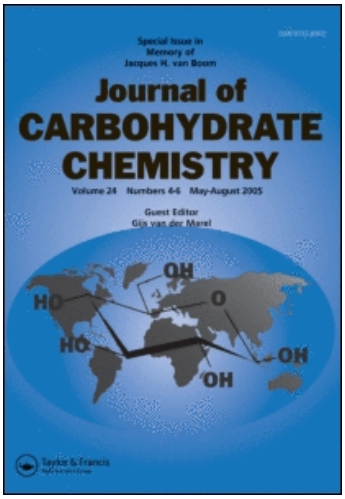

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α-D anomeric configuration and in which the non-carbohydrate portion is a one-carbon, reactive, functional group.

Many of the methods described for synthesis of *C*-pyranosyl compounds give predominately 1,2-*trans* products. BeMiller *et al.*[1] used photoamidation of glycals with formamide to produce carboxamides with the α-D-galacto and α-D-gluco configurations (1,2-*cis* products). However, the analogous reaction with the glycal prepared from di-*N*-acetyl-2-amino-2-deoxy-D-glucose, according to Pravdic *et al.*,[2] was unsuccessful (unpublished).

Glycosyl cyanides are also useful as intermediates in the preparation of *C*-glycosyl compounds, especially those that are isosteric substrate analogs and which have biochemical interest as pseudo-substrates[3-5] and as competitive[6] and irreversible inhibitors[7-9] of enzymes that make and break glycosidic bonds; but, while their preparation by reaction of glycosyl halides with mercuric cyanide in an aprotic, polar solvent[10-19] seemed to be a reasonable approach to meeting the objective, neither is it devoid of problems when applied to the synthesis of "*N*-acetyl-α-D-glucosaminyl" and "*N*-acetyl-α-D-galactosaminyl" cyanides, the desired intermediates for synthesis of the target compounds. Kolb *et al.*[20] prepared 2-deoxy-3,5-di-*O*-(*p*-toluoyl)-β-D-*erythro*-pentofuranosyl cyanide from the corresponding α-D-glycosyl chloride using sodium cyanide in various polar solvents. However, preparation of glycosyl cyanides with the α-D configuration by S_N2-type nucleophilic displacement with cyanide ion would require an 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glycopyranosyl halide. When such compounds with the β-D configuration are prepared, an oxazolidone ring forms spontaneously via attack by the neighboring acetamido group. Subsequent attack of nucleophiles gives products with the β-D configuration.[21-23] An S_N1 reaction using a heavy metal ion to remove the halide ion from either an α- or β-D-glycosyl halide also gives products of β-D configuration.[19] When a "nonparticipating" group is used to block the amino group, i.e., when D-glucosamine is converted into a phthalimido derivative, the β-D-glycosyl bromide can be prepared,[24,25] but treatment of it with mercuric cyanide gives only the β-D cyanide.[19,25,26]

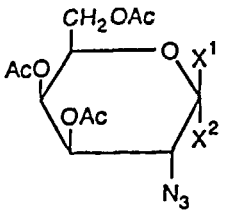
From other work, it was known that per-*O*-acetyl-D-galactopyranosyl cyanides are prepared in better yield than are the corresponding D-glucopyranosyl or D-mannopyranosyl cyanides.[19] Hence, it was decided that the first synthetic attempt should be conducted with D-galactose as the starting compound and that the procedure, once established, should subsequently be extended to the preparation of sugar derivatives with the D-gluco and D-manno configurations because, unfortunately, the use of D-galactosamine itself as a starting compound is cost prohibitive and because it was thought desirable to have a common method that could be used for the general synthesis of *C*-glycosyl analogs of amino sugars. It appeared that, in order to make an α-D-glycosyl cyanide (1,2-*cis* product) of a 2-amino-2-deoxyhexopyranose, it would be necessary, but not necessarily sufficient, to use a nonparticipating functional group at C-2 that could be converted to an amino group after preparation of the glycosyl cyanide. Two such types of precursors with nonparticipating functional groups on C-2 were considered, those with an oximino group[27] and those with an azido group;[28,29] the latter type was selected. Use of the oximino group was rejected because of the lack of stereochemical control associated with the reduction of that group to an amino group.[30,31]

Lemieux and Ratcliffe converted "tri-*O*-acetyl-D-galactal"[28] and "tri-*O*-acetyl-D-glucal"[29] into their azidonitration products; the latter reaction was not reported in detail and ^{1}H NMR chemical shifts of H-1 protons were the only physical constants given. Similar reactions have been conducted with "lactal",[32] "maltal",[33] and "cellobial"[34] hexaacetates. In all these cases, the "2-azido-2-deoxy 1-nitrates" were converted into α-D-glycosyl halides in good yield using either a lithium or a tetraalkylammonium halide. Some of the same glycosyl halides have been made by reaction of 3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-D-aldohexopyranosyl acetates with titanium tetrabromide[35-39] and by reaction of "tri-*O*-acetyl-D-glycals" with chloroazide.[40] The resultant glycosyl halides have been used in a variety of *O*-glycosidation reactions to give 2-azido-2-deoxy glycosides[38,39,41-46] which are subsequently reduced to 2-acetamido-2-deoxy glycosides.[38,39,41-46]

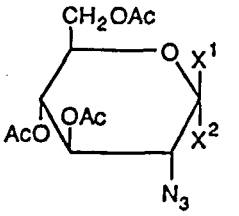
RESULTS AND DISCUSSION

Azidonitration of 3,4,6-tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-*lyxo*-hex-1-enitol with ceric ammonium nitrate and sodium azide according to the procedure of Lemieux and Ratcliffe[28] produced primarily 3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α,β-D-galactopyranosyl nitrates (1,2) in 48% combined isolated yield from 2,3,4,6-tetra-O-acetyl-α-D-galactopyranosyl bromide, the immediate precursor of the hex-1-enitol, and a lesser amount of 3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α-D-talopyranosyl nitrate (3). Isolated glycosyl nitrates (1-3) were converted with lithium bromide in acetonitrile (also by the procedure described by Lemieux and Ratcliffe[28]) into 3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α-D-galactopyranosyl bromide (4) and 3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α-D-talopyranosyl bromide (6). Compound 4 was isolated by column chromatography in ~60% yield from the reaction products obtained from a mixture of 1, 2 and 3. Reaction of 4 with 1.5 equivalents of mercuric cyanide gave 3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α,β-D-galactopyranosyl cyanide (7,8), isolated as an anomeric mixture in 49% yield by column chromatography. The α:β ratio was ~2.7:1 as determined by ^{1}H NMR spectroscopy. In a separate experiment, 7 and 8 were obtained pure by column chromatography and fractional crystallization, yield of the α-D anomer (7) 24.9% and the β-D anomer (8) 17.0% (from 4). In an attempt to improve the yield of the glycosyl cyanide, a more reactive halide was tried. Compound 1 was treated with lithium iodide to give, presumably, the glycosyl iodide 5. The product was reacted directly with 1.0 equivalent of mercuric cyanide to give 7 and 8 in ~24% combined yield (from 1).

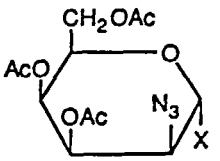
Azidonitration of 3,4,6-tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-*arabino*-hex-1-enitol gave an 80% combined isolated yield of a mixture of 3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α,β-D-glucopyranosyl nitrate (9,10) and 3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α-D-mannopyranosyl nitrate (11).[29] Separation of 9, 10 and 11 was ineffective; so for synthetic purposes, the crude reaction mixture was subjected to column chromatography and an isolated mixture of 9, 10 and 11 was reacted with lithium bromide to give the corresponding 3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α-D-aldohexopyranosyl bromides (12,14) in a 75% combined isolated yield. Because of the anomeric effect, only α-D-aldohexopyranosyl bromides were



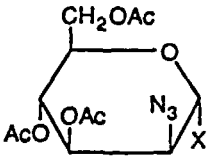
	X^1	X^2
1:	H	ONO_2
2:	ONO_2	H
4:	H	Br
5:	H	I
7:	H	CN
8:	CN	H



	X^1	X^2
9:	H	ONO_2
10:	ONO_2	H
12:	H	Br
13:	H	I
16:	H	CN
17:	CN	H



	X
3:	ONO_2
6:	Br



	X
11:	ONO_2
14:	Br
15:	I
18:	CN

formed; in this way, the number of major products was reduced by one. Separation of 12 from 14 by chromatography could be effected more easily than separation of 9 and 10 from 11. Reaction of 12 with 1.5 equivalents mercuric cyanide gave 3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α,β-D-glucopyranosyl cyanides (16,17) in ~30% yield with an α:β ratio of ~2:1 as determined by ^{1}H NMR. In a separate synthesis, the anomers were isolated by column chromatography and fractional crystallization to give the α-D anomer (16) in 18.5% yield and the β-D anomer (17) in 9.6% yield (from 12). Alternatively, crystalline 9 was reacted with lithium iodide to give, presumably, the glucosyl iodide (13) which was reacted directly

with 1.1 equivalents mercuric cyanide to give **16** and **17** in 26% combined isolated yield (from **9**).

Treatment of **14** with 1.1 equivalents of mercuric cyanide gave 3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α-D-mannopyranosyl cyanide (**18**) in ~28% yield; none of the β-D anomer was detected. Compound **11** was also reacted with lithium iodide to give, presumably, the mannosyl iodide (**15**), which was reacted directly with 1.1 equivalents of mercuric cyanide to give **18** in ~22% yield (from **11**).

For purposes of comparison with published physical data, **1** and **4** were isolated by fractional crystallization. The melting point (101-102 °C), optical rotation ($[\alpha]^{25}D$ +116° (*c* 1.85, $CHCl_3$)) (Table I) and ^1H NMR (Table II) data for compound **1** agreed with that reported [lit.[28,41] mp 103-104 °C, $[\alpha]^{25}D$ +125° (*c* 1.0, $CHCl_3$)]. Compound **1** was also examined by ^{13}C NMR spectroscopy (Table III). The melting point of **4** (102-103 °C) and optical rotation ($[\alpha]^{25}D$ +174° (*c* 1.20, $CHCl_3$)) agreed with those reported [97-98 °C[28], 101.5 °C[40]; $[\alpha]^{25}D$ +188.6° (*c* 1.95, $CHCl_3$)[40]], as did the ^1H NMR data.[28]

H-1 chemical shifts of isolated **9**, **10** and **11** matched those reported.[29] Compounds **9** and **11** were also examined by ^{13}C NMR spectroscopy; the $^1J_{C-1,H-1}$ values of **9** and **11** (180.40 Hz for **9** and 181.13 for **11**) were of the same magnitude as the $^1J_{C-1,H-1}$ values for **1** (180.40) Hz) and 3,6-di-*O*-acetyl-2-azido-2-deoxy-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-α-D-mannopyranosyl nitrate ($^1J_{C-1,H-1}$ 182 Hz),[33] indicative of the α-D configuration.[33,47] The 2,3,4-tri-*O*-acetyl-2-azido-2-deoxy-aldohexopyranosyl nitrates of α-D configuration (**1**,**9**,**11**) were crystalline; the corresponding β-D anomers (**2**,**10**) could not be crystallized, in accord with the report of Lemieux and Ratcliffe.[28]

Configurations of the glycosyl cyanides (**7**,**8**,**16**-**18**) were determined by ^1H and ^{13}C NMR spectroscopy. $^1J_{C-1,H-1}$ values of **7**, **16** and **18** were 160.3, 160.7 and 160.2 Hz, respectively, indicative of the α-D configuration. $^1J_{C-1,H-1}$ values for **8** and **17** were 151.4 and 149.4 Hz, respectively, indicating the β-D configuration.[47]

Anomeric configurations were determined from anomeric proton spin coupling constants which, in increasing order of magnitude, were α-D-manno $J_{1e,2e}$ = 1.3 and 2.3 Hz for compounds **11** and **18** respectively, α-D-galacto,gluco $J_{1e,2a}$ = 5.4, 4.2 and 6.0 Hz for compounds **7**, **9** and **16**,

TABLE I. Physical Constants of 2-Azido-2-deoxyhexopyranosyl Derivatives

Configuration and anomeric constituent	R_f				Melting Point, °C	Calculated, %			Found, %			$[\alpha]^{25}$ D (c, $CHCl_3$)		IR $\nu(-N_3)$, cm^{-1} (solvent)
	C	D(2X)	E	F		C	H	N	C	H	N			
α-Glc-NO_3 (9)	0.35	0.28	0.39	0.51	138.5-140.5	38.30	4.29	14.89	38.28	4.24	14.81	139°	(2.81)	2120.5[a]
β-Glc-NO_3 (10)	0.35	0.26	0.35	0.50								18.8°	(1.08)	
α-Man-NO_3 (11)	0.37	0.30	0.41	0.48	87.0-87.5	38.30	4.29	14.89	38.23	4.22	14.85	105°	(1.35)	2115.6[a]
α-Man-Br (14)	0.38	0.35	0.45	0.50										
α-Gal-CN (7)	0.24	0.26	0.38	0.41	107-108	45.89	4.74	16.46	45.55	4.68	16.21	83.1°	(2.42)	2119.6 (CCl_4)
β-Gal-CN (8)	0.26	0.21	0.34	0.34	128.5-129.5	45.89	4.74	16.46	45.79	4.72	16.42	3.83°	(2.41)	2117.5 ($CHCl_3$)
α-Glc-CN (16)	0.23	0.25	0.36	0.37								85.3°	(2.85)	2118.2 ($CHCl_3$)
β-Glc-CN (17)	0.24	0.20	0.30	0.33	129.5-130 124-125[b]	45.89	4.74	16.46	45.77	4.67	16.27	15.5° -21.0°	(0.515) (2.73)	2118.2 ($CHCl_3$)
α-Man-CN (18)	0.28	0.28	0.40	0.42								67.9°	(2.76)	2110.7 (CCl_4)

[a] KBr pellet
[b] From CH_2Cl_2-hexane

TABLE II. ^{1}H NMR Chemical Shifts and Coupling Constants of 2-Azido-2-deoxyhexopyranosyl Derivatives

	9 α-Glc-NO_3	10 β-Glc-NO_3	11 α-Man-NO_3	7 α-Gal-CN	8 β-Gal-CN	16 α-Glc-CN	17 β-Glc-CN	18 α-Man-CN
H-1	6.33(d)	5.60(d)	6.20(d)	4.96(d)	4.04(d)	4.94(d)	4.05(d)	4.85(d)
H-2	3.87(dd)	3.69(t)	4.06	4.15(m)	4.05(m)	3.95(dd)	3.90(dd)	4.31(m)
H-3	5.40(t)	5.17(t)	5.41(t)	5.18(dd)	4.87-4.92	5.38(t)	5.10(t)	5.40(dd)
H-4	5.13(t)	5.05(t)	5.24(dd)	5.48(bd)	5.34(bd)	5.05(t)	5.02(t)	5.36(t)
H-5	--	3.86(ddd)	4.19	4.27(bt)	3.88(bt)	4.09(ddd)	3.69(ddd)	4.03(ddd)
H-6	4.33(dd)	4.12(dd)	4.35(dd)	4.12	4.09(bd)	4.14(dd)	4.12(dd)	4.15(dd)
H-6'	--	4.31(dd)	4.12	4.18	--	4.33(dd)	4.25(dd)	4.28(m)
$COCH_3$	2.06-2.11	2.04-2.11	2.07-2.13	2.06-2.16	2.05-2.18	2.06-2.11	2.03-2.12	2.08-2.13
Couplings								
H-1, H-2	4.24	8.8	1.3	5.9	--	6.0	10.0 2.3	
H-2, H-3	10.7	9.2	--	11.1	--	9.7	9.7 --	
H-3, H-4	10.0	9.5	9.6	3.2	2.8	9.7	9.7 9.5	
H-4, H-5	9.83	9.5	9.7	1.0	1.0	9.7	9.7 9.5	
H-5, H-6	--	2.1	--	6.1	6.3	2.3	2.2 2.0	
H-5, H-6'	--	4.6	4.9	--	--	4.4	4.5 5.0	
H-6, H-6'	--	12.5	--	--	--	12.9	12.2 12.5	

TABLE III. ^{13}C NMR Chemical Shifts and Coupling Constants ($^{1}J_{C-1,H-1}$) of 2-Azido-2-deoxyhexopyranosyl Derivatives

	1 α-Gal-NO_3	9 α-Glc-NO_3	11 α-Man-NO_3	7 α-Gal-CN	8 β-Gal-CN	16 α-Glc-CN	17 β-Glc-CN	18 α-Man-CN
C-1	96.88	96.85	97.07	66.79	67.39	66.27	67.13	65.86
C-2	55.95	59.96	58.80	55.25	58.09	58.96	61.58	60.12
C-3	68.61	70.94	70.41	70.76	72.34	72.53	73.74	70.93
C-4	66.63	68.03	64.79	66.25	66.04	67.20	67.21	64.66
C-5	69.49	71.13	71.77	72.47	75.29	73.69	76.77	74.25
C-6	60.92	61.62	61.38	60.93	61.21	61.08	61.35	61.26
CN	--	--	--	113.7	114.8	113.4	114.5	113.6
C=O	169.5 169.7 170.3	169.4 169.7 170.4	169.3 169.8 170.6	169.2 169.6 170.2	169.5 169.8 170.3	170.3 169.6 169.5	170.4 169.7 169.4	170.5 169.6 169.3
CH_3	20.6 20.6 20.6	20.5 20.6 20.6	20.4 20.6 20.6	20.5 20.5 20.6	20.5 20.5 20.6	20.6 20.5 20.5	20.6 20.5 20.4	20.6 20.5 20.4
$^{1}J_{C-1,H-1}$	180.4	180.4	181.1	160.3	151.4	160.7	149.4	160.2

respectively, and β-D-galacto,gluco $J_{1a,2a}$ = 8.8, 10 Hz for compounds 10 and 11, respectively. Assigned configurations[28,48] were confirmed by the chemical shifts of H-1.

Infrared spectra of glycosyl cyanides 7, 8, 17 and 18 showed a characteristic azide peak at ~2110-2120 cm^{-1}, but no absorption in the 2800-1900 cm^{-1} region for cyanide, in agreement with previous reports.[15,16,19,26] Optical rotations of the compounds obeyed Hudson's rule of isorotation.

Myers and Lee[19] reported yields of 2.9% for preparation of the α-D anomer (the 1,2-*cis* product) and 79% for preparation of the β-D anomer (the 1,2-*trans* product) of 2,3,4,6-tetra-*O*-acetyl-D-galactopyranosyl cyanide from 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide. By comparison, reported yields for the preparation of 2,3,4,6-tetra-*O*-acetyl-D-glucopyranosyl cyanides from 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide were 1.1% for the α-D anomer and 20% for the β-D anomer.[19] Reported yields of 2,3,4,6-tetra-*O*-acetyl-D-mannopyranosyl cyanides prepared from the corresponding glycosyl bromide were 37% for the α-D anomer and 3.3% for the β-D anomer.[19]

The increase in the proportion of the α-D anomer in the case of the 2-azido-2-deoxy compound is probably due to the absence of a participating group (an acyloxyl group) on C-2. The overall lower yield in the case of the 2-azido-2-deoxy cyanides may reflect a decreased reactivity of the corresponding glycosyl bromide that results from the relatively greater electron-withdrawing effect of the azido group as compared to an acetoxyl group. Paulsen and Kolar[49] reported that 2-azido-2-deoxy sugars required a more reactive catalyst for *O*-glycosidation than did the corresponding sugars with a protected amino or hydroxyl group on C-2. The ground state azido group exerts an electron-withdrawing effect by induction.[50,51] The decreased yield may also be due to the azido group being transformed by the weak Lewis acid, mercuric cyanide, into a highly reactive nitrene which decomposes rapidly. Use of a more reactive halide, the glycosyl iodide, improved the yields of the 2-azido-2-deoxyglycosyl cyanides only slightly. However, the increased reactivity of the 2-azido-2-deoxyglycosyl iodides also make them more sensitive to moisture, resulting in more by-products. However, since the glycosyl iodide was not isolated, this method saved considerable time and gave yields comparable to those

obtained by the method involving glycosyl bromide preparation. Comparative yields of the per-*O*-acetyl-2-azido-2-deoxyglycosyl cyanides, based on the glycosyl nitrate as the starting compound, were as follows: (via glycosyl iodides) D-galacto (24%), D-gluco (26%), D-manno (22%); (via glycosyl bromides) D-galacto (19%), D-gluco (20%), D-manno (19%).

We have hereby demonstrated that reaction of 3,4,6-tri-*O*-acetyl-2-azido-2-deoxyaldohexopyranosyl halides with mercuric cyanide in nitromethane provides a regioselective synthesis of the corresponding 3,4,6-tri-*O*-acetyl-2-azido-2-deoxyaldohexopyranosyl cyanides. The reaction is more stereoselective than the reaction of the corresponding 2-acetoxyglycosyl halides with mercuric cyanide and, thereby, provides a higher percentage of the α-D-anomer in lower overall yields, as compared to those obtained with the 2-acetoxyglycosyl halides, for compounds with the D-galacto and D-manno configuration and in slightly greater overall yield for compounds with the D-gluco configuration.

None of the yields were optimized.

EXPERIMENTAL

Materials. The following materials were obtained from the sources indicated and used without further treatment: Celite filter aid 545 (Fisher Scientific Co.), molecular sieves type 4Å (Aldrich Chemical Co.), Sephadex LH-20 (Pharmacia), silica gel 60 (E. Merck), mercuric cyanide, 99.7% (Aldrich Chemical Co.), tri-*O*-acetyl-D-glucal (Aldrich Chemical Co.). Acetonitrile (Aldrich Chemical Co.) was distilled from CaH_2 and stored over molecular sieves. Nitromethane (Aldrich Chemical Co.) was distilled from anhydrous $CaSO_4$ and stored over molecular sieves.

General Methods. Melting points were determined with a Thomas-Hoover Uni-melt apparatus and are uncorrected. Optical rotations were determined at 25±2 °C with a Perkin Elmer 241 digital polarimeter using a 1-dm cell. Infrared spectra were recorded with a Nicolet 20DX FT-IR spectrophotometer in the solvents indicated. NMR spectra (^1H and ^{13}C) of $CDCl_3$ solutions were recorded with a Nicolet NT-200 (200 MHz) FT-NMR or a Varian XL 400 (400 MHz) FT-NMR spectrometer. Chemical shifts (δ) are reported with references to tetramethylsilane. Two-dimensional,

neterocorrelated spectra were obtained using the Varian instrument and the Varian Hetcor program. The $^{1}J_{C-1,H-1}$ values were measured by means of gated decoupling. High-resolution mass spectra were obtained from the Midwest Center for Mass Spectrometry (Lincoln, Nebraska). Microanalyses were performed by Micronal (Tucson, Arizona). Solutions were evaporated under reduced pressure at <40 °C.

Column chromatography was conducted on silica gel 60 (230-400 mesh, E. Merck). Compounds purified by gel filtration were chromatographed on a 2.0 X 190-cm column of Sephadex LH-20 equilibrated and eluted with 95% ethanol; a loading of less than 2.5 g was used, and 7-mL fractions were collected. The solvent systems used for both column and thin-layer chromatography were as follows (v/v): A, 7:3 benzene-ethyl acetate; B, 8:2 toluene-ethyl acetate; C, 7:3 pet. ether-ethyl acetate; D, 6:4 pet. ether-diethyl ether; E, 9:1 chloroform-diethyl ether; F, 100:1 chloroform-methanol; G, 7:3 toluene-ethyl acetate. TLC was conducted on silica gel 60 F254 precoated aluminum sheets (E. Merck). Components on TLC plates were detected by spraying with 15% (v/v) sulfuric acid in 50% (v/v) aqueous ethanol and heating for several minutes at ~150 °C.

3,4,6-Tri-*o*-acetyl-1,5-anhydro-2-deoxy-D-*lyxo*-[52] and -D-*arabino*-hex-1-enitol,[28] 3,4,6-tri-*o*-acetyl-2-azido-2-deoxy-α,β-D-galactopyranosyl nitrate (1,2),[28] 3,4,6-tri-*o*-acetyl-2-azido-2-deoxy-α-D-talopyranosyl nitrate (3),[28] and 3,4,6-tri-*o*-acetyl-2-azido-2-deoxy-α-D-galactopyranosyl bromide (4)[28] were prepared as previously described.

3,4,6-Tri-O-acetyl-2-azido-2-deoxy-α,β-D-galactopyranosyl Cyanide (7,8). Method A. A mixture of mercuric cyanide (1.58 g, 6.26 mmol), 4 Å molecular sieves (0.5 g) and nitromethane (15 mL) was stirred at room temperature for 20 min before adding crystalline 3,4,6-tri-*o*-acetyl-2-azido-2-deoxy-α-D-galactopyranosyl bromide (4) (2.445 g, 6.203 mmol). After stirring for 60 h in the dark, the mixture was diluted with dichloromethane (100 mL) and filtered through Celite, which was then washed with dichloromethane (100 mL). The filtrate was washed with M KBr (3 X 33 mL), dried with anhydrous sodium sulfate, filtered, and concentrated to a syrup (2.55 g). Compounds 7 and 8 were isolated by silica gel 60 column chromatography (2.5-cm diam., 100 g) using solvent E (500 mL). The β-D anomer 8 was crystallized from 95% ethanol to give 0.360 g (1.058 mmol) of 4 (17.05%). The α-D anomer (7) was also crystallized from 95% ethanol to give 0.429 g of material. The mother

liquor was purified by Sephadex LH-20 chromatography. In this way, an additional 0.096 g was recovered; total recovered yield of α-D anomer was 0.525 g (1.542 mmol) (24.9% from 14), calculated for MH^+ 341.1098, measured by mass spectral analysis 341.1095.

Method B. Crystalline 1 (4.0 g, 10.63 mmol) was added to a solution of lithium iodide (9.96 g, 74.4 mmol) in dry acetonitrile (40 mL). This solution was stirred at room temperature for 20 min. (The next steps until the addition of mercuric cyanide were done as quickly as possible.) The reaction solution was then diluted with dichloromethane (80 mL) and washed with cold, saturated, aqueous sodium thiosulfate (80 mL). The organic layer was collected, washed with ice water (2 X 80 mL), dried with anhydrous sodium sulfate, filtered, and concentrated to a syrup. 3,4,6-Tri-*O*-acetyl-2-azido-2-deoxy-α-D-galactopyranosyl iodide (5) was not purified. It was immediately dissolved in dry nitromethane (40 mL) and reacted with mercuric cyanide (2.68 g, 10.63 mmol) in the dark. After 57 h at room temperature, no starting material was detected by TLC (solvents C, E), and the reaction mixture was diluted with dichloromethane (100 mL) and filtered through Celite. The filter cake was washed with dichloromethane (150 mL). The filtrate was washed with 120 mL of M KBr (3 X 40 mL), dried with anhydrous sodium sulfate, filtered, and concentrated to a syrup (2.86 g). The syrup was purified by column chromatography on a 110-g silica gel 60 column (3-cm diam.) to give 0.92 g of recovered material. The syrup was further purified by gel filtration on a Sephadex LH-20 column to afford 0.875 g (2.57 mmol) of 7 and 8 (24% from 1).

3,4,6-Tri-O-acetyl-2-azido-2-deoxy-α,β-D-glucopyranosyl Nitrate (9,10) and 3,4,6-Tri-O-acetyl-2-azido-2-deoxy-α-D-mannopyranosyl Nitrate (11). At -20 °C in a dry argon atmosphere, 3,4,6-tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-*arabino*-hex-1-enitol (27.2 g, 100 mmol) in 500 mL of acetonitrile (0.2 M solution) was added to a mixture of sodium azide (150 mmol, 9.75 g) and ceric ammonium nitrate (300 mmol, 164.74 g). The reaction mixture was stirred under argon (~20.5 h) until no starting material was detected by TLC (solvent A or B) [9 and 10 appear on TLC as one spot (R_f 0.57, solvent A); 11 has a slightly higher R_f (0.61, solvent A).] The reaction mixture was poured into a 2-L separatory funnel containing diethyl ether (600 mL) and ice water (600 mL). The organic layer was collected, and the aqueous portion was extracted with

additional diethyl ether (200 mL). The organic extracts were combined, washed with water (3 X 600 mL), dried with anhydrous sodium sulfate, filtered, and concentrated to a yellow syrup (33.19 g) that was dissolved in diethyl ether (90 mL) and allowed to crystallize overnight at 0 °C; 11.44 g (30.40 mmol) of a crystalline mixture of 9 and 11 was recovered. The mother liquor (21.75 g) was chromatographed on a 340-g silica gel 60 column (5-cm diam.) using 1 L of solvent G to give additional pure azidonitration products (9-11); yield 18.84 g (50.0 mmol). The syrupy mixture was dissolved in diethyl ether (50 mL) and allowed to crystallize as before to give an additional 5.01 g (13.31 mmol) of a crystalline mixture of 9 and 11. The mother liquor contained primarily 10 and lesser amounts of 9 and 11. The overall isolated yield of the azidonitration products (9-11) from "tri-*O*-acetyl-D-glucal" was 80% (30.28 g), of which 55% (16.54 g) was crystalline 9 + 11.

3,4,6-Tri-O-acetyl-2-azido-2-deoxy-α-D-glucopyranosyl Nitrate (9). Compound 9 was obtained from a crystalline mixture (11.44) of 9 and 11 by fractional recrystallization from dichloromethane (25 mL) at -10 °C (24 h). The recovered crystals (2.96 g) were found by TLC (solvent A) to contain primarily 9 and a small amount of 11 which was removed by two recrystallizations (dissolution in dichloromethane, concentration, evaporation, and addition of 10 mL of diethyl ether). In this way an analytically pure sample of 2.22 g of 10 was obtained.

3,4,6-Tri-O-acetyl-2-azido-2-deoxy-β-D-glucopyranosyl Nitrate (10) and 3,4,6-Tri-O-acetyl-2-azido-2-deoxy-α-D-mannopyranosyl Nitrate (11). A syrupy mixture of 10, 11 and some 9 (6.0 g, obtained by concentration of the mother liquor from the original crystallization of 9 and 11) was dissolved in a minimal amount of ethyl acetate; hexane was added to opalescence, and the solution was allowed to crystallize at room temperature for several hours before being held at 0 °C overnight. The recovered crystals (4.6 g) contained 11 contaminated with some 9, which was removed by recrystallization from ethyl acetate-hexane as before. The mother liquor (1.4 g), which contained 10 contaminated by 9 and 11, was chromatographed on a 80-g silica gel 60 column (3-cm diam.) using solvent E (400 mL) to give ~60 mg of pure 10.

3,4,6-Tri-O-acetyl-2-azido-2-deoxy-α-D-glucopyranosyl Bromide (12). Anhydrous lithium bromide (25 mmol, 2.17 g) and powdered Drierite (1 g) were stirred in dry acetonitrile (19 mL) under argon at room

temperature for 30 min before addition of 9 (5 mmol, 1.88 g). The reaction was conducted in the dark and followed by TLC using a double development system; the chromatogram was first developed in solvent D, then dried, then developed in solvent E. This system revealed a by-product with a slightly higher R_f (0.55) value then the product (R_f 0.53) and three by-products with much lower R_f values. After 9.5 h, the reaction mixture was diluted with dichloromethane (35 mL), washed with water (3 X 15 mL), dried with anhydrous sodium sulfate, and concentrated. Compound 21 was isolated from the residue by silica gel 60 chromatography using 3:1 v/v pet. ether-ethyl acetate. The yield was 1.43 g (3.6 mmole, 72%).

3,4,6-Tri-O-acetyl-2-azido-2-deoxy-α,β-D-glucopyranosyl Cyanide (16,17). Method A. Mercuric cyanide (2.0 g, 7.9 mmol) was added to a solution of 12 (2.18 g, 5.5 mmol) in nitromethane (21 mL), and the mixture was stirred for 77 h in the dark. The reaction was followed by TLC using either solvent C or E. The mixture was diluted with dichloromethane (50 mL) and filtered through Celite, which was then washed with dichloromethane (100 mL). The filtrate was washed with M KBr (3 X 30 mL), dried with anhydrous sodium sulfate, and concentrated. Compounds 16 and 17 were isolated by silica gel 60 column chromatography (3-cm diam., 90 g) using solvent E. The β-D anomer (17) crystallized from 95% ethanol to give 0.18 g (0.53 mmol, 9.6%). The α-D anomer (16) was purified by Sephadex LH-20 chromatography using 95% ethanol. The yield was 0.348 g (1.02 mmol, 18.5%) of syrup; calculated for MH^+ 341.1098, measured by mass spectral analysis 341.1095.

Method B. Crystalline 9 (3.33 g, 8.84 mmol) was added to a mixture of anhydrous lithium iodide (9.22 g, 68.89 mmol) and powdered 4 Å molecular sieves (0.5 g) in dry acetonitrile (35 mL). The mixture was stirred at room temperature for 20 min, diluted with dichloromethane (80 mL) and washed with cold, saturated, aqueous sodium thiosulfate (80 mL). The organic layer was collected and washed with ice water (2 X 80 mL), dried with anhydrous sodium sulfate, filtered, and concentrated to a syrup. 3,4,6-Tri-*O*-acetyl-2-azido-2-deoxy-α-D-glucopyranosyl iodide (13) was not purified. It was immediately dissolved in nitromethane (35 mL) and reacted with mercuric cyanide (2.50 g, 9.90 mmol). After 57.5 h in the dark, no starting material was observed by TLC, and the reaction mixture was diluted with dichloromethane (100 mL) and filtered through

Celite. The filter cake was washed with additional dichloromethane (150 mL). The filtrate was washed with 120 mL of M KBr (3 X 40 mL), dried with anhydrous sodium sulfate, filtered, and concentrated to a brown residue. Compounds **16** and **17** (0.75 g of syrup) were isolated by column chromatography on a 110-g silica gel 60 column (2.5-cm diam.). The syrup was further purified by chromatography on a Sephadex LH-20 column to give 0.5898 g (1.733 mmol) of **16** and **17** (19.6% from **10**).

3,4,6-Tri-O-acetyl-2-azido-2-deoxy-α-D-mannopyranosyl Bromide (14). Crystalline **11** (2.5 g, 6.64 mmol) was added to a suspension of lithium bromide (2.9 g, 33.4 mmol) in dry acetonitrile (25 mL), and the suspension was stirred at room temperature. The reaction was followed by a double development system; the chromatograph was first developed in solvent D, then dried, then developed in solvent E. After 8 h in the dark, no starting material was detected by TLC. The reaction mixture was diluted with dichloromethane (100 mL), washed with ice water (4 X 20 mL), dried with anhydrous sodium sulfate, filtered, and the solvent evaporated. The residue was purified on a 90-g column of silica gel 60 (3-cm diam.) using solvent C (500 mL); 1.99 g of **14** (76% from **11**) was recovered.

3,4,6-Tri-O-acetyl-2-azido-2-deoxy-α-D-mannopyranosyl Cyanide (18). Method A. 3,4,6-Tri-*o*-acetyl-2-azido-2-deoxy-α-D-mannopyranosyl bromide (**14**) (0.7040 g, 1.786 mmol) was dissolved in nitromethane (17 mL). Mercuric cyanide (0.5 g, 1.98 mmol) was added, and the reaction mixture was stirred for 60 h in the dark. The reaction mixture was diluted with dichloromethane (50 mL) and washed twice with M KBr (15 mL); the combined aqueous KBr washings were extracted with dichloromethane (10 mL). The combined organic extracts were washed with additional M KBr (15 mL), dried with anhydrous sodium sulfate, filtered, and concentrated to give 0.73 g of a syrup. The syrup was dissolved in solvent C (1 mL) and placed on a 40 g silica gel 60 column (2-cm diam.) and eluted with solvent C (500 mL) to afford 0.27 g of crude **18**. The crude syrup was further purified by gel filtration to give 0.167 g of pure **18** (0.49 mmol, 28% from **14**). Calculated for MH^+ 341.1098, measured by mass spectral analysis 341.1098.

Method B. Crystalline **11** (2.50 g, 6.64 mmol) and lithium iodide (7.47 g, 55.8 mmol) were dissolved in acetonitrile (25 mL) and stirred in the dark at room temperature for 20 min. (The solution became warm

during the course of the reaction.) The mixture was then poured into a separatory funnel containing cold saturated sodium thiosulfate solution (50 mL) and dichloromethane (50 mL). The organic layer was washed with cold water (2 X 50 mL) and dried with anhydrous sodium sulfate, filtered, and concentrated to give 2.41 g of a yellow foam. 3,4,6-Tri-*O*-acetyl-2-azido-2-azido-2-deoxy-α-D-mannopyranosyl iodide (15) was not purified. It was immediately dissolved in nitromethane (20 mL) and reacted with mercuric cyanide (1.70 g, 6.73 mmol) in the dark. The reaction mixture was stirred for 64.5 h and then was filtered through Celite. The filter cake was washed with dichloromethane (100 mL). The filtrate was washed with 100 mL of M KBr (3 X 33 mL) dried with anhydrous sodium sulfate, filtered, and the solvent evaporated to give 2.48 g of a yellow syrup. The syrup was purified by column chromatography on a 80-g silica gel 60 column (3-cm diam.), recovering 0.62 g of material. Chromatography of this material on a Sephadex LH-20 column gave 0.499 g (1.47 mmol) of pure 18 (22% from 11).

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