaction mixture was quenched with alkaline hydrogen peroxide, a mixture of products was formed. The chromatographic mobilities of these substances indicated retention of a silyl substituent. Since treatment of these substances with tetrabutylammonium fluoride gave **13** as the sole product, it is probable that intramolecular silyl migration, from O-7 to O-6, had taken place.

In the *manno* series, preparation of the TBDMS derivative **21** from **7** was followed by Swern oxidation (11) to the 6-ulose, reduction with L-selectride, and *O*-desilylation to give the D-*glycero* epimer **8** as the only detectable product and in 80% isolated yield.

Diastereoselectivity in C-6 homologation of altrose and galactose derivatives

Treatment of methyl 2,3,4-tri-*O*-benzyl-α-D-altropyranoside with oxalyl chloride and methyl sulfoxide gave a mixture of hexodialdo-1,5-pyranosides, as judged by the appearance of two aldehydic protons in the ^1H nmr spectrum and, most prominently in the ^{13}C nmr spectrum, of two sets of resonances assignable to ring carbons of the expected methyl 2,3,4-tri-*O*-benzyl-α-D-*altro*-hexodialdo-1,5-pyranoside (**22**) and the C-5 epimer, methyl 2,3,4-tri-*O*-benzyl-β-L-*galacto*-hexodialdo-1,5-pyranoside (**23**) in the approximate ratio of 1:4. The correctness of this conclusion was confirmed by reduction of the mixture of hexodialdo-1,5-pyranosides with $NaBH_4$ followed by acetylation to give a mixture of methyl 6-*O*-acetyl-2,3,4-tri-*O*-benzyl-hexopyranosides in the somewhat altered ratio of 2:3 with glc retention times coincident with those of standard α-D-altrose and β-D-galactose derivatives. Confirmation of the L-*galacto* configuration for the main component was obtained by *O*-debenzylation of the mixture of tri-*O*-benzyl glycosides followed by hydrolysis and conversion of the resulting reducing sugars into acetates of chiral 2-butyl glycosides (15). These results confirmed that epimerization at C-5 had occurred, leading to the formation of the β-L-*galacto* isomer as the major component of the mixture of hexodialdo-1,5-pyranosides. Mixtures of **22** and **23** in the same proportions were obtained on oxidation of methyl 2,3,4-tri-*O*-benzyl-α-D-altropyranoside with periodinane (14), indicating that the epimerization was not just a base-catalyzed reaction promoted by the use of triethylamine in the Swern oxidation.

A rapid interconversion of **22** and **23**, with the composition of isomers on further reaction dependent on the relative rates of formation of different products, was indicated in the above-mentioned reduction to give stereoisomeric products in changed proportions. In an exploration of the stereochemical consequences of the C-6 homologation with TMSthiazole, reaction of the mixture of **22** and **23** gave only one detectable product, which was assigned the structure methyl (6*R*)-2,3,4-tri-*O*- benzyl-6-(2-thiazolyl)-β-L-galactopyranoside (**24**) on the basis of the following evidence. The ^{13}C nmr spectra of **24** and the derived methyl 2,3,4-tri-*O*-benzyl-L-*glycero*-



β-L-*galacto*-heptopyranoside (**25**) showed resonances for carbon atoms of the β-*galacto* ring configuration and none for those of the α-*altro* configuration. *O*-Debenzylation of **25** followed by hydrolysis, reduction, and acetylation gave a single heptitol heptaacetate coincident on glc with that formed from the enantiomeric L-*glycero*-D-*manno*-heptose (= D-*glycero*-D-*galacto*-heptose) and therefore confirmed the relative configuration of the chiral centres.

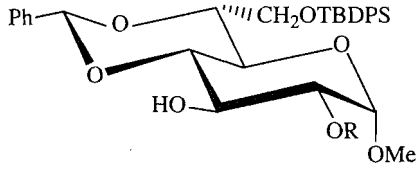
The reversibility of the *altro–galacto* interconversion was also examined in the formation of hexodialdo-1,5-pyranose derivatives in the more accessible D-galactose series. In a re-examination of the oxidation of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose as reported by Dondoni et al. (5, 6), the ^1H and ^{13}C nmr spectra of the corresponding hexodialdo-1,5-pyranose (**3**) showed only the *galacto* isomer with no trace of the *altro* derivative. TMSthiazole homologation likewise gave only the reported (6*S*)-1,2:3,4-di-*O*-isopropylidene-6-(2-thiazolyl)-α-D-galactopyranose (**4**). In confirmation of this observation, independent evidence for the configurational assignments at C-6 in **4** and in its C-6 epimer (**18**) was obtained by their conversions into 1,2:3,4-di-*O*-isopropylidene-D-*glycero*-D- *galacto*-heptopyranose (**26**) and the corresponding L-*glycero*-D- *galacto* compound (**27**), and thence into heptitol heptaacetates that were identical (gc) to samples prepared from the corresponding D-*glycero*-D-*galacto*-heptose and L-*glycero*-D-*gluco*- heptose (= L-*glycero*-D-*galacto*-heptose).

As expected, a parallel series of oxidation and TMSthiazole homologation reactions starting from methyl 2,3,4-tri-*O*-benzyl-β-D-galactopyranoside afforded compounds enantiomeric with those described above that were derived from methyl 2,3,4-tri-*O*-benzyl-α-D-altropyranoside. Comment here is restricted to a few salient points and details are given later. Oxidation of the D-galactopyranoside gave the corresponding mixture of *galacto* and *altro* dialdohexopyranosides in the ratio of 3:1 and, as expected, only a single product (**28**) with the D-*glycero*-α-D-*galacto* configuration was isolated from the ensuing TMSthiazole homologation. Although there were small differences in the magnitudes of the optical rotations of **28** and the corresponding methyl 2,3,4-tri-*O*-benzylheptopyranoside **29**, compared with those of the L-*galacto* compounds **24** and **25**, the enantiomeric pairs were chromatographically indistinguishable and ^1H and ^{13}C nmr spectra showed no significant differences.

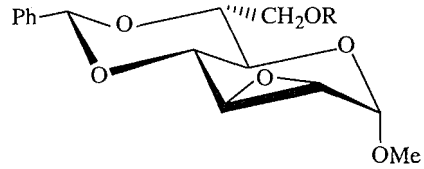
The stereoselectivity of configurational inversion at C-6 of **28** by oxidation and subsequent reduction with L-selectride was also examined. Two fractions were separated by preparative tlc and the structures of the products, which were obtained in insufficient quantity and purity for elemental analysis, were established from nmr spectra data and conversions to the corresponding heptitol heptaacetates. The nmr spectra of the derivative from the first fraction showed the presence of a single component with the *galacto* configuration, and further processing furnished L-*glycero*-D-*galacto*-heptitol heptaacetate derived from the product of C-6 inversion. The ^{13}C nmr spectrum of the second fraction showed the presence of compounds with α-*altro* and β-*galacto* configurations, and further processing of the fraction afforded a mixture of two heptitol heptaacetates. Comparison of their glc retention times with those of reference compounds with the D-*glycero*-D-*galacto* and the D-*glycero*-D-*altro* configurations showed that the second fraction of the oxidation–reduction sequence consisted of the product from unchanged starting compound **28** and only one of two possible products arising from epimerization at C-5 of the 6-ulose, that with the L-*glycero*-L-*altro* configuration.

Synthesis of derivatives of D-glycero-D-altro-*heptose*

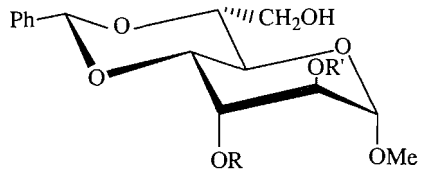
The preceding studies of C-6 homologations of D-hexodialdo-1,5-pyranose derivatives provided abundant evidence that route B is the only practical strategy for the synthesis of D-*glycero*-D-*altro*-heptose derivatives and ruled out any reac-



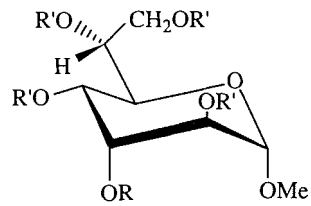
32 R = H
33 R = Ts



34 R = TBDPS
35 R = H



36 R = R' = H
37 R = R' = Ac
40 R = Me; R' = H
41 R = Me; R' = Ac



38 R = R' = H
39 R = R' = Ac
42 R = Me; R' = H
43 R = Me; R' = Ac

tions involving carbonyl groups at C-6 of compounds having the *altro* ring configuration. Methyl 7-*tert*-butyldiphenylsilyl-D-*glycero*-α-D-*gluco*-heptopyranoside (**31**) was best prepared by *O*-silylation of methyl glycoside **15**, since silylation of **13** to give the TBDPS derivative (**30**) followed by hydrogenolysis was accompanied by ~25% *O*-desilylation. Reaction of **31** with benzaldehyde dimethylacetal in the presence of catalytic amounts of *p*-toluenesulfonic acid gave the 4,6-*O*-benzylidene derivative **32**. Several methods for the preparation of methyl 2,3-anhydro-4,6-*O*-benzylidene-D-*glycero*-α-D-*manno*-heptopyranoside (**35**) were explored. In the course of these experiments samples of the 2-tolylsulfonyl ester **33** and the *O*-silyl epoxide **36** were obtained in adequate purity for structural characterization by nmr but not for elemental analysis. These samples were of value in monitoring the procedure of Hicks and Fraser-Reid (16) in which treatment of **32** with sodium hydride and tosyl imidazole led to the formation in a single operation of a derivative with the desired 2,3-anhydro-*manno* configuration but this reaction was accompanied by *O*-desilylation to give the epoxide **35**. The initially formed tosyl ester **33** was rapidly converted into the silylated epoxide **34**, but by the time all starting material (**32**) had reacted, much **34** had undergone *O*-desilylation. Prolongation of the reaction led to complete conversion into the epoxide **35**. This further reaction turned out to be advantageous since the 7-*O*-silyl expoxide (**34**) proved to be quite unreactive under normal conditions of epoxide opening. The *O*-desilylated epoxide **35** underwent normal diaxial opening on reaction with aqueous sodium hydroxide to yield methyl 4,6-*O*-benzylidene-D-*glycero*-α-D-*altro*-heptopyranoside (**36**), and *O*-debenzylidenation gave methyl D-*glycero*-α-D-*altro*-heptopyranoside (**38**). The nmr data for the respective acetylated derivatives (**37** and **39**) of these two compounds supported the *gluco* to *altro* configurational change. Confirmation of the relative configuration was obtained by hydrolysis of the glycoside **38**, followed by reduction to give the heptitol and a mixture of 1,6- and 1,7-anhydroheptoses, whose acetylated derivatives were coincident on glc with those derived from the *C. jejuni* O:36 LPS (7). A sample of the heptose was converted into the (*R*)- and (*S*)-2-butyl glycosides whose acetylated derivatives were identical (glc) with those similarly derived from the polysaccharide, thus confirming the absolute configuration of the naturally occurring sugar as D-*glycero*-D-*altro*-heptose. In like manner, methoxide opening of epoxide **35** afforded methyl 4,6-*O*-benzylidene-3-*O*-methyl-D-*glycero*-D-*altro*-heptopyranoside (**40**) and the derived compounds **41–43** were characterized in the same way as for compounds **36–38**. Conversion of a sample of methyl glycoside **41** into (*R*)- and (*S*)-2-butyl glycosides followed by acetylation for glc comparison with those derived from the *C. jejuni* O:23 LPS (7) confirmed that the naturally occurring heptose was 3-*O*-methyl-D-*glycero*-D-*altro*-heptose.

In summary, these studies have shown that the high diastereoselectivity observed by Dondoni et al. (5, 6) in the C-6 homologation of a hexodialdo-1,5-pyranose derivative using 2-trimethylsilylthiazole as a one-carbon synthon is restricted to the galactose series. The unidirectional attack at the *si* face of the 6-aldehyde in this series is presumably governed by the steric effect of the axial oxygen substituent at C-4. No such stereoselectivity was found with glucose and mannose derivatives. In the galactose series a further observation was made that might have escaped attention if experiments had not also been performed in the altrose series. Oxidation of methyl 2,3,4-tri-*O*-benzyl-α-D-altropyranoside was accompanied by epimerization at C-5 with the formation of an equilibrium mixture of 5-epimeric hexodialdo-1,5-pyranosides favouring the β-L-*galacto* isomer **23** over the α-D-*altro* isomer **22** in the ratio of 3:1. In the opposite direction, oxidation of the enantiomeric β-D-galactoside gave the corresponding mixture of products with the α-L-altropyranoside as the minor component. For the monocyclic methyl 2,3,4-tri-*O*-benzyl hexopyranosides, rapid equilibration may be presumed with product composition on further reaction being kinetically determined. Thus rapid and irreversible reduction with sodium borohydride gave back a mixture of hexopyranosides in approximately the same proportions from glc analysis as indicated by nmr for the hexodialdo-1,5-pyranosides. In contrast the TMSthiazole addition, of presumably reversible character, gave a single detectable product with the β-*galacto* ring configuration. In the D-series high diastereoselectivity, as reported by Dondoni et al. (5, 6), led to the formation of the 6-(*S*) thiazolyl derivative **28** and thence of the D-*glycero*-D-*galacto*-heptopyranoside **29**. In reexamining the preparation of 1,2;3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose (**3**), nmr showed no evi-

dence for epimerization at C-5 in this conformationally more rigid fused ring derivative. The enolization mechanism for epimerization would require the adoption of a trigonal carbon at C-5 with energetically unfavourable conformational changes in the fused ring system. It is noteworthy that no evidence was obtained for C-5 epimerization in the preparation of hexodialdo-1,5-pyranosides in the mannose and glucose series.

The conversion of (6*S*)- (**4**) into the epimeric (6*R*)-1,2;3,4-di-*O*-isopropylidene-6-(2-thiazolyl)-α-D-galactopyranose (**18**) by oxidation to the thiazolyl heptose-6-ulose followed by stereoselective reduction with L-selectride (5, 6) appeared to establish in principle a route for conversion of D-*glycero*- to the 6-epimeric L-*glycero*-D-heptopyranose derivatives. In our hands this stereoselectivity is not general and seems to be restricted to the conformationally rigid fused ring system in **18** where reduction of the thiazolyl heptose-6-ulose would require unidirectional attack on the *re* face at C-6 analogous to that on the *si* face of the hexodialdo-1,5-pyranose **3** in the formation of thiazolyl derivative **4**. Reaction starting from the (6*S*)-(2-thiazolyl)-β-D-galactopyranoside **28** gave a mixture of products that could be converted into derivatives of D-*glycero*- and L-*glycero*-β-D-galactopyranosides, and L-*glycero*-α-L-altropyranosides. The analogous reaction sequence with the corresponding thiazolyl derivatives in the glucose and mannose series showed no stereoselectivity. Stereoselective reductions were achieved here, but in the *opposite direction* when the heptoside-6-uloses from the severely hindered 7-TBDMS L-*glycero*-α-D-*manno*- (**19**) and α-D-*gluco*- (**20**) heptopyranosides were treated with L-selectride.

In reaching our initial objective, that of developing a synthesis of D-*glycero*-D-*altro*-heptose to confirm the absolute configuration of the O antigen constituent in the LPS of *C. jejuni* serotype O:36, the C-6 homologation was achieved first with the formation of derivatives of D-*glycero*-D-*gluco*-heptose. The well-known series of transformations from D-glucopyranosides to D-altropyranosides with inversions at C-2 and C-3 presented unexpected difficulties in the formation, and subsequent ring opening, of the intermediate 2,3-anhydro-*manno*-heptose derivative bearing a 7-*O*-TBDMS substituent until that protecting group could be removed after its purpose had been served.

Experimental

General methods

The following solvents were dried and purified by distillation over the reagents specified in parentheses: dichloromethane (phosphorus pentoxide), oxolane (lithium aluminum hydride), methanol (magnesium–iodine), toluene (sodium). Light petroleum (bp 30–60°C) and ethyl acetate used as chromatographic solvents were freshly distilled immediately before use. Acetonitrile, *N,N*-dimethylformamide, and methyl sulfoxide were purchased already dried and glass-distilled. Evaporations were conducted under diminished pressure at <40°C. Thin-layer chromatography (tlc) was conducted on plates coated with Silica Gel $60F_{254}$ (Merck). Optical rotations were measured with a Perkin–Elmer 141 polarimeter, for solutions in $CHCl_3$ at ~20°C unless otherwise stated.

^1H, ^{13}C (often in the JMODXH mode), and 2D ^1H nmr spectra were recorded with a Bruker AM 300 spectrometer. Solutions in chloroform-*d* were referenced to internal tetramethylsilane as internal reference. Solutions in D_2O were referenced to internal acetone (δ_H 2.17 ppm and δ_C 30.5 ppm). Chemical shifts and coupling constants are first-order values and assignments in ^1H nmr spectra on the basis of double resonance or COSY experiments are specified in parentheses. Spectra are reported only in sufficient detail to substantiate chemical changes effected and for configurational assignments. The following characteristic resonances were observed consistently and are not cited individually other than when the groups were first incorporated: for thiazolyl derivatives at δ_H ~ 7.7 (H-4′) and 7.3 (H-5′), and δ_C ~171 (C-2′), 142 (C-4′) and 119 (C-5′), for benzyl ethers at δ_H ~ 7.4–7.2 (Ph-H) and 5.0–4.8 (CH_2Ph), and δ_C ~137 and 127 (aromatic C) and 75–72 (Ph-CH_2); and for *O*-isopropylidene derivatives at δ_H 1.5–1.3 ($(CH_3)_2C$), and δ_C ~108 ($(CH_3)_2C$) and 26–24 ($(CH_3)_2C$). The glc analyses were carried out on a Hewlett–Packard model 5890 A chromatograph. Separations were performed using a DB-23 (30 m × 0.25 mm) column with the following programs: (A) for alditol acetates, isothermally at 220°C unless specified at 200°C; (B) for 2-butyl glycoside acetates, 200°C (10 min), 200° → 240°C at 2°/min. Microanalyses were by Canadian Microanalytical Service, Ltd., Delta, B.C.

Preparations of hexodialdo-1,5-pyranose derivatives

Typical oxidations were performed by the addition of freshly distilled methyl sulfoxide (0.23 mL, 3 mmol) in dichloromethane (4 mL) to oxalyl chloride (1.2 mL, 2.4 mmol) in dichloromethane (10 mL) at −60°C. After 5 min substrate (~0.5 g, 1 mmol) in dichloromethane was added dropwise. After 30 min the reaction was quenched by the addition of triethylamine (2 mL) in dichloromethane (5 mL), and the solution was allowed to rise to room temperature, washed twice with water, dried, and concentrated. Completeness of reaction was checked by tlc for disappearance of initial substrate and, if necessary, by nmr (appearance of an aldehydic proton singlet at δ ~9.7 in the ^1H spectrum, appearance of aldehydic carbonyl resonance at δ ~198, and disappearance of C-6 resonance of substrate at δ ~62 in the ^{13}C spectrum). The hexodialdo-1,5-pyranose derivative was used directly without further purification in the TMSthiazole homologation reaction.

*Addition of 2-(trimethylsilyl)thiazole to methyl 2,3,4-tri-*O*-benzyl-α-D-manno-hexodialdo-1,5-pyranoside 2*

2-(Trimethylsilyl)thiazole (0.4 mL) was added to **2** (from methyl 2,3,4-tri-*O*-benzyl-α-D-mannopyranoside (17) (0.5 g)) in dichloromethane (10 mL) at 0°C under nitrogen. The mixture was kept at 0°C overnight and then at room temperature for 3 h. Solvents were evaporated, and the residue in oxolane (10 mL) was treated with 1 M tetrabutylammonium fluoride (2.8 mL) for 30 min. Solvent was partly evaporated and the residue was treated with aqueous sodium hydrogen carbonate and extracted with ethyl acetate. The extract was dried, concentrated, and chromatographed on silica gel (dichloromethane containing 3% of acetone) to give, in order of elution, **5** (320 mg, 55%) and **6** (216 mg, 37%). Methyl (6*R*)-2,3,4-tri-*O*-benzyl-6-(2-thiazolyl)-α-D-mannopyranoside (**5**) had $[\alpha]_D$ +29 (*c* 1.0); ^1H nmr, δ: 5.33 (s, 1H, H-6), 4.64 (s, 1H, H-1), 3.04 (s, 3H, OCH_3); ^{13}C nmr, δ_C: 99.3 (C-1), 80.1, 74.7, 74.2, 73.6, 70.3 (C-2 to C-6), 54.7 (OCH_3). Anal. calcd. for $C_{31}H_{33}NO_6S$: C 67.98, H 6.07, N 2.55, S 5.85; found: C 67.96, H 5.98, N 2.55, S 5.85. Methyl (6*S*)-2,3,4-tri-*O*-benzyl-6-(2-thiazolyl)-α-D-mannopyranoside (**6**) had $[\alpha]_D$ +31 (*c* 1.0); ^1H nmr, δ: 5.39 (d, 1H, $J_{5,6}$ 3.4 Hz, H-6), 4.75 (d, 1H, $J_{1,2}$ 1.7 Hz, H-1), 3.28 (s, 3H, OCH_3); ^{13}C nmr, δ_C: 98.9 (C-1), 80.1, 75.1, 74.6, 73.8, 72.3 (C-2 to C-6), 54.9 (OCH_3). Anal. calcd. for $C_{13}H_{33}NO_6S$: C 67.98, H 6.07, N 2.55, S 5.85; found: C 67.75, H 6.00, N 2.55, S 5.85.

*Methyl 2,3,4-tri-*O*-benzyl-L-glycero- (7) and methyl 2,3,4-tri-*O*-benzyl-D-glycero- (8) α-D-manno-heptopyranoside*

Formyl deblocking from the thiazole ring and subsequent reduction were carried in four successive steps. (1) Compounds **5** and **6** (150 mg, 0.27 mmol each) were separately treated with methyl iodide (0.17 mL, 2.7 mmol) in boiling acetonitrile (7 mL) for 24 h. (2) After removal of solvent, the residues in methanol (5 mL) were each treated with $NaBH_4$ (21 mg, 2 equiv.) at −10°C for 30 min, after which acetone (2 mL) was added to destroy excess of hydride. Solvent was evaporated, the residue were treated with saturated aqueous NaCl and extracted into ethyl acetate, and the extracts were concentrated. (3) The separate residues in acetonitrile (0.4 mL) were added to solutions of

$HgCl_2$ (90 mg, 1.2 equiv.) in acetonitrile–water (4:1, 5 mL), and the solutions were stirred at room temperature for 15 min. Reaction mixtures were filtered, and the filtrates were concentrated. The residues were treated with saturated aqueous NaCl, extracted with chloroform, and the extracts were concentrated. (4) $NaBH_4$ (21 mg each, 2 equiv.) was added portionwise during 30 min to the crude aldehydic products in methanol (10 mL) at room temperature. Acetic acid – water (1:1) was added dropwise to each solution to destroy excess of hydride and bring the solutions to pH 7, the respective solutions were concentrated, and the residues were chromatographed on silica gel.

Methyl 2,3,4-tri-*O*-benzyl-L-*glycero*-α-D-*manno*-heptopyranoside (**7**) (82 mg, 61%), formed from **5**, was eluted with dichloromethane containing 6% of acetone and had $[\alpha]_D$ +25 (*c* 1.0) (lit. $[\alpha]_D$ +30 (18), $[\alpha]_D$ +23 (19)); ^{1}H nmr, δ: 4.65 (s, 1H, H-1), 4.11 (t, 1H, $J_{3,4} \sim J_{4,5} \sim$ 9.5 Hz, H-4), 3.94 (m, 1H, H-6), 3.84 (dd, 1H, $J_{2,3}$ 3.0 Hz, $J_{3,4}$ 9.4 Hz, H-3), 3.80–3.60 (m, 3H, H-2, H-7), 3.55 (dd, 1H, $J_{5,6}$ 1.4 Hz, $J_{4,5}$ 9.7 Hz, H-5); ^{13}C nmr, δ_C: 99.5 (C-1), 80.0, 74.5, 74.3, 72.5, 69.4 (C-2 to C-6), 65.0 (C-7) (lit. (17, 18) for similar nmr data).

Methyl 2,3,4-tri-*O*-benzyl-D-*glycero*-α-D-*manno*-heptopyranoside (**8**) (76 mg, 57%), formed from **6**, was eluted with dichloromethane containing 4% of acetone and had $[\alpha]_D$ +35 (*c* 1.0); ^{1}H nmr, δ: 4.68 (d, 1H, $J_{1,2}$ 2.1 Hz, H-1), 4.02 (t, 1H, $J_{3,4} \sim J_{4,5} \sim$ 9.3 Hz, H-4), 3.93 (m, 2H, H-3, H-6), 3.80–3.63 (m, 4H, H-2, H-5, H-7); ^{13}C nmr, δ_C: 99.0 (C-1), 80.5, 76.9, 74.4, 72.5, 71.1 (C-2 to C-6), 62.9 (C-7) (lit. (20) for similar data).

Samples of **7** and **8** were each hydrogenolyzed in ethanol over palladium 5% on charcoal, the resulting methyl glycosides were hydrolyzed, and the heptoses were reduced and acetylated. The glc analysis showed the formation, respectively, of heptaacetates of L-*glycero*-D-*manno*-heptitol and D-*glycero*-D-*manno*-heptitol.

*Addition of 2-(trimethylsilyl)thiazole to methyl 2,3,4-tri-*O*-benzyl-α-D-gluco-hexodialdo-1,5-pyranoside* **9**

Treatment of **9** (from methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (21) (18 g, 38.8 mmol)) in dichloromethane (125 mL) with TMSthiazole (6.5 mL, 39.2 mmol) with subsequent processing, as described for **2**, afforded a mixture of **10** and **11** that was chromatographed on silica gel (light petroleum – ethyl acetate, 2:1). Methyl (6*R*)-2,3,4-tri-*O*-benzyl-6-(2-thiazolyl)-α-D-glucopyranoside (**10**) (11.57 g, 54.3%) had mp 110–112°C, and $[\alpha]_D$ +35 (*c* 1.0); ^{1}H nmr, δ: 5.24 (bs, 1H, H-6), 4.48 (d, 1H, $J_{1,2}$ 3.4 Hz, H-1), 4.16 (m, 1H, H-5), 4.06 (t, 1H, *J* 9.3 Hz, H-3 or H-4), 3.77 (t, 1H, *J* 9.6 Hz, H-4 or H-3), 3.51 (dd, 1H, $J_{1,2}$ 3.5 Hz, $J_{2,3}$ 9.5 Hz, H-2); ^{13}C nmr, δ_C: 98.1 (C-1), 81.9, 79.6, 76.9, 72.4, 69.8 (C-2 to C-6). Anal. calcd. for $C_{31}H_{33}NO_6S$: C 67.98, H 6.07, N 2.55, S 5.85; found: C 67.77, H 5.89, N 2.53, S 6.05.

Methyl (6*S*)-2,3,4-tri-*O*-benzyl-6-(2-thiazolyl)-α-D-glucopyranoside (**11**) (3.84 g, 18%) had $[\alpha]_D$ +33 (*c* 1.0); ^{1}H nmr, δ: 5.30 (d, 1H, $J_{5,6}$ 3.5 Hz, H-6), 4.60 (d, 1H, $J_{1,2}$ 3.8 Hz, H-1), 4.11 (dd, 1H, $J_{5,6}$ 3.5 Hz, $J_{4,5}$ 10 Hz, H-5), 4.04 (t, 1H, *J* 9.2 Hz, H-3 or H-4), 3.67 (t, 1H, *J* 9.4 Hz, H-4 or H-3), 3.43 (dd, 1H, $J_{1,2}$ 3.4 Hz, $J_{2,3}$ 9.5 Hz, H-2); ^{13}C nmr, δ_C: 97.8 (C-1), 82.0, 79.9, 78.6, 72.4, 71.9 (C-2 to C-6). Anal. calcd. for $C_{31}H_{33}NO_6S$: C 67.98, H 6.07, N 2.55, S 5.85; found: C 67.89, H 5.93, N 2.50; S 6.20.

Methyl 2,3,4-tri-*O*-benzyl-L-*glycero*-α-D-*gluco*-heptopyranoside (**12**) (4.5 g, 71%), formed from **10** (7 g), as described for **7** and **8**, was eluted with dichloromethane containing 8% of acetone and had $[\alpha]_D$ +53 (*c* 1.0); ^{1}H nmr, δ: 4.54 (d, 1H, $J_{1,2}$ 3.5 Hz, H-1), 3.97–3.50 (m, 7H, H-2 to H-7′); ^{13}C nmr, δ_C: 97.4 (C-1), 81.1, 79.0, 76.5, 69.9, 68.3 (C-2 to C-6), 64.0 (C-7). Anal. calcd. for $C_{29}H_{34}O_7$: C 70.42, H 6.92; found: C 70.49, H 7.06.

Methyl 2,3,4-tri-*O*-benzyl-D-*glycero*-α-D-*gluco*-heptopyranoside (**13**) (1.1 g, 71%), formed from **11** (2 g), as described for **7** and **8**, was eluted with dichloromethane containing 8% of acetone and had $[\alpha]_D$ +55 (*c* 1.0); ^{1}H nmr, δ: 4.53 (d, 1H, $J_{1,2}$ 3.4 Hz, H-1), 4.05–3.50 (m, 7H, H-2 to H-7′); ^{13}C nmr, δ_C: 97.7 (C-1), 82.1, 80.2, 79.7, 72.6, 69.8 (C-2 to C-6), 62.8 (C-7). Anal. calcd. for $C_{29}H_{34}O_7$: C 70.42, H 6.92; found: C 70.41, H 6.82.

Methyl L-*glycero*-α-D-*gluco*-heptopyranoside (**14**) (40 mg), from hydrogenolysis of **12** (100 mg) in ethanol (50 mL) over palladium 5% on charcoal, had mp 153–155°C, $[\alpha]_D$ +157 (*c* 1.0 MeOH); ^{1}H nmr (D_2O), δ: 4.73 (d, 1H, $J_{1,2}$ 3.66 Hz), 3.32 (s, 3H, OCH_3). The derived pentaacetate (**16**) had $[\alpha]_D$ +86 (*c* 1.0); ^{1}H nmr, δ: 5.46 (t, 1H, $J_{2,3} \sim J_{3,4} \sim$ 9.8 Hz, H-3 or H-4), 5.27 (m, 1H, H-6), 5.04 (t, 1H, $J_{3,4} \sim J_{4,5} \sim$ 9.8 Hz, H-4 or H-3), 4.99 (d, 1H, $J_{1,2}$ 3.7 Hz, H-1), 4.90 (dd, 1H, $J_{1,2}$ 3.7 Hz, $J_{2,3}$ 10 Hz, H-2), 4.29 (dd, 1H, $J_{6,7}$ 5.7 Hz, $J_{7,7'}$ 11.2 Hz, H-7), 4.21 (dd, 1H, $J_{6,7'}$ 7.5 Hz, $J_{7,7'}$ 11.2 Hz, H-7′), 4.08 (dd, 1H, $J_{5,6}$ 2.0 Hz, $J_{4,5}$ 10.2 Hz, H-5), 3.40 (s, 3H, OCH_3), 2.12, 2.08, 2.05, 2.01, 2.00 (5 s, 15H, $OCOCH_3$). Anal. calcd. for $C_{18}H_{26}O_{12}$: C 49.76, H 6.03; found: C 49.56, H 5.86.

Methyl D-*glycero*-α-D-*gluco*-heptopyranoside (**15**) (20 mg), from hydrogenolysis of **13** (60 mg) in ethanol (25 mL) over palladium 5% on charcoal, had $[\alpha]_D$ +107 (*c* 1.0, MeOH); ^{1}H nmr (D_2O), δ: 4.72 (d, 1H, $J_{1,2}$ 3.4 Hz), 3.35 (s, 3H, OCH_3). The derived pentaacetate (**17**) had $[\alpha]_D$ +127 (*c* 1.0); ^{1}H nmr, δ: 5.44 (t, 1H, *J* 10.1 Hz, H-3 or H-4), 5.22–5.17 (overlapping ddd, 1H, $J_{5,6}$ 2.8 Hz, $J_{6,7}$ 4.1 Hz, $J_{6,7'}$ 7.2 Hz, H-6), 5.08 (dd, 1H, *J* 9.2 and 10.2 Hz, H-4 or H-3), 4.94 (d, 1H, $J_{1,2}$ 3.6 Hz, H-1), 4.84 (dd, 1H, $J_{1,2}$ 3.7 Hz, $J_{2,3}$ 10.3 Hz, H-2), 4.36 (dd, 1H, $J_{7,7'}$ 11.8 Hz and $J_{6,7}$ 4.0 Hz, H-7a), 4.19 (dd, 1H, $J_{7,7'}$ 11.8 and $J_{6,7'}$ 7.23 Hz, H-7′), 4.01 (dd, 1H, $J_{5,6}$ 2.8 Hz, $J_{4,5}$ 10.1 Hz, H-5), 3.40 (s, 3H, OCH_3), 2.12, 2.08, 2.05, 2.01, 2.00 (5 s, 15H, $OCOCH_3$). Anal. calcd. for $C_{18}H_{26}O_{12}$: C 49.76, H 6.03; found: C 49.57, H 5.92.

Methyl glycosides **14** and **15** were hydrolyzed, and the heptoses were reduced and acetylated. The glc analysis showed the formation, respectively, of heptaacetates of L-*glycero*-D-*gluco*-heptitol and D-*glycero*-D-*gluco*-heptitol.

*Configurational inversions at C-6 of derivatives of methyl 2,3,4-tri-*O*-benzyl-L-*glycero*-α-D-*gluco*-heptopyranoside by an oxidation–reduction sequence*

(A) Thiazolyl derivative **10** (3.7 g, 6 mmol) in dichloromethane (10 mL) was added to periodinane (3.4 g, 8 mmol) at 0°C and the solution was kept for 30 min at 0°C and then at room temperature for 3.5 h. The solution was diluted with ether (100 mL) and poured with stirring into saturated aqueous $NaHCO_3$ (75 mL) containing $Na_2S_2O_3 \cdot 5H_2O$, and shaken for 5 min. The organic layer was separated, washed successively with saturated aqueous $NaHCO_3$, water, and aqueous sodium chloride, dried, and concentrated. L-Selectride (1 M in oxolane, 14 mL) was added to the resulting syrup (3.7 g) in oxolane at −78°C and stirred for 1 h. The reaction was quenched with a solution of aqueous 10% NaOH (20 mL) and 30% hydrogen peroxide (10 mL), and the mixture was stirred at room temperature for 2 h. Solvents were evaporated, the mixture was extracted with ethyl acetate, and the extract was washed with saturated aqueous NaCl, dried, and concentrated. Column chromatography, as above, furnished **10** (1.6 g) and **11** (1.4 g), characterized by tlc and their ^{1}H and ^{13}C nmr spectra, and incompletely separated mixture (0.5 g).

(B) Methyl glycoside (**12**) (4 g, 8 mmol) in *N,N*-dimethylformamide (30 mL) containing imidazole (1.2 g, 17.8 mmol) was treated with *tert*-butyldimethylsilyl chloride (1.34 g, 8.8 mmol) for 1 h at room temperature. The solution was diluted with ether, washed with water, dried, and concentrated. The product was chromatographed on silica gel (light petroleum – ethyl acetate, 2:1) to yield methyl 2,3,4-tri-*O*-benzyl-7-*O*-*tert*-butyldimethylsilyl-L-*glycero*-α-D-*gluco*-heptopyranoside (**19**) (4.9 g, 99%), $[\alpha]_D$ +7.4; ^{1}H nmr, δ: 4.52 (d, 1H, $J_{1,2}$ 3.47 Hz, H-1), 3.26 (s, 3H, OCH_3), 0.82 (s, 9H, $(CH_3)_3Si$), −0.012, −0.014 (2 s, 6H, CH_3Si). Anal. calcd. for $C_{35}H_{48}O_7Si$: C 69.04, H 7.94; found: C 69.00, H 7.85.

Methyl 2,3,4-tri-*O*-benzyl-7-*O*-*tert*-butyldimethylsilyl-D-*glycero*-α-D-*gluco*-heptopyranoside (**20**), similarly prepared as a reference sample, had $[\alpha]_D$ +11 (*c* 1.0); ^{1}H nmr, δ: 4.56 (d, 1H, $J_{1,2}$ 3.4 Hz, H-1), 3.37 (s, 3H, OCH_3), 0.85 (s, 9H, $(CH_3)_3Si$), 0.00 (2 s, 6H, CH_3Si). Anal. calcd. for $C_{35}H_{48}O_7Si$: C 69.04, H 7.94; found: C 68.94, H 7.74.

Oxidation of **19** (4.9 g, 7.9 mmol) with oxalyl chloride (9 mL, 18 mmol) and methyl sulfoxide (1.63 mL, 24.5 mmol) as described above and monitored by tlc afforded the 6-ulose, which was treated directly in oxolane (30 mL) with L-selectride (1 M in oxolane, 16 mL). After 30 min tlc showed the formation of an altered product with the mobility of **20** and only trace amounts of **19**. When the reaction was

quenched with alkaline hydrogen peroxide, tlc showed the formation of modified products without loss of silyl substituent. *O*-Desilylation (22) on treatment of the mixture in oxolane (30 mL) with tetrabutylammonium fluoride (1 M in oxolane, 15 mL) gave **13** (3.6 g, 90%), $[\alpha]_D$ +55 (*c* 1.0), identical (tlc, ^1H and ^{13}C nmr, and diastereomeric purity by conversion to the heptitol heptaacetate for glc analysis) to the previously prepared sample.

Configurational inversion at C-6 of methyl 2,3,4-tri-O-benzyl-L-glycero-α-D-manno-heptopyranoside by oxidation–reduction

Methyl heptoside **7** (47 mg, 0.09 mmol) in *N,N*-dimethylformamide (3 mL) containing imidazole (14 mg, 0.2 mmol) was treated with *tert*-butyldimethylsilyl chloride (16 mg, 0.1 mmol) for 4 h at room temperature. Thin-layer chromatography showed that reaction was incomplete, and further TBDMS (16 mg) and imidazole (14 mg) were added and reaction was continued for another 2 h. The solution was diluted with ether, washed with water, dried, concentrated, and chromatographed on silica gel (light petroleum – ethyl acetate, 3:1) to give methyl 2,3,4-tri-*O*-benzyl-7-*O*-*tert*-butyldimethylsilyl-L-*glycero*-α-D-*manno*-heptopyranoside (**21**) (53 mg, 90%), $[\alpha]_D$ +24 (*c* 1.0); ^1H nmr, δ: 4.56 (d, 1H, $J_{1,2}$ 2.78 Hz, H-1), 3.22 (s, 3H, OMe), 0.83 (s, 9H, $(CH_3)_3Si$), 0.00, −0.01 (2 s, 6H, CH_3Si). Anal. calcd. for $C_{35}H_{48}O_7Si$: C 69.04, H 7.94; found: C 68.92, H 7.97.

Oxidation of **21** (40 mg, 0.06 mmol) with oxalyl chloride (184 μL) and methyl sulfoxide (33 μL) in dichloromethane at −78°C, as described above and monitored by tlc, afforded the 6-ulose, which was treated directly in oxolane (5 mL) with L-selectride (1 M in oxolane, 136 μL) for 1 h. The reaction was quenched by the addition of alkaline hydrogen peroxide (10% aqueous NaOH and 30% H_2O_2, 2:1) to give a mixture of compounds that was treated with tetrabutylammonium fluoride (1 M in oxolane, 133 μL). The residue was chromatographed on silica gel to give **8** (26 mg, 80%), $[\alpha]_D$ +33 (*c* 1.0), as the sole detectable product, which was indistinguishable (tlc, ^1H and ^{13}C nmr) from the previous sample, and was further characterized by conversion into D-*glycero*-D-*manno*-heptitol heptaacetate (glc analysis). Treatment of the above-mentioned 6-ulose with sodium borohydride in methanol gave configurationally altered silyl ether (DDManHep) and **21** (LDManHep) in the approximate ratio of 9:1.

Oxidation of methyl 2,3,4-tri-O-benzyl-α-D-altropyranoside and addition of 2-(trimethylsilyl)thiazole to the resulting hexodialdo-1,5-pyranoside mixture

Methyl 2,3,4-tri-*O*-benzyl-α-D-altropyranoside (23) (250 mg, 0.53 mmol) was oxidized with oxalyl chloride (0.6 mL, 1.2 mmol) and methyl sulfoxide (0.11 mL, 1.43 mmol), as described previously, and gave a mixture of products (**22** and **23**) as indicated by the appearance of two aldehydic protons in the ^1H nmr spectrum at δ 9.76 and 9.59 in the approximate ratio of 1:4. The ^{13}C nmr spectrum showed inter alia two sets of resonances in the same relative proportions corresponding to those of ring carbon atoms of methyl glycosides having the β-galactopyranose (δ_C 104.6 (C-1), 80.8, 78.8, 78.5, and 74.7 (C-2 to C-5)) and α-altropyranose (δ_C 101.1 (C-1), 75.8, 74.6, 74.0, and 71.5 (C-2 to C-5)) configurations. Part of the mixture was reduced with $NaBH_4$ in methanol. One portion of the reduction product was acetylated and gc analysis on column B showed the presence of two components with the retention times of 6-*O*-acetyl-2,3,4-tri-*O*-benzyl derivatives of methyl β-D-galactopyranoside and methyl α-D-altropyranoside in the approximate ratio of 3:2. Another portion of the reduction product was *O*-debenzylated for hydrolysis, followed by (*a*) reduction and acetylation to give the corresponding mixtures of galactitol and altritol hexaacetates, and (*b*) glycosidation with (*R*)- and (*S*)-2-butanol and acetylation to give products with the retention times (glc on a DB-5 (15 m × 0.25 mm) column, 230°C (5 min), 230° → 260°C, 2°/min, 260°C) of derivatives of L-galactose and D-altrose.

2-TMSthiazole (0.12 mL was added to the remaining mixture of hexodialdo-1,5-pyranosides **22** and **23** (150 mg) as described previously, and chromatography on silica gel (light petroleum – ethyl acetate, 2:1) gave methyl (6*R*)-2,3,4-tri-*O*-benzyl-6-(2-thiazolyl)-β-L-galactopyranoside (**24**) (103 mg, 59%), $[\alpha]_D$ −4 (*c* 1.0); ^1H nmr, δ: 4.26 (d, 1H, $J_{1,2}$ 7.7 Hz, H-1), 3.87 (dd, 1H, $J_{1,2}$ 7.7 Hz, $J_{2,3}$ 9.7 Hz, H-2), 3.53 (s, 3H, OCH_3); ^{13}C nmr, δ_C: 105.2 (C-1), 81.8, 79.3, 75.9, 73.8, 70.1 (C-2 to C-6), 57.4 (OCH_3). Anal. calcd. for $C_{31}H_{33}NO_6S$: C 67.98, H 6.07, N 2.55; found: C 67.82, H 6.15, N 2.55.

Methyl 2,3,4-tri-*O*-benzyl-L-*glycero*-α-L-*galacto*-heptopyranoside (**25**) (50 mg, 74%), formed from **24** (75 mg), as described for **7** and **8**, was chromatographed on silica gel with dichloromethane containing 8% of acetone and had $[\alpha]_D$ +13 (*c* 1.0); ^1H nmr, δ: 4.24 (d, 1H, $J_{1,2}$ 7.6 Hz, H-1), 3.51 (s, 3H, OCH_3); ^{13}C nmr, δ_C: 105.0 (C-1), 82.1, 79.5, 74.0, 71.9, 69.1 (C-2 to C-6), 63.8 (C-7). Anal. calcd. for $C_{29}H_{34}O_7$: C 70.42, H 6.92; found: C 70.28, H 6.94.

A sample of **25** was hydrogenolyzed in ethanol over palladium 5% on charcoal, the resulting methyl glycoside was hydrolyzed, and the heptose was reduced and acetylated. The glc analysis showed the formation, respectively, of a heptitol heptaacetate with the retention time of the corresponding derivative of L-*glycero*-D-*manno*-heptitol (= enantiomer of L-*glycero*-L-*galacto*-heptitol).

*2-(Trimethylsilyl)thiazole homologation of 1,2:3,4-di-O-isopropylidene-α-D-galacto-hexadialdo-1,5-pyranose **3** and configurational inversion of product **4** at C-6*

A solution in dichloromethane (10 mL) of compound **3** (1 g, 3.84 mmol), from oxidation of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose with oxalyl chloride and methyl sulfoxide showed ^{13}C nmr, δ_C: 199.0 (CHO), 108.3 (C-1), 95.5, 72.5, 70.9, 69.7 (C-2 to C-5), and was reacted with TMS thiazole (0.72 mL, 4.37 mmol), as described previously, and silica gel chromatography (light petroleum – ethyl acetate, 2:1) furnished (6*S*)-1,2:3,4-di-*O*-isopropylidene-6-(2-thiazolyl)-α-D-galactopyranose (**4**) (780 mg, 60%), mp 178–180°C (lit. (6) mp 170–172°C), $[\alpha]_D$ −67 (*c* 1.0); ^1H nmr, δ: 5.57 (d, 1H, $J_{1,2}$ 4.9 Hz, H-1), 5.14 (d, 1H, $J_{5,6}$ 7.9 Hz, H-6), 4.65 (dd, 1H, $J_{2,3}$ 2.3 Hz, H-2), 4.54 (dd, 1H, $J_{4,5}$ 1.3 Hz, H-4), 4.33 (dd, 1H, H-2), 4.10 (dd, 1H, H-5); ^{13}C nmr, δ_C: 96.2 (C-1), 70.7, 70.4, 70.3, 69.4, 68.0 (C-2 to C-6).

1,2:3,4-Di-*O*-isopropylidene-D-*glycero*-α-D-*galacto*-heptopyranose (**26**) (182 mg, 72%), formed from **4** (300 mg), as described for **7** and **8**, was chromatographed on silica gel (dichloromethane containing 10% of acetone) and had $[\alpha]_D$ −57 (*c* 1.0); ^1H nmr: δ: 5.50 (d, 1H, $J_{1,2}$ 4.9 Hz, H-1), 4.63 (dd, 1H, $J_{2,3}$ 2.3 Hz, $J_{3,4}$ 7.9 Hz, H-3), 4.46 (dd, 1H, $J_{4,5}$ 1.6 Hz, H-4), 4.30 (dd, 1H, H-2), 3.88–3.68 (m, 4H, H-5, 6, 7, 7′); ^{13}C nmr, δ_C: 96.2 (C-1), 70.7, 70.6, 70.5, 69.9, 67.3 (C-2 to C-6), 63.8 (C-7). Anal. calcd. for $C_{13}H_{22}O_7$: C 53.78, H 7.64; found: C 53.46, H 7.74. Compound **26** was hydrolyzed, and the resulting heptose was reduced and acetylated. The glc analysis showed the formation, respectively, of the heptaacetate of D-*glycero*-D-*galacto*-heptitol (= L-*glycero*-D-*manno*-heptitol).

Thiazole adduct **4** (49 mg) was oxidized with oxalyl chloride and methyl sulfoxide and the product, without further purification, was reduced with L-selectride, as reported by Dondoni et al. (13), and the isolated (6*R*)-1,2:3,4-di-*O*-isopropylidene-6-(2-thiazolyl)-α-D-galactopyranose (**18**) (30 mg, 60%) had mp 102–104°C (lit. (13) mp 98–100°C); ^1H nmr, δ: 5.57 (d, 1H, $J_{1,2}$ 4.8 Hz, H-1), 5.34 (d, 1H, $J_{5,6}$ 4.8 Hz, H-6), 4.63 (dd, 1H, $J_{2,3}$ 2.4 Hz, $J_{3,4}$ 8.0 Hz, H-3), 4.46 (dd, 1H, $J_{4,5}$ 1.6 Hz, H-4), 4.32 (dd, 1H, H-2), 4.15 (dd, 1H, H-5); ^{13}C nmr, δ_C: 96.4 (C-1), 72.4, 71.9, 70.9, 70.8, 69.8 (C-2 to C-6).

1,2:3,4-Di-*O*-isopropylidene-L-*glycero*-α-D-*galacto*-heptopyranose (**27**) (13 mg, 63%), formed from **18** (25 mg), as described for **7** and **8**, was chromatographed on silica gel (dichloromethane containing 10% of acetone) and had mp 98–100°C, $[\alpha]_D$ −41 (*c* 1.0); ^1H nmr, δ: 5.59 (d, 1H, $J_{1,2}$ 5.0 Hz, H-1), 4.62 (dd, 1H, $J_{2,3}$ 2.3 Hz, $J_{3,4}$ 7.9 Hz, H-3), 4.36–4.33 (m, 2H), 3.79–3.77 (m, 4H); ^{13}C nmr, δ_C: 96.4 (C-1), 71.6, 71.3, 70.8, 70.5, 67.5 (C-2 to C-6), 62.4 (C-7). Anal. calcd. for $C_{13}H_{22}O_7$: C 53.78, H 7.64; found: C 53.93, H 7.63. Compound **27** was hydrolyzed, and the resulting heptose was reduced and acetylated. The glc analysis showed the formation of the heptaacetate of L-*glycero*-D-*galacto*-heptitol (= L-*glycero*-D-*gluco*-heptitol).

Oxidation of methyl 2,3,4-tri-O-benzyl-β-D-galactopyranoside and addition of 2-(trimethylsilyl)thiazole to the resulting hexodialdo-1,5-pyranoside mixture

Methyl 2,3,4-tri-*O*-benzyl-β-D-galactopyranoside (24) (1.09 g,

2.3 mmol) was oxidized with oxalyl chloride (2.4 mL, 4.8 mmol) and methyl sulfoxide (0.47 mL, 6.1 mmol), as described previously, and gave a mixture of products corresponding to enantiomers **22** and **23**, as indicated by the appearance of two aldehydic protons in the ^{1}H nmr spectrum at δ 9.68 and 9.53 in the approximate ratio of 1:6. The ^{13}C nmr spectrum showed inter alia two sets of resonances in the same relative proportions corresponding to those of ring carbon atoms of methyl glycosides having the β-galactopyranose (δ_C 104.6 (C-1), 80.8, 78.8, 78.5, and 74.7 (C-2 to C-5)) and α-altropyranose (δ_C 101.1 (C-1), 75.8, 74.6, 74.0, and 71.5 (C-2 to C-5)) configurations. A portion of the mixture was reduced with $NaBH_4$ in methanol, the reduction product was acetylated, and glc analysis on column B showed the presence of components with the retention times of 6-*O*-acetyl-2,3,4-tri-*O*-benzyl derivatives of methyl β-D-galactopyranoside and methyl α-D-altropyranoside in the approximate ratio of 3:1. 2-TMSthiazole (0.45 mL) was added to the remaining mixture of hexodialdo-1,5-pyranosides (950 mg) was described previously, and chromatography on silica gel (light petroleum – ethyl acetate, 2:1) gave methyl (6*S*)-2,3,4-tri-*O*-benzyl-6-(2-thiazolyl)-β-D-galactopyranoside (**28**) (853 mg, 76%), $[\alpha]_D$ +2.5 (*c* 1.0); ^{1}H nmr, δ: 4.20 (d, 1H, $J_{1,2}$ 7.6 Hz, H-1), 3.46 (s, 3H, OCH_3); ^{13}C nmr, δ_C: 104.7 (C-1), 81.4, 78.9, 75.8, 73.5, 69.3 (C-2 to C-6), 56.9 (OCH_3). Within experimental limits these spectra were identical to those of the enantiomer **24**. Anal. calcd. for $C_{31}H_{33}NO_6S$: C 67.98, H 6.07, N 2.55; found: C 67.92, H 6.14, N 2.53.

Methyl 2,3,4-tri-*O*-benzyl-D-*glycero*-α-D-*galacto*-heptopyranoside (**29**) (220 mg, 60%), formed from **28** (407 mg), as described for **7** and **8**, was eluted from silica gel with dichloromethane containing 5% of acetone and had mp 101–103°C and $[\alpha]_D$ −18 (*c* 1.0); ^{1}H nmr, δ: 4.21 (d, 1H, $J_{1,2}$ 7.6 Hz, H-1), 3.47 (s, 3H, OCH_3); ^{13}C nmr, δ_C: 104.8 (C-1), 81.9, 79.3, 73.8, 72.4, 69.0 (C-2 to C-6), 63.6 (C-7). Anal. calcd. for $C_{29}H_{34}O_7$: C 70.42, H 6.92; found: C 70.41, H 6.88. A sample of **29** was hydrogenolyzed in ethanol over palladium 5% on charcoal, the resulting methyl glycoside was hydrolyzed, and the heptose was reduced and acetylated. The glc analysis showed the formation of a heptitol heptaacetate with the retention time of the corresponding derivative of L-*glycero*-D-*manno*-heptitol (= enantiomer of L-*glycero*-L-*galacto*-heptitol).

Configurational inversions at C-6 and C-5 of methyl (6S)-2,3,4-tri-O-benzyl-6-(2-thiazolyl)-β-D-galactopyranoside (28)

Thiazolyl derivative **28** (85 mg, 0.15 mmol) was oxidized as described previously with oxalyl chloride (0.175 mL, 0.35 mmol) and methyl sulfoxide (0.03 mL, 0.45 mmol). The product (84 mg), without purification, was reduced with L-selectride (0.3 mL, 0.33 mmol) in oxolane. The resulting syrup was separated by preparative layer chromatography (multiple development in light petroleum – ether–methanol, 14:6:1) to give two main fractions.

Fraction 1 (15 mg) had $[\alpha]_D$ +5 (*c* 1.0); ^{1}H nmr, δ: 5.25 (d, 1H, $J_{5,6}$ 3.58 Hz, H-6), 4.22 (d, 1H, $J_{1,2}$ 7.7 Hz, H-1), 3.84 (d, 1H, $J_{2,3}$ 9.7 Hz and $J_{1,2}$ 7.7 Hz, H-2), 3.52 (dd, 1H, $J_{2,3}$ 9.7 Hz and $J_{3,4}$ 2.8 Hz, H-3), 3.41 (s, 3H, OCH_3); ^{13}C nmr, δ_C: 105.1 (C-1), 81.9, 79.1, 75.9, 75.6, 72.4 (C-2 to C-5), 57.0 (OCH_3). The sequence of operations, formyl deblocking, *O*-debenzylation, hydrolysis, reduction, and acetylation, gave a single heptitol heptaacetate coincident on glc analysis (column A) with the corresponding derivative from L-*glycero*-D-*galacto*-heptose. The ^{13}C nmr spectrum of fraction 2 (39 mg) showed the presence of signals assignable to anomeric C-1 resonances of compounds with β-galacto (δ_C 104.3) and α-altro (δ_C 99.6) ring configurations and, without individual specifications, to two sets of carbon atoms 2 to 6. Formyl deblocking furnished a mixture of methyl tri-*O*-benzyl heptopyranosides whose ^{13}C nmr spectrum likewise showed anomeric carbon resonances at δ_C 105.1 and 100.5 consistent with the presence of β-*galacto* and α-*altro* configurational isomers together with two sets of other carbon resonances. This mixture of compounds was *O*-debenzylated by formic acid with 5% palladium on charcoal as catalyst, hydrolyzed, reduced, and acetylated. The glc analysis (column A) showed the presence of two heptitol heptaacetates coincident with those from D-*glycero*-D-*galacto*-heptose and D-*glycero*-D-*altro*-heptose.

Conversion of methyl D-glycero-D-gluco-heptopyranoside into methyl D-glycero-D-altro-heptopyranoside derivatives

Methyl 2,3,4-tri-*O*-benzyl-7-*O*-*tert*-butyldiphenylsilyl-D-*glycero*-α-D-*gluco*-heptopyranoside (**30**) was prepared as described for **19** and had $[\alpha]_D$ +9 (*c* 1.0); ^{1}H nmr, δ: 7.63–7.10 (m, 25H, Ph-H), 4.61 (d, 1H, $J_{1,2}$ 3.60 Hz, H-1), 3.24 (s, 3H, OCH_3), 1.05 (s, 9H, $(CH_3)_3Si$) Anal. calcd. for $C_{45}H_{52}O_7Si$: 73.73, H 7.15; found: C 73.45, H 7.04.

Similarly, silylation of methyl D-*glycero*-α-D-*gluco*-heptopyranoside (**15**) (2 g, 8.9 mmol) followed by chromatography on silica gel (dichloromethane–methanol, 9:1) afforded methyl 7-*O*-*tert*-butyldiphenylsilyl-D-*glycero*-α-D-*gluco*-heptopyranoside (**31**) (2.9 g, 71%), $[\alpha]_D$ +59 (*c* 1.0, methanol); ^{1}H nmr, δ: 7.68–7.32 (m, 10H, Ph-H), 4.61 (d, 1H, $J_{1,2}$ 3.6 Hz, H-1), 3.24 (s, 3H, OCH_3). Exact Mass calcd. for $C_{24}H_{34}O_7Si$ + H: 463.2135; found: 463.2152; calcd. for $C_{24}H_{34}O_7Si$ + Na: 485.1941; found: 485.1971.

A solution of **31** (1 g, 2.16 mmol), benzaldehyde dimethyl acetal (0.67 mL, 2 equiv., 3.9 mmol), and *p*-toluenesulfonic acid (50 mg) in toluene (50 mL) was kept at 30°C for 1 h under reduced pressure (aspirator), to ensure removal of methanol. Solid $NaHCO_3$ was added, the solution was concentrated, the residue was partitioned between dichloromethane and water, and the organic layer was dried and concentrated. The residue was chromatographed on silica gel (dichloromethane containing 1% of methanol) to give methyl 4,6-*O*-benzylidene-7-*O*-*tert*-butyldiphenylsilyl-D-*glycero*-α-D-*gluco*-heptopyranoside (**32**) (913 mg, 76%), $[\alpha]_D$ +94 (*c* 1.0); ^{1}H nmr, δ: 7.60–7.22 (m, 15H, Ph-H), 5.57 (s, 1H, C*H*Ph), 4.69 (d, 1H, $J_{1,2}$ 3.10 Hz, H-1), 3.34 (s, 3H, OCH_3), 1.03 (s, 9H, $(CH_3)_3Si$). Exact Mass calcd. for $C_{31}H_{38}O_7Si$ + H: 551.2465; found: 551.2465.

Compound **32** (630 mg, 1.14 mmol) was added to sodium hydride (55 mg, 2 equiv.) in *N*,*N*-dimethylformamide (10 mL) and the mixture was stirred for 30 min. *N*-Tosylimidazole (280 mg, 1.1 equiv.) was added and the mixture was stirred at room temperature for 4 days. Thin-layer chromatography showed the successive formation after 1 h of 2-*O*-tosyl derivative (**33**) and *O*-silyl epoxide (**34**), and, after 24 h, complete reaction of **32** and conversion of **33** into **34**, but now the appearance of *O*-desilylated epoxide (**35**). After 84 h conversion of **34** into **35** was complete. The reaction mixture was poured into ice-water, the product was extracted with dichloromethane, and the organic layer was washed with water, concentrated, and chromatographed on silica gel (light petroleum – ethyl acetate, 9:1) to give methyl 2,3-anhydro-4,6-*O*-benzylidene-D-*glycero*-α-D-*manno*-heptopyranoside (**35**) (236 mg, 70%), $[\alpha]_D$ +20 (*c* 1.0); ^{1}H nmr (including ^{1}H–^{1}H COSY), δ: 7.52–7.25 (m, 5H, Ph-H), 5.69 (s, 1H, C*H*Ph), 4.92 (d, 1H, H-1), 3.49 (d, 1H, $J_{2,3}$ 3.7 Hz, H-3), 3.34 (s, 3H, OCH_3), 3.18 (d, 1H, $J_{2,3}$ 3.7 Hz, H-2), 1.03 (s, 9H, $(CH_3)_3Si$). Anal. calcd. for $C_{15}H_{18}O_6$: C 61.21, H 6.16; found: C 61.16, H 6.18.

The ^{1}H nmr spectrum of **33** showed inter alia resonances at δ 7.8–7.2 (m, 14H, Ph-H), 5.57 (s, 1H, acetal C*H*Ph), 4.83 (d, 1H, $J_{1,2}$ 3.7 Hz, H-1), 4.39 (dd, 1H, $J_{1,2}$ 3.8 Hz, $J_{2,3}$ 9.4 Hz, H-2), 4.16 (t, 1H, $J_{2,3} \sim J_{3,4}$ = 9.3 Hz, H-3), 3.31 (s, 3H, OCH_3), 2.43 (s, 3H, CH_3-$C_6H_4SO_2$), 1.03 (s, 9H, $(CH_3)_3C$). On acetylation the resonance of H-3 is shifted to δ 5.60. The ^{1}H nmr spectrum of **34** showed inter alia resonances at δ 7.7–7.2 (m, 10H, Ph-H), 5.66 (s, 1H, acetal C*H*Ph), 4.89 (s, 1H, H-1), 3.51 (d, 1H, $J_{2,3}$ 3.7 Hz, H-3), 3.40 (s, 3H, OCH_3), 3.17 (d, 1H, $J_{2,3}$ 3.7 Hz, H-2), 1.06 (s, 9H, $(CH_3)_3C$).

Compound **35** (151 mg) was heated at 100°C in 1 M aqueous sodium hydroxide for 12 h. Liquid–liquid extraction of the solution with chloroform afforded methyl 4,6-*O*-benzylidene-D-*glycero*-α-D-*altro*-heptopyranoside (**36**) (140 mg, 87%), which crystallized from ether–methanol and had mp 209–211°C, $[\alpha]_D$ +92 (*c* 1.0, methanol); ^{1}H nmr (D_2O), δ: 7.55–7.42 (m, 5H, Ph-H), 5.85 (s, 1H, Ph-C*H*), 4.67 (s, 1H, H-1), 3.35 (s, 3H, OMe); ^{13}C nmr, δ: 129.4, 128.2, 126.0 (aromatic C), 101.4 (Ph-*C*H), 101.0 (C-1), 79.0, 74.3, 69.5, 67.5, 58.3 (C-2 to C-6), 60.1 (C-7), 54.7 (OCH_3). Anal. calcd. for $C_{15}H_{22}O_7$: C 57.68, H 6.45; found: C 57.34, H, 6.33. Acetylation of **36** under standard conditions afforded the tri-*O*-acetyl derivative **37**, which had $[\alpha]_D$ +92 (*c* 1.0); $[\alpha]_D$ +55 (*c* 1.0); ^{1}H nmr (1 D with decoupling and ^{1}H–^{1}H COSY), δ: 7.47–7.26 (m, 5H, Ph-H), 5.23 (1H, br s, H-3), 5.00 (d, 1H, $J_{2,3}$ 2 Hz, H-2), 4.60 (s, 1H, H-1), 4.49 (d, 1H, $J_{7,7'}$ 12 Hz, H-7), 4.27

(dd, 1H, $J_{7,7'}$ 12 Hz, $J_{6,7'}$ 5 Hz, H-7'), 4.06 (m, 3H, H-4, H-5, H-6), 3.36 (s, 3H, OMe), 2.14, 2.12, 2.10 (3 s, 9H, OAc).

O-Benzylidene compound **36** (110 mg) was heated in acetic acid – water (4:1) for 2 h at 80°C and concentration of the solution gave methyl D-*glycero*-α-D-*altro*-heptopyranoside (**38**) (70 mg, 86%), $[\alpha]_D$ +68 (*c* 1.0, methanol); ^{1}H nmr (D_2O), δ: 4.61 (s, 1H, H-1), 3.24 (s, 3H, OMe); ^{13}C nmr, δ_C: 100.4 (C-1), 70.8, 70.0, 69.4, 69.1, 65.0 (C-2 to C-6), 61.3 (C-7), 55.0 (OCH_3). The penta-*O*-acetyl derivative **39** had $[\alpha]_D$ +50 (*c* 1.0); ^{1}H nmr (1 D with decoupling and ^{1}H–^{1}H COSY), δ: 4.94 (dd, 1H, $J_{1,2}$ 1.7 Hz, $J_{2,3}$ 4.1 Hz, H-2), 4.62 (d, 1H, $J_{1,2}$ 1.3 Hz, H-1), 4.43 (dd, 1H, $J_{7,7'}$ 12 Hz, $J_{6,7}$ 3.8 Hz, H-7), 4.18 (dd, 1H, $J_{7,7'}$ 12 Hz, $J_{6,7'}$ 7.2 Hz, H-7'), 3.40 (s, 3H, OMe), 2.13, 2.12, 2.10, 2.07, 2.05 (5 s, 15H, OAc); ^{13}C nmr, δ_C: 99.2 (C-2), 69.8, 69.4, 67.3, 66.6, 65.8 (C-2 to C-6), 61.9 (C-7), 55.6 (OCH_3). Anal. calcd. for $C_{18}H_{26}O_{12}$: C 49.76, H 6.03; found: C 49.83, H 5.95.

Hydrolysis of methyl heptoside (**38**), followed by treatment of the product with $NaBH_4$ and acetylation, gave products that were coincident on gc with the heptitol heptaacetate formed from the O:36 glycan with accompanying 1,6- and 1,7-anhydroheptose tetraacetates. Further samples of the hydrolyzate were converted into glycoside acetates on reaction with (*R*)- and (*S*)-2-butanol followed by acetylation. Comparison (gc on column A) of these glycoside acetates with those similarly derived from the hydrolysate of the O:36 glycan showed that the natural heptose was D-*glycero*-D-*altro*-heptose.

Anhydro glycoside **35** (34 mg) was boiled with methanolic 2 M sodium methoxide (10 mL) for 16 h. Solvent was evaporated and the residue in dichloromethane was washed successively with water, saturated NaCl, and again water, dried, concentrated, and chromatographed on silica gel (light petroleum – ethyl acetate, 4:1, later 2:1) to give methyl 4,6-*O*-benzylidene-3-*O*-methyl-D-*glycero*-α-D-*altro*-heptopyranoside (**40**) (28 mg, 74%), $[\alpha]_D$ +81 (*c* 1.0); ^{1}H nmr, δ: 7.52–7.26 (m, 5H, Ph-H), 5.67 (s, 1H, Ph-C*H*), 4.60 (s, 1H, H-1), 3.58, 3.41 (2 s, 6H, OMe). Acetylation of **40** gave the di-*O*-acetyl derivative **41**, $[\alpha]_D$ +45 (*c* 0.5); ^{1}H nmr (1 D with decoupling and ^{1}H–^{1}H COSY), δ: 7.52–7.26 (m, 5H, Ph-H), 5.67 (s, 1H, Ph-C-*H*), 5.09 (d, 1H, $J_{2,3}$ 2.5 Hz, H-2), 4.58 (s, 1H, H-1), 4.47 (dd, 1H, $J_{7,7'}$ 12 Hz, $J_{6,7}$ 1.7 Hz, H-7), 4.26 (dd, 1H, $J_{7,7'}$ 12 Hz, $J_{6,7}$ 5.9 Hz, H-7'), 4.15 (t, 1H, $J_{4,5} \sim J_{5,6} \sim$ 9.6 Hz, H-5), 4.05–3.99 (m, 1H, H-6), 3.95 (dd, 1H, $J_{4,5}$ 9.5 Hz, $J_{3,4}$ 2.9 Hz, H-4), 3.71 (t, 1H, *J* 2.4 Hz, H-3), 3.58, 3.39 (2 s, 6H, OMe), 2.14, 2.09 (2 s, 6H, OAc); ^{13}C nmr, δ_C: 137.2 (quat. aromatic C), 129.2, 128.3, 126.4 (aromatic C), 101.9 (Ph-*C*-H), 99.4 (C-1), 77.5, 76.3, 75.6, 70.0, 60.1 (C-2 to C-6), 63.2 (C-7), 59.2, 55.8 (2 OCH_3). Anal. calcd. for $C_{20}H_{26}O_9$: C 58.51, H 6.38; found: C 58.24, H 6.35.

Hydrolysis of **40** (27 mg) in acetic acid – water (4:1) for 1 h at 80°C gave methyl heptoside (**42**) (18 mg), $[\alpha]_D$ +92 (*c* 1.0, methanol), which was converted into the acetylated derivative (**43**), $[\alpha]_D$ +86 (*c* 1.0); ^{1}H nmr (1 D with decoupling and ^{1}H–^{1}H COSY), δ: 5.33 (ddd (apparent quintet), 1H, $J_{5,6} = J_{6,7'} \sim$ 3.8 Hz, H-6), 5.11 (dd, 1H, $J_{3,4}$ 3.5 Hz, $J_{4,5}$ 9.1 Hz, H-4), 5.04 (dd, 1H, $J_{1,2}$ 1.7 Hz, $J_{2,3}$ 4.5 Hz, H-2), 4.60 (s, 1H, H-1), 4.43 (dd, 1H, $J_{6,7}$ 3.6 Hz, $J_{7,7'}$ 12.0 Hz, H-7), 4.28 (dd, 1H, $J_{4,5}$ 9.1 Hz, $J_{5,6}$ 4.0 Hz, H-5), 4.18 (dd, 1H, $J_{6,7'}$ 7.4 Hz, $J_{7,7'}$ 12.0 Hz, H-7'), 3.66 (t, 1H, $J_{2,3} = J_{3,4} \sim$ 3.9 Hz, H-3), 3.45, 3.40 (2 s, 6H, OCH_3), 2.14, 2.13, 2.10, 2.05 (4 s, 12H, OAc). Anal. calcd. for $C_{17}H_{26}O_{11}$: C 50.24, H 6.45; found: C 50.44, C 6.47.

Hydrolysis of methyl heptoside (**42**), followed by treatment of the product with $NaBH_4$ and acetylation, gave products that were coincident on gc with the *O*-methylheptitol hexaacetate formed from the O:23 glycan with accompanying 1,6- and 1,7-anhydro-3-*O*-methylheptose triacetates. Further samples of the hydrolyzate were converted into glycoside acetates on reaction with (*R*)- and (*S*)-2-butanol followed by acetylation. Comparison (gc on column A) of these glycoside acetates with those similarly derived from the hydrolysate of the O:23 glycan showed that the natural heptose was 3-*O*-methyl-D-*glycero*-D-*altro*-heptose.

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