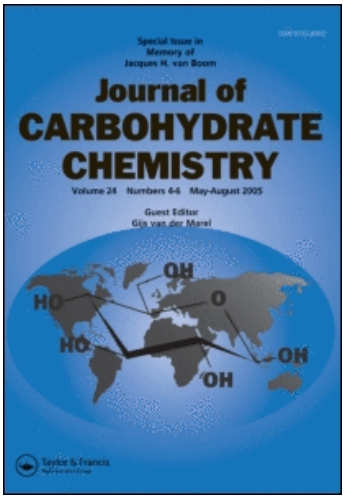

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O-ACETYL PROTECTION OF 6-AMINOALDOPYRANOSIDES AND 1-AMINOALDITOLS

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ABSTRACT

Methyl 6-amino-6-deoxy-α-D-glycopyranosides having the D-*gluco*, D-*manno* and D-*galacto* configurations (**1a-3a**), 2-aminoethanol (**4a**), 1-amino-1-deoxy-D-glucitol (**5a**), and 1-amino-1-deoxy-4-*O*-ß-D-glucopyranosyl-D-glucitol (**6a**) were transformed into the corresponding per-*O*-acetyl amine hydrochlorides **1d-6d** in excellent yields by using the 2,2-(diethoxycarbonyl)vinyl group for temporary amine protection. Deprotection of the peracetylated enamines **1c-6c** was effected with chlorine in chloroform and no O→N acetyl migration occurred when short reaction times were used. Treatment of **1d-6d** with thiophosgene resulted in the formation of peracetyl isothiocyanates (**1e-6e**).

INTRODUCTION

O-Protected amino sugars and sugar isothiocyanates have proved to be the best carbohydrate synthons for condensation reactions with suitable haptens in the synthesis of *N*-linked glycoconjugate analogues.[1] The acetyl group has been universally employed for hydroxyl protection whenever possible, as the reagents are inexpensive, provide high yields and easy manipulation, and the group can be selectively removed under mild conditions.

In the framework of a program concerning *neo-N*-glycoconjugate synthesis, we have been interested in the preparation of per-*O*-acetyl derivatives of hexopyranosides

and alditols bearing a reactive amino group at a primary carbon atom. The former have been claimed as convenient synthons for the preparation of amide pseudo cord factors,[2] and sugar-peptide conjugates in which an amino acid residue is *N*-linked to a primary carbon atom of the carbohydrate portion have been recently found in nature.[3] In addition, *O*-protected 1-amino-1-deoxy alditols have been proposed as flexible spacers for the solid-phase synthesis of *neo*-*N*-glycopeptides.[4]

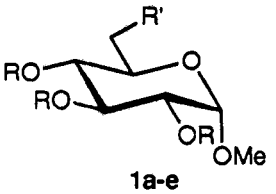
The synthesis of *O*-acetyl glycosylamines and amino sugars bearing the amino group on a secondary carbon atom is currently achieved by direct reduction of the corresponding azides or by using a variety of temporary *N*-protecting groups which generally involve the formation of carbamate derivatives.[1b,5] In contrast, attempts to prepare per-*O*-acetyl derivatives of 6-amino-6-deoxy aldopyranosides or amino alditols using these methodologies have been reported to be unsuccessful as a result of acetyl migration to the more basic primary amino group.[2,4a]

We have previously shown[5d,6] that sugar enamines can be subjected to halogenolysis, following the procedure of Gómez-Sánchez et al.,[7] to give the corresponding amino sugar hydrochlorides in high yield. The method is compatible with the *O*-acetyl protection of the hydroxyl groups in both glycosylamine and 2-amino-2-deoxy sugar derivatives. We have now examined the application of this strategy to the title compounds and report on the preparation of the corresponding per-*O*-acetyl amine hydrochlorides. The transformation of the latter into peracetyl isothiocyanates has also been effected.

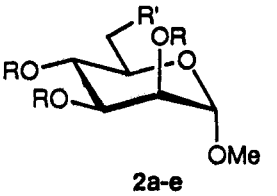
RESULTS AND DISCUSSION

To have complete insight into the scope of the enamine strategy for the preparation of per-*O*-acetyl aminoaldose derivatives, the methyl 6-amino-6-deoxy-α-D-hexopyranosides **1a-3a**, having respectively the D-*gluco*,[8] D-*manno*,[9] and D-*galacto*[10] configuration, have been considered in our study. The primary amines were obtained from the corresponding commercial-grade methyl glycopyranosides through an efficient, three-step synthetic scheme involving direct replacement of the primary hydroxyl group by iodine, nucleophilic displacement by sodium azide, and Staudinger reduction of the 6-azido-6-deoxy derivatives with triphenylphosphine (60-80% overall yields).[11] For

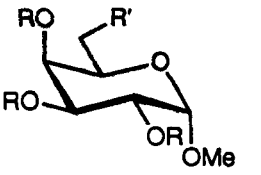
temporary *N*-protection, the amines **1a-3a** were treated with diethyl ethoxymethylenemalonate in methanol. Although the resulting 6-deoxy-6-(2',2'-diethoxycarbonylvinyl)amino glycopyranosides **1b-3b** could be obtained in pure form (65-70% yield) after chromatographic purification, it was generally advantageous to perform the *O*-acetylation step on the crude reaction mixture. Flash chromatography then provided overall yields higher than 80% for the **1a-3a**→**1c-3c** transformations.



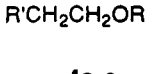
1a-e



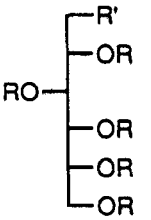
2a-e



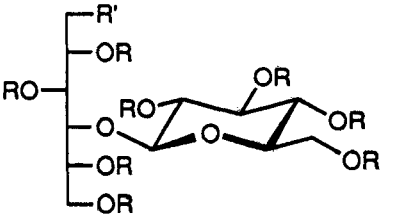
3a-e



4a-e

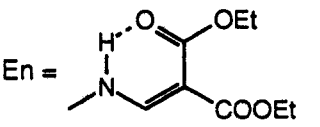


5a-e



6a-e

a R = H, R' = NH_2
b R = H, R' = En
c R = Ac, R' = En
d R = Ac, R' = NH_2·HCl
e R = Ac, R' = NCS



In previous work,[6] deprotection of sugar enamines was effected by treatment with chlorine in humid chloroform for several hours to ensure complete hydrolysis. In the case of the 6-enamino derivatives **1c-3c** control of the reaction time was however crucial. After 1 h reaction time total consumption of the starting material was observed (TLC), and work-up of the reaction mixtures provided virtually quantitative yields of the target tri-*O*-acetyl amine hydrochlorides **1d-3d**. Higher reaction times (>3 h) resulted in complex mixtures which likely contained *N*-acetyl derivatives and further trans-*O*-acetylation products, as seen from ^{13}C NMR. These side-reactions were particularly

evident for the D-*galacto* derivative **3d**, probably due to a faster acetyl transfer from the axial O-4 to the nitrogen atom as compared with the O-4 equatorial isomers **1d** and **2d**. Nevertheless, all salts were stable as solids and could be stored at 5 °C for several weeks without any appreciable decomposition.

Treatment of **1d-3d** with thiophosgene, using a 1:3 amine hydrochloride-thiophosgene molar ratio,[12] resulted in fast conversions (85-90% yield) into the corresponding peracetyl 6-deoxy-6-isothiocyanato aldopyranosides **1e-3e**. Compounds **1e-3e** had been previously obtained by conventional acetylation of the respective fully unprotected isothiocyanates,[11] and this was an additional confirmation for the proposed structures.

Our next interest was to examine this synthetic methodology in the case of aminomethyl polyols, from which ethanolamine (**4a**) is the simplest representative. Acetyl migration from the ß-located acetoxy group to the more basic amino group through a five-membered cyclic intermediate should now be a very favoured process. Nevertheless, application of the above commented reaction sequence starting from **4a** afforded 2-aminoethyl acetate hydrochloride (**4d**) in good yield, via the corresponding enamine derivatives **4b** and **4c**. Definitive confirmation for the validity of this approach was obtained by performing this same reaction on 1-amino-1-deoxy-D-glucitol (glucamine, **5a**) and on its 4-*O*-ß-D-glucopyranosyl derivative (**6a**). Reaction with diethyl ethoxymethylenemalonate (→**5b**, **6b**), acetylation (→**5c**, **6c**), and deprotection with chlorine gave the per-*O*-acetyl amino polyol hydrochlorides **5d** and **6d** in 65% overall yield. No formation of *N*-acetyl derivatives was detected provided the reaction times were kept to about 1 h.

Compounds **4d-6d** reacted with a three-fold excess of thiophosgene to give the corresponding peracetyl isothiocyanates **4e-6e** in ~80% yield. To our best knowledge, these are the first examples of alditol isothiocyanate derivatives. It must be noted that ß-acetoxy isothiocyanates cannot be obtained by acetylation of the corresponding unprotected derivatives, as ß-hydroxy isothiocyanates are unstable.[11,13] The thiophosgene reaction additionally confirms the presence of the nonacetylated amino group in **4d-6d**.

The proposed structures for all new compounds were supported by both analytical and spectroscopic data (Tables 1-4 and Experimental).

Table 1. ^{1}H NMR Spectral Data (300 MHz) for Methyl Aldopyranoside Derivatives 1b-3b and 1c-3c.

Comp.	H-1	H-2	H-3	H-4	H-5	H-6a	H-6b
1b[a]	4.69d	3.39dd	3.60t	3.15t	3.59ddd	3.74dd	3.50dd
2b[a]	4.64d	3.78dd	<-3.53-3.51m->		3.64m	3.76m	3.47m
3b[a]	4.72d	3.78dd	3.71dd	<-3.85-3.81m->		3.62dd	3.54dd
1c[b]	4.95d	4.83dd	5.50t	4.87t	3.83ddd	<----3.40bs----->	
2c[b]	4.71d	5.20dd	5.36dd	5.14t	3.80ddd	<----3.41bs----->	
3c[b]	5.01d	5.15dd	5.33dd	5.42dd	4.04ddd	<-3.48-3.33m-->	
	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6a}$	$J_{5,6b}$	$J_{6a,6b}$
1b	3.7	9.6	9.6	9.6	2.3	6.7	13.5
2b	1.6	3.3	---	---	---	---	---
3b	3.5	10.0	3.1	0	8.6	4.2	13.8
1c	3.5	10.0	10.0	10.0	5.0	4.1	---
2c	1.7	3.4	10.0	10.0	4.5	3.6	---
3c	3.6	10.8	3.3	1.0	4.0	8.1	---

a. In CD_3OD.
b. In $CDCl_3$.

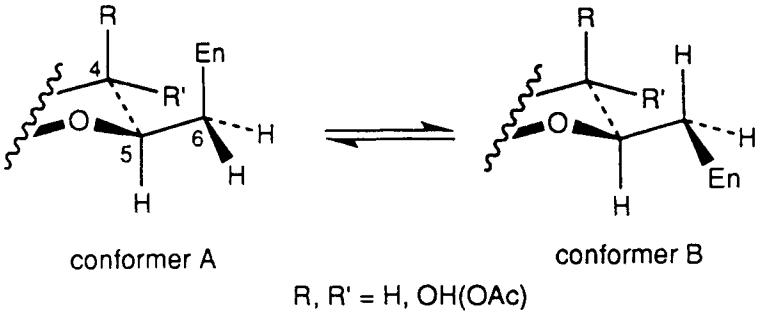


Figure 1. Conformational equilibrium about the C-5–C-6 linkage for compounds 1b-3b and 1c-3c.

Table 2. ^{13}C NMR Spectral Data (δ values) for Methyl Aldopyranoside Derivatives 1b-3b, 1c-3c and 1d-3d.

Comp.	C-1	C-2	C-3	C-4	C-5	C-6
1b[a,c]	101.4	73.4	74.9	72.6	71.9	51.2
2b[a,c]	103.7	72.4	73.0	69.6	71.9	51.5
3b[a,c]	101.5	71.3	70.9	71.4	70.0	51.5
1c[b,c]	95.5	69.7	70.6	69.3	67.8	49.5
2c[b,c]	98.1	69.1	69.1	67.1	68.3	49.3
3c[b,c]	96.9	67.8	67.7	68.8	67.3	49.4
1d[b,d]	96.4	69.7	70.0	69.0	65.1	39.8
2d[b,c]	98.4	68.1	69.0	65.6	66.4	40.6
3d[b,c]	97.0	67.5	67.1	68.4	64.8	39.4

a. In CD_3OD.
b. In $CDCl_3$.
c. At 75.5 MHz.
d. At 125.7 MHz.

The $^3J_{H,H}$ values for methyl aldopyranoside enamino derivatives **1b-3b** and **1c-3c** (Table 1) around the pyranose ring indicated that it adopts the expected $^4C_1$(D) conformation in all cases. The coupling constant values between H-5 and the methylene protons supported a conformational equilibrium between the staggered rotamers A and B in the case of D-*gluco* (**1**) and D-*manno* (**2**) derivatives, whereas conformation B, with C-4 and the bulky enamino group in *trans* relative disposition, was almost the only form present in the case of D-galacto derivatives (**3**) (Figure 1). Both conformations A and B avoid 1,3-parallel arrangements between the substituent at C-4 and the enamino group.

The absence of such unfavourable 1,3-parallel interactions also governs the conformational equilibrium of the peracetylated D-glucitol derivatives **5c,e** and **6c,e** in $CDCl_3$ solutions. In agreement with reported results for related compounds,[14] the J values (Table 3) supported a conformational equilibrium between the $_2G^-$ and the $_3G^+$,$_4G^+$ conformations for the backbone chain (Figure 2).

Table 3. ^{1}H NMR Spectral Data ($CDCl_3$) for Alditol Derivatives 5c, 6c, 5e and 6e.

Comp.	H-1a	H-1b	H-2	H-3	H-4	H-5	H-6a	H-6b
5c[a]	3.56 dt	3.44 dt	5.07 dt	5.32 dd	5.36 dd	5.01 ddd	4.23 dd	4.12 dd
6c[a,c] unit g	3.57 ddd	3.52 dt	5.28 td	5.26 d	4.05 t	5.07 ddd	4.40 dd	4.00 dd
unit a	4.36 d	---	4.97 dd	5.17 t	5.07 t	3.70 ddd	4.20 m	4.20 m
5e[a]	3.80 dd	3.77 dd	5.06 dt	5.44 dd	5.32 dd	5.01 ddd	4.23 dd	4.12 dd
6e[b,c] unit g	3.91 dd	3.84 dd	5.32 dt	5.42 dd	4.07 dd	5.12 m	4.53 dd	4.04 dd
unit a	4.70 d	---	4.49 dd	5.21 t	5.08 t	3.73 ddd	4.26 dd	4.19 dd

	$J_{1a,1b}$	$J_{1a,2}$	$J_{1b,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6a}$	$J_{5,6b}$	$J_{6a,6b}$
5c	14.2	5.3	7.1	5.3	4.2	6.5	3.5	5.0	12.5
6c unit g	14.3	5.9	6.3	6.3	4.4	4.9	3.2	6.2	12.3
unit a	---	7.9	---	8.9	8.9	8.9	3.3	7.3	---
5e	15.1	4.5	4.5	6.8	3.5	7.7	3.2	4.7	12.5
6e unit g	15.3	4.5	4.5	7.4	3.4	6.1	3.1	5.6	12.4
unit a	---	7.9	---	9.5	9.5	9.5	2.6	5.1	12.4

a. At 500 MHz.
b. At 300 MHz.
c. Unit g and unit a refer to the glucitol and glucopyranosyl subunits, respectively.

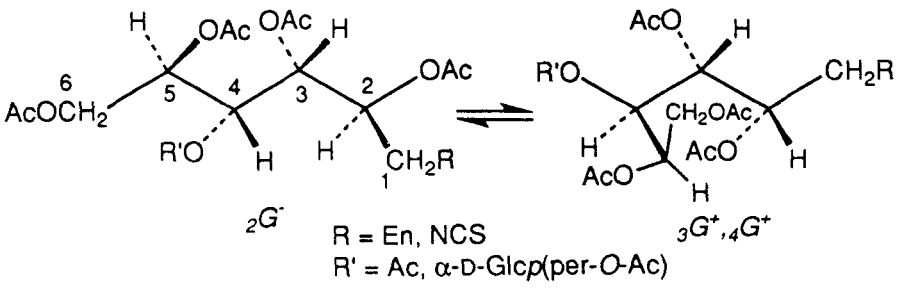


Figure 2. Conformational equilibrium for compounds 5c,e and 6c,e.

Table 4. ^{13}C NMR Spectral Data (δ values) for Alditol Derivatives 5b-e and 6b-e.

Comp.	C-1	C-2	C-3	C-4	C-5	C-6
5b[a,d]	52.0	71.9	70.1	71.4	71.2	63.4
6b[a,e,f] unit g	51.7	71.1[g]	69.8	80.2	70.3	62.0
unit a	103.2	73.8	77.1[h]	70.9[g]	76.6[h]	61.2
5c[b,e]	48.9	70.2	68.7	68.4	67.8	61.0
6c[b,e] unit g	49.2	69.9	69.6	75.8	69.9	61.2
unit a	100.7	71.1	72.4	67.9	72.1	61.6
5d[c,e]	39.3	68.7	68.1	68.4	68.4	61.2
6d[b,e] unit g	55.2	70.4	68.1	75.6	69.5	62.9
unit a	100.3	71.3	72.6	67.8	71.8	62.9
5e[b,d]	45.1	69.1	68.1	68.2	68.2	61.1
6e[b,d] unit g	45.2	69.3	69.6	75.1	68.5	61.2
unit a	100.4	71.2	72.4	67.9	72.1	61.5

a. In Me_2SO-d_6.
b. In $CDCl_3$.
c. In D_2O
d. At 75.5 MHz.
e. At 125.7 MHz.
f. Unit g and unit a refer to the glucitol and glucopyranosyl subunits, respectively.
g, h. Assignments may be reversed.

The relative proportions between both conformers changed significantly from the enamino (**5c**, **6c**) to the isothiocyanato (**5e**, **6e**) derivatives. Thus, the $J_{2,3}$ and $J_{4,5}$ values for **5e** and **6e** (6.1-7.7 Hz) agreed with quasi-*trans* relationships for the respective protons, indicating a high contribution of the $_2G^-$ conformer. In the case of **5c** and **6c**, the corresponding J values (5.3-6.5 Hz) were indicative of a higher contribution of the $_3G^+$,$_4G^+$ sickle conformer. This difference on the conformational properties must obviously be related to the bulkiness of the 2,2-diethoxycarbonylvinylaminomethyl group. The existence of a *gauche* arrangement between the CH_2R group and C-4 probably unstabilizes the $_2G^-$ conformation in the case of **5c** and **6c** (Figure 2).

It is also noteworthy that the presence of the ß-D-glucopyranosyl substituent at C-4 in **6c,e** results in lower $J_{4,5}$ values as compared to **5c,e**. A deviation from the above

discussed staggered conformations through rotation about C-4–C-5, in order to avoid the gauche interaction between the glucopyranosyl and acetoxymethyl groups, probably explains this result.

EXPERIMENTAL

General Methods. Concentrations were performed at <40 °C (bath). Melting points were determined with a Gallenkamp MFB 595 apparatus and are uncorrected. Optical rotations were measured with a Perkin-Elmer 141 MC polarimeter using 1 cm cells. UV spectra were recorded with a Philips PU 8710 spectrophotometer. Infrared spectra were recorded on a Bomem Michelson MB-120 FTIR spectrophotometer. ^{1}H NMR (300 and 500 MHz) and ^{13}C NMR spectra (75.5 and 125.7 MHz) were obtained on Bruker 300 AMX and 500 AMX spectrometers. Tetramethylsilane (Me_4Si) was used as internal ($CDCl_3$ or Me_2SO-d_6) or external reference (D_2O). The spectra are reported as chemical shifts downfield from Me_4Si. Assigments of ^{1}H signals were confirmed by 2D COSY, decoupling, and H/D exchange experiments. 2D HETCOR experiments were carried out to assign on ^{13}C signals. Mass spectra were taken on a Kratos MS-80 RFA instrument. In the EI mode, opperating conditions were: ionizing energy 35 eV, ionizing current 100 μA, accelerating voltage 4 kV, resolution 1000 (10% valley definition). In the CI mode, isobutane (0.8 bar) was used as ionizing agent, with ionizing energy 150 eV and ionizing current 500 μA. In the FAB mode, the primary beam consisted of xenon atoms with a maximum energy of 8 keV. The samples were dissolved in thioglycerol (*unprotected* derivatives) or *m*-nitrobenzyl alcohol (per-*O*-acetates), and the positive ions were separated and accelerated over a potential of 7 kV. NaI was added as cationizing agent. TLC was performed on silica gel 30 F_{254} (Merck) plates with visualization by UV light or/and by charring with 10% sulphuric acid, and column chromatography was carried out with silica gel 60 (Merck, 70-230 mesh).

Preparation of Methyl 6-Deoxy-6-(2',2'-diethoxycarbonylvinyl)amino-α-D-glycopyranosides (1b-3b). To a solution of methyl 6-amino-6-deoxy-α-D-glycopyranosides (**1a-3a**, 1 g, 5.4 mmol) in dry MeOH (20 mL), diethyl ethoxymethylenemalonate (1.65 mL, 8.2 mmol) was added. The mixture was stirred at 40 °C for 12 h, and concentrated. Column chromatography (EtOAc-EtOH-H_2O 45:5:3) of the resulting syrupy residue yielded pure **1b-3b** as white foams.

Methyl 6-Deoxy-6-(2',2'-diethoxycarbonylvinyl)amino-α-D-glucopyranoside (**1b**, 1.38 g, 70%) had $[\alpha]_D^{22}$ +72.2° (*c* 1.1, MeOH); UV (MeOH) 279 and 223 nm (ϵ_{mM} 22.0 and 13.6); IR 3383 (OH), 1715 (C=O free), 1655 (C=O chelated), 1630 (C=C and NH), and 1233 cm^{-1} (C-O-C); ^1H NMR (300 MHz, CD_3OD) Table 1 and δ 8.11 (s, 1H, =CH), 4.20, 4.14 (2q, each 2H, $^3J_{H,H}$ = 7.1 Hz, CH_2CH_3), 3.35 (s, 3H, OCH_3), 1.28 and 1.27 (2t, each 3H, $2CH_2CH_3$); ^{13}C NMR (75.5 MHz, CD_3OD) Table 2 and δ 169.2 (C=O chelated), 168.2 (C=O free), 161.9 (=CH), 90.0 (=C), 60.8, 60.7 ($2CH_2$), 55.6 (OCH_3), 14.5 and 14.4 ($2CH_3$).

Anal. Calcd for $C_{15}H_{25}NO_9$: C, 49.58; H, 6.93; N, 3.85. Found: C, 49.50; H, 7.04; N, 3.79.

A FABMS spectrum showed a pseudomolecular $[M+Na]^+$ ion at *m/z* 386.

Methyl 6-Deoxy-6-(2',2'-diethoxycarbonylvinyl)amino-α-D-mannopyranoside (**2b**, 1.4 g, 70%) had $[\alpha]_D^{22}$ +43.8° (*c* 0.9, MeOH); UV (MeOH) 279 and 223 nm (ϵ_{mM} 16.4 and 9.8); IR 3389 (OH), 1715 (C=O free), 1659 (C=O chelated), 1632 (C=C and NH), and 1229 cm^{-1} (C-O-C); ^1H NMR (300 MHz, CD_3OD) Table 1 and δ 8.13 (s, 1H, =CH), 4.19, 4.14 (2q, each 2H, $^3J_{H,H}$ = 7.1 Hz, CH_2CH_3), 3.31 (s, 3H, OCH_3), 1.27 and 1.26 (2t, each 3H, $2CH_2CH_3$); ^{13}C NMR (75.5 MHz, CD_3OD) Table 2 and δ 169.8 (C=O chelated), 168.3 (C=O free), 161.9 (=CH), 89.9 (=C), 60.7, 60.6 ($2CH_2$), 55.2 (OCH_3), and 14.8 ($2CH_3$).

Anal. Found: C, 49.41; H, 6.75; N, 3.85.

A FABMS spectrum showed a pseudomolecular $[M+Na]^+$ ion at *m/z* 386.

Methyl 6-Amino-6-deoxy-*N*-(2,2-diethoxycarbonylvinyl)-α-D-galactopyranoside (**3b**, 1.0 g, 65%) had $[\alpha]_D^{22}$ +101.5° (*c* 1.1, MeOH); UV (MeOH) 279 and 223 nm (ϵ_{mM} 20.9 and 14.7); IR 3437 (OH), 1715 (C=O free), 1659 (C=O chelated), 1630 (C=C and NH), and 1225 cm^{-1} (C-O-C); ^1H NMR (300 MHz, CD_3OD) Table 1 and δ 8.10 (s, 1H, =CH), 4.18, 4.13 (2q, each 2H, $^3J_{H,H}$ = 7.1 Hz, CH_2CH_3), 3.32 (s, 3H, OCH_3), 1.27 and 1.26 (2t, each 3H, $2CH_2CH_3$); ^{13}C NMR (75.5 MHz, CD_3OD) Table 2 and δ 169.9 (C=O chelated), 168.2 (C=O free), 161.8 (=CH), 89.9 (=C), 60.7, 60.6 ($2CH_2$), 55.6 (OCH_3), and 14.8 ($2CH_3$).

Anal. Found: C, 49.48; H, 6.79; N, 3.91.

A FABMS spectrum showed a pseudomolecular $[M+Na]^+$ ion at *m/z* 386.

Diethyl (2-Hydroxyethyl)aminomethylenemalonate (4b). Reaction of 2-aminoethanol (**4a**, 0.15 mL, 2.58 mmol) with diethyl ethoxymethylenemalonate (0.23 mL, 3.87 mmol), following the protocol above described for the preparation of 6-deoxy-6-enaminoaldopyranosides, and column chromatography (EtOAc-light petroleum ether 3:2) of the residue yielded **4b** (0.83 g, 93%) as an oil; UV (CH_2Cl_2) 281 and 227 nm (ϵ_{mM} 7.0 and 4.2); IR 3441 (OH), 1676 (C=O free), 1630 (C=O chelated), 1597 (C=C and NH), and 1217 cm^{-1} (C-O-C); ^1H NMR (500 MHz, $CDCl_3$): δ 9.29 (dd, 1H, $J_{NH,=CH}$ = 14.2 Hz, $J_{CH_2,NH}$ = 5.6 Hz, NH), 8.00 (s, 1H, =CH), 4.22, 4.15 (2q, each 2H, $^3J_{H,H}$ = 7.1 Hz, CH_2CH_3), 3.77 (bs, 2H, CH_2OH), 3.47 (q, 2H, $^3J_{H,H}$ = 5.6 Hz, CH_2NH), 2.94 (bs, 1H, OH), 1.32 and 1.27 (2t, each 3H, $2CH_3$); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 169.1 (C=O chelated), 166.1 (C=O free), 160.4 (=CH), 89.6 (=C), 59.7, 59.5 ($2CH_2$), and 14.2 ($2CH_3$). EIMS, *m/z* 231 (38% M^+).

Anal. Calcd for $C_{10}H_{17}NO_5$: C, 51.94; H, 7.41; N, 6.05. Found: C, 51.94; H, 7.51; N, 6.04.

1-Deoxy-1-(2',2'-diethoxycarbonylvinyl)amino-D-glucitol (5b). Reaction of 1-amino-1-deoxy-D-glucitol (**5a**, 0.71 g, 3.9 mmol) with diethyl ethoxymethylenemalonate (0.35 mL, 5.85 mmol), following the protocol above described, and column chromatography (EtOAc-EtOH-H_2O 45:5:3) of the residue yielded **5b** (1.06 g, 77%); mp 131-133 °C (from EtOH); $[\alpha]_D^{22}$ -26.3° (*c* 0.9, Me_2SO); UV (Me_2SO) 281 nm (ϵ_{mM} 14.6); IR 3412 (OH), 1680 (C=O free), 1657 (C=O chelated), 1605 (C=C and NH), and 1269 cm^{-1} (C-O-C); ^1H NMR (300 MHz, Me_2SO-d_6) δ 9.17 (dt, 1H, $J_{NH,=CH}$ = 14.0 Hz, $J_{1a,NH}$ = $J_{1b,NH}$ = 6.0 Hz, NH), 7.96 (d, 1H, =CH), 4.99-4.32 (5 OH), 3.65-3.25 (m, 8H, H-1a to H-6b), 4.08, 4.02 (2q, each 2H, $^3J_{H,H}$ = 7.1 Hz, CH_2CH_3), 1.19 and 1.17 (2t, each 3H, $2CH_3$); ^{13}C NMR (75.5 MHz, Me_2SO-d_6) Table 4 and δ 167.9 (C=O chelated), 165.3 (C=O free), 160.3 (=CH), 87.9 (=C), 58.8, 58.7 ($2CH_2$), 14.5 and 14.4(2C) ($2CH_3$).

Anal. Calcd for $C_{14}H_{25}NO_9$: C, 47.81; H, 7.16; N, 3.98. Found: C, 48.07; H, 7.04; N, 3.70.

A FABMS spectrum showed a pseudomolecular $[M+Na]^+$ ion at *m/z* 374.

1-Deoxy-1-(2',2'-diethoxycarbonylvinyl)amino-4-*O*-ß-D-glucopyranosyl-D-glucitol (6b). Reaction of 1-amino-1-deoxy-4-*O*-ß-D-glucopyranosyl-D-glucitol[15] (**6a**, 0.8 g, 2.34 mmol) with diethyl ethoxymethylenemalonate (0.21 mL, 3.51 mmol), following

the protocol above described, and column chromatography (EtOAc-EtOH 1:1) of the residue yielded **6b** (0.84 g, 70%) as an amorphous solid; $[\alpha]_D^{22}$ -15.2° (*c* 0.63, MeOH); UV (MeOH) 280 nm (ϵ_{mM} 17.1); IR 3380 (OH), 1707 (C=O free), 1630 (C=O chelated), and 1287 cm^{-1} (C-O-C); ^1H NMR (500 MHz, Me_2SO-d_6) δ 9.12 (dt, 1H, $J_{NH,=CH}$ = 14.6 Hz, $J_{1a,NH}$ = $J_{1b,NH}$ = 6.1 Hz, NH), 7.98 (d, 1H, =CH), 5.27 (d, 1H, OH), 5.09 (dd, 1H, CH_2OH), 4.84 (dd, 1H, CH_2OH), 4.58 (m, 2H, 2 OH), 4.42 (d, 1H, OH), 4.18 (m, 2H, 2 OH), 4.07, 4.00 (2q, each 2H, $^3J_{H,H}$ = 7.0 Hz, CH_2CH_3), 3.71-2.97 (m, 15H, H-1a to H-6b), 1.18 and 1.16 (2t, each 3H, $2CH_3$); ^{13}C NMR (125.7 MHz, Me_2SO-d_6) Table 4 and δ 167.9 (C=O chelated), 165.4 (C=O free), 160.4 (=CH), 87.8 (=C), 58.7, 58.6 ($2CH_2$), 14.5 and 14.4(2C) ($2CH_3$).

Anal. Calcd for $C_{20}H_{25}NO_{14}$: C, 46.78; H, 6.87; N, 2.73. Found: C, 46.69; H, 7.00; N, 2.59.

Preparation of Methyl 2,3,4-Tri-*O*-acetyl-6-deoxy-6-(2',2'-diethoxycarbonylvinyl)amino-α-D-glycopyranosides (1c-3c). The crude reaction mixtures arising from treatment of **1a-3a** with diethyl ethoxymethylenemalonate, as described above, were acetylated (Ac_2O-pyridine 1:1, 12 mL, overnight). The peracetylated product was purified by flash chromatography using EtOAc-light petroleum ether 1:1 as eluent.

Methyl 2,3,4-Tri-*O*-Acetyl-6-deoxy-6-(2',2'-diethoxycarbonylvinyl)amino-α-D-glucopyranoside (1c, 2.16 g, 82%) had mp 109-111 °C (from EtOH); $[\alpha]_D^{22}$ +91.7° (*c* 0.9, CH_2Cl_2); UV (CH_2Cl_2) 280 and 227 nm (ϵ_{mM} 10.6 and 5.6); IR 3246 (NH), 1755 (C=O acetate), 1676 (C=O free), 1642 (C=O chelated), 1605 (C=C and NH), and 1240 cm^{-1} (C-O-C); ^1H NMR (300 MHz, $CDCl_3$) Table 1 and δ 9.37 (dt, 1H, $J_{NH,=CH}$ = 14.0 Hz, $J_{6,NH}$ = $J_{6',NH}$ = 7.0 Hz, NH), 7.95 (d, 1H, =CH), 4.26, 4.19 (2q, each 2H, $^3J_{H,H}$ = 7.1 Hz, CH_2CH_3), 3.37 (s, 3H, OCH_3), 2.08, 2.07, 2.01 (3s, each 3H, 3Ac), 1.34 and 1.30 (2t, each 3H, $2CH_2CH_3$); ^{13}C NMR (75.5 MHz, $CDCl_3$) Table 2 and δ 170.0, 169.9, 169.7 ($3COCH_3$), 168.8 (C=O chelated), 166.0 (C=O free), 160.5 (=CH), 90.6 (=C), 59.7, 59.6 ($2CH_2$), 55.4 (OCH_3), 20.5 (3C) ($3COCH_3$), 14.3 and 14.2 ($2CH_3$). EIMS, *m/z* 489 (25%, M^+), 444 (20, M^+-EtO·), 200 (45, $[CH_2NHCH{=}C(CO_2Et)_2]^+$), 43 (100, Ac^+).

Anal. Calcd for $C_{21}H_{31}NO_{12}$: C, 51.53; H, 6.38; N, 2.86. Found: C, 51.32 ; H, 6.43 ; N, 2.73.

Methyl 2,3,4-Tri-*O*-acetyl-6-deoxy-6-(2',2'-diethoxycarbonylvinyl)amino-α-D-mannopyranoside (**2c**, 2.11 g, 80%) had mp 129-131 °C (from $CHCl_3$-hexane); $[\alpha]_D^{22}$ +33.9° (*c* 0.9, CH_2Cl_2); UV (CH_2Cl_2) 280 and 227 nm (ϵ_{mM} 23.2 and 11.6); IR 3262 (NH), 1753 (C=O acetate), 1690 (C=O free), 1645 (C=O chelated), 1611 (C=C and NH), and 1227 cm^{-1} (C-O-C); ^1H NMR (300 MHz, $CDCl_3$) Table 1 and δ 9.43 (dt, 1H, $J_{NH,=CH}$ = 14.0 Hz, $J_{6,NH}$ = $J_{6',NH}$ = 6.9 Hz, NH), 7.99 (d, 1H, =CH), 4.25, 4.19 (2q, each 2H, $^3J_{H,H}$ = 7.0 Hz, CH_2CH_3), 3.41 (s, 3H, OCH_3), 2.10, 2.09, 1.99 (3s, each 3H, 3Ac), 1.33 and 1.29 (2t, each 3H, $2CH_2CH_3$); ^{13}C NMR (75.5 MHz, $CDCl_3$) Table 2 and δ 170.2, 169.8, 169.6 ($3COCH_3$), 168.8 (C=O chelated), 166.1 (C=O free), 160.5 (=CH), 90.3 (=C), 59.6, 59.5 ($2CH_2$), 55.2 (OCH_3), 20.5 (3C) ($3COCH_3$), 14.3 and 14.2 ($2CH_3$). EIMS, *m/z* 489 (30%, M^+), 444 (20, M^+-EtO·), 200 (40, $[CH_2NHCH=C(CO_2Et)_2]^+$), 43 (100, Ac^+).

Anal. Found: C, 51.42; H, 6.28; N, 2.94.

Methyl 2,3,4-Tri-*O*-acetyl-6-deoxy-6-(2',2'-diethoxycarbonylvinyl)amino-α-D-galactopyranoside (**3c**, 2.3 g, 87%) had $[\alpha]_D^{22}$ +116.4° (*c* 0.7, CH_2Cl_2); UV (CH_2Cl_2) 281 and 227 nm (ϵ_{mM} 21.9 and 8.9); IR 3285 (NH), 1751 (C=O acetate), 1701 (C=O free), 1659 (C=O chelated), 1611 (C=C and NH), and 1225 cm^{-1} (C-O-C); ^1H NMR (300 MHz, $CDCl_3$) Table 1 and δ 9.30 (dt, 1H, $J_{NH,=CH}$ = 13.9 Hz, $J_{6,NH}$ = $J_{6',NH}$ = 6.9 Hz, NH), 7.96 (d, 1H, =CH), 4.23, 4.18 (2q, each 2H, $^3J_{H,H}$ = 7.1 Hz, CH_2CH_3), 3.34 (s, 3H, OCH_3), 2.18, 2.09, 1.99 (3s, each 3H, 3Ac), 1.29 and 1.26 (2t, each 3H, $2CH_2CH_3$); ^{13}C NMR (75.5 MHz, $CDCl_3$) Table 2 and δ 170.2, 170.1, 169.7 ($3COCH_3$), 168.8 (C=O chelated), 165.6 (C=O free), 160.0 (=CH), 90.5 (=C), 59.7, 59.5 ($2CH_2$), 55.3 (OCH_3), 20.6, 20.4 (2C) ($3COCH_3$), 14.2 and 14.1 ($2CH_3$). EIMS, *m/z* 489 (15%, M^+), 444 (13, M^+-EtO), 200 (25, $[CH_2NHCH=C(CO_2Et)_2]^+$), 43 (100, Ac^+).

Anal. Found: C, 51.57; H, 6.40; N, 2.71.

Diethyl (2-Acetoxyethyl)aminomethylenemalonate (4c). The reaction mixture arising from the treatment of **4a** with diethyl ethoxymethylenemalonate, as described above, was acetylated (Ac_2O-pyridine 1:1, 6 mL, overnight) and subjected to column chromatography (EtOAc-light petroleum ether 3:2) to give **4c** (0.51 g, 72%) as an oil; UV (CH_2Cl_2) 280 and 228 nm (ϵ_{mM} 48.3 and 23.1); IR 3287 (NH), 1744 (C=O acetate),

1680 (C=O free), 1661 (C=O chelated), 1615 (C=C and NH), and 1227 cm^{-1} (C-O-C); ^1H NMR (500 MHz, $CDCl_3$): δ 9.23 (dt, 1H, $J_{NH,=CH}$ = 12.9 Hz, $J_{CH2,NH}$ = 6.5 Hz, NH), 7.97 (d, 1H, =CH), 4.22, 4.17 (2q, each 2H, $^3J_{H,H}$ = 7.1 Hz, CH_2CH_3), 4.16 (t, 2H, $^3J_{H,H}$ = 6.6 Hz, CH_2OAc), 3.56 (q, 2H, CH_2NH), 2.07 (s, 3H, Ac), 1.34 and 1.27 (2t, each 3H, $2CH_3$); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 170.4 ($COCH_3$), 168.9 (C=O chelated), 165.7 (C=O free), 159.9 (=CH), 90.4 (=C), 59.7, 59.5 ($2CH_2$), 20.5 ($COCH_3$), 14.2 and 14.1 (CH_3). EIMS, *m/z* 273 (27%, M^+), 228 (40, M^+-EtO·), 200 (20, $[CH_2NHCH=C(CO_2Et)_2]^+$), and 154 (100, 200-EtOH).

Anal. Calcd for $C_{12}H_{19}NO_6$: C, 52.74; H, 7.01; N, 5.12. Found: C, 52.70; H, 6.91; N, 5.10.

2,3,4,5,6-Penta-*O*-acetyl-1-deoxy-1-(2',2'-diethoxycarbonylvinyl)amino-D-glucitol (5c). The reaction mixture arising from the treatment of **5a** with diethyl ethoxymethylenemalonate, as described above, was acetylated (Ac_2O-pyridine 1:1, 12 mL, overnight) and subjected to column chromatography (EtOAc-light petroleum ether 3:2) to give **5c** (1.6 g, 76%) as a syrup having $[\alpha]_D^{22}$ -1.9° (*c* 0.9, CH_2Cl_2); UV (CH_2Cl_2) 280 and 227 nm (ϵ_{mM} 33.7 and 15.6); IR 3289 (NH), 1755 (C=O acetate), 1701 (C=O free), 1659 (C=O chelated), 1611 (C=C and NH), and 1219 cm^{-1} (C-O-C); ^1H NMR (500 MHz, $CDCl_3$) Table 3 and δ 9.18 (dt, 1H, $J_{NH,=CH}$ = 13.7 Hz, $J_{1a,NH}$ = $J_{1b,NH}$ = 6.5 Hz, NH), 7.88 (d, 1H, =CH), 4.21, 4.15 (2q, each 2H, $^3J_{H,H}$ = 7.1 Hz, CH_2CH_3), 2.12, 2.08, 2.07, 2.04, 2.03 (5s, each 3H, 5Ac), 1.30 and 1.26 (2t, each 3H, $2CH_3$); ^{13}C NMR (125.7 MHz, $CDCl_3$) Table 4 and δ 170.2, 169.9, 169.7, 169.6, 169.5 ($5COCH_3$), 168.6 (C=O chelated), 165.5 (C=O free), 159.9 (=CH), 91.2 (=C), 59.7, 59.5 ($2CH_2$), 20.5 (2C), 20.4(2C), 20.2 ($5COCH_3$), 14.2 and 14.1 ($2CH_3$). EIMS, *m/z* 561 (16%, M^+), 516 (22, M^+-EtO·), 200 (60, $[CH_2NHCH=C(CO_2Et)_2]^+$), 154 (80, 200-EtOH), and 43 (100, Ac^+).

Anal. Calcd for $C_{24}H_{35}NO_{14}$: C, 51.33; H, 6.28; N, 2.49. Found: C, 51.37; H, 6.10; N, 2.48.

2,3,5,6-Tetra-*O*-acetyl-1-deoxy-1-(2',2'-diethoxycarbonylvinyl)amino-4-*O*-(2,3,4,6-tetra-*O*-acetyl-ß-D-glucopyranosyl)-D-glucitol (6c). The reaction mixture arising from the treatment of **6a** with diethyl ethoxymethylenemalonate, as described above, was acetylated (Ac_2O-pyridine, 10 mL, overnight) and subjected to column chromatography (EtOAc-light petroleum ether 3:2) to give **6c** (1.49 g, 75%) as a syrup

having $[\alpha]_D^{22}$ +4.9° (*c* 0.9, CH_2Cl_2); UV (CH_2Cl_2) 281 nm (ϵ_{mM} 2.1); IR 3293 (NH), 1753 (C=O acetate), 1700 (C=O free), 1655 (C=O chelated), 1616 (C=C and NH), and 1223 cm^{-1} (C-O-C); ^1H NMR (500 MHz, $CDCl_3$) Table 3 and δ 9.16 (ddd, 1H, $J_{NH,=CH}$ = 13.8 Hz, $J_{1b,NH}$ = 6.3 Hz, $J_{1a,NH}$ = 4.7 Hz, NH), 7.87 (d, 1H, =CH), 4.21, 4.15 (2q, each 2H, $^3J_{H,H}$ = 7.1 Hz, CH_2CH_3), 2.04 (s, 6H, 2 Ac), 2.03, 2.02, 2.00, 1.99, 1.97, 1.96 (6s, each 3H, 6Ac), 1.30 and 1.26 (2t, each 3H, $2CH_3$); ^{13}C NMR (125.7 MHz, $CDCl_3$) Table 4 and δ 170.3, 170.0, 169.9, 169.6, 169.5, 169.4, 169.0, 168.9, (8 $COCH_3$), 168.6 (C=O chelated), 165.6 (C=O free), 160.0 (=CH), 90.8 (=C), 59.7, 59.4 ($2CH_2$), 20.5, 20.4, 20.3, 20.2 (5C) (8 $COCH_3$), 14.2 and 14.0 ($2CH_3$).

Anal. Calcd for $C_{36}H_{51}NO_{22}$: C, 50.88; H, 6.05; N, 1.65. Found: C, 51.04; H, 5.95; N, 1.70.

A FABMS spectrum showed a pseudomolecular $[M+Na^+]$ ion at *m/z* 872.

Preparation of Methyl 2,3,4-Tri-*O*-acetyl-6-amino-6-deoxy-α-D-glycopyranoside Hydrochlorides (1d-3d). Cl_2 was bubbled through solutions of enamines **1c-3c** (0.4 g, 0.82 mmol) in $CHCl_3$ (15 mL) containing 3 drops of water at 0 °C until saturation. The reaction mixtures were kept for 1 h at 5 °C and then concentrated. Ether (3 x 20 mL) was added and evaporated, and the resulting solids were suspended in ether, filtered and dried.

Methyl 2,3,4-Tri-*O*-acetyl-6-amino-6-deoxy-α-D-glucopyranoside Hydrochloride (1d, 0.28 g, 95%) had $[\alpha]_D^{22}$ +127.1° (*c* 0.9, MeOH); IR 3133-2544 (NH_3^+), 1746 (C=O acetate), and 1240 cm^{-1} (C-O-C); ^1H NMR (500 MHz, $CDCl_3$) δ 8.04 (bs, 3H, NH_3^+), 5.33 (dd, 1H, $J_{2,3}$ = $J_{3,4}$ = 9.7 Hz, H-3), 4.78 (m, 1H, H-1), 4.66 (m, 2H, H-2,4), 3.89 (m, 1H, H-5), 3.26 (s, 3H, CH_3), 2.96 (m, 1H, H-6a), 2.78 (m, 1H, H-6b), 1.86 and 1.80 (3s, each 3H, 3Ac); ^{13}C NMR (125.7 MHz, $CDCl_3$), Table 2 and δ 170.3, 170.2, 170.0 ($3COCH_3$), 55.5 (OCH_3), and 19.9 (3C) ($3COCH_3$).

Anal. Calcd for $C_{13}H_{22}NO_8Cl$: C, 43.89; H, 6.23; N, 3.94; Cl, 9.96. Found: C, 43.71; H, 6.51; N, 3.85; Cl, 9.74.

A FABMS spectrum showed a pseudomolecular $[M+Na-HCl]^+$ ion at *m/z* 342.

Methyl 2,3,4-Tri-*O*-acetyl-6-amino-6-deoxy-α-D-mannopyranoside Hydrochloride (2d, 0.26 g, 90%) had $[\alpha]_D^{22}$ +20.4° (*c* 1.1, MeOH); IR 3200-2500 (NH_3^+), 1755 (C=O acetate), and 1223 cm^{-1} (C-O-C); ^1H NMR (300 MHz, $CDCl_3$) δ

8.44 (bs, 3H, NH_3^+), 5.28 (bd, 1H, H-3), 5.20 (bs, 1H, H-2), 5.04 (t, 1H, $J_{3,4} = J_{4,5}$ = 9.0 Hz, H-4), 4.70 (bs, 1H, H-1), 4.05 (m, 1H, H-5), 3.47 (s, 3H, CH_3), 3.18 (m, 1H, H-6a), 3.07 (m, 1H, H-6b), 2.11, 2.05, and 1.94 (3s, each 3H, 3Ac); ^{13}C NMR (75.5 MHz, $CDCl_3$), Table 2 and δ 170.3, 169.7, 169.5 (3*C*OCH_3), 56.2 (OCH_3), 20.7 (2C), and 20.4 (3CO*C*H_3).

Anal. Found: C, 43.85; H, 6.10; N, 3.71; Cl, 9.85.

A FABMS spectrum showed a pseudomolecular $[M+Na-HCl]^+$ ion at *m/z* 342.

Methyl 2,3,4-Tri-*O*-acetyl-6-amino-6-deoxy-α-D-galactopyranoside Hydrochloride (**3d**, 0.28 g, 98%) had $[\alpha]_D^{22}$ +132.3° (*c* 1.1, MeOH); IR 3650-2473 (NH_3^+), 1751 (C=O acetate), and 1229 cm^{-1} (C-O-C); ^1H NMR (300 MHz, $CDCl_3$) δ 8.33 (bs, 3H, NH_3^+), 5.46 (d, 1H, $J_{3,4}$ = 3.1 Hz, $J_{4,5}$ = 0 Hz, H-4), 5.30 (dd, 1H, H-3), 5.11 (dd, 1H, $J_{2,3}$ = 10.8 Hz, $J_{1,2}$ = 3.4 Hz, H-2), 5.02 (d, 1H, H-1), 4.41 (m, 1H, H-5), 3.50 (s, 3H, CH_3), 3.15 (bs, 2H, H-6a,6b), 2.17, 2.07, and 1.96 (3s, each 3H, 3Ac); ^{13}C NMR (75.5 MHz $CDCl_3$), Table 2 and δ 170.4, 170.1, 169.8 (3*C*OCH_3), 56.3 (OCH_3), 20.5 (2C), and 20.4 (3CO*C*H_3).

Anal. Found: C, 43.58; H, 6.28; N, 3.91; Cl, 10.02.

A FABMS spectrum showed a pseudomolecular $[M+Na-HCl]^+$ ion at *m/z* 342.

2-Aminoethyl Acetate Hydrochloride (4d). Treatment of **4c** (0.62 g, 2.27 mmol) with Cl_2, as described above, yielded **4d** (0.23 g, 77%); mp 124-126 °C (from CH_2Cl_2:ether); IR 3459-2508 (NH_3^+), 1736 (C=O acetate), and 1246 cm^{-1} (C-O-C); ^1H NMR (300 MHz, Me_2SO-d_6): δ 8.37 (bs, 3H, NH_3^+), 4.19 (t, 2H, $^3J_{H,H}$ = 5.3 Hz, *C*H_2OAc), 3.01 (bs, 2H, *C*$H_2NH_3^+$), and 2.03 (s, 3H, Ac); ^{13}C NMR (75.5 MHz Me_2SO-d_6): δ 170.3 (*C*OCH_3), 60.4 (C-1), 37.7 (C-2), and 20.8 (CO*C*H_3).

Anal. Calcd for $C_4H_{10}NO_2Cl$: C, 31.98; H, 7.49; N, 10.41; Cl, 26.34. Found: C, 32.13; H, 7.58; N, 10.28; Cl, 26.41.

A FABMS spectrum showed a pseudomolecular $[M+Na+thioglycerol]^+$ ion at *m/z* 229.

2,3,4,5,6-Penta-*O*-acetyl-1-amino-1-deoxy-D-glucitol Hydrochloride (5d). Treatment of **5c** (0.56 g, 1.0 mmol) with Cl_2, as described above, yielded pure **5d** (0.38 g, 88%); mp 178-180 °C (from EtOH-H_2O); $[\alpha]_D^{22}$ +1.5° (*c* 0.7, H_2O); IR 3300-2419 (NH_3^+), 1751 (C=O acetate), and 1232 cm^{-1} (C-O-C); ^1H NMR (300 MHz, Me_2SO-d_6) δ 8.34 (bs, 3H, NH_3^+), 4.96 (dt, 1H, $J_{5,6b}$ = 10.5 Hz, $J_{5,6a} = J_{4,5}$ =5.1 Hz, H-5),

4.28-4.23 (m, 2H, H-3,4), 4.19 (dd, 1H, $J_{6a,6b}$ = 20.7 Hz, H-6a), 4.17 (m, 1H, H-2), 4.04 (dd, 1H, H-6b), 3.03-2.40 (m, 2H, H-1a,1b), 2.10, 2.04, 2.02, 1.98 and 1.97 (5s, each 3H, 5Ac); ^{13}C NMR (125.7 MHz Me_2SO-d_6), Table 4 and δ 173.1, 172.4, 172.1, 172.0, 171.9 (5*C*OCH$_3$), 19.8, 19.7, 19.8, 19.5, and 19.4 (5CO*C*H$_3$).

Anal. Calcd for $C_{16}H_{26}NO_{10}Cl$: C, 44.92; H, 6.12; N, 3.27; Cl, 8.29. Found: C, 45.06; H, 6.04; N, 3.37; Cl, 8.29.

A FABMS spectrum showed a pseudomolecular $[M+Na-HCl]^+$ ion at *m/z* 414.

2,3,5,6-Tetra-*O*-acetyl-1-amino-1-deoxy-4-*O*-(2,3,4,6-tetra-*O*-acetyl-ß-D-glucopyranosyl)-D-glucitol Hydrochloride (6d). Tratment of **6c** (0.59 g, 0.69 mmol) with Cl_2 yielded pure **6d** (0.42 g, 84%); $[\alpha]_D^{22}$ +6.5° (*c* 0.85, CH_2Cl_2); IR 3300-2400 (NH_3^+), 1750 (C=O acetate), and 1215 cm^{-1} (C-O-C); ^{1}H NMR (500 MHz, Me_2SO-d_6) δ 8.30 (bs, 3H, NH_3^+), 5.45-3.99 (m, 15H, H-1a to H-6b), 2.12, 2.09, 2.05 (6H), 2.03 (9H) and 1.96 (5s, 8Ac); ^{13}C NMR (125.7 MHz Me_2SO-d_6), Table 4 and δ 171.0, 170.7, 170.4, 170.0, 169.9, 169.7, 169.2, 169.1 (8*C*OCH$_3$), 21.0, 20.7, 20.6, 20.5, 20.4, and 20.3 (3C) (8CO*C*H$_3$).

Anal. Calcd for $C_{28}H_{42}NO_{18}Cl$: C, 46.96; H, 5.91; N, 1.96; Cl, 4.95. Found: C, 46.71; H, 6.28; N, 2.04; Cl, 4.94.

A FABMS spectrum showed a pseudomolecular $[M+Na-HCl]^+$ ion at *m/z* 702.

Preparation of Methyl 2,3,4-Tri-*O*-acetyl-6-deoxy-6-isothiocyanato-α-D-glycopyranosides (1e-3e). To a heterogeneous mixture of the corresponding per-*O*-acetyl amino sugar hydrochloride **1d-3d** (0.2 g, 0.56 mmol) in $CHCl_3$ (7 mL), $CaCO_3$ (0.17 g, 1.68 mmol), and H_2O (7 mL) was added $CSCl_2$ (0.2 mL, 1.68 mmol). The mixture was vigorously stirred for 3 h in a round bottom flask provided with a system for evacuation of gases, and then filtered. The organic layer was separated, washed with water, dried ($MgSO_4$), and concentrated to dryness. The residue was subjected to column chromatography using EtOAc-light petroleum ether 2:1 as eluent.

Methyl 2,3,4-Tri-*O*-acetyl-6-deoxy-6-isothiocyanato-α-D-glucopyranoside (**1e**, 0.17 g, 85%) had the physical and spectroscopic data reported in the literature.[11]

Methyl 2,3,4-Tri-*O*-acetyl-6-deoxy-6-isothiocyanato-α-D-mannopyranoside (2e, 0.17 g, 87%) had the physical and spectroscopic data reported in the literature.[11]

Methyl 2,3,4-Tri-*O*-acetyl-6-deoxy-6-isothiocyanato-α-D-galactopyranoside (3e, 0.16 g, 80%) had the physical and spectroscopic data reported in the literature.[11]

2-Isothiocyanatoethyl Acetate (4e). Reaction of **4d** (0.15 g, 1.11 mmol) with $CSCl_2$, following the above procedure, yielded **4e** (0.10 g, 62%) as an oil having bp 40 °C (0.05 Torr); IR 2116 (NCS), 1744 (C=O acetate), and 1227 cm^{-1} (C-O-C); ^1H NMR (500 MHz, $CDCl_3$) δ 4.26 (t, 2H, $^3J_{H,H}$ = 5.2 Hz, CH_2OAc), 3.77 (t, 2H, CH_2NCS), and 2.13 (s, 3H, Ac); ^{13}C NMR (125.7 MHz $CDCl_3$) δ 170.4 ($COCH_3$), 134.0 (NCS), and 20.6 ($COCH_3$). EIMS, *m/z* 145 (4%, M^+), 85 (35, M^+-AcOH), 43 (100, Ac^+).

Anal. Calcd for $C_5H_7NO_2S$: C, 41.36; H, 4.86; N, 9.65; S, 22.09. Found: C, 41.10; H, 4.92; N, 9.51; S, 21.94.

2,3,4,5,6-Penta-*O*-acetyl-1-deoxy-1-isothiocyanato-D-glucitol (5e). Treatment of **5d** (0.2 g, 0.5 mmol) with $CSCl_2$, as described above, and column chromatography (EtOAc-light petroleum ether 3:2) of the resulting syrupy residue yielded **5e** (0.14 g, 70%) as a syrup having $[\alpha]_D^{22}$ +58.8° (*c* 0.6, CH_2Cl_2); IR 2103 (NCS), 1751 (C=O acetate), and 1215 cm^{-1} (C-O-C); ^1H NMR (500 MHz, $CDCl_3$) Table 3 and δ 2.12, 2.11, 2.08, 2.07 ,and 2.06 (5s, each 3H, 5Ac); ^{13}C NMR (75.5 MHz $CDCl_3$), Table 4 and δ 170.3, 169.8, 169.7, 169.6, 169.5 ($5COCH_3$), 135.3 (NCS), 20.6, 20.5 (3C), and 20.2 ($5COCH_3$). CIMS *m/z* 434 (70%, $[M+H]^+$), 433 (20, M^+), 432 (80, $[M-H]^+$). EIMS *m/z* 313 (10%, M^+-2AcOH), 211 (35, 313-Ac_2O), 169 (15, 211-CH_2CO), 43 (100, Ac+).

Anal. Calcd for $C_{17}H_{23}NO_{10}S$: C, 47.11; H, 5.35; N, 3.23; S, 7.40. Found: C, 47.10; H, 5.41; N, 3.54; S, 7.50.

2,3,5,6-Tetra-*O*-acetyl-1-deoxy-1-isothiocyanato-4-*O*-(2,3,4,6-tetra-*O*-acetyl-ß-D-glucopyranosyl)-D-glucitol (6e). Treatment of **6d** (0.41 g, 0.57 mmol) with $CSCl_2$, as described above, and column chromatography (EtOAc-light petroleum ether 1:2) of the resulting syrupy residue yielded **6e** (0.26 g, 65%) as a syrup having $[\alpha]_D^{22}$ +25° (*c* 0.9, CH_2Cl_2); IR 2124 (NCS), 1751 (C=O acetate), and 1229 cm^{-1} (C-O-C); ^1H NMR (300 MHz, $CDCl_3$) Table 3 and δ 2.13, 2.11, 2.10, 2.09, 2.08, 2.07, 2.04, and 2.01 (8s, each 3H, 8Ac); ^{13}C NMR (75.5 MHz $CDCl_3$), Table 4 and δ 170.5, 170.1, 170.0, 169.5 (3C), 169.1, 168.9 ($8COCH_3$), 134.5 (NCS), 20.6 (3C), and 20.4 (5C) ($8COCH_3$).

Anal. Calcd for $C_{29}H_{39}NO_{18}S$: C, 48.26; H, 5.45; N, 1.94; S, 4.44. Found: C, 48.40; H, 5.41; N, 1.71; S, 4.62.

A FABMS spectrum showed a pseudomolecular $[M+Na]^+$ ion at *m/z* 744.

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resulted in concommitant O→N Acetyl migration particularly significant in the case of **3d**.

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