Application of asymmetric aqueous aldol reaction using water-compatible organocatalysts: Stereoselective synthesis of carbohydrates and spiroacetals

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Contents

Introduction

Chirality of carbohydrates affords their functions in chemical and biological systems, and increasing knowledge about the structure and reactivity of the carbohydrate molecules is providing a greater understanding of stereochemistry on almost all important organic compounds, hence stereochemical principles in carbohydrate chemistry can be superimposed on aliphatic and heterocyclic chemistry.

In nature, carbohydrates occupy central roles on biosynthesis because of the existence of their abundant stereoisomers, due to the several chiral centers, affords inductive determinations of a shape of natural molecules in which the conformational disposition of hydroxyls of the sugar chain would present favorable orientations, and in synthesis, the synthesis of optically active molecules of biological significance, often containing several or more chiral centers, makes extensive use of intermediates derived from carbohydrates. The use of natural carbohydrates for the synthesis of enantiomerically pure compounds has been of particularly interest since many sugars are available with a variety of relative and absolute stereochemistries, and are capable of undergoing a wide range of synthetic transformations.

As a result of their immense importance in many different sectors, the structure and properties of carbohydrates have been widely studied and it is the intension of this research to extent of applications of the carbohydrate chemistry to development of a new approach for construction of carbohydrate chains by stereoselective aldol reaction using the carbohydrate-based organocatalysts in water; water is regarded as an ideal solvent in terms of its environmental influence and low cost, however, achievements of stereocontrolling the stereoselective reactions in water are elusive.

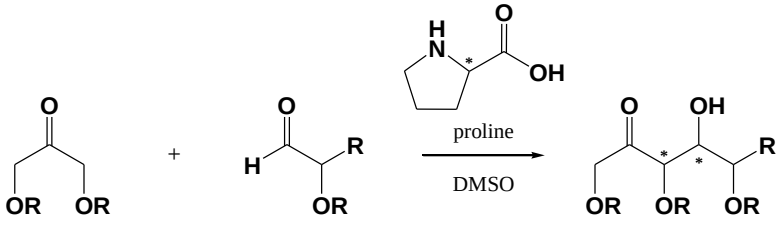
Prolinamido-glycosides in which the sugar component is the chiral auxiliary have been of sustained synthetic interest as the catalysts, as such products should in principle be effective to asymmetric aldol reactions in water.[1]

This thesis comprises stereoselective synthesis of carbohydrates by aldol reaction using the prolinamido-glycosides, namely, methyl 2-(L-prolyl)-amido-α-D-glucopyranoside **7** and methyl 2-(D-prolyl)-amido-α-D-glucopyranoside **8**, catalysts that have been exploited for the aldol reaction in water (Figure 1). Because of the fixed hydroxyls of the sugar ring, such hydroxyl groups are capable of interacting with aldehyde acceptors in the transition state, they would be expected acting as water compatible organocatalysts.

7 **8**

Figure 1. Prolinamido-glycoside catalysts

The proline catalyzes cross aldol reaction[2] is one of the easiest procedures for the controlled introduction of a carbon-carbon bond, possesses hydroxyl groups as substituents, from a carbonyl compound. This reaction has found significant use in the carbohydrate synthesis as a convenient route to uloses[3] (Scheme 1). Suitably protected aldoses are readily convertible by the aldol reaction of dihydroxyacetone derivatives into the corresponding uloses.



Scheme 1. Carbohydrate synthesis *via* carbohydrates by proline catalyzed aldol reaction.

A disadvantage of this and related methods is that they do not allow stereoselective aldol reaction in water. Since proline and the analogues have shown decreased selectivities in water[4], the conventional methods, using either hydrophilic or hydrophobic substrates, require an organic solvent for stereoselective aldol reactions. In the midst of wide-ranging research on the role of organocatalysts in asymmetric aldol reactions, and the attendant focus on design of such catalysts, the important role of which in water is overlooked in the tedious 'hydrophobic active pocket' theory. This persistence is spread in some 'organocatalytic chemists', albeit mechanistic pathway of the aldol reaction essentially requires participation of water molecules as Janda described.[4(b),(c)] Regarding the cause of the stereoselectivity of proline catalyzes aldol reaction, previous reports[5] showed a proposed transition state involves interactions of substrates and the catalyst, in which a large substituent of an aldehyde predominantly poses a pseudo equatorial orientation, and water is known to inhibit the asymmetric aldol reactions by interrupting hydrogen bonds of the stabilized transition state. A proposed transition state of the proline catalyzed aldol reaction was illustrated in Figure 2.

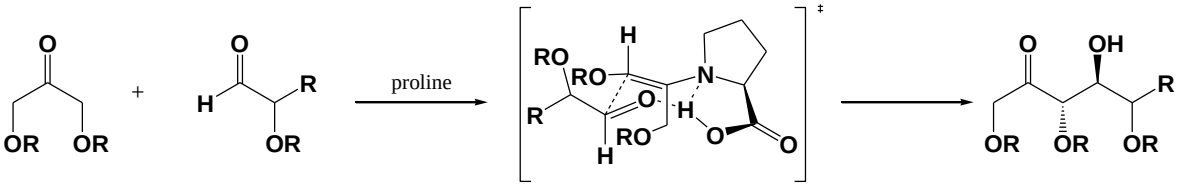
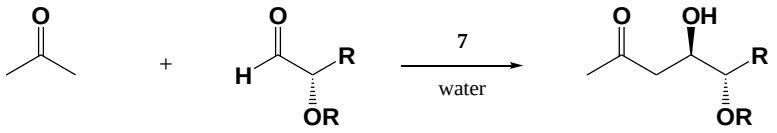


Figure 2. Mechanistic pathway for the proline catalyzed aldol reaction.

This limited solvent compatibility of the proline catalyzed asymmetric aldol reaction is one of the reasons that much effort has been put into developing other asymmetric organocatalysts[6], especially, development of the asymmetric catalysts catalyzing asymmetric aldol reaction in an aqueous media has focused on.

In this context, prolinamido-glycoside catalyzed aldol reaction has been of particular value. With a view to achieving stereoselective cross aldol reaction in an aqueous medium, **7** and **8** were prepared. The first chapter sets the scene by illustrating synthesis of **7** and **8**.

In aqueous media, they exhibited catalyzing the formation of aldol products with stereocontrol, and the observed stereoselectivity in their aldol reaction on acetone, using **7** or **8**, was in general accordance with the empirical Felkin-Anh theory,[7] especially if the conformational disposition of the chiral aldehydes had presented a favorable conformation by avoiding eclipsing bulky substituent along the C-1–C-2 bond, in which L-prolinamido-glycoside **7** selectively catalyzed *re*-facial attack, it has shown increased selectivity in the reactions with (*2S*)-aldehydes which possess a less hindered *re*-face, and D-prolinamido-glycoside **8** selectively catalyzed *si*-facial attack and prefers (*2R*)-aldehyde favor *si*-facial selective aldol reaction. For example, reaction of the (*2S*)-aldehydes, e.g., 2,3-*O*-isopropylidene-L-glyceraldehyde and 2,3:4,5-di-*O*-isopropylidene-D-arabinose, with acetone in the presence of 0.1 equivalent of **7** was successful in bringing about desired reaction in terms of diastereoselectivity (Scheme 2).

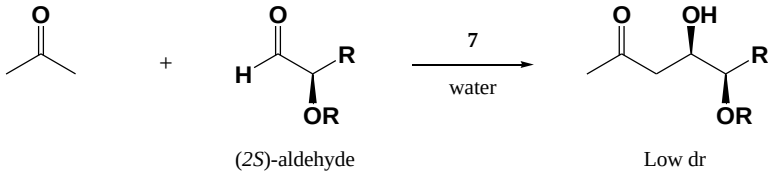


(*2S*)-aldehyde High dr

Scheme 2. Favored facial attack mode for the (*2S*)-aldehyde catalyzed by **7**.

In contrast, reaction of the (*2R*)-aldehydes, e.g., 2,3-*O*-isopropylidene-D-glyceraldehyde and 2,3:4,5-di-*O*-isopropylidene-L-arabinose, with acetone under the same conditions gave the corresponding aldol product in low disatereoselectivity, because the steric hindrance of a *re*-face of (*2R*)-aldehyde significantly decreased the stereoselectivity of L-prolinamido-glycoside **7** catalyzed

re-facial selective aldol reaction (Scheme 3).



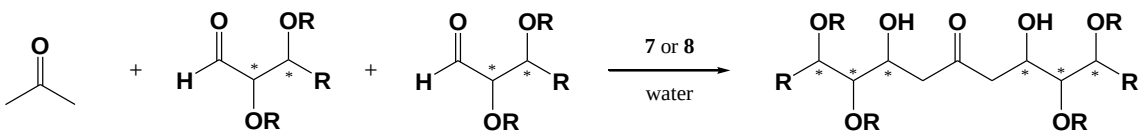
Scheme 3. Less favored facial attack mode for the (*2R*)-aldehyde catalyzed by **7**.

It appears that effective stereocontrol of the aldol reactions using L-prolinamido-glycoside **7** and D-prolinamido-glycoside **8** requires a suitable combination of both the catalyst and also the chiral center at C-2 of the aldehydes. The second chapter was devoted to the studies of the stereoselective synthesis of uloses, arbitrary define as monoaldol products, which possess a distal oxo group including higher carbon carbohydrates[8] from *aldehydo*-sugars by prolinamido-glycoside catalyzed aldol reactions, and conformations of the acyclic uloses in solution were studied in detail by high-field NMR spectroscopy. Having different configurations and conformations depending on the parent sugars and protecting groups, these *aldehydo*-sugars offer useful potential as tools for elucidating the stereochemical pathways of the asymmetric aldol reactions. Many established synthetic methods[9] permit the elaboration of steremchemically complex carbohydrate molecules, but frequently involve the use of tedious protection-deprotection sequences and expensive or hazardous reagent. Such carbohydrate-based prolinamide catalysts are easy to handle and recover, are nontoxic, and can offer interesting possibilities for preparing various carbohydrates in asymmetric aldol reactions. The work allows predictive understanding of the steric factor dictating product distribution in the reaction. Further, it provides a methodology for utilizing readily available sugars as chiral precursors to higher-carbon sugars in enantiomerically pure forms and having functional substituents capable of differential elaboration.

Organocatalysts capable of catalyzing the aldol reaction of aldoses in the unprotected form, that

exist predominantly as acyclic hemiacetals but which nevertheless participate well in aldol reaction, are of interest as potential mimics of enzyme, and also have significant practical implications in connection with of theoretical interests of formation of ketoses in the nature, but such stereocontrolled reactions catalyzed by organocatalysts have never been achieved in aqueous media. Therefore, with convenient access to ketoses, the possibility of the aldol reaction of unprotected aldoses has been investigated using the prolinamide catalysts and the aldol reaction of acetone with the unprotected aldoses stereoselectively gave the 1,3-dideoxy-uloses. The stereochemistry of the aldol products depends on pH of the solvent, and the observed pH dependency may suggest the conformational changes of free aldoses. Changes in the conformation of the aldoses may modify the stereochemical course of the reaction predicted by the Felkin-Anh model. The product distribution was explained on the basis of conformational mobility of the free aldoses and a correlation established between the influence of steric effects in aldoses and the diastereofacial selectivity of the prolinamido-glycoside. Stereoselectivity observed in the aldol reaction of free aldoses under prolinamide catalyzed conditions is discussed in terms of effects of pH of solvent, diastereofacial selectivity of the catalysts, and the nature of the aldoses. The factors discussed as being responsible for the product distribution during the aldol reactions are allowed to predict the stereochemistry of the aldol products.

An advantage of the prolinamido-glycoside catalyzed aldol reaction was found in the occurrence of the tandem aldol-aldol reaction when the reaction carried out using 2 equivalents of aldehyde (Scheme 4), and this type of reaction was hardly observed in organocatalytic aldol reactions.[10]



Scheme 4. Prolinamido-glycoside catalyzed tandem aldol-aldol reaction.

A double introduction of hydroxyl groups at β and β' positions of a ketone was attempted in some investigations[11], however, the procedures involved complex mechanisms in which they occur some difficulties. Considering the ease of procedure of the prolinamido-glycoside catalyzes tandem aldol-aldol reaction due to the simple mechanism of which, development of a facilitate route to β,β-dihydroxyls substituted ketones has achieved. The third chapter deals exclusively with studies of stereoselective tandem aldol-aldol reactions.

In the chapter, the convenient synthesis of C_2 symmetrical uloses by one-step tandem aldol-aldol reaction and the synthesis of asymmetric higher carbon uloses, possess a central oxo group in the molecule, by crossed tandem aldol-aldol reaction were described.

As an acidic treatment of the tandem aldol-aldol products, described in chapter 3, gave the corresponding spiroacetals (Scheme 5), found in the skeleton of many biologically active natural products[12], the last chapter deals with studies on spiroacetals

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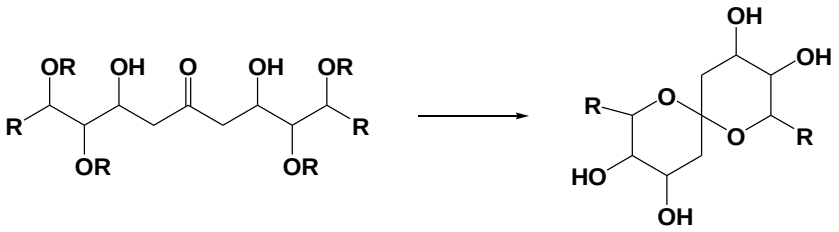


Scheme 5. Spiroacetalyzation of bis-aldol adduct.

A simple approach to the chiral synthesis of spiroacetals has been developed from bis aldol products, readily available from the prolinamido-glycoside catalyzed tandem aldol-aldol reaction, in which the chirality of the hydroxyls determine that of the spiro center in the products (Figure 3).

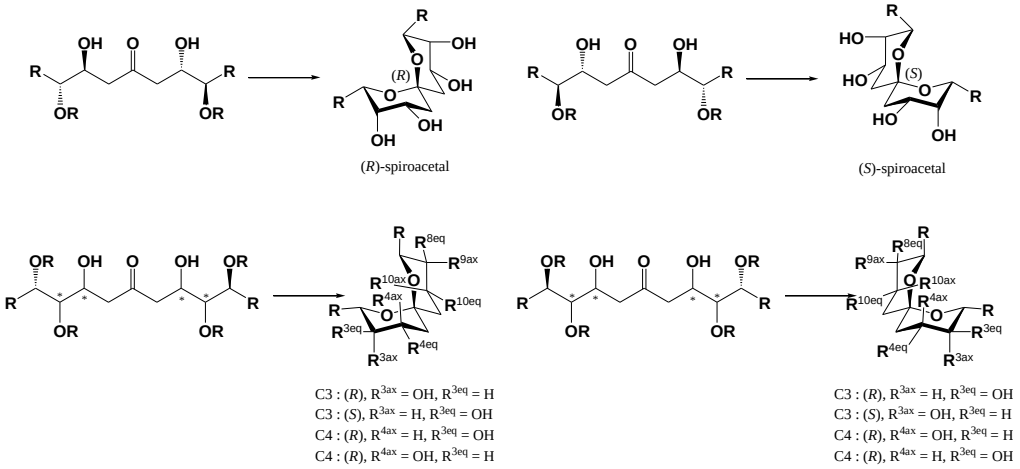


Figure 3. Stereospecific spiroacetalization.

In the last decade, a number of simple spiroacetals have been reported as components of insect sex pheromone[13] etc., and a number of methods have been reported for their synthesis.[14] A particularly interested compound is 1,7-dioxaspiro[5,5]undecane, which functions as the main sex pheromone of the olive fruit fly, in which it occurs together with its 3- and 4-hydroxyl derivatives in the rectal gland of the female insect. The chirality of this compound is due solely to the spiro center (Figure 4), and therefore the enantiospecific synthesis of each of its antipodes or the resolution of the racemic spiroundecane poses special problems. The published synthesis[15] of the (*R*) and (*S*) enantiomers has relied upon the spontaneous cyclization of either a chiral ketotriol or ketotetrol to give a separable mixture of diastereomers differing in configuration at the spiro center.

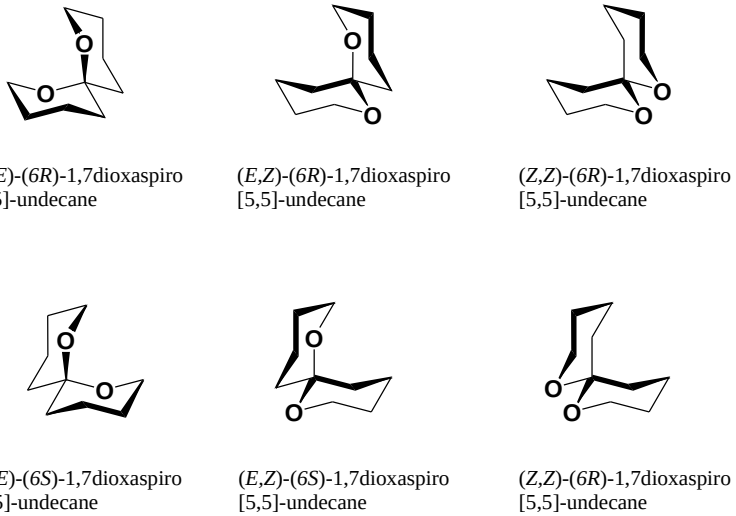


Figure 4. Stereoisomers of 1,7-dioxaspiro[5,5]undecane.

As the published synthetic procedures of chiral ketopolyols have entailed a long synthetic sequence from a commercially available chiral compound, the stereospecific synthesis of poly hydroxyl substituted spiroacetals *via* prolinamide catalyzed tandem aldol-aldol procedure represents a significant improvement if with a limited view to preparing the insect pheromones.

In common with higher carbon polyhydroxyketones, the tandem aldol-aldol adducts, e.g., the 5-nonulose utilizes two of its hydroxyls to act as nucleophiles in intramolecular acetalization, *via* the hemiacetal which allows β-equatorial, γ-axial-diol or β-axial, γ-equatorial-diol but not diaxial-diol on a pyranose chair conformation. This ring structure originates from the open chain *keto* form by reversible reaction between the ketone function at C-5 and the hydroxyl at C-1 or C-9 (Figure 5). Configurational studies on spiroacetals through X-ray crystallography, it revealed that an avoidance of a 1,3-diaxial interaction is a determining factor of orientations of the hydroxyls on the pyranose ring, in which β-equatorial, γ-axial form is more favored than β-axial, γ-equatorial form.

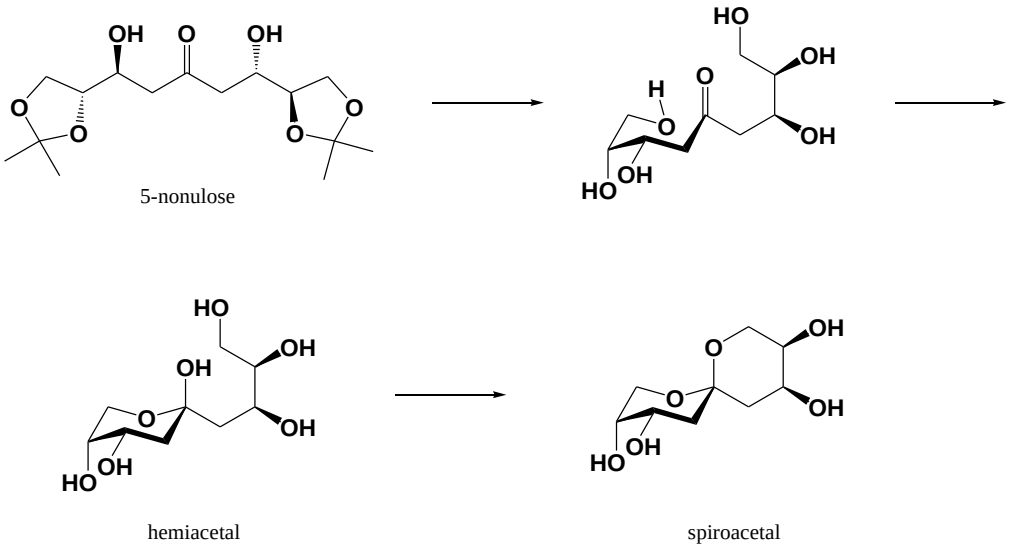


Figure 5. Effects of 1,3-diaxial interaction on spiroacetalization.

Enantiospecific synthesis of some spiroacetals, of which spirocenters were formed by avoiding the 1,3-diaxial interactions, and determinations its absolute configurations were described.

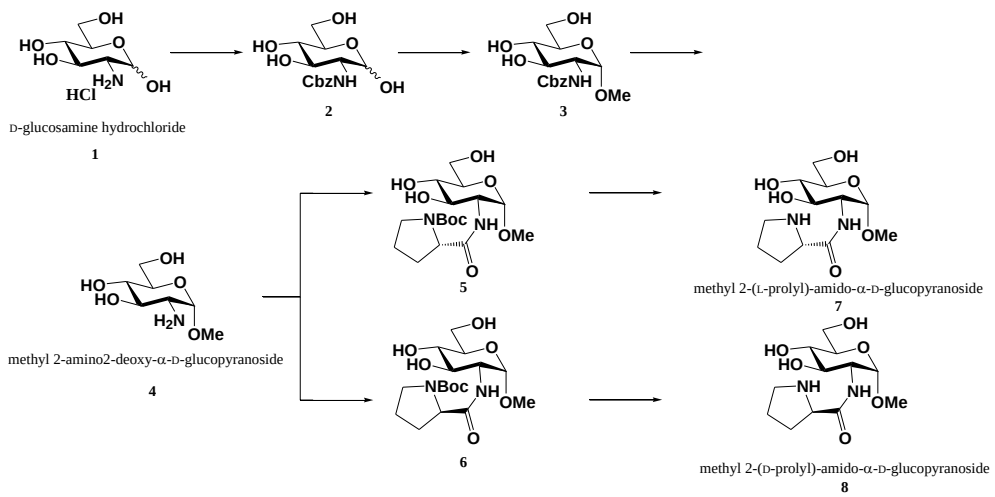
Chapter 1

Synthesis of prolinamido-glycoside catalysts

1.1 Introduction

The prolinamido-glycosides were designed as the proline-based catalysts bearing carbohydrate moiety, but difficulties have been experienced in obtaining a reliable preparation in initial studies.[1] Consequently, a minor modification of the method of preparation was investigated and provides an improved synthesis.

Methyl 2-(L-prolyl)-amido-α-D-glucopyranoside **7** and methyl 2-(D-prolyl)-amido-α-D-glucopyranoside **8** were obtained from D-glucosamine hydrochloride **1** *via* methyl 2-amino-2-deoxy-α-D-glucopyranoside **4**, followed by condensation with *N*-Boc-proline (Scheme 1.1).



Scheme 1.1.1. Preparation of **7** and **8**.

Methyl 2-amino-2-deoxy-α-D-glucopyranoside **4** was prepared from D-glucosamine hydrochloride **1** by adapting the procedure described by Suami.[16]

Compound **4** was coupled to *N*-Boc-proline by treatment with EDCI as a coupling reagent in an ice cooling mixture of methanol and dichloromethane.

The conventional method using EDCI as a coupling reagent for the synthesis has usually entailed using DMF as a solvent when the substrates possess a lack of lipophilicity. As the coupled compounds **5** and **6** were hydrophilic, separation of product from residual reagents poses problems when used DMF as a solvent. Therefore the investigation was commenced with a view to using other solvents, instead of DMF.

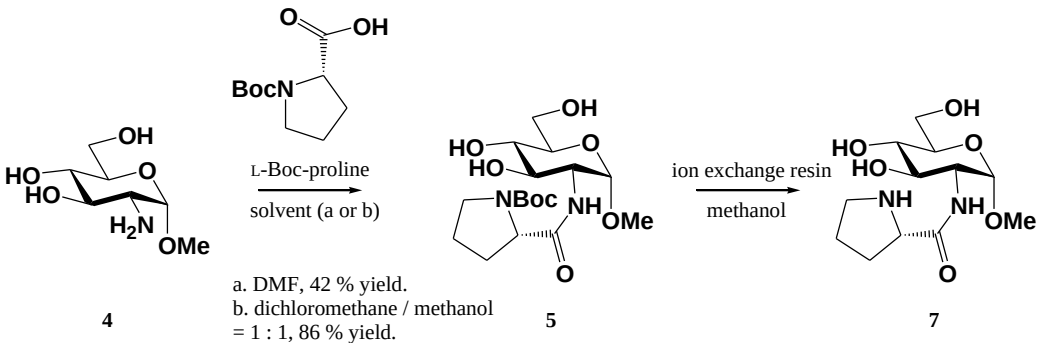
Two solvent systems, DMF and dichloromethane-methanol solution, were compared. The latter has the distinct advantage of ease of purification of the product by facilitating the removal of residual reagents without conventional column chromatography.

1.2 Synthesis of methyl 2-(L-prolyl)-amido-α-D-glucopyranoside **7**

Methyl 2-amono-2-deoxy-α-D-glucopyranoside **4** was coupled to *N*-Boc-L-proline by treatment with EDCI in DMF at room temperature for 5 hours. Despite TLC indicated that the complete reaction, the desired **5** was isolated in only 42 % yield after extraction with n-butanol, followed by a silica gel column chromatography. The extraction of the product with *n*-butanol and water, in which it entailed troublesome emulsion, was difficult. However, the pure **5** was obtained in high yield by adapting the procedure, using ice cooling mixture of dichloromethane and methanol as a solvent, which next described.

Methyl 2-amono-2-deoxy-α-D-glucopyranoside **4** was coupled to *N*-Boc-L-proline by treatment with EDCI in an ice cooling dichloromethane-methanol solution for 1 hour. As the time required for complete reaction was shorter than that for the reaction in DMF, over reactions of undesired

hydroxyls and *N*-Boc-L-proline were not observed. Subsequent concentration of the reaction mixture results in precipitation of the crude **5** and recrystallization from ethanol gave pure **5** in up to 80 % yield. Methyl 2-(L-prolyl)-amido-α-D-glucopyranoside **7** was obtained by hydrogenolysis of the Boc-protecting group from **5** followed by neutralization of resulting hydrochloride of **7** with ion-exchange resin (Scheme 1.2.1).



Scheme 1.2.1. Preparation of **7**.

The ^{1}H NMR spectrum of **7** showed the anticipated signals for a prolyl residue; H-β resonated as a multiplet at δ 1.91 which is characteristic of a proline in basic solution.

The conformation of **7** in water was indicated by NOESY experiment, which showed large NOE signals between H3 of the sugar component and Hα of prolyl residue, and between H-6 and H-α. A relatively large NOE signal between H-3 and H-γ also supporting the conformational aspects in **7**, in which the C-3 hydroxyl and prolyl NH groups, should participate in the aldol reaction by formation of enamines, face each other, and hence the L-prolyl residue positioned below the sugar ring. The NOESY spectrum of **7** was illustrated in Figure 1.2.1.

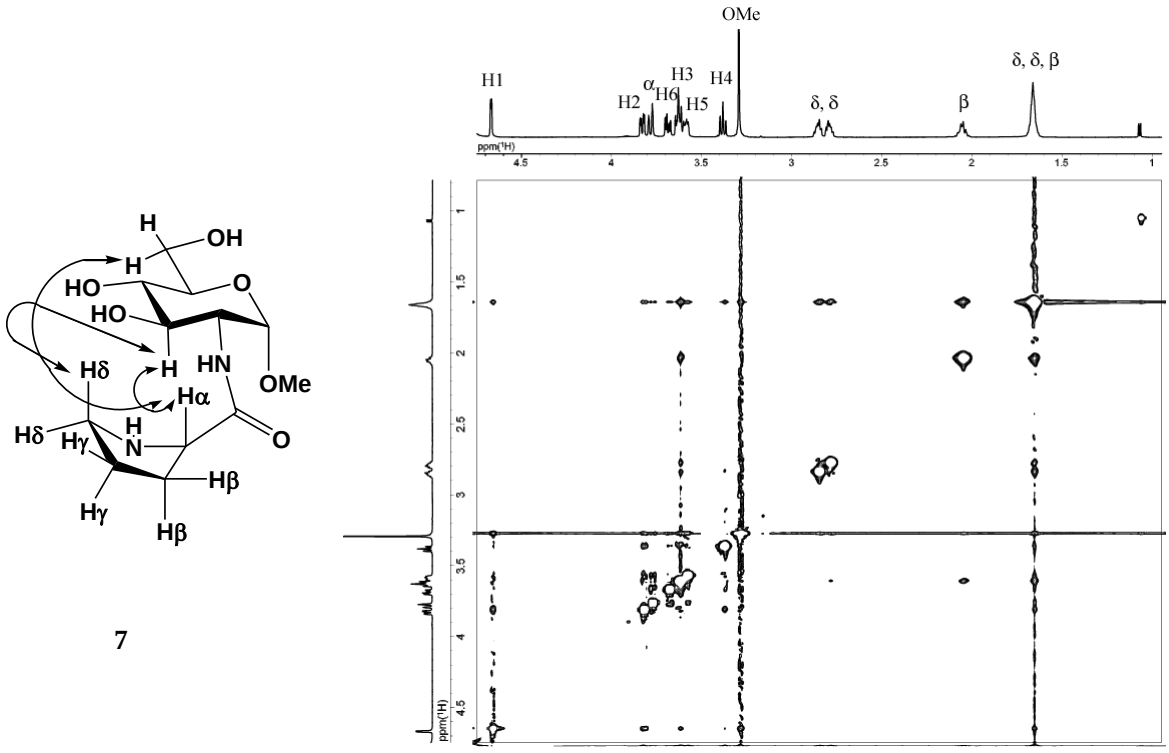
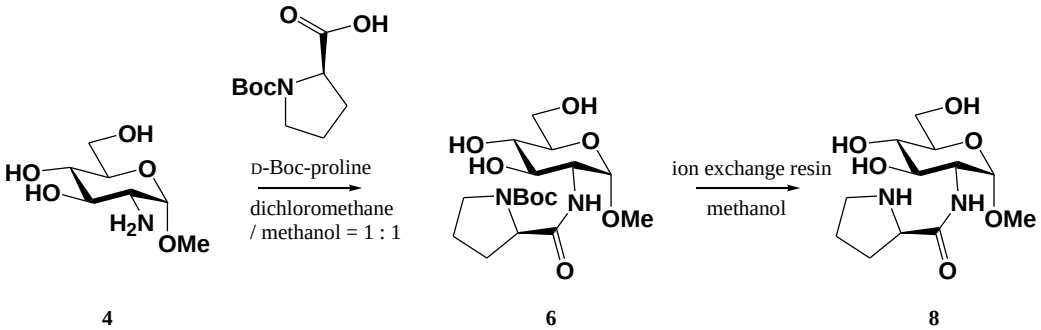


Figure 1.2.1. NOESY spectrum of **7**.

1.3 Synthesis of methyl 2-(D-prolyl)-amido-α-D-glucopyranoside **8**

Methyl 2-amono-2-deoxy-α-D-glucopyranoside **4** was coupled to the *N*-Boc-D-proline exactly as described for the analogue of L-diastereomer (Scheme 1.3.1).



Scheme 1.3.1. Preparation of **8**.

The anomeric proton signal of **8** in ^{1}H NMR spectrum fall at lower field than the anomeric proton of its L-diastereomer. This shift is attributable to steric interactions of the prolyl residue.

NOESY experiment was also used in conformational assignments. NOE signals for H-α of the proline residue appeared at H-2 and H-4 of the sugar component. These results suggesting the D-prolyl residue positioned above the sugar ring in contrast of L-analogue (Figure 1.3.1).

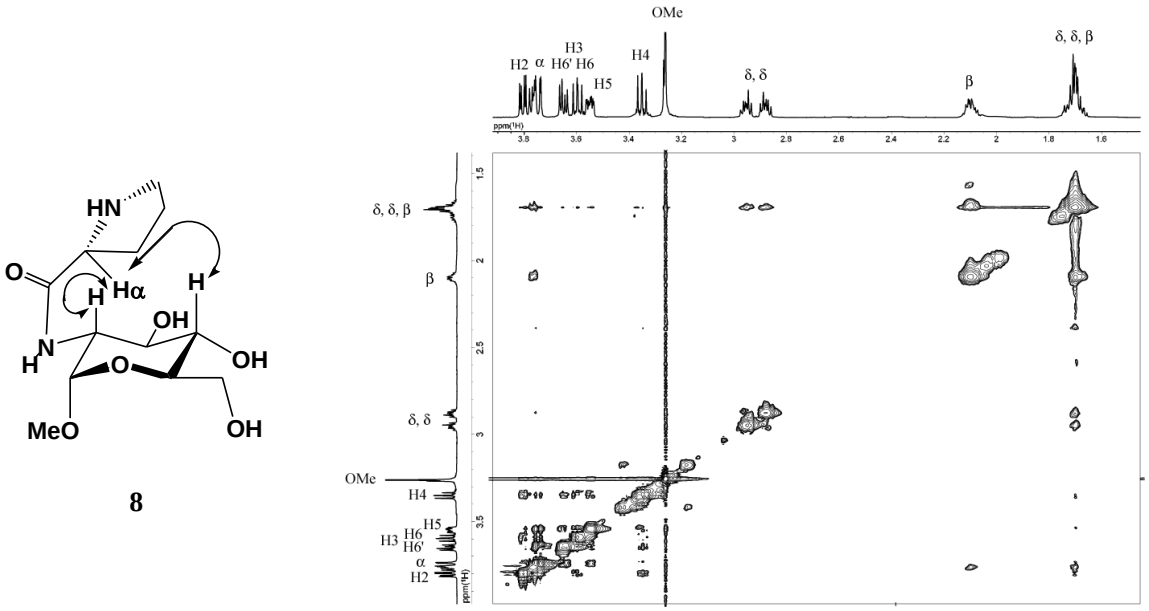


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Figure 1.3.1. NOESY spectrum of **8**.

With the conformation of the catalysts **7** and **8** clearly established, it was of interest to investigate the mechanism of stereoselective aldol reaction.

In previous studies on the aminoacyl derivatives of glucoside catalyzed aldol reaction of acetone with aromatic aldehyde, our group reported that the stereochemistry at C-4 of the product was markedly depended upon the steric effects between the sugar ring and the aminoacly residue, and that the reaction appeared to occur *via* an enamine intermediate.[1]

To test this hypothesis, chiral aldehydes were treated with **7** and **8**. The following chapter described the results in terms of facial selectivities.

Chapter 2

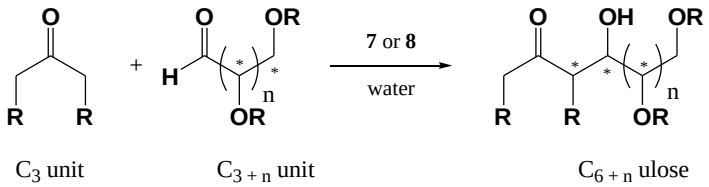
Synthesis of carbohydrates from *aldehydo*-sugars

2.1 Introduction

In the last three decades organic synthesis entered its stereoselective stage, in which it is important not only to manipulate and control relative stereochemistry of substituents, but to control their absolute stereochemistry. Toward this objective, carbohydrates were discovered as suitable source and of which original chiralcenters were utilized to synthesis of more stereochemically intricate natural compounds. For example, chain extension of *aldehydo*-sugars has attempted by Wittig reaction[17], Diels-Alder cycloaddition[18], and aldol reaction[9] in the carbohydrate field as a convenient route to higher-carbon carbohydrates, as such sugars having biological properties are of sustained synthetic interest.

As part of a general program on synthetic transformations of sugars having potential value for access to enantiomerically pure, higher-sugars and polysubstituted spiroacetals, this chapter describes a systematic study of the reaction of ketones with sugar derived aldehydes, having different configurations and conformations depending on the parent sugars and protecting groups, under the prolinamido-glycoside catalyzed aqueous conditions.

The simple acyclic *aldehydo*-sugar, 2,3-*O*-isopropylidene-D-glyceraldehyde was chosen as a starting point of this work both for its ease of synthesis and a clue to the expected behavior of the aldehyde by the Felkin-Anh model. And then reactions of easily available *aldehydo*-pentoses were investigated (Scheme 2.1).



Scheme 2.1.1. Synthesis of uloses.

Conformational studies on acyclic forms of the aldopentoses have been achieved by Horton[19] through NMR spectroscopy of their dithioacetals, thymine, uracil, cytosine, adenine, and *aldehydo*-derivatives to determine major conformer in solution. High-field NMR spectroscopy of the acetylated *aldehyde*-pentoses in conjunction with selective proton decoupling values being consistent with substantial population of more than one rotameric state.

The systematic conformational studies on the acyclic-sugar chain systems as a function of stereochemical substitution mode in solution have revealed in the majority of instances a high degree of conformational homogeneity. The extended planar zigzag conformation favored for a linear alkane chain on the basis of maximal separation of large groups along each carbon-carbon bond is subjected to perturbation in polysubstituted systems, notably by unfavorable parallel 1,3-interactions, namely, *syn*-axial interactions, between bulky substituents as well as by polar effects and by solvent interactions. Poly substituted systems may thus favor nonextended (sickle, gauche, *G*) conformations or conformational mixtures, according to the substitution mode. By adopting these established aspects, it allowed unambiguous assignments of the conformations of the aldol adducts from which the transition states of the aldol reactions were discussed.

In water, the prolinamido-glycosides catalyzed these aldol reactions with high degree of stereoselectivity, and the results demonstrate that the configurations and conformations of the

catalysts and aldehydes are a determining factor in the stereochemical outcome of the reaction. The quantitative distribution of adducts as a function of stereochemistry of the chiral aldehydes was discussed.

In the initial study, employing prochiral isobutyraldehyde, the aldol product of which is well known and it permitted omitted determinations of the enantiomeric excess using chiral HPLC analysis, the high enantiofacial selectivities were observed in the both cases of the prolinamido-glycosides aldol reaction. As such prochiral aldehydes possesse two enantiotopic faces, namely *re*-face and *si*-face, of which reactivities are considered as equivalent, the absolute stereochemistry at C-4 of the product has directly influenced by the attack of a preference of the catalyst; the L-prolinamide **7** selectively catalyzes *re*-face attack, and the D-prolinamide **8** catalyzes *si*-face selective aldol reaction.

For comparative studies, chiral aldehydes derived from sugars were also used in the aldol reaction. It is evident from these results that the prolinamido-glycoside catalyzed aldol reaction using *aldehydo*-sugars in acetate and isopropylidene forms favors the anti aldol products throughout. As regards diastereofacial selectivity, (*2S*)-chiral aldehydes that have less hindered *re*-face at C-2 position show the tendency for favored attack at the *re*-face catalyzed by the L-prolinamido-catalysts **7**. In contrast, (*2R*)-chiral aldehydes possess less hindered *si*-face, show favored *si*-face attack catalyzed by the D-catalyst **8**. The observed stereoselectivity in these aldol reactions and also that encountered in the tandem aldol-aldol reactions, described in the chapter 3, on acetone, using either L-prolinamido-glycoside **7** or D-prolinamido-glycoside **8**, was in general accordance with the empirical Felkin-Anh theory, apart from the reaction of 2.3:4,5-di-*O*-isopropylidene-*aldehydo*-D-ribose, 2,3,4,5-tetra-*O*-acetyl-*aldehydo*-D-ribose, D-arabinose, and L-arabinose.

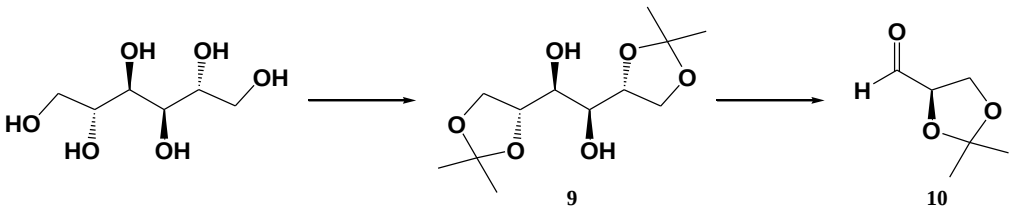
Conventional methods for preparing higher-uloses by the organocatalytic aldol route require several steps: conversion of the aldose precursor into the acyclic form as the dithioacetal,

protection of the chain through acylation or acetalization, deprotection of the carbonyl group, and finally reaction with the appropriate ketone. Although aldoses in the free forms are frequently used in Wittig reaction, and enzymatic aldol reaction by aldolase mostly utilizes free aldose substrates, there have been few reports of organocatalytic aldol reaction using free sugars. Therefore, the aldol reactions of aldoses in the free forms, that exists predominantly as cyclic acetals, formed as the result of dimerlization or hemiacetalization, which nevertheless participates well in aldol reaction under proline catalyzes condition, have been investigated. Each of commercially available nine aldoses reacts in the unprotected form with acetone in water or phosphate buffer under prolinamido-glycoside catalyzed conditions to give stereoselectively the corresponding 1,3-dideoxy-uloses.

2.2 Substrates preparation

2,3-*O*-Isopropylidene-D-glyceraldehyde **10**

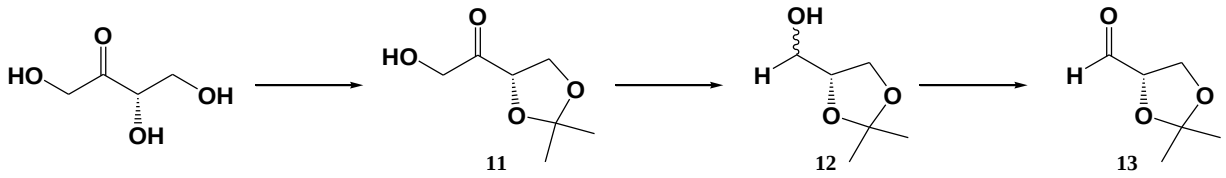
2,3-*O*-Isopropylidene-D-glyceraldehyde was prepared from D-mannitol *via* 1,2:3,4-di-*O*-isopropylidene-D-mannitol **9**, followed by periodate cleavage according to the procedure of Schmid[20] (Scheme 2.2.1). It was obtained as homogeneous syrups after purification by high-vacuum distillation and of which NMR spectrum confirmed that it was single compound free from any contaminants.



Scheme 2.2.1. Preparation of 2,3-*O*-isopropyliden-D-glyceraldehyde **10**.

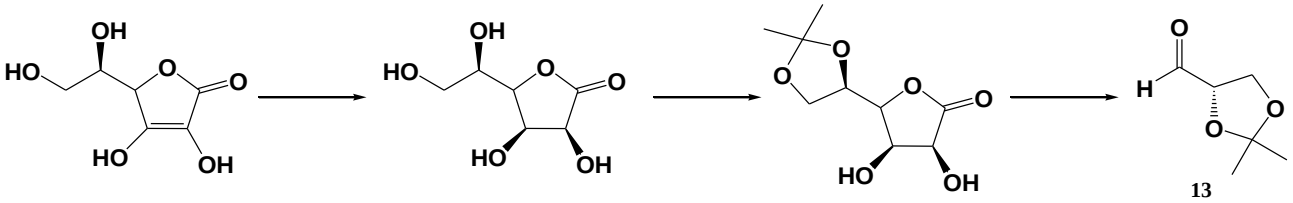
2,3-*O*-Isopropylidene-L-glyceraldehyde **13**

2,3-*O*-Isopropylidene-L-glyceraldehyde was prepared from L-erythulose *via* isopropylidene acetalization with anhydrous copper sulfate in anhydrous acetone and followed by periodate cleavage as described by Vandewalle[21] (Scheme 2.2.2). It was obtained as homogeneous syrups after purification by high-vacuum distillation and of which NMR spectrum confirmed that it was single compound free from any contaminants.



Scheme 2.2.2 Preparation of 2,3-*O*-isopropyliden-L-glyceraldehyde **13**.

An alternative procedure,[22] periodate cleavage of 5,6-isopropylidene-L-gulono-1,4-lactone, obtained from D-ascorbic acid *via* 5,6-O-isopropylidene-L-ascorbic acid, was failed, because it entailed low yield and troublesome byproducts (Scheme 2.2.3).



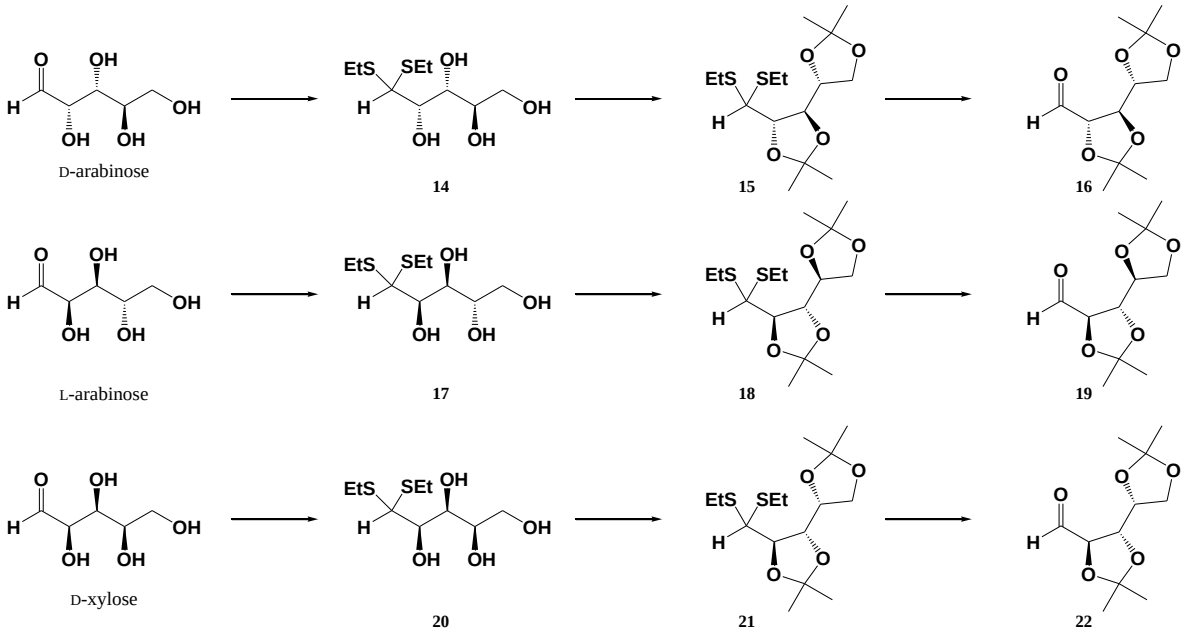
Scheme 2.2.3. The alternative procedure to **13**.

2,3:4,5-Di-*O*-isopropylidene-*aldehydo*-D-arabinose **16**,

2,3:4,5-di-*O*-isopropylidene-*aldehydo*-L-arabinose **19**,

2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-xylose **22**

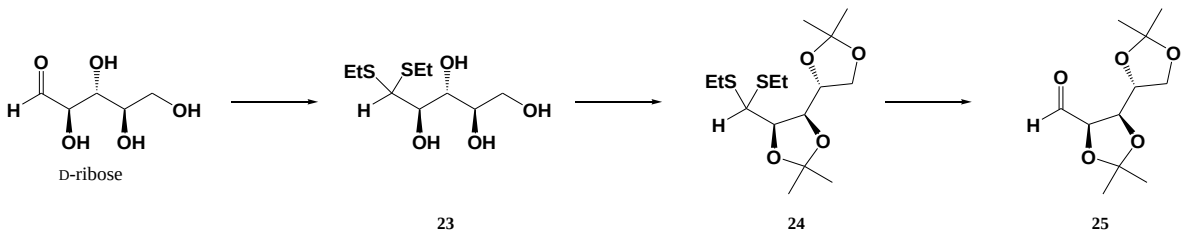
2,3:4,5-Di-*O*-isopropylidene-*aldehydo*-D-arabinose **16**, L-arabinose **19** and D-xylose **22** were prepared by adapting the procedure described by Horton.[23] They were obtained from D-arabinose, L-arabinose and D-xylose *via* the dithioacetals **14**, **17**, and **20** and 2,3:4,5-di-*O*-isopropylidene-1-dithioacetals **15**, **18**, and **21**, followed by hydrogenolysis with mercuric oxide and mercuric chloride (Scheme 2.2.4). They were obtained as homogeneous syrups after purification by high-vacuum distillation and their NMR spectra confirmed that they were single compounds free from any contaminants.



Scheme 2.2.4. Preparation of 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-arabinose **16**, L-arabinose **19** and D-xylose **22**.

2,3:4,5-Di-*O*-isopropylidene-*aldehydo*-D- ribose **25**

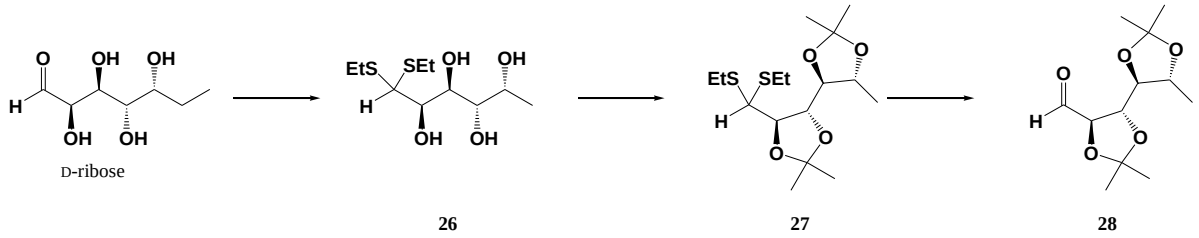
2,3:4,5-Di-*O*-isopropylidene-*aldehydo*-D-ribose **25** was prepared by the method of Aslani-Shotorbani et al[24] from D-ribose *via* the 1-dithioacetal **23** and 2,3:4,5-di-*O*-isopropylidene-1-dithioacetal **24** (Scheme 2.2.5). Isopropylidene acetalization of **23** to the acetonide **24**, with either conc H_2SO_4 in dry acetone condition, or 2,2-dimethoxypropan-DMF condition was unsatisfactory. The former reaction was very slow and the latter reaction formed the undesired regioisomer.



Scheme 2.2.5. Preparation of 2,3:4,5-di-*O*-isopropyliden-*aldehydo*-D-ribose **25**.

2,3:4,5-Di-*O*-isopropylidene-*aldehydo*-D- fucose **28**

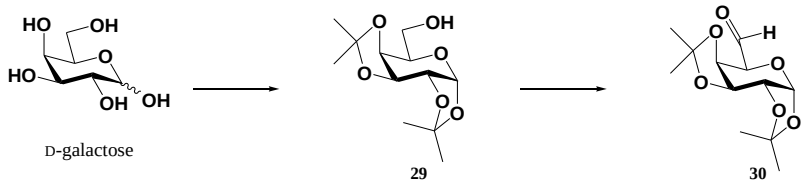
2,3:4,5-Di-*O*-isopropylidene-*aldehydo*-D-fucose **28** was prepared by adapting the procedure described by Lichtenthaler[25] from D-fucose *via* the dithioacetal **26** and 2,3:4,5-di-*O*-isopropylidene-diethyldithioacetal **27**, followed by hydrogenolysis with mercuric oxide and mercuric chloride (Scheme 2.2.6). It was obtained as homogeneous syrups after purification by high-vacuum distillation and the NMR spectrum confirmed that it was single compound free from any contaminants.



Scheme 2.2.6. Preparation of 2,3:4,5-di-*O*-isopropyliden-*aldehydo*-D-fucose **28**.

1,2:3,4-Di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose **30**

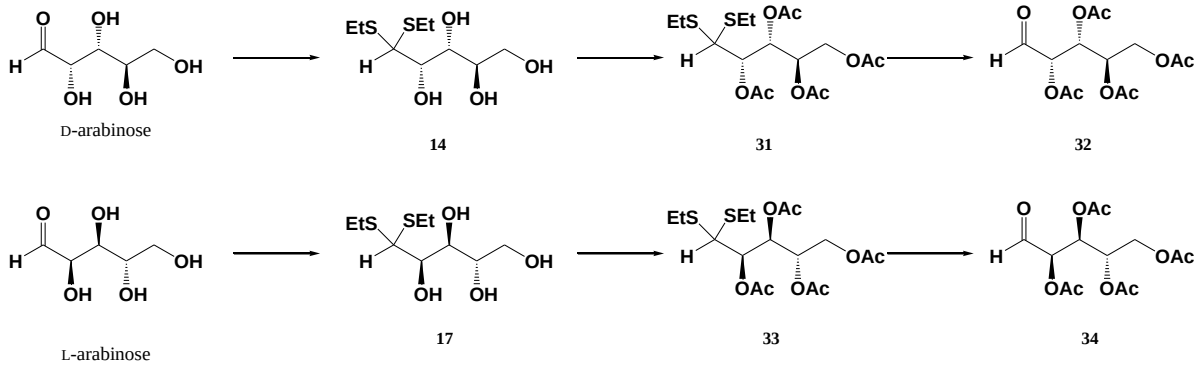
1,2:3,4-Di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose was prepared by the Horton's prodecure[28] from D-galactose *via* isopropyliden-acetalization with the acidic mixture of 2,2-dimethoxypropane and DMF, followed by oxidation with PDC in dichloromethane (Scheme 2.2.7).



Scheme 2.2.7. Preparation of 1,2:3,4-Di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose **30**.

2,3,4,5-Tetra-*O*-acetyl-*aldehydo*-D-arabinose **32** and 2,3,4,5-tetra-*O*-acetyl-*aldehydo*-L-arabinose **34**.

2,3,4,5-Tetra-*O*-acetyl-*aldehydo*-D-arabinose **32** and 2,3,4,5-tetra-*O*-acetyl-*aldehydo*-L-arabinose **34** were prepared by adapting the procedure described by Wolfrom.[26] They were obtained from D-arabinose, L-arabinose and D-xylose *via* the dithioacetals **14** and **17** and 2,3,4,5-tetra-*O*-acetyl-1-dithioacetals **31** and **33**, followed by hydrogenolysis with mercuric oxide and mercuric chloride (Scheme 2.2.8).

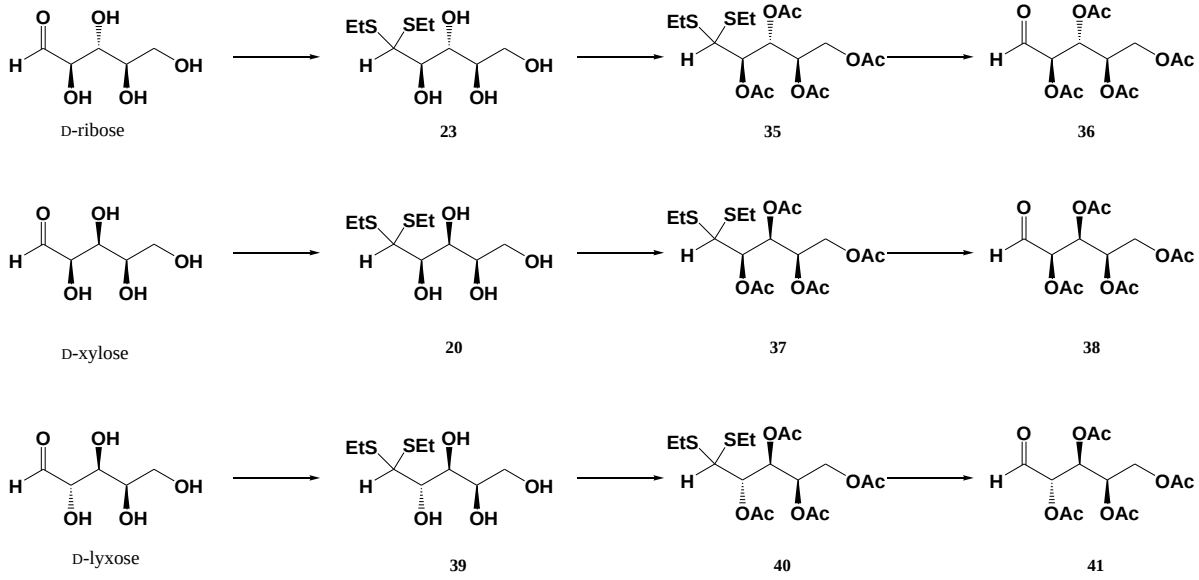


Scheme 2.2.8. Preparation of 2,3,4,5-tetra-*O*-acetyl-*aldehydo*-D-arabinose **32** and L-arabinose **34**.

2,3,4,5-Tetra-*O*-acetyl-*aldehydo*-D-ribose **36**, 2,3,4,5-tetra-*O*-acetyl-*aldehydo*-D-xylose **38**, and 2,3,4,5-tetra-*O*-acetyl-*aldehydo*-D-lyxose **41**.

2,3,4,5-Tetra-*O*-acetyl-*aldehydo*-D-ribose **36**, 2,3,4,5-tetra-*O*-acetyl-*aldehydo*-D-xylose **38**, and 2,3,4,5-tetra-*O*-acetyl-*aldehydo*-D-lyxose **41** were prepared by adapting the procedure described by Zinner.[27] They were obtained from D-arabinose, L-arabinose and D-xylose *via* the dithioacetals **23**, **20**, and **39** and 2,3,4,5-tetra-*O*-acetyl-diethyldithioacetals **35**, **37**, and **40**, followed by

hydrogenolysis with mercuric oxide and mercuric chloride (Scheme 2.2.9).

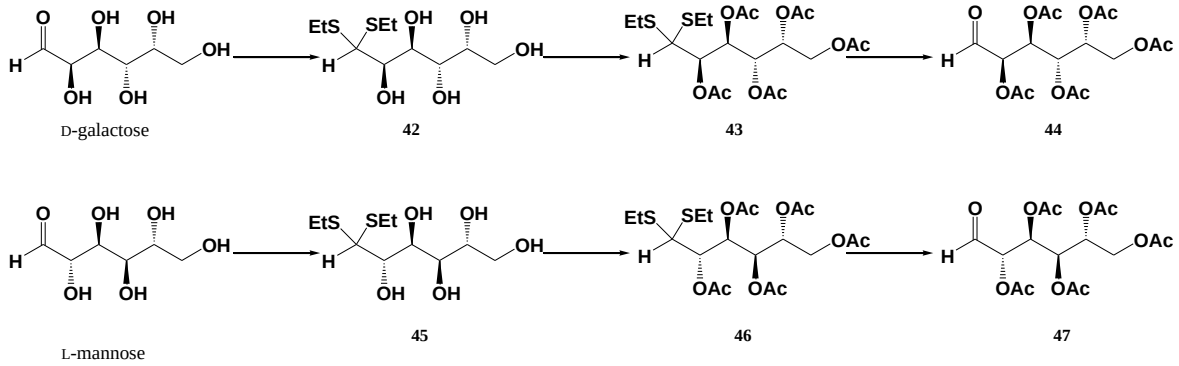


Scheme 2.2.9. Preparation of 2,3,4,5-tetra-*O*-acetyl-*aldehydo*-D-ribose **36**, D-xylose **38**, and D-lyxose **41**.

2,3,4,5,6-Penta-*O*-acetyl-*aldehydo*-D-galactose **44** and 2,3,4,5,6-penta-*O*-acetyl-*aldehydo*-D-mannose **47**.

2,3,4,5,6-Penta-*O*-acetyl-*aldehydo*-D-galactose **44** and 2,3,4,5,6-penta-*O*-acetyl-*aldehydo*-D-mannose **47** were prepared by adapting the procedure described by Wolfrom.[29] They were obtained from D-galactose and D-mannose *via* the dithioacetals, **42** and **45** and 2,3,4,5,6-penta-*O*-acetyl-1-dithioacetals, **43** and **46**, followed by hydrogenolysis with mercuric oxide and mercuric chloride (Scheme 2.2.10). They were obtained as pure crystals after purification by recrystallization and their NMR spectra confirmed that they were single

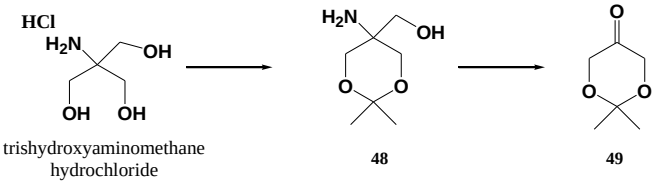
compounds free from any contaminants.



Scheme 2.2.10. Preparation of 2,3,4,5,6-penta-*O*-acetyl-*aldehydo*-D-galactose **44** and D-mannose **47**.

2,2-Dimethyl-1,3-dioxan-5-one **49**

2,2-Dimethyl-1,3-dioxan-5-one was prepared from trishydroxyaminomethane hydrochloride *via* isopropylidene acetalization with 2,2-dimethoxypropane in anhydrous DMF, followed by periodate cleavage as described by Doyle[30] (Scheme 2.2.11). It was obtained as homogeneous syrups after purification by high-vacuum distillation and of which NMR spectrum confirmed that it was single compound free from any contaminants.



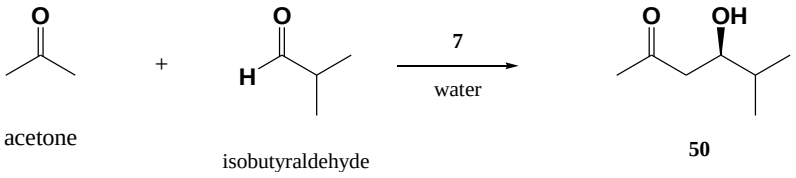
Scheme 2.2.11. Preparation of 2,2-dimethyl-1,3-dioxan-5-one **49**.

2.3 Crossed aldol reaction between acetone and isobutyraldehyde

Various conditions were evaluated for the selective aldol reaction of acetone with the enantiotopic isobutyraldehyde, and the results are summarized in Table 2.3.1; the best results were obtained when the reaction was performed using 0.1 equivalent of the catalyst. When the amount of catalyst was decreased from 0.3 to 0.05 equivalents, the yield significantly decreased, and the reaction time increased. Further, a simple change of solvent from water to DMSO markedly altered the course of the foregoing reactions. Formations of the aldol condensation product nor the self aldol product were not observed.

When the isobutyraldehyde was reacted with acetone in the presence of 0.1 equivalent of the catalyst and 10 equivalents of water, desired aldol product was formed within 30 min in the both cases of D- and L-prolinamido-glycoside.

The (*R*)-enantiomer **50** was obtained in almost quantitative yield with 86 % ee by L-prolinamido-glycoside **7** catalyzed *re*-facial* selective aldol reaction (Scheme 2.3.1).

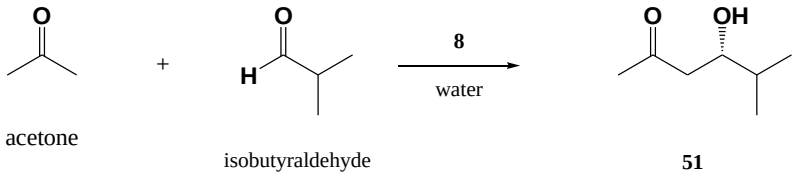


Scheme 2.3.1. Aldol reaction between acetone and isobutyraldehyde.

The same aldol reaction was next performed using D-prolinamido-glycoside **8**. As the (*S*)-enantiomer **51** was formed in 98 % yield with 89 % ee (Scheme 2.3.2), the attack of acetone

* In the aldehydes, the configuration of the carbonyl carbon was assigned by the convention of the Cahn-Ingold-Prelog rule. For the C-O double-bond, priorities are set so that the carbonyl carbon is the first, and the carbon chain is the second. Therefore, *re*-face is adopted when the carbonyl group was illustrated on the left side, and the opposite face is *si*-face.

was selectively took place at *si*-face of isobutyraldehyde.



Scheme 2.3.2. Aldol reaction between acetone and isobutyraldehyde.

The enantiomeric excesses of **50** and **51** were determined by chiral HPLC analysis using Chiralpak AS and AD as chiral columns (280 nm, IPA / hexane), and the conditions of which were previously reported by Barbas III.[2a]

entry	catalyst	amount of catalyst (equivallent)	solvent	time (h)	yield (%)	ee (%)
1	**7**	0.3	water	0.5	quant	86 (*R*)
2	**7**	0.1	water	0.5	91	89 (*R*)
3	**7**	0.05	water	2	82	89 (*R*)
4	**7**	0.1	DMSO	48	11	19 (*R*)
5	**8**	0.3	water	0.5	quant	89 (*S*)
6	**8**	0.1	water	0.5	89	91 (*S*)
7	**8**	0.05	water	2	81	87 (*S*)
8	**8**	0.1	DMSO	48	23	31 (*S*)

Table 2.3.1 Aldol reaction between acetone and isobutyraldehyde.

Considering the conformation of prochiral isobutyraldehyde by adopting the Felkin-Anh model, the two enantiotopic faces are equivalent (Figure 2.3.1), hence the enantioselectivity of the reaction was due solely to the preference of the catalyst.

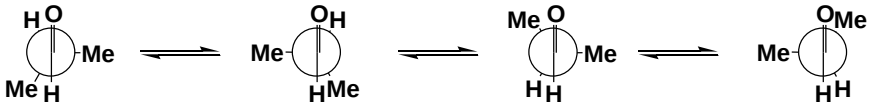


Figure 2.3.1. Conformers of isobutyraldehyde.

As the (*R*)-enantiomer **50** was obtained by the L-prolinamido-glycoside catalyzed aldol reaction, it considered that the attack of the enamine of L-prolinamido-glycoside was selectively took place at the *re*-face of isobutyraldehyde and the conformer of which would be considered as **A** in Figure 2.3.2.

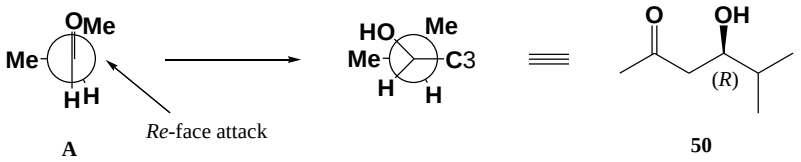


Figure 2.3.2. L-prolinamido-glycoside **7** catalyzed *re*-face attack for isobutyraldehyde.

In the case of D-prolinamido-glycoside, it considered that the *si*-face of isobutyraldehyde on the conformer **B** was selectively took place attack of the enamine and formed (*S*)-enantiomer **51** of the product (Figure 2.3.3).

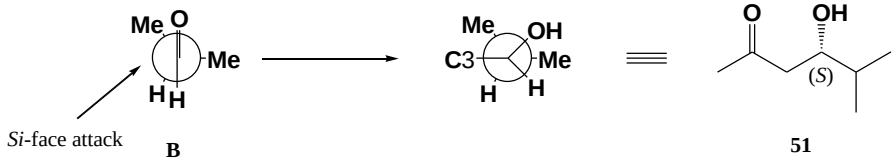
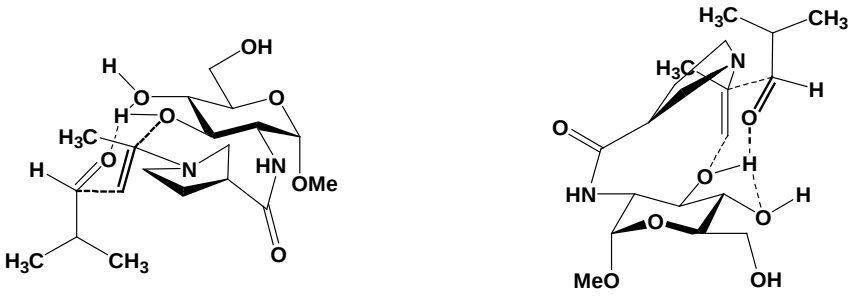


Figure 2.3.3. D-prolinamido-glycoside **8** catalyzed *si*-face attack for isobutyraldehyde.

Based on the conformational aspects, described in Chapter 1, proposed transition states were illustrated in Figure 2.3.4.



Re-face attack catalyzed by **7** *Si*-face attack catalyzed by **8**

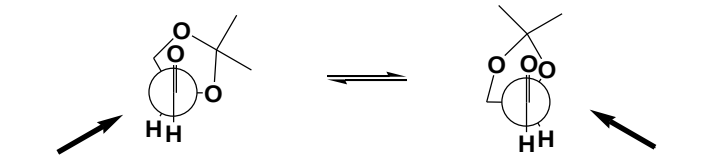
Figure 2.3.4. A proposed transition states for prolinamid-glycoside catalyzed aldol reaction with isobutyraldehyde.

After the reactions completed, the catalyst **1** and **2** could be separated by an extraction. Concentration of the aqueous layers, followed recrystallizations from 2-propanol gave up to 75 % recovery of the catalysts. Use of recovered **1** and **2** for the aldol reactions showed that the second aldol reactions were indistinguishable from the first aldol reactions in terms of yield and diastereoselectivity.

2.4 Aqueous aldol reaction for isopropylidene *aldehydo*- aldoses

2.4.1 Crossed aldol reaction between acetone and 2,3-*O*-isopropylidene-D-glyceraldehyde **10**

Differences between 2,3-*O*-isopropylidene-D-glyceraldehyde **10** and isobutyraldehyde converge that the existence or not of the chiral center at C-2. 2,3-*O*-Isopropylidene-D-glyceraldehyde belongs to point group C_1 and is asymmetric, the two diastereotopic faces are not equivalent. Because of their greater accessibility due to the asymmetric effects, less hindered *si*-faces of (*2R*)-aldehydes are on the whole significantly more reactive than more crowded *re*-faces (Figure 2.4.1.1).



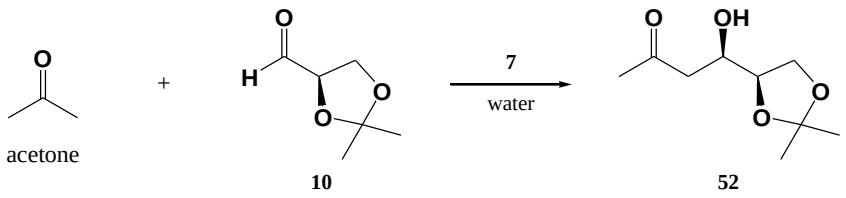
Favored conformer **10A** Less favored conformer **10B**

Figure 2.4.1.1. Conformers of 2,3- *O*-isopropylidene-D-glyceraldehyde **10**.

Thus nucleophilic addition with hindered nucleophiles results in the introduction of the substituent groups stereoselectively at *si*-faces. Crossed aldol reactions of acetone with (*2R*)-aldehydes under the prolinamdo-glycoside condition, similarly show a preference for *si*-faces and then often a high degree of selectivity toward *re*-faces. Considering this aspect and the results of the enantiotopic facial selectivities of prolinamido-glycosides catalyze aldol reactions on isobutyraldehyde, in which the L-prolinamido-glycoside catalyzed *re*-facial selective aldol reaction and D-prolinamido-glycoside catalyzed *si*-facial selective reaction, it allowed a prediction that an only

combination of the D-prolinamido-glycoside and (*2R*)-aldehydes should be matched.

As expected, the reaction between acetone and 2,3-*O*-isopropylidene-D-glyceraldehyde **10** under L-prolinamido-glycoside **7** catalyzed conditions gave the 1,3-dideoxy-4,5-di-*O*-isopropylidene-D-erythro-hexulose[31] **52** with low (24 %) de (Scheme 2.4.1).



Scheme 2.4.1.1. Aldol reaction between acetone and 2,3-*O*-isopropylidene-D-glyceraldehyde **10**.

Interestingly, a high yield was observed, albeit in low diastereoselectivity, hence it suggested the rivalry of the *re*-face attack and crowded *re*-face of the aldehyde in the fast reaction, in which it considered that the majority of the prefer configuration of 2,3-*O*-isopropylidene-D-glyceraldehyde, enough to destroy inter-relationships of the transition state, reversed the selectivity (Figure 2.6).

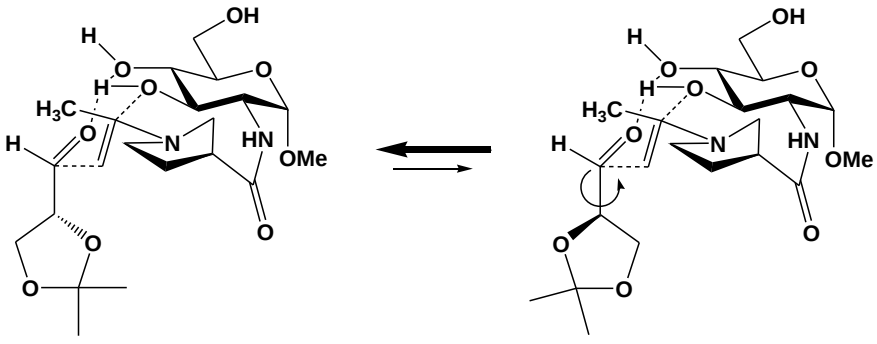
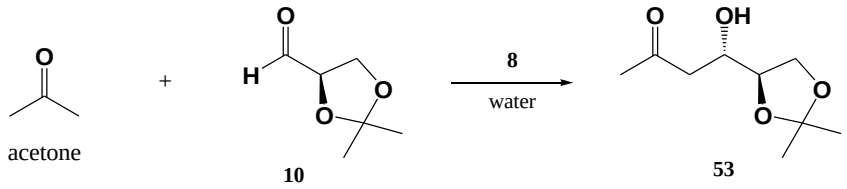


Figure 2.4.1.2. A proposed transition states for reaction with **10**.

In contrast, feasible reaction of the same substrate was carried out using D-prolinamido-glycoside. The 1,3-dideoxy-4,5-di-*O*-isopropylidene-D-erythro-hexulose **53** was obtained in 88% yield with 95% de (Scheme 2.4.1.2), in the matched case, the *si*-facial attack took place almost exclusively at *si*-face (Figure 2.4.1.3).



Scheme 2.4.1.2. Aldol reaction between acetone and 2,3-*O*-isopropylidene-D-glyceraldehyde **10**.

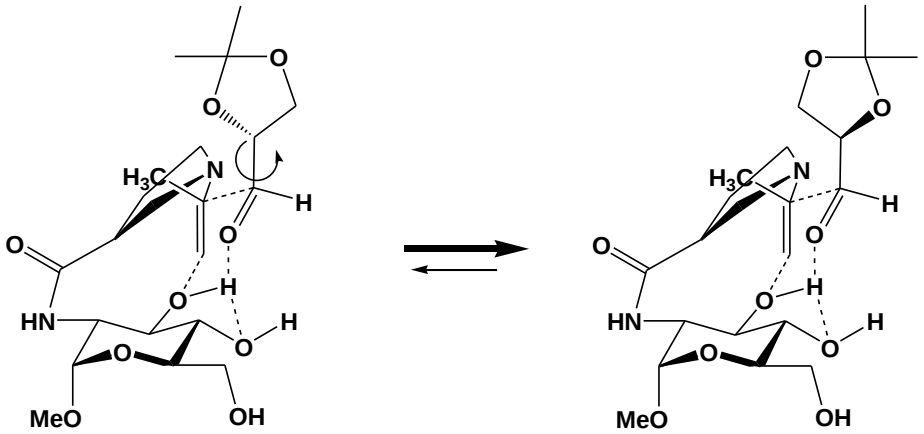


Figure 2.4.1.3. A proposed transition states for reaction with **10**.

The ^{1}H NMR analysis of the mixture of **53** and its diastereomer, 1.3-dideoxy-5,6-*O*-isopropylidene-L-*threo*-hexulose **52** showed distinctive resonance for the H-3

and isopropylidene methyl groups in both *erythro* and *threo* configurations, permitting accurate determination of the *erythro* : *threo* ratio of the product in the mixture (Figure 2.4.4).

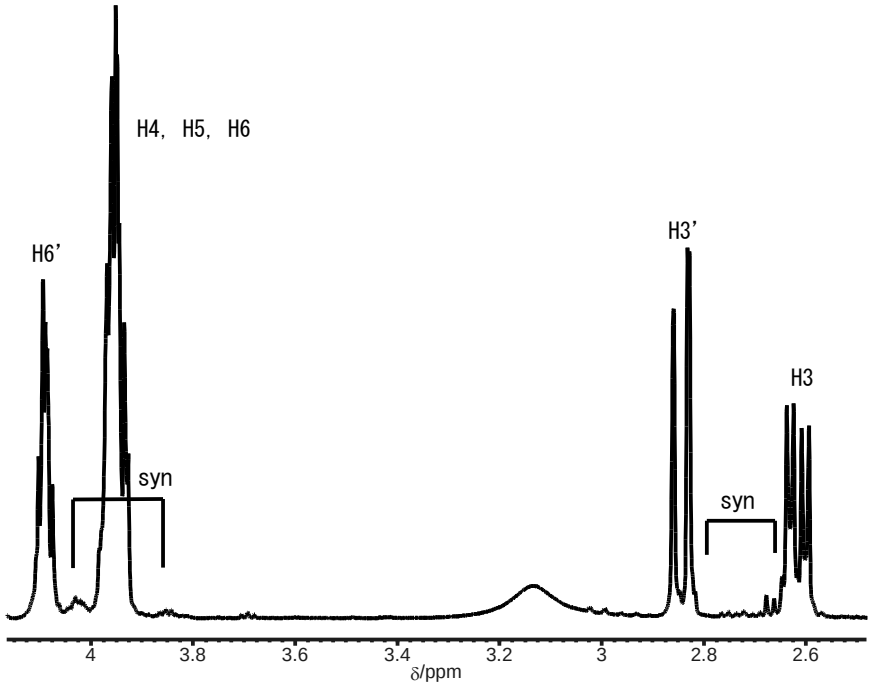


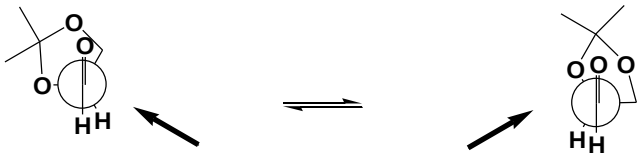
Figure 2.4.1.4. 1H NMR spectrum of 1.3-dideoxy-5,6-*O*-isopropylidene-D-*erythro*-hexulose **53**.

To provide a chemical proof of the stereochemistry at C-4 of **53**, acyclic 1,3-dideoxyhexulose **53** was converted into the crystalline spiroacetal derivative *via* its bisaldol product that would permit unambiguous assignment by X-ray crystallography of the orientation of the C-4 substituent. The X-ray crystallography of the spiroacetal was described in the chapter 4.

2.4.2 Crossed aldol reaction between acetone and 2,3-*O*-isopropylidene-L-glyceraldehyde **13**

As 2,3-*O*-isopropylidene-L-glyceraldehyde **13** is the enantiomer of 2,3-*O*-isopropylidene-D-glyceraldehyde, greater reactive diastereotopic face should be the *re*-face (Figure 2.4.2.1). Therefore, the less hindered *re*-face of which allows the preferential *re*-face

attacks catalyzed by L-prolinamido-glycoside.

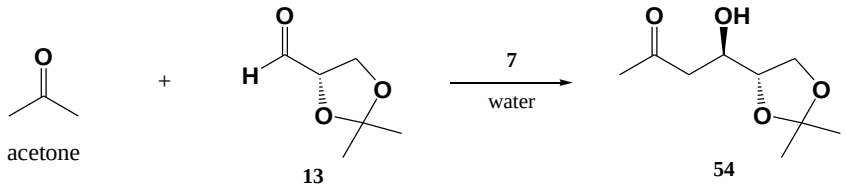


Favored *re*-face attack Less favored *si*-face attack

Favored conformer **13A** Less favored conformer **13B**

Figure 2.4.2.1. Conformers of 2,3- *O*-isopropylidene-L-glyceraldehyde **13**.

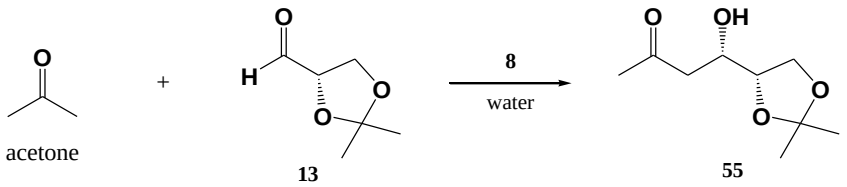
The 1,3-dideoxy-4,5-di-*O*-isopropylidene-L-erythro-hexulose **54** was obtained in 96% yield with 80% de by L-prolinamido-glycoside catalyzed aldol reaction of acetone and 2,3-*O*-isopropylidene-L-glyceraldehyde (Scheme 2.4.2.1).



Scheme 2.4.2.1. Aldol reaction between acetone and 2,3-*O*-isopropylidene-L-glyceraldehyde **13**.

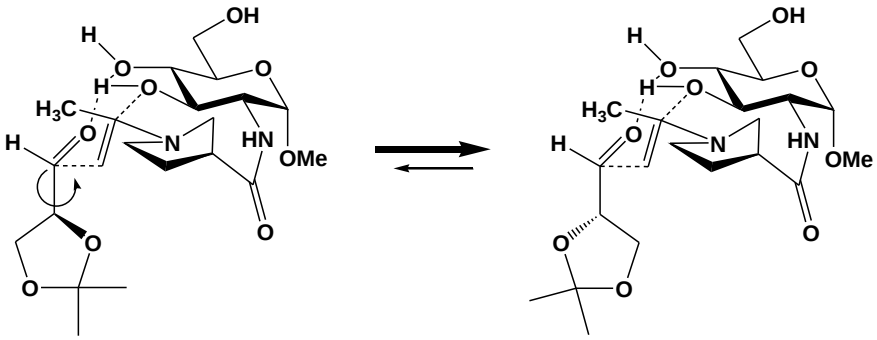
A higher diastereomeric excess has been observed in the combination of L-prolinamido-glycoside **7** and 2,3-*O*-isopropylidene-L-glyceraldehyde **13** in the reaction on acetone. The optical rotation measurements of **53** and **54** allowed an empirical assignment of the absolute configuration of **54**. Also, the reaction between acetone and 2,3-*O*-isopropylidene-L-glyceraldehyde under the D-prolinamido-glycoside conditions gave

1,3-dideoxy-4,5-di-*O*-isopropylidene-L-erythro-hexulose **55** in 75% yield with moderate 63% de (Schme 2.4.2.2).



Scheme 2.4.2.2. Aldol reaction between acetone and 2,3-*O*-isopropylidene-L-glyceraldehyde **13**.

Configurational changes at C-2 of the aldehyde revealed different results. Attachment of the catalyst, *via* enamine, to the chiral aldehyde acceptor, where C-1-C-2 rotamer of aldehyde reside on the opposite area toward the sugar ring, will of necessity, be highly stereoselective (Figure 2.4.2.2).



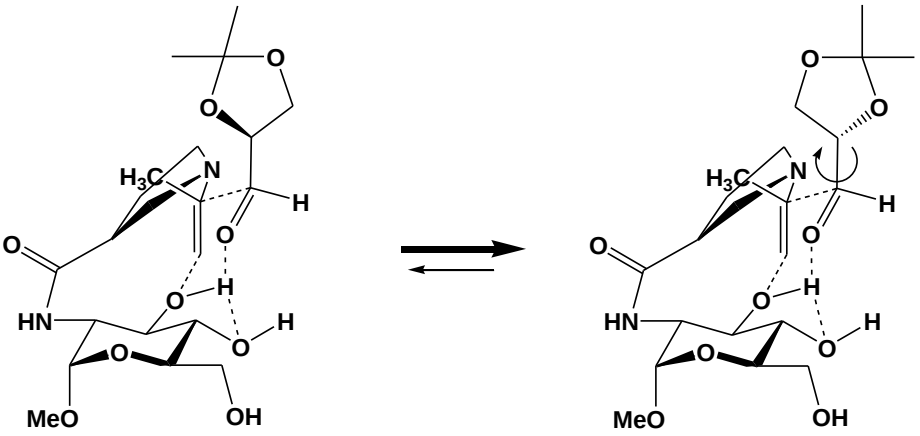
Si-face attack
(Less favored)

Re-face attack
(Favored)

Figure 2.4.2.2. A proposed transition states for reaction with **13**.

Decreased selectivity was similarly observed in a combination of D-prolinamido-glycoside **8** and (*2S*)-aldehyde whereas steric inhibition of *si*-face inhibits catalyzed *si*-face attack. This attack

requires a clockwise rearrangement of aldehyde acceptor (Figure 2.4.2.3).

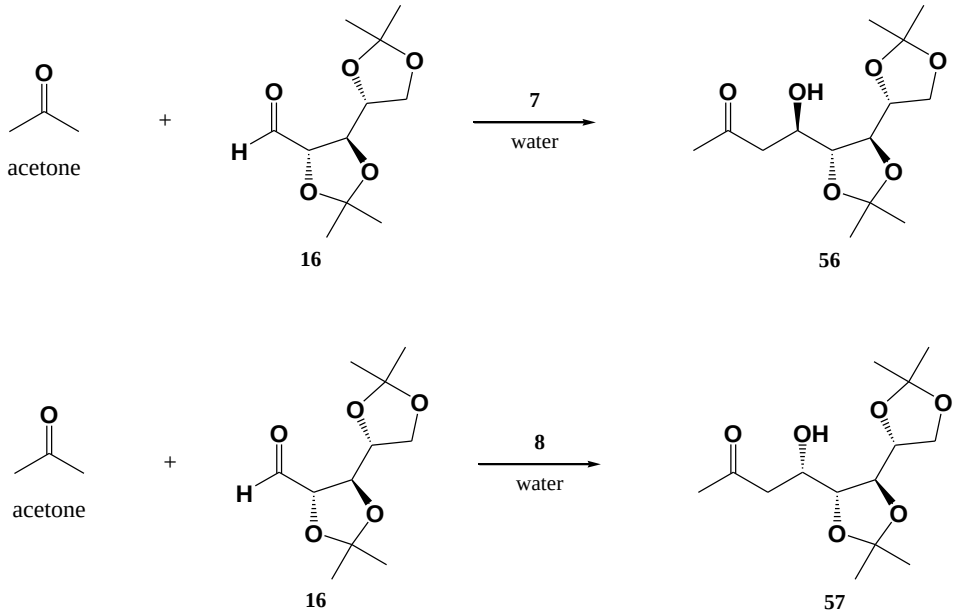


Re-face attack *Si*-face attack

Figure 2.4.2.3. A proposed transition states for reaction with **13**.

2.4.3 Crossed aldol reaction between acetone and 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-arabinose **16**

The reaction of 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-arabinose **16** in an aqueous solution of 0.1 equivalent of **7** gave, as expected, mainly the syrupy 1.3-dideoxy-D-*glycero*-D-*ribo*-octulose **56** (Scheme 2.4.3.1) in 82% yield with 95% de together with the corresponding bisaldol product, 6.8-dideoxy-D-*allo*-D-*allo*-7-trideculose, as a consequence of the tandem aldol-aldol reaction, **102** in 14% yield as a single diastereomer, this type of compounds were described in the chapter 3. In this case, the high diastereoselectivity was observed when the reaction carried out using **8** as the catalyst.



Scheme 2.4.3.1. Aldol reaction between acetone and 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-arabinose **16**

.

The spectra of both epimers were amenable to first-order analysis and the diastereomeric ratio was indicated by ^{1}H NMR analysis of the initial mixture of **56** and **57**, in which upfield shifts of the H-3

and the isopropylidene methyl groups resonances were observed relative to its *syn*-diastereomer. The vicinal proton-proton couplings for both epimers deviate significantly from those values diagnostic of preponderantly antiperiplanar or gauche, and are indicative of conformational mixtures with substantial contributions from more than one conformer. The H-4 resonance for the epimer **56** was narrow doubled doublet of doublets ($J_{4,5}$ Hz) at δ 4.2, indicating that H-4 and H-5 are essentially antiparallel. The $J_{5,6}$ value is 2.1 Hz, indicating an essentially gauche disposition between H-5 and H-6, and the $J_{6,7}$ large coupling (11.8 Hz) is consistent with exclusive antiperiplanar orientation of H-6 and H-7. These data indicate that the epimer **56** favors an extended, planar zigzag conformation (*P* conformation) having all backbone carbon atoms in the same plane (Figure 2.4.3.1).

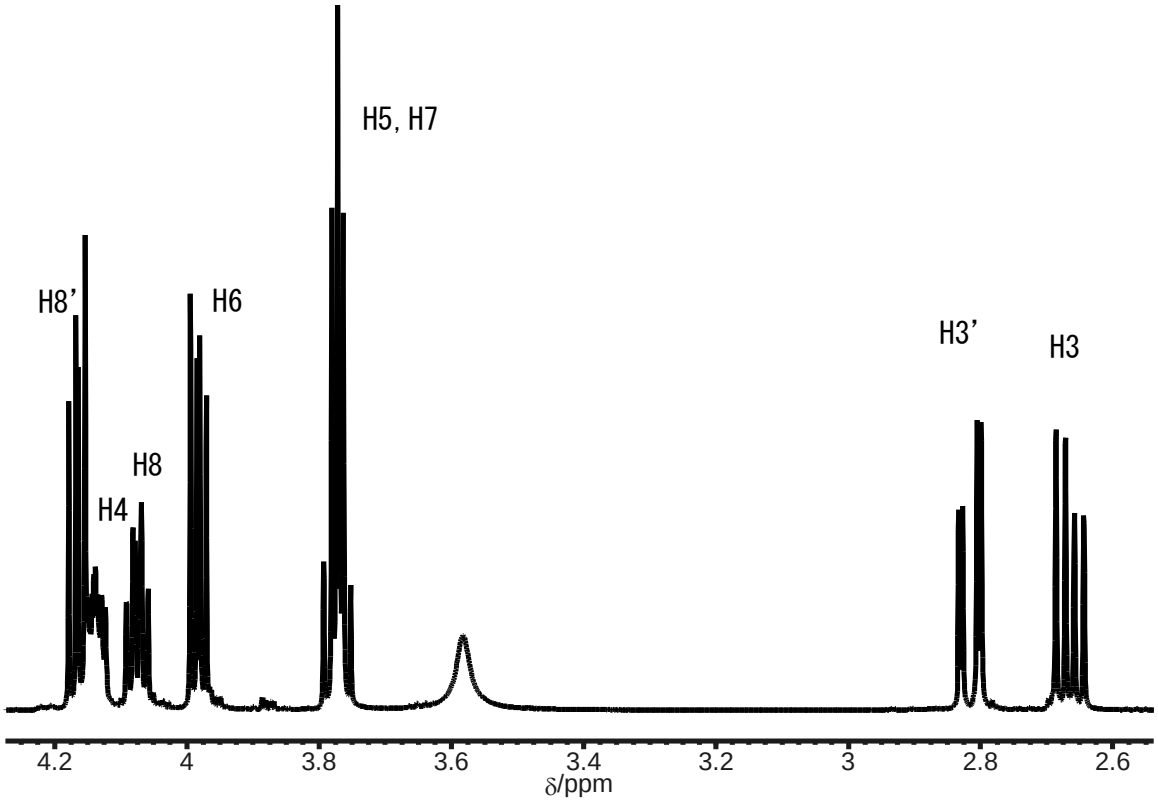


Figure 2.4.3.1. 1H NMR spectrum of 1.3-dideoxy-D-*glycero*-D-*ribo*-octulose **56**.

Coupling constants (Hz)

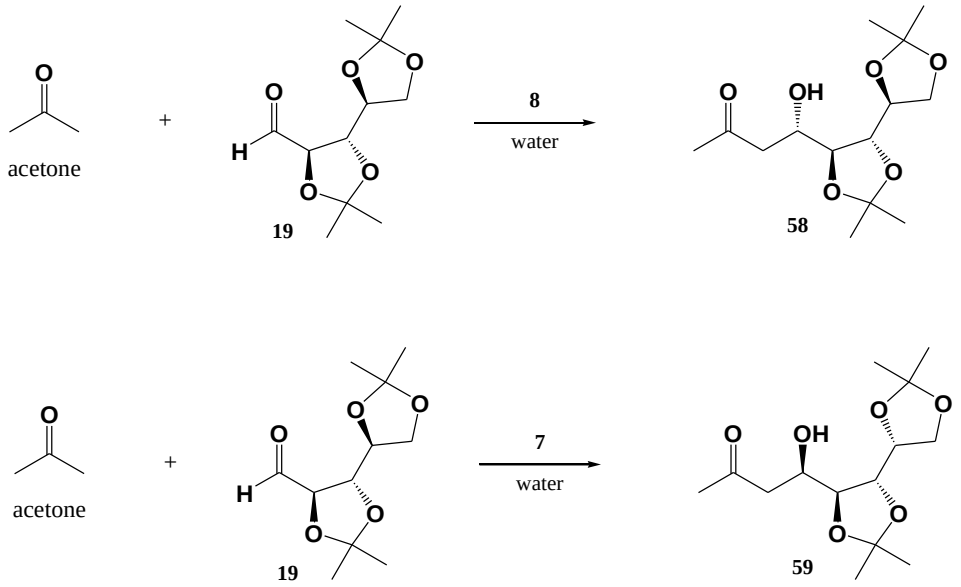
H3a	H3b	H4	H5	H6	H7	H8a	H8b
$J_{3a,4}$	$J_{3b,4}$	$J_{3a,4}$	$J_{4,5}$	$J_{5,6}$	$J_{6,7}$	$J_{7,8a}$	$J_{7,8b}$
$J_{3a,3b}$	$J_{3a,3b}$	$J_{3b,4}$	$J_{5,6}$	$J_{6,7}$	$J_{7,8a}$	$J_{8a,8b}$	$J_{8a,8b}$
		$J_{4,5}$			$J_{7,8b}$		
3.40 (dd)	8.81 (dd)	3.40 (dt)	9.10 (dd)	2.10 (dd)	9.32 (ddd)	3.20(dd)	6.20 (dd)
16.6	16.6	8.81	1.91	11.8	3.20	8.74	8.74
					6.20		

Table 2.4.3.1.

To determine the absolute configuration of which, the bisaldol product **102** was converted into the crystalline spiroacetal as described in the chapter 4.

2.4.4 Crossed aldol reaction between acetone and 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-L-arabinose **19**

Similarly, the reaction of 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-L-arabinose **19** under the same conditions (Scheme 2.4.4.1) afforded stereoselectively the corresponding 1.3-dideoxy-L-*glycero*-L-*ribo*-octulose **58** (83% yield, 96% de) along with bisaldol product, 6.8-dideoxy-L-*allo*-L-*allo*-7-trideculose, **103** using D-prolinamido-glycoside **8**. The NMR spectra and MS spectrum of **58** and its dextrorotatory D-enantiomer **56** were identical.

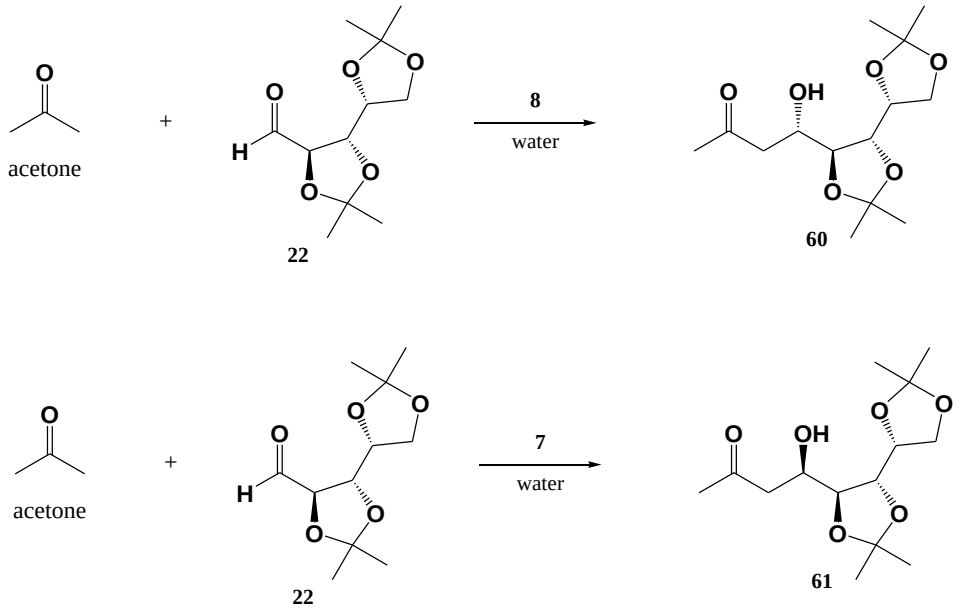


Scheme 2.4.4.1. Aldol reaction between acetone and 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-L-arabinose **19**

.

2.4.5 Crossed aldol reaction between acetone and 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-xylose **22**

Treatment of 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-xylose **22** with acetone in aqueous solution of **8** for 1 hour gave 1,3-dideoxy-D-*glycero*-L-*ribo*-octulose **60** in 77% yield with 96% de (Scheme 2.4.5.1) together with bisaldol product, 6,8-dideoxy-D-*talo*-D-*talo*-7-trideculose in 13% yield. The diastereomeric ratio of **60** and **61** was determined by ^{1}H NMR integration of the H-5 and the isopropylidene methyl peaks in the product mixture. The *anti*-diastereomer **60** showed its H-3b and H-4 signals at lower-field (2.93 and 4.45 ppm) than the *syn*-diastereomer, 1.3-dideoxy-D-*glycero*-L-*arabino*-octulose **61,** (2.86 and 4.18 ppm), affording the diastereomeric ratio.



Scheme 2.4.5.1. Aldol reaction between acetone and 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-xylose **22**

.

The conformationally diagnostic spin couplings, $J_{4,5}$ and $J_{6,7}$ are respectively, 7.9 and 6.9 Hz, and the latter indicates that H-6 and H-7 are preponderantly gauche, with rotation about the C-6–C-7 bond to alleviate the *syn*-axial interaction between O-5 and O-7 in the *P* conformation (Figure 2.4.5.1), and generating the sickle* ($_6G^-$) conformer as a significant contributor to the conformational equilibrium, and the former is consistent with essentially exclusive antiperiplanar orientation of H-4 and H-5, and it clearly indicates the newly formed chiral center at C-4 as (*S*).

* The term ‘‘sickle’’ was introduced by Horton to designate the conformation generated from the extended, planar, zigzag, form by rotation through 120º about an internal carbon-carbon bond. $_6G^-$ denoted the sickle form obtained by 120 º clockwise rotation of the remote atom along C-6–C7 bond.

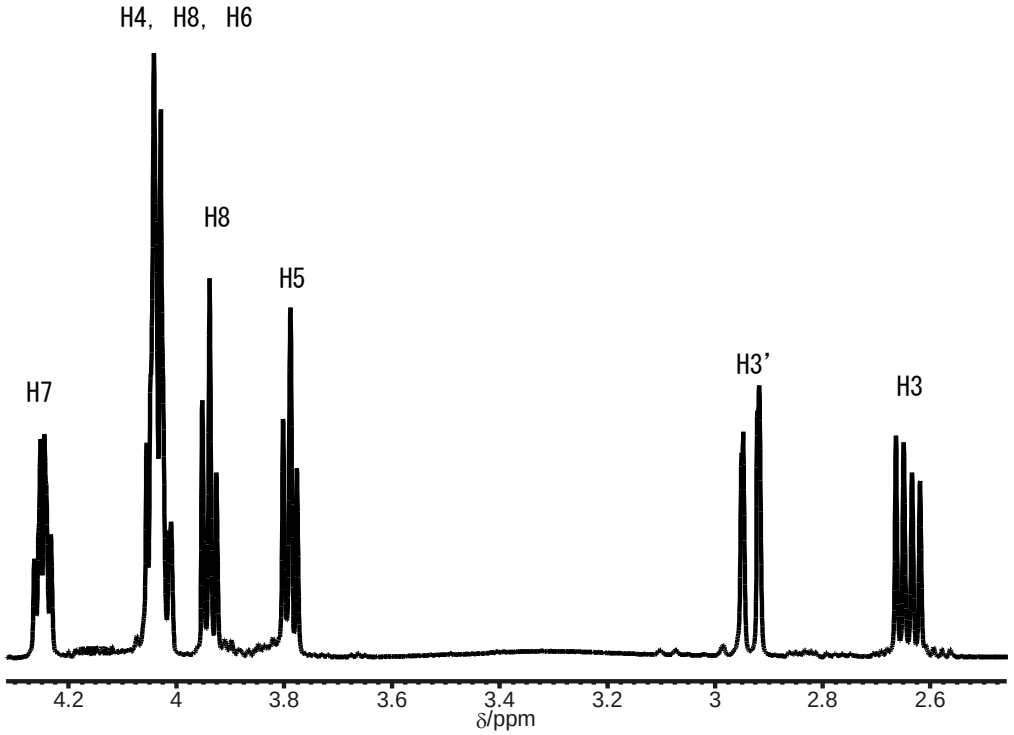


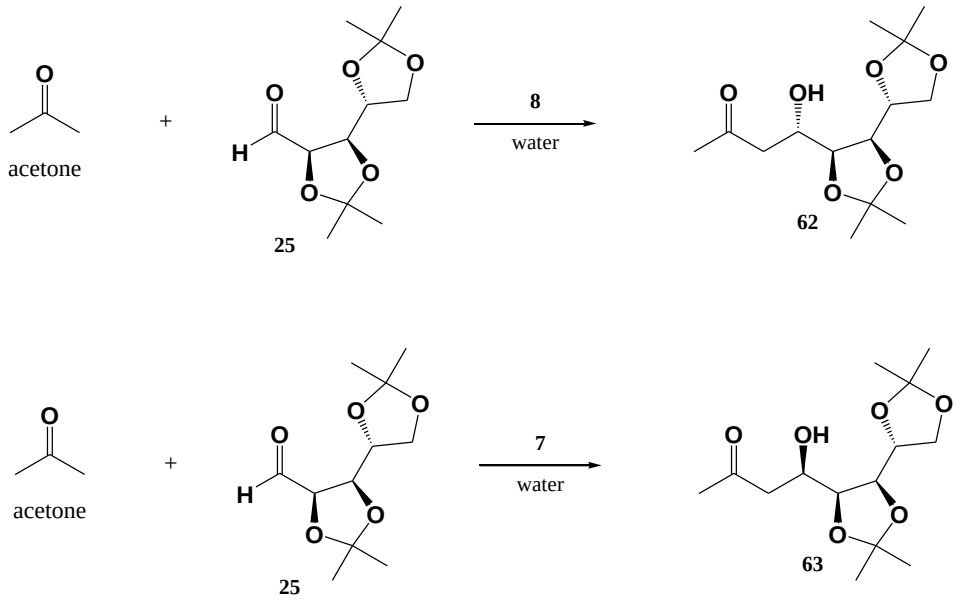
Figure 2.4.5.1. 1H NMR spectrum of 1,3-dideoxy-5,6:7,8-*O*-isopropylidene-L-*glycero*-L-*ribo*-octulose **60**.

	Coupling constants (Hz)						
H3a	H3b	H4	H5	H6	H7	H8a	H8b
$J_{3a,4}$	$J_{3b,4}$	$J_{3a,4}$	$J_{4,5}$	$J_{5,6}$	$J_{6,7}$	$J_{7,8a}$	$J_{7,8b}$
$J_{3a,3b}$	$J_{3a,3b}$	$J_{3b,4}$	$J_{5,6}$	$J_{6,7}$	$J_{7,8a}$	$J_{8a,8b}$	$J_{8a,8b}$
		$J_{4,5}$			$J_{7,8b}$		
2.46 (dd) 17.1	9.10 (dd) 17.1	2.46 (dt) 9.10 9.01	9.10 (dd) 1.91	1.91 (dd) 9.32	9.32 (ddd) 4.62 2.49	4.62 (dd) 12.5	2.49 (dd) 12.5

Table 2.4.5.1. [1]H NMR data for1,3-dideoxy-5,6,7,8-tetra-*O*-acetyl-D-*glycero*-D-*ribo*-octulose **60**.

2.4.6 Crossed aldol reaction between acetone and 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-ribose **25**

D-Prolinamido-glycoside **8** catalyzed aldol reaction between acetone and 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-ribose **25** predictably gave the corresponding 1,3-dideoxy-D-*glycero*-D-*lyxo*-octluose **62** in 81% net yield as a crystalline single diastereomer together with its bisaldol adduct, 6,8-dideoxy-D-*mannno*-D-*mannno*-7-trideculose **108** in 9% yield. The diastereofacial selectivity was again accorded with the Felkin-Anh model. The D-ribo aldehyde **25** subjected to the same aldol reaction conditions using L-prolinamido-glycoside **7** gave, *syn*-aldol adduct, syrupy 1,3-dideoxy-D-*gluco*-octluose **63** in 71% yield with, surprisingly, 92 % de together with 6,8-dideoxy-L-*gluco*-D-*gluco*-7-trideculose in 22% yield (Scheme 2.4.6.1).



Scheme 2.4.6.1. Aldol reaction between acetone and 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-ribose **25**

.

Distinctive mobilities of **62** and **63** on TLC (Rf, 0.3 and Rf, 0.5) were observed in this case and it allowed complete separation of each of the two diastereomers by silica gel column chromatography. In ^{1}H NMR spectra, the relative chemical shifts of the H-3 signals between the *anti* and *syn* isomer were considered stereochemically diagnostic, with the *anti*-isomer showing doublet of doublets for H-3 at δ 2.7 and δ 2.8 (Figure 2.4.6.1), and the *syn* isomer showing a narrow doublet for H-3 at δ 2.75 (Figure 2.4.6.2). The large (9.2 Hz) value of $J_{6,7}$ is consistent with essentially exclusive antiperiplanar orientation of H-6 and H-7, but the $J_{5,6}$ value of 5.4 Hz is indicative of conformational instability with an appreciable contribution of both the planar zigzag conformer having H-5 and H-6 antiperiplanar, and a larger contribution of the sickle form ($_5G^-$ form*), arising through rotation about the C-5–C-6 bond to alleviate the 1,3-interaction between each IP groups (Figure 2.4.6.4).

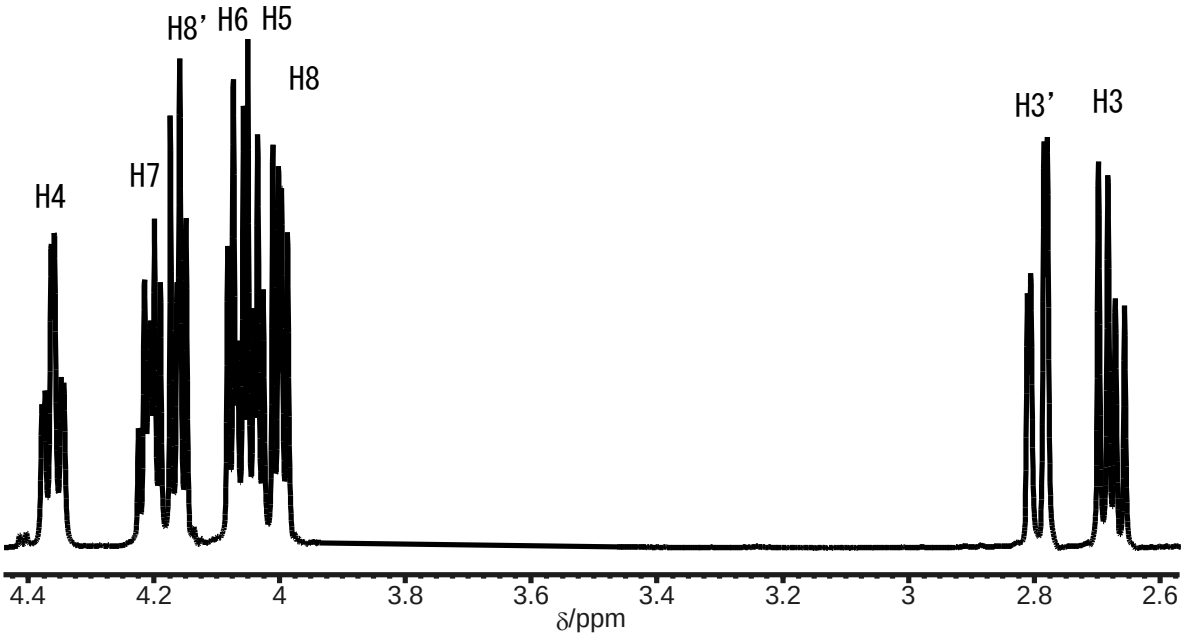


Figure 2.4.6.1. 1H NMR spectrum of 1.3-dideoxy-5,6:7,8-*O*-isopropylidene-L-*glycero*-L-*ribo*-octulose **62**.

* $_5G^-$ denotes the sickle obtained by 120º clockwise rotation of the remote atom along C-5–C-6 bond.

Coupling constants (Hz)							
H3a	H3b	H4	H5	H6	H7	H8a	H8b
$J_{3a,4}$	$J_{3b,4}$	$J_{3a,4}$	$J_{4,5}$	$J_{5,6}$	$J_{6,7}$	$J_{7,8a}$	$J_{7,8b}$
$J_{3a,3b}$	$J_{3a,3b}$	$J_{3b,4}$	$J_{5,6}$	$J_{6,7}$	$J_{7,8a}$	$J_{8a,8b}$	$J_{8a,8b}$
		$J_{4,5}$			$J_{7,8b}$		
9.20 (dd)	2.91 (dd)	9.20 (dt)	6.33 (dd)	5.60 (dd)	9.22 (dt)	5.44 (dd)	6.31 (dd)
15.9	15.9	2.91	5.60	9.22	5.44	8.73	8.73
		6.33			6.31		

Table 2.4.6.1. ^{1}H NMR data for1.3-dideoxy-5,6,7,8-tetra-*O*-acetyl-D-*glycero*-D-*ribo*-octulose **62**.

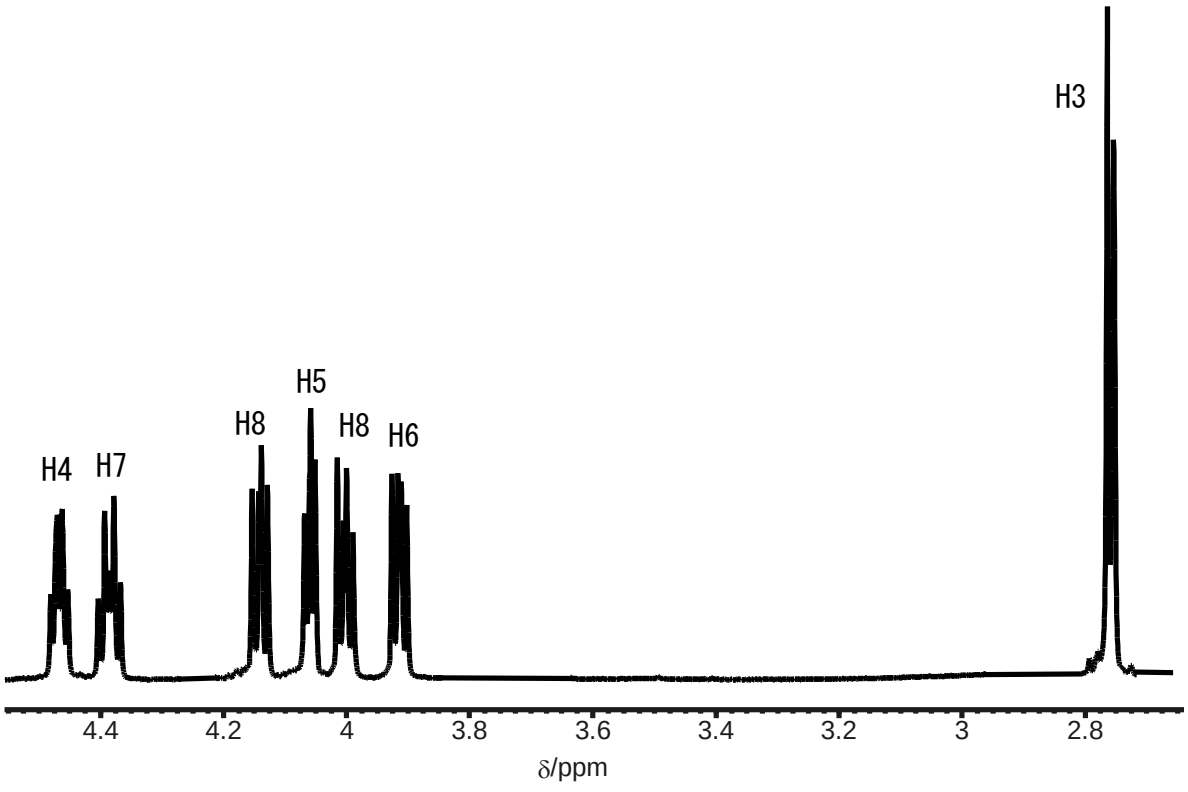


Figure 2.4.6.2. 1H NMR spectrum of 1.3-dideoxy-5,6:7,8-*O*-isopropylidene-D-*glycero*-L-*ribo*-octulose **63**.

	Coupling constants (Hz)					
H3b	H4	H5	H6	H7	H8a	H8b
$J_{3,4}$	$J_{3,4}$ $J_{4,5}$	$J_{4,5}$ $J_{5,6}$	$J_{5,6}$ $J_{6,7}$	$J_{6,7}$ $J_{7,8a}$ $J_{7,8b}$	$J_{7,8a}$ $J_{8a,8b}$	$J_{7,8b}$ $J_{8a,8b}$
6.2(dd)	6.20 (dt) 5.82	6.20 (dd) 5.71	5.71 (dd) 5.93	5.93 (dt) 5.70 6.22	5.70 (dd) 8.74	6.22(dd) 8.74

Table 2.4.6.2. [1]H NMR data for1.3-dideoxy-5,6,7,8-tetra-*O*-acetyl-D-*glycero*-D-*ribo*-octulose **63**.

The behavior of the D-*ribo*-aldehyde was quite different from that of other diastereomers, due to the conformational instability. As for the highly anti Felkin-Anh controlled *re*-facial selectivity, evident by formation of the *anti*-aldol adduct, the favored conformation of the *aldehydo*-D-ribose was considered as **25A** in Figure 2.4.6.3.

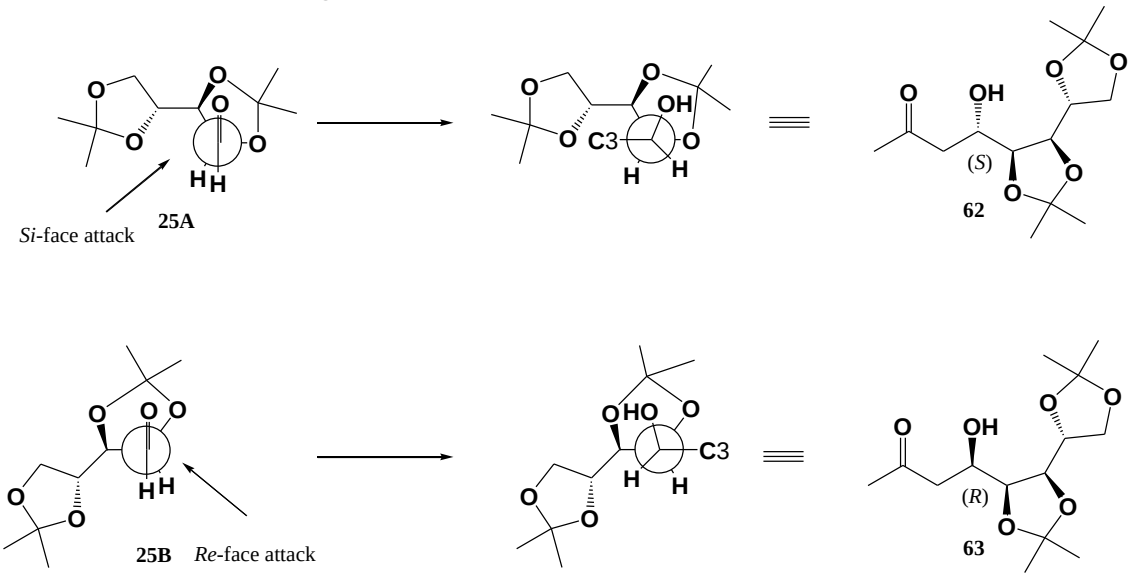
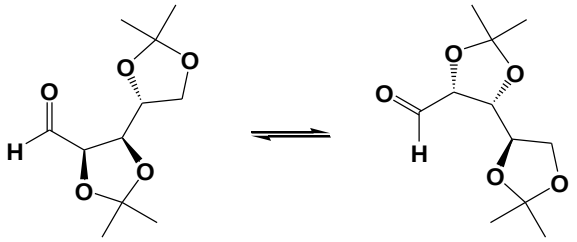


Figure 2.4.6.3. Formation of each epimers.

And this result suggesting that the two sickle* conformers of 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-ribose, i.e. $_2G^-$ and $_2G^+$, are easily exchangeable in the aldol reaction (Figure 2.4.6.4).

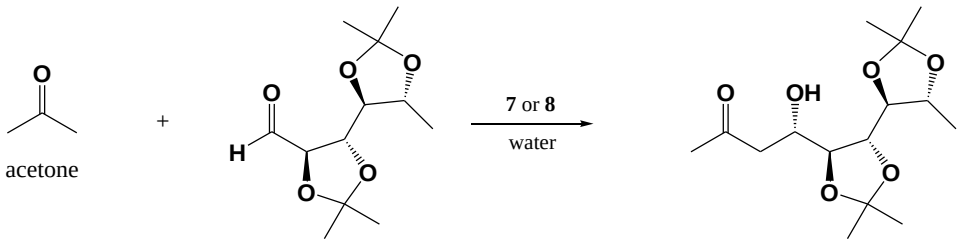


$_2G^-$ conformation $_2G^+$ conformation

Figure 2.4.6.4. The sickle conformers of the D-ribo aldehyde.

2.4.7 Crossed aldol reaction between acetone and 2,3:4,5-di-*O*-isopropylidene-D-fucose **28**

Likewise, the aldol reaction of 2,3:4,5-di-*O*-isopropylidene-D-fucose **28** afforded expected 1,3,9-trideoxy-5,6:7,8-di-*O*-isopropylidene-L-*glycero*-D-*tallo*-nonulose **64** in 75% yield as a single diastereomer under the D-prolinamide catalyzed conditions, whereas the L-prolinamide catalyzed condition gave a diastereomeric mixture (Scheme 2.4.7.1).



28 **64**

* $_2G^-$ denotes the sickle obtained by 120º clockwise rotation of the remote atom along C-2–C-3 bond; $_2G^+$ denotes the sickle obtained by 120º counterclockwise rotation of the remote atom along C-2–C-3 bond.

Scheme 2.4.7.1. Aldol reaction between acetone and 2,3:4,5-di-*O*-isopropylidene-D-fucose **28**.

The ^{1}H NMR spectrum of nonulose **64** was of first order and showed expected patterns for each signals of the sugar chain (Figure 2.4.7.1).

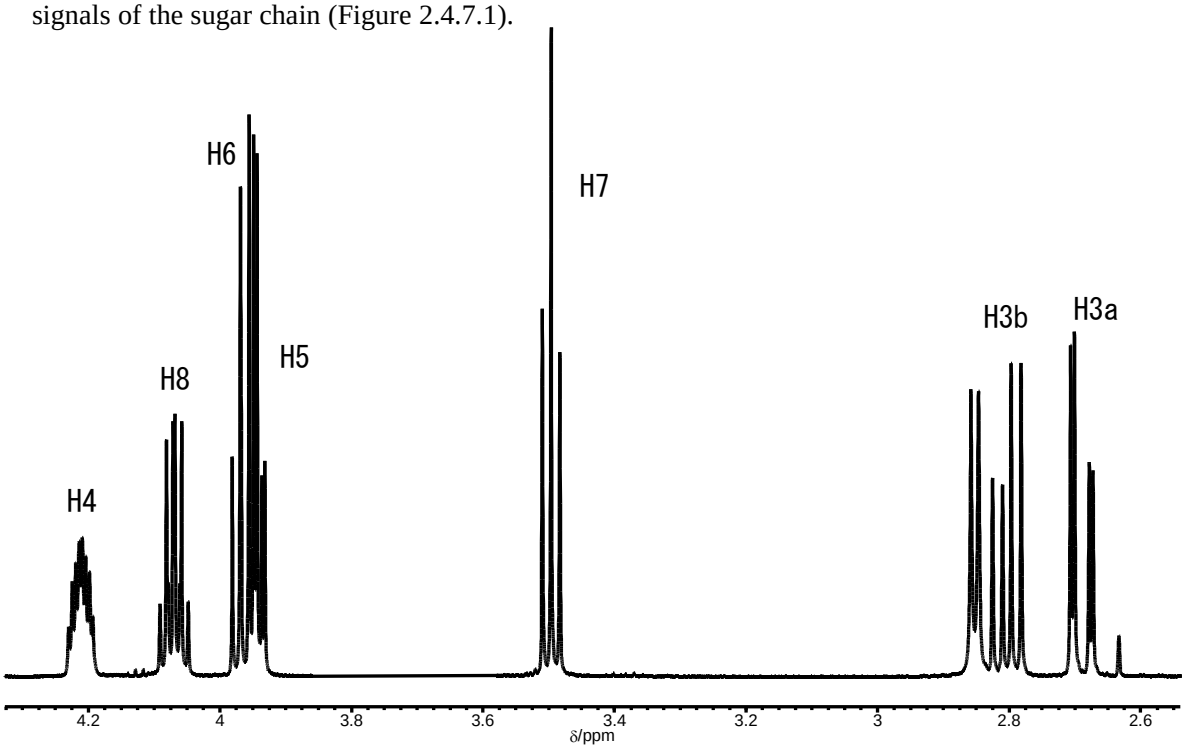


Figure 2.4.7.1. 1H NMR spectrum of 1,3,9-trideoxy-5,6:7,8-di-*O*-isopropylidene-L-*glycero*-D-*tallo*-nonulose **64**.

The L-*glycero*-D-*tallo*-sugar chain has no *syn*-axial interactions, and hence the conformation of which is considered essentially *P* form, however, the large (7.9 Hz) $J_{5,6}$ value consists ${}_{5}G^{+}$ conformation may be caused by the two isopropylidene rings (Table 2.4.7.1).

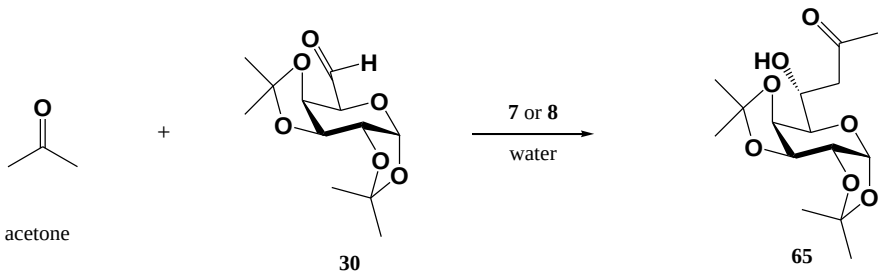
	Coupling constants (Hz)						
H3a	H3b	H4	H5	H6	H7	H8	H9
$J_{3a,4}$ $J_{3a,3b}$	$J_{3b,4}$ $J_{3a,3b}$	$J_{3a,4}$ $J_{3b,4}$ $J_{4,5}$	$J_{4,5}$ $J_{5,6}$	$J_{5,6}$ $J_{6,7}$	$J_{6,7}$ $J_{7,8}$	$J_{7,8}$ $J_{8,9}$	$J_{8.9}$
3.51 (dd) 15.1	7.91 (dd) 15.1	3.51 (ddd) 7.91 3.02	3.02 (dd) 8.11	8.11 (t) 7.93	7.93 (t) 7.93	7.93 (dq) 6.01	6.01 (d)

Table 2.4.7.1. ^{1}H NMR data for

1,3,9-trideoxy-5,6:7,8-di-*O*-isopropylidene-L-*glycero*-D-*tallo*-nonulose **64**.

2.4.8 Crossed aldol reaction between acetone and 1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose **30**.

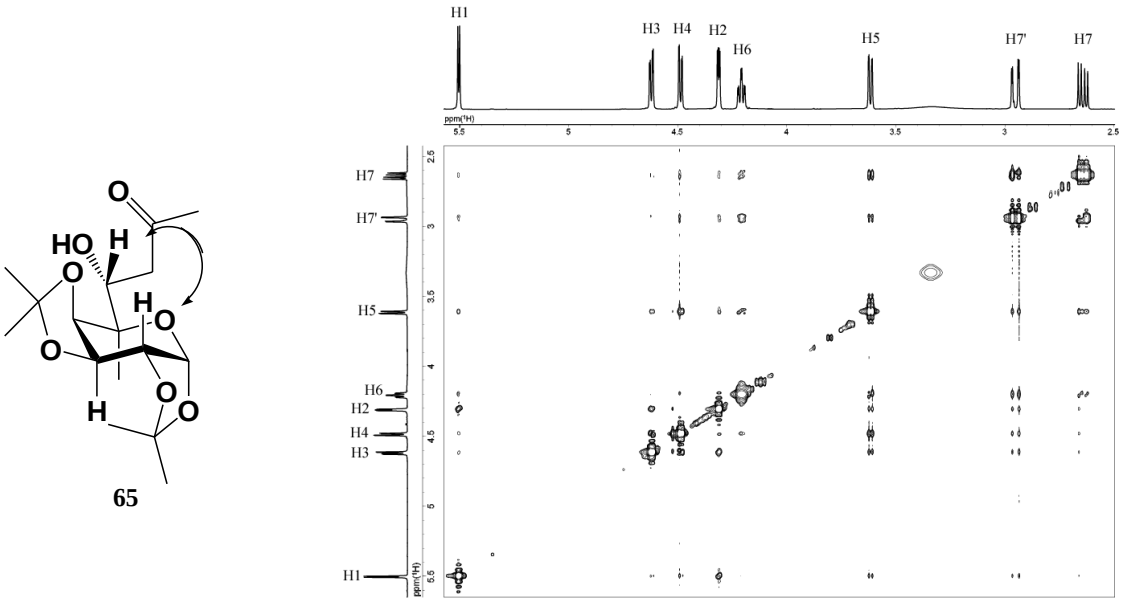
Aldol reaction of 1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose **30** under L-prolinamido-glycoside **7** catalyzed conditions gave 7,8-didoxy-1,2:3,4-di-*O*-isopropylidene-8-oxo-D-*glycero*-D-*galacto*-nonopyranose **65** in 73% yield, accompanied by a very small proportion of another isomer, as a syrup (Scheme 2.4.8.1).



Scheme 2.4.8.1. Aldol reaction between acetone and

1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose **30**.

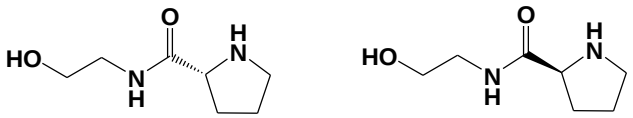
The relative configuration at the newly formed carbon center C-6 was assigned by NOESY experiment as (*6R*), which is accorded with Felkin-Anh theory. NOE signals for H-7 and H-7’ were observed at H-2, H-3, H-4 and anomeric proton. Thus, C-6–C-9 chain on the **65** places above the ring (Figure 2.4.8.1).



65

Figure 2.4.8.1. NOESY spectrum of **64**.

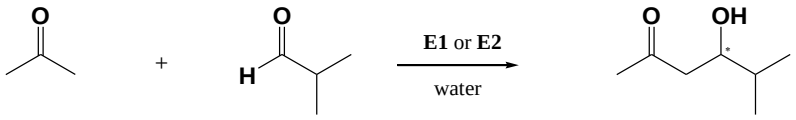
2.5 The aqueous aldol reaction under prolinamido-ethanol catalyzed conditions.



E1 **E2**

Figure 2.5.1. Prolinamido-etnanol catalysts

In a parallel series of experiments, known[32] prolinamido-ethanols **E1** and **E2** (Figure 2.5.1), which have no chiral, rigid hydroxyls, were also used as catalyst in the aqueous aldol reaction of isobutyraldehyde and the isopropylidene-D-glyceraldehyde **10** (Schemes 2.5.1 and 2.5.2, Tables 2.5.1 and 2.5.2). The yields and stereoselectivities were reduced when compared with prolinamido-glycoside catalyzed conditions, suggesting the efficiency of the carbohydrate auxiliaries in aqueous aldol reaction.

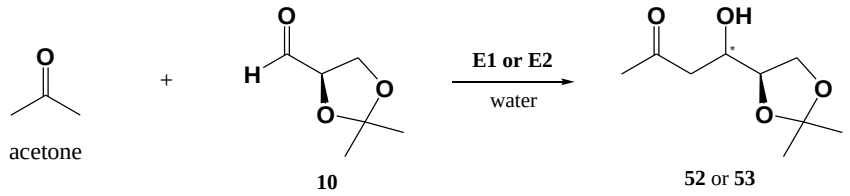


acetone isobutyraldehyde **50** or **51**

Scheme 2.5.1. Aldol reaction between acetone and isobutyraldehyde.

entry	catalyst	amount of catalyst (equivallent)	solvent	time (h)	yield (%)	ee (%)
1	**7**	0.3	water	24	32	83 (*R*)
2	**7**	0.1	water	24	25	76(*R*)
3	**7**	0.05	water	48	26	81 (*R*)
4	**7**	0.1	DMSO	48	11	68 (*R*)
5	**8**	0.3	water	24	36	83 (*S*)
6	**8**	0.1	water	24	22	79 (*S*)
7	**8**	0.05	water	48	24	75 (*S*)
8	**8**	0.1	DMSO	48	12	61 (*S*)

Table 2.5.1. Aldol reaction between acetone and isobutyraldehyde.



Scheme 2.5.2. Aldol reaction between acetone and **10**.

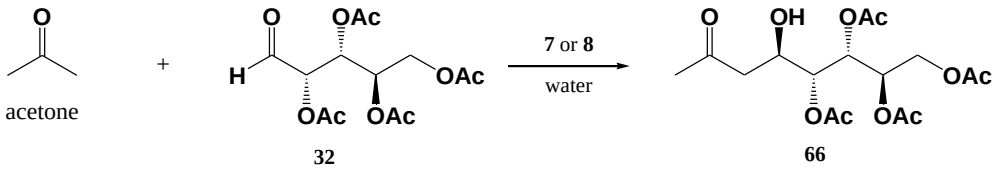
entry	catalyst	amount of catalyst (equivallent)	solvent	time (h)	yield (%)	de (%)
1	**7**	0.3	water	24	64	79 (3*R*)
2	**7**	0.1	water	48	48	71 (3*R*)
3	**7**	0.3	phosphate buffer	24	61	77 (3*R*)
4	**7**	0.1	phosphate buffer	48	51	70 (3*R*)
5	**8**	0.3	water	24	69	81 (3*S*)
6	**8**	0.1	water	48	52	79 (3*S*)
7	**8**	0.3	phosphate buffer	24	66	72 (3*S*)
8	**8**	0.1	phosphate buffer	48	50	69 (3*S*)

Table 2.5.2. Aldol reaction between acetone and **10**.

2.6 Aqueous aldol reaction for acetyl *aldehydo*-aldoses

2.6.1 Crossed aldol reaction between acetone and 2,3,4,5-tetra-*O*-acetyl-*aldehydo*-D-arabinose **32**

L-Prolinamido-glycoside **7** catalyzed aldol reaction of acetone with 2,3,4,5-tetra-*O*-acetyl-*aldehydo*-D-arabinose **32** gave, after chromatographic resolution, a 95% yield of **66** as a single diastereomer (Scheme 2.6.1.1).



Scheme 2.6.1.1. Aldol reaction between acetone and 2,3,4,5-tetra-*O*-acetyl-*aldehydo*-D-arabinose **32**

.

The observed values for $J_{3,4}$ (9.1 Hz), $J_{4,5}$ (9.0 Hz), and $J_{5,6}$ (1.9 Hz) gave clear support for the extended planar zigzag (*P*) conformation for X (Figure 2.6.1.1, Table2.6.1.1).

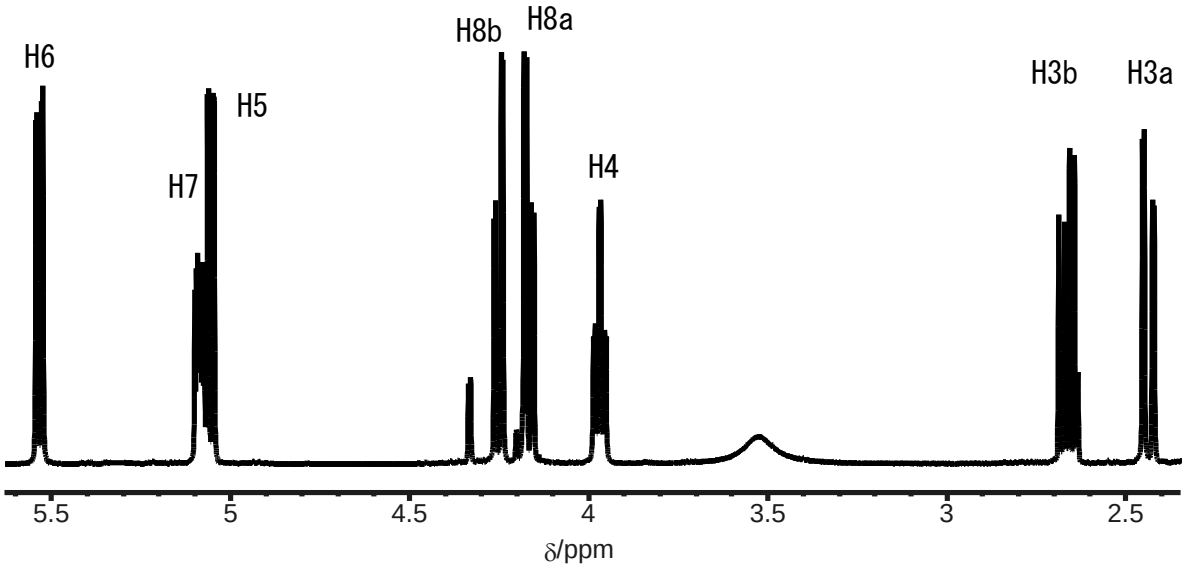


Figure 2.6.1.1. 1H NMR spectrum of 1.3-dideoxy-5,6,7,8-tetra-*O*-acetyl-D-*glycero*-D-*ribo*-octulose **66**.

	Coupling constants (Hz)							
H3a	H3b	H4	H5	H6	H7	H8a	H8b
$J_{3a,4}$	$J_{3b,4}$	$J_{3a,4}$	$J_{4,5}$	$J_{5,6}$	$J_{6,7}$	$J_{7,8a}$	$J_{7,8b}$
$J_{3a,3b}$	$J_{3a,3b}$	$J_{3b,4}$	$J_{5,6}$	$J_{6,7}$	$J_{7,8a}$	$J_{8a,8b}$	$J_{8a,8b}$
		$J_{4,5}$			$J_{7,8b}$		
2.46 (dd) 17.1	9.10 (dd) 17.1	2.46 (dt) 9.10 9.01	9.10 (dd) 1.91	1.91 (dd) 9.32	9.32 (ddd) 4.62 2.49	4.62 (dd) 12.5	2.49 (dd) 12.5

Table 2.6.1.1. [1]H NMR data for1.3-dideoxy-5,6,7,8-tetra-*O*-acetyl-D-*glycero*-D-*ribo*-octulose **66**.

Further, as illustrated in Figure, relatively large NOE signals (Figure 2.6.1.2) were observed between H-3 and H-5, and also H-6 and H-8. Assignment of the absolute configuration was achieved by X-ray crystallography (Figure2.6.1.3).

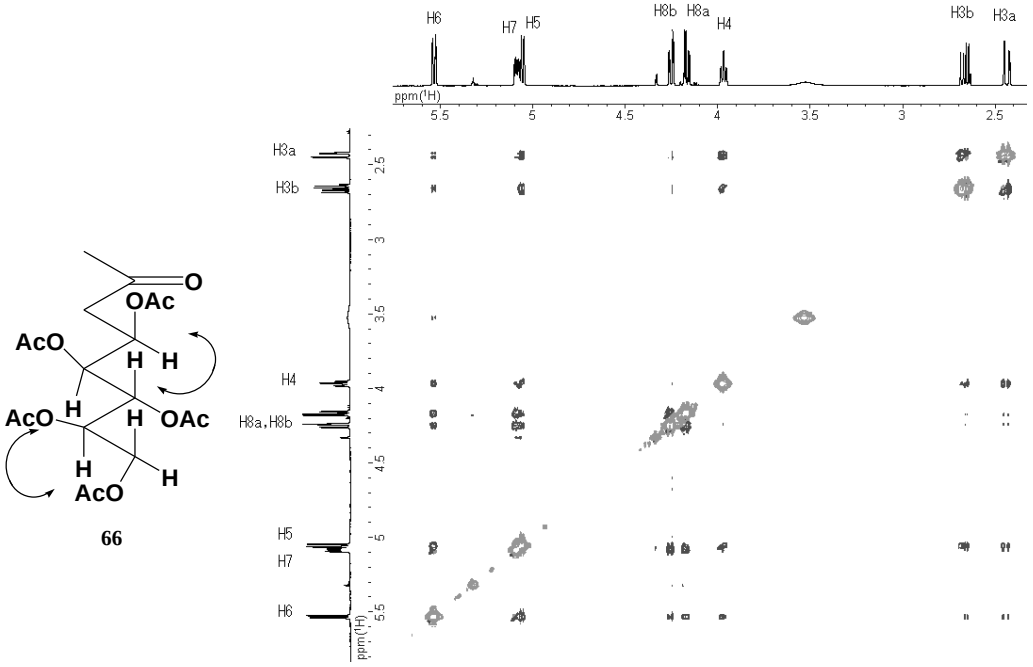


Figure 2.6.1.2. NOESY spectrum of 1.3-dideoxy-5,6,7,8-tetra-*O*-acetyl-D-*glycero*-D-*ribo*-octulose **66**.

It crystallizes in the orthorhombic space group $P2_12_12_1$ with cell parameters a = 7.931 (12) Å, b = 13.464 (3) Å, c = 15.825 (3) Å, and Z = X. The crystal structure is in good agreement with the NMR data. The observed torsion angles in crystalline **66** were compared in Table 2.6.1.2 with the ^{1}H NMR couplings observed chloroform-*d* solution.

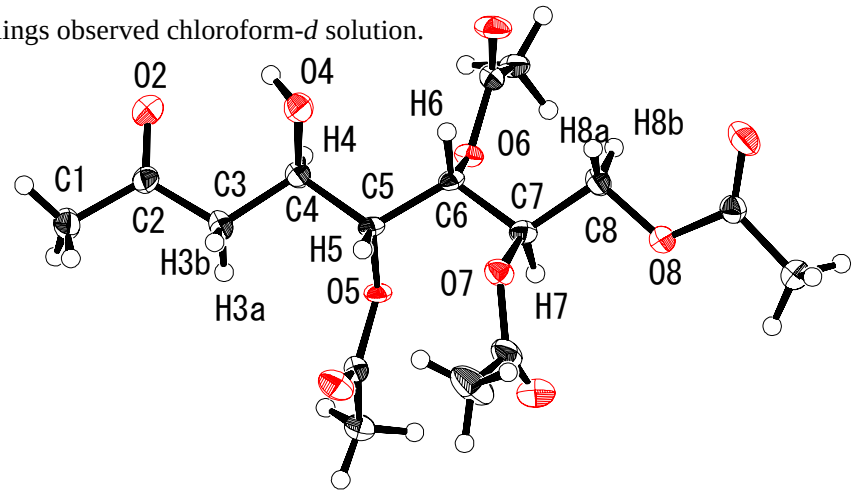


Figure 2.6.1.3. ORTEP representation of **66**.

Torsion angles (°)		coupling constants (Hz)	
H3a-C3-C4-H4	61.70	$J_{3a,4}$	2.46
H3b-C3-C4-H4	-178.30	$J_{3b,4}$	9.10
H4-C4-C5-H5	-174.60	$J_{4,5}$	9.01
H5-C5-C6-H6	-67.25	$J_{5,6}$	1.91
H6-C6-C7-H7	-167.37	$J_{6,7}$	9.32
H7-C7-C8-H8a	167.43	$J_{7,8a}$	4.62
H7-C7-C8-H8b	67.81	$J_{7,8b}$	2.49

Table 2.6.1.2. Selected torsion angles and coupling constants.

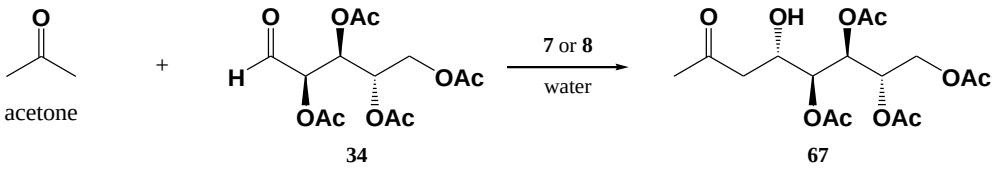
D-Prolinamido-glycoside **8** catalyzed reaction gave the same *anti* adduct **66**, as a consequence of anti Felkin-Anh controlled attack, with high (91%) diastereoselectivity, albeit in low (26%) yield.

Differences in selectivity between the acetate form and the isopropylidene form may be attributed to the different conformational mobilities of the chain depending on the protecting groups.

2.6.2 Crossed aldol reaction between acetone and 2,3,4,5-tetra-*O*-acetyl-*aldehydo*-L-arabinose **34**

Likewise, the enantiomer of **66** was obtained from the enantiomer of **32**, 2,3,4,5-tetra-*O*-acetyl-*aldehydo*-L-arabinose **34** (Scheme 2.6.2.1). L-Prolinamido-glycoside **7** catalyzed aldol reaction of acetone with 2,3,4,5-tetra-*O*-acetyl-*aldehydo*-L-arabinose **34** gave, as expected, **67** in 71% yield with 92% de. The spectral data of **67** was identical with the enantiomer of which, except sign of the optical rotation. The same reaction catalyzed D-prolinamido-glycoside **8** gave enantiomerically pure **67** in 89 % net yield.

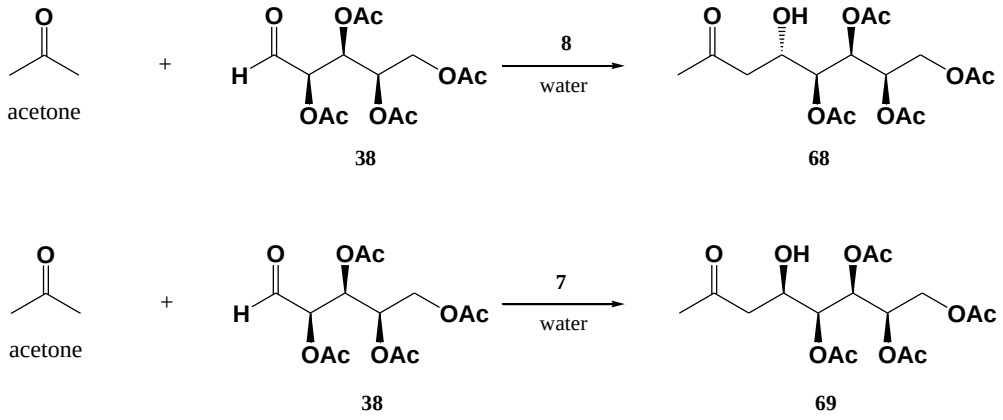
In the case of 2,3,4,5-tetra-*O*-acetly-aldehydo-D-arabonose **32** and 2,3,4,5-tetra-*O*-acetly-aldehydo-L-arabonose **34**, the high diastereofacial selectivities were observed under both D-prolinamido-glycoside **8** and L-prolinamido-glycoside **7** catalyzed conditions. These high diastereofacial selectivities may be ascribed to the low mobility of the chains possess the *arabino* configuration, because the stable planar zigzag orientation of the chain is favored only in those chains having the *arabino* stereochemistry. The absolute configuration of **66** was determined by X-ray crystallography and the backbone chain is revealed as planar zigzag conformation.



Scheme 2.6.2.1. Aldol reaction between acetone and 2,3,4,5-tetra-*O*-acetyl-*aldehydo*-L-arabinose **34**

2.6.3 Crossed aldol reaction between acetone and 2,3,4,5-tetra-*O*-acetyl-*aldehydo*-D-xylose **38**

The favored conformation of 2,3,4,5-tetra-*O*-acetyl-*aldehydo*-D-xylose **38** is ${}_3G^-$ conformation, the high diastereofacial selectivity was observed when the aldol reaction carried out using D-prolinamido-glycoside **8** as the catalyst. When the same reaction was performed using L-prolinamido-glycoside **7**, negligible facial selectivity was observed, and it may be attributed to the conformational instability of the *xylo*-chain.



Scheme 2.6.3.1. Aldol reaction between acetone and 2,3,4,5-tetra-*O*-acetyl-*aldehydo*-D-xylose **38**

The vicinal proton-proton couplings for **68** deviate significantly from those values diagnostic of preponderantly antiperiplanar or gauche, and are indicative of conformational mixtures with substantial contributions from more than one conformer. The $J_{4,5}$ coupling of 8.4 Hz of **68** indicates comparably weighted contributions from antiperiplanar and gauche dispositions of those protons. Likewise the respective $J_{5,6}$ and $J_{6,7}$ values are 2.8 and 7.3 Hz, again demonstrating conformational mixing with no principal conformation (Figure 2.6.3.1, Table 2.6.3.1).

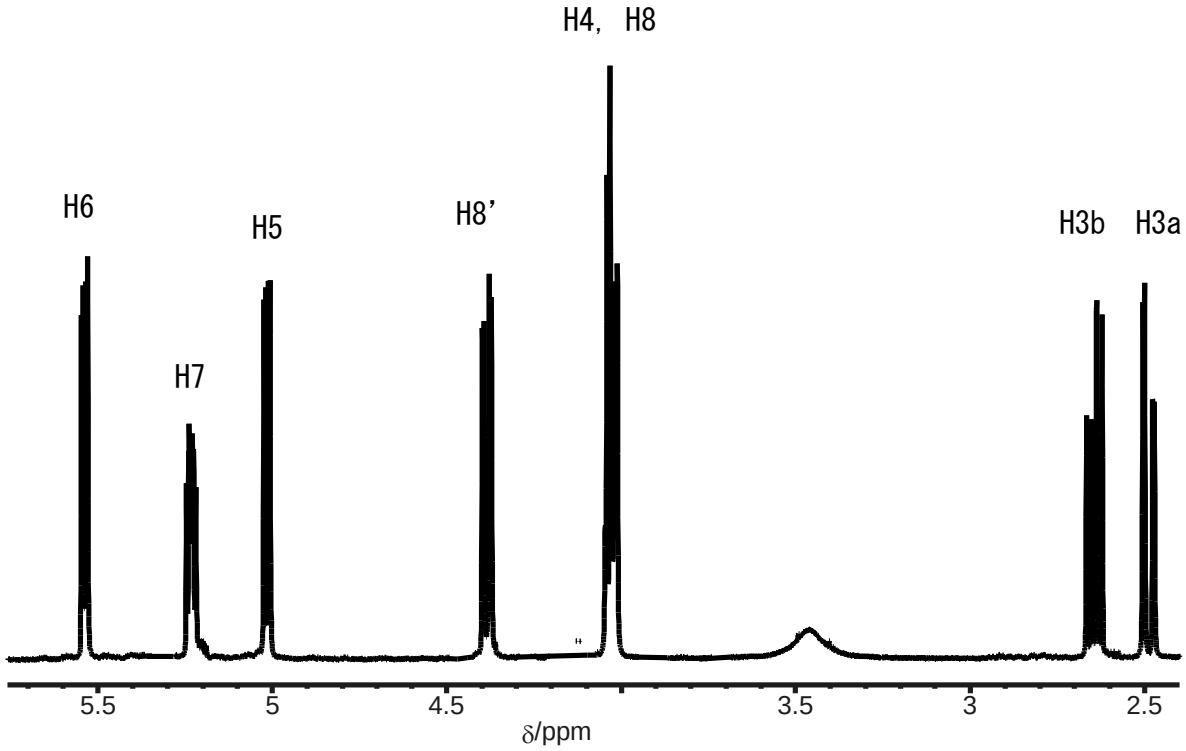


Figure 2.6.3.1. 1H NMR spectrum of 1.3-dideoxy-5,6,7,8-tetra-*O*-acetyl-D-*tallo*-octulose **68**.

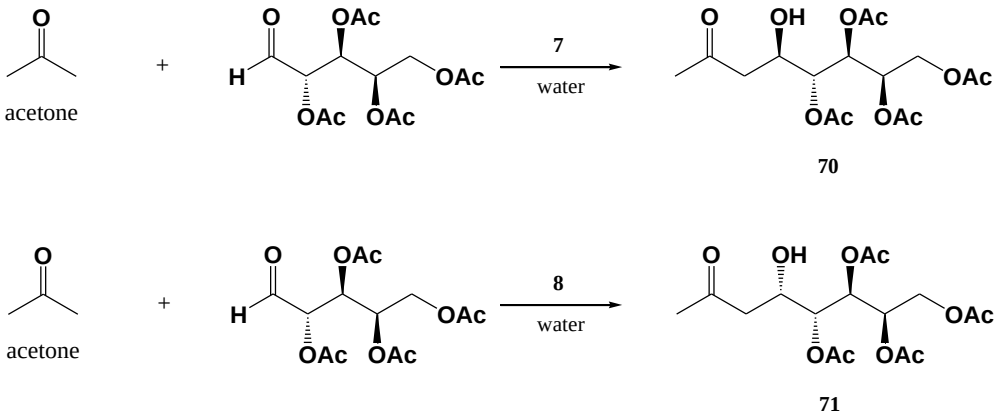
		Coupling constants (Hz)					
H3a	H3b	H4	H5	H6	H7	H8a	H8b
$J_{3a,4}$	$J_{3b,4}$	$J_{3a,4}$	$J_{4,5}$	$J_{5,6}$	$J_{6,7}$	$J_{7,8a}$	$J_{7,8b}$
$J_{3a,3b}$	$J_{3a,3b}$	$J_{3b,4}$	$J_{5,6}$	$J_{6,7}$	$J_{7,8a}$	$J_{8a,8b}$	$J_{8a,8b}$
		$J_{4,5}$			$J_{7,8b}$		
2.64 (dd)	9.02 (dd)	9.02 (m)	8.37 (dd)	2.79 (dd)	7.34 (ddd)	5.72 (dd)	3.67 (dd)
17.4	17.4	2.46	2.79	7.34	5.72	12.2	12.2
		8.37			3.67		

Table 2.6.3.1. [1]H NMR data for1.3-dideoxy-5,6,7,8-tetra-*O*-acetyl-D-*tallo*-octulose **68**.

2.6.4 Crossed aldol reaction between acetone and 2,3,4,5-tetra-*O*-acetyl-*aldehydo*-D-lyxose **41**

In the case of 2,3,4,5-tetra-*O*-acetyl-*aldehydo*-D-lyxose **41**, the extended, planar zigzag

conformation is the most favored, however, conformational instability was observed when compared with the *arabino* isomer and the result of the prolinamide catalyzed reactions has been correlated with those previously observed (Scheme 2.6.4.1). L-Prolinamido-glyxoside **7** catalyzed condition gave the D-*gulo* epimer **70** in 74% yield with 83% de. Analysis of the ^{1}H NMR spectra was of first order. The conformationally diagnostic spin couplings for **70** show, respectively, large (8.4 Hz) and medium (7.3Hz) values for $J_{4,5}$ and $J_{6,7}$, leading to assignment of the *P* conformation depicted in Scheme 2.6.4.1, as the most favored, but not exclusive at the limits expected for exclusive antiperiplanar and gauche dispositions, respectively.

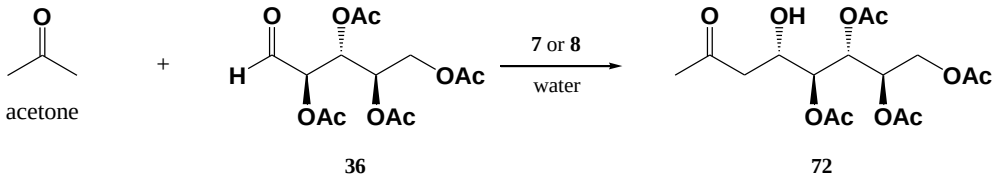


Scheme 2.6.4.1. Aldol reaction between acetone and 2,3,4,5-tetra-*O*-acetyl-*aldehydo*-D-lyxose **41**

.

2.6.5 Crossed aldol reaction between acetone and 2,3,4,5-tetra-*O*-acetyl-*aldehydo*-D-ribose **36**

As the configuration of D-ribose is (*2R*,*3R*,*4R*), the favored conformation of 2,3,4,5-tetra-*O*-acetyl-*aldehydo*-D-ribose **36** is sickle ($_{2}G^{-}$), and hence the *re*-face of **36** is crowded. Therefore, the attack of enamine of acetone occurred selectively from *si*-face to afford octulose **72** in both D-prolinamide **8** and L-prolinamide **7** catalyzed conditions (Scheme 2.6.5.1).



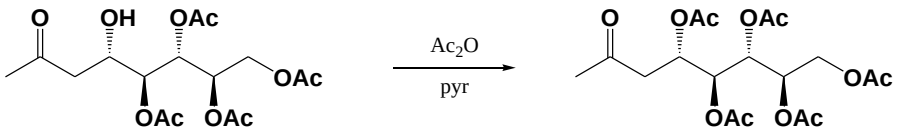
36 **72**

Scheme 2.6.5.1. Aldol reaction between acetone and 2,3,4,5-tetra-*O*-acetyl-*aldehydo*-D-ribose **36**

.

On the ^{1}H NMR spectrum of octulose **72**, overlap of The H-6 and H-7 signals of backbone chain precluded rigorous conformational assignments, hence the octulose was derived to the acetate form to determine the accurate spin-spin coupling for H-5, H-6, and H-7.

Acetylation of **72** with acetic anhydride and pyridine gave the expected acetate in 86% yield (Scheme 2.6.5.2), and the 1H NMR spectrum of which was amenable to first-order analysis and proton assignments paralleled those made for 4-OH octuloses.



72 **73**

Scheme 2.6.5.2. Acetylation of **72**.

The ^{1}H NMR spectrum of the syrupy product of the aldol reaction showed narrow doublet of doublets signals at δ 2.7 and δ 2.6 ppm in 94 : 4 ratio, assigned to the H-3 signals of the (*4R*) and (*4S*) diastereomeric products. The coupling constant between H-5 and H-6 was small, indicative of a nonplanar carbon chain rotated out of the plane of C-6–C-8 to the $_{5}G^{-}$ orientation, as depicted in Xa, alleviating the unfavorable *syn*-axial interactions between O-4 and O-6, and between O-5 and O-7 that would have resulted in the fully extended planar zigzag conformation of the sugar chain

(Figure 2.6.5.1, Table 2.6.5.1).

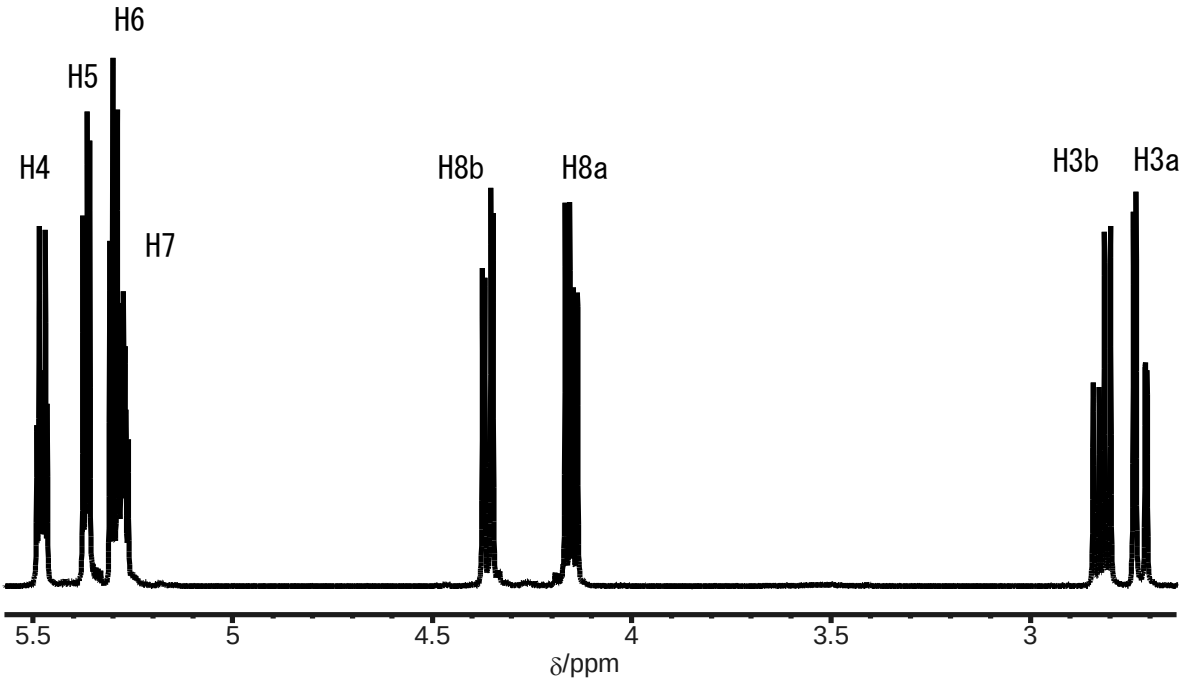


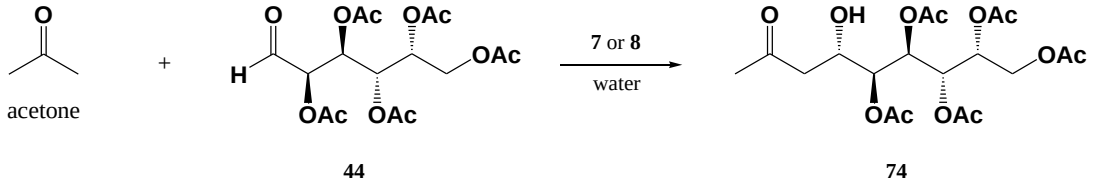
Figure 2.6.5.1. 1H NMR spectrum of 1.3-dideoxy-4,5,6,7,8-penta-*O*-acetyl-D-*mannno*-octulose **73**.

		Coupling constants (Hz)					
H3a	H3b	H4	H5	H6	H7	H8a	H8b
$J_{3a,4}$	$J_{3b,4}$	$J_{3a,4}$	$J_{4,5}$	$J_{5,6}$	$J_{6,7}$	$J_{7,8a}$	$J_{7,8b}$
$J_{3a,3b}$	$J_{3a,3b}$	$J_{3b,4}$	$J_{5,6}$	$J_{6,7}$	$J_{7,8a}$	$J_{8a,8b}$	$J_{8a,8b}$
		$J_{4,5}$			$J_{7,8b}$		
3.70(dd)	8.92 (dd)	3.70 (dt)	3.72 (dd)	6.40 (dd)	4.62(ddd)	6.81 (dd)	3.40 (dd)
17.1	17.1	8.92	6.40	4.62	6.81	12.3	12.3
		3.72			3.40		

Table 2.6.5.1. ^{1}H NMR data for1.3-dideoxy-4,5,6,7,8-penta-*O*-acetyl-D-*mannno*-octulose **73**.

2.6.6 Cossed aldol reaction between acetone and 2,3,4,5,6-penta-*O*-acetyl-*aldehydo*-D-galactose **44**.

The same procedure with acetylated *aldehydo*-D-galactose **44** using D-prolinamido-glycoside **8** afforded, after chromatographic purification, a syrupy 51 : 1 mixture of *anti* and *syn* 1,3-dideoxy-nonulose **74** in 72% yield, from which there crystallized the pure *anti* isomer. The ratio of the two epimers was determined by comparison of the H-3a and H-3b signals in the ^{1}H NMR spectra of the initial mixture and the spectrum of the crystalline *anti* product (Scheme 2.6.6.1).



44 **74**

Scheme 2.6.6.1. Aldol reaction between acetone and 2,3,4,5,6-penta-*O*-acetyl-*aldehydo*-D-galactose **44**.

The ^{1}H NMR spectrum of the dideoxynonulose **74** was of first order. Singlet signal near δ 2.18 was assigned to C-1 methyl group, and the protons of the sugar chain showed anticipated doublet of doublets for H-3a, H-3b, H-5, H-6, H-7, H-9a, H-9b, and the expected ABXY system for H-4 and H-8. The sugar chain showed large values for $J_{4,5}$ and $J_{6,7}$ and small values $J_{5,6}$ and $J_{7,8}$, consistent with the expected planar zigzag conformation of the carbon backbone chain (Figure 2.6.6.1, Table 2.6.6.1).

A definitive assignment is provided by an X-ray crystallographic structure analysis of the single crystal of **74** (Figure 2.6.6.2). The structure demonstrates an ambiguously that the newly formed chiral center at C-4 is (*S*), and indicates an extended planar zigzag conformation for the sugar chain, in good agreement with the ^{1}H NMR spectral data.

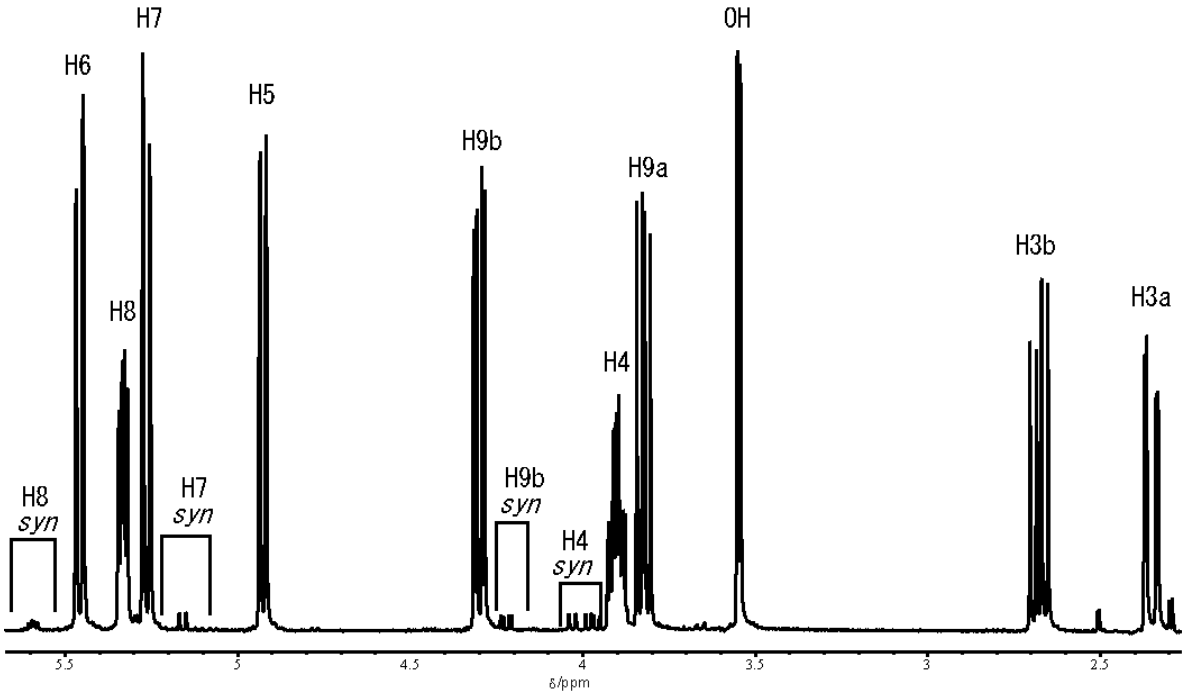


Figure 2.6.6.1. 1H NMR spectrum of 1,3-dideoxy-5,6,7,8,9-penta-*O*-acetyl-L-*glycero*-D-*ido*-nonulose **74**.

	Coupling constants (Hz)								
	H3a	H3b	H4	H5	H6	H7	H8	H9a	H9b
	$J_{3a,4}$ $J_{3a,3b}$	$J_{3b,4}$ $J_{3a,3b}$	$J_{3a,4}$ $J_{3b,4}$ $J_{4,5}$	$J_{4,5}$ $J_{5,6}$	$J_{5,6}$ $J_{6,7}$	$J_{6,7}$ $J_{7,8}$	$J_{7,8}$ $J_{8,9a}$ $J_{8,9b}$	$J_{8,9a}$ $J_{9a,9b}$	$J_{8,9b}$ $J_{9a,9b}$
	2.50(dd) 16.7	9.31 (dd) 16.7	2.50(ddd) 9.31 6.70	7.72(dd) 1.51	1.51 (dd) 10.2	1.51(dd) 1.93	1.93(ddd) 7.93 4.50	7.93 (dd) 11.8	4.50(dd) 11.8

Table 2.6.6.1. ^{1}H NMR data for 1,3-dideoxy-5,6,7,8,9-penta-*O*-acetyl-L-*glycero*-D-*ido*-nonulose **74**.

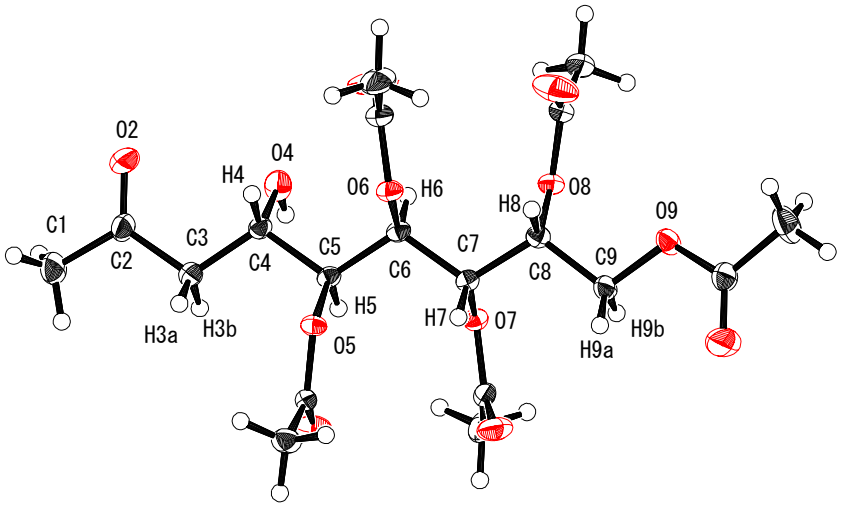


Figure 2.6.6.2. ORTEP representation of

1,3-dideoxy-5,6,7,8,9-penta-*O*-acetyl-L-*glycero*-D-*ido*-nonulose **74**.

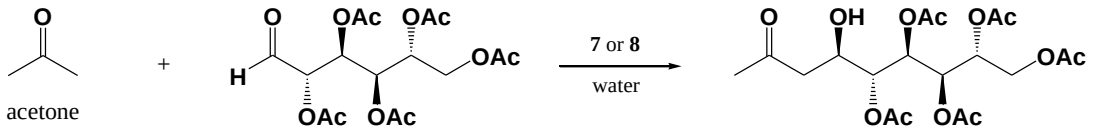
Torsion angles (°)		coupling constants (Hz)	
H3a-C3-C4-H4	-59.76	$J_{3a,4}$	2.50
H3b-C3-C4-H4	-179.43	$J_{3b,4}$	9.31
H4-C4-C5-H5	-176.29	$J_{4,5}$	6.70
H5-C5-C6-H6	65.38	$J_{5,6}$	1.51
H6-C6-C7-H7	-178.61	$J_{6,7}$	10.2
H7-C7-C8-H8	-60.92	$J_{7,8}$	1.93
H8-C8-C9-H9a	-175.18	$J_{8,9b}$	7.93
H8-C8-C9-H9b	60.94	$J_{8,9b}$	4.50

Table 2.6.6.2. Selected torsion angles and coupling constants.

2.6.7 Crossed aldol reaction between acetone and 2,3,4,5,6-penta-*O*-acetyl-*aldehydo*-D-mannnose **47**

From the acetylated *aldehydo*-D-mannose **47**, There was obtained in 76% yield a 49 : 1 mixture of

diastereomers, and the major diastereomer was assigned as 1,3-dideoxy-5,6,7,8,9-penta-*O*-acetyl D-*glycero*-D-*allo*-nonulose **75** by ^{1}H NMR analysis of the diagnostic H-3 methylene protons for *anti* isomer (Scheme 2.6.7.1).



47 **75**

Scheme 2.6.7.1. Aldol reaction between acetone and 2,3,4,5,6-penta-*O*-acetyl-*aldehydo*-D-mannnose **47**

.

The ^{1}H NMR spectrum of the dideoxy-D-*glycero*-D-*allo*-nonulose **75** showed the expected doublet of doublets for H-3a and H-3b, which are diagnostic for *anti* isomers of those observed for the 1,3-dideoxy-uloses. The respective $J_{4,5}$ and $J_{5,6}$ values are 4.9 and 7.9 Hz for *anti* epimer **75** demonstrating conformational mixing with no clear single, principal conformation. Avoidance of the 1,3-*syn* axial interaction of the hydroxyl and acetoxy groups at C-4 and C-6 that would have been present in the *P* conformation would seem to be the driving force in establishing the most favored disposition of the chain, and from the possible contributions to the equilibrium population, a major contributor for the **75** appears to be the ${}_{5}G^{-}$ conformer.

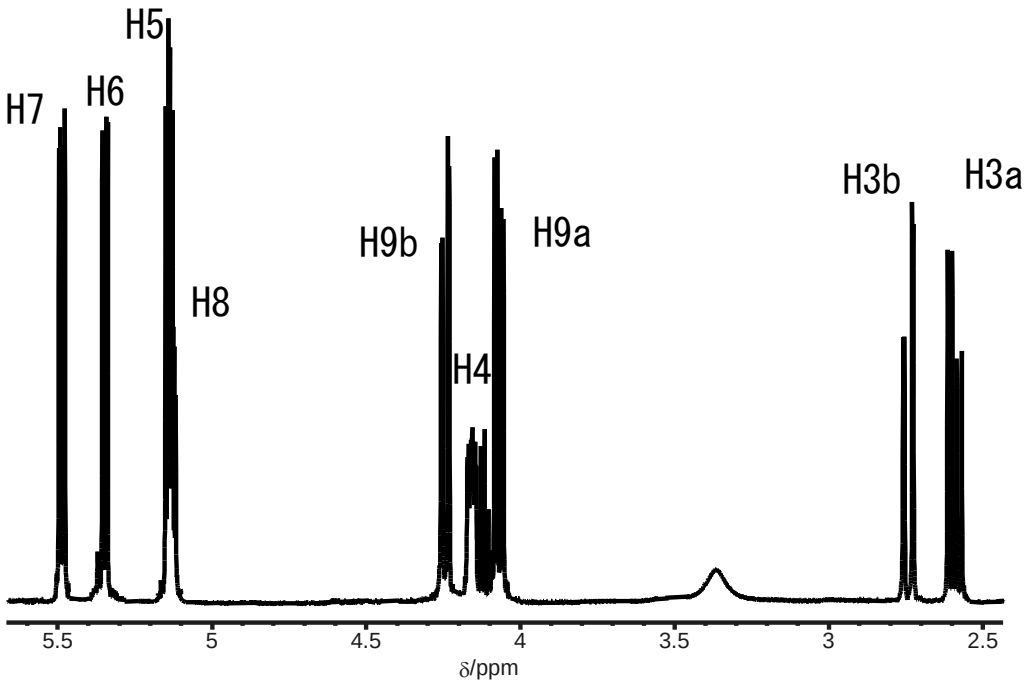


Figure 2.6.7.1. 1H NMR spectrum of 1,3-dideoxy-5,6,7,8,9-penta-*O*-acetyl D-*glycero*-D-*allo*-nonulose **75**.

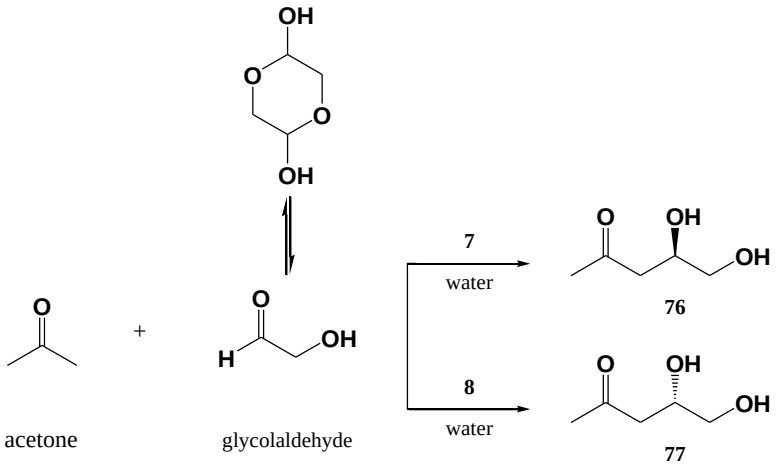
		Coupling constants (Hz)						
H3a	H3b	H4	H5	H6	H7	H8	H9a	H9b
$J_{3a,4}$ $J_{3a,3b}$	$J_{3b,4}$ $J_{3a,3b}$	$J_{3a,4}$ $J_{3b,4}$ $J_{4,5}$	$J_{4,5}$ $J_{5,6}$	$J_{5,6}$ $J_{6,7}$	$J_{6,7}$ $J_{7,8}$	$J_{7,8}$ $J_{8,9a}$ $J_{8,9b}$	$J_{8,9a}$ $J_{9a,9b}$	$J_{8,9b}$ $J_{9a,9b}$
9.44(dd) 17.7	2.30 (dd) 17.7	9.44(ddd) 2.30 4.91	4.91(dd) 7.93	7.93 (dd) 2.63	2.63(dd) 8.54	8.54(ddd) 5.63 2.81	5.63 (dd) 12.4	2.81(dd) 12.4

Table 2.6.7.1. ^{1}H NMR data for 1,3-dideoxy-5,6,7,8,9-penta-*O*-acetyl D-*glycero*-D-*allo*-nonulose **75**.

2.7 Aqueous aldol reaction for aldoses in free forms

2.7.1 Crossed aldol reaction between acetone and glycolaldehyde dimer

Treatment of an aqueous solution of glycolaldehyde dimer and acetone with catalytic amount of the prolinamido-glycoside **7** and **8** gave, aftere chromatographic separation, the expected 1,3-dideoxy-pentulose[33] **76** and **77** in 81% and 84% yields, respectively (Scheme 2.7.1.1).



Scheme 2.7.1.1. Aldol reaction acetone and glycolaldehyde dimer.

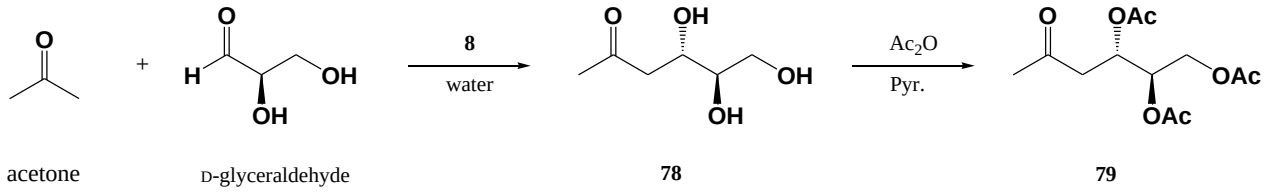
The ^{1}H NMR spectra of both enantiomers were amenable to first-order analysis, and showed expected doublet of doublets for H-3a, H-3b, H-5a, and H-5b, and the anticipated doubled doublet of doublets for H-4. The chirality at C-4 in the pentulose **76** and **77** was assigned on the basis of the Mosher's method [39] using ^{1}H and ^{19}F NMR spectroscopy.

2.7.2 Crossed aldol reaction between acetone and D-glyceraldehyde in the free form.

The same method was applied to D-glyceraldehyde in the free form, and the results are shown in

Table 2.7.2.1. Although the relatively low diastereofacial selectivities exhibited by the free sugar-chain may be attributed to the conformational mobility of the chain, the reaction rates were still fast.

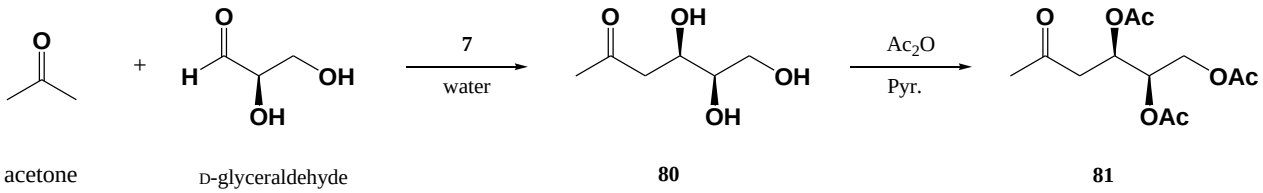
Reaction of D-glyceraldehyde with acetone in an aqueous solution of **8** gave mainly the *anti*-diastereomer, 1,3-dideoxy-D-*erythro*-hexulose[34] **78** (94% yield, 76% de), from which the tri-acetate **79**, which was used for the determination of the diastereomeric ratio of **78**, was obtained (Scheme 2.7.2.1).



Scheme 2.7.2.1. Aldol reaction between acetone and D-glyceraldehyde in the free form.

Since the corresponding bisaldol product, the result of the tandem aldol-aldol reaction, was not afforded, the 1,3-dideoxyhexulose **78** hemiacetalized in the reaction mixture, and was resistant to successive aldol reaction. However, the tri-acetate **79** was isolated as the acyclic form. In ^{13}C NMR spectrum of **79**, the resonance due to the 2-carbonyl group was at lowest field (216 ppm). The preference of diastereofacial selectivity of **8** for formation of *erythro*-product *via re*-facial attack was maintained in this matched case.

Similarly, the reaction of D-glyceraldehyde with acetone under the L-prolinamido-glycoside **7** catalyzed condition afforded mainly the *syn*-diastereomer, 1,3-dideoxy-D-*threo*-hexulose **80** in 87% yield with 67% de.



Scheme 2.7.2.2. Aldol reaction between acetone and D-glyceraldehyde in the free form.

NMR spectral analysis of the mixture of **79** and **81** showed distinctive resonances for C-3 methylene and C-5 methyne groups in both *anti* and *syn* configurations, permitting accurate determination of the *anti* : *syn* ratio of the products in the mixture (Figure 2.7.2.1).

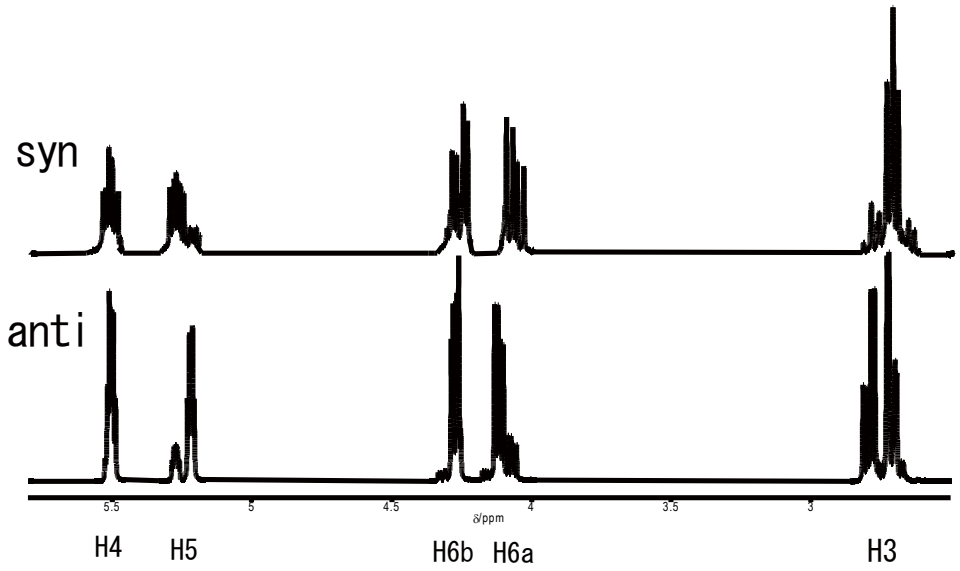


Figure 2.7.2.1. ^{1}H NMR spectra of **79** and **81**.

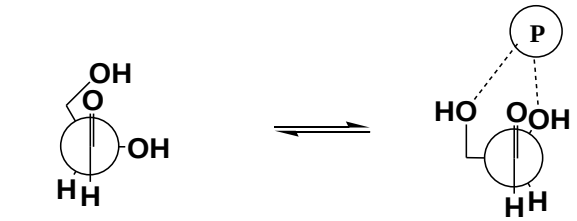
When the same reaction was carried out using phosphate buffer as a solvent, instead of water, an increased diastereoselectivity was observed (Entries 3 and 4). Because of the high conformational mobility, it was thought that the conformation of D-glyceraldehyde would be changed in the buffered condition, and it allowed the *re*-facial attack catalyzed by **7**. Clarke and co-workers[6b] observed similar phenomenon in their research, in which the use of phosphate buffer significantly

increased the enantiomeric excess of the dimerisation of the TIPS-protected glycolaldehyde under organocatalytic conditions. They postulated that non-selective general base-mediated mechanism was suppressed by increased acidity.

entry	catalyst	amount of catalyst (equivallent)	solvent	time (h)	yield (%)	de (%)
1	**7**	0.1	water	0.5	87	67 (3*R*)
2	**7**	0.05	water	2	82	58 (3*R*)
3	**7**	0.1	phosphate buffer	0.5	89	78 (3*R*)
4	**7**	0.05	phosphate buffer	2	84	71 (3*R*)
5	**8**	0.1	water	0.5	94	76 (3*S*)
6	**8**	0.05	water	1	84	69 (3*S*)
7	**8**	0.1	phosphate buffer	0.5	86	68 (3*S*)
8	**8**	0.05	phosphate buffer	1	56	62 (3*S*)

Table 2.7.2.1. Aldol reaction between acetone and D-glyceraldehyde in the free form.

In the presence a phosphoric acid molecule, a proposed transition state, could account for its reversed facial selectivity of the L-prolinamide aldol reaction, was illustrated in Figure 2.7.2.2. Like an enzymatic reaction, it would be expected to be acting in conjunction with free hydroxyls of substrate. Bridged attachment of the glyceraldehyde, *via* a phosphoric acid, to the catalyst, where 3-OH group on the sugar ring, will of necessity, be reversed stereoselectivity. This docking requires a clockwise or counterclockwise rearrangement of D-glyceraldehyde, when viewed from the active site of the catalyst. Thus, buffered condition is *si*-face attack selective whereas normal condition in which no bridged binding is *re*-face attack selective, in contrast to 2,3-*O*-isopropylidene derivatives which have no free hydroxyl groups.

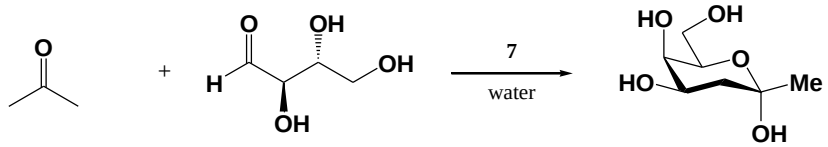


aqueous condition bufferd condition

Figure 2.7.2.2. Conformation of D-glyceraldehyde

2.7.3Crossed aldol reaction between acetone and D-erythrose in the free form.

L-prolinamido-glycoside **7** catalyzed aldol reaction of unprotected D-erythrose with acetone in water gave, after chromatographic resolution, a 85% yield of crystalline cyclic **82** as a single diastereomer (Scheme 2.7.3.1).



acetone D-erythrose **82**

Scheme 2.7.3.1. Aldol reaction between acetone and D-erythrose in the free form.

The reaction proceeds essentially in the Felkin-Anh product mode, however, the tendency of the L-prolinamide for favored attack at the *re*-face of aldehyde acceptor was changed in this case. The absolute configuration at C-4 was affirmed by proton-proton couplings and NOESY experiment. Axial-equatorial couplings between H-4 and H-3_{eq}, and between H-4 and H-5 are 5.1 Hz and 2.1 Hz, respectively, showed that they are in the *cis* relationships (^{1}H NMR spectrum is Figure 2.7.3.1, proton-proton couplings are in Table 2.7.3.1). Moreover, very large NOE signals for H-4 at H-3 and

H-5 were observed (Figure 2.7.3.2). This information permits assignment of the newly formed C-4 as (*S*). In aqueous solution, it exists an equilibrium mixture of cyclic and acyclic forms in which the pyranose predominates (90 %).

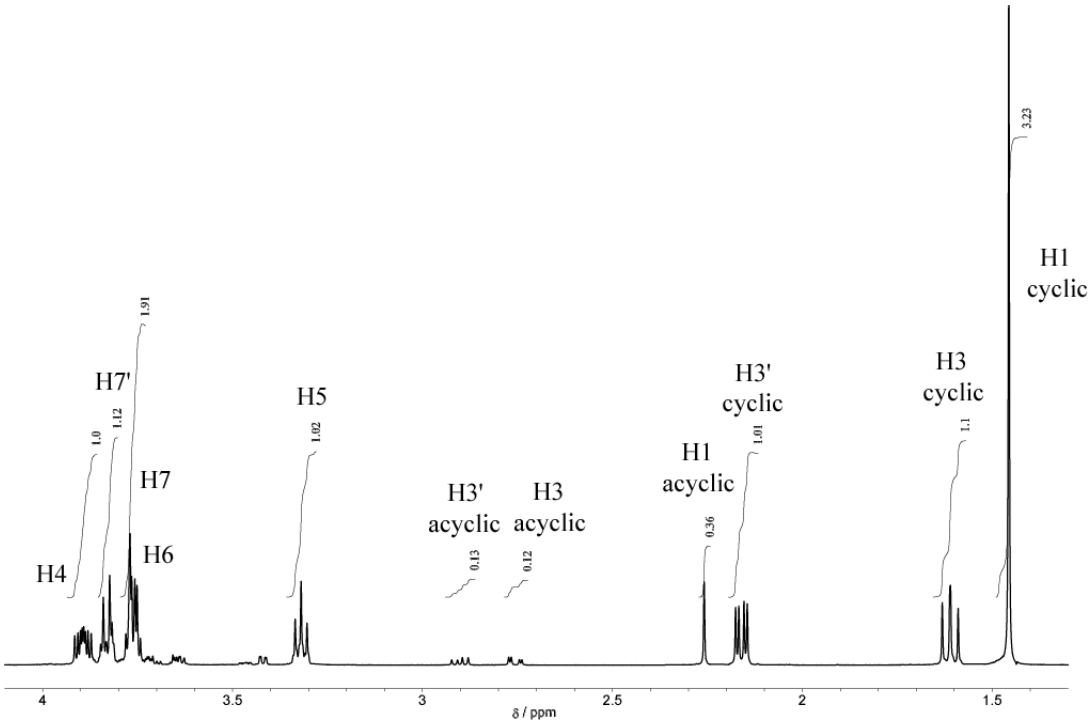


Figure 2.7.3.1. 1H NMR spectrum of cyclic and acyclic 1,3-dideoxy-D-*lyxo*-heptuloses **82**.

Coupling constants (Hz)

H3a	H3b	H4	H5	H6	H7a	H7b
$J_{3a,4}$	$J_{3b,4}$	$J_{3a,4}$	$J_{4,5}$	$J_{5,6}$		$J_{6,7b}$
$J_{3a,3b}$	$J_{3a,3b}$	$J_{3b,4}$	$J_{5,6}$	$J_{6,7b}$		$J_{7a,7b}$
		$J_{4,5}$				
12.3 (dd)	5.12 (d)	12.3(ddd)	2.10(t)	9.3 (m)	(m)	5.5 (dd)
13.2	13.2	5.12	9.30	5.5		8.7
		2.10				

Table 2.7.3.1. ^{1}H NMR data for 1,3-dideoxy-D-*lyxo*-heptuloses **82**.

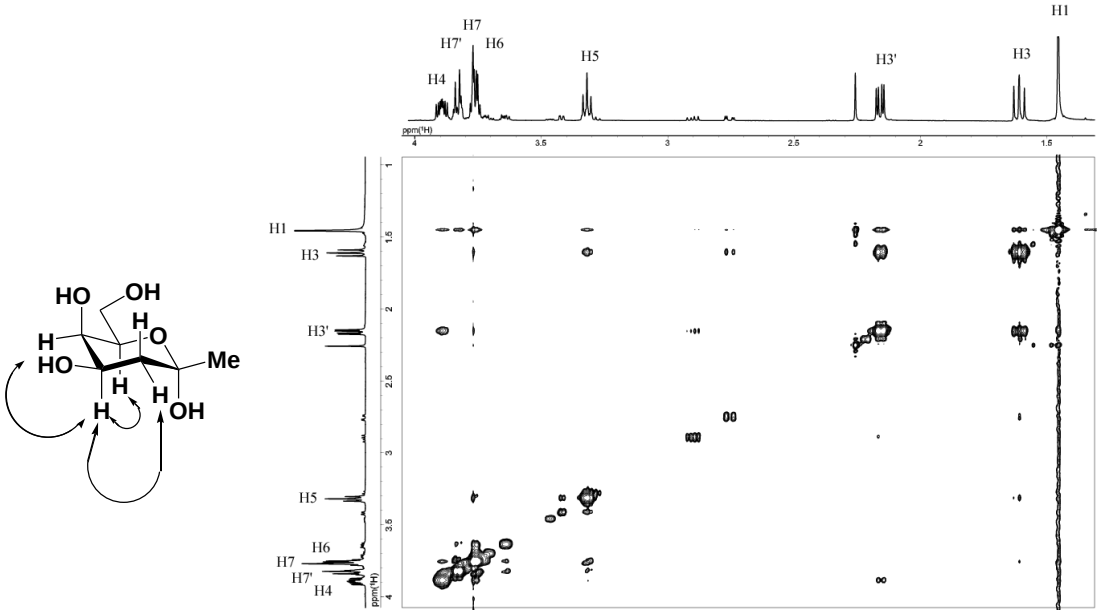
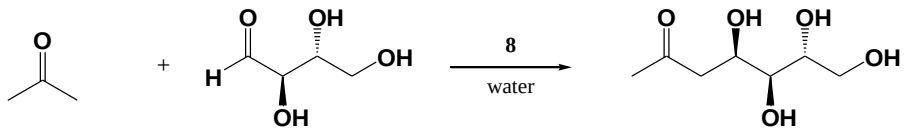


Figure 2.7.3.2. NOESY spectrum of **82**.

In contrast, D-prolinamide catalyzed condition gave mainly syrupy acyclic diastereomer, compound name **83**, in 76% yield as a single diastereomer (Scheme 2.7.3.2).



acetone D-erythrose **83**

Scheme 2.7.3.2. Aldol reaction between acetone and D-erythrose in the free form.

For the D-*xylo* isomer **83**, the small $J_{4,5}$ coupling supports the gauche disposition of H-4 and H-5, while the large value of $J_{5,6}$ indicates antiperiplanar relationship between H-5 and H-6, and the *P* conformation depicted can be assigned as the major conformer (Figure 2.7.3.3).

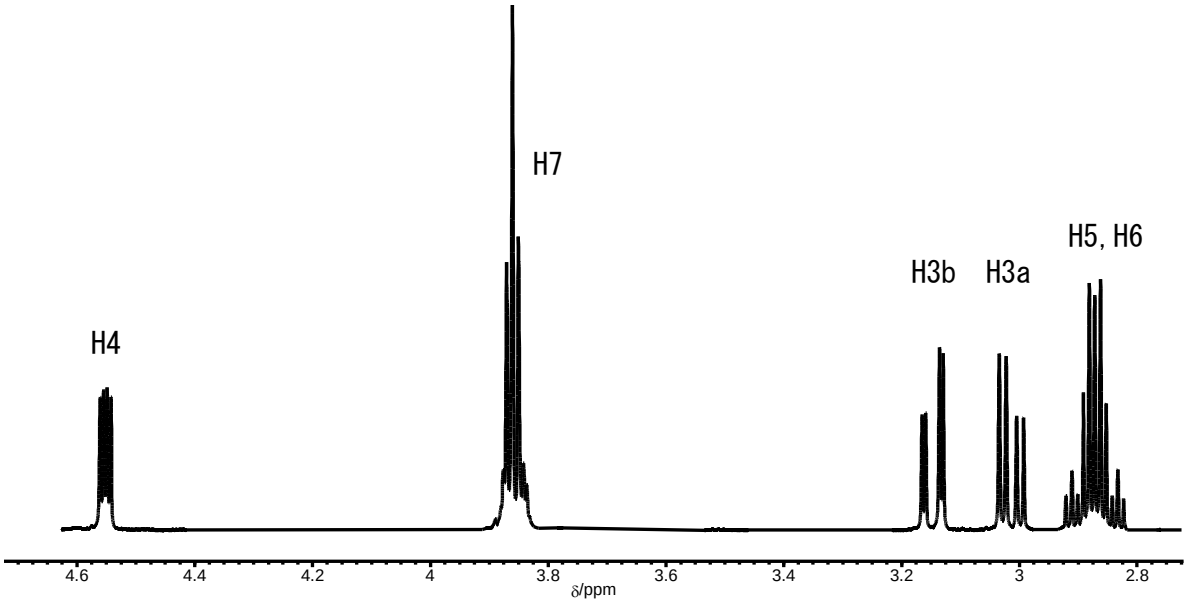
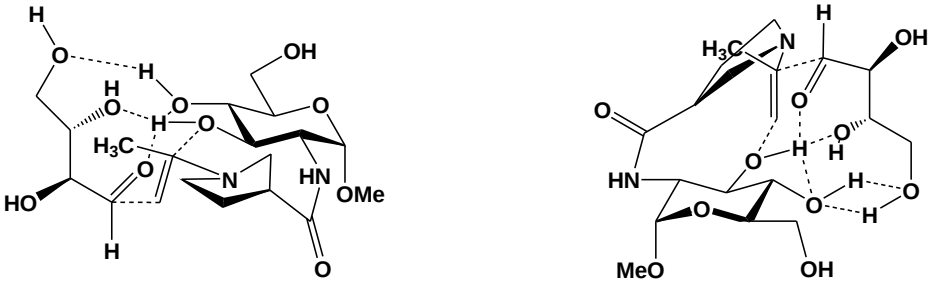


Figure 2.7.3.3. 1H NMR spectrum of psicofuranoses and acyclic psicose **83**.

This diastereofacial selectivities exhibited by the free acyclic sugar-chain may be attributed to the conformational mobility of the chain and intermolecular H-bonds, one between the 3-OH of the catalyst and 3-O of the D-erythrose, and the other from 4-OH on the catalyst to 4-O of the aldose. The following schematic illustration (Figure 2.7.3.4) satisfactorily interprets the observed behavior.

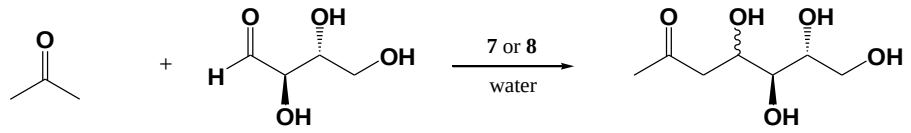


Si-face attack
(Exclusive)

Re-face attack

Figure 2.7.3.4. A proposed transition states for reaction with D-erythrose.

2.7.4 Crossed aldol reaction between acetone and D-threose in the free form.



acetone D-threose

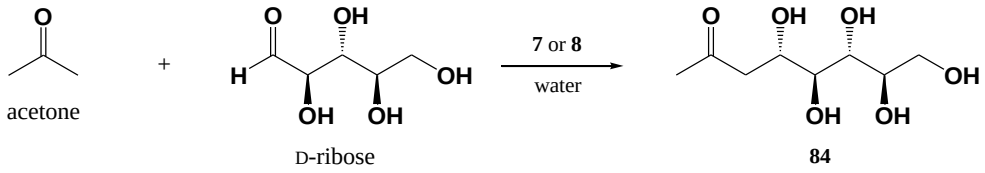
When the aldol reaction was performed with D-threose, using neither **7** nor **8**, the desired deoxyheptose was obtained as a mixture of two diastereomer (Scheme 2.7.4.1). Increasing selectivity was not observed when the reactions carried out in the phosphate buffer in these cases.

2.7.5 Crossed aldol reaction between acetone and D-ribose in the free form.

When the same procedure was performed with aldopentoses, the desired octuloses were obtained but only in low yield. In all instances, the reaction rate was extremely slow. Among the reaction of aldopentoses, L-prolinamide catalyzed reaction of D-lyxose was the fastest and the reaction of D-xylose was the slowest. The preference for formation of 3,4-*anti* products was observed in these cases of D-aldopentoses, and the selectivities were in accord with Felkin-Anh model. As for the diasetereofacial selectivity, D-prolinamido-glycoside **8** shown catalyzing favored *si*-face attack for D-ribose and D-xylose having *R* configuration at C-2 position, and in contrast, L-prolinamido-glycoside **7** shown favored *re*-face attack for D-arabinose and D-lyxose having *S* configuration at C-2 position.

D-Ribose underwent the aldol reaction of acetone under D-prolinamide catalyzed conditions gave 1,3-dideoxy-octulose **84** in 31% yield with 82% de after 2 weeks. The same aldol reaction under

L-prolinamide gave the octulose **84** in 36% yield with 60% de.



Scheme 2.7.5.1. Aldol reaction between acetone and D-ribose in the free form.

The 600 MHz ^{1}H NMR spectrum of the syrupy initial product of the mixture of two diastereomers in acyclic and cyclic forms showed narrow doublet of doublets signals at δ 2.64 and δ 2.81 in 23 : 1 ratio, assigned to acyclic H-3a signals of the (*4S*) and (*4R*) diastereomers, and in aqueous solution, the octulose **84** exists an equilibrium mixture of acyclic and cyclic forms in 2.6 : 1 ratio (Figure 2.7.5.1).

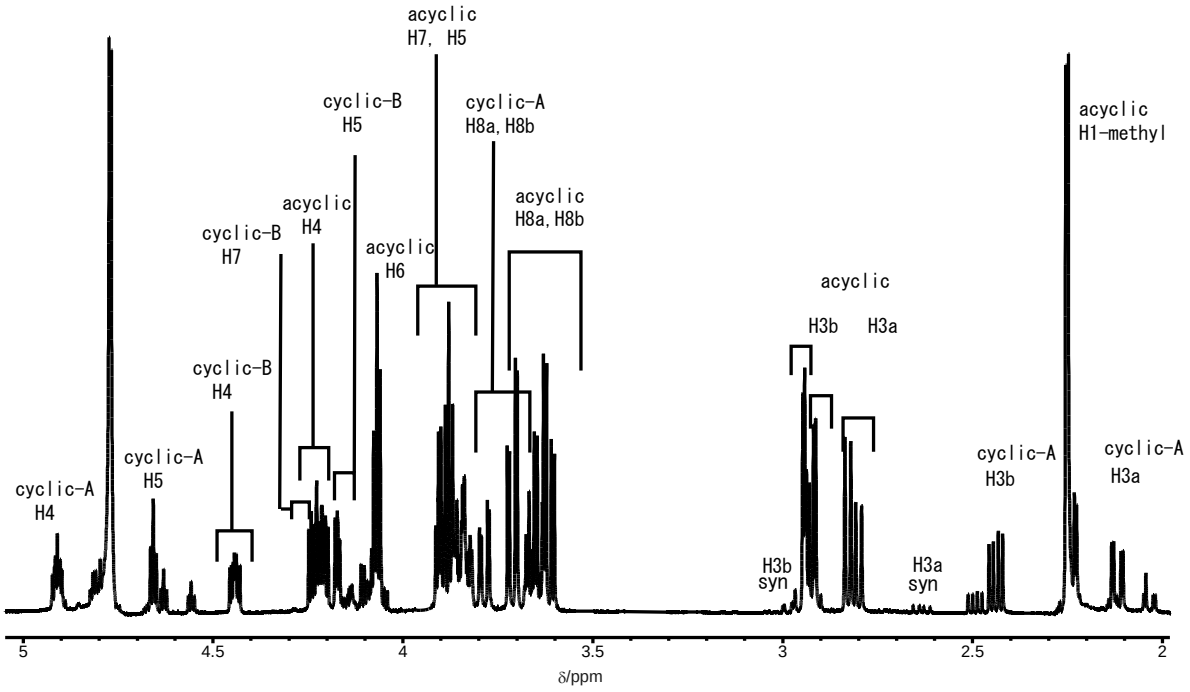
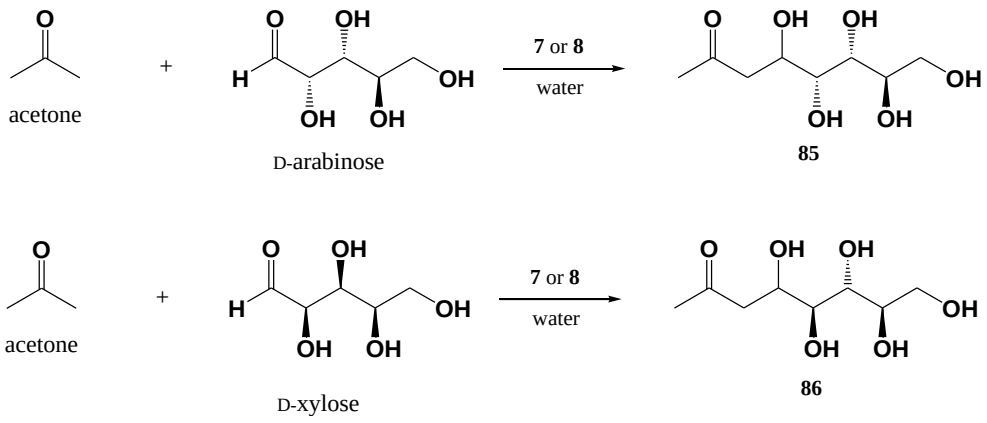


Figure 2.7.5.1. 1H NMR spectrum of **84**.

The signals for the acyclic octulose showed expected 2-proton pattern for the C-3 methylene group, upfield by ~ 1.0 ppm from that for H-3 in the acyclic form, and also expected ddd pattern for the methyne group at C-4, downfield by ~ 0.7 ppm from acyclic H-4 proton. The large $J_{5,6}$ and the medium coupling constants might have confirmed that product was not $^1C_4$ conformation, which would have small $J_{5,6}$ coupling constant because of the axial-equatorial disposition of two protons in the pyranoside ring.

2.7.6 Crossed aldol reaction between acetone and D-arabinose, and D-xylose in the free forms.

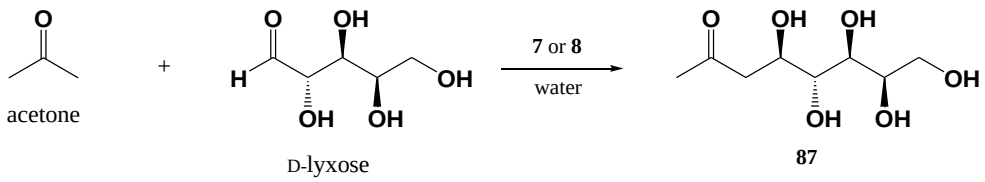
The aldol reactions of D-arabinose, and D-xylose with acetone under prolinamide catalyzed conditions were slow, and TLC analysis revealed only production of highly polar products, and the purifications of which gave only trace amounts of the products together with recovered starting materials. The reason for these outcomes may be readily rationalized by the fact that the stable ring forms of D-arabinose and D-xylose; the five-membered-ring of D-arabinose, and also, six-membered-ring of D-xylose are stable and were hindered the aldol reaction.



Scheme 2.7.6.1. Aldol reaction between acetone and D-arabinose, and D-xylose in the free forms.

2.7.7 Crossed aldol reaction between acetone and D-lyxose in the free form.

D-Lyxose underwent the aldol reaction under the L-prolinamide catalyzed condition to give 1,3-dideoxy-D-*glycero*- D-*xylo*-octulose **87** in 42% yield with 56% de (Scheme 2.7.7.1).



Scheme 2.7.7.1. Aldol reaction between acetone and D-lyxose in the free form.

In aqueous solution, the octulose **87** exists only in acyclic form, and hence the ^{1}H NMR spectrum was of first order (Figure 2.7.7.1).

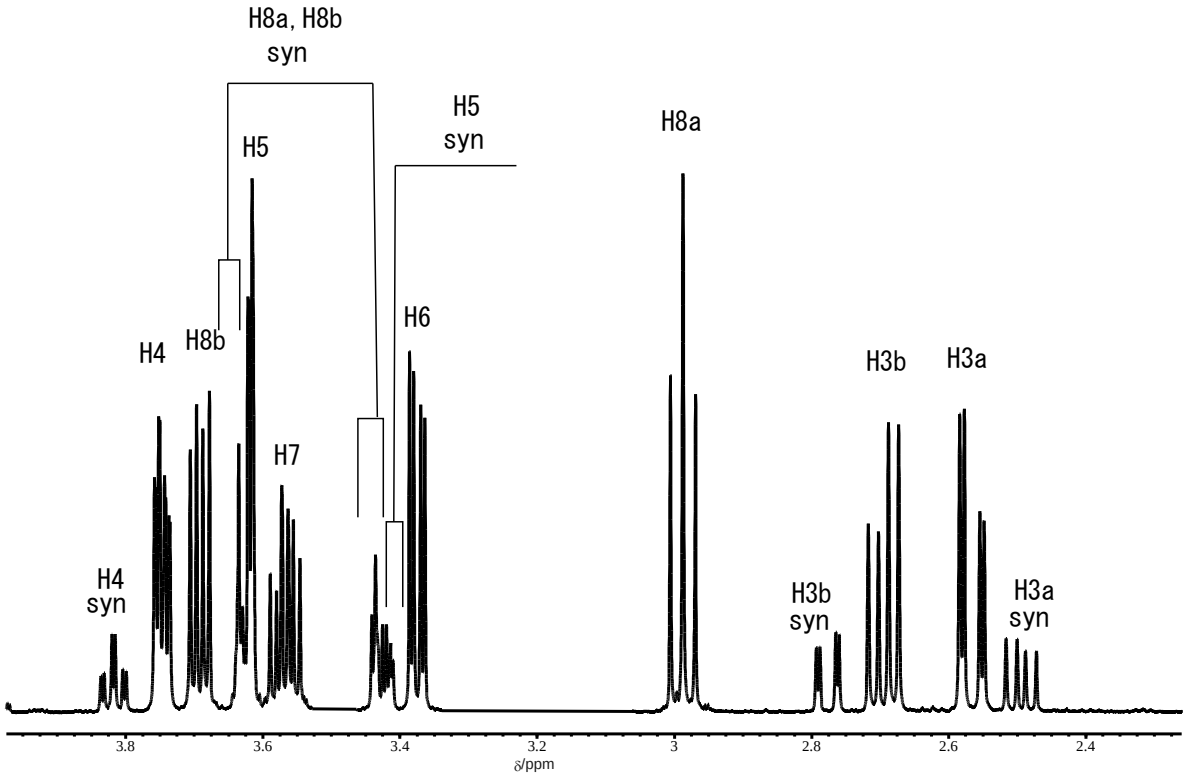


Figure 2.7.7.1. 1H NMR spectrum of 1,3-dideoxy-D-*glycero*- D-*xylo*-octulose **87**.

Coupling constants (Hz)							
H3a	H3b	H4	H5	H6	H7	H8a	H8b
$J_{3a,4}$ $J_{3a,3b}$	$J_{3b,4}$ $J_{3a,3b}$	$J_{3a,4}$ $J_{3b,4}$ $J_{4,5}$	$J_{4,5}$ $J_{5,6}$	$J_{5,6}$ $J_{6,7}$	$J_{6,7}$ $J_{7,8a}$ $J_{7,8b}$	$J_{7,8a}$ $J_{8a,8b}$	$J_{7,8b}$ $J_{8a,8b}$
3.96(dd) 17.5	8.80 (dd) 17.5	3.96(ddd) 8.80 8.89	8.89 (dd) 4.90	4.90 (dd) 9.80	9.80(dt) 10.9 5.58	10.9 (dd) 16.6	5.58 (dd) 16.6

Table 2.7.7.1. ^{1}H NMR data for 1,3-dideoxy-D-*glycero*- D-*xylo*-octulose **87**.

The anticipated signals for H-3a and H-3b of each diastereomers in acyclic form were observed, and the ratio of the two diastereomers was determined to be 3.6 : 1. The H-4 signal for the major *anti* isomer **87** was a narrow ddd consistent with the *anti* and *gauche* disposition ($J_{3a,4}$ = 3.9 Hz, $J_{3b,4}$ = 8.8 Hz) of H-3a–H-4 and H-3b–H-4, respectively, whereas that the signal for the *syn* isomer was narrow dt, and showed a $J_{3,4}$ value of 6.7 Hz, indicating a major but not exclusive contribution of the conformer. For both epimers, the $J_{5,6}$ and $J_{6.7}$ values were similar (4.9 and 9.8 Hz, respectively, for *anti*-isomer and 4.8 and 9.1 Hz, respectively, for *syn*-isomer), indicating the extended planar orientation of the carbon backbone for each epimers.

When the same aldol reaction was performed under the D-prolinamide catalyzed condition, the diastereofacial selectivity was negligible.

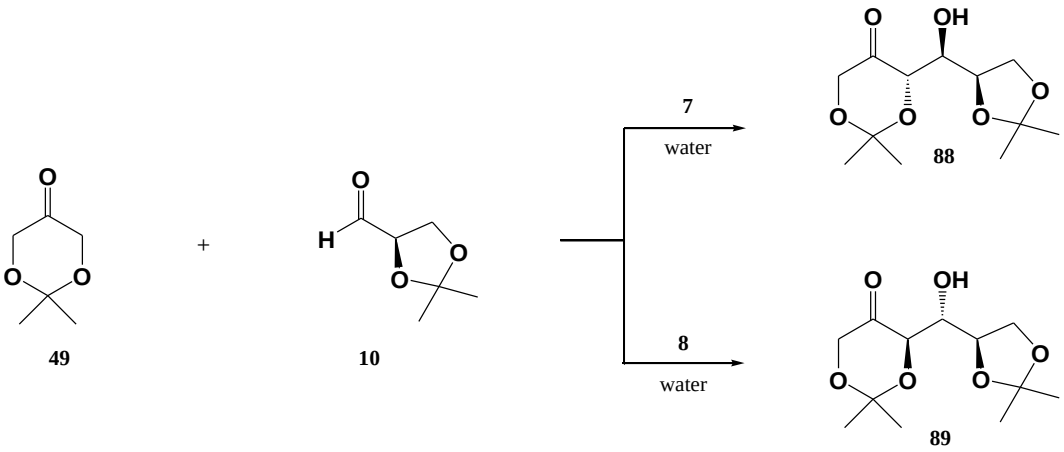
2.8 Aqueous aldol reaction using dihydroxyacetone in protected and unprotected forms

2.8.1 The crossed aldol reaction between 2,2-dimethyl-1,3-dioxan-5-one **49** and 2,3-*O*-isopropylidene-D-glyceraldehyde **10**.

Various applications of 2,2-dimethyl-1,3-dioxan-5-one **49** for useful preparations of carbohydrates by organocatalytic aldol reaction have detailed previously, and it was of interest to evaluate the stereoselective aldol reaction of **49** with 2,3-*O*-isopropylidene-D-glyceraldehyde **10** employing the prolinamido-glycoside catalysts in aqueous media, as the conformations of **10** in addition reaction are easy to predict by adopting the Felkin-Anh model.

Each of isopropylidene protected D-psicose **89** and D-tagatose **88** was obtained by treating 2,2-dimethyl-1,3-dioxan-5-one **49** with 2,3-*O*-isopropylidene-D-glyceraldehyde **10** in the presence of the prolinamido-glycoside in water at room temperature (Scheme 2.8.1.1). As shown in Table 2.8.1.1, a simple change of solvent from water to DMSO markedly altered the stereoselectivity of this reaction (entries 4 and 8). This result may imply that water molecule plays an important role in the aldol reaction. When the amount of catalyst was decreased from 0.1 to 0.05 equivalents, the yield significantly decreased (entries 3 and 7). The best results were obtained when 0.1 equiv. of the prolinamide catalyst was used. When 0.1 equiv. of the catalyst was used, D-prolinamido-glycoside **8** catalyzed condition gave protected D-psicose **89** in 69 % yield with 91 % de, and L-prolinamido-glycoside **7** catalyzed condition gave protected D-tagatose **88** in 72 % yield with 76 % de, respectively. The isopropylidene protected D-psicose **89** and D-tagatose **88** had properties concordant with those already reported. The product ratio of **88** and **89** was determined by ^{1}H NMR integration of the singlet methyl peaks of the isopropylidene groups in the product mixture, and signals attributable to the *syn*-diastereomers, isopropylidene-D-fructose and isopropylidene-D-sorbose, were not observed in the products. It is noteworthy that the foregoing

reactions did not proceed at all when commercial 2,2-dimethyl-1,3-dioxan-5-one **49** and 2,3-*O*-isopropylidene-D-glyceraldehyde **10** were used, but when the reagents were freshly prepared, and distilled before use, the reactions progressed satisfactorily.

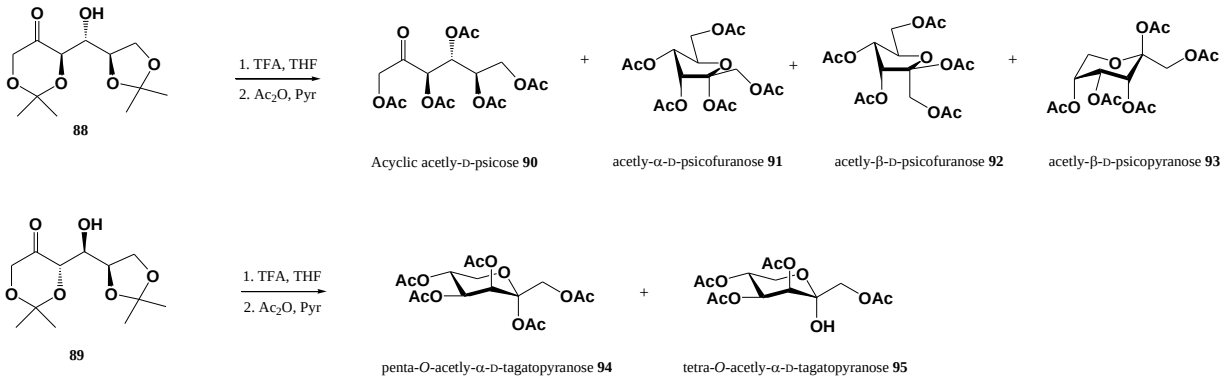


Scheme 2.8.1.1. Aldol reaction between 2,2-dimethyl-1,3-dioxan-5-one **49** and 2,3-*O*-isopropylidene-D-glyceraldehyde **10**.

entry	catalyst	amount of catalyst (equivallent)	solvent	time (h)	yield (%)	dr (**89** : *fructo* : *sorbo* : **88**)
1	**8**	0.3	water	5	72	9 : 0 : 0 : 1
2	**8**	0.1	water	6	69	9.6 : 0 : 0 : 4
3	**8**	0.05	water	24	42	8.1 : 0 : 0 : 1.9
4	**8**	0.1	DMSO	48	23	1.2 : 1 : 1 : 1.1
5	**7**	0.3	water	4	76	8 : 0 : 0 : 2
6	**7**	0.1	water	4	72	1.2 : 0 : 0 : 8.8
7	**7**	0.05	water	24	32	2.8 : 0 : 0 : 7.2
8	**7**	0.1	DMSO	48	19	1 : 1 : 1 : 1.2

Table 2.8.1.1. Aldol reaction between 2,2-dimethyl-1,3-dioxan-5-one **49** and 2,3-*O*-isopropylidene-D-glyceraldehyde **10**.

The absolute stereochemistry of **88** and **89** was confirmed by acetylation of the equilibrated mixture of the deprotected products (Scheme 2.8.1.2). The stereochemistry at C-3 and C-4 was assigned by ^{1}H NMR analysis through spectroscopic comparison with the ^{1}H NMR spectra of authentic samples of D-psicose and D-tagatose in the acetate forms.



Scheme 2.8.1.2. Deprotection and acetylation of **88** and **89**.

Acid-catalyzed hydrogenolysis of **89** with 80 vol % aqueous trifluoroacetic acid in ice cooling THF, followed by acetylation of the resultant α, and β-D-psicofuranoses and α,and β-D-psicopyranose with acetic anhydride-pyridine, afforded 72 % of a 1.5:1:1 mixture of acyclic penta-*O*-acetyl-D-psicose **90**, penta-*O*-acetyl-α-D-psicofuranose **91** and penta-*O*-acetyl-β-D-psicofuranose[35] **92**, which were not separated chromatographically (Figure 2.8.1.1), and penta-*O*-acetyl-β-D-psicopyranose **93** in 15 % yield, along with traces of *tagato* isomer (4 %). The ^{1}H NMR spectra of which were identical with the product obtained by similar treatment of an authentic sample of D-psicose, apart from the presence of the H-1, H-5 and H6 signals of its diastereomer, penta-*O*-acetyl-α-D-tagatopyranose, and signals attributable to the *syn*-diastereomers, penta-*O*-acetyl-D-fructose and penta-*O*-acetyl-D-sorbose, were not observed in the products.

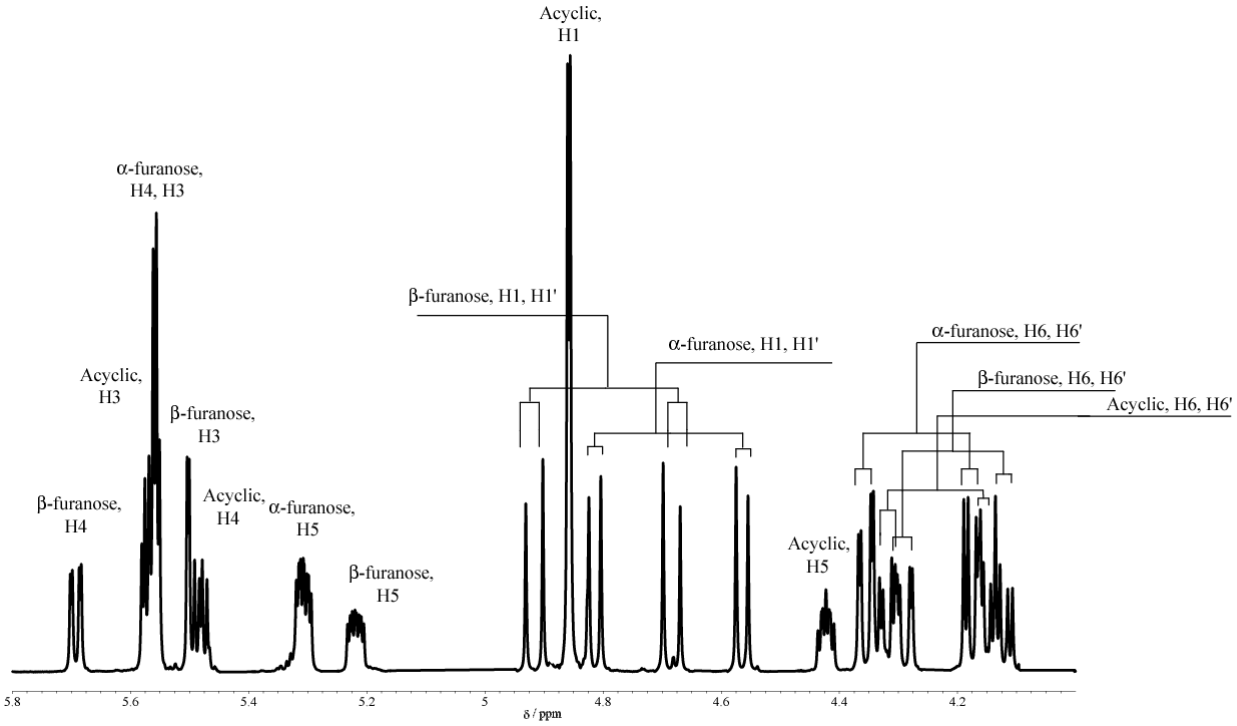


Figure 2.8.1.1. ^{1}H NMR spectrum of mixture of psicofuranoses and acyclic psicose.

Inspection of the ^{1}H NMR spectra of each of the four hexuloses, D-psicose, D-tagatose, D-fructose and L-sorbose in the acetate forms enabled the diastereomeric ratios of **88** and **89** to be determined. The small $J_{5,6}$ coupling constants (3.0 Hz and 4.4 Hz) might have confirmed that **93** was not the $^{4}C_{1}$ conformation, which would have had a large axial-axial coupling (Figure 2.8.1.2 and Table 2.8.1.2).

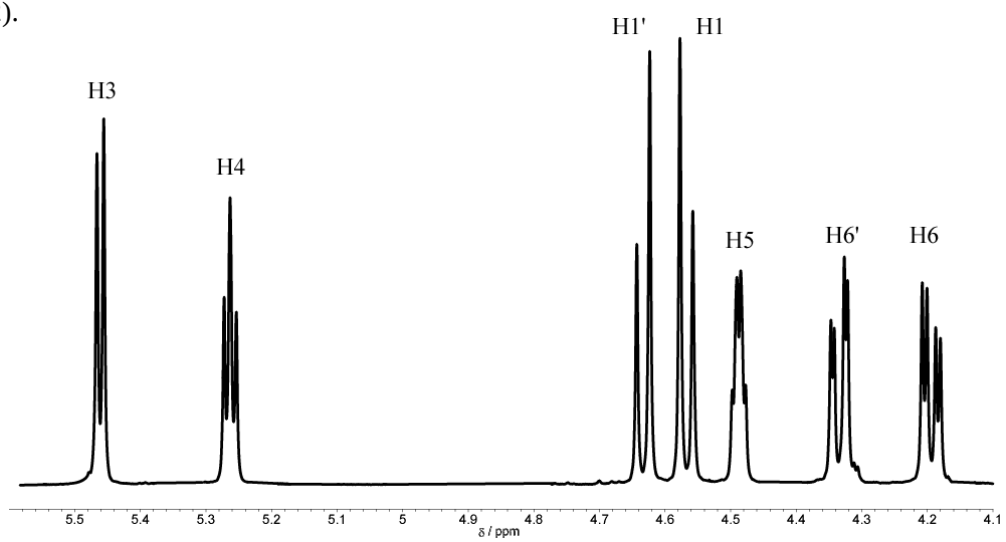
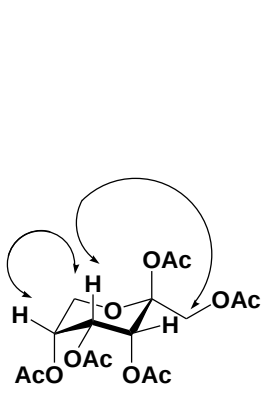


Figure 2.8.1.2. ^{1}H NMR spectrum of β-D-psicopyranose 93.

	Coupling constants (Hz)					
H1	H1	H3	H4	H5	H6	H6'
$J_{1,1'}$	$J_{1,1'}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6}$	$J_{5,6}$
				$J_{5,6'}$	$J_{6,6'}$	$J_{6,6'}$
4.57 (d)	4.49 (d)	5.46 (d)	5.26 (d)	4.49 (dd)	4.22 (dd)	4.33 (dd)
11.8	11.8	6.10	0	4.40	4.40	3.00
				3.00	12.3	12.3

Table 2.8.1.2. ^{1}H NMR data for penta-*O*-acetly-β-D-psicopyranose **X**.

Strong supporting evidence that **93** is the *psico* product was obtained from NOESY experiment, which showed large NOE singals between H-3 and H-4, and also between H-4 and H-5 (Figure 2.8.1.3).



93

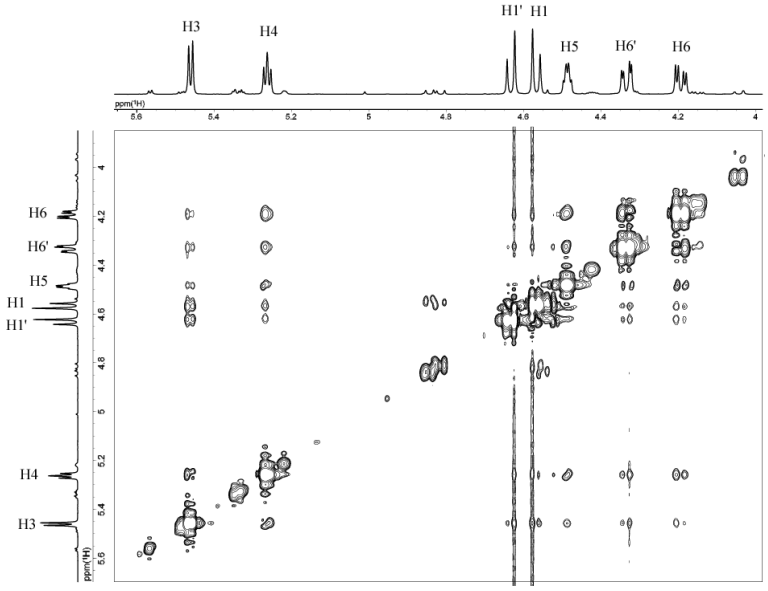


Figure 2.8.1.3. NOESY spectrum of **93**.

Rigorous assignments in the X-ray crystallography of D-psicose have been made previously and our NMR results are in general agreement with those.

The isopropylidene groups in **88** were deprotected exactly as described for the *psico* analogue, with subsequent acetylation. Two major products were formed, along with the **93** and the mixture of **90**-**92** (14 %), and were separated by silica gel column chromatography. The fast moving spot was the penta-*O*-acetyl-α-D-tagatopyranose **94** (15 %), which had the same spectral data as the compound prepared from an authentic sample. The ^{1}H NMR couplings (Figure 2.8.1.4 and Table 2.8.1.3) and the NOESY spectrum (Figure 2.8.1.5) of **94** clearly showed the relative configuration; a large NOE signal between H-3 and H-4.

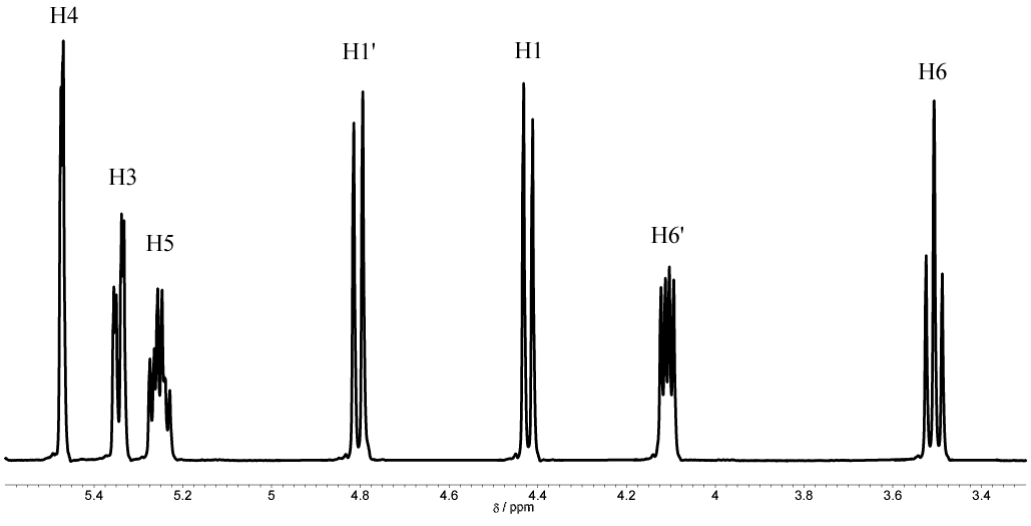


Figure 2.8.1.4. ^{1}H NMR spectrum of penta-*O*-acetyl-α-D-tagatopyranose **94**.

	Coupling constants (Hz)					
H1	H1'	H3	H4	H5	H6	H6'
$J_{1,1'}$	$J_{1,1'}$	$J_{3,4}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$
			$J_{4,5}$	$J_{5,6}$	$J_{6,6'}$	$J_{6,6'}$
				$J_{5,6'}$		
4.42 (d)	4.80 (d)	5.47 (d)	5.35 (dd)	5.25 (dt)	3.51 (t)	4.11 (dd)
12.2	12.2	3.23	3.23	10.5	10.7	5.94
			10.5	10.7	11.2	11.2
				5.94		

Table 2.8.1.3. ^{1}H NMR data for penta-*O*-acetly-α-D-tagatopyranose **94**.

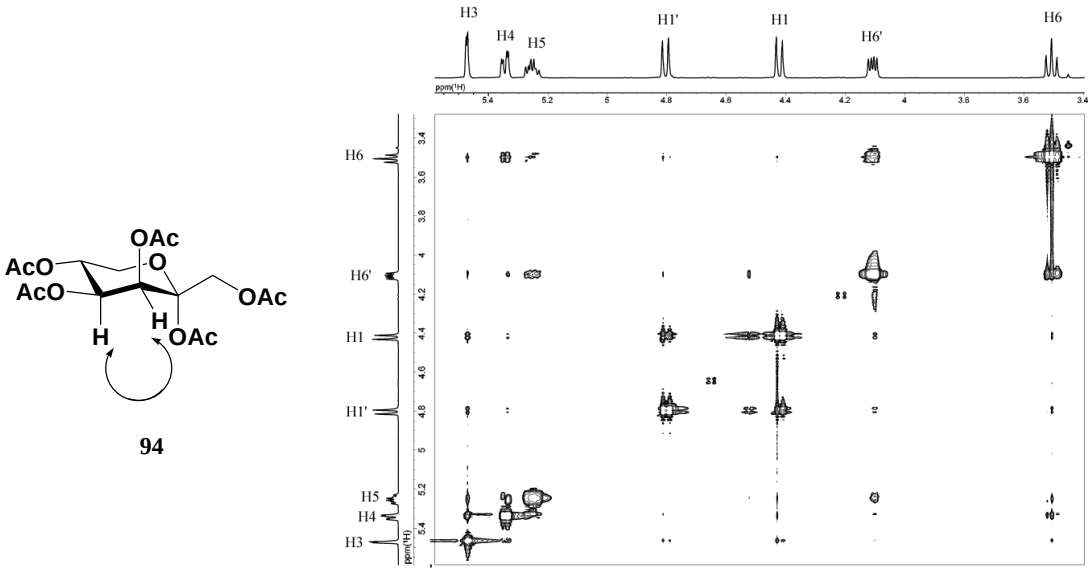


Figure 2.8.1.5. NOESY spectrum of **94**.

The slow moving spot was identified by ^{1}H-^{13}C HMBC experiment as the tetra-*O*-acetyl-α-D-tagatopyranose **95**, produced in 75 % yield. Configuration of the α-anomeric carbon of **95** was determined by X-ray crystallography. It crystallizes in the orthorhombic space

group $P2_12_12_1$ with cell parameters a = 7.931 (12) Å, b = 13.464 (3) Å, c = 15.825 (3) Å, and Z = 4. The ORTEP representation of **95** was illustrated in Figure 2.8.1.6. Table 2.8.1.4 and 2.8.1.5 record selected torsion angles and bond lengths data, respectively, and relevant crystal data are recorded in experimental section. As shown in Fig. 2.8.1.6, the ORTEP representation of the acetyl-tagatose clearly shows $^4C_1$ conformation of the sugar ring which is also the most favored conformation of the free form, and the hydroxyl group at C-3 of the sugar ring (C1 in the molecular structure) occupying the axial position; the observed small (3.28 Hz) $J_{3,4}$ coupling constant in ^{1}H NMR spectrum was in good agreement with the crystallographic data. The O5 – C12 – C6 – O3 and O5 – C12 – C6 – C1 torsion angles (167.54º and 47.13º, respectively) indicate the orientation of C12 – O5 hydroxymethyl group is *trans-gauche*. As the result of the anomeric effect, the anomeric hydroxyl group occupies the axial position in which the relationship between C12 – O5 and C6 – O6 bonds is synclinal (torsion angle of O5 – C12 – C6 – O6 is -71.34º).

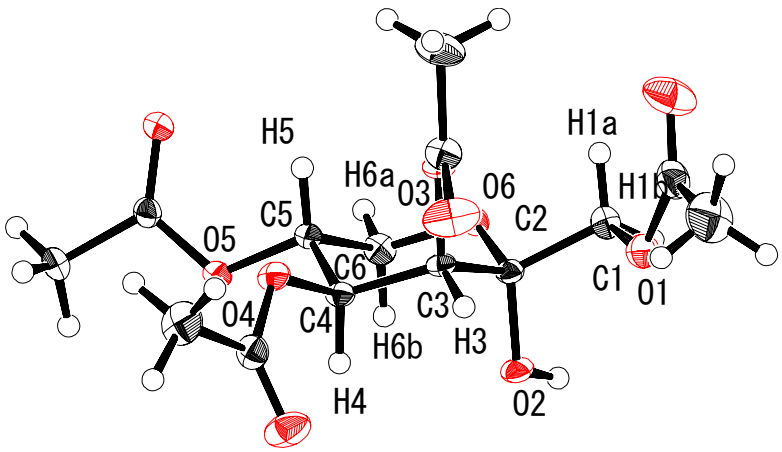


Figure 2.8.1.6. ORTEP representation of Tetra-*O*-acetly-α-D-tagatopyranose **95**.

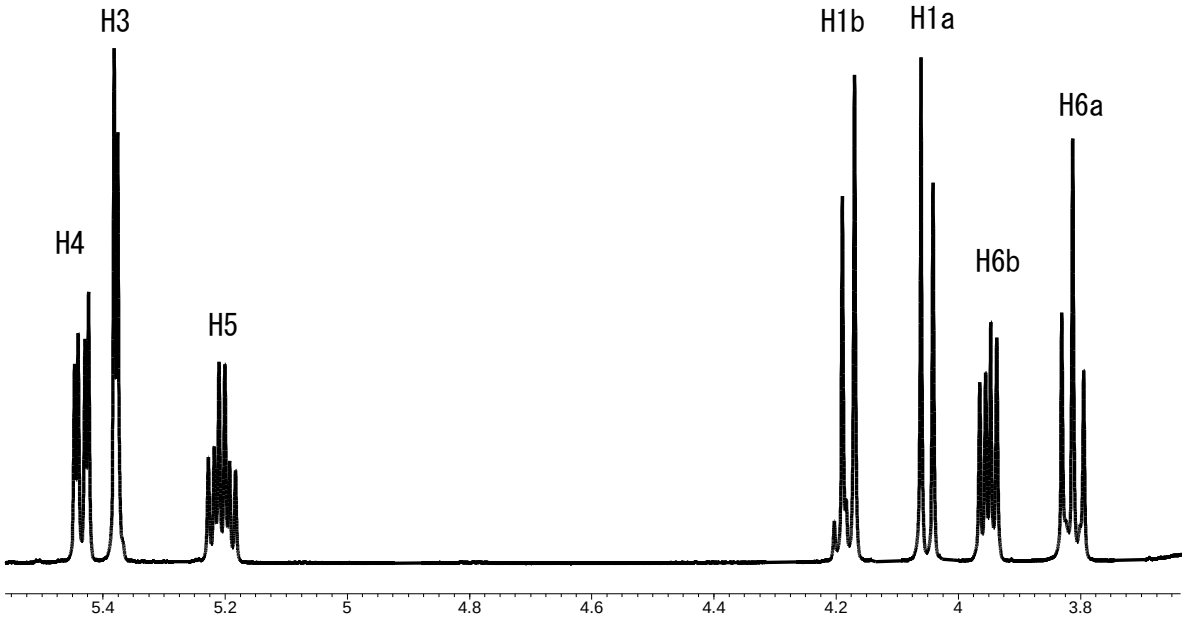


Figure 2.8.1.7. ^{1}H NMR spectrum of tetra-*O*-acetyl-α-D-tagatopyranose **95**.

	Coupling constants (Hz)					
H1	H1'	H3	H4	H5	H6	H6'
$J_{1,1'}$	$J_{1,1'}$	$J_{3,4}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$
			$J_{4,5}$	$J_{5,6}$	$J_{6,6'}$	$J_{6,6'}$
				$J_{5,6'}$		
11.9 (d)	11.9 (d)	3.38 (d)	3.38 (dd) 10.4	10.4(dt) 10.7 5.94	10.7 (t) 10.7	5.94 (dd) 10.7

Table 2.8.1.4. ^{1}H NMR data for tetra-*O*-acetyl-α-D-tagatopyranose **95**.

Torsion angles (°)		coupling constants (Hz)	
H3-C3-C4-H4	-54.41	$J_{3,4}$	3.38
H4-C4-C5-H5	174.09	$J_{4,5}$	10.4
H5-C5-C6-H6a	-177.17	$J_{5,6}$	10.7
H5-C5-C6-H6b	-54.43	$J_{6,7}$	5.94

Table 2.8.1.5. Selected torsion angles and coupling constants.

^{1}H NMR spectral analysis of the mixture of penta-*O*-acetyl-β-D-psicopyranose **93** and penta-*O*-acetyl-α-D-tagatopyranose **94** again showed distinctive resonance for the H-1, H-5 and H-6 ring protons in both *psico* and *tagato* configurations, permitting accurate determination of the ratio of the diastereomers in the mixture.

These two assignments of absolute configuration of **88** and **89** revealed that the D-prolinamido-glycoside **7** catalyzed the aldol reaction selectively from the *si*-face of **10**, and the L-prolinamido-glycoside **8** selectively catalyzed *re*-face attack. Considering the most stable conformation predicted by the Felkin-Anh model, as shown in Fig. 2.8.1.8, the *aldehydo*-sugar **10** possessing the *R* configuration at the C-2 position favors *si*-face attack, and the other aldehydes possessing the *S* configuration favor *re*-face attack. The conformer **10A** is expected to be overwhelmingly more favored than **10B**. The ketone **49** thus attacks preferentially from the *si*-face of the favored conformer **4A** to give the D-psicose **89** with high diastereoselectivity in the case of D-prolinamido-glycoside **8** catalyzed condition. In contrast, the less favored conformer **10B** decreased the diastereofacial selectivity of the L-prolinamido-glycoside **7** catalyzed *re*-face attack and gave D-tagatose **88** with relatively low diastereomeric ratio.

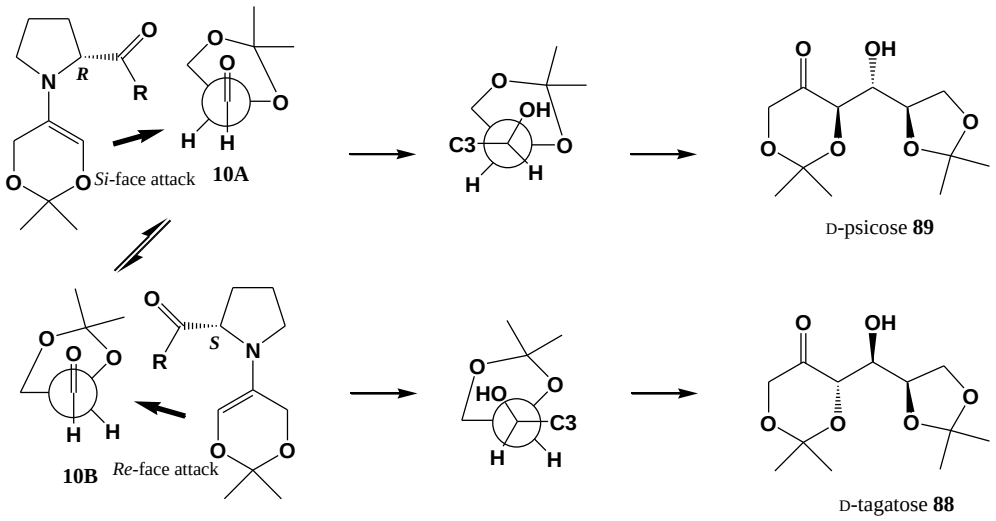


Figure 2.8.1.8. A proposed transition states for reaction with **10**.

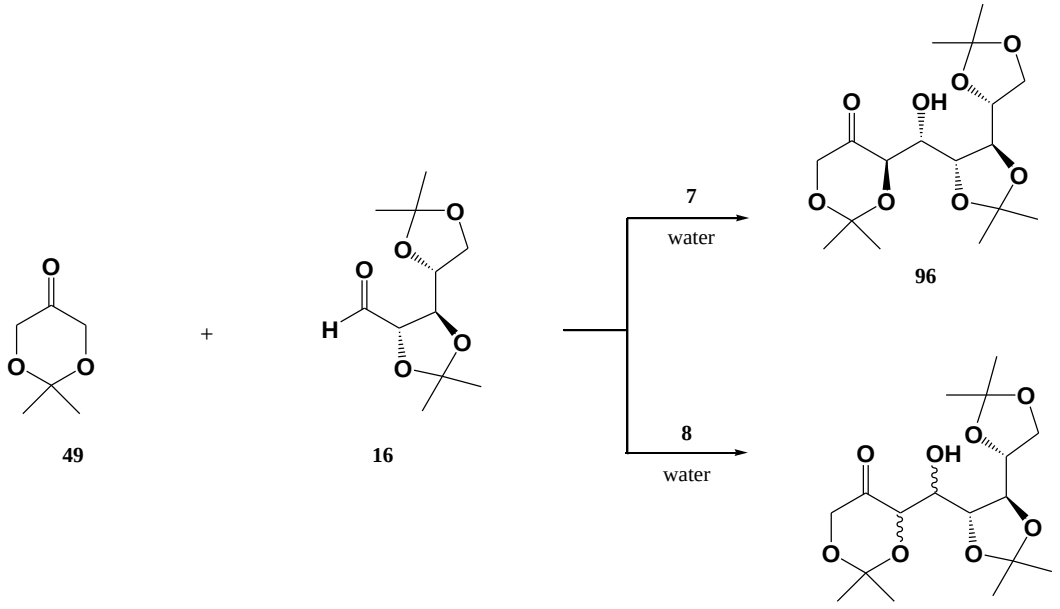
When the reactions were performed in DMSO, the observed products comprised a mixture of all four possible isomers. The isolative separation of each diastereomer out of the mixture of products was difficult, and hence the deprotection and acetylation method was used to determine the accurate *psico* : *fructo* : *sorbo* : *tagato* ratios, as all four hexuloses are commercially available in enantiomerically pure form, and each of their acetates was readily obtained. Inspection of the ^{1}H NMR spectra of each of the four hexuloses, D-psicose, D-tagatose, D-fructose, and L-sorbose in the acetate forms enabled the diastereomeric ratio of the products to be determined.

2.8.2 Crossed aldol reaction between 2,2-dimethyl-1,3-dioxan-5-one **49** and 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-arabinose **16**

In a parallel, 2,3;4,5-di-*O*-isopropylidene-*aldehydo*-D-arabinoses **16** was reacted to the

2,2-dimethyl-1,3-dioxan-5-one **49** by treatment with **7** and **8** in an aqueous solution over night at room temperature (Scheme 2.8.2.1). As the time required for proceed reaction was greater than that for the reaction between **49** and **10**, decomposition of the starting aldehyde slightly occurred. However, the octulose **96** was obtained, after chromatographic resolution, up to 65 % yield, thereby providing a convenient synthesis of octulose derivatives.

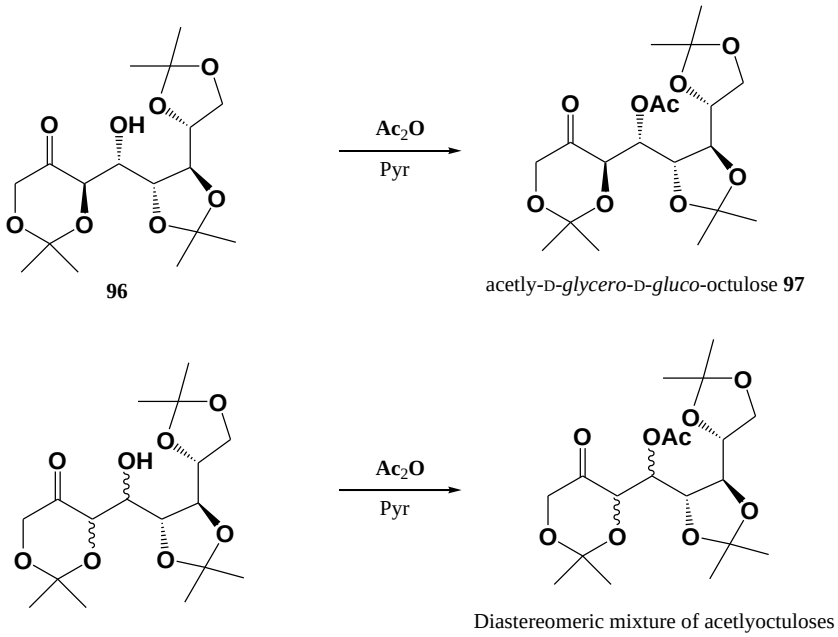
L-Prolinamido-glycoside **7** catalyzed aldol reaction between 2,2-dimethyl-1,3-dioxan-5-one **49** and 2,3;4,5-di-*O*-isopropylidene-*aldehydo*-D-arabinose **16** gave 68 % of the isopropylidene protected D-*glycero*-D-*gluco*-octulose[36] **96** and recovered **16** in 11 % yield.



Scheme 2.8.2.1. Aldol reaction between 2,2-dimethyl-1,3-dioxan-5-one **49** and 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-arabinose **16**.

The yield of **96** in the aldol reaction was diminished when less-fresh samples of *aldehydo*-sugar **16** were used. The ratio of the two diastereomeres in the product was approximately 10 : 1 from ^{1}H

NMR analysis (only two diastereomers were detected). Acetylation of the product **96** with acetic anhydride and pyridine gave the expected acetate **97** in 86 % yield (Scheme 2.8.2.2).



Scheme 2.8.2.2. Acetylation of octose.

The ^{1}H NMR spectrum of **97** confirmed that an acetyl group was present, and the fact that the conversion of **96** into the acetate had involved a substantial downfield shift of the H-4 signal confirmed that the acetyl group was indeed attached at C-4. The ^{1}H NMR spectrum clearly showed signals for protons in isopropylidene methyl groups and the H4 proton in the ratio of 9.6 : 1.

Recrystallization of the mixture of two diastereomers gave the crystalline single diastereomer, suitable for X-ray structure analysis and the absolute configuration of which was determined as (*3R*,*4R*,*5S*,*6R*,*7R*). The ORTEP representation of octulose **96** (Figure 2.8.2.1) clearly shows the absolute configurations at the newly formed chiral centers, C-3 and C-4.

It crystallizes in the orthorhombic space group $P2_12_12_1$ with cell parameters a = 9.553 (2) Å, b =

10.880 (18) Å, *c* = 18.020 (3) Å, and *Z* = 4. Table 2.8.2.1 records selected torsion angles and NMR data, respectively, and relevant crystal data are recorded in experimental section.

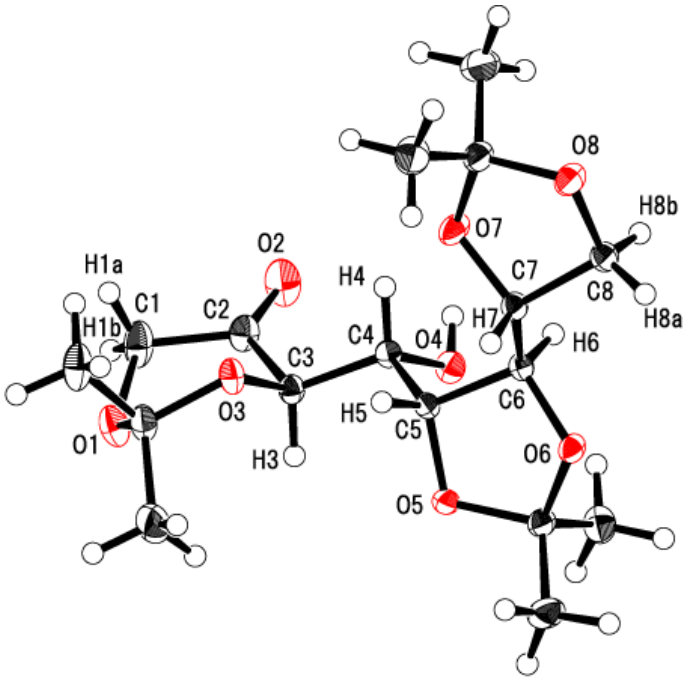


Figure 2.8.2.1. ORTEP representation of D-*glycero*-D-*gluco*-octulose **96**.

Avoidance of the *syn*-axial interaction of the newly formed hydroxyl group at C-4 and O-6, that would have been present in the *P* conformation, would seem to be the driving force in establishing the most favored disposition of the diastereomer, and form the possible contributors to the equilibrium population, a major contributor for the **96** appears to be ${}_5G^-$ conformer* in the crystalline state.

* ${}_5G^-$ denotes the sickle conformation obtained by 120° clockwise rotation of the remote atom along C-5 – C-6 bond.

The ^{1}H NMR couplings (Figure 2.8.2.2 and Table 2.8.2.1) for compound **96** were in good agreement with the crystallographic data.

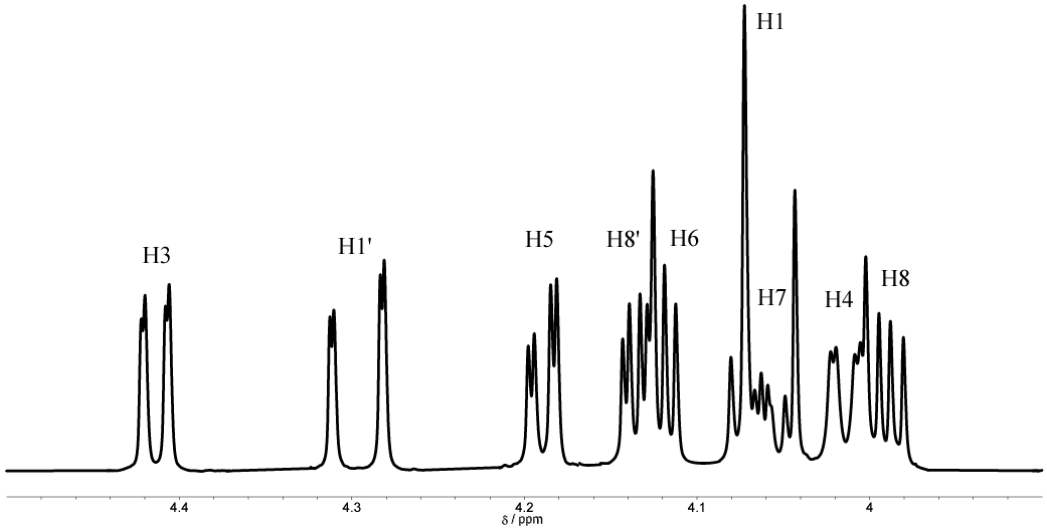


Figure 2.8.2.2. ^{1}H NMR spectrum of D-*glycro*-D-*gluco*-octulose **96**.

Coupling constants (Hz)

H1a, 1b	H3	H4	H5	H6	H7	H8a	H8b
$J_{1a,1b}$	$J_{1b,3}$ $J_{3,4}$	$J_{3,4}$ $J_{4,5}$	$J_{4,5}$ $J_{5,6}$	$J_{5,6}$ $J_{6,7}$	$J_{6,7}$ $J_{7,8a}$ $J_{7,8b}$	$J_{7,8a}$ $J_{8a,8b}$	$J_{7,8b}$ $J_{8a,8b}$
17.5 (d)	1.30 (dd) 8.50	8.50 (dd) 1.90	1.90 (dd) 7.80	7.77 (t) 7.77	7.77 (ddd) 4.51 2.40	4.51 (dd) 12.5	2.40 (dd) 12.5

Table 2.8.2.1. ^{1}H NMR data for D-*glycro*-D-*gluco*-octulose **96**.

Torsion angles (°)		coupling constants (Hz)	
H3-C3-C4-H4	178.19	$J_{3,4}$	8.50
H4-C4-C5-H5	66.47	$J_{4,5}$	1.90
H5-C5-C6-H6	-144.80	$J_{5,6}$	7.80
H6-C6-C7-H7	-171.92	$J_{6,7}$	7.77
H7-C7-C8-H8a	164.32	$J_{7,8a}$	4.51
H7-C7-C8-H8b	38.72	$J_{7,8b}$	2.40

Table 2.8.2.2. Selected torsion angles and coupling constants.

The backbone chain of **96** is sickle ($_5G^-$) conformation as predicted by consideration of avoidance of a parallel disposition of O-4 and O-6 on the same side of the chain; the observed small (1.8 Hz) $J_{4,5}$ coupling and large (9.2 Hz) $J_{3,4}$ coupling indicate that the sickle conformation is also favored in solution. The ^{1}H NMR couplings for compound **96** were in good agreement with the crystallographic data. The H-3–C-3–C-4–H-4 torsion angle (178.20º) is near the expected value in the antiperiplanar relationship of the H-3 and its vicinal H-4 ($J_{3,4}$ 8.4 Hz) in the ^{1}H NMR spectrum of **96**. Also, the synperiplanar relationship of H-4 and H-5 ($J_{4,5}$ 1.8 Hz) was allowed determination by the H-4–C-4–C-5–H-5 torsional angle (66.47º). Two adjacent IP groups of the octulose are antiperiplanar on the sugar chain (H-6–C-6–C-7–H-7 torsion angle is 172.54 º). Avoiding a *syn*-axial interaction, H-5 and H-7, and also H-6 and one of H-8 are closely placed. Further support of this $_5G^-$ conformation of **96** in solution was made through NOESY experiment. A relatively large NOE signals were observed between H-5 and H-7, and also between H-6 and H-8 (Figure 2.8.2.3).

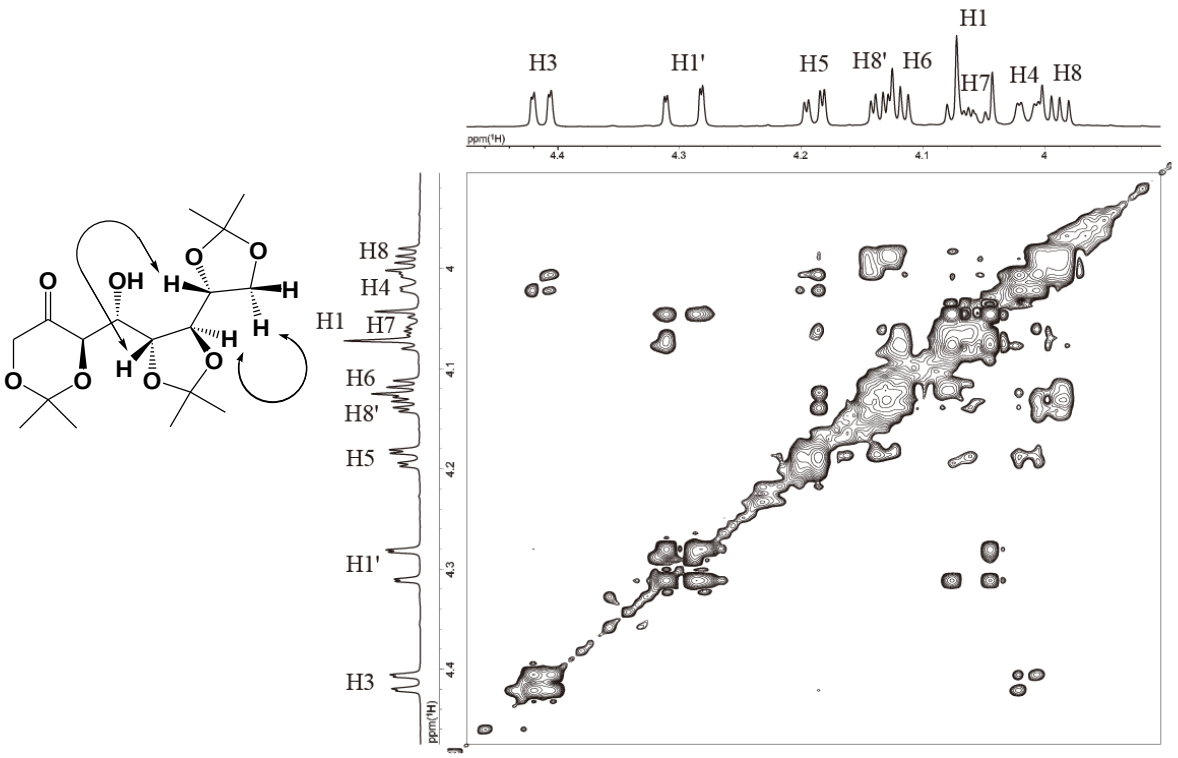
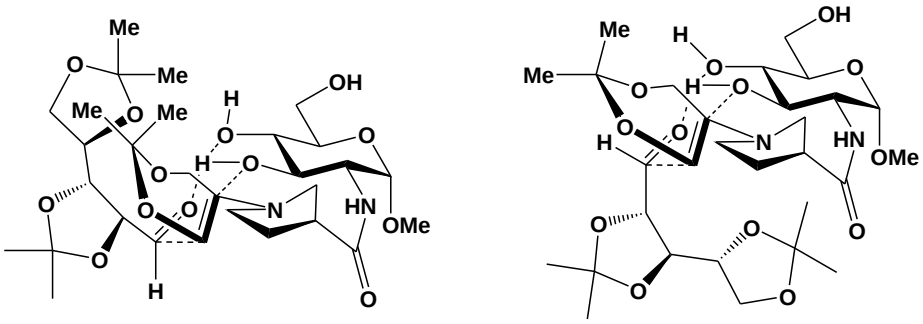


Figure 2.8.2.3. NOESY spectrum of **96**.

The proposed transition states, in which 3-OH of the sugar ring is capable of interacting with the aldehyde acceptor *via* enamine, with either 3-O or 3-O-H, and in each case hydrophobic pieces on the aldehyde avoided the hydrophilic sugar ring (Figure 2.8.2.4), are not accorded with this case.

This result requires an additional explaining for the reversal facial selectivity. Thus, additional binding of the *exo*-IP group of the aldehyde to the enamine intermediate arises *via* the IP group of its constituent hydrophobic piece, by van der Waals force, determines the transition state (Figure 2.8.2.4).



Si-face attack
(Favored)

Re-face attack
(Less favored)

Figure 2.8.2.4. A proposed transition states for reaction with **16**.

D-Prolinamido-glycoside **8** catalyzed aldol reaction between **49** and **16** gave an inseparable mixture of all four possible diastereomers, as detected by ^{13}C NMR analysis, in 72 % yield (Scheme 2.8.2.1). The diastereofacial selectivity of attack on **16** was very small (approximately 2 : 1 : 1 : 1). This very low diastereofacial selectivity may be ascribed to the competing effect of the hindered *si*-face of **16** and the *si*-face attack catalyzed by D-prolinamido-glycoside **8**. According to the Felkin-Anh model, the *aldehydo*-D-arabinose having *S* configuration at C-2 position should show tendency for favored attack at the *re*-face, however, the former reaction proceeded via the attack preferentially from the *si*-face of the less favored conformer **16A** to give **96** (Fig. 2.8.2.5). This result shows that *re*-face attack to the less-hindered *re*-face of **16** does not selectively occur, suggesting that the conformation of **16** was **16A** in the transition state, and this differing diastereofacial selectively may be attributed to the conformational mobility of the C-3–C-4 chain of **16**. Because of the two isopropylidene groups, favored conformation of **16** is sickle. Steric hindrances between the 4,5-isopropylidene ring in **16** and the enamine of **49** constrain the *si*-face attack toward less favored conformer **16B**.

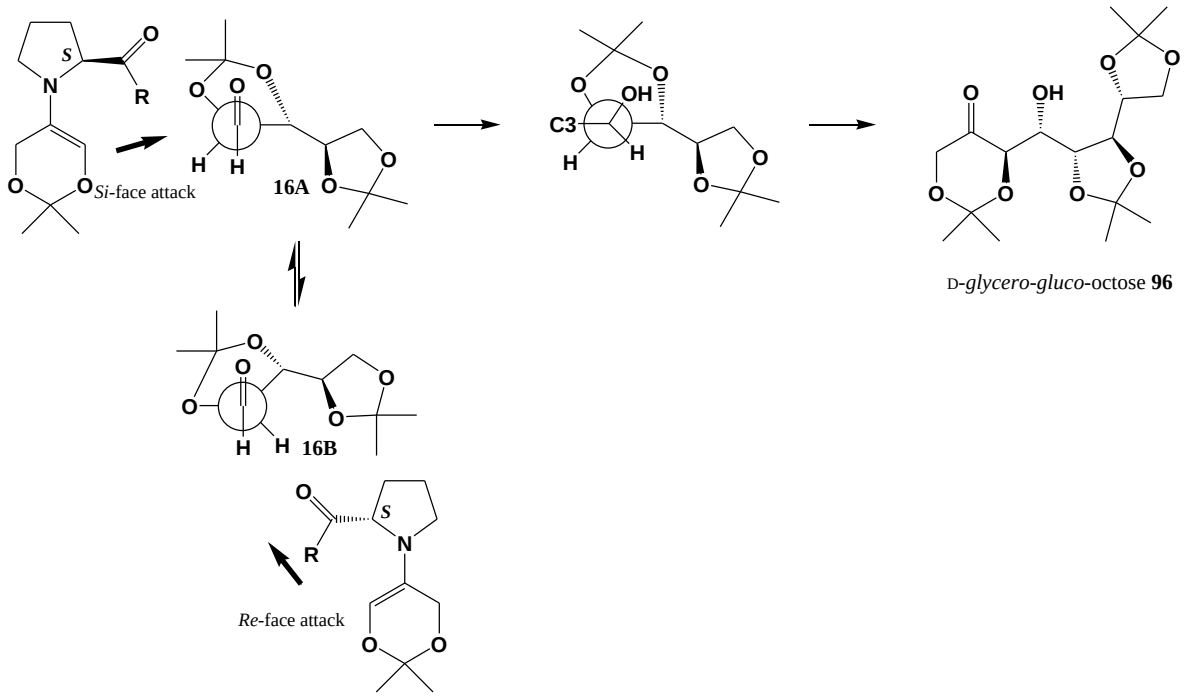
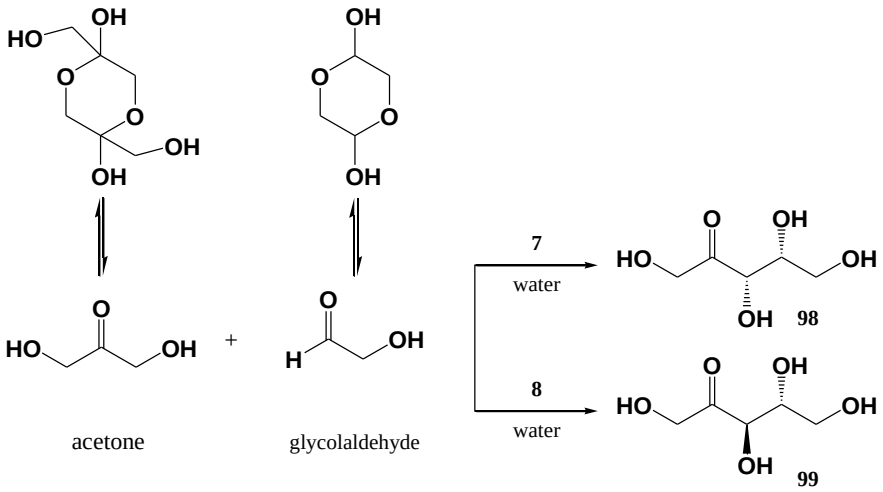


Figure 2.8.2.5. A proposed transition states for reaction with **16**.

Interestingly, aldol reactions of 2,3;4,5-di-*O*-isopropylidene-*aldehydo*-L-arabinose **19** under the same conditions, using either **8** nor **7**, was failed. Because of its extremely slow reaction rate when compared with its enantiomer, only trace amounts of aldol product were observed.

2.8.3 Crossed aldol reaction between dihydroxyacetone dimer and glycolaldehyde dimer

When the two dimers, dihydroxyacetone and glycolaldehyde were treated under prolinamido-glycoside catalyzed conditions in aqueous media, each of D-xylulose[37] **98** and D-ribulose[38] **99** was selectively obtained from L-prolinamide **7** and D-prolinamide **8** conditions, respectively, but in low to moderate yields (Scheme 2.8.3.1).



Scheme 2.8.3.1. Aldol reaction between dihydroxyacetone dimer and glycolaldehyde dimer

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As shown Table 2.8.3.1, variations in aqueous solvent system, amounts of the catalyst, or of temperature did not significantly affect the stereoselectivities. The ^{1}H NMR spectra of which were

identical with the authentic samples of D-xylulose **98** and D-ribulose **99**, and the ratios of the two epimers were determined by comparison of the H-1 signals in the ^{1}H NMR spectra of the initial mixtures.

entry	catalyst	amount of catalyst (equivallent)	solvent	time (h)	yield (%)	dr (**98** : **99**)
1	**D**	0.3	water	72	38	1 : 9
2	**D**	0.1	water	72	37	1 : 9
3	**D**	0.05	water	96	28	1 : 9
4	**D**	0.1	DMSO	96	trace	n.d.
5	**D**	0.3	phoshate buffer	72	39	8 : 1
6	**L**	0.3	water	72	38	8 : 1
7	**L**	0.1	water	72	39	8 : 1
8	**L**	0.05	water	96	30	8 : 1
9	**L**	0.3	DMSO	96	trace	n.d.
5	**L**	0.3	phoshate buffer	72	36	8 : 1

Table 2.8.3.1. Aldol reaction between dihydroxyacetone dimer and glycolaldehyde dimer

Chapter 3

Stereoselective tandem aldol-aldol reaction

3.1 Introduction

Attempts to provide bisaldol products by tandem aldol-aldol reaction were centered initially on the choice of enolates. For example, a sequential treatment with lithium and boron enolates[40] and asymmetric Mukaiyama aldol reaction[41], in which involved nucleophilic addition of enol silyl ether as an enolate equivalent, were utilized for the purpose, albeit the former posed diastereoselective problems and the latter entailed low yields.

Envisaging the target of poly hydroxylated chiral bisaldol products incorporating attributes favorable to high selectivity for following spiroacetalization, the *aldehydo*-sugars having rigid chiral centers depending upon the parent sugars would be suitable to adapt as aldehyde acceptors, as there would be predictable requirement for a stereoselective reaction by Felkin-Anh model. The introduction of carbohydrate moieties into the bisaldol products should increase the stereoselectivity of following spiroacetalization as well as versatility for formation of various favored diastereomers of spiroacetal depending upon the chirality of the sugars.

With that aim, a novel approach to the chiral synthesis of bisaldol products has been developed by utilizing prolinamido-glycoside catalyzes tandem aldol-aldol reaction, in which it involves simple organocatalytic aldol reaction. Two types of the tandem aldol-aldol-reaction, ‘symmetrical’ and ‘asymmetrical’ were described. The former derived to the C_2 symmetrical uloses and the latter derived to the asymmetrical higher carbon uloses, possess a central oxo group (Scheme). In all cases of the tandem aldol-aldol reactions, the diastereofacial selectivity of its second aldol reactions was followed the first aldol reactions, the diastereofacial selectivity of which was predictable by

adopting the Felkin-Anh model.

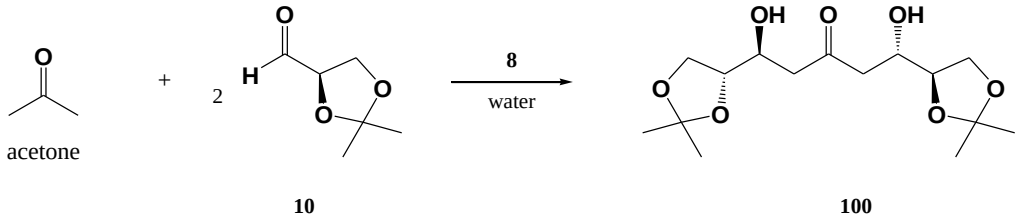
These compounds were used as a model to evaluate the stereospecific formation of enantiomerically pure spiroacetals, embedded in a rigid chiral matrix, in a variety of representative reactions of potential utility in synthetic transformations of sugars.

With a view to synthesizing spirosugar, the tandem aldol-aldol reactions on acetone with a representative series of *aldehydo*-sugars as a route to its precursor have been investigated, and the advantages and the disadvantages of these reactions were described.

3.2 Tandem aldol reaction between acetone and 2,3-*O*-isopropylidene-D-glyceraldehyde **10**

The starting compound was again 2,3-*O*-isopropylidene-D-glyceraldehyde **10** due to its simple system.

When 2 equiv. of the 2,3-*O*-isopropylidene-D-glyceraldehyde **10** was treated with acetone in the presence of matched catalyst, D-prolinamido-glycoside **8,** in 10 equiv. of water, the expected bisaldol adduct **100** was produced crystalline single diastereomer in 77% yield together with a small proportion of the monoaldol adduct **53** (Scheme 3.2.1).



Scheme 3.2.1. Tandem aldol-aldol reaction acetone and 2,3-*O*-isopropylidene-D-glyceraldehyde **10**.

The ^{1}H and ^{13}C NMR spectra are very simple, and are similar to its monoaldol adduct apart from the absence of C-1 methyl signals, hence the bisaldol adduct is C_2 symmetry (Figure 3.2.1)

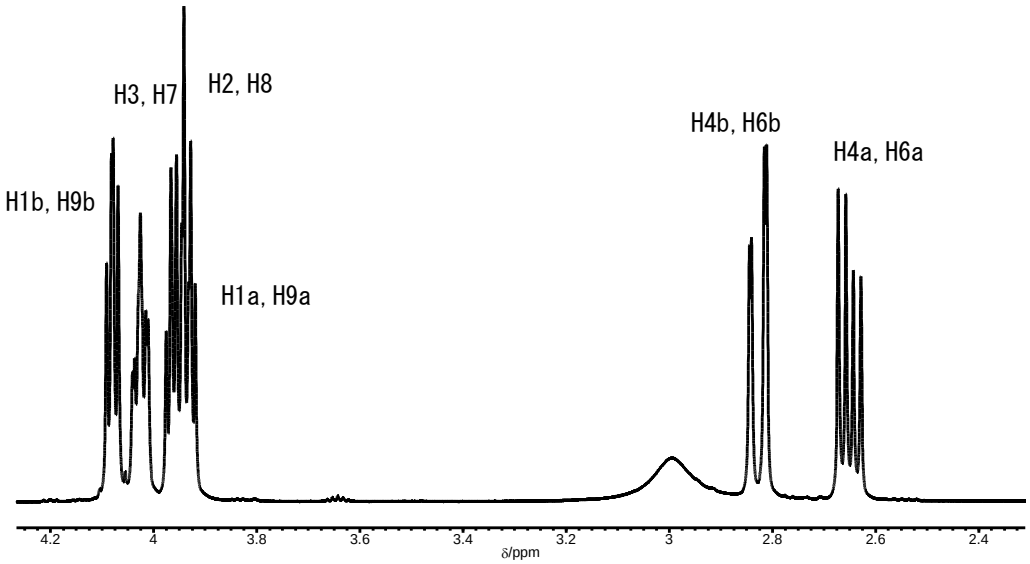


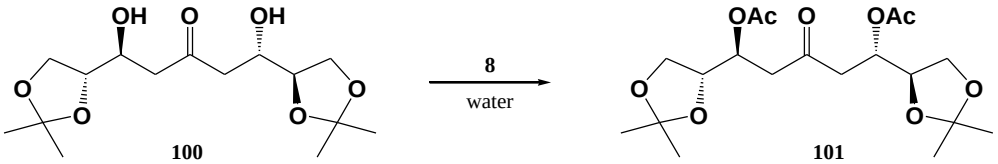
Figure 3.2.1. ^{1}H NMR spectrum of

4,6-dideoxy-1,2:8,9-di-*O*-isopropylidene-D-*galacto*-5-nonulose **100**.

Examination of symmetry properties of this compound shows that it has only a C_2 axis and hence belongs to point group C_2, and it caused significant simplification of the signals of the backbone.

Although the C_2 symmetrical structure of **100** caused simplification of the ^{1}H NMR spectrum, signal overlaps precluded specific assignment of the favored conformation of the sugar-chain, and hence, the C_2 symmetrical diol **100** was subjected to acetylation to determine the favored conformation.

Acetylation of **100** with acetic anhydride-pyridine gave, after chromatographic resolution, a 89% yield of expected diacetate **101** as a syrup (Scheme 3.2.2).



Scheme 3.2.2. Acetylation of **100**.

The ^{1}H NMR spectrum (Figure 3.2.2) of which showed for the methylene protons of C-4 and C-6 the anticipated downfield shift and changed splitting pattern relative to the precursor **100**, along with a comparable downfield shift of the methyne protons at C-3 and C-7.

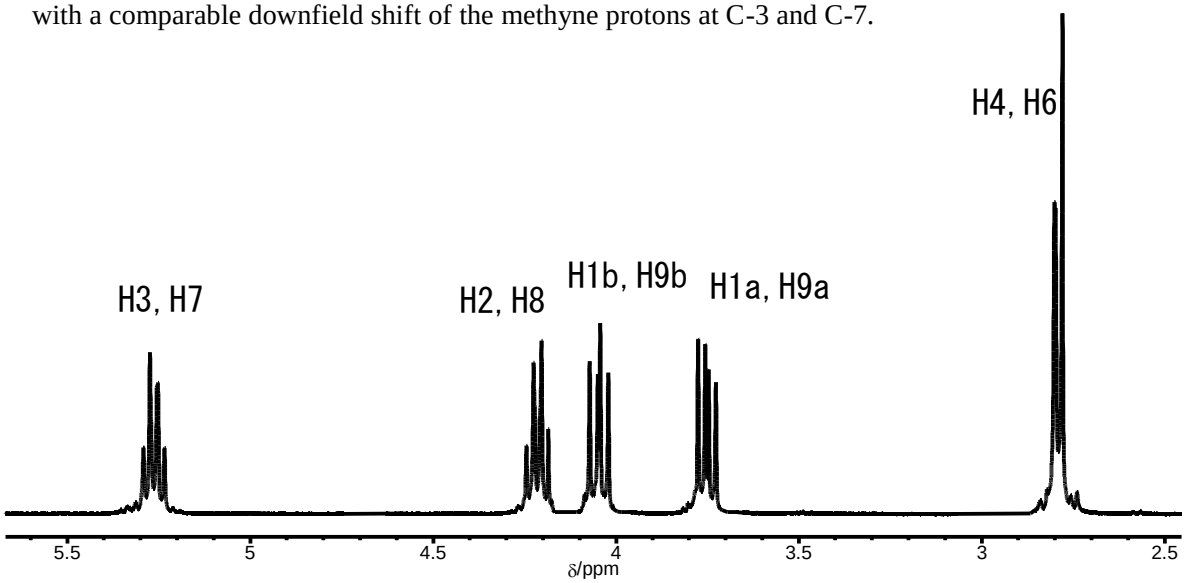


Figure 3.2.2. ^{1}H NMR spectrum of **101**.

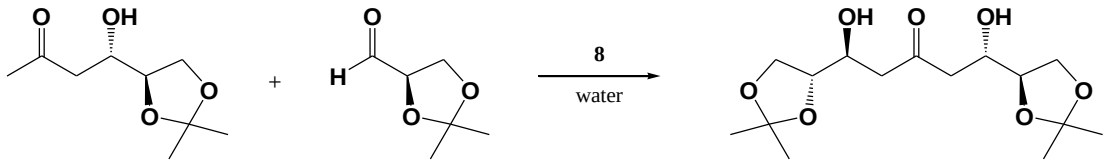
The vicinal proton-proton couplings for the diacetate **101** deviates significantly from those values diagnostic of preponderantly antiperiplanar or gauche, and is indicative of conformational mixture with substantial contributions from more than one conformer. The respective $J_{2,3} = J_{7,8}$ and $J_{3,4} = J_{6,7}$ values are 5.6 and 6.3 Hz, suggesting ${}_3G^-$, ${}_6G^-$ conformation of the carbon backbone chain.

To provide chemical proof of the stereochemistry at C-5 and C-9, the acyclic bisaldol adduct was

converted into a crystalline spiroacetal that would permit unambiguous assignment by X-ray crystallography.

There are two plausible mechanistic pathways for the tandem aldol-aldol reaction, one proceeds *via* tautomerization of the resulting imine to enamine, and the other proceeds *via* hydrogenolysis of the imine (Figure 3.2.3). The latter requires reattachment of the catalyst *via* the imine for the next aldol reaction.

An understanding of this mechanism only requires a simple experiment. When a chromatographically purified monoaldol adduct was treated with 1.1 equiv. of aldehyde **10** in the presence of 0.3 equiv. of catalyst 8 in water (10 equiv.), the yield of bisaldol adduct was markedly reduced (Scheme 3.2.3).



53 **10** **100**

Scheme 3.2.3. Aldol reaction acetone and 2,3-*O*-isopropylidene-D-glyceraldehyde **10**.

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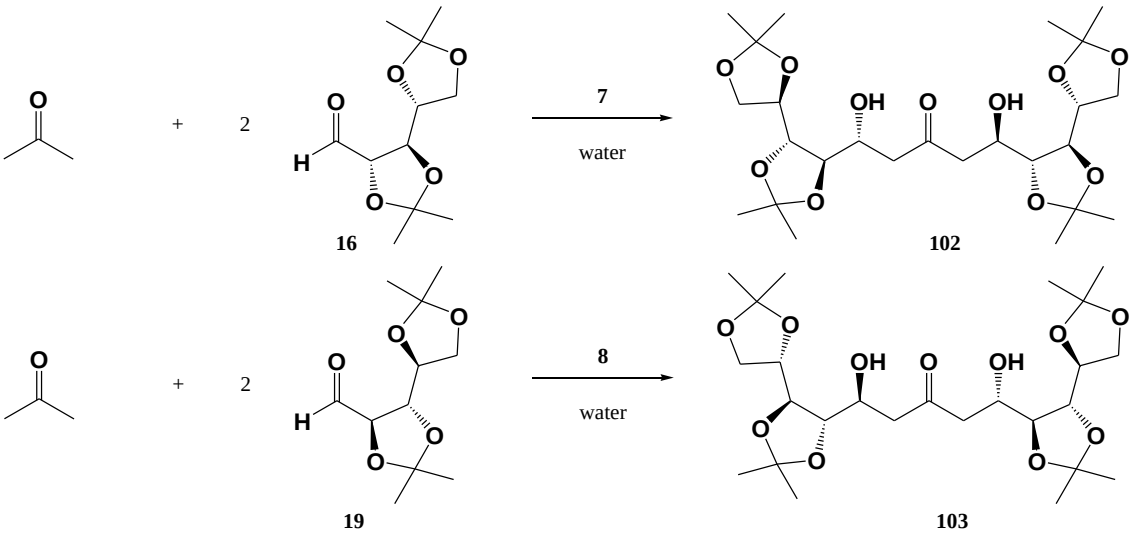
Concordant with the former aspect, the present result show that the tautomerization of intermediate imine plays an important role in the outcome of the tandem aldol-aldol reaction.

3.3 Tandem aldol reaction between acetone and 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-arabinoses **16** and **19**

The same procedure with the isopropylidene protected D-arabinose **16**, using L-prolinamide **7**,

afforded a single, crystalline, dextrorotatory product in 72% yield assigned (see Chapter 4) as 6.8-dideoxy-D-*allo*-D-*allo*-7-trideculose **102** together with its monoaldol adduct (11%), and similar treatment of the L-enantiomer **19**, but with D-prolinamide catalyst, gave the L-*allo*-L-*allo* analogue **103** (76% yield), which was likewise crystalline (Scheme 3.3.1).



Scheme 3.3.1. Tandem aldol reaction between acetone and 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-arabinoses **16** and **19**

The ^{1}H NMR spectra of the *allo*-*allo*-7-trideculose **102** and **103** indicated that they were single diastereomers. The protons of the sugar chain showed the anticipated doublet of doublets for H-1, H-1', H-3, H-6, H-6', H-8, H-8', H-11, H-13, and H-13', and the spin coupling data for **102** and **103** were consistent with the *P* conformation of the sugar chain, but overlap of the H-2, H-4, H-10, and H-12 signals precluded rigorous conformational assignment (Figure 3.3.1).

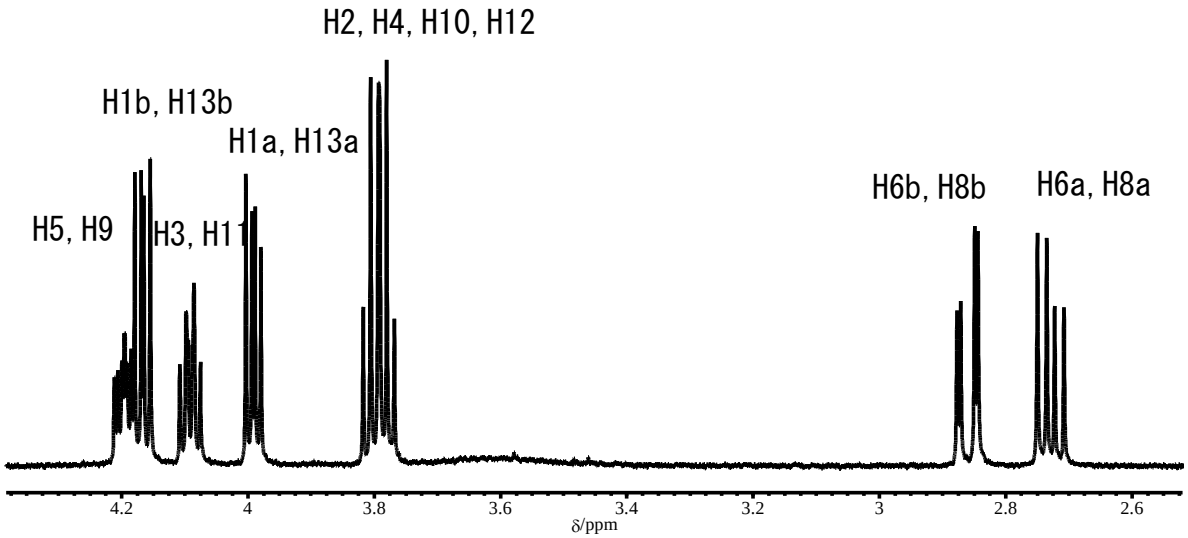
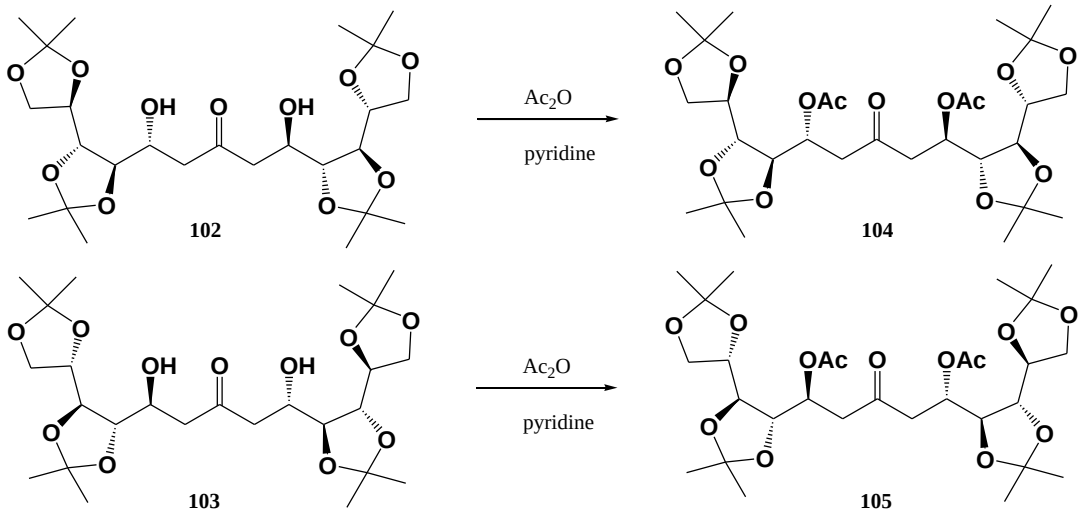


Figure 3.3.1. ^{1}H NMR spectrum of

6,8-dideoxy-1,2:3,4:10,11:12,13-tetra-*O*-isopropylidene-D-*allo*-D-*allo*-7-tridexulose **102**.

Acetylation of **102** and **103** gave expected acetates **104** and **105** in 84% and 81% yield, respectively (Scheme 3.3.2).



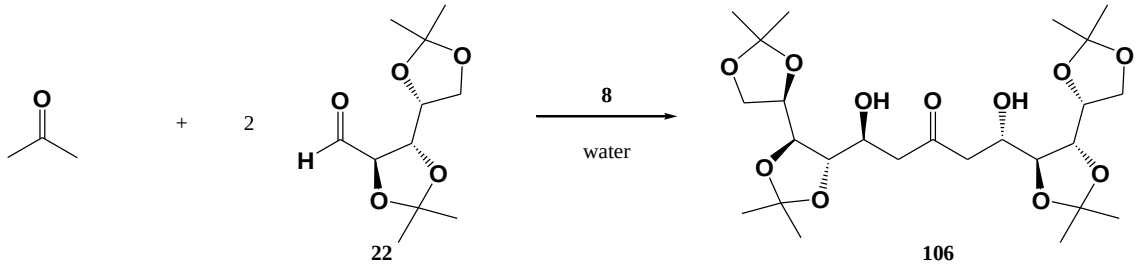
Scheme 3.3.2. Acetylation of **102** and **103**.

An expected downfield shift of the signal for H-5 and H-6 confirmed the acetate form, however,

close overlap of the resonances for H-1', H4, H-10, and H-13' of the sugar backbone chain precluded extractions of spin-spin coupling date and conformational assignment.

3.4 Tandem aldol reaction between acetone and 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D- xylose **22**

2,3:4,5-Di-*O*-isopropylidene-*aldehydo*-D-xylose **22**, when subjected to the action of enamine formed from acetone and D-prolinamido-glycoside **8** in water gave a single product, isolated initially as an oil and subsequently as crystals in 73% yield, which was characterized as 6,8-dideoxy-1,2:3,4:10,11:12,13-tetra-*O*-isopropylidene-D-*altro*-D-*tallo*-7-tridexulose **106** (Scheme 3.4.1).



Scheme 3.4.1. Tandem aldol-aldol reaction between acetone and 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D- xylose **22**.

It was isomeric with **103**, had the same mass spectrum, and was as single diastereomeric isomer, as evidenced by a single narrow doublet of doubldets for H-6 and H-8 at δ 2.73 and 2.92 in its NMR spectrum (Figure 3.4.1). Close overlap of the H-1', 4, 5, 9, 11, and 13' on the sugar backbone chain in **106** precluded extraction of spin-spin coupling data and conformational assignment.

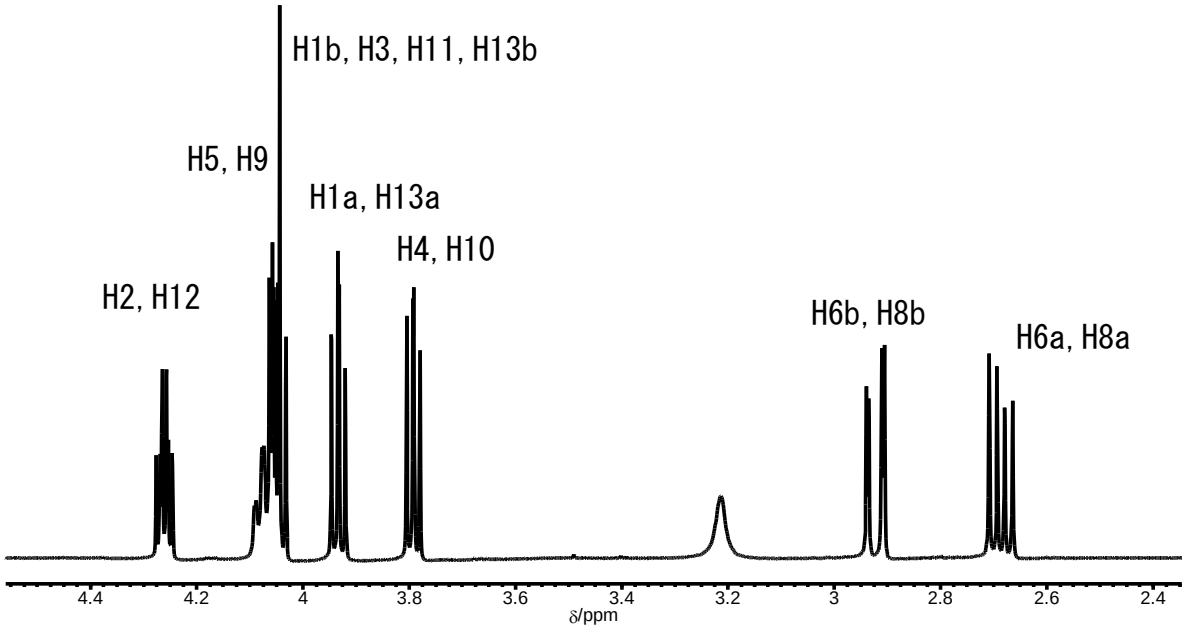
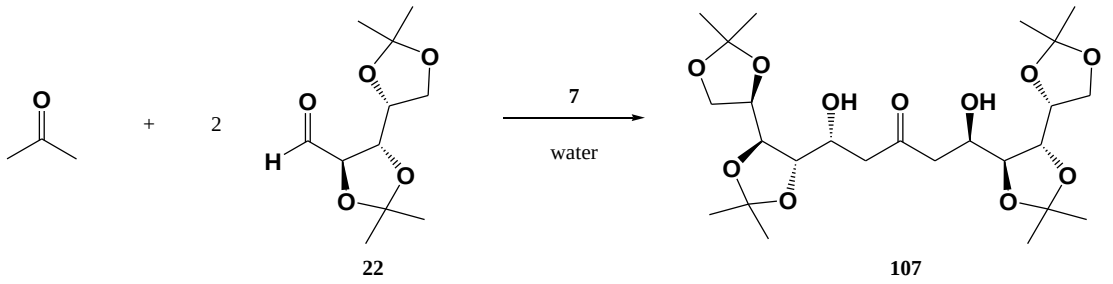


Figure 3.4.1. ^{1}H NMR spectrum of tetra-*O*-acetyl-α-D-tagatopyranose **106**.

When the same reaction was performed under L-prolinamide catalyzed condition, the D-*glycero*-D-*lyxo* isomer **107** was isolated in 63% yield with 79% de (Scheme 3.4.2).

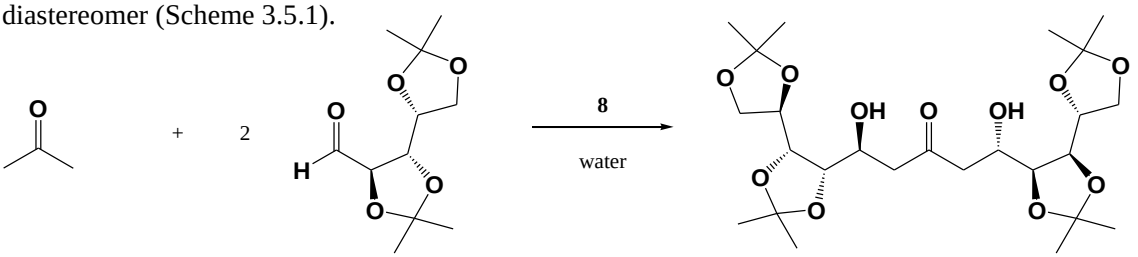


Scheme 3.4.2. Tandem aldol-aldol reaction between acetone and **22**.

The L-prolinamide catalyzed reaction proceeded in the *anti* Felkin-Anh mode, and the result may be attributed to the conformational mobility of the D-*xylo* chain of **22**. The ratio of the diastereomers was determined by comparison of the methylene protons at C-6 and C-8. The signals for H-6a and H-8a in the ^{1}H NMR spectrum of **107** are significantly shifted upfield, whereas the signals for H-6b and H-8b are shifted downfield, respectively, relative to L-*glycero*-D-*lyxo* isomer **106**, and hence, the integrations of which are clear to determine the ratio of two diastereomers.

3.5 Tandem aldol reaction between acetone and 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-ribose **25**

When the tandem aldol-aldol reaction was performed with 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-ribose **25**, the corresponding 6,8-dideoxy-D-*manno*-L-*manno*-7-trideculose **108** was obtained in 75% yield as a crystalline single diastereomer (Scheme 3.5.1).



25 **108**

Scheme 3.5.1. Tandem aldol-aldol reaction between acetone and 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-ribose **25**.

The anticipated signals δ 2.75 and δ 2.88 in ^{1}H NMR spectrum were assigned to H-6 and H-8 as expected A_2X system in common with α-deoxy *anti*-aldol adducts (Figure 3.5.1)

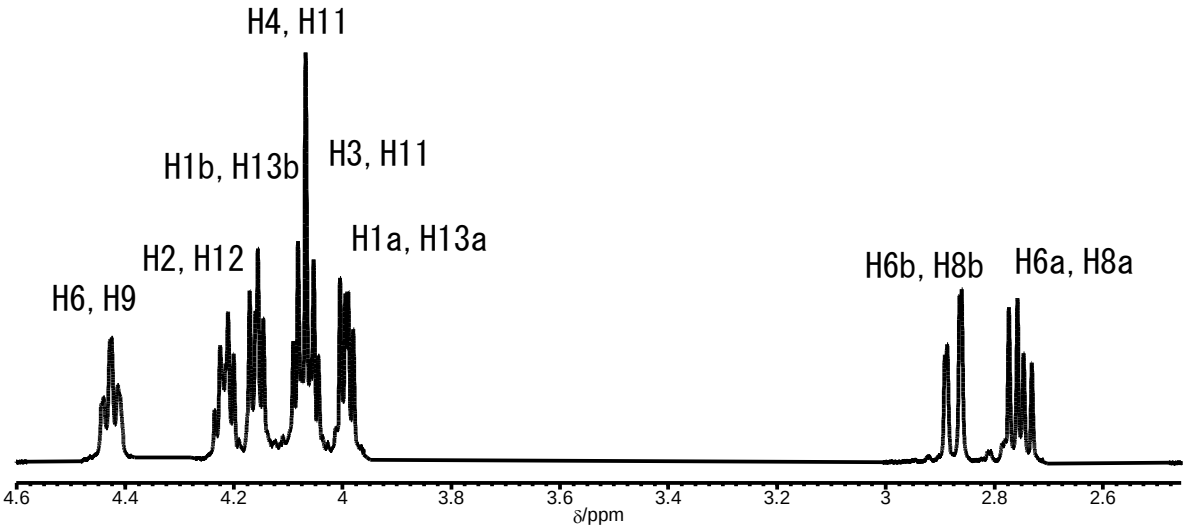
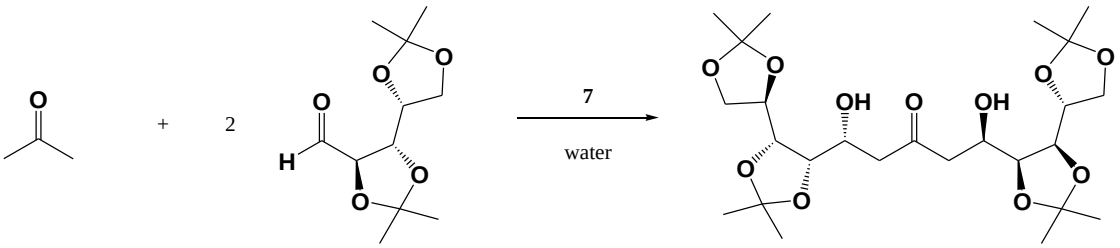


Figure 3.5.1. ^{1}H NMR spectrum of 6,8-dideoxy-1,2:3,4:10,11:12,13-tetra-*O*-isopropylidene-D-*manno*-L-*manno*-7-tridexulose **108**.

When the same reaction was performed, but with L-prolinamido-glycoside **7**, the *anti* Felkin-Anh product was obtained (Scheme 3.5.2). The *syn* diastereomer, 6,8-dideoxy-D-*gulo*-D-*gluco* -7-trideculose **109** was obtained in high (76%) yield with high (92%) diastereofacial selectivity (Scheme 3.5.2).



Scheme 3.5.2. Tandem aldol-aldol reaction between acetone and 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-ribose **25**.

Formation of the *syn*-diastereomer suggests that stereochemically less-favored *re*-face attack toward the *re*-face hindered *aldehydo*-D-ribose selectively occurred, and it was not in accord with the Felkin-Anh theory but the preference for stereoselectivity of the L-prolinamido-glycoside was appeared; conformational stability of the sickle form on the *ribo* stereochemistry may allow both selective *re*- and *si*-face attack catalyzed by D- and L-prolinamido-glycosides. As shown in Figure 3.5.2, the ^{1}H NMR spectrum of the *syn* isomer **109** was of first order, and a diagnostic coupling pattern for the H-6 and H-8 methylene peak was observed as a single doublet of doublets peak at δ 2.8. The H-2, 5, 9, and 12 signals generally appear as an ABX type of multiplet in related compounds possessing the same structure, but taking the *anti*-isomer **109** as a reference for chemical shifts, it is noteworthy that in the *syn*-isomer **108**, H-2 and H-12 are shifted downfield by about 0.2 ppm, whereas H-5 and H-9 are little affected. This may be attributed to deshielding

because of the close proximity of the O-5 and O-9 to H-2 and H-12, respectively; this results also indicated that the ${}_3G^-$, ${}_{10}G^-$ sickle conformation is favored. The spectrum showed the large values for $J_{2,3}$ and $J_{11,12}$ and small values for $J_{3,4}$, $J_{4,5}$, $J_{9,10}$, and $J_{10,11}$ consistent with the ${}_3G^-$, ${}_{10}G^-$ sickle conformation of the carbon backbone chain.

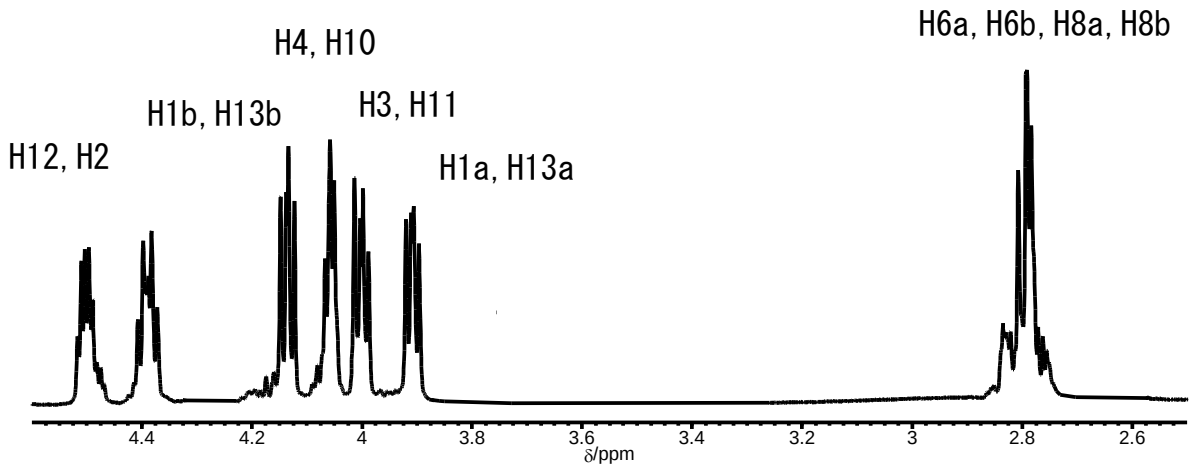
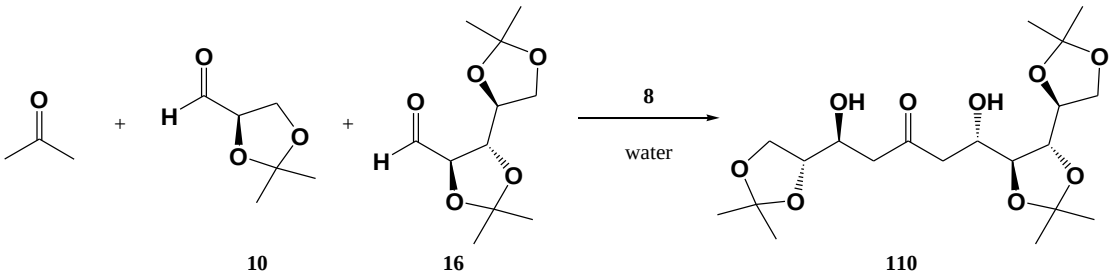


Figure 3.5.2. ^{1}H NMR spectrum of 6,8-dideoxy-1,2:3,4:10,11:12,13-tetra-*O*-isopropylidene-D-*gulo*-D-*gluco*-7-tridexulose **109**.

3.6 Tandem aldol reactionof acetone with 2,3-*O*-isopropylidene-D-glyceraldehyde **10** and 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-arabinose **16**

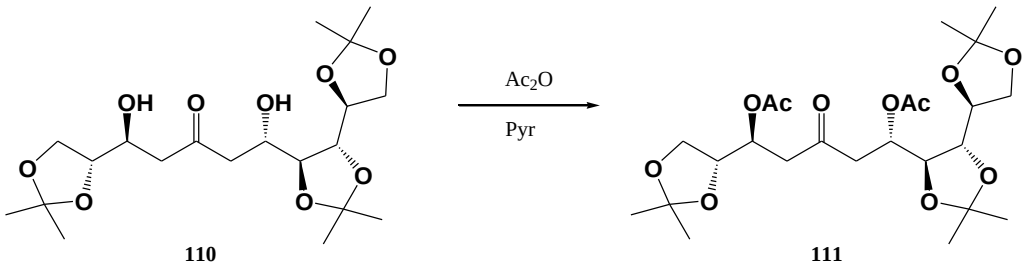
The stereoisomerically pure undeculose **110** was obtained in high yield (69%) by consecutive aldol reaction of acetone with 2,3-*O*-isopropylidene-D-glyceraldehyde **10** and 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-arabinose **16** under the D-prolinamide catalyzed condition (Scheme 3.6.1).



Scheme 3.6.1. Tandem aldol reactionof acetone with 2,3-*O*-isopropylidene-D-glyceraldehyde **10** and 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-arabinose **16**

.

As ^{1}H NMR spectrum of asymmetric undeculose **110** is complicated due to close overlap of the signals of the sugar chain, the undeculose **110** was next subjected to acetylation to determine the accurate diastereofacial selectivity. Acetylation of **110** with acetic anhydride and pyridine gave the expected diacetate **111** in 88% yield (Scheme 3.6.2).



Scheme 3.6.2. Acetylation of **110**.

NMR spectral analysis of the diacetate showed single singlet peaks for both two acetyl groups and for each of the isopropylidene methyl peaks (Figure 3.6.1).

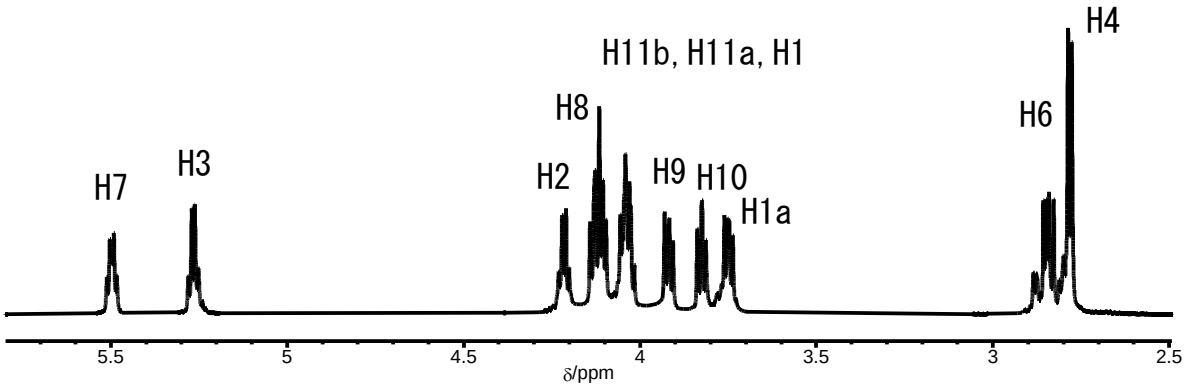


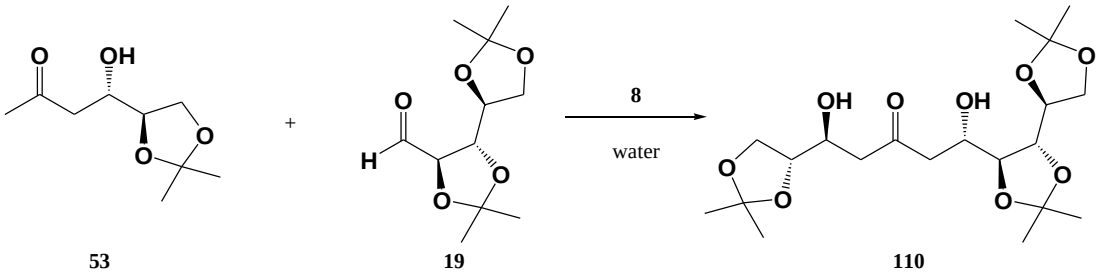
Figure 3.6.1. ^{1}H NMR spectrum of

4,6-dideoxy-3,7-di-*O*-acetyl-1,2:8,9:10,11-tri-*O*-isopropylidene-L-*threo*-D-*manno*-5-undeculose

111.

Down field shifted doublet of doublets signals near δ 5.27 and δ 5.49 were easily assigned to the newly formed chiral centers H-3 and H-7, respectively, by considering their COSY correlations with the help of the diagnostic signals of H-4 and H-7. The other protons of the sugar chain showed the anticipated doublet of doublets for H-1, H-2, and H-6, and the expected AB_2 system for H-9. The diagnostic spin coupling of antiperiplanar orientation are observed for $J_{2,3}$, $J_{7,8}$, and $J_{9,10}$. The sugar chain of **111** has no *syn*-axial interactions, however, the $J_{8,9}$ value is 5.6 Hz, indicating an essentially gauche disposition between H-8 and H-9, due to the isopropylidene ring, and is consistent with ${}_8G^+$ conformation.

For comparative studies, the hexulose **53** separately prepared by the reaction of acetone and 2,3-*O*-isopropylidene-D-glyceraldehyde was reacted with the *aldehydo*-L-arabinose **19**. The second aldol reaction was proceeded by catalyzing the D-prolinamido-glycoside, however, the yield was decreased from 69% to 31% (Scheme 3.6.3).

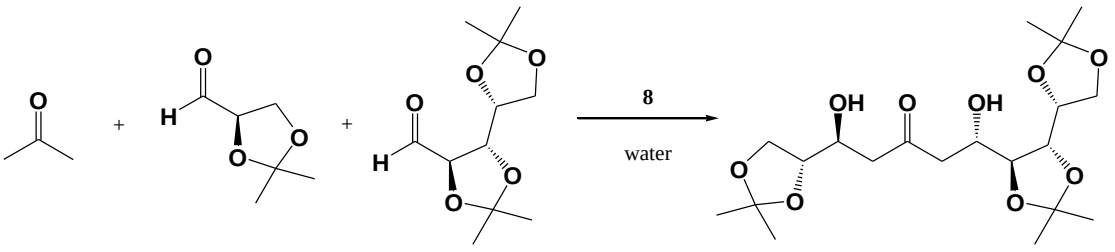


53 19 110

Scheme 3.6.3. Aldol reaction between **53** and **19**.

3.7 Tandem aldol reactionof acetone with 2,3-*O*-isopropylidene-D-glyceraldehyde **10** and 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-xylose **22**

The *aldehydo*-D-xylose showed an increased yield in the desired product **112** in the tandem aldol reaction when the D-prolinamido-glycoside was present. When the same tandem aldol reaction was performed, but with 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-xylose, the undeculose **112** was obtained in 71% yield as a crystalline single diastereomer (Scheme 3.7.1).



10 22 112

Scheme 3.7.1. Tandem aldol reactionof acetone with 2,3-*O*-isopropylidene-D-glyceraldehyde **10** and 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-xylose **22**

.

The ^{1}H NMR spectrum showed well separated single singlet signals for protons in the isopropylidene methyl groups of the single diastereomer (Figure 3.7.1).

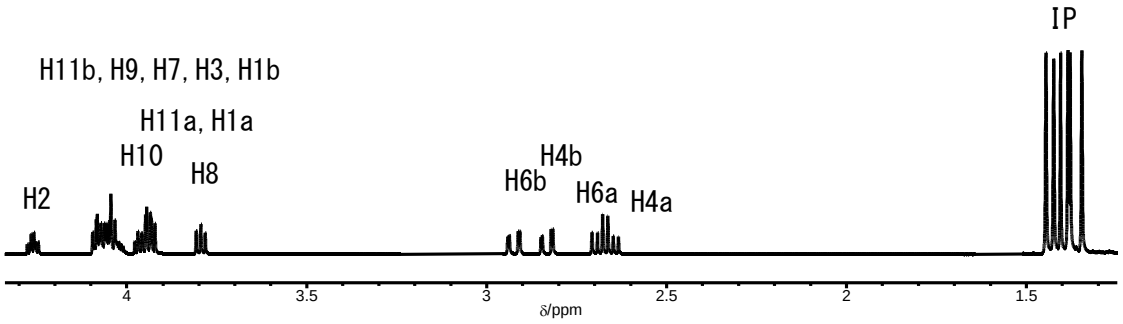
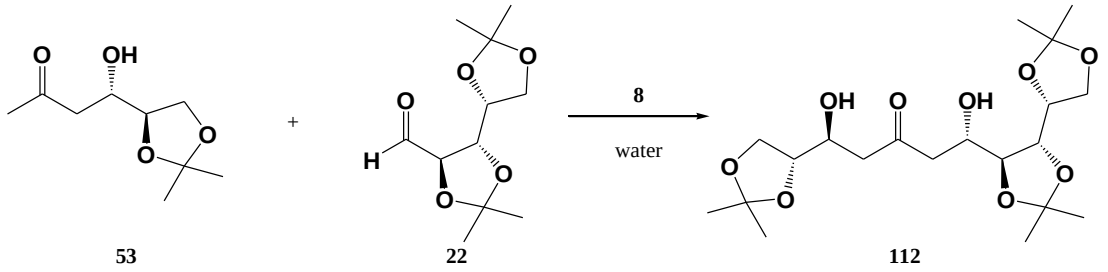


Figure 3.7.1. ^{1}H NMR spectrum of

4,6-dideoxy-1,2:8,9:10,11-tri-*O*-isopropylidene-L-*threo*-D-*tallo*-5-undeculose **112**.

Treatment of the hexulose **53** with 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-xylose **22** under the D-prolinamido-glycoside **8** catalyzed condition gave the same undeculose (Scheme 3.7.2). The net yield by this route is more than double (66%) of the case of the *aldehydo*-L-arabinose. Formation of an alternative aldol dimerization compound was not observed nor expected, as such compound has never been observed in the prolinamide catalyzed conditions.

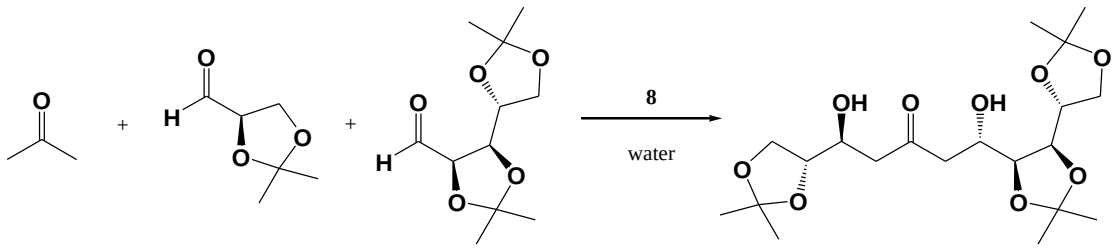


53 **22** **112**

Scheme 3.7.2. Aldol reaction between **53** and **22**.

3.7 Tandem aldol reactionof acetone with 2,3-*O*-isopropylidene-D-glyceraldehyde **10** and 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-ribose **25**

Similarly, the tandem reaction with *aldehydo*-D-ribose gave, after chromatographic separation, the expected 4,5-dideoxy-L-*threo*-D-*manno*-5-undeculose **113** in 59% yield as a 91 : 1 mixture of two diastereomers, from which there crystallized the pure, levorotatory L-*thero*-D-*manno* diastereomer (Scheme 3.7.1.).



10 **25** **113**

Scheme 3.7.1. Tandem aldol reactionof acetone with 2,3-*O*-isopropylidene-D-glyceraldehyde **10** and 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-ribose **25**

.

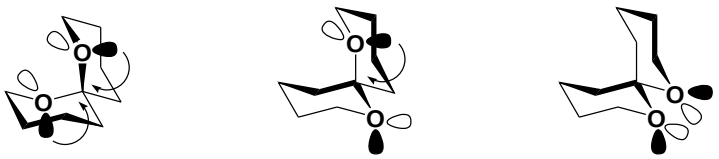
The ratio of the two diastereomers was determined by comparison of H-4 and H-6 methylene signals in the ^{1}H NMR spectra of the initial mixture and the spectrum of the crystalline L-*threo*-D-*manno* product. The methylene protons at C-4 and C-5 showed the anticipated doublet of doublets, respectively, however, overlap of the signals of the sugar chain in **113** precluded extraction of spin-spin coupling data and conformational assignment.

Chapter 4

Enantiospecific synthesis of spiroacetals

4.1 Introduction

The chirality of the non-substituted spiroacetal linkage, namely, 1,7-dioxaspiro[5,5]undecane, which functions as the main sex pheromone of the olive fruit fly, is due solely to the spiro ring junction. Examination of its symmetry property shows that 1,7-dioxaspiro[5,5]undecane has only a C_2 axis and hence belongs to point group C_2 and is chiral. Differing in configuration at the spiro center, 1,7-dioxaspiro[5,5]undecane also has three diastereomers, and therefore, six stereoisomers exist in the structure of which. The (*E*,*E*)-diastereomer, of which double chair conformation is stabilized by a double anomeric effect, is the most stable diastereomer and the (*Z*,*Z*)-diastereomer which has no anomeric effects is the most unstable (Figure 4.1.1).



(*E*,*E*)-(*6R*)-diastereomer
Anomeric effects × 2

(*Z*,*E*)-(*6R*)-diastereomer
Anomeric effects × 1

(*Z*,*Z*)-(*6R*)-diastereomer
Anomeric effects × 0

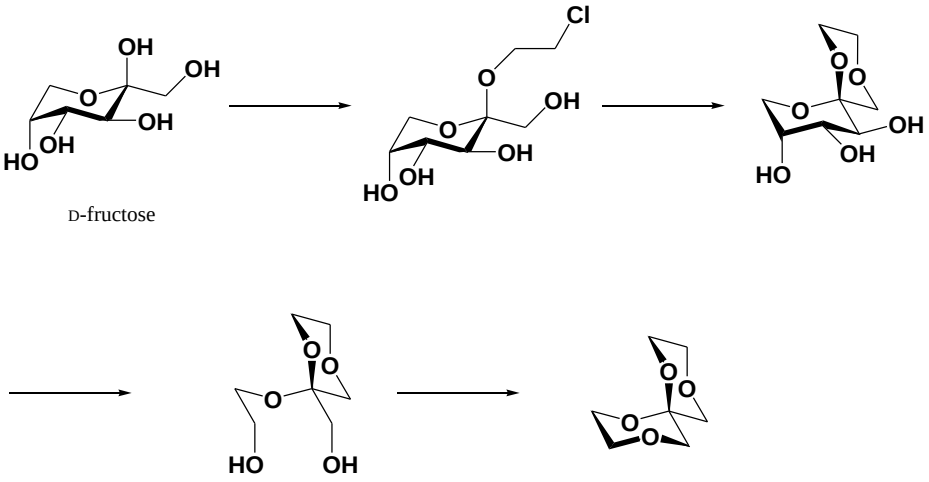
Figure 4.1.1. Conformation and anomeric effects of spiroacetal.

When a spiroacetal skeleton is formed, joined by two intramolecular C-O bonds, the double anomeric effect is normally regarded as highly stabilization.

The enantioselective synthesis of the spiroacetal linkage poses special problems due to its several stereoisomers formed in a reaction, albeit it occurs widely in nature and is present in several

biologically active compounds.

The first enantiospecific creation of an acetal carbon atom at a spiro-ring junction was achieved by Hough and Richardson[42] from D-fructose *via* 2-chloroethyl β-D-fructopyranoside, in which the chirality of the spiro-ring junction is defined by the configuration of the anomeric carbon atom of the glycoside. They synthesized (*R*)-1,4,7-trioxaspiro[5,5]undecane from D-fructose, the spirocenter of which was due to the configuration at the ring junction and was predetermined by β-configuration of the precursor and the β-configuration was predetermined by the original chiral centers of D-fructose (Scheme 4.1.1).



Scheme 4.1.1. Enantiospecific synthesis of (*R*)-spiro-1,4-dioxan from D-fructose.

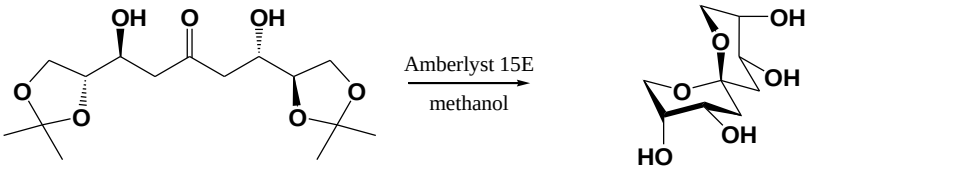
The enantiospecific synthesis of spiroacetals *via* bisaldol products, described in the chapter 3, utilizing its chiral centers from starting sugars and the chiral centers created by the tandem aldol-aldol reaction was described in this chapter.

The acid catalyzed spiroacetalization of bisaldol product, in which the chirality of the anomeric carbon defines that of the acetal carbon in the target spiroacetal by avoiding 1,3-diaxial interactions of hydroxyls in the bisaldol product, of which orientations predetermine the configuration of the double chair form, afforded single diastereomer of the spiroactal. The chair conformation for

pyranosides would determine by the orientations of the ring substituents, hence the prevalent chair conformations of pyranosides with all or the majority of the large hydroxyls in equatorial positions rather than unfavorable crowded axial positions. (*S*)-spiroacetals are $^{4}C_{1}$, i.e. a chair conformation in which C-2, C-4, C-5 and the ring oxygen are coplanar, with C-3 and the spirocenter lying above and below this plane respectively. And in contrast, (*R*)-spiroacetals adopt $^{1}C_{4}$ conformation (Figure 4.2). From this aspect it was concluded that the chirality of carbohydrates occupies a central role in enantiospecific synthesis of spiroacetals.

4.2 Spiroacetalization of 4,6-dideoxy-1,2:8,9-di-*O*-isopropylidene-D-*galacto*-5-nonulose **100**

Stereospecific spiroacetalization was achieved by acid-catalyzed hydrolysis, and followed by spontaneous cyclization. Attempted catalytic hydrogenation of **100** with Amberlyst 15E ion-exchange resin in methanol gave a crystalline (*6R*)-1,7-dioxaspiro[5,5]undecan-3,4,9,10 tetrol **114** in almost quantitative yield (Scheme 4.2).



100 (*6R*)-1,7-dioxaspiro[5,5]undecan-3,4,9,10-tetrol **114**

Scheme 4.2.1. Spiroacetalization of 4,6-dideoxy-1,2:8,9-di-*O*-isopropylidene-D-galacto-5nonulose **100**.

The (*R*)-spiroacetal **114** was formed as a result of intramolecular diacetalization which allows α-equatorial and β-axial diols on the both pyranose rings to avoid 1,3-diaxial interactions between α-axial hydroxyl groups and spiro-oxygens. This spiroacetalization requires ${}_2G^-$, ${}_3G^-$, ${}_5G^-$, and ${}_6G^-$ arrangement of the chain. As shown in Figure 4.1, the C-1 and C-9 hydroxyl groups on this sickle conformation is capable of interacting with the C-4 oxo-group.

The (*R*)-spiroacetal **114** is strongly levorotatory. The ^{1}H NMR spectrum showed the presence of only six apparent proton signals, indicating the C_2 symmetrical form of the molecule (Figure 4.2.1).

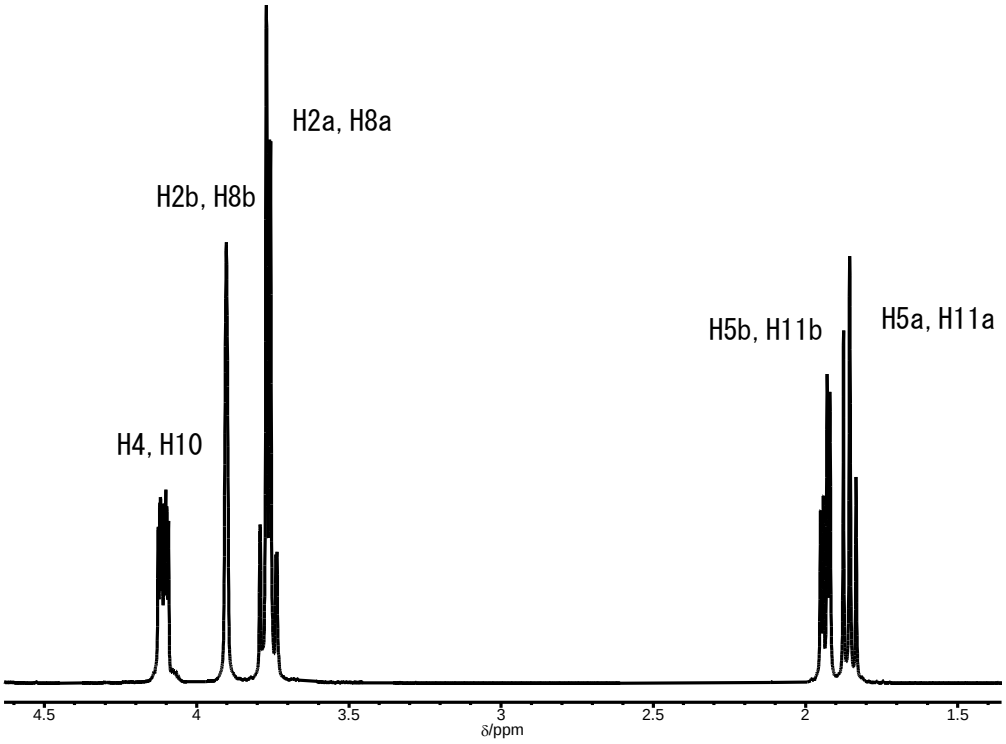


Figure 4.2.1. ^{1}H NMR spectrum of the spiroacetal **114**.

The spectrum showed expected A_2X patterns for the methylene groups at C-5 and C-11 as a triplet and doublet of doublets, respectively. The H-2 and H-8 signals also showed expected A_2B patterns and the H-4 and H-10 signals showed ABX_2 patterns both as doubled doublet of doublets. From this aspect, the double chair conformation of which was determined by ^{1}H-^{13}C HMBC analysis, but configurational assignment of the C_2 symmetrical spiroacetals by NMR analysis has proved difficult; the C_2 symmetrical spiroacetal showed signals on only one chair ring in ^{1}H NMR spectrum, therefore, the assignment of the absolute stereochemistry by NOESY or ROESY experiments has not allowed. Assignment of the absolute stereochemistry at spirocenter, and also C-4 and C-10 on the double chair was unambiguously achieved by crystallographic analysis of single crystals of **114** grown from methanol. The spiroacetal **114** is tetragonal, space group $P4_12_12$, and cell dimensions $a = b = 7.225(2)$ Å, $c = 19.523(6)$ Å, and $Z = 4$. The crystallographic structure establishes that the stereochemistry about the spirocenter is (*R*) in **114**. The observed proton-proton dihedral angles in crystalline **114** are compared in Table 4.2.1 with the proton-proton spin-spin couplings observed in aqueous solution, and are in accord with the Karplus relationship. Each

pyranose ring in **114** is held rigidly in a $^{1}C_{4}$ conformation by the chirality of spirocenter and the stereochemistry at C-4 and C-10. Avoiding 1,3-diaxial interactions, (*6S*)-(*E*,*E*)-3-axial-4-equatorial isomer was exclusively formed in the six isomers (Scheme 4.2.3).

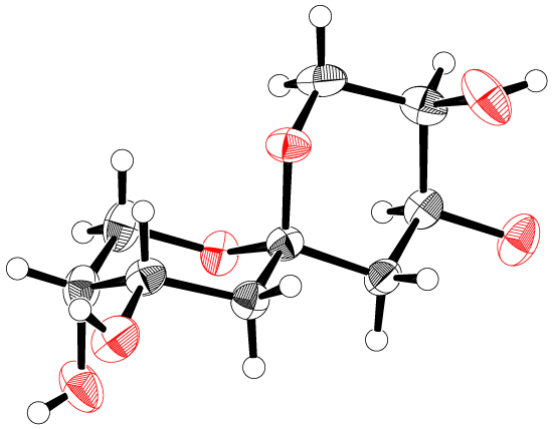
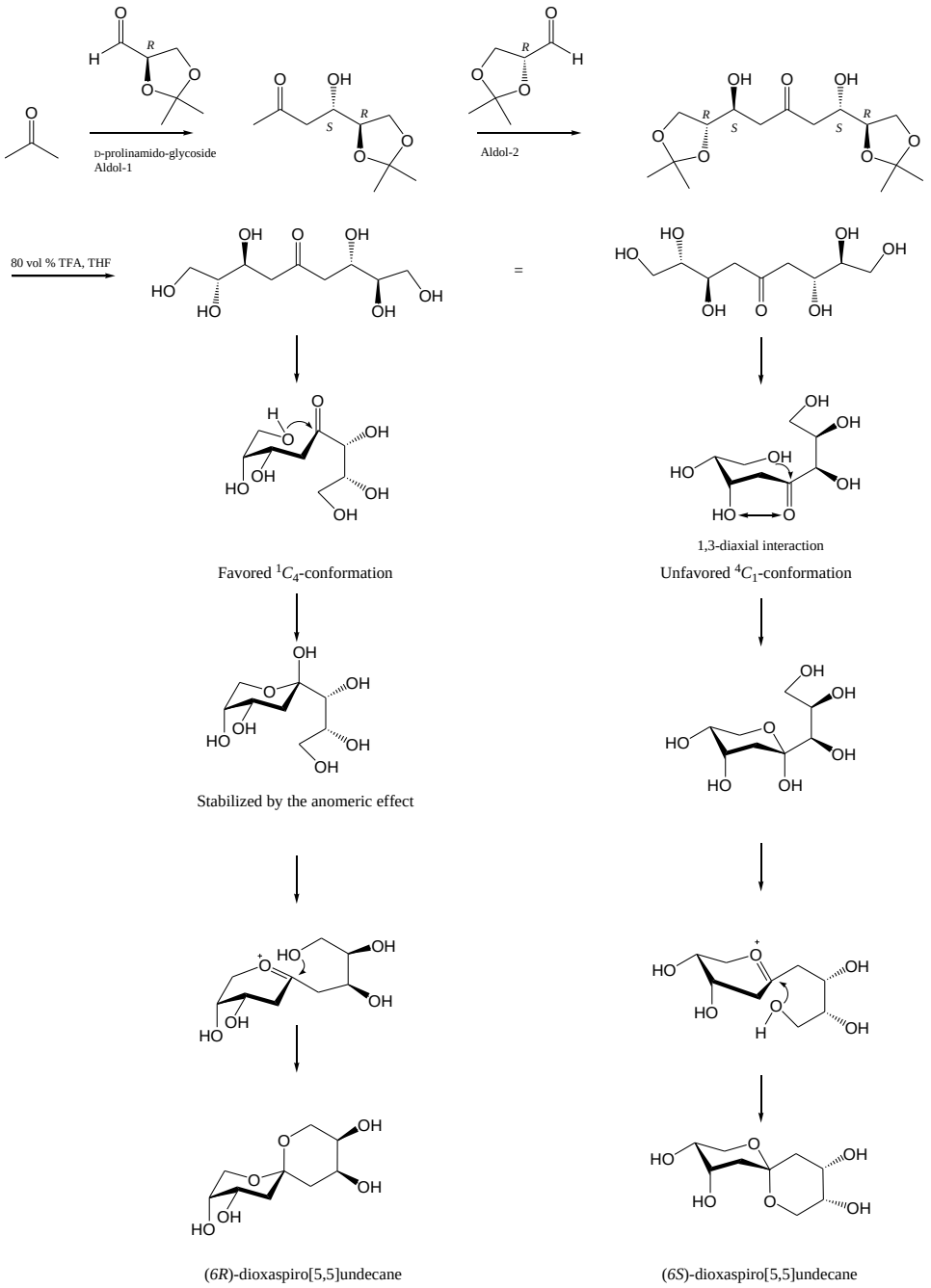


Figure 4.2.2. ORTEP representation of (*6R*)-1,7-dioxaspiro[5,5]undecan-3,4,9,10-tetrol **114**.

Torsion angles (°)		coupling constants (Hz)	
H2a-C2-C3-H3 H8a-C8-C9-H9	59.20	$J_{2a,3}$	2.00
H2b-C2-C3-H3 H8b-C8-C9-H9	-60.50	$J_{2b,3}$	2.00
H3-C3-C4-H4 H9-C9-C10-H10	-56.70	$J_{3,4}$	1.90
H4-C4-C5-H5a H10-C10-C11-H11a	173.89	$J_{4,5a}$	12.9
H4-C4-C5-H5b H10-C10-C11-H11b	54.89	$J_{4,5b}$	5.20

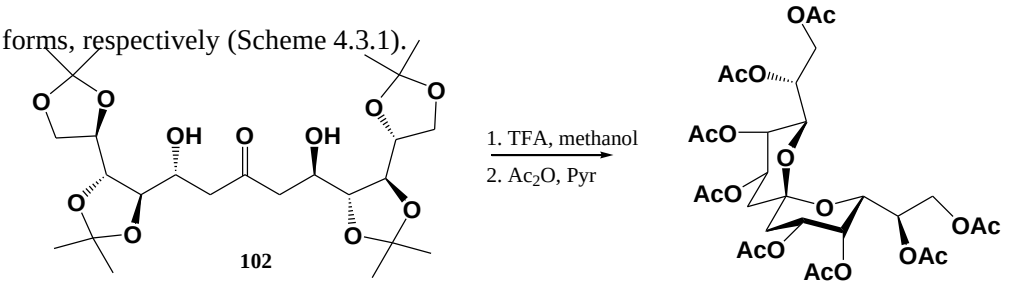
Table 4.2.1. Selected torsion angles and coupling constants.



Scheme 4.2.3. Stereospecific formation of (*6R*)-1,7-Dioxaspiro[5,5]undecan-3,4,9,10-tetrol.

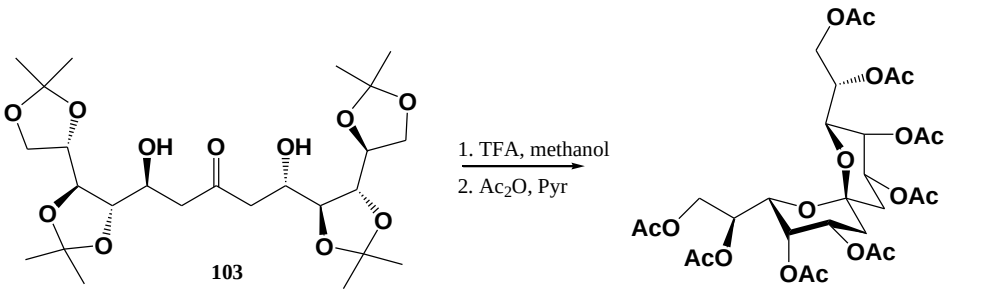
4.3 Spiroacetalization of 6,8-dideoxy-1,2:3,4:10,11:12,13-tetra-*O*-isopropylidene-*gluco-gulo*-7-tridexulose **102** and **103**.

Earlier efforts to remove the isopropylidene groups from acyclic-sugars similar to compound **102-109** by a variety of reagents have in many instances led to elimination of β-hydroxyl groups. Therefore, several reagents and various conditions were evaluated for stereospecific spiroacetalization. In the present work it was found that the individual enantiomers **102** or **103**, on treatment with 50 vol % aqueous trifluoroacetic acid in methanol for 24 h, led to clean removal of the isopropylidene groups to afford the corresponding enantiomerically pure spiroacetals, purified in acetate forms, respectively (Scheme 4.3.1).



102

(*3S,4R,6R,9S,10R*)-2,8-di[(*1R*)-1,2-dihydrocyethyl]-1,7-dioxaspiro[5,5]-undecan-3,4,9,10-tetrol octaacetate **115**

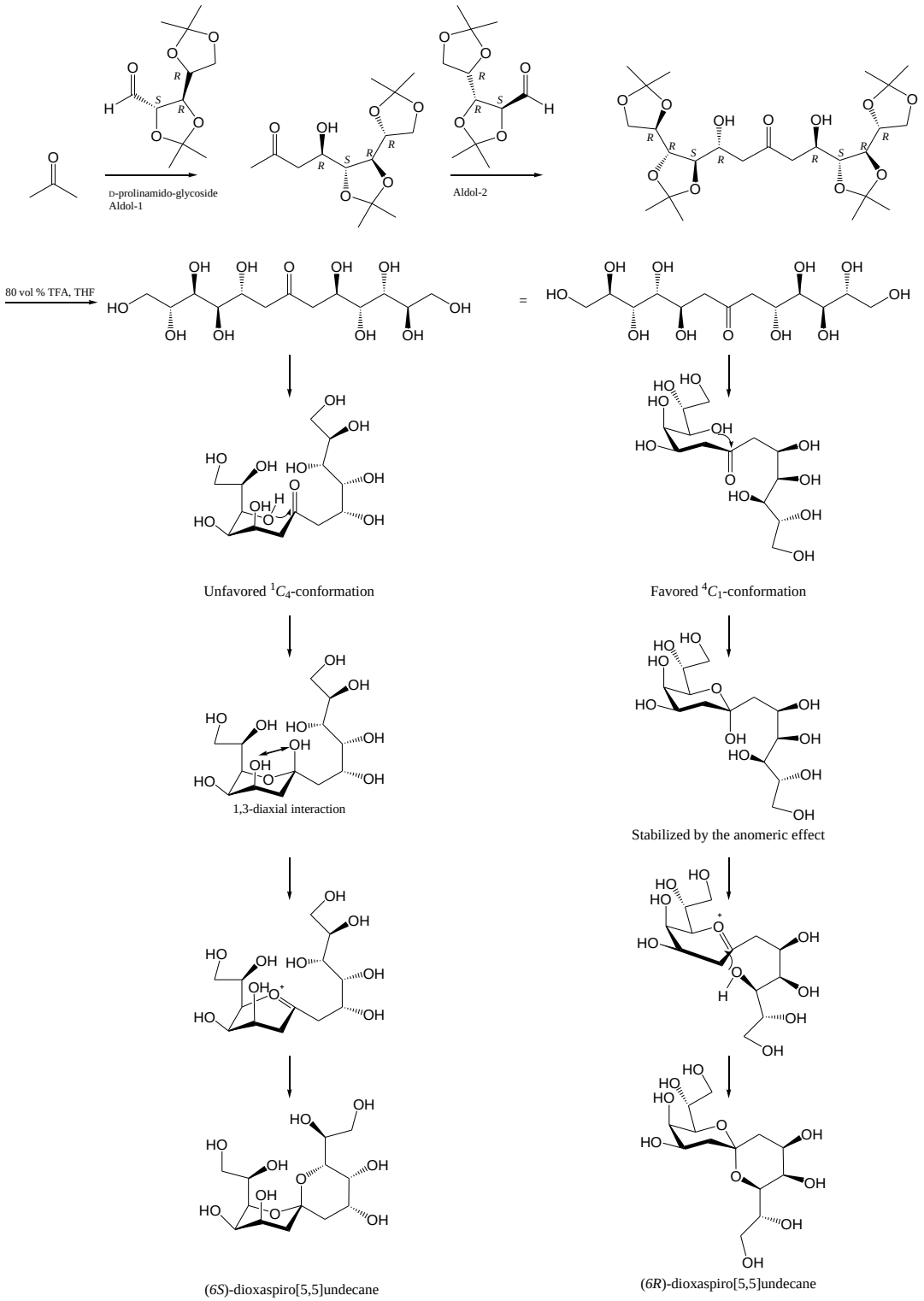


103

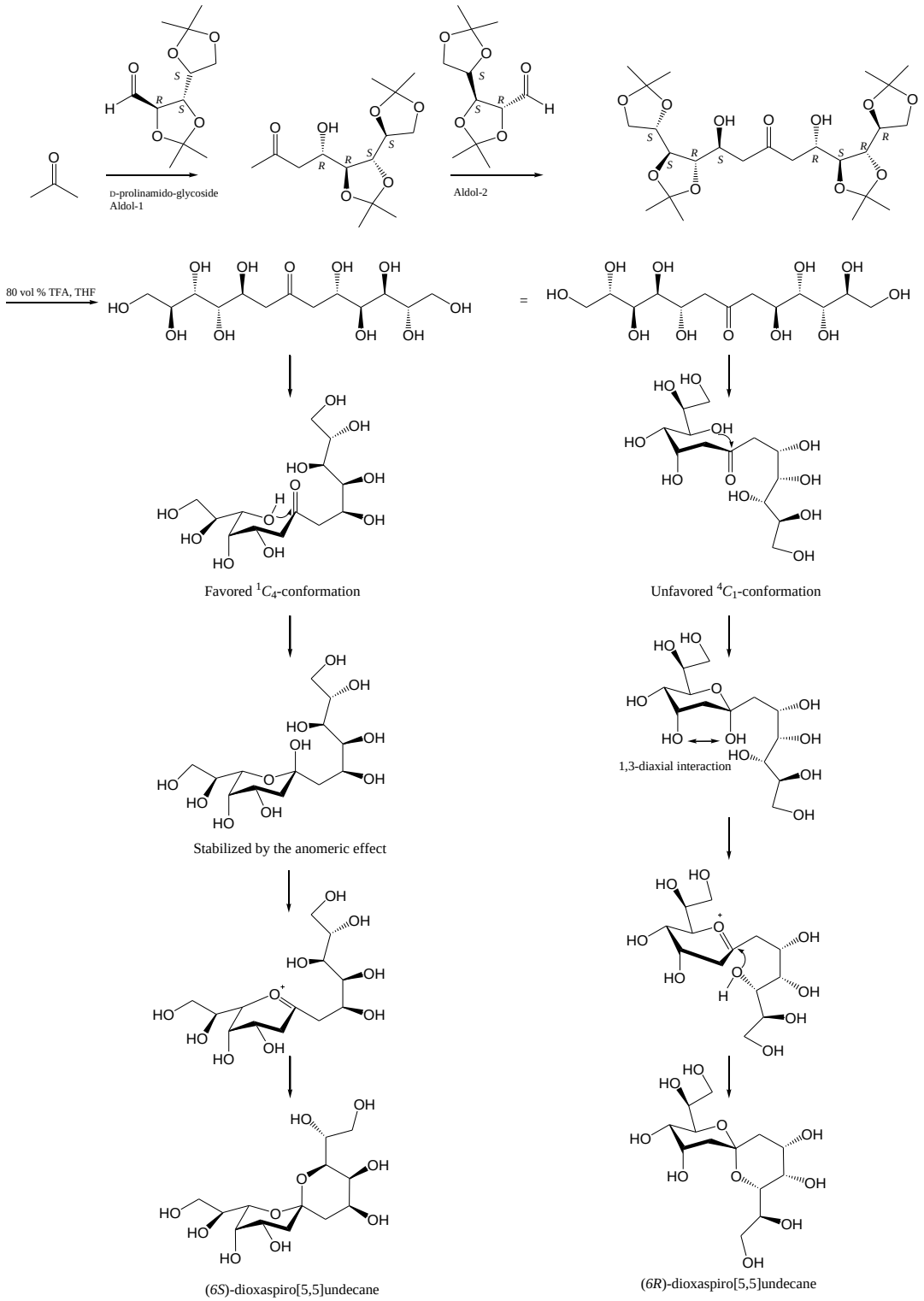
(*3R,4S,6S,9R,10S*)-2,8-di[(*1S*)-1,2-dihydrocyethyl]-1,7-dioxaspiro[5,5]-undecan-3,4,9,10-tetrol octaacetate **116**

Scheme 4.3.1. Spiroacetalization of 6,8-dideoxy-1,2:3,4:10,11:12,13-tetra-*O*-isopropylidene-*gluco-gulo*-7-tridexulose **102** and **103**.

With a new asymmetric spirocenter in the molecule, six possible stereoisomers could, in principle, be formed, but only as single isomer was isolated (Scheme 4.3.2 and 4.3.3).

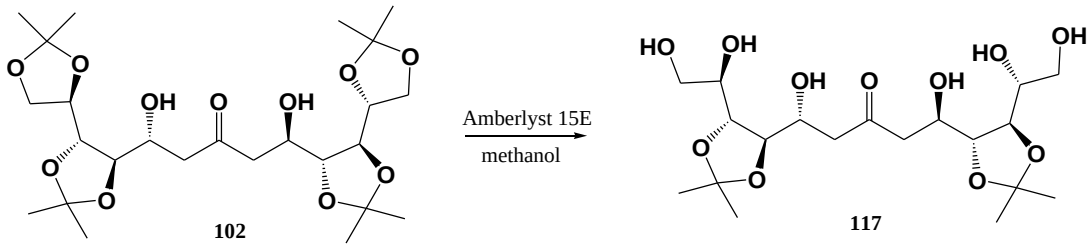


Scheme 4.3.2. Stereospecific formation of (*3S,4R,6R,9S,10R*)-2,8-di[(*1R*)-1,2-dihydrocyethyl]-1,7-dioxaspiro[5,5]-undecan-3,4,9,10-tetrol octaacetate **115**.



Scheme 4.3.3. Stereospecific formation of (*3R,4S,6S,9R,10S*)-2,8-di[(*1S*)-1,2-dihydrocyethyl]-1,7-dioxaspiro[5,5]-undecan-3,4,9,10-tetrol octaacetate **116**.

Attempts to hydrolyze by neither 80 vol % aqueous trifluoroacetic acid nor 80 vol % boiling aqueous acetic acid led to decomposition and the formation of a tarry product from which no discrete products could be identified. Treatment of a methanoic solution of **102** with trace of hydrochloric acid gave the same compound, but in low yield. Attempted catalytic hydrolysis of **102** with various acids, for instance, *p*-toluene sulfonic acid, camphor sulfonic acid, and ion-exchange resins in methanol failed. In these conditions, the *endo*-isopropylidene groups of **102** were inert toward hydrolysis, and 3,4:10,11-di-*O*-isopropylidene-trideculose **117** was only isolated (Scheme 4.3.4).



102 **117**

Scheme 4.3.4. Deprotection of the isopropylidene group in **102** by weak acids.

Assignment of absolute stereochemistry was achieved by X-ray crystallography of single crystals of **115** and **116**. The (*S*)-spiroacetal **115** is orthorhombic, space group $P2_12_12_1$, and cell dimensions a = 9.063 (2) Å, b = 14.273 (3) Å, c = 25.018 (4) Å, and Z = 4. The (*R*)-spiroacetal **116** is orthorhombic, space group $P2_12_12_1$, and cell dimensions a = 9.064 (17) Å, b = 14.275 (3) Å, c = 25.022 (4) Å, and Z = 4. The crystallographic structures established that the stereochemistry about the double chair is (*E*,*E*) in **115** and **116** (Figure 4.3.1).

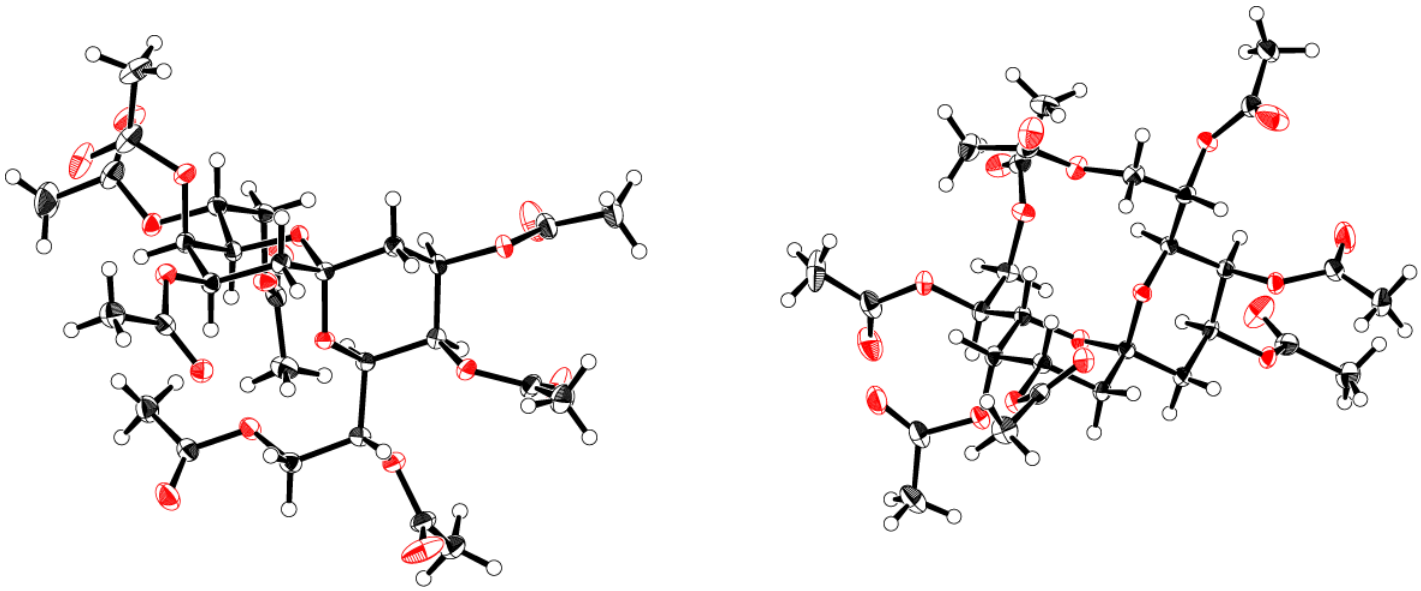
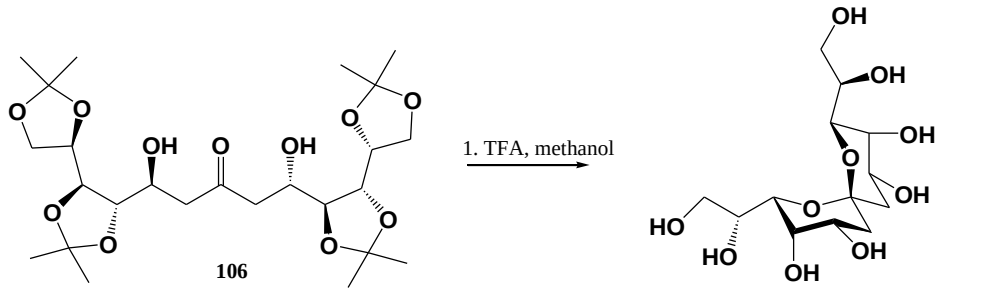


Figure 4.3.1 ORTEP representation of 2,8-di[1,2-dihydrocyethyl]-1,7-dioxaspiro[5,5]-undecan-3,4,9,10-tetrol octaacetates **115** and **116**.

4.4 Spiroacetalization of 6,8-dideoxy-1,2:3,4:10,11:12,13-tetra-*O*-isopropylidene-D-*altro*-D-*tallo*-7-tridexulose **106**

Spiroacetalization of **106**, under conditions similar to the experiment performed on the arabino diastereomer **103** but with trideculose **106** derived from D-xylose, afforded the spiroacetal **118** in 62% yield as a single diastereomer (Scheme 4.4.1).



(*3R,4S,6S,9R,10S*)-2,8-di[(*1R*)-1,2-dihydrocyethyl]-1,7-dioxaspiro[5,5]-undecan-3,4,9,10-tetrol **118**

Scheme 4.4.1. Spiroacetalization of 4,6-dideoxy-1,2:8,9-di-*O*-isopropylidene-D-galacto-5nonulose **106**.

The ^{1}H NMR spectrum of **118** showed a A_2B pattern for the methylene groups and ABX_2 pattern for the methyne groups of bulky chains of both pyranose ring, but otherwise there was very close resemblance of the spectrum to that of the spiroacetal **114**, emphasizing the underling similarity of structure (Figure 4.4.1). The depiction of the spiroacetal **118** as having $^1C_4$ conformation stems from the small (3.0 Hz) coupling constant between H-3, H-9 and H-4, H-8 in the ^{1}H NMR.

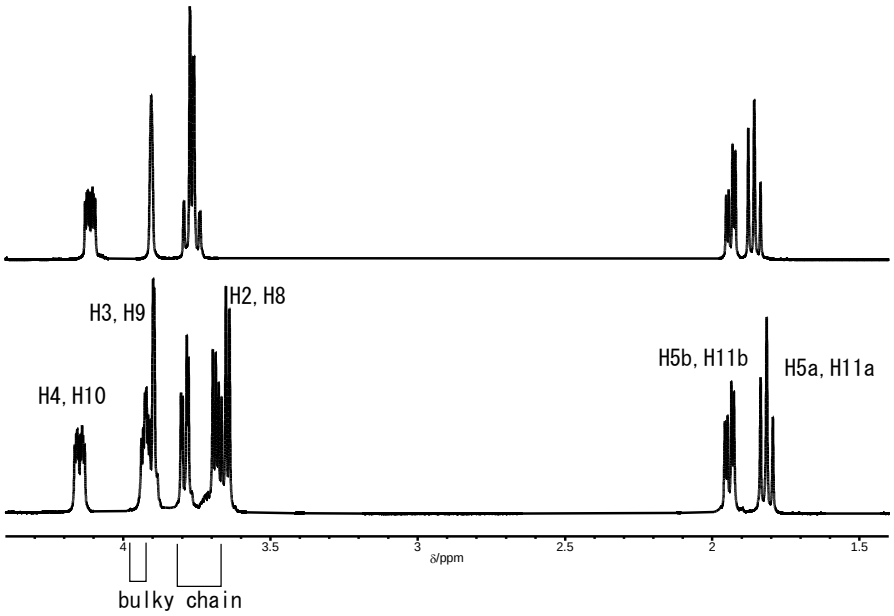


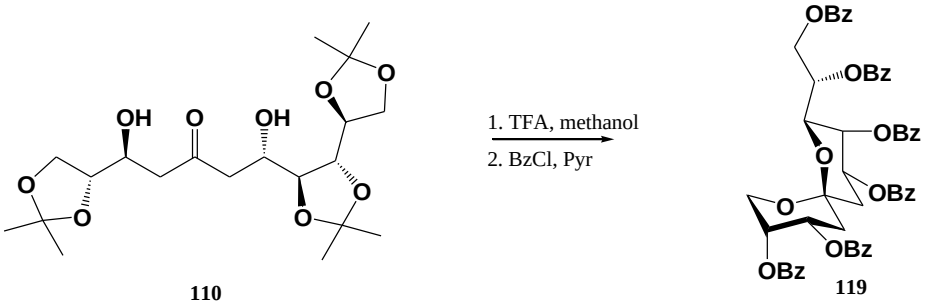
Figure 4.4.1. ^{1}H NMR spectra of the spiroacetals **114** and **118**.

Firm assignment of the stereochemistry of **118** was achieved by single-crystal X-ray structural analysis. The spiroacetal **118** is tetragonal, space group $P4_3$, and cell dimensions $a = b =$ 7.5855(16) Å, c = 25.354(6) Å, and Z = 4. The ORTEP representation of the spiroacetal **118** (Figure 4.4.2) clearly shows the OH groups at C-4 and C-8 occupying the equatorial position of the sugar rings, respectively, and provides independent verification of the structural assignments for the octulose **60**, the trideculose **106**, and the spiroacetal **118** derived from isopropylidene-D-xylose **22** by chemical means.

Figure 4.4.2 ORTEP representation of 2,8-di[1,2-dihydrocyethyl]-1,7-dioxaspiro[5,5]-undecan-3,4,9,10-tetrol octaacetate **118**.

4.5 Spiroacetalization of 4,6-dideoxy-1,2:8,9:10,11-tri-*O*-isopropylidene-L-*threo*-D-*manno*-5-undeculose **110**

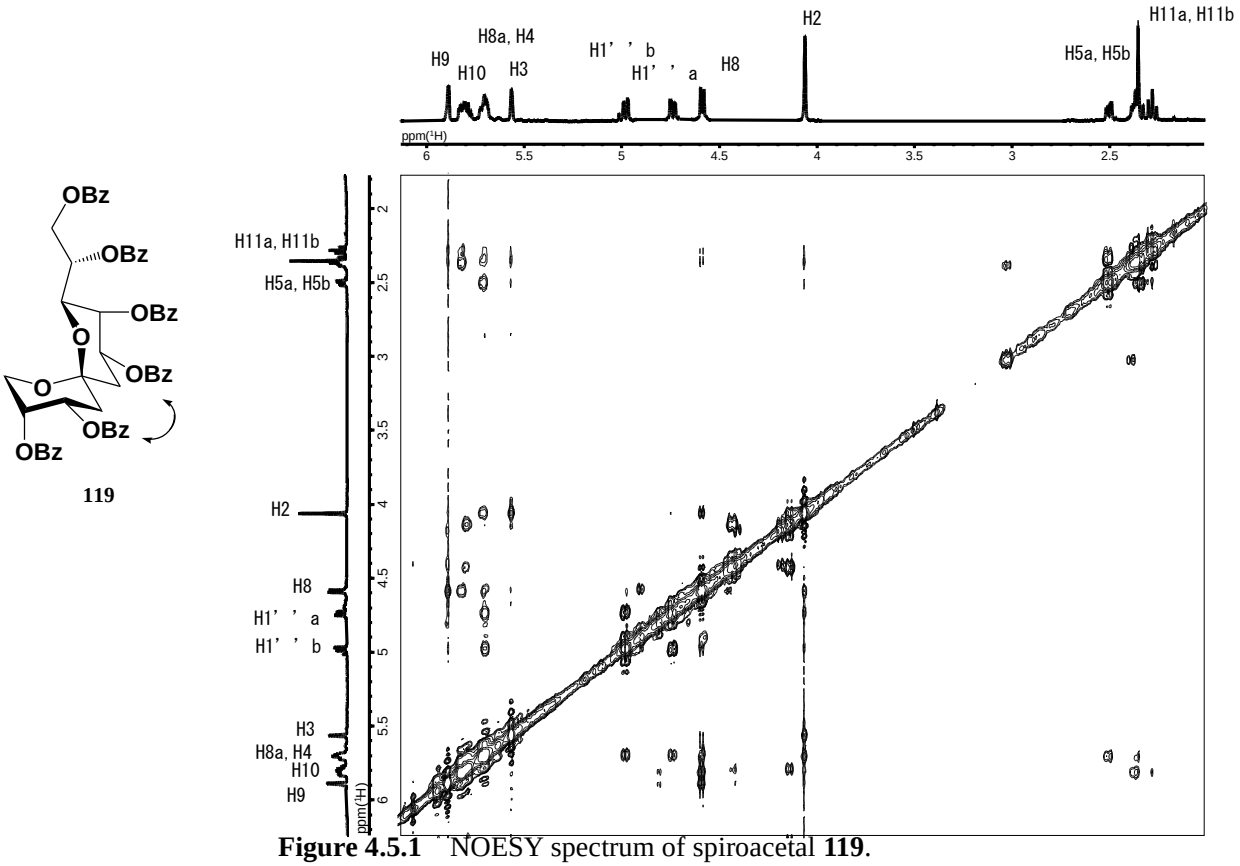
Acid hydrogenolysis of the isopropylidene groups of **110**, followed by benzylation with benzoyl chloride-pyridine, afforded, after chromatographic separation, the non C_2-symmetrical spiroacetal **119** in 42% yield as a single diastereomer (Scheme 4.5.1).



110 **119**

Scheme 4.5.1. Spiroacetalization of 4,6-dideoxy-1,2:8,9-di-*O*-isopropylidene-D-galacto-5nonulose **110**.

Stereochemical assignment of the non C_2-symmetrical spiroacetal **119** was made possible by use of ^{1}H NMR spin-coupling and NOE data. The $^1C_4$ sugar rings of **119** are indicated from H-2 – H-3 and H-8 – H-9 coupling constants of 0 Hz in the ^{1}H NMR spectrum. The NOE enhancements shown in Figure 4.5.1 support this structural assignment. Relatively strong NOE enhancements indicated in Figure 4.5.1 established the proximity between C-5 and C-11 methylene groups in the $^1C_4$ sugar rings, and thence the skeleton of the spiroacetal is (*E*,*E*), suggesting the stereochemistry of the spiroacetalization of non C_2-symmetrical ulose **110** controlled by the same manner that of C_2-symmetrical uloses on acid catalyzed spiroacetalization.

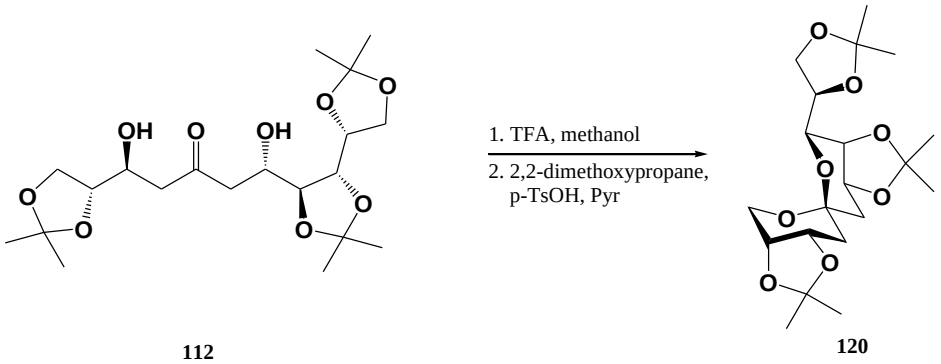


119

Figure 4.5.1 NOESY spectrum of spiroacetal **119**.

4.6 Spiroacetalization of 4,6-dideoxy-1,2:8,9:10,11-tri-*O*-isopropylidene-L-*threo*-D-*tallo*-5-undeculose **112**

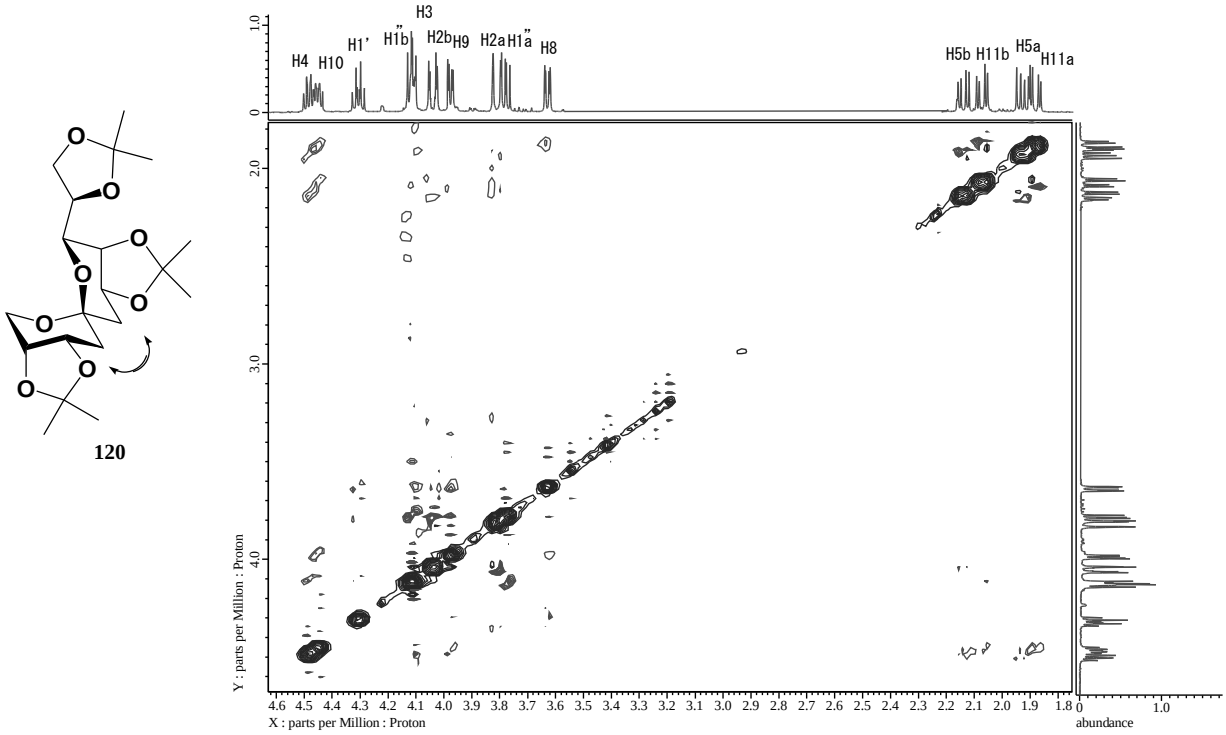
Acid hydrolysis of 4,6-dideoxy-1,2:8,9:10,11-tri-*O*-isopropylidene-L-*threo*-D-*tallo*-5-undeculose **112**, followed by isopropylidene acetalization gave, after chromatographic separation, spiroacetal **120** in triisopropylidene form in 46% yield as a single diastereomer (Figure 4.6.1).



112 **120**

Scheme 4.6.1. Spiroacetalization of 4,6-dideoxy-1,2:8,9:10,11-tri-*O*-isopropylidene-L-*threo*-D-*tallo*-5-undeculose **112**.

The absolute configuration of the newly formed spirocenter C-6 in **120** was assigned by NOESY experiment as shown in Figure 4.6.1. The NOESY spectrum indicated the proximity between C-5 and C-11 methylene protons in $^{1}C_{4}$ rings, and hence the skeleton of spiroacetal **120** is (*E*,*E*).



120

Figure 4.6.1 NOESY spectrum of spiroacetal **120**.

Conclusion

Prolinamido-glycosides catalyzed stereoselective aldol reaction of aldoses in aqueous media, and uloses were stereoselectively synthesized. The diastereofacial selectivities in the aldol reaction were mainly controlled by the stereocenter at the prolyl residue of the catalysts and the conformational disposition of substrate aldoses, and were in general accordance with the Felkin-Anh model, if the conformational disposition of the chiral aldoses had presented a favorable conformation by avoiding eclipsing bulky substituents along C-1 – C-2 bond. L-Prolinamido-glycoside selectively catalyzed *re*-face attack, and it prefers (*2S*)-aldoses. In contrast, D-prolinamido-glycoside catalyzed selective *si*-face attack, and prefers (*2R*)-aldoses.

Prolinamido-glycosides were also capable of catalyzing the aldol reaction of aldoses in unprotedted form that exist predominantly as cyclic hemiacetals or acetals, which nevertheless participate well in those aldol reaction, and hence the prolinamido-glycosides catalyzed aldol reaction has potential for understanding prebiotic routes of carbohydrates.

When two equivalents of *aldehydo*-aldoses in the isopropylidene protected form were used in the aqueous aldol reaction, tandem aldol-aldol reaction was occurred and stereochemically pure higher-uloses were obtained, and the stereoselectivities in the tandem aldol-aldol reaction were also in general accordance with Felkin-Anh model.

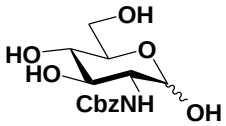
Acidic treatment of those tandem aldol-aldol adducts gave the corresponding spiroacetals, and the stereochemistry of these spiroacetalizations was predetermined by the configuration of the precursors. Configurational and conformational studies on the spiroacetals through X-ray crystallography revealed that avoidance of a 1,3-diaxial interaction was a determining factor of the orientation of hydroxyl groups on pyranose ring in transition states, and was determined the chirality of spiroacetals.

Experimental section

General methods.

NMR spectra were recorded on JEOL JNM-A500 and Varian NB 600 spectrometers. All chemical shifts are quoted in ppm and were referenced to TMS and residual solvent as internal standards. Splitting patterns are designated: s, singlet; d, doublet; dd, doublet of doublets; ddd, doubled doublet of doublets; t, triplet; dt, double triplets; q, quartet; dq, double quartet; m, multiplet. Where appropriate, signal assignments were deduced by COSY, DQCOSY, TOCSY, HSQC, HMQC, HMBC, ROESY, and NOESY experiments. In ^{1}H NMR spectra of products containing two diastereomers, protons at related centers in the isomers that give rise to resolved and assignable signals are distinguished by subscripts 'A' and 'B', otherwise no distinction is made. HPLC analysis was performed using a Shimazu LC-10AD vp using Chiralpack AS-H and AD-H from Daicel Chemical Industries, Ltd. Mass spectra were recorded on JEOL JMS-T100CS spectrometer. Optical rotations were measured on JASCO Model DIP-1000 polarimeter. X-ray crystallographic analysis was preformed on Rigaku AXIS-RAPID Imaging Plate diffractometer with graphite monochromated Mo-Kα radiation. Melting points were determined in open glass capillaries in Yazawa apparatus, and are uncorrected. Evaporations were performed under diminished pressure with a rotary evaporator at 40º C or less unless otherwise stated. Thin-layer chromatography (TLC) was preformed on pre-coated plates of silica gel (DC-Fertigpettenkiesge 160F 256, Merck). Spots were detected by spraying the plate with 10% aqueous H_2SO_4 or molybdic acid followed by heating. Column chromatography was preformed on Wacogel C-200. When mixed solvents were used as eluent, the ratios given are volume / volume except if otherwise stated. Solvents for reactions were dried appropriately when required anhydrous. Dichloromethane, pyridine and DMF were dried by storage over 4Å molecular sieves. All anhydrous reactions were carried out under argon atmospheres.

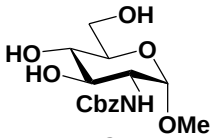
2-Benzyloxycarbonylamino-2-deoxy-D-glucose **2**



2

To a solution of D-glucosamine hydrochloride **1** (50.0 g, 2.32 mmole), $NaHCO_3$ (43.0 g, 5.47 mole) in 20 vol % aqueous methanol (1000 ml) was added benzyloxycarbonyl chloride (42.0 ml, 0.294 mole), and the mixture was stirred at room temperature for 4 h and then resultant precipitate was filtered. The crude **2** was recrystallized from 70 vol % aqueous methanol; yield 54.4 g (76.2%), mp, $[\alpha]_D$, R_f = 0.39 (chloroform-methanol, 4 : 1), The ^1H and ^{13}C NMR spectra and also MS spectrum were identical to the already reported.

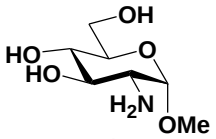
Methyl 2-benzyloxycarbonylamino-2-deoxy-α-D-glucose **3**



3

To a solution of **1** (40.0 g, 0.128 mole) in methanol (800 ml) was added 4N-dioxane HCl (30.4 ml, 255 mmole), and the solution was heated under reflux for 3 h, when TLC indicated that the reaction was completed. Concentration of the reaction mixture afforded a slightly yellowish solid. Recrystallization from 2-propanol gave pure **3** as white needles; yield 34.4 g (82.1%), mp , $[\alpha]_D$, R_f = 0.55 (chloroform-methanol, 4 : 1), The ^1H and ^{13}C NMR spectra and also MS spectrum were identical to the already reported.

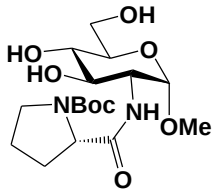
Methyl 2-amino-2-deoxy-α-D-glucose **4**



4

To a solution of **3** (10 g, 30.6 mmole) in methanol (100 ml) was added 10 % Pd / C (5.01 g), and hydrogen was gently bubbled into the stirred mixture. TLC after 3 h showed the consumption of starting material. The mixture was filtered through Hyflo-Super cell, the cake washed with methanol and filtrate evaporated. The residue was purified by recrystallization from 2-propanol to give pure **4** as white needles; yield 5.37 g (91.0%), mp , $[\alpha]_D$, R_f = 0.37 (BAPW), The ^1H and ^{13}C NMR spectra and also MS spectrum were identical to the already reported.

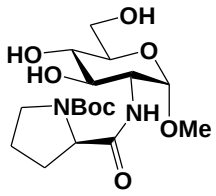
Methyl 2-(*tert*-butoxycarbonyl-L-prolyl)-amido-α-D-glucopyranoside **5**



5

A mixture of *tert*-butoxycarbonyl-L-proline (1.67 g, 7.78 mmole) and EDCI (1.88 g, 9.82 mmole) in dry dichloromethane (16.7 ml) was stirred for 30 min under argon at 0 ºC. A solution of **5** (1.00 g, 5.30 mmole) in methanol (10.0 ml) was added slowly and the mixture was stirred at the same temperature for 1 h, when TLC indicated that the reaction was completed and that one major product had been formed. Concentration of the reaction mixture afforded colorless syrup which was purified by column chromatography over silica gel. The amorphous product crystallized from methanol - IPA solution as colorless crystals, ; yield 1.71 g (82.0%), mp 176-179 ºC, $[\alpha]_D^{27}$ 78º (*c* = 1.0, methanol), R_f = 0.55 (chloroform-methanol, 4 : 1). The ^1H and ^{13}C NMR spectra and also MS spectrum were identical to the already reported.

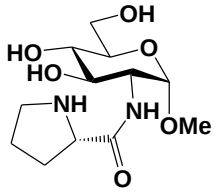
Methyl 2-(*tert*-butoxycarbonyl-D-prolyl)-amido-α-D-glucopyranoside **6**



6

This compound was obtained from Boc-D-proline by an identical procedure used for the L-diastereomer; yield 91.0%. The ^{1}H and ^{13}C NMR spectra and also MS spectrum were identical to the already reported.

Methyl 2-(L-prolyl)-amido-α-D-glucopyranoside **7**



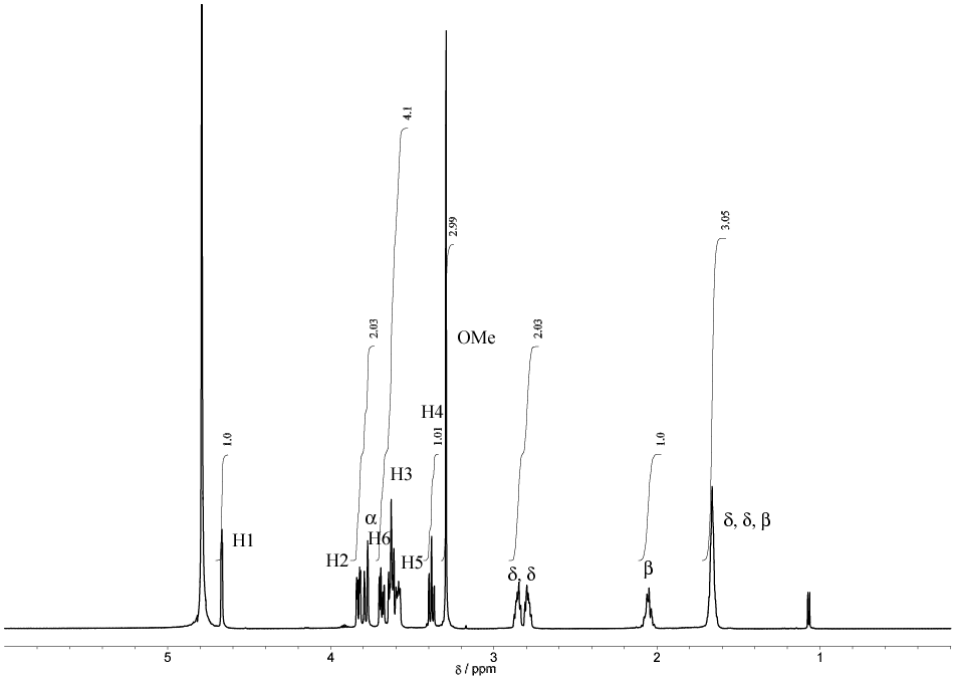
7

To a solution of **5** (100 mg, 0.256 mmole) in methanol (2.00 ml) at room temperature was added 4N-dioxane HCl (0.130 ml, 0.510 mmole), and the solution was kept overnight under stirring. The mixture was neutralized using Amberlite-400 ion exchange resin and filtered. Evaporation gave the product as a colorless syrup, which was recrystallized from 2-propanol; yield 64.7 mg (87.1%), mp 143-144 ºC, $[\alpha]_D^{27}$ 127º (*c* = 1.0, methanol), R_f = 0.32 (BAPW).

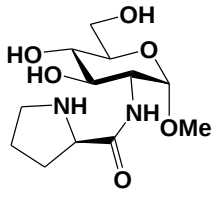
^{1}H NMR (D_2O, 600 MHz), δ 1.52 (m, 3H, prolyl H_β, prolyl $H_{\gamma a}$, $H_{\gamma b}$), 1.91 (m, 1H, prolyl H_β), 2.66 (m, 1H, prolyl H_δ), 2.71 (m, 1H, prolyl H_δ), 3.15 (s, 3H, 1-OMe), 3.24 (t, 1H, $J_{4,5}$ = 10 Hz, H4), 3.45 (dd, 1H, $J_{4,5}$ = 10 Hz, $J_{5,6a}$ = 5.5 Hz, H5), 3.50 (m, 2H, $J_{2,3}$ = 9.7 Hz, H3, H6b), 3.55 (dd, 1H, $J_{5,6a}$ = 5.5 Hz, $J_{6a,6b}$ = 12 Hz, H6a), 3.64 (d, 1H, $J_{H\alpha,H\beta}$ = 12 Hz, prolyl H_α), 3.68 (dd, 1H, $J_{1,2}$ = 3.5 Hz, $J_{2,3}$ = 9.7 Hz, H2), 4.52 (d, 1H, $J_{1,2}$ = 3.5 Hz, H1).

^{13}C NMR (D_2O, 150MHz), δ 27.7 (prolyl C_γ), 33.0 (prolyl C_β), 48.8 (prolyl C_δ), 55.8 (C2), 57.5 (C-OMe), 62.5 (C6), 62.9 (prolyl C_α), 72.3 (C4), 73.5 (C3), 74.1 (C5), 100 (C1), 180 (carbonyl). ESI-TOFMS *m/z*: calcd for $[C_{12}H_{22}N_2O_6+H]^+$, 291.15561; found, 291.16116.

^{1}H NMR spectrum



Methyl 2-(D-prolyl)-amido-α-D-glucopyranoside **8**



8

To a solution of **6** (100 mg, 0.256 mmole) in methanol (2.00 ml) at room temperature was added 4N-dioxane HCl (0.260 ml, 1.02 mmole), and the solution was stirred at room temperature for 3 days. The mixture was neutralized using Amberlite 400 ion exchange resin and filtered. Evaporation gave the product as a colorless syrup, which was recrystallized from 2-propanol; yield

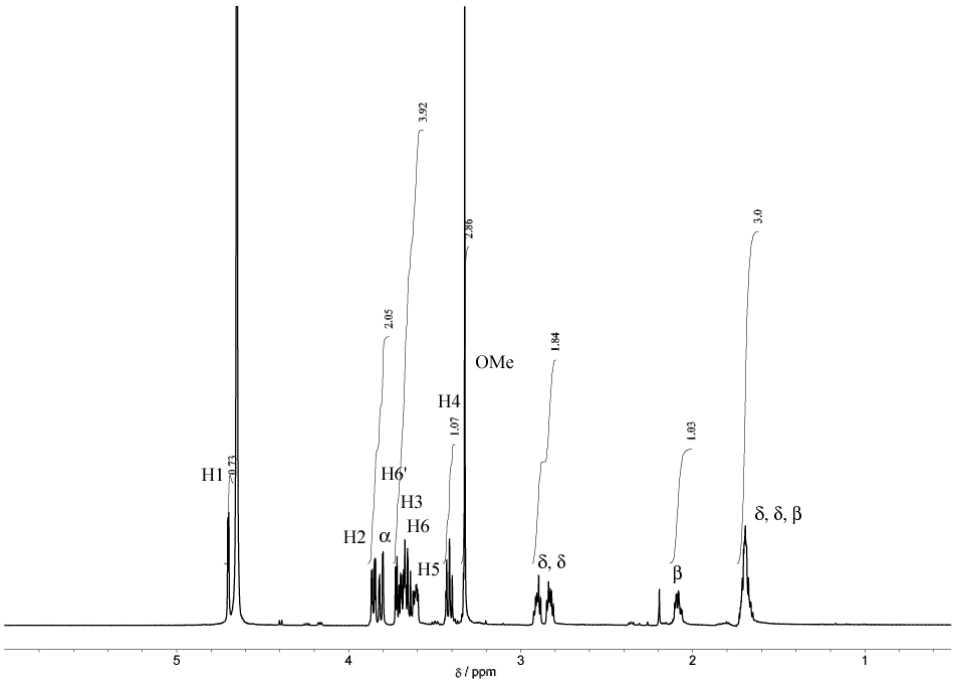
73.8 mg (99.3 %), mp 141-142 ºC, $[\alpha]_D^{27}$ 147º (*c* = 1.0, methanol), R_f = 0.33 (BAPW).

^{1}H NMR (D_2O, 600 MHz), δ 1.69 (m, 3H, prolyl $H_{\beta a}$, prolyl $H_{\gamma a}$, $H_{\gamma b}$), 2.08 (m, 1H, prolyl $H_{\beta b}$), 2.84 (m, 1H, prolyl $H_{\delta a}$), 2.90 (m, 1H, prolyl $H_{\delta b}$), 3.33 (s, 3H, 1-OMe), 3.41 (t, 1H, $J_{3,4}$ = 10 Hz , $J_{4,5}$ = 9.5 Hz, H4), 3.61 (ddd, 1H, $J_{4,5}$ = 9.5 Hz, $J_{5,6a}$ = 5.5 Hz, $J_{5,6b}$ = 2.3 Hz, H5), 3.67 (m, 2H, $J_{2,3}$ = 11 Hz, $J_{3,4}$ = 10 Hz, H3, H6b), 3.72 (dd, 1H, $J_{5,6a}$ = 5.5 Hz, $J_{6a,6b}$ = 12 Hz, H6a), 3.81 (dd, 1H, $J_{H\alpha,H\beta}$ = 12 Hz, prolyl H_α), 3.86 (dd, 1H, $J_{1,2}$ = 3.6 Hz, $J_{2,3}$ = 11 Hz, H2), 4.70 (d, 1H, $J_{1,2}$ = 3.6 Hz, H1).

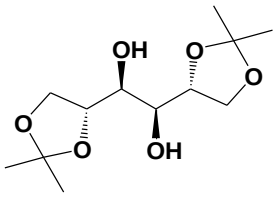
^{13}C NMR (D_2O, 150MHz), δ 28.0 (prolyl C_γ), 33.4 (prolyl C_β), 49.1 (prolyl C_δ), 56.3 (C2), 58.1 (C-OMe), 62.8 (C6), 63.4 (prolyl C_α), 72.7 (C4), 73.8 (C3), 74.5 (C5), 101 (C1), δ 180 (carbonyl).

ESI-TOFMS *m*/*z*: calcd for $[C_{12}H_{22}N_2O_6+H]^+$, 291.15561; found, 291.15053.

^{1}H NMR spectrum

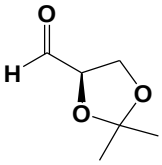


2,3:4,5-Di-*O*-isopropylidene-D-mannitol **9**



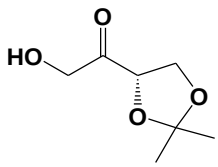
To a solution of D-mannitol (20.0 g, 0.110 mmole) in dry pyridine (80 ml) at room temperature were added 2,2-dimethoxypropane (43.3 ml) and a catalytic amount of *p*-toluenesulphonic acid, and the solution was left overnight under stirring to warm to 100 ºC. Removal of the solvent using toluene for azeotropic distillation of pyridine gave a slightly yellowish solid, which was purified by recrystallization from hexane; yield 21.3 g (73.8%). The properties and spectral data of which were identical to the already reported.

2,3-*O*-Isopropylidene-D-glyceraldehyde **10**



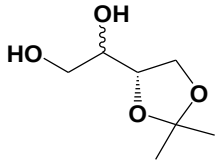
To a suspension of the $NaIO_4$ (5.68g, 26.5 mmole) in dichloromethane (56.8), containing 4 vol % of saturated aqueous $NaHCO_3$ solution, was added **9** (3.48 g, 13.3 mmole). After 30 min, an excess amount of Na_2SO_4 was added to the suspension and the inorganic material was filtered off, the filtrate was concentrated under diminished pressure at 0 ºC. Vacuum distillation gave pure **10**; yield 2.61 g (75.4%). The properties and spectral data of which were identical to the already reported.

3,4-*O*-Isopropylidene-L-glycero-tetrulose **11**



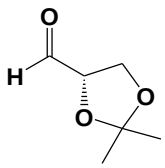
To a stirred solution of L-erythrulose (3.50 g, 29.1 mmole) in dry acetone was added anhydrous $CuSO_4$ (4.09 g, 25.6 mmole) under argon atmosphere, and the suspension was stirred at 40 ºC for 3 days after which time TLC indicated that the reaction was complete and that a major faster moving product had been formed. The inorganic material was filtered off and the filtrate was concentrated to dryness. The crude **11** was used next step without further purification.

Diastereomeric mixture of 1,2-*O*-isopropylidene-1,2,3,4-butan-tetrol **12**



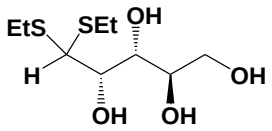
A solution of **11** (5.39 g, 33.7 mmole) in methanol (54.0 ml) was cooled to at 0 ºC and $NaBH_4$ (1.91 g, 50.6 mmole) was added. It was stirred at this temperature for 1 h and then allowed to warm slowly to room temperature. The excess of $NaBH_4$ was decomposed by dropwise addition of acetone until effervescence ceased. The solvent was removed in vacuo, and the residue was purified by silicagel column chromatography, to give pure **12**; yield 5.03 g (92.0%). The properties and spectral data of which were identical to the already reported.

2,3-*O*-Isopropylidene-L-glyceraldehyde **13**



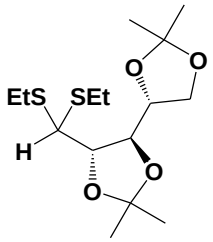
To a suspension of the $NaIO_4$ (5.28 g, 24.6 mmole) in dichloromethane (52.8 ml), containing 4 vol % of saturated aqueous $NaHCO_3$ solution, was added **12** (2.02 g, 12.3 mmole). After 30 min, an excess amount of Na_2SO_4 was added to the suspension and the inorganic material was filtered off, the filtrate was concentrated under diminished pressure at 0 ºC. Vacuum distillation gave pure **13**; yield 240 mg (15.0%). The properties and spectral data of which were identical to the already reported.

D-Arabinose diethyl dithioacetal **14**



D-Arabinose (25 g, 0.150 mole) was dissolved in concentrated HCl (25 ml) and cooled to 0 ºC. Ethanthiol (25 ml) was added and the two layers were vigorously shaken. Copious crystallization occurred after about 15 min. After 30 min, the crude D-arabinose diethyl dithioacetal was recovered by vacuum filtration and then recrystallized from water; yield 29.1 g (85.7%). The properties and spectral data of which were identical to the already reported.

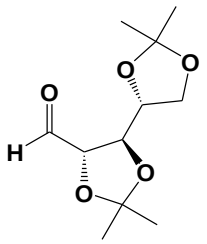
2,3:4,5-Di-*O*-isopropylidene-D-arabinose diethyl dithioacetal **15**



To a suspension of **14** (20.0 g, 88.4 mmole) in dry acetone (200 ml) was added 5.00 ml of concentrated H_2SO_4. The mixture was stirred overnight at room temperature, neutralized with aqueous ammonia, filtered, and the filtrate

evaporated to dryness. The residue was extracted with dichloromethane, which was washed with water, dried (Na_2SO_4), filtered, and then evaporated to slightly brown syrup that was purified by silica gal column chromatography to afford pure **15**; yield 18.9 g (63.5%). The properties and spectral data of which were identical to the already reported.

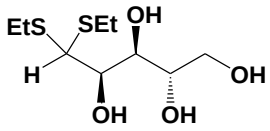
2,3:4,5-Di-*O*-isopropylidene-*aldehydo*-D-arabinose **16**



The 2,3:4,5-di-*O*-isopropylidene-D-arabinose diethyl dithioacetal **15** (7.20 g, 23.5 mmole) was dissolved in acetone (144 ml) and then to the stirred mixture of HgO (yellow, 14.2 g, 65.7 mmole),

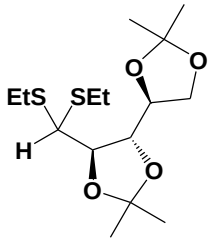
HgCl (14.0 g, 51.7 mmole), and water (ml) were added in succession. After heating for 2h at 56 ºC the mixture was dried (Na_2SO_4), and filtered. The resultant mixture was evaporated to dryness, filtered again, extracted with dichloromethane, washed with 5 wt % NaI solution (ml), filtered, and then washed twice with water. Evaporation gave slightly yellowish syrup, which was purified by vacuum distillation to give pure **16**; yield 1.91g (35.1%). The properties and spectral data of which were identical to the already reported.

L-Arabinose diethyl dithioacetal **17**



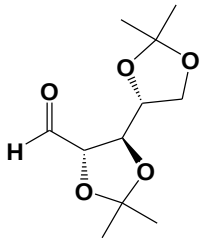
L-Arabinose diethyl dithioacetal was prepared exactly as described for the analogue of L-enantiomer; yield 80.1%. The properties and spectral data of which were identical to the already reported.

2,3:4,5-Di-*O*-isopropylidene-L-arabinose diethyl dithioacetal **18**



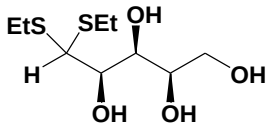
2,3:4,5-Di-*O*-isopropylidene-L-arabinose diethyl dithioacetal was prepared exactly as described for the analogue of L-enantiomer; yield 69.1%. The properties and spectral data of which were identical to the already reported.

2,3:4,5-Di-*O*-isopropylidene-*aldehydo*-L-arabinose **19**



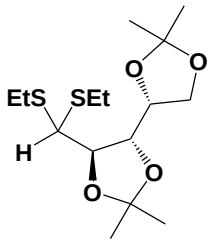
2,3:4,5-Di-*O*-isopropylidene-*aldehydo*-L-arabinose **19** was prepared exactly as described for the analogue of D-enantiomer; yield 66.1%. The properties and spectral data of which were identical to the already reported.

D-Xylose diethyl dithioacetal **20**



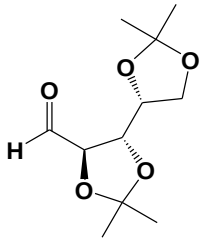
D-Xylose (25 g, 0.150mole) was dissolved in concentrated HCl (25 ml) and cooled to 0 ºC. Ethanthiol (25 ml) was added and the two layers were vigorously shaken. After 30 min, TLC indicated that the reaction was complete and that a major faster moving product had been formed. The mixture was diluted with methanol, basic $PbCO_3$ was added, and the suspension was kept overnight under stirring and warming to room temperature. The mixture was filtered through Hyflo-super cell. The solvent was removed, and the residue was purified by recrystallization from ethanol; yield 31.1 g (91.7%). The properties and spectral data of which were identical to the already reported.

2,3:4,5-Di-*O*-isopropylidene-D-xylose diethyl dithioacetal **21**



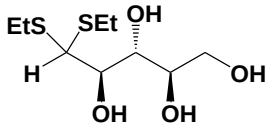
2,3:4,5-Di-*O*-isopropylidene-D-xylose diethyl dithioacetal **21** was prepared as described for the *arabino*-analogue; yield 69.9%. The properties and spectral data of which were identical to the already reported.

2,3:4,5-Di-*O*-isopropylidene-*aldehydo*- D-xylose **22**



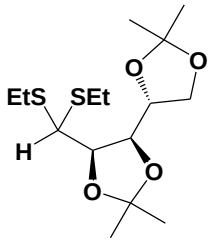
2,3:4,5-Di-*O*-isopropylidene-*aldehydo*-D-xylose **22** was prepared as described for the *arabino*-analogue; yield 46.5%. The properties and spectral data of which were identical to the already reported.

D-Ribose diethyl dithioacetal **23**



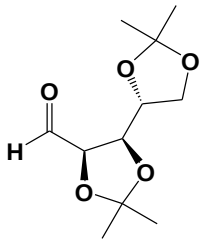
D-Ribose diethyl dithioacetal **23** was prepared as described for the *xylo*-analogue; yield 88.3%. The properties and spectral data of which were identical to the already reported.

2,3:4,5-Di-*O*-isopropylidene-D-ribose diethyl dithioacetal **24**



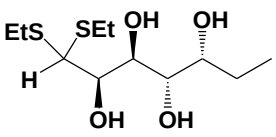
2,3:4,5-Di-*O*-isopropylidene-D-xylose diethyl dithioacetal **24** was prepared as described for the *xylo*-analogue; yield 71.3%. The properties and spectral data of which were identical to the already reported.

2,3:4,5-Di-*O*-isopropylidene-*aldehydo* -D-ribose **25**



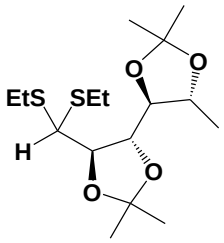
2,3:4,5-Di-*O*-isopropylidene-*aldehydo*-D-ribose **25** was prepared as described for the *arabino*-analogue; yield 40.7%. The properties and spectral data of which were identical to the already reported.

D-Fucose diethyl dithioacetal **26**



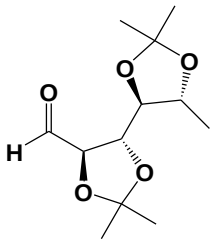
D-Fucose diethyl dithioacetal **26** was prepared as described for the *ribo*-analogue; yield 80.9%. The properties and spectral data of which were identical to the already reported.

2,3:4,5-Di-*O*-isopropylidene-D-fucose diethyl dithioacetal **27**



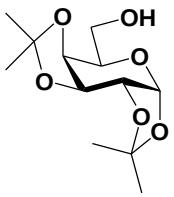
2,3:4,5-Di-*O*-isopropylidene-D-fucose diethyl dithioacetal **27** was prepared as described for the *ribo*-analogue; yield 79.2%. The properties and spectral data of which were identical to the already reported.

2,3:4,5-Di-*O*-isopropylidene-D-fucose **28**



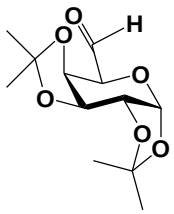
2,3:4,5-Di-*O*-isopropylidene-*aldehydo*-D-fucose **28** was prepared as described for the *ribo*-analogue; yield 39.4%. The properties and spectral data of which were identical to the already reported.

1,2:3,4-Di-*O*-isopropylidene-α-D-*galacto*pyranose **29**



To a stirred solution of D-galactose (5.01 g, 27.8 mmole) in dry acetone (50.0 ml) were added 2,2-dimethoxypropane (10.0 ml), a catalytic amount of H_2SO_4 acid and anhydrous zinc chloride (6.04 g), and the solution was left overnight under stirring at ambient temperature. The solvents were removed by evaporation, and the residue was dissolved in ethyl acetate, washed with water, dried (Na_2SO_4), filtered, and concentrated under vacuo. The crude product was purified by silica gel column chromatography (chloroform-acetone, 10 : 1) to give 1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*pyranose **29**; yield 4.51 g (62.3%). The properties and spectral data of which were identical to the already reported.

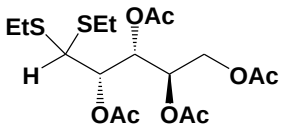
1,2:3,4-Di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose **30**



To a stirred solution of PDC (3.96 g) in dichloromethane (45 ml) were added acetic anhydride (5.7 ml), DMF (11.0 ml), and dichloromethane solution of **29** (4.51 g / 20ml), and the solution was stirred at reflux temperature for two hours. After which time, the solution was poured into 450 ml of toluene, and then filtered through Hyflo-super cell. Then the solvent was evaporated to oil which was extracted with successive portions of dichloromethane, and again filtered. The filtrate was

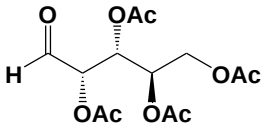
washed with saturated $NaHCO_3$ aq., water, and brine and then dried ($NaSO_4$). Evaporation afforded crude X as a slightly yellowish oil, which was purified by high-vacuum distillation to give pure **30** as a colorless oil (4.01 g, 88.9 %). The properties and spectral data of which were identical to the already reported.

2,3,4,5-Tetra-*O*-acetyl-D-arabinose diethyl dithioacetal **31**



D-Arabinose diethyl dithioacetal **14** (20.0 g, 88.4 mmole) was dissolved in pyridine (200 ml), and Ac_2O (100 ml) was added. The mixture was stirred at ambient temperature for 24 h. The solvents were removed by evaporation, and the residue was dissolved in ethyl acetate, washed with water, dried (Na_2SO_4), filtered, and concentrated under vacuo. The crude product was purified by silica gel column chromatography (eluent) to give 2,3,4,5-tetra-*O*-acetyl-D-arabinose diethyl dithioacetal **31**; yield 34.3 g (91.4%). The properties and spectral data of which were identical to the already reported.

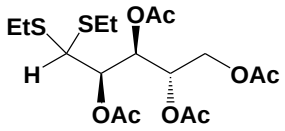
2,3,4,5-Tetra-*O*-acetyl-*aldehydo*-D-arabinose **32**



The 2,3,4,5-Tetra-*O*-acetyl-*aldehydo*-D-arabinose **31** (100 mg, 0.236 mmole) was dissolved in acetone (2.00 ml) and then to the stirred mixture of HgO (yellow, 142 mg, 0.660 mmole), HgCl (141 mg, 0.518 mmole), and water (50 μl) were added in succession. After heating for 2h at 56 ºC

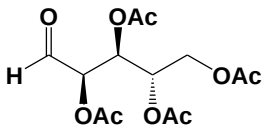
the mixture was dried (Na_2SO_4), and filtered. The resultant mixture was evaporated to dryness, filtered again, extracted with dichloromethane, washed with 5 wt % NaI solution (2.00 ml), filtered, and then washed twice with water. Evaporation gave slightly yellowish crystals, which were recrystallized from ethanol to give pure **32** (61.6 mg, 69.5%). The properties and spectral data of which were identical to the already reported.

2,3,4,5-Tetra-*O*-acetyl-L-arabinose diethyl dithioacetal **33**



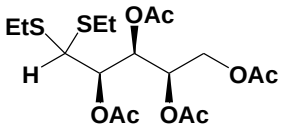
2,3,4,5-Tetra-*O*-acetyl-D-arabinose diethyl dithioacetal **33** was prepared exactly as described for the analogue of D-enantiomer; yield 89.2%. The properties and spectral data of which were identical to the already reported.

2,3,4,5-Tetra-*O*-acetyl-*aldehydo*-L-arabinose **34**



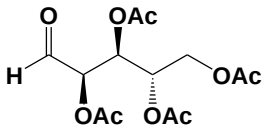
2,3,4,5-Tetra-*O*-acetyl-*aldehydo*-L-arabinose **34** was prepared exactly as described for the analogue of D-enantiomer; yield 70.3%. The properties and spectral data of which were identical to the already reported.

2,3,4,5-Tetra-*O*-acetyl-D-xylose diethyl dithioacetal **37**



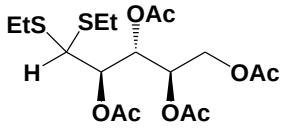
2,3,4,5-Tetra-*O*-acetyl-D-xylose diethyl dithioacetal **37** was prepared as described for the *arabino*-analogue; yield 86.1%. The properties and spectral data of which were identical to the already reported.

2,3,4,5-Tetra-*O*-acetyl-*aldehydo*-D-xylose **38**



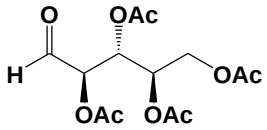
2,3,4,5-Tetra-*O*-acetyl-*aldehydo*-D-xylose **38** was prepared as described for the *arabino*-analogue; yield 72.2%. The properties and spectral data of which were identical to the already reported.

2,3,4,5-Tetra-*O*-acetyl-D-ribose diethyl dithioacetal **35**



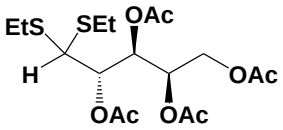
2,3,4,5-Tetra-*O*-acetyl-D-ribose diethyl dithioacetal **35** was prepared as described for the *arabino*-analogue; yield 79.2%. The properties and spectral data of which were identical to the already reported.

2,3,4,5-Tetra-*O*-acetyl-*aldehydo*-D-ribose **36**



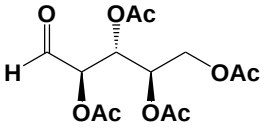
2,3,4,5-Tetra-*O*-acetyl-*aldehydo*-D-ribose **36** was prepared as described for the *arabino*-analogue; yield 66.4%. The properties and spectral data of which were identical to the already reported.

2,3,4,5-Tetra-*O*-acetyl-D-lyxose diethyl dithioacetal **40**



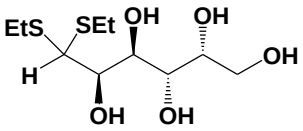
2,3,4,5-Tetra-*O*-acetyl-D-lyxose diethyl dithioacetal **40** was prepared as described for the *arabino*-analogue; yield 92.5%. The properties and spectral data of which were identical to the already reported.

2,3,4,5-Tetra-*O*-acetyl-*aldehydo*-D-lyxose **41**



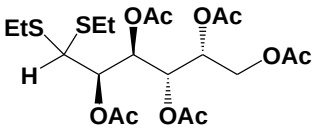
2,3,4,5-Tetra-*O*-acetyl-*aldehydo*-D-lyxose **41** was prepared as described for the *arabino*-analogue; yield 68.4%. The properties and spectral data of which were identical to the already reported.

D-Galactose diethyl dithioacetal **42**



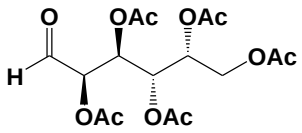
D-Galactose (25 g, 0.139 mmole) was dissolved in concentrated HCl (25 ml) and cooled to 0 ºC. Ethanthiol (25 ml) was added and the two layers were vigorously shaken. After 30 min, TLC indicated that the reaction was complete and that a major faster moving product had been formed. The mixture was diluted with methanol, basic $PbCO_3$ was added, and the suspension was kept overnight under stirring and warming to room temperature. The mixture was filtered through Hyflo-super cell. The solvent was removed, and the residue was purified by recrystallization from ethanol; yield 33.5 g (84.1%). The properties and spectral data of which were identical to the already reported.

2,3,4,5,6-Penta-*O*-acetyl-D-galactose diethyl dithioacetal **43**



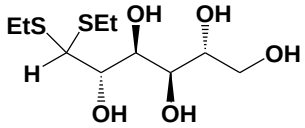
D-Galactose diethyl dithioacetal **42** (1.03 g, 3.60 mmole) was dissolved in pyridine (10.0 ml), and Ac_2O (5.00 ml) was added. The mixture was stirred at ambient temperature for 24 h. The solvents were removed by evaporation, and the residue was dissolved in ethyl acetate, washed with water, dried (Na_2SO_4), filtered, and concentrated under vacuo. The crude product was purified by silica gel column chromatography (chloroform-acetone, 10 : 1) to give 2,3,4,5-tetra-*O*-acetyl-D-arabinose diethyl dithioacetal **43**; yield 1.89 g (92.4%). The properties and spectral data of which were identical to the already reported.

2,3,4,5,6-Penta-*O*-acetyl-*aldehydo*-D-galactose **44**



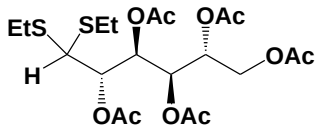
2,3,4,5,6-Penta-*O*-acetyl-D-galactose diethyl dithioacetal **43** (500 mg, 0.840 mmole) was dissolved in acetone (4.00 ml) and then to the stirred mixture of $CdCO_3$ (900 mg, 5.22 mmole), HgCl (900 mg, 3.31 mmole), and water (40 μl) were added in succession. After heating for 2h at 56 ºC the mixture was dried (Na_2SO_4), and filtered. The resultant mixture was evaporated to dryness, filtered again, extracted with dichloromethane, washed with 5 wt % NaI solution (4.00 ml), filtered, and then washed twice with water. Evaporation gave slightly yellowish crystals, which were recrystallized from ethanol to give pure **44** (301 mg, 91.8%). The properties and spectral data of which were identical to the already reported.

D-Mannose diethyl dithioacetal **45**



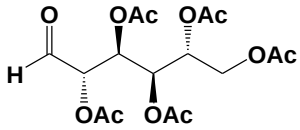
D-Mannose diethyl dithioacetal **45** was prepared as described for the *galacto*-analogue; yield 72.5%. The properties and spectral data of which were identical to the already reported.

2,3,4,5,6-Penta-*O*-acetyl-D-mannose diethyl dithioacetal **46**



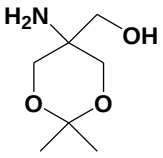
D-Mannose diethyl dithioacetal **46** was prepared as described for the *galacto*-analogue; yield 89.9%. The properties and spectral data of which were identical to the already reported.

2,3,4,5,6-Penta-*O*-acetyl-*aldehydo*-D-mannose **47**



2,3,4,5,6-Penta-*O*-acetyl-*aldehydo*-D-mannose **47** was prepared as described for the *galacto*-analogue; yield 71.4%. The properties and spectral data of which were identical to the already reported.

Isopropylidene-tris(hydroxymethyl)aminomethane **48**

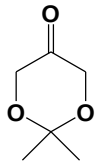


48

To a solution of tris(hydroxymethyl)aminomethane hydrochloride (10.0 g, 63.5 mmole) in dry DMF was added *p*-TsOH (1.02 g, 5.30 mmole), and 2,2-dimethoxypropane (8.50 ml) was added and the mixture was stirred at room temperature. After 24 h, the solution made neutral by stirring for 15 min with triethylamine. Evaporation afforded **48** as a slightly yellow solid. Recrystallization from toluene gave pure **48** (5.13g, 98.0%). The properties and spectral data of which were identical

to the already reported.

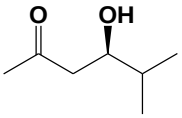
2,2-dimethyl-1,3-dioxane-5-one **49**

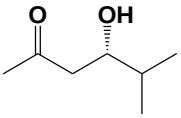


49

To an ice-cold solution of **48** (5.13 g, 32.0 mmole) in dichloromethane (40 ml) was added an aqueous solution of $NaIO_4$ (6.84 g, 32.0 mole, 70 ml in water) in one portion. After stirring for 30 min at 0 ˚C, the solution was partitioned between dichloromethane and water. The aqueous layer was extracted twice with dichloromethane (50 ml), and the combined organic layer was washed with saturated $NaHCO_3$, and brine and then dried (Na_2SO_4). Evaporation at 0 ˚C afforded **49** as a yellow syrup. Crude **49** was purified by vacuum distillation to give pure **49** (3.55g, 85.2%). The properties and spectral data of which were identical to the already reported.

(*R*)- and (*S*)-4-hydroxy-5-methyl-2-haxanones **50** and **51**

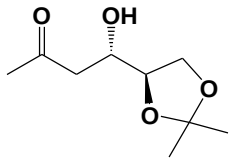




To a solution of **7** or **8** (15.9 mg, 0.0550mmole) in water were added acetone (1.33 ml, 1.84 mmole) and isobutyraldehyde (50 μl, 0.550 mmole), and the solution was stirred at room temperature for 30 min. The excess of acetone was removed by evaporation, and the residue was

dissolved in ethyl acetate (1.40 ml). The resulting solution was washed with water. The organic layer was dried ($NaSO_4$), and the solvent removed to an oil. The crude product was chromatographied over silica gel (dichloromethane-acetone, 10 : 1) to give pure **50** or **51**. The properties and spectral data of which were identical to the already reported.

1.3-Dideoxy-5,6-*O*-isopropylidene-D-*erythro*-hexulose **53**



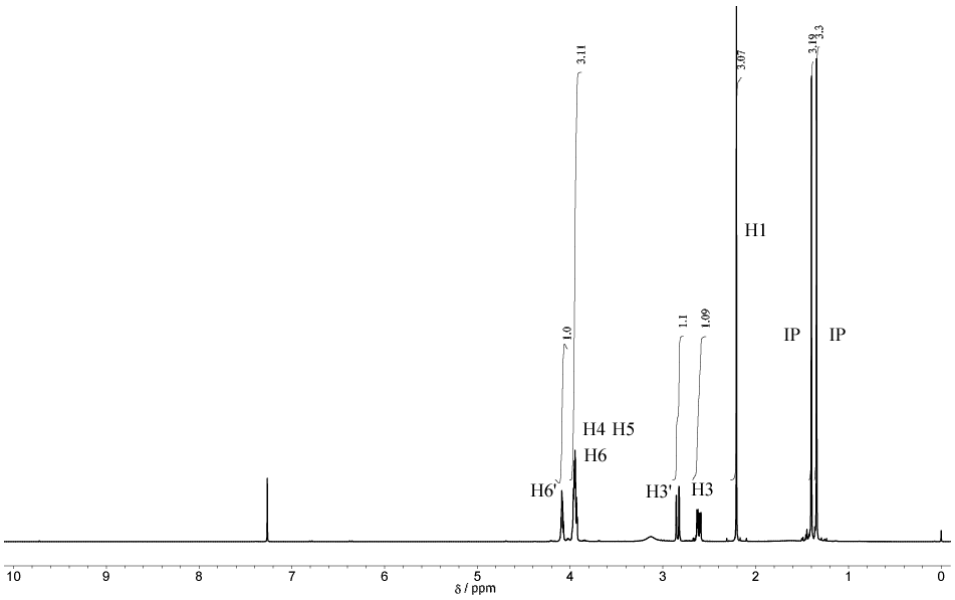
To a solution of **8** (11.7 mg, 0.0403 mmole) in water (72.3 μl) were added acetone (0.980 ml, 12.1 mmole) and 2.3-*O*-isopropylidene-D-glyceraldehyde **10** (50 μl, 0.402 mmole), and the solution was stirred at room temperature for 1 h. The excess of acetone was removed by evaporation, and the residue was dissolved in ethyl acetate (0.70 ml). The resulting solution was washed with water. The organic layer was dried ($NaSO_4$), and the solvent removed to an oil. The crude product was chromatographied over silica gel (dichloromethane-acetone, 10 : 1) to give pure **53**; yield 66.5 mg (87.8%), $[\alpha]_D^{27}$ -23.0º (*c* = 1.0, chloroform), R_f = 0.54 (dichloromethane-acetone, 10 : 1).

^{1}H NMR ($CDCl_3$, 600 MHz), δ 1.34 (s, 3H, IP), 1.40 (s, 3H, IP), 2.21 (s, 3H, 1-CH_3), 2.61 (dd, 1H, $J_{3,4}$ = 8.2 Hz, $J_{3a,3b}$ = 17.5 Hz, H3a), 2.84 (dd, 1H, $J_{3,4}$ = 2.2 Hz, $J_{3a,3b}$ = 17.5 Hz, H3b), 3.97 (m, 3H, H4, H5, H6a), 4.09 (m, 1H, H6b).

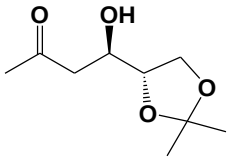
^{13}C NMR ($CDCl_3$, 150MHz) δ 25.1 (IP), 26.6 (IP), 30.7 (C1), 46.2 (C3), 66.8 (C6), 69.0, δ 73.4, δ 109, δ 209

ESI-TOFMS *m*/*z*: calcd for $[C_9H_{16}O_4+Na]^+$, 211.09463; found, 211.09515.

^{1}H NMR spectrum



1.3-Dideoxy-5,6-*O*-isopropylidene-L-*erythro*-hexulose **54**



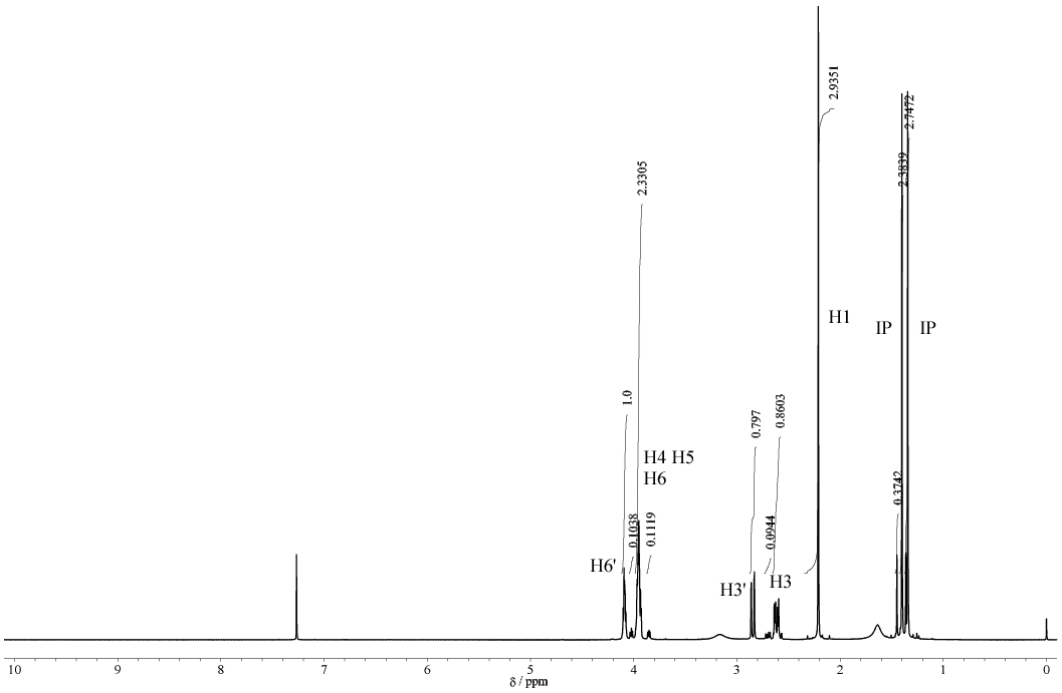
To a solution of **7** (11.7 mg, 0.0403 mmole) in water (72.3 μl) were added acetone (0.980 ml, 12.1 mmole) and 2.3-*O*-isopropylidene-L-glyceraldehyde **13** (50 μl, 0.402 mmole), and the solution was stirred at room temperature for 1 h. The excess of acetone was removed by evaporation, and the residue was dissolved in ethyl acetate (0.70 ml). The resulting solution was washed with water. The organic layer was dried ($NaSO_4$), and the solvent removed to an oil. The crude product was chromatographied over silica gel (dichloromethane-acetone, 10 : 1) to give pure **54**; yield 61.7 mg (81.4%), $[\alpha]_D^{27}$ 23.0º (*c* = 1.0, chloroform), R_f = 0.54 (dichloromethane-acetone, 10 : 1).

^{1}H NMR ($CDCl_3$, 600 MHz), δ 1.34 (s, 3H, IP), 1.40 (s, 3H, IP), 2.21 (s, 3H, 1-CH_3), 2.61 (dd, 1H, $J_{3,4}$ = 8.2 Hz, $J_{3a,3b}$ = 17.5 Hz, H3a), 2.84 (dd, 1H, $J_{3,4}$ = 2.2 Hz, $J_{3a,3b}$ = 17.5 Hz, H3b), 3.97 (m, 3H, H4, H5, H6a), 4.09 (m, 1H, H6b).

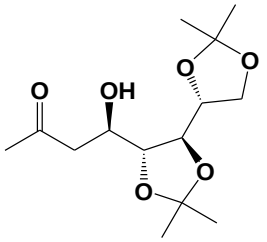
^{13}C NMR ($CDCl_3$, 150MHz) δ 25.1 (IP), 26.6 (IP), 30.7 (C1), 46.2 (C3), 66.8 (C6), 69.0, 73.4, 109, 209

ESI-TOFMS *m*/*z*: calcd for $[C_9H_{16}O_4+Na]^+$, 211.09463; found, 211.09435.

^{1}H NMR spectrum



1.3-Dideoxy-5,6:7,8-*O*-isopropylidene-D-*glycero*-D-*ribo*-octulose **56**

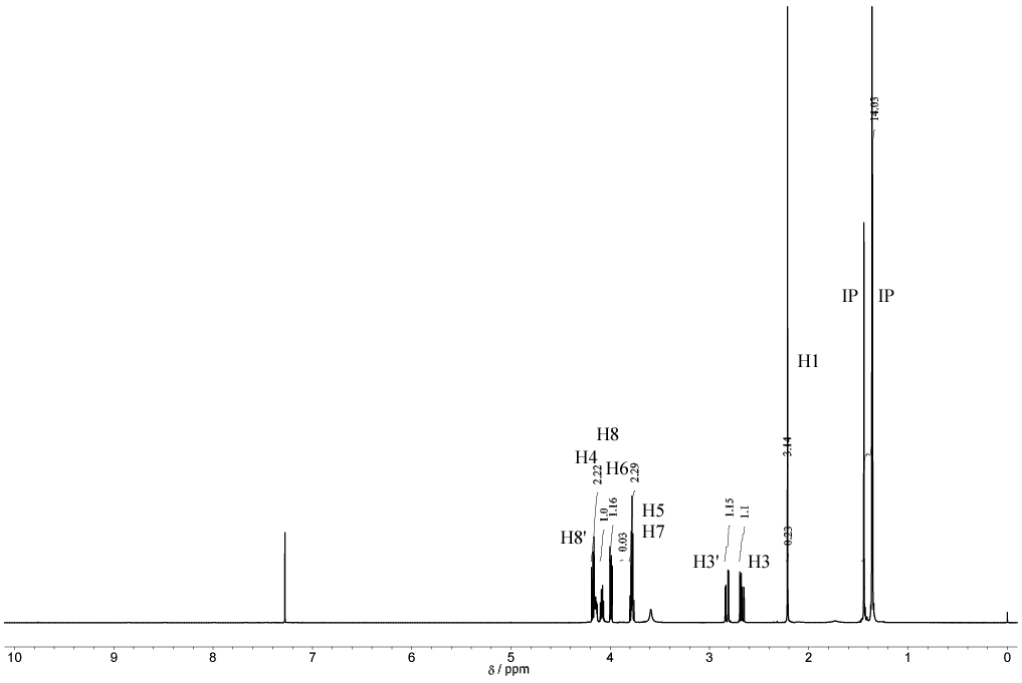


To a stirred solution of freshly distilled 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-arabinose **16** (50 mg, 0.22 mmole) in acetone (0.53 ml, 6.5 mmole) was added 6.3 mg (0.0217 mole) of

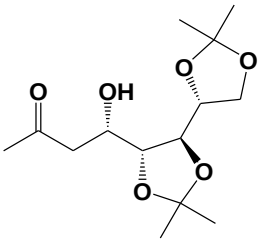
L-prolinamido-glycoside **7** in ml of distilled water (0.04 ml), and the solution was stirred at ambient temperature for 1h, when TLC (chloroform-acetone, 10 : 1) indicated that the reaction was complete. The mixture was concentrated to remove excess amount of acetone, and the residue was diluted with ethyl acetate, washed with water, dried ($NaSO_4$), and concentrated to dryness. The crude product was then purified by column chromatography on silica gel (chloroform-acetone, 10 : 1), to give pure **56** as a colorless syrup; yield 56 mg (89%), $[\alpha]_D^{27}$ +13.5° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$, 600 MHz), δ 1.36 (s, 3H, IP), 1.36 (s, 6H, IP), 1.44 (s, 3H, IP), 2.21 (s, 3H,1-CH_3), 2.67 (dd, 1H, $J_{3,4}$ = 8.8 Hz, $J_{3a,3b}$ = 16.6 Hz, H3a), 2.82 (dd, 1H, $J_{3,4}$ = 3.4 Hz, $J_{3a,3b}$ = 16.6 Hz, H3b), 3.78 (m, 2H, H5, H7), 3.99 (dd, 1H, $J_{7,8a}$ = 3.2 Hz, $J_{8a,8b}$ = 8.7 Hz, H8a) , 4.08 (ddd, 1H, $J_{5,6}$ = 2.1 Hz, $J_{6,7}$ = 11.8 Hz, H6), 4.15 (m, 1H, $J_{3a,4}$ = 8.8 Hz, $J_{3b,4}$ = 3.4 Hz, H4), 4.18 (dd, 1H, $J_{7,8b}$ = 6.2 Hz, $J_{8a,8b}$ = 8.7 Hz, H8a); ^{13}C NMR ($CDCl_3$, 150MHz) δ 25.1 (IP), 26.3 (IP), 26.8 (IP), 30.9 (C1), 47.0 (C3), 67.6 (C8), 68.7 (C4), 76.3 (C6), 80.6, 82.3, 109 (IP), 110 (IP), 208 (C2).

ESI-TOFMS *m/z*: calcd for $[C_{14}H_{24}O_6+Na]^+$, 311.1465; found, 311.1466.

^{1}H NMR spectrum



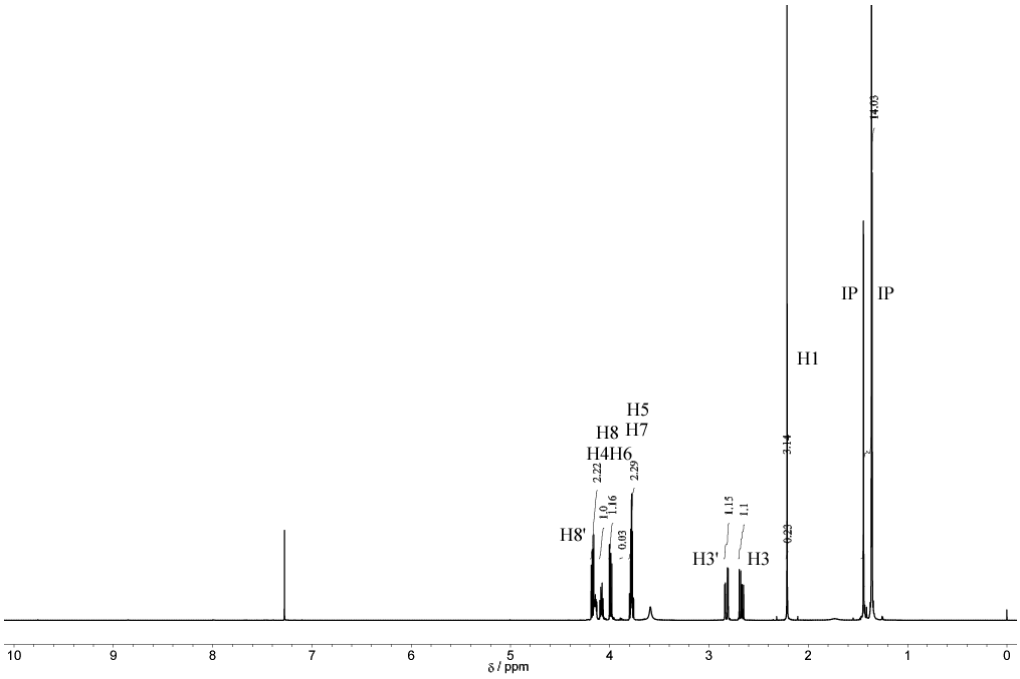
1.3-Dideoxy-5,6:7,8-*O*-isopropylidene-L-*glycero*-L-*ribo*-octulose **57**



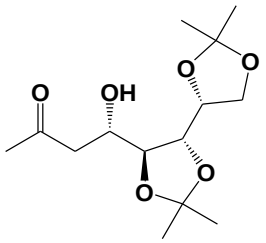
This compound was obtained from 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-L-arabinose **19** by an identical procedure used for the D-enantiomer, $[\alpha]_D^{27}$ -32.0° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$, 600 MHz), δ 1.36 (s, 3H, IP), 1.36 (s, 6H, IP), 1.44 (s, 3H, IP), 2.21 (s, 3H,1-CH_3), 2.67 (dd, 1H, $J_{3,4}$ = 8.8 Hz, $J_{3a,3b}$ = 16.6 Hz, H3a), 2.82 (dd, 1H, $J_{3,4}$ = 3.4 Hz, $J_{3a,3b}$ = 16.6 Hz, H3b), 3.78 (m, 2H, H5, H7), 3.99 (dd, 1H, $J_{7,8a}$ = 3.2 Hz, $J_{8a,8b}$ = 8.7 Hz, H8a) , 4.08 (ddd, 1H, $J_{5,6}$ = 2.1 Hz, $J_{6,7}$ = 11.8 Hz, H6), 4.15 (m, 1H, $J_{3a,4}$ = 8.8 Hz, $J_{3b,4}$ = 3.4 Hz, H4), 4.18 (dd, 1H, $J_{7,8b}$ = 6.2 Hz, $J_{8a,8b}$ = 8.7 Hz, H8a); ^{13}C NMR ($CDCl_3$, 150MHz) δ 25.1 (IP), 26.3 (IP), 26.8 (IP), 30.9 (C1), 47.0 (C3), 67.6 (C8), 68.7 (C4), 76.3 (C6), 80.6, 82.3, 109 (IP), 110 (IP), 208 (C2).

ESI-TOFMS *m*/*z*: calcd for $[C_{14}H_{24}O_6+Na]^+$, 311.1465; found, 311.1479.

^{1}H NMR spectrum



1.3-Dideoxy-5,6:7,8-*O*-isopropylidene-L-*glycero*-L-*ribo*-octulose **60**

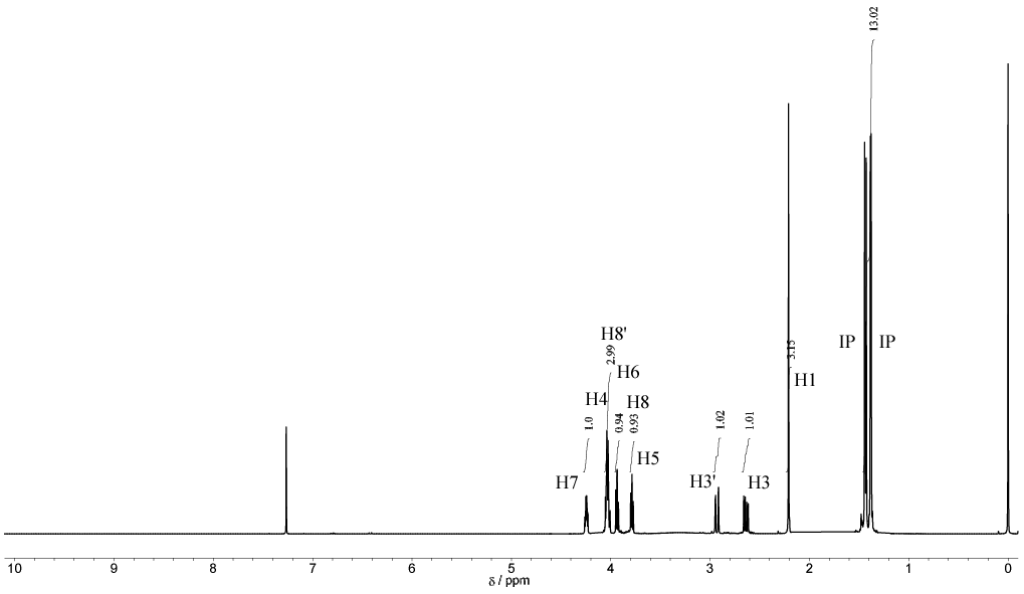


This compound was obtained from 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-xylose **22** by an identical procedure used for the *arabono*-diastereomer; $[\alpha]_D^{27}$ -33.0° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$, 600 MHz), δ 1.36 (s, 3H, IP), 1.38 (s, 3H, IP), 1.43 (s, 3H, IP), 1.44 (s, 3H, IP), 2.21 (s, 3H,1-CH_3), 2.64 (dd, 1H, $J_{3a,4}$ = 9.1 Hz, $J_{3a,3b}$ = 18.0 Hz, H3a), 2.93 (dd, 1H, $J_{3b,4}$ = 1.9 Hz, $J_{3a,3b}$ = 18.0 Hz, H3b), 3.78 (t, 1H, $J_{4,5}$ = 7.9 Hz, $J_{4,6}$ = 7.4 Hz, H5), 3.91 (t, 1H, $J_{7,8a}$ = 7.9 Hz, $J_{8a,8b}$ = 15.7 Hz, H8a) , 4.01 – 4.05 (m, 3H, $J_{3a,4}$ = 9.1 Hz, $J_{4,5}$ = 4.8 Hz, $J_{5,6}$ = 7.4 Hz, $J_{6,7}$ = 6.9 Hz, $J_{7,8b}$ = 4.7 Hz, $J_{8a,8b}$ = 15.7 Hz, H4, H6, H8b), 4.25 (dt, 1H, $J_{6,7}$ = 6.9 Hz, $J_{7,8a}$ = 7.9 Hz, $J_{7,8b}$ = 4.7 Hz, H7); ^{13}C NMR ($CDCl_3$, 150MHz) δ 22.4 (IP), 23.1 (IP), 23.9 (IP), 24.1 (IP), 47.6 (C1), 63.7 (C3), 82.8

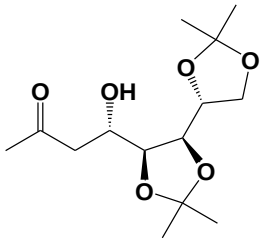
(C8), 86.8, 92.9 (C7), 95.6, 97.2, 127 (IP), 127 (IP), 227 (C2).

ESI-TOFMS *m*/*z*: calcd for $[C_{14}H_{24}O_6+Na]^+$, 311.1465; found, 311.1488.

^{1}H NMR spectrum



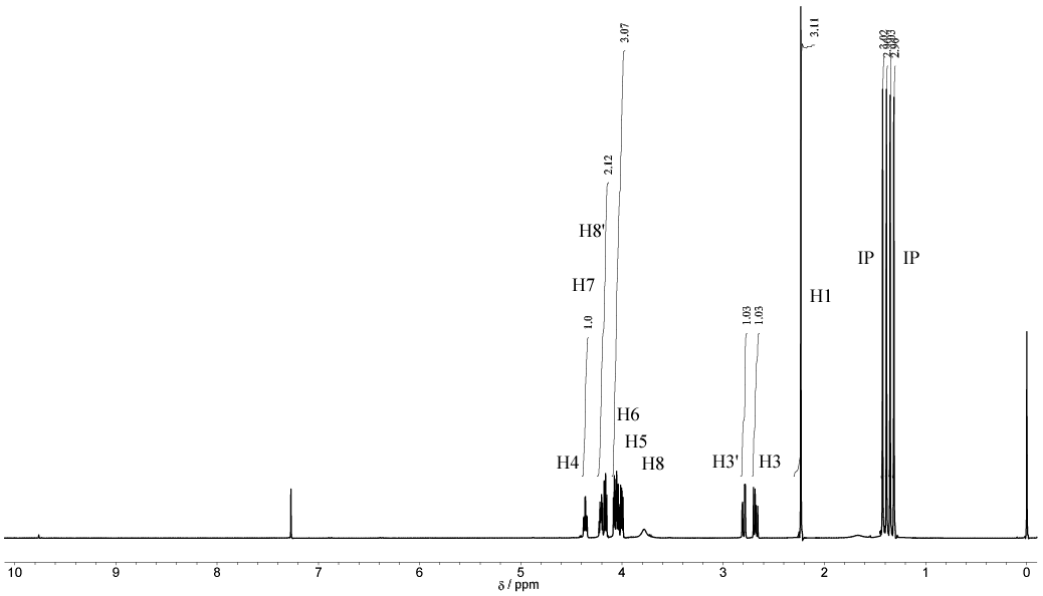
1.3-Dideoxy-5,6:7,8-*O*-isopropylidene-L-*glycero*-L-*ribo*-octulose **62**



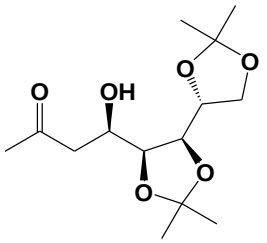
Freshly distilled 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-ribose **25** (100 mg, 0.434 mmole) was dissolved in acetone, and D-prolinamido-glycoside **8** (12.6 mg, 0.0433mole) and distilled water were added. The solution was kept stirring for 3 h at room temperature, after which TLC (chloroform-ethyl acetate, 10 : 1) indicated the formation of an aldol adduct. The reaction mixture was evaporated, and the residue was dissolved in ethyl acetate, washed with water, dried ($NaSO_4$), and concentrated to dryness. The crude product was purified by column chromatography on silica gel (chloroform-ethyl acetate, 10 : 1), to give **62**. the amorphous product was recrystallized from hexane to give needles; yield 51.0 mg (81.0%), $[\alpha]_D^{23.5}$ +37.3° (*c* 1.0, chloroform); mp 57.5 – 58.5 ºC; ^{1}H NMR ($CDCl_3$, 600 MHz), δ 1.31 (s, 3H, IP), 1.35 (s, 3H, IP), 1.39 (s, 3H, IP), 1.42 (s, 3H, IP), 2.23 (s, 3H,1-CH_3), 2.68 (dd, 1H, $J_{3a,4}$ = 9.2 Hz, $J_{3a,3b}$ = 15.9 Hz, H3a), 2.80 (dd, 1H, $J_{3b,4}$ = 2.9 Hz, $J_{3a,3b}$ = 15.9 Hz, H3b), 4.00 (dd, 1H, $J_{7,8a}$ = 5.4 Hz, $J_{8a,8b}$ = 8.7 Hz, H8a), 4.04 (dd, 1H, $J_{4,5}$ = 6.3 Hz, $J_{5,6}$ = 5.6 Hz, H5) , 4.07 (dd, 1H, $J_{5,6}$ = 5.6 Hz, $J_{6,7}$ = 9.2 Hz, H6), 4.15 (dd, 1H, $J_{7,8b}$ = 6.3 Hz, $J_{8a,8b}$ = 8.7 Hz, H8b), 4.21 (dt, 1H, $J_{6,7}$ = 9.2 Hz, $J_{7,8a}$ = 5.4 Hz, $J_{7,8b}$ = 6.3 Hz,H7), 4.36 (dt, 1H, $J_{3a,4}$ = 9.2 Hz, $J_{3b,4}$ = 2.9 Hz, $J_{4,5}$ = 6.3 Hz,H4); ^{13}C NMR ($CDCl_3$, 150MHz) δ 25.3 (IP), 25.4 (IP), 26.5 (IP), 27.9 (IP), 31.2 (C1), 47.9 (C3), 65.9 (C4), 67.9 (C8), 73.1 (C7), 78.5 (C6), 80.0 (C5), 109 (IP), 111 (IP), 207 (C2).

ESI-TOFMS *m*/*z*: calcd for $[C_{14}H_{24}O_6+Na]^+$, 311.1465; found, 311.1472.

^{1}H NMR spectrum



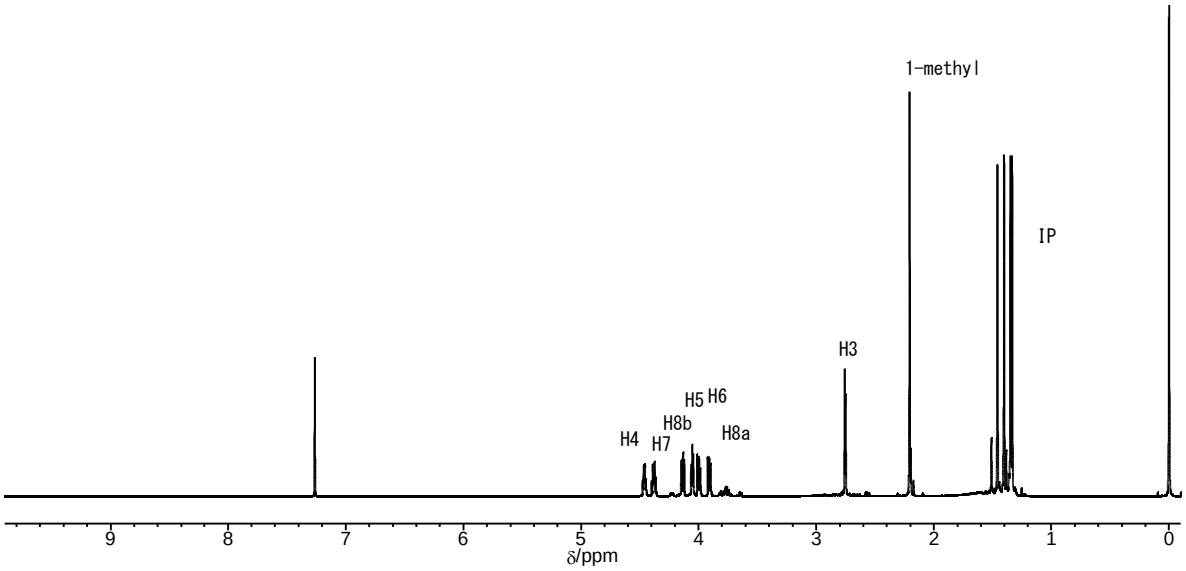
1.3-Dideoxy-5,6:7,8-*O*-isopropylidene-L-*glycero*-L-*ribo*-octulose **63**



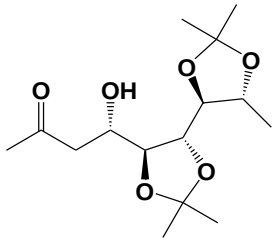
Freshly distilled 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-ribose **25** (50.0 mg, 0.217 mmole) was dissolved in acetone, and L-prolinamido-glycoside **7** (18.9 mg, 0.0650 mmole) and distilled water were added. The solution was kept stirring for 3 h at room temperature, after which TLC (chloroform-ethyl acetate, 10 : 1) indicated the formation of an aldol adduct. The reaction mixture was evaporated, and the residue was dissolved in ethyl acetate, washed with water, dried ($NaSO_4$), and concentrated to dryness. The crude product was purified by column chromatography on silica gel (chloroform-ethyl acetate, 10 : 1), to give **63**. the amorphous product was recrystallized from hexane to give needles; yield 36.5 mg (58.0%), $[\alpha]_D^{23.5}$ +5.18° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$, 600 MHz), δ 1.33 (s, 3H, IP), 1.35 (s, 3H, IP), 1.40 (s, 3H, IP), 1.42 (s, 3H, IP), 2.20 (s,

3H,1-CH_3), 2.75 (d, 1H, $J_{3,4}$ = 6.2 Hz, H3), 3.91 (dd, 1H, $J_{7,8a}$ = 5.7 Hz, $J_{8a,8b}$ = 8.7 Hz, H8a), 4.00 (dd, 1H, $J_{5,6}$ = 4.5 Hz, $J_{6,7}$ = 5.9 Hz, H6) , 4.05 (dd, 1H, $J_{4,5}$ = 5.8 Hz, $J_{5,6}$ = 5.7 Hz, H5), 4.13 (dd, 1H, $J_{7,8b}$ = 6.2 Hz, $J_{8a,8b}$ = 8.7 Hz, H8b), 4.30 (dt, 1H, $J_{6,7}$ = 5.9 Hz, $J_{7,8a}$ = 5.7 Hz, $J_{7,8b}$ = 6.2 Hz,H7), 4.46 (dt, 1H, $J_{3,4}$ = 6.2 Hz, $J_{4,5}$ = 5.8 Hz,H4); ^{13}C NMR ($CDCl_3$, 150MHz) δ 25.2 (IP), 25.4 (IP), 26.8 (IP), 27.4 (IP), 30.7 (C1), 47.7 (C3), 65.7 (C4), 68.2 (C8), 73.3 (C7), 78.2 (C6), 79.4 (C5), 109 (IP), 110 (IP), 208 (C2); ESI-TOFMS *m*/*z*: calcd for $[C_{14}H_{24}O_6+Na]^+$, 311.1465; found, 311.1451.

^{1}H NMR spectrum



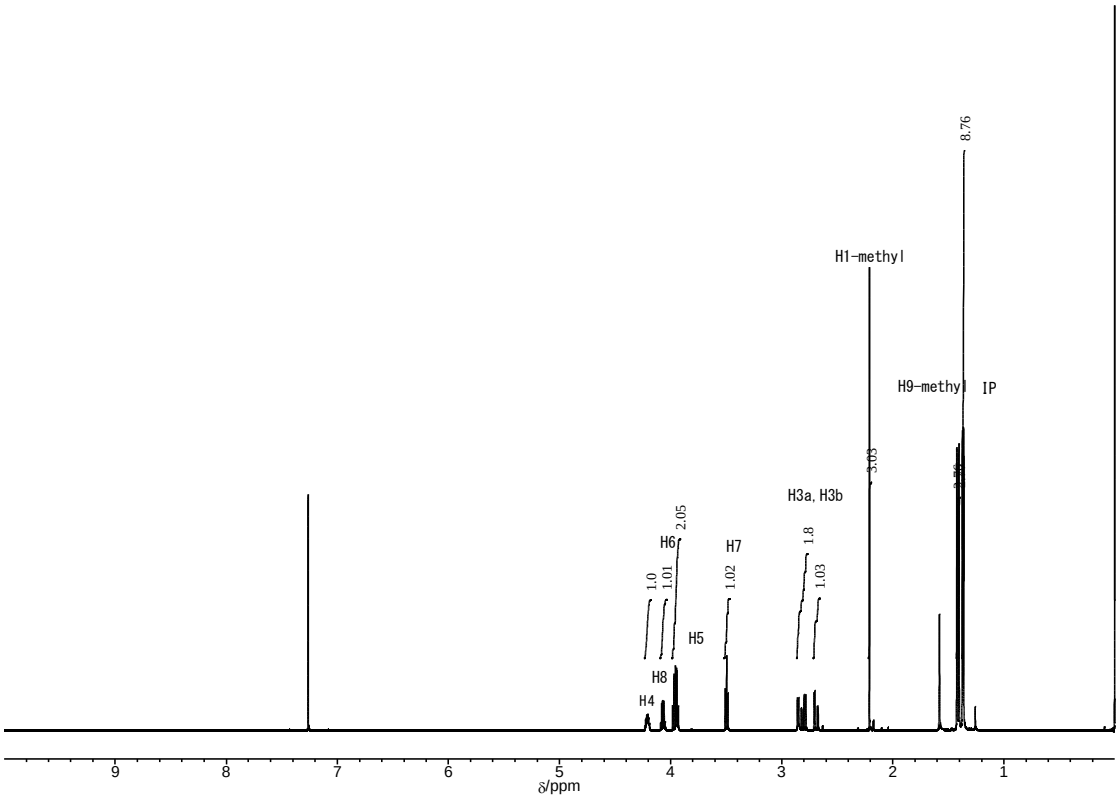
1,3,9-Trideoxy-5,6:7,8-di-*O*-isopropylidene-L-*glycero*-D-*tallo*-nonulose **64**



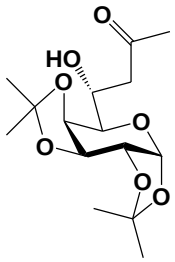
Freshly distilled 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-fucose **28** (50.0 mg, 0.205 mmole) was dissolved in acetone, and D-prolinamido-glycoside **8** (17.8 mg, 0.0614 mmole) and distilled water

were added. The solution was kept stirring for 2 h at room temperature, after which TLC (chloroform-ethyl acetate, 10 : 1) indicated the formation of an aldol adduct. The reaction mixture was evaporated, and the residue was dissolved in ethyl acetate, washed with water, dried ($NaSO_4$), and concentrated to dryness. The crude product was purified by column chromatography on silica gel (chloroform-ethyl acetate, 10 : 1), to give **64** as a syrup. Yield 45.1 mg (74.5%), $[\alpha]_D^{23.5}$ – 1.2° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$, 600 MHz), δ 1.36 (s, 3H, IP), 1.37 (d, 3H, $J_{8,9}$ = 6.0 Hz, H9), 1.37 (s, 3H, IP), 1.40 (s, 3H, IP), 1.42 (s, 3H, IP), 2.21 (s, 3H,1-CH_3), 2.69 (dd, 1H, $J_{3a,4}$ = 3.5 Hz, $J_{3a,3b}$ = 15.1 Hz, H3a), 2.80 (dd, 1H, $J_{3b,4}$ = 7.9 Hz, $J_{3a,3b}$ = 15.1 Hz, H3b), 3.50 (t, 1H, $J_{6,7}$ = 7.9 Hz, H7), 3.94 (dd, 1H, $J_{4,5}$ = 3.0 Hz, $J_{5,6}$ = 7.9 Hz, H5) , 3.97 (t, 1H, $J_{5,6}$ = 7.9 Hz, $J_{6,7}$ = 7.9 Hz, H6), 4.07 (dq, 1H, $J_{7,8}$ = 7.9 Hz, $J_{8,9}$ = 6.0 Hz, H8), 4.36 (ddd, 1H, $J_{3a,4}$ = 3.5 Hz, $J_{3b,4}$ = 7.9 Hz, $J_{4,5}$ = 3.0 Hz,H4); ^{13}C NMR ($CDCl_3$, 150MHz) δ 18.5 (C9), 26.8 (IP), 26.9 (IP), 27.2 (IP), 27.4 (IP), 30.7 (C1), 47.6 (C3), 66.8 (C4), 76.9 (C8), 77.7 (C6), 82.8 (C7), 83.2 (C5), 109 (IP), 111 (IP), 208 (C2). ESI-TOFMS *m*/*z*: calcd for $[C_{15}H_{26}O_6+Na]^+$, 325.1622; found, 325.1672.

^{1}H NMR spectrum



7,8-Didoxy-1,2:3,4-di-*O*-isopropylidene-8-oxo-D-*glycero*-D-*galacto*-nonopyranose **65**

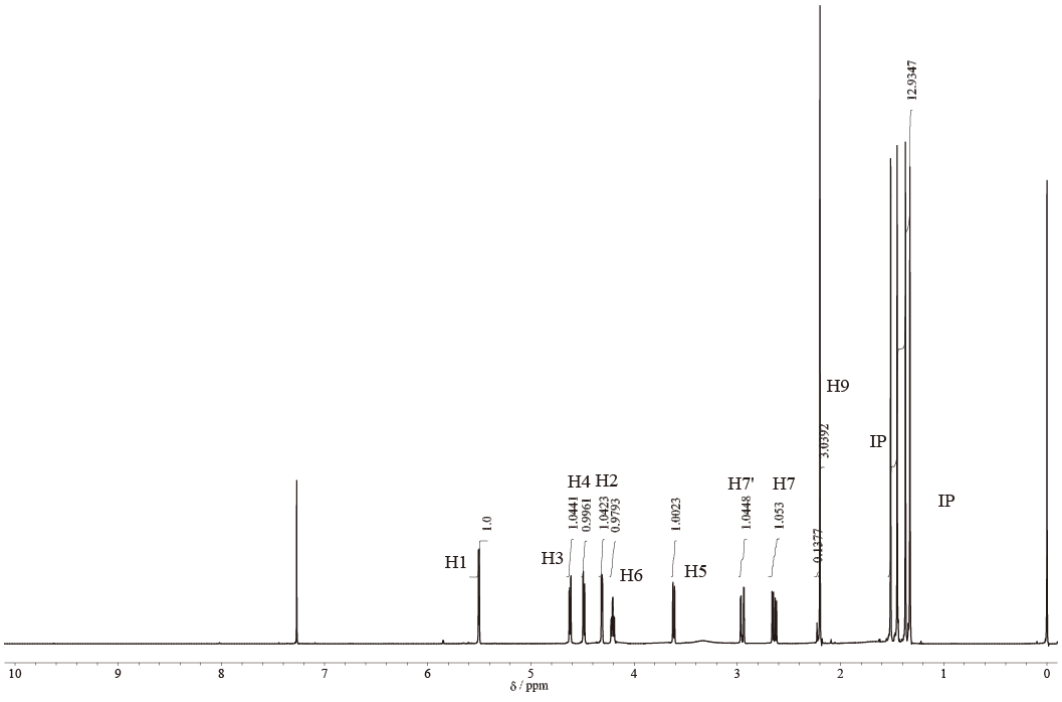


Freshly distilled 1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose **30** (100 mg, 0.387 mmole) was dissolved in acetone, and D-prolinamido-glycoside **8** (33.7 mg, 0.116 mmole) and distilled water were added. The solution was kept stirring for 2 h at room temperature, after which TLC (chloroform-ethyl acetate, 10 : 1) indicated the formation of an aldol adduct. The reaction mixture was evaporated, and the residue was dissolved in ethyl acetate, washed with water, dried ($NaSO_4$), and concentrated to dryness. The crude product was purified by column

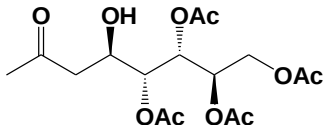
chromatography on silica gel (chloroform-ethyl acetate, 10 : 1), to give **65** as a syrup. Yield 89.4 mg (73.3%), $[\alpha]_D^{23.5}$ – 52.3° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$, 600 MHz), δ 1.33 (s, 3H, IP), 1.37 (s, 3H, IP), 1.45 (s, 3H, IP), 1.51 (s, 3H, IP), 2.20 (s, 3H, 9-CH_3), 2.64 (dd, 1H, $J_{6,7a}$ = 8.3 Hz, $J_{7a,7b}$ = 17.8 Hz, H7a), 2.93 (dd, 1H, $J_{6,7b}$ = 2.7 Hz, $J_{7a,7b}$ = 17.8 Hz, H7b), 3.62 (dd, 1H, $J_{4,5}$ = 1.6 Hz, $J_{5,6}$ = 8.3 Hz, H5), 4.21 (dt, 1H, $J_{5,6}$ = 8.3 Hz, $J_{6,7a}$ = 8.3 Hz, $J_{6,7b}$ = 2.7 Hz, H6) , 4.31 (dd, 1H, $J_{1,2}$ = 5.1 Hz, $J_{2,3}$ = 2.4 Hz, H2), 4.49 (dd, 1H, $J_{3,4}$ = 7.9 Hz, $J_{4,5}$ = 1.6 Hz, H4), 4.62 (dd, 1H, $J_{2,3}$ = 2.4 Hz, $J_{3,4}$ = 7.9 Hz, H3), 5.50 (1H, d, $J_{1,2}$ = 5.0 Hz, H1); ^{13}C NMR ($CDCl_3$, 150MHz) δ 24.4 (IP), 24.9 (IP), 26.0 (IP), 31.0 (C9), 46.1 (C7), 66.3 (C6), 69.2 (C5), 70.2 (C4), 70.6 (C3), 70.8 (C2), 96.4 (C1), 109 (IP), 109 (IP), 211 (C2).

ESI-TOFMS *m*/*z*: calcd for $[C_{15}H_{24}O_7+Na]^+$, 339.1414; found, 339.1477.

^{1}H NMR spectrum



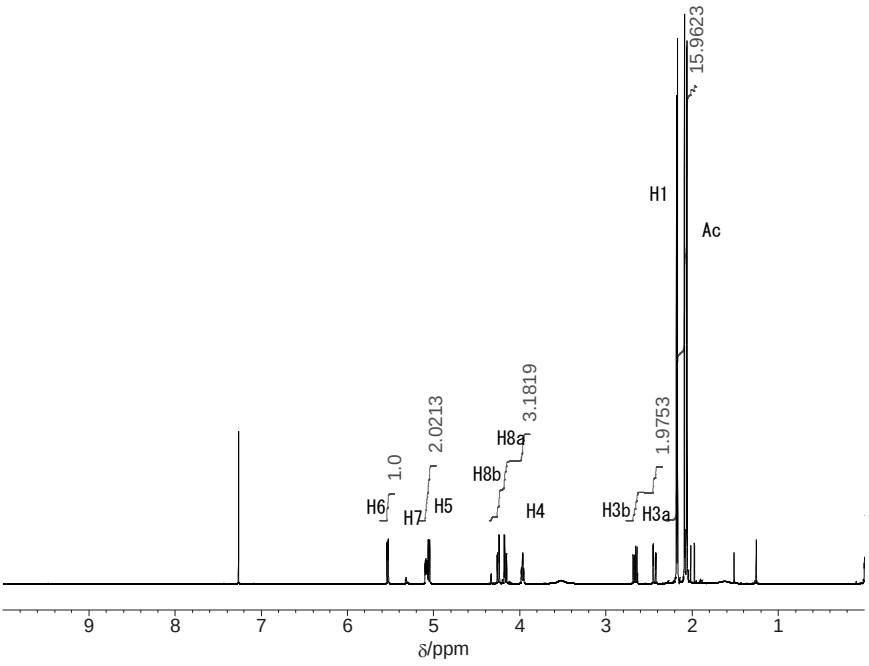
1.3-Dideoxy-5,6,7,8-tetra-*O*-acetyl-D-*glycero*-D-*ribo*-octulose **66**



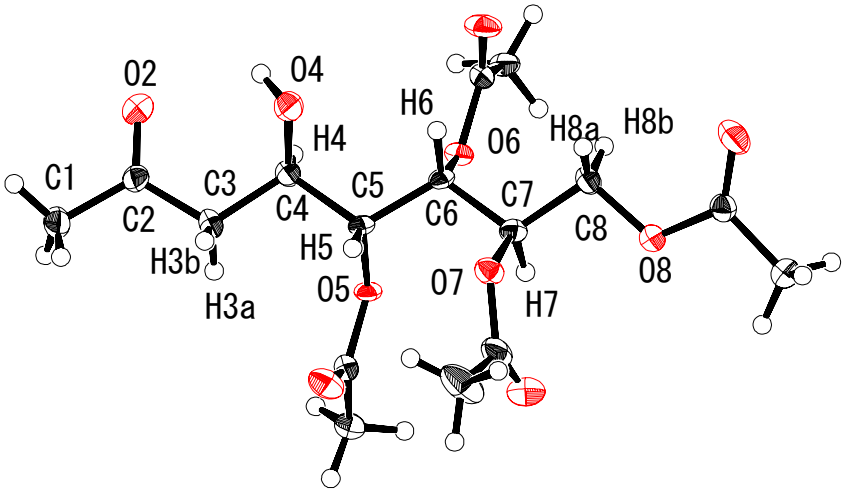
To a stirred solution of freshly prepared 2,3,4,5-tetra-*O*-acetyl-*aldehydo*-D-arabinose **32** (50 mg, 0.157 mmole) in acetone (0.380 ml, 4.71 mmole) was added 6.3 mg (0.0217 mole) of L-prolinamido-glycoside **7** in ml of distilled water (28.0 μl), and the solution was stirred at ambient temperature for 1h, when TLC (chloroform-acetone, 10 : 1) indicated that the reaction was complete. The mixture was concentrated to remove excess amount of acetone, and the residue was diluted with ethyl acetate, washed with water, dried ($NaSO_4$), and concentrated to dryness. The crude product was then purified by column chromatography on silica gel (chloroform-acetone, 10 : 1), to give pure **64** as a colorless syrup; yield 56.0 mg (94.5%), $[\alpha]_D^{27}$ +41.9° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$, 600 MHz), δ 2.06 (s, 3H, Ac), 2.06 (s, 3H, Ac), 2.17 (s, 3H, Ac), 2.17 (s, 3H, Ac), 2.18 (s, 3H,1-CH_3), 2.43 (dd, 1H, $J_{3,4}$ = 2.6 Hz, $J_{3a,3b}$ = 17.1 Hz, H3a), 2.66 (dd, 1H, $J_{3b,4}$ = 9.1 Hz, $J_{3a,3b}$ = 17.1 Hz, H3b), 3.97 (dt, 1H, $J_{3,4}$ = 2.6 Hz, $J_{3b,4}$ = 9.1 Hz, $J_{3,4}$ = 2.6 Hz, $J_{4,5}$ = 9.0 Hz, H4), 4.17 (dd, 1H, $J_{7,8a}$ = 4.6 Hz, $J_{8a,8b}$ = 12.5 Hz, H8a) , 4.25 (dd, 1H, $J_{7,8b}$ = 2.5 Hz, $J_{8a,8b}$ = 12.5 Hz, H8b), 5.05 (dd, 1H, $J_{4,5}$ = 9.0 Hz, $J_{5,6}$ = 1.9 Hz, H5), 5.89 (ddd, 1H, $J_{6,7}$ = 9.3 Hz, $J_{7,8a}$ = 4.6 Hz, $J_{7,8b}$ = 2.5 Hz, H7), 5.54 (dd, 1H, $J_{5,6}$ = 1.9 Hz, $J_{6,7}$ = 9.3 Hz, H6); ^{13}C NMR ($CDCl_3$, 150MHz) δ 20.7 (Ac), 20.8 (Ac), 20.8 (Ac), 20.8 (Ac), 31.2 (C1), 45.7 (C3), 61.9 (C8), 65.5 (C4), 67.9 (C7), 68.2 (C6), 71.6 (C5), 169.9 (Ac), 170.3 (Ac), 170.6 (Ac), 170.9 (Ac), 208 (C2).

ESI-TOFMS *m*/*z*: calcd for $[C_{16}H_{24}O_{10}+Na]^+$, 377.1369; found, 377.1379.

^{1}H NMR spectrum



Crystal structure of 1.3-dideoxy-5,6,7,8-tetra-*O*-acetyl-D-*glycero*-D-*ribo*-octulose



Empirical Formula $C_{16}H_{24}O_{10}$

Formula Weight 376.36

Crystal Color, Habit colorless, block

Crystal Dimensions 0.200 X 0.200 X 0.200 mm

Crystal System monoclinic

Lattice Type Primitive

Lattice Parameters a = 8.636(3) Å

b = 8.045(3) Å

c = 13.771(5) Å

V = 3236.2(9) Å3

Space Group $P12_11$

Z value 2

Dcalc 1.349 g/cm3

R-factor 4.87%

Temperature 123 K

ω oscillation Range (c=45.0, f=180.0) 0.0 - 160.0o

No. of Reflections Measured Total: 5398

Atomic coordinates and Biso/Beq and occupancy

atom	x	y	z	B_{eq}
O3 O	0.88828(18)	0.44688(19)	0.64273(10)	0.0185(4)
O6 O	0.54051(19)	0.7461(3)	0.84159(11)	0.0240(4)
O8 O	0.9360(3)	0.6665(3)	0.55150(14)	0.0314(5)
O4 O	0.84244(18)	0.34682(19)	0.82415(10)	0.0190(4)
O5 O	0.80819(19)	0.7860(2)	0.75927(11)	0.0224(4)
O2 O	1.2367(2)	0.4644(3)	0.85284(12)	0.0285(5)
O7 O	0.5194(3)	0.7896(3)	0.99859(13)	0.0339(5)
O9 O	0.9386(2)	0.3463(3)	0.99068(12)	0.0293(4)
O1 O	1.4219(3)	0.2244(3)	0.76590(14)	0.0356(5)

O10 O	0.6108(3)	0.7835(4)	0.61931(14)	0.0418(6)
C6 C	0.9022(3)	0.5128(3)	0.81565(14)	0.0173(5)
C13 C	0.8631(3)	0.2784(3)	0.91639(15)	0.0201(5)
C9 C	0.4670(3)	0.8052(3)	0.90977(16)	0.0219(5)
C5 C	0.9935(3)	0.5119(3)	0.73384(14)	0.0175(4)
C7 C	0.7560(3)	0.6281(3)	0.79020(15)	0.0193(5)
C4 C	1.1452(3)	0.4053(3)	0.75958(16)	0.0205(5)
C14 C	0.7814(3)	0.1143(3)	0.91079(16)	0.0225(5)
C2 C	1.3827(3)	0.3210(3)	0.69499(16)	0.0224(5)
C3 C	1.2345(3)	0.4243(4)	0.67766(17)	0.0256(6)
C8 C	0.6879(3)	0.6583(3)	0.88043(16)	0.0229(5)
C1 C	1.4819(3)	0.3423(4)	0.62019(18)	0.0300(6)
C11 C	0.8724(3)	0.5329(3)	0.55511(16)	0.0225(5)
C12 C	0.7718(3)	0.4398(4)	0.46843(16)	0.0270(6)
C10 C	0.3141(3)	0.8919(4)	0.86055(18)	0.0295(6)
C15 C	0.7269(4)	0.8478(4)	0.67015(18)	0.0307(6)
C16 C	0.8063(5)	1.0032(4)	0.6463(3)	0.0459(9)

Bond lengths (Å)

atom	atom	distance
O3	C5	1.451(3)
O3	C11	1.368(3)
O6	C9	1.344(3) .
O6	C8	1.438(3)

O8	C11	1.214(4)
O4	C6	1.447(3)
O4	C13	1.355(3)
O5	C7	1.447(3)
O5	C15	1.348(3)
O2	C4	1.412(3)
O7	C9	1.200(3)
O9	C13	1.199(3)
O1	C2	1.228(3)
O10	C15	1.189(4)
C6	C5	1.527(4) .
C6	C7	1.535(3)
C13	C14	1.490(4)
C9	C10	1.498(4)
C5	C4	1.532(3)
C7	C8	1.521(4)
C4	C3	1.524(4)
C2	C3	1.495(4)
C2	C1	1.504(4)
C11	C12	1.491(3) .
C15	C16	1.502(5)

Bond angles (o)

atom	atom	atom	angle
C5	O3	C11	118.95(17)
C9	O6	C8	116.25(16)
C6	O4	C13	118.97(15)
C7	O5	C15	117.51(18)
O4	C6	C5	108.37(17)
O4	C6	C7	106.64(16)
C5	C6	C7	112.37(17)
O4	C13	O9	122.1(3)
O4	C13	C14	111.18(17)
O9	C13	C14	126.7(2)
O6	C9	O7	123.4(2)
O6	C9	C10	111.40(19)
O7	C9	C10	125.2(3)
O3	C5	C6	108.21(17)
O3	C5	C4	108.28(17)
C6	C5	C4	113.63(17)
O5	C7	C6	107.39(18)
O5	C7	C8	108.23(18)
C6	C7	C8	111.92(17)
O2	C4	C5	105.93(18)
O2	C4	C3	111.61(19)

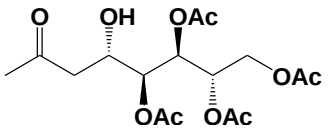
C5	C4	C3	109.49(18)
O1	C2	C3	122.3(3)
O1	C2	C1	121.7(3)
C3	C2	C1	1 16.0(2)
C4	C3	C2	113.4(2)
O6	C8	C7	105.14(17)
O3	C11	O8	122.48(19)
O3	C11	C12	111.3(2)
O8	C11	C12	126.2(3)
O5	C15	O10	123.2(3)
O5	C15	C16	110.1(3)
O10	C15	C16	126.7(3)

Torsion Angles(o) (Those having bond angles > 160 or < 20 degrees are excluded.)

atom1	atom2	atom3	atom4	angle
C5	O3	C11	O8	-4.2(4)
C5	O3	C11	C12	174.81(16)
C11	O3	C5	C6	130.54(18)
C11	O3	C5	C4	-105.9(2)
C9	O6	C8	C7	-172.07(17)
C8	O6	C9	O7	1.0(4)
C8	O6	C9	C10	-179.18(16)
C6	O4	C13	O9	-5.1(3)

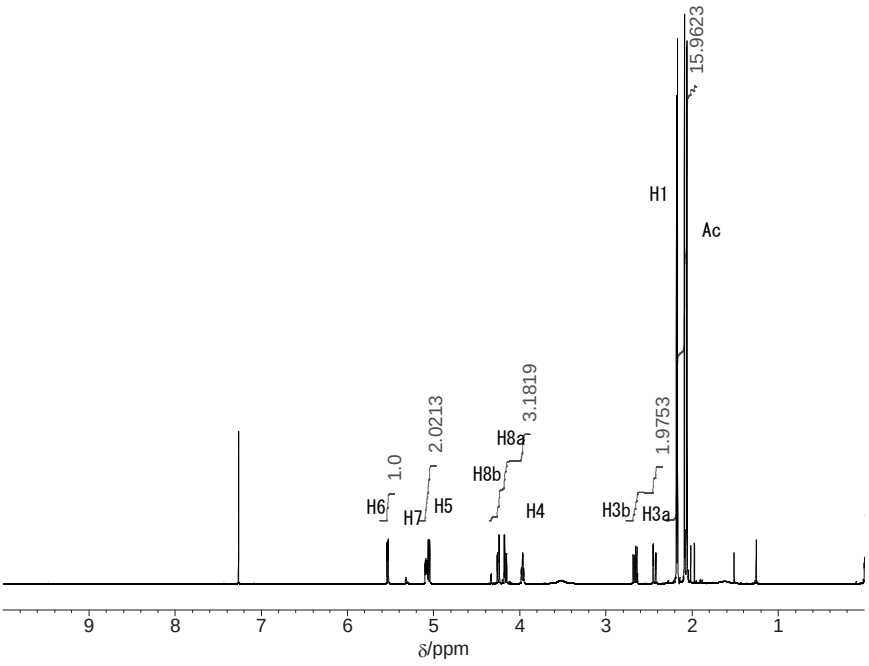
C6	O4	C13	C14	174.92(15)
C13	O4	C6	C5	132.92(17)
C13	O4	C6	C7	-105.89(18)
C7	O5	C15	O10	4.2(4)
C7	O5	C15	C16	-174.88(17)
C15	O5	C7	C6	126.6(2)
C15	O5	C7	C8	-112.4(2)
O4	C6	C5	O3	54.73(18)
O4	C6	C5	C4	-65.56(18)
O4	C6	C7	O5	-167.31(13)
O4	C6	C7	C8	74.05(18)
C5	C6	C7	O5	-48.7(2)
C5	C6	C7	C8	-167.34(15)
C7	C6	C5	O3	-62.8(2)
C7	C6	C5	C4	176.86(14)
O3	C5	C4	O2	-175.03(15)
O3	C5	C4	C3	64.5(2)
C6	C5	C4	O2	-54.8(3)
C6	C5	C4	C3	-175.26(15)
O5	C7	C8	O6	70.16(18)
C6	C7	C8	O6	-171.70(15)
O2	C4	C3	C2	64.5(3)
C5	C4	C3	C2	-178.51(16)
O1	C2	C3	C4	3.7(3)
C1	C2	C3	C4	-176.26(18)

1.3-Dideoxy-5,6,7,8-tetra-*O*-acetyl-L-*glycero*-L-*ribo*-octulose **67**

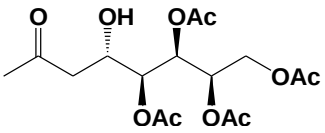


This compound was obtained from 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-L-arabinose **34** by an identical procedure used for the D-enantiomer, $[\alpha]_D^{27}$ -41.9° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$, 600 MHz), δ 2.06 (s, 3H, Ac), 2.06 (s, 3H, Ac), 2.17 (s, 3H, Ac), 2.17 (s, 3H, Ac), 2.18 (s, 3H,1-CH_3), 2.43 (dd, 1H, $J_{3,4}$ = 2.6 Hz, $J_{3a,3b}$ = 17.1 Hz, H3a), 2.66 (dd, 1H, $J_{3b,4}$ = 9.1 Hz, $J_{3a,3b}$ = 17.1 Hz, H3b), 3.97 (dt, 1H, $J_{3,4}$ = 2.6 Hz, $J_{3b,4}$ = 9.1 Hz, $J_{3,4}$ = 2.6 Hz, $J_{4,5}$ = 9.0 Hz, H4), 4.17 (dd, 1H, $J_{7,8a}$ = 4.6 Hz, $J_{8a,8b}$ = 12.5 Hz, H8a) , 4.25 (dd, 1H, $J_{7,8b}$ = 2.5 Hz, $J_{8a,8b}$ = 12.5 Hz, H8b), 5.05 (dd, 1H, $J_{4,5}$ = 9.0 Hz, $J_{5,6}$ = 1.9 Hz, H5), 5.89 (ddd, 1H, $J_{6,7}$ = 9.3 Hz, $J_{7,8a}$ = 4.6 Hz, $J_{7,8b}$ = 2.5 Hz, H7), 5.54 (dd, 1H, $J_{5,6}$ = 1.9 Hz, $J_{6,7}$ = 9.3 Hz, H6); ^{13}C NMR ($CDCl_3$, 150MHz) δ 20.7 (Ac), 20.8 (Ac), 20.8 (Ac), 20.8 (Ac), 31.2 (C1), 45.7 (C3), 61.9 (C8), 65.5 (C4), 67.9 (C7), 68.2 (C6), 71.6 (C5), 169.9 (Ac), 170.3 (Ac), 170.6 (Ac), 170.9 (Ac), 208 (C2); ESI-TOFMS *m*/*z*: calcd for $[C_{16}H_{24}O_{10}+Na]^+$, 377.1369; found, 377.1361.

^{1}H NMR spectrum



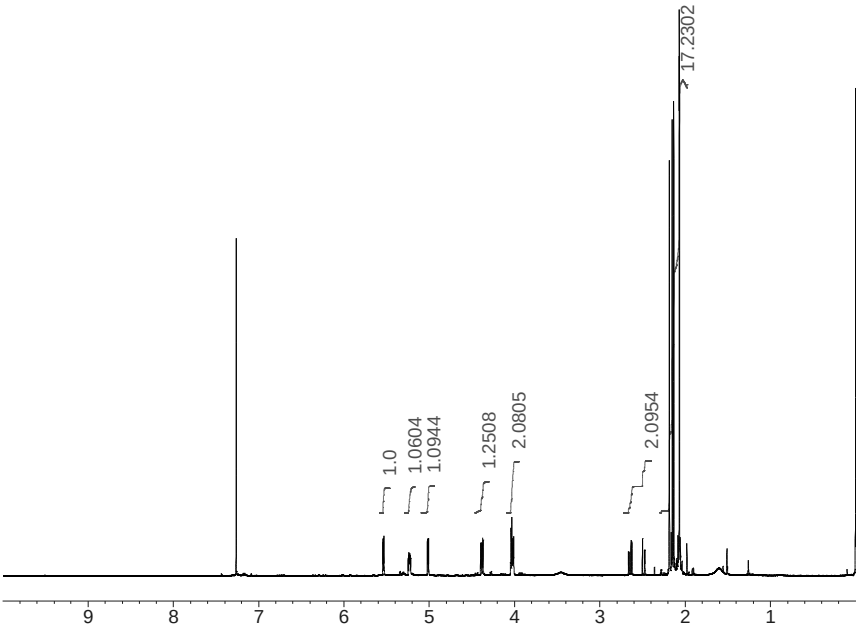
1.3-Dideoxy-5,6,7,8-tetra-*O*-acetyl-D-*tallo*-octulose **68**



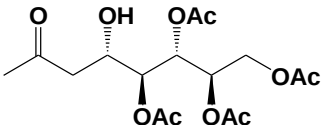
To a stirred solution of freshly prepared 2,3,4,5-tetra-*O*-acetyl-*aldehydo*-D-xylose **38** (61.6 mg, 0.194 mmole) in acetone (0.427 ml, 5.81 mmole) was added 6.3 mg (0.0217 mmole) of L-prolinamido-glycoside **7** in 35 µl of distilled water, and the solution was stirred at ambient temperature for 1h, when TLC (chloroform-acetone, 10 : 1) indicated that the reaction was complete. The mixture was concentrated to remove excess amount of acetone, and the residue was diluted with ethyl acetate, washed with water, dried ($NaSO_4$), and concentrated to dryness. The crude product was then purified by column chromatography on silica gel (chloroform-acetone, 10 : 1), to give pure **68** as a colorless syrup; yield 45.6 mg (77.3%), $[\alpha]_D^{27}$ -28.6° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$, 600 MHz), δ 2.05 (s, 3H, Ac), 2.06 (s, 3H, Ac), 2.13 (s, 3H, Ac), 2.15 (s, 3H, Ac),

2.18 (s, 3H,1-CH_3), 2.48 (dd, 1H, $J_{3,4}$ = 2.6 Hz, $J_{3a,3b}$ = 17.4 Hz, H3a), 2.64 (dd, 1H, $J_{3b,4}$ = 9.0 Hz, $J_{3a,3b}$ = 17.4Hz, H3b), 4.01-4.04 (m, 2H, $J_{3a,4}$ = 9.2 Hz, $J_{3b,4}$ = 2.6 Hz, $J_{8a,8b}$ = 12.2 Hz, H4, H8), 4.39 (dd, 1H, $J_{7,8b}$ = 3.7 Hz, $J_{8a,8b}$ = 12.2 Hz, H8b) , 5.01 (dd, 1H, $J_{4,5}$ = 8.4 Hz, $J_{5,6}$ = 2.8 Hz, H5), 5.23 (ddd, 1H, $J_{6,7}$ = 7.3 Hz, $J_{7,8a}$ = 5.7 Hz, $J_{7,8b}$ = 3.7 Hz, H7), 5.54 (dd, 1H, $J_{5,6}$ = 2.8 Hz, $J_{6,7}$ = 7.3 Hz, H6); ^{13}C NMR ($CDCl_3$, 150MHz) δ 20.7 (Ac), 20.7 (Ac), 20.8 (Ac), 20.9 (Ac), 31.1 (C1), 45.5 (C3), 61.9 (C8), 66.1 (C4), 69.2 (C6), 70.0 (C7), 72.2 (C5), 169 (Ac), 170 (Ac), 170 (Ac), 170.9 (Ac), 208 (C2); ESI-TOFMS *m*/*z*: calcd for $[C_{16}H_{24}O_{10}+Na]^+$, 377.1369; found, 377.1351.

^{1}H NMR spectrum



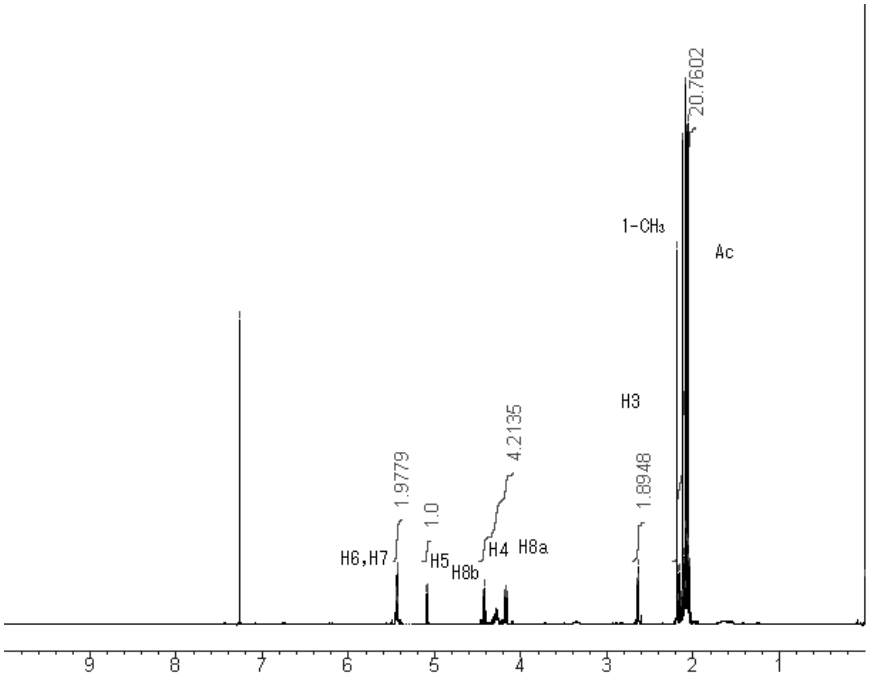
1.3-Dideoxy-5,6,7,8-tetra-*O*-acetyl-D-*mannno*-octulose **72**



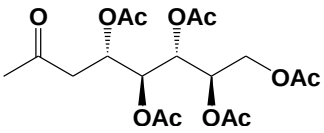
To a stirred solution of freshly prepared 2,3,4,5-tetra-*O*-acetyl-*aldehydo*-D-ribose **36** (50.4 mg, 0.157 mmole) in acetone (0.380 ml, 4.71 mmole) was added 6.30 mg (0.0217 mole) of

L-prolinamido-glycoside **7** in 28 μl of distilled water, and the solution was stirred at ambient temperature for 1h, when TLC (chloroform-acetone, 10 : 1) indicated that the reaction was complete. The mixture was concentrated to remove excess amount of acetone, and the residue was diluted with ethyl acetate, washed with water, dried ($NaSO_4$), and concentrated to dryness. The crude product was then purified by column chromatography on silica gel (chloroform-acetone, 10 : 1), to give pure **72** as a colorless syrup; yield 46.9 mg (79.5%), $[\alpha]_D^{27}$ +1.50° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$, 600 MHz), δ 2.05 (s, 3H, Ac), 2.08 (s, 3H, Ac), 2.09 (s, 3H, Ac), 2.12 (s, 3H, Ac), 2.19 (s, 3H,1-CH_3), 2.63 (t, 2H, $J_{3,4}$ = 8.8 Hz, H3), 4.17 (dd, 1H, $J_{7,8a}$ = 6.8 Hz, $J_{8a,8b}$ = 12.3Hz, H8a), 4.28 (dt, 1H, $J_{3,4}$ = 8.8 Hz, $J_{4,5}$ = 4.1 Hz, H4), 4.12 (dd, 1H, $J_{7,8b}$ = 2.6 Hz, $J_{8a,8b}$ = 12.3 Hz, H8b) , 5.08 (dd, 1H, $J_{4,5}$ = 4.1 Hz, $J_{5,6}$ = 7.0 Hz, H5), 5.42 – 5.46 (m, 2H, H6, H7); ^{13}C NMR ($CDCl_3$, 150MHz) δ 20.7 (Ac), 20.7 (Ac), 20.8 (Ac), 20.9 (Ac), 31.1 (C1), 45.5 (C3), 61.9 (C8), 66.1 (C4), 69.2 (C6), 70.0 (C7), 72.2 (C5), 169 (Ac), 170 (Ac), 170 (Ac), 170.9 (Ac), 208 (C2); ESI-TOFMS *m*/*z*: calcd for $[C_{16}H_{24}O_{10}+Na]^+$, 377.1369; found, 377.1351.

^{1}H NMR spectrum



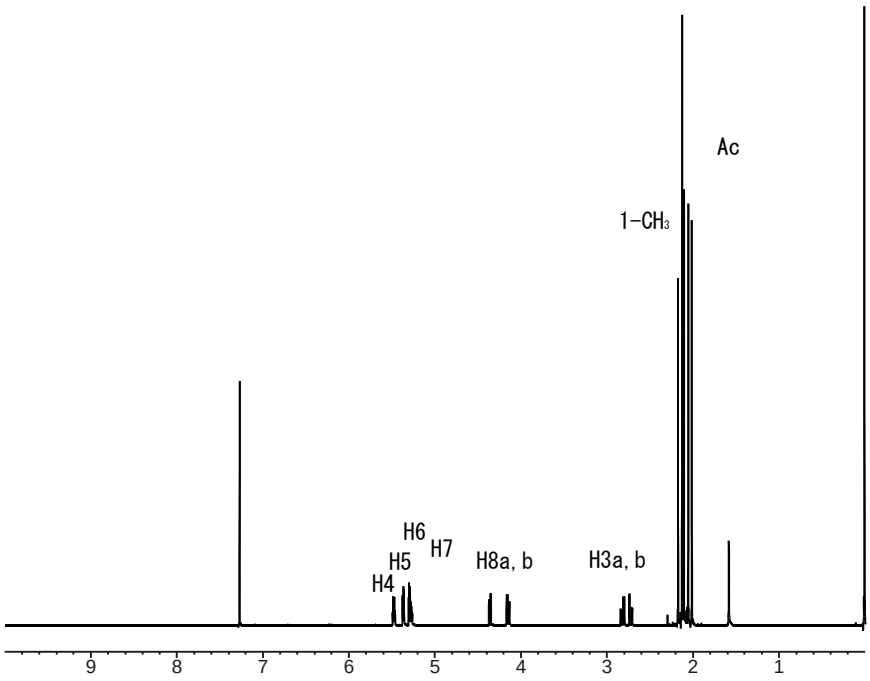
1.3-Dideoxy-4,5,6,7,8-penta-*O*-acetyl-D-*mannno*-octulose **73**



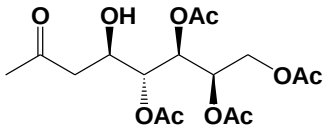
The deoxy-hexulose **72** (40.0 mg, 0.106 mmole) was dissolved in pyridine (400 μl), and Ac_2O (200 μl) was added. The mixture was stirred at ambient temperature for 24 h. After which time, the solvents were removed by azeotropic concentration with toluene, to give a light-brown syrup which was purified by silica gel column chromatography (dichloromethane-acetone, 10 : 1) to give pure **73** as a colorless syrup; yield 27.1 mg (59.4%), $[\alpha]_D^{26}$ +3.74º (*c* = 1.0, chloroform), R_f = 0.51 (dichloromethane-acetone, 10 : 1); ^{1}H NMR ($CDCl_3$, 600 MHz), δ 2.01 (s, 3H, Ac), 2.04 (s, 3H, Ac), 2.10 (s, 3H, Ac), 2.12 (s, 6H, Ac), 2.16 (s, 3H,1-CH_3), 2.71 (dd, 1H, $J_{3a,4}$ = 3.7 Hz, $J_{3a,3b}$ = 17.1 Hz, H3a), 2.81 (dd, 1H, $J_{3b,4}$ = 8.9 Hz, $J_{3a,3b}$ = 17.1 Hz, H3b), 4.15 (dd, 1H, $J_{7,8}$ = 6.3 Hz, $J_{8a,8b}$ = 12.3, H8a), 4.35 (dd, 1H, $J_{7,8a}$ = 3.4 Hz, $J_{8a,8b}$ = 12.3 Hz, H8b) , 5.26 (ddd, 1H, $J_{6,7}$ = 4.6 Hz, $J_{7,8a}$ = 6.8 Hz, $J_{7,8b}$ = 3.4 Hz, H7), 5.29 (dd, 1H, $J_{5.6}$ = 6.4 Hz, $J_{6,7}$ = 4.6 Hz, H6), 5.36 (dd, 1H, $J_{4,5}$ = 3.7 Hz, $J_{5,6}$ = 6.4 Hz, H5), 5.47 (dt, 1H, $J_{3a,4}$ = 3.7 Hz, $J_{3b,4}$ = 8.9 Hz, $J_{4,5}$ = 3.7 Hz, H4); ^{13}C NMR ($CDCl_3$, 150MHz) δ 20.8 (Ac), 20.9 (Ac), 20.9 (Ac), 21.0 (Ac), 31.4 (C1), 43.1 (C3), 61.7 (C4), 68.0 (C6), 69.4 (C7), 68.2 (C6), 70.9 (C5), 169.7 (Ac), 169.8 (Ac), 170.2 (Ac), 170.7 (Ac), 203.9 (C2).

ESI-TOFMS *m*/*z*: calcd for $[C_{18}H_{26}O_{11}+Na]^+$, 418.1475; found, 418.1491.

^{1}H NMR spectrum



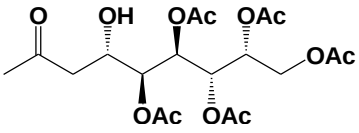
1.3-dideoxy-5,6,7,8-tetra-*O*-acetyl-D-*gulo*-octulose **70**



To a stirred solution of freshly prepared 2,3,4,5-tetra-*O*-acetyl-*aldehydo*-D-lyxose **41** (50.0 mg, 0.157 mmole) in acetone (0.380 ml, 4.71 mmole) was added 6.37 mg (0.0217 mole) of L-prolinamido-glycoside **7** in 28 μl of distilled water, and the solution was stirred at ambient temperature for 1h, when TLC (chloroform-acetone, 10 : 1) indicated that the reaction was complete. The mixture was concentrated to remove excess amount of acetone, and the residue was diluted with ethyl acetate, washed with water, dried ($NaSO_4$), and concentrated to dryness. The crude product was then purified by column chromatography on silica gel (chloroform-acetone, 10 : 1), to give pure **70** as a colorless syrup; yield 43.6 mg (73.9%), $[\alpha]_D^{27}$ +27.4° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$, 600 MHz), δ 2.05 (s, 3H, Ac), 2.07 (s, 3H, Ac), 2.08 (s, 3H, Ac), 2.19 (s, 3H,1-CH_3), 2.59 (dd, 1H, $J_{3a,4}$ = 9.5 Hz, $J_{3a,3b}$ = 17.9 Hz,H3a), 2.71 (dd, 1H, $J_{3b,4}$ = 2.3 Hz, $J_{3a,3b}$ =

17.9 Hz,H3a), 4.09 (dd, 1H, $J_{7,8a}$ = 6.5 Hz, $J_{8a,8b}$ = 11.8Hz, H8a), 4.22 (ddd, 1H, $J_{3a,4}$ = 9.5 Hz, $J_{3b,4}$ = 2.3 Hz, $J_{4,5}$ = 6.8 Hz, H4), 4.25 (dd, 1H, $J_{7,8b}$ = 4.6 Hz, $J_{8a,8b}$ = 11.8 Hz, H8b) , 5.09 (dd, 1H, $J_{4,5}$ = 6.8 Hz, $J_{5,6}$ = 5.9 Hz, H5), 5.37 (dd, 1H, $J_{5,6}$ = 5.9 Hz, $J_{6,7}$ = 4.1 Hz, H7); ^{13}C NMR ($CDCl_3$, 150MHz) δ 37.5 (Ac), 37.6 (Ac), 37.6 (Ac), 37.7 (Ac), 47.6 (C1), 61.8 (C3), 79.0 (C8), 83.3 (C4), 85.5 (C7), 86.4 (C6), 88.6 (C5), 187 (Ac), 187 (Ac), 187 (Ac), 187 (Ac), 226 (C2); ESI-TOFMS *m*/*z*: calcd for $[C_{16}H_{24}O_{10}+Na]^+$, 377.1369; found, 377.1391.

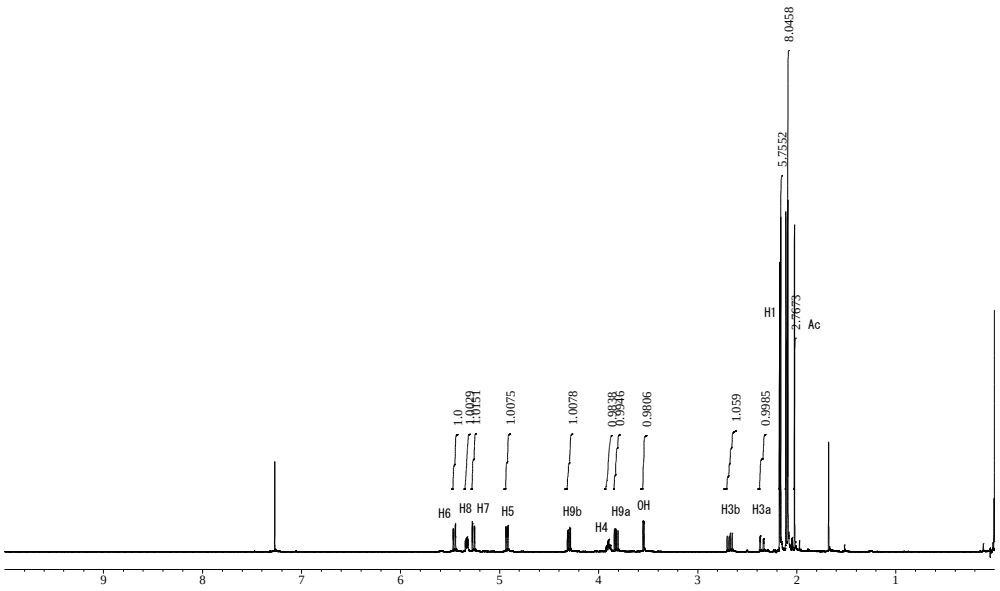
1,3-Dideoxy-5,6,7,8,9-penta-*O*-acetyl-L-*glycero*-D-*ido*-nonulose **74**



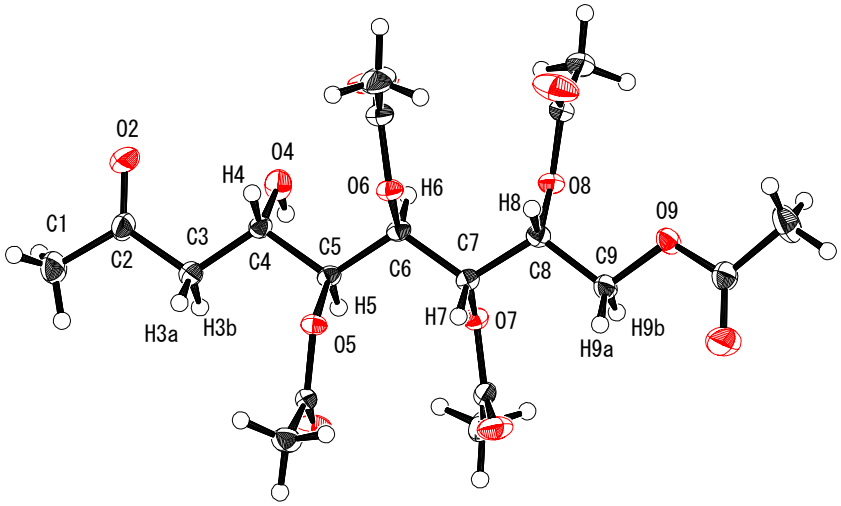
To a stirred solution of freshly prepared 2,3,4,5,6-penta-*O*-acetyl-*aldehydo*-D-galactose **44** (32.0 mg, 0.0820 mmole) in acetone (0.200 ml, 2.46 mmole) was added 2.67 mg (0.00919 mmole) of L-prolinamido-glycoside **7** in 30 μl of distilled water, and the solution was stirred at ambient temperature for 1h, when TLC (chloroform-acetone, 10 : 1) indicated that the reaction was complete. The mixture was concentrated to remove excess amount of acetone, and the residue was diluted with ethyl acetate, washed with water, dried ($NaSO_4$), and concentrated to dryness. The crude product was then purified by column chromatography on silica gel (chloroform-acetone, 10 : 1), to give pure **74** as a colorless syrup; yield 28.6 mg (71.4%), $[\alpha]_D^{26.8}$ +3.93° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$, 500 MHz), δ 2.02 (s, 3H, Ac), 2.09 (s, 3H, Ac), 2.09 (s, 3H, Ac), 2.11 (s, 3H, Ac), 2.16 (s, 3H, Ac), 2.18 (s, 3H,1-CH_3), 2.36 (dd, 1H, $J_{3a,4}$ = 2.5 Hz, $J_{3a,3b}$ = 16.7 Hz,H3a), 2.68 (dd, 1H, $J_{3b,4}$ = 9.3 Hz, $J_{3a,3b}$ = 16.7 Hz,H3b), 3.82 (dd, 1H, $J_{8,9a}$ = 7.9 Hz, $J_{9a,9b}$ = 11.8Hz, H9a), 3.90 (ddd, 1H, $J_{3a,4}$ = 2.5 Hz, $J_{3b,4}$ = 9.3 Hz, $J_{4,5}$ = 6.7 Hz, H4), 4.30 (dd, 1H, $J_{8,9b}$ = 4.5 Hz, $J_{9a,9b}$ = 11.8 Hz, H9b) , 4.92 (dd, 1H, $J_{4,5}$ = 7.7 Hz, $J_{5,6}$ = 1.5 Hz, H5), 5.26 (dd, 1H, $J_{6,7}$ = 10.2 Hz, $J_{7,8}$ = 1.9 Hz, H7), 5.33 (ddd, 1H, $J_{7,8}$ = 1.9 Hz, $J_{8,9a}$ = 7.9 Hz, $J_{8,9b}$ = 4.5 Hz, H8), 5.46 (dd,

1H, $J_{5,6}$ = 1.5 Hz, $J_{6,7}$ = 10.2 Hz, H6); ^{13}C NMR ($CDCl_3$, 125MHz) δ 20.6 (Ac), 20.7 (Ac), 20.7 (Ac), 20.8 (Ac), 20.9 (Ac), 31.3 (C1), 45.8 (C3), 62.4, 65.4, 67.4, 67.6, 67.8, 71.3, 170 (Ac), 170 (Ac), 171 (Ac), 171 (Ac), 172 (Ac), 208 (C2); ESI-TOFMS *m*/*z*: calcd for $[C_{16}H_{24}O_{10}+Na]^+$, 448.1581; found, 448.1601.

^{1}H NMR spectrum



Crystal structure of **74**



Empirical Formula $C_{19}H_{28}O_{12}$

Formula Weight 448.42

Crystal Color, Habit colorless, block

Crystal Dimensions 0.250 X 0.200 X 0.200 mm

Crystal System monoclinic

Lattice Type Primitive

Lattice Parameters *a* = 8.608(3) Å

b = 8.155(3) Å

c = 15.649(5) Å

V = 1094.9(6) Å^3

Space Group $P12_11$

Z value 4

*D*calc 1.360 g/cm3

R-factor 4.18%

Temperature 123 K

ω oscillation Range (c=45.0, f=180.0) 0.0 - 160.0o

No. of Reflections Measured Total: 6153

Atomic coordinates and Biso/Beq and occupancy

atom	x	y	z	B_{eq}
O1 O	0.14787(12)	0.84303(15)	0.87872(7)	0.0180(3)
O2 O	0.25132(12)	0.89046(14)	0.71589(7)	0.0193(3)
O3 O	0.24030(12)	0.47117(14)	0.78822(7)	0.0183(3)
O4 O	0.66303(12)	0.46072(17)	0.66851(7)	0.0228(3)
O5 O	0.34895(12)	0.52729(14)	0.62590(7)	0.0186(3)
O6 O	0.38804(15)	0.45017(19)	0.91325(8)	0.0329(4)
O7 O	0.07713(15)	0.64303(17)	0.96731(8)	0.0297(4)
O8 O	0.84919(16)	0.3877(3)	0.76921(10)	0.0553(5)
O9 O	0.10256(19)	0.9016(3)	0.59097(9)	0.0492(5)
O10 O	-0.15282(13)	0.77839(17)	0.70535(8)	0.0284(3)
O11 O	0.4400(2)	0.7280(2)	0.54464(9)	0.0462(5)
O12 O	-0.3422(3)	1.0528(3)	0.74137(11)	0.0723(7)
C1 C	0.31469(16)	0.62412(18)	0.76846(9)	0.0160(4)
C2 C	0.06637(16)	0.7636(2)	0.80558(9)	0.0162(3)
C3 C	-0.07444(16)	0.8690(2)	0.77323(9)	0.0178(4)
C4 C	0.18014(16)	0.73719(19)	0.73741(9)	0.0169(4)
C5 C	-0.18365(17)	0.8993(3)	0.84310(10)	0.0217(4)
C6 C	0.43106(17)	0.5956(2)	0.70186(9)	0.0176(4)
C7C	0.28146(18)	0.4014(2)	0.86529(10)	0.0218(4)

C8 C	0.20532(19)	0.9581(3)	0.63827(10)	0.0253(4)
C9 C	-0.32646(18)	0.9962(3)	0.81180(11)	0.0254(4)
C11 C	0.55778(17)	0.4768(3)	0.73470(10)	0.0219(4)
C12 C	0.14167(17)	0.7710(2)	0.95692(10)	0.0180(4)
C14 C	0.1792(2)	0.2570(3)	0.87918(14)	0.0334(5)
C15 C	0.2862(3)	0.5112(3)	0.47732(10)	0.0308(5)
C16 C	0.80853(18)	0.4147(3)	0.69522(11)	0.0277(4)
C17 C	0.3678(2)	0.6034(3)	0.54998(10)	0.0237(4)
C19 C	0.2981(3)	1.1071(3)	0.62230(14)	0.0361(5)
C20 C	0.9092(2)	0.4030(4)	0.62279(13)	0.0390(6)
C21 C	-0.4490(2)	1.0192(3)	0.87370(12)	0.0330(5)
C22 C	0.22441(19)	0.8738(3)	1.02548(10)	0.0257(4)

Bond lengths (Å)

atom	atom	distance
O1	C2	1.4457(18)
O1	C12	1.362(2)
O2	C4	1.444(2)
O2	C8	1.363(2)
O3	C1	1.4470(19)
O3	C7	1.354(2)
O4	C11	1.437(2)
O4	C16	1.341(2)
O5	C6	1.4439(18)

O5	C17	1.362(2)
O6	C7	1.204(2)
O7	C12	1.200(3)
O8	C16	1.202(3)
O9	C8	1.198(3)
O10	C3	1.419(2)
O11	C17	1.198(3)
O12	C9	1.192(3)
C1	C4	1.528(2)
C1	C6	1.522(3)
C2	C3	1.538(2)
C2	C4	1.522(2)
C3	C5	1.519(3)
C5	C9	1.509(3)
C6	C11	1.516(3)
C7	C14	1.497(3)
C8	C19	1.486(3)
C9	C21	1.501(3)
C12	C22	1.495(3)
C15	C17	1.490(3)
C16	C20	1.485(3)

Bond angles (o)

C2	O1	C12	117.76(13)
C4	O2	C8	117.41(12)

C1	O3	C7	117.66(12)
C11	O4	C16	115.39(13)
C6	O5	C17	117.22(13)
O3	C1	C4	104.53(11)
O3	C1	C6	110.01(13)
C4	C1	C6	113.51(12)
O1	C2	C3	109.18(13)
O1	C2	C4	108.67(12)
C3	C2	C4	112.56(12)
O10	C3	C2	105.60(13)
O10	C3	C5	109.82(12)
C2	C3	C5	111.80(12)
O2	C4	C1	105.75(11)
O2	C4	C2	110.53(13)
C1	C4	C2	112.16(12)
C3	C5	C9	112.77(14)
O5	C6	C1	108.52(12)
O5	C6	C11	108.83(13)
C1	C6	C11	111.18(13)
O3	C7	O6	123.16(16)
O3	C7	C14	110.23(14)
O6	C7	C14	126.59(16)
O2	C8	O9	122.75(18)
O2	C8	C19	111.09(15)
O9	C8	C19	126.17(18)

O12	C9	C5	122.06(18)
O12	C9	C21	121.03(18)
C5	C9	C21	116.92(15)
O4	C11	C6	107.01(13)
O1	C12	O7	123.34(15)
O1	C12	C22	110.57(14)
O7	C12	C22	126.09(16)
O4	C16	O8	122.83(16)
O4	C16	C20	111.62(15)
O8	C16	C20	125.55(16)
O5	C17	O11	123.16(15)
O5	C17	C15	110.70(15)

Torsion Angles(o)

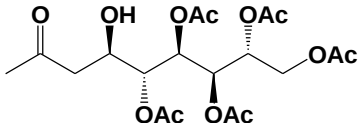
(Those having bond angles > 160 or < 20 degrees are excluded.)

atom1	atom2	atom3	atom4	angle
C2	O1	C12	O7	2.8(2)
C2	O1	C12	C22	-176.89(11)
C12	O1	C2	C3	110.74(13)
C12	O1	C2	C4	-126.14(13)
C4	O2	C8	O9	5.1(3)
C4	O2	C8	C19	-175.13(11)
C8	O2	C4	C1	130.93(12)
C8	O2	C4	C2	-107.46(14)

C1	O3	C7	O6	-8.6(3)
C1	O3	C7	C14	172.82(11)
C7	O3	C1	C4	-130.45(12)
C7	O3	C1	C6	107.35(13)
C11	O4	C16	O8	0.3(3)
C11	O4	C16	C20	-179.40(13)
C16	O4	C11	C6	155.54(14)
C6	O5	C17	O11	-4.9(3)
C6	O5	C17	C15	175.53(11)
C17	O5	C6	C1	127.61(13)
C17	O5	C6	C11	-111.28(14)
O3	C1	C4	O2	-179.13(10)
O3	C1	C4	C2	60.32(14)
O3	C1	C6	O5	58.88(14)
O3	C1	C6	C11	-60.77(14)
C4	C1	C6	O5	-57.83(16)
C4	C1	C6	C11	-177.49(11)
C6	C1	C4	O2	-59.24(15)
C6	C1	C4	C2	-179.80(11)
O1	C2	C3	O10	-176.54(10)
O1	C2	C3	C5	-57.15(15)
O1	C2	C4	O2	-55.46(14)
O1	C2	C4	C1	62.28(15)
C3	C2	C4	O2	65.60(15)
C3	C2	C4	C1	-176.66(11)

C4	C2	C3	O10	62.69(15)
C4	C2	C3	C5	-177.92(11)
O10	C3	C5	C9	-60.59(17)
C2	C3	C5	C9	-177.46(12)
C3	C5	C9	O12	-5.7(3)
C3	C5	C9	C21	174.46(13)
O5	C6	C11	O4	61.77(15)
C1	C6	C11	O4	-178.76(12)

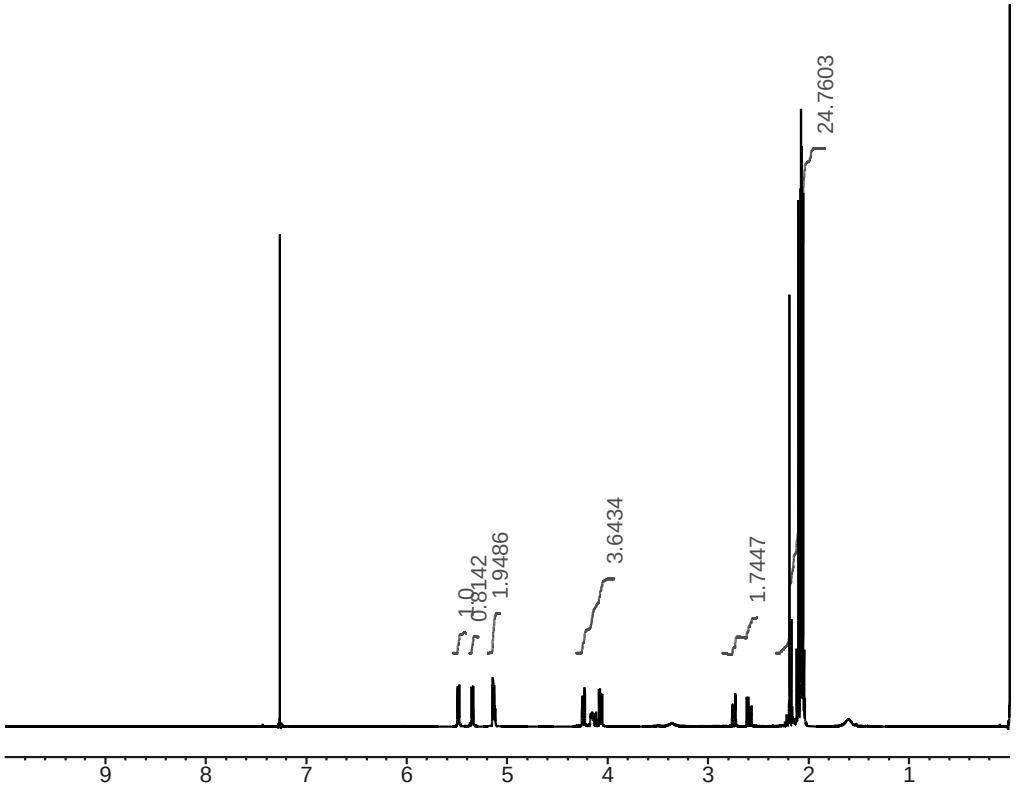
1,3-Dideoxy-5,6,7,8,9-penta-*O*-acetyl D-*glycero*-D-*allo*-nonulose **75**



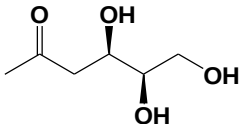
To a stirred solution of freshly prepared 2,3,4,5,6-penta-*O*-acetyl-*aldehydo*-D-mannnose **47** (32.0 mg, 0.0820 mmole) in acetone (0.200 ml, 2.46 mmole) was added 2.67 mg (0.00919 mmole) of L-prolinamido-glycoside **7** in 30 μl of distilled water, and the solution was stirred at ambient temperature for 1h, when TLC (chloroform-acetone, 10 : 1) indicated that the reaction was complete. The mixture was concentrated to remove excess amount of acetone, and the residue was diluted with ethyl acetate, washed with water, dried ($NaSO_4$), and concentrated to dryness. The crude product was then purified by column chromatography on silica gel (chloroform-acetone, 10 : 1), to give pure **74** as a colorless syrup; yield 30.3 mg (75.6%), $[\alpha]_D^{23.4}$ +31.3° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$, 600 MHz), δ 2.07 (s, 3H, Ac), 2.07 (s, 3H, Ac), 2.08 (s, 3H, Ac), 2.10 (s, 3H, Ac), 2.19 (s, 3H,1-CH_3), 2.59 (dd, 1H, $J_{3a,4}$ = 9.4 Hz, $J_{3a,3b}$ = 17.7 Hz,H3a), 2.74 (dd, 1H, $J_{3b,4}$ = 2.3 Hz, $J_{3a,3b}$ = 17.7 Hz,H3b), 4.06 (dd, 1H, $J_{8,9a}$ = 5.6 Hz, $J_{9a,9b}$ = 12.4 Hz, H9a), 4.16 (ddd, 1H, $J_{3a,4}$ = 9.4 Hz, $J_{3b,4}$ = 2.3 Hz, $J_{4,5}$ = 4.9 Hz, H4), 4.24 (dd, 1H, $J_{8,9b}$ = 2.8 Hz, $J_{9a,9b}$ = 12.4

Hz, H9b) , 5.13 (ddd, 1H, $J_{7,8}$ = 8.5 Hz, $J_{8,9a}$ = 5.6 Hz, $J_{8,9b}$ = 2.8 Hz, H8), 5.14 (dd, 1H, $J_{4,5}$ = 4.9 Hz, $J_{5,6}$ = 7.9 Hz, H5), 5.46 (dd, 1H, $J_{5,6}$ = 7.9 Hz, $J_{6,7}$ = 2.6 Hz, H6), 5.49 (dd, 1H, $J_{6,7}$ = 2.6 Hz, $J_{7,8}$ = 8.5 Hz, H7); ^{13}C NMR ($CDCl_3$, 150MHz) δ 20.5 (Ac), 20.6 (Ac), 20.6 (Ac), 20.7 (Ac), 20.7 (Ac), 30.6 (C1), 45.4 (C3), 61.8 (C9), 66.7 (C4), 67.6 (C7), 67.9 (C8), 68.1 (C6), 68.6 (C5), 169 (Ac), 169 (Ac), 170 (Ac), 171 (Ac), 172 (Ac), 208 (C2); ESI-TOFMS *m*/*z*: calcd for $[C_{16}H_{24}O_{10}+Na]^+$, 448.1581; found, 448.1666.

^{1}H NMR spectrum



1,3-Dideoxy-D-*threo*-hexulose **80**



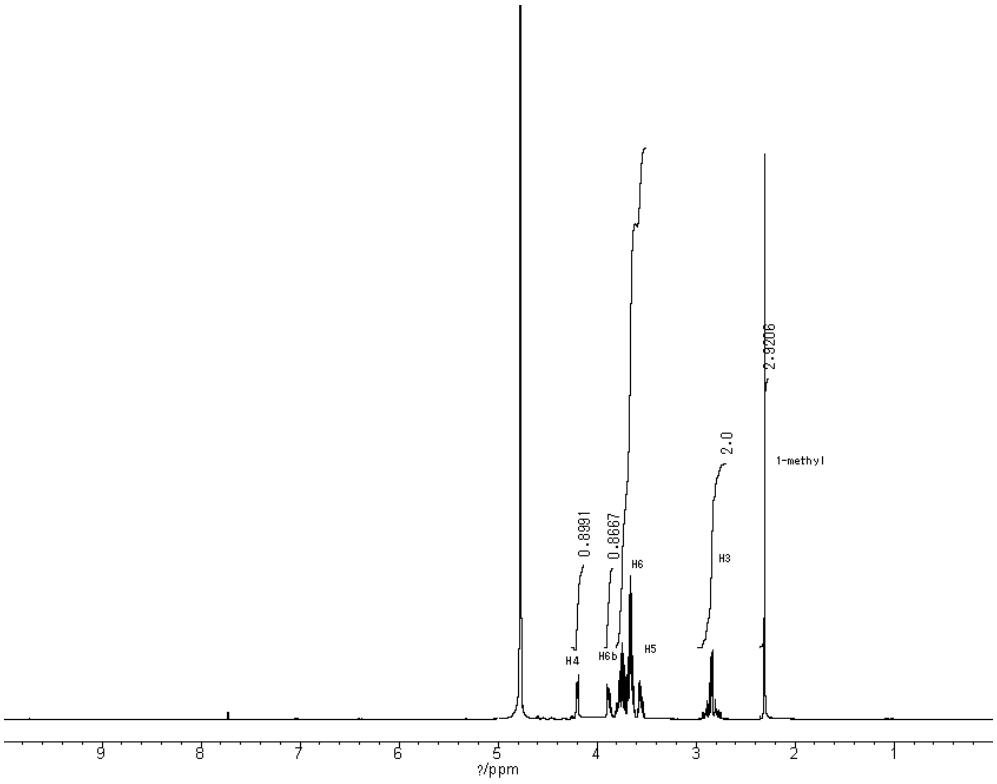
To a solution of D-glyceraldehyde (25.1 mg, 0.278 mmole) in water (500 μl) and acetone (0.680ml, 8.33 mmole) was added L-prolinamido-glycoside **7** (8.10 mg, 0.0278 mmole), and the mixture was stirred at ambient temperature for 1h, after which TLC (chloroform-methanol, 4 : 1) indicated that the reaction was complete and that one major product had been formed. The mixture was concentrated to dryness, and the residue was subjected to column chromatography on silica gel (chloroform – methanol, 10 : 1), to give pure **80** as a colorless syrup; yield 36.4 mg (86.5%), $[\alpha]_D^{26}$ 9.6º (*c* = 1.0, methanol), R_f = 0.46 (chloroform-methanol, 4 : 1).

^{1}H NMR ($CDCl_3$, 600 MHz), δ 2.31 (s, 3H, H1), 2.84 (dd, 2H, $J_{3,4}$ = 4.6 Hz, $J_{3,3'}$ = 8.9 Hz, H3), 3.57 (m, 1H, $J_{4,5}$ = 3.6 Hz, H5), 3.66 (dd, 1H, $J_{5,6}$ = 4.3 Hz, $J_{6,6'}$ = 11 Hz, H6), 3.74 (dd, 1H, $J_{5,6'}$ = 5.7 Hz, $J_{6,6'}$ = 11 Hz, H6'), 4.20 (m, 1H, $J_{3,4}$ = 4.6 Hz, $J_{3',4}$ = 8.9 Hz, $J_{4,5}$ = 3.6 Hz, H4);

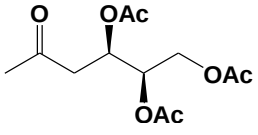
^{13}C NMR ($CDCl_3$, 150MHz) δ 32.7 (C1), 49.3 (C3), 65.1 (C6), 70.1 (C4), 216 (C2);

ESI-TOFMS *m*/*z*: calcd for $[C_9H_{16}O_4+Na]^+$, 211.09463; found, 211.09435.

^{1}H NMR spectrum



4,5,6-Tri-*O*-acetyl-1,3-dideoxy-D-*threo*-hexulose **81**



The deoxy-hexulose **80** (21.6 mg, 0. 145 mmole) was dissolved in pyridine (200 μl), and Ac_2O (100 μl) was added. The mixture was stirred at ambient temperature for 24 h. After which time, the

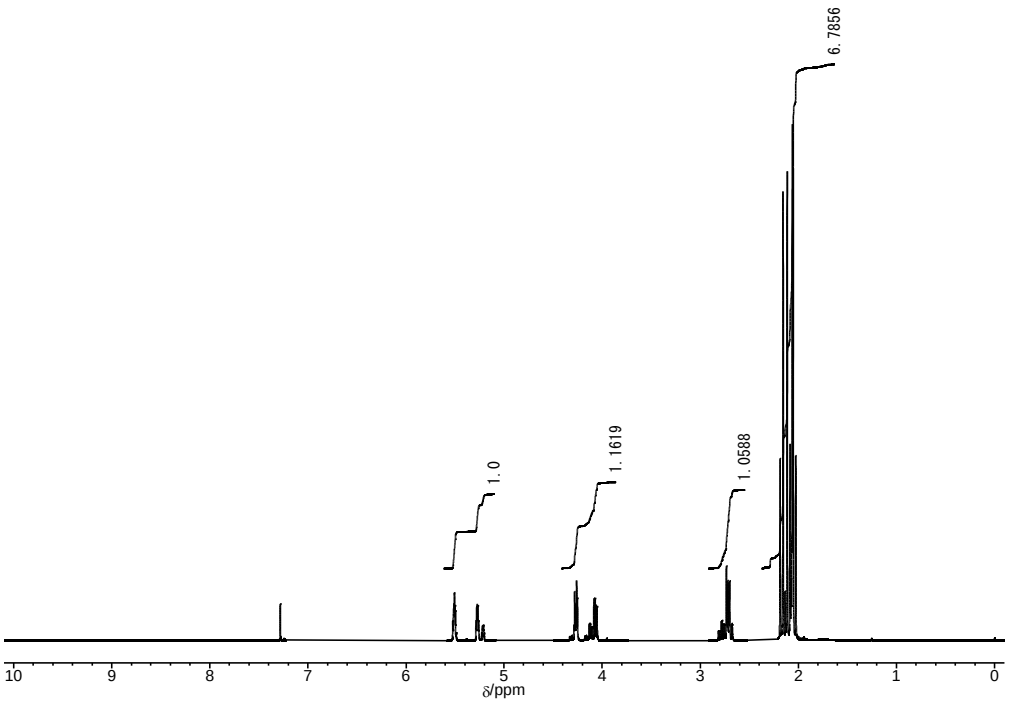
solvents were removed by azeotropic concentration with toluene, to give a light-brown syrup which was purified by silica gel column chromatography (dichloromethane-acetone, 10 : 1) to give pure **81** as a colorless syrup; yield 23.0 mg (57.9%), $[\alpha]_D^{26}$ 26º (*c* = 1.0, chloroform), R_f = 0.36 (dichloromethane-acetone, 10 : 1).

^{1}H NMR ($CDCl_3$, 600 MHz), δ 2.05 (s, 3H, Ac), 2.06 (s, 3H, Ac), 2.11 (s, 3H, Ac), 2.16 (s, 3H, H1), 2.84 (dd, 2H, $J_{3,4}$ = 5.8, H3), 4.07 (dd, 1H, $J_{5,6}$ = 6.9 Hz, $J_{6,6}$ = 12 Hz, H6), 4.27 (dd, 1H, $J_{5,6'}$ = 4.7 Hz, $J_{6,6'}$ = 12 Hz, H6'), 5.27 (m, 1H, $J_{4,5}$ = 3.6 Hz, $J_{5,6}$ = 6.9 Hz, $J_{5,6'}$ = 12 Hz, H5), 5.51 (m, 1H, $J_{3,4}$ = 5.8 Hz, $J_{4,5}$ = 3.6 Hz, H4);

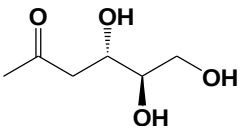
^{13}C NMR ($CDCl_3$, 150MHz) δ 20.5 (Ac), 20.6 (Ac), 20.6 (Ac), 30.1 (C1), 43.8 (C3), 62.1 (C6), 67.6 (C4), 70.5 (C5), 169 (Ac), 170 (Ac), 170 (Ac), 216 (C2);

ESI-TOFMS *m*/*z*: calcd for $[C_9H_{16}O_4+Na]^+$, 211.09463; found, 211.09435.

^{1}H NMR spectrum



1,3-Dideoxy-D-*erythro*-hexulose **78**



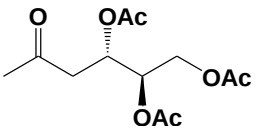
To a solution of D-glyceraldehyde (25.6 mg, 0.278 mmole) in water (500 μl) and acetone (0.680ml, 8.33 mmole) was added D-prolinamido-glycoside **7** (8.50 mg, 0.0278 mmole), and the mixture was stirred at ambient temperature for 1h, after which TLC (chloroform-methanol, 4 : 1) indicated that the reaction was complete and that one major product had been formed. The mixture was concentrated to dryness, and the residue was subjected to column chromatography on silica gel (chloroform – methanol, 10 : 1), to give pure **78** as a colorless syrup; yield 31.9 mg (94.0%), $[\alpha]_D^{26}$ 9.6º (*c* = 1.0, methanol), R_f = 0.4 (chloroform-methanol, 4 : 1).

^{1}H NMR ($CDCl_3$, 600 MHz), δ 2.31 (s, 3H, H1), 2.84 (dd, 2H, $J_{3,4}$ = 4.6 Hz, $J_{3,3'}$ = 8.9 Hz, H3), 3.57 (dt, 1H, $J_{4,5}$ = 3.6 Hz, H5), 3.66 (dd, 1H, $J_{5,6}$ = 4.3 Hz, $J_{6,6'}$ = 11 Hz, H6), 3.74 (dd, 1H, $J_{5,6'}$ = 5.7 Hz, $J_{6,6'}$ = 11 Hz, H6'), 4.20 (ddd, 1H, $J_{3,4}$ = 4.6 Hz, $J_{3',4}$ = 8.9 Hz, $J_{4,5}$ = 3.6 Hz, H4);

^{13}C NMR ($CDCl_3$, 150MHz) δ 32.7 (C1), 49.3 (C3), 65.1 (C6), 70.1 (C4), 216 (C2);

ESI-TOFMS *m*/*z*: calcd for $[C_9H_{16}O_4+Na]^+$, 211.09463; found, 211.09435.

4,5,6-Tri-*O*-acetyl-1,3-dideoxy-D-*erythro*-hexulose **79**

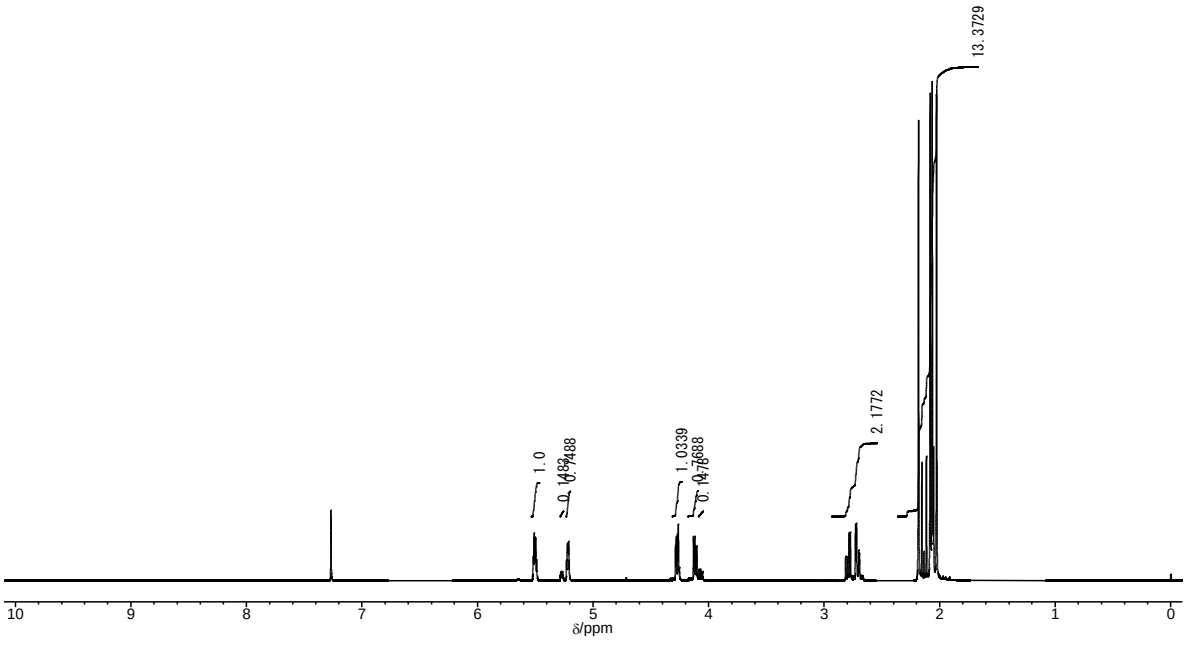


The deoxy-hexulose **78** (39.1 mg, 0.264 mmole) was dissolved in pyridine (390 μl), and Ac_2O

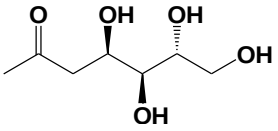
(200 μl) was added. The mixture was stirred at ambient temperature for 24 h. After which time, the solvents were removed by azeotropic concentration with toluene, to give a light-brown syrup which was purified by silica gel column chromatography (dichloromethane-acetone, 10 : 1) to give pure **79** as a colorless syrup; yield 42.8 mg (59.1%), $[\alpha]_D^{26}$ 26º (*c* = 1.0, chloroform), R_f = 0.X (dichloromethane-acetone, 10 : 1).

^{1}H NMR ($CDCl_3$, 600 MHz), δ 2.05 (s, 3H, Ac), 2.06 (s, 3H, Ac), 2.11 (s, 3H, Ac), 2.16 (s, 3H, H1), 2.84 (dd, 2H, $J_{3,4}$ = 5.8, H3), 4.07 (dd, 1H, $J_{5,6}$ = 6.9 Hz, $J_{6,6}$ = 12 Hz, H6), 4.27 (dd, 1H, $J_{5,6'}$ = 4.7 Hz, $J_{6,6'}$ = 12 Hz, H6'), 5.27 (m, 1H, $J_{4,5}$ = 3.6 Hz, $J_{5,6}$ = 6.9 Hz, $J_{5,6'}$ = 12 Hz, H5), 5.51 (m, 1H, $J_{3,4}$ = 5.8 Hz, $J_{4,5}$ = 3.6 Hz, H4); ^{13}C NMR ($CDCl_3$, 150MHz) δ 20.5 (Ac), 20.6 (Ac), 20.6 (Ac), 30.1 (C1), 43.8 (C3), 62.1 (C6), 67.6 (C4), 70.5 (C5), 169 (Ac), 170 (Ac), 170 (Ac), 216 (C2); ESI-TOFMS *m*/*z*: calcd for $[C_9H_{16}O_4+Na]^+$, 211.09463; found, 211.09435.

^{1}H NMR spectrum



1,3-Dideoxy-D-*xylo*-heptulose **83**



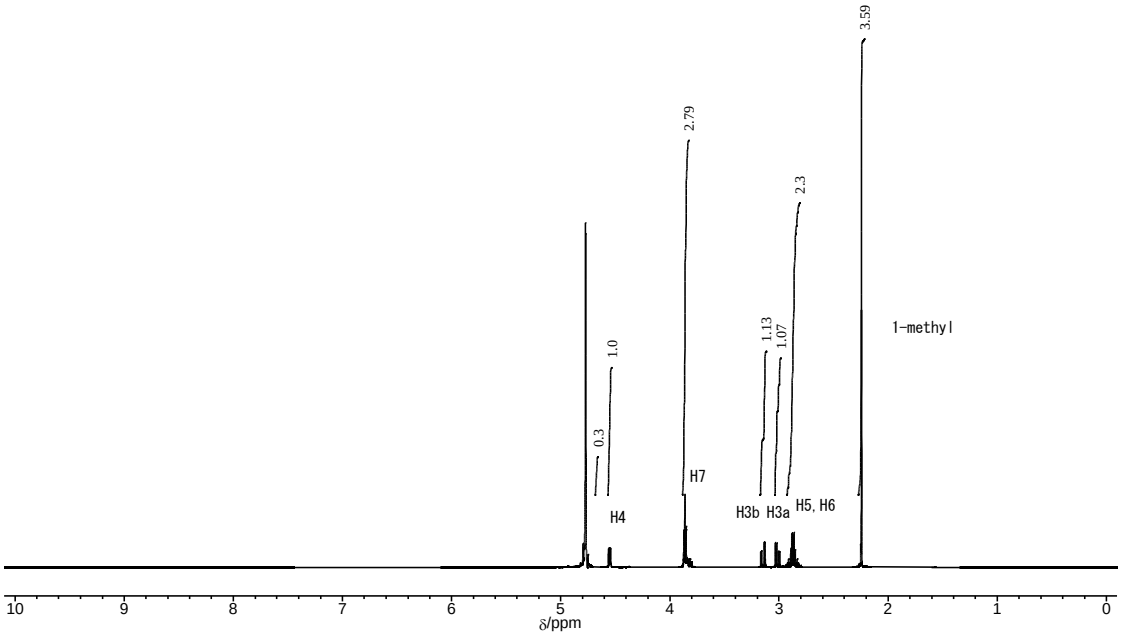
To a solution of D-erythrose (25.0 mg, 0.208 mmole) in water (500 μl) and acetone (0.510 ml, 6.24 mmole) was added D-prolinamido-glycoside **8** (6.03 mg, 0.0208 mmole), and the mixture was stirred at ambient temperature for 1h, after which TLC (chloroform-methanol, 4 : 1) indicated that the reaction was complete and that one major product had been formed. The mixture was concentrated to dryness, and the residue was subjected to column chromatography on silica gel (chloroform – methanol, 10 : 4), to give pure **83** as a colorless syrup; yield 28.1 mg (75.8%), $[\alpha]_D^{26}$ -26.4º (*c* = 0.5, methanol), R_f = 0.3 (chloroform-methanol, 4 : 1).

^{1}H NMR ($CDCl_3$, 600 MHz), δ 2.25 (s, 3H, H1), 2.87 – 2.92 (m, 2H, H5, H6), 3.01 (dd, 1H, $J_{3a,4}$ = 7.1 Hz, $J_{3a,3b}$ = 17.8 Hz, H3a), 3.15 (dd, 1H, $J_{3b,4}$ = 3.7 Hz, $J_{3a,3b}$ = 17.8 Hz, H3b), 3.86 (t, 2H, $J_{6,7}$ = 5.9 Hz, H7), 4.20 (dd, 1H, $J_{3a,4}$ = 7.1 Hz, $J_{3b,4}$ = 3.7 Hz, $J_{4,5}$ = 11.0 Hz, H4);

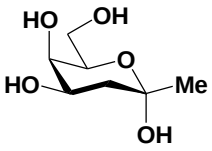
^{13}C NMR ($CDCl_3$, 150MHz) δ 32.4 (C1), 42.9 (C5), 42.9 (C6), 48.6 (C3), 59.0 (C7), 216 (C2);

ESI-TOFMS *m*/*z*: calcd for $[C_7H_{14}O_5+Na]^+$, 201.0733; found, 201.0745.

^{1}H NMR spectrum



1,3-Dideoxy-D-*lyxo*-heptulose **82**



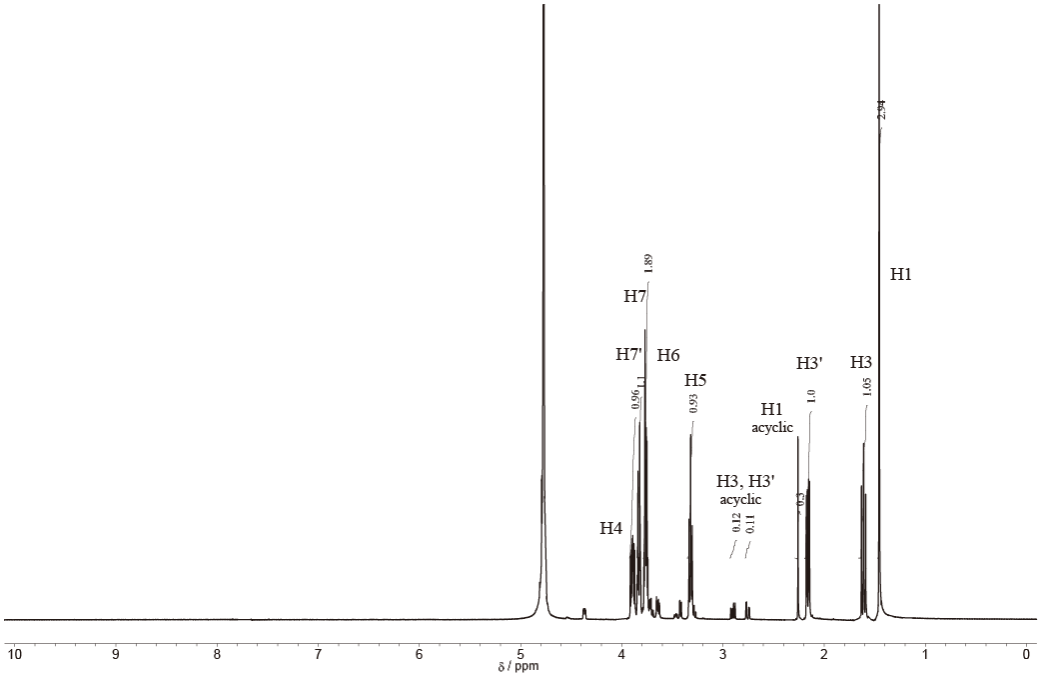
To a solution of D-erythrose (25.2 mg, 0.208 mmole) in water (500 μl) and acetone (0.510 ml, 6.24 mmole) was added L-prolinamido-glycoside **7** (6.03 mg, 0.0208 mmole), and the mixture was stirred at ambient temperature for 1h, after which TLC (chloroform-methanol, 4 : 1) indicated that the reaction was complete and that one major product had been formed. The mixture was concentrated to dryness, and the residue was subjected to column chromatography on silica gel (chloroform – methanol, 10 : 4), to give pure **82** as a colorless syrup; yield 31.6 mg (85.3%), $[\alpha]_D^{26}$ 45.9º (*c* = 0.5, methanol), R_f = 0.28 (chloroform-methanol, 4 : 1).

^{1}H NMR ($CDCl_3$, 600 MHz), δ 1.46 (s, 3H, H1), 1.61 (t, 1H, $J_{3a,4}$ = 12.3 Hz, $J_{3a,3b}$ = 13.2 Hz, H3a), 2.16 (dd, 1H, $J_{3b,4}$ = 5.1 Hz, $J_{3a,3b}$ = 13.2 Hz, H3b), 3.32 (t, 1H, $J_{5,6}$ = 9.3 Hz, H5), 3.74 – 3.78 (m, 2H, $J_{5,6}$ = 9.3 Hz, $J_{6,7b}$ = 5.5 Hz, H6, H7a), 3.83 (dd, 1H, $J_{6,7b}$ = 5.5 Hz, $J_{7a,7b}$ = 8.7 Hz, H7b), 3.89

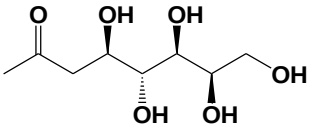
(ddd, 1H, $J_{3a,4}$ = 12.3 Hz, $J_{3b,4}$ = 5.1 Hz, $J_{4,5}$ = 2.1 Hz, H4);

^{13}C NMR ($CDCl_3$, 150MHz) δ 30.6 (C1), 44.6 (C3), 63.5 (C7), 71.7 (C4), 73.8 (C5), 75.7 (C6), 99.6 (C2);

ESI-TOFMS *m*/*z*: calcd for $[C_7H_{14}O_5+Na]^+$, 201.0733; found, 201.0745.



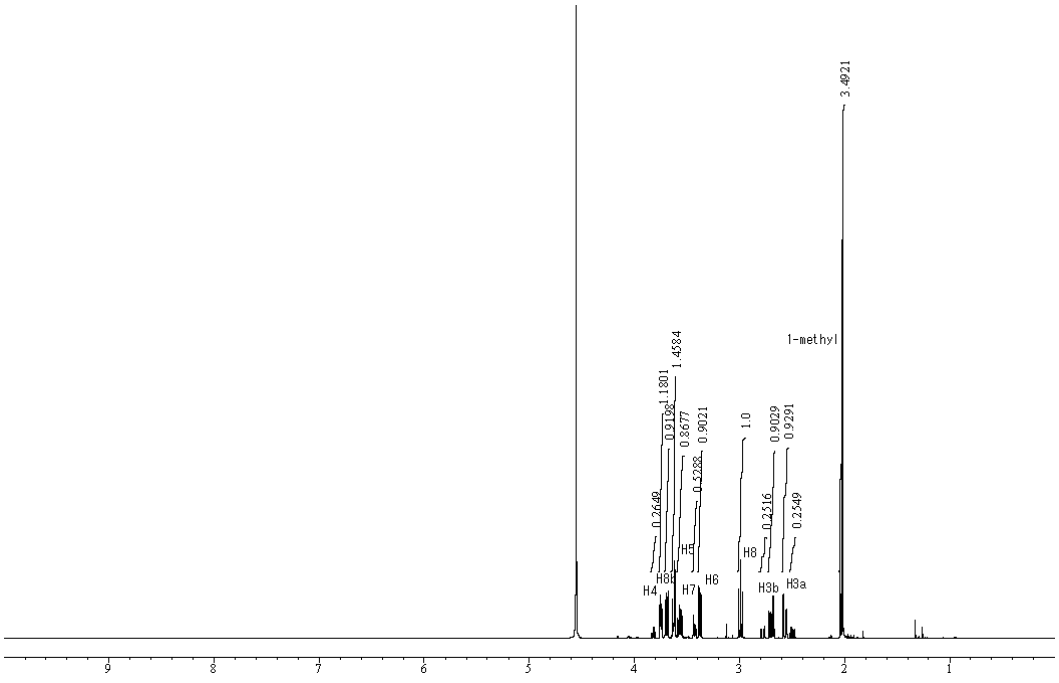
1,3-Dideoxy-D-*glycero*- D-*xylo*-octulose **87**



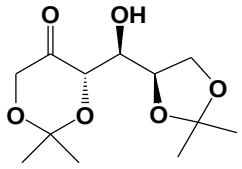
To a stirred solution of D-lyxose (25.3 mg, 0.168 mmole) in acetone (0.53 ml, 6.5 mmole) was added 14.5 mg (0.0500 mole) of L-prolinamido-glycoside **7** in 0.410 ml of distilled water, and the solution was stirred at ambient temperature for two weeks, when TLC (chloroform-methanol, 4 : 1) indicated that the reaction was complete. The mixture was concentrated to remove excess amount of acetone, and the the crude product was then purified by column chromatography on silica gel

(chloroform-acetone, 4 : 1), to give pure **87** as a colorless syrup; yield 14.7 mg (41.9%), $[\alpha]_D^{27}$ +X° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$, 600 MHz), δ 2.02 (s, 3H,1-CH_3), 2.57 (dd, 1H, $J_{3a,4}$ = 3.9 Hz, $J_{3a,3b}$ = 17.5 Hz,H3a), 2.70 (dd, 1H, $J_{3b,4}$ = 8.8 Hz, $J_{3a,3b}$ = 17.5 Hz,H3a), 2.99 (t, 1H, $J_{7,8a}$ = 10.9 Hz, $J_{8a,8b}$ = 16.6Hz, H8a), 3.37 (dd, 1H, $J_{5,6}$ = 4.9 Hz, $J_{6,7}$ = 9.8 Hz, H6), 3.57 (dt, 1H, $J_{6,7}$ = 9.8 Hz, $J_{7,8a}$ = 10.9 Hz, $J_{7,8b}$ = 5.6 Hz, H7), 3.69 (dd, 1H, $J_{7,8b}$ = 5.6 Hz, $J_{8a,8b}$ = 16.6 Hz, H8b) , 5.09 (dd, 1H, $J_{4,5}$ = 6.8 Hz, $J_{5,6}$ = 5.9 Hz, H5), 3.75 (ddd, 1H, $J_{3a,4}$ = 3.9 Hz, $J_{3b,4}$ = 8.8 Hz, $J_{4,5}$ = 8.9 Hz, H4); ^{13}C NMR ($CDCl_3$, 150MHz) δ 32.5 (C1), 47.2 (C3), 69.0 (C7), 71.8 (C8), 73.4 (C5), 74.5 (C6), 76.7 (C4), 215 (C2); ESI-TOFMS *m*/*z*: calcd for $[C_{16}H_{24}O_{10}+Na]^+$, 377.1369; found, 377.1391.

^{1}H NMR spectrum

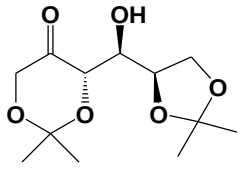


1,3:5,6-Di-*O*-isopropylidene-D-tagatose **88**



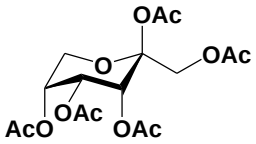
To a solution of freshly distilled 2,3-*O*-isopropylidene-D-glyceraldehyde **10** (52.3 mg, 0.402 mmole) in distilled water at ambient temperature were added freshly distilled 2,2-dimethyl-1,3-dioxan-5-one (72.0 μl, 0.603 mmole) and a catalytic amount (35.0 mg, 0.121 mole) of L-prolinamido-glycoside **7**, and the solution was stirred for 6 h. After which time, the mixture was poured into water, and extracted with ethyl acetate in the usual way. The extract was dried over anhydrous Na_2SO_4, and concentrated to dryness. The colorless syrup was then purified by column chromatography on silica gel (toluene – acetone, 20 : 1) to give **88** as a colorless syrup; yield 75.3 mg (72.0%). The properties and spectral data of which were identical to the already reported.

1,3:5,6-Di-*O*-isopropylidene-D-psicose **89**



Processing as described for the *psico*-analogue using L-prolinamido-glycoside **8** gave pure **89** as a colorless syrup.

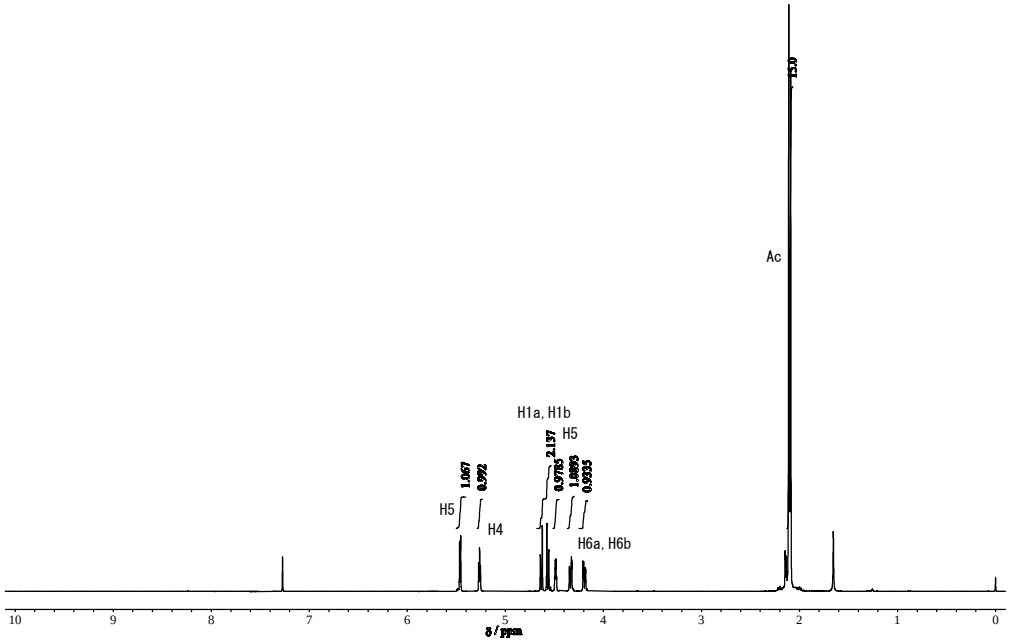
Penta-*O*-acetly-β-D-psicopyranose **93**



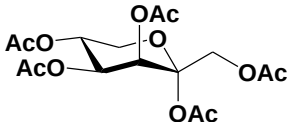
To a solution of **89** (50.0 mg, 0.192 mmole) in ice-cooling THF (500 μl) was added 80 vol % aqueous trifluoroacetic acid (500 μl) so that the pH was 0-1. The mixture was stirred at room temperature for 30 min and TLC then indicated completion of the reaction. The mixture was concentrated by azeotropic distillation with toluene to give a syrupy psicose, a solution of which in pyridine (500 μl ml) at ambient temperature was treated with Ac_2O (250 μl ml). The mixture was kept at the same temperature for 4 h and worked up in the usual way to give a syrupy product that was purified by column chromatography (solid charged, toluene – ethyl acetate, 10 : 1) to afford **93** as a syrup together with a mixture of acyclic pentaacetly psicose and pentaacetyl psicofuranoses; $[\alpha]_D^{26.4}$ +22º (c 1.0, chloroform);

^{1}H NMR (600 MHz, chloroform-*d*): δ 2.09 (s, 3H, Ac), 2.10 (s, 3H, Ac), 2.11 (s, 3H, Ac), 4.20 (dd, 1H, $J_{5,6a}$ 4.40 Hz, $J_{6a,6b}$ 12.3 Hz, H6a), 4.33 (dd, 1H, $J_{5,6b}$ 3.00 Hz, $J_{6a,6b}$ 12.3 Hz, H6b), 4.49 (dd, 1H, $J_{5,6a}$ 4.40 Hz, $J_{5,6b}$ 3.00 Hz, H5), 4.57 (d, 1H, $J_{1a,1b}$ 11.8 Hz, H1a), 4.63 (d, 1H, $J_{1a,1b}$ 11.8 Hz, H1b), 5.26 (t, 1H, $J_{3,4}$ 6.10 Hz, H4), 5.46 (d, 1H, $J_{3,4}$ 6.10 Hz, H3); ^{13}C NMR (150 MHz, chloroform-*d*): δ 20.2 (Ac), 20.4 (Ac), 20.5 (Ac), 20.6 (Ac), 21.5 (Ac), 62.8 (C6), 62.9 (C1), 70.0 (C4), 71.0 (C3), 80.2 (C5), 106.2 (C2), 168.4 (Ac), 168.9 (Ac), 169.6 (Ac), 169.6 (Ac), 170.3 (Ac).

^{1}H NMR spectrum

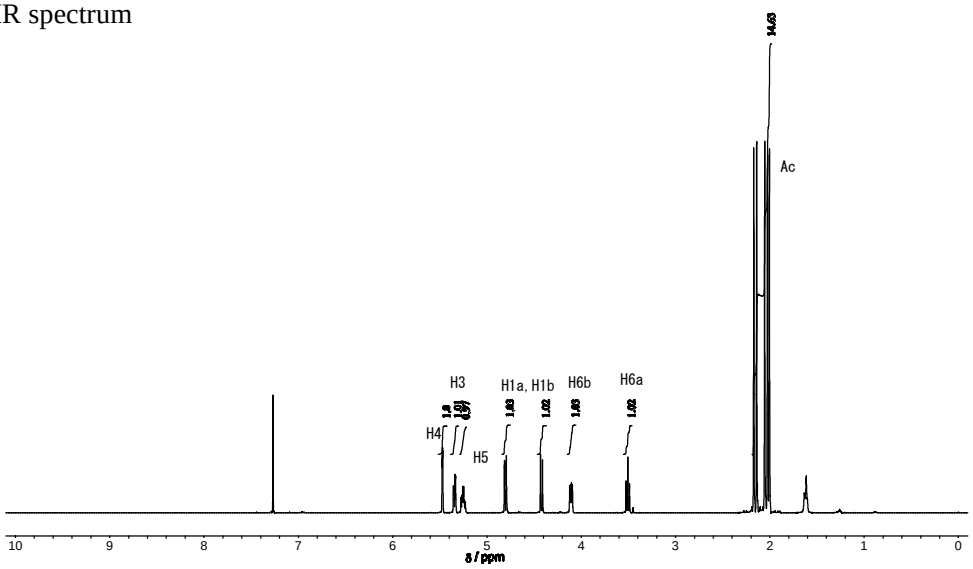


Penta-*O*-acetly-α-D-tagatopyranose **94**

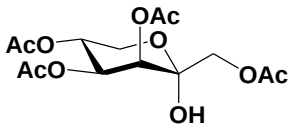


This compound was obtained from **89** by an identical procedure used for the *psico*-analogue along with tetra-*O*-acetyl-α-D-tagatopyranose **94**; ^{1}H NMR (600 MHz, chloroform-*d*): δ 2.00 (s, 3H, Ac), 2.03 (s, 3H, Ac), 2.06 (s, 3H, Ac), 2.14 (s, 3H, Ac), 2.17 (s, 3H, Ac), 3.51 (t, 1H, $J_{5,6a}$ 10.7 Hz, $J_{6a,6b}$ 11.2 Hz, H6a), 4.11 (dd, 1H, $J_{5,6b}$ 5.94 Hz, $J_{6a,6b}$ 11.2 Hz, H6b), 4.42 (d, 1H, $J_{1a,1b}$ 12.2 Hz, H1a), 4.80 (d, 1H, $J_{1a,1b}$ 12.2 Hz, H1b), 5.25 (dt, 1H, $J_{4,5}$ 10.5 Hz, $J_{5,6a}$ 10.7 Hz, $J_{5,6b}$ 5.94 Hz, H5), 5.35 (dd, 1H, $J_{3,4}$ 3.23 Hz, $J_{4,5}$ 10.5 Hz, H4), 5.47 (d, 1H, $J_{3,4}$ 3.23 Hz, H3); ^{13}C NMR (150 MHz, chloroform-*d*): δ 20.4 (Ac), 20.5 (Ac), 20.6 (Ac), 20.6 (Ac), 21.7 (Ac), 60.0 (C1), 61.4 (C6), 65.4 (C5), 66.9 (C4), 68.5 (C3), 102.0 (C2), 167.9 (Ac), 169.5 (Ac), 169.8 (Ac), 169.8 (Ac), 169.9 (Ac).

^{1}H NMR spectrum

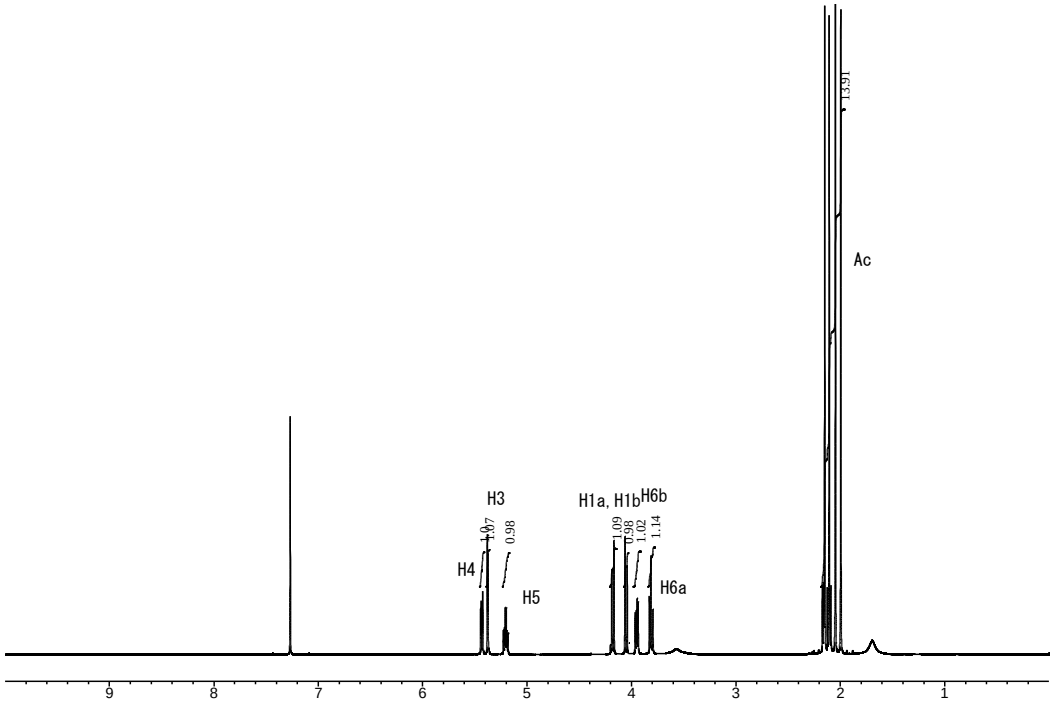


Tetra-*O*-acetly-α-D-tagatopyranose **95**

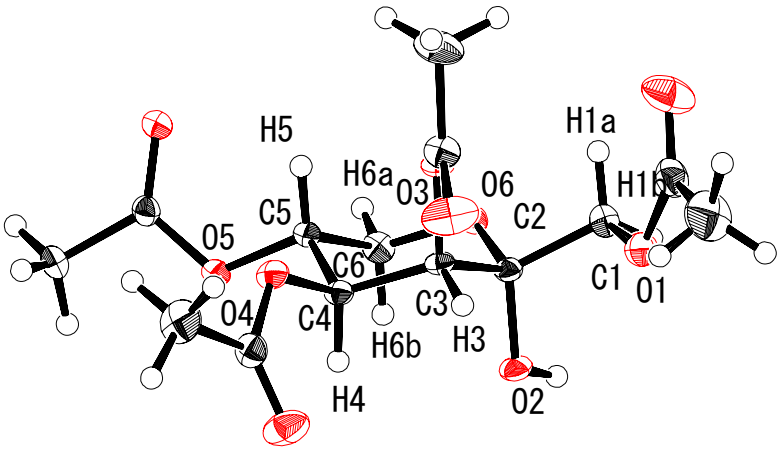


$[\alpha]_D^{26.4}$ +15.6º (c 1.0, chloroform); mp 126.5 – 128.5 ºC; ^{1}H NMR (600 MHz, chloroform-*d*): δ 2.00 (s, 3H, Ac), 2.05 (s, 3H, Ac), 2.11 (s, 3H, Ac), 2.15 (s, 3H, Ac), 3.81 (t, 1H, $J_{5,6a}$ 10.7 Hz, $J_{6a,6b}$ 10.7 Hz, H6a), 3.95 (dd, 1H, $J_{5,6b}$ 5.94 Hz, $J_{6a,6b}$ 10.7 Hz, H6b), 4.05 (d, 1H, $J_{1a,1b}$ 11.9 Hz, H1a), 4.18 (d, 1H, $J_{1a,1b}$ 11.9 Hz, H1b), 5.21 (dt, 1H, $J_{4,5}$ 10.4 Hz, $J_{5,6a}$ 10.7 Hz, $J_{5,6b}$ 5.94 Hz, H5), 5.38 (d, 1H, $J_{3,4}$ 3.38 Hz, H3), 5.44 (dd, 1H, $J_{3,4}$ 3.28 Hz, $J_{4,5}$ 10.4 Hz, H4); ^{13}C NMR (150 MHz, chloroform-*d*): δ 20.6 (Ac), 20.6 (Ac), 20.7 (Ac), 60.1 (C6), 65.4 (C1), 66.2 (C5), 68.8 (C3), 69.0 (C4), 96.1 (C2), 169.8 (Ac), 169.9 (Ac), 170.1 (Ac), 171.3 (Ac). It crystallizes in the orthorhombic space group $P2_12_12_1$ with cell parameters a = 9.553 (2) Å, b = 10.880 (18) Å, c = 18.020 (3) Å, and Z = 4.

^{1}H NMR spectrum



Crystal structure of tetra-*O*-acetly-α-D-tagatopyranose **95**



Empirical Formula $C_{14}H_{20}O_{10}$

Formula Weight 348.31

Crystal Color, Habit colorless, block

Crystal Dimensions 0.200 X 0.200 X 0.200 mm

Crystal System orthorhombic

Lattice Type Primitive

Lattice Parameters *a* = 7.939(3) Å

b = 13.469(3) Å

c = 15.825(5) Å

V = 1692.2(5) $Å^3$

Space Group $P2_12_12_1$

Z value 4

*D*calc 1.367 g/cm3

R-factor 3.13%

Temperature 123 K

ω oscillation Range (c=45.0, f=180.0) 0.0 - 160.0o

No. of Reflections Measured Total: 4941

Atomic coordinates and Biso/Beq

atom	x	y	z	B_{eq}
O1 O	-0.09777(9)	0.56703(6)	0.57653(5)	0.01598(18) 4
O2 O	-0.03697(12)	0.68502(8)	0.28584(6)	0.0250(3)
O3 O	0.10182(10)	0.74814(6)	0.56230(5)	0.01710(18)
O4 O	0.08366(11)	0.46811(6)	0.45322(6)	0.01965(19)
O5 O	0.03852(11)	0.61365(7)	0.75439(6)	0.0247(3)
O6 O	0.31302(10)	0.65685(7)	0.63014(6)	0.0206(2)
O7 O	0.19059(10)	0.63144(7)	0.35794(5)	0.0198(2)
O8 O	0.31157(14)	0.38102(8)	0.49239(8)	0.0355(3)
O17 O	-0.24117(14)	0.63526(10)	0.76973(9)	0.0435(4)
O18 O	-0.10028(14)	0.41190(8)	0.63024(8)	0.0375(3)
C1 C	0.08352(13)	0.56819(8)	0.58060(7)	0.0146(3)
C4 C	0.17797(17)	0.38407(9)	0.45738(8)	0.0220(3)
C5 C	0.17024(15)	0.73782(9)	0.47901(7)	0.0188(3)
C6 C	0.13934(13)	0.66831(8)	0.61775(7)	0.0152(3)
C7 C	0.10420(15)	0.65127(9)	0.28662(7)	0.0180(3)
C8 C	-0.17452(16)	0.48210(9)	0.60295(8)	0.0218(3)
C9 C	0.15377(14)	0.55542(8)	0.49177(7)	0.0153(3)

C10	C	0.10560(13)	0.64331(9)	0.43776(7)	0.0156(3)
C11	C	-0.11470(18)	0.59108(11)	0.78679(9)	0.0278(3)
C12	C	0.04415(16)	0.69724(9)	0.69751(7)	0.0209(3)
C13	C	0.0908(2)	0.29959(10)	0.41406(11)	0.0345(4)
C14	C	-0.36139(17)	0.49080(11)	0.59492(12)	0.0341(4)
C15	C	-0.1052(3)	0.50294(14)	0.84422(11)	0.0453(5)
C16	C	0.20349(16)	0.62250(11)	0.21103(8)	0.0251(3)

Bond lengths (Å)

atom	atom	distance
O1	C1	1.4408(13)
O1	C8	1.3618(15)
O2	C7	1.2095(16)
O3	C5	1.4324(14)
O3	C6	1.4194(14)
O4	C4	1.3587(16)
O4	C9	1.4369(14)
O5	C11	1.3546(17)
O5	C12	1.4421(16)
O6	C6	1.4013(14)
O7	C7	1.3474(14)
O7	C10	1.4410(14)
O8	C4	1.1974(18)

O17	C11	1.1980(19)
O18	C8	1.1949(17)
C1	C6	1.5364(16)
C1	C9	1.5221(16)
C4	C13	1.498(2)
C5	C10	1.5198(17)
C6	C12	1.5219(16)
C7	C16	1.4841(18)
C8	C14	1.4937(19)
C9	C10	1.5093(16)
C11	C15	1.497(3)

Bond angles (o)

atom	atom	atom	angle
C1	O1	C8	116.25(9)
C5	O3	C6	114.57(9)
C4	O4	C9	116.60(10)
C11	O5	C12	116.06(11)
C7	O7	C10	118.29(9)
O1	C1	C6	108.35(9)
O1	C1	C9	108.88(9)
C6	C1	C9	110.30(9)
O4	C4	O8	122.63(12)

O4	C4	C13	110.86(12)
O8	C4	C13	126.51(13)
O3	C5	C10	110.39(10)
O3	C6	O6	112.11(9)
O3	C6	C1	111.58(9)
O3	C6	C12	102.39(9)
O6	C6	C1	103.93(9)
O6	C6	C12	113.63(10)
C1	C6	C12	113.51(9)
O2	C7	O7	123.69(11)
O2	C7	C16	125.60(11)
O7	C7	C16	110.67(10)
O1	C8	O18	123.70(12)
O1	C8	C14	110.64(11)
O18	C8	C14	125.65(13)
O4	C9	C1	110.04(9)
O4	C9	C10	107.65(9)
C1	C9	C10	109.97(9)
O7	C10	C5	108.14(9)
O7	C10	C9	106.90(9)
C5	C10	C9	109.15(9)
O5	C11	O17	123.77(14)
O5	C11	C15	111.25(13)
O17	C11	C15	124.96(15)
O5	C12	C6	109.46(10)

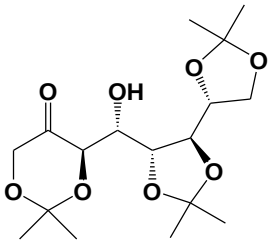
Torsion Angles(o)

(Those having bond angles > 160 or < 20 degrees are excluded.)

atom1	atom2	atom3	atom4	angle
C1	O1	C8	O18	1.75(16)
C1	O1	C8	C14	-179.68(8)
C8	O1	C1	C6	-135.73(9)
C8	O1	C1	C9	104.29(10)
C5	O3	C6	O6	60.76(11)
C5	O3	C6	C1	-55.35(11)
C5	O3	C6	C12	-177.09(8)
C6	O3	C5	C10	58.70(11)
C4	O4	C9	C1	-96.69(11)
C4	O4	C9	C10	143.47(10)
C9	O4	C4	O8	1.29(17)
C9	O4	C4	C13	-179.39(9)
C11	O5	C12	C6	-131.03(11)
C12	O5	C11	O17	1.08(19)
C12	O5	C11	C15	179.59(9)
C7	O7	C10	C5	-105.11(10)
C7	O7	C10	C9	137.48(10)
C10	O7	C7	O2	5.29(17)
C10	O7	C7	C16	-172.57(9)

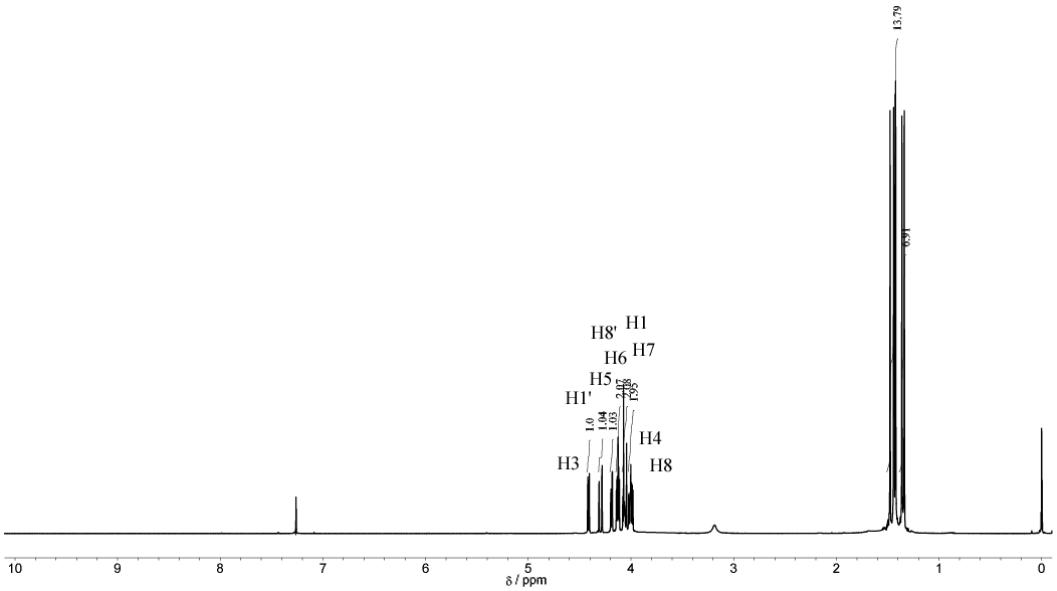
O1	C1	C6	O3	-67.00(11)
O1	C1	C6	O6	171.99(8)
O1	C1	C6	C12	48.06(11)
O1	C1	C9	O4	-53.75(11)
O1	C1	C9	C10	64.67(10)
C6	C1	C9	O4	-172.51(8)
C6	C1	C9	C10	-54.09(11)
C9	C1	C6	O3	52.08(11)
C9	C1	C6	O6	-68.93(10)
C9	C1	C6	C12	167.14(8)
O3	C5	C10	O7	-174.41(8)
O3	C5	C10	C9	-58.46(11)
O3	C6	C12	O5	167.54(8)
O6	C6	C12	O5	-71.34(12)
C1	C6	C12	O5	47.13(12)
O4	C9	C10	O7	-66.08(10)
O4	C9	C10	C5	177.18(8)
C1	C9	C10	O7	174.04(8)
C1	C9	C10	C5	57.30(11)

1,3:5,6:7,8-Tri-*O*-isipropylidene- D-*glycero*-D-*gluco*-octulose **96**



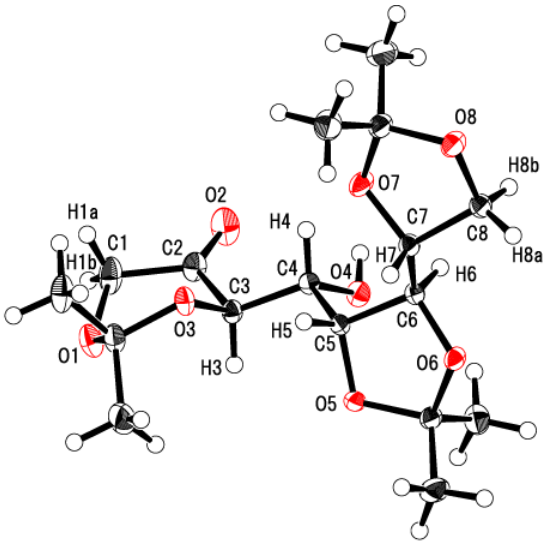
To a solution of freshly distilled 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-arabinose **16** (200 mg, 0.869 mmole) in freshly distilled 2,2-dimethyl-1,3-dioxan-5-one (155 μl, 1.30 mmole) was added 25.2 mg (0.0 869 mmole) of L-prolinamido-glycoside **7** in water (ml, mole), and the solution was stirred at room temperature for 24 h. The mixture was poured into water, and extracted with ethyl acetate. The extract was dried (Na_2SO_4), and concentrated to dryness. The slightly yellowish syrup was then purified by column chromatography on silica gel (solid charged, toluene-ethyl acetate, 20 : 1) to give amorphous **96**. The amorphous was crystallized from hexane to give needles; yield 213 mg (68.0%), $[\alpha]_D^{26.1}$ +99º (c 1.0, chloroform); mp 94.0-95.5 ºC; ^{1}H NMR (600 MHz, chloroform-*d*): δ 1.34 (s, 3H, IP), 1.36 (s, 3H, IP), 1.42 (s, 3H, IP), 1.43 (s, 3H, IP), 1.44 (s, 3H, IP), 1.48 (s, 3H, IP), 3.18 d, 1H, $J_{4,4\text{-OH}}$ 3.38 Hz, 4-OH), 3.98 - 4.02 (m, 2H, H4, H8a), 4.04 – 4.08 (m, 2H, H6, H8b), 4.19 (dd, 1H, $J_{4,5}$ 1.83 Hz, H5), 4.30 (d, 1H, $J_{1a,1b}$ 17.5 Hz, H1b), 4.42 (d, 1H, $J_{3,4}$ 9.20 Hz, H3); ^{13}C NMR (150 MHz, chloroform-*d*): δ 23.4 (IP), 23.6 (IP), 25.3 (IP), 26.6 (IP), 26.6 (IP), 27.0 (IP), 66.6 (C1), 67.7 (C8), 68.3 (C4), 72.8 (C3), 75.8 (C6), 77.2 (C7), 78.4 (C5), 101.3 (IP), 109.1 (IP), 109.7 (IP), 211.5 (C2). It crystallizes in the orthorhombic space group $P2_12_12_1$ with cell parameters a = 9.553 (2) Å, b = 10.880 (18) Å, c = 18.020 (3) Å, and Z = 4, CCDC-931166.

^{1}H NMR spectrum



IP

Crystal structure of 1,3:5,6:7,8-tri-*O*-isipropylidene- D-*glycero*-D-*gluco*-octulose **96**



Empirical Formula $C_{17}H_{28}O_8$

Formula Weight 360.40

Crystal Color, Habit colorless, prism

Crystal Dimensions 0.300 X 0.250 X 0.200 mm

Crystal System orthorhombic

Lattice Type Primitive

Lattice Parameters *a* = 9.553(2) Å

b = 10.8801(18) Å

c = 18.020(3) Å

V = 1872.9(6) Å3

Space Group $P2_12_12_1$

Z value 4

*D*calc 1.278 g/cm3

R-factor 2.96%

Temperature 123 K

ω oscillation Range (c=45.0, f=210.0) 0.0 - 159.0o

No. of Reflections Measured Total: 5478

Atomic coordinates and Biso/Beq

atom	x	y	z	B_{eq}
O1 O	0.64453(7)	0.16649(6)	0.87849(4)	0.01816(16)
O2 O	0.49090(7)	0.28788(6)	0.81545(4)	0.01822(16)
O3 O	0.20712(8)	0.08583(7)	0.86664(4)	0.02382(18)
O4 O	0.53293(8)	-0.08146(6)	0.99238(4)	0.01986(17)
O5 O	0.04356(7)	0.21805(7)	0.81806(5)	0.02600(19)

O6 O	0.60171(8)	-0.04555(6)	0.79521(4)	0.01985(16)
O7 O	0.69876(9)	-0.21714(7)	1.04109(4)	0.02752(19)
O19 O	0.59501(11)	-0.29335(7)	0.85878(4)	0.0348(3)
C1 C	0.52857(9)	-0.03235(8)	0.86339(5)	0.01536(19)
C2 C	0.51235(10)	0.10428(8)	0.88046(5)	0.01440(19)
C3 C	0.42260(10)	0.17191(8)	0.82300(5)	0.01519(19)
C4 C	0.27559(10)	0.19853(9)	0.84875(5)	0.0170(2)
C5 C	0.17827(10)	0.25082(9)	0.78996(5)	0.0199(3)
C7 C	0.61458(11)	-0.23785(9)	0.91557(5)	0.0214(3)
C8 C	0.60871(10)	-0.09824(8)	0.92463(5)	0.0162(2)
C9 C	0.60857(12)	-0.11653(9)	1.05764(5)	0.0226(3)
C10 C	0.63761(10)	0.26692(9)	0.82693(5)	0.0185(2)
C11 C	0.70825(11)	0.23246(11)	0.75457(6)	0.0269(3)
C12 C	-0.00505(14)	-0.00077(11)	0.82156(7)	0.0328(3)
C13 C	-0.00376(13)	0.13135(11)	0.93695(6)	0.0301(3)
C14 C	0.05915(11)	0.10755(10)	0.86126(6)	0.0228(3)
C15 C	0.64036(15)	-0.30130(10)	0.98928(6)	0.0294(3)
C16 C	0.49764(15)	-0.15049(12)	1.11398(6)	0.0324(3)
C17 C	0.70004(13)	0.38012(10)	0.86243(7)	0.0298(3)
C18 C	0.70186(17)	-0.01240(12)	1.08313(7)	0.0390(4)

Bond lengths (Å)

atom	atom	distance

O1	C2	1.4331(12)
O1	C10	1.4358(12)
O2	C3	1.4270(12)
O2	C10	1.4349(12)
O3	C4	1.4266(13)
O3	C14	1.4365(14)
O4	C8	1.4310(12)
O4	C9	1.4320(13)
O5	C5	1.4281(12)
O5	C14	1.4400(14)
O6	C1	1.4207(12)
O7	C9	1.4246(14)
O7	C15	1.4217(14)
O19	C7	1.2028(12)
C1	C2	1.5259(13)
C1	C8	1.5224(13)
C2	C3	1.5325(13)
C3	C4	1.5071(14)
C4	C5	1.5200(14)
C7	C8	1.5287(14)
C7	C15	1.5171(15)
C9	C16	1.5134(17)
C9	C18	1.5129(18)
C10	C11	1.5153(15)
C10	C17	1.5106(15)

C12	C14	1.5089(17)
C13	C14	1.5128(16)

Bond angles (o)

atom	atom	atom	angle
C2	O1	C10	109.57(7)
C3	O2	C10	107.00(7)
C4	O3	C14	107.13(8)
C8	O4	C9	114.29(8)
C5	O5	C14	107.87(8)
C9	O7	C15	113.27(9)
O6	C1	C2	108.83(7)
O6	C1	C8	109.39(8)
C2	C1	C8	111.33(8)
O1	C2	C1	111.45(8)
O1	C2	C3	104.44(7)
C1	C2	C3	112.85(8)
O2	C3	C2	103.48(8)
O2	C3	C4	106.59(8)
C2	C3	C4	113.93(8)
O3	C4	C3	109.37(8)
O3	C4	C5	101.46(8)

C3	C4	C5	115.30(8)
O5	C5	C4	102.16(8)
O19	C7	C8	125.73(9)
O19	C7	C15	122.80(10)
C8	C7	C15	111.38(8)
O4	C8	C1	107.69(8)
O4	C8	C7	103.68(7)
C1	C8	C7	114.14(8)
O4	C9	O7	109.76(8)
O4	C9	C16	105.23(10)
O4	C9	C18	110.31(9)
O7	C9	C16	112.11(9)
O7	C9	C18	106.42(10)
C16	C9	C18	113.06(10)
O1	C10	O2	105.02(8)
O1	C10	C11	110.37(9)
O1	C10	C17	109.16(8)
O2	C10	C11	110.50(8)
O2	C10	C17	108.49(9)
C11	C10	C17	112.97(9)
O3	C14	O5	106.00(8)
O3	C14	C12	107.67(9)
O3	C14	C13	110.99(9)
O5	C14	C12	110.72(9)
O5	C14	C13	107.66(9)

C12	C14	C13	113.56(10)
O7	C15	C7	110.22(9)

Torsion Angles(o)

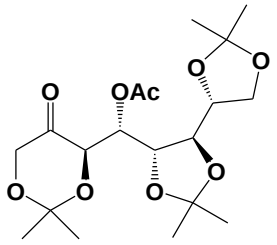
(Those having bond angles > 160 or < 20 degrees are excluded.)

atom1	atom2	atom3	atom4	angle
C2	O1	C10	O2	17.33(9)
C2	O1	C10	C11	-101.78(8)
C2	O1	C10	C17	133.49(7)
C10	O1	C2	C1	124.22(7)
C10	O1	C2	C3	2.07(9)
C3	O2	C10	O1	-31.29(9)
C3	O2	C10	C11	87.73(8)
C3	O2	C10	C17	-147.91(7)
C10	O2	C3	C2	32.04(8)
C10	O2	C3	C4	152.48(7)
C4	O3	C14	O5	18.03(10)
C4	O3	C14	C12	136.56(7)
C4	O3	C14	C13	-98.59(9)
C14	O3	C4	C3	-157.04(7)
C14	O3	C4	C5	-34.80(9)
C8	O4	C9	O7	-32.74(10)
C8	O4	C9	C16	-153.54(7)

C8	O4	C9	C18	84.21(9)
C9	O4	C8	C1	-168.02(7)
C9	O4	C8	C7	70.69(9)
C5	O5	C14	O3	7.84(10)
C5	O5	C14	C12	-108.64(8)
C5	O5	C14	C13	126.69(8)
C14	O5	C5	C4	-28.56(9)
C9	O7	C15	C7	62.28(12)
C15	O7	C9	O4	-36.03(11)
C15	O7	C9	C16	80.52(10)
C15	O7	C9	C18	-155.39(8)
O6	C1	C2	O1	-53.42(9)
O6	C1	C2	C3	63.74(9)
O6	C1	C8	O4	179.23(6)
O6	C1	C8	C7	-66.26(9)
C2	C1	C8	O4	58.92(9)
C2	C1	C8	C7	173.43(7)
C8	C1	C2	O1	67.22(9)
C8	C1	C2	C3	-175.63(7)
O1	C2	C3	O2	-20.68(9)
O1	C2	C3	C4	-136.00(7)
C1	C2	C3	O2	-141.90(7)
C1	C2	C3	C4	102.78(8)
O2	C3	C4	O3	-172.54(7)
O2	C3	C4	C5	73.94(9)

C2	C3	C4	O3	-59.06(10)
C2	C3	C4	C5	-172.59(7)
O3	C4	C5	O5	38.51(8)
C3	C4	C5	O5	156.55(7)
O19	C7	C8	O4	136.61(11)
O19	C7	C8	C1	19.75(15)
O19	C7	C15	O7	163.37(11)
C8	C7	C15	O7	-19.89(13)
C15	C7	C8	O4	-40.01(11)
C15	C7	C8	C1	-156.87(9)

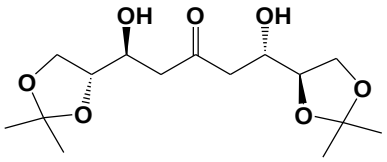
3-*O*-Acetyl-1,3:5,6:7,8-tri-*O*-isipropylidene- D-*glycero*-D-*gluco*-octulose **97**



To a solution of the octulose **96** (50.1 mg, 0.139 mmole) in pyridine (500 μl) was added Ac_2O (250 μl), and the solution was stirred at room temperature for 1 h, after which TLC (toluene – ethyl acetate, 10 : 1) indicated the formation of the single product. The mixture was poured into ice-cooling water, and extracted with chloroform. The extract was washed with aqueous $NaHCO_3$, water, and brine, dried (Na_2SO_4), and concentrated to dryness. The light yellow syrup was then purified by silica gel column chromatography (toluene-ethyl acetate, 10 : 1) to give syrupy acetate **97**; yield 48.2 mg (86.0%), $[\alpha]_D^{25.2}$ +27º (c 1.0, chloroform);

^{1}H NMR (600 MHz, chloroform-*d*): δ 1.33 (s, 3H, IP), 1.37 (s, 3H, IP), 1.41 (s, 3H, IP), 1.42 (s, 3H, IP), 1.46 (s, 3H, IP), 1.47 (s, 3H, IP), 2.11 (s, 3H, Ac),δ 3.72 (t, 1H, $J_{5,6}$ 7.27 Hz, H6), 3.95 (q, 1H, $J_{7,8a}$ 7.27 Hz, $J_{8a,8b}$ 8.30 Hz, H8a), 4.01 (d, 1H, $J_{1a,1b}$ 17.3 Hz, H1a), 4.10 – 4.13 (m, 2H, H7, H8b), 4.28 (d, 1H, 1H, $J_{1a,1b}$ 17.3 Hz, H1b), 4.44 (dd, 1H, $J_{4,5}$ 2.56 Hz, $J_{5,6}$ 7.27 Hz, H5), 4.53 (d, 1H, $J_{3,4}$ 8.45 Hz, H3), 5.34 (dd, 1H, $J_{3,4}$ 8.45 Hz, $J_{4,5}$ 2.57 Hz, H4); ^{13}C NMR (150 MHz, chloroform-*d*): δ 20.9 (Ac), 23.4 (IP), 24.2 (IP), 25.1 (IP), 26.2 (IP), 26.6 (IP), 27.3 (IP), 66.9 (C1), 67.2 (C8), 69.0 (C4), 71.8 (C3), 76.8 (C7), 77.0 (C6), 77.3 (C5), 101.2 (IP), 109.7 (IP), 109.8 (IP), 170.0 (Ac), 206.7 (C2).

4,6-Dideoxy-1,2:8,9-di-*O*-isopropylidene-D-*galacto*-5nonulose **100**

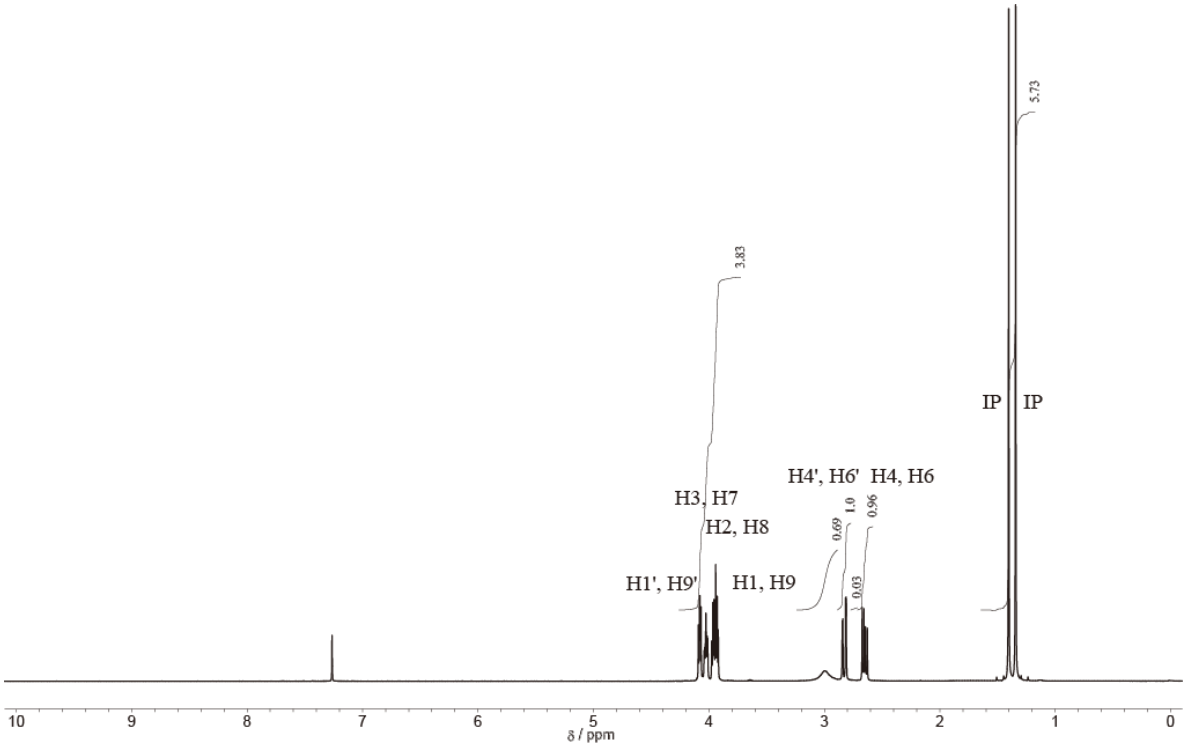


D-Prolinamide **8** (7 mg, 0.025 mmole) was added to a solution of freshly distilled 2,3-*O*-isopropylidene-D-glyceraldehyde **10** (65 mg, 0.5 mmole) and acetone (0.02 ml, 0.25 mmole) in water (0.44 ml). After the reaction solution was stirred at room temperature for 24 h, crude product that deposited was corrected by filtration. Recrystallization from IPE gave pure **100** as fine needles; yield 60 mg (77 %), $[\alpha]_D^{28}$ -37.0° (*c* 1.0, chloroform); m p 98-99 °C; ^{1}H NMR ($CDCl_3$, 600 MHz), δ 1.34 (s, 6H, IP), 1.40 (s, 6H, IP), 2.65 (dd, 2H, $J_{3,4b}$ = $J_{6b,7}$ = 8.9 Hz, $J_{4a,4b}$= $J_{6a,6b}$ = 17.4 Hz, H4a, H6a), 2.83 (dd, 2H, $J_{3,4a}$ = $J_{6a,7}$ = 2.6 Hz, $J_{4a,4b}$ = $J_{6a,6b}$ = 17.4 Hz, H4b, H6b), 3.94 (dd, 2H, $J_{1a,1b}$ = J_{9a-9b} = 7.8 Hz, $J_{1b,2}$ = $J_{8,9a}$ = 2.3 Hz, H1b, H9b), 3.96 (dd, 2H, $J_{1a,2}$ = $J_{8,9b}$ = 5.9 Hz,

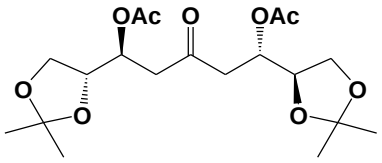
$J_{2,3}$ = $J_{8,9}$ = 6.5 Hz, H2, H8), 4.03 (dt, 2H, $J_{2,3}$ = $J_{7,8}$ = 6.5 Hz, $J_{3,4a}$ = $J_{6a,7}$ = 2.5 Hz, $J_{3,4a}$ = $J_{6b,7}$ =8.9 Hz, H3, H7), 4.08 (dd, 2H, $J_{1a,2}$ = $J_{9a,8}$ = 5.9 Hz, $J_{1a,1b}$ = $J_{9a,9b}$ =7.8 Hz, H1a, H9a).

^{13}C NMR ($CDCl_3$, 150 MHz) δ 26.8 (IP), 26.8 (IP), 46.6 (C4, C6), 66.8 (C1, C9), 69.0 (C3, C7) 77.7 (C2, C8), 109 (IP), 211 (C5); ESI-TOFMS *m*/*z*: calcd for $[C_{15}H_{26}O_7+Na]^+$, 341.1576; found, 341.1570.

^{1}H NMR spectrum



3,7,-Di-*O*-acetyl-4,6-dideoxy-1,2:8,9-di-*O*-isopropylidene-D-*galacto*-5nonulose **101**

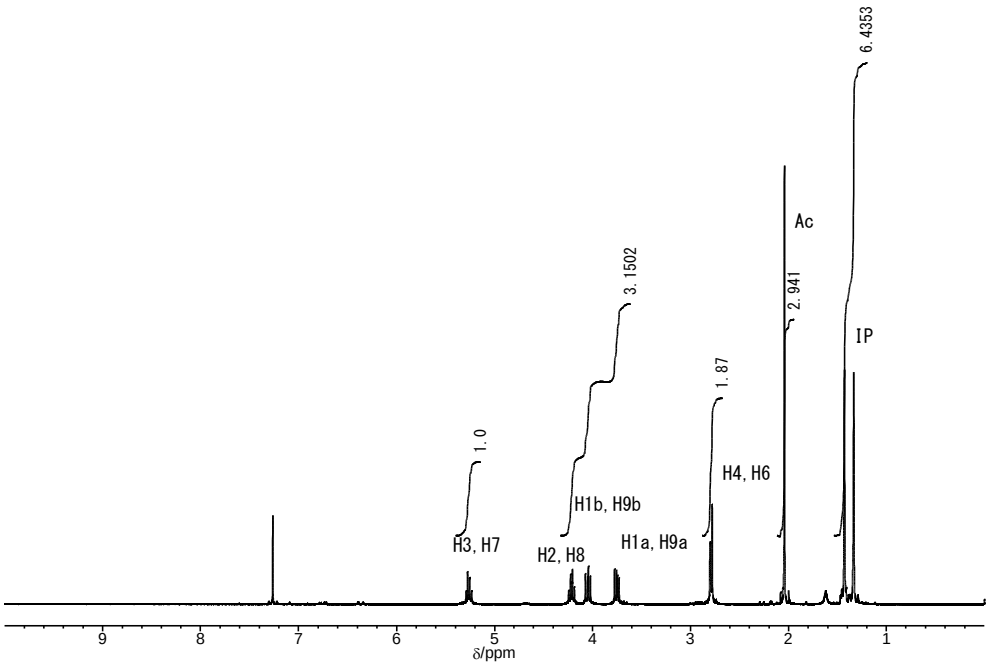


To a solution of the 5-nonulose **100** (50.3 mg, 0.158 mmole) in pyridine (500 µl) was added Ac_2O

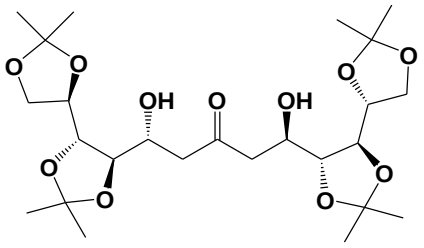
(250 μl), and the solution was stirred at room temperature for 1 h, after which TLC (toluene – ethyl acetate, 10 : 1) indicated the formation of the single product. The mixture was poured into ice-cooling water, and extracted with chloroform. The extract was washed with aqueous $NaHCO_3$, water, and brine, dried (Na_2SO_4), and concentrated to dryness. The light yellow syrup was then purified by silica gel column chromatography (toluene-ethyl acetate, 10 : 1) to give syrupy acetate **101**; yield 61.0 mg (95.5%); ^{1}H NMR ($CDCl_3$, 600 MHz), δ 1.34 (s, 3H, IP), 1.43 (s, 6H, IP), 2.04 (s, 6H, Ac), 2.79 (d, 4H, $J_{3,4} = J_{6,7}$ = 6.3 Hz, H4, H6), 3.75 (dd, 2H, $J_{1a,2} = J_{8,9a}$ = 5.6 Hz, $J_{1a,1b} = J_{9a,9b}$ = 8.8 Hz, H1a, H9a), 4.05 (dd, 2H, $J_{1b,2} = J_{8,9b}$ = 6.8 Hz, $J_{1a,1b} = J_{9a,9b}$ = 8.8 Hz, H1b, H9b), 4.21 (ddd, 2H, $J_{1a,2} = J_{8,9a}$ = 5.6 Hz, $J_{1b,2} = J_{8,9b}$ = 6.8 Hz, $J_{2,3} = J_{7,8}$ =5.6 Hz, H2, H8), 5.26 (dd, 2H, $J_{2,3} = J_{7,8}$ = 5.6 Hz, $J_{3,4} = J_{6,7}$ =6.3 Hz, H3, H8).

^{13}C NMR ($CDCl_3$, 150 MHz) δ 20.9 (Ac), 24.9 (IP), 26.3 (IP), 43.5 (C4, C6), 66.2 (C1, C9), 69.9 (C3, C7) 76.1 (C2, C8), 109 (IP), 170 (Ac), 203 (C5); ESI-TOFMS *m*/*z*: calcd for $[C_{19}H_{30}O_9+Na]^+$, 425.1782; found, 425.1770.

^{1}H NMR



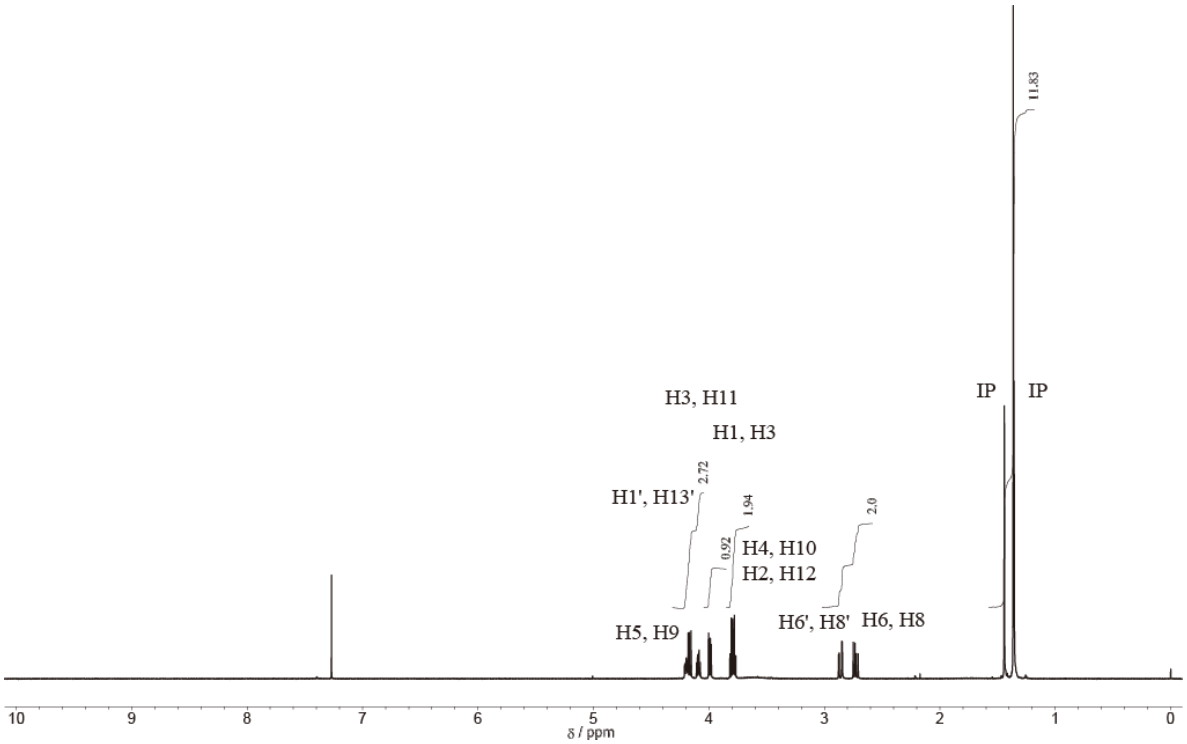
6,8-Dideoxy-1,2:3,4:10,11:12,13-tetra-*O*-isopropylidene-D-*allo*-D-*allo*-7-tridexulose **102**



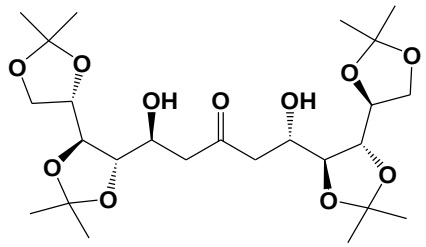
L-Prolinamide catalyst **7** (14.0 mg, 0.0490 mmole) was added to an aqueous solution of freshly distilled D-arabinose acetonide **16** (227 mg, 0.990 mmole) and acetone (40.0 µl, 0.490 mmole) in water (0.890 ml). The reaction solution was stirred at ambient temperature for 24 hours and extracted with ethyl acetate (5.0 ml). The organic extract was washed with water (3.0 ml), dried over $NaSO_4$ and concentrated in vacuo to give a white solid. Recrystallization from hexane gave pure **102** as colorless needles (263 mg, 72 %), $[\alpha]_D^{27}$ +23 ° (*c* 1.0, chloroform); mp 82-83°C; ^{1}H NMR ($CDCl_3$, 600 MHz), δ 1.36 (s, 3H, IP), 1.36 (s, 6H, IP), 1.44 (s, 3H, IP), 2.73 (dd, 2H, $J_{5,6a}$ = $J_{8a,9}$ =8.9 Hz, $J_{6a,6b}$ = $J_{8a,8b}$ =16.5 Hz, H6a, H8a), 2.86 (dd, 2H, $J_{5,6b}$ = $J_{8b,9}$ =3.3 Hz, $J_{6a,6b}$ = $J_{8a,8b}$ =16.5 Hz, H6b, H8b), 3.79 (m, 4H, H2, H4, H10, H12), 3.99 (dd, 2H, $J_{1a,2}$ = $J_{12,13a}$ =5.4 Hz, $J_{1a,1b}$ = $J_{13a,13b}$ =8.7 Hz, H1a, H13a), 4.10 (dd, 2H, H3, H11), 4.16 (dd, 2H, $J_{1b,2}$ = $J_{12,13b}$ =6.2 Hz, $J_{1a,1b}$ = $J_{13a,13b}$ =8.7 Hz, H1b, H13b), 4.19 (ddd, 1H, $J_{5,6a}$ = $J_{8a,9}$ =8.9 Hz, $J_{5,6b}$ = $J_{8b,9}$ =3.3 Hz, H5, H9).

^{13}C NMR ($CDCl_3$, 150MHz) 25.1 (IP), 26.4 (IP), 26.7 (IP), 26.7 (IP), 47.1 (C6, C9), 67.5 (C1, C13), 68.7 (C5, C9), 76.3 (C3, C11), 76.3 (C6), 80.5, 82.3, 109 (IP), 109 (IP), 110 (IP), 209 (C7); ESI-TOFMS *m*/*z*: calcd for $[C_{25}H_{42}O_{11}+Na]^+$, 541.2619; found, 541.269.

^{1}H NMR spectrum



6,8-Dideoxy-1,2:3,4:10,11:12,13-tetra-*O*-isopropylidene-L-*allo*-L-*allo*-7-tridexulose **103**

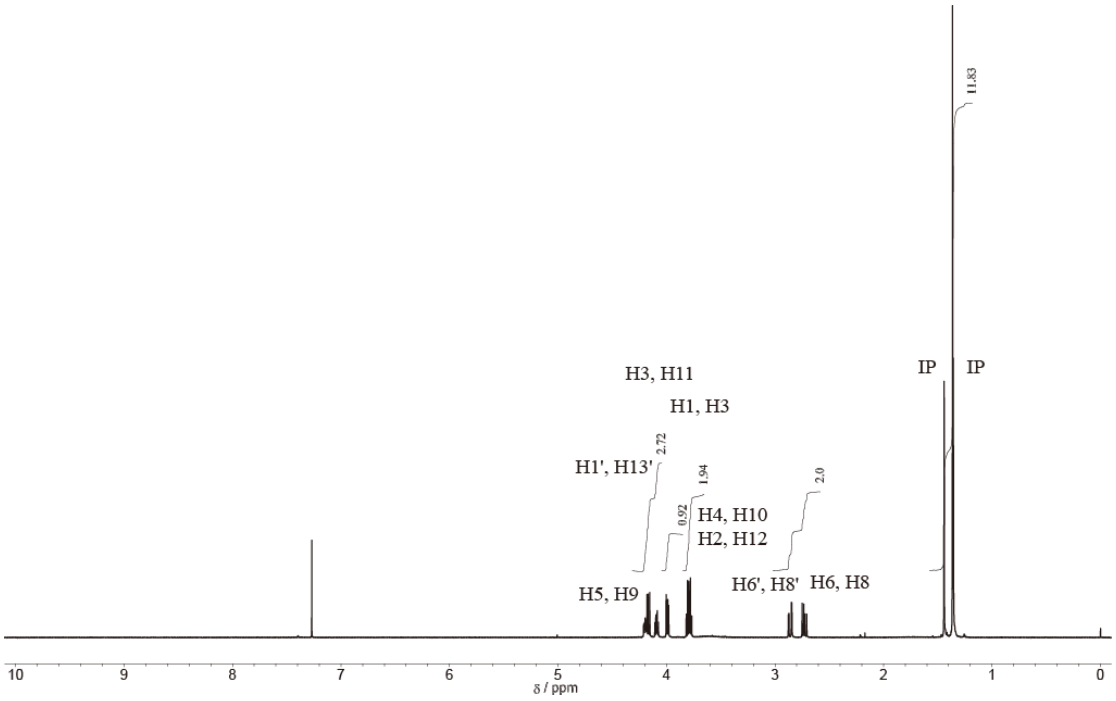


This compound was obtained from 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-L-arabinose **19** by an identical procedure used for the D-enantiomer, $[\alpha]_D^{27}$ -23 ° (*c* 1.0, chloroform); mp 82-83°C; ^{1}H NMR ($CDCl_3$, 600 MHz), δ 1.36 (s, 3H, IP), 1.36 (s, 6H, IP), 1.44 (s, 3H, IP), 2.73 (dd, 2H, $J_{5,6a}$ = $J_{8a,9}$ =8.9 Hz, $J_{6a,6b}$ = $J_{8a,8b}$ =16.5 Hz, H6a, H8a), 2.86 (dd, 2H, $J_{5,6b}$ = $J_{8b,9}$ =3.3 Hz, $J_{6a,6b}$ = $J_{8a,8b}$ =16.5 Hz, H6b, H8b), 3.79 (m, 4H, H2, H4, H10, H12), 3.99 (dd, 2H, $J_{1a,2}$ = $J_{12,13a}$ =5.4 Hz, $J_{1a,1b}$ = $J_{13a,13b}$ =8.7 Hz, H1a, H13a), 4.10 (dd, 2H, H3, H11), 4.16 (dd, 2H, $J_{1b,2}$ = $J_{12,13b}$ =6.2 Hz, $J_{1a,1b}$ = $J_{13a,13b}$ =8.7 Hz, H1b, H13b), 4.19 (ddd, 1H, $J_{5,6a}$ = $J_{8a,9}$ =8.9 Hz, $J_{5,6b}$ = $J_{8b,9}$ =3.3 Hz, H5, H9).

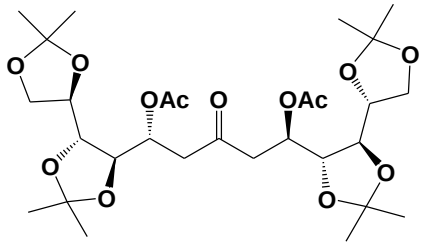
^{13}C NMR ($CDCl_3$, 150MHz) δ 25.1 (IP), 26.4 (IP), 26.7 (IP), 26.7 (IP), 47.1 (C6, C9), 67.5 (C1,

C13), 68.7 (C5, C9), 76.3 (C3, C11), 76.3 (C6), 80.5, 82.3, 109 (IP), 109 (IP), 110 (IP), 209 (C7); ESI-TOFMS *m*/*z*: calcd for $[C_{25}H_{42}O_{11}+Na]^+$, 541.2619; found, 541.273.

^{1}H NMR spectrum



5,9-Di-*O*-acetyl-6,8-dideoxy-1,2:3,4:10,11:12,13-tetra-*O*-isopropylidene-D-*allo*-D-*allo*-7-tridexulose **104**

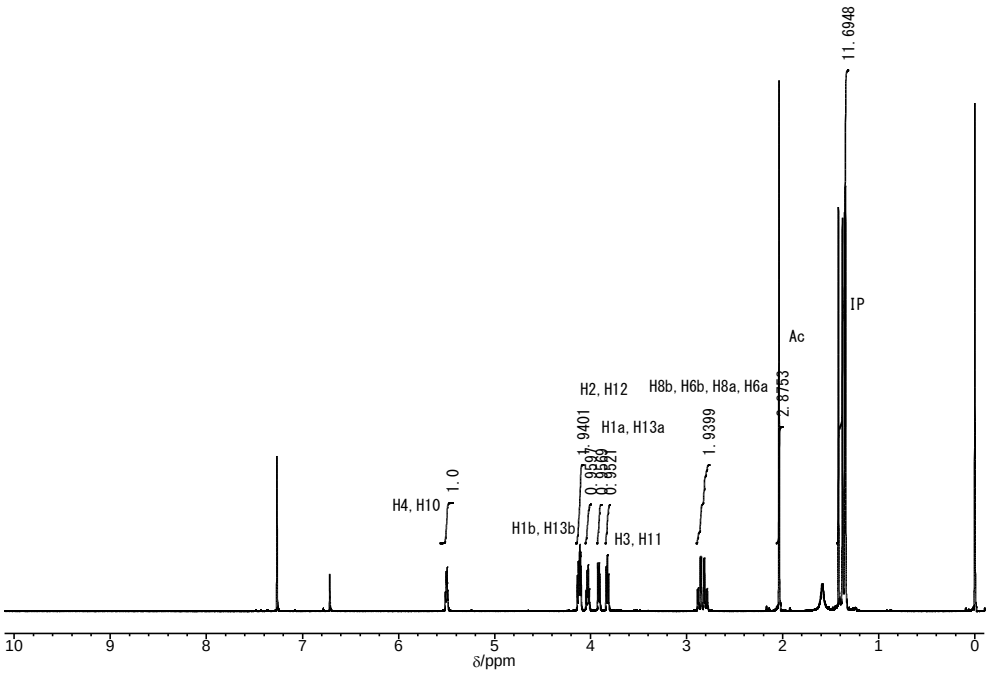


To a solution of the 5-nonulose **102** (50.7 mg, 0.0978 mmole) in pyridine (500 μl) was added Ac_2O (250 μl), and the solution was stirred at room temperature for 1 h, after which TLC (toluene – ethyl acetate, 10 : 1) indicated the formation of the single product. The mixture was poured into ice-cooling water, and extracted with chloroform. The extract was washed with aqueous $NaHCO_3$, water, and brine, dried (Na_2SO_4), and concentrated to dryness. The light yellow syrup was then

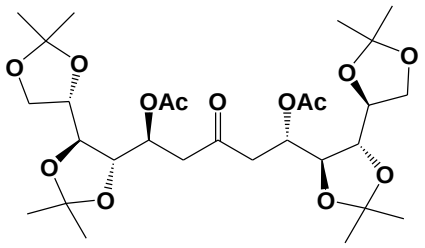
purified by silica gel column chromatography (toluene-ethyl acetate, 10 : 1) to give syrupy acetate **104**; yield 56.6 mg; $[\alpha]_D^{27}$ -17.2 ° (*c* 1.0, chloroform); mp 106.0-107.0°C; ^{1}H NMR ($CDCl_3$, 600 MHz), δ 1.35 (s, 6H, IP), 1.36 (s, 6H, IP), 1.38 (s, 6H, IP), 1.42 (s, 6H, IP), 2.04 (s, 6H, Ac), 2.80 (dd, 2H, $J_{5,6a} = J_{8a,9} = 7.4$ Hz, $J_{6a,6b} = J_{8a,8b} = 17.1$ Hz, H6a, H8a), 2.87 (dd, 2H, $J_{5,6b} = J_{8b,9} = 5.0$ Hz, $J_{6a,6b} = J_{8a,8b} = 17.1$ Hz, H6b, H8b), 3.86 (dd, 2H, $J_{3,4} = J_{10,11} = 6.8$ Hz, $J_{2,3} = J_{11,12} = 7.9$ Hz, H3, H11), 3.91 (dd, 2H, $J_{1a,2} = J_{12,13a} = 5.9$ Hz, $J_{1a,1b} = J_{13a,13b} = 8.5$ Hz, H1a, H13a), 4.03 (dd, 2H, $J_{1a,2} = J_{12,13a} = 5.9$ Hz, $J_{2,3} = J_{11,12} = 7.9$ Hz, H2, H12), 4.11 (dd, 2H, $J_{3,4} = J_{10,11} = 6.8$ Hz, $J_{4,5} = J_{9,11} = 5.0$ Hz, H4, H10), 4.13 (dd, 2H, $J_{1b,2} = J_{12,13b} = 6.2$ Hz, $J_{1a,1b} = J_{13a,13b} = 8.5$ Hz, H1b, H13b) 4.19 (dt, 2H, $J_{5,6a} = J_{8a,9} = 7.4$ Hz, $J_{5,6b} = J_{8b,9} = 5.0$ Hz, $J_{4,5} = J_{9,11} = 5.0$ Hz, H4, H10).

^{13}C NMR ($CDCl_3$, 150MHz) δ 17.0 (Ac), 21.1 (IP), 25.3 (IP), 26.6 (IP), 27.1 (IP), 27.3 (IP), 43.6 (C6, C8), 67.6 (C1, C13), 69.1 (C5, C9), 77.0 (C2, C12), 78.9 (C3, C11), 80.9 (C4, C10), 109 (IP), 110 (IP), 203 (C7); ESI-TOFMS *m*/*z*: calcd for $[C_{29}H_{46}O_{13}+Na]^+$, 625.2831; found, 625.2844.

^{1}H NMR spectrum



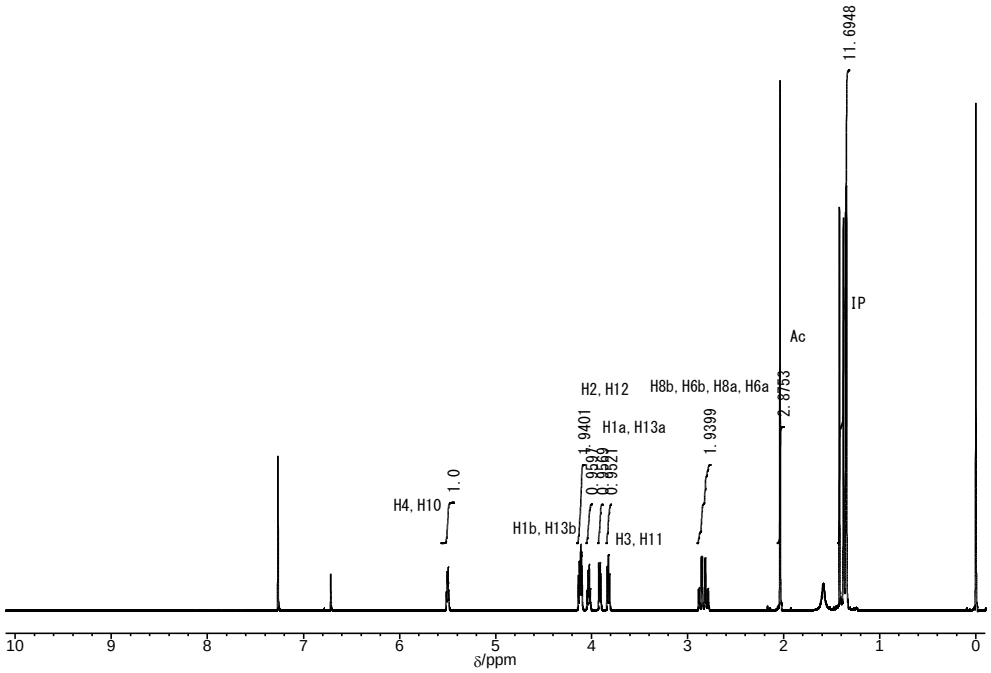
5,9-Di-*O*-acetyl-6,8-dideoxy-1,2:3,4:10,11:12,13-tetra-*O*-isopropylidene-D-*allo*-D-*allo*-7-tridexulos e **105**



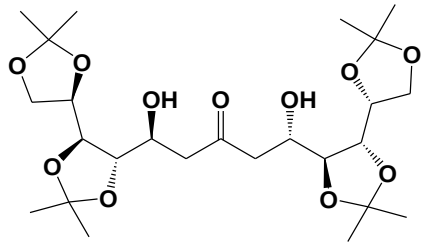
This compound was obtained from 6,8-Dideoxy-1,2:3,4:10,11:12,13-tetra-*O*-isopropylidene-L-*gluco*-L-*gulo*-7-tridexulose **103** by an identical procedure used for the D-enantiomer; yield g; $[\alpha]_D^{27}$ +17.4 ° (*c* 1.0, chloroform); mp 108.5-109.5°C; ^{1}H NMR ($CDCl_3$, 600 MHz), δ 1.35 (s, 6H, IP), 1.36 (s, 6H, IP), 1.38 (s, 6H, IP), 1.42 (s, 6H, IP), 2.04 (s, 6H, Ac), 2.80 (dd, 2H, $J_{5,6a} = J_{8a,9}$ = 7.4 Hz, $J_{6a,6b} = J_{8a,8b}$ =17.1 Hz, H6a, H8a), 2.87 (dd, 2H, $J_{5,6b} = J_{8b,9}$ = 5.0 Hz, $J_{6a,6b} = J_{8a,8b}$ =17.1 Hz, H6b, H8b), 3.86 (dd, 2H, $J_{3,4} = J_{10,11}$ = 6.8 Hz, $J_{2,3} = J_{11,12}$ = 7.9 Hz, H3, H11), 3.91 (dd, 2H, $J_{1a,2} = J_{12,13a}$ =5.9 Hz, $J_{1a,1b} = J_{13a,13b}$ =8.5 Hz, H1a, H13a), 4.03 (dd, 2H, $J_{1a,2} = J_{12,13a}$ =5.9 Hz, $J_{2,3} = J_{11,12}$ = 7.9 Hz, H2, H12), 4.11 (dd, 2H, $J_{3,4} = J_{10,11}$ = 6.8 Hz, $J_{4,5} = J_{9,11}$ = 5.0 Hz, H4, H10), 4.13 (dd, 2H, $J_{1b,2} = J_{12,13b}$ = 6.2 Hz, $J_{1a,1b} = J_{13a,13b}$ = 8.5 Hz, H1b, H13b) 4.19 (dt, 2H, $J_{5,6a} = J_{8a,9}$ = 7.4 Hz, $J_{5,6b} = J_{8b,9}$ = 5.0 Hz, $J_{4,5} = J_{9,11}$ = 5.0 Hz, H4, H10).

^{13}C NMR ($CDCl_3$, 150MHz) δ 17.0 (Ac), 21.1 (IP), 25.3 (IP), 26.6 (IP), 27.1 (IP), 27.3 (IP), 43.6 (C6, C8), 67.6 (C1, C13), 69.1 (C5, C9), 77.0 (C2, C12), 78.9 (C3, C11), 80.9 (C4, C10), 109 (IP), 110 (IP), 203 (C7); ESI-TOFMS *m*/*z*: calcd for $[C_{29}H_{46}O_{13}+Na]^+$, 625.2831; found, 625.2844.

^{1}H NMR spectrum



6,8-dideoxy-1,2:3,4:10,11:12,13-tetra-*O*-isopropylidene-D-*altro*-D-*tallo*-7-tridexulose **106**

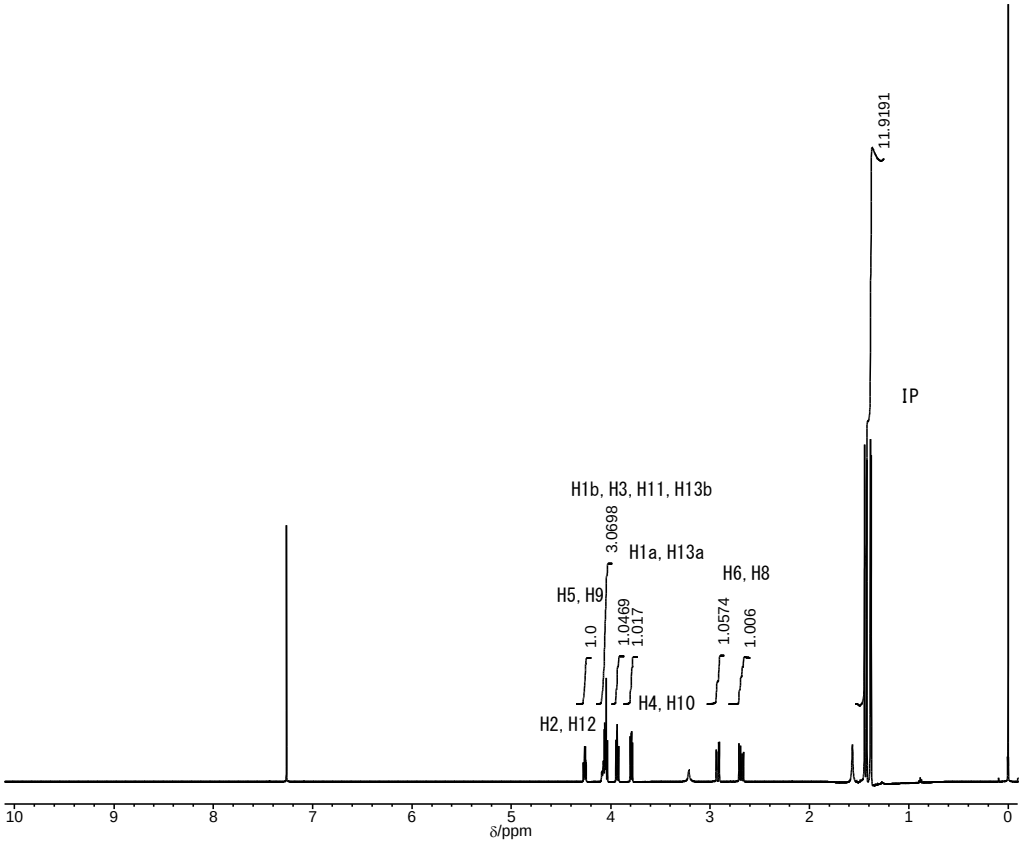


D-Prolinamide catalyst **7** (14.3 mg, 0.0491 mmole) was added to an aqueous solution of freshly distilled D-xylose acetonide **22** (229 mg, 0.991 mmole) and acetone (40.0 μl, 0.490 mmole) in water (0.890 ml). The reaction solution was stirred at ambient temperature for 24 hours and extracted with ethyl acetate (5.0 ml). The organic extract was washed with water (3.0 ml), dried over $NaSO_4$ and concentrated in vacuo to give a syrpu. Recrystallization from IPA gave pure **106** as colorless needles (265 mg, 73 %), $[\alpha]_D^{27}$ -32.1 ° (*c* 1.0, chloroform); mp 82-83°C; ^{1}H NMR ($CDCl_3$, 600 MHz), δ 1.38 (s, 6H, IP), 1.38 (s, 6H, IP), 1.42 (s, 6H, IP), 1.44 (s, 6H, IP), 2.73 (dd, 2H, $J_{5,6a}$ = $J_{8a,9}$ =9.0 Hz, $J_{6a,6b}$ = $J_{8a,8b}$ =17.4 Hz, H6a, H8a), 2.92 (dd, 2H, $J_{5,6b}$ = $J_{8b,9}$ =2.5 Hz, $J_{6a,6b}$ = $J_{8a,8b}$ =17.4 Hz, H6b, H8b), 3.79 (t, 2H, $J_{3,4}$ = $J_{10,11}$ =7.5 Hz, H4, H10), 3.99 (t, 2H, $J_{1a,2}$ = $J_{12,13a}$ = 7.5 Hz,

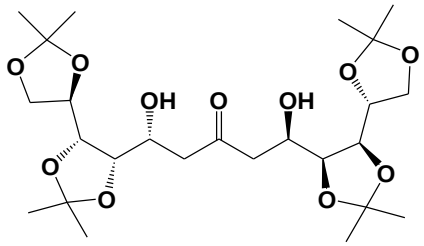
H1a, H13a), 4.01-4.06 (m, 4H, H1b, H3, H11, H13b), 4.08 (2H, dd, $J_{5,6a}$ = $J_{8a,9}$ = 7.5 Hz, $J_{5,6b}$ = $J_{8b,9}$ = 2.5 Hz, H5, H9), 4.26 (dt, 2H, $J_{1b,2}$ = $J_{12,13b}$ = 7.5 Hz, $J_{2,3}$ = $J_{11,12}$ = 4.4 Hz, H2, H12).

^{13}C NMR ($CDCl_3$, 150MHz) 25.5 (IP), 26.1 (IP), 26.7 (IP), 27.2 (IP), 47.2 (C6, C8), 65.9 (C1, C13), 69.8 (C5, C9), 75.8 (C2, C12), 78.8 (C4, C10), 80.1 (C3, C11), 109 (IP), 110 (IP), 212 (C7); ESI-TOFMS *m/z*: calcd for $[C_{25}H_{42}O_{11}+Na]^+$, 541.2619; found, 541.269.

^{1}H NMR spectrum



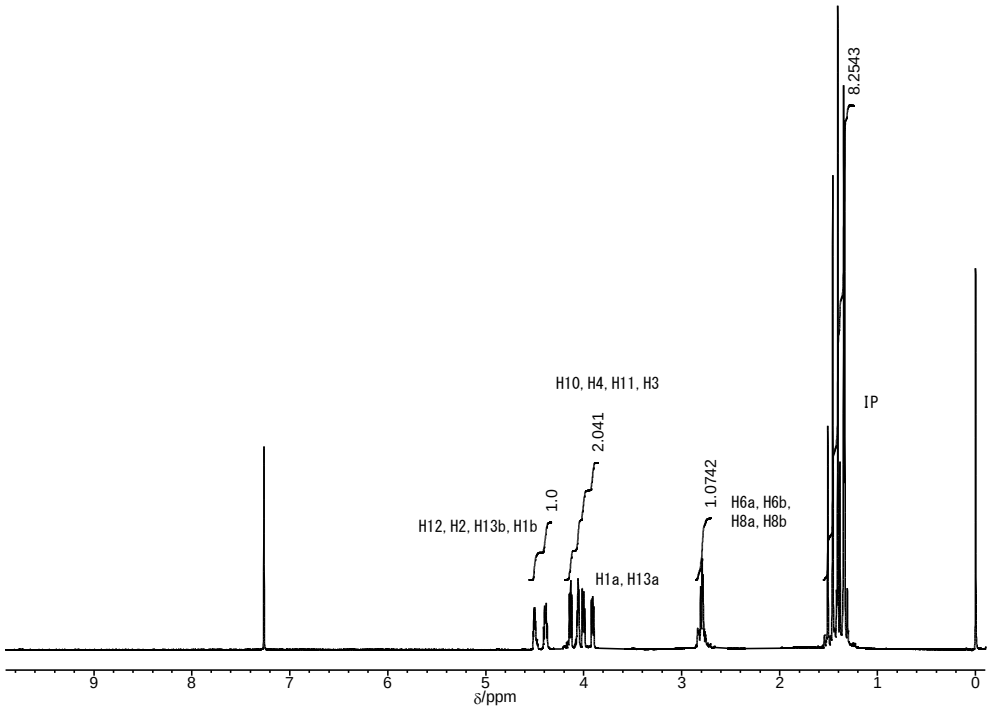
6,8-dideoxy-1,2:3,4:10,11:12,13-tetra-*O*-isopropylidene-D-*gulo*-D-*gluco*-7-tridexulose **109**



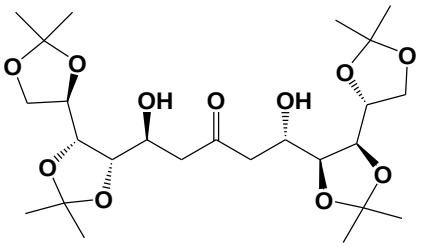
L-Prolinamide catalyst **7** (14.4 mg, 0.0491 mmole) was added to an aqueous solution of freshly distilled D-ribose acetonide **22** (228 mg, 0.991 mmole) and acetone (0.04 ml, 0.490 mmole) in water (0.890 ml). The reaction solution was stirred at ambient temperature for 24 hours and extracted with ethyl acetate (5.0 ml). The organic extract was washed with water (3.0 ml), dried over $NaSO_4$ and concentrated in vacuo to give a syrup which was purified by column chromatography, yield; (205 mg, 56.0 %), $[\alpha]_D^{24}$ +8.6 ° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$, 600 MHz), δ 1.34 (s, 6H, IP), 1.35 (s, 6H, IP), 1.41 (s, 6H, IP), 1.46 (s, 6H, IP), 2.75-2.85 (m, 4H, H6a, H6b, H8a, H8b), 3.91 (dd 2H, $J_{1a,2} = J_{12,13a}$ = 5.8 Hz, $J_{1a,1b} = J_{13a,13b}$ = 8.6 Hz, H1a, H13a), 4.00 (dd, 2H, $J_{2,3} = J_{11,12}$ =9.2 Hz, $J_{3,4} = J_{10,11}$ = 6.1 Hz, H3, H11), 4.06 (t, 2H, $J_{3,4} = J_{10,11}$ = 6.1 Hz, H4, H10), 4.14 (dd, 2H, $J_{1b,2} = J_{12,13b}$ = 5.8 Hz, $J_{1a,1b} = J_{13a,13b}$ = 8.6 Hz, H1b, H13b), 4.39 (dt, 2H, $J_{1b,2} = J_{12,13b}$ = 5.8 Hz, $J_{2,3} = J_{11,12}$ = 9.2 Hz, H2, H12).

^{13}C NMR ($CDCl_3$, 150MHz) 25.3 (IP), 25.4 (IP), 26.8 (IP), 27.4 (IP), 47.7 (C6, C8), 65.6 (C5, C9), 68.2 (C1, C13), 73.3 (C2, C12), 78.2 (C3, C11), 79.4 (C4, C10), 100 (IP), 100 (IP), 108 (IP), 110 (IP) 209 (C7); ESI-TOFMS *m*/*z*: calcd for $[C_{25}H_{42}O_{11}+Na]^+$, 541.2619; found, 541.269.

^{1}H NMR spectrum



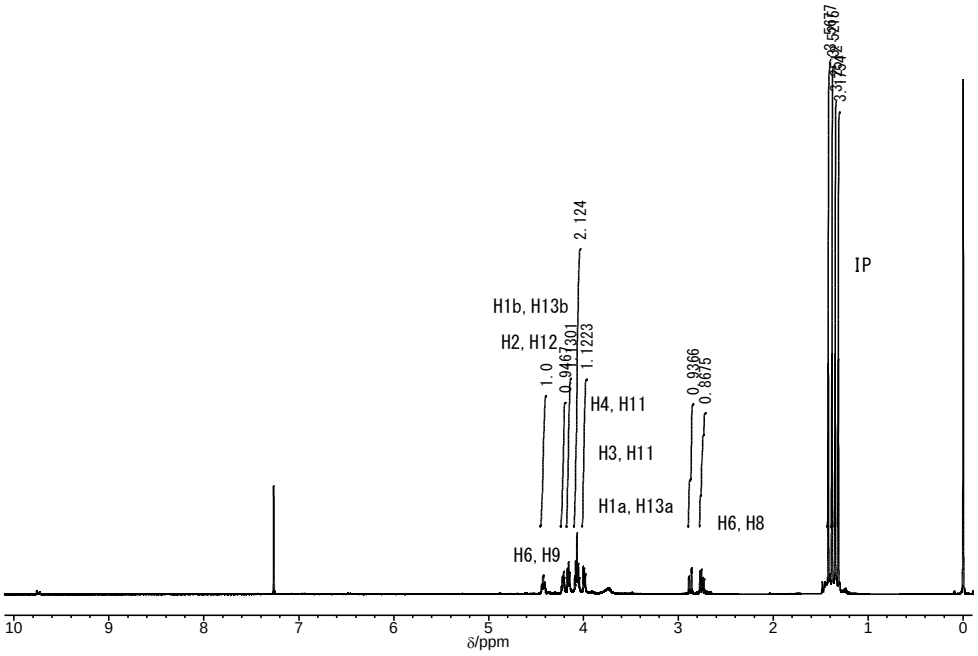
6,8-Dideoxy-1,2:3,4:10,11:12,13-tetra-*O*-isopropylidene-D-*manno*-L-*manno*-7-tridexulose **108**



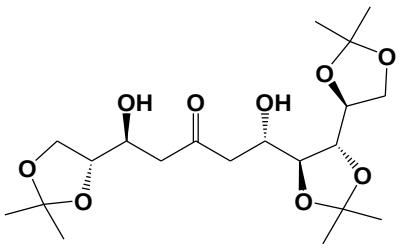
D-Prolinamide catalyst **7** (14.0 mg, 0.0490 mmole) was added to an aqueous solution of freshly distilled D-ribose acetonide **25** (227 mg, 0.990 mmole) and acetone (40.0 μl, 0.490 mmole) in water (0.890 ml). The reaction solution was stirred at ambient temperature for 24 hours and extracted with ethyl acetate (5.0 ml). The organic extract was washed with water (3.0 ml), dried over $NaSO_4$ and concentrated in vacuo to give a syrup which was purified by column chromatography, yield; (273 mg, 75 %), $[\alpha]_D^{27}$ +19.1 ° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$, 600 MHz), δ 1.31 (s, 6H, IP), 1.34 (s, 6H, IP), 1.38 (s, 6H, IP), 1.42 (s, 6H, IP), 2.75 (dd, 2H, $J_{5,6a} = J_{8a,9} = 9.2$ Hz, $J_{6a,6b} = J_{8a,8b} = 16.1$ Hz, H6a, H8a), 2.88 (dd, 2H, $J_{5,6b} = J_{8b,9} = 2.4$ Hz, $J_{6a,6b} = J_{8a,8b} = 16.1$ Hz, H6b, H8b), 3.99 (dd 2H, $J_{1a,2} = J_{12,13a} = 5.7$ Hz, $J_{1a,1b} = J_{13a,13b} = 8.8$ Hz, H1a, H13a), 4.06 (dd, 2H, $J_{3,4} = J_{10,11} = 5.5$

Hz, $J_{4,5}$ = $J_{9,10}$ = 9.3 Hz, H4, H10), 4.08 (dd, 2H, $J_{2,3}$ = $J_{11,12}$ = 9.0 Hz, $J_{3,4}$ = $J_{10,11}$ = 5.5 Hz, H3, H11), 4.16 (dd, 2H, $J_{1b,2}$ = $J_{12,13b}$ = 6.3 Hz, $J_{1a,1b}$ = $J_{13a,13b}$ = 8.8 Hz, H1b, H13b), 4.22 (dt, 2H, $J_{1b,2}$ = $J_{12,13b}$ = 5.7 Hz, $J_{2,3}$ = $J_{11,12}$ = 9.0 Hz, H2, H12), 4.43 (dt, 2H, $J_{4,5}$ = $J_{9,10}$ = 9.2 Hz, $J_{5,6a}$ = $J_{8a,9}$ = 9.2 Hz, $J_{5,6b}$ = $J_{8b,9}$ = 2.4 Hz,H5, H9); ^{13}C NMR ($CDCl_3$, 150MHz) 25.3 (IP), 25.4 (IP), 26.6 (IP), 27.9 (IP), 48.2 (C6, C8), 65.6 (C5, C9), 67.9 (C1, C13), 73.2 (C2, C12), 78.5 (C4, C11), 79.9 (C3, C10), 109 (IP), 111 (IP), 209 (C7); ESI-TOFMS *m*/*z*: calcd for $[C_{25}H_{42}O_{11}+Na]^+$, 541.2619; found, 541.269.

^{1}H NMR spectrum

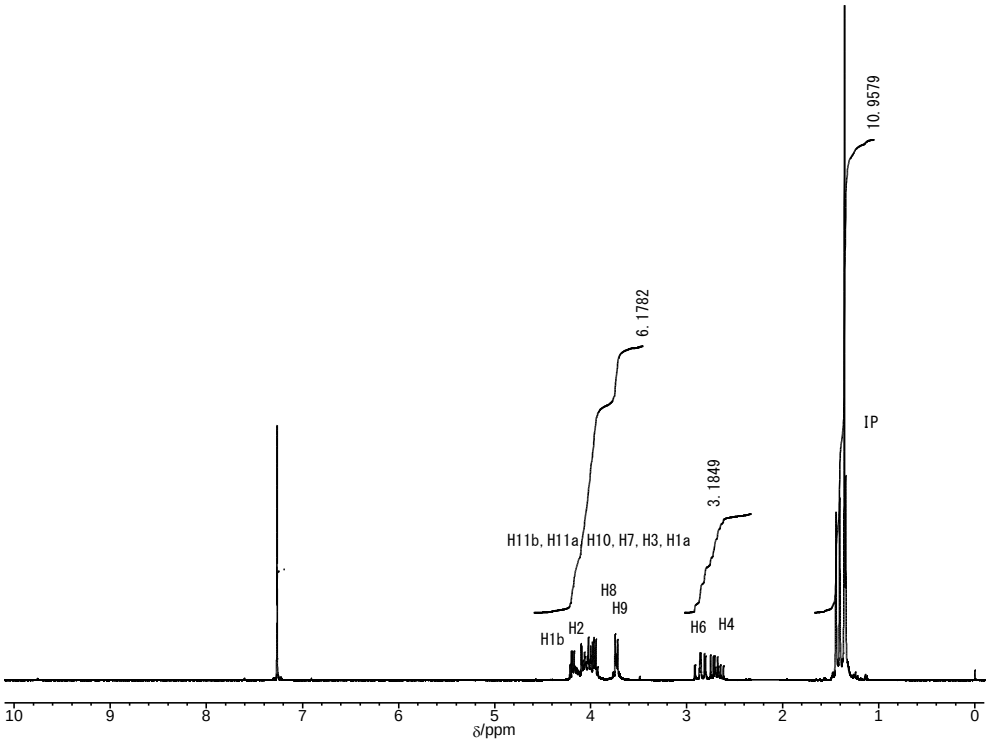


4,6-Dideoxy-1,2:8,9:10,11-tri-*O*-isopropylidene-L-*threo*-D-*manno*-5-undeculose **110**



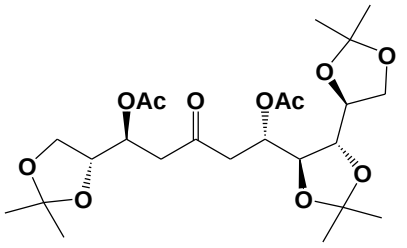
$[\alpha]_D^{27}$ +-34.4 ° (*c* 1.0, chloroform); m.p. 88.0-89.0˚C ^{1}H NMR ($CDCl_3$, 600 MHz), δ 1.35 (s, 3H, IP), 1.36 (s, 9H, IP), 1.40 (s, 3H, IP), 1.45 (s, 3H, IP), 2.71 (dd, 1H, $J_{3,4}$ = 8.4 Hz, $J_{4a,4b}$ = 13.6 Hz, H4), 2.84 (dd 1H, $J_{6,7}$ = 2.5 Hz, $J_{6a,6b}$ = 17.6 Hz, H6), 3.73 (dd, 1H, $J_{8,9}$ = 9.2 Hz, $J_{9,10}$ = 10.6 Hz, H9), 3.73 (d, 1H, $J_{7,8}$ = 9.2 Hz, H8), 3.92 – 4.10 (m, 5H, H1a, H3, H7, H10, H11a, H11b), 4.14 (dd, 1H, $J_{1,2}$ = 5.5 Hz, $J_{2,3}$ = 7.3 Hz, H2), 4.19 (dd, 1H, $J_{1,2}$ = 5.5 Hz, $J_{1a,1b}$ = 7.7 Hz, H1); ^{13}C NMR ($CDCl_3$, 150MHz) δ 25.0 (IP), 25.2 (IP), 26.4 (IP), 26.7 (IP), 26.8 (IP), 30.9 (IP), 47.0 (C6), 47.1 (C4), 66.9 (C11), 67.9 (C1), 69.0 (C10), 69.0 (C2), 76.2 (C7), 77.2 (C3), 81.0 (C9), 82.6 (C8), 109 (IP), 110 (IP), 110 (IP), 211 (C5); ESI-TOFMS *m*/*z*: calcd for $[C_{20}H_{34}O_9+Na]^+$, 441.2095; found, 441.2071.

^{1}H NMR spectrum



4,6-Dideoxy-3,7-di-*O*-acetyl-1,2:8,9:10,11-tri-*O*-isopropylidene-L-*threo*-D-*manno*-5-undeculose

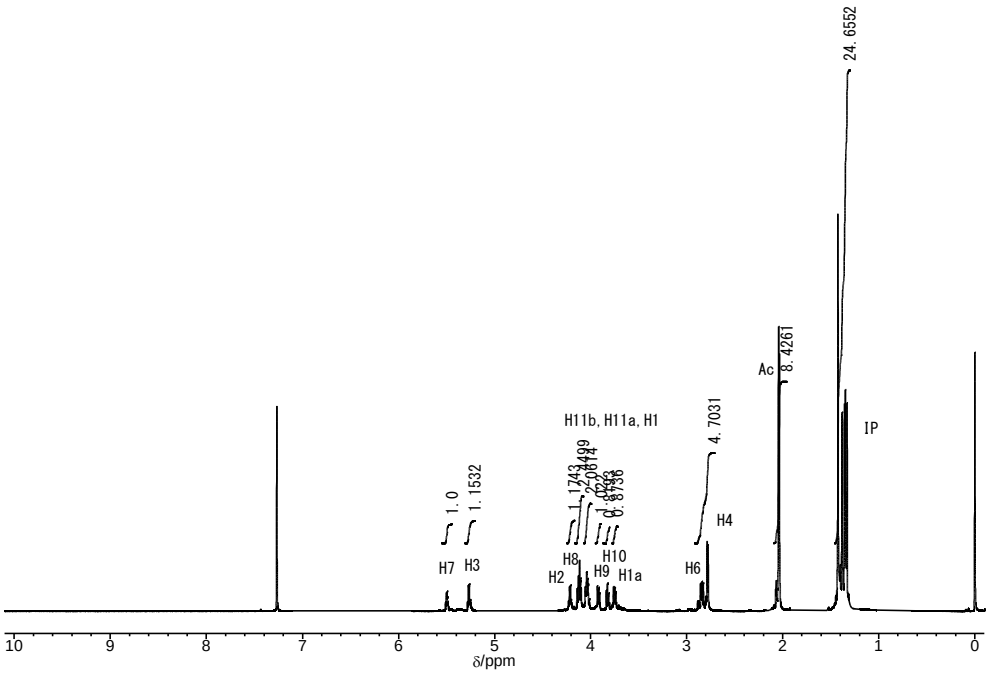
111



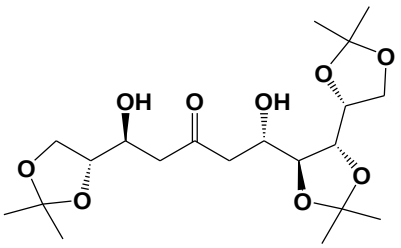
To a solution of the 5-nonulose **110** (25.2 mg, 0.0602 mmole) in pyridine (250 μl) was added Ac_2O (125 μl), and the solution was stirred at room temperature for 1 h, after which TLC (toluene – ethyl acetate, 10 : 1) indicated the formation of the single product. The mixture was poured into ice-cooling water, and extracted with chloroform. The extract was washed with aqueous $NaHCO_3$, water, and brine, dried (Na_2SO_4), and concentrated to dryness. The light yellow syrup was then

purified by silica gel column chromatography (toluene-ethyl acetate, 10 : 1) to give syrupy acetate **111**; yield g; $[\alpha]_D^{27}$ -19.1 ° (*c* 0.5, chloroform); ^{1}H NMR ($CDCl_3$, 600 MHz), δ 1.33 (s, 3H, IP), 1.35 (s, 3H, IP), 1.36 (s, 3H, IP), 1.38 (s, 3H, IP), 1.38 (s, 3H, IP), 1.42 (s, 6H, IP), 2.03 (s, 3H, Ac), 2.04 (s, 3H, Ac), 2.78 (d, 2H, $J_{3,4}$ = 6.0 Hz, H4), 2.84 (dd 2H, $J_{6,7}$ = 5.3 Hz, $J_{6a,6b}$ = 7.0 Hz, H6), 3.75 (dd, 1H, $J_{1a,2}$ = 5.6 Hz, $J_{1a,1b}$ = 8.8 Hz, H1a), 3.82 (dd, 1H, $J_{9,10}$ = 8.0 Hz, $J_{10,11}$ = 6.6 Hz, H10), 3.92 (dd, 1H, $J_{8,9}$ = 5.6 Hz, $J_{9,10}$ = 8.0 Hz, H9), 4.00 – 4.10 (m, 3H, H1b, H11a, H11b), 4.13 (dd, 1H, $J_{7,8}$ = 8.1 Hz, $J_{8,9}$ = 5.6 Hz, H8), 4.22 (ddd, 1H, $J_{1a,2}$ = 5.6 Hz, $J_{1b,2}$ = 11.2 Hz, $J_{2,3}$ = 5.6 Hz, H2), 5.27 (dd, 1H, $J_{2,3}$ = 5.6 Hz, $J_{3,4}$ = 6.0 Hz, H3), 5.50 (dd, 1H, $J_{6,7}$ = 5.3 Hz, $J_{7,8}$ = 8.1 Hz, H7). ^{13}C NMR ($CDCl_3$, 150MHz) δ 24.9 (IP), 25.3 (IP), 26.2 (IP), 26.5 (IP), 27.0 (IP), 27.2 (IP), 43.4 (C4), 43.6 (C6), 66.2 (C1), 67.5 (C11), 69.1 (C7), 69.9 (C3), 76.1 (C2), 77.2 (C9), 78.9 (C6), 80.8 (C8), 109 (IP), 110 (IP), 110 (IP), 169 (Ac), 170 (Ac), 203 (C5); ESI-TOFMS *m*/*z*: calcd for $[C_{24}H_{36}O_{11}+Na]^+$, 525.2306; found, 525.2311.

^{1}H NMR spectrum

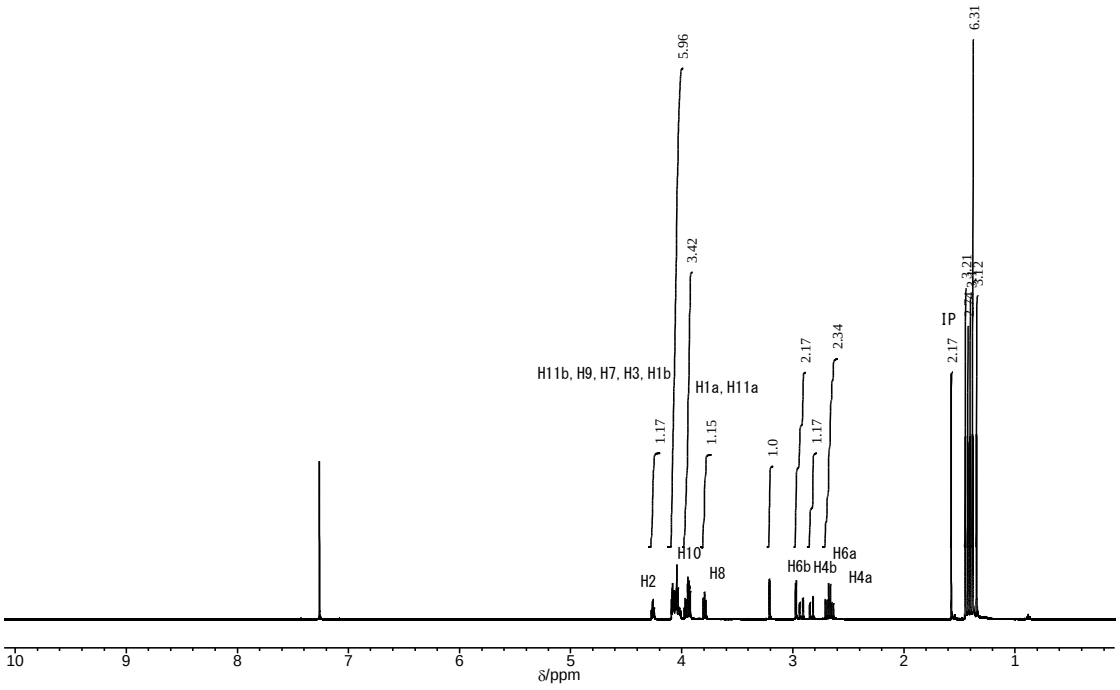


4,6-Dideoxy-1,2:8,9:10,11-tri-*O*-isopropylidene-L-*threo*-D-*tallo*-5-undeculose **112**

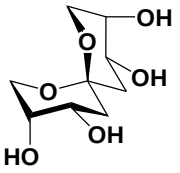


$[\alpha]_D^{27}$ -36.2 ° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$, 600 MHz), δ 1.35 (s, 3H, IP), 1.38 (s, 3H, IP), 1.38 (s, 3H, IP), 1.38 (s, 3H, IP), 1.40 (s, 3H, IP), 1.42 (s, 3H, IP), 1.45 (s, 3H, IP), 2.66 (dd, 1H, $J_{3,4a}$ = 9.0 Hz, $J_{4a,4b}$ = 17.6 Hz, H4a), 2.69 (dd 1H, $J_{6a,7}$ = 8.9 Hz, $J_{6a,6b}$ = 17.6 Hz, H6a), 2.83 (dd, 1H, $J_{3,4b}$ = 2.9 Hz, $J_{4a,4b}$ = 17.6 Hz, H4b), 2.92 (dd, 1H, $J_{6b,7}$ = 2.8 Hz, $J_{6a,6b}$ = 17.6 Hz, H6b), 3.79 (t, 1H, $J_{7,8}$ = 7.2 Hz, H8), 3.92 – 3.97 (m, 2H, H1a, H11a), 3.97 (t, 1H, $J_{9,10}$ = 5.9 Hz, H10), 4.00 – 4.10 (m, 5H, H1b, H3, H7, H9, H11b), 4.26 (dt, 1H, $J_{1,2}$ = 7.0 Hz, $J_{2,3}$ = 4.5 Hz, H2); ^{13}C NMR ($CDCl_3$, 150MHz) δ 25.1 (IP), 25.5 (IP), 26.2 (IP), 26.7 (IP), 27.1 (IP), 27.2 (IP), 46.5 (C4), 47.2 (C6), 65.9 (C11), 66.7 (C1), 68.9 (C3), 69.8 (C7), 75.8 (C2), 77.5 (C10), 78.8 (C8), 80.1 (C9), 109 (IP), 110 (IP), 110 (IP), 110 (IP), 212 (C5); ESI-TOFMS *m*/*z*: calcd for $[C_{20}H_{34}O_9+Na]^+$, 441.2095; found, 441.2099.

^{1}H NMR spectrum



(*6R*)-1,7-Dioxaspiro[5,5]undecan-3,4,9,10-tetrol **114**



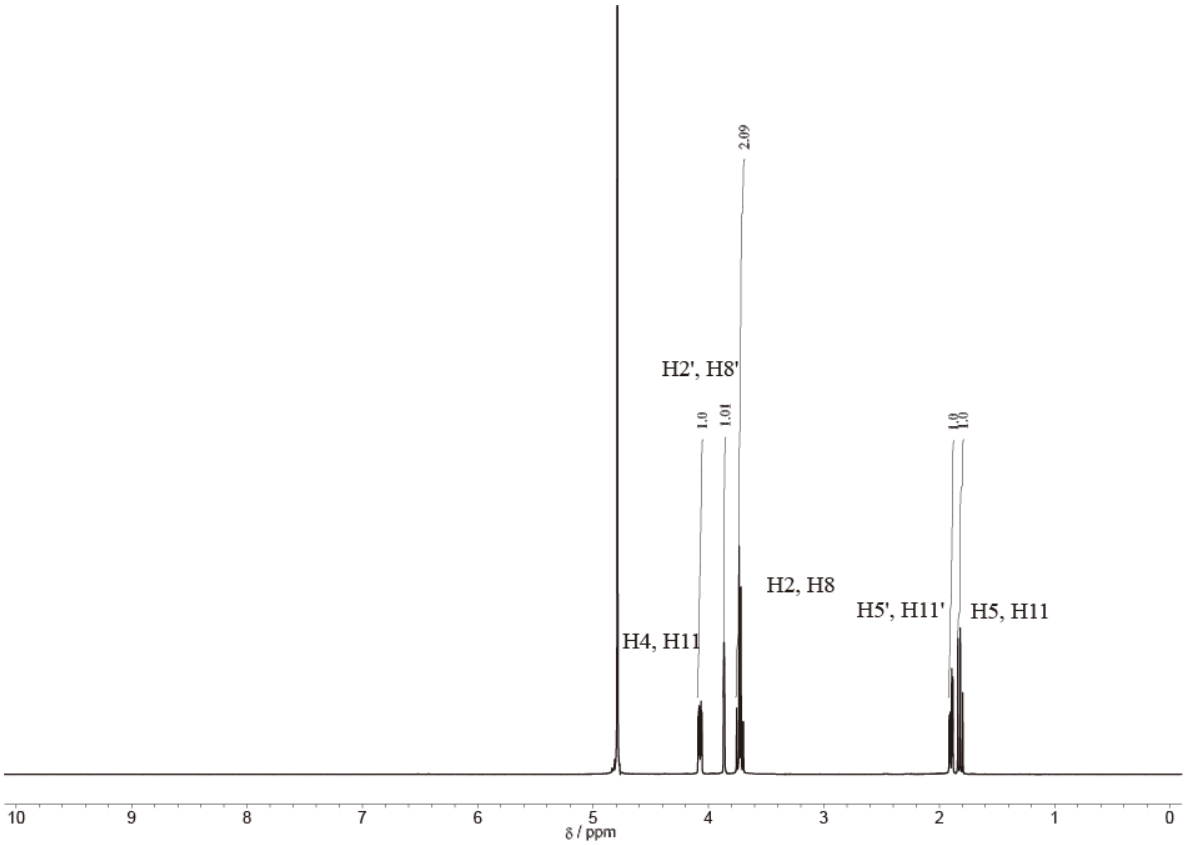
To a solution of **100** (38 mg) in methanol (7.5 ml) was added Amberlyst 15E (70 mg) and the mixture was stirred at room temperature for 48 h. The suspension was filtered and the filtrate was evaporated to deposit the crude product as a white solid. Recrystallization from methanol afforded pure **4** as colorless prisms; yield 20 mg (79 %), $[\alpha]_D^{27}$ -218° (*c* 1.0, methanol); mp 224 °C (dec); ^{1}H NMR (D_2O, 600 MHz), δ 1.86 (t, 2H, $J_{5a,5b} = J_{11a,11b}$ = 12.9 Hz, H5, H11), 1.94 (dd, 2H, $J_{5a,5b} = J_{11a,11b}$ = 12.9 Hz, $J_{4,5b} = J_{10,11b}$ = 5.2 Hz, H5, H11), 3.75 (dd, 2H, $J_{2a,3} = J_{8a,9}$ = 2.0 Hz, $J_{2a,2b} = J_{8a,8b}$ = 12.7 Hz, H2, H8), 3.78 (broad d, 2H, $J_{2a,3} = J_{8a,9}$ = 2.0 Hz, H3, H9), 3.90 (m, 2H, H3, H9), 4.11 (ddd, 2H, $J_{2a,3} = J_{8a,9}$ = 2.0 Hz, $J_{4,5b} = J_{10,11b}$ = 5.2 Hz, H4, H10).

^{13}C NMR (D_2O, 150MHz) δ 39.2 (C5, C11), 66.6 (C2, C8), 67.2 (C3, C9), 69.7 (C4, C10), 102

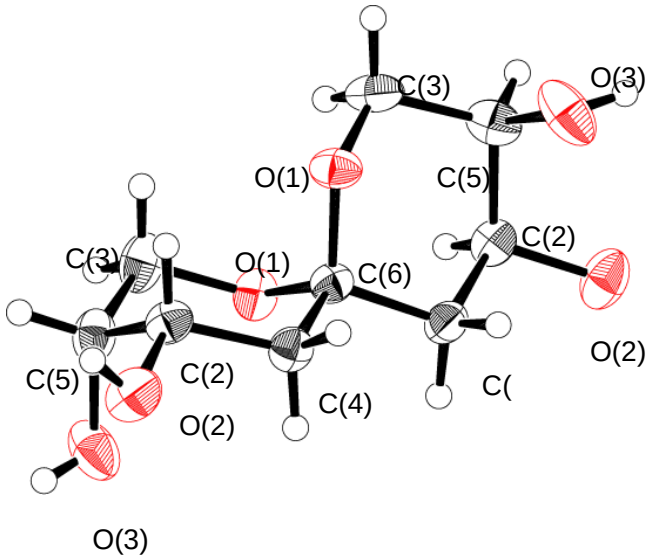
(C6); ESI-TOFMS *m*/*z*: calcd for $[C_9H_{16}O_6+Na]^+$, 243.0845; found, 243.0846.

CCDC-931133.

^{1}H NMR spectrum



Crystal structure of (*6R*)-1,7-Dioxaspiro[5,5]undecan-3,4,9,10-tetrol **114**



Empirical Formula $C_9H_{16}O_6$

Formula Weight 220.22

Crystal Color, Habit colorless, prism

Crystal Dimensions 0.300 X 0.200 X 0.200 mm

Crystal System tetragonal

Lattice Type Primitive

Lattice Parameters *a* = 7.225(2) Å

c = 19.523(6) Å

V = 1019.1(5) Å3

Space Group $P4_12_12$

Z value 4

*D*calc 1.435 g/cm3

R-factor 3.26%

Temperature 296 K

ω oscillation Range (c=45.0, f=210.0) 0.0 - 159.0o

No. of Reflections Measured Total: 11568

Atomic coordinates and Biso/Beq and occupancy

atom	x	y	z	B_{eq}	occ
O(1)	0.1621(1)	0.3584(1)	0.53035(3)	2.41(2)	1
O(2)	0.2333(2)	0.6136(2)	0.34138(4)	3.35(2)	1
O(3)	0.0097(2)	0.6654(2)	0.46024(4)	3.81(2)	1
C(2)	0.2085(2)	0.4701(2)	0.39063(5)	2.30(2)	1
C(3)	0.0134(2)	0.3404(2)	0.48228(6)	2.96(2)	1
C(4)	0.3664(2)	0.4780(2)	0.44182(5)	2.28(2)	1
C(5)	0.0240(2)	0.4891(2)	0.42765(6)	2.72(2)	1
C(6)	0.3404(2)	0.3404(2)	0.5000	1.97(2)	1/2

Bond lengths (Å)

atom	atom	distance	atom	atom	distance
O(1)	C(3)	1.4321(14)	O(1)	C(6)	1.4238(12)
O(2)	C(2)	1.4255(14)	O(3)	C(5)	1.4272(16)
C(2)	C(4)	1.5181(15)	C(2)	C(5)	1.5223(16)
C(3)	C(5)	1.5156(18)	C(4)	C(6)	1.5215(13)

Bond angles (o)

atom	atom	atom	angle	atom	atom	atom	angle
C(3)	O(1)	C(6)	113.41(7)	O(2)	C(2)	C(4)	108.79(9)
O(2)	C(2)	C(5)	111.38(9)	C(4)	C(2)	C(5)	110.01(9)
O(1)	C(3)	C(5)	111.04(10)		C(2)	C(4)	C(6) 111.94(9)
O(3)	C(5)	C(2)	110.83(10)		O(3)	C(5)	C(3) 108.36(10)
C(2)	C(5)	C(3)	108.32(10)		O(1)	C(6)	$O(1)^1$ 109.83(8)
O(1)	C(6)	C(4)	111.27(8)	O(1)	C(6)	$C(4)^1$	105.63(6)
$O(1)^1$	C(6)	C(4)	105.63(6)	$O(1)^1$	C(6)	$C(4)^1$	111.27(8)
C(4)	C(6)	$C(4)^1$	113.29(9)				

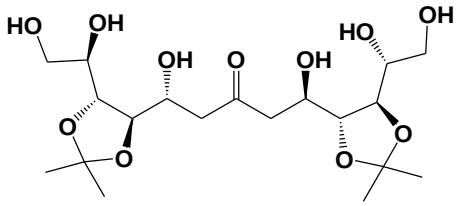
Torsion Angles(o)

(Those having bond angles > 160 or < 20 degrees are excluded.)

atom1	atom2	atom3	atom4	angle
C(3)	O(1)	C(6)	O(1)1	-60.82(9)
C(3)	O(1)	C(6)	C(4)1	179.09(8)
O(2)	C(2)	C(4)	C(6)	174.67(7)
O(2)	C(2)	C(5)	C(3)	-176.14(8)
C(4)	C(2)	C(5)	C(3)	-55.43(11)
O(1)	C(3)	C(5)	O(3)	-60.81(11)
C(2)	C(4)	C(6)	O(1)	-51.49(10)
C(2)	C(4)	C(6)	C(4)1	-170.32(7)

atom1	atom2	atom3	atom4	angle
C(3)	O(1)	C(6)	C(4)	55.77(10)
C(6)	O(1)	C(3)	C(5)	-60.94(11)
O(2)	C(2)	C(5)	O(3)	-57.40(11)
C(4)	C(2)	C(5)	O(3)	63.31(11)
C(5)	C(2)	C(4)	C(6)	52.41(11)
O(1)	C(3)	C(5)	C(2)	59.48(12)
C(2)	C(4)	C(6)	O(1)[1]	67.64(10)

4,6-Dideoxy-3,4:10,11-di-*O*-isopropylidene-D-*allo*-D-*allo*-7-trideculose **117**

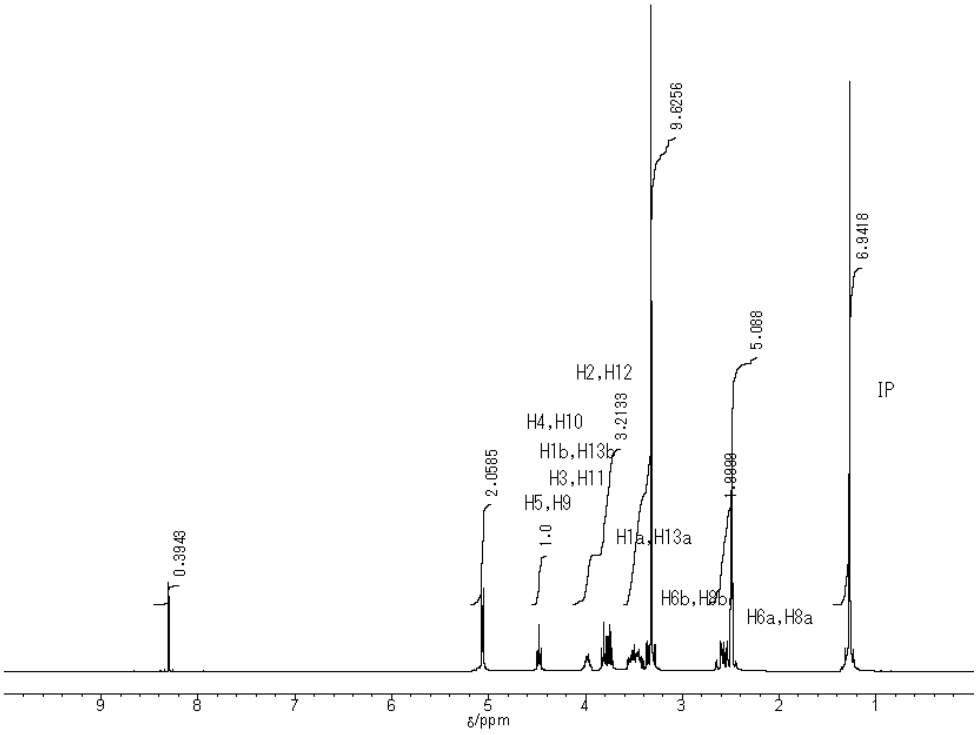


To a solution of **102** (38 mg) in methanol (7.5 ml) was added Amberlyst 15E (70 mg) and the mixture was stirred at room temperature for 48 h. The suspension was filtered and the filtrate was evaporated to deposit the crude product of **117** as a white solid; ^{1}H NMR ($CDCl_3$, 600 MHz), δ 1.27 (s, 12H, IP), 2.45-2.57 (m, 2H, H6a, H8a), 2.62 (dd, 2H, $J_{5,6a} = J_{8a,9} = 3.6$ Hz, $J_{6a,6b} = J_{8a,8b}$ =16.0 Hz, H6b, H8b), 3.28-3.36 (m, 2H, H1a, H13a), 3.40-3.47 (m, 2H, H2, H12), 3.50-3.55 (m, 2H, H1b, H13b), 3.75 (t, 2H, $J_{2,3} = J_{11,12} = 6.4$ Hz, H3, H11), 3.81 (t, 2H, $J_{3,4} = J_{10,11} = 6.4$ Hz, H4, H10), 3.98 (dt, 2H, $J_{4,5} = J_{9,10} = 6.4$ Hz, $J_{5,6} = J_{8,9} = 8.9$ Hz, H5, H9).

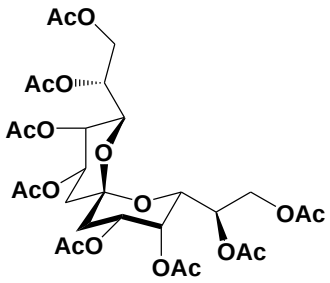
^{13}C NMR ($CDCl_3$, 150MHz) 28.4 (IP), 28.4 (IP), 48.4 (C6, C8), 64.2 (C1, C13), 69.0 (C5, C9), 74.0 (C2, C12), 80.3 (C3, C11), 83.0 (C4, C10), 109 (IP), 209 (C7); ESI-TOFMS *m*/*z*: calcd for

$[C_{19}H_{34}O_{11}+Na]^+$, 438.2101; found,438.2169.

^1H NMR spectrum



(*3S*,*4R*,*6R*,*9S*,*10R*)-2,8-Di[(*1R*)-1,2-dihydrocyethyl]-1,7-dioxaspiro[5,5]-undecan-3,4,9,10-tetrol octaacetate **115**

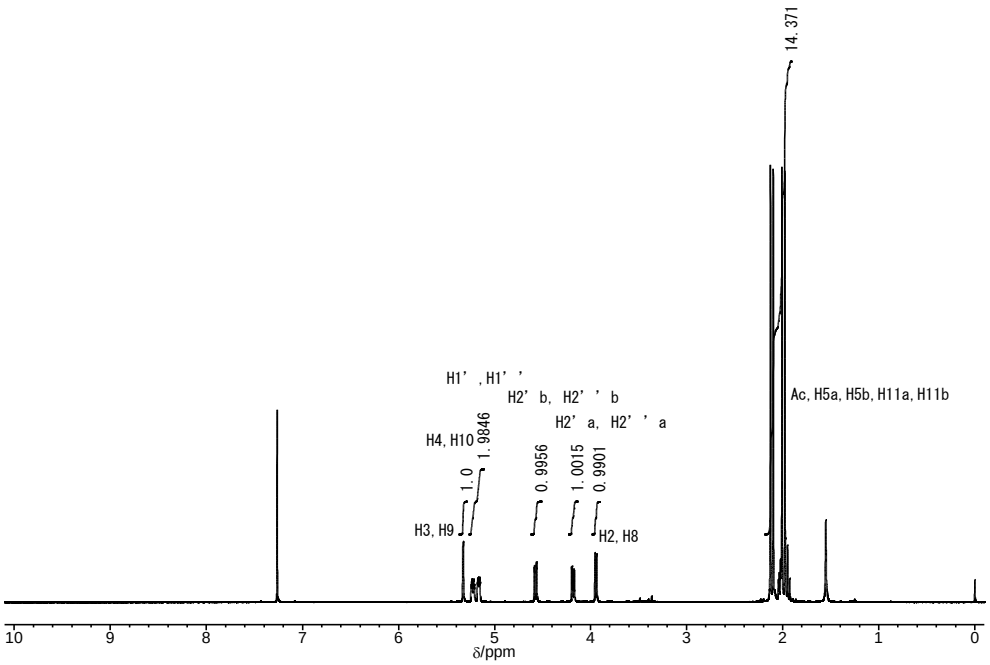


To a stirred solution of **102** (92.0 mg) in methanol was added 50 % trifluoroacetic acid (2.0 ml) at 0 °C, and the solution was stirred at room temperature for 24 h. Azeotropic concentration of the reaction mixture with toluene gave crude [5,5]spiroketal-octol as a hygroscopic solid. The compound was immediately acetylated with acetic anhydride (0.25 ml) in pyridine (0.5 ml) at room temperature. After stirring for 3 h, the reaction mixture was quenched with ice-water (2.5 ml) and extracted with dichloromethane (2.5 ml). The combined organic extract was washed successively with 5% aq $NaHSO_4$, saturated aq $NaHCO_3$, water, brine, and dried ($NaHSO_4$). The organic solution was concentrated to a syrup that was purified by silica gel column chromatography (chloroform-acetone, 10 : 1) to give **115** as a white solid. Recrystallization from methanol afforded pure **115** as fine needles; yield 98 mg (84%), $[\alpha]_D^{27}$ +85.2° (*c* 1.0, chloroform); mp 200.5-201.5 °C; ^{1}H NMR ($CDCl_3$, 600 MHz), δ 2.13 (m, 28H, Ac, H5a, H5b, H11a, H11b), 3.94 (d, 2H, $J_{2,1'} = J_{8,1''}$ = 9.8 Hz, H2, H8), 4.18 (dd, 2H, $J_{1',2'a} = J_{1'',2''a}$ = 4.6 Hz, $J_{2'a,2'b} = J_{2''a,2''b}$ = 12.3 Hz, H2'a, H2''a), 4.57 (dd, 2H, $J_{1',2'b} = J_{1'',2''b}$ = 2.2 Hz, $J_{2'a,2'b} = J_{2''a,2''b}$ = 12.3 Hz, H2'b, H2''b), 5.17 (ddd, 2H, $J_{2,1'} = J_{8,1''}$ = 9.8 Hz, $J_{1',2'a} = J_{1'',2''a}$ = 4.6 Hz, $J_{1',2'b} = J_{1'',2''b}$ = 2.2 Hz, H1', H1''), 5.23 (ddd, 2H, H4, H10), 5.23 (s, 2H, H3, H9); ^{13}C NMR ($CDCl_3$, 150MHz) δ 20.5 (Ac), 20.5 (Ac), 20.6 (Ac), 20.7 (Ac), 34.2 (C5, C11), 62.4 (C2', C2''), 64.4 (C3, C9), 66.0 (C4, C10), δ67.4 (C1', C1''), 68.2 (C2, C8), 99.8 (C6), 170 (Ac), 170 (Ac), 170 (Ac), 170 (Ac); ESI-TOFMS *m*/*z*: calcd

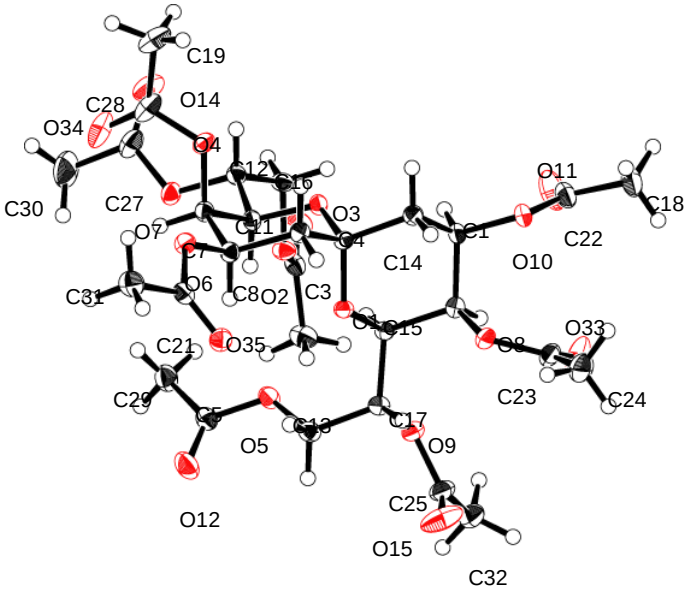
for $[C_{29}H_{40}O_{18}+Na]^+$, 699.2107; found, 699.2108.

CCDC-931132.

^{1}H NMR spectrum



Crystal structure of (*3S*,*4R*,*6R*,*9S*,*10R*)-2,8-Di[(*1R*)-1,2-dihydrocyethyl]-1,7-dioxaspiro[5,5]-undecan-3,4,9,10-tetrol octaacetate **115**



Empirical Formula $C_{29}H_{40}O_{18}$

Formula Weight 676.62

Crystal Color, Habit colorless, block

Crystal Dimensions 0.350 X 0.250 X 0.200 mm

Crystal System orthorhombic

Lattice Type Primitive

Lattice Parameters *a* = 9.063(2) Å

b = 14.273(3) Å

c = 25.018(4) Å

V = 3236.2(9) Å3

Space Group $P2_12_12_1$ (#19)

Z value 4

*D*calc 1.389 g/cm3

R-factor 3.41%

Temperature 123 K

ω oscillation Range (c=45.0, f=180.0) 0.0 - 160.0o

No. of Reflections Measured Total: 38269

Atomic coordinates and Biso/Beq and occupancy

atom	x	y	z	Beq
O1	0.4020(1)	0.66638(6)	0.27936(4)	1.30(2)
O2	0.7817(1)	0.83406(7)	0.27497(4)	1.67(2)
O3	0.4731(1)	0.79998(6)	0.23071(4)	1.30(2)
O4	0.4616(1)	0.77911(7)	0.11346(4)	1.56(2)
O5	0.7344(1)	0.58947(6)	0.30772(4)	1.53(2)
O6	0.3161(1)	0.61687(7)	0.11648(4)	1.56(2)
O7	0.8128(1)	0.79665(7)	0.15710(4)	1.59(2)
O8	0.2397(1)	0.70758(7)	0.37739(4)	1.61(2)
O9	0.5881(1)	0.62926(7)	0.40393(4)	1.61(2)
O10	0.2333(1)	0.89991(6)	0.35958(4)	1.49(2)
O11	0.2915(2)	1.02037(7)	0.30513(4)	1.86(2)
O12	0.8743(2)	0.45976(7)	0.31283(5)	2.20(3)
O13	0.8548(2)	0.96167(7)	0.31975(5)	2.61(3)
O14	0.8284(2)	0.9286(1)	0.10847(6)	3.70(3)
O15	0.4789(2)	0.51225(9)	0.44886(5)	3.28(3)
O33	0.3120(2)	0.7031(1)	0.46366(4)	3.03(3)

O34	0.5634(2)	0.7050(1)	0.04303(4)	3.43(3)
O35	0.4495(2)	0.48430(9)	0.10898(5)	3.35(3)
C1	0.3275(2)	0.84000(9)	0.32769(5)	1.34(3)
C3	0.2808(2)	0.6969(1)	0.19809(5)	1.44(3)
C4	0.3528(2)	0.74203(9)	0.24646(5)	1.27(3)
C5	0.8602(2)	0.5410(1)	0.30142(6)	1.55(3)
C6	0.3728(2)	0.75764(9)	0.36200(5)	1.39(3)
C7	0.5213(2)	0.7087(1)	0.14925(5)	1.37(3)
C8	0.3936(2)	0.64464(9)	0.16459(5)	1.38(3)
C11	0.5846(2)	0.75623(9)	0.19876(5)	1.26(3)
C12	0.6876(2)	0.83706(9)	0.18449(5)	1.41(3)
C13	0.6060(2)	0.53745(9)	0.32381(6)	1.53(3)
C14	0.2502(2)	0.80692(9)	0.27700(5)	1.37(3)
C15	0.4714(2)	0.69385(9)	0.32830(5)	1.29(3)
C16	0.7387(2)	0.8950(1)	0.23151(5)	1.58(3)
C17	0.5092(2)	0.60219(9)	0.35630(5)	1.35(3)
C18	0.1440(2)	1.0494(1)	0.38298(7)	2.17(3)
C19	0.3792(2)	0.8218(2)	0.02763(6)	2.69(4)
C20	0.8645(2)	0.8125(1)	0.36325(6)	2.21(3)
C21	0.3556(2)	0.5359(1)	0.09265(6)	1.98(3)
C22	0.2304(2)	0.99100(9)	0.34461(5)	1.52(3)
C23	0.2217(2)	0.6856(1)	0.42988(6)	2.14(3)
C24	0.0779(2)	0.6375(2)	0.43912(7)	2.82(4)
C25	0.5609(2)	0.5775(2)	0.44846(6)	2.21(3)
C26	0.8346(2)	0.8785(1)	0.31825(6)	1.68(3)

C27	0.8757(2)	0.8525(2)	0.11933(6)	2.08(3)
C28	0.4798(2)	0.7628(2)	0.06044(6)	2.03(3)
C29	0.9788(2)	0.6009(1)	0.27802(7)	2.20(3)
C30	1.0105(2)	0.8090(2)	0.09569(6)	2.49(4)
C31	0.2677(2)	0.5214(2)	0.04258(6)	2.61(4)
C32	0.6499(3)	0.6123(2)	0.49421(7)	4.15(5)

Bond lengths (Å)

atom	atom	distance	atom	atom	distance
O1	C4	1.4291(16)	O1	C15	1.4312(17)
O2	C16	1.4463(17)	O2	C26	1.3430(18)
O3	C4	1.4244(16)	O3	C11	1.4319(17)
O4	C7	1.4504(17)	O4	C28	1.3568(19)
O5	C5	1.3432(17)	O5	C13	1.4373(17)
O6	C8	1.4486(17)	O6	C21	1.3491(19)
O7	C12	1.4452(17)	O7	C27	1.3614(19)
O8	C6	1.4536(18)	O8	C23	1.3599(19)
O9	C17	1.4424(17)	O9	C25	1.3593(19)
O10	C1	1.4480(17)	O10	C22	1.3533(16)
O11	C22	1.2073(17)	O12	C5	1.2015(18)
O13	C26	1.2021(18)	O14	C27	1.199(3)
O15	C25	1.192(3)	O33	C23	1.203(2)
O34	C28	1.202(3)	O35	C21	1.197(2)

C1	C6	1.5124(19)	C1	C14	1.5238(19)
C3	C4	1.5179(19)	C3	C8	1.5183(19)
C4	C14	1.5186(19)	C5	C29	1.492(3)
C6	C15	1.5290(19)	C7	C8	1.524(2)
C7	C11	1.5242(19)	C11	C12	1.5264(19)
C12	C16	1.5111(19)	C13	C17	1.5114(19)
C15	C17	1.5232(19)	C18	C22	1.493(3)
C19	C28	1.488(3)	C20	C26	1.493(3)
C21	C31	1.499(3)	C23	C24	1.491(3)
C25	C32	1.486(3)	C27	C30	1.493(3)

Bond angles (o)

atom	atom	atom	angle	atom	atom	atom	angle
C4	O1	C15	115.02(10)	C16	O2	C26	114.71(11)
C4	O3	C11	116.21(10)	C7	O4	C28	116.05(12)
C5	O5	C13	117.02(10)	C8	O6	C21	118.24(11)
C12	O7	C27	115.09(11)	C6	O8	C23	117.95(11)
C17	O9	C25	116.20(12)	C1	O10	C22	115.23(11)
O10	C1	C6	107.84(10)	O10	C1	C14	111.74(11)
C6	C1	C14	110.87(11)	C4	C3	C8	111.05(11)
O1	C4	O3	111.05(11)	O1	C4	C3	105.85(11)
O1	C4	C14	111.23(11)	O3	C4	C3	110.78(11)
O3	C4	C14	104.70(10)	C3	C4	C14	113.36(12)

O5	C5	O12	123.97(13)	O5	C5	C29	111.29(12)
O12	C5	C29	124.74(14)	O8	C6	C1	107.89(11)
O8	C6	C15	109.76(11)	C1	C6	C15	107.97(11)
O4	C7	C8	106.73(11)	O4	C7	C11	109.50(11)
C8	C7	C11	110.37(11)	O6	C8	C3	105.49(11)
O6	C8	C7	108.84(10)	C3	C8	C7	110.81(11)
O3	C11	C7	112.46(11)	O3	C11	C12	103.45(10)
C7	C11	C12	112.11(11)	O7	C12	C11	106.81(11)
O7	C12	C16	110.31(11)	C11	C12	C16	114.79(11)
O5	C13	C17	107.73(11)	C1	C14	C4	109.04(11)
O1	C15	C6	112.22(11)	O1	C15	C17	104.90(10)
C6	C15	C17	112.92(11)	O2	C16	C12	109.77(11)
O9	C17	C13	108.68(11)	O9	C17	C15	105.16(10)
C13	C17	C15	114.11(11)	O6	C21	O35	124.38(15)
O6	C21	C31	110.25(14)	O35	C21	C31	125.35(15)
O10	C22	O11	123.45(13)	O10	C22	C18	111.60(12)
O11	C22	C18	124.95(13)	O8	C23	O33	123.30(15)
O8	C23	C24	111.16(14)	O33	C23	C24	125.54(15)
O9	C25	O15	123.02(15)	O9	C25	C32	110.56(15)
O15	C25	C32	126.39(16)	O2	C26	O13	123.09(14)
O2	C26	C20	112.01(13)	O13	C26	C20	124.91(15)
O7	C27	O14	122.58(15)	O7	C27	C30	111.98(14)
O14	C27	C30	125.39(16)	O4	C28	O34	123.27(15)
O4	C28	C19	111.57(14)	O34	C28	C19	125.11(14)

Torsion Angles (o)

(Those having bond angles > 160 or < 20 degrees are excluded.)

atom1	atom2	atom3	atom4	angle
C4	O1	C15	C6	55.55(13)
C15	O1	C4	O3	60.95(13)
C15	O1	C4	C14	-55.23(13)
C16	O2	C26	C20	175.03(10
C4	O3	C11	C7	53.74(13)
C11	O3	C4	O1	62.48(13)
C11	O3	C4	C14	-177.38(9)
C7	O4	C28	C19	163.20(11
C28	O4	C7	C11	143.29(11
C13	O5	C5	O12	-6.7(2)
C8	O6	C21	O35	1.1(2)
C21	O6	C8	C3	-147.70(11
C12	O7	C27	O14	-2.0(2)
C27	O7	C12	C11	148.40(11
C6	O8	C23	O33	-2.3(2)
C23	O8	C6	C1	-130.90(11
C17	O9	C25	O15	1.2(2)
C25	O9	C17	C13	-94.90(13)
C1	O10	C22	O11	5.80(18)
C22	O10	C1	C6	154.69(10

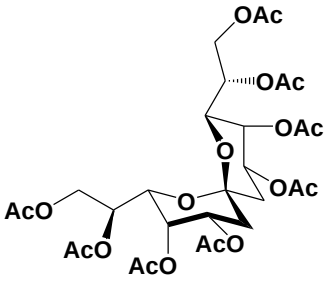
O10	C1	C6	O8	61.02(12)
O10	C1	C14	C4	-178.11(9)
C14	C1	C6	O8	-61.61(13)
C4	C3	C8	O6	-172.05(10
C8	C3	C4	O1	-66.23(13)
C8	C3	C4	C14	171.58(10
O3	C4	C14	C1	-65.13(12)
O8	C6	C15	O1	62.64(13)
C1	C6	C15	O1	-54.72(14)
O4	C7	C8	O6	48.80(13)
O4	C7	C11	O3	66.44(13)
C8	C7	C11	O3	-50.77(14)
C11	C7	C8	O6	167.71(10
O3	C11	C12	O7	173.70(9)
C7	C11	C12	O7	-64.89(13)
O7	C12	C16	O2	-76.06(13)
O5	C13	C17	O9	-63.29(13)

atom1	atom2	atom3	atom4	angle
C4	O1	C15	C17	178.51(9)
C15	O1	C4	C3	-178.77(9)
C16	O2	C26	O13	-5.08(19)
C26	O2	C16	C12	177.57(10)
C4	O3	C11	C12	174.91(9)
C11	O3	C4	C3	-54.83(13)

C7	O4	C28	O34	-14.3(2)
C28	O4	C7	C8	-97.23(13)
C5	O5	C13	C17	149.67(11)
C13	O5	C5	C29	172.65(10)
C8	O6	C21	C31	-177.68(10)
C21	O6	C8	C7	93.35(13)
C12	O7	C27	C30	175.77(10)
C27	O7	C12	C16	-86.23(13)
C6	O8	C23	C24	178.08(10)
C23	O8	C6	C15	111.68(12)
C17	O9	C25	C32	179.50(10)
C25	O9	C17	C15	142.52(11)
C1	O10	C22	C18	-173.82(10)
C22	O10	C1	C14	-83.21(13)
O10	C1	C6	C15	179.58(9)
C6	C1	C14	C4	-57.78(13)
C14	C1	C6	C15	56.95(14)
C4	C3	C8	C7	-54.42(13)
C8	C3	C4	O3	54.23(14)
O1	C4	C14	C1	54.88(13)
C3	C4	C14	C1	174.02(10)
O8	C6	C15	C17	-55.67(13)
C1	C6	C15	C17	-173.04(10)
O4	C7	C8	C3	-66.76(12)
O4	C7	C11	C12	-49.64(14)

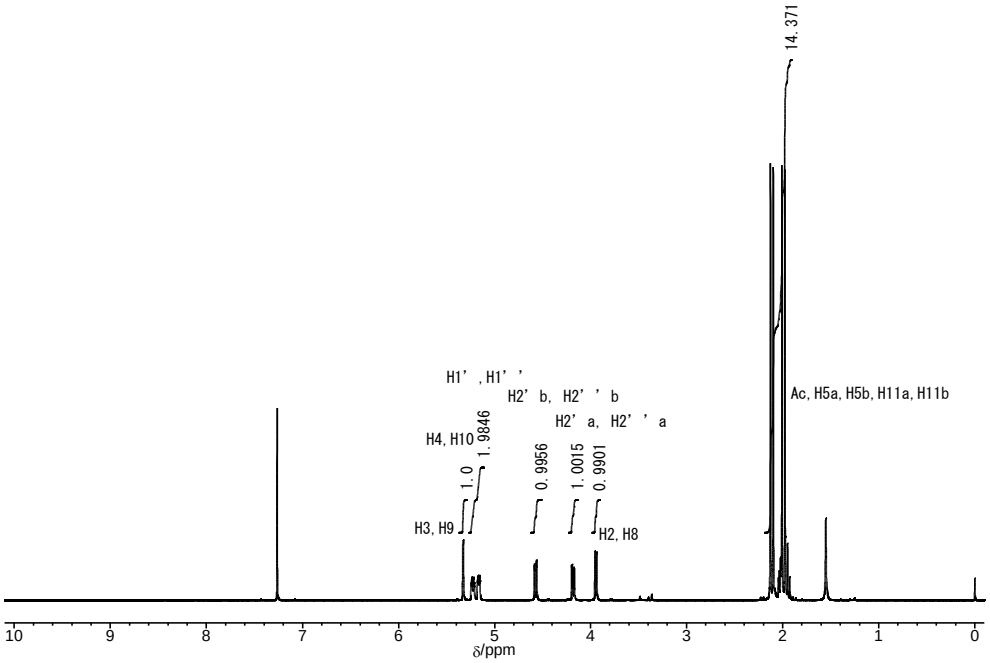
C8	C7	C11	C12	-166.85(10)
C11	C7	C8	C3	52.15(14)
O3	C11	C12	C16	51.09(13)
C7	C11	C12	C16	172.50(10)
C11	C12	C16	O2	44.65(15)
O5	C13	C17	C15	53.70(14)

(*3R,4S,6S,9R,10S*)-2,8-Di[(*1S*)-1,2-dihydrocyethyl]-1,7-dioxaspiro[5,5]-undecan-3,4,9,10-tetrol octaacetate **116**

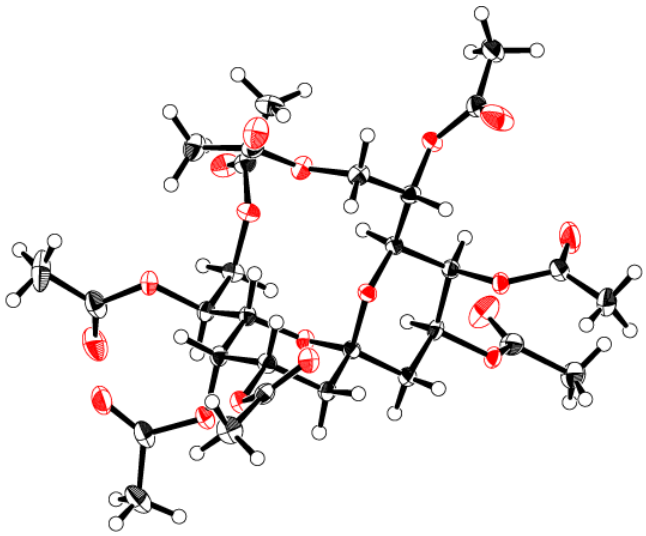


This compound was prepared exactly as described for the analogue of *R*-enantiomer; yield 76%, $[\alpha]_D^{27}$ -85.2° (*c* 1.0, chloroform); mp 198.0-199.0 °C; ^{1}H NMR ($CDCl_3$, 600 MHz), δ 2.13 (m, 28H, Ac, H5a, H5b, H11a, H11b), 3.94 (d, 2H, $J_{2,1'} = J_{8,1''}$ = 9.8 Hz, H2, H8), 4.18 (dd, 2H, $J_{1',2'a} = J_{1'',2''a}$ = 4.6 Hz, $J_{2'a,2'b} = J_{2''a,2''b}$ = 12.3 Hz, H2'a, H2''a), 4.57 (dd, 2H, $J_{1',2'b} = J_{1'',2''b}$ = 2.2 Hz, $J_{2'a,2'b} = J_{2''a,2''b}$ = 12.3 Hz, H2'b, H2''b), 5.17 (ddd, 2H, $J_{2,1'} = J_{8,1''}$ = 9.8 Hz, $J_{1',2'a} = J_{1'',2''a}$ = 4.6 Hz, $J_{1',2'b} = J_{1'',2''b}$ = 2.2 Hz, H1', H1''), 5.23 (ddd, 2H, H4, H10), 5.23 (s, 2H, H3, H9); ^{13}C NMR ($CDCl_3$, 150MHz) δ 20.5 (Ac), 20.5 (Ac), 20.6 (Ac), 20.7 (Ac), 34.2 (C5, C11), 62.4 (C2', C2''), 64.4 (C3, C9), 66.0 (C4, C10), δ67.4 (C1', C1''), 68.2 (C2, C8), 99.8 (C6), 170 (Ac), 170 (Ac), 170 (Ac), 170 (Ac); ESI-TOFMS *m/z*: calcd for $[C_{29}H_{40}O_{18}+Na]^+$, 699.2107; found, 699.2108.

^{1}H NMR spectrum



Crystal structure of (*3R*,*4S*,*6S*,*9R*,*10S*)-2,8-Di[(*1S*)-1,2-dihydrocyethyl]-1,7-dioxaspiro[5,5]-undecan-3,4,9,10-tetrol octaacetate **116**



Empirical Formula $C_{29}H_{40}O_{18}$

Formula Weight 676.62

Crystal Color, Habit colorless, block

Crystal Dimensions 0.150 X 0.150 X 0.100 mm

Crystal System orthorhombic

Lattice Type Primitive

Lattice Parameters *a* = 9.064(13) Å

b = 14.275(3) Å

c = 25.022(4) Å

V = 3237.4(9) Å3

Space Group $P2_12_12_1$ (#19)

Z value 4

*D*calc 1.388 g/cm3

R-factor 4.64%

Temperature 123 K

ω oscillation Range (c=45.0, f=180.0) 0.0 - 160.0o

No. of Reflections Measured Total: 9439

Atomic coordinates and Biso/Beq and occupancy

atom	x	y	z	Beq
O1 O	0.59790(17)	0.16645(10)	0.27932(6)	0.0168(4)
O2 O	0.21814(18)	0.33414(10)	0.27487(6)	0.0220(4)
O3 O	0.52707(17)	0.30018(10)	0.23067(6)	0.0166(4)
O4 O	0.53846(18)	0.27896(10)	0.11350(6)	0.0199(4)
O5 O	0.26553(17)	0.08928(10)	0.30759(6)	0.0197(4)

O6 O	0.68370(17)	0.11661(11)	0.11669(6)	0.0193(4)
O7 O	0.18701(18)	0.29664(11)	0.15706(6)	0.0205(4)
O8 O	0.76029(18)	0.20711(11)	0.37722(6)	0.0204(4)
O9 O	0.41182(18)	0.12931(11)	0.40392(6)	0.0213(4)
O10 O	0.76703(18)	0.40009(10)	0.35945(6)	0.0194(4)
O11 O	0.70865(19)	0.52018(11)	0.30513(6)	0.0231(4)
O12 O	0.12536(19)	-0.04040(11)	0.31260(8)	0.0282(5)
O13 O	0.1447(3)	0.46178(12)	0.31961(7)	0.0334(5)
O14 O	0.1718(3)	0.42880(15)	0.10852(9)	0.0483(7)
O15 O	0.5504(3)	-0.01576(14)	0.10906(8)	0.0422(6)
O16 O	0.5210(3)	0.01190(14)	0.44875(8)	0.0423(6)
O32 O	0.4369(3)	0.20440(18)	0.04320(7)	0.0457(6)
O33 O	0.6887(3)	0.20278(16)	0.46356(7)	0.0396(6)
C1 C	0.6721(3)	0.33972(15)	0.32760(8)	0.0176(5)
C3 C	0.7191(3)	0.19665(16)	0.19815(8)	0.0191(6)
C4 C	0.6474(3)	0.24215(15)	0.24632(9)	0.0164(5)
C5 C	0.4786(3)	0.20890(15)	0.14937(8)	0.0171(5)
C6 C	0.6066(3)	0.14458(15)	0.16467(9)	0.0178(6)
C7 C	0.1400(3)	0.04083(16)	0.30133(9)	0.0206(6)
C8 C	0.6272(3)	0.25727(15)	0.36202(9)	0.0175(5)
C10 C	0.3128(3)	0.33718(15)	0.18471(9)	0.0182(5)
C11 C	0.3941(3)	0.03734(15)	0.32394(10)	0.0194(6)
C12 C	0.4149(3)	0.25585(14)	0.19875(9)	0.0162(5)
C13 C	0.7496(3)	0.30714(15)	0.27693(8)	0.0173(5)
C14 C	0.5288(3)	0.19393(15)	0.32818(8)	0.0166(5)

C15 C	0.4909(3)	0.10245(15)	0.35639(8)	0.0174(6)
C16 C	0.2617(3)	0.39529(15)	0.23142(9)	0.0208(6)
C17 C	0.8560(3)	0.54899(17)	0.38301(11)	0.0285(7)
C18 C	0.7698(3)	0.49083(15)	0.34464(9)	0.0196(6)
C19 C	0.6208(4)	0.3217(2)	0.02783(10)	0.0337(7)
C20 C	0.9220(4)	0.1378(2)	0.43886(12)	0.0353(8)
C21 C	0.1355(3)	0.31240(18)	0.36301(10)	0.0287(7)
C22 C	0.1653(3)	0.37819(16)	0.31817(9)	0.0213(6)
C23 C	0.6439(3)	0.03569(17)	0.09276(10)	0.0254(6) .
C24 C	0.7789(3)	0.18524(17)	0.42971(10)	0.0264(7)
C25 C	0.4385(3)	0.07703(19)	0.44829(10)	0.0289(7)
C26 C	0.1245(3)	0.35235(19)	0.11932(10)	0.0276(7)
C27 C	0.0212(3)	0.10089(17)	0.27768(11)	0.0289(7)
C28 C	0.5208(3)	0.2623(2)	0.06044(9)	0.0277(7)
C29 C	-0.0097(3)	0.3092(2)	0.09556(10)	0.0313(7)
C30 C	0.7322(4)	0.0211(2)	0.04273(10)	0.0327(7)
C31 C	0.3495(5)	0.1122(3)	0.49409(11)	0.0521(10)

Bond lengths (Å)

atom	atom	distance
O1	C4	1.432(3)
O1	C14	1.429(3)

O2	C16	1.449(3)
O2	C22	1.341(3)
O3	C4	1.425(3)
O3	C12	1.440(3)
O4	C5	1.449(3)
O4	C28	1.358(3)
O5	C7	1.341(3)
O5	C11	1.441(3)
O6	C6	1.445(3)
O6	C23	1.350(3)
O7	C10	1.454(3)
O7	C26	1.358(3)
O8	C8	1.453(3)
O8	C24	1.360(3)
O9	C15	1.440(3)
O9	C25	1.359(3)
O10	C1	1.455(3)
O10	C18	1.347(3)
O11	C18	1.209(3)
O12	C7	1.201(3)
O13	C22	1.208(3)
O14	C26	1.203(4)
O15	C23	1.193(4)
O16	C25	1.193(4)
O32	C28	1.203(4)

O33	C24	1.204(4)
C1	C8	1.514(3)
C1	C13	1.522(3)
C3	C4	1.516(3)
C3	C6	1.515(4)
C4	C13	1.518(3)
C5	C6	1.529(3)
C5	C12	1.520(3)
C7	C27	1.498(4)
C8	C14	1.527(4)
C10	C12	1.525(3)
C10	C16	1.506(4)
C11	C15	1.514(4)
C14	C15	1.524(3)
C17	C18	1.490(4)
C19	C28	1.485(4)
C20	C24	1.481(4)
C21	C22	1.488(4)
C23	C30	1.501(4)
C25	C31	1.489(5)
C26	C29	1.487(4)

Bond angles (o)

atom	atom	atom	angle

C4	O1	C14	115.07(16)
C16	O2	C22	114.90(17)
C4	O3	C12	115.96(16)
C5	O4	C28	116.14(18)
C7	O5	C11	117.02(17)
C6	O6	C23	118.39(18)
C10	O7	C26	115.15(18)
C8	O8	C24	117.94(18)
C15	O9	C25	116.08(18)
C1	O10	C18	115.46(17)
O10	C1	C8	107.92(17)
O10	C1	C13	111.37(18)
C8	C1	C13	111.12(18)
C4	C3	C6	111.18(19)
O1	C4	O3	110.93(18)
O1	C4	C3	105.64(17)
O1	C4	C13	111.18(18)
O3	C4	C3	111.04(18)
O3	C4	C13	104.51(17)
C3	C4	C13	113.66(19)
O4	C5	C6	106.57(17)
O4	C5	C12	109.97(17)
C6	C5	C12	110.47(18)
O6	C6	C3	105.64(18)

O6	C6	C5	108.96(18)
C3	C6	C5	110.79(18)
O5	C7	O12	124.4(2)
O5	C7	C27	111.16(19)
O12	C7	C27	124.5(3)
O8	C8	C1	107.99(18)
O8	C8	C14	109.78(17)
C1	C8	C14	107.58(18)
O7	C10	C12	106.40(17)
O7	C10	C16	110.33(18)
C12	C10	C16	115.27(19)
O5	C11	C15	107.76(17)
O3	C12	C5	112.12(18)
O3	C12	C10	102.81(16)
C5	C12	C10	112.26(19)
C1	C13	C4	108.99(18)
O1	C14	C8	112.39(18)
O1	C14	C15	105.07(17)
C8	C14	C15	112.48(17)
O9	C15	C11	108.55(18)
O9	C15	C14	105.46(17)
C11	C15	C14	114.10(18)
O2	C16	C10	109.53(17)
O10	C18	O11	123.3(2)
O10	C18	C17	111.6(2)

O11	C18	C17	125.1(2)
O2	C22	O13	122.8(2)
O2	C22	C21	112.2(2)
O13	C22	C21	125.0(3)
O6	C23	O15	124.4(3)
O6	C23	C30	110.2(2)
O15	C23	C30	125.4(3)
O8	C24	O33	123.2(3)
O8	C24	C20	111.3(3)
O33	C24	C20	125.5(3)
O9	C25	O16	123.2(3)
O9	C25	C31	110.3(3)
O16	C25	C31	126.5(3)
O7	C26	O14	122.6(3)
O7	C26	C29	112.1(3)
O14	C26	C29	125.3(3)
O4	C28	O32	123.0(3)
O4	C28	C19	111.4(3)
O32	C28	C19	125.5(3)

Torsion Angles (o)

(Those having bond angles > 160 or < 20 degrees are excluded.)

atom	atom	atom	atom	angle

C4	O1	C14	C8	-55.7(3)
C4	O1	C14	C15	-178.36(15)
C14	O1	C4	O3	-60.9(3)
C14	O1	C4	C3	178.70(15)
C14	O1	C4	C13	54.9(3)
C16	O2	C22	O13	5.4(3)
C16	O2	C22	C21	-174.78(16)
C22	O2	C16	C10	-177.66(17)
C4	O3	C12	C5	-54.1(2)
C4	O3	C12	C10	-174.85(15)
C12	O3	C4	O1	-62.4(3)
C12	O3	C4	C3	54.8(3)
C12	O3	C4	C13	177.73(15)
C5	O4	C28	O32	14.4(4)
C5	O4	C28	C19	-163.62(17)
C28	O4	C5	C6	96.9(2)
C28	O4	C5	C12	-143.34(18)
C7	O5	C11	C15	-149.68(17)
C11	O5	C7	O12	6.4(3)
C11	O5	C7	C27	-172.74(16)
C6	O6	C23	O15	-1.4(4)
C6	O6	C23	C30	177.76(16)
C23	O6	C6	C3	147.81(17)
C23	O6	C6	C5	-93.1(2)
C10	O7	C26	O14	1.8(4)

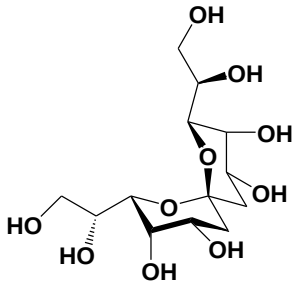
C10	O7	C26	C29	-175.86(16)
C26	O7	C10	C12	-148.27(17)
C26	O7	C10	C16	86.0(2)
C8	O8	C24	O33	2.4(4)
C8	O8	C24	C20	-177.75(16)
C24	O8	C8	C1	130.84(18)
C24	O8	C8	C14	-112.1(2)
C15	O9	C25	O16	-0.7(4)
C15	O9	C25	C31	-179.77(16)
C25	O9	C15	C11	94.3(2)
C25	O9	C15	C14	-143.02(18)
C1	O10	C18	O11	-6.0(3)
C1	O10	C18	C17	173.56(15)
C18	O10	C1	C8	-154.66(16)
C18	O10	C1	C13	83.1(2)
O10	C1	C8	O8	-61.1(2)
O10	C1	C8	C14	-179.55(15)
O10	C1	C13	C4	178.21(14)
C8	C1	C13	C4	57.9(3)
C13	C1	C8	O8	61.3(3)
C13	C1	C8	C14	-57.2(3)
C4	C3	C6	O6	171.87(16)
C4	C3	C6	C5	54.0(3)
C6	C3	C4	O1	66.4(2)
C6	C3	C4	O3	-54.0(3)

C6	C3	C4	C13	-171.46(16)
O1	C4	C13	C1	-54.5(2)
O3	C4	C13	C1	65.23(19)
C3	C4	C13	C1	-173.55(16)
O4	C5	C6	O6	-48.8(2)
O4	C5	C6	C3	67.0(2)
O4	C5	C12	O3	-66.1(2)
O4	C5	C12	C10	49.1(3)
C6	C5	C12	O3	51.3(3)
C6	C5	C12	C10	166.41(16)
C12	C5	C6	O6	-168.20(16)
C12	C5	C6	C3	-52.4(3)
O8	C8	C14	O1	-62.3(2)
O8	C8	C14	C15	56.0(3)
C1	C8	C14	O1	54.9(3)
C1	C8	C14	C15	173.30(16)
O7	C10	C12	O3	-174.05(15)
O7	C10	C12	C5	65.3(2)
O7	C10	C16	O2	76.1(2)
C12	C10	C16	O2	-44.4(3)
C16	C10	C12	O3	-51.4(3)
C16	C10	C12	C5	-172.09(16)
O5	C11	C15	O9	63.6(2)
O5	C11	C15	C14	-53.7(3)
O1	C14	C15	O9	-176.06(15)

O1	C14	C15	C11	-57.0(2)
C8	C14	C15	O9	61.4(3)
C8	C14	C15	C11	-179.61(16)

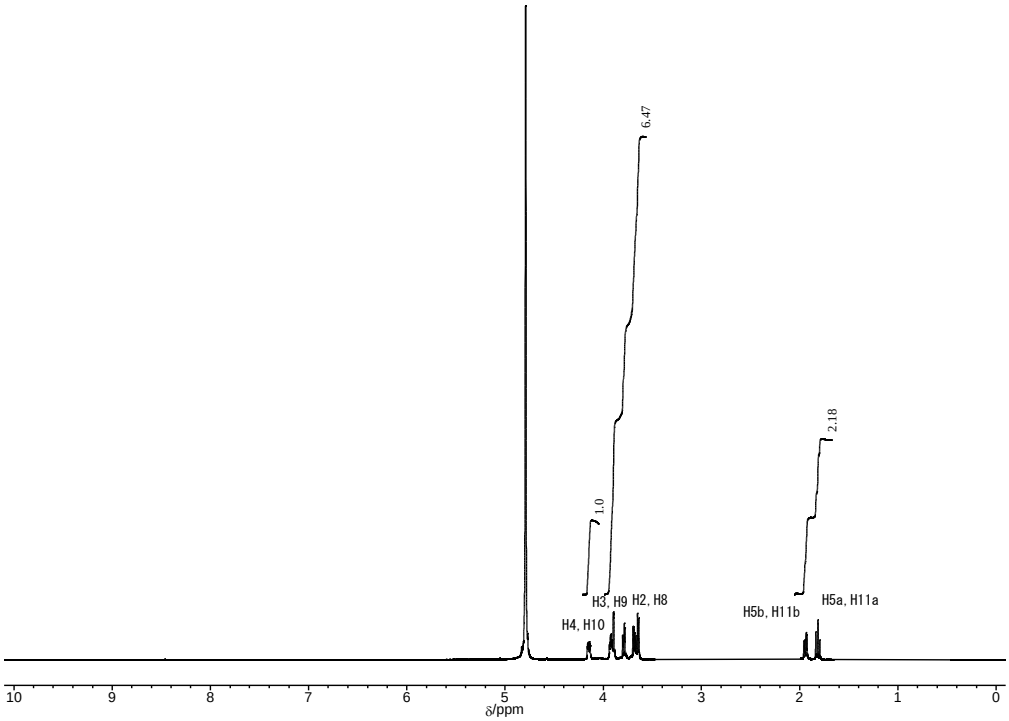
(*3R,4S,6S,9R,10S*)-2,8-Di[(*1R*)-1,2-dihydrocyethyl]-1,7-dioxaspiro[5,5]-undecan-3,4,9,10-tetrol

118

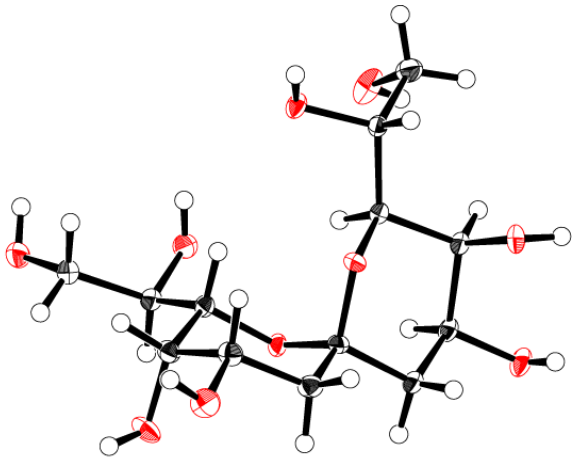


To a stirred solution of **102** (101 mg, 0.195 mmole) in methanol was added 50 % trifluoroacetic acid (2.0 ml) at 0 °C, and the solution was stirred at room temperature for 24 h. Azeotropic concentration of the reaction mixture with toluene gave crude [5,5]spiroketal-octol as a hygroscopic solid. Recrystallization from methanol afforded pure **118** as colorless crystals; yield 62.5 mg (94.3%), $[\alpha]_D^{26}$ -44.3° (*c* 1.0, chloroform); mp 218.2-218.6 °C; ^{1}H NMR (D_2O, 600 MHz), δ 1.79 (t, 2H, $J_{5a,5b} = J_{11a,\ 11b}$ = 12.5 Hz, H5a, H11a), 1.92 (dd, 2H, $J_{4,5b} = J_{10,11b}$ = 5.1 Hz, $J_{5a,5b} = J_{11a,11b}$ = 12.5 Hz, H5b, H11b), 3.62 (d, 2H, $J_{1',2} = J_{2',8}$ = 6.3 Hz, $J_{1''a,1''b} = J_{2''a,2''b}$ = 12.0 Hz, H1''a, H2''a), 3.77 (dd, 2H, $J_{1',1''b} = J_{2',2''b}$ = 3.0 Hz, $J_{1''a,1''b} = J_{2''a,2''b}$ = 12.0 Hz, H1''b, H2''b), 3.88 (d, 2H, $J_{3,4} = J_{8,9}$ = 2.6 Hz, H3, H9), 3.91 (dt, $J_{1',2} = J_{2',8}$ = 7.4 Hz, $J_{1',1''a} = J_{2',2''a}$ = 6.3 Hz, $J_{1',1''b} = J_{2',2''b}$ = 3.0 Hz, H1', H2'), 4.13 (ddd, 2H, $J_{3,4} = J_{8,9}$ = 2.6 Hz, $J_{4,5a} = J_{10,11a}$ = 7.4 Hz, $J_{4,5b} = J_{10,11b}$ = 5.1 Hz, H4, H10); ^{13}C NMR (D_2O, 150MHz) δ 38.9 (C5, C11), 64.5 (C1'', C2''), 68.1 (C4, C10), 70.3 (C3, C9), 74.4 (C2, C8), 74.5 (C1', C2'), 101.5 (C6); ESI-TOFMS *m*/*z*: calcd for $[C_{29}H_{40}O_{18}+Na]^+$, 699.2107; found, 699.2108.

^{1}H NMR spectrum



Crystal structure of (*3R*,*4S*,*6S*,*9R*,*10S*)-2,8-Di[(*1R*)-1,2-dihydrocyethyl]-1,7-dioxaspiro[5,5]-undecan-3,4,9,10-tetrol **118**



Empirical Formula $C_{13}H_{24}O_{10}$

Formula Weight 340.33

Crystal Color, Habit colorless, block

Crystal Dimensions 0.200 X 0.150 X 0.100 mm

Crystal System tetragonal

Lattice Type Primitive

Lattice Parameters *a* = 7.586(16) Å

b = 7.586(16) Å

c = 25.354(6) Å

V = 1458.9(6) Å3

Space Group $P2_12_12_1$ (#19)

Z value 4

*D*calc 1.549 g/cm3

R-factor 3.71%

Temperature 123 K

ω oscillation Range (c=45.0, f=180.0) 0.0 - 160.0o

No. of Reflections Measured Total: 4261

Atomic coordinates and Biso/Beq and occupancy

atom	x	y	z	Beq
O1 O	1.12495(16)	0.62361(16)	0.40770(4)	0.0185(3)
O2 O	1.17227(16)	0.61986(16)	0.64176(4)	0.0197(3)

O3 O	0.90365(15)	0.54354(14)	0.49578(4)	0.0140(3)
O4 O	0.65501(16)	0.32990(15)	0.44051(5)	0.0213(3)
O5 O	0.80650(14)	0.80726(13)	0.53299(4)	0.0128(3)
O6 O	1.00684(18)	0.50888(16)	0.30857(5)	0.0225(3)
O7 O	0.96195(15)	0.93782(15)	0.62353(4)	0.0171(3)
O8 O	0.89342(15)	1.07351(15)	0.46080(4)	0.0163(3)
O9 O	0.36243(16)	0.51308(18)	0.48585(5)	0.0242(3)
O10 O	1.26627(17)	1.0674(2)	0.48573(5)	0.0265(4)
C1 C	0.8324(2)	0.5907(2)	0.44507(6)	0.0142(4)
C2 C	0.8841(3)	0.5447(2)	0.34929(6)	0.0182(4)
C3 C	0.8084(2)	0.61873(19)	0.53865(6)	0.0140(3)
C4 C	0.9647(2)	0.5270(2)	0.40391(6)	0.0148(4)
C5 C	0.98097(19)	0.88274(19)	0.53077(6)	0.0119(3)
C6 C	0.9622(2)	1.07381(19)	0.51342(6)	0.0130(3)
C7 C	1.0866(2)	0.6569(2)	0.59311(6)	0.0142(4)
C8 C	0.5324(2)	0.5911(2)	0.48447(6)	0.0169(4)
C9 C	1.0695(2)	0.8554(2)	0.58408(5)	0.0131(3)
C10 C	1.1376(3)	1.1686(3)	0.51451(6)	0.0197(4)
C11 C	0.9061(2)	0.5673(2)	0.58929(6)	0.0150(4)
C13 C	0.6460(2)	0.5171(2)	0.43972(6)	0.0158(4)
C16 C	0.6178(2)	0.5592(2)	0.53787(6)	0.0171(4)

Bond lengths (Å)

atom	atom	distance

O1	C4	1.423(2)
O2	C7	1.4223(19)
O3	C1	1.4398(19)
O3	C3	1.4243(19)
O4	C13	1.422(2)
O5	C3	1.4373(18)
O5	C5	1.4431(18)
O6	C2	1.417(2)
O7	C9	1.4339(18)
O8	C6	1.4325(19)
O9	C8	1.419(2)
O10	C10	1.441(3)
C1	C4	1.526(3)
C1	C13	1.526(3)
C2	C4	1.520(3)
C3	C11	1.533(3)
C3	C16	1.515(3)
C5	C6	1.521(2)
C5	C9	1.523(2)
C6	C10	1.512(3)
C7	C9	1.529(3)
C7	C11	1.532(3)
C8	C13	1.532(3)
C8	C16	1.521(3)

Bond angles (o)

atom	atom	atom	angle
C1	O3	C3	113.06(12)
C3	O5	C5	112.91(11)
O3	C1	C4	106.58(12)
O3	C1	C13	109.65(12)
C4	C1	C13	115.64(13)
O6	C2	C4	112.50(14)
O3	C3	O5	109.11(12)
O3	C3	C11	106.99(12)
O3	C3	C16	110.77(12)
O5	C3	C11	109.99(12)
O5	C3	C16	106.60(12)
C11	C3	C16	113.34(13)
O1	C4	C1	110.65(13)
O1	C4	C2	111.09(13)
C1	C4	C2	109.31(13)
O5	C5	C6	107.67(12)
O5	C5	C9	108.39(12)
C6	C5	C9	115.30(13)
O8	C6	C5	107.57(12)
O8	C6	C10	109.76(12)
C5	C6	C10	111.43(13)

O2	C7	C9	111.31(12)
O2	C7	C11	112.06(13)
C9	C7	C11	110.60(13)
O9	C8	C13	112.15(13)
O9	C8	C16	107.40(13)
C13	C8	C16	111.18(13)
O7	C9	C5	108.00(12)
O7	C9	C7	111.91(12)
C5	C9	C7	107.72(12)
O10	C10	C6	109.47(13)
C3	C11	C7	111.83(13)
O4	C13	C1	108.64(13)
O4	C13	C8	112.48(13)
C1	C13	C8	108.78(13)
C3	C16	C8	111.78(13)

Torsion Angles (o)

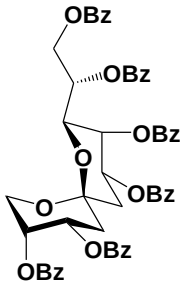
(Those having bond angles > 160 or < 20 degrees are excluded.)

atom	atom	atom	atom	angle
C1	O3	C3	O5	-57.40(15)
C1	O3	C3	C11	-176.36(10)
C1	O3	C3	C16	59.65(14)
C3	O3	C1	C4	170.71(10)

C3	O3	C1	C13	-63.45(14)
C3	O5	C5	C6	168.34(10)
C3	O5	C5	C9	-66.31(13)
C5	O5	C3	O3	-57.82(14)
C5	O5	C3	C11	59.25(14)
C5	O5	C3	C16	-177.49(10)
O3	C1	C4	O1	-66.78(14)
O3	C1	C4	C2	170.58(10)
O3	C1	C13	O4	-64.36(15)
O3	C1	C13	C8	58.38(14)
C4	C1	C13	O4	56.12(16)
C4	C1	C13	C8	178.86(11)
C13	C1	C4	O1	171.08(12)
C13	C1	C4	C2	48.44(16)
O6	C2	C4	O1	50.25(17)
O6	C2	C4	C1	172.63(11)
O3	C3	C11	C7	67.76(14)
O3	C3	C16	C8	-52.28(15)
O5	C3	C11	C7	-50.62(15)
O5	C3	C16	C8	66.30(14)
C11	C3	C16	C8	-172.55(11)
C16	C3	C11	C7	-169.84(11)
O5	C5	C6	O8	-64.58(14)
O5	C5	C6	C10	175.07(10)
O5	C5	C9	O7	-58.36(14)

O5	C5	C9	C7	62.69(13)
C6	C5	C9	O7	62.37(15)
C6	C5	C9	C7	-176.59(11)
C9	C5	C6	O8	174.30(11)
C9	C5	C6	C10	53.95(16)
O8	C6	C10	O10	-67.58(15)
C5	C6	C10	O10	51.47(16)
O2	C7	C9	O7	-62.84(16)
O2	C7	C9	C5	178.59(11)
O2	C7	C11	C3	175.72(11)
C9	C7	C11	C3	50.89(15)
C11	C7	C9	O7	62.42(15)
C11	C7	C9	C5	-56.15(15)
O9	C8	C13	O4	-52.79(16)
O9	C8	C13	C1	-173.18(11)
O9	C8	C16	C3	173.38(11)
C13	C8	C16	C3	50.35(16)
C16	C8	C13	O4	67.48(16)
C16	C8	C13	C1	-52.92(16)

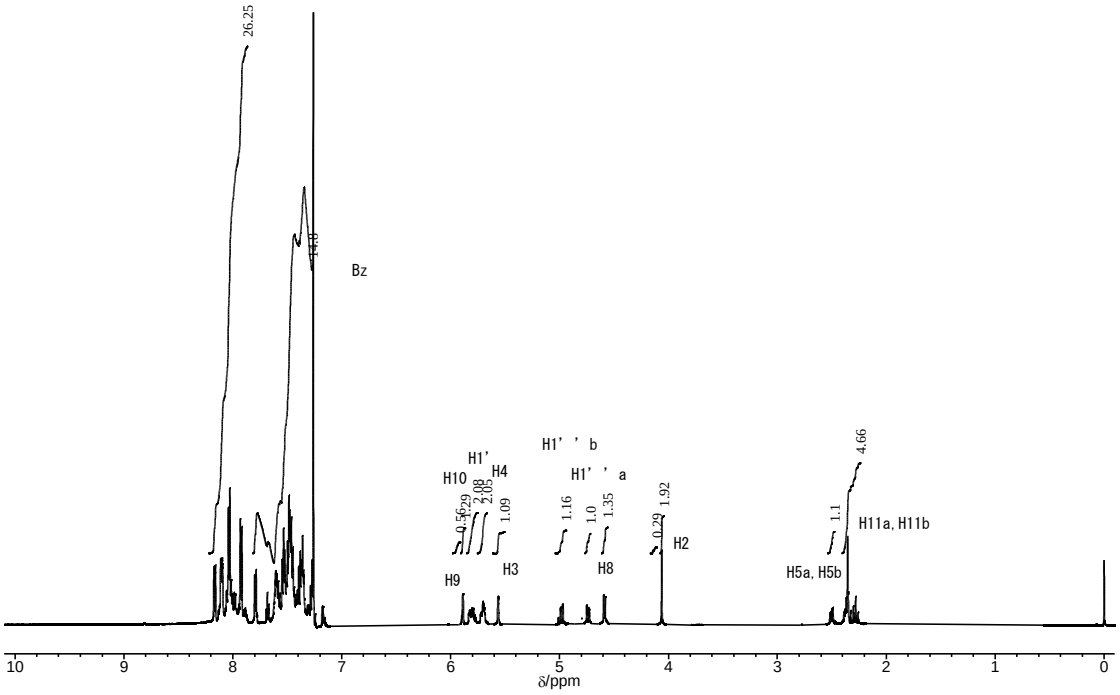
Spiroacetal **119**



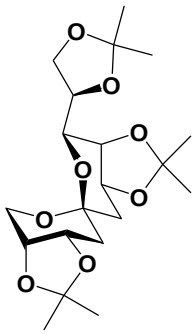
To a stirred solution of **110** (31.1 mg, 0.0743 mmole) in methanol (600 µl) was added 50 % trifluoroacetic acid (2.0 ml) at 0 °C, and the solution was stirred at room temperature for 24 h. Azeotropic concentration of the reaction mixture with toluene gave crude [5,5]spiroketal-octol as a hygroscopic solid. The compound was immediately benzylated with benzoyl chloride (0.25 ml) in pyridine (0.5 ml) at room temperature. After stirring for 24 h, the reaction mixture was quenched with ice-water (2.5 ml) and extracted with dichloromethane (2.5 ml). The combined organic extract was washed successively with 5% aq $NaHSO_4$, saturated aq $NaHCO_3$, water, brine, and dried ($NaHSO_4$). The organic solution was concentrated to a syrup that was purified by silica gel column chromatography (chloroform-acetone, 10 : 1) to give **119** as a colorless syrup.; yield 29.3 mg, $[\alpha]_D^{26}$ -200° (*c* 0.5, chloroform); ^{1}H NMR ($CDCl_3$, 600 MHz), δ 2.28 (t, 1H, $J_{10,11a}$ = 12.3 Hz, H11a), 2.34 (d, 1H, $J_{4,5a}$ = 12.6 Hz, H5a), 2.37 (dd, 1H, $J_{10,11b}$ = 5.1 Hz, $J_{11a,11b}$ = 12.3 Hz, H11b), 2.50 (dd, 1H, $J_{4,5b}$ = 4.8 Hz, $J_{5a,5b}$ = 12.6 Hz, H5b), 4.06 (s, 2H, H2), 4.59 (d, 1H, $J_{8,9}$ = 10.0 Hz, H8), 4.74 (dd, 1H, $J_{1',1''a}$ = 3.7 Hz, $J_{1''a,1''b}$ = 12.3 Hz, H1''a), 4.98 (dd, 1H, $J_{1',1''b}$ = 2.2 Hz, $J_{1''a,1''b}$ = 12.3 Hz, H1''b), 5.17 (s, 1H, H3), 5.60 – 5.83 (m, 3H, H1', H4, H10), 5.57 (s, 1H, H9), 7.16 – 8.17 (m, 30H, Bz); ^{13}C NMR ($CDCl_3$, 150MHz) δ 35.4 (C5), 35.5 (C11), 62.3 (C2), 62.6 (C1''), 65.6 (C9), 66.8 (C4), 67.3 (C3), 67.6 (C10), 68.6 (C1'), 99.7 (C6), 128.1 (Bz), 128.1 (Bz), 128.2 (Bz), 128.2 (Bz), 128.3 (Bz), 128.3 (Bz), 128.4 (Bz), 128.4 (Bz), 128.5 (Bz), 128.5 (Bz), 128.5

(Bz), 128.6 (Bz), 129.3 (Bz), 129.4 (Bz), 129.4 (Bz), 129.5 (Bz), 129.6 (Bz), 129.6 (Bz), 129.6 (Bz), 129.6 (Bz), 129.7 (Bz), 129.7 (Bz), 129.7 (Bz), 129.8 (Bz), 133.1 (Bz), 133.2 (Bz), 133.2 (Bz), 133.2 (Bz), 133.3 (Bz), 133.3 (Bz), 133.4 (Bz), 165.0 (Bz), 165.3 (Bz), 165.4 (Bz), 165.5 (Bz), 165.7 (Bz), 166.0 (Bz); ESI-TOFMS *m*/*z*: calcd for $[C_{53}H_{44}O_{14}+Na]^+$, 927.2623; found, 927.2608.

^{1}H NMR spectrum



Spiroacetal **120**

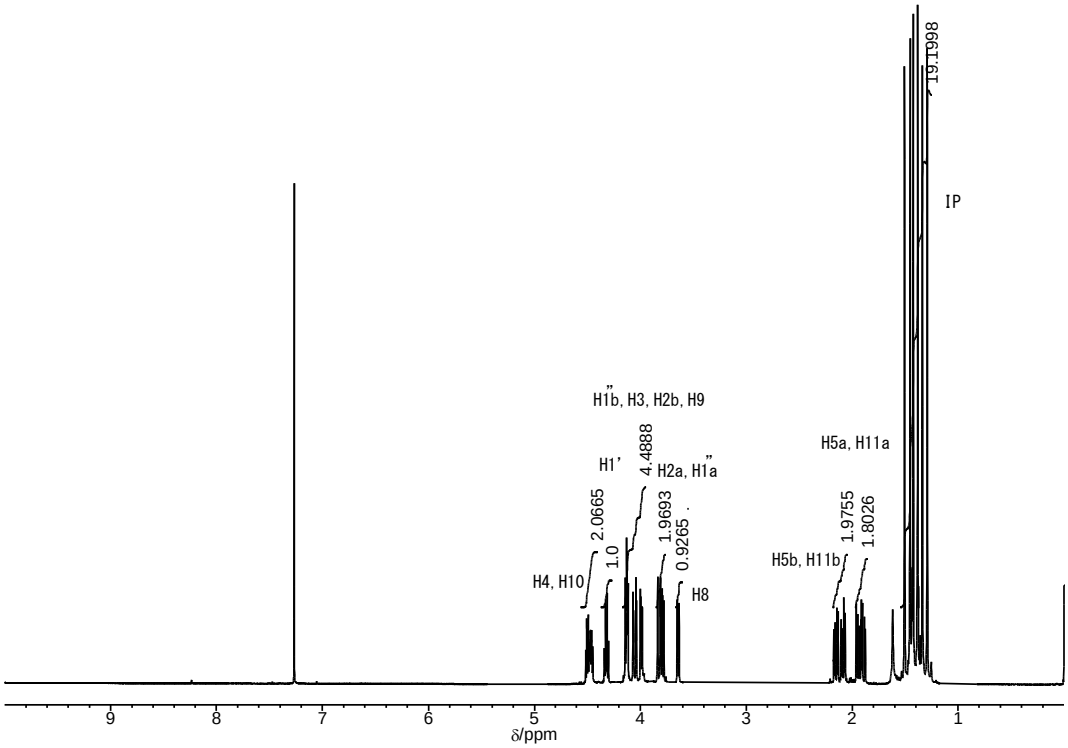


120

To a stirred solution of **112** (80.6 mg, 0.193 mmole) in methanol (900 μl) was added 50 % trifluoroacetic acid (4.0 ml) at 0 °C, and the solution was stirred at room temperature for 24 h. Azeotropic concentration of the reaction mixture with toluene gave crude [5,5]spiroketal-octol as a hygroscopic solid. The compound was immediately treated with 2,2-dimethoxypropane (410 μl) and *p*-toluenesulfonic acid in DMF (820 μl) at 50 ˚C. After stirring for 24 h, the reaction mixture was quenched with ice-water (5.0 ml) and extracted with dichloromethane (5.0 ml). The combined organic extract was washed successively with saturated aq $NaHCO_3$, water, brine, and dried ($NaHSO_4$). The organic solution was concentrated to a syrup that was purified by silica gel column chromatography (chloroform-acetone, 20 : 1) to give **120** as a colorless syrup.; yield 35.6 mg (46%), $[\alpha]_D^{22}$ -52.0° (*c* 0.5, chloroform); ^{1}H NMR ($CDCl_3$, 600 MHz), δ 1.29 (s, 3H, IP), 1.34 (s, 3H, IP), 1.37 (s, 3H, IP), 1.42 (s, 3H, IP), 1.45 (s, 3H, IP), 1.51 (s, 3H, IP), 1.89 (dd, 1H, $J_{10,11a}$ = 4.6 Hz, $J_{11a,11b}$ = 14.7 Hz,H11a), 1.94 (dd, 1H, $J_{4,5a}$ = 7.3 Hz, $J_{5a,5b}$ = 14.2 Hz, H5a), 2.85 (dd, 1H, $J_{10,11b}$ = 5.5 Hz, $J_{11a,11b}$ = 14.7 Hz, H11b), 2.15 (dd, 1H, $J_{4,5b}$ = 5.5 Hz, $J_{5a,5b}$ = 14.2 Hz, H5b), 3.59 (dd, 1H, $J_{1',8}$ = 8.7 Hz, $J_{8,9}$ = 2.3 Hz, H8), 3.79 (dd, 1H, $J_{1',1''a}$ = 6.4 Hz, $J_{1''a.1''b}$ = 8.7 Hz, H1''a), 3.82 (dd, 1H, $J_{2a,3}$ = 0.9 Hz, $J_{2a,2b}$ = 13.3 Hz, H2a), 3.99 (dd, 1H, $J_{8,9}$ = 2.3 Hz, $J_{9,10}$ = 6.9 Hz, H9), 4.05 (dd, 1H, $J_{2b,3}$ = 2.3 Hz, $J_{2a,2b}$ = 13.3 Hz, H2b), 4.12 (ddd, 1H, $J_{2a,3}$ = 0.9 Hz, $J_{2b,3}$ = 2.3 Hz, $J_{3,4}$

= 5.5 Hz, H3), 4.13 (dd, 1H, $J_{1',1''b}$ = 6.4 Hz, $J_{1''a.1''b}$ = 8.7 Hz, H1''b), 4.32 (dt, 1H, $J_{8,1'}$ = 8.7 Hz, $J_{1'.1''}$ = 6.4 Hz, H1'), 4.46 (ddd, 1H, $J_{9,10}$ = 6.9 Hz, $J_{10,11a}$ = 4.6 Hz, $J_{10,11b}$ = 5.5 Hz, H10), 4.49 (dt, 1H, $J_{3,4}$ = 5.5 Hz, $J_{4,5a}$ = 7.3 Hz, $J_{4,5b}$ = 5.5 Hz, H4); ^{13}C NMR ($CDCl_3$, 150MHz) δ 25.8 (IP), 25.8 (IP), 26.0 (IP), 27.1 (IP), 27.8 (IP), 36.6 (C11), 38.4 (C5), 60.7 (C2), 65.8 (C1"), 70.1 (C4), 71.2 (C10), 71.6 (C8), 71.8 (C3), 72.3 (C9), 75.9 (C1'), 97.7 (C6), 108.6 (IP), 109.5 (IP), 109.6 (IP); ESI-TOFMS *m*/*z*: calcd for $[C_{53}H_{44}O_{14}+Na]^+$, 423.1989; found, 423.1977.

^{1}H NMR spectrum



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