Stereoselective Homologation–Amination of Aldehydes by Addition of Their Nitrones to C-2 Metalated Thiazoles— A General Entry to α-Amino Aldehydes and Amino Sugars

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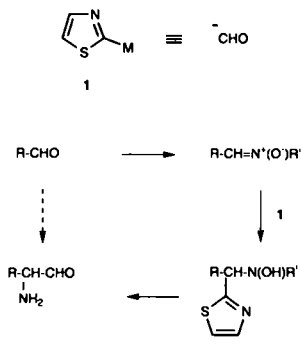
Abstract: A general method for the homologation of aldehydes to α-amino aldehydes (aminohomologation) has been developed, which employs nitrones as iminium derivatives of the aldehydes. Key operations include a) the addition of a thiazole metalated at C-2 to the *N*-benzylnitrone derived from the aldehyde, b) the reductive dehydroxylation of the resultant thiazolyl *N*-benzylhydroxylamine, and c) the unmasking of the formyl group from the thiazole ring. The homologation sequence was studied by employing nitrones derived from various chiral polyalkoxy aldehydes and dialdoses. The addition of 2-lithiothiazole to these nitrones was *syn*-selective, whereas the reaction with the same nitrones precomplexed with Lewis acids was *anti*-selective. Hence, from each nitrone a pair of diastereoisomeric hydroxylamines was obtained. These compounds were then converted by the above sequence into α-epimeric α-amino aldehydes. Model elaborations of some of these products afforded the amino sugars D-glucosamine, D-mannosamine, D-nojirimycin, and advanced intermediates for the synthesis of destomic acid and lincosamine.

Keywords
amino aldehydes · aminohomologation · amino sugars · nitrones · thiazoles

Introduction

The stereoselective introduction of an amino group at a saturated carbon center is a central transformation in synthetic methodologies toward various classes of bioactive molecules, mainly amino acids[1] and amino sugars.[2] Amination is also a crucial step in various approaches to polyhydroxylated piperidines and pyrrolidines, a class of nitrogen-containing sugar analogues (aza sugars)[3] that are attracting increasing interest as glycosidase inhibitors of potential therapeutic utility against viral infections, including that from HIV-1, the virus responsible for the AIDS disease.[4] Among the methods available, the most common are the nucleophilic amination by substitution or addition,[5] the electrophilic amination of ester enolates,[6] the alkylation of nucleophilic[7] and electrophilic[8] glycinate derivatives bearing a chiral template, the asymmetric hydrogenation of dehydroamino compounds,[9] the addition of organometallic reagents to the same dehydroamino compounds followed by removal of the substituent(s) on nitrogen,[10] and the stereoselective alkylation of metalated amidines.[11] Inspired by previous work on the use of 2-(trimethylsilyl)thiazole (**1a**) (M = $SiMe_3$) as a formyl anion equivalent[12] to homologate aldehydes into α-hydroxy aldehydes,[13] we sought an extension of the methodology to nitrones derived from aldehydes with the aim of achieving both homologation and amination (aminohomologation) and thus obtaining α-amino aldehydes (Scheme 1). After the addition of a suitable thiazole metalated at C-2 (**1**) to the nitrone, the reaction sequence would then involve the reductive dehydroxylation of the resultant hydroxylamine and the conversion of the thiazole ring to the formyl group. We report in this account details of our studies[14] on the synthetic scope and stereochemical aspects of this aminohomologation route for aldehydes and illustrate the versatility of our approach for the synthesis of amino and aza sugars. This synthetic strategy could in principle be extended to other C=N derivatives of aldehydes, such as imines, iminium ions, hydrazones, and oximes, as well as to other interesting heterocycles serving as functional group equivalents, such as furyl derivatives as carboxyl group equivalents.[15]



Scheme 1. Synthetic strategy for aldehyde homologation to α-amino aldehyde by addition of a thiazole to a nitrone.

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Results and Discussion

Synthesis of *N*-Benzyl Nitrones: It is mainly within the area of 1,3-dipolar cycloaddition chemistry that nitrones (azomethine oxides) have served as reagents in recent years.[16] Since the nitrone functionality incorporates a modified iminium moiety capable of undergoing facile nucleophilic attack, increasing attention is now being given to the reactions with carbon- and heteroatom-centered nucleophiles.[17] Among the possible nitrogen derivatives of aldehydes, nitrones therefore appeared to be very promising substrates for the aminohomologation strategy. In the course of our study this proved to have been a good choice, since all chiral nitrones employed were readily available, stable compounds, which did not require particular care with regard to handling and storage and were nevertheless sufficiently reactive towards a range of metalated thiazoles **1**.

We have recently described a fairly general synthesis of *N*-benzylnitrones by condensation of aldehydes with *N*-benzylhydroxylamine in the presence of a heterogeneous drying agent such as sodium or magnesium sulfate.[18] *N*-Benzylnitrones **2**–**11** derived from chiral alkoxy aldehydes and dialdoses were prepared in fairly good yields and on a multigram scale by this method (Fig. 1). Compounds **2**–**11** were solid materials, which could readily be purified by crystallization. The (*Z*) isomer was obtained in all cases; the configuration was assigned based on the ^{1}H NMR spectra in non-aromatic ($CDCl_3$) and aromatic solvents[19] (C_6D_6), and on the nuclear Overhauser effect[20] between $CH{=}N^+$ and CH_2Ph signals (8–10% enhancement) in the difference spectra.

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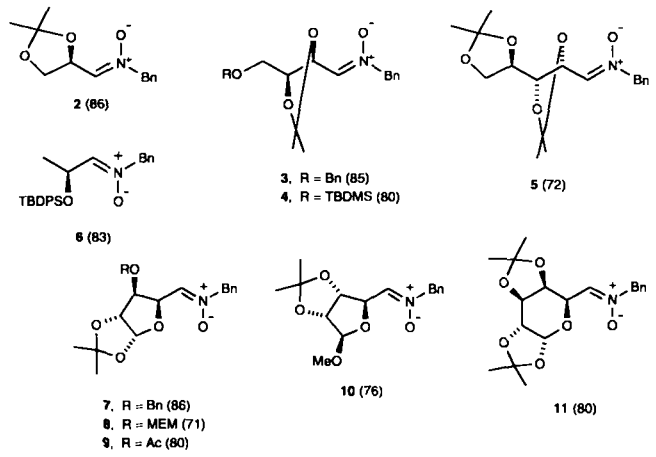
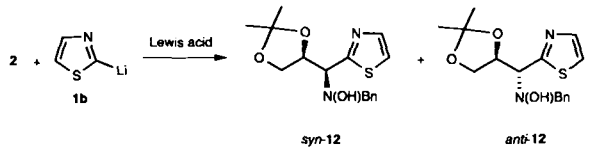


Fig. 1. Nitrones prepared by reaction of aldehydes with benzylhydroxylamine (yields are shown in parentheses). Bn = benzyl; Ac = acetyl; MEM = methoxyethoxymethyl; TBDMS = *tert*-butyldimethylsilyl; TBDPS = *tert*-butyldiphenylsilyl.

Addition Reaction:

Scope and Stereochemistry: Although very facile reactions of 2-(trimethylsilyl)thiazole (**1a**) with various carbon electrophiles (aldehydes, ketones, ketenes, carboxylic acid chlorides, and azaaryl cations) have been reported,[13, 21] it turned out to be unreactive toward nitrones[22] including compound **2** derived from D-glyceraldehyde acetonide. However, 2-lithiothiazole (**1b**) reacted rapidly with **2** at low temperature and in diethyl ether or tetrahydrofuran as solvent[23] to give *N*-benzyl hydroxylamines **12** (Scheme 2) with good overall yield and *syn* selectivity[24] (Table 1). The configurations at the newly formed stereocenters were unequivocally established by the X-ray structure determination of *anti*-**12** (see below). It is worth mentioning that in our first report[14a] we erroneously assigned the *anti* configuration to the major stereoisomer based on its conversion into an *erythro* oxazolidinone. A correction has been reported.[14b]



Scheme 2. Addition of 2-lithiothiazole (**1b**) to the nitrone **2** (see Table 1 for reaction conditions).

Aiming at a reversal of diastereoselectivity, we studied the reaction of **1b** with **2** under different conditions (Table 1). The presence of Me_3SiCl, which was expected to give a highly activated *N*-siloxyiminium intermediate by *O*-silylation of the nitrone,[25] had very little effect on stereoselectivity. Lithium iodide was ineffective as well. In contrast, the Lewis acids $MgBr_2$, $ZnCl_2$, and $ZnBr_2$ induced the formation *anti*-**12** in slight excess over *syn*-**12**. Fortunately, very high *anti* selectivity was obtained with Et_2AlCl and $TiCl_4$. The use of other metalated thiazoles **1c**–**f** either in the absence or presence of nitrone-complexing agents proved to be unsatisfactory. These reagents were quite sluggish and consequently required long reaction times and high temperatures. In all cases the chemical yield and/or stereoselectivity were much lower than with 2-lithiothiazole (**1b**).

Guided by the above results, we next examined the addition of **1b** to nitrones derived from other alkoxy aldehydes and from

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Table 1. Product studies and diastereoselectivities for the addition of 2-metalated thiazoles **1** to the nitrone **2**.

Thiazole [a]	M	Solvent	T/°C	t/h	Lewis acid [b]	*syn*-**12**:*anti*-**12** [c]	Yield/% [d]
1a	$SiMe_3$	CH_2Cl_2	25	24	–	– [e]	– [e]
1b	Li	Et_2O	−80	0.25	–	92:8	82
1b	Li	THF	−80	0.25	–	93:7	70
1b	Li	Et_2O	−80	0.5	Me_3SiCl	73:27	71
1b	Li	Et_2O	−80	0.5	LiI	88:12	78
1b	Li	Et_2O	−80	0.5	$MgBr_2$	46:54	81
1b	Li	Et_2O	−80	0.5	$ZnCl_2$	35:65	75
1b	Li	Et_2O	−80	0.5	$ZnBr_2$	44:56	78
1b	Li	Et_2O	−80	0.5	Et_2AlCl	3:97	84
1b	Li	Et_2O	−80	0.5	$TiCl_4$	5:95	69
1c	$CuLi)_{1/2}$	Et_2O	−80	1	–	75:25	66
1d	MgBr	Et_2O	−50	1	–	89:11	40 [f]
1d	MgBr	Et_2O	−50	1	$MgBr_2$	45:55	56 [f]
1e	$AlEt_2$	Et_2O	−20	1	–	83:17	73 [f]
1e	$AlEt_2$	Et_2O	−20	1	Et_2AlCl	57:43	70 [f]
1f	ZnBr	Et_2O	−40	12	$ZnBr_2$	55:45	35 [g]

[a] In all cases 3 equiv of **1** were used. [b] Precomplexation of the nitrone with 1.0 equiv of Lewis acid was carried out at ambient temperature for 15 min. [c] Ratio determined by ^1H NMR integration of the characteristic proton signals of the crude mixture. [d] Isolated yield of diastereomeric mixture. [e] Unchanged **2** was recovered totally. [f] No product was formed at lower temperatures. [g] No product was formed in THF as solvent or in the presence of $ZnCl_2$.

dialdoses. The hydroxylamines obtained are presented in Figure 2 and the corresponding diastereoselectivities[26] and yields in Table 2. The reactions of nitrones **3** and **4**, both derived from L-threose, had similar stereochemical outcomes to the reactions of **2**, that is, the *syn*:*anti* selectivity depended on whether the reagents alone were employed or the nitrones were precomplexed with Lewis acids. In contrast, the reaction of the nitrone **5** derived from D-arabinose was *anti*-selective under both conditions, while the reaction of **6** derived from L-lactaldehyde lacked selectivity in both cases. The overall chemical yields ranged from good to excellent.

Conditions for high levels of diastereoselectivity were obtained in reactions of **1b** with nitrones derived from protected D-dialdoses (*C*-glycosyl nitrones). Without added Lewis acids, the *C*-xylosyl derivatives **7**–**9**, which differ in the protective groups at the C-3 hydroxyl, afforded the corresponding adducts

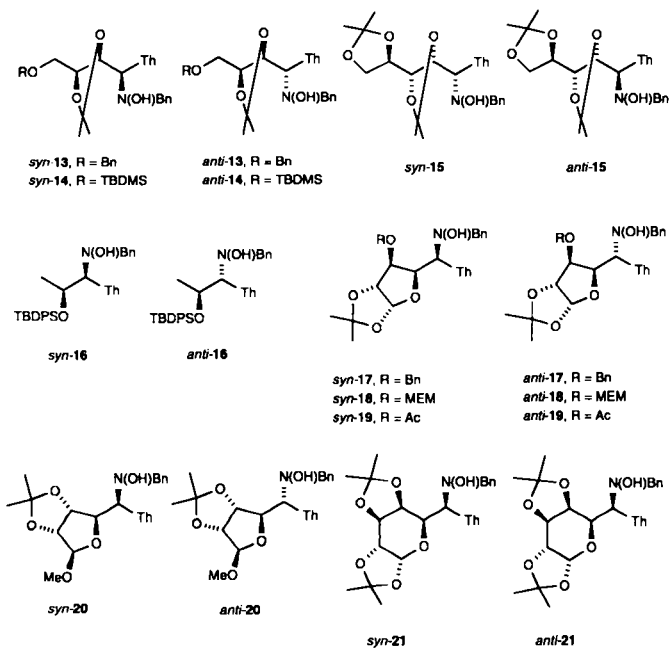


Fig. 2. Hydroxylamines prepared by addition of **1b** to nitrones **3**–**11** (see Table 2). Th = 2-thiazolyl.

Table 2. Product studies and diastereomeric ratios (*syn*:*anti*) for the addition of 2-lithiothiazole (**1b**) to the nitrones **3**–**11** [a].

Nitrone	Lewis acid [b]	Product	*syn*:*anti* [c]	Yield/% [d]
3	–	**13**	70:30	76
3	$ZnCl_2$	**13**	55:45	75
3	Et_2AlCl	**13**	13:87	80
4	–	**14**	60:40	77
4	Et_2AlCl	**14**	33:67	72
5	–	**15**	28:72	80
5	$ZnCl_2$	**15**	24:76	75
5	Me_3SiCl	**15**	30:70	64
5	Et_2AlCl	**15**	25:75	80
6	–	**16**	53:47	88
6	Et_2AlCl	**16**	51:49	86
7	–	**17**	90:10	90
7	$ZnCl_2$	**17**	69:31	86
7	Et_2AlCl	**17**	4:96	90
8	–	**18**	88:12	81
8	$ZnCl_2$	**18**	62:38	77
8	Et_2AlCl	**18**	10:90	83
9	–	**19**	88:12	23
10	–	**20**	84:16	77
10	$ZnCl_2$	**20**	84:16	82
10	$MgBr_2$	**20**	76:24	80
10	$TiCl_4$	**20**	49:51	60
10	Et_2AlCl	**20**	35:65	90
11	–	**21**	58:42	86
11	LiI	**21**	63:37	85
11	$MgBr_2$	**21**	68:32	82
11	$ZnCl_2$	**21**	75:25	80
11	$ZnBr_2$	**21**	79:21	88
11	$TiCl_4$	**21**	11:89	68
11	Et_2AlCl	**21**	9:91	90

[a] All reactions in Et_2O as solvent at −80 °C for 15 min with 3.0 equiv of 2-lithiothiazole (**1b**). [b] Nitrone complexation with the Lewis acid (1.0 equiv) at ambient temperature. [c] Determined by integration of the ^1H NMR spectrum of the crude reaction mixture. [d] Isolated yield of the diastereomeric mixture.

syn-**17**, *syn*-**18**, and *syn*-**19**, respectively, as major isomers. While the overall yields for nitrones **7** and **8** were fairly good, the yield for compound **9** was less satisfactory, because of the competing reaction of **1b** with the *O*-acetyl group of the nitrone to form 2-acetylthiazole as a by-product.[27] The *C*-ribosyl and *C*-galactosyl nitrones **10** and **11** also afforded the hydroxylamines *syn*-**20** and *syn*-**21**, respectively, as major products, although the latter formed with low selectivity. Reactions in the presence of

complexing agents led to variable *syn*:*anti* ratios. The above *syn* adducts were still the major products in the presence of zinc and magnesium halides, whereas the isomers *anti*-**17**, *anti*-**18**, *anti*-**20**, and *anti*-**21** were favored in the presence of $TiCl_4$ or Et_2AlCl. Good to excellent overall yields of isolated products were registered in all cases.

Transition-State Models: From the few reports dealing with the 1,3-addition of organometallic reagents to chiral alkoxy nitrones,[17a,c] it appears that transition-state models similar to those developed for alkenes (Houk model)[28] and enolates (Fleming–McGarvey model)[29] are more consistent with the observed diastereofacial selectivities than that developed for carbonyl addition (Felkin–Anh).[30] A similar conclusion has been reached for addition reactions to chiral imines[31] and iminium cations.[32] Accordingly, models **A** and **B** (Fig. 3) were

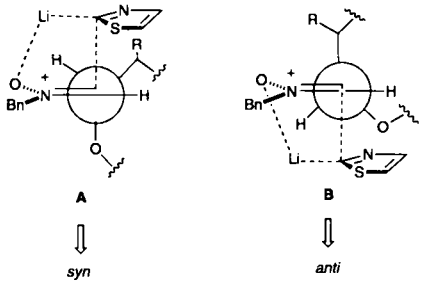


Fig. 3. Proposed transition states for the addition of 2-lithiothiazole (**1b**) to the nitrones **2**–**5** and **7**–**11**.

considered to account for the stereochemical outcome of the addition of **1b** to the above nitrones in the absence of complexing agents.[33] In model **A** the nitrone conformation is such that the largest group is perpendicular to the C=N bond and the medium-size substituent occupies the outer rather than the inner position in order to avoid the steric interaction with the *N*-substituents.[34] However, it has been already pointed out by Kita and co-workers[17a,c] that this model predicts that severe steric interactions may occur between the incoming nucleophile and the substituent R. In this case, the reactive nitrone adopts the conformation shown in **B**. Thus, the level of *syn* selectivity (model **A**) is considerably higher for nitrone **2** (R = H, Fig. 3) derived from D-glyceraldehyde than for compounds **3** (R = CH_2OBn) and **4** (R = $CH_2OTBDMS$) derived from L-threose. The *anti* selectivity[35] found with the nitrone **5** derived from D-arabinose (R = 1,3-dioxolane ring) suggests that in this case the organometallic reagent **1b** is forced to attack primarily the less reactive but less hindered nitrone conformer shown in model **B**.[36] The high levels of *syn* selectivity observed with the *C*-glycosyl nitrones **7**–**10** are also consistent with model **A**, whereas the low selectivity with **11** indicates that model **B** is equally important here. Finally, the lack of selectivity observed with the nitrone **6** derived from L-lactaldehyde leads us to consider the transition-state models **C** and **D** (Fig. 4), both involving the *tert*-butyldiphenylsilyl group as the largest substituent while methyl or hydrogen occupy the inner position. In this case, the difference in size between methyl and hydrogen is not sufficient that one of these structures predominates.

Stereochemical models involving nitrone/Lewis acid associations were considered for reactions carried out in the presence of complexing agents. NMR spectra provide evidence for the mode of complexation of **2** by three different Lewis acids (Table 3).[37] The substantial deshielding of H_a, H_e, and C_1 indicates a coor-

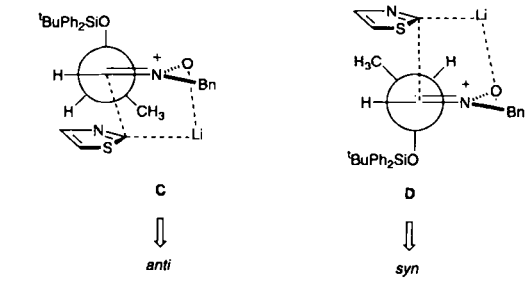
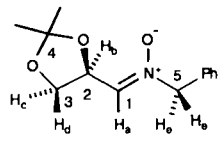


Fig. 4. Proposed transition states for the addition of 2-lithiothiazole (**1b**) to the nitrone **6**.

Table 3. Chemical shift differences ($\Delta\delta$ in ppm) induced by complexing agents in the NMR spectra ($CDCl_3$) of the nitrone **2**.



2

Lewis acid[b]	^{1}H NMR [b]					^{13}C NMR				
	H_a	H_b	H_c	H_d	H_e	C_1	C_2	C_3	C_4	C_5
Et_2AlCl	0.28	0.13	0.05	0.24	0.26	14.89	0.00	0.16	1.46	−1.50
$ZnBr_2$	0.26	0.21	0.07	0.24	0.29	12.20	0.08	0.02	1.02	−0.25
Me_3SiCl	0.39	0.05	0.02	0.15	0.25	8.39	−0.20	0.36	0.37	−1.28

[a] 1.0 equiv. [b] H_c and H_d signals were assigned on the basis of NOE experiments; H_c protons appeared as a singlet in all cases.

dination of the metal to the nitrone oxygen in all cases, while deshielding of H_b and H_d induced by Et_2AlCl and $ZnBr_2$ indicates additional coordination of aluminum and zinc to the oxygen atoms of the dioxolane ring. Hence, transition-state structures **E** and **F** were postulated (Fig. 5), arising from coordi-

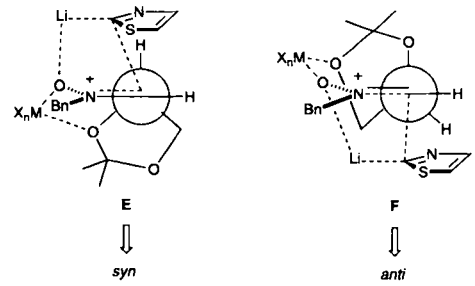


Fig. 5. Proposed transition states for the addition of 2-lithiothiazole (**1b**) to the nitrone **2** in the presence of Et_2AlCl and $ZnBr_2$.

nation of the Lewis acid to the nitrone oxygen and to the α-alkoxy (α-chelation) and β-alkoxy (β-chelation) groups, respectively.[38] The observed *anti* selectivity (Table 1) is in agreement with the β-chelate model **F** featuring a less crowded arrangement than in the α-chelate structure **E**. Similar structures can be employed to explain the results with the other precomplexed nitrones **3**–**10**, although the presence of various oxygen atoms in these substrates leaves room for conjecture. Even for compound **2**, the postulated structures **E** and **F** may be an oversimplification since the ^{27}Al chemical shifts of the nitrone/Et_2AlCl mixture show the presence of four- and five-coordinated species.

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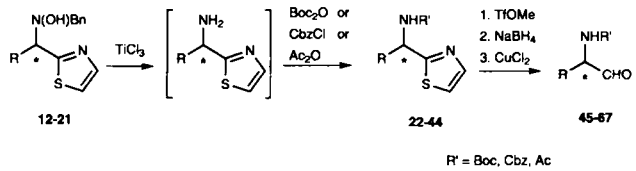
Synthesis of α-Amino Aldehydes: We next examined the reductive dehydroxylation of 2-thiazolyl *N*-benzylhydroxylamines to give the corresponding amines, as a further step toward the synthesis of α-aminoaldehydes (Scheme 3). Various methods have been reported for the reduction of *N*,*N*-dialkylhydroxylamines, including catalytic hydrogenation,[39] reduction with



Scheme 3. Conversion of 2-thiazolyl *N*-benzyl hydroxylamines to amines and α-amino aldehydes (see Fig. 6 and Table 4 for products and yields).

SmI_2,[39] Zn/HCl,[39] Raney Ni,[39,40] and aqueous $TiCl_3$,[41,42] and reduction of phosphate or carbonate esters with Li in liquid ammonia.[17e] Problems with catalyst poisoning by thiazole precluded the use of catalytic hydrogenation with our compounds. Reduction under strongly acidic conditions was not an option, owing to the presence of acid-sensitive protective groups. A recent method for dehydroxylation with carbon disulfide under neutral conditions[43] was also unsuccessful. Fortunately, the reaction proceeded smoothly with aqueous $TiCl_3$ at room temperature and rapidly went to completion. While the formation of secondary amines has been reported under these conditions,[41] in our case, both dehydroxylation and debenzylation occurred readily to give primary amines (Scheme 3).[44] These compounds were isolated and characterized through their *N*-protected *tert*-butoxycarbonyl (Boc), benzyloxycarbonyl (Cbz), and acetyl (Ac) derivatives. In this way, all diastereomeric pairs of *syn* and *anti* hydroxylamines **12–21** were converted into the corresponding pairs of *N*-monoprotected amines **22–44** (Fig. 6). Chemical yields of individual isolated products are collected in Table 4.

What remained to complete the homologation sequence was the liberation of the formyl group from the thiazole ring. This operation was based on a simple and amply documented one-pot protocol[45] involving *N*-methylation, reduction, and metal-assisted hydrolysis. Previous work on the thiazole–aldehyde synthesis[13] had demonstrated that the almost neutral conditions under which these reactions take place leave the various oxygen and nitrogen protective groups and the stereocenters of the substrate untouched.[46] Hence, α-aminoalkylthiazoles **22–44** were transformed into the corresponding α-amino aldehydes **45–67** (Fig. 6) in good overall yields (Table 4). In some cases, the NMR spectra of isolated product revealed the presence of 5–6% of the α-epimer. Attempts at removing this by-product by column chromatography on silica gel led to complete epimerization. Therefore, crude compounds were immediately used for further transformations or stored at −30 °C under an argon atmosphere.

Stereochemical Assignments and Synthetic Applications: Characterization of the *syn* and *anti* isomers of hydroxylamines **12–21** or their derivatives was achieved by X-ray crystallography or chemical transformations. Single crystal X-ray analyses[47] established unequivocally the structures of hydroxylamines *anti*-**12**, *syn*-**20**, *anti*-**21**, and *N*-acetyl amine **36**. The oxidation of the α-amino aldehyde **49** with sodium chlorite and hydrogen peroxide produced the carboxylic acid **68** (Scheme 4), which was identical to the product derived from the 2-furyl derivative **69** employed as an advanced intermediate for the synthesis of polyoxamic acid.[15] The reduction of *N*-acetyl α-amino aldehydes **52** (from *syn*-**15**) and **53** (from *anti*-**15**) with $NaBH_4$ and

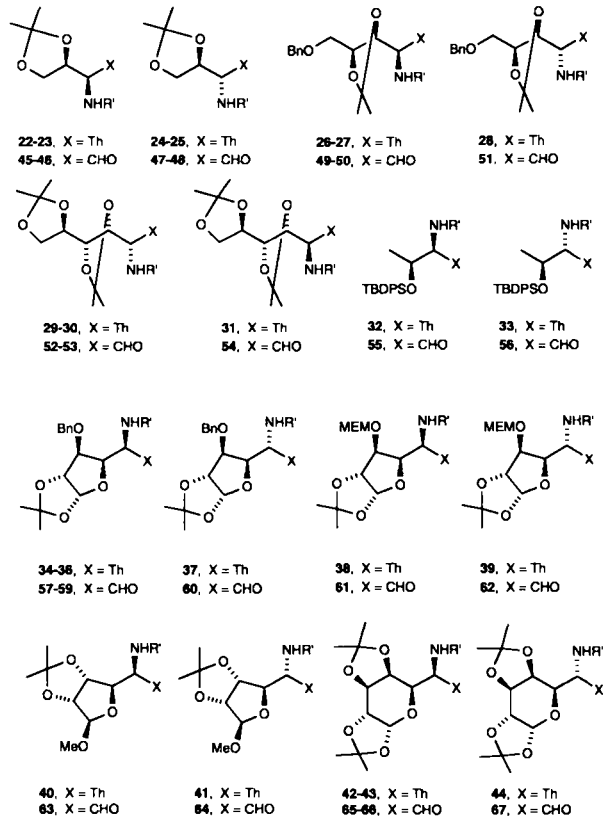
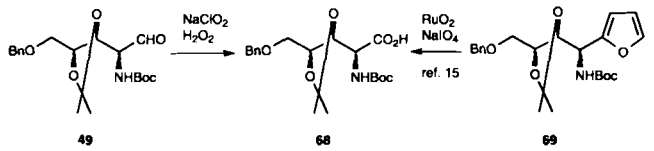


Fig. 6. α-Aminoalkylthiazoles and α-amino aldehydes obtained from hydroxylamines **12–21**. R′ = Ac, Boc, and Cbz (see Table 4).

Table 4. Products obtained from the elaboration of 2-thiazolyl *N*-benzyl hydroxylamines **12–21**.

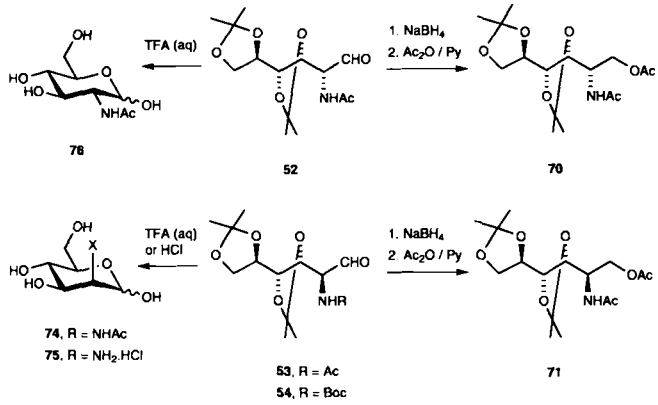
Hydroxylamine	R′[a]	α-Aminoalkylthiazole (yield/% [b])		α-Aminoaldehyde (yield/% [b])	
syn-**12**	Boc	**22**	(74)	**45**	(64)
syn-**12**	Cbz	**23**	(86)	**46**	(70)
anti-**12**	Boc	**24**	(78)	**47**	(70)
anti-**12**	Cbz	**25**	(80)	**48**	(76)
syn-**13**	Boc	**26**	(78)	**49**	(75)
syn-**13**	Cbz	**27**	(72)	**50**	(80)
anti-**13**	Cbz	**28**	(76)	**51**	(73)
syn-**15**	Ac	**29**	(72)	**52**	(60)
anti-**15**	Ac	**30**	(76)	**53**	(64)
anti-**15**	Boc	**31**	(81)	**54**	(72)
syn-**16**	Boc	**32**	(85)	**55**	(73)
anti-**16**	Boc	**33**	(82)	**56**	(75)
syn-**17**	Boc	**34**	(72)	**57**	(81)
syn-**17**	Cbz	**35**	(84)	**58**	(89)
syn-**17**	Ac	**36**	(72)	**59**	[c]
anti-**17**	Cbz	**37**	(81)	**60**	(76)
syn-**18**	Cbz	**38**	(87)	**61**	(72)
anti-**18**	Cbz	**39**	(72)	**62**	(63)
syn-**20**	Cbz	**40**	(86)	**63**	(79)
anti-**20**	Cbz	**41**	(82)	**64**	(76)
syn-**21**	Cbz	**42**	(81)	**65**	(90)
syn-**21**	Ac	**43**	(86)	**66**	(83)
anti-**21**	Ac	**44**	(78)	**67**	(70)

[a] Cbz = benzyloxycarbonyl; Boc = *tert*-butoxycarbonyl; Ac = acetyl. [b] Isolated yield of crude material. [c] Not formed.



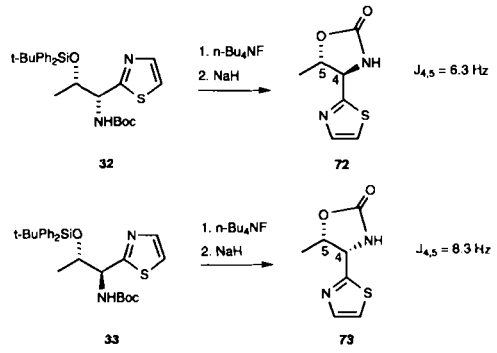
Scheme 4.

acetylation of the resultant alcohols with Ac_2O and pyridine gave the acetamides **70** and **71**, respectively (Scheme 5), whose properties were identical to those reported in the literature.[48] The deprotection of the hydroxyl group in compounds **32** and



Scheme 5. Synthesis of **74**, **75**, and **76**.

33 (Scheme 6) with nBu$_4$NF and base-induced ring-closure in the resultant amino alcohols formed the diastereomeric oxazolidinones **72** and **73** whose ^{1}H NMR spectra showed $^3J_{4,5}$ values[49] consistent with the assigned stereochemistry.[50]

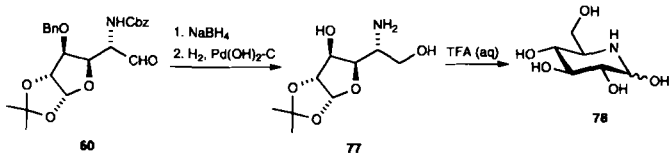


Scheme 6.

The stereochemical assignments were confirmed and the synthetic utility of the aminohomologation methodology illustrated by means of the synthesis of model natural products or their advanced intermediates as detailed below.

D-Mannosamine and D-Glucosamine: Derivatives of D-mannosamine are key intermediates in the chemical or enzymatic syntheses of *N*-acetyl neuraminic acid (Neu5Ac),[51] the most widely encountered member of the sialic acid family.[52] For instance, *N*-acetyl-D-mannosamine diacetonide **53** (Scheme 5) has previously been prepared from D-gluconolactone (52%),[53] while *N*-acetyl-D-mannosamine **74** has been obtained by enzymatic epimerization of the more readily available *gluco* isomer **76**.[54] Both compounds **53** and **74** were then converted to Neu5Ac by coupling with pyruvic acid or synthetic equivalents.[53, 54, 55] Hence, a sample of compound **53**, prepared as described above by the aminohomologation route from D-arabinose diacetonide in 20% yield, was cleanly converted into **74** (76%) by treatment with aqueous trifluoroacetic acid, while the *N*-Boc analogue **54** was converted into D-mannosamine hydrochloride **75** (Scheme 5).[56] In a similar way, deacetonization of **52** with aqueous trifluoroacetic acid afforded *N*-acetyl-D-glucosamine **76**. Physical and spectral properties of compounds **74**, **75**, and **76** were in accordance with the literature values.

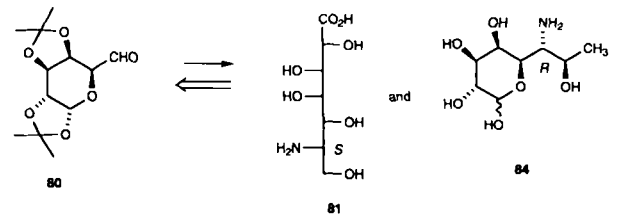
D-Nojirimycin: A simple three-step manipulation (Scheme 7) of the α-amino aldehyde **60** (46% from D-*xylo*-dialdose) led to the naturally occurring aza sugar D-nojirimycin (**78**), which showed



Scheme 7. Synthesis of D-nojirimycin (**78**).

physical characteristics identical to literature values.[57, 58] The reaction sequence involved the reduction of **60** with sodium borohydride followed by simultaneous deprotection of the C-3 hydroxyl and amino groups by $Pd(OH)_2$-catalyzed hydrogenolysis[59] to give the amino alcohol **77**. This compound, upon deprotection of the C-1 and C-2 hydroxyl groups by deacetonization with aqueous trifluoroacetic acid, afforded **78** in 68% overall yield. In addition to providing proof for the structure of **60**, this model reaction sequence represents a new approach to aza sugars involving the aminohomologation of sugar-derived aldehydes.

Destomic Acid and Lincosamine: The polyhydroxylated ε-amino acid **81** (destomic acid) (Scheme 8) is a component of the antibiotic natural products destomycin[60] and hygromycin,[61] while the amino sugar **84** (lincosamine) is a key structural unit of the anticancer antibiotic lincomycin.[62] Both compounds have been the targets of various synthetic approaches. For instance, the first total synthesis of destomic acid **81** was reported by Hashimoto and co-workers[63] and involved the cyanomesylation of α-D-*galacto*-hexodialdo-1,5-pyranose diacetonide **80**. The diastereoselectivity of the reaction was 63% and the overall yield of the isolated amino acid 21.4%. More recently, Jurczak and co-workers[64] described the synthesis of **81** by the hetero-Diels–Alder reaction of a protected α-amino aldehyde derived from L-serine. The reported syntheses of lincosamine (**84**)[65] include the construction of the pyranose ring by elaboration of



Scheme 8. Retrosynthesis of the amino sugars destomic acid (**81**) and lincosamine (**84**).

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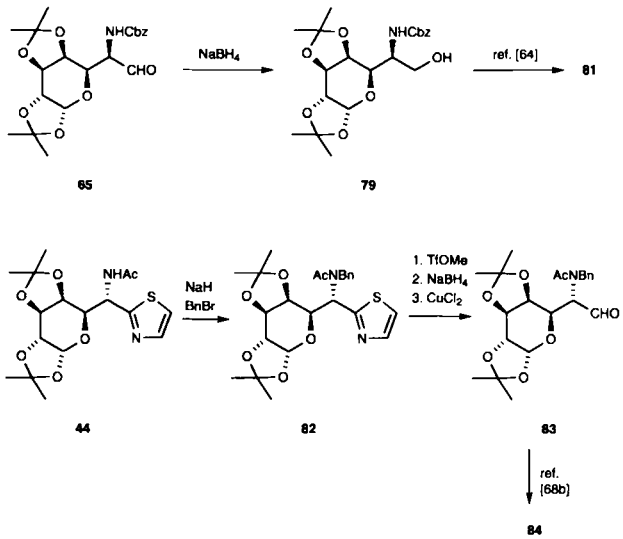
a furan derivative[66] or by hetero-Diels–Alder reaction,[67] and the chain-elongation of D-*galacto*-dialdose derivatives.[68]

Compounds **81** and **84** feature an aminomethylene group, but with opposite configuration at the carbon atom attached to the polyhydroxylated carbon chain with the *galacto* configuration. These features suggested that these amino sugars could be synthesized by stereoselective aminohomologation of the D-*galacto*-dialdose **80** (Scheme 8).[69] Indeed, conditions have been described above under which 2-lithiothiazole (**1b**) and the nitrone **11**, derived from **80**, stereoselectively afforded either of the hydroxylamines *syn*-**21** or *anti*-**21** (Table 2). The transformation of these compounds into the corresponding amines and aldehydes was also described (Table 4). Hence, suitable elaborations of these intermediates were needed to complete the formal synthesis of **81** and **84**. To this end, the α-amino aldehyde **65** was reduced with $NaBH_4$ (Scheme 9) to give the amino alcohol **79** (39.7% from **80**), which had been previously converted into



Scheme 9. Synthesis of advanced intermediates for the preparation of destomic acid (**81**) and lincosamine (**84**).

destomic acid **81**.[64] Benzylation of the *N*-acetyl amine **44** gave **82**, which was converted to the galactosyl amino aldehyde **83** (27.3% from **80**) by the conventional thiazolyl-to-formyl unmasking protocol. The use of **83** as an intermediate for the synthesis of lincosamine has been previously described.[68b]

Conclusion

The aminohomologation of aldehydes through nitrone intermediates is an interesting synthetic methodology whose main operation involves the Lewis acid stereocontrolled reaction with a metalated thiazole to give hydroxylamine derivatives. Also in this synthetic route the thiazole ring plays a key role as a masked formyl group, since it tolerates the reaction conditions employed to transform the hydroxylamino group into an amino group[46] and can readily be cleaved to give the aldehyde. The syntheses of D-mannosamine, D-glucosamine, D-nojirimycin, and the formal synthesis of lincosamine and destomic acid illustrate the potential of this methodology in the construction of various types of natural amino sugars and their unnatural analogues.

Experimental Procedure

General: The reaction flasks and other glass equipment were heated in an oven at 130 °C overnight and assembled in a stream of argon. Syringes were assembled and fitted with needles while hot and cooled in a stream of argon. Special techniques were used in handling moisture- and air-sensitive materials, as described in ref. [70]. All solvents were dried by the usual methods [71]. Preparative chromatography was performed on columns of silica gel (60–240 mesh) and with solvents that were distilled prior to use. Reactions were monitored by TLC on silica gel 60F254; the positions of the spots were detected with 254 nm UV light and by charring with 50% methanolic sulfuric acid as staining system. Melting points were determined on a Büchi 510 melting-point apparatus and are uncorrected. Optical rotations were measured on a Perkin Elmer 241 polarimeter at 20 °C in the stated solvent. Elemental analyses were performed on a Perkin Elmer 240 B microanalyzer. IR spectra were recorded with a Perkin Elmer FT1600 infrared spectrophotometer. ^1H and ^{13}C NMR spectra were recorded on a Varian 300 Unity spectrometer operating at 300 and 75.5 MHz, respectively, at 20 °C in $CDCl_3$ unless otherwise specified. Chemical shifts are expressed in ppm positive values downfield from internal TMS.

Materials: *N*-Benzyl nitrones **2–11** were prepared as described in ref. [18]. 2-Bromothiazole was either obtained commercially (Aldrich or Acros) and distilled twice prior to use, or prepared from 2-aminothiazole as described in ref. [13c]. New compounds obtained as solid materials by column chromatography were not recrystallized.

2-Lithiothiazole (1b): A solution of freshly distilled 2-bromothiazole (2.46 g, 1.35 mL, 15 mmol) in diethyl ether (30 mL) was added slowly to a stirred solution of butyllithum (10 mL of a 1.6 M solution in hexanes, 16 mmol) in diethyl ether (30 mL), cooled to −78 °C. During this operation, the temperature of the solution was not allowed to rise above −70 °C. The mixture was stirred for 15 min at −78 °C and the resulting pale yellow solution of 2-lithiothiazole (**1b**) (ca. 0.2 M) was used immediately [72].

Addition of 2-Lithiothiazole (1b) to Nitrones 2–11:

Method A (without Lewis acid): A cooled (−90 °C) and stirred solution of 2-lithiothiazole (**1b**) in diethyl ether (from 15 mmol of 2-bromothiazole) was treated with a solution of the nitrone (5 mmol) in THF (60 mL) added dropwise. During the addition, the temperature of the reaction mixture was not allowed to rise above −80 °C. The mixture was stirred for 15 min at −80 °C, quenched with saturated aq NH_4Cl (15 mL), stirred again at ambient temperature for 10 min, and diluted with diethyl ether (25 mL). The organic layer was separated and the aqueous layer extracted with diethyl ether (3 × 50 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$), and the solvent evaporated in vacuo. The diastereoselectivity (d.s./%) was determined on the residue by ^1H NMR analysis. The crude product was purified by column chromatography on silica gel.

Method B (with Lewis acid): To a stirred solution of the nitrone (5 mmol) in diethyl ether (100 mL) was added the Lewis acid (5 mmol) in one portion at room temperature, and stirring was continued for 15 min. The mixture was transferred under argon atmosphere into a dropping funnel and added dropwise to a cooled (−90 °C) and stirred solution of 2-lithiothiazole (**1b**) in diethyl ether (from 15 mmol of 2-bromothiazole). The mixture was stirred for 30 min at −80 °C and then treated with 1 N aq NaOH (100 mL). After additional stirring for 15 min at ambient temperature, the mixture was extracted with diethyl ether (3 × 50 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$) and concentrated in vacuo. The d.s. was determined on the residue by ^1H NMR analysis. The crude product was purified by column chromatography on silica gel.

***N*-Benzyl-1-deoxy-1-(hydroxyamino)-2,3-*O*-isopropylidene-1-(2-thiazolyl)-D-*threo*-triitol** (*syn*-**12**): Formed from the nitrone **2** (1.18 g, 5 mmol) by method A. Column chromatography (70:30, hexane:diethyl ether) of the residue afforded *syn*-**12** (1.18 g, 74%, d.s. = 93%) as an oil; $[\alpha]_D^{20} = -7.8$ ($c = 0.74$ in $CHCl_3$); ^1H NMR: $\delta = 1.25$ (s, 3H), 1.28 (s, 3H), 3.70 (dd, $^2J(H,H) = 8.2$, $^3J(H,H) = 5.3$ Hz, 1H), 3.84 (d, $^2J(H,H) = 12.0$ Hz, 1H), 3.94 (dd, $^2J(H,H) = 8.2$, $^3J(H,H) = 5.7$ Hz, 1H), 3.98 (d, $^2J(H,H) = 12.0$ Hz, 1H), 4.38 (d, $^3J(H,H) = 6.8$ Hz, 1H), 4.72 (ddd, $^3J(H,H) = 6.8$, 5.7, 5.3 Hz, 1H), 6.45 (bs, ex. D_2O), 7.20–7.35 (m, 5H), 7.38 (d, $^3J(H,H) = 3.2$ Hz, 1H), 7.82 (d, $^3J(H,H) = 3.2$ Hz, 1H); ^{13}C NMR: $\delta = 25.50$, 26.49, 61.73, 66.97, 68.57, 76.25, 109.62, 120.31, 127.50, 128.39, 129.39, 136.81, 142.01, 164.71; $C_{16}H_{20}N_2O_3S$ (320.41): calcd C 59.98; H 6.29; N 8.74; found C 60.05; H 6.17; N 8.65.

***N*-Benzyl-1-deoxy-1-(hydroxyamino)-2,3-*O*-isopropylidene-1-(2-thiazolyl)-D-*erythro*-triitol** (*anti*-**12**): Formed from the nitrone **2** (1.18 g, 5 mmol) and Et_2AlCl (5 mL of a 1 M solution in hexanes, 5 mmol) by method B. Column chromatography (70:30, hexane:diethyl ether) of the residue afforded *anti*-**12** (1.30 g, 81%, d.s. = 97%) as a white solid; m.p. 157–159 °C; $[\alpha]_D^{20} = -9.0$ ($c = 0.39$ in $CHCl_3$); ^1H NMR: $\delta = 1.28$ (s, 3H), 1.32 (s, 3H), 3.71 (d, $^2J(H,H) = 13.2$ Hz, 1H), 3.79 (d, $^2J(H,H) = 13.2$ Hz, 1H), 4.05 (dd, $^2J(H,H) = 8.5$, $^3J(H,H) = 5.3$ Hz, 1H), 4.15 (dd, $^2J(H,H) = 8.5$, $^3J(H,H) = 5.5$ Hz, 1H), 4.16 (d, $^3J(H,H) = 7.7$ Hz, 1H), 4.72 (dt, $^3J(H,H) = 7.7$, 5.4 Hz, 1H), 6.43 (bs, 1H, ex. D_2O), 7.26 (bs, 5H), 7.39 (d, $^3J(H,H) = 3.2$ Hz, 1H), 7.82 (d, $^3J(H,H) = 3.2$ Hz, 1H); ^{13}C NMR: $\delta = 25.21$,

26.65, 62.09, 67.70, 69.00, 76.55, 109.77, 120.08, 127.48, 128.34, 129.20, 136.89, 141.72, 165.52; $C_{16}H_{20}N_2O_3S$ (320.41): calcd C 59.98; H 6.29; N 8.74; found C 60.11; H 6.53; N 9.02.

***N*-Benzyl-4-*O*-benzyl-1-deoxy-1-(hydroxyamino)-2,3-*O*-isopropylidene-1-(2-thiazolyl)-L-*xylo*-tetritol** (*syn*-**13**): Formed from the nitrone **3** (1.78 g, 5 mmol) by method A. Column chromatography (98:2, dichloromethane:diethyl ether) of the residue afforded *syn*-**13** (1.17 g, 53%, d.s. = 70%) as an oil; $[\alpha]_D^{20} = -31.7$ ($c = 0.30$ in $CHCl_3$); ^{1}H NMR: $\delta = 1.26$ (s, 3H), 1.31 (s, 3H), 3.01 (dd, ^2J(H,H) = 10.5, ^3J(H,H) = 3.0 Hz, 1H), 3.09 (dd, ^2J(H,H) = 10.5, ^3J(H,H) = 5.9 Hz, 1H), 3.74 (d, ^2J(H,H) = 12.8 Hz, 1H), 3.96 (d, ^2J(H,H) = 12.8 Hz, 1H), 4.21–4.23 (m, 1H), 4.36 (d, ^2J(H,H) = 12.5 Hz, 1H), 4.38 (d, ^2J(H,H) = 12.5 Hz, 1H), 4.44–4.48 (m, 2H), 6.80 (bs, 1H, ex. D_2O), 7.16–7.34 (m, 11H), 7.75 (d, ^3J(H,H) = 3.2 Hz, 1H); ^{13}C NMR: $\delta = 26.86$, 27.29, 61.59, 69.17, 70.31, 73.19, 77.71, 78.21, 109.89, 120.72, 127.43, 127.66, 127.75, 128.23, 128.29, 129.41, 136.61, 137.69, 141.78, 163.45; $C_{24}H_{28}N_2O_4S$ (440.56): calcd C 65.43; H 6.41; N 6.36; found C 65.56; H 6.49; N 6.51.

***N*-Benzyl-4-*O*-benzyl-1-deoxy-1-(hydroxyamino)-2,3-*O*-isopropylidene-1-(2-thiazolyl)-L-*lyxo*-tetritol** (*anti*-**13**): Formed from the nitrone **3** (1.78 g, 5 mmol) and Et_2AlCl (5 mL of a 1 M solution in hexanes, 5 mmol) by method B. Column chromatography (98:2, dichloromethane:diethyl ether) of the residue afforded *anti*-**13** (1.54 g, 70%, d.s. = 87%) as a white solid; m.p. 83–84 °C; $[\alpha]_D^{20} = -26.3$ ($c = 0.38$ in $CHCl_3$); ^{1}H NMR: $\delta = 1.28$ (s, 3H), 1.34 (s, 3H), 3.70 (d, ^2J(H,H) = 13.4 Hz, 1H), 3.74 (d, ^2J(H,H) = 13.4 Hz, 1H), 3.75 (dd, ^2J(H,H) = 10.3, ^3J(H,H) = 6.1 Hz, 1H), 3.81 (dd, ^2J(H,H) = 10.3, ^3J(H,H) = 5.1 Hz, 1H), 4.30 (d, ^3J(H,H) = 8.3 Hz, 1H), 4.37 (ddd, ^3J(H,H) = 6.8, 6.1, 5.1 Hz, 1H), 4.56 (dd, ^3J(H,H) = 8.3, 6.8 Hz, 1H), 4.59 (s, 2H), 6.36 (bs, 1H, ex. D_2O), 7.24–7.30 (m, 10H), 7.40 (d, ^3J(H,H) = 3.2 Hz, 1H), 7.85 (d, ^3J = 3.2 Hz, 1H); ^{13}C NMR: $\delta = 26.90$, 27.13, 61.33, 70.01, 71.61, 73.71, 78.24, 80.03, 109.89, 120.33, 127.30, 127.78, 127.86, 128.30, 128.46, 129.01, 137.17, 137.19, 141.67, 165.06; $C_{24}H_{28}N_2O_4S$ (440.56): calcd C 65.43; H 6.41; N 6.36; found C 65.06; H 6.24; N 6.62.

***N*-Benzyl-4-*O*-(*tert*-butyldimethylsilyl)-1-deoxy-1-(hydroxyamino)-2,3-*O*-isopropylidene-1-(2-thiazolyl)-L-*xylo*-tetritol** (*syn*-**14**): Prepared from the nitrone **4** (1.90 g, 5 mmol) by method A. Column chromatography (90:10, hexane:diethyl ether) of the residue afforded *syn*-**14** (1.07 g, 46%, d.s. = 60%) as an oil; $[\alpha]_D^{20} = -62.5$ ($c = 0.12$ in $CHCl_3$); ^{1}H NMR: $\delta = -0.04$ (s, 3H), −0.02 (s, 3H), 0.81 (s, 9H), 1.23 (s, 3H), 1.37 (s, 3H), 3.34 (dd, ^2J(H,H) = 10.8 Hz, ^3J(H,H) = 4.0 Hz, 1H), 3.53 (dd, ^2J(H,H) = 10.8 Hz, ^3J(H,H) = 5.0 Hz, 1H), 3.78 (d, ^2J(H,H) = 13.1 Hz, 1H), 3.92 (d, ^2J(H,H) = 13.1 Hz, 1H), 4.20–4.23 (m, 1H), 4.56-4.60 (m, 2H), 6.30 (bs, 1H, ex. D_2O), 7.20–7.36 (m, 5H), 7.40 (d, ^3J(H,H) = 3.2 Hz, 1H), 7.84 (d, ^3J(H,H) = 3.2 Hz, 1H); ^{13}C NMR: $\delta = -5.55$, −5.46, 18.33, 25.92, 27.07, 27.32, 61.60, 63.79, 69.19, 78.62, 78.74, 109.53, 120.54, 127.37, 128.25, 129.42, 136.98, 141.88, 164.05; $C_{23}H_{36}N_2O_4SSi$ (464.70): calcd C 59.45; H 7.81; N 6.03; found C 59.20; H 7.61; N 6.34.

***N*-Benzyl-4-*O*-(*tert*-butyldimethylsilyl)-1-deoxy-1-(hydroxyamino)-2,3-*O*-isopropylidene-1-(2-thiazolyl)-L-*lyxo*-tetritol** (*anti*-**14**): Formed from the nitrone **4** (1.90 g, 5 mmol) and Et_2AlCl (5 mL of a 1 M solution in hexanes, 5 mmol) by method B. Column chromatography (90:10, hexane:diethyl ether) of the residue afforded *anti*-**14** (1.12 g, 48%, d.s. = 67%) as an oil; $[\alpha]_D^{20} = -31.7$ ($c = 0.12$ in $CHCl_3$); ^{1}H NMR: $\delta = -0.01$ (s, 3H), 0.04 (s, 3H), 0.83 (s, 9H), 1.27 (s, 3H), 1.29 (s, 3H), 3.64 (d, ^2J(H,H) = 13.4 Hz, 1H), 3.68 (d, ^2J(H,H) = 13.4 Hz, 1H), 3.80 (dd, ^2J(H,H) = 10.7, ^3J(H,H) = 6.2 Hz, 1H), 3.95 (dd, ^2J(H,H) = 10.7, ^3J(H,H) = 4.0 Hz, 1H), 4.19 (td, ^3J(H,H) = 6.5, 4.2 Hz, 1H), 4.30 (d, ^3J(H,H) = 8.1 Hz, 1H), 4.57 (dd, ^3J(H,H) = 8.1, 6.5 Hz, 1H), 6.45 (bs, 1H, ex. D_2O), 7.22–7.28 (m, 5H), 7.38 (d, ^3J(H,H) = 3.2 Hz, 1H), 7.82 (d, ^3J(H,H) = 3.2 Hz, 1H); ^{13}C NMR: $\delta = -5.54$, −5.45, 18.46, 25.93, 26.99, 27.17, 61.05, 65.15, 70.07, 79.49, 80.37, 109.61, 120.38, 127.28, 128.25, 129.21, 137.18, 141.68, 165.07; $C_{23}H_{36}N_2O_4SSi$ (464.70): calcd C 59.45; H 7.81; N 6.03; found C 59.25; H 7.99; N 6.17.

***N*-Benzyl-1-deoxy-1-(hydroxyamino)-2,3:4,5-di-*O*-isopropylidene-1-(2-thiazolyl)-D-*gluco*-pentitol** (*syn*-**15**): Formed from the nitrone **5** (1.68 g, 5 mmol) following method A. Column chromatography (80:20, hexane:diethyl ether) of the residue afforded *syn*-**15** (0.93 g, 22%, d.s. = 28%) as a white solid; m.p. 92–94 °C; $[\alpha]_D^{20} = +23.4$ ($c = 0.96$ in $CHCl_3$); ^{1}H NMR: $\delta = 1.04$ (s, 3H), 1.12 (s, 3H), 1.19 (s, 3H), 1.34 (s, 3H), 3.69 (d, ^2J(H,H) = 12.6 Hz, 1H), 3.87 (d, ^2J = 12.6 Hz, 1H), 3.89 (dd, ^2J(H,H) = 7.9, ^3J(H,H) = 5.1 Hz, 1H), 3.95 (ddd, ^3J(H,H) = 7.5, 5.2, 5.1 Hz, 1H), 4.05 (dd, ^2J(H,H) = 7.9, ^3J(H,H) = 5.2 Hz, 1H), 4.19 (dd, ^3J(H,H) = 7.5, 4.4 Hz, 1H), 4.58 (d, ^3J = 7.2 Hz, 1H), 4.68 (dd, ^3J(H,H) = 7.2, 4.4 Hz, 1H), 6.96 (bs, 1H, ex. D_2O), 7.30 (bs, 5H), 7.38 (d, ^3J(H,H) = 3.2 Hz, 1H), 7.81 (d, ^3J(H,H) = 3.2 Hz, 1H); ^{13}C NMR: $\delta = 25.20$, 26.17, 27.28, 27.75, 61.63, 67.38, 69.04, 78.68, 78.75, 81.08, 109.79, 110.30, 120.40, 127.27, 128.15, 129.41, 137.21, 141.87, 164.27; $C_{21}H_{28}N_2O_5S$ (420.53): calcd C 59.98; H 6.71; N 6.66; found C 60.37; H 6.61; N 6.30.

***N*-Benzyl-1-deoxy-1-(hydroxyamino)-2,3:4,5-di-*O*-isopropylidene-1-(2-thiazolyl)-D-*manno*-pentitol** (*anti*-**15**): Prepared from the nitrone **5** (1.68 g, 5 mmol) and Et_2AlCl (5 mL of a 1 M solution in hexanes, 5 mmol) by method B. Column chromatography (80:20, hexane:diethyl ether) of the residue afforded *anti*-**15** (1.26 g, 60%, d.s. = 75%) as a white solid; m.p. 140–141 °C; $[\alpha]_D^{20} = +30.6$ ($c = 0.46$ in $CHCl_3$); ^{1}H NMR: $\delta = 1.24$ (s, 3H), 1.30 (bs, 9H), 3.61 (d, ^2J(H,H) = 12.6 Hz, 1H), 3.71 (d, ^2J(H,H) = 12.6 Hz, 1H), 4.03–4.05 (m, 1H), 4.16–4.21 (m, 2H), 4.27 (dd, ^2J(H,H) = 7.9, ^3J(H,H) = 5.4 Hz, 1H), 4.36 (d, ^3J(H,H) = 8.7 Hz, 1H), 4.63 (dd, ^3J(H,H) = 8.7, 5.4 Hz, 1H), 6.61 (bs, 1H, ex. D_2O), 7.31 (bs, 5H), 7.41 (d, ^3J(H,H) = 3.2 Hz, 1H), 7.84 (d, ^3J(H,H) = 3.2 Hz, 1H); ^{13}C NMR: $\delta = 25.27$, 25.89, 26.96, 27.31, 60.95, 68.11, 71.02, 78.12, 80.02, 82.29, 110.30, 110.35, 120.43, 127.27, 128.16, 129.38, 137.24, 141.72, 164.95; $C_{21}H_{28}N_2O_5S$ (420.53): calcd C 59.98; H 6.71; N 6.66; found C 59.89; H 6.65; N 6.47.

***N*-Benzyl-2-*O*-(*tert*-butyldiphenylsilyl)-1,3-dideoxy-1-(hydroxyamino)-1-(2-thiazolyl)-L-*threo*-triitol** (*syn*-**16**) **and *N*-Benzyl-2-*O*-(*tert*-butyldiphenylsilyl)-1,3-dideoxy-1-(hydroxyamino)-1-(2-thiazolyl)-L-*erythro*-triitol** (*anti*-**16**): Formed from the nitrone **6** (2.09 g, 5 mmol) by method A. Column chromatography (90:10, hexane:diethyl ether) of the residue afforded *syn*-**16** (1.18 g, 47%, d.s. = 53%) as a white solid; m.p. 105–106 °C; $[\alpha]_D^{20} = -56.4$ ($c = 0.58$ in $CHCl_3$); ^{1}H NMR: $\delta = 1.00$ (d, ^3J(H,H) = 6.3 Hz, 3H), 1.04 (s, 9H), 3.33 (d, ^2J(H,H) = 12.6 Hz, 1H), 3.52 (d, ^2J(H,H) = 12.6 Hz, 1H), 3.76 (bs, 1H, ex. D_2O), 4.32–4.35 (m, 2H), 6.80–6.83 (m, 1H), 7.12–7.20 (m, 4H), 7.23 (d, ^3J(H,H) = 3.2 Hz, 1H), 7.30–7.48 (m, 7H), 7.58–7.61 (m, 1H), 7.70–7.78 (m, 2H), 7.79 (d, ^3J(H,H) = 3.2 Hz, 1H); ^{13}C NMR: $\delta = 19.50$, 21.02, 26.95, 61.76, 70.01, 75.43, 120.34, 127.56, 127.64, 127.82, 129.51, 129.55, 129.69, 129.88, 133.64, 135.38, 135.74, 135.94, 137.08, 141.30, 164.71.; $C_{29}H_{34}N_2O_2SSi$ (502.75): calcd C 69.28; H 6.82; N 5.57; found C 69.50; H 6.69; N 5.39.

The second fraction to be eluted contained *anti*-**16** (1.03 g, 41%, d.s. = 47%) isolated as a white solid; m.p. 52–54 °C; $[\alpha]_D^{20} = -41.7$ ($c = 0.48$ in $CHCl_3$); ^{1}H NMR: $\delta = 0.96$ (d, ^3J(H,H) = 6.4 Hz, 3H), 1.00 (s, 9H), 3.56 (d, ^2J(H,H) = 13.2 Hz, 1H), 3.70 (d, ^2J(H,H) = 13.2 Hz, 1H), 4.08 (d, ^3J(H,H) = 4.6 Hz, 1H), 4.56 (dq, ^3J(H,H) = 4.6, 6.4 Hz, 1H), 5.00 (bs, 1H, ex. D_2O), 7.18–7.40 (m, 12H), 7.61–7.69 (m, 4H), 7.81 (d, ^3J(H,H) = 3.2 Hz, 1H); ^{13}C NMR: $\delta = 19.07$, 21.00, 26.91, 62.15, 68.73, 74.46, 120.52, 127.20, 127.51, 127.67, 127.84, 128.21, 128.68, 129.07, 129.70, 135.65, 135.76, 135.95, 136.06, 141.39, 166.65.; $C_{29}H_{34}N_2O_2SSi$ (502.75): calcd C 69.28; H 6.82; N 5.57; found C 68.99; H 6.71; N 5.99.

***N*-Benzyl-3-*O*-benzyl-5-deoxy-5-(hydroxyamino)-1,2-*O*-isopropylidene-5-(2-thiazolyl)-β-L-*ido*-1,4-pentofuranoside** (*syn*-**17**): Prepared from the nitrone **7** (1.92 g, 5 mmol) by method A. Column chromatography (60:40, hexane:diethyl ether) of the residue afforded *syn*-**17** (1.90 g, 81%, d.s. = 90%) as a white solid; m.p. 45–46 °C; $[\alpha]_D^{20} = -49.0$ ($c = 0.77$ in $CHCl_3$); ^{1}H NMR: $\delta = 1.31$ (s, 3H), 1.51 (s, 3H), 3.87 (d, ^3J(H,H) = 3.2 Hz, 1H), 3.84 (d, ^2J(H,H) = 13.4 Hz, 1H), 3.93 (d, ^2J = 13.4 Hz, 1H), 4.17 (d, ^2J(H,H) = 11.2 Hz, 1H), 4.38 (d, ^2J(H,H) = 11.2 Hz, 1H), 4.55 (d, ^3J = 3.7 Hz, 1H), 4.86 (d, ^3J(H,H) = 9.8 Hz, 1H), 5.00 (dd, ^3J(H,H) = 9.8, 3.4 Hz, 1H), 5.82 (bs, 1H, ex. D_2O), 6.03 (d, ^3J(H,H) = 3.7 Hz, 1H), 7.15-7.36 (m, 11H), 7.79 (d, ^3J(H,H) = 3.2 Hz, 1H); ^{13}C NMR: $\delta = 26.28$, 26.86, 60.96, 65.84, 72.06, 79.96, 81.66, 82.29, 105.28, 111.86, 119.90, 127.11, 127.72, 127.79, 128.13, 128.26, 129.24, 137.15, 137.67, 142.02, 164.97; $C_{25}H_{28}N_2O_5S$ (468.57): calcd C 64.08; H 6.02; N 5.98; found C 64.04; H 5.97; N 6.20.

***N*-Benzyl-3-*O*-benzyl-5-deoxy-5-(hydroxyamino)-1,2-*O*-isopropylidene-5-(2-thiazolyl)-α-D-*gluco*-1,4-pentofuranoside** (*anti*-**17**): Formed from the nitrone **7** (1.92 g, 5 mmol) and Et_2AlCl (5 mL of a 1 M solution in hexanes, 5 mmol) by method B. Column chromatography (60:40, hexane:diethyl ether) of the residue afforded *anti*-**17** (2.01 g, 86%, d.s. = 96%) as an oil; $[\alpha]_D^{20} = -26.5$ ($c = 0.46$ in $CHCl_3$); ^{1}H NMR: $\delta = 1.26$ (s, 3H), 1.45 (s, 3H), 3.76 (d, ^2J(H,H) = 13.2 Hz, 1H), 3.82 (d, ^2J(H,H) = 13.2 Hz, 1H), 4.29 (d, ^3J(H,H) = 2.7 Hz, 1H), 4.54 (d, ^3J(H,H) = 3.9 Hz, 1H), 4.67 (s, 2H), 4.78 (d, ^3J(H,H) = 9.5 Hz, 1H), 4.86 (dd, ^3J(H,H) = 9.5, 2.7 Hz, 1H), 5.86 (d, ^3J(H,H) = 3.9 Hz, 1H), 6.64 (bs, 1H, ex. D_2O), 7.25–7.31 (m, 10H), 7.35 (d, ^3J(H,H) = 3.2 Hz, 1H), 7.84 (d, ^3J(H,H) = 3.2 Hz, 1H); ^{13}C NMR: $\delta = 26.24$, 26.78, 62.19, 64.08, 72.68, 80.89, 81.70, 82.15, 104.91, 111.74, 119.85, 127.31, 127.43, 127.69, 128.20, 128.36, 129.19, 136.91, 137.75, 141.69, 165.98; $C_{25}H_{28}N_2O_5S$ (468.57): calcd C 64.08; H 6.02; N 5.98; found C 63.90; H 5.80; N 6.12.

***N*-Benzyl-5-deoxy-5-(hydroxyamino)-1,2-*O*-isopropylidene-3-*O*-(methoxy-ethoxymethyl)-5-(2-thiazolyl)-β-L-*ido*-1,4-pentofuranoside** (*syn*-**18**): Prepared from the nitrone **8** (1.91 g, 5 mmol) by method A. Column chromatography (20:80, hexane:diethyl ether) of the residue afforded *syn*-**18** (1.66 g, 71%, d.s. = 88%) as an oil; $[\alpha]_D^{20} = -11.1$ ($c = 1.82$ in $CHCl_3$); ^{1}H NMR: $\delta = 1.29$ (s, 3H), 1.49 (s, 3H), 3.31 (s, 3H), 3.35–3.41 (m, 3H), 3.59–3.61 (m, 1H), 3.74 (d, ^2J(H,H) = 13.4 Hz, 1H), 3.88 (d, ^2J(H,H) = 13.4 Hz, 1H), 3.96 (d, ^3J(H,H) = 2.7 Hz, 1H), 4.30 (d, ^3J(H,H) = 7.1 Hz, 1H), 4.60 (d, ^3J(H,H) = 7.1 Hz, 1H), 4.66 (d, ^3J(H,H) = 3.6 Hz, 1H), 4.76 (d, ^3J(H,H) = 9.8 Hz, 1H), 4.94 (dd, ^3J(H,H) = 9.8, 2.7 Hz, 1H), 5.76 (bs, 1H, ex. D_2O), 5.98 (d, ^3J(H,H) = 3.6 Hz, 1H), 7.26-7.37 (m, 6H), 7.78 (d, ^3J(H,H) = 3.2 Hz, 1H); ^{13}C NMR: $\delta = 26.22$, 26.84, 58.94, 60.89, 66.22, 67.44, 71.50, 79.78, 81.40, 82.62, 95.83, 105.07, 111.85, 120.20, 127.10, 128.11, 129.22, 137.60, 141.88, 164.83: $C_{22}H_{30}N_2O_7S$ (466.56): calcd C 56.64; H 6.48; N 6.00; found C 56.88; H 6.82; N 5.94.

***N*-Benzyl-5-deoxy-5-(hydroxyamino)-1,2-*O*-isopropylidene-3-*O*-(methoxyethoxymethyl)-5-(2-thiazolyl)-α-D-*gluco*-1,4-pentofuranoside** (*anti*-**18**): Formed from the nitrone **8** (1.91 g, 5 mmol) and Et_2AlCl (5 mL of a 1 M solution in hexanes, 5 mmol)

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by method B. Column chromatography (20:80, hexane:diethyl ether) of the residue afforded *anti*-**18** (1.75 g, 75%, d.s. = 90%) as an oil; $[\alpha]_D^{20} = -9.0$ ($c = 1.34$ in $CHCl_3$); ^1H NMR: $\delta = 1.25$ (s, 3H), 1.44 (s, 3H), 3.27 (s, 3H), 3.39–3.46 (m, 3H), 3.58–3.62 (m, 1H), 3.67 (d, $^2J(H,H) = 12.6$ Hz, 1H), 3.76 (d, $^2J = 12.6$ Hz, 1H), 4.40 (d, $^3J(H,H) = 2.7$ Hz, 1H), 4.60–4.66 (m, 3H), 4.78–4.82 (m, 2H), 5.80 (d, $^3J(H,H) = 3.7$ Hz, 1H), 6.81 (bs, 1H, ex. D_2O), 7.23 (bs, 5H), 7.37 (d, $^3J = 3.2$ Hz, 1H), 7.82 (d, $^3J(H,H) = 3.2$ Hz, 1H); ^{13}C NMR: $\delta = 26.25$, 26.81, 58.92, 61.86, 64.20, 67.20, 71.63, 79.95, 80.80, 82.73, 95.54, 104.75, 111.76, 119.80, 127.37, 128.15, 129.60, 136.87, 141.85, 166.02; $C_{22}H_{30}N_2O_7S$ (466.56): calcd C 56.64; H 6.48; N 6.00; found C 56.84; H 6.67; N 6.19.

3-*O*-Acetyl-*N*-benzyl-5-deoxy-5-(hydroxyamino)-1,2-*O*-isopropylidene-5-(2-thiazolyl)-β-L-*ido*-1,4-pentofuranoside (*syn*-**19**): Prepared from the nitrone **9** (1.68 g, 5 mmol) by method A. Column chromatography (30:70, hexane:ethyl acetate) of the residue afforded *syn*-**19** (0.42 g, 20%, d.s. = 88%) as an sticky oil; $[\alpha]_D^{20} = -38.6$ ($c = 0.51$ in $CHCl_3$); ^1H NMR: $\delta = 1.22$ (s, 3H), 1.41 (s, 3H), 2.00 (s, 3H), 3.73 (d, $^2J(H,H) = 13.3$ Hz, 1H), 3.90 (d, $^2J(H,H) = 13.3$ Hz, 1H), 4.40 (d, $^3J(H,H) = 8.3$ Hz, 1H), 4.50 (d, $^3J(H,H) = 3.7$ Hz, 1H), 4.52 (d, $^3J(H,H) = 3.0$ Hz, 1H), 4.69 (dd, $^3J(H,H) = 3.0$, 8.3 Hz, 1H), 4.76 (bs, 1H, ex. D_2O), 5.84 (d, $^3J(H,H) = 3.7$ Hz, 1H), 7.21–7.32 (m, 5H), 7.38 (d, $^3J(H,H) = 3.2$ Hz, 1H), 7.83 (d, $^3J(H,H) = 3.2$ Hz, 1H); ^{13}C NMR: $\delta = 26.20$, 26.86, 31.66, 53.71, 61.69, 75.63, 82.26, 84.77, 105.06, 11.64, 119.98, 127.98, 128.72, 129.29, 136.04, 142.02, 166.10, 167.60; $C_{20}H_{24}N_2O_6S$ (420.49): calcd C 57.13; H5.75; N 6.66; found C 57.19; H 5.90; N 6.90.

Methyl *N*-benzyl-5-deoxy-5-(hydroxyamino)-2,3-*O*-isopropylidene-5-(2-thiazolyl)-α-L-*talo*-1,4-pentofuranoside (*syn*-**20**): Prepared from the nitrone **10** (1.54 g, 5 mmol) by method A. Column chromatography (20:80, hexane:diethyl ether) of the residue afforded *syn*-**20** (1.28 g, 65%, d.s. = 84%) as a white solid; m.p. 105–106 °C; $[\alpha]_D^{20} = -21.3$ ($c = 0.31$ in $CHCl_3$); ^1H NMR: $\delta = 1.20$ (s, 3H), 1.43 (s, 3H), 3.38 (s, 3H), 3.66 (d, $^2J(H,H) = 13.0$ Hz, 1H), 3.74 (d, $^2J(H,H) = 13.0$ Hz, 1H), 4.54 (d, $^3J(H,H) = 9.0$ Hz, 1H), 4.58 (s, 2H), 4.69 (d, $^3J(H,H) = 9.0$ Hz, 1H), 5.04 (s, 1H), 6.30 (bs, 1H, ex. D_2O), 7.24–7.35 (m, 5H), 7.44 (d, $^3J(H,H) = 3.2$ Hz, 1H), 7.87 (d, $^3J = 3.2$ Hz, 1H); ^{13}C NMR: $\delta = 24.77$, 26.33, 55.31, 61.47, 70.42, 82.06, 84.93, 87.19, 110.00, 112.21, 121.09, 127.24, 128.15, 129.51, 137.10, 141.66, 163.91; $C_{19}H_{24}N_2O_5S$ (392.48): calcd C 58.15; H 6.16; N 7.14; found C 57.85; H 6.00; N 7.29.

Methyl *N*-benzyl-5-deoxy-5-(hydroxyamino)-2,3-*O*-isopropylidene-5-(2-thiazolyl)-β-D-*allo*-1,4-pentofuranoside (*anti*-**20**): Formed from the nitrone **10** (1.54 g, 5 mmol) and Et_2AlCl (5 mL of a 1 M solution in hexanes, 5 mmol) by method B. Column chromatography (20:80, hexane:diethyl ether) of the residue afforded *anti*-**20** (1.16 g, 59%, d.s. = 65%) as a sticky foam; $[\alpha]_D^{20} = -23.9$ ($c = 0.31$ in $CHCl_3$); ^1H NMR: $\delta = 1.33$ (s, 3H), 1.46 (s, 3H), 3.13 (s, 3H), 3.62 (d, $^2J(H,H) = 13.7$ Hz, 1H), 3.78 (d, $^2J(H,H) = 13.7$ Hz, 1H), 4.35 (d, $^3J(H,H) = 10.8$ Hz, 1H), 4.62 (d, $^3J(H,H) = 6.0$ Hz, 1H), 4.79 (d, $^3J(H,H) = 10.8$ Hz, 1H), 4.90 (s, 1H), 5.22 (d, $^3J(H,H) = 6.0$ Hz, 1H), 5.09 (bs, 1H, ex. D_2O), 7.20-7.35 (m, 5H), 7.41 (d, $^3J(H,H) = 3.2$ Hz, 1H), 7.83 (d, $^3J(H,H) = 3.2$ Hz, 1H); ^{13}C NMR: $\delta = 25.27$, 26.56, 55.68, 61.83, 69.28, 82.21, 85.06, 87.79, 109.87, 112.52, 120.31, 127.45, 128.32, 129.24, 137.12, 141.74, 165.17; $C_{19}H_{24}N_2O_5S$ (392.48): calcd C 58.15; H 6.16; N 7.14; found C 57.78; H 6.05; N 6.99.

***N*-Benzyl-6-deoxy-6-(hydroxyamino)-1,2:3,4-*O*-isopropylidene-6-(2-thiazolyl)-β-L-*glycero*-D-*galacto*-1,5-hexopyranoside** (*syn*-**21**): Prepared from the nitrone **11** (1.82 g, 5 mmol) and $ZnBr_2$ (1.13 g, 5 mmol) by method B. Treatment of the crude product with a 1:1 mixture of hexane:diethyl ether gave pure *anti*-**21** as a crystalline white solid, which was filtered off. Evaporation of the mother liquors afforded pure *syn*-**21** (1.57 g, 70%, d.s. = 79%) as a white solid; m.p. 45–46 °C; $[\alpha]_D^{20} = -59.4$ ($c = 1.12$ in $CHCl_3$); ^1H NMR: $\delta = 1.23$ (s, 3H), 1.32 (s, 3H), 1.46 (s, 3H), 1.56 (s, 3H), 3.70 (d, $^2J(H,H) = 13.4$ Hz, 1H), 3.78 (d, $^2J(H,H) = 13.4$ Hz, 1H), 3.92 (dd, $^3J(H,H) = 7.8$, 1.5 Hz, 1H), 4.33 (dd, $^3J(H,H) = 4.9$, 2.4 Hz, 1H), 4.50–4.55 (m, 2H), 4.85 (d, $^3J(H,H) = 10.5$ Hz, 1H), 5.55 (bs, 1H, ex. D_2O), 5.65 (d, $^3J(H,H) = 4.9$ Hz, 1H), 7.26–7.40 (m, 6H), 7.81 (d, $^3J(H,H) = 3.2$ Hz, 1H); ^{13}C NMR: $\delta = 24.34$, 25.01, 25.90, 25.88, 60.29, 65.43, 66.46, 68.57, 70.63, 70.86, 96.92, 108.99, 109.58, 120.16, 127.11, 128.10, 129.34, 137.82, 142.17, 159.80. $C_{22}H_{28}N_2O_6S$ (448.54): calcd C 58.91; H 6.29; N 6.25; found C 58.60; H 6.30; N 6.38.

***N*-Benzyl-6-deoxy-6-(hydroxyamino)-1,2:3,4-*O*-isopropylidene-6-(2-thiazolyl)-α-D-*glycero*-D-*galacto*-1,5-hexopyranoside** (*anti*-**21**): Prepared from the nitrone **11** (1.82 g, 5 mmol) and Et_2AlCl (5 mL of a 1 M solution in hexanes, 5 mmol) by method B. Treatment of the crude product with a 1:1 mixture of hexane:diethyl ether gave a crystalline white solid, which proved to be pure *anti*-**21** (1.84 g, 82%, d.s. = 91%); m.p. 196–198 °C; $[\alpha]_D^{20} = -60.2$ ($c = 1.03$ in $CHCl_3$); ^1H NMR: $\delta = 1.21$ (s, 3H), 1.38 (s, 6H), 1.44 (s, 3H), 3.79 (d, $^2J(H,H) = 13.2$ Hz, 1H), 3.85 (d, $^2J(H,H) = 13.2$ Hz, 1H), 4.23 (dd, $^3J(H,H) = 4.9$, 2.2 Hz, 1H), 4.45 (dd, $^3J(H,H) = 9.8$, 1.5 Hz, 1H), 4.54 (d, $^3J(H,H) = 9.8$ Hz, 1H), 4.63 (dd, $^3J(H,H) = 8.1$, 2.2 Hz, 1H), 4.72 (dd, $^3J(H,H) = 8.1$, 1.5 Hz, 1H), 5.38 (d, $^3J(H,H) = 4.9$ Hz, 1H), 6.34 (bs, 1H, ex. D_2O), 7.30 (bs, 5H), 7.38 (d, $^3J(H,H) = 3.2$ Hz, 1H), 7.80 (d, $^3J(H,H) = 3.2$ Hz, 1H); ^{13}C NMR: $\delta = 22.62$, 24.46, 24.97, 25.93, 62.20, 65.00, 68.70, 70.68, 70.76, 70.99, 96.46, 108.71, 109.06, 119.82, 127.28, 128.12, 129.12, 137.20, 141.53, 166.01; $C_{22}H_{28}N_2O_6S$ (448.54): calcd C 58.91; H 6.29; N 6.25; found C 58.94; H 6.10; N 6.37.

Reduction of *N*-Benzyl Hydroxylamines 12–21 with Titanium(III) Chloride: A solution of the hydroxylamine (4 mmol) in MeOH (50 mL) was treated with a 20% aq solution of $TiCl_3$ (1.55 g, 10 mmol of $TiCl_3$ in 6.2 mL of water) at ambient temperature for 15 min. Then, 5 M aq NaOH was added and stirring was continued for additional 5 min. After extraction with ethyl acetate (4 × 25 mL), the combined extracts were washed with brine, dried ($MgSO_4$), and concentrated in vacuo to afford the crude amine, which was used in the next step without purification.

Protection of Amines as *N*-(*tert*-Butoxycarbonyl) Derivatives. The above crude amine obtained from 4 mmol of hydroxylamine, was taken up in 1,4-dioxane (30 mL) and treated with Boc_2O (1.92 g, 8.8 mmol). The resulting solution was stirred at ambient temperature for 12 h. The mixture was partitioned between saturated aq $NaHCO_3$ (80 mL) and CH_2Cl_2 (50 mL), and the organic layer separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 25 mL). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product, which was purified by column chromatography on silica gel. The overall yield from the corresponding hydroxylamine and the mixture of solvents employed for chromatography are reported below for each compound.

1-(*tert*-Butoxycarbonylamino)-1-deoxy-2,3-*O*-isopropylidene-1-(2-thiazolyl)-D-*threo*-triitol (22) (0.93 g, 74%; 60:40, hexane:diethyl ether); white solid; m.p. 75–76 °C; $[\alpha]_D^{20} = -18.6$ ($c = 0.88$ in $CHCl_3$); ^1H NMR: $\delta = 1.32$ (s, 3H), 1.43 (s, 3H), 1.45 (s, 9H), 3.87 (dd, $^2J(H,H) = 8.5$ Hz, $^3J(H,H) = 5.7$ Hz, 1H), 4.10 (dd, $^2J(H,H) = 8.5$ Hz, $^3J(H,H) = 6.7$ Hz, 1H), 4.70 (ddd, $^3J(H,H) = 7.7$, 6.7, 5.7 Hz, 1H), 5.08 (dd, $^3J(H,H) = 7.7$, 2.6 Hz, 1H), 5.42 (d, $^3J(H,H) = 2.6$ Hz, 1H), 7.24 (d, $^3J(H,H) = 3.2$ Hz, 1H), 7.73 (d, $^3J(H,H) = 3.2$ Hz, 1H); ^{13}C NMR: $\delta = 24.98$, 26.28, 28.35, 54.58, 66.54, 80.44, 85.06, 110.05, 119.00, 142.88, 155.51, 170.54; $C_{14}H_{22}N_2O_4S$ (314.41): calcd C 53.48; H 7.05; N 8.91; found C 53.72; H 7.34; N 8.70.

1-(*tert*-Butoxycarbonylamino)-1-deoxy-2,3-*O*-isopropylidene-1-(2-thiazolyl)-D-*erythro*-triitol (24) (0.98 g, 78%; 60:40, hexane:diethyl ether); white solid; m.p. 93–95 °C; $[\alpha]_D^{20} = +3.5$ ($c = 0.75$ in $CHCl_3$); ^1H NMR: $\delta = 1.31$ (s, 3H), 1.37 (s, 3H), 1.42 (s, 9H), 3.98–4.06 (m, 2H), 4.46 (c, $^2J(H,H)$ and $^3J(H,H) = 5.7$ Hz, 1H), 5.13 (dd, $^2J(H,H) = 8.1$ Hz, $^3J(H,H) = 5.7$ Hz, 1H), 5.52 (bd, $^3J(H,H) = 8.1$ Hz, 1H), 7.22 (d, $^3J(H,H) = 3.2$ Hz, 1H), 7.72 (d, $^3J(H,H) = 3.2$ Hz, 1H); ^{13}C NMR: $\delta = 24.96$, 26.38, 28.24, 54.55, 65.95, 77.23, 80.28, 110.116, 119.35, 142.41, 155.35, 168.79; $C_{14}H_{22}N_2O_4S$ (314.41): calcd C 53.48; H 7.05; N 8.91; found C 53.56; H 7.20; N 8.88.

4-*O*-Benzyl-1-(*tert*-butoxycarbonylamino)-1-deoxy-2,3-*O*-isopropylidene-1-(2-thiazolyl)-L-*xylo*-tetriitol (26) (1.36 g, 78%; 70:30, hexane:diethyl ether); oil; $[\alpha]_D^{20} = -30.0$ ($c = 0.31$ in $CHCl_3$); ^1H NMR: $\delta = 1.37$ (s, 3H), 1.39 (s, 3H), 1.44 (s, 9H), 3.58 (dd, $^2J(H,H) = 10.3$ Hz, $^3J(H,H) = 4.8$ Hz, 1H), 3.62 (dd, $^2J(H,H) = 10.3$ Hz, $^3J(H,H) = 5.0$ Hz, 1H), 4.11 (dt, $^3J(H,H) = 8.1$, 4.9 Hz, 1H), 4.49 (dd, $^3J(H,H) = 8.1$, 2.6 Hz, 1H), 4.58 (s, 2H), 5.20 (dd, $^3J(H,H) = 8.7$, 2.6 Hz, 1H), 5.60 (bs, 1H), 7.22–7.35 (m, 6H), 7.72 (d, $^3J(H,H) = 3.2$ Hz, 1H); ^{13}C NMR: $\delta = 26.91$, 27.05, 28.36, 53.36, 70.49, 73.68, 76.67, 79.93, 80.39, 110.06, 118.00, 127.65, 127.74, 128.40, 138.08, 142.84, 153.97, 168.72; $C_{22}H_{30}N_2O_5S$ (434.56): calcd C 60.81; H 6.96; N 6.45; found C 60.64; H 7.22; N 6.36.

1-(*tert*-Butoxycarbonylamino)-1-deoxy-2,3:4,5-di-*O*-isopropylidene-1-(2-thiazolyl)-D-*manno*-pentitol (31) (1.34 g, 81%; 60:40, hexane:diethyl ether); white solid; m.p. 90–92 °C; $[\alpha]_D^{20} = +10.07$ ($c = 1.07$ in $CHCl_3$); ^1H NMR: $\delta = 1.24$ (s, 3H), 1.32 (s, 3H), 1.33 (s, 3H), 1.39 (s, 9H), 1.48 (s, 3H), 3.92 (dd, $^2J(H,H) = 8.1$ Hz, $^3J(H,H) = 4.2$ Hz, 1H), 4.03 (dd, $^2J(H,H) = 8.1$ Hz, $^3J(H,H) = 6.3$ Hz, 1H), 4.08–4.12 (m, 2H), 4.32 (t, $^3J(H,H) = 6.0$ Hz, 1H), 5.16 (dd, $^3J(H,H) = 7.8$, 6.8 Hz, 1H), 5.72 (bs, 1H), 7.25 (d, $^3J(H,H) = 3.2$ Hz, 1H), 7.72 (d, $^3J(H,H) = 3.2$ Hz, 1H); ^{13}C NMR: $\delta = 25.14$, 26.45, 26.86, 27.35, 28.27, 54.87, 67.64, 77.10, 79.03, 80.05, 81.61, 110.04, 110.60, 119.12, 142.48, 154.90, 169.12; $C_{19}H_{30}N_2O_6S$ (414.52): calcd C 55.05; H 7.30; N 6.76; found C 54.86; H 7.61; N 6.97.

1-(*tert*-Butoxycarbonylamino)-2-*O*-(*tert*-butyldiphenylsilyl)-1,3-dideoxy-1-(2-thiazolyl)-L-*threo*-triitol (32) (1.48 g, 85%; 80:20, hexane:diethyl ether); white solid; m.p. 60–62 °C; $[\alpha]_D^{20} = +4.7$ ($c = 1.33$ in $CHCl_3$); ^1H NMR: $\delta = 0.90$ (s, 9H), 1.02 (d, $^3J(H,H) = 6.4$ Hz, 3H), 1.49 (s, 9H), 4.60 (dq, $^3J(H,H) = 2.5$, 6.4 Hz, 1H), 4.91 (dd, $^3J(H,H) = 8.8$, 5.5 Hz, 1H), 5.72 (d, $^3J(H,H) = 8.8$ Hz, 1H), 7.26–7.42 (m, 7H), 7.58–7.64 (m, 4H), 7.71 (d, $^3J(H,H) = 3.2$ Hz, 1H); ^{13}C NMR: $\delta = 19.14$, 20.18, 26.77, 28.35, 58.69, 71.83, 80.09, 118.60, 127.50, 127.56, 129.66, 129.70, 132.62, 134.12, 135.77, 135.81, 142.75, 155.82, 168.23; $C_{27}H_{36}N_2O_3SSi$ (496.60): calcd C 65.28; H 7.31; N 5.64; found C 65.46; H 7.02; N 5.56.

1-(*tert*-Butoxycarbonylamino)-2-*O*-(*tert*-butyldiphenylsilyl)-1,3-dideoxy-1-(2-thiazolyl)-L-*erythro*-triitol (33) (1.43 g, 82%; 80:20, hexane:diethyl ether); oil; $[\alpha]_D^{20} = -10.5$ ($c = 1.05$ in $CHCl_3$); ^1H NMR: $\delta = 1.00$ (d, $^3J(H,H) = 6.2$ Hz, 3H), 1.04 (s, 9H), 1.40 (s, 9H), 4.32 (dq, $^3J(H,H) = 3.9$, 6.2 Hz, 1H), 5.01 (dd, $^3J(H,H) = 8.1$, 4.2 Hz, 1H), 5.38 (d, $^3J(H,H) = 8.1$ Hz, 1H), 7.30–7.40 (m, 7H),

7.60–7.66 (m, 4H), 7.71 (d, ^3J(H,H) = 3.2 Hz, 1H); ^{13}C NMR: δ = 19.24, 19.49, 26.90, 28.28, 58.30, 71.42, 79.79, 118.96, 127.54, 127.80, 129.70, 129.90, 133.22, 133.82, 135.83, 135.84, 142.31, 155.03, 168.10; $C_{27}H_{36}N_2O_3SSi$ (496.60): calcd C 65.28; H 7.31; N 5.64; found C 65.40; H 7.03; N 5.89.

3-*O*-Benzyl-5-(*tert*-Butoxycarbonylamino)-5-deoxy-1,2-*O*-isoprylidene-5-(2-thiazolyl)-β-L-*ido*-1,4-pentofuranoside (34) (1.33 g, 72%; 50:50, hexane:diethyl ether); oil; $[\alpha]_D^{20} = -7.5$ (c = 0.83 in $CHCl_3$); ^{1}H NMR: δ = 1.28 (s, 3H), 1.40 (s, 9H), 1.44 (s, 3H), 4.00 (d, ^3J(H,H) = 3.4 Hz, 1H), 4.41 (d, ^2J(H,H) = 11.7 Hz, 1H), 4.52 (d, ^2J(H,H) = 11.7 Hz, 1H), 4.58 (d, ^3J(H,H) = 3.9 Hz, 1H), 4.67 (dd, ^3J(H,H) = 7.0, 3.4 Hz, 1H), 5.38 (t, ^3J(H,H) = 7.0 Hz, 1H), 5.43 (bs, 1H), 5.95 (d, ^3J(H,H) = 3.9 Hz, 1H), 7.25–7.32 (m, 6H), 7.69 (d, ^3J(H,H) = 3.2 Hz, 1H); ^{13}C NMR: δ = 26.17, 26.76, 28.21, 51.49, 71.92, 79.06, 81.14, 81.99, 82.03, 104.98, 111.87, 119.16, 127.67, 127.74, 128.36, 137.04, 142.48, 155.24, 170.25; $C_{23}H_{30}N_2O_6S$ (462.57): calcd C 59.72; H 6.54; N 6.06; found C 59.97; H 6.45; N 5.99.

Protection of Amines as *N*-Benzyloxycarbonyl Derivatives: The crude amine, obtained as described above from 4 mmol of hydroxylamine, was taken up in 1,4-dioxane (50 mL) and treated with 7% aq $NaHCO_3$ (20 mL). The resulting solution was stirred at 0 °C for 10 min, then treated with benzyl chloroformate (0.64 mL, 4.4 mmol). After the reaction had been stirred at 0 °C for 20 min, water (80 mL) was added and the mixture was extracted with CH_2Cl_2 (3 × 20 mL). The combined extracts were dried ($MgSO_4$) and the solvent evaporated under reduced pressure to give the crude product, which was purified by column chromatography on silica gel. The overall yield from the corresponding hydroxylamine and the mixture of solvents employed for chromatography are reported below for each compound.

1-(Benzyloxycarbonylamino)-1-deoxy-2,3-*O*-isopropylidene-1-(2-thiazolyl)-D-*threo*-triitol (23) (1.20 g, 86%; 50:50, hexane:diethyl ether); oil; $[\alpha]_D^{20} = -10.8$ (c = 2.22 in $CHCl_3$); ^{1}H NMR: δ = 1.29 (s, 3H), 1.41 (s, 3H), 3.83 (dd, ^2J(H,H) = 8.6, ^3J(H,H) = 6.4 Hz, 1H), 4.07 (dd, ^2J(H,H) = 8.6, ^3J(H,H) = 6.6 Hz, 1H), 4.72 (ddd, ^3J(H,H) = 6.6, 6.4, 3.9 Hz, 1H), 5.11 (d, ^2J(H,H) = 12.6 Hz, 1H), 5.14 (d, ^2J(H,H) = 12.6 Hz, 1H), 5.18 (dd, ^3J(H,H) = 8.6, 3.9 Hz, 1H), 5.88 (bd, ^3J(H,H) = 8.6 Hz, 1H), 7.25 (d, ^3J(H,H) = 3.2 Hz, 1H), 7.29 (bs, 5H), 7.70 (d, ^3J(H,H) = 3.2 Hz, 1H); ^{13}C NMR: δ = 24.66, 26.09, 54.45, 66.18, 67.19, 76.58, 109.96, 119.20, 127.94, 128.12, 128.43, 135.99, 142.81, 156.12, 169.47; $C_{17}H_{20}N_2O_4S$ (348.42): calcd C 58.60; H 5.79; N 8.04; found C 58.38; H 6.01; N 7.92.

1-(Benzyloxycarbonylamino)-1-deoxy-2,3-*O*-isopropylidene-1-(2-thiazolyl)-D-*erythro*-triitol (25) (1.11 g, 80%; 50:50, hexane:diethyl ether); m.p. 71–72 °C; $[\alpha]_D^{20} = +2.0$ (c = 0.30 in $CHCl_3$); ^{1}H NMR: δ = 1.30 (s, 3H), 1.35 (s, 3H), 4.04 (d, ^3J(H,H) = 5.9 Hz, 2H), 4.48 (q, ^3J(H,H) = 5.9 Hz, 1H), 5.09 (d, 1H, ^2J(H,H) = 12.4 Hz, 1H), 5.14 (d, ^2J(H,H) = 12.4 Hz, 1H), 5.21 (dd, ^3J(H,H) = 8.3, 5.9 Hz, 1H), 5.84 (d, ^3J(H,H) = 8.3 Hz, 1H), 7.28 (d, ^3J(H,H) = 3.2 Hz, 1H), 7.30–7.38 (m, 5H), 7.73 (d, ^3J(H,H) = 3.2 Hz, 1H); ^{13}C NMR: δ = 24.86, 26.28, 55.08, 65.90, 67.23, 77.09, 110.15, 119.50, 128.16, 128.20, 128.49, 136.03, 142.51, 156.01, 167.80; $C_{17}H_{20}N_2O_4S$ (348.42): calcd C 58.60; H 5.79; N 8.04; found C 58.75; H 5.50; N 7.75.

4-*O*-Benzyl-1-(benzyloxycarbonylamino)-1-deoxy-2,3-*O*-isopropylidene-1-(2-thiazolyl)-L-*xylo*-tetritol (27) (1.35 g, 72%; 60:40, hexane:diethyl ether); oil; $[\alpha]_D^{20} = -23.0$ (c = 0.88 in $CHCl_3$); ^{1}H NMR: δ = 1.23 (s, 3H), 1.36 (s, 3H), 3.54 (dd, ^2J(H,H) = 10.3 Hz, ^3J(H,H) = 5.0 Hz, 1H), 3.62 (dd, ^2J(H,H) = 10.3 Hz, ^3J(H,H) = 5.3 Hz, 1H), 4.08 (dt, ^3J = 8.2, 5.1 Hz, 1H), 4.50 (dd, ^3J(H,H) = 8.2, 2.0 Hz, 1H), 4.54 (d, ^2J(H,H) = 12.8 Hz, 1H), 4.60 (d, ^2J(H,H) = 12.8 Hz, 1H), 5.12 (d, ^2J(H,H) = 12.9 Hz, 1H), 5.16 (d, ^2J(H,H) = 12.9 Hz, 1H), 5.30 (dd, ^3J(H,H) = 9.0, 2.0 Hz, 1H), 5.95 (d, ^3J(H,H) = 9.0 Hz, 1H), 7.20–7.40 (m, 11H), 7.72 (d, ^3J(H,H) = 3.2 Hz, 1H); ^{13}C NMR: δ = 26.77, 29.20, 53.13, 67.27, 70.06, 73.53, 76.20, 79.58, 110.06, 119.26, 127.65, 127.69, 128.05, 128.19, 128.34, 128.49, 136.00, 137.60, 142.83, 154.10, 169.60; $C_{25}H_{28}N_2O_5S$ (468.57): calcd C 64.08; H 6.02; N 5.98; found C 64.39; H 6.11; N 6.18.

4-*O*-Benzyl-1-(benzyloxycarbonylamino)-1-deoxy-2,3-*O*-isopropylidene-1-(2-thiazolyl)-L-*lyxo*-tetritol (28) (1.42 g, 76%; 60:40, hexane:diethyl ether); oil; $[\alpha]_D^{20} = -20.4$ (c = 0.66 in $CHCl_3$); ^{1}H NMR: δ = 1.27 (s, 3H), 1.37 (s, 3H), 3.53 (dd, ^2J(H,H) = 10.5 Hz, ^3J(H,H) = 4.6 Hz, 1H), 3.87 (dd, ^2J(H,H) = 10.5, ^3J(H,H) = 4.6 Hz, 1H), 4.22-4.33 (m, 2H), 4.54 (s, 2H), 5.08 (d, ^2J(H,H) = 13.0 Hz, 1H), 5.11 (d, ^2J(H,H) = 13.0 Hz, 1H), 5.27 (dd, ^3J(H,H) = 8.7, 5.5 Hz, 1H), 5.84 (d, ^3J(H,H) = 8.7 Hz, 1H), 7.20–7.37 (m, 11H), 7.72 (d, ^3J(H,H) = 3.2 Hz, 1H); ^{13}C NMR: δ = 26.82, 27.16, 55.27, 67.21, 70.58, 73.66, 77.26, 79.98, 110.23, 119.37, 127.66, 127.73, 128.05, 128.12, 128.38, 128.48, 136.39, 138.00, 142.43, 155.74, 168.03; $C_{25}H_{28}N_2O_5S$ (468.57): calcd C 64.08; H 6.02; N 5.98; found C 64.31; H 6.35; N 5.61.

3-*O*-Benzyl-5-(benzyloxycarbonylamino)-5-deoxy-1,2-*O*-isopropylidene-5-(2-thiazolyl)-β-L-*ido*-1,4-pentofuranoside (35) (1.67 g, 84%; 60:40, hexane:diethyl ether); white solid; m.p. 58–60 °C; $[\alpha]_D^{20} = -21.5$ (c = 0.65 in $CHCl_3$); ^{1}H NMR: δ = 1.26 (s, 3H), 1.44 (s, 3H), 4.00 (d, ^3J(H,H) = 3.4 Hz, 1H), 4.38 (d, ^2J(H,H) = 11.5 Hz, 1H), 4.50 (d, ^2J(H,H) = 11.5 Hz, 1H), 4.58 (d, ^3J(H,H) = 3.7 Hz, 1H), 4.74 (dd, ^3J(H,H) = 6.6, 3.4 Hz, 1H), 5.00 (d, ^2J(H,H) = 12.2 Hz, 1H), 5.08 (d, ^2J(H,H) = 12.2 Hz, 1H), 5.48 (dd, ^3J(H,H) = 7.1, 6.6 Hz, 1H), 5.64 (d, ^3J(H,H) = 7.1 Hz, 1H), 5.94 (d, ^3J(H,H) = 3.4 Hz, 1H), 7.26-7.31 (m, 11H), 7.68 (d, ^3J(H,H) = 3.2 Hz, 1H); ^{13}C NMR: δ = 26.29, 26.34, 52.36, 67.02, 72.28, 81.27, 82.43, 82.51, 105.19, 112.10, 119.25, 127.89, 127.97, 128.10, 128.36, 128.41, 128.54, 136.55, 137.26, 142.62, 155.98, 169.92; $C_{26}H_{28}N_2O_6S$ (496.58): calcd C 62.87; H 5.68; N 5.64; found C 63.01; H 5.69; N 5.29.

3-*O*-Benzyl-5-(benzyloxycarbonylamino)-5-deoxy-1,2-*O*-isopropylidene-5-(2-thiazolyl)-α-D-*gluco*-1,4-pentofuranoside (37) (1.61 g, 81%; 60:40, hexane:diethyl ether); sticky oil; $[\alpha]_D^{20} = -4.9$ (c = 0.76 in $CHCl_3$); ^{1}H NMR: δ = 1.29 (s, 3H), 1.50 (s, 3H), 4.10 (d, ^3J(H,H) = 3.7 Hz, 1H), 4.28 (d, ^2J(H,H) = 11.5 Hz, 1H), 4.45 (d, ^2J(H,H) = 11.5 Hz, 1H), 4.52 (d, ^3J(H,H) = 3.9 Hz, 1H), 4.90 (dd, ^3J(H,H) = 5.8, 3.7 Hz, 1H), 5.12 (s, 2H), 5.66 (dd, ^3J(H,H) = 9.0, 5.8 Hz, 1H), 5.94 (d, ^3J(H,H) = 3.9 Hz, 1H), 6.40 (d, ^3J(H,H) = 9.0 Hz, 1H), 7.18-7.29 (m, 11H), 7.64 (d, ^3J(H,H) = 3.2 Hz, 1H); ^{13}C NMR: δ = 26.31, 26.90, 53.21, 66.83, 72.31, 79.41, 81.63, 83.11, 105.08, 112.00, 119.02, 127.84, 127.96, 127.98, 128.16, 128.43, 128.57, 136.40, 136.59, 142.99, 156.41, 170.50; $C_{26}H_{28}N_2O_6S$ (496.58): calcd C 62.87; H 5.68; N 5.64; found C 62.88; H 5.91; N 5.76.

5-(Benzyloxycarbonylamino)-5-deoxy-1,2-*O*-isopropylidene-3-*O*-(methoxyethoxymethyl)-5-(2-thiazolyl)-β-L-*ido*-1,4-pentofuranoside (38) (1.72 g, 87%; 40:60, hexane:diethyl ether); oil; $[\alpha]_D^{20} = -1.4$ (c = 0.64 in $CHCl_3$); ^{1}H NMR: δ = 1.27 (s, 3H), 1.45 (s, 3H), 3.34 (s, 3H), 3.42–3.51 (m, 3H), 3.61–3.64 (m, 1H), 4.37 (d, ^3J(H,H) = 3.4 Hz, 1H), 4.54 (d, ^2J(H,H) = 7.1 Hz, 1H), 4.65 (d, ^2J(H,H) = 7.1 Hz, 1H), 4.70 (d, ^3J(H,H) = 3.7 Hz, 1H), 4.74 (dd, ^3J(H,H) = 7.3, 3.7 Hz, 1H), 5.07 (d, ^2J(H,H) = 12.5 Hz, 1H), 5.13 (d, ^2J(H,H) = 12.5 Hz, 1H), 5.40 (dd, ^3J(H,H) = 7.3, 6.4 Hz, 1H), 5.82 (d, ^3J(H,H) = 6.4 Hz, 1H), 5.92 (d, ^3J(H,H) = 3.4 Hz, 1H), 7.29 (m, 6H), 7.72 (d, ^3J(H,H) = 3.2 Hz, 1H); ^{13}C NMR: δ = 26.10, 26.73, 51.94, 58.92, 66.93, 97.48, 71.51, 80.71, 81.09, 82.91, 95.53, 104.83, 111.92, 119.28, 128.00, 128.36, 128.41, 136.23, 142.66, 156.02, 169.80; $C_{23}H_{30}N_2O_8S$ (494.57) calcd C 55.86; H 6.11; N 5.66; found C 55.94; H 5.78; N 5.57.

5-(Benzyloxycarbonylamino)-5-deoxy-1,2-*O*-isopropylidene-3-*O*-(methoxyethoxymethyl)-5-(2-thiazolyl)-α-D-*gluco*-1,4-pentofuranoside (39) (1.42 g, 72%; 40:60, hexane:diethyl ether); oil; $[\alpha]_D^{20} = +9.0$ (c = 0.78 in $CHCl_3$); ^{1}H NMR: δ = 1.28 (s, 3H), 1.48 (s, 3H), 3.31 (s, 3H), 3.33–3.41 (m, 3H), 3.53-3.61 (m, 1H), 4.24 (d, ^3J(H,H) = 3.1 Hz, 1H), 4.43 (d, ^2J(H,H) = 7.0 Hz, 1H), 4.61–4.68 (m, 2H), 4.88 (dd, ^3J(H,H) = 5.9, 3.1 Hz, 1H), 5.11 (d, ^2J(H,H) = 12.1 Hz, 1H), 5.14 (d, ^2J(H,H) = 12.1 Hz, 1H), 5.63 (t, ^3J(H,H) = 7.0 Hz, 1H), 5.92 (d, ^3J(H,H) = 3.5 Hz, 1H), 6.22 (d, ^3J(H,H) = 9.4 Hz, 1H), 7.23 (d, ^3J(H,H) = 3.3 Hz, 1H) 7.24–7.40 (m, 5H), 7.71 (d, ^3J(H,H) = 3.3 Hz, 1H); ^{13}C NMR: δ = 26.23, 26.87, 52.83, 58.99, 67.10, 67.71, 71.52, 79.44, 81.86, 82.56, 95.52, 104.95, 111.94, 119.07, 128.15, 128.33, 128.48, 136.35, 142.89, 156.35, 170.09; $C_{23}H_{30}N_2O_8S$ (494.57): calcd C 55.86; H 6.11; N 5.66; found C 56.09; H 6.07; N 5.53.

Methyl 5-(benzyloxycarbonylamino)-5-deoxy-2,3-*O*-isopropylidene-5-(2-thiazolyl)-α-L-*talo*-1,4-pentofuranoside (40) (1.45 g, 86%; 60:40, hexane:diethyl ether); oil; $[\alpha]_D^{20} = -8.0$ (c = 0.78 in $CHCl_3$); ^{1}H NMR: δ = 1.27 (s, 3H), 1.44 (s, 3H), 3.32 (s, 3H), 4.55 (d, ^3J(H,H) = 5.7 Hz, 1H), 4.76 (d, ^3J(H,H) = 5.7 Hz, 1H), 4.94 (s, 1H), 4.97 (dd, ^3J(H,H) = 5.7, 4.6 Hz, 1H), 5.12 (d, ^2J(H,H) = 12.3 Hz, 1H), 5.16 (d, ^2J(H,H) = 12.3 Hz, 1H), 5.25 (dd, ^3J(H,H) = 8.2, 4.6 Hz, 1H), 6.62 (d, ^3J(H,H) = 8.2 Hz, 1H), 7.20–7.40 (m, 6H), 7.78 (d, ^3J(H,H) = 3.2 Hz, 1H); ^{13}C NMR: δ = 24.94, 26.40, 55.34, 55.95, 67.10, 81.85, 85.45, 89.02, 110.48, 112.73, 118.89, 127.00, 127.97, 128.14, 128.48, 143.28, 156.40, 170.40; $C_{20}H_{24}N_2O_6S$ (420.49): calcd C 57.13; H5.75; N 6.66; found C 57.18; H 5.66; N 6.72.

Methyl 5-(benzyloxycarbonylamino)-5-deoxy-2,3-*O*-isopropylidene-5-(2-thiazolyl)-β-D-*allo*-1,4-pentofuranoside (41) (1.38 g, 82%; 60:40, hexane:diethyl ether); oil; $[\alpha]_D^{20} = -39.1$ (c = 0.88 in $CHCl_3$); ^{1}H NMR: δ = 1.28 (s, 3H), 1.44 (s, 3H), 3.30 (s, 3H), 4.47 (dd, ^3J(H,H) = 10.0, 1.1 Hz, 1H), 4.64 (d, ^3J(H,H) = 5.5 Hz, 1H), 4.92–4.97 (m, 2H), 5.10 (s, 2H), 5.15 (d, ^3J(H,H) = 9.5 Hz, 1H), 5.82 (bd, ^3J(H,H) = 8.0 Hz, 1H), 7.29 (d, ^3J(H,H) = 3.2 Hz, 1H), 7.30–7.40 (m, 5H), 7.77 (d, ^3J(H,H) = 3.2 Hz, 1H); ^{13}C NMR: δ = 25.16, 26.54, 54.49, 56.23, 67.31, 81.47, 85.11, 89.24, 110.40, 112.67, 119.32, 128.10, 128.21, 128.50, 135.99, 142.67, 156.02, 167.68; $C_{20}H_{24}N_2O_6S$ (420.49): calcd C 57.13; H5.75; N 6.66; found C 57.28; H 5.62; N 6.63.

6-(Benzyloxycarbonylamino)-6-deoxy-1,2:3,4-di-*O*-isopropylidene-6-(2-thiazolyl)-β-L-*glycero*-D-*galacto*-1,5-hexopyranoside (42) (1.54 g, 81%; 50:50, hexane:diethyl ether); white solid; m.p. 156–157 °C; $[\alpha]_D^{20} = -59.9$ (c = 1.06 in $CHCl_3$); ^{1}H NMR: δ = 1.26 (s, 6H), 1.33 (s, 3H), 1.45 (s, 3H), 4.22 (bd, ^3J(H,H) = 7.8 Hz, 1H), 4.28 (dd, ^3J(H,H) = 4.9, 2.2 Hz, 1H), 4.39 (bs, 1H), 4.57 (dd, ^3J(H,H) = 7.8, 2.2 Hz, 1H), 5.08 (d, ^2J(H,H) = 12.5 Hz, 1H), 5.14 (d, ^2J(H,H) = 12.5 Hz, 1H), 5.50 (t, ^3J(H,H) = 5.4 Hz, 1H), 5.48 (d, ^3J(H,H) = 4.9 Hz, 1H), 5.84 (bs, 1H), 7.25 (d, ^3J(H,H) = 3.2 Hz, 1H), 7.30 (bs, 5H), 7.72 (d, ^3J(H,H) = 3.2 Hz, 1H); ^{13}C NMR: δ = 24.14, 24.92, 25.79, 25.92, 54.03, 66.93, 68.79, 70.78, 70.93, 71.77, 96.34, 109.03, 109.59, 119.24, 128.02, 128.40, 128.05, 136.35, 142.61, 156.40, 170.78; $C_{23}H_{28}N_2O_7S$ (476.55): calcd C 57.97; H5.92; N 5.88; found C 57.87; H 5.75; N 6.23.

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Protection of Amines as *N*-acetyl Derivatives: The crude amine, obtained as described above fr m 4 mmol of hydroxylamine, was taken up in pyridine (7 mL), and treated with acetic anhydride (7 mL) and DMAP (12.2 mg, 0.1 mmol) at ambient temperature. The solution was stirred for 12 h at the same temperature. The solvent was partially distilled at reduced pressure and the residue was partitioned between saturated aq $NaHCO_3$ (30 mL) and CH_2Cl_2 (30 mL). The organic layer was washed sequentially with saturated aq $CuSO_4$ and brine, dried ($MgSO_4$), and evaporated under reduced pressure to give the crude product, which was purified by column chromatography on silica gel. The overall yield from the corresponding hydroxylamine and the mixture of solvents employed for chromatography are reported below for each compound.

1-Acetamido-1-deoxy-2,3:4,5-di-*O*-isopropylidene-1-(2-thiazolyl)-D-*gluco*-pentitol (29) (1.03 g, 72%; 5:95, hexane:diethyl ether); white solid; m.p. 124–126 °C; $[\alpha]_D^{20} = +25.2$ ($c = 0.73$ in $CHCl_3$); ^1H NMR: $\delta = 1.32$ (s, 3H), 1.34 (s, 6H), 1.46 (s, 3H), 2.08 (s, 3H), 3.70 (t, $^2J(H,H)$ and $^3J(H,H) = 8.1$ Hz, 1H), 3.93–3.98 (m, 1H), 4.05–4.19 (m, 2H), 4.56 (dd, $^3J(H,H) = 8.2$, 2.2 Hz, 1H), 5.73 (dd, $^3J(H,H) = 9.0$, 2.2 Hz, 1H), 6.75 (d, $^3J(H,H) = 9.0$ Hz, 1H), 7.26 (d, $^3J(H,H) = 3.3$ Hz, 1H), 7.74 (d, $^3J(H,H) = 3.3$ Hz, 1H); ^{13}C NMR: $\delta = 23.23$, 25.23, 26.57, 26.79, 26.95, 50.79, 67.71, 76.95, 77.73, 81.11, 109.89, 110.21, 119.20, 142.71, 168.84, 169.46; $C_{16}H_{24}N_2O_5S$ (356.44): calcd C 53.92; H 6.79; N 7.86; found C 54.05; H 6.68; N 8.18.

1-Acetamido-1-deoxy-2,3:4,5-di-*O*-isopropylidene-1-(2-thiazolyl)-D-*manno*-pentitol (30) (1.08 g, 76%; 5:95, hexane:diethyl ether); white solid; m.p. 118–120 °C; $[\alpha]_D^{20} = -5.6$ ($c = 0.45$ in $CHCl_3$); ^1H NMR: $\delta = 1.26$ (s, 3H), 1.32 (s, 3H), 1.34 (s, 3H), 1.45 (s, 3H), 2.00 (s, 3H), 3.88 (dd, $^2J(H,H) = 8.4$, $^3J = 5.6$ Hz, 1H), 3.98 (dd, $^2J(H,H) = 8.4$, $^3J(H,H) = 6.1$ Hz, 1H), 4.04 (ddd, $^3J(H,H) = 6.1$, 5.6, 4.9 Hz, 1H), 4.14 (dd, $^3J(H,H) = 7.6$, 4.9 Hz, 1H), 4.35 (t, $^3J(H,H) = 7.7$ Hz, 1H), 5.50 (t, $^3J(H,H) = 7.8$ Hz, 1H), 6.64 (d, $^3J(H,H) = 8.0$ Hz, 1H), 7.27 (d, $^3J(H,H) = 3.2$ Hz, 1H), 7.77 (d, $^3J(H,H) = 3.2$ Hz, 1H); ^{13}C NMR: $\delta = 23.23$, 25.23, 26.63, 26.91, 27.37, 53.04, 63.71, 67.81, 79.16, 81.77, 109.96, 110.62, 119.34, 142.44, 167.54, 169.26; $C_{16}H_{24}N_2O_5S$ (356.44): calcd C 53.92; H 6.79; N 7.86; found C 54.12; H 6.97; N 7.92.

5-Acetamido-3-*O*-benzyl-5-deoxy-1,2-*O*-isopropylidene-5-(2-thiazolyl)-β-L-*ido*-1,4-pentofuranoside (36) (1.16 g, 72%; 5:95, hexane:diethyl ether); colorless crystals; m.p. 136 °C; $[\alpha]_D^{20} = -19.3$ ($c = 0.61$ in $CHCl_3$); ^1H NMR: $\delta = 1.30$ (s, 3H), 1.48 (s, 3H), 1.92 (s, 3H), 3.93 (d, $^3J(H,H) = 3.3$ Hz, 1H), 4.33 (d, $^2J(H,H) = 11.6$ Hz, 1H), 4.50 (d, $^2J(H,H) = 11.6$ Hz, 1H), 4.59 (d, $^3J(H,H) = 3.7$ Hz, 1H), 4.76 (dd, $^3J(H,H) = 7.1$, 3.3 Hz, 1H), 5.70 (t, $^3J(H,H) = 7.3$ Hz, 1H), 5.96 (d, $^3J(H,H) = 3.7$ Hz, 1H), 6.37 (bd, $^3J(H,H) = 7.5$ Hz, 1H), 7.25–7.33 (m, 6H), 7.68 (d, $^3J(H,H) = 3.2$ Hz, 1H); ^{13}C NMR: $\delta = 23.21$, 26.21, 26.81, 38.70, 49.99, 72.09, 80.93, 82.06, 105.08, 112.05, 119.42, 127.89, 128.11, 130.88, 136.85, 142.29, 168.98, 169.83; $C_{20}H_{24}N_2O_5S$ (404.41): calcd C 59.40; H 5.98; N 6.93; found C 59.60; H 5.79; N 6.81.

6-Acetamido-6-deoxy-1,2:3,4-di-*O*-isopropylidene-6-(2-thiazolyl)-β-L-*glycero*-D-*galacto*-1,5-hexopyranoside (43) (1.32 g, 86%; diethyl ether); white solid; m.p. 127–129 °C; $[\alpha]_D^{20} = -42.2$ ($c = 0.45$ in $CHCl_3$); ^1H NMR: $\delta = 1.28$ (s, 6H), 1.42 (s, 3H), 1.49 (s, 3H), 2.02 (s, 3H), 4.20 (dd, $^3J(H,H) = 8.1$, 1.7 Hz, 1H), 4.27 (dd, $^3J(H,H) = 4.9$, 2.2 Hz, 1H), 4.43 (dd, $^3J(H,H) = 5.1$, 1.7 Hz, 1H), 4.56 (dd, $^3J(H,H) = 8.1$, 2.2 Hz, 1H), 5.51 (d, $^3J(H,H) = 4.9$ Hz, 1H), 5.56 (dd, $^3J(H,H) = 7.1$, 5.1 Hz, 1H), 6.55 (bd, $^3J(H,H) = 7.1$ Hz, 1H), 7.22 (d, $^3J(H,H) = 3.2$ Hz, 1H), 7.71 (d, $^3J(H,H) = 3.2$ Hz, 1H); ^{13}C NMR: $\delta = 23.15$, 23.94, 24.87, 25.83, 25.89, 52.02, 68.44, 70.74, 70.90, 71.68, 96.30, 108.99, 109.36, 119.15, 142.30, 170.00, 170.14; $C_{17}H_{24}N_2O_6S$ (384.45): calcd C 53.11; H 6.29; N 7.29; found C 53.50; H 6.35; N 7.29.

6-Acetamido-6-deoxy-1,2:3,4-di-*O*-isopropylidene-6-(2-thiazolyl)-α-D-*glycero*-D-*galacto*-1,5-hexopyranoside (44) (1.20 g, 78%; diethyl ether); white solid; m.p. 50–52 °C; $[\alpha]_D^{20} = -69.8$ ($c = 0.45$ in $CHCl_3$); ^1H NMR: $\delta = 1.26$ (s, 3H), 1.28 (s, 3H), 1.50 (s, 3H), 1.54 (s, 3H), 2.02 (s, 3H), 4.27 (dd, $^3J(H,H) = 7.9$, 1.6 Hz, 1H), 4.28 (dd, $^3J(H,H) = 5.0$, 2.2 Hz, 1H), 4.45 (dd, $^3J(H,H) = 5.5$, 1.6 Hz, 1H), 4.54 (d, $^3J(H,H) = 7.9$, 2.2 Hz, 1H), 5.53 (d, $^3J(H,H) = 5.0$ Hz, 1H), 5.66 (dd, $^3J(H,H) = 8.2$, 5.5 Hz, 1H), 7.23 (d, $^3J(H,H) = 3.2$ Hz, 1H), 7.43 (d, $^3J(H,H) = 8.2$ Hz, 1H), 7.70 (d, $^3J(H,H) = 3.2$ Hz, 1H); ^{13}C NMR: $\delta = 23.33$, 24.08, 24.94, 25.81, 26.08, 53.65, 66.64, 70.50, 71.01, 71.66, 96.75, 108.99, 109.46, 119.10, 142.80, 169.52, 169.94; $C_{17}H_{24}N_2O_6S$ (384.45): calcd C 53.11; H 6.29; N 7.29; found C 53.24; H 6.69; N 7.11.

Thiazolyl-to-Formyl Deblocking—Preparation of α-Aminoaldehydes: A mixture of the *N*-protected α-aminoalkylthiazole (3 mmol) and activated 4 Å molecular sieves (6.0 g) and CH_3CN (50 mL) was stirred at ambient temperature for 10 min. Methyl trifluoromethanesulfonate (0.36 mL, 3.3 mmol) was added to the mixture and stirring was continued for an additional 20 min. period. The solvent was removed under reduced pressure. The residue was taken up in MeOH (50 mL), cooled to 0 °C and treated with $NaBH_4$ (0.252 g, 6.6 mmol). The mixture was stirred at room temperature for 15 min, diluted with acetone (6 mL), filtered through Celite, and concentrated in vacuo. The residue was taken up in 10:1 $CH_3CN:H_2O$ (50 mL) and then treated with CuO (0.72 g, 9 mmol) and $CuCl_2 \cdot 2H_2O$ (0.56 g, 3.3 mmol). The resulting suspension was stirred at ambient temperature for 10 min, then filtered through Celite and concentrated in vacuo below 30 °C. The residue was partitioned between brine (80 mL) and diethyl ether (80 mL). The organic layer was separated and the aqueous layer was extracted with diethyl ether (2 × 50 mL). The combined extracts were washed with saturated aq EDTA (disodium salt) and brine, dried ($MgSO_4$), and passed through a plug of Florisil eluting with diethyl ether. The solvent was then evaporated under reduced pressure to give essentially pure α-aminoaldehyde.

2-(*tert*-Butoxycarbonylamino)-2-deoxy-3,4-*O*-isopropylidene-D-threose (45) (0.498 g, 64%); oil; $[\alpha]_D^{20} = +8.1$ ($c = 0.49$ in $CHCl_3$); IR (Nujol): $\tilde{\nu} = 1711\ cm^{-1}$; ^1H NMR: $\delta = 1.31$ (s, 3H), 1.39 (s, 3H), 1.43 (s, 9H), 3.76 (dd, $^2J(H,H) = 8.5$, $^3J(H,H) = 6.9$ Hz, 1H), 4.09 (dd, $^2J(H,H) = 8.5$, $^3J(H,H) = 6.6$ Hz, 1H), 4.30 (dd, $^3J(H,H) = 8.1$, 2.7 Hz, 1H), 4.62 (ddd, $^3J(H,H) = 6.9$, 6.6, 2.7 Hz, 1H), 5.25 (d, $^3J(H,H) = 8.1$ Hz, 1H), 9.66 (s, 1H); ^{13}C NMR: $\delta = 24.74$, 26.02, 28.20, 60.67, 65.73, 66.29, 73.12, 110.10, 156.20, 198.40.

2-(Benzyloxycarbonylamino)-2-deoxy-3,4-*O*-isopropylidene-D-threose (46) (0.616 g, 70%); oil; $[\alpha]_D^{20} = +11.5$ ($c = 2.17$ in $CHCl_3$); IR (Nujol): $\tilde{\nu} = 1720\ cm^{-1}$; ^1H NMR: $\delta = 1.30$ (s, 3H), 1.38 (s, 3H), 3.77 (dd, $^2J(H,H) = 8.7$, $^3J(H,H) = 6.5$ Hz, 1H), 4.10 (dd, $^2J(H,H) = 8.7$, $^3J(H,H) = 6.5$ Hz, 1H), 4.39 (dd, $^3J(H,H) = 8.1$, 3.0 Hz, 1H), 4.66 (ddd, $^3J(H,H) = 6.8$, 6.5, 3.0 Hz, 1H), 5.12 (AB quartet, $^2J(H,H) = 12.1$ Hz, $\Delta\delta = 0.06$, 2H), 5.56 (d, $^3J(H,H) = 8.1$ Hz, 1H), 7.32 (bs, 5H), 9.62 (s, 1H); ^{13}C NMR: $\delta = 24.62$, 25.95, 61.05, 65.62, 67.38, 72.91, 109.90, 128.06, 128.27, 128.52, 135.85, 156.62, 197.76.

2-(*tert*-Butoxycarbonylamino)-2-deoxy-3,4-*O*-isopropylidene-D-erythrose (47) (0.545 g, 70%); oil; $[\alpha]_D^{20} = -22.5$ ($c = 4.76$ in $CHCl_3$); IR (Nujol): $\tilde{\nu} = 1715\ cm^{-1}$; ^1H NMR: $\delta = 1.28$ (s, 3H), 1.38 (s, 3H), 1.39 (s, 9H), 4.05–4.11 (m, 2H), 4.22 (q, $^3J(H,H) = 5.7$ Hz, 1H), 4.26–4.30 (m, 1H), 5.40 (d, $^3J(H,H) = 5.9$ Hz, 1H), 9.69 (s, 1H); ^{13}C NMR: $\delta = 24.81$, 26.28, 28.13, 61.54, 65.70, 73.12, 80.43, 110.24, 158.50, 198.61.

2-(Benzyloxycarbonylamino)-2-deoxy-3,4-*O*-isopropylidene-D-erythrose (48) (0.668 g, 76%); oil; $[\alpha]_D^{20} = -20.9$ ($c = 0.76$ in $CHCl_3$); IR (Nujol): $\tilde{\nu} = 1720\ cm^{-1}$; ^1H NMR: $\delta = 1.29$ (s, 3H), 1.39 (s, 3H), 4.27 (q, $^3J(H,H) = 5.2$ Hz, 1H), 4.36 (t, $^3J(H,H) = 5.8$ Hz, 1H), 4.70 (d, $^3J(H,H) = 5.2$ Hz, 2H), 5.08 (s, 2H), 5.78 (d, $^3J(H,H) = 6.2$ Hz, 1H), 7.20–7.40 (m, 5H), 9.68 (s, 1H); ^{13}C NMR: $\delta = 26.63$, 26.18, 61.79, 66.38, 67.14, 75.70, 110.28, 128.00, 128.14, 128.40, 135.82, 156.12, 198.12.

5-*O*-Benzyl-2-(*tert*-butoxycarbonylamino)-2-deoxy-3,4-*O*-isopropylidene-L-xylose (49) (0.854 g, 75%); oil; $[\alpha]_D^{20} = -3.3$ ($c = 0.33$ in $CHCl_3$); IR (Nujol): $\tilde{\nu} = 1717\ cm^{-1}$; ^1H NMR: $\delta = 1.38$ (s, 3H), 1.39 (s, 3H), 1.41 (s, 9H), 3.63 (dd, $^2J(H,H) = 10.5$ Hz, $^3J(H,H) = 4.7$ Hz, 1H), 3.68 (dd, $^2J(H,H) = 10.5$ Hz, $^3J(H,H) = 4.7$ Hz, 1H), 4.03 (dd, $^3J(H,H) = 8.4$, 4.7 Hz, 1H), 4.32–4.44 (m, 2H), 4.57 (s, 2H), 5.26 (bs, 1H), 7.20–7.40 (m, 5H), 9.60 (s, 1H); ^{13}C NMR: $\delta = 26.69$, 26.77, 28.22, 59.42, 69.22, 73.59, 75.37, 75.95, 80.50, 110.09, 127.70, 127.76, 128.42, 138.12, 153.85, 198.16.

5-*O*-Benzyl-2-(benzyloxycarbonylamino)-2-deoxy-3,4-*O*-isopropylidene-L-xylose (50) (0.992 g, 80%); oil; $[\alpha]_D^{20} = -1.5$ ($c = 1.6$ in $CHCl_3$); IR (Nujol): $\tilde{\nu} = 1719\ cm^{-1}$; ^1H NMR: $\delta = 1.21$ (s, 3H), 1.39 (s, 3H), 3.54 (dd, $^2J(H,H) = 10.4$, $^3J(H,H) = 5.1$ Hz, 1H), 3.60 (dd, $^3J(H,H) = 9.0$, 5.1 Hz, 1H), 3.68 (dd, $^2J(H,H) = 10.4$ Hz, $^3J(H,H) = 4.5$ Hz, 1H), 4.01 (ddd, $^3J(H,H) = 8.0$, 5.1, 4.5 Hz, 1H), 4.44 (dd, $^3J(H,H) = 9.0$, 8.0 Hz, 1H), 4.55 (s, 2H), 5.12 (s, 2H), 5.54 (bd, $^3J(H,H) = 5.1$ Hz, 1H), 7.25–7.34 (m, 10H), 9.58 (s, 1H); ^{13}C NMR: $\delta = 26.57$, 29.32, 54.04, 59.89, 67.26, 69.52, 73.62, 75.79, 109.82, 127.62, 127.89, 127.98, 128.09, 128.28, 128.36, 137.68, 136.08, 156.52, 197.34.

5-*O*-Benzyl-2-(benzyloxycarbonylamino)-2-deoxy-3,4-*O*-isopropylidene-L-lyxose (51) (0.905 g, 73%); oil; $[\alpha]_D^{20} = -25.1$ (c 0.82 in $CHCl_3$); IR (Nujol): $\tilde{\nu} = 1716\ cm^{-1}$; ^1H NMR: $\delta = 1.37$ (s, 3H), 1.39 (s, 3H), 3.56 (dd, $^2J(H,H) = 10.1$ Hz, $^3J(H,H) = 5.4$ Hz, 1H), 3.63 (dd, $^2J(H,H) = 10.1$ Hz, $^3J(H,H) = 4.7$ Hz, 1H), 4.05 (dd, $^3J(H,H) = 7.5$, 6.0 Hz, 1H), 4.32 (dt, $^3J(H,H) = 7.8$, 5.0 Hz, 1H), 4.42 (t, $^3J(H,H) = 6.6$ Hz, 1H), 4.52 (d, $^2J(H,H) = 12.0$ Hz, 1H), 4.54 (d, $^2J(H,H) = 12.0$ Hz, 1H), 5.09 (s, 2H), 5.55 (bs, 1H), 7.20–7.40 (m, 10H), 9.7 (s, 1H); ^{13}C NMR: $\delta = 26.74$, 26.83, 61.45, 67.34, 70.27, 73.81, 77.49, 78.60, 110.36, 127.81, 128.12, 128.24, 128.33, 128.46, 128.54, 136.25, 137.71, 156.13, 197.72.

2-Acetamido-2-deoxy-3,4:5,6-di-*O*-isopropylidene-D-glucose (52) (0.542 g, 60%); oil; $[\alpha]_{578}^{20} = +2.0$ to $+3.1$ ($c = 0.64$ in MeOH) [ref. [48]: $[\alpha]_{578}^{20} = +2.07$ ($c = 8.25$ in MeOH)]; IR (Nujol): $\tilde{\nu} = 1725\ cm^{-1}$; ^1H NMR: $\delta = 1.31$ (s, 3H), 1.32 (s, 3H), 1.38 (s, 3H), 1.41 (s, 3H), 2.08 (s, 3H), 3.65 (t, $^2J(H,H)$ and $^3J(H,H) = 8.1$ Hz, 1H), 3.96 (dd, $^2J(H,H) = 8.1$, $^3J(H,H) = 4.0$ Hz, 1H), 4.06 (ddd, $^3J(H,H) = 8.1$, 6.3, 4.0 Hz, 1H), 4.15 (dd, $^3J(H,H) = 8.0$, 6.3 Hz, 1H), 4.50 (dd, $^3J(H,H) = 8.0$, 2.0 Hz, 1H), 4.98 (dd, $^3J(H,H) = 9.0$, 2.0 Hz, 1H), 6.18 (d, $^3J(H,H) = 9.0$ Hz, 1H), 9.64 (bs, 1H); ^{13}C NMR: $\delta = 23.07$, 25.12, 26.47, 26.60, 26.93, 58.34, 67.66, 76.58, 77.43, 77.54, 110.02, 110.26, 170.33, 197.82.

2-Acetamido-2-deoxy-3,4:5,6-di-*O*-isopropylidene-D-mannose (53) (0.579 g, 64%); oil; $[\alpha]_D^{20} = +34.0$ to $+37.5$ ($c = 0.86$ in $CHCl_3$) [ref. [53]: $[\alpha]_D^{20} = +36.8°$ to $+40.1$ ($c = 1$ in $CHCl_3$)]; IR (Nujol): $\tilde{\nu} = 1740\ cm^{-1}$; ^1H NMR: $\delta = 1.32$ (s, 3H), 1.34 (s, 3H), 1.40 (s, 3H), 1.41 (s, 3H), 2.03 (s, 3H), 3.94–4.22 (m, 5H), 4.66 (dt, $^3J(H,H) = 6.4$, 0.6 Hz, 1H), 6.45 (d, $^3J(H,H) = 6.4$ Hz, 1H), 9.70 (d, $^3J(H,H) = 0.6$ Hz, 1H); ^{13}C NMR: $\delta = 22.40$, 25.20, 26.64, 26.70, 26.90, 59.72, 67.60, 76.80, 79.02, 79.69, 110.08, 110.52, 170.20, 197.82. The ^1H and ^{13}C NMR data were in agreement with those reported [64].

2-(*tert*-Butoxycarbonylamino)-2-deoxy-3,4:5,6-di-*O*-isopropylidene-D-mannose (54) (0.776 g, 72%); oil; $[\alpha]_D^{20} = +21.4$ to $+24.7$ ($c = 0.70$ in $CHCl_3$); IR (Nujol): $\tilde{\nu} = 1718$; ^1H NMR (55 °C): $\delta = 1.31$ (s, 3H), 1.33 (s, 3H), 1.36 (s, 3H), 1.41 (s, 9H), 1.42 (s, 3H), 3.91–4.18 (m, 5H), 4.29–4.32 (m, 1H), 5.50 (bs, 1H), 9.62 (s, 1H); ^{13}C NMR (55 °C): $\delta = 25.01$, 26.37, 26.77, 26.93, 28.21, 61.20, 67.81, 76.77, 79.11, 79.28, 80.27, 110.26, 110.66, 155.46, 198.53.

2-(*tert*-Butoxycarbonylamino)-3-*O*-(*tert*-butyldiphenylsilyl)-2,4-dideoxy-L-threose (55). (0.967 g, 73%); oil; $[\alpha]_D^{20} = -11.8$ ($c = 1.02$ in $CHCl_3$); IR (Nujol): $\tilde{\nu} = 1725\ cm^{-1}$; ^1H NMR (55 °C mixture of rotamers): $\delta = 1.02$ (s, 9H), 1.08 (d, $^3J(H,H) = 6.4$ Hz, 3H), 1.43 (s, 9H), 4.14 (bs, 0.67H), 4.46–4.49 (m, 0.67H), 4.59–4.62 (m, 0.33H), 4.92–4.95 (m, 0.33H), 5.22 (bs, 0.67H), 5.64 (bs, 0.33H), 7.26–7.41 (m, 6H), 7.56–7.70 (m, 4H), 9.60 (bs,1H); ^{13}C NMR (55 °C mixture of rotamers): $\delta = 19.23$, 19.30, 20.16, 26.95, 27.05, 28.36, 28.42, 65.64, 65.74, 68.77, 71.95, 80.09, 127.55, 127.61, 127.66, 127.88, 129.63, 129.70, 129.88, 130.09, 132.94, 133.12, 133.92, 134.30, 135.88, 135.93, 155.86, 200.12.

2-(*tert*-Butoxycarbonylamino)-3-*O*-(*tert*-butyldiphenylsilyl)-2,4-dideoxy-L-erythrose (56) (0.993 g, 75%); oil; $[\alpha]_D^{20} = +27.8$ ($c = 0.54$ in $CHCl_3$); IR (Nujol): $\tilde{\nu} = 1720\ cm^{-1}$; ^1H NMR (55 °C): $\delta = 1.02$ (s, 9H), 1.29 (d, $^3J(H,H) = 6.5$ Hz, 3H), 1.40 (s, 9H), 4.18–4.23 (m, 2H), 5.34 (bs, 1H), 7.27–7.41 (m, 6H), 7.56–7.68 (m, 4H), 9.81 (bs, 1H); ^{13}C NMR (55 °C): $\delta = 19.26$, 20.56, 26.95, 28.29, 65.46, 71.15, 80.12, 127.67, 127.83, 129.87, 129.97, 133.20, 133.96, 135.80, 135.83, 155.20, 198.78.

3-*O*-Benzyl-5-(*tert*-butoxycarbonylamino)-5-deoxy-1,2-*O*-isopropylidene-β-L-*ido*-hexodialdo-1,4-furanose (57) (0.99 g, 81%); oil; $[\alpha]_D^{20} = -60.0$ ($c = 3.7$ in $CHCl_3$); IR (Nujol): $\tilde{\nu} = 1725\ cm^{-1}$; ^1H NMR: $\delta = 1.28$ (s, 3H), 1.40 (s, 9H), 1.43 (s, 3H), 4.00 (d, $^3J(H,H) = 3.2$ Hz, 1H), 4.36–4.40 (m, 2H), 4.50–4.61 (m, 3H), 5.10 (d, $^3J(H,H) = 6.3$ Hz, 1H), 5.90 (d, $^3J(H,H) = 3.7$ Hz, 1H), 7.23–7.38 (m, 5H), 9.64 (s, 1H); ^{13}C NMR: $\delta = 26.24$, 26.79, 28.19, 57.70, 71.98, 79.23, 80.61, 81.89, 81.94, 104.92, 112.16, 128.08, 128.35, 128.63, 136.42, 155.81, 197.60.

3-*O*-Benzyl-5-(benzyloxycarbonylamino)-5-deoxy-1,2-*O*-isopropylidene-β-L-*ido*-hexodialdo-1,4-furanose (58) (1.18 g, 89%); oil; $[\alpha]_D^{20} = -63.1$ ($c = 2.74$ in $CHCl_3$); IR (Nujol): $\tilde{\nu} = 1731\ cm^{-1}$; ^1H NMR: $\delta = 1.28$ (s, 3H), 1.44 (s, 3H), 4.02 (d, $^3J(H,H) = 3.2$ Hz, 1H), 4.39 (d, $^2J(H,H) = 11.7$ Hz, 1H), 4.46 (dd, $^3J(H,H) = 6.1$, 5.9 Hz, 1H), 4.52 (d, $^2J(H,H) = 11.7$ Hz, 1H), 4.53 (d, $^3J(H,H) = 4.1$ Hz, 1H), 4.66 (dd, $^3J(H,H) = 5.9$, 3.2 Hz, 1H), 5.04 (d, $^2J(H,H) = 12.2$ Hz, 1H), 5.09 (d, $^2J(H,H) = 12.2$ Hz, 1H), 5.36 (d, $^3J(H,H) = 6.1$ Hz, 1H), 5.90 (d, $^3J(H,H) = 4.1$ Hz, 1H), 7.25–7.32 (m, 10H), 9.67 (s, 1H); ^{13}C NMR: $\delta = 26.21$, 26.82, 58.34, 67.08, 72.19, 79.04, 81.23, 82.16, 105.03, 119.18, 127.66, 127.91, 128.03, 128.19, 128.40, 128.59, 136.19, 136.42, 156.10, 196.80.

3-*O*-Benzyl-5-(benzyloxycarbonylamino)-5-deoxy-1,2-*O*-isopropylidene-α-D-*gluco*-hexodialdo-1,4-furanose (60) (1.01 g, 76%); oil; $[\alpha]_D^{20} = -26.1$ ($c = 2.98$ in $CHCl_3$); IR (Nujol): $\tilde{\nu} = 1730\ cm^{-1}$; ^1H NMR: $\delta = 1.30$ (s, 3H), 1.45 (s, 3H), 4.37 (d, $^2J(H,H) = 11.9$ Hz, 1H), 4.45–4.55 (m, 3H), 4.60 (d, $^3J(H,H) = 3.9$ Hz, 1H), 4.65 (d, $^2J(H,H) = 11.9$ Hz, 1H), 5.09 (s, 2H), 5.38 (d, $^3J(H,H) = 6.8$ Hz, 1H), 5.91 (d, $^3J(H,H) = 3.9$ Hz, 1H), 7.27–7.32 (m, 10H), 9.68 (bs, 1H); ^{13}C NMR: $\delta = 26.11$, 26.68, 59.03, 67.20, 72.28, 81.56, 81.79, 82.60, 104.94, 111.98, 127.87, 127.96, 128.22, 128.36, 128.54, 128.56, 136.33, 136.43, 156.15, 198.93.

5-(Benzyloxycarbonylamino)-5-deoxy-1,2-*O*-isopropylidene-3-*O*-(methoxyethoxymethyl)-β-L-*ido*-hexodialdo-1,4-furanose (61) (0.949 g, 72%); oil; $[\alpha]_D^{20} = -66.6$ ($c = 4.10$ in $CHCl_3$); IR (Nujol): $\tilde{\nu} = 1716\ cm^{-1}$; ^1H NMR: $\delta = 1.28$ (s, 3H), 1.47 (s, 3H), 3.24 (s, 3H), 3.42–3.50 (m, 2H), 3.52–3.59 (m, 2H), 4.27 (d, $^3J(H,H) = 2.5$ Hz, 1H), 4.50 (d, $^2J(H,H) = 7.1$ Hz, 1H), 4.58 (d, $^3J(H,H) = 3.4$ Hz, 1H), 4.62–4.65 (m, 2H), 4.67 (d, $^2J(H,H) = 7.1$ Hz, 1H), 5.10 (s, 2H), 5.90 (d, $^3J(H,H) = 3.6$ Hz, 1H), 6.10 (bs, 1H), 7.28–7.33 (m, 5H), 9.68 (s, 1H); ^{13}C NMR: $\delta = 26.08$, 26.66, 57.83, 58.95, 67.15, 67.83, 71.51, 78.59, 79.49, 82.20, 93.76, 104.70, 112.13, 128.11, 128.19, 128.38, 135.96, 156.52, 196.92.

5-(Benzyloxycarbonylamino)-5-deoxy-1,2-*O*-isopropylidene-3-*O*-(methoxyethoxymethyl)-α-D-*gluco*-hexodialdo-1,4-furanose (62) (0.831 g, 63%); oil; $[\alpha]_D^{20} = -3.5$ ($c = 4.78$ in $CHCl_3$); IR (Nujol): $\tilde{\nu} = 1723\ cm^{-1}$; ^1H NMR: $\delta = 1.27$ (s, 3H), 1.47 (s, 3H), 3.30 (s, 3H), 3.39–3.50 (m, 4H), 4.24 (d, $^3J(H,H) = 2.5$ Hz, 1H), 4.45–4.80 (m, 5H), 5.05 (s, 2H), 5.84 (d, $^3J(H,H) = 3.6$ Hz, 1H), 5.90 (bd, $^3J(H,H) = 9.0$ Hz, 1H), 7.20–7.35 (m, 5H), 9.70 (s, 1H); ^{13}C NMR: $\delta = 26.73$, 29.23, 53.87, 58.95, 67.10, 67.94, 71.56, 77.31, 81.32, 82.42, 95.47, 105.00, 112.07, 128.06, 128.17, 128.48, 136.15, 156.20, 198.84.

5-(Benzyloxycarbonylamino)-5-deoxy-2,3-*O*-isopropylidene-1-*O*-methyl-α-L-*talo*-hexodialdo-1,4-furanose (63) (0.866 g, 79%); oil; $[\alpha]_D^{20} = -37.7$ ($c = 1.03$ in $CHCl_3$); IR (Nujol): $\tilde{\nu} = 1719\ cm^{-1}$; ^1H NMR: $\delta = 1.24$ (s, 3H), 1.43 (s, 3H), 3.26 (s, 3H), 4.47 (d, $^3J(H,H) = 6.0$ Hz, 1H), 4.48 (dd, $^3J(H,H) = 9.2$, 3.2 Hz, 1H), 4.69 (d, $^3J(H,H) = 6.0$ Hz, 1H), 4.88 (s, 1H), 4.94 (d, $^3J(H,H) = 3.2$ Hz, 1H), 5.08 (d, $^2J(H,H) = 12.3$ Hz, 1H), 5.12 (d, $^2J(H,H) = 12.3$ Hz, 1H), 6.25 (d, $^3J(H,H) = 9.2$ Hz, 1H), 7.20–7.38 (m, 5H), 9.57 (s, 1H); ^{13}C NMR: $\delta = 24.66$, 26.26, 55.69, 62.20, 67.04, 81.53, 84.62, 85.32, 110.27, 112.70, 127.90, 128.06, 128.39, 136.16, 156.60, 197.00.

5-(Benzyloxycarbonylamino)-5-deoxy-2,3-*O*-isopropylidene-1-*O*-methyl-β-D-*allo*-hexodialdo-1,4-furanose (64) (0.833 g, 76%); oil; $[\alpha]_D^{20} = -2.9$ ($c = 1.37$ in $CHCl_3$); IR (Nujol): $\tilde{\nu} = 1720\ cm^{-1}$; ^1H NMR: $\delta = 1.23$ (s, 3H), 1.42 (s, 3H), 3.35 (s, 3H), 4.20 (dd, $^3J(H,H) = 9.2$, 1.2 Hz, 1H), 4.40 (t, $^3J(H,H) = 8.8$ Hz, 1H), 4.62 (d, $^3J(H,H) = 5.8$ Hz, 1H), 4.92 (dd, $^3J(H,H) = 5.8$, 1.2 Hz, 1H), 5.0 (s, 1H), 5.08 (d, $^2J(H,H) = 12.2$ Hz, 1H), 5.12 (d, $^2J(H,H) = 12.2$ Hz, 1H), 5.57 (d, $^3J(H,H) = 8.8$ Hz, 1H), 7.22–7.38 (m, 5H), 9.72 (s, 1H); ^{13}C NMR: $\delta = 24.89$, 26.33, 54.03, 61.40, 67.27, 81.67, 84.78, 86.81, 110.52, 112.79, 127.91, 128.08, 128.38, 135.98, 156.55, 198.34.

6-(Benzyloxycarbonylamino)-6-deoxy-1,2:3,4-di-*O*-isopropylidene-β-L-*glycero*-D-*galacto*-heptodialdo-1,5-pyranose (65) (1.14 g, 90%); white solid; m.p. 46–47 °C; $[\alpha]_D^{20} = -63.6$ ($c = 4.2$ in $CHCl_3$); IR (Nujol): $\tilde{\nu} = 1731\ cm^{-1}$; ^1H NMR: $\delta = 1.24$ (s, 3H), 1.31 (s, 3H), 1.35 (s, 3H), 1.54 (s, 3H), 4.26 (dd, $^3J(H,H) = 7.5$, 1.5 Hz, 1H), 4.31 (dd, $^3J(H,H) = 4.9$, 2.3 Hz, 1H), 4.35 (t, $^3J(H,H) = 5.5$ Hz, 1H), 4.49 (dd, $^3J(H,H) = 5.4$, 1.5 Hz, 1H), 4.59 (dd, $^3J(H,H) = 7.5$, 2.3 Hz, 1H), 5.07 (d, $^2J(H,H) = 11.7$ Hz, 1H), 5.10 (d, $^2J(H,H) = 11.7$ Hz, 1H), 5.54 (d, $^3J(H,H) = 4.9$ Hz, 1H), 5.72 (d, $^3J(H,H) = 5.6$ Hz, 1H), 7.30 (bs, 5H), 9.71 (s, 1H); ^{13}C NMR: $\delta = 24.00$, 24.93, 25.57, 25.91, 60.07, 67.06, 67.26, 70.24, 70.44, 70.51, 96.34, 109.31, 109.62, 128.06, 128.16, 128.47, 136.22, 153.78, 197.09.

6-Acetamido-6-deoxy-1,2:3,4-di-*O*-isopropylidene-β-L-*glycero*-D-*galacto*-heptodialdo-1,5-pyranose (66) (0.82 g, 83%); oil; $[\alpha]_D^{20} = -120.0$ ($c = 0.30$ in $CHCl_3$); IR (Nujol): $\tilde{\nu} = 1732$, $1665\ cm^{-1}$; ^1H NMR: $\delta = 1.28$ (s, 3H), 1.32 (s, 3H), 1.39 (s, 3H), 1.57 (s, 3H), 2.05 (s, 3H), 4.24 (dd, $^3J(H,H) = 7.8$, 1.7 Hz, 1H), 4.33 (dd, $^3J(H,H) = 4.9$, 2.4 Hz, 1H), 4.48 (t, $^3J(H,H) = 5.6$ Hz, 1H), 4.56 (dd, $^3J(H,H) = 5.6$, 1.7 Hz, 1H), 4.61 (dd, $^3J(H,H) = 7.8$, 2.4 Hz, 1H), 5.54 (d, $^3J(H,H) = 4.9$ Hz, 1H), 6.38 (bd, $^3J(H,H) = 5.6$ Hz, 1H), 9.72 (s, 1H); ^{13}C NMR: $\delta = 23.03$, 24.10, 25.04, 25.70, 25.96, 59.20, 66.87, 70.51, 70.60, 96.45, 109.51, 109.69, 153.86, 170.57, 197.68.

6-Acetamido-6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*glycero*-D-*galacto*-heptodialdo-1,5-pyranose (67) (0.692 g, 70%): white solid; m.p. 34–35 °C; $[\alpha]_D^{20} = +12.2$ ($c = 0.49$ in $CHCl_3$); IR (Nujol): $\tilde{\nu} = 1734$, $1653\ cm^{-1}$; ^1H NMR: $\delta = 1.28$ (s, 3H), 1.35 (s, 3H), 1.44 (s, 6H), 2.02 (s, 3H), 4.21 (bt, $^3J(H,H) = 2.4$, 1.7 Hz, 1H), 4.28 (dd, $^3J(H,H) = 4.8$, 2.5 Hz, 1H), 4.51 (dd, $^3J(H,H) = 8.1$, 1.7 Hz, 1H), 4.64 (dd, $^3J(H,H) = 8.1$, 2.5 Hz, 1H), 4.72 (dd, $^3J(H,H) = 6.8$, 2.4 Hz, 1H), 5.42 (d, $^3J(H,H) = 4.8$ Hz, 1H), 6.66 (bd, $^3J(H,H) = 6.8$ Hz, 1H), 9.86 (s, 1H); ^{13}C NMR: $\delta = 22.99$, 24.02, 24.95, 25.75, 25.95, 60.26, 69.59, 70.39, 70.98, 71.94, 96.36, 109.05, 109.76, 170.30, 198.26.

Oxidation of the Aldehyde 49 to 5-*O*-Benzyl-2-(*tert*-butoxycarbonylamino)-2-deoxy-3,4-*O*-isopropylidene-L-xylonic acid (68): A solution of **49** (0.259 g, 1 mmol) in acetonitrile (3 mL) was treated sequentially with 35% aq H_2O_2 (0.21 mL, 1.04 mmol), 1.2 M aq NaH_2PO_4 (1 mL), and 0.17 M aq sodium chlorite (7 mL). Then the mixture was stirred for 2 h at ambient temperature, acidified to pH = 3 with 1 N aq HCl and diluted with ethyl acetate (10 mL). The organic layer was separated, and the aqueous layer extracted with ethyl acetate (3 × 5 mL). The combined organic phases were extracted with saturated aq $NaHCO_3$ (3 × 10 mL). The aqueous extract was washed with CH_2Cl_2 (1 × 5 ml) and then acidified to pH = 3 with 1 N aq HCl and extracted with CH_2Cl_2 (3 × 5 mL). The combined organic extracts were dried ($MgSO_4$), and the solvent evaporated under reduced pressure to give the acid **68** (0.277 g, 70%) as a sticky foam; $[\alpha]_D^{20} = -4.6$ ($c = 1.17$ in $CHCl_3$); ^1H NMR ($CDCl_3 + D_2O$): $\delta = 1.38$ (s, 3H), 1.41 (s, 3H), 1.44 (s, 9H), 3.62 (dd, $^2J(H,H) = 10.5$ Hz, $^3J(H,H) = 4.8$ Hz, 1H), 3.67 (dd, $^2J(H,H) = 10.5$ Hz, $^3J(H,H) = 4.8$ Hz, 1H), 4.04 (dt, $^3J(H,H) = 8.3$, 4.8 Hz, 1H), 4.37 (d, $^3J(H,H) = 8.3$ Hz, 1H), 4.45 (d, $^3J(H,H) = 9.3$ Hz, 1H), 4.57 (s, 2H), 5.35 (bs, 1H), 7.20–7.37 (m, 5H); ^{13}C NMR ($CDCl_3 + D_2O$): $\delta = 26.80$, 28.19, 29.00, 52.86, 69.99, 73.38, 76.09, 77.67, 80.36, 109.91, 127.59, 127.70, 128.32, 137.74, 155.99, 173.99; $C_{20}H_{29}NO_7$ (395.45): calcd found C 60.75; H 7.39; N 3.45; found C 60.91; H, 7.60; N 3.59.

Reduction of the Amino Aldehyde 52 to 2-Acetamido-2-deoxy-3,4:5,6-di-*O*-isopropylidene-D-glucitol (70): To a solution of the aldehyde **52** (0.3 g, 1 mmol) in MeOH (20 mL), $NaBH_4$ (92 mg, 2.42 mmol) was added at 0 °C. After stirring for 1 h at 0 °C, acetone (1 mL) was added, and the solvent evaporated under reduced pressure. The residue was partitioned between saturated aq $NaHCO_3$ (20 mL) and CH_2Cl_2 (20 mL). The organic layer was separated, and the aqueous layer extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layers were dried ($MgSO_4$), and the solvent was removed in vacuo. The crude alcohol was dissolved in pyridine (2 mL) and treated sequentially with Ac_2O (2 mL) and DMAP (11 mg, 0.1 mmol). The

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mixture was stirred for 12 h at ambient temperature. The solvent was distilled in vacuo, and the residue partitioned between saturated aq $NaHCO_3$ (20 mL) and CH_2Cl_2 (20 mL). The organic layer was washed with saturated aq $CuSO_4$ and brine, dried ($MgSO_4$), and the solvent evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (20:1, diethyl ether:methanol) to give **70** (0.318 g, 92%) as a white solid; m.p. 59–60 °C; $[\alpha]_D^{20} = +7.9$ ($c = 1.2$ in MeOH) [ref. [48]: m.p. 61–62 °C; $[\alpha]_D^{20} = +6.7$ ($c = 1$ in MeOH)]; ^{1}H NMR: $\delta = 1.32$ (s, 3H), 1.33 (s, 3H), 1.38 (s, 3H), 1.41 (s, 3H), 1.98 (s, 3H), 2.04 (s, 3H), 3.60 (t, $^3J(H,H) = 7.9$ Hz, 1H), 3.92–3.94 (m, 1H), 3.98–4.06 (m, 3H), 4.15 (dd, $^3J(H,H) = 8.2$, 6.1 Hz, 1H), 4.28 (dd, $^2J(H,H) = 11.1$ Hz, $^3J(H,H) = 6.9$ Hz, 1H), 4.53 (dddd, $^3J(H,H) = 9.4$, 6.9, 5.5, 1.6 Hz, 1H), 5.88 (d, $^3J(H,H) = 9.4$ Hz, 1H); ^{13}C NMR: $\delta = 20.85$, 23.31, 25.19, 26.50, 26.76, 26.94, 47.74, 64.22, 67.59, 77.20, 77.75, 78.80, 109.50, 110.10, 169.65, 170.88; $C_{16}H_{27}NO_7$ (345.31): calcd C 55.64; H 7.88; N 4.06; found C 55.87; H 8.00; N 4.25.

Reduction of the Amino Aldehyde 53 to 2-Acetamido-1-*O*-acetyl-2-deoxy-3,4:5,6-di-*O*-isopropylidene-D-mannitol (71): The same procedure described above for the conversion of **52** to **70** was applied to the aldehyde **53** (0.3 g, 1 mmol) to give, after column chromatography (20:1, diethyl ether:methanol), pure **71** (0.325 g, 94%) as colorless needles; m.p. 78–79 °C; $[\alpha]_D^{20} = +32.5$ ($c = 0.9$ in MeOH) [ref. [48]: m.p. 77–78 °C; $[\alpha]_D^{20} = +31.0$ ($c = 1$ in MeOH)]; ^{1}H NMR: $\delta = 1.34$ (bs, 6H), 1.36 (s, 3H), 1.39 (s, 3H), 1.96 (s, 3H), 2.06 (s, 3H), 3.81–3.87 (m, 2H), 3.95–4.03 (m, 2H), 4.14 (dd, $^3J(H,H) = 8.4$, 5.9 Hz, 1H), 4.23–4.33 (m, 3H), 5.85 (d, $^3J(H,H) = 7.4$ Hz, 1H); ^{13}C NMR: $\delta = 20.87$, 23.39, 25.28, 26.60, 27.19, 27.44, 50.74, 63.29, 67.89, 76.57, 79.21, 80.07, 109.82, 110.40, 169.70, 170.87; $C_{16}H_{27}NO_7$ (345.31): calcd C 55.64; H 7.88; N 4.06; found C 55.41; H 7.68; N 4.15.

***N*-Acetyl-D-glucosamine (76)**: The aldehyde **52** (0.2 g, 0.66 mmol) was treated with 80% aq TFA (8 mL), and the mixture stirred at ambient temperature for 30 min. The solvent was distilled under reduced pressure at a temperature below 20 °C. The residue was dissolved in methanol (10 mL) and then treated with Amberlyst A-26 basic ion exchange resin for 30 min at ambient temperature. The resin was removed by filtration and washed with MeOH (10 mL). The combined methanol solutions were concentrated on a rotatory evaporator below 20 °C, and the residue was dissolved in water (10 mL) and washed with CH_2Cl_2 (1 × 10 mL). The aqueous layer was then lyophilized, and the residue recrystallized from the minimal quantity of water by adding ethanol and diethyl ether to incipient turbidity to give *N*-Ac-D-glucosamine **76** (117 mg, 80%) as colorless needles; m.p. 208–215 °C (decomp.); $[\alpha]_D^{20} = +40.2$ ($c = 0.53$ in H_2O, equilibrium) [ref. [73]: m.p. 210 °C; $[\alpha]_D^{20} = +41$ ($c = 1$ in H_2O)]. Compound **76** showed identical physical and spectroscopic properties to those of an authentic sample of *N*-Ac-D-glucosamine purchased from Sigma (ref. A 8625).

***N*-Acetyl-D-mannosamine (74)**: The method described above to convert **52** to **76** was applied to the aldehyde **53** (0.2 g, 0.66 mmol) to give, after lyophilization and recrystallization of the crude product (solution in the minimal quantity of 50% aq ethanol, and addition of acetone to incipient turbidity), *N*-Ac-D-mannosamine **74** (111 mg, 76%) as an amorphous white solid; m.p. 124–127 °C (decomp.); $[\alpha]_D^{20} = +10.4$ ($c = 0.41$ in H_2O, equilibrium) [ref. [74]: m.p. 128–129 °C; $[\alpha]_D^{20} = +9.7$ ($c = 1$ in H_2O)]. Compound 74 showed identical physical and spectroscopic properties to those of an authentic sample of *N*-Ac-D-mannosamine purchased from Sigma (ref. A 9816).

D-Mannosamine Hydrochloride (75): A solution of the aldehyde **54** (0.2 g, 0.56 mmol) in ethyl acetate (15 mL) was treated with 3 N aq HCl (15 mL) at ambient temperature. The resulting mixture was vigorously stirred for 1 h and then allowed to stand until the organic and aqueous layers were well separated. The aqueous layer was washed with CH_2Cl_2 (1 × 10 mL) and distilled under reduced pressure at a temperature below 20 °C. The residue was recrystallized from the minimal quantity of 50% aq ethanol by adding acetone to incipient turbidity. D-Mannosamine hydrochloride **75** (90 mg, 75%) was thus obtained as a crystalline colorless solid that liquified shortly after contact with air; $[\alpha]_D^{20} = -3.0$ ($c = 0.39$ in H_2O, equilibrium) [ref. [56]: $[\alpha]_D^{20} = -3.2$ ($c = 10$ in H_2O)]. Compound **75** showed identical physical and spectroscopic properties to those of an authentic sample of D-mannosamine hydrochloride purchased from Sigma (ref. M 4500).

(4*R*,5*S*)-5-Methyl-4-(2-thiazolyl)-oxazolidin-2-one (72): A solution of compound **32** (0.4 g, 0.8 mmol) in THF (15 mL) was treated with 1 M solution of Bu_4NF in THF (1 mL, 1 mmol) at ambient temperature. After 2 h, saturated aq $NaHCO_3$ (10 mL) was added and the mixture was extracted with diethyl ether (3 × 10 mL). The combined organic layers were washed with brine, dried ($MgSO_4$), and distilled under reduced pressure to give the crude aminoalcohol, which was dissolved in DMF (5 mL), treated with NaH (32 mg, 60% dispersion in mineral oil, 0.8 mmol), and stirred at ambient temperature for 4 h. The resulting solution was diluted with water (15 mL), extracted with diethyl ether (2 × 15 mL), dried ($MgSO_4$), and concentrated in vacuo. Column chromatography (diethyl ether) of the residue afforded the oxazolidinone **72** (118 mg, 80%) as a sticky foam; $[\alpha]_D^{20} = +11.9$ ($c = 1.13$ in $CHCl_3$); ^{1}H NMR: $\delta = 1.58$ (d, $^3J(H,H) = 6.3$ Hz, 3H), 4.63 (dq, $^3J(H,H) = 6.3$, 6.3 Hz, 1H), 4.87 (dd, $^3J(H,H) = 6.3$, 1.3 Hz, 1H), 6.83 (bs, 1H), 7.35 (d, $^3J(H,H) = 3.3$ Hz, 1H), 7.75 (d, $^3J(H,H) = 3.3$ Hz, 1H); ^{13}C NMR: $\delta = 19.81$, 61.19, 80.08, 119.16, 143.19, 168.54, 169.70; $C_7H_8N_2O_2S$ (184.22): calcd C 45.64; H 4.38; N 15.21; found C 45.72; H 4.17; N 15.12.

(4*S*,5*S*)-5-Methyl-4-(2-thiazolyl)-oxazolidin-2-one (73): The method described above for the conversion of **32** to **72** was applied to compound **33** (0.4 g, 0.8 mmol). After column chromatography (diethyl ether) of the crude product, pure **73** (112 mg, 76%) was obtained as a sticky foam; $[\alpha]_D^{20} = -49.1$ ($c = 0.29$ in $CHCl_3$); ^{1}H NMR: $\delta = 1.06$ (d, $^3J(H,H) = 6.2$ Hz, 3H); 5.08 (dq, $^3J(H,H) = 8.3$, 6.2 Hz, 1H), 5.31 (d, $^3J(H,H) = 8.3$ Hz, 1H), 6.65 (bs, 1H), 7.38 (d, $^3J(H,H) = 3.2$ Hz, 1H), 7.80 (d, $^3J(H,H) = 3.2$ Hz, 1H); ^{13}C NMR: $\delta = 16.01$, 57.83, 76.82, 119.85, 143.66, 168.32, 170.92; $C_7H_8N_2O_2S$ (184.22): calcd C 45.64; H 4.38; N 15.21; found C 45.80; H 4.30; N 15.42.

Reduction of the Amino Aldehyde 60 to 5-Amino-5-deoxy-1,2-*O*-isopropylidene-α-D-glucofuranose (77): A solution of **60** (0.44 g, 1 mmol) in MeOH (20 mL) at 0 °C was treated with $NaBH_4$ (92 mg, 2.42 mmol). After 1 h of stirring at 0 °C, acetone (1 mL) was added, and the solvent evaporated under reduced pressure. The residue was partitioned between saturated aq $NaHCO_3$ (20 mL) and CH_2Cl_2 (20 mL). The organic layer was separated, and the aqueous layer extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layers were dried ($MgSO_4$) and distilled in vacuo to give the crude alcohol, which was dissolved in ethanol (2 mL) and treated with $Pd(OH)_2$ (25 mg, 0.2 mmol) and cyclohexene (0.41 g, 5 mmol). The resulting solution was refluxed for 6 h. The mixture was filtered through Celite with ethanol as eluant (20 mL). The solvent was evaporated under reduced pressure to give pure **77** (0.22 g, 100%) as a white solid; m.p. 124–125 °C; $[\alpha]_D^{20} = -14.2$ ($c = 1.1$ in MeOH) [ref. [75]: m.p. 125–126 °C; $[\alpha]_D^{20} = -13.0$ ($c = 1$ in MeOH)]; ^{1}H NMR (D_2O): $\delta = 1.14$ (s, 3H), 1.29 (s, 3H), 3.51–3.57 (m, 1H), 3.63 (dd, $^2J(H,H) = 12.2$ Hz, $^3J(H,H) = 7.1$ Hz, 1H), 3.74 (dd, $^2J(H,H) = 12.2$ Hz, $^3J(H,H) = 4.0$ Hz, 1H), 4.15 (dd, $^3J(H,H) = 5.8$, 3.0 Hz, 1H), 4.19 (d, $^3J(H,H) = 3.0$ Hz, 1H), 4.51 (d, $^3J(H,H) = 3.5$ Hz, 1H), 5.87 (d, $^3J(H,H) = 3.4$ Hz, 1H); ^{13}C NMR (D_2O): $\delta = 24.97$, 25.49, 51.99, 58.51, 73.83, 76.18, 84.69, 104.12, 112.86; $C_9H_{17}NO_5$ (219.18): calcd C 49.31; H 7.82; N 6.39; found C 49.22; H 7.71; N 6.45.

D-Nojirimycin (78): The amino alcohol **77** (0.1 g, 0.46 mmol) was treated with 90% aq TFA (5 mL), and the mixture stirred at ambient temperature for 30 min. The solvent was distilled under reduced pressure at a temperature below 20 °C. The residue was dissolved in water (10 mL) and passed through a column of Amberlyst A-26 basic ion exchange resin and eluted with water. The resulting solution was lyophilized to give D-nojirimycin (**78**) (67 mg, 81%) as an amorphous white powder; m.p. 123–128 °C (decomp.); $[\alpha]_D^{20} = +73.3$ ($c = 0.43$ in H_2O, equilibrium) [ref. [13e]: m.p. 124–131 °C; $[\alpha]_D^{20} = +71.2$ ($c = 0.17$ in H_2O)].

Reduction of the Amino Aldehyde 65 to 6-(Benzyloxycarbonyl)-6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*glycero*-D-*galacto*-heptopyranose (79): A solution of **65** (0.42 g, 1 mmol) in MeOH (20 mL) was treated with $NaBH_4$ (92 mg, 2.42 mmol) at 0 °C. After 1 h of stirring at 0 °C, acetone (1 mL) was added, and the solvent evaporated under reduced pressure. The residue was partitioned between saturated aq $NaHCO_3$ (20 mL) and CH_2Cl_2 (20 mL). The organic layer was separated, and the aqueous layer extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layers were dried ($MgSO_4$) and distilled in vacuo to give the crude alcohol, which was purified by column chromatography (40:60, hexane:diethyl ether) to give pure **79** (415 mg, 98%) as an oil; $[\alpha]_D^{20} = -48.2$ ($c = 1.20$ in $CHCl_3$) [ref. [64b]: $[\alpha]_D^{20} = -47.3$ ($c = 0.2$ in $CHCl_3$)]; ^{1}H NMR: $\delta = 1.29$ (s, 3H), 1.39 (s, 3H), 1.47 (s, 3H), 1.49 (s, 3H), 3.40 (bs, 1H, ex. D_2O), 3.70 (m, 1H), 3.84 (m, 2H), 4.07 (dd, $^3J(H,H) = 5.8$, 1.5 Hz, 1H), 4.27 (dd, $^3J(H,H) = 4.9$, 2.5 Hz, 1H), 4.32 (dd, $^3J(H,H) = 8.2$, 1.5 Hz, 1H), 4.59 (dd, $^3J(H,H) = 8.2$, 2.5 Hz, 1H), 5.08 (s, 2H), 5.47 (bs, 1H), 5.50 (d, $^3J(H,H) = 4.9$ Hz, 1H), 7.32 (bs, 5H); ^{13}C NMR: $\delta = 24.11$, 24.90, 25.73, 25.85, 53.52, 61.30, 66.75, 66.90, 70.67, 70.80, 70.86, 96.41, 108.82, 109.31, 128.01, 128.07, 128.38, 136.30, 156.65; $C_{21}H_{29}NO_8$ (423.37): calcd C 59.56; H 6.90; N 3.31; found C 59.70; H 7.01; N 3.66. The ^{1}H and ^{13}C NMR data were in agreement with those reported [64b].

Preparation of 6-Acetamido-*N*-benzyl-6-deoxy-1,2:3,4-di-*O*-isopropylidene-6-(2-thiazolyl)-β-L-*glycero*-D-*galacto*-1,5-hexopyranoside (82): A well-stirred suspension of NaH (45 mg, 60% dispersion in mineral oil, 1.13 mmol) in DMF (5 mL) cooled to −10 °C was treated with a solution of **44** (0.38 g, 1 mmol) in DMF (10 mL). The mixture was stirred at −10 °C for 15 min and then at ambient temperature for 2 h. The mixture was poured into water (50 mL) and extracted with diethyl ether (3 × 20 mL). The combined organic layers were washed with brine twice, dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed on silica gel (50:50, hexane:diethyl ether) to give compound **82** (428 mg, 91%) as an oil; $[\alpha]_D^{20} = -36.8$ ($c = 1.0$ in $CHCl_3$); IR (Nujol): $\tilde{\nu} = 1640$ cm^{-1}; ^{1}H NMR ([D$_6$]DMSO, 98 °C): $\delta = 1.23$ (s, 3H), 1.30 (s, 3H), 1.37 (s, 3H), 1.50 (s, 3H), 2.07 (s, 3H), 4.28 (dd, $^3J(H,H) = 5.1$, 2.1 Hz, 1H), 4.42–4.56 (m, 4H), 4.64–4.73 (m, 2H), 5.37 (d, $^3J(H,H) = 5.1$ Hz, 1H), 7.18 (d, $^3J(H,H) = 3.4$ Hz, 1H), 7.20–7.25 (m, 5H), 7.54 (d, $^3J(H,H) = 3.4$ Hz, 1H); ^{13}C NMR ([D$_6$]DMSO, 98 °C): $\delta = 21.62$, 23.81, 24.42, 25.25, 25.27, 59.90, 60.02, 66.99, 69.56, 69.87, 70.09, 95.38, 107.80, 108.21, 120.15, 124.26, 126.22, 126.77, 127.42, 140.52, 165.76, 170.73; $C_{24}H_{30}N_2O_6S$ (474.58): calcd C 60.74; H 6.37; N 5.90; found C 60.82; H 6.29; N 5.76.

Preparation of 6-Acetamido-*N*-benzyl-6-deoxy-1,2:3,4-di-*O*-isopropylidene-β-L-*glycero*-D-*galacto*-heptodialdo-1,5-pyranose (83): The thiazolyl-to-formyl deblocking procedure described above was applied to compound **82** (0.4 g, 0.9 mmol) to

give, after column chromatography (50:50, hexane:diethyl ether), the aldehyde **83** (315 mg, 84%) as a sticky oil; $[\alpha]_D^{20} = -56.1$ ($c = 0.50$ in $CHCl_3$) [ref. [68b]: $[\alpha]_D^{20} = -54.4$ ($c = 0.94$ in $CHCl_3$)]; IR (Nujol): $\tilde{\nu} = 1730, 1647\ cm^{-1}$; ^1H NMR: $\delta = 1.29$ (s, 3H), 1.35 (s, 3H), 1.42 (s, 3H), 1.51 (s, 3H), 2.07 (s, 3H), 3.56 (d, $^3J(H,H) = 9.0$ Hz, 1H), 4.22 (dd, $^3J(H,H) = 7.8$, 1.5 Hz, 1H), 4.29 (dd, $^3J(H,H) = 4.9$, 2.4 Hz, 1H), 4.63 (dd, $^3J(H,H) = 7.8$, 2.4 Hz, 1H), 4.64 (d, $^2J(H,H) = 16.6$ Hz, 1H), 4.68 (d, $^2J(H,H) = 16.6$ Hz, 1H), 4.78 (dd, $^3J(H,H) = 9.0$, 1.5 Hz, 1H), 5.49 (d, $^3J(H,H) = 4.9$ Hz, 1H), 7.28 (bs, 5H), 9.65 (s, 1H); ^{13}C NMR: $\delta = 21.33, 25.04, 25.96, 25.98, 29.30, 53.84, 54.06, 64.46, 64.57, 70.78, 71.14, 96.65, 109.30, 109.46, 127.43, 127.76, 128.73, 136.51, 171.30, 196.41$; $C_{22}H_{29}NO_7$(419.39): calcd C 62.99; H 6.97; N 3.34: found C 63.12; H 6.88; N 3.45.

Crystal Structure Analysis: The data for compounds *anti*-**12**, *syn*-**20**, and *anti*-**21** were collected at room temperature on an Enraf-Nonius CAD-4 diffractometer with graphite monochromated $Mo_{K\alpha}$ radiation, $\omega/2\theta$ scan technique ($2 \le \theta \le 27°$). All data were corrected for Lorentzian polarization. The structures were solved by direct methods with the SIR 88 program package [76]. All other calculations were accomplished by the MolEN program package [77]. The data for compound **36** were collected at room temperature on a Siemens P-4 diffractometer with graphite monochromated $Mo_{K\alpha}$ radiation, $\theta/2\theta$ scan technique. The data were corrected for Lorentzian polarization. The structure was solved by direct methods with SHELXS 86 [78]. All other calculations were accomplished by using the SHELX 93 program package [79].

Crystal data : *anti*-**12**: $C_{16}H_{20}N_2O_3S$, hexagonal $P6_1$ (no. 169), $a = 9.818(2)$, $c = 30.980(16)$ Å, $V = 2587(2)$ Å^3, $Z = 6$, $D_{calcd} = 1.24\ g\,cm^{-3}$, $\mu = 1.91\ cm^{-1}$. Of the 1927 unique measured reflections, 711 with $I \ge 3\sigma(I)$ were used in the refinement. Full-matrix least-squares refinement (in two blocks for final cycles) with all non-hydrogen atoms anisotropic and hydrogens in calculated positions, except the hydrogen bonded to O1, which was refined isotropically. R(on F) = 0.029, $R_w = 0.031$.

syn-**20**: $C_{19}H_{24}NO_5S$, orthorhombic $C222_1$ (no. 20), $a = 18.411(6)$, $b = 22.544(7)$, $c = 10.367(3)$ Å, V = 4303(2) Å^3, $Z = 8$. $D_{calcd} = 1.17\ cm^{-1}$, $\mu = 1.68\ cm^{-1}$. Of the 2617 unique measured reflections, 1435 with $I \ge 3\sigma(I)$ were used in the refinement. Full-matrix least-squares refinement with all non-hydrogen atoms anisotropic and hydrogen atoms in calculated positions, except the hydrogen bonded to O1, which was refined isotropically. R(on F) = 0.061, $R_w = 0.082$.

anti-**21**: $C_{22}H_{28}N_2O_6S$, orthorhombic $P2_12_12_1$ (no. 19), $a = 10.664(5)$, $b = 10.722(2)$, $c = 20.339(3)$ Å, $V = 2325(1)$ Å^3, $Z = 4$, $D_{calcd} = 1.28\ g\,cm^{-3}$, $\mu = 1.69\ cm^{-1}$. Of the 2786 unique measured reflections 1214 with $I \ge 3\sigma(I)$ were used in the refinement. Full-matrix least squares refinement with all non-hydrogen atoms anisotropic and hydrogen atoms in calculated positions, except the hydrogen bonded to O1, which was refined isotropically. R(on F) = 0.049, $R_w = 0.058$.

36: $C_{20}H_{24}N_2O_5S$, monoclinic, $P2_1$ (no. 4), $a = 8.437(2)$, $b = 9.252(2)$, $c = 14.277(3)$ Å, $\beta = 106.29(3)°$, $V = 1069.7(4)$ Å^3, $Z = 2$, $D_{calcd} = 1.26\ g\,cm^{-3}$, $\mu = 1.83\ cm^{-1}$. Of the 1706 measured reflections 1456 with $I \ge 2\sigma(I)$ were used in the refinement. Full-matrix refinement with all non-hydrogen atoms anisotropic and hydrogen atoms in calculated positions. R(on F^2) = 0.037, $R_w = 0.089$.

Further details of the crystal structure investigation may be obtained from the Director of the Cambridge Crystallographic Data Centre, 12 Union Road, GB-Cambridge CB2 1EZ (UK), on quoting the full journal citation.

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[1] a) G. C. Barret, *Chemistry and Biochemistry of the Amino Acids*; Chapman and Hall, London, **1985**; b) R. M. Williams in *Synthesis of Optically Active α-Amino Acids* (Eds.: J. E. Baldwin, P. D. Magnus), Pergamon, Oxford, **1989**; c) R. O. Duthaler, *Tetrahedron* **1994**, *50*, 1539–1650.

[2] a) F. M. Hauser, S. R. Ellenberger, *Chem. Rev.* **1986**, *86*, 35–67; b) D. Horton, J. D. Wander in *The Carbohydrates, Chemistry/Biochemistry*; *Vol. 1 B* (Eds.: W. Pigman, D. Horton, J. D. Wandert), Academic Press, New York, **1980**, pp. 643–760; c) J. Jurczak, A. Golebiowski in *Studies in Natural Products Chemistry, Vol. 4* (Ed.: A. Raman), Elsevier, Amsterdam, **1989**, pp. 111–156; d) I. F. Pelyvas, C. Monneret, P. Herczegh, *Synthetic Aspects of Aminodeoxy Sugars of Antibiotics*; Springer, Berlin, **1988**.

[3] a) L. E. Fellows, *Chem. Br.* **1987**, *23*, 842–844; b) G. W. J. Fleet, *ibid.* **1989**, *25*, 287–292; c) G. W. J. Fleet, S. K. Namgoong, C. Berker, S. Baines, G. S. Jacob, B. Winchester, *Tetrahedron Lett.* **1989**, *30*, 4439–4442; d) M. L. Sinnott, *Chem. Rev.* **1990**, *90*, 1171–1202; e) G. C. Look, C. H. Fotsch, C.-H. Wong, *Acc. Chem. Res.* **1993**, *26*, 182–190; f) L. A. G. H. van den Broek, D. J. Vermaas, B. M. Heskamp, C. A. A. van Boeckel, M. C. A. A. Tan, J. G. M. Bolscher, H. L. Ploegh, F. J. van Kemenade, R. E. Y. de Goede, F. Miedema, *Recl. Trav. Chim. Pays-Bas* **1993**, *112*, 82–94.

[4] This activity appears to arise from the inhibition of glycoprotein processing necessary for virus replication. Natural castanospermine, 1-deoxynojirimycin, and 1-deoxymannojirimycin and synthetic analogues have been shown to be potentially useful for the treatment of AIDS. See: a) A. Karpas, G. W. J. Fleet, R. A. Dwek, S. Peturrson, S. K. Namgoong, N. G. Ramsden, G. S. Jacob, T. W. Rademacher, *Proc. Natl. Acad. Sci. USA* **1988**, *85*, 9229–9233; b) P. S. Sunkara, D. L. Taylor, M. S. Kang, T. L. Bowlin, P. S. Liu, A. S. Tymes, A. Sjoedsma, *Lancet* **1989**, 1206; c) G. W. J. Fleet, A. Karpas, R. A. Dwek, L. E. Fellows, A. S. Tyms, S. Petursson, S. K. Namgoong, N. G. Ramsden, P. W. Smith, J. C. Son, F. Wilson, D. R. Witty, G. S. Jacob, T. W. Rademacher, *FEBS Lett.* **1988**, *237*, 128–132; d) D. C. Montefiori, W. E. Robinson Jr., W. M. Mitchell, *Proc. Natl. Acad. Sci. USA* **1988**, *85*, 9248–9252.

[5] Substitution on halides or sulfonates by N_3^-: a) M. E. C. Biffin, J. Miller, D. B. Paul in *The chemistry of the Azido Group, Vol. 2* (Ed.: S. Patai), Wiley-Interscience, London, **1971**. Mitsunobu reaction: b) O. Mitsunobu, *Synthesis* **1981**, 1–28; c) D. L. Hughes, *Org. React.* **1992**, *42*, 335; d) M. C. Viaud, P. Rollin, Synthesis **1990**, 130–132; e) A. S. Thompson, G. R. Humphrey, A. DeMarco, D. J. Mathre, E. J. Grabowski, *J. Org. Chem.* **1993**, *58*, 5886–5888. Oxirane opening: f) N. Minami, S. S. Ko, Y. Kishi, *J. Am. Chem. Soc.* **1982**, *104*, 1109–1111; g) S. Saito, N. Bunya, M. Inaba, T. Moriwake, S. Torii, *Tetrahedron Lett.* **1985**, *26*, 5309–5312; h) S. J. Danishefsky, E. Larson, J. P. Springer, *J. Am. Chem. Soc.* **1985**, *107*, 1274–1280; i) M. Caron, P. R. Carlier, K. B. Sharpless, *J. Org. Chem.* **1988**, *53*, 5185–5187; j) E. J. Corey, D. H. Lee, S. Choi, *Tetrahedron Lett.* **1992**, *33*, 6735–6738. Addition of amines or metal amides to activated alkenes: k) I. Dyong, H. Bendlin, *Chem. Ber.* **1979**, *112*, 717–726; l) G. Fronza, C. Fuganti, P. Grasselli, L. Majori, G. Pedrocchi-Fantoni, F. Spreafico, *J. Org. Chem.* **1982**, *47*, 3289–3296; m) H. Matsunaga, T. Sakamaki, H. Nagaoka, Y. Yamada, *Tetrahedron Lett.* **1983**, *17*, 3009–3012; n) A. Dondoni, G. Fantin, M. Fogagnolo, P. Merino, *Tetrahedron* **1990**, *46*, 6167–6184; o) J. M. Hawkins, T. A. Lewis, *J. Org. Chem.* **1992**, *57*, 2114–2121; p) Y. Yamamoto, N. Asao, T. Uyehara, *J. Am. Chem. Soc.* **1992**, *114*, 5427–5429; q) T. Uyehara, N. Shida, Y. Yamamoto, *J. Org. Chem.* **1992**, *57*, 3139–3145; r) A. Dondoni, A. Boscarato, A. Marra, *Synlett* **1993**, 256–258; s) A. Dondoni, A. Boscarato, A. Marra, *Tetrahedron: Asymm.* **1994**, *6*, 2209–2212.

[6] a) D. A. Evans, T. C. Britton, R. L. Dorow, J. F. Dellaria, *J. Am. Chem. Soc.* **1986**, *108*, 6395–6397; b) D. A. Evans, T. C. Britton, *ibid.* **1987**, *109*, 6881–6883; c) C. Gennari, L. Colombo, G. Bertolini, *ibid.* **1986**, *108*, 6394–6395; d) L. A. Trimble, J. C. Vederas, *ibid.* **1986**, *108*, 6397–6399; e) W. Oppolzer, R. Moretti, *Helv. Chim. Acta* **1986**, *69*, 1923–1926; f) M. A. Loreto, L. Pellacani, P. A. Tardella, *Tetrahedron Lett.* **1989**, *30*, 2975–2978; g) D. A. Evans, D. A. Evrard, S. D. Rychnovsky, T. Früh, *ibid.* **1992**, *33*, 1189–1192; h) W. Oppolzer, O. Tamura, J. Deerberg, *Helv. Chim. Acta* **1992**, *75*, 1965–1978.

[7] a) U. Schöllkopf, *Top. Curr. Chem.* **1983**, *109*, 66–84; b) D. Seebach, E. Dziadulewicz, L. Behrendt, S. Cantoreggi, R. Fitzi, *Liebigs Ann. Chem.* **1983**, *109*, 65–84; c) D. Seebach, S. G. Müller, V. Gysel, J. Zimmermann, *Helv. Chim. Acta* **1988**, *71*, 1303–1318; d) R. Fitzi, D. Seebach, *Tetrahedron* **1988**, *44*, 5277–5292; e) S. Ikegami, T. Hayama, T. Katsuki, M. Yamaguchi, *Tetrahedron Lett.* **1986**, *27*, 3403–3406; f) D. A. Evans, A. E. Weber, *J. Am. Chem. Soc.* **1986**, *108*, 6757–6761; g) Y. N. Belokon', A. G. Bulychev, S. V. Vitt, Y. T. Struchkov, A. S. Batsanov, T. V. Timofeeva, V. A. Tsyryapkin, M. G. Ryzhov, L. A. Lysova, V. I. Bakhmutov, V. M. Belikov, *ibid.* **1985**, *107*, 4252–4259; h) J. M. McIntosh, R. K. Leavitt, P. Mishra, K. C. Cassidy, J. E. Drake, R. Chadha, *J. Org. Chem.* **1988**, *53*, 1947–1952; i) M. Tabcheh, A. El Achqar, L. Pappalondo, M. L. Roumestant, P. Viallefont, *Tetrahedron* **1991**, *47*, 4611–4618; j) M. El Hadrami, J. P. Lavergne, P. Viallefont, A. Chiaroni, C. Riche, A. Hasnaoui, *Synth. Commun.* **1993**, *23*, 157–163; k) S. Kanemasa, T. Mori, E. Wada, A. Tatsukawa, *Tetrahedron Lett.* **1993**, *34*, 677–670; l) G. Jommi, G. Miglierini, R. Pogliarin, G. Sello, M. Sisti, *Tetrahedron: Asymmetry* **1992**, *3*, 1131–1134; m) S. Kanemasa, A. Tatsukawa, E. Wada, *J. Org. Chem.* **1991**, *56*, 2875–2883; n) A. Tatsukawa, M. Dan, M. Ohbatake, K. Kawatake, T. Fukata, E. Wada, S. Kanemasa, S. Kakei, *ibid.* **1993**, *58*, 4221–4227.

[8] a) P. J. Sinclair, D. Zhai, J. Reibenspies, R. M. Williams, *J. Am. Chem. Soc.* **1986**, *108*, 1103–1104; b) R. M. Williams, *Aldrichimica Acta* **1992**, *25*, 11–25; c) R. Kober, K. Papadopoulos, W. Miltz, D. Enders, W. Steglich, H. Reuter, H. Puff, *Tetrahedron* **1985**, *41*, 1683–1701; d) P. Ermert, J. Meyer, C. Stucki, J. Schneebeli, J.-P. Obrecht, *Tetrahedron Lett.* **1988**, *29*, 1265–1268; e) K. E. Harding, C. S. Davis, *ibid.* **1988**, *29*, 1891–1894.

[9] For reviews, see: a) R. O. Hutchins, M. K. Hutchins in *Comprehensive Organic Synthesis, Vol. 8* (Eds.: B. M. Trost, I. Fleming), Pergamon, Oxford, **1990**, pp. 25–74; b) R. C. Larock, *Comprehensive Organic Transformations*, VCH, New York, **1989**. See also: c) D. Enders, R. Funk, M. Klatt, G. Raabe, E. R. Hovestreydt, *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 418–421; d) A. Alexakis, N. Lensen, P. Mangeney, *Tetrahedron Lett.* **1993**, *34*, 1171–1172.

[10] For reviews, see: a) R. A. Volkman in *Comprehensive Organic Synthesis, Vol. 1* (Eds.: B. M. Trost, I. Fleming), Pergamon Press, Oxford, **1990**, pp. 355–396; b) E. F. Kleinman, R. A. Volkmann in *Comprehensive Organic Synthesis, Vol. 2* (Eds.: B. M. Trost, I. Fleming), Pergamon Press, Oxford, **1990**, pp. 975–1006.

[11] A. I. Meyers, *Aldrichimica Acta* **1985**, *18*, 59–68.

[12] For a review on formyl anion and cation equivalents, see: A. Dondoni, L. Colombo in *Advances in the Use of Synthons in Organic Chemistry* (Ed.: A. Dondoni), JAI, Greenwich, **1993**.

[13] a) A. Dondoni, G. Fantin, M. Fogagnolo, A. Medici, *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 835; b) A. Dondoni, G. Fantin, M. Fogagnolo, A. Medici, P. Pedrini, *J. Org. Chem.* **1989**, *54*, 693–702; c) A. Dondoni, G. Fantin,

M. Fogagnolo, P. Pedrini, *ibid.* **1990**, *55*, 1439–1446; d) A. Dondoni, J. Orduna, P. Merino, *Synthesis* **1992**, 201–210; e) A. Dondoni, P. Merino, D. Perrone, *Tetrahedron* **1993**, *49*, 2939–2956; f) A. Dondoni, D. Perrone, T. Semola, *Synthesis*, **1995**, 181–186. For overviews on the "thiazole-aldehyde synthesis", see: g) A. Dondoni, *Pure Appl. Chem.* **1990**, *62*, 643–652; h) A. Dondoni in *Modern Synthetic Methods* (Ed.: R. Scheffold), Verlag Helvetica Chimica Acta, Basel, **1992**, pp. 377–437.

[14] For preliminary accounts, see: a) A. Dondoni, F. Junquera, F. L. Merchan, P. Merino, T. Tejero, *Tetrahedron Lett.* **1992**, *33*, 4221–4224; b) A. Dondoni, S. Franco, F. L. Merchan, P. Merino, T. Tejero, *ibid.* **1993**, *34*, 5475–5478.

[15] A. Dondoni, S. Franco, F. L. Merchan, P. Merino, T. Tejero, *Tetrahedron Lett.* **1993**, *34*, 5479–5482.

[16] For reviews see: a) J. J. Tufariello in *1,3-Dipolar Cycloaddition Chemistry, Vol. 2* (Ed.: A. Padwa), Wiley, New York, **1984**, pp. 83–168; b) K. B. G. Torssel, *Nitrile Oxides, Nitrones, and Nitronates in Organic Synthesis*, VCH, New York, **1988**; c) P. DeShong, S. W. Lander Jr., J. M. Leginus, C. M. Dicken in *Advances in Cycloaddition, Vol. 1* (Ed.: D. P. Curran), JAI, Greenwich, **1988**, pp. 87–128; d) P. N. Confalone, E. M. Huie, *Org. React.* **1988**, *36*, 1–173. See also:e) R. Annunziata, M. Cinquini, F. Cozzi, L. Raimondi, *Gazz. Chim. Ital.* **1989**, *119*, 253–269; f) L. Fisera, U. A. R. Al-Timari, P. Ertl, *ACS Symp. Ser.* **1992**, *494*, 158–171; g) P. DeShong, W. Li, J. W. Kennington, H. L. Ammon, *J. Org. Chem.* **1991**, *56*, 1364–1373; h) D. D. Dhavale, C. Trombini, *J. Chem. Soc. Chem. Commun.* **1992**, 1268–1270.

[17] a) Y. Kita, F. Itoh, O. Tamura, Y. Ke, Y. Tamura, *Tetrahedron Lett.* **1987**, *28*, 1431–1434; b) M. P. Cowling, P. R. Jenkins, K. Cooper, *J. Chem. Soc. Chem. Commun.* **1988**, 1503–1504; c) Y. Kita, O. Tamura, F. Itoh, H. Kishino, T. Miki, M. Kohno, Tamura *ibid.* **1988**, 761–763; d) R. Huber, A. Vasella, *Tetrahedron* **1990**, *46*, 33–58; e) Z.-Y. Chang, R. M. Coates, *J. Org. Chem.* **1990**, *55*, 3464–3474 and 3475–3483; f) A. Basha, J. D. Ratjczyk, D. W. Brooks, *Tetrahedron Lett.* **1991**, *32*, 3783–3786; g) F. Manconi, M. G. Piazza, C. Trombini, *J. Org. Chem.* **1991**, *56*, 4246–4252; h) R. Ballini, E. Marcantoni, M. Petrini, *ibid.* **1992**, *57*, 1316–1318; i) S. G. Pyne, A. R. Hajipour, *Tetrahedron* **1992**, *48*, 9385–9590; j) D. D. Dhavale, L. Gentilucci, M. G. Piazza, C. Trombini, *Liebigs Ann. Chem.* **1992**, 1289–1295; k) S.-I. Murahashi, J. Sun, T. Tsuda, *Tetrahedron Lett.* **1993**, *34*, 2645–2648; l) W. G. Hollis, P. L. Smith Jr., D. K. Hood, S. M. Cook, *J. Org. Chem.* **1994**, *59*, 3485–3486

[18] A. Dondoni, S. Franco, F. Junquera, F. L. Merchan, P. Merino, T. Tejero, *Synth. Commun.* **1994**, *24*, 2537–2550.

[19] H. G. Aurich, M. Franzke, H. P. Kesselheim, *Tetrahedron* **1992**, *48*, 663–668.

[20] P. DeShong, C. M. Dicken, R. R. Staib, A. J. Freyer, S. Weinreb, *J. Org. Chem.* **1982**, *47*, 4397–4403.

[21] a) A. Dondoni, G. Fantin, M. Fogagnolo, A. Medici, P. Pedrini, *J. Org. Chem.* **1988**, *43*, 1748–1761; b) A. Dondoni, A. Boscarato, P. Formaglio, J.-P. Bégué, F. Benayoud, *Synthesis* **1995**, 654–658.

[22] Treatment of *N*-benzyl nitrones derived from benzaldehyde and *i*-butyraldehyde with **1a** in ether at room temperature or under reflux failed to give the desired product. Instead unchanged starting material was recovered.

[23] Due to the limited solubility of the nitrone **2** in diethyl ether (about 20 mg mL^{-1}), a mixture of diethyl ether/tetrahydrofuran in a 1:1 ratio was employed as solvent in multigram-scale reactions (more than 2 g of **2**).

[24] A reversed ratio was quoted in our first report (ref. [14a]), owing to the opposite, but incorrect, structural assignment to the major stereoisomer. For a prompt correction, see ref. [14b].

[25] a) P. G. M. Wuts, Y. W. Jung, *J. Org. Chem.* **1988**, *53*, 1957–1965; b) D. D. Dhavale, C. Trombini, *Heterocycles* **1992**, *34*, 2253–2258.

[26] For stereochemical assignements, see the section below.

[27] The reaction of 2-lithiothiazole (**1b**) with esters is well established. See: a) A. Dondoni, D. Perrone, P. Merino, *J. Chem. Soc. Chem. Commun.* **1991**, 1313–1314; b) A. Dondoni, P. Merino, D. Perrone, *ibid.* **1991**, 1576–1578; c) A. Dondoni, D. Perrone, *Synthesis* **1993**, 1162–1176.

[28] For a review, see: K. N. Houk, N. M. Paddon-Row, N. G. Rondan, Y. D. Wu, F. K. Brown, D. C. Spellmeyer, J. T. Metz, Y. Li, R. J. Loncharich, *Science* **1986**, *231*, 1108–1117.

[29] a) I. Fleming, J. J. Lewis, *J. Chem. Soc. Chem. Commun.* **1985**, 149–151; b) I. Fleming, J. H. M. Hill, D. Parker, D. Waterson, *ibid.* **1985**, 318–321; c) G. J. McGarvey, J. M. Wiliams, *J. Am. Chem. Soc.* **1985**, *107*, 1435–1437.

[30] a) M. Cherest, H. Felkin, N. Prudent, *Tetrahedron Lett.* **1968**, 2199–2202; b) H. B. Bürgi, J. D. Dunitz, J. M. Lehn, G. Wipff, *Tetrahedron* **1974**, *30*, 1563–1572; c) N. J. Ahn, O. Eisenstein, *Nouv. J. Chem.* **1977**, *1*, 61–70; d) N. J. Anh, *Top. Curr. Chem.* **1980**, *88*, 145–162; e) Y. D. Wu, N. K. Houk, *J. Am. Chem. Soc.* **1987**, *109*, 908–910. For a recent concise overview of the so-called Cram rule, see: f) H. J. Altenbach in *Organic Synthesis Highlights* (Eds.: J. Mulzer, H. J. Altenbach, M. Braun, K. Krohn, H. U. Reissig), VCH, Weinheim, **1991**, pp. 3–8.

[31] Y. Yamamoto, S. Nishi, K. Maruyama, T. Komatsu, W. Ito, *J. Am. Chem. Soc.* **1986**, *108*, 7778–7786.

[32] M. Nagi, J. J. Gaudino, C. S. Wilcox, *Synthesis* **1992**, 163–168.

[33] Although 2-lithiothiazole (**1b**) is represented for simplicity as a monomer having the metal covalently linked to C-2, recent X-ray crystallographic studies on a lithiated thiazole have shown a dimeric structure with the lithium positioned halfway between C-2 and nitrogen. See: G. Boche, C. Hilf, K. Harms, M. Marsch, M. J. C. W. Lohrenz, *Angew. Chem. Int. Ed.* **1995**, *34*, 487–489.

[34] The same conformation has been assumed to explain the stereoselection of cycloaddition reactions. See also ref. [16g].

[35] This selectivity has been observed in cycloaddition reactions as well. See: M. J. Fray, R. H. Jones, E. J. Thomas, *J. Chem. Soc. Perkin Trans 1* **1985**, 2753–2761.

[36] a) B. M. Trost, J. Lynch, P. Renaut, D. H. Steinman, *J. Am. Chem. Soc.* **1986**, *108*, 284–291; b) Y. Yamamoto, S. Nishi, T. Ibuka, *J. Chem. Soc. Chem. Commun.* **1987**, 464–466 and 1572–1573.

[37] The NMR experiments were performed at 300 MHz. The complexing agent was added through a syringe to a septum-sealed 5-mm NMR tube containing a solution of **2** (0.05 mmol) in 0.8 mL of $CDCl_3$. The sample was quickly inserted into the NMR probe, and spectra were recorded at different temperatures (from −40 to 20 °C). Identical spectra were obtained in CD_2Cl_2 from −80 °C to 20 °C. Also, the addition of diethyl ether as a cosolvent (up to 1:1 v/v) did not cause substantial changes in the ^{13}C NMR spectra.

[38] A similar situation has been recently described for the complexation between α,β-dialkoxy esters and Et_2AlCl. See: S. Castellino, D. E. Volk, *Tetrahedron Lett.* **1993**, *34*, 967–970.

[39] S.-I. Murahashi, H. Mitsui, T. Shiota, T. Tsuda, S. Watanabe, *J. Org. Chem.* **1990**, *55*, 1736–1744.

[40] S.-I. Murahashi, T. Tsuda, *Tetrahedron Lett.* **1993**, *34*, 2645–2648.

[41] S.-I. Murahashi, Y. Kodera, *Tetrahedron Lett.* **1985**, *26*, 4633–4636.

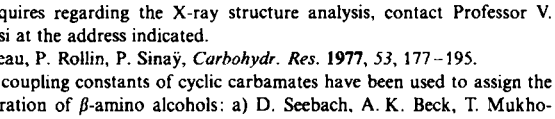
[42] L. S. Liebeskind, M. E. Welker, R. W. Fengl, *J. Am. Chem. Soc.* **1986**, *108*, 6328–6343.

[43] M. A. Schwartz, J. Gu, X. Hu, *Tetrahedron Lett.* **1992**, *33*, 1687–1690.

[44] The application of the same $TiCl_3$-based methodology to *N*-benzyl hydroxylamines bearing a 2-furyl group afforded benzaldimines, which were hydrolyzed to amines on treatment with wet silica gel. In no instances was the formation of the isomeric ketimine observed, arising from the removal of the proton α to the furyl group (A. Dondoni, F. Junquera, F. L. Merchan, P. Merino, T. Tejero, *Synthesis* **1994**, 1450–1456). Whether the same reaction pathway is also operative for reaction with 2-thiazolyl-substituted hydroxylamines is a subject under investigation in our laboratories.

[45] A. Dondoni, A. Marra, D. Perrone, *J. Org. Chem.* **1993**, *58*, 275–277.

[46] It is worth pointing out here that the stability of the thiazole ring under various reaction conditions provides another substantial advantage, which amply justifies the use of this heterocycle as a masked formyl group in this methodology. In contrast, the use of the 1,3-dithiane ring appeared to be quite problematical. For instance, we have been unable to convert the *N*-benzylhydroxylamine shown below to amine under the conditions employed for the thiazole analogue.



[47] For enquires regarding the X-ray structure analysis, contact Professor V. Bertolasi at the address indicated.

[48] J. M. Beau, P. Rollin, P. Sinaÿ, *Carbohydr. Res.* **1977**, *53*, 177–195.

[49] Vicinal coupling constants of cyclic carbamates have been used to assign the configuration of β-amino alcohols: a) D. Seebach, A. K. Beck, T. Mukhopadhlyay, E. Thomas, *Helv. Chim Acta* **1982**, *65*, 1101–1133; b) D. J. Kempf, T. J. Sowin, E. M. Doherty, S. M. Hannick, L. Covadoci, R. F. Henry, B. E. Green, S. G. Spanton, D. W. Norbeck, *J. Org. Chem.* **1992**, *55*, 5692–5700.

[50] Normally for 5-(2-thiazolyl)-4-substituted-1,3-oxazolidin-2-ones $J_{trans} < 5.0$ Hz and $J_{cis} > 8.0$ Hz; see ref. [13c].

[51] For a review on the synthesis and reactivity of Neu5Ac, see: M. P. DeNinno, *Synthesis* **1991**, 583–593.

[52] *Sialic Acids. Chemistry, Metabolism, and Function* in *Cell Biology Monographs, Vol. 10* (Ed.: R. Schauer) Springer, Wien, New York, **1982**.

[53] R. Csuk, M. Hugener, A. Vasella, *Helv. Chim. Acta* **1988**, *71*, 609–618.

[54] U. Kragl, D. Gygax, O. Ghisalba, C. Wandrey, *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 827–828.

[55] J. Kim, W. J. Hennen, H. M. Sweers, C.-H. Wong, *J. Am. Chem. Soc.* **1988**, *110*, 6481–6486.

[56] J. C. Sowden, M. L. Oftedahl, *J. Am. Chem. Soc.* **1960**, *82*, 2303–2304.

[57] A. Vasella, R. Voeffray, *Helv. Chim. Acta* **1982**, *65*, 1134–1144.

[58] a) H. Ida, N. Yamazaki, C. Kibayashi, *J. Org. Chem.* **1987**, *52*, 3337–3342; b) Y. Tsuda, Y. Okuno, K. Kanemitsu, *Heterocycles* **1988**, *27*, 63–66; c) N. Chida, Y. Furuno, Y. Ogawa, *J. Chem. Soc. Chem. Commun.* **1989**, 1230–1231; d) B. Rajanikanth, R. Seshadri, *Tetrahedron Lett.* **1989**, *30*, 755–758.

[59] S. Hanessian, T. J. Liak, B. Vanasse, *Synthesis* **1981**, 396–397.

[60] a) S. Kondo, K. Inuma, H. Naganawa, H. Shimura, Y. Sekizawa, *J. Antibiot.* **1975**, *28*, 79–82; b) H. Shimura, Y. Sekizawa, K. Inuma, H. Naganawa, S. Kondo, *Agric. Biol. Chem.* **1976**, *40*, 611–618.

[61] N. Neuss, K. F. Koch, B. B. Molloy, W. Day, L. L. Huckstep, D. E. Dorman, J. D. Roberts, *Helv. Chim. Acta* **1970**, *53*, 2314–2319.

[62] R. E. Hornish, R. E. Gosline, J. M. Nappier, *Drug Metab. Rev.* **1987**, *18*, 177–214.
[63] H. Hashimoto, K. Asanu, F. Fuji, J. Yoshimura, *Carbohydr. Res.* **1982**, *104*, 87–104.
[64] a) A. Golebiowski, J. Jurczak, *J. Chem. Soc. Chem. Commun.* **1989**, 263–264; b) A. Golebiowski, J. Kozak, J. Jurczak, *J. Org. Chem.* **1991**, *56*, 7344–7347.
[65] For a review, see: A. Golebiowski, J. Jurczak, *Total Synthesis of Lyncomycin and Related Chemistry* in *Recent Progress in the Chemical Synthesis of Antibiotics* (Eds.: G. Lukacs, M. Ohno), Springer, Berlin–Heidelberg, **1990**, pp 366–385.
[66] B. Szechner, *Tetrahedron* **1981**, *37*, 949–952.
[67] a) E. Larson, S. J. Danishefsky, *J. Am. Chem. Soc.* **1983**, *105*, 6715–6716; b) S. J. Danishefsky, E. Larson, J. P. Springer, *ibid.* **1985**, *107*, 1274–1280.
[68] a) H. Saeki, E. Ohki, *Chem. Pharm. Bull.* **1970**, *18*, 789–802; b) T. Atsumi, T. Fukumaru, T. Ogawa, M. Matsui, *Agric. Biol. Chem.* **1973**, *37*, 2621–2626; c) R. V. Stick, D. M. G. Tilbrook, *Aust. J. Chem.* **1990**, *43*, 1643–1655; d) L. M. Engelhardt, B. W. Skelton, R. V. Stick, D. M. G. Tilbrook, A. H. White, *ibid.* **1990**, *43*, 1657–1680.
[69] For a preliminary report on this work, see: A. Dondoni, S. Franco, F. L. Merchan, P. Merino, T. Tejero, *Synlett* **1993**, 78–80.
[70] D. F. Shriver, M. A. Drezdzon, *The manipulation of Air-Sensitive Compounds*; 2nd ed., Wiley-Interscience, New York, **1986**.
[71] D. D. Perrin, W. L. F. Armarego, *Purification of Laboratory Chemicals*; 3rd ed., Pergamon, Oxford, **1988**.
[72] For a cautionary note on the preparation of 2-lithiothiazole (**1b**) from 2-bromothiazole in situ, see: A. Dondoni, M.-C. Scherrmann, *J. Org. Chem.* **1994**, *59*, 6404–6412 (ref. [16]).
[73] S. Roseman, J. Ludowieg, *J. Am. Chem. Soc.* **1954**, *76*, 301–302.
[74] C. T. Spivak, S. Roseman, *J. Am. Chem. Soc.* **1959**, *81*, 2403–2404.
[75] H. Kayakiri, T. Oku, M. Hashimoto, *Chem. Pharm. Bull.* **1991**, *39*, 1397–1401.
[76] M. C. Burla, M. Camalli, G. Cascarano, C. Giacovazzo, G. Polidori, R. Spagna and D. Viterbo, *J. Appl. Crystallogr.* **1989**, *22*, 389–391.
[77] MolEN, Enraf-Nonius, Delft, The Netherlands, **1990**.
[78] G. M. Sheldrick, SHELXS86. Program for the Solution of Crystal Structures, Univ. of Göttingen, Germany, **1985**.
[79] G. M. Sheldrick, SHELX93. Program for the Crystal Structure Refinement, Univ. of Göttingen, Germany, **1993**.

0947-6539/95/0108-0520 $ 30.00+.25/0