described above. Kugelrohr distillation (75 °C/30 mm) afforded propanoyl iodide[6a,7] (165 mg, 88%) in the form of a slightly yellowish liquid. NMR: δ 3.11 (q, J = 7.4, 2 H), 1.13 (t, J = 7.4, 3 H).

Palmitoyl Iodide from Palmitoyl Chloride. DIS (330 mg, 1.16 mmol) was added to a solution of palmitoyl chloride (290 mg, 1.06 mmol) in $CHCl_3$ (5 mL). The mixture was stirred at 50 °C for 2 h and then worked up as described above. Kugelrohr distillation (200 °C/1 mm) afforded palmitoyl iodide[10] (338.5 mg, 87.5%) in the form of a colorless oil. NMR: δ 3.05 (t, J = 6.6, 2 H), 1.64 (quintet, J = 6.7, 2 H), 1.25 (br s, 24 H), 0.88 (t, J = 6.5, 3 H). IR: 1800 (br, s). Anal. Calcd for $C_{16}H_{31}IO$: C, 52.46; H, 8.53; I, 34.64. Found: C, 52.81; H, 8.99; I, 34.10.

Methyl Butyrate from Butyric Acid. A reaction similar to the one described above was carried out with butyric acid, DIS, and iodine. After 45 min at 50 °C excess of methanol was added. The NMR spectrum taken after 1 h at room temperature showed quantitative conversion to methyl butyrate.

***tert*-Butyl Heptanoate from Isopropyl Heptanoate.** DIS (305 mg, 1.07 mmol) and iodine (135 mg, 1.06 mmol) were added to a stirred solution of isopropyl heptanoate (180.5 mg, 1.05 mmol) in CH_2Cl_2 (3 mL). The mixture was stirred at 50 °C for 1 h and then cooled to room temperature. Pyridine (200 mg, 2.5 mmol) and then *tert*-butyl alcohol (100 mg, 1.35 mmol) were added, and the mixture was stirred for 1 h at room temperature and then worked up with ether and water. The organic layer was washed with water and dried over sodium sulfate, and the solvent was removed under reduced pressure. Kugelrohr distillation of the residue (150 °C/30 mm) afforded *tert*-butyl heptanoate (180 mg, 92%) in the form of a colorless oil. NMR: δ 2.20 (t, J = 7.6, 2 H), 1.56 (m, 2 H), 1.44 (s, 9 H), 1.30 (m, 6 H), 0.88 (t, J = 6.8, 3 H).

NMR Data. Iodosilyl Propanoate, III (R = Et, SiQ_3 = $SiIH_2$). NMR: δ 2.43 (q, J = 7.4, 2 H), 1.13 (t, J = 7.4, 3 H).

Iodosilyl 4-Iodobutyrate, VIa (SiQ_3 = $SiIH_2$). NMR: δ 4.2 (br s, 2 H), 3.25 (t, J = 6.7, 2 H), 2.60 (t, J = 7.2, 2 H), 2.44 (br quintet, J = 7, 2 H).

Trimethylsilyl 4-Iodobutyrate,[14a] VIa (SiQ_3 = $SiMe_3$). NMR: δ 3.23 (t, J = 6.7, 2 H), 2.55 (t, J = 7.2, 2 H), 2.13 (br quintet, J = 7, 2 H), 0.26 (s, 9 H).

Iodosilyl 4-Iodovalerate, VIb (SiQ_3 = $SiIH_2$). NMR: δ 4.2 (br s, 2 H), 4.23 (m, 1 H), 2.62 (m, 2 H), 1.98 (m, 2 H), 1.95 (d, J = 6.8, 3 H).

Trimethylsilyl 4-Iodovalerate, VIb (SiQ_3 = $SiMe_3$). NMR: δ 4.20 (m, 1 H), 2.59 (m, 2 H), 1.98 (m, 2 H), 1.93 (d, J = 6.9, 3 H), 0.26 (s, 9 H).

4-Iodovaleryl Iodide, VIIb. NMR: δ 4.16 (m, 1 H), 3.3 (m, 2 H), 1.98 (m, 2 H), 1.93 (d, J = 6.8, 3 H).

Aldolase-Catalyzed C–C Bond Formation for Stereoselective Synthesis of Nitrogen-Containing Carbohydrates[1]

Alexander Straub,[2] Franz Effenberger,* and Peter Fischer[†]

Institut für Organische Chemie, Universität Stuttgart, Pfaffenwaldring 55, D-7000 Stuttgart 80, FRG

Received October 26, 1989

Rabbit muscle aldolase was found to catalyze stereoselective aldol addition of dihydroxyacetone phosphate (**1**) to 3-azido-2-hydroxypropanal (**2**). The ketose 1-phosphates were isolated as barium salts, **4a**/**4b**, and hydrolyzed with acid phosphatase. The mixture of 6-azido-6-deoxy-D-fructose (**5**) and 6-azido-6-deoxy-L-sorbose (**6**) thus obtained was separated by anion-exchange chromatography. Reductive amination of **5** and **6** yielded, respectively, 1-deoxymannojirimycin (**7**) and 1-deoxynojirimycin (**8**), with high diastereoselectivity (>98:2). Analogous aldol addition of **1** to 3-azido-2-hydroxybutanal (**9**) (*E*:*Z* = 92:8) afforded a mixture of the 6-azido-6,7-dideoxyheptuloses **12** and **13**, which contained 88% of 6-azido-6,7-dideoxy-D-*altro*-heptulose (**13**). After anion-exchange chromatography, **13** was isolated as a 18:82 mixture of the β/α anomers. Reductive amination of pure **13** gave a mixture of 2,6,7-trideoxy-2,6-imino-D-*glycero*-D-*manno*- and -D-*gluco*-heptitols (**14** and **15**) (3:2 molar ratio), which likewise was separated by anion-exchange chromatography. If a mixture of **12** and **13** was hydrogenated under identical conditions, 2,6,7-trideoxy-2,6-imino-L-*glycero*-L-*gulo*-heptitol (**16**) could be isolated besides **14** and **15**.

Introduction

The use of rabbit muscle aldolase (EC 4.1.2.13; RAMA) in stereoselective syntheses has been reviewed by Whitesides et al.[3] and Wong et al.[4] Systematic investigations of C–C coupling reactions showed that this enzyme permits virtually no structural variation of the *C*-nucleophile, dihydroxyacetone phosphate (DHAP). The natural substrate D-glyceraldehyde 3-phosphate, on the other hand, may be substituted by various other aldehydes as *C*-electrophiles.[3,5] A broad field thus is opened up for applying this *enzymatic* reaction, particularly for the stereoselective synthesis of polyhydroxycarbonyl compounds. However, many *chemical* aldol additions have been reported in the last few years which likewise proceed with very high stereoselectivity.[6]

In our investigations on the use of enzyme-active compounds, a major objective has been the optimum combination of chemical *and* enzymatic steps. DHAP generally is obtained from D-fructose 1,6-diphosphate (FDP) by enzymatic cleavage with RAMA, and subsequent enzymatic isomerization with triose phosphate isomerase (EC 5.3.1.1; TIM).[3,4] We have developed a chemical synthesis

[†] NMR and MS spectroscopic analyses.

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for 2,5-bis[(phosphonooxy)methyl]-2,5-diethoxy-1,4-dioxane dibarium salt, which may conventiently be up-graded to the scale of several hundred grams. DHAP is liberated from this stable storage form in high purity by simple treatment with an acid ion exchange resin.[5] A favorable starting point thus is given for preparative exploitation of RAMA-catalyzed C–C coupling reactions.[5]

Pyranoses and furanoses in which the ring oxygen atom has been replaced by an imino group[7] have been isolated from numerous natural substances with an interesting spectrum of biological activities. 1-Deoxymannojirimycin (7), for instance, inhibits α-mannosidase and α-fucosidase.[8] 1-Deoxynojirimycin (8) inhibits α- and β-glucosidases as well as β-xylosidase and has found use in the therapy of diabetes mellitus, hyperlipoproteinemia, cancer, and arthritis, in caries prophylaxis, and as a herbicide, fungicide, or bactericide.[8,9] Recent investigations have shown its *N*-butyl derivative to be highly active against HIV in cultured cells.[10] Consequently, many research groups have become interested in the preparation of polyhydroxypiperidines and -pyrrolidines,[7,9,11,12] starting as a rule from carbohydrates which already incorporate the requisite chirality centers. However, this frequently necessitates multistage reaction sequences since protecting-group techniques have to be used extensively in this approach.

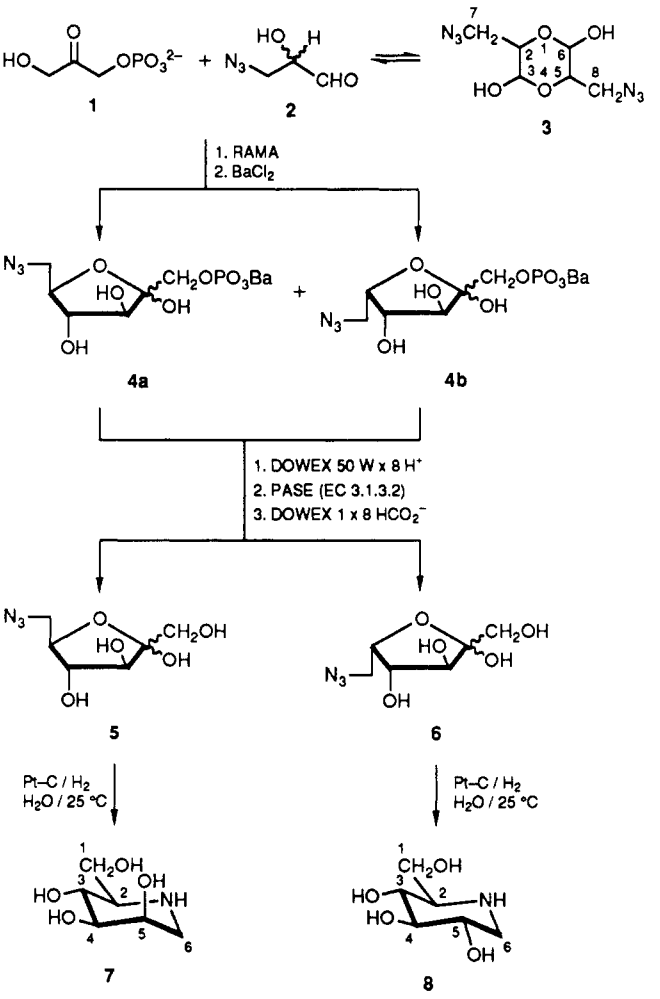
We have recently shown that, by combining enzymatic and chemical steps, 1-deoxymannojirimycin (7) and 1-deoxynojirimycin (8) are readily accessible from achiral precursors.[1] Almost simultaneously, and independently from our work, Wong et al. reported the same synthetic route;[4b,c] they obtained a mixture of 7 and 8 and determined the percentage composition by NMR spectroscopy without isolating the individual compounds.[4c]

In the present paper, we describe the preparation of the 3,4,5-trihydroxy-2-(hydroxymethyl)piperidines **7** (1-deoxymannojirimycin) and **8** (1-deoxynojirimycin), as well as of some 2,6,7-trideoxy-2,6-iminoheptitols, i.e. 2,6,7-trideoxy-2,6-imino-D-*glycero*-D-*manno*- and D-*gluco*-heptitols (**14** and **15**) and 2,6,7-trideoxy-2,6-imino-L-*glycero*-L-*gulo*-heptitol (**16**), all as pure compounds and on a preparatively useful scale.

Synthesis of 1-Deoxymannojirimycin (7) and 1-Deoxynojirimycin (8)

Compounds **7** and **8**, each containing four centers of asymmetry, were prepared from DHAP (**1**) and 3-azido-2-hydroxypropanal (**2**) via the reaction steps outlined in Scheme I.

Scheme I



The preparation of the aldehyde **2** has been described previously;[4b] only the diethyl acetal was characterized, however. We have now found that **2**, which in aqueous solution exists as the hydrate, slowly crystallizes from aqueous solutions as the dimer **3**. Despite its bis(hemiacetal) structure, the 1,4-dioxane **3** represents a stable storage form for the aldehyde **2**. For the RAMA-catalyzed syntheses of compounds **7** and **8**, though, only freshly prepared aqueous solutions of **2** and DHAP (**1**) were allowed to react (1:1 molar ratio; 12 h; 25 °C; pH 6.5). The enzymatically determined turnover under these conditions was almost quantitative (>99%), with 8.6 units aldolase consumed for formation of 1 mmol of **4**.

The resulting diastereoisomeric 6-azido-6-deoxy-D-fructose and -L-sorbose 1-phosphates were precipitated as a mixture of the barium salts, **4a**/**4b**, in 70% crude yield. Subsequent hydrolysis of the phosphate esters with acid phosphatase (EC 3.1.3.2; PASE) under mild conditions afforded a mixture of the corresponding 6-azido-6-deoxyhexuloses (**5**, **6**) which were purified and separated by chromatography on DOWEX 1×8, HCO_2^-. The combined yield of **5**/**6** was ca. 80%. Capillary GC analyses of the tetrakis(trimethylsilyl) derivatives demonstrated the purity of the products and established the percentage composition of the anomeric mixtures as α-**5**/β-**5** = 28:72 and α-**6**/β-**6** = 87:13.

Catalytic hydrogenation of 6-azido-6-deoxyfuranuloses is known to give initially the corresponding 6-amino-6-deoxyfuranuloses which, in turn, undergo ring opening and

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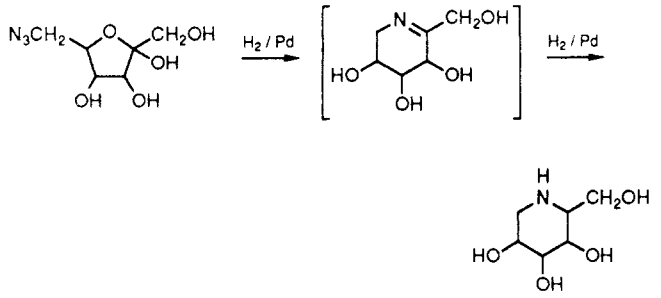
subsequent reclosure to pyranose hemiaminals. By elimination of water, Schiff bases are formed and hydrogenated to the corresponding amines under the hydrogenolytic reaction conditions.[7c] The stereochemistry of this ultimate



hydrogenation step is controlled by the configuration of the optically active centers in the molecule.

Although the reduction of 6-azido-6-deoxy-D-fructose (**5**) is mentioned in the literature, no detailed reaction conditions are given, and neither substrate nor product are characterized unequivocally.[12e] Catalytic hydrogenation of 6-azido-6-deoxy-L-sorbose (**6**) in basic medium with platinum according to Adams, on the other hand, has been reported to proceed with high optical induction.[5c] We have now hydrogenated the 6-azido-6-deoxyhexuloses **5** and **6** with a Pt/C catalyst in aqueous medium at ambient temperature, and from this reaction isolated **7** and **8** as the respective hydrochlorides. The diastereomeric purity of both products was once more established as >98:2 by capillary GC analysis of the tetrakis(trimethylsilyl) derivatives.

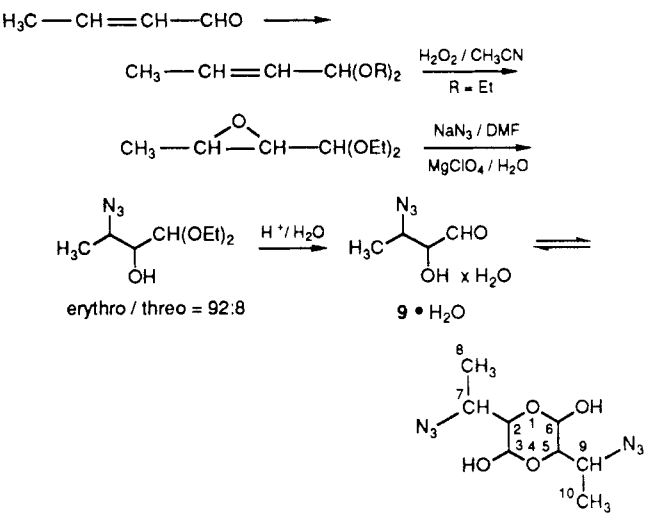
Synthesis of 2,6,7-Trideoxy-2,6-heptitols 14–16

The "chiral pool" offers no heptoses as starting materials for the synthesis of 2,6,7-trideoxy-2,6-iminoheptitols which hitherto were prepared, therefore, from the corresponding hexoses by either Grignard[13] or Wittig[14] reactions. α-Homonojirimycin (2,6-dideoxy-2,6-imino-D-*glycero*-L-*gulo*-heptitol) was isolated as the first naturally occurring heptulose-derived piperidino derivative from *Omphalea diandra* L.[15]

A major advantage of the enzymatic C–C coupling described here is the wide variation possible for the aldehyde component. This very flexibility makes it attractive for the synthesis of compounds for which no appropriate, naturally occurring chiral starting compounds are available. We have therefore applied the synthetic route, described above for the piperidinoses **7** and **8**, to a RAMA-catalyzed synthesis of the 2,6,7-trideoxy-2,6-iminoheptitols **14–16** by using 3-azido-2-hydroxybutanal (**9**) as starting material.

This aldehyde is accessible from crotonaldehyde diethyl acetal[16] via epoxidation[17] and subsequent ring opening with sodium azide, in analogy to the preparation of 3-azido-2-hydroxypropanal (**2**). Crotonaldehyde acetals are not formed as pure *E* isomers, however; even after distillation, 8% and 18% of the *Z* isomer was present in the diethyl and ethylene acetals, respectively (see the Experimental Section). Since this stereochemistry is preserved upon epoxidation, and since the epoxide ring is opened regioselectively with azide, a mixture of *erythro*- and *threo*-3-azido-2-hydroxybutyraldehyde diethyl acetal was obtained (92:8 as determined by capillary GC of the 2-*O*-(trimethylsilyl) derivatives). Acid cleavage of the acetal leaves the stereochemistry at C-2 and C-3 intact. Thus, **9** is formed as the identical 92:8 mixture of diastereoisomers. The aldehyde **9**, like its homologue **2**, exists as the hydrate in aqueous solution; upon prolonged standing at 5 °C, a crystalline precipitate of the dimer **10** is formed (Scheme II). The carbohydrates, formed in the ensuing steps from the small amount of threo component (8%), are easily removed by chromatography.

Scheme II



R	*E*:*Z*
Et	92:8
—CH_2—	82:18

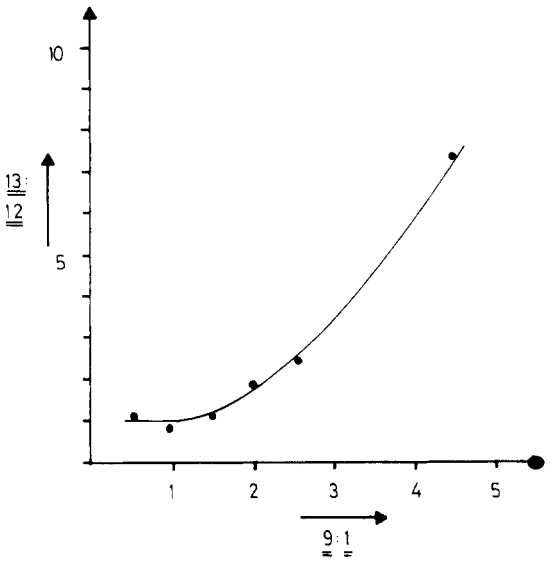


Figure 1. Dependence of the ratio of 6-azido-6,7-dideoxy-D-*altro*-heptulose (**13**) to 6-azido-6,7-dideoxy-L-*gluco*-heptulose (**12**) on the ratio of 3-azido-2-hydroxybutanal (**9**) to hydroxyacetone phosphate (DHAP; **1**) employed [capillary GC analyses of the tetrakis(trimethylsilyl) derivatives; GC conditions: see the Experimental Section].

Some RAMA-catalyzed reactions of DHAP (**1**) with aldehydes show substantial kinetic diastereoselectivity.[3b,4c,18] We have tested, therefore, whether the rate of the RAMA-catalyzed reaction of **1** with **9** likewise is de-

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Table I. ^{1}H NMR Spectral Data[a] of 1-Deoxymannojirimycin (7), and 1-Deoxynojirimycin (8), as Well as 2,6,7-Trideoxy-2,6-imino-D-*glycero*-D-*manno*-heptitol, -D-*glycero*-D-*gluco*-heptitol, and -L-*glycero*-L-*gulo*-heptitol (14, 15, and 16, Respectively)

	δ, ppm					
	7	8	14	15	16	
H-1a	3.150	2.44	1.14	1.12	1.10	H-7
H-1e	2.932	3.11	3.152	2.836	2.529	H-6
H-2	4.088	3.48	3.822	3.441	2.97	H-5
H-3	3.615	3.22	3.754	3.923	3.262	H-4
H-4	3.702	3.31	3.627	3.891	3.172	H-3
H-5	2.715	2.53	2.717	3.008	2.556	H-2
H-6A	3.852	3.82	3.811	3.598	3.778	H-1A
H-6B	3.788	3.62	3.684	3.574	3.527	H-1B
	J, Hz					
	7	8	14	15	16	
$^2J_{1a,1e}$	−14.1	−12.6				
$^3J_{1a,2}$	1.3	5.2	7.3	6.4	6.3	$^3J_{6,7}$
$^3J_{1e,2}$	2.8	10.9	2.6	10.2	9.3	$^3J_{5,6}$
$^3J_{2,3}$	3.1	9.4	3.1	3.0	8.8	$^3J_{4,5}$
$^3J_{3,4}$	9.6	8.9	9.5	3.8	9.2	$^3J_{3,4}$
$^3J_{4,5}$	9.8	9.4	9.8	1.5	9.6	$^3J_{2,3}$
$^3J_{5,6A}$	3.3	6.5	4.2	6.9	6.7	$^3J_{1A,2}$
$^3J_{5,6B}$	5.2	2.9	3.1	6.5	3.0	$^3J_{1B,2}$
$^2J_{6A,6B}$	−12.1	−11.9	−11.8	−11.2	−11.6	$^2J_{1A,1B}$

[a] 300 MHz, 25 °C, 0.1 M in D_2O, digital resolution 0.1 Hz; for the numerical analyses, the Bruker spin simulation program PANIC was used.

pendent on the absolute configuration of the substrate. When **9** was reacted, in increasing molar ratio, with **1** under RAMA catalysis, 6-azido-6,7-dideoxy-D-*altro*-heptulose (**13**) was formed with increasing preference as shown in Figure 1. The diastereoisomer ratio of the 6-azido-6,7-dideoxyheptuloses **12**:**13** was determined by capillary GC, after PASE-catalyzed hydrolysis of the phosphate esters, and persilylation of the product mixture. The small amounts of heptuloses resulting from the reaction of *threo*-**9** were neglected. With a 3.5-fold excess of **9**, the mixture of heptuloses **12**/**13** contained 88% of **13**.

As in the case of **2**, freshly prepared aqueous solutions of aldehyde **9** were always employed (obtained from the 3-azido-2-hydroxybutyraldehyde diethyl acetal by acid hydrolysis). An excess of **9** was found to be essential, however, for high turnover in the RAMA-catalyzed reaction with **1** (6.5 h; 31 °C; pH 6.5; 13.6 units of aldolase being consumed for the formation of 1 mmol of **11**). As outlined above, **9** reacts preferentially under aldehyde excess. Therefore, after precipitation of the mixture of barium salts **11a**/**11b**, PASE-catalyzed hydrolysis, and column chromatography on DOWEX 1×8 (formate form), the mixture of the isolated 6-azido-6,7-dideoxyheptuloses **12**/**13** (combined yield 90% relative to DHAP employed) contained 88% of the diastereoisomer **13**. Repeated chromatography of this mixture afforded pure **13**.

The synthesis of the 2,6,7-trideoxy-2,6-iminoheptitols **14**–**16** followed the same route as in the preparation of **7** and **8** (see Scheme I): hydrogenation of the azides, formation of the Schiff bases, and subsequent hydrogenation (Scheme III). However, catalytic hydrogenation of **13** with platinum dioxide proceeded with considerably lower diastereoselectivity than in the case of **5** and yielded 88% of a mixture of D-*manno*- and D-*gluco*-heptitol **14** and **15**.

The ratio of the diastereoisomers was only 3:2 in this case, as determined by ^{1}H NMR spectroscopy as well as by capillary GC and GC/MS analyses of the tetrakis(trimethylsilyl) derivatives.

Upon cation exchange chromatography, **14** was obtained in crystalline form, and **15** as a viscous oil. When the mixture of the 6-azido-6,7-dideoxyheptuloses **12**/**13** was subjected to catalytic hydrogenation under the same conditions, 2,6,7-trideoxy-2,6-imino-L-*glycero*-L-*gulo*-heptitol (**16**) was isolated in addition to the 2,6,7-trideoxy-2,6-iminoheptitols **14** and **15**.

NMR Spectroscopic Structural Assignment for Compounds 14–16

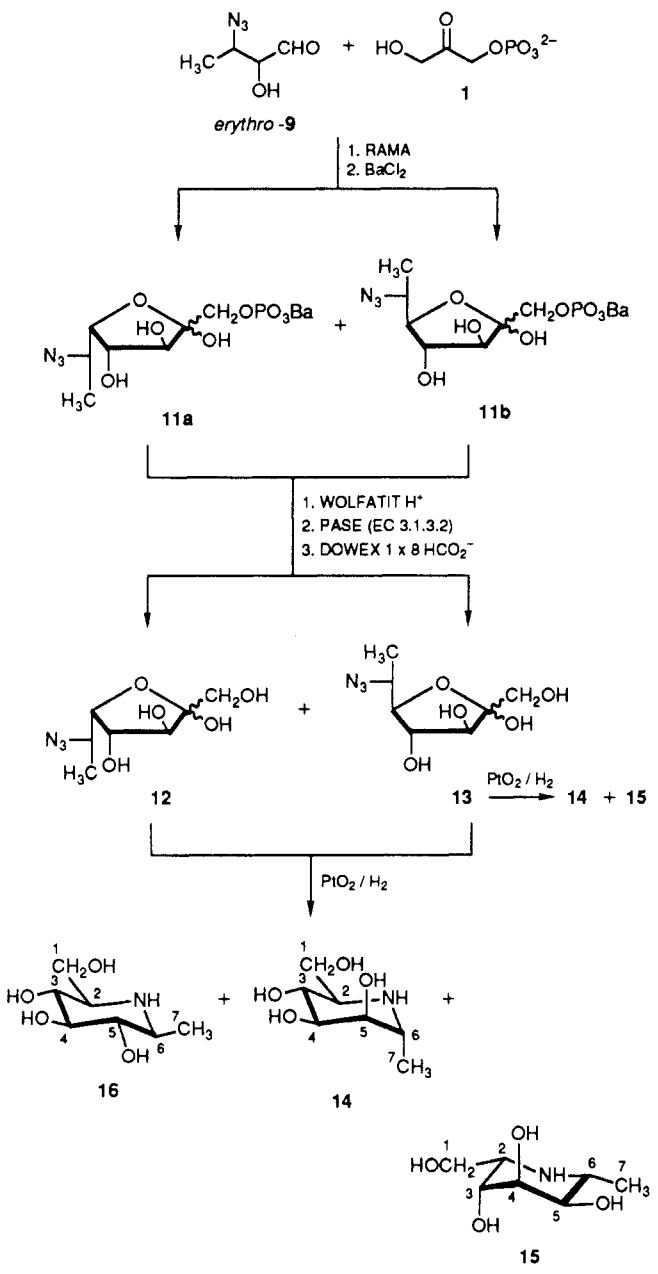
The absolute configuration of the four centers of chirality in the hexuloses **7** and **8** was determined from their ^{1}H NMR spectra and by comparing the optical rotation with the literature values.[7c,12a] The data from numerical analyses of these ^{1}H spectra are collected in Table I.

The 2- and 6-H multiplets of **16** appear superimposed at highest field (see Table I). Large (9.6 Hz) couplings between 2- and 6-H and the vicinal ring protons at C-3 and C-5 constitute definite proof for equatorial OH groups at C-3,5. The 4-H triplet likewise shows two large ^3J coupling constants. Consequently, the OH group at C-4 is equatorial, and **16** can be unequivocally assigned a conformation with all five substituents of the piperidine ring in equatorial position, as shown in Scheme III.

Since for **15** the 6-H/5-H vicinal coupling once again has a typical $^3J_{trans}$ value, CH_3 at C-6 and OH at C-5 must both be equatorial. This is confirmed nicely by the almost identical ^{13}C resonances of the methyl carbons in **15** and **16** (20.02 and 19.81 ppm, respectively). The small values for all other vicinal couplings demand either e,a or e,e orientation for the respective ring protons. Thus, 4-H must be equatorial. Since the relative configuration at C-3 and C-4 is determined by the enzymatic process, it must be identical in **15** and **16**, i.e. the *trans*-OH groups in **15** are axial. The extremely small (1.5 Hz) ^3J coupling between the equatorial 3- and the 2-H appears reasonable if 2-H is in axial position, with the OH group at C-3, trans to the C-2/2-H bond, exerting the well-known diminishing effect on ^3J coupling. If the C^1H_2OH group were axially oriented, **15** would have three substituents in an axial, and only two in equatorial position, and consequently would invert the conformation of the piperidine ring.

This is exactly the situation for the third isomer, **14**. The large vicinal coupling constants show that the C^1H_2OH group and both the C-3,4 OH substituents are equatorial while the 5-OH group is axial (the 3.1-Hz coupling between 4- and 5-H is typical for a,e orientation). Finally, the 3 ppm up-field shift for the C-7 resonance (17.06 ppm) shows

Scheme III



the C-6 methyl group in **14** to be axial. A comparison of the individual coupling constants between the two sets of homologous pyridinoses **7**/**14** and **8**/**16** clearly shows the configurational and conformational identity and constitutes further proof for these structures.

Only the heptitols **14** and **15**, which differ in the absolute configuration at the anomeric carbon C-2, were isolated when pure **13** was employed as precursor (as a 1:4 α/β mixture, but with pure stereochemistry at C-5). Reductive amination of a mixture of α/β-**12** and α/β-**13** affords, in addition to **14** and **15**, only one of the other two diastereoisomers, viz. **16**.

Experimental Section

Melting points were determined on a silicon bath (Büchi SMP 20) and are uncorrected. ^{1}H NMR spectra were recorded at 60, 80, or 300 MHz; ^{13}C NMR spectra were obtained at 75 MHz. GC analyses for reaction monitoring were run on a 2-mm glass column; OV 17, 101, or 225 or Chromosorb W. High-resolution GC analyses, especially for the determination of isomer ratios, were run with split injection (1:20, 300 °C) on a 20-m PS 086 glass capillary column; or with split- (1:20, 220 °C) or on-column injection on a 20-m OV 1701 glass capillary column. High-resolution mass determinations were performed by the peak-matching technique. For preparative column chromatography, silica gel A 60, 0.032–0.063 mm (Riedel-de Haen), DOWEX 50 W×8 200–400 mesh p.A. (Serva), and DOWEX 1×8 200–400 mesh p.A. (Serva) were used as stationary phases. For centrifugation a "Labofuge" GL (6242g) (Heraeus) was used. For both high-resolution GC and GC/MS analyses, the respective compounds (1–5 mg) were dissolved in pyridine (50 μL) in a Reacti-Vial (Serva), and *N,O*-bis(trimethylsilyl)trifluoroacetamide (Fluka) (50 μL) was added. The mixture was thoroughly mixed by shaking and heated to 90 °C for 5–10 min (N_2 atmosphere). The reaction mixture was cooled to ambient temperature, diluted with chloroform, and injected on-column.

Dihydroxyacetone Phosphate (DHAP, 1). 1 was synthesized according to ref 5 from 2,5-bis(hydroxymethyl)-2,5-diethoxy-1,4-dioxane. A round-bottomed flask, equipped with a P_2O_5 drying tube, was carefully heated in a N_2 atmosphere with a stream of warm air to melt the substrate without discoloration. The clear melt was maintained for 30 min by occasional heating, and worked up as described in ref 5.

3-Azido-2-hydroxypropanal Hydrate (2·H_2O) and 2,5-Bis(azidomethyl)-3,6-dihydroxy-1,4-dioxane (3). 3-Azido-2-hydroxypropionaldehyde diethyl acetal[4b] (8.0 g, 42.5 mmol), DOWEX 50 W×8 H^+ (10.0 g), and demineralized water (128 mL) were stirred for 2 h at 60 °C. The resulting solution was employed directly after removal of DOWEX for the enzyme-catalyzed transformations. The aldehyde can be isolated as the hydrate 2·H_2O by chromatography on silica gel (R_f = 0.15, CH_2Cl_2/Et_2O, 9.5:0.5, v/v). ^{1}H NMR (D_2O): δ 3.42, 3.52 (AB spin system, $^2J_{AB}$ = −13.2 Hz, 3-$H_{A,B}$), 3.68 (ddd, J = 7.0, 3.3, 5.6 Hz, 2-H), 4.95 (d, J = 5.6 Hz, 1-H). ^{13}C NMR (H_2O): δ 55.24 (C-3), 75.75 (C-2), 92.80 (C-1). When the solution was kept at ambient temperature for 1–3 days, a precipitate of **3** was formed, colorless crystals, mp 129 °C. ^{1}H NMR (DMSO-d_6): δ 3.26 (d, J = 6.4 Hz, 7-, 8-CH_2), 4.13 (t, broadened by unresolved small couplings to 3-H [1.6 Hz], OH [0.5 Hz], J = 6.4 Hz, 2-, 5-H), 4.83 (dd, J = 5.1, 1.6 Hz, 3-, 6-H), 6.70 (dd, J = 5.1, 0.6 Hz, 3-, 6-OH). ^{13}C NMR (DMSO-d_6): δ 50.78 (C-7, -8), 66.97 (C-2, -5), 88.30 (C-3, -6). Anal. Calcd for $C_6H_{10}N_6O_4$: C, 31.31; H, 4.38; N, 36.51. Found: C, 31.46; H, 4.36; N, 36.53.

6-Azido-6-deoxy-D-fructose-1-phosphate and 6-Azido-6-deoxy-L-sorbose-1-phosphate Barium Salts (4a/4b). Freshly prepared aqueous solutions of DHAP (**1**)[5] (40 mmol) and 2·H_2O (obtained from 42.5 mmol of 4-azido-3-hydroxypropionaldehyde diethyl acetal) were combined, and the resulting solution was adjusted to pH 6.5 with 2 N NaOH. Aldolase (EC 4.1.2.13, RAMA; 1000 units) was added, and the reaction mixture was incubated for 12 h at 25 °C. The reaction mixture was adjusted to pH 7, a solution of $BaCl_2 \cdot 2H_2O$ (22.0 g, 90 mmol) in water (100 mL) was added, and the mixture was refrigerated for 1 h at 0 °C. The precipitate was separated by centrifugation, and the supernatant was diluted with ethanol (500 mL). After 5 h at 0 °C, the precipitated barium salts **4a**/**4b** were separated by centrifugation and dried in high vacuo; yield, 11.8 g (70%).

6-Azido-6-deoxy-D-fructose (5) and 6-Azido-6-deoxy-L-sorbose (6). The mixture of barium salts **4a**/**4b** (11.77 g, 28 mmol) was dissolved in demineralized water (300 mL), DOWEX 50 W×8 H^+ (80 mL) was added, and the solution was filtered. The filtrate was adjusted to pH 4.5 with 2 N NaOH and filtered once more, PASE (acid phosphatase EC 3.1.3.2, Fa. Boehringer, Mannheim) (400 units) was added, and the mixture was incubated for 48 h at 38 °C. The reaction mixture was adjusted to pH 7 with an aqueous solution of $Ba(OH)_2$ and centrifugated. The supernatant was chromatographed in 40-mL portions on a DOWEX column 1×8 HCO_2^- (3 × 40 cm; 200–400 mesh; eluent H_2O; polarimetric flow-cell detection at 365 nm). The separated diastereoisomers **5** and **6** were obtained with a total yield of 4.6 g (77%) (**5**/**6** = 1:1). Anal. Calcd for $C_6H_{11}O_5N_3 \cdot {}^1/_2H_2O$: C, 33.65; H, 5.61; N, 19.62. Found: C, 33.61; H, 5.72; N, 19.46. **5**. $[\alpha]^{20}_D$: +52.5° (*c* 2.1, H_2O). ^{1}H NMR (D_2O) β-**5**: δ 3.64 (dd, J = −13.4, 3.5 Hz, 6-H_A), 3.59, 3.55 (AB spin system, J = −12.2 Hz, 1-$H_{A,B}$), 3.45 (dd, J = −13.4, 6.2 Hz, 6-H_B). ^{13}C NMR (D_2O) β-**5**: δ 55.41 (C-6) 65.51 (C-1) 77.95 (C-3, -4), 81.82 (C-5), 104.68 (C-2). α-**5**: δ 54.45 (C-6), 65.69 (C-1), 79.94 (C-4), 82.68, 84.76 (C-3, -5), 107.57 (C-2). **6**. $[\alpha]^{20}_D$: −60.0° (*c* 5.9, H_2O). ^{1}H NMR (D_2O) α-**6**: δ 4.10

(d, J = 5.6 Hz, 3-H), 3.62, 3.60 (AB spin system, J = −12.2 Hz, 1-$H_{A,B}$), 3.56 (dd, J = −13.3, 3.4 Hz, 6-H_A), 3.43 (dd, J = −13.3, 6.1 Hz, 6-H_B). **β-6**: δ 4.17 (d, J = 3.1 Hz, 3-H). The isomer ratio was determined from the two well-separated 3-H doublets as **α/β-6** = 80:20. ^{13}C NMR (D_2O) **α-6**: δ 53.55 (C-6), 66.05 (C-1), 77.95, 78.78, 79.15 (C-3, -4, -5), 104.77 (C-2). **β-6**: δ 54.22 (C-6), 65.34 (C-1), 78.58 (C-5), 82.48, 82.84 (C-3, -4), 108.48 (C-2).

1,2,3,4-Tetrakis(trimethylsilyl) Derivatives of 5 and 6. A mixture of the four diastereoisomers of **5** and **6** (**5:6** = 1:1) was subjected to capillary GC and CI(CH_4)–GC/MS analyses. Capillary GC (OV 1701, 20 m, on-column injection) in the order of increasing retention time: **α-5**, 15%; **β-5**, 39%; **α-6**, 40%; **β-6**, 6%. The four MS spectra showed no significant differences: m/z (%) 494 (3) $[MH]^+$, 478 (3) $[MH - CH_4]^+$, 466 (5) $[MH - N_2]^+$, 450 (13) $[MH - CH_4 - N_2]^+$, 376 (10) $[MH - N_2 - TMSOH]^+$, 286 (12) $[MH - N_2 - 2TMSOH]^+$, 217 (15), 172 (68), and peaks originating from the TMS groups.

1,5-Dideoxy-1,5-imino-D-mannitol (1-Deoxymannojirimycin) (7). A stirred mixture of 5% Pt/C (water content 50%) (100 mg), K_2CO_3 (2 mg), a little activated charcoal (washed with HCl), and demineralized water (40 mL) was saturated with H_2 (60 bar) at 25 °C for 5 min. A solution of **5** (300 mg, 1.46 mmol) in demineralized water (10 mL) was added rapidly, and the mixture was hydrogenated (60 bar H_2, 25 °C, 12 h). The reaction mixture was filtered over Celite and Duolite, the filtrate was adjusted to pH 1.5 with 1 N HCl and concentrated in vacuo, and the residue was dissolved in little methanol. By slowly condensing diethyl ether into this solution, **7**·HCl was precipitated; yield 231 mg (79%) colorless needles, mp 174 °C [lit.[12a] mp 172.5–173.5 °C]. $[\alpha]^{20}_D$: −12.01° (c 1.64, H_2O) [lit.[12a] $[\alpha]^{20}_D$ −14.5° (c 0.01, H_2O)]. Treatment of **7**·HCl with 2 N NaOH afforded the free base **7**. ^{1}H NMR of **7**, see Table I. ^{13}C NMR (D_2O) of **7**·HCl: δ 50.43, 61.00, 63.26, 68.64, 68.77, 75.32. Anal. Calcd for $C_6H_{14}ClNO_4$: C, 36.10; H, 7.07; N, 7.02. Found: C, 36.00; H, 7.08; N, 6.83. CI(CH_4)-GC/MS of the 2,3,4,6-tetrakis(trimethylsilyl) derivative of **7** (obtained from **7**·HCl): m/z (%) 492 (2) $[M + C_3H_5]^+$, 480 (7) $[M + C_2H_5]^+$, 452 (42) $[MH]^+$, 436 (100) $[MH - CH_4]^+$, 362 (4) $[MH - TMSOH]^+$, 346 (24) $[MH - CH_4 - TMSOH]^+$, 272 (78) $[MH - 2TMSOH]^+$.

1,5-Dideoxy-1,5-imino-D-glucitol (1-Deoxynojirimycin) (8). A sitrred mixture of 5% Pt/C (water content 50%) (140 mg), K_2CO_3 (100 mg), activated charcoal (270 mg), and demineralized water (35 mL) was saturated twice with H_2 (100 bar) at 25 °C for 7 min. A solution of **6** (217 mg, 1.06 mmol) in demineralized water (35 mL) was added rapidly, the mixture was hydrogenated (100 to 20 bar H_2, 25 °C, 12 h), and the catalyst was removed by filtering over Celite. The filtrates was adjusted to pH 2 with 1 N HCl and concentrated in vacuo. The residue was crystallized as described for **7**·HCl. Yield 137 mg (65%) **8**·HCl, mp 205 °C [lit.[19] mp 208–209 °C]. Treatment of **8**·HCl with 2 N NaOH afforded the free base **8**. $[\alpha]^{20}_D$: +45.2° (c 1.04, H_2O) [lit.[7c] $[\alpha]^{20}_D$ +46.5° (c 0.61, H_2O)]. High-resolution mass spectrum (EI) calcd for $C_6H_{13}NO_4$ 163.0845, found 163.0843. ^{1}H NMR of **8** see Table I. ^{13}C NMR (D_2O) of **8**·HCl: δ 49.15, 60.99, 63.23, 70.10, 71.04, 79.43. Anal. Calcd for $C_6H_{14}ClNO_4$: C, 36.10; H, 7.07; N, 7.02. Found: C, 36.27; H, 7.04; N, 6.71. CI(CH_4)-GC/MS of the 2,3,4,6-tetrakis(trimethylsilyl) derivative of **8** (obtained from **8**·HCl): m/z (%) 492 (2) $[M + C_3H_5]^+$, 480 (7) $[M + C_2H_5]^+$, 452 (42) $[MH]^+$, 436 (100) $[MH - CH_4]^+$, 362 (9) $[MH - TMSOH]^+$, 346 (18) $[MH - CH_4 - TMSOH]^+$, 272 (34) $[MH - 2TMSOH]^+$.

3-Azido-2-hydroxybutanal (9). Crotonaldehyde diethyl acetal and ethylene acetal, as well as 2,3-epoxybutyraldehyde diethyl acetal, were synthesized according to refs 16 and 17, and the E/Z ratio of the distilled products were determined by capillary GC (PS 086, 20 m, 40–200 °C, 4°/min).

3-Azido-2-hydroxybutyraldehyde Diethyl Acetal. To the stirred solution of 2,3-epoxybutyraldehyde diethyl acetal (17.4 g, 109 mmol) in dimethylformamide (50 mL) were added sodium azide (28.3 g, 435 mmol), $MgClO_4 \cdot 2H_2O$ (14.6 g, 56.3 mmol), and water (25 mL). The reaction mixture was heated to 85 °C for 48 h and concentrated in vacuo. The residue was diluted with water and extracted with chloroform; the extract was dried with Na_2SO_4 and distilled in high vacuo. Yield: 13.7 g (62%). Bp: 64 °C (0.001 Torr). ^{13}C NMR ($CDCl_3$) *erythro* form: δ 14.24 (C-4), 15.34, 15.37 (2 CH_3CH_2O), 58.04 (C-3), 63.40, 63.83 (2 CH_3CH_2O), 74.16 (C-2), 101.95 (C-1). *threo* form: δ 14.24 (C-4) 15.44, 15.82 (2 CH_3CH_2O), 56.67 (C-3), 63.44, 64.40 (2 CH_3CH_2O), 74.85 (C-2), 102.94 (C-1). Anal. Calcd for $C_8H_{17}N_3O_3$: C, 47.28; H, 8.43; N, 20.68; C_2H_5O, 44.34. Found: C, 47.40; H, 8.41; N, 20.74; C_2H_5O, 44.39.

2-*O*-(Trimethylsilyl) Derivative of 3-Azido-2-hydroxybutyraldehyde Diethyl Acetal. The *erythro/threo* ratio was determined from a capillary GC (PS 086, 20 m, 40–200 °C, 4 °C/min) of the TMS derivatives as 92:8 (retention time 490, 500 s). The CI(CH_4)-GC/MS spectra of the two diastereoisomers showed no significant differences: m/z (%) 232 (8) $[MH - CH_4 - N_2]^+$, 230 (3) $[MH - C_2H_5OH]^+$, 202 (22) $[MH - N_2 - C_2H_5OH]^+$, 186 (4) $[MH - TMSOH]^+$.

3-Azido-2-hydroxybutanal Hydrate (9·H_2O) and 2,5-Bis(1-azidoethyl)-3,6-dihydroxy-1,4-dioxane (10). A mixture of 3-azido-2-hydroxybutyraldehyde diethyl acetal (10.73 g, 52.7 mmol) and 0.1 N HCl (200 mL) was emulsified by ultrasound. After stirring at 60 °C for 2 h, a clear solution of **9**·H_2O was obtained. ^{13}C NMR (H_2O): δ 15.54 (C-4), 60.67 (C-3), 78.59 (C-2), 92.55 (C-1). When the solution was kept at 5 °C for some days, colorless crystals of **10** were precipitated, mp 144.5 °C. ^{1}H NMR (DMSO-d_6): δ 1.26 (d, J = 6.4 Hz, 8-, 10-CH_3), 3.60 (dq, J = 9.0, 6.4 Hz, 7-, 9-H), 3.72 (d, broadened by unresolved small couplings, J = 9.0 Hz, 2-, 5-H), 4.95 (dd, J = 5.2, 1.5 Hz, 3-, 6-H), 6.72 (d, 3-, 6-OH). ^{13}C NMR (DMSO-d_6): δ 15.73 (C-8, -10), 56.67 (C-7, -9), 69.47 (C-2, -5), 88.53 (C-3, -6). Anal. Calcd for $C_8H_{14}N_6O_4$: C, 37.21; H, 5.46; N, 32.54. Found: C, 37.19; H, 5.45; N, 32.43.

6-Azido-6,7-dideoxy-D-*altro*-heptulose-1-phosphate and 6-Azido-6,7-dideoxy-L-*gluco*-heptulose-1-phosphate Barium Salts (11a/11b). Freshly prepared solutions of DHAP (**1**)[5] (30 mmol) and **9**·H_2O, obtained from 3-azido-2-hydroxybutyraldehyde diethyl acetal (52.7 mmol), in demineralized water were combined and adjusted to pH 6.5 with 2 N NaOH (total volume 510 mL). RAMA (1020 units) was added, and the reaction mixture was incubated at 31 °C for 400 min and for 12 h at ambient temperature. A concentrated aqueous solution of $BaCl_2 \cdot 2H_2O$ (15 g, 61.4 mmol) was added, and after 3 h at 0 °C, the precipitate was separated by centrifugation. Ethanol (1 L) was added to the supernatant, and the mixture was kept at 0 °C for 12 h. The precipitate was separated by centrifugation and dried in high vacuo, yielding 11.3 g (87%).

6-Azido-6,7-dideoxy-D-*altro*-heptulose (13). A solution of the mixture of barium salts **11a/11b** (11.3 g) in demineralized water (400 mL) was adjusted to pH 1.7 by addition of WOLFATIT H^+ (100 mL). The resin was removed by filtering over Celite, and the pH of the filtrate was adjusted to pH 4.5 with 2 N NaOH. Sodium azide—to prevent microbic contamination—(50 mg) and PASE (320 units) were added, and the mixture was incubated at 37 °C for 60 h. The reaction mixture was neutralized with barium hydroxide solution, the precipitate was removed by filtering over Celite, and the filtrate was evaporated in vacuo. The residue was chromatographed on DOWEX 1×8 HCO_2^- (200–400 mesh; 3.5 × 30 cm; eluent water; polarimetric detection), yielding 5.9 g of the 6-azido-6,7-dideoxyheptuloses **12/13** (90% with respect to **1**), which contained 88% **13**. The main fraction was rechromatographed on the same column, yielding pure **13**, $[\alpha]^{20}_D$ +12.5° (c 8.85, H_2O). ^{1}H NMR (D_2O) **β-13**: δ 4.22 (dd, J = 8.2, 7.5 Hz, 4-H), 4.08 (d, J = 8.2 Hz, 3-H), 3.81 (dq, J = 6.7, 4.8 Hz, 6-H), 3.74 (dd, J = 7.4, 4.8 Hz, 5-H), 3.56, 3.52 (AB spin system, J = −12.1 Hz, 1-$H_{A,B}$), 1.26 (d, J = 6.7 Hz, 7-CH_3). **α-13**: δ 3.88 (dq, J = 6.8, 4.2 Hz, 6 H), 3.69, 3.64 (AB spin system, J = −12.0 Hz, 1-$H_{A,B}$), 1.25 (d, J = 6.8 Hz, 7-CH_3). ^{13}C NMR (D_2O) **β-13**: δ 17.03 (C-7), 61.76 (C-6), 65.46 (C-1), 77.86, 78.35 (C-3, -4), 84.93 (C-5), 104.38 (C-2); **α-13**: δ 17.28 (C-7), 60.60 (C-6), 65.60 (C-1), 79.67, 84.93 (C-3, -4), 87.06 (C-5), 107.58 (C-2). Anal. Calcd for $C_7H_{13}N_3O_5$: C, 38.36; H, 5.98; N, 19.17. Found: C, 38.16; H, 6.00; N, 18.94. CI(CH_4)-GC/MS (OV 1701; 20 m; 50–300 °C, 5°/min; on-column injection) of the 1,2,3,4-Tetrakis(trimethylsilyl) derivative of pure **13**: m/z (%) 508 (1) $[MH]^+$, 492 (0.5) $[MH - CH_4]^+$, 480 (1) $[MH - N_2]^+$, 464 (11) $[MH - CH_4 - N_2]^+$, 390 (4) $[MH - N_2 - TMSOH]^+$, 374 (4) $[MH - CH_4 - N_2 - TMSOH]^+$, 300 (25) $[MH - N_2 - 2TMSOH]^+$, 260 (22), 186 (48) [m/z 260 − $CH_2{=}SiMe_2]^+$, and peaks originated from TMS groups. From the capillary GC, the ratio of **β-13/α-13** was determined as 82:18 (retention times 30.75, 30.82 min).

Dependence of the Ratio of 6-Azido-6,7-dideoxy-D-*altro*-heptulose (13) to 6-Azido-6,7-dideoxy-L-*glyco*-heptulose (12)

on the Ratio of 3-Azido-2-hydroxybutanal Hydrate (9·H_2O) to Hydroxyacetone Phosphate (DHAP, 1) Employed (see Figure 1). 1 (60 mM), variable concentrations of 9·H_2O, and RAMA (4 units/mL) were incubated for 2 days at pH 6.2 and 25 °C as described above. The barium salts **11a/11b** were precipitated by addition of a solution of $BaCl_2 \cdot 2H_2O$ (0.2 mmol/mL) and ethanol (1 mmol/mL), and hydrolyzed with PASE. The reaction mixture was evaporated, and aliquots of the residue were persilylated. The diastereoisomer ratio of the TMS_4 derivatives of **12/13** was determined by capillary GC (OV 1701; 20 m; 40–300 °C, 5°/min; on-column injection).

2,6,7-Trideoxy-2,6-imino-D-*glycero*-D-*manno*-heptitol (14) and 2,6,7-Trideoxy-2,6-imino-D-*glycero*-D-*gluco*-heptitol (15). A suspension of $PtO_2 \cdot 2H_2O$ (200 mg) and activated charcoal (700 mg) in demineralized water (60 mL) was stirred and saturated twice with H_2 (100 bar) at 25 °C for 7 min. A solution of **13** (1.0 g, 4.56 mmol) in glacial acetic acid (1 mL) and demineralized water (15 mL) was added rapidly. The mixture was hydrogenated at 25 °C for 12 h (50–80 bar H_2) and filtered over Celite. The filtrate was adjusted to pH 2 with 1 N HCl, the solvent was evaporated in vacuo, and the residue was dissolved in ethanol. By addition of ether, **14**·HCl/**15**·HCl were precipitated (855 mg, 88%). The colorless oil was applied to a WOLFATIT H^+ column, which was washed with water and eluted with 10% ammonia. The eluate was evaporated in vacuo. Anal. Calcd for $C_7H_{15}N_4 \cdot 0.2H_2O$: C, 46.50; H, 8.47; N, 7.75. Found: C, 46.33; H, 8.51; N, 7.60. High-resolution mass spectrum (EI): calcd for $C_7H_{15}NO_4$ 177.1001, found 177.1000. MS (EI, 70 eV): *m/z* (%) 177 (1.5) $[M]^{+\cdot}$, 160 (1.6) $[M - OH]^+$, 159 (1.5) $[M - H_2O]^{+\cdot}$, 146 (100) $[M - CH_2OH]^+$. CI(CH_4)-3,4,5,7-tetrakis(trimethylsilyl) derivatives of **14** and **15** (obtained from the mixture **14**·HCl/**15**·HCl): *m/z* (%) 466 (7) $[MH]^+$, 464 (4) $[M - H]^+$, 450 (19) $[MH - CH_4]^+$, 378 (2.4), 362 (6.6), 286 (11.7), 216 (6), besides 75 (100) $[HOSiMe_2]^+$ and 73 (83) $[SiMe_3]^+$. The mixture of **14**·HCl/**15**·HCl in water (2 mL) was acidified with diluted formic acid and separated on DOWEX 50 W×8 NH_4^+ (200–400 mesh; 2.5 × 50 cm; conditioned with 0.75 M ammonium formate, pH 4.0; eluent 0.75 M ammonium formate buffer, applied with a gradient: 50 mL pH 4.0, 75 mL pH 5.0, 180 mL pH 5.0–5.6; polarimetric detection). The individual fractions were applied to a WOLFATIT H^+ column (2 × 15 cm), washed with water, and eluted with 10% ammonia. The eluates were concentrated in vacuo, yielding **15** as an oil and **14** as colorless crystals. **15**. $[\alpha]^{20}_D$: +38.7° (*c* 1, H_2O). ^1H NMR see Table I. ^{13}C NMR (D_2O): δ 20.02 (C-7), 52.64 (C-6), 56.92, 64.12, 72.39, 73.64, 74.17. **14** (dried over P_2O_5 and potassium hydroxide). Mp 141 °C. $[\alpha]^{20}_D$: −11.3° (*c* 1, H_2O). ^1H NMR see Table I. ^{13}C NMR (D_2O): δ 17.06 (C-7), 55.15 (C-6), 57.28, 63.32, 71.33, 73.91, 75.80.

2,6,7-Trideoxy-2,6-imino-L-*glycero*-L-*gulo*-heptitol (16). A mixture of **12/13** (1.0 g, 4.56 mmol) was hydrogenated, and the reaction mixture was worked up chromatographically as described for **14/15**. The products were eluted from the DOWEX NH_4^+ column in the order **14**, **16**, **15**. The fraction containing **16** was concentrated in vacuo, yielding pure **16** as a colorless oil. $[\alpha]^{20}_D$: +17.3° (*c* 1, H_2O). ^1H NMR see Table I. ^{13}C NMR (D_2O): δ 19.81 (C-7), 57.14 (C-6), 62.82, 64.42, 74.61, 79.11, 80.87.

Acknowledgment. Support of this research by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie is gratefully acknowledged. A.S. is indebted to the Robert Bosch Stiftung for a generous grant.

Prespacer Glycosides in Glycoconjugate Chemistry. Dibromoisobutyl Glycosides for the Synthesis of Neoglycolipids, Neoglycoproteins, Neoglycoparticles, and Soluble Glycosides

Göran Magnusson,* Stefan Ahlfors, Jan Dahmén,† Karl Jansson, Ulf Nilsson, Ghazi Noori,† Kristina Stenvall,† and Ann Tjörnebo†

Organic Chemistry 2, Chemical Center, The Lund Institute of Technology, University of Lund, P.O. Box 124, S-221 00 Lund, Sweden, and Symbicom AB, Research Park Ideon, 223 70 Lund, Sweden

Received October 30, 1989

3-Bromo-2-(bromomethyl)propyl (dibromoisobutyl or DIB) mono- to tetrasaccharide glycosides were prepared in moderate to high yields by treatment of the corresponding 1-*O*-acetyl saccharides with 3-bromo-2-(bromomethyl)propanol (DIBOL) and boron trifluoride etherate. Treatment of the DIB glycosides with alkyl- and ω-methoxycarbonylalkyl thiols gave the corresponding bis-sulfide glycolipids and spacer arm sugars, respectively. Oxidation of the sulfides with *m*-chloroperbenzoic acid gave the corresponding bis-sulfones. Treatment of the DIB glycosides with tetrabutylammonium fluoride gave the corresponding allylic bromide glycosides, and addition of thiols gave the allylic sulfides. Prolonged fluoride treatment gave the allylic fluorides. Hydrogenation of DIB glycosides under basic conditions gave the corresponding isobutyl glycosides. Spacer arm and allylic bromide glycosides were coupled to bovine serum albumin and derivatized silica gel, thereby providing artificial glycoproteins and glycoparticles.

The aim of the present report is to show that the combination of 2-(trimethylsilyl)ethyl (TMSET) glycosides for anomeric blocking during oligosaccharide synthesis,[1] followed by transformation into 3-bromo-2-(bromomethyl)-propyl (dibromoisobutyl or DIB) glycosides and further conversion to glycolipids, spacer glycosides, and soluble glycosides, represents a coherent and systematic approach to the rational synthesis of glycoconjugates. By this strategy, the number of synthesis steps can be minimized and the desired glycoconjugates can be obtained in high yield. The general concept is depicted in Scheme I.

Biochemical and medical research on the function of glycolipids and glycoproteins depends to a great extent on the availability of synthetic glycoconjugates both with the sugar portion intact and in the form of analogues that emulate the natural compounds. For example, synthetic glycolipids are useful for the coating of cells and surfaces

† Symbicom AB.

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0022-3263/90/1955-3932$02.50/0 © 1990 American Chemical Society