Carbohydrate Research, 132 (1984) 61–82
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

SYNTHESIS AND CHARACTERIZATION OF SOME ANOMERIC PAIRS OF PER-*O*-ACETYLATED ALDOHEXOPYRANOSYL CYANIDES (PER-*O*-ACETYLATED 2,6-ANHYDROHEPTONONITRILES). ON THE REACTION OF PER-*O*-ACETYLALDOHEXOPYRANOSYL BROMIDES WITH MERCURIC CYANIDE IN NITROMETHANE*

ROBERT WALTER MYERS** AND YUAN CHUAN LEE***
Department of Biology and The McCollum-Pratt Institute, The Johns Hopkins University, Baltimore, Maryland 21218 (U.S.A.)

(Received February 14th, 1984; accepted for publication, March 8th, 1984)

ABSTRACT

The synthesis and characterization of the anomeric pairs of the per-*O*-acetylaldohexopyranosyl cyanides of D-galactose, L-fucose, D-glucose, and D-mannose, as well as of 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl cyanide, are described. Cyanation of the readily available, per-*O*-acetylaldohexopyranosyl bromides with mercuric cyanide in nitromethane, and subsequent purification, gave the corresponding, crystalline glycosyl cyanides with a high degree of 1,2-*trans* stereoselectivity. Thus, per-*O*-acetylated aldohexopyranosyl cyanides of the 1,2-*trans* configuration were obtained in yields ranging from 20 to 79%, whereas the corresponding 1,2-*cis* anomers were obtained in yields of ≤8.4%, the ratios of the 1,2-*trans*:1,2-*cis* anomers so prepared being ≥8.5:1. The principal by-products of these irreversible, cyanation reactions were the per-*O*-acetylated 1,2-*O*-[1-(*exo*- and *endo*-cyano)ethylidene]aldohexopyranoses, obtained in yields of up to 40%. The structural assignments of the per-*O*-acetylaldohexopyranosyl cyanides were unequivocally established by elemental analysis, chemical transformation, vibrational spectroscopy, and ^{13}C- and ^{1}H-nuclear magnetic resonance spectroscopy. Correlations between the physical properties and the anomeric configurations of these *C*-aldohexopyranosyl compounds are described.

INTRODUCTION

Aldohexopyranosyl cyanides (2,6-anhydroheptononitriles) are anomerically functionalized, one-carbon-extended *C*-glycosyl compounds that have been utilized for the preparation of carbohydrate analogs having biochemical interest,

*Contribution No. 1246 from The McCollum-Pratt Institute, The Johns Hopkins University. Supported by USPHS, NIH Research Grants AM 9970 and CA 21091.
**Supported by NIH National Research Service Award GM 07231.
***To whom all correspondence should be addressed.

0008-6215/84/$ 03.00

including pseudo-substrates[1], competitive inhibitors[2], and irreversible inhibitors[3]. These synthetically versatile compounds are of further interest as alternative precursors to other *C*-aldohexopyranosyl compounds synthesized as potential, reversible[4] and irreversible[5] inhibitors, and as synthons for the preparation of pyranoid analogs of *C*-nucleoside antibiotics[6]. Moreover, aldohexopyranosyl cyanides are promising intermediates for the stereospecific synthesis of natural products containing a polyhydroxytetrahydropyran moiety having functionalized alkyl substituents at C-2 and C-6 of the pyranoid ring[7]. In an even broader sense, these carbohydrate derivatives may be regarded as chiral synthons useful for the asymmetric synthesis of a variety of target molecules[8].

As part of a synthetic program[9] for the preparation of a series of *C*-glycosyl compounds that might potentially be used as mechanism-based, irreversible inhibitors and (photo)affinity-labeling reagents for glycosidases and other carbohydrate-binding proteins, we needed the 1,2-*trans*- and 1,2-*cis*-glycosyl cyanide derivatives of several, naturally occurring aldohexopyranoses. However, relatively few aldohexopyranosyl cyanides had been described when this project was initiated. To the best of our knowledge, the only examples were 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl cyanide[10–13], 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl cyanide[13–15], and the 2,3,4-tri-*O*-benzoyl-α,β-L-rhamnopyranosyl cyanides[16]. We now detail the results of our initial studies on the synthesis of the anomeric pairs of the per-*O*-acetylaldohexopyranosyl cyanides of D-galactose, L-fucose, D-glucose, and D-mannose, as well as of 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl cyanide (compounds **1–9**), by using the well known[6,10,11,14,16] reaction of per-*O*-acylglycosyl bromides with mercuric cyanide in nitromethane. A preliminary account of this work has been presented[9].

While this report was in preparation, Grynkiewicz and BeMiller[17,18] reported the synthesis of several new aldohexopyranosyl cyanides by dehydration of the corresponding, per-*O*-acetylated 2,6-anhydroheptonamides[19] with chloromethylenedimethylforminium chloride, and the preparation of 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl cyanide in low yield from the reaction of the corresponding glycosyl bromide with mercuric cyanide in acetonitrile. The latter nitrile had been reported by Lemieux *et al.*[20] in 1976 as "the major product" resulting from the attempted glycosylation of trichloroethanol with the same β-bromide, using mercuric cyanide as the catalyst, but no further details have yet been made available by them.

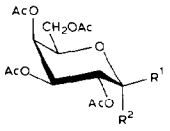
RESULTS AND DISCUSSION

Preparation of per-O-acetylaldohexopyranosyl cyanides **1–9**. — Treatment of 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide with one equivalent of mercuric cyanide in dry nitromethane for 48 h at room temperature according to the method originally described by Helferich and Bettin[10] gave, after fractional crystallization, the expected 1,2-*trans* product, namely, 2,3,4,6-tetra-*O*-acetyl-β-D-

galactopyranosyl cyanide[10–13] (**2**), in 79% yield. Similar treatment of 2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl bromide gave the analogous 1,2-*trans* product of the L-*galacto* configuration, *viz.*, 2,3,4-tri-*O*-acetyl-β-L-fucopyranosyl cyanide (**4**), in 60% yield by fractional crystallization (71% total yield following purification of the resulting mother liquor). In addition, crystalline 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl bromide was similarly converted into the 1,2-*trans* product, namely, 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl cyanide (**7**), obtained in 67% yield by fractional crystallization. Alternatively, use of the more readily available, syrupy mixture of the 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-α,β-D-glucopyranosyl bromides gave **7** in 62% yield following purification by chromatography on silica gel and subsequent crystallization.

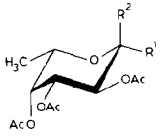
Compound **7** should prove useful as a precursor to various *N*-acylated *C*-(2-amino-2-deoxy-β-D-glucopyranosyl) derivatives by the application of well established[20] deblocking and selective *N*-acylation procedures. Interestingly, treatment of 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-gluco- and -galacto-pyranosyl chlorides with mercuric cyanide in nitromethane failed to produce the corresponding glycosyl cyanide derivatives[21]. In contrast, application of the Helferich procedure[10] to the 2,3,4,6-tetra-*O*-acetyl-α-D-gluco- and -manno-pyranosyl bromides generated complex reaction-mixtures from which the crystalline 1,2-*trans* nitriles, *viz.*, 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl cyanide[13,14] (**6**) and 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl cyanide (**8**), were obtained in yields of 20 and 37%, respectively, following chromatographic purification (see later).

Cyanation of the per-*O*-acetylaldohexopyranosyl bromide derivatives of α-D-galactose, α-L-fucose, α-D-glucose, and α-D-mannose with mercuric cyanide in nitromethane *also* generated (albeit in low yields) the corresponding 1,2-*cis*-glycosyl cyanides, namely, 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl cyanide (**1**), 2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl cyanide (**3**), 2,3,4,6-tetra-*O*-acetyl-α-D-gluco-pyranosyl cyanide (**5**), and 2,3,4,6-tetra-*O*-acetyl-β-D-mannopyranosyl cyanide (**9**). It was of interest to develop facile and efficient methods for the purification of these previously unknown 1,2-*cis*-glycosyl cyanides to homogeneity. This was accomplished, despite the complexity of the reaction mixtures in which these minor products were found, by using the purification methods to be described.



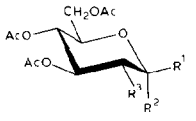
1 $R^1 = H, R^2 = CN$
2 $R^1 = CN, R^2 = H$

D-*galacto*



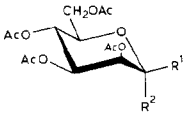
3 $R^1 = H, R^2 = CN$
4 $R^1 = CN, R^2 = H$

6-deoxy-L-*galacto*



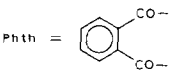
5 $R^1 = H, R^2 = CN, R^3 = OAc$
6 $R^1 = CN, R^2 = H, R^3 = OAc$
7 $R^1 = CN, R^2 = H, R^3 = NPhth$

D-*gluco*



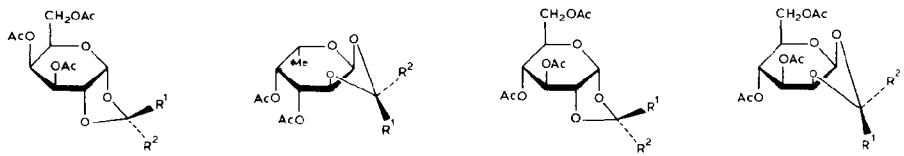
8 $R^1 = H, R^2 = CN$
9 $R^1 = CN, R^2 = H$

D-*manno*



Per-*O*-acetylated 1,2-*O*-[1-(*exo*- and *endo*-cyano)ethylidene]aldohexopyranoses[14,22] were by-products of some of these cyanation reactions. Similarities in the physical properties of the per-*O*-acetylated aldohexopyranosyl cyanides and their 1,2-*O*-(1-cyanoethylidene) regioisomers complicated the (preparative scale) isolation and purification of the desired glycosyl cyanides from such mixtures. Accordingly, purification of the 2,3,4,6-tetra-*O*-acetyl-α,β-D-glucopyranosyl cyanides (**5**, **6**), as well as of 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl cyanide (**1**) employed selective, acid hydrolysis of the corresponding per-*O*-acetylated 1,2-*O*-[1-(*exo*- and *endo*-cyano)ethylidene]-α-D-glucopyranose (**12A** and **12B**) and -galactopyranose (**10A** and **10B**) contaminants. Preliminary experiments[21] demonstrated that treatment of **10A/B** (ref. 22) or **12A/B** (ref. 22) with 9:1 (v/v) trifluoroacetic acid–water (~0.25M "orthocyanide" derivative) for 30 min at 55° effected complete cleavage of the α-oriented 1,2-*O*-(1-cyanoethylidene) linkage. Per-*O*-acetylated aldohexopyranosyl cyanides (**1**, **2**) and (**5**, **6**) were stable to these conditions. Treatment of Helferich reaction-products containing mixtures of these regioisomers (**1**, **2** and **10A/B**; **5**, **6** and **12A/B**) essentially as just described gave similar results. The multiple hydrolysis products arising from the 1,2-*O*-(1-cyanoethylidene) derivatives (**10A/B** and **12A/B**) were readily removed by gel filtration, or chromatography on silica gel, from the unaltered, less polar glycosyl cyanides (**1**, **2** and **5**, **6**), thereby facilitating the preparative-scale isolation of compounds **1**, **5**, and **6** without lowering their yields. These results are reflected in the higher yield of 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl cyanide (**6**) obtained by our purification procedure (20%) relative to that previously reported[14] (12%).

Selective, acid hydrolysis could not be employed in the purification of the 2,3,4,6-tetra-*O*-acetyl-α,β-D-mannopyranosyl cyanides (**8**, **9**), owing to the marked resistance of the 3,4,6-tri-*O*-acetyl-1,2-*O*-[1-(*exo*- and *endo*-cyano)ethylidene]-β-D-mannopyranoses (**13A** and **13B**) to cleavage by aqueous acid[21]. Thus, although treatment[22] of **13A** or **13B** in 9:1 (v/v) trifluoroacetic acid–water (~0.25M "orthocyanide" derivative) for 90 min at 55° effected hydrolysis of the majority of the β-oriented, 1,2-*O*-(1-cyanoethylidene) linkages, these conditions also resulted in considerable hydrolysis of the desired glycosyl cyanides **8** and **9**. Therefore, more-tedious methods were required for purification of the per-*O*-acetyl-α,β-D-mannopyranosyl cyanides. Interestingly, the conditions needed in order to hydrolyze both the α- and β-oriented 1,2-*O*-(1-cyanoethylidene) linkages are considerably



10A R^1 = CN, R^2 = Me
10B R^1 = Me, R^2 = CN
D-*galacto*

11A R^1 = CN, R^2 = Me
11B R^1 = Me, R^2 = CN
6-deoxy-L-*galacto*

12A R^1 = CN, R^2 = Me
12B R^1 = Me, R^2 = CN
D-*gluco*

13A R^1 = CN, R^2 = Me
13B R^1 = Me, R^2 = CN
D-*manno*

A = *exo*-cyano, B = *endo*-cyano

more vigorous than those required for the cleavage of isopropylidene and benzylidene acetals, using the same reagent[21,23].

Following crystallization and recrystallization, or selective acid hydrolysis where applicable, or both, the remaining per-*O*-acetylaldohexopyranosyl cyanides were purified by chromatographic methods. Gel-filtration chromatography using Sephadex LH-20 provided a most efficacious method of purifying the anomeric per-*O*-acetylaldohexopyranosyl cyanides. These compounds were retarded similarly under the conditions of elution, owing to their relatively enhanced hydrophobicity, whereas most of the by-products, either present in the crude reaction-mixtures or generated by selective acid hydrolysis of the 1,2-*O*-(1-cyanoethylidene) derivatives, were eluted earlier. However, the anomeric per-*O*-acetylaldohexopyranosyl cyanides and their 1,2-*O*-[1-(*exo*- and *endo*-cyano)ethylidene] regioisomers were co-eluted in gel-filtration chromatography. Separate experiments utilized[21] this result to establish the approximate yield of the 1,2-*O*-(1-cyanoethylidene) derivatives from these reactions (see later). Chromatography on silica gel was therefore employed to separate the per-*O*-acetylated 1,2-*cis*-aldohexopyranosyl cyanides from the corresponding, more readily crystallizable 1,2-*trans* anomers, and also to separate glycosyl cyanides **8** and **9** from 1,2-*O*-[1-(*exo*- and *endo*-cyano)ethylidene] derivatives **13A** and **13B**. Although the diethyl ether–petroleum ether solvent systems provided the best resolution, we generally elected to use the less hazardous 100:1 (v/v) chloroform–methanol for column chromatography. However, silica-gel chromatography with 2:1 (v/v) diethyl ether–petroleum ether as the eluant had to be employed to separate 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl cyanide (**8**) from the more readily crystallizable **13A** (which exhibited a slightly lower R_F value in this solvent). Purification of 2,3,4,6-tetra-*O*-acetyl-β-D-mannopyranosyl cyanide (**9**) from the lower R_F **13B** was most readily accomplished by using 3:1 (v/v) toluene–ethyl acetate as the eluant.

After chromatographic purification, per-*O*-acetylated 1,2-*trans*-aldohexopyranosyl cyanides **6** and **8**, as well as the 1,2-*cis* anomers **1**, **3**, **5**, and **9**, crystallized. The yields of crystalline per-*O*-acetylaldohexopyranosyl cyanides **1–9**, and some other salient features of these syntheses, are summarized in Table I.

*Structural analysis of per-*O*-acetylaldohexopyranosyl cyanides* **1–9**. — The structural assignments of per-*O*-acetylaldohexopyranosyl cyanides **1–9** were unequivocally established by elemental analysis, chemical transformation, vibrational spectroscopy, and ^{13}C- and ^{1}H-n.m.r. spectroscopy. A synopsis of the analytical data obtained for these compounds is presented in Table II. Inspection of Table II reveals that each of the previously unknown compounds (**1**, **3**, **4**, **5**, **7**, **8**, and **9**) gave the elemental analysis expected for a per-*O*-acetylhexopyranosyl cyanide. The physical properties of compounds **2** and **6** were in complete agreement with those reported for 2,3,4,6-tetra-*O*-acetyl-β-D-galacto-[10–13] and -gluco-[13,14] pyranosyl cyanides, respectively.

Chemical transformation[9,21] provided evidence for the structure of several of the products obtained. Thus, compounds (**1**, **2**), (**5**, **6**), and (**8**, **9**) were stable to

TABLE I

RESULTS OF THE REACTIONS OF VARIOUS PER-*O*-ACETYLATED ALDOHEXOPYRANOSYL BROMIDES WITH MERCURIC CYANIDE IN NITROMETHANE[a]

Starting bromide		*Per-O-acetylated aldohexopyranosyl cyanides produced*					*Per-O-acetylated 1,2-O-(1-cyano-ethylidene)aldohexopyranose produced*			*Glycosyl cyanide: "orthocyanide"*	*Glycosyl cyanide + "orthocyanide"[c] (%)*
Parent sugar	*Anomer*	*Compound*	*Anomer*	*Yield[b] (%)*	*1,2*-trans: *1,2*-cis	*Total yield (%)*	*Compound*	*Anomer*	*Total yield[c] (%)*		
D-Gal	α	**1**	α	2.9	27:1	82	**10A/B**	α	5	16:1	90
		2	β	79							
L-Fuc	α	**3**	α	8.4	8.5:1	79	**11A/B**	α	0	—	80
		4	β	71							
D-Glc	α	**5**	α	1.1	18:1	21	**12A/B**	α	25	0.8:1	45
		6	β	20							
D-Man	α	**8**	α	37	11:1	40	**13A/B**	β	40	1:1	80
		9	β	3.3							
D-GlcNPhth	β	**7**	β	67[d]	—	67	—	—	—	—	67

[a]Reaction conditions: 1 mmol $Hg(CN)_2$/mmol bromide, 2 mL CH_3NO_2/mmol bromide, room temperature, 48 h. [b]Yield of crystalline product. [c]Approximate yields[21]. [d]No other cyanated glycoses were detected.

TABLE II

PROPERTIES OF PER-*O*-ACETYLATED ALDOHEXOPYRANOSYL CYANIDES **1–9**

Compound	*Parent sugar*	*Anomer*	R_F[a] *in t.l.c.*	*Melting point*[b] *(°C)*	$[\alpha]_D$ *(degrees)*[c] *(c, in $CHCl_3$)*	*Analytical data*						ν(-C≡N)[d] *(cm^{-1})*	^{1}H-N.m.r.[e]		^{13}C-N.m.r.[e,f]	
						Calculated			*Found*				*δ H-1 (p.p.m.)*	$J_{1,2}$ *(Hz)*	*δ-C≡N (p.p.m.)*	*δ C-1 (p.p.m.)*
						C	*H*	*N*	*C*	*H*	*N*					
1	D-Gal	*α*	0.30[A], 0.46[D]	93–94	+131.0 (3.50)	50.39	5.36	3.92	50.32	5.31	3.85	2244	5.182	5.6	114.1	65.0
2	D-Gal	*β*	0.19[A], 0.38[D]	169–170	+35.7 (3.74)	50.39	5.36	3.92		n.d.[g]		2257	4.298	10.1	114.5	66.1
3	L-Fuc	*α*	0.30[B], 0.54[D]	97–98	−161.9 (3.50)	52.15	5.72	4.68	52.29	5.73	4.64	2242	5.123	5.8	114.5	65.1
4	L-Fuc	*β*	0.18[B], 0.47[D]	124–125	−33.1 (2.98)	52.15	5.72	4.68	52.20	5.60	4.63	2262	4.264	10.4	114.9	66.2
5	D-Glc	*α*	0.29[A], 0.45[D]	111–112	+125.0 (3.43)	50.39	5.36	3.92	50.42	5.37	4.11	2243	5.138	6.2	113.8	65.2
6	D-Glc	*β*	0.20[A], 0.38[D]	114–115	+10.7 (3.28)	50.39	5.36	3.92		n.d.		2256	4.330	10.1	114.3	66.4
8	D-Man	*α*	0.24[A], 0.45[D]	58–60	+28.6 (3.36)	50.39	5.36	3.92	50.34	5.32	4.07	2242	4.906	2.0	113.6	65.1
9	D-Man	*β*	0.15[A], 0.37[D]	142–144	−20.9 (3.76)	50.39	5.36	3.92	50.40	5.26	4.00	2259	4.588	1.4	113.9	64.9
7	D-GlcNPhth	*β*	0.21[A], 0.39[D]	176–178	+68.8 (1.03)	56.73	4.53	6.30	56.74	4.60	6.19	—	5.38	10.5	114.3	64.4

[a]Solvent systems: (*A*) 3:1 (v/v) diethyl ether–petroleum ether, (*B*) 3:2 (v/v) diethyl ether–petroleum ether, and (*D*) 100:1 (v/v) chloroform–methanol. [b]Uncorrected. [c]Room temperature. [d]See ref. 26. [e]In $CDCl_3$. [f]C-1 assignments tentative. [g]n.d., not determined.

aqueous acid under conditions where the acetal linkage of the corresponding 1,2-*O*-(1-cyanoethylidene) derivatives is hydrolyzed. Glycosyl isocyanides would be expected to be transformed into *N*-glycosylformamides and, possibly, into reducing sugars under these conditions[24a]. Zemplén deacetylation of compounds **2** and **6**, followed by alkaline hydrolysis, gave the corresponding sodium 2,6-anhydroheptonates. This derivative (of **2**) had previously been described[25]. These sodium carboxylates were readily converted into the corresponding, known free acids[15] by treatment with an appropriate ion-exchange resin. Acetylation of the carboxylates by using acetic anhydride–*p*-toluenesulfonic acid gave the corresponding per-*O*-acetyl-2,6-anhydroheptonic acids. This derivative of **2** was recently described by Fritz *et al.*[1]. In addition, treatment of compounds **1, 2, 5,** and **6** with hydrogen bromide in glacial acetic acid yielded the corresponding per-*O*-acetyl-2,6-anhydroheptonamides, which can be deamidinated with dinitrogen tetraoxide to the corresponding per-*O*-acetyl-2,6-anhydroheptonic acids. The per-*O*-acetyl-2,6-anhydroheptonamide derivatives of compounds **1** and **5**, as well as several others, were reported by BeMiller and co-workers[19].

Direct evidence for the per-*O*-acetylaldohexopyranosyl cyanide structure of compounds **1–9** was obtained from ^{13}C-n.m.r. spectroscopy. Coxon[13] had demonstrated the value of this technique in the structural analysis of glycosyl cyanides and 1,2-*O*-(1-cyanoethylidene)glycoses. The 20-MHz, proton-noise-decoupled, ^{13}C-n.m.r. spectra of compounds **1–9** in $CDCl_3$ exhibited signals for the following carbon atoms: (1) -CO*C*H$_3$, 20.3–20.7 p.p.m., generally one high-intensity peak, often with a shoulder, although three closely spaced peaks were observed for **7**; (2) C-1–C-6 ("ring-carbon atoms"), 61–77 p.p.m., with the exception of C-6 of **3** and **4** (16.1 p.p.m.) and C-2 of **7** (52.4 p.p.m.); (3) -*C*≡N, one signal, of low-to-moderate intensity, from 113.6–114.9 p.p.m. (see Table II); and (4) -*C*OCH$_3$, 169–170.5 p.p.m., generally one signal per acetoxyl substituent present. In addition, the spectrum of **7** exhibited signals for the phthalimido substituent, that is, for the carbonyl (167.1 p.p.m.) and aromatic (124–135 p.p.m.) carbon atoms. In contrast, the ^{13}C-n.m.r. spectra of aldohexopyranosyl isocyanides exhibit no -*C*≡N resonance, but, instead, show[24] a low-intensity, -N≡*C* signal in the region of 162.3 to 166.1 p.p.m. Thus, compounds **1–9** are not isonitriles.

On the other hand, the ^{13}C-n.m.r. spectra[21] of the per-*O*-acetyl-1,2-*O*-[1-(*exo*- and *endo*-cyano)ethylidene]aldohexopyranose derivatives of α-D-galactose (**10A** and **10B**), α-D-glucose (**12A** and **12B**), and β-D-mannose (**13A** and **13B**) in $CDCl_3$ exhibit a -*C*≡N resonance in the region of 116.5 to 117.5 p.p.m. These signals are consistently 2.2–3.4 p.p.m. downfield from those of the corresponding glycosyl cyanides[21]. The spectra of **10A/B**, **12A/B**, and **13A/B** also display two signals in the midfield region, from 97.0 to 101.7 p.p.m., corresponding to the two carbon atoms that are each singly bonded to two oxygen atoms (C-1 of the pyranoid ring and C-2 of the 1,3-dioxolane ring), as well as two signals at high field, 20.5–20.7 (-CO*C*H$_3$) and 24.3–27.1 p.p.m. (1,3-dioxolane ring, C-2 methyl resonance). Compounds **1–9** gave no signals in the region from 80 to 110 p.p.m., and

displayed only the -CO*C*H$_3$ resonance (20.3–20.7 p.p.m.). Thus, compounds **1–9** are not "orthocyanide" derivatives. The relatively high-field, anomeric-carbon resonances of compounds **1–9** (64.4–66.4 p.p.m.; see Table II) provide strong evidence that the cyano group is bonded to C-1. Tentative assignments for the remaining ring-carbon resonances provide further confirmation of the *C*-aldohexopyranosyl structure of compounds **1–9**, and support their conformational and configurational assignments[21]. For a given anomeric pair of glycosyl cyanides, the relative chemical-shift values of several of the skeletal-carbon resonances are correlated with the configuration of the anomeric center[21].

Vibrational spectroscopy was also employed for the analysis of per-*O*-acetylaldohexopyranosyl cyanides **1–9**. The i.r. spectra of compounds **1–9** in $CHCl_3$ show no absorption bands in the 2800–1900-cm^{-1} region. In agreement with this result, it is well documented that the i.r. spectra of glycosyl cyanides[11,14,16,18], as well as of 1,2-*O*-(1-cyanoethylidene)aldohexopyranoses[14,22] generally do not exhibit the expected -C≡N stretching-vibration (~2265–2240 cm^{-1}) as a result of quenching, whereas glycosyl isocyanides[24] display a -N≡C stretching-vibration in the region of 2146–2123 cm^{-1}. Compounds **1–6, 8,** and **9** were also examined by laser-Raman spectroscopy[26]. Each of the resulting spectra exhibited a single, sharp, -C≡N stretching-vibration in the region of 2262–2242 cm^{-1} (see Table II), but none exhibited a -N≡C stretching-vibration band. Moreover, the relatively large differences in the values of ν(-C≡N) of compounds **1–6, 8,** and **9** are dependent upon the stereochemistry of the anomeric cyano group (axial *versus* equatorial orientation). Thus, laser-Raman spectroscopy provided further confirmation of the assignment of the anomeric configuration and the conformation of compounds **1–6, 8,** and **9**. A more-detailed discussion of these results has been published[26].

The ^{1}H-n.m.r. spectra of the per-*O*-acetylaldohexopyranosyl cyanides **1–9** in $CDCl_3$ were entirely consistent with the structures assigned. Chemical-shift and integration data demonstrated the expected number of skeletal protons, as well as acetoxyl and phthalimido substituents for each compound. Each of the signals for the skeletal protons in compounds **1–9** was sufficiently resolved to allow for their identification from the spin–spin coupling-splitting patterns and vicinal-coupling constants, and, where necessary, from the results of double-resonance experiments. Interpretation of the resulting data revealed that compounds **1–9** were aldohexopyranoses of either the $^4C_1$(D), or $^1C_4$(L) conformation (compare, ref. 19). The relative configurations of the asymmetric centers C-2, 3, 4, and 5 were unchanged from those of the starting per-*O*-acetylaldohexopyranosyl bromides. The signals of the anomeric protons of compounds **1–9** appeared as resolved doublets, with chemical-shift values (see Table II) upfield from those generally observed for "typical" aldohexopyranosides, 1-thiohexopyranosides, and aldohexopyranosylamines, providing additional support for their *C*-aldohexopyranosyl structure. The anomeric configuration of each compound was deduced from a first-order analysis of the vicinal-coupling constants. The values of $J_{1,2}$ were as follows (see Table II): (1) 10.1–10.5 Hz, $J_{1a,2a}$ [β-D-*galacto* (**2**), β-L-*galacto* (**4**),

β-D-*gluco* (**6**, **7**) configurations]; (2) 5.6–6.2 Hz, $J_{1e,2a}$ [α-D-*galacto* (**1**), α-L-*galacto* (**3**), α-D-*gluco* (**5**) configurations]; (3) 1.4 Hz, $J_{1a,2e}$ [β-D-*manno* configuration (**9**)]; and (4) 2.0 Hz, $J_{1e,2e}$ [α-D-*manno* configuration (**8**)]. The chemical shift of H-1 of the α anomer (H-1 equatorial) of a given anomeric pair is consistently downfield from that of the β anomer (H-1 axial) (see Table II). Additional confirmation of the anomeric configuration of compounds **1–6, 8,** and **9** was obtained from the relative chemical-shifts of the ring protons at C-2, 3, and 5 for a given anomeric pair[21].

Inspection of Table II reveals some additional correlations between the physical properties of per-*O*-acetylaldohexopyranosyl cyanides **1–6, 8,** and **9** and their anomeric configuration. Compounds **1–6, 8,** and **9** obey Hudson's[27] rules of isorotation. Thus, the α-D or α-L anomer (-C≡N axial) of a given anomeric pair of glycosyl cyanides was more dextrorotary or levorotary than the β-D or β-L anomer (-C≡N equatorial). In addition, the α anomers had consistently higher mobility in t.l.c., and lower melting points, than the corresponding β anomers. Similar trends in ^{1}H-n.m.r., optical rotational, and m.p. data were reported by Igolen and coworkers[16] for the anomeric 2,3,4-tri-*O*-benzoyl-L-rhamnopyranosyl cyanides.

Reaction results. — Cyanation of the per-*O*-acetylaldohexopyranosyl bromide derivatives of α-D-galactose, α-L-fucose, α-D-glucose, α-D-mannose, and 2-deoxy-2-phthalimido-β-D-glucose with one equivalent of mercuric cyanide in nitromethane gave the results summarized in Table I. Inspection of Table I reveals that these reactions generated per-*O*-acetylaldohexopyranosyl cyanides having a high degree of 1,2-*trans* stereoselectivity, irrespective of the stereochemistry of the per-*O*-acetylglycosyl bromide employed. Thus, the corresponding per-*O*-acetyl-1,2-*trans*-aldohexopyranosyl cyanides (**2, 4, 6, 7,** and **8**) were obtained in yields of 20–79%, whereas the yields of the corresponding 1,2-*cis* anomers, **1, 3, 5,** and **9** (no 1,2-*cis* analog of **7** was detected), were 1.1–8.4%.

The stereoselectivity of *C*-glycosylation by the per-*O*-acetylaldohexopyranosyl bromides showed the following trend (ratio of 1,2-*trans*- to 1,2-*cis*-glycosyl cyanide obtained): 2-deoxy-2-phthalimido-β-D-glucose (no 1,2-*cis*-glycosyl cyanide detected) > α-D-galactose (27:1) > α-D-glucose (18:1) > α-D-mannose (11:1) > α-L-fucose (8.5:1). Thus, increases in the 1,2-*trans* stereoselectivity of the Helferich procedure[10] result from the use of per-*O*-acetylglycosyl bromides having (*1*) a 6-*C*-acetoxyl substituent [*cf.*, α-D-galactose with α-L-fucose (6-deoxy-L-*galacto*)], (*2*) the sterically demanding, neighboring-group-active, phthalimido substituent at C-2 [*cf.*, 2-deoxy-2-phthalimido-β-D-glucose with 2-*O*-acetyl-α-D-glucose; note that the former bromide has the 1,2-*trans* disposition], (*3*) an axial acetoxyl substituent on C-4 (*cf.*, α-D-galactose with α-D-glucose), and (*4*) an equatorial acetoxyl group on C-2, *i.e.*, 1,2-*cis* stereochemistry (*cf.*, α-D-glucose with α-D-mannose). The high yield of the 1,2-*trans* product, namely, 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl cyanide (**7**), was anticipated from the results of studies employing the corresponding 1,2-*trans* bromide as an *O*-glycosylating reagent[20] (see also, for a mechanistic interpretation of these results). Moreover, the low stereoselectivity exhibited by 2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl bromide

agrees well with the report of Igolen and co-workers[16], who demonstrated that the reaction of 2,3,4-tri-*O*-benzoyl-α-L-rhamnopyranosyl bromide (L-*manno* configuration) with mercuric cyanide in nitromethane gave both the per-*O*-benzoylated 1,2-*trans*- and 1,2-*cis*-rhamnopyranosyl cyanides in 72% overall yield, with a 1,2-*trans* to 1,2-*cis* ratio of 4.5:1 (*cf.*, 2,3,4,6-tetra-*O*-acetyl-α- and -β-D-mannopyranosyl cyanides, 11:1). The mechanistic rationale for the (generally observed) stereoselective formation of 1,2-*trans* glycosylation products from per-*O*-acylglycosyl halides of both the 1,2-*cis* and 1,2-*trans* disposition has been reviewed in detail[28].

In contrast, the total yield of the per-*O*-acetylaldohexopyranosyl cyanides varied considerably with the stereochemistry of the per-*O*-acetylaldohexopyranosyl bromide employed and the nature of its C-2 substituent. Thus, the per-*O*-acetylaldohexopyranosyl cyanide derivatives of D-galactose (**1**, **2**), L-fucose (**3**, **4**), and 2-deoxy-2-phthalimido-D-glucose (**7**) were obtained in much higher overall yields (82, 79, and 67%, respectively) than the corresponding derivatives of D-mannose (**8**, **9**) and D-glucose (**5**, **6**), 40 and 21%, respectively (see Table I).

The lower overall yields of the per-*O*-acetylated D-manno- and -gluco-pyranosyl cyanides from the Helferich procedure[10] is due, in large part, to the co-production of considerable proportions of the per-*O*-acetyl-1,2-*O*-[1-(*exo*- and *endo*-cyano)ethylidene]-β-D-manno- and -α-D-gluco-pyranoses. These regioisomers are formed by nucleophilic attack of cyanide ion on the dioxolenium carbon atom of the corresponding, ambidentate 1,2-acetoxonium ion intermediates[28,29]. They are stable under the conditions of the Helferich procedure (*i.e.* cyanation is irreversible)[14,21]. Coxon and Fletcher[14] reported that treatment of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide with mercuric cyanide in nitromethane, according to the method of Helferich and Bettin[10], generated **6**, as well as a crystalline 3,4,6-tri-*O*-acetyl-1,2-*O*-(1-cyanoethylidene)-α-D-glucopyranose (now known to be the *exo*-cyano isomer[22]) in equivalent, but low, yields (12%). We have independently established[21] that the combined yield of the 3,4,6-tri-*O*-acetyl-1,2-*O*-[1-(*exo*- and *endo*-cyano)ethylidene]-α-D-glucopyranoses (**12A** and **12B**)[22] from this reaction is ~25%, whereas the combined yield of the 3,4,6-tri-*O*-acetyl-1,2-*O*-[1-(*exo*- and *endo*-cyano)ethylidene]-β-D-mannopyranoses (**13A** and **13B**)[22] is ~40%. In contrast, we have determined[21] that treatment of 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide with mercuric cyanide in nitromethane yields only ~5% of the 3,4,6-tri-*O*-acetyl-1,2-*O*-[1-(*exo*- and *endo*-cyano)ethylidene]-α-D-galactopyranoses (**10A** and **10B**)[22], whereas the 3,4-di-*O*-acetyl-1,2-*O*-[1-(*exo*- and *endo*-cyano)ethylidene]-α-L-fucopyranoses (**11A** and **11B**)[21] were not detected as products of the analogous reaction employing 2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl bromide. Moreover, no evidence was obtained for the formation of cyanated products other than 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl cyanide (**7**) from treatment of the corresponding glycosyl bromide according to the Helferich procedure[10].

Thus, the per-*O*-acetylaldohexopyranosyl bromides from α-D-galactose, α-L-fucose, and 2-deoxy-2-phthalimido-β-D-glucose exhibited much higher C-1 regioselectivity than their α-D-mannose and α-D-glucose counterparts under identical conditions (see Table I). Clearly, the C-1 regioselectivity of the Helferich procedure[10] increases when applied to per-*O*-acetylglycosyl bromides possessing (*1*) an axial 4-acetoxyl substituent (*cf.*, α-D-galactose with α-D-glucose), and (*2*) the sterically demanding phthalimido substituent at C-2 (*cf.*, 2-deoxy-2-phthalimido-β-D-glucose with α-D-glucose). Our results suggest that, under these conditions, the relative configuration at C-1 and C-2 of the per-*O*-acetylaldohexopyranosyl bromide examined (1,2-*trans* or 1,2-*cis*) may be of little consequence to the regioselectivity exhibited, *i.e.*, that other factors are more important.

The combined yields of the anomeric glycosyl cyanides and 1,2-*O*-[1-(*exo*- and *endo*-cyano)ethylidene] regioisomers from application of the Helferich procedure[10] to the per-*O*-acetylaldohexopyranosyl bromide derivatives of α-D-galactose, α-L-fucose, α-D-mannose, 2-deoxy-2-phthalimido-β-D-glucose, and α-D-glucose were ~90, 80, 80, 67, and 45%, respectively (see Table I). Clearly, the reaction of glycosyl bromides with one equivalent of mercuric cyanide in nitromethane is an intrinsically effective method for synthesizing cyanated glycoses (not the corresponding isocyano species). In contrast, the reaction of glycosyl bromides with silver cyanide in less-polar solvents (dichloromethane or xylene) generates appreciable proportions of the corresponding glycosyl isocyanides[24a,b]. It is not known why 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide is selectively prone to side reactions under the conditions of the Helferich procedure[10]. However, we have found[21] that 1,2,3,4,6-penta-*O*-acetyl-α-D-glucopyranose (identified by t.l.c., m.p., and ^{13}C- and ^{1}H-n.m.r. spectroscopy) is formed in ~10% yield by this reaction.

A mechanism for the reaction of mercuric cyanide with 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide in nitromethane has been proposed[6,14]. Comprehensive reviews on the mechanism of *O*-glycosylation reactions have been published[28].

EXPERIMENTAL

Materials. — The following materials were obtained from the sources indicated and were used without further treatment: Celite filter aid (Johns–Manville); molecular sieves Type 4 A (Davison Chemical); Sephadex LH-20 (Pharmacia); silica gel 60, 15–40 μm (E. Merck, Cat. No. 15111); L-fucose, D-galactose, D-mannose, and 2-amino-2-deoxy-D-glucose hydrochloride (Sigma Chemical Co.); D-glucose and petroleum ether (b.p. 30–75°) (J. T. Baker Chem. Co.); hydrogen bromide (Linde Division, Union Carbide); nitromethane, 99%, and trifluoroacetic acid, 99% (Aldrich Chem. Co.); all other compounds used in this study were of reagent grade. Mercuric cyanide, 99.7% (Alfa Products) was vacuum-dried for 18 h at 100° over sodium hydroxide prior to use.

The following compounds were prepared as previously described: the

2,3,4,6-tetra-*O*-acetylaldohexopyranosyl bromide derivatives of α-D-galactose, α-D-glucose, and α-D-mannose[30]; 2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl bromide[31] from the 1,2,3,4-tetra-*O*-acetyl-α,β-L-fucopyranoses[32]; crystalline 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl bromide and the syrupy α,β mixture of that bromide[20]; and the 3,4,6-tri-*O*-acetyl-1,2-*O*-[1-(*exo*- and *endo*-cyano)ethylidene]aldohexopyranose derivatives of α-D-galactose, α-D-glucose, and β-D-mannose[22].

General methods. — Where indicated, solvents were dried over molecular sieves Type 4 A. Conventional processing of organic solutions refers to drying with anhydrous sodium sulfate, filtering, washing the solid with additional organic solvent, and evaporating the combined filtrates. All evaporations were conducted in a rotary evaporator under diminished pressure at 20–40°. Where indicated, compounds were purified by gel-filtration chromatography on a column measuring either 5.0 × 195 cm (samples of 2–18 g) or 2.0 × 190 cm (samples <2 g) of Sephadex LH-20 equilibrated in, and eluted with, 95% ethanol, with collection of 20- and 8-mL fractions, respectively. Preparative liquid chromatography (p.l.c.) of samples (3–18 g) was performed as previously described[33] with a Jobin–Yvonne Chromatospac Prep 100 apparatus, using silica gel 60 (15–40 μm) and the solvents indicated. Conventional chromatography on silica gel (samples <3 g) was executed on columns (2.0 or 2.5 cm i.d.) of silica gel 60 (15–40 μm), using the solvents indicated and an adsorbent-to-sample ratio of 40:1. T.l.c. was conducted on layers (0.20 mm) of silica gel 60 F_{254} pre-coated on aluminum sheets (E. Merck, Cat. No. 5534). The following solvent systems were employed for chromatography: (*A*) 3:1 (v/v) diethyl ether–petroleum ether, (*B*) 3:2 (v/v) diethyl ether–petroleum ether, (*C*) 2:1 (v/v) diethyl ether–petroleum ether, (*D*) 100:1 (v/v) chloroform–methanol, and (*E*) 3:1 (v/v) toluene–ethyl acetate. Components on t.l.c. plates were detected by spraying with 15% (v/v) sulfuric acid in 50% (v/v) aqueous ethanol, and heating for several minutes at 140°. This process was repeated for the per-*O*-acetylaldohexopyranosyl cyanides, which were charred to give reddish-brown to brown spots. Less-vigorous conditions were sufficient to visibilize other carbohydrate derivatives present, which appeared as dark-brown to black spots.

Elemental analyses were performed by Guelph Chem. Lab., Guelph, Ontario, Canada, or Galbraith Lab., Inc., Knoxville, TN, USA. Instrumental analyses were conducted with the following equipment: Fisher–Johns melting-point apparatus, Perkin-Elmer 141 spectropolarimeter and 599B infrared spectrophotometer, Varian CFT-20 nuclear magnetic resonance spectrometer (20-MHz, broad-band-decoupled, ^{13}C-n.m.r. spectroscopy, and 80-MHz, ^{1}H-n.m.r. spectroscopy), and Bruker WM-300 wide-bore, n.m.r. spectrometer (300-MHz, ^{1}H-n.m.r. spectroscopy). Melting points reported are uncorrected; optical rotations were determined for solutions at room temperature (~25°). ^{1}H-N.m.r. and ^{13}C-n.m.r. chemical-shifts are reported in parts per million from an internal standard of tetramethylsilane. Vicinal-coupling constants reported are from a first-order analysis of the observed, spin–spin-coupling pattern. Tentative assignments of the ^{13}C-n.m.r. resonances are based on literature analogies.

Preparation of per-O-acetylaldohexopyranosyl cyanides: general procedure. — These compounds were prepared by a modification of the method described by Helferich and Bettin[10]. A mixture of the appropriate, freshly prepared per-*O*-acetylaldohexopyranosyl bromide (5–150 mmol) and mercuric cyanide (1.0 mmol/mmol of bromide) in dry nitromethane (2 mL/mmol of bromide) was stirred for 48 h at room temperature, and the mixture was filtered through Celite, which was then washed with nitromethane, and the combined filtrates were evaporated. Unless otherwise indicated, the resulting thick paste was partitioned between chloroform (~4 mL/mmol of bromide) and M aqueous potassium bromide (1 mL/mmol of bromide), the chloroform solution washed twice with additional M aqueous potassium bromide (1 mL/mmol of bromide), and conventionally processed, to yield a syrup that was further treated as described next.

*2,3,4,6-Tetra-*O*-acetyl-α- and -β-*D*-galactopyranosyl cyanide* (**1** *and* **2**). — Filtration and evaporation of the mixture resulting from the reaction of 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide (61.7 g, 150 mmol) with mercuric cyanide (37.9 g, 150 mmol) in dry nitromethane (300 mL) for 48 h at room temperature yielded a thick paste which crystallized directly by a modification of the method of Helferich and Bettin[10]. Dissolution of the paste in hot methanol (675 mL) followed by successive addition, with stirring, of M aqueous potassium bromide (375 mL) and chilled water (375 mL) resulted in the immediate formation of crystals. After the suspension had been stirred overnight at 4°, the crystals were filtered off, and washed successively at 4° with 1:1 (v/v) methanol–water (100 mL) and water (100 mL), to give **2** (42.1 g, 118 mmol; 79% yield); m.p. 167–168°; homogeneous by t.l.c. (solvent *A*). Subsequently, it was found that an alternative procedure, in which the reaction mixture is processed as described under *General methods* and compound **2** then crystallized by addition of diethyl ether, gave it in comparable yield and purity. The mother liquor is easier to evaporate, thus facilitating the isolation of **1**.

Recrystallization of **2** (1.07 g, 3.0 mmol) from dichloromethane (6 mL)–diethyl ether (6 mL) gave 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl cyanide (3,4,5,7-tetra-*O*-acetyl-2,6-anhydro-D-*glycero*-L-*manno*-heptononitrile) (0.92 g, 2.58 mmol; 86% recovery); m.p. 169–170° (lit.[10] m.p. 168–169°), $[\alpha]_D$ +35.7° (*c* 3.74, $CHCl_3$), {lit.[10] $[\alpha]_D^{22}$ +37.2° (*c* 2.5, $CHCl_3$)}; R_F 0.19 (solvent *A*) and 0.38 (solvent *D*); $\nu_{max}^{CHCl_3}$ 3025, 2970, 2870, 1750 (OAc), 1430, 1370 (OAc), 1240 (OAc), 1160, 1110, 1060, 1020, 960, and 900 cm^{-1}; ^{1}H-n.m.r. data (300-MHz, $CDCl_3$): δ 2.008, 2.071, 2.130, 2.195 (4 s, 12 H, 4 $COCH_3$), 3.950 (dt, 1 H, $J_{5,6} = J_{5,6'} = 6.4$ Hz, H-5), 4.128 (d, 2 H, H-6,6′), 4.298 (d, 1 H, $J_{1,2}$ 10.1 Hz, H-1), 5.013 (dd, 1 H, $J_{3,4}$ 3.3 Hz, H-3), 5.442 (dd, 1 H, $J_{4,5}$ 1.1 Hz, H-4), and 5.544 (t, 1 H, $J_{2,3}$ 10.2 Hz, H-2) (in agreement with the lit.[12] 100-MHz, ^{1}H-n.m.r. spectrum); ^{13}C-n.m.r. data ($CDCl_3$): δ 19.7 (shoulder), 20.5 ($COCH_3$), 61.3 (C-6), and 66.1 (C-1), 66.8 (C-2,4), 70.9 (C-3), 75.4 (C-5), 114.5 (C≡N), and 168.8, 170.0, 170.4 ($COCH_3$) (in agreement with the lit.[13] 22.6-MHz, ^{13}C-n.m.r. spectrum); ^{13}C-n.m.r. data (Me_2SO-d_6): δ 20.2, 20.4 (shoulder) ($COCH_3$), 61.6 (C-6), 65.1 (C-1), 65.9 (C-4), 67.3 (C-2), 69.8 (C-3), 74.5 (C-5), 115.6 (C≡N), and 169.0, 169.3, and 169.8 ($COCH_3$).

The mother liquor from the crystallization of **2** was evaporated, the residue partitioned between chloroform (250 mL) and water (100 mL), the chloroform solution washed with additional water (100 mL), the aqueous washes combined, and back-extracted with chloroform (50 mL), and the combined organic phases washed with M aqueous potassium bromide (100 mL) and then processed in the conventional way. Purification by p.l.c. (solvent *D* as eluant, solvent *A* for t.l.c. analysis) gave fractions containing mainly **1**, as well as the 3,4,6-tri-*O*-acetyl-1,2-*O*-[1-(*exo*- and *endo*-cyano)ethylidene]-α-D-galactopyranoses[22] and a third component of unknown structure, which were combined and evaporated. No attempt was made to recover the remaining **2** present in later-eluting fractions. The resulting syrup (~4.3 g) was dissolved in 9:1 (v/v) trifluoroacetic acid–water (25 mL) freshly prepared at 55°, and stirred for 30 min at 55°. At that time, the solution was evaporated, followed by azeotropic evaporation with toluene (2 × 20 mL). The hydrolyzate was immediately dissolved in chloroform (75 mL), and the solution successively washed with water, cold saturated sodium hydrogencarbonate, and water (15 mL each), and then processed conventionally. Purification by p.l.c., as before, gave fractions (containing almost exclusively **1**) which were pooled, evaporated, and crystallized from diethyl ether (10 mL) to give **1** (1.06 g, 2.97 mmol; 2.0% yield); m.p. 92–93°; homogeneous by t.l.c. (solvent *A*). Purification of the mother liquor by gel filtration and subsequent crystallization from diethyl ether (4 mL) gave additional **1** (0.51 g, 1.43 mmol; 1.0% yield); m.p. 90–92°. The total yield of crystalline **1** was 2.9%. Subsequently, it was found that direct treatment of the syrupy mother liquor from the crystallization of **2** with trifluoroacetic acid, followed by purification by gel filtration, chromatography on silica gel (solvent *D*) to separate **1** from **2**, and then crystallization gives comparable yields of pure **1** with increased ease.

Recrystallization of **1** (0.71 g, 2.0 mmol) by dissolution in chloroform, evaporation, and addition of diethyl ether (4 mL) gave an analytical sample of 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl cyanide (3,4,5,7-tetra-*O*-acetyl-2,6-anhydro-D-*glycero*-L-*gluco*-heptononitrile) (0.47 g, 1.32 mmol; 66% recovery); m.p. 93–94° (lit.[18] m.p. 97°), $[\alpha]_D$ +131.0° (*c* 3.50, $CHCl_3$) {lit.[18] $[\alpha]_D$ +120° (*c* 1.0, CH_2Cl_2)}; R_F 0.30 (solvent *A*) and 0.46 (solvent *D*); $\nu_{max}^{CHCl_3}$ 3025, 2940, 1750 (OAc), 1425, 1370 (OAc), 1230 (OAc), 1130, 1070, 950, 920, and 900 cm^{-1}; ^{1}H-n.m.r. data (300-MHz, $CDCl_3$): δ 2.024, 2.073 (2 s, 6 H, 2 $COCH_3$), 2.152 (s, 6 H, 2 $COCH_3$), 4.134 (m, 2 H, H-6,6'), 4.314 (dt, 1 H, $J_{5,6} \simeq J_{5,6'} \simeq 6.3$ Hz, H-5), 5.182 (d, 1 H, $J_{1,2}$ 5.6 Hz, H-1), 5.246 (dd, 1 H, $J_{2,3}$ 10.6 Hz, H-2), 5.312 (dd, 1 H, $J_{3,4}$ 2.9 Hz, H-3), and 5.534 (dd, 1 H, $J_{4,5}$ 1.1 Hz, H-4) (in agreement with the lit.[18] 200-MHz, ^{1}H-n.m.r. spectrum); ^{13}C-n.m.r. data ($CDCl_3$): δ 19.9 (shoulder), 20.5 ($COCH_3$), 61.1 (C-6), 65.0 (C-1), 65.7 (C-2), 67.0 (C-4), 68.4 (C-3), 72.5 (C-5), 114.1 (C≡N), and 169.5, 169.8, and 170.2 ($COCH_3$); ^{13}C-n.m.r. data (Me_2SO-d_6): δ 20.2, 20.4 (shoulder) ($COCH_3$), 61.5 (C-6), 64.1 (C-1), 65.3 (C-2), 67.2 (C-4), 68.1 (C-3), 72.4 (C-5), 115.1 (C≡N), and 169.1, 169.2, 169.8, and 169.9 ($COCH_3$).

Anal. Calc. for $C_{15}H_{19}NO_9$ (357.18): C, 50.39; H, 5.36; N, 3.92. Found: C, 50.32; H, 5.31; N, 3.85.

2,3,4-Tri-O-acetyl-α- and -β-L-fucopyranosyl cyanide (**3** *and* **4**). — The syrupy product resulting from the reaction of 2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl bromide (9.33 g, 26.4 mmol) with mercuric cyanide crystallized spontaneously. The crystals were collected, washed with 1:1 (v/v) diethyl ether–petroleum ether (40 mL), and dried, to give **4** (4.72 g, 15.8 mmol; 60% yield); m.p. 123–125°; homogeneous by t.l.c. (solvents *B, D*). Additional pure **4** (0.88 g, 2.94 mmol; 11% yield) was obtained as described later. The total yield of crystalline **4** was 71%.

Recrystallization of **4** (0.45 g, 1.50 mmol) by dissolution in dichloromethane, evaporation, and addition of diethyl ether (5 mL) gave an analytical sample of 2,3,4-tri-*O*-acetyl-β-L-fucopyranosyl cyanide (3,4,5-tri-*O*-acetyl-2,6-anhydro-7-deoxy-L-*glycero*-D-*manno*-heptononitrile) (0.39 g, 1.31 mmol; 87% recovery); m.p. 124–125°, $[\alpha]_D$ −33.1° (*c* 2.98, $CHCl_3$); R_F 0.18 (solvent *B*) and 0.47 (solvent *D*); $\nu_{max}^{CHCl_3}$ 3020. 2990, 2860, 1750 (OAc), 1430, 1375 (OAc), 1310, 1245 (OAc), 1165, 1100, 1065, 1020, 960, 930, and 900 cm^{-1}; ^{1}H-n.m.r. data (300-MHz, $CDCl_3$): δ 1.227 (d, 3 H, 3 H-6), 2.004, 2.119, 2.211 (3 s, 9 H, 3 $COCH_3$), 3.829 (dq, 1 H, $J_{5,6}$ 6.4 Hz, H-5), 4.264 (d, 1 H, $J_{1,2}$ 10.4 Hz, H-1), 5.006 (dd, 1 H, $J_{3,4}$ 3.3 Hz, H-3), 5.281 (dd, 1 H, $J_{4,5}$ 0.9 Hz, H-4), and 5.514 (t, 1 H, $J_{2,3}$ 10.2 Hz, H-2); ^{13}C-n.m.r. data ($CDCl_3$): δ 16.1 (C-6), 20.5 ($COCH_3$), 66.2 (C-1), 66.7 (C-2), 69.8 (C-4), 71.3 (C-3), 74.3 (C-5), 114.9 (C≡N), and 168.9, 169.9, and 170.4 ($COCH_3$); ^{13}C-n.m.r. data (Me_2SO-d_6): δ 15.6 (C-6), 20.2 ($COCH_3$), 65.1 (C-1), 66.0 (C-2), 69.8 (C-4), 70.2 (C-3), 73.1 (C-5), 115.9 (C≡N), and 169.1, 169.4, and 170.1 ($COCH_3$).

Anal. Calc. for $C_{13}H_{17}NO_7$ (299.16): C, 52.15; H, 5.72; N, 4.68. Found: C, 52.20; H, 5.60; N, 4.63.

The mother liquor from the crystallization of **4** was evaporated, and the mixture purified by gel filtration. Fractions containing **3** and **4** (solvent *B* for t.l.c. analysis) were combined, evaporated, and crystallized by dissolution in dichloromethane, evaporation, and addition of diethyl ether (5 mL), to give **4** (0.73 g, 2.44 mmol; 9.2% yield); m.p. 123–125°; homogeneous by t.l.c. (solvents *B, D*). The remaining mother liquor was further purified by conventional chromatography on silica gel with solvent *D* as the eluant. Fractions containing **4** were pooled, evaporated, and crystallized from diethyl ether to give **4** (0.15 g, 0.50 mmol; 1.9% yield); m.p. 124–125°; homogeneous by t.l.c. (solvents *B, D*).

Fractions eluted earlier that contained **3** and were devoid of **4** were combined, and evaporated to a syrup which failed to crystallize. Gel filtration of this syrup yielded **3** (0.66 g, 2.21 mmol; 8.4% yield), homogeneous by t.l.c. (solvents *B, D*). A portion of syrupy **3** so prepared crystallized upon prolonged storage in a vacuum desiccator to give, after trituration with 1:2 (v/v) diethyl ether–petroleum ether at 4°, an analytical sample of 2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl cyanide (3,4,5-tri-*O*-acetyl-2,6-anhydro-7-deoxy-L-*glycero*-D-*gluco*-heptononitrile) (0.41 g, 1.37 mmol, 5.2% yield; 62% recovery); m.p. 97–98°, $[\alpha]_D$ −161.9° (*c* 3.50,

$CHCl_3$); R_F 0.30 (solvent *B*) and 0.54 (solvent *D*); $\nu_{max}^{CHCl_3}$ 3020, 1750 (OAc), 1420, 1370 (OAc), 1240 (OAc), 1130, 1100, 1070, 970, 920, and 900 cm^{-1}; ^{1}H-n.m.r. data (300-MHz, $CDCl_3$): δ 1.223 (d, 3 H, 3 H-6), 2.021, 2.145, 2.176 (3 s, 9 H, 3 $COCH_3$), 4.233 (dq, 1 H, $J_{5,6}$ 6.3 Hz, H-5), 5.123 (d, 1 H, $J_{1,2}$ 5.8 Hz, H-1), 5.227 (dd, 1 H, $J_{2,3}$ 10.6 Hz, H-2), 5.304 (dd, 1 H, $J_{3,4}$ 2.9 Hz, H-3), and 5.372 (dd, 1 H, $J_{4,5}$ 1.0 Hz, H-4); ^{13}C-n.m.r. data ($CDCl_3$): δ 16.0 (C-6), 20.6 ($COCH_3$), 65.1 (C-1), 65.8 (C-2), 68.9 (C-3), 69.9 (C-4), 71.0 (C-5), 114.5 (C≡N), and 169.6, 169.9, and 170.2 ($COCH_3$); ^{13}C-n.m.r. data (Me_2SO-d_6): δ 15.6 (C-6), 20.2 ($COCH_3$), 64.0 (C-1), 65.3 (C-2), 68.5 (C-3), 69.6 (C-4), 70.7 (C-5), 115.5 (C≡N), and 169.1, 169.3, and 170.0 ($COCH_3$).

Anal. Calc. for $C_{13}H_{17}NO_7$ (299.16): C, 52.15; H, 5.72; N, 4.68. Found: C, 52.29; H, 5.73; N, 4.64.

2,3,4,6-Tetra-O-acetyl-α- and -β-D-glucopyranosyl cyanide (**5** *and* **6**). — The syrupy product resulting from the reaction of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (20.6 g, 50.0 mmol) with mercuric cyanide was dissolved in 9:1 (v/v) trifluoroacetic acid–water (100 mL), freshly prepared at 55°, and stirred for 30 min at 55°. The solution was then cooled, and evaporated, and azeotropically evaporated with toluene (2 × 25 mL). The hydrolyzate was immediately dissolved in chloroform (200 mL), and the solution successively washed at 4° with water, saturated sodium hydrogencarbonate, and water (50 mL each), and then processed by the standard method. Purification by p.l.c. (solvent *E* as the eluant, solvent *A* for t.l.c. analysis) gave fractions containing mainly **5** and **6**, contaminated with 1,2,3,4,6-penta-*O*-acetyl-α-D-glucopyranose[21], which were combined and evaporated. Further purification by gel filtration gave fractions containing only **5** and **6**, which were pooled, evaporated, and crystallized from ethanol (25 mL) to give **6** (3.29 g, 9.21 mmol; 18% yield), m.p. 111–114°; additional **6** (0.29 g, 0.81 mmol; 1.6% yield) was obtained as described later. The total yield of crystalline **6** was 20%. Subsequent experiments demonstrated that the p.l.c. step prior to gel filtration is unnecessary.

Recrystallization of **6** (1.07 g, 3.0 mmol) from ethanol (7 mL) gave 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl cyanide (3,4,5,7-tetra-*O*-acetyl-2,6-anhydro-D-*glycero*-D-*gulo*-heptononitrile) (0.95 g, 2.66 mmol; 89% recovery); m.p. 114–115° (lit.[14] m.p. 116°), $[\alpha]_D$ +10.7° (*c* 3.28, $CHCl_3$) {lit.[14] $[\alpha]_D^{20}$ +10.1° (*c* 2.64, $CHCl_3$)}; R_F 0.20 (solvent *A*) and 0.38 (solvent *D*); $\nu_{max}^{CHCl_3}$ 3030, 2960, 2880, 1760 (OAc), 1430, 1370 (OAc), 1225 (OAc), 1140, 1070, 1040, 965, and 900 cm^{-1}; ^{1}H-n.m.r. data (300-MHz, $CDCl_3$): δ 2.028, 2.038 (2 s, 6 H, 2 $COCH_3$), 2.114 (s, 6 H, 2 $COCH_3$), 3.722 (dddd, 1 H, $J_{5,6}$ 2.3, $J_{5,6'}$ 4.8 Hz, H-5), 4.148 (dd, 1 H, $J_{6,6'}$ 12.8 Hz, H-6), 4.243 (dd, 1 H, H-6'), 4.330 (d, 1 H, $J_{1,2}$ 10.1 Hz, H-1), 5.106 (t, 1 H, $J_{4,5}$ 9.6 Hz, H-4), 5.181 (t, 1 H, $J_{3,4}$ 9.3 Hz, H-3), and 5.318 (t, 1 H, $J_{2,3}$ 9.3 Hz, H-2); ^{13}C-n.m.r. data ($CDCl_3$): δ 20.5 ($COCH_3$), 61.5 (C-6), 66.4 (C-1), 67.4 (C-4), 69.0 (C-2), 72.8 (C-3), 76.7 (C-5), 114.3 (C≡N), and 168.8, 169.2, 170.0, and 170.5 ($COCH_3$) (in agreement with the lit.[13] 22.6-MHz, ^{13}C-n.m.r. spectrum); ^{13}C-n.m.r. data (Me_2SO-d_6): δ 20.2, 20.4 ($COCH_3$), 61.6 (C-6), 64.7 (C-1), 67.3 (C-4),

68.5 (C-2), 71.9 (C-3), 75.2 (C-5), 115.5 (C≡N), and 168.8, 169.1, 169.5, and 170.0 ($COCH_3$).

The mother liquor from crystallization of **6** was evaporated and purified by conventional chromatography on silica gel with solvent *D* as the eluant. Fractions containing **6** were pooled, evaporated, and crystallized from ethanol (3 mL), to give **6** (0.29 g, 0.81 mmol; 1.6% yield); m.p. 114–115°. Fractions, eluted earlier, that contained **5** and were devoid of **6**, were combined, evaporated, and crystallized from diethyl ether (4 mL), to give **5** (0.20 g, 0.56 mmol; 1.1% yield); m.p. 109–111°.

Recrystallization of **5** so prepared (0.54 g, 1.50 mmol) from ethanol (4 mL) gave an analytical sample of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl cyanide (3,4,5,7-tetra-*O*-acetyl-2,6-anhydro-D-*glycero*-D-*ido*-heptononitrile) (0.30 g, 0.84 mmol; 56% recovery); m.p. 111–112° (lit.[18] m.p. 112°), $[\alpha]_D$ +125.0° (*c* 3.43, $CHCl_3$) {lit.[18] $[\alpha]_D$ +76° (*c* 1.0, CH_2Cl_2)}; R_F 0.29 (solvent *A*) and 0.45 (solvent *D*); $\nu_{max}^{CHCl_3}$ 3020, 2955, 1755 (OAc), 1430, 1370 (OAc), 1235 (OAc), 1110, 1070, 1040, 960, 915, and 900 cm^{-1}; ^{1}H-n.m.r. data (300-MHz, $CDCl_3$): δ 2.045, 2.060, 2.103, 2.137 (4 s, 12 H, 4 $COCH_3$), 4.106 (dddd, 1 H, $J_{5,6}$ 2.2, $J_{5,6'}$ 4.3 Hz, H-5), 4.164 (dd, 1 H, $J_{6,6'}$ 12.7 Hz, H-6), 4.320 (dd, 1 H, H-6'), 5.032 (dd, 1 H, $J_{2,3}$ 9.8 Hz, H-2), 5.087 (t, 1 H, $J_{4,5}$ 9.8 Hz, H-4), 5.138 (d, 1 H, $J_{1,2}$ 6.2 Hz, H-1), and 5.460 (t, 1 H, $J_{3,4}$ 9.6 Hz, H-3) (in agreement with the lit.[18] 200-MHz, ^{1}H-n.m.r. spectrum); ^{13}C-n.m.r. data ($CDCl_3$): δ 20.5 ($COCH_3$), 61.2 (C-6), 65.2 (C-1), 67.3 (C-4), 67.9 (C-2), 70.7 (C-3), 73.6 (C-5), 113.8 (C≡N), and 169.4, 169.6, and 170.4 ($COCH_3$); ^{13}C-n.m.r. data (Me_2SO-d_6): δ 20.2, 20.4 ($COCH_3$), 61.4 (C-6), 64.9 (C-1), 66.4 (C-4), 66.8 (C-2), 70.4 (C-3), 73.2 (C-5), 114.9 (C≡N), and 168.8, 169.1, 169.5, and 169.9 ($COCH_3$).

Anal. Calc. for $C_{15}H_{19}NO_9$ (357.18): C, 50.39; H, 5.36; N, 3.92. Found: C, 50.42; H, 5.37; N, 4.11.

*2,3,4,6-Tetra-*O*-acetyl-α- and -β-*D*-mannopyranosyl cyanide* (**8** *and* **9**). — The syrupy product resulting from the reaction of 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl bromide (19.2 g, 46.7 mmol) with mercuric cyanide was fractionated by p.l.c. (solvent *D* as eluant, solvent *A* for t.l.c. analysis). Two pools were thus obtained. The first pool contained mainly **8**, contaminated with 3,4,6-tri-*O*-acetyl-1,2-*O*-[1-(*exo*-cyano)ethylidene]-β-D-mannopyranose[22] (**13A**), as well as a trace of the corresponding *endo* isomer[22] (**13B**), but was devoid of **9**. The second pool contained mainly **9**, contaminated with **13B** and a trace of **13A**, as well as several unidentified polar species of low R_F value.

The first pool was further purified by gel filtration. Fractions containing **8**, contaminated with **13A/B** were combined and evaporated. All attempts to obtain **8** at this stage by fractional crystallization failed. However, repeated chromatography on silica gel (solvent *C* as eluant) of a small portion of this mixture, followed by crystallization from ethanol at 4°, provided seed crystals of pure **8** (see later). The bulk of the (more readily crystallized) 1,2-*O*-[1-(*exo*-cyano)ethylidene] contaminant was therefore removed by fractional crystallization from diethyl ether (46 mL), and then methanol (30 mL), using seed crystals of authentic **13A**.

The remaining mother liquor (containing mainly **8**) was evaporated, dissolved in hot ethanol (42 mL), and the solution cooled to 4°. The material crystallized upon addition of a seed crystal of authentic compound to give **8** (4.89 g, 13.7 mmol; 29% yield); m.p. 57–59°; homogeneous by t.l.c. (solvent *A*). Further fractional crystallization of **8** was not possible. The mixture was therefore purified by conventional chromatography on silica gel with solvent *C* as the eluant. Fractions containing only **8** were pooled, and evaporated. Fractions containing **8** as well as **13A** were pooled, and evaporated, and the bulk of the contaminant was removed by fractional crystallization from diethyl ether (5 mL). The mother liquor resulting was again purified by conventional chromatography on silica gel with solvent *C* as the eluant. Fractions containing only **8** were combined with those from the first such column treatment and evaporated. Crystallization from ethanol (10 mL), as before, gave additional **8** (1.19 g, 3.33 mmol; 7.1% yield); m.p. 54–59°; homogeneous by t.l.c. (solvent *A*). The total yield of **8** was 37%.

Recrystallization of **8** (0.71 g, 2.0 mmol) from ethanol (4 mL) gave an analytical sample of 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl cyanide (3,4,5,7-tetra-*O*-acetyl-2,6-anhydro-D-*glycero*-D-*talo*-heptononitrile) (0.50 g, 1.40 mmol; 70% recovery); m.p. 58–60°, $[\alpha]_D$ +28.6° (*c* 3.36, $CHCl_3$); R_F 0.24 (solvent *A*) and 0.45 (solvent *D*); $\nu_{max}^{CHCl_3}$ 3025, 2960, 1755 (OAc), 1430, 1370 (OAc), 1230 (OAc), 1130, 1080, 1050, 1015, 985, 960, 920, and 890 cm^{-1}; ^{1}H-n.m.r. data (300-MHz, $CDCl_3$): δ 2.034, 2.084, 2.117, 2.197 (4 s, 12 H, 4 $COCH_3$), 4.086 (dddd, 1 H, $J_{5,6}$ 2.3, $J_{5,6'}$ 5.3 Hz, H-5), 4.165 (dd, 1 H, $J_{6,6'}$ 12.6 Hz, H-6), 4.340 (dd, 1 H, H-6'), 4.906 (d, 1 H, $J_{1,2}$ 2.0 Hz, H-1), 5.306 (t, 1 H, $J_{4,5}$ 9.4 Hz, H-4), 5.372 (dd, 1 H, $J_{3,4}$ 9.5 Hz, H-3), and 5.433 (dd, 1 H, $J_{2,3}$ 3.0 Hz, H-2); ^{13}C-n.m.r. data ($CDCl_3$): δ 20.6 ($COCH_3$), 61.8 (C-6), 65.1 (C-1), 65.7 (C-4), 68.7 (C-2), 69.0 (C-3), 74.3 (C-5), 113.6 (C≡N), and 169.5 and 170.4 ($COCH_3$); ^{13}C-n.m.r. data (Me_2SO-d_6): δ 20.4 ($COCH_3$), 61.6 (C-6), 64.5 (C-1), 65.4 (C-4), 67.9 (C-2), 68.8 (C-3), 73.8 (C-5), 114.7 (C≡N), and 169.2, 169.4, 169.6, and 170.0 ($COCH_3$).

Anal. Calc. for $C_{15}H_{19}NO_9$ (357.18): C, 50.39; H, 5.36; N, 3.92. Found: C, 50.34; H, 5.32; N, 4.07.

The second pool from the initial p.l.c. (solvent *D*), containing **9**, was dissolved in the minimal volume of chloroform, and further purified by conventional chromatography on silica gel with solvent *E* as the eluant. Fractions containing mainly **9** were combined, evaporated, and crystallized from chloroform (1 mL)–diethyl ether (4 mL), to give **9** (0.47 g, 1.32 mmol; 2.8% yield); m.p. 142–143°; homogeneous by t.l.c. (solvent *A*). Rechromatography of the mother liquor on silica gel (solvent *E* as eluant), and subsequent crystallization from ethanol (3 mL), gave additional **9** (0.08 g, 0.21 mmol; 0.5% yield); m.p. 142–144°; homogeneous by t.l.c. (solvent *A*). The total yield of **9** was 3.3%.

Recrystallization of **9** so prepared (0.71 g, 2.0 mmol) by dissolution in dichloromethane, evaporation, and addition of diethyl ether (4 mL) gave an analytical sample of 2,3,4,6-tetra-*O*-acetyl-β-D-mannopyranosyl cyanide (3,4,5,7-tetra-*O*-acetyl-2,6-anhydro-D-*glycero*-D-*galacto*-heptononitrile) (0.62 g, 1.74 mmol; 87%

recovery); m.p. 142–144°, $[\alpha]_D$ −20.9° (*c* 3.76, $CHCl_3$); R_F 0.15 (solvent *A*) and 0.37 (solvent *D*); $\nu_{max}^{CHCl_3}$ 3025, 2960, 2880, 2865, 1750 (OAc), 1430, 1370 (OAc), 1230 (OAc), 1120, 1060, 960, and 905 cm^{-1}; ^{1}H-n.m.r. data (300-MHz, $CDCl_3$): δ 2.001, 2.059, 2.119, 2.259 (4 s, 12 H, 4 $COCH_3$), 3.699 (dddd, 1 H, $J_{5,6}$ 2.4, $J_{5,6'}$ 5.7 Hz, H-5), 4.165 (dd, 1 H, $J_{6,6'}$ 12.6 Hz, H-6), 4.259 (dd, 1 H, H-6'), 4.588 (d, 1 H, $J_{1,2}$ 1.4 Hz, H-1), 5.047 (dd, 1 H, $J_{3,4}$ 10.0 Hz, H-3), 5.255 (t, 1 H, $J_{4,5}$ 9.9 Hz, H-4), and 5.622 (dd, 1 H, $J_{2,3}$ 3.4 Hz, H-2); ^{13}C-n.m.r. data ($CDCl_3$): δ 20.5 ($COCH_3$), 62.2 (C-6), 64.9 (C-1), 66.7 (C-4), 67.7 (C-2), 70.6 (C-3), 77.0 (C-5), 113.9 (C≡N), and 169.4, 169.8, 170.0, and 170.6 ($COCH_3$); ^{13}C-n.m.r. data (Me_2SO-d_6): δ 20.2 ($COCH_3$), 61.8 (C-6), 64.8 (C-1), 65.9 (C-4), 67.9 (C-2), 69.7 (C-3), 75.3 (C-5), 115.0 (C≡N), and 169.3, and 170.0 ($COCH_3$).

Anal. Calc. for $C_{15}H_{19}NO_9$ (357.18): C, 50.39; H, 5.36; N, 3.92. Found: C, 50.40; H, 5.26; N. 4.00.

Grynkiewicz and BeMiller[18] reported the synthesis of a 2,3,4,6-tetra-*O*-acetyl-D-mannopyranosyl cyanide with physical constants {m.p. 149–150°; $[\alpha]_D$ −28° (*c* 1.0, CH_2Cl_2); 200-MHz, ^{1}H-n.m.r. spectrum; and t.l.c. R_F} in complete agreement with those now found for 2,3,4,6-tetra-*O*-acetyl-β-D-mannopyranosyl cyanide (**9**), but which they designated as the corresponding α anomer. Subsequent examination[34] revealed this report[18] to be in error. The compound had been produced by dehydration of 3,4,5,7-tetra-*O*-acetyl-2,6-anhydro-D-*glycero*-D-*galacto*-heptonamide to give 2,3,4,6-tetra-*O*-acetyl-β-D-mannopyranosyl cyanide[34].

3,4,6-Tri-O-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl cyanide (**7**). — *Method a. From crystalline 3,4,6-tri-O-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl bromide.* The syrupy product resulting from the reaction of 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl bromide (2.49 g, 5.0 mmol) with mercuric cyanide crystallized from ethanol (35 mL) to give **7** (1.61 g, 3.62 mmol; 72% yield). T.l.c. (solvent *D*) demonstrated that **7** so prepared was slightly contaminated with several compounds having low R_F values.

Recrystallization of **7** (1.61 g, 3.62 mmol) from ethanol (36 mL) gave an analytically pure sample of 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl cyanide (4,5,7-tri-*O*-acetyl-3-deoxy-3-phthalimido-2,6-anhydro-D-*glycero*-D-*gulo*-heptononitrile) (1.49 g, 3.35 mmol; 67% yield, 92% recovery); m.p. 176–178° (lit.[18] m.p. 178°), $[\alpha]_D$ +68.8° (*c* 1.03, $CHCl_3$) {lit.[18] $[\alpha]_D$ +78° (*c* 1.0, CH_2Cl_2)}; R_F 0.21 (solvent *A*) and 0.39 (solvent *D*); $\nu_{max}^{CHCl_3}$ 3025, 2960, 2940, 2880, 1780 (Phth), 1750 (OAc), 1720 (Phth), 1610 (Phth), 1470 (Phth), 1430, 1370 (OAc), 1235 (OAc), 1080, 1045, 975, 960, and 900 cm^{-1}; ^{1}H-n.m.r. data (80-MHz, $CDCl_3$): δ 1.87, 2.04, 2.13 (3 s, 9 H, 3 $COCH_3$), 3.88 (dddd, 1 H, $J_{5,6}$ 2.6, $J_{5,6'}$ 4.4 Hz, H-5), 4.25 (m, 2 H, H-6,6'), 4.65 (t, 1 H, $J_{2,3}$ 10.5 Hz, H-2), 5.19 (dd, 1 H, $J_{4,5}$ 10.0 Hz, H-4), 5.38 (d, 1 H, $J_{1,2}$ 10.5 Hz, H-1), 5.76 (dd, 1 H, $J_{3,4}$ 9.2 Hz, H-3), and 7.84 (m, 4 H, Phth) (in agreement with the lit.[18] 200-MHz, ^{1}H-n.m.r. spectrum); ^{13}C-n.m.r. data ($CDCl_3$): δ 20.3, 20.5, 20.7 ($COCH_3$), 52.4 (C-2), 61.6 (C-6), 64.4 (C-1), 67.9 (C-4), 70.3 (C-3), 76.8 (C-5), 114.3 (C≡N), 124.1, 131.0, 134.9 (aromatic), 167.1 (Phth carbonyl), and 169.2, 169.9, and 170.5 ($COCH_3$).

Anal. Calc. for $C_{21}H_{20}N_2O_9$ (444.20): C, 56.73; H, 4.53; N, 6.30. Found: C, 56.74; H, 4.60; N, 6.19.

Method b. From syrupy 3,4,6-tri-O-acetyl-2-deoxy-2-phthalimido-α,β-D-glucopyranosyl bromides. The syrupy product resulting from the reaction of crude 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-α,β-D-glucopyranosyl bromide (10.0 g, 20.2 mmol) with mercuric cyanide was purified by p.l.c. (solvent *D* as eluant; and for t.l.c. analysis). Fractions containing a preponderance of **7** were combined, evaporated, and crystallized from ethanol (140 mL), to give **7** (5.84 g, 13.2 mmol; 65% yield) slightly contaminated with a compound of lower R_F value. Recrystallization from ethanol (120 mL) gave pure **7** (5.56 g, 12.5 mmol; 62% yield, 95% recovery), m.p. 176–178°. T.l.c. (solvents *A*, *D*, and *E*) and 80-MHz, ^{1}H-n.m.r. analyses confirmed that the homogeneous product so obtained was identical to that prepared by method a.

ACKNOWLEDGMENTS

The authors thank Dr. L. S. Kan of The Johns Hopkins University Baltimore N.M.R. Biomedical Research Center and Dr. C. A. Townsend of The Johns Hopkins University Department of Chemistry for the use of their instrumental facilities. We want especially to acknowledge the contribution of Dr. Martin Hulce and Dr. Siegfried Christensen for their invaluable instruction in the use of the instrumentation made available by The Johns Hopkins University Department of Chemistry, and that of Mr. Joe Cousins for his expert technical assistance in obtaining the 300-MHz, ^{1}H-n.m.r. spectra. Dr. A. T. Tu and Mr. W. K. Liddle of the Department of Biochemistry of the Colorado State University kindly recorded the laser-Raman spectra. We are grateful to Dr. J. N. BeMiller of the Department of Chemistry and Biochemistry of the Southern Illinois University at Carbondale for providing us with a preprint of his group's studies on the synthesis of per-*O*-acetylated aldohexopyranosyl cyanides, and for helpful discussions on this subject.

REFERENCES

1 H. FRITZ, J. LEHMANN, AND P. SCHLESSELMANN, *Carbohydr. Res.*, 113 (1983) 71–92; P. SCHLESSELMANN, H. FRITZ, J. LEHMANN, T. UCHIYAMA, C. F. BREWER, AND E. J. HEHRE, *Biochemistry*, 21 (1982) 6606–6614; and references cited in these articles.

2 H.-M. DETTINGER, G. KURZ, AND J. LEHMANN, *Carbohydr. Res.*, 74 (1979) 301–307.

3 M. BROCKHAUS AND J. LEHMANN, *Carbohydr. Res.*, 63 (1978) 301–306; J. LEHMANN AND B. SCHWESINGER, *ibid.*, 110 (1982) 181–185; O. P. VAN DIGGELEN, H. GALJAARD, M. L. SINNOTT, AND P. J. SMITH, *Biochem. J.*, 188 (1980) 337–343; and references cited in these articles.

4 M. CHMIELEWSKI, J. N. BEMILLER, AND D. P. CERRETTI, *Carbohydr. Res.*, 97 (1981) c1–c4; F. NICOTRA, F. RONCHETTI, AND G. RUSSO, *J. Org. Chem.*, 47 (1982) 4459–4462.

5 M. L. SHULMAN, S. D. SHIYAN, AND A. YA KHORLIN, *Carbohydr. Res.*, 33 (1974) 229–235; S. D. SHIYAN, O. E. LAKHTINA, M. L. SHULMAN, AND A. YA. KHORLIN, *Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 25 (1976) 188–190.

6 For a review, see: S. HANESSIAN AND A. G. PERNET, *Adv. Carbohydr. Chem. Biochem.*, 33 (1976) 111–188.

7 For examples, see S. HANESSIAN, T. J. LIAK, AND D. M. DIXIT, *Carbohydr. Res.*, 88 (1981) c14–c19; J. K. CHA, W. J. CHRIST, J. M. FINAN, Y. KISHI, L. L. KLEIN, S. S. KO, J. LEDER, W. W. MCWHORTER, JR., K.-P. PFAFF, M. YONAGA, D. UEMURA, AND Y. HIRATA, *J. Am. Chem. Soc.*, 104 (1982) 7369–7371, and references cited therein; N. J. BARNES, A. H. DAVIDSON, L. R. HUGHES, G. PROCTER, AND V. RAJCOOMAR, *Tetrahedron Lett.*, (1981) 1751–1754; J. WESTLEY, *Adv. Appl. Microbiol.*, 22 (1977) 177–223.
8 For reviews, see: B. FRASER-REID, *Acc. Chem. Res.*, 8 (1975) 192–201; S. HANESSIAN, *ibid.*, 12 (1979) 159–165; B. FRASER-REID AND R. C. ANDERSON, *Fortschr. Chem. Org. Naturst.*, 39 (1980) 1–61; A. VASELLA, in R. SHEFFOLD (Ed.), *Modern Synthetic Methods*, Vol. 2, Verlag Sauerlander, Aarau, Switzerland, 1980, pp. 173–267; *R. Soc. Chem., Spec. Period. Rep., Carbohydr. Chem.*, 9–15, Part 1 (1977–1983).
9 R. W. MYERS AND Y. C. LEE, *Abstr. Int. Symp. Carbohydr. Chem., 11th*, Vancouver, B. C., Canada, 1982, I-30.
10 B. HELFERICH AND K. L. BETTIN, *Chem. Ber.*, 94 (1961) 1159–1160.
11 B. COXON AND H. G. FLETCHER, JR., *J. Am. Chem. Soc.*, 86 (1964) 922–926.
12 B. COXON AND H. G. FLETCHER, JR., *Chem.Ind. (London)*, (1964) 662–663.
13 B. COXON, *Ann. N Y. Acad. Sci.*, 222 (1973) 952–970.
14 B. COXON AND H. G. FLETCHER, JR., *J. Am. Chem. Soc.*, 85 (1963) 2637–2642.
15 E.-F. FUCHS AND J. LEHMANN, *Chem. Ber.*, 108 (1975) 2254–2260.
16 T. HUYNH-DINH, C. GOUYETTE, AND J. IGOLEN, *Tetrahedron Lett.*, (1980) 4499–4502.
17 G. GRYNKIEWICZ AND J. N. BEMILLER, *Abstr. Int. Symp. Carbohydr. Chem., 11th*, Vancouver, B. C., Canada, 1982, I-18.
18 G. GRYNKIEWICZ AND J. N. BEMILLER, *Carbohydr. Res.*, 112 (1983) 324–327; 124 (1983) c30.
19 M. CHMIELEWSKI, J. N. BEMILLER, AND D. P. CERRETTI, *J. Org. Chem.*, 46 (1981) 3903–3908.
20 R. U. LEMIEUX, T. TAKEDA, AND B. Y. CHUNG, *Am. Chem. Soc. Symp. Ser.*, 39 (1976) 90–115, and references cited therein.
21 R. W. MYERS AND Y. C. LEE, unpublished results.
22 V. I. BETANELI, M. V. OVCHINNIKOV, L. V. BACKINOWSKY, AND N. K. KOCHETKOV, *Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 28 (1979) 2561–2567.
23 J. E. CHRISTENSEN AND L. GOODMAN, *Carbohydr. Res.*, 7 (1968) 510–512.
24 (a) P. BOULLANGER, D. MARMET, AND G. DESCOTES, *Tetrahedron*, 35 (1979) 163–167; (b) M. MARTIN-LOMAS AND M. E. CHACÓN-FUERTES, *Carbohydr. Res.*, 59 (1977) 604–606; (c) R. J. M. NOLTE, J. A. J. VAN ZOMEREN, AND J. W. ZWIKKER, *J. Org. Chem.*, 43 (1978) 1972–1975.
25 B. HELFERICH AND K. L. BETTIN, *Chem. Ber.*, 104 (1971) 1701–1702.
26 A. T. TU, W. K. LIDDLE, Y. C. LEE, AND R. W. MYERS, *Carbohydr. Res.*, 117 (1983) 291–297.
27 C. S. HUDSON, *J. Am. Chem. Soc.*, 31 (1909) 66–86.
28 See for examples, G. WULFF AND G. ROHLE, *Angew. Chem., Int. Ed. Engl.*, 13 (1974) 157–170; H. PAULSEN, *ibid.*, 21 (1982) 155–173; K. IGARASHI, *Adv. Carbohydr. Chem. Biochem.*, 34 (1977) 243–283; A. F. BOCHKOV AND G. E. ZAIKOV, *Chemistry of the O-Glycosidic Bond: Formation and Cleavage*, Pergamon Press, Oxford, England, 1979; C. SCHUERCH, *Am. Chem. Soc. Symp. Ser.*, 87 (1979) 80–94.
29 H. PAULSEN, *Adv. Carbohydr. Chem. Biochem.*, 26 (1971) 127–195.
30 R. U. LEMIEUX, *Methods Carbohydr. Chem.*, 2 (1963) 221–222.
31 J.-H. TSAI AND E. J BEHRMAN, *Carbohydr. Res.*, 64 (1978) 297–301.
32 D. H. LEABACK, E. C. HEATH, AND S. ROSEMAN, *Biochemistry*, 8 (1969) 1351–1359.
33 D. T. CONNOLLY, S. ROSEMAN, AND Y. C. LEE, *Carbohydr. Res.*, 87 (1980) 227–239.
34 J. N. BEMILLER, personal communication.