Linear total synthetic routes to beta-D-C-(1,6)-linked oligoglucoses and oligogalactoses up to pentaoses by iterative Wittig olefination assembly.

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New Synthesis of Pyrrolidine Homoazasugars via Aminohomologation of Furanoses and Their Use for the Stereoselective Synthesis of Aza-*C*-disaccharides

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The introduction of a formyl group at the anomeric center of 2,3,5-tri-*O*-benzyl furanoses and substitution of the ring oxygen with a basic nitrogen atom (aminohomologation) was carried out via stereoselective addition of 2-lithiothiazole to *N*-benzyl, *N*-furanosylhydroxylamines (masked *N*-benzyl sugar nitrones), followed by reductive dehydroxylation of the resulting open-chain adducts, and then ring closure via intramolecular displacement of the free hydroxy group by the amino group and unmasking of the formyl group from the thiazole ring. The resulting formyl aza-*C*-glycosides were transformed into 2,5-dideoxy-2,5-imino-hexitols (pyrrolidine homoazasugars) by reduction of the formyl to the hydroxymethyl group and removal of the *O*- and *N*-benzyl groups by hydrogenolysis. This reaction sequence was applied to four furanoses (D-*arabino*, D-*ribo*, D-*lyxo*, L-*xylo*) to give the hydroxy- and amino-free homoazasugars, including the natural product 2,5-dideoxy-2,5-imino-D-mannitol, in 17% overall yields (six steps). The formyl aza-*C*-glycosides proved to be valuable intermediates for the synthesis of more complex derivatives. In fact, these sugar aldehydes were employed in Wittig-type coupling reactions with galactose and ribose phosphoranes to give bis-glycosylated alkenes, which upon reduction of the double bond were transformed into methylene isosteres of (1→6)- and (1→5)-linked disaccharides in which one of the two sugar moieties was an azasugar (aza-(1→*x*)-*C*-disaccharides).

Introduction

Given the potent and specific inhibitory activity toward carbohydrate processing enzymes such as glycosylhydrolases and transferases, polyhydroxylated piperidines and pyrrolidines currently referred to as azasugars or iminosugars[1] have emerged in recent years as highly promising candidates for the development of new efficient drugs against diabetes,[2] cancer metastasis,[3] and viral infections, particularly that of the human immunodeficiency virus (HIV).[4] Of the several azasugars developed, those having an hydroxymethyl group or a polyhydroxylated carbon chain linked to the carbon adjacent to nitrogen, the anomeric carbon, so that homoazasugars (aza-*C*-glycosides) are formed,[5] have gained special importance because they retain the same type of biological activity of the parent azasugars and, in some cases, exhibit higher selectivity and potency. Another positive aspect of homoazasugars is represented by their stability toward chemical and enzymatic degradation, a limitation of the parent azasugars containing an anomeric hydroxyl as carbohydrate mimics due to the lability of the *O,N*-acetal function. Homoazasugars are natural products widely diffused in plants and microorganisms,[6] as various pyrrolidine and piperidine derivatives have been isolated and duly characterized. Typically, 2,5-dihydromethyl-3,4-dihydroxypyrrolidine (DMDP, **1**, 2,5-dideoxy-2,5-imino-D-mannitol) (Figure 1) was found at first in the leaves of some legumes[7] in 1976, and the one-carbon higher homologue

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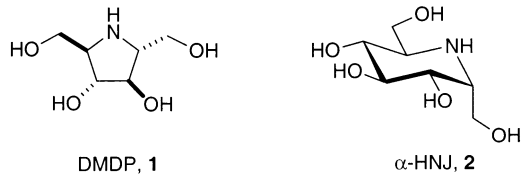

FIGURE 1.

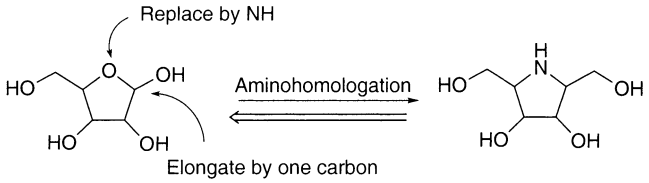

FIGURE 2.

of deoxynojirimycin, α-homonojirimycin (α-HNJ, **2**, 2,6-dideoxy-2,6-imino-D-*glycero*-L-*gulo*-heptitol), was isolated in 1988 from a neotropical liana of the family Euphorbiaceae.[8] The chemical synthesis of these compounds that was reported shortly after the isolation confirmed their structures.[9−11]

Various synthetic routes to different pyrrolidine and piperidine homoazasugars have been reported from academic and industrial laboratories, including those of Fleet, Liu, Martin, Vogel, Wong, and others.[12] Simple analogues such as C-1 aminomethyl[13] and aryl derivatives [14] have been also described by Wong and Johnson and their co-workers, respectively. Recent research has been focused on the construction of more complex aza-*C*-glycosyl compounds in which the polyhydroxylated piperidine or pyrrolidine ring is linked through the α-carbon atom to another carbohydrate residue by an all-carbon tether.[5,15] Interest in this special class of stable glycoconjugate mimics, which are currently named aza-*C*-disaccharides, is mainly based on the suggestion that the attachment of a second aglycone-mimicking sugar unit to an azasugar would result in increased potency and specificity.[15,16] Hence, in the context of this general interest in aza-*C*-glycosyl compounds, we report in full in the first part of this paper the results of our efforts dealing with a new and general entry to homoazasugars of the pyrrolidine family (2,5-dideoxy-2,5-imino-hexitols) using a thiazole-based aminohomologation protocol of furanoses.[17] In the second part, we will describe the synthesis of (1→6)- and (1→5)-linked aza-*C*-disaccharides via Wittig coupling of azasugar aldehydes (formyl *C*-aza-glycosides) with pyranose and furanose phosphoranes.[18]

Results and Discussion

Synthesis of 2,5-Dideoxy-2,5-imino-hexitols. Our first objective was to develop a stereoselective chemical synthesis of pyrrolidine homoazasugars from furanoses (Figure 2) via the aldehyde aminohomologation sequence exploiting the nitrone and thiazole chemistry.[19] In this methodology the aldonitrone is allowed to react with lithiothiazole; then, the resulting hydroxylamine is reduced to amine, and the thiazole is transformed into the formyl group. The application of the aminohomologation sequence to furanose-derived nitrones en route to 2,5-dihydroxymethyl 3,4-dihydroxypyrrolidines will require an extra step in which the amino group replaces the ring oxygen by an intramolecular substitution reaction with inversion of the configuration of the C-4 stereocenter.

The feasibility of this approach was tested starting from the readily available 2,3,5-tri-*O*-benzyl-D-arabino-furanose **3** (Scheme 1). Heating this compound with *N*-benzylhydroxylamine at 110 °C for 30 min under solvent-free conditions afforded the corresponding arabinosyl hydroxylamine **4** as the single α-anomer in very good yield.[20] The configuration at the anomeric center of **4** was assigned on the basis of a strong NOE between H-1 and H-3 and the absence of a NOE between H-1 and

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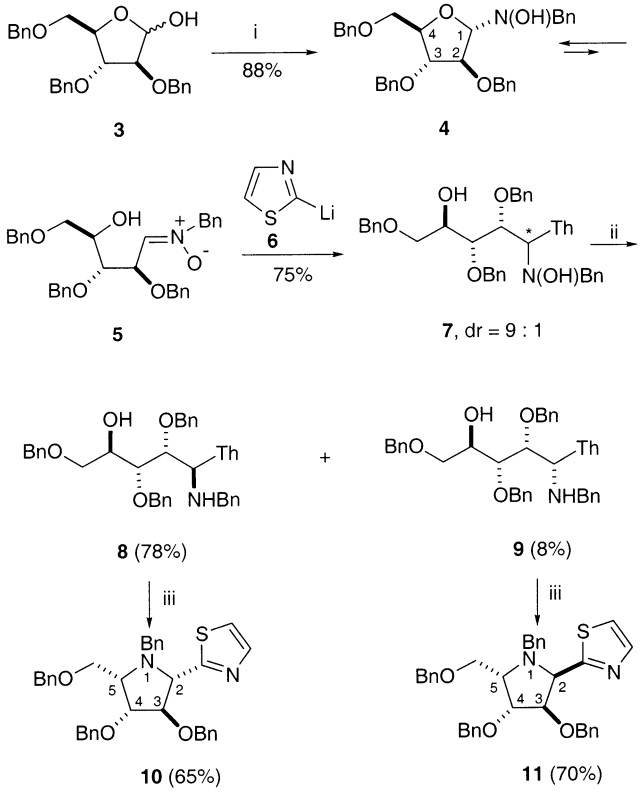
(20) This method appears to be more practical and efficient than an earlier procedure of Merino and co-workers (Merino, P.; Franco, S.; Merchán, F. L.; Tejero, T. *Synth. Commun.* **1997**, *27*, 3529) employing a mixture of a drying agent ($MgSO_4$) and a Lewis acid ($ZnCl_2$), which in fact requires very long reaction times (48−72 h) and gives lower yields.

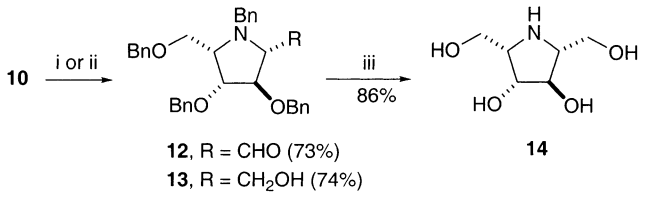
SCHEME 1[a]



[a] Key: Th = 2-thiazolyl. Reagents: (i) BnNHOH. (ii) $(AcO)_2Cu$, Zn. (iii) Tf_2O, pyridine.

H-4. Although the open-chain nitrone **5** in equilibrium with **4** could not be detected by NMR spectroscopy, the slow addition of an excess of 2-lithiothiazole **6** (3−5 equiv) in diethyl ether at low temperatures (−70 °C) afforded the formal product of addition to **5**, i.e., the open-chain thiazolyl hydroxylamine **7** as a mixture of diastereoisomers (9:1 ratio) in 75% combined yield. Due to the difficult separation of these diastereoisomers, the product **7** was subjected to reductive dehydroxylation using a Zn−Cu couple as we have described in an earlier work.[21] The resulting *N*-benzylamines **8** (78%) and **9** (8%) were individually isolated by flash chromatography. The configuration at the newly formed amino group-bearing stereocenter of these compounds was established following their transformation into pyrrolidines. To this aim, the free hydroxyl group of **8** and **9** was activated as an *O*-triflate by treatment with triflic anhydride[22] and the product heated in pyridine to give the corresponding 2-thiazolylpyrrolidines **10** (65%) and **11** (70%), respectively, in satisfactory isolated yields. The *cis*-relationship between the thiazole ring and the CH_2OBn group in **10** was assigned on the basis of a strong NOE of H-2 with H-4 and H-5, while these effects were not observed in the trans epimer **11**. Consequently, on the basis of the reasonable assumption that the ring closure occurred via an S_N2-like mechanism involving the displacement of the OSO_2CF_3 group with inversion, the stereochemistry of

SCHEME 2[a]



[a] Reagents: (i) TfOMe; then $NaBH_4$; then $AgNO_3$ in MeCN−H_2O. (ii) i, then $NaBH_4$. (iii) H_2, 20% $Pd(OH)_2$/C; then Dowex (OH^-).

the γ-amino alcohols **8** and **9** was assigned as shown. It thus appears that the major isomer (90%) in the mixture of *N*-benzylhydroxylamines **7** is an anti adduct. Attempts to increase the anti selectivity[19] by silylation or precomplexation of the nitrone with Lewis acids (Et_2AlCl, $ZnCl_2$, $Ti(O\text{-}^iPr)_4$, $TiCl(O\text{-}^iPr)_3$) failed since, under these conditions, the system became unreactive. Variable stereochemical outcomes have been reported for the addition of nucleophiles to nitrones depending on the presence of additives and the nature of the α-substituent.[19,23] We observed that nitrones derived from polyalkoxy aldehydes and aldehydo sugars give preferentially syn adducts, while anti adducts are obtained when the nitrones are precomplexed with Lewis acids.[19c] However, there were some exceptions to this general trend since the nitrone derived from D-arabinose bis-acetonide underwent the addition of 2-lithiothiazole with a preferential anti selectivity.[19c] Hence the anti selectivity observed in the addition of **6** to **5** appears to follow the same behavior. However, in the present case, it is also possible that the nitrone **5** exists in a preferential conformation due to the lithium coordination to the nitrone oxygen and the free hydroxyl group and that the addition of **6** occurs to the less hindered side of this complex.

The completion of the aminohomologation process required the unmasking of the formyl group from the thiazole ring as the final step. Only the 2-thiazolyl pyrrolidine **10** arising from the main stereochemical course of the amination sequence was considered for this final transformation (Scheme 2). However, at the outset of this operation, we wondered whether the thiazole-to-formyl unmasking protocol (N-methylation, reduction, hydrolysis) was compatible with the presence of the nucleophilic *N*-benzylamino group.[24] Nevertheless, to our delight, the submission of **10** to the improved thiazole-to-formyl conversion protocol[25] afforded the 2-formyl pyrrolidine **12** (formyl aza-*C*-glycoside) in good yield (73%). This compound turned out to be an isolable product sufficiently stable to storage for several days.[26]

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(24) Accordingly, methylation by methyl triflate of the *N*-benzylamino group was observed to take place so that 2 equiv of the methylating agent was required. However, demethylation of the ammonium quaternary salt took place by treatment with sodium borohydride in the subsequent reductive step.

(25) Improvement of the unmasking sequence relies on the use of silver ion ($AgNO_3$) for the thiazolidine hydrolysis. For a comment on this issue, see: Dondoni, A.; Marra, A.; Scherrmann, M.-C.; Bertolasi, V. *Chem. Eur. J.* **2001**, *7*, 1371.

(26) We stated in our first publication (ref 17) that this compound was an unstable product. The erroneous belief was corrected in a subsequent report (ref 18).

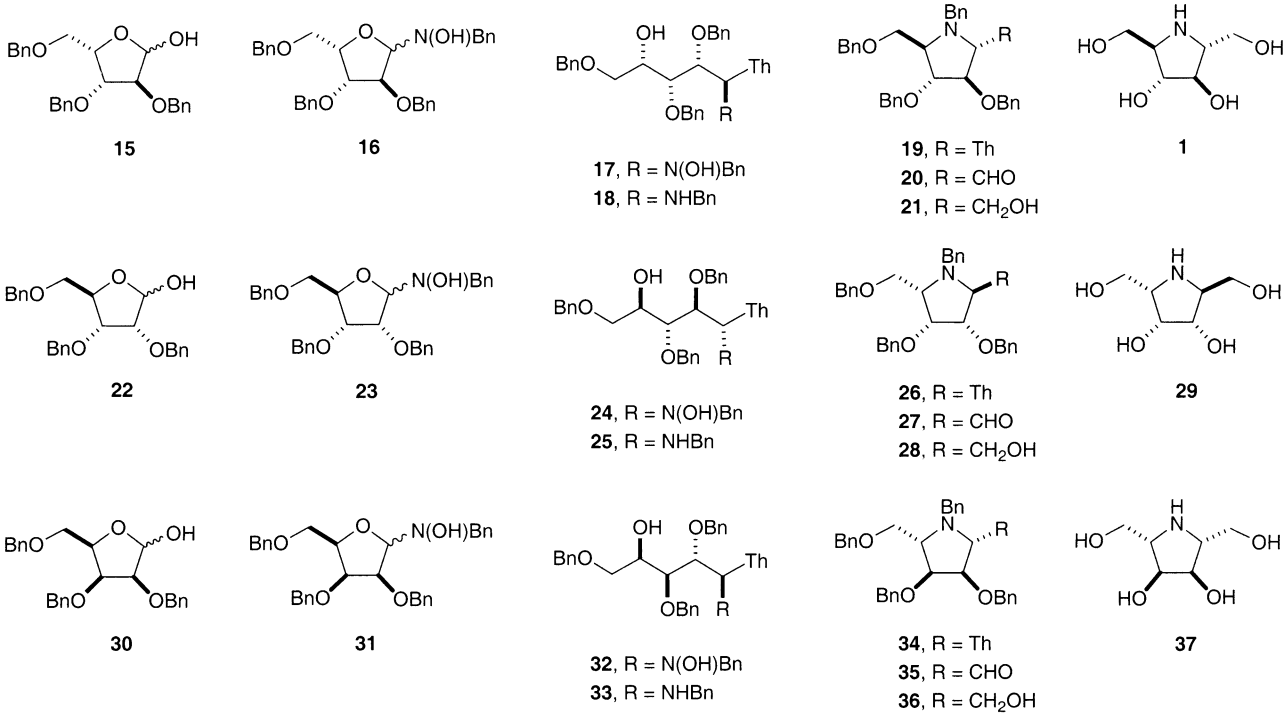


FIGURE 3. 2,5-Dideoxy-2,5-imino-hexitols **1**, **29**, and **37** and the corresponding intermediates prepared via aminohomologation of furanoses **15**, **22**, and **30** (Th = 2-thiazolyl).

However, the aldehyde **12** was reduced in situ ($NaBH_4$) to give the alcohol **13** in good overall yield (74%). This compound upon O- and N-debenzylation by hydrogenolysis afforded the known (2*R*,5*S*)-dihydroxymethyl-(3*R*,4*R*)-dihydroxypyrrolidine (**14**, 2,5-dideoxy-2,5-imino-D-glucitol), whose physical and spectroscopic data were identical to those reported in the literature (see Experimental Section). The overall yield of the pyrrolidine homoazasugar **14** from **3** was 21% (six steps).

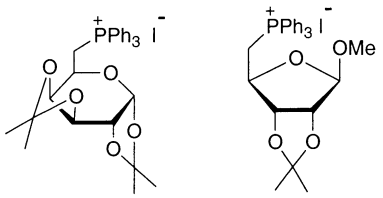
The scope of the above aminohomologation strategy was examined by the conversion of three more furanoses into the corresponding homoazasugars (Figure 3). At first, we decided to prepare another known compound, i.e., the natural product DMDP **1**, for an easy confirmation of the structure of the final product. A retrosynthetic analysis taking into account the stereochemical course of the two bond-forming reactions in Scheme 1, i.e., anti addition of 2-lithiothiazole **6** to the sugar nitrone and inversion of configuration at C-4 of the γ-amino alcohol in the ring closure reaction, indicated the 2,3,5-tri-*O*-benzyl-L-xylofuranose **15** as the starting material in this synthesis. Succintly, the sugar **15** was transformed into its hydroxylamine derivative[27] **16**, which was treated with 2-lithiothiazole **6** to give the anti adduct **17** and the syn isomer (not shown) in 4:1 ratio and 72% overall yield. These adducts were separated, and the major isomer **17** was transformed into the amino alcohol **18**, which in turn was cyclized to the 2-thiazolyl pyrrolidine **19**, the structure of which was assigned by the aid of NOE experiments. Finally, the aldehyde **20** was liberated by cleavage of the thiazole ring and reduced in situ to the alcohol **21**, whose hydrogenolysis afforded the natural product **1** in 17% overall yield from the xylofuranose **15**. By the same reaction sequence were prepared the hitherto unreported 2,5-dideoxy-2,5-imino-L-altritol **29** (23% yield) from the D-ribofuranose derivative **22** and 2,5-dideoxy-2,5-imino-allitol **37** (19% yield) from the D-*lyxo* isomer **30**. Since the overall yields of the isolated homoazasugars **1**, **29**, and **37** are comparable to that of **14**, it can be deduced that all steps in each reaction sequence occurred with similar efficiencies.

Synthesis of Aza-*C*-disaccharides. In contrast to our earlier belief,[17] the formyl *N*-benzyl pyrrolidines **12**, **20**, and **27**, precursors of imino alditols **14**, **1**, and **29**, respectively, turned out to be sufficiently stable products suitable for synthetic elaborations. Compound **12** could be purified, whereas the isomers **20** and **27** were used as crude material. On the other hand, the aldehyde **35** appeared to be a rather unstable compound manipulatable with some difficulty. Thus, we were stimulated to employ only the stable aldehydes in a synthetic route leading to more complex aza-*C*-glycosides such aza-*C*-disaccharides.[15] In analogy to our earlier synthesis of *C*-disaccharides,[28] we intended to pursue this objective via Wittig olefination using the sugar phosphoranes derived from the readily available galactose and ribose phosphonium iodides **38** and **39**, respectively. We planned to obtain by this approach (1→6)- and (1→5)-linked aza-*C*-disaccharides, i.e., genuine methylene isosteres of *O*-disaccharides.

The Wittig reaction of the aldehyde **12** with a slight excess (1.2 equiv) of the ylide generated in situ from the D-galactopyranose phosphonium iodide **38** (Scheme 3) occurred smoothly at −30 °C in THF−HMPA as a solvent

(27) In this case, the presence of the open-chain nitrone form was substantiated by the NMR spectrum showing a doublet at δ 6.75 ppm corresponding to the C*H* proton of the nitrone group.

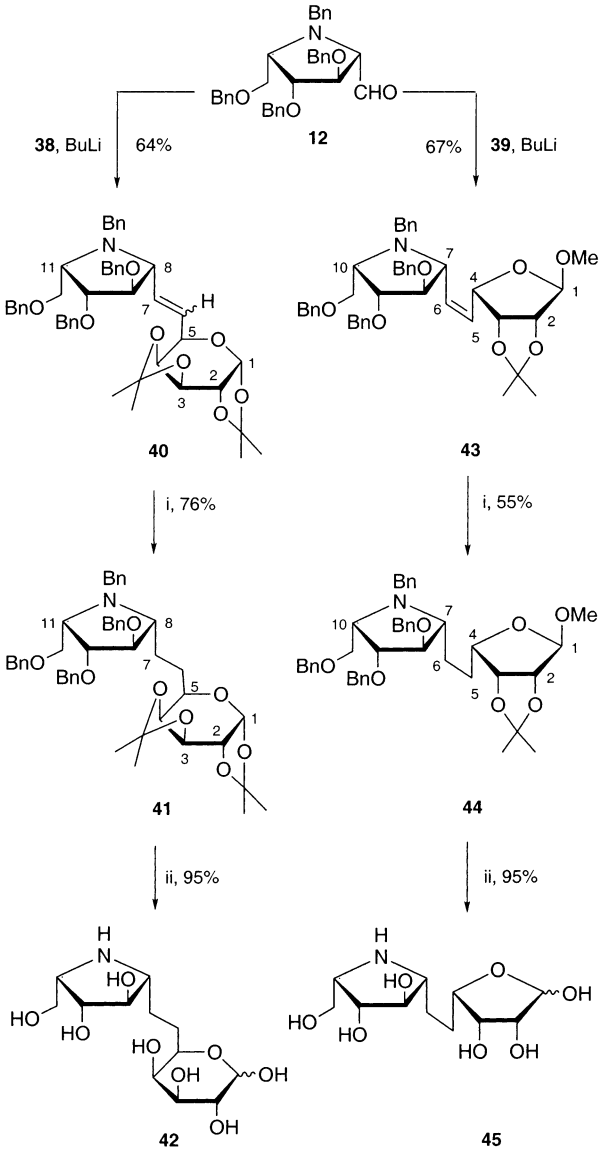
(28) Dondoni, A.; Zuurmond, H. M.; Boscarato, A. *J. Org. Chem.* **1997**, *62*, 8114.



38 **39**

to give, after 2 h, the olefin **40** as a mixture of (*E*)- and (*Z*)-isomers in a ca. 1:1 ratio by NMR analysis and 64% overall yield. Guided by our previous work,[28] we reduced the double bond of these alkenes by in situ-generated diimide from *p*-toluensulfonylhydrazine, thus producing the alkane **41** (76%). The NMR spectrum of this compound confirmed the stereochemistry of its α-D-galactopyranose residue since it exhibited a coupling constant value between H-4 and H-5 ($J_{4,5}$ = 1.8 Hz) almost identical to that of the corresponding protons in the phosphonium salt **38** ($J_{4,5}$ = 2.0 Hz). This finding is in line with earlier observations[28] showing the conservation of the configuration at C-5 in the galactose 6-phosphorane generated from **38**. The removal of the O- and N-protective group in **41** was then carried out in two steps, i.e., by catalytic hydrogenation over $Pd(OH)_2$ for debenzylation and treatment with Amberlite IR 120 for deacetonization. The free aza-(1→6)-*C*-disaccharide **42** featuring D-galactose and 4-amino-L-xylofuranose moieties linked by a methylene bridge was released from the resin with aqueous HCl and purified and characterized as hydrochloride. The same reaction sequence was applied to the synthesis of the aza-(1→5)-*C*-disaccharide **45**, which proved by NMR analysis of its precursor **44** to be constituted by L-lyxo and 4-amino-L-xylofuranose moieties linked by a methylene bridge. The assignment of the L-*lyxo* configuration of the furanose residue in **44** was based on the coupling constant value $J_{3,4}$ = 3.6 Hz, whereas a much lower value ($J_{3,4}$ < 0.5 Hz) was observed in the ribofuranosyl phosphonium iodide **39**. Hence, the original D-ribo configuration of **39** appeared to have been not retained in the course of the Wittig reaction, an observation that has already been made in earlier work from another[29] and this laboratory.[28,30] It has been suggested[29] that epimerization of the *β*-D-*ribo* ylide to the α-L-*lyxo* isomer takes place through an open-chain intermediate arising from the cleavage of the O−C-4 bond.

SCHEME 3[a]



[a] Reagents: (i) $TsNHNH_2$, AcONa. (ii) H_2, 20% $Pd(OH)_2$ then Amberlite IR 120.

Reaction sequences similar to those shown in Scheme 3 were followed to transform the aldehydes **20** and **27** into the (1→6)- and (1→5)-linked aza-*C*-disaccharides **48** and **51** (Figure 4) and **54** and **57** (Figure 5), respectively. The yields of alkenes produced in the Wittig reactions were lower than those registered in Scheme 3 very likely because the aldehydes **20** and **27** were less stable than the isomer **12**. It is worth noting that compounds **48** and **51** contain the same azasugar moiety as that in the natural product DMDP, **1**. Thus, it has been demonstrated that polyhydroxylated chiral pyrrolidine aldehydes **12**, **20**, and **27** can be used as convenient precursors to more complex aza-*C*-glycosides. Therefore, the synthesis of other carbon-linked glycoconjugates by the use of these aldehydes now becomes of interest.

In conclusion, a viable route has been outlined that permits the transformation of furanoses into nitrogen analogues bearing one or more carbon atoms at the anomeric center. The stereochemistry of the asymmetric reactions involved in the aminohomologation sequence appears to be reproducible and predictable so that the synthesis of target products can be planned with some accuracy and confidence. The scope of the methodology has been tested by the synthesis of four homoazasugars starting from furanoses with D-*arabino*, D-*ribo*, D-*lyxo*, and L-*xylo* configurations. A larger collection of these compounds should be accessible either by changing the configuration of the above starting furanoses or by the use of other sugar derivatives in the furanose form. In fact, the method appeared so far applicable only to furanose derivatives since *N*-benzyl hydroxylamines derived from pyranoses have been unreactive in our hands unreactive toward low-temperature-reacting or-

(29) Secrist, J. A., III; Wu, S.-R. *J. Org. Chem.* **1977**, *42*, 4084.
(30) Dondoni, A.; Kleban, M.; Marra, A. *Tetrahedron Lett.* **1997**, *38*, 7801.

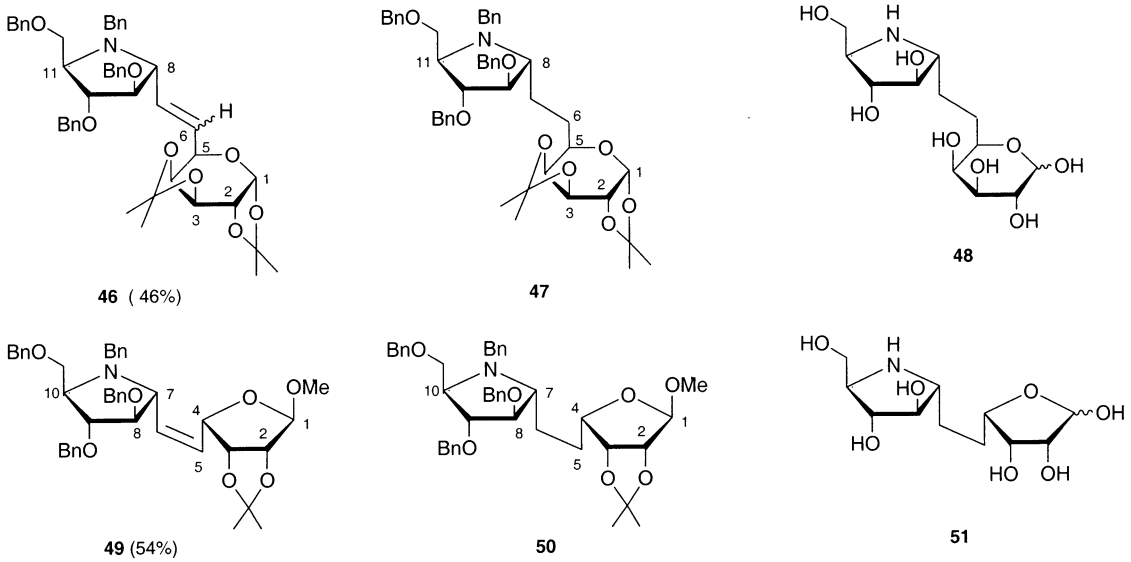


FIGURE 4. Aza-*C*-disaccharides **48** and **51** and the corresponding precursors obtained by Wittig reaction of the aldehyde **20** with the phosphoranes derived from **38** (first raw) and **39** (second raw).

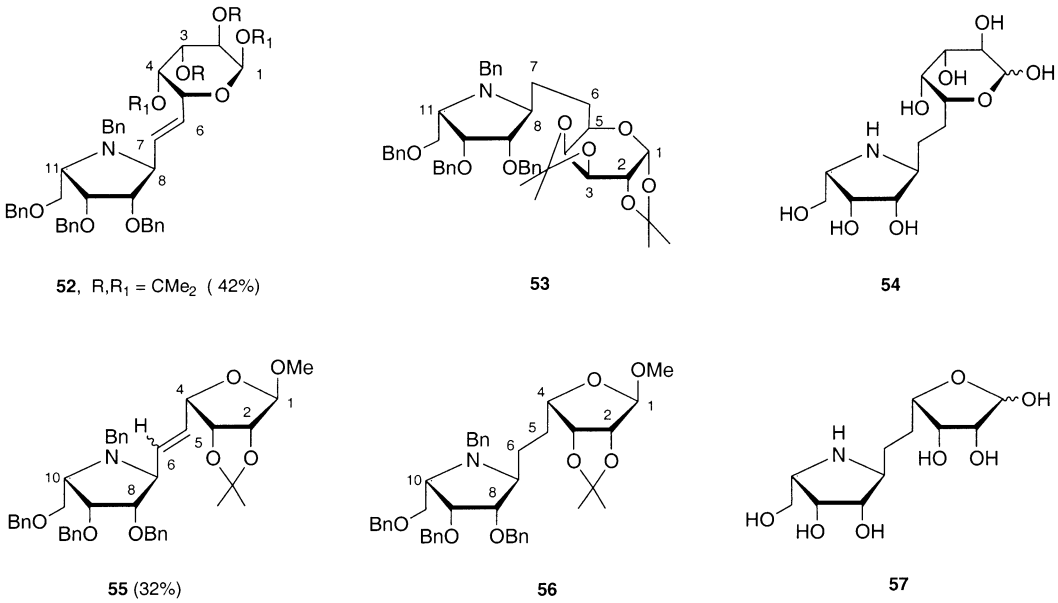


FIGURE 5. Aza-*C*-disaccharides **54** and **57** and the corresponding precursors obtained by Wittig reaction of the aldehyde **27** with the phosphoranes derived from **38** (first raw) and **39** (second raw).

ganometallic species such as 2-lithiothiazole **6**. This indicates a less favorable nitrone−hydroxylamine equilibrium for pyranoses than for furanoses.

An additional interesting feature of the above methodology is the formation of formyl aza-*C*-glycosides as intermediates. These compounds constitute a class of almost unknown azasugar derivatives[31] that, through reactions of the formyl group, can be employed for the construction of a variety of complex azasugar conjugates. It has been demonstrated in this work that these aldehydes are convenient reagents for the preparation of methylene isosteres of (1→6)- and (1→5)-linked disaccharides in which one sugar residue is an azasugar.

Experimental Section

All moisture-sensitive reactions were performed under a nitrogen atmosphere using oven-dried glassware. Solvents were dried over a standard drying agent[32] and freshly distilled prior to use. Commercially available powdered 4 Å molecular sieves (5 μm average particle size) were used without further activation. Reactions were monitored by TLC on silica gel 60 F_{254} with detection by charring with sulfuric acid. Flash column chromatography[33] was performed on silica gel 60 (230−400 mesh). Melting points were determined with a capillary apparatus. Optical rotations were measured at 20 ± 2 °C in the stated solvent; $[\alpha]_D$ values are given in 10^{-1} deg cm^2 g^{-1}. ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra were recorded for $CDCl_3$ solutions at room temperature unless otherwise

(31) We are aware of only one sufficiently stable formyl pyrrolidine, which was prepared by oxidation of the corresponding 2,5-dideoxy-2,5-imino-glucitol. See ref 13.

(32) Armarego, W. L. F.; Perrin, D. D. *Purification of Laboratory Chemicals*, 4th ed.; Butterworth−Heinemann; Oxford, 1996.

(33) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

specified. Assignments were aided by homo-two-dimensional experiments. MALDI-TOF mass spectra were acquired using α-cyano-4-hydroxycinnamic acid as the matrix. Arabinofuranoside **3**,[34] xylofuranoside **15**,[34] ribofuranoside **22**,[34] lyxofuranoside **30**,[34] galactose phosphonium iodide **38**,[35] and ribose phosphonium iodide **39**[29] were synthesized as described.

1-(*N*-Benzylhydroxylamino)-2,3,5-tri-*O*-benzyl-1-deoxy-α-D-arabinose (4). A mixture of **3** (10.0 g, 23.8 mmol) and *N*-benzylhydroxylamine (3.50 g, 28.4 mmol) was stirred at 110 °C for 30 min. The resulting residue was crystallized from cyclohexane to give **4** (11.0 g, 88%) as a white solid. Mp 68−70 °C. $[\alpha]_D^{20}$ = +29.6 (*c* 1.0, $CHCl_3$). ^{1}H NMR: δ 7.45−7.20 (m, 20 H, 4 Ph), 4.78 (d, 1 H, $J_{1,2}$ = 4.5 Hz, H-1), 4.73−4.51 (m, 6 H, 3 PhCH_2), 4.48 (dd, 1 H, $J_{2,3}$ = 5.2 Hz, H-2), 4.33 (ddd, 1 H, $J_{3,4}$ = 7.1, $J_{4,5a}$ = 3.2, $J_{4,5b}$ = 5.2 Hz, H-4), 4.22 and 3.95 (2 d, 2 H, *J* = 13.0 Hz, PhCH_2N), 4.13 (d, 1 H, H-3), 3.70 (dd, 1 H, $J_{5a,5b}$ = 11.0 Hz, H-5a), 3.59 (dd, 1 H, H-5b). Anal. Calcd for $C_{33}H_{35}NO_5$: C, 75.40; H, 6.71; N, 2.66. Found: C, 75.51; H, 6.53; N, 2.84.

(1*S*,2*R*,3*R*,4*R*)- and (1*R*,2*R*,3*R*,4*R*)-1-*N*-Benzylhydroxylamino-2,3,5-tribenzyloxy-1-(2-thiazolyl)-4-pentanol (7). To a cooled (−78 °C) and stirred solution of *n*-BuLi (19.6 mL, 31.4 mmol of a 1.6 M solution in hexane) in dry Et_2O (110 mL) was added dropwise a solution of freshly distilled 2-bromothiazole (2.83 mL, 31.4 mmol) in dry Et_2O (23.0 mL). The rate of addition was adjusted so as to keep the temperature of the reaction mixture below −70 °C. After the pale yellow solution of 2-lithiothiazole (**6**) had been stirred at this temperature for 20 min, a solution of the D-arabinose-derived *N*-benzylhydroxylamine **4** (3.00 g, 5.71 mmol) in dry THF (30.0 mL) was added slowly while the temperature of the mixture was maintained below −65 °C. The reaction mixture was stirred at −70 °C for 5 h, and then aqueous phosphate buffer (50 mL, pH 7) was added the mixture allowed to warm to room temperature. The layers were separated, and the aqueous layer was extracted with AcOEt (3 × 50 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated. The crude residue was eluted from a column of silica gel with 2:1 cyclohexane−AcOEt to give **7** (2.60 g, 75%) as a mixture of diastereoisomers in a 9:1 ratio (by ^{1}H NMR analysis). ^{1}H NMR (selected data): δ 7.90 (d, 1 H, *J* = 3.2 Hz, Th), 7.42−7.15 and 6.98−6.90 (m, 21 H, 4 Ph, Th), 6.62 (s, 0.9 H, NO*H*), 5.99 (s, 0.1 H, NO*H*). Anal. Calcd for $C_{36}H_{38}N_2O_5S$: C, 70.79; H, 6.27; N, 4.59. Found: C, 70.44; H, 6.39; N, 4.44.

(1*S*,2*R*,3*R*,4*R*)- and (1*R*,2*R*,3*R*,4*R*)-1-*N*-Benzylamino-2,3,5-tribenzyloxy-1-(2-thiazolyl)-4-pentanol (8) and (9). To a solution of $(AcO)_2Cu{\cdot}H_2O$ (0.17 g, 0.85 mmol) in AcOH (10.0 mL) was added Zn dust (2.78 g, 42.5 mmol). The resulting suspension was vigorously stirred at room temperature for 15 min, and then a solution of benzylhydroxylamines **7** (2.60 g, 4.26 mmol) in 3:1 AcOH/H_2O (12.0 mL) was added and the suspension warmed to 70 °C for 45 min. The suspension was filtered through Celite, and the collected solution was neutralized with an aqueous solution of NaOH (3 M), extracted with AcOEt (3 × 10 mL), and washed with a saturated aqueous solution of EDTA (30 mL). The organic phase was dried (Na_2SO_4) and concentrated. Chromatography on silica gel of the residue with 3:2 cyclohexane−AcOEt afforded as the first eluate the *N*-benzylamine **9** (0.20 g, 8%) as a syrup. $[\alpha]_D^{20}$ = +29.1 (*c* 2.5, $CHCl_3$). ^{1}H NMR: δ 7.79 and 7.40 (2d, 2 H, *J* = 3.2 Hz, Th), 7.38−7.10 (m, 20 H, 4 Ph), 4.72 (s, 1 H, O*H*), 4.59 and 4.37 (2 d, 2 H, *J* = 10.5 Hz, PhCH_2), 4.60−4.46 (m, 5H, H-1, 2 PhCH_2), 4.01 (ddd, 1 H, $J_{3,4}$ = 6.7, $J_{4,5a}$ = 4.5, $J_{4,5b}$ = 5.6 Hz, H-4), 3.97 (dd, 1 H, $J_{1,2}$ = 3.4, $J_{2,3}$ = 4.2 Hz, H-2), 3.87 (dd, 1 H, H-3), 3.80 and 3.70 (2 d, 2 H, *J* = 12.5 Hz, PhCH_2N), 3.69 (dd, 1 H, $J_{5a,5b}$ = 9.8 Hz, H-5a), 3.61 (dd, 1 H, H-5b). Anal. Calcd for $C_{36}H_{38}N_2O_4S$: C, 72.70; H, 6.44; N, 4.71. Found: C, 72.91; H, 6.52; N, 4.52.

Eluted next was the *N*-benzylamine **8** (1.98 g, 78%) as a syrup. $[\alpha]_D^{20}$ = +20.9 (*c* 1.1, $CHCl_3$). ^{1}H NMR: δ 7.82 (d, 1 H, *J* = 3.2 Hz, Th), 7.40−7.10 (m, 21 H, 4 Ph, Th), 4.63 and 4.45 (2 d, 2 H, *J* = 11.0 Hz, PhCH_2), 4.52 and 4.28 (2 d, 2 H, *J* = 11.5 Hz, PhCH_2), 4.52−4.46 (m, 3 H, H-1, PhCH_2), 4.04 (dd, 1 H, $J_{1,2}$ = 6.5, $J_{2,3}$ = 3.5 Hz, H-2), 4.01−3.93 (m, 1 H, H-4), 3.81 (dd, 1 H, $J_{3,4}$ = 7.5 Hz, H-3), 3.75 and 3.59 (2 d, 2 H, *J* = 13.0 Hz, PhCH_2N), 3.63−3.58 (m, 2 H, H-5a, H-5b), 2.92 (s, 1 H, O*H*). Anal. Calcd for $C_{36}H_{38}N_2O_4S$: C, 72.70; H, 6.44; N, 4.71. Found: C, 72.98; H, 6.72; N, 4.65.

(2*S*,3*R*,4*R*,5*S*)-*N*-Benzyl-3,4-dibenzyloxy-5-benzyloxymethyl-2-(2-thiazolyl)pyrrolidine (10). To a solution of the *N*-benzylamine **8** (0.66 g, 1.11 mmol) in dry pyridine (2.0 mL) were added activated 4 Å powdered molecular sieves (0.20 g) and Tf_2O (0.78 g, 2.77 mmol). The resulting mixture was stirred at 40 °C for 30 min, treated with CH_3OH (0.3 mL), and cooled to room temperature. After being stirred for 10 min at room temperature, the mixture was filtered through Celite and concentrated. Chromatography on silica gel of the residue with 4:1 cyclohexane−AcOEt afforded the thiazolylpirrolidine **10** (0.42 g, 65%) as a syrup. $[\alpha]_D^{20}$ = +28.7 (*c* 0.4, $CHCl_3$). ^{1}H NMR: δ 7.67 and 7.17 (2d, 2 H, *J* = 3.2 Hz, Th), 7.40−7.20 and 7.10−7.00 (m, 20 H, 4 Ph), 4.67 and 4.53 (2 d, 2 H, *J* = 12.0 Hz, PhCH_2), 4.45 (s, 2H, PhCH_2), 4.42 (d, 1 H, $J_{2,3}$ = 2.5 Hz, H-2), 4.40 and 4.35 (2 d, 2 H, *J* = 12.0 Hz, PhCH_2), 4.25 (dd, 1 H, $J_{3,4}$ = 2.5 Hz, H-3), 4.08 (dd, 1 H, $J_{4,5}$ = 5.0 Hz, H-4), 4.03 and 3.96 (2 d, 2 H, *J* = 13.0 Hz, PhCH_2N), 3.81 (dd, 1 H, $J_{5,5'a}$ = 8.9, $J_{5'a,5'b}$ = 11.0 Hz, H-5′a), 3.61−3.53 (m, 2 H, H-5, H-5′b). Anal. Calcd for $C_{36}H_{36}N_2O_3S$: C, 74.97; H, 6.29; N, 4.86. Found: C, 74.81; H, 6.35; N, 4.66.

(2*R*,3*R*,4*R*,5*S*)-*N*-Benzyl-3,4-dibenzyloxy-5-benzyloxymethyl-2-(2-thiazolyl)pyrrolidine (11). The reaction was carried out as described above for **10** starting from **9** (0.11 g, 0.18 mmol) to give after flash chromatography (4:1 cyclohexane−AcOEt) the thiazolylpyrrolidine **11** (73.0 mg, 70%) as a syrup. $[\alpha]_D^{20}$ = −79.3 (*c* 0.5, $CHCl_3$). ^{1}H NMR: δ 7.75 (d, 1 H, *J* = 3.2 Hz, Th), 7.40−7.20 and 7.10−7.00 (m, 21 H, 4 Ph, Th), 5.02 (d, 1 H, $J_{2,3}$ = 8.1 Hz, H-2), 4.67 (dd, 1 H, $J_{3,4}$ = 7.4 Hz, H-3), 4.62 and 4.49 (2 d, 2 H, *J* = 12.0 Hz, PhCH_2), 4.56 (s, 2 H, PhCH_2), 4.51 and 4.38 (2 d, 2 H, *J* = 11.5 Hz, PhCH_2), 4.38 (dd, 1 H, $J_{4,5}$ = 7.4 Hz, H-4), 3.86 and 3.76 (2 d, 2 H, *J* = 13.5 Hz, PhCH_2N), 3.68 (dd, 1 H, $J_{5,5'a}$ = 3.4 Hz, $J_{5'a,5'b}$ = 10.0 Hz, H-5′a), 3.54 (dd, 1 H, $J_{5,5'b}$ = 2.0 Hz, H-5′b) 3.35 (ddd, 1 H, H-5). Anal. Calcd for $C_{36}H_{36}N_2O_3S$: C, 74.97; H, 6.29; N, 4.86. Found: C, 74.79; H, 6.35; N, 4.78.

***N*-Benzyl-3,4,6-tri-*O*-benzyl-2,5-dideoxy-2,5-imino-D-glucitol (13).** A mixture of the thiazolylpirrolidine **10** (0.50 g, 0.87 mmol) and activated 4 Å powdered molecular sieves (1.74 g) in dry CH_3CN (9.0 mL) was stirred at room temperature for 10 min and then treated with methyl triflate (0.20 mL, 1.74 mmol). The suspension was stirred for 30 min and then concentrated to dryness. The residue was suspended in CH_3OH (9.0 mL), cooled (ice-bath), and treated with $NaBH_4$ (72.0 mg, 1.91 mmol). The resulting mixture was stirred at room temperature for 10 min, diluted with acetone (1 mL) filtered through Celite, and concentrated. To a solution of the residue in 10:1 CH_3CN-H_2O (9.0 mL) was added $AgNO_3$ (0.18 g, 1.04 mmol). The yellow mixture was stirred at room temperature for 10 min, cooled (ice-bath), and treated with $NaBH_4$ (72.0 mg, 1.91 mmol). The dark mixture was stirred at room temperature for 15 min, diluted with acetone (1 mL), filtered through a pad of Florisil (100−200 mesh), and concentrated. Chromatography on silica gel of the residue with 4:1 cyclohexane−AcOEt afforded the alcohol **13** (0.34 g, 74%) as a syrup. $[\alpha]_D^{20}$ = +25.7 (*c* 1.5, $CHCl_3$). ^{1}H NMR: δ 7.40−7.20 (m, 20 H, 4 Ph), 4.61 and 4.52 (2 d, 2 H, *J* = 12.0 Hz, PhCH_2), 4.59 and 4.51(2 d, 2 H, *J* = 12.0 Hz, PhCH_2), 4.45 (s, 2 H, PhCH_2), 4.07 (dd, 1 H, $J_{2,3}$ = $J_{3,4}$ = 3.5 Hz, H-3), 4.02 (dd, 1 H, $J_{4,5}$ = 5.5 Hz, H-4), 3.93 and 3.80 (2 d, 2 H, *J* = 14.0 Hz, PhCH_2N), 3.61 (dd, 1 H, $J_{5,6a}$ = 6.5, $J_{6a,6b}$ = 9.5 Hz, H-6a), 3.52−3.34 (m, 4 H, H-1a, H-1b, H-5, H-6b), 3.02−2.97 (m, 1

(34) Dondoni, A.; Marra, A. *Tetrahedron Lett.* **1993**, *34*, 7327.
(35) Secrist, J. A., III; Wu, S.-R. *J. Org. Chem.* **1979**, *44*, 1434.

H, H-2), 2.80 (s, 1 H, OH). Anal. Calcd for $C_{34}H_{37}NO_4$: C, 77.98; H, 7.12; N, 2.67. Found: C, 78.25; H, 7.31; N, 2.95.

A separated experiment afforded the crude aldehyde **12** when after the addition of $AgNO_3$, the resulting yellow mixture, stirred for 10 min at room temperature, was diluted with aqueous phosphate buffer (5 mL, pH 7) and filtered through Celite. The filtrate was extracted with AcOEt (3 × 20 mL), and the organic phase was dried (Na_2SO_4) and concentrated. The residue was eluted from a short column (1 × 10 cm, d × h) of silica gel with 8:1 cyclohexane−AcOEt to afford the aldehyde **12** (0.33 g, 73%) in ca. 95% purity by ^{1}H NMR analysis. ^{1}H NMR: δ 9.34 (d, 1 H, J = 1.5 Hz, CHO), 4.61 and 4.53 (2 d, 2 H, J = 11.5 Hz, PhCH_2), 4.59, (s, 2 H, PhCH_2), 4.49 and 4.37 (2 d, 2 H, J = 11.5 Hz, PhCH_2), 4.28 and 3.74 (2 d, 2 H, J = 13.0 Hz, PhCH_2N), 4.14−4.08 (m, 2 H, H-3, H-4), 3.94 (dd, 1 H, $J_{5,5'a}$ = 7.0, $J_{5'a,5'b}$ = 9.0 Hz, H-5′a), 3.77 (dd, 1 H, $J_{5,5'b}$ = 5.0 Hz, H-5′b), 3.59 (ddd, 1 H, $J_{4,5}$ = 4.0 Hz, H-5), 3.39−3.37 (m, 1 H, H-2).

2,5-Dideoxy-2,5-imino-D-glucitol (14). A solution of the alcohol **13** (0.35 g, 0.67 mmol) in AcOH (5.0 mL) was debenzylated with H_2 over 20% $Pd(OH)_2$ (0.20 g) at atmospheric pressure for 12 h. The mixture was filtered through Celite and concentrated, and then the crude residue was purified by ion-exchange chromatography Dowex 1 × 8 (100−200 mesh) and eluted with H_2O to give **14** (87.0 mg, 80%) as a white solid. Mp 138−140 °C (lit.[36] 139−142.5). $[\alpha]_D^{20}$ = +25.1 (*c* 1.5, H_2O) (lit.[37] $[\alpha]_D^{23}$ = +25.75 (*c* 4.00, H_2O). ^{1}H NMR (D_2O): δ 3.93 (dd, 1 H, $J_{3,4}$ = 3.0 Hz, $J_{4,5}$ = 5.0 Hz, H-4), 3.68 (dd, 1 H, $J_{2,3}$ = 5.2 Hz, H-3), 3.60 (dd, 1 H, $J_{5,6a}$ = 6.0 Hz, $J_{6a,6b}$ = 11.0 Hz, H-6a), 3.55 (dd, 1 H, $J_{1a,1b}$ = 11.0 Hz, $J_{1a,2}$ = 5.0 Hz, H-1a), 3.48 (dd, 1 H, $J_{5,6b}$ = 6.5 Hz, H-6b), 3.45 (dd, 1 H, $J_{1b,2}$ = 6.0 Hz, H-1b), 3.14 (q, 1 H, H-5), 2.83 (q, 1 H, H-2). Anal. Calcd for $C_6H_{13}NO_4$: C, 44.16; H, 8.03; N, 8.58. Found: C, 44.35; H, 8.27; N, 8.36.

1-(*N*-Benzylhydroxylamino)- 2,3,5-tri-*O*-benzyl-1-deoxy-L-xylose (16). The reaction was carried out as descibed above for **4** starting from **15** (10.0 g, 23.8 mmol) to give after flash chromatography (5:1 cyclohexane−AcOEt) the hydroxylamine **16** (10.25 g, 82%) as a syrup: $[\alpha]_D^{20}$ = +18.7 (*c* 2.4, $CHCl_3$). Compound **16** appeared by ^{1}H NMR analysis as a complex mixture of the two C-1 anomers besides the open-chain derivative. ^{1}H NMR (selected data for the open-chain form): δ 6.73 (d, 1 H, $J_{1,2}$ = 7.0 Hz, H-1). Anal. Calcd for $C_{33}H_{35}NO_5$: C, 75.40; H, 6.71; N, 2.66. Found: C, 75.55; H, 6.83; N, 2.48.

(1*S*,2*R*,3*R*,4*S*)-1-*N*-Benzylhydroxylamino-2,3,5-tribenzyloxy-1-(2-thiazolyl)-4-pentanol (17). The addition of 2-lithiothiazole **6** to the hydroxylamine **16** (3.00 g, 5.71 mmol) was carried out as described for **7**. The crude residue was a 4:1 mixture of **17** and its C-1 epimer (by ^{1}H NMR analysis). Chromatography on silica gel of the crude residue with 3:1 cyclohexane−AcOEt afforded as the first eluate the benzylhydroxylamine **17** (1.90 g, 55%) as a syrup: $[\alpha]_D^{20}$ = +9.6 (*c* 1.5 $CHCl_3$). ^{1}H NMR: δ 7.91 and 7.42 (2 d, 2H, J = 3.2 Hz, Th), 7.40−7.15 and 6.95−6.85 (m, 20 H, 4 Ph), 6.52 (s, 1 H, OH), 4.92 (s, 1 H, OH), 4.67 (d, 1 H, $J_{1,2}$ = 9.0 Hz, H-1), 4.66 and 4.58 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.57 and 4.49 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.32 and 4.05 (2 d, 2 H, J = 11.5 Hz, PhCH_2), 4.32−4.27 (m, 1 H, H-4), 4.25 (dd, 1 H, $J_{2,3}$ = 4.0 Hz, H-2), 4.04 (dd, 1 H, $J_{3,4}$ = 2.5 Hz, H-3), 3.76 and 3.60 (2 d, 2 H, J = 13.5 Hz, PhCH_2N), 3.66 (dd, 1 H, $J_{4,5a}$ = 5.5, $J_{5a,5b}$ = 9.5 Hz, H-5a), 3.58 (dd, 1 H, $J_{4,5b}$ = 7.5 Hz, H-5b). Anal. Calcd for $C_{36}H_{38}N_2O_5S$: C, 70.79; H, 6.27; N, 4.59. Found: C, 70.95; H, 6.39; N, 4.49.

Eluted next was the C-1 epimer of **17** (0.6 g, 17%) as a white solid. Mp 134−135 °C (CH_3CN). $[\alpha]_D^{20}$ = −4.8 (*c* 1.1, $CHCl_3$). ^{1}H NMR: δ 7.90 and 7.42 (2 d, 2 H, J = 3.2 Hz, Th), 7.40−7.15 (m, 20 H, 4 Ph), 6.12 (s, 1 H, OH), 4.90 (d, 1 H, $J_{1,2}$ = 4.0 Hz, H-1), 4.70 and 4.62 (2 d, 2 H, J = 11.0 Hz, PhCH_2), 4.61 and 4.56 (2 d, 2 H, J = 11.5 Hz, PhCH_2), 4.52 and 4.45 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.23 (dd, 1 H, $J_{2,3}$ = 6.5 Hz, H-2), 4.24−4.17 (m, 1 H, H-4), 3.96 (s, 1 H, OH), 3.89 (dd, 1 H, $J_{3,4}$ = 2.5 Hz, H-3), 3.85 and 3.79 (2 d, 2 H, J = 13.0 Hz, PhCH_2N), 3.57 (dd, 1 H, $J_{4,5a}$ = 6.0, $J_{5a,5b}$ = 9.0 Hz, H-5a), 3.49 (dd, 1 H, $J_{4,5b}$ = 7.0 Hz, H-5b). Anal. Calcd for $C_{36}H_{38}N_2O_5S$: C, 70.79; H, 6.27; N, 4.59. Found: C, 70.88; H, 6.11; N, 4.68.

(1*S*,2*R*,3*R*,4*S*)-1-*N*-Benzylamino-2,3,5-tribenzyloxy-1-(2-thiazolyl)-4-pentanol (18). The benzylhydroxylamine **17** (2.50 g, 4.09 mmol) was processed as described above for **7** to give the crude syrup **18** (2.30 g, 95%) in ca. 95% purity by ^{1}H NMR analysis. The crude product was used for the next reaction without further purification. A pure sample of **18** was obtained by flash chromatograpy with 3:2 cyclohexane−AcOEt. $[\alpha]_D^{20}$ = +5.6 (*c* 1.3, $CHCl_3$). ^{1}H NMR: δ 7.82 (d, 1 H, J = 3.2 Hz, Th), 7.40−7.10 (m, 21 H, 4 Ph, Th), 4.68 and 4.49 (2 d, 2 H, J = 11.0 Hz, PhCH_2), 4.55 and 4.38 (2 d, 2 H, J = 11.0 Hz, PhCH_2), 4.51 and 4.44 (2 d, 2 H, J = 11.5 Hz, PhCH_2), 4.46 (d, 1 H, $J_{1,2}$ = 6.0 Hz, H-1), 4.12 (dd, 1 H, $J_{2,3}$ = 5.5 Hz, H-2), 4.08 (ddd, 1 H, $J_{3,4}$ = 2.5 Hz, $J_{4,5a}$ = $J_{4,5b}$ = 6.0 Hz, H-4), 3.81 (dd, 1 H, H-3), 3.73 and 3.63 (2 d, 2 H, J = 13.0 Hz, PhCH_2N), 3.56 (d, 1 H, $J_{5a,5b}$ = 10.0 Hz, H-5a), 3.50 (d, 1 H, H-5b), 3.20−3.00 (m, 1 H, OH). Anal. Calcd for $C_{36}H_{38}N_2O_4S$: C, 72.70; H, 6.44; N, 4.71. Found: C, 72.98; H, 6.67; N, 4.68.

(2*S*,3*R*,4*R*,5*R*)-*N*-Benzyl-3,4-dibenzyloxy-5-benzyloxymethyl-2-(2-thiazolyl)pyrrolidine (19). The reaction was carried out as described above for **10** starting from crude **18** (1.0 g, 1.68 mmol) to give after flash chromatography (4:1 cyclohexane−AcOEt) the thiazolylpyrrolidine **19** (0.69 g, 71%) as a syrup. $[\alpha]_D^{20}$ = +19.7 (*c* 1.2, $CHCl_3$). ^{1}H NMR: δ 7.75 (d, 1 H, J = 3.2 Hz, Th), 7.40−7.15 (m, 21 H, 4 Ph, Th), 4.70 (d, 1 H, $J_{2,3}$ = 5.5 Hz, H-2), 4.62 and 4.42 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.51 (s, 2 H, PhCH_2), 4.48 and 4.44 (2 d, 2 H, J = 11.0 Hz, PhCH_2), 4.24 (dd, 1 H, $J_{3,4}$ = 3.5 Hz, $J_{4,5}$ = 2.5 Hz, H-4), 4.17 (dd, 1 H, H-3), 3.81 and 3.70 (2 d, 2 H, J = 14.5 Hz, PhCH_2N), 3.63 (dd, 1 H, $J_{5,5'a}$ = 5.0, $J_{5'a,5'b}$ = 9.5 Hz, H-5′a), 3.50 (dd, 1 H, $J_{5,5'b}$ = 3.5 Hz, H-5′b), 3.44−3.50 (m, 1 H, H-5). Anal. Calcd for $C_{36}H_{36}N_2O_3S$: C, 74.97; H, 6.29; N, 4.86. Found: C, 74.88; H, 6.25; N, 4.89.

***N*-Benzyl-3,4,6-tri-*O*-benzyl-2,5-dideoxy-2,5-imino-D-mannitol (21).** The thiazolylpyrrolidine **19** (0.60 g, 1.04 mmol) was processed as described above for the synthesis of **13**. Chromatography on silica gel with 4:1 cyclohexane−AcOEt afforded the alcohol **21** (0.39 g, 72%) as a syrup. $[\alpha]_D^{20}$ = −19.3 (*c* 1.5, $CHCl_3$). ^{1}H NMR: δ 7.40−7.20 (m, 20 H, 4 Ph), 4.57 and 4.46 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.55 and 4.45 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.52 (s, 2 H, PhCH_2), 4.12−4.08 (m, 1 H, H-3), 4.08−4.05 (m, 1 H, H-4), 3.94 and 3.84 (2 d, 2 H, J = 14.0 Hz, PhCH_2N), 3.76 (dd, 1 H, $J_{1a,1b}$ = 11.5 Hz, $J_{1a,2}$ = 3.5 Hz, H-1a), 3.68−3.54 (m, 3 H, H-1b, H-6a, H-6b), 3.50−3.44 (m, 1 H, H-5), 3.24−3.19 (m, 1 H, H-2), 2.90−2.50 (m, 1 H, OH). Anal. Calcd for $C_{34}H_{37}NO_4$: C, 77.98; H, 7.12; N, 2.67. Found: C, 78.28; H, 7.23; N, 2.58.

A separated experiment afforded the crude aldehyde **20** (0.46 g, 85%; ca. 90% pure by ^{1}H NMR analysis) as described above for the synthesis of the aldehyde **12**. ^{1}H NMR: δ 9.52 (d, 1 H, J = 3.5 Hz, CHO), 7.40−7.15 (m, 20 H, 4 Ph), 4.58−4.42 (m, 6 H, 3 PhCH_2), 4.12 (dd, 1 H, $J_{3,4}$ = 2.0 Hz, $J_{4,5}$ = 4.5 Hz, H-4), 4.06 and 3.92 (2 d, 2 H, J = 14.0 Hz, PhCH_2N), 4.06 (dd, 1 H, $J_{2,3}$ = 4.0 Hz, H-3), 3.65 (dd, 1 H, H-2), 3.62−3.52 (m, 3 H, H-5, H-5′a, H-5′b). Attempts to purify this compound by a short column (1 × 10 cm, d × h) of silica gel led to extensive decomposition.

2,5-Dideoxy-2,5-imino-D-mannitol (1). A solution of the alcohol **21** (0.35 g, 0.67 mmol) in AcOH (5.0 mL) was debenzylated and purified as described above for **13** to give **1** (85.0 mg, 78%) as an hygroscopic gum. $[\alpha]_D^{20}$ = +54.2 (*c* 1.0, H_2O) (lit.[7] $[\alpha]_D^{20}$ = +56.4 (*c* 7.0, H_2O). ^{1}H NMR (D_2O): δ 3.66−3.74 (m, 2 H, H-3, H-4), 3.59 (dd, 2 H, J = 4.5, 11.5 Hz, H-1a, H-6a), 3.49 (dd, 2 H, J = 6.0, 11.5 Hz, H-1b, H-6b), 2.94−2.84 (m, 2 H, H-2, H-5). Anal. Calcd for $C_6H_{13}NO_4$: C, 44.16; H, 8.03; N, 8.58. Found: C, 43.92; H, 8.29; N, 8.48.

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1-(*N*-Benzylhydroxylamino)-2,3,5-tri-*O*-benzyl-1-deoxy-D-ribose (23). The reaction was carried out as descibed above for **4** starting from **22** (10.0 g, 23.8 mmol) to give after crystallization from cyclohexane the hydroxylamine **23** (10.0 g, 80%) as a white solid: mp 84−85 °C (cyclohexane); $[\alpha]_D^{20} = +39.2$ (*c* 0.9, $CHCl_3$). Compound **23** appeared by NMR analysis as a complex mixture of the two C-1 anomers besides the open-chain derivative. ^{1}H NMR (selected data for the open-chain form): δ 6.93 (d, 1 H, $J_{1,2} = 6.5$ Hz, H-1). Anal. Calcd for $C_{33}H_{35}NO_5$: C, 75.40; H, 6.71; N, 2.66. Found: C, 75.27; H, 6.59; N, 2.45.

(1*R*,2*S*,3*R*,4*R*)-1-*N*-Benzylhydroxylamino-2,3,5-tribenzyloxy-1-(2-thiazolyl)-4-pentanol (24). The addition of 2-lithiothiazole **6** to the hydroxylamine **23** (3.00 g, 5.71 mmol) was carried out as described for **7**. Chromatography on silica gel of the crude residue with 3:1 cyclohexane−AcOEt afforded the benzylhydroxylamine **24** (2.51 g, 72%) as a syrup. $[\alpha]_D^{20} = +22.1$ (*c* 0.8, $CHCl_3$). ^{1}H NMR: δ 7.88 and 7.40 (2 d, 2 H, $J =$ 3.2 Hz, Th), 7.38−7.15 and 6.96−6.87 (m, 21, OH, 4 Ph), 4.83 and 4.49 (2 d, 2 H, $J = 10.0$ Hz, PhCH_2), 4.76 and 4.58 (2 d, 2 H, $J = 11.5$ Hz, PhCH_2), 4.52−4.45 (m, 2 H, H-1, H-2), 4.48−4.16 (2 d, 2 H, $J = 11.5$ Hz, PhCH_2), 4.50−4.22 (m, 1 H, H-4), 4.08 (dd, 1 H, $J_{2,3} = 1.2$ Hz, $J_{3,4} = 8.0$ Hz, H-3), 3.92−3.88 (m, 1 H, OH), 3.87 and 3.74 (2 d, 2 H, $J = 14.0$ Hz, PhCH_2N), 3.69 (dd, 1 H, $J_{4,5a} = 3.8$ Hz, $J_{5a,5b} = 9.0$ Hz, H-5a), 3.59 (dd, 1 H, $J_{4,5b} = 5.0$ Hz, H-5b). Anal. Calcd for $C_{36}H_{38}N_2O_5S$: C, 70.79; H, 6.27; N, 4.59. Found: C, 70.53; H, 6.43; N, 4.38.

(1*R*,2*S*,3*R*,4*R*)-1-*N*-Benzylamino-2,3,5-tribenzyloxy-1-(2-thiazolyl)-4-pentanol (25). The benzylhydroxylamine **24** (2.50 g, 4.10 mmol) was processed as described above for **7** to give the crude syrup **25** (2.30 g, 95%) in ca. 95% purity by ^{1}H NMR analysis. The crude product was used for the next reaction without further purification. A pure sample of **25** was obtained by flash chromatography with 3:2 cyclohexane−AcOEt. $[\alpha]_D^{20} = +12.3$ (*c* 0.5, $CHCl_3$). ^{1}H NMR: δ 7.78 (d, 1 H, $J =$ 3.2 Hz, Th), 7.40−7.20 and 7.05−6.95 (m, 21 H, 4 Ph, Th), 4.68 and 4.58 (2 d, 2 H, $J = 12.0$ Hz, PhCH_2), 4.52 (s, 2 H, PhCH_2), 4.50 (d, 1 H, $J_{1,2} = 8.0$ Hz, H-1), 4.44 and 4.23 (2 d, 2 H, $J = 11.5$ Hz, PhCH_2), 4.10 (ddd, 1 H, $J_{3,4} = 6.0$ Hz, $J_{4,5a} = J_{4,5b} = 5.0$ Hz, H-4), 4.04 (dd, 1 H, $J_{2,3} = 2.0$ Hz, H-2), 3.99 (dd, 1 H, H-3), 3.77 and 3.70 (2 d, 2 H, $J = 12.5$ Hz, PhCH_2N), 3.60 (dd, 1 H, $J_{5a,5b} = 11.5$ Hz, H-5a), 3.57 (dd, 1 H, H-5b). Anal. Calcd for $C_{36}H_{38}N_2O_4S$: C, 72.70; H, 6.44; N, 4.71. Found: C, 72.57; H, 6.22; N, 4.69.

(2*R*,3*S*,4*R*,5*S*)-*N*-Benzyl-3,4-dibenzyloxy-5-benzyloxymethyl-2-(2-thiazolyl)pyrrolidine (26). The reaction was carried out as described above for **10** starting from crude **25** (1.0 g, 1.68 mmol) to give after flash chromatography (4:1 cyclohexane−AcOEt) the thiazolylpyrrolidine **26** (0.66 g, 68%) as a syrup. $[\alpha]_D^{20} = -20.4$ (*c* 1.2, $CHCl_3$). ^{1}H NMR: δ 7.75 (d, 1 H, $J =$ 3.2 Hz, Th), 7.35−7.20 (m, 21 H, 4 Ph, Th), 4.82 and 4.70 (2 d, 2 H, $J = 12.0$ Hz, PhCH_2), 4.59 (d, 1 H, $J_{2,3} = 1.8$ Hz, H-2), 4.53 (s, 2 H, PhCH_2), 4.45 (s, 2 H, PhCH_2), 4.26 (dd, 1 H, $J_{3,4} = J_{4,5} = 6.0$ Hz, H-4), 4.03 (dd, 1 H, $J_{5,5'a} = 7.1$ Hz, $J_{5'a,5'b} = 10.6$ Hz, H-5′a), 3.93 (dd, 1 H, H-3), 3.92−3.88 (m, 1 H, H-5′b), 4.11 and 3.86 (2 d, 2 H, $J = 14.0$ Hz, PhCH_2N), 3.75 (ddd, 1 H, $J_{5,5'b} = 3.0$ Hz, H-5). Anal. Calcd for $C_{36}H_{36}N_2O_3S$: C, 74.97; H, 6.29; N, 4.86. Found: C, 74.69; H, 6.35; N, 4.79.

***N*-Benzyl-3,4,6-tri-*O*-benzyl-2,5-dideoxy-2,5-imino-L-altritol (28).** The thiazolylpyrrolidine **26** (0.60 g, 1.04 mmol) was processed as described above for the synthesis of **13**. Chromatography on silica gel with 4:1 cyclohexane−AcOEt afforded the alcohol **28** (0.40 g, 74%) as a syrup. $[\alpha]_D^{20} = -22.2$ (*c* 0.5, $CHCl_3$). ^{1}H NMR: δ 7.40−7.20 (m, 20 H, 4 Ph), 4.75 and 4.57 (2 d, 2 H, $J = 12.0$ Hz, PhCH_2), 4.60 (s, 2 H, PhCH_2), 4.51 (s, 2 H, PhCH_2), 4.24 and 3.68 (2 d, 2 H, $J = 14.0$ Hz, PhCH_2N), 4.06−3.88 (m, 4 H, H-3, H-4, H-5, H-6a), 3.72−3.66 (m, 1 H, H-6b), 3.36 (dd, 1 H, $J_{1a,1b} = 10.5$ Hz, $J_{1a,2} = 3.0$ Hz, H-1a), 3.30 (dd, 1 H, $J_{1b,2} = 3.0$ Hz, H-1b), 3.12−3.07 (m, 1 H, H-2). Anal. Calcd for $C_{34}H_{37}NO_4$: C, 77.98; H, 7.12; N, 2.67. Found: C, 78.15; H, 7.27; N, 2.51.

A separate experiment afforded the crude aldehyde **27** (0.48 g, 89%; ca. 90% pure by ^{1}H NMR analysis) as described above for the synthesis of the aldehyde **12**. ^{1}H NMR: δ 9.03 (d, 1 H, $J = 3.5$ Hz, CHO), 7.15−7.40 (m, 20 H, 4 Ph), 4.67 and 4.60 (2 d, 2 H, $J = 11.0$ Hz, PhCH_2), 4.60 and 4.55 (2 d, 2 H, $J = 12.0$ Hz, PhCH_2), 4.53 (s, 2 H, PhCH_2), 4.33 and 3.75 (2 d, 2 H, $J =$ 13.0 Hz, PhCH_2N), 4.01 (dd, 1 H, $J_{3,4} = J_{4,5} = 5.5$ Hz, H-4), 3.97−3.92 (m, 2 H, H-5′a, H-5′b), 3.90 (dd, 1 H, $J_{2,3} = 2.0$ Hz, H-3), 3.83−3.79 (m, 1 H, H-5), 3.52 (dd, 1 H, H-2). Attempts to purify this compound by a short column (1 × 10 cm, d × h) of silica gel led to extensive decomposition.

2,5-Dideoxy-2,5-imino-L-altritol (29). A solution of the alcohol **28** (0.35 g, 0.67 mmol) in AcOH (5.0 mL) was debenzylated and purified as described above for **13** to give **29** (91.0 mg, 83%) as a white solid. Mp 70−72 °C. $[\alpha]_D^{20} = -29.1$ (*c* 0.5, H_2O). ^{1}H NMR (D_2O): δ 4.04 (dd, 1 H, $J_{3,4} = 4.5$ Hz, $J_{4,5} = 4.0$ Hz, H-4), 3.85 (dd, 1 H, $J_{2,3} = 8.5$ Hz, H-3), 3.65 (dd, 1 H, $J_{5,6a} = 7.0$ Hz, $J_{6a,6b} = 11.0$ Hz, H-6a), 3.60 (dd, 1 H, $J_{1a,1b} = 11.5$ Hz, $J_{1a,2} = 4.0$ Hz, H-1a), 3.50 (dd, 1 H, $J_{1b,2} = 6.0$ Hz, H-1b), 3.49 (dd, 1 H, $J_{5,6b} = 6.5$ Hz, H-6b), 3.16 (ddd, 1 H, H-5), 2.97 (ddd, 1 H, H-2). Anal. Calcd for $C_6H_{13}NO_4$: C, 44.16; H, 8.03; N, 8.58. Found: C, 43.95; H, 8.19; N, 8.49.

1-(*N*-Benzylhydroxylamino)-2,3,5-tri-*O*-benzyl-1-deoxy-D-lyxose (31). The reaction was carried out as descibed above for **4** starting from **30** (10.0 g, 23.8 mmol) to give after crystallization from cyclohexane the hydroxylamine **31** (10.3 g, 82%) as a white solid: mp 95−96 °C; $[\alpha]_D^{20} = -25.8$ (*c* 1.6, $CHCl_3$). Compound **31** appeared by ^{1}H NMR analysis as a complex mixture of the two C-1 anomers besides the open-chain derivative. ^{1}H NMR (selected data for the open-chain form): δ 6.81 (d, 1 H, $J_{1,2} = 6.5$ Hz, H-1). Anal. Calcd for $C_{33}H_{35}NO_5$: C, 75.40; H, 6.71; N, 2.66. Found: C, 75.68; H, 6.87; N, 2.74.

(1*S*,2*R*,3*S*,4*R*)-1-*N*-Benzylhydroxylamino-2,3,5-tribenzyloxy-1-(2-thiazolyl)-4-pentanol (32). The addition of 2-lithiothiazole **6** to the hydroxylamine **31** (3.00 g, 5.71 mmol) was carried out as described for **7**. The crude residue was a 2.5:1 mixture of **32** and its C-1 epimer (by ^{1}H NMR analysis). Chromatography on silica gel of the crude residue with 3:1 cyclohexane−AcOEt afforded as the first eluate the benzylhydroxylamine **32** (1.85 g, 52%) as a white solid. Mp 93−94 °C (cyclohexane). $[\alpha]_D^{20} = -27.9$ (*c* 1.4, $CHCl_3$). ^{1}H NMR: δ 7.92 and 7.42 (2 d, 2 H, $J = 3.2$ Hz, Th), 7.40−7.20 and 7.00−6.95 (m, 20 H, 4 Ph), 6.60 (s 1 H, OH), 4.82 and 4.61 (2 d, 2 H, $J = 11.5$ Hz, PhCH_2), 4.58 and 4.20 (2 d, 2 H, $J = 11.0$ Hz, PhCH_2), 4.57−4.44 (m, 4 H, H-1, OH, PhCH_2), 4.17−4.07 (m, 3 H, H-2, H-3, H-4), 3.87 and 3.70 (2 d, 2 H, $J = 14.0$ Hz, PhCH_2N), 3.63 (dd, 1 H, $J_{4,5a} = 5.0$ Hz, $J_{5a,5b} = 9.0$ Hz, H-5a), 3.57 (dd, 1 H, $J_{4,5b} = 6.5$ Hz, H-5b). Anal. Calcd for $C_{36}H_{38}N_2O_5S$: C, 70.79; H, 6.27; N, 4.59. Found: C, 70.64; H, 6.07; N, 4.65.

Eluted next was the C-1 epimer of **32** (0.76 g, 22%) as a syrup. $[\alpha]_D^{20} = -25.7$ (*c* 2.0, $CHCl_3$). ^{1}H NMR: δ 7.88 and 7.39 (2d, 2 H, $J = 3.2$ Hz, Th), 7.38−7.21 and 7.20−7.15 (m, 20 H, 4 Ph), 5.80 (s, 1 H, OH), 4.78 and 4.68 (2 d, 2 H, $J =$ 11.0 Hz, PhCH_2), 4.75 (d, 1 H, $J_{1,2} = 6.0$ Hz, H-1), 4.51 and 4.38 (2 d, 2 H, $J = 11.5$ Hz, PhCH_2), 4.47 and 4.40 (2 d, 2 H, $J = 11.5$ Hz, PhCH_2), 4.36 (dd, 1 H, $J_{2,3} = 6.0$ Hz, H-2), 4.09 (dddd, 1 H, $J_{3,4} = 2.0$, $J_{4,5a} = J_{4,OH} = 6.0$, $J_{4,5b} = 7.0$ Hz, H-4), 3.87 and 3.74 (2 d, 2 H, $J = 13.5$ Hz, PhCH_2N), 3.83 (dd, 1 H, H-3), 3.56 (dd, 1 H, $J_{5a,5b} = 9.5$ Hz, H-5a), 3.49 (dd, 1 H, H-5b), 3.14 (d, 1 H, OH). Anal. Calcd for $C_{36}H_{38}N_2O_5S$: C, 70.79; H, 6.27; N, 4.59. Found: C, 70.58; H, 6.35; N, 4.49.

(1*S*,2*R*,3*S*,4*R*)-1-*N*-Benzylamino-2,3,5-tribenzyloxy-1-(2-thiazolyl)-4-pentanol (33). The benzylhydroxylamine **32** (2.00 g, 3.27 mmol) was processed as described above for **7** to give the crude syrup **33** (1.85 g, 95%) in ca. 95% purity by ^{1}H NMR analysis. The crude product was used for the next reaction without further purification. A pure sample of **33** was obtained by flash chromatography with 3:2 cyclohexane−AcOEt. $[\alpha]_D^{20} = -13.4$ (*c* 0.5, $CHCl_3$). ^{1}H NMR: δ 7.82 and 7.40 (2d, 2 H, $J = 3.2$ Hz, Th), 7.38−7.20 and 7.05−7.18 (m,

20 H, 4 Ph), 4.83 and 4.51 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.73 (s, 1 H, OH), 4.55 and 4.44 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.55 and 4.32 (2 d, 2 H, J = 11.5 Hz, PhCH_2), 4.43 (d, 1 H, $J_{1,2}$ = 7.0 Hz, H-1), 4.03 (dd, 1 H, $J_{2,3}$ = 3.5, $J_{3,4}$ = 1.5 Hz, H-3), 4.00 (ddd, 1 H, $J_{4,5a}$ = 6.0, $J_{4,5b}$ = 7.0 Hz, H-4), 3.95 (dd, 1 H, H-2), 3.73 and 3.68 (2 d, 2 H, J = 13.5 Hz, PhCH_2N), 3.59 (dd, 1 H, $J_{5a,5b}$ = 10.0 Hz, H-5a), 3.54 (dd, 1 H, H-5b). Anal. Calcd for $C_{36}H_{38}N_2O_4S$: C, 72.70; H, 6.44; N, 4.71. Found: C, 72.85; H, 6.30; N, 4.58.

(2*S*,3*R*,4*S*,5*S*)-*N*-Benzyl-3,4-dibenzyloxy-5-benzyloxymethyl-2-(2-thiazolyl)pyrrolidine (34). The reaction was carried out as described above for **10** starting from crude **33** (1.0 g, 1.68 mmol) to give after flash chromatography (4:1 cyclohexane−AcOEt) the thiazolylpyrrolidine **34** (0.64 g, 66%) as a white solid. Mp 98−100 °C (cyclohexane). $[\alpha]_D^{20}$ = +14.7 (*c* 1.0 $CHCl_3$). ^{1}H NMR: δ 7.78 (d, 1 H, J = 3.2 Hz, Th), 7.40−7.15 (m, 21 H, 4 Ph, Th), 4.63 (d, 1 H, $J_{2,3}$ = 4.0 Hz, H-2), 4.57 and 4.53 (2 d, 2 H, J = 10.0 Hz, PhCH_2), 4.55 (s, 2H, PhCH_2), 4.42 (s, 2H, PhCH_2), 4.06 and 3.89 (2 d, 2 H, J = 13.0 Hz, PhCH_2N), 4.01 (dd, 1 H, $J_{3,4}$ = 5.0 Hz, H-3), 3.93 (dd, 1 H, $J_{4,5}$ = 5.0 Hz, H-4), 3.42 (ddd, 1 H, $J_{5,5'a}$ = , $J_{5,5'b}$ = 5.0 Hz, H-5), 3.34−3.26 (m, 2 H, H-5′a, H-5′b). Anal. Calcd for $C_{36}H_{36}N_2O_3S$: C, 74.97; H, 6.29; N, 4.86. Found: C, 74.89; H, 6.30; N, 4.59.

***N*-Benzyl-3,4,6-tri-*O*-benzyl-2,5-dideoxy-2,5-imino-D-allitol (36).** The thiazolylpyrrolidine **34** (0.60 g, 1.04 mmol) was processed as described above for the synthesis of **13**. Chromatography on silica gel with 4:1 cyclohexane−AcOEt afforded the alcohol **36** (0.47 g, 87%) as a syrup. $[\alpha]_D^{20}$ = +15.1 (*c* 0.5, $CHCl_3$). ^{1}H NMR: δ 7.40−7.20 (m, 20 H, 4 Ph), 4.58 and 4.55 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.54 and 4.50 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.38 and 4.34 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 3.98−3.90 (m, 2 H, H-3, H-4), 3.92 and 3.82 (2 d, 2 H, J = 13.0 Hz, PhCH_2N), 3.48 (ddd, 1 H, $J_{1a,1b}$ = 11.0 Hz, $J_{1a,2}$ = 1.3 Hz, $J_{1a,OH}$ = 8.0 Hz, H-1a), 3.42 (dd, 1 H, $J_{1b,2}$ = 3.2 Hz, H-1b), 3.30−3.22 (m, 2 H, H-2, H-5), 3.18 (dd, 1 H, $J_{5,6a}$ = 4.0 Hz, $J_{6a,6b}$ = 9.5 Hz, H-6a) 3.13 (dd, 1 H, $J_{5,6b}$ = 6.2 Hz, H-6b), 2.90 (d, 1 H, OH). Anal. Calcd for $C_{34}H_{37}NO_4$: C, 77.98; H, 7.12; N, 2.67. Found: C, 77.73; H, 7.08; N, 2.41.

A separate experiment afforded the crude aldehyde **35** (0.42 g, 78%; ca. 90% pure by ^{1}H NMR analysis) as described above for the synthesis of the aldehyde **12**. ^{1}H NMR: δ 9.15 (d, 1 H, J = 3.0 Hz, CHO), 7.20−7.40 (m, 20 H, 4 Ph), 4.60 and 4.55 (2 d, 2 H, J = 11.0 Hz, PhCH_2), 4.54 and 4.50 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.48 (s, 2 H, PhCH_2), 4.06 and 3.77 (2 d, 2 H, J = 13.0 Hz, PhCH_2N), 3.98 (dd, 1 H, $J_{2,3}$ = 6.0 Hz, $J_{3,4}$ = 4.0 Hz, H-3), 3.82 (dd, 1 H, $J_{4,5}$ = 3.0 Hz, H-4), 3.56 (dd, 1 H, H-2), 3.44−3.34 (m, 3 H, H-5, H-5′a, H-5′b). Attempts to purify this compound by a short column (1 × 10 cm, d × h) of silica gel led to extensive decomposition.

2,5-Dideoxy-2,5-imino-D-allitol (37). A solution of the alcohol **36** (0.35 g, 0.67 mmol) in AcOH (5.0 mL) was debenzylated and purified as described above for **13** to give **37** (88.0 mg, 81%) as a hygroscopic gum. ^{1}H NMR (D_2O): δ 3.72−3.63 (m, 2 H, H-3, H-4), 3.57 (dd, 2 H, $J_{1a(6a),1b(6b)}$ = 12.0 Hz, $J_{1a(6a),2(5)}$ = 4.5 Hz, H-1a, H-6a), 3.47 (dd, 2 H, $J_{1b(6b),2(5)}$ = 5.5 Hz, H-1b, H-6b), 2.96−2.86 (m, 2 H, H-2, H-5). Anal. Calcd for $C_6H_{13}NO_4$: C, 44.16; H, 8.03; N, 8.58. Found: C, 43.95; H, 8.31; N, 8.42.

Alkene 40. A mixture of the phosphonium salt **38** (0.38 g, 0.60 mmol) and activated 4 Å powdered molecular sieves (0.25 g) in anhydrous THF (2.2 mL) and HMPA (1.1 mL) was cooled to −30 °C. To this suspension was added *n*-BuLi (0.37 mL, 0.60 mmol of 1.6 M solution in hexane) followed by a solution of the aldehyde **12** (0.26 g, 0.50 mmol) in anhydrous THF (1.0 mL). The reaction mixture was stirred for 2 h at −30 °C, filtered through Celite, diluted with 1.0 M phosphate buffer (5.0 mL, pH 7.0), and extracted with Et_2O (3 × 10 mL). The organic phase was dried (Na_2SO_4) and concentrated and the residue chromatographated (7:1 cyclohexane−AcOEt with 0.3% of triethylamine) to afford the syrup **40** (0.24 g, 64%) as a mixture of (*Z*)- and (*E*)-olefins in a 1:1 ratio (by ^{1}H NMR analysis). **(*Z*)-40.** ^{1}H NMR (selected data): δ 5.78 (dd, 1 H, J = 10.1, 11.1 Hz), 5.65 (dd, 1 H, J = 8.8, 11.1 Hz), 5.57 (d, 1 H, J = 5.1 Hz, H-1). **(*E*)-40.** ^{1}H NMR (selected data): δ 5.94 (dd, 1 H, J = 5.9, 15.8 Hz), 5.80 (dd, 1 H, J = 8.5, 15.8 Hz), 5.64 (d, 1 H, J = 5.2 Hz, H-1).

Aza-*C*-disaccharide 41. To a solution of olefins **40** (0.24 g, 0.32 mmol) in dimethoxyethane (3.5 mL) was added freshly recrystallized (*p*-toluenesulfonyl)hydrazide (0.24 g, 1.3 mmol). The solution was warmed to 85 °C, and an aqueous solution of AcONa (1.3 mL, 1.0 M) was added dropwise over 2 h. After an additional 3 h at 85 °C, the reaction mixture was diluted with H_2O (5.0 mL), extracted with CH_2Cl_2 (3 × 10 mL), dried (Na_2SO_4), and concentrated. Flash chromatography (5:1 cyclohexane−AcOEt with 0.3% of triethylamine) of the residue gave 0.18 g (76%) of **41** as a syrup. $[\alpha]_D^{20}$ = −12.2 (*c* 1.8, $CHCl_3$). ^{1}H NMR: δ 7.38−7.20 (m, 20 H, 4 Ph), 5.52 (d, 1 H, $J_{1,2}$ = 5.0 Hz, H-1), 4.59 and 4.54 (2 d, 2 H, J = 11.5 Hz, PhCH_2), 4.53 (dd, 1 H, $J_{2,3}$ = 2.3 Hz, $J_{3,4}$ = 8.0 Hz, H-3), 4.47 and 4.43 (2 d, 2 H, J = 12.5 Hz, PhCH_2), 4.46 (s, 2 H, PhCH_2), 4.28 (dd, 1 H, H-2), 3.99 (dd, 1 H, $J_{9,10}$ = 2.0 Hz, $J_{10,11}$ = 5.0 Hz, H-10), 3.92 and 3.80 (2 d, 2 H, J = 14.0 Hz, PhCH_2N), 3.89 (dd, 1 H, $J_{4,5}$ = 1.8 Hz, H-4), 3.77 (dd, 1 H, $J_{11,12a}$ = 8.0 Hz, $J_{12a,12b}$ = 9.2 Hz, H-12a), 3.73 (dd, 1 H, $J_{8,9}$ = 2.5 Hz, H-9), 3.55−3.49 (m, 1 H, H-5), 3.49 (dd, 1 H, $J_{11,12b}$ = 4.5 Hz, H-12b), 3.30 (ddd, 1 H, H-11), 2.86−2.78 (m, 1 H, H-8), 1.70−1.45 (m, 4 H, H-6a, H-6b, H-7a, H-7b), 1.48, 1.44, 1.33, 1.30 (4 s, 12 H, 4 CH_3). Anal. Calcd for $C_{46}H_{55}NO_8$: C, 73.67; H, 7.39; N, 1.87. Found: C, 73.91; H, 7.51; N, 1.93.

Aza-*C*-disaccharide 42. A solution of compound **41** (0.15 g, 0.20 mmol) in AcOH (5.0 mL) was debenzylated with H_2 over 20% $Pd(OH)_2$ (0.10 g) for 4 h at a pressure of 7 bar. The mixture was filtered through a pad of cotton and concentrated to afford 78 mg (100%) of a crude product (95% pure by ^{1}H NMR analysis). ^{1}H NMR (CD_3OD) (selected data): δ 5.54 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1), 4.49 (dd, 1 H, $J_{2,3}$ = 1.0 Hz, $J_{3,4}$ = 4.0 Hz, H-3), 4.30 (dd, 1 H, H-2), 3.50−3.42 (m, 1 H, H-5), 3.07−2.98 (m, 1 H, H-8), 1.53, 1.47, 1.36, 1.31 (4 s, 12 H, 4 CH_3). To a mixture of debenzylated product (78 mg, 0.20 mmol) in H_2O (5 mL) was added Amberlite IR-120 (H^+) ion-exchange resin (1.5 g), previously washed with hot water (70 °C). The mixture was heated at 70 °C for 1 h and then cooled to room temperature, and the resin was removed by filtration and washed with 1 M aqueous HCl. The filtrate was concentrated and the residue purified by gel permeation column chromatography on Sephadex LH-20 (10:1 CH_3OH-H_2O) to obtain the pure compound **42** (66 mg, 95%) as a colorless syrup. $[\alpha]_D^{20}$ = +35.6 (*c* 0.3, H_2O). ^{1}H NMR (D_2O) (selected data): δ 5.80 (d, 0.3 H, $J_{1\alpha,2\alpha}$ = 3.5 Hz, H-1α), 4.40 (d, 0.7 H, $J_{1\beta,2\beta}$ = 7.8 Hz, H-1β), 3.63 (dd, 0.3 H, $J_{2\alpha,3\alpha}$ = 10.0 Hz, H-2α), 3.31 (dd, 0.7 H, $J_{2\beta,3\beta}$ = 10.0 Hz, H-2β), 1.95−1.50 (m, 4 H, 2 H-6α, 2 H-6β, 2 H-7α, 2 H-7β). MALDI-TOF MS (345.77): 311.5 (M + H − Cl). Anal. Calcd for $C_{12}ClH_{24}NO_8$: C, 41.68; H, 7.00; N, 4.05. Found: C, 41.81; H, 7.22; N, 4.16.

Alkene 43. A mixture of phosphonium salt **39** (0.35 g, 0.60 mmol) and activated 4 Å powdered molecular sieves (0.25 g) in anhydrous THF (2.2 mL) and HMPA (1.1 mL) was cooled to −50 °C. To this suspension was added *n*-BuLi (0.37 mL, 0.60 mmol of 1.6 M solution in hexane) followed by a solution of the aldehyde **12** (0.26 g, 0.50 mmol) in anhydrous THF (1.0 mL). The reaction mixture was stirred for 2 h at −50 °C, filtered through Celite, diluted with 1.0 M phosphate buffer (5.0 mL, pH 7.0), and extracted with Et_2O (3 × 10 mL). The organic phase was dried (Na_2SO_4) and concentrated and the residue chromatographated (5:1 cyclohexane−AcOEt with 0.3% of triethylamine) to afford the syrup **43** (0.23 g, 67%) as a (*Z*)-olefin (by ^{1}H NMR analysis). $[\alpha]_D^{20}$ = −20.8 (*c* 1.1, $CHCl_3$). ^{1}H NMR: (C_6D_6) δ 7.40−7.00 (m, 20 H, 4 Ph), 6.13 (dd, 1 H, $J_{4,5}$ = 9.0, $J_{5,6}$ = 11.0 Hz, H-5), 5.84 (dd, 1 H, $J_{6,7}$ = 9.5 Hz, H-6), 5.02 (s, 1 H, H-1), 4.99 (dd, 1 H, $J_{3,4}$ = 3.5 Hz, H-4), 4.53 (d, 1 H, $J_{2,3}$ = 6.0 Hz, H-2), 4.50 and 4.40 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.49 (s, 2 H, PhCH_2), 4.44 (dd, 1 H, H-3), 4.27 and 4.22 (2 d, 2 H, J = 11.8 Hz, PhCH_2), 4.40 and 3.70 (2

d, 2 H, J = 14.3 Hz, PhCH_2N), 3.94 (dd, 1 H, $J_{8,9}$ = 4.5, $J_{9,10}$ = 7.0 Hz, H-9), 3.87 (dd, 1 H, $J_{7,8}$ = 7.0 Hz, H-8), 3.80 (dd, 1 H, $J_{10,11a}$ = 6.8, $J_{11a,11b}$ = 9.3 Hz, H-11a), 3.63 (dd, 1 H, H-7), 3.49 (dd, 1 H, $J_{10,11b}$ = 4.5 Hz, H-11b), 3.38 (ddd, 1 H, H-10), 3.15 (s, 3 H, OCH_3), 1.47, 1.06 (2 s, 6 H, 2 CH_3). Anal. Calcd for $C_{43}H_{49}NO_7$: C, 74.65; H, 7.14; N, 2.02. Found: C, 74.51; H, 7.22; N, 2.12.

Aza-*C*-disaccharide 44. The olefin **43** (0.23 g, 0.33 mmol) was reduced as described for the preparation of **41** to afford after flash chromatography (5:1 cyclohexane−AcOEt with 0.3% of triethylamine) 0.13 g (55%) of **44** as a syrup. $[\alpha]_D^{20} = -6.4$ (*c* 0.9, $CHCl_3$). ^{1}H NMR: δ 7.40−7.20 (m, 20 H, 4 Ph), 4.85 (s, 1 H, H-1), 4.60 (s, 2 H, PhCH_2), 4.55−4.40 (m, 6 H, H-2, H-3, 2 PhCH_2), 4.00 (dd, 1 H, $J_{8,9}$ = 2.5 Hz, $J_{9,10}$ = 5.5 Hz, H-9), 3.88 (s, 2 H, PhCH_2), 3.80−3.72 (m, 3 H, H-4, H-8, H-11a), 3.48 (dd, 1 H, $J_{10,11b}$ = 4.5 Hz, $J_{11a,11b}$ = 9.2 Hz, H-11b), 3.34−3.25 (m, 1 H, H-10), 3.31 (s, 3 H, CH_3), 2.84−2.77 (m, 1 H, H-7), 1.85−1.57 (m, 4 H, H-6a, H-6b, H7a, H-7b), 1.24, 1.30 (2 s, 6 H, 2 CH_3). Anal. Calcd for $C_{43}H_{51}NO_7$: C, 74.43; H, 7.41; N, 2.02. Found: C, 74.65; H, 7.30; N, 1.91.

Aza-*C*-disaccharide 45. Compound **44** (0.14 g, 0.20 mmol) was hydrogenated as described for the preparation of **42** to afford 67 mg (100%) of a crude product (95% pure by ^{1}H NMR analysis). ^{1}H NMR (CD_3OD): δ 4.82 (s, 1 H, H-1), 4.69 (dd, 1 H, $J_{2,3}$ = 6.0 Hz, $J_{3,4}$ = 3.5 Hz, H-3), 4.56 (d, 1 H, H-2), 4.04 (dd, 1 H, $J_{8,9}$ = 2.0 Hz, $J_{9,10}$ = 4.2 Hz, H-9), 3.96 (ddd, 1 H, $J_{4,5a} = J_{4,5b}$ = 6.0 Hz, H-4), 3.86 (dd, 1 H, $J_{10,11a}$ = 5.8 Hz, $J_{11a,11b}$ = 11.5 Hz, H-11a), 3.80 (dd, 1 H, $J_{10,11b}$ = 6.5 Hz, H-11b), 3.77 (dd, 1 H, $J_{7,8}$ = 4.0 Hz, H-8), 3.40−3.32 (m, 1 H, H-10), 3.32 (s, 3 H, OCH_3), 3.04−2.96 (m, 1 H, H-7), 2.00−1.70 (m, 4 H, H-5a, H-5b, H-6a, H-6b), 1.88, 1.62 (2 s, 6 H, 2 CH_3). The debenzylated product (67 mg, 0.20 mmol) was treated with Amberlite IR-120 (H^+) ion-exchange resin as described for the preparation of **42** to obtain after gel permeation column chromatography on Sephadex LH-20 (10:1 CH_3OH-H_2O) the pure compound **45** (53 mg, 95%) as a colorless syrup. $[\alpha]_D^{20}$ = +5.5 (*c* 0.3, H_2O). ^{1}H NMR (D_2O) (selected data): δ 4.20−3.90 (m, 3 H), 3.86−3.58 (m, 3 H), 3.56−3.30 (m, 1 H), 3.10−2.90 (m, 1 H), 1.95−1.35 (m, 4 H, 2 H-5, 2 H-6). MALDI-TOF MS (315.75): 281.6 (M + H − Cl). Anal. Calcd for $C_{11}ClH_{22}NO_7$: C, 41.84; H, 7.02; N, 4.44. Found: C, 41.60; H, 6.94; N, 4.32.

Alkene 46. The Wittig reaction was carried out as described above for the aza-*C*-disaccharide **40** starting from the aldehyde **20** (0.26 g, 0.50 mmol) and the phosphonium salt **38** (0.38 g, 0.60 mmol) to afford after flash chromatography (10:1 cyclohexane−AcOEt with 0.3% of triethylamine) the syrup **46** (0.17 g, 46%) as a mixture of (*Z*)- and (*E*)-olefins in a 1:1 ratio (by ^{1}H NMR analysis). **(*Z*)-46.** ^{1}H NMR (selected data): δ 5.92−5.79 (m, 2 H, H-6, H-7), 5.52 (d, 1 H, $J_{1,2}$ = 5.0 Hz, H-1), 4.43 (dd, 1 H, $J_{2,3}$ = 2.3 Hz, $J_{3,4}$ = 8.0 Hz, H-3), 4.38−4.30 (m, 1 H, H-5), 4.24 (dd, 1 H, H-2), 4.14−4.08 (m, 1 H, H-8), 4.08 and 3.66 (2 d, 2 H, J = 14.0 Hz, PhCH_2N), 3.99 (dd, 1 H, $J_{9,10}$ = 2.7 Hz, $J_{10,11}$ = 4.3 Hz, H-10), 3.87 (dd, 1 H, $J_{8,9}$ = 2.7 Hz, H-9), 3.66−3.56 (m, 3 H, H-4, H-12a, H-12b), 3.32−3.24 (m, 1 H, H-11). **(*E*)-46.** ^{1}H NMR (selected data): δ 5.85 (dd, 1 H, $J_{6,7}$ = 15.0 Hz, $J_{7,8}$ = 6.5 Hz, H-7), 5.77 (dd, 1 H, $J_{5,6}$ = 5.5 Hz, H-6), 5.60 (d, 1 H, $J_{1,2}$ = 5.0 Hz, H-1), 4.63 (dd, 1 H, $J_{2,3}$ = 2.5, $J_{3,4}$ = 8.0 Hz, H-3), 4.63 and 4.52 (2 d, 2 H, J = 11.5 Hz, PhCH_2), 4.54 and 4.50 (2 d, 2 H, J = 11.5 Hz, PhCH_2), 4.48 and 4.43 (2 d, 2 H, J = 12.5 Hz, PhCH_2), 4.33 (dd, 1 H, H-2),4.33−4.29 (m, 1 H, H-5), 4.20 (dd, 1 H, $J_{4,5}$ = 2.0 Hz, H-4), 4.06 (dd, 1 H, $J_{9,10} = J_{10,11}$ = 3.2 Hz, H-10), 3.99 and 3.65 (2 d, 2 H, J = 14.5 Hz, PhCH_2N), 3.89 (dd, 1 H, $J_{8,9}$ = 5.0 Hz, H-9), 3.66 (dd, 1 H, H-8), 3.56−3.48 (m, 2 H, H-12a, H-12b), 3.31−3.23 (m, 1 H, H-11).

Aza-*C*-disaccharide 47. Olefins **46** (0.17 g, 0.23 mmol) were reduced as described for the preparation of **41** to afford after flash chromatography (8:1 cyclohexane−AcOEt with 0.3% triethylamine) the compound **47** (0.13 g, 77%) as a syrup. $[\alpha]_D^{20} = -47.9$ (*c* 0.6, $CHCl_3$). ^{1}H NMR: δ 7.40−7.20 (m, 20 H, 4 Ph), 5.53 (d, 1 H, $J_{1,2}$ = 5.0 Hz, H-1), 4.55 and 4.47 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.54 (dd, 1 H, $J_{2,3}$ = 2.3 Hz, $J_{3,4}$ = 8.0 Hz, H-3), 4.53 and 4.45 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.44 (s, 2 H, PhCH_2), 4.28 (dd, 1 H, H-2), 4.03−4.39 (m, 2 H, H-4, H-10), 4.02 and 3.72 (2 d, 2 H, J = 14.0 Hz, PhCH_2N), 3.86 (dd, 1 H, $J_{8,9}$ = 4.5 Hz, $J_{9,10}$ = 2.0 Hz, H-9), 3.64−3.60 (m, 1 H, H-5), 3.59 (dd, 1 H, $J_{11,12a}$ = 4.5 Hz, $J_{12a,12b}$ = 10.0 Hz, H-12a), 3.53 (dd, 1 H, $J_{11,12b}$ = 6,5 Hz, H-12b), 3.31−3.25 (m, 1 H, H-11), 3.15−3.07 (m, 1 H, H-8), 2.00−1.88 (m, 1 H, H-7a), 1.70−1.40 (m, 3 H, H-6a, H-6b, H-7b), 1.49, 1.40, 1.33, 1.30 (4 s, 12 H, 4 CH_3). Anal. Calcd for $C_{46}H_{55}NO_8$: C, 73.67; H, 7.39; N, 1.87. Found: C, 73.89; H, 7.51; N, 1.98.

Aza-*C*-disaccharide 48. Compound **47** (0.15 g, 0.20 mmol) was hydrogenated as described for the preparation of **42** to afford 74 mg (95%) of a crude product (95% pure by ^{1}H NMR analysis). ^{1}H NMR (CD_3OD): δ 5.01 (d, 1 H, $J_{1,2}$ = 5.0 Hz, H-1), 4.65 (dd, 1 H, $J_{2,3}$ = 2.2 Hz, $J_{3,4}$ = 8.0 Hz, H-3), 4.37 (dd, 1 H, H-2), 4.20 (dd, 1 H, $J_{4,5}$ = 1.7 Hz, H-4), 3.98 (dd, 1 H, $J_{9,10} = J_{10,11}$ = 5.8 Hz, H-10), 3.91−3.76 (m, 4 H, H-5, H-9, H-12a, H-12b), 3.46 (ddd, 1 H, $J_{11,12a}$ = 4.2 Hz, $J_{11,12b}$ = 6.2 Hz, H-11), 3.38−3.31 (m, 2 H, H-8, NH), 2.10−1.70 (m, 4 H, H-6a, H-6b, H-7a, H-7b), 1.53, 1.44 (2 s, 6 H, 2 CH_3), 1.36 (s, 6 H, 2 CH_3). The debenzylated product (74 mg, 0.19 mmol) was treated with Amberlite IR-120 (H^+) ion-exchange resin as decribed for the preparation of **42** to obtain after gel permeation column chromatography on Sephadex LH-20 (10:1 CH_3OH-H_2O) the pure compound **48** (52 mg, 79%) as a colorless syrup. $[\alpha]_D^{20}$ = +42.5 (*c* 1.5, H_2O). ^{1}H NMR (D_2O) (selected data): δ 5.10 (d, 0.3 H, $J_{1\alpha,2\alpha}$ = 3.8 Hz, H-1α), 4.42 (d, 0.7 H, $J_{1\beta,2\beta}$ = 8.0 Hz, H-1β), 3.63 (dd, 0.3 H, $J_{2\alpha,3\alpha}$ = 10.0 Hz, H-2α), 3.32 (dd, 0.7 H, $J_{2\beta,3\beta}$ = 10.0 Hz, H-2β), 1.95−1.50 (m, 4 H, 2 H-6α, 2 H-6β, 2 H-7α, 2 H-7β). MALDI-TOF MS (345.77): 311.9 (M + H − Cl). Anal. Calcd for $C_{12}ClH_{24}NO_8$: C, 41.68; H, 7.00; N, 4.05. Found: C, 41.48; H, 6.91; N, 4.00.

Alkene 49. The Wittig reaction was carried out as described above for aza-*C*-disaccharide **43** starting from the aldehyde **20** (0.26 g, 0.50 mmol) and the phosphonium salt **39** (0.35 g, 0.60 mmol) to afford after flash chromatography (7:1 cyclohexane−AcOEt with 0.3% of triethylamine) the syrup **49** (0.19 g, 54%) as (*Z*)-olefin contaminated by a small amount of the (*E*)-isomer (by ^{1}H NMR analysis). **(*Z*)-49.** ^{1}H NMR (selected data): δ 5.88 (dd, 1 H, $J_{5,6}$ = 11.0 Hz, $J_{6,7}$ = 8.0 Hz, H-6), 5.81 (dd, 1 H, $J_{4,5}$ = 9.0 Hz, H-5), 4.14 (dd, 1 H, $J_{8,9} = J_{9,10}$ = 3.2 Hz, H-9), 4.02 (dd, 1 H, $J_{7,8}$ = 6.0 Hz, H-7), 3.98 and 3.65 (2 d, 2 H, J = 14.0 Hz, PhCH_2N), 3.92 (dd, 1 H, H-8), 3.61 (dd, 1 H, $J_{10,11a}$ = 5.8 Hz, $J_{11a,11b}$ = 9.5 Hz, H-11a), 3.51 (dd, 1 H, $J_{10,11b}$ = 3.5 Hz, H-11b), 3.34−3.25 (m, 1 H, H-10), 3.28 (s, 3 H, OCH_3), 1.44, 1.24 (2 s, 6 H, 2 CH_3).

Aza-*C*-disaccharide 50. The olefin **49** (0.19 g, 0.27 mmol) was reduced as described for the preparation of **41** to afford after flash chromatogrphy (5:1 cyclohexane−AcOEt with 0.3% of triethylamine) the compound **50** (0.11 g, 60%) as a syrup. $[\alpha]_D^{20} = -39.1$ (*c* 1.4, $CHCl_3$). ^{1}H NMR: δ 7.45−7.22 (m, 20 H, 4 Ph), 4.86 (s, 1 H, H-1), 4.57 and 4.48 (2 d, 2 H, J = 11.8 Hz, PhCH_2), 4.56 and 4.51 (2 d, 2 H, J = 11.5 Hz, PhCH_2), 4.56−4.52 (m, 2 H, H-2, H-3), 4.58 (s, 2 H, PhCH_2), 4.03 and 3.73 (2 d, 2 H, J = 14.0 Hz, PhCH_2N), 4.03 (dd, 1 H, $J_{8,9} = J_{9,10}$ = 2.5 Hz, H-9), 3.90 (dd, 1 H, $J_{7,8}$ = 4.5 Hz, H-8), 3.88−3.80 (m, 1 H, H-4), 3.62 (dd, 1 H, $J_{10,11a}$ = 5.0 Hz, $J_{11a,11b}$ = 9.5 Hz, H-11a), 3.56 (dd, 1 H, $J_{10,11b}$ = 6.5 Hz, H-11b), 3.32−3.28 (m, 1 H, H-10), 3.30 (s, 3 H, OCH_3), 3.18−3.12 (m, 1 H, H-7), 1.92−1.63 (m, 4 H, H-5a, H-5b, H-6a, H-6b), 1.42, 1.46 (2 s, 6 H, 2 CH_3). Anal. Calcd for $C_{43}H_{51}NO_7$: C, 74.43; H, 7.41; N, 2.02. Found: C, 74.59; H, 7.53; N, 2.13.

Aza-*C*-disaccharide 51. Compound **50** (0.14 g, 0.20 mmol) was hydrogenated as described for the preparation of **42** to afford 69 mg (100%) of a crude product (95% pure by ^{1}H NMR analysis). ^{1}H NMR (CD_3OD): δ 4.82 (s, 1 H, H-1), 4.68 (dd, 1 H, $J_{2,3}$ = 6.0 Hz, $J_{3,4}$ = 3.5 Hz, H-3), 4.55 (d, 1 H, H-2), 3.98−3.91 (m, 1 H, H-4), 3.79 (dd, 1 H, $J_{8,9} = J_{9,10}$ = 6.5 Hz, H-9), 3.70 (dd, 1 H, $J_{10,11a}$ = 4.2 Hz, $J_{11a,11b}$ = 11.5 Hz, H-11a), 3.65 (dd, 1 H, $J_{7,8} = J_{8,9}$ = 6.5 Hz, H-8), 3.62 (dd, 1 H, $J_{10,11b}$ = 6.0 Hz, H-11b), 3.35−3.30 (m, 1 H, NH), 3.32 (s, 3 H, OCH_3), 3.03 (ddd, 1 H, H-10), 3.01−2.93 (m, 1 H, H-7), 1.97−1.71 (m, 3 H,

H-5a, H-5b, H-6a), 1.65−1.50 (m, 1 H, H-6b), 1.43, 1.30 (2 s, 6 H, 2 CH_3). The debenzylated product (69 mg, 0.20 mmol) was treated with Amberlite IR-120 (H^+) ion-exchange resin as described for the preparation of **42** to obtain after gel permeation column chromatography on Sephadex LH-20 (10:1 CH_3OH-H_2O) the pure compound **51** (42 mg, 75%) as a colorless syrup. $[\alpha]_D^{20} = +19.7$ (*c* 0.3, H_2O). ^1H NMR (D_2O) (selected data): δ 3.80 (dd, 1 H, $J = 3.5, 12.5$ Hz), 3.72 (dd, 1 H, $J = 5.8$ Hz, $J = 12.5$ Hz), 3.50−3.30 (m, 2 H), 2.00−1.60 (m, 4 H, 2 H-5, 2 H-6). MALDI-TOF MS (315.75): 282.0 (M + H − Cl). Anal. Calcd for $C_{11}ClH_{22}NO_7$: C, 41.84; H, 7.02; N, 4.44. Found: C, 41.98; H, 7.11; N, 4.56.

Alkene 52. The Wittig reaction was carried out as described above for the aza-*C*-disaccharide **40** starting from the aldehyde **27** (0.26 g, 0.50 mmol) and the phosphonium salt **38** (0.38 g, 0.60 mmol) to afford after flash chromatography (5:1 cyclohexane−AcOEt with 0.3% of triethylamine) the compound **52** (0.16 g, 42%) as a syrup ((*Z*)-olefin by ^1H NMR analysis). $[\alpha]_D^{20} = -42.0$ (*c* 0.7, $CHCl_3$). ^1H NMR: δ 7.40−7.10 (m, 20 H, 4 Ph), 5.76 (dd, 1 H, $J_{5,6} = 6.5$ Hz, $J_{6,7} = 15.5$ Hz, H-6), 5.60 (dd, 1 H, $J_{7,8} = 8.5$ Hz, H-8), 5.60 (d, 1 H, $J_{1,2} = 5.0$ Hz, H-1), 4.68 (s, 2 H, PhCH_2), 4.61 (s, 2 H, PhCH_2), 4.60 (dd, 1 H, $J_{2,3} = 2.3$ Hz, $J_{3,4} = 7.5$ Hz, H-3), 4.49 (s, 2 H, PhCH_2), 4.33 (dd, 1 H, H-2), 4.23 (dd, 1 H, $J_{4,5} = 1.5$ Hz, H-5), 4.10 (dd, 1 H, $J_{9,10} = J_{10,11} = 6.0$ Hz, H-10), 4.09 (dd, 1 H, H-4), 3.99 and 3.87 (2 d, 2 H, $J = 14.0$ Hz, PhCH_2N), 3.92−3.88 (m, 2 H, H-12a, H-12b), 3.84 (dd, 1 H, $J_{8,9} = 2.5$ Hz, H-9), 3.63 (dd, 1 H, H-8), 3.61−3.53 (m, 1 H, H-11), 1.48, 1.58, 1.39, 1.35 (4 s, 12 H, 4 CH_3). Anal. Calcd for $C_{46}H_{53}NO_8$: C, 73.87; H, 7.14; N, 1.87. Found: C, 74.01; H, 7.20; N, 1.98.

Aza-*C*-disaccharide 53. The olefin **52** (0.16 g, 0.21 mmol) was reduced as described for the preparation of **41** to afford after flash chromatogrphy (5:1 cyclohexane−AcOEt with 0.3% of triethylamine) the compound **53** (0.12 g, 76%) as a syrup. $[\alpha]_D^{20} = -20.0$ (*c* 0.7, $CHCl_3$). ^1H NMR: δ 7.40−7.18 (m, 20 H, 4 Ph), 4.76 and 4.57 (2 d, 2 H, $J = 12.0$ Hz, PhCH_2), 4.62 and 4.54 (2 d, 2 H, $J = 12.0$ Hz, PhCH_2), 4.56 (dd, 1 H, $J_{2,3} = 2.3$ Hz, $J_{3,4} = 7.8$ Hz, H-3), 4.45 (s, 2 H, PhCH_2), 4.28 (dd, 1 H, H-2), 4.05 and 3.84 (2 d, 2 H, $J = 14.0$ Hz, PhCH_2N), 4.05 (dd, 1 H, $J_{9,10} = 5.5$ Hz, $J_{10,11} = 6.0$ Hz, H-10), 3.97 (dd, 1 H, $J_{4,5} = 1.8$ Hz, H-4), 3.94 (dd, 1 H, $J_{11,12a} = 6.5$ Hz, $J_{12a,12b} = 10.8$ Hz, H-12a), 3.85 (dd, 1 H, $J_{11,12b} = 3.0$ Hz, H-12b), 3.77 (dd, 1 H, $J_{8,9} = 2.2$ Hz, H-9), 3.60−3.57 (m, 1 H, H-5), 3.57 (ddd, 1 H, H-11), 3.03−2.97 (m, 1 H, H-8), 1.80−1.25 (m, 4 H, H-6a, H-6b, H-7a, H-7b), 1.50, 1.45, 1.33, 1,31, (4 s, 12 H, 4 CH_3). Anal. Calcd for $C_{46}H_{55}NO_8$: C, 73.67; H, 7.39; N, 1.87. Found: C, 73.95; H, 7.47; N, 1.95.

Aza-*C*-disaccharide 54. Compound **53** (0.15 g, 0.20 mmol) was hydrogenated as described for the preparation of **42** to afford 74 mg (95%) of a crude product (95% pure by ^1H NMR). ^1H NMR (CD_3OD): δ 5.52 (d, 1 H, $J_{1,2} = 5.0$ Hz, H-1), 4.65 (dd, 1 H, $J_{2,3} = 2.3$ Hz, $J_{3,4} = 8.0$ Hz, H−0.3), 4.37 (dd, 1 H, H-2), 4.19 (dd, 1 H, $J_{4,5} = 1.8$ Hz, H-4), 4.17 (dd, 1 H, $J_{9,10} = J_{10,11} = 3.5$ Hz, H-10), 3.99 (dd, 1 H, H-9), 3.96−3.88 (m, 2 H, H-12a, H-12b), 3.86−3.80 (m, 1 H, H-5), 3.70−3.63 (m, 1 H, H-11), 3.55−3.44 (m, 1 H, H-8), 3.36−3.30 (m, 1 H, NH), 3.32 (s, 3 H, OCH_3), 2.10−2.00 (m, 1 H, H-7a), 1.92−1.60 (m, 3 H, H-6a, H-6b, H-7b), 1.54, 1.42, 1.33, 1.32 (4 s, 12 H, 4 CH_3). The debenzylated product (74 mg, 0.19 mmol) was treated with Amberlite IR-120 (H^+) ion-exchange resin as described for the preparation of **42** to obtain after gel permeation column chromatography on Sephadex LH-20 (10:1 CH_3OH-H_2O) the pure compound **54** (59 mg, 90%) as a colorless syrup. $[\alpha]_D^{20} = +3.2$ (*c* 0.4, H_2O). ^1H NMR (D_2O) (selected data): δ 5.80 (d, 0.4 H, $J_{1\alpha,2\alpha} = 3.5$ Hz, H-1α), 4.43 (d, 0.6 H, $J_{1\beta,2\beta} = 8.0$ Hz, H-1β), 3.50 (dd, 0.4 H, $J_{2\alpha,3\alpha} = 10.0$ Hz, H-2α), 3.32 (dd, 0.6 H, $J_{2\beta,3\beta} = 10.0$ Hz, H-2β), 2.05−1.47 (m, 4 H, 2 H-6α, 2 H-6β, 2 H-7α, 2 H-7β). MALDI-TOF MS (345.77): 311.8 (M + H − Cl). Anal. Calcd for $C_{12}ClH_{24}NO_8$: C, 41.68; H, 7.00; N, 4.05. Found: C, 41.55; H, 6.93; N, 4.01.

Alkene 55. The Wittig reaction was carried out as described above for the aza-*C*-disaccharide **43** starting from the aldehyde **27** (0.52 g, 1.0 mmol) and the phosphonium salt **39** (0.70 g, 1.2 mmol) to afford after flash chromatography (8:1 cyclohexane−AcOEt with 0.3% of triethylamine) the syrup **55** (0.22 g, 32%) as a mixture of (*Z*)- and (*E*)-olefins in a 5:1 ratio (by ^1H NMR analysis). **(*Z*)-55.** ^1H NMR (selected data): δ 5.82 (dd, 1 H, $J_{4,5} = 8.7$ Hz, $J_{5,6} = 11.0$ Hz, H-5), 5.62 (dd, 1 H, $J_{6,7} = 10.5$ Hz, H-6), 4.87 (s, 1 H, H-1), 4.26 (dd, 1 H, $J_{2,3} = 6.0$ Hz, $J_{3,4} = 3.5$ Hz, H-3), 4.12 (dd, 1 H, $J_{8,9} = J_{9,10} = 6.0$ Hz, H-9), 4.02 (dd, 1 H, $J_{7,8} = 3.8$ Hz, H-7), 3.82 (dd, 1 H, H-8). **(*E*)-55.** ^1H NMR (selected data): δ 5.88 (dd, 1 H, $J = 7.0, 15.5$ Hz), 5.66 (dd, 1 H, $J = 8.0, 15.5$ Hz).

Aza-*C*-disaccharide 56. The olefin **55** (0.22 g, 0.32 mmol) was reduced as described for the preparation of **41** to afford after flash chromatogrphy (5:1 cyclohexane−AcOEt with 0.3% triethylamine) compound **56** (0.17 g, 76%) as a syrup. $[\alpha]_D^{20} = -14.8$ (*c* 0.6, $CHCl_3$). ^1H NMR: δ 7.40−7.20 (m, 20 H, 4 Ph), 4.84 (s, 1 H, H-1), 4.76 and 4.55 (2 d, 2 H, $J = 11.8$ Hz, PhCH_2), 4.66 and 4.58 (2 d, 2 H, $J = 11.5$ Hz, PhCH_2), 4.54−4.51 (m, 2 H, H-2, H-3), 4.46 (s, 2 H, PhCH_2), 4.06 and 3.82 (2 d, 2 H, $J = 14.0$ Hz, PhCH_2N), 4.05 (dd, 1 H, $J_{8,9} = 6.0$ Hz, $J_{9,10} = 6.5$ Hz, H-9), 3.95 (dd, 1 H, $J_{10,11a} = 6.5$ Hz, $J_{11a,11b} = 10.5$ Hz, H-11a), 3.86 (dd, 1 H, $J_{10,11b} = 3.0$ Hz, H-11b), 3.79 (dd, 1 H, $J_{7,8} = 2.0$ Hz, H-8), 3.89−3.73 (m, 1 H, H-4), 3.58 (ddd, 1 H, H-10), 3.29 (s, 3 H, OCH_3), 3.08−3.02 (m, 1 H, H-7), 1.83−1.72 (m, 1 H, H-5a), 1.71−1.51 (m, 2 H, H-5b, H-6a), 1.49−1.30 (m, 1 H, H-6b), 1.41, 1.30 (2 s, 6 H, 2 CH_3). Anal. Calcd for $C_{43}H_{51}NO_7$: C, 74.43; H, 7.41; N, 2.02. Found: C, 74.20; H, 7.33; N, 1.98.

Aza-*C*-disaccharide 57. Compound **56** (0.14 g, 0.20 mmol) was hydrogenated as described for the preparation of **42** to afford 63 mg (95%) of a crude product (95% pure by ^1H NMR analysis). ^1H NMR (CD_3OD): δ 4.82 (s, 1 H, H-1), 4.70 (dd, 1 H, $J_{2,3} = 6.0$ Hz, $J_{3,4} = 5.2$ Hz, H-3), 4.58 (dd, 1 H, H-2), 4.21−4.16 (m, 1 H), 4.03−3.88 (m, 4 H), 3.75−3.66 (m, 1 H), 3.54−3.43 (m, 1 H), 3.38−3.28 (m, 1 H), 3.33 (s, 3 H, OCH_3), 2.08−1.85 (m, 4 H, H-5a, H-5b, H-6a, H-6b), 1.44, 1.32 (2 s, 6 H, 2 CH_3). The debenzylated product (63 mg, 0.19 mmol) was treated with Amberlite IR-120 (H^+) ion-exchange resin as described for the preparation of **42** to obtain after gel permeation column chromatography on Sephadex LH-20 (10:1 CH_3OH-H_2O) the pure compound **57** (51 mg, 95%) as a colorless syrup. $[\alpha]_D^{20} = -11.5$ (*c* 0.2, H_2O). ^1H NMR (D_2O) (selected data): δ 5.12 (d, 1 H, $J = 4.5$ Hz), 3.84 (dd, 1 H, $J = 5.0, 11.5$ Hz), 3.42−3.32 (m, 1 H), 1.87−1.44 (m, 4 H, 2 H-5, 2 H-6). MALDI-TOF MS (315.75): 281.7 (M + H − Cl). Anal. Calcd for $C_{11}ClH_{22}NO_7$: C, 41.84; H, 7.02; N, 4.44. Found: C, 41.99; H, 7.15; N, 4.53.

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