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Synthesis of 3-*C*-carbamoyl-3-*C*-cyano-3-deoxyhexopyranosides by cyclization of dialdehydes with cyanoacetamide

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ABSTRACT

The dialdehydes **1** and **11** obtained by periodate oxidation of methyl α- and β-D-glucopyranoside underwent cyclization with cyanoacetamide to give 3-deoxyhexopyranosides bearing a carbamoyl and a cyano group at C-3. Three products formed from **1** and were isolated as 4,6-benzylidene acetals and found to have the α-D-*gluco*, α-D-*manno*, and β-L-*gluco* configurations. From **11** was obtained a normal cyclization product having the β-D-*gluco* configuration, its 4-methyl ether, and a 1:2 addition product.

INTRODUCTION

In continuation of our work on the synthesis of *C*-glycosides[1,2] and *O*-glycosides[2,3] bearing two branches at C-3, achieved by cyclization of 1,5-dialdehydes with reactive methylene compounds, we report the preparation of methyl 3-deoxyhexopyranosides substituted at C-3 by a carbamoyl and a cyano group. Such compounds can be converted into 3-amino-3-aminomethyl-3-deoxy sugars by Hofmann degradation of the amide function and reduction of the cyano group[4]; sugars of this type are of interest as reactants for condensation with anthracyclinones in connection with our studies[5] on the synthesis of novel, modified anthracycline antitumor agents.

RESULTS AND DISCUSSION

Various 1,5-dialdehydes have previously been condensed with cyanoacetamide, to give acceptable yields of cyclic products bearing geminal carbamoyl and cyano groups. In fact, the first use of this reagent with the dialdehyde **1** [α-(*S*)-methoxy-α'-(*R*)-hydroxymethyldiglycolaldehyde; (2*S*,4*R*)-2-methoxy-4-hydroxymethyl-3-oxapentanedial] was reported by Nemal'tsev and co-workers[6], who obtained the crystalline α-D-*gluco** (**2**) and α-D-*manno** (**3**) derivatives in 51 and 33% yields by sodium methoxide-

* According to the IUPAC-IUB 1980 Recommendations for branched chain sugars, the C-3 substituent of higher priority according to the sequence rules is considered to replace hydroxyl, and that of lower priority to replace hydrogen, in the parent monosaccharide.

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catalyzed cyclization at −5° for 15–18 min. After a reaction time of 90–100 min, the proportions of isolated **2** and **3** were 54 and 9%, suggesting the occurrence of retro-addition in thermodynamically less stable **3**. No other products were observed. When we repeated the reaction under the same conditions, but with a reaction time of 4 h (in the hope of augmenting the yield of the more stable **2**), the product mixture obtained in 51% yield could not be resolved by column chromatography using the reported[6] or other solvent systems. However, the presence of the glycosides **2** and **3**, and additionally, the β-L-*gluco* isomer **4**, was established by benzylidenation of the mixture with α,α-dimethoxytoluene, followed by chromatography, to give 16% (based on **1**) of the α-D-*gluco* acetal **5** that contained a small proportion (less than one-tenth, removable by recrystallization) of the α-D-*manno* isomer **7**, and 12% of the β-L-*gluco* acetal **9**. Cyclization of **1** with cyanoacetamide at room temperature during 96 h, in the presence of piperidine as the catalyst, gave a product mixture (41%) from which, following benzylidenation, a 2.5:1 mixture of **5** and **7** (23% based on **1**) and pure **9** (6%) were chromatographically isolated. Acetylation of **5** and **9** furnished the corresponding 2-acetates **6** and **10**, whereas acetylation of the mixture of **5** and **7** gave the 2-acetate **8** of the latter, isolated by chromatography.

Similar experiments were performed with the dialdehyde **11** [α-(*R*)-methoxy-α'-(*R*)-hydroxymethyldiglycolaldehyde; (2*R*,4*R*)-2-methoxy-4-hydroxymethyl-3-oxapentanedial]. Under the conditions of sodium methoxide catalysis employed for **1**, but with a reaction time of only 0.5 h, **11** gave a mixture from which chromatography yielded the β-D-*gluco* derivative **12** (41%), its 4-methyl ether **14** (4.6%), and a mixed fraction consisting of **12** and a product of 1:2 addition, namely **16**. Acetylation of this fraction furnished the triacetate **13** of **12** (16% based on **11**) and the diacetate **17** (9.5%) of **16**, both crystalline. Under conditions of catalysis by piperidine as employed for **1**, but with a reaction time of 46 h, **11** gave **12**, which was chromatographically separated from unidentified by-products and isolated crystalline in 51% yield. Benzylidenation of pure **12** afforded the 4,6-acetal **18** (87%), characterized further as its 2-acetate **19**. Compounds **12**, **18**, and **19** were shown by their physical constants and spectra to be the enantiomers of **4**, **9**, and **10**, respectively.

The structures of the new compounds were established on the basis of elemental analysis and spectroscopic data. Thus, the $J_{1,2}$ values (see Table I) for **5**, **6**, and **8** (3.9, 3.6, and 1.2 Hz) indicated H-1*eq*–H-2*ax* and H-1*eq*–H-2*eq* relationships in agreement with the proposed structures, and the $J_{1,2}$ values of 7.8–8.2 Hz for **9** and **10** as well as for **12**–**15** and **17** signified H-1*ax*–H-2*ax* orientations. All of the new compounds had $J_{4,5}$ values in the range of 9.3–10.7 Hz, indicating H-4*ax*–H-5*ax* arrangements. The configurations at C-2 and C-4 were thus established. As far as the configuration at C-3 is concerned, Nemal'tsev and co-workers[6] had already determined the axial orientation of the cyano group in **2** and **3** by measuring the heteronuclear C-H couplings $^3J_{CN\text{-}3,H\text{-}4}$ and $^3J_{CN\text{-}3,H\text{-}2}$. The *C*N signal for **2** was a triplet with $J = 8.7$, and for **3** a doublet of doublets with $J =$ 8.6 and 1.2 Hz. The ^{13}C-n.m.r. data (Table II) supported the assignments. In particular, the C-1 chemical shifts of **5** and **6** (98.1 and 96.1 p.p.m.) indicated axial anomeric groups, whereas the shifts of C-1 for all other compounds (except for the dicarbamoyl

TABLE I

^{1}H-N.m.r. data for 3-*C*-carbamoyl-3-*C*-cyano-3-deoxyglycosides

Compound	*Chemical shifts (δ) and multiplicities*								
	H-1	*H-2*	*H-4*	*H-5*	*H-6*	*H-6'*	OCH_3[a]	NH_2[b]	*Others*
5[c,d]	4.80d	4.27dd[e]	3.93d	4.10dt	4.34dd	3.74~t	3.51	6.50, 5.81	5.50[f], 3.05d (O*H*)
6[d,g]	5.07d	5.52d	———	——4.50–3.75m——		———	3.48	6.50, 5.70	5.55[f], 2.15s (Ac)
8[d,g]	4.65d	5.55d	———	——4.40–3.70m——		———	3.50	6.70, 5.80	5.70[f], 2.10s (Ac)
9,18[c,h]	4.52d	3.88d	3.90d	3.80dt	4.31dd	3.71~t	3.50		5.45[f]
10,19[c,d]	5.41d	4.67d	4.05d	3.90dt	4.41dd	3.80~t	3.51	6.30, 5.70	5.52[f], 2.11s (Ac)
12[c,i]	4.25d	3.54dd	3.76dd	——3.66–3.36m——		———	3.42	7.59, 7.48	6.90d (O*H*-2), 5.96d (O*H*-4), 4.64t (O*H*-6)
13[c,i]	4.65d	5.27d	5.39dd	4.02m	4.19dd	4.05dd	3.41	7.98, 7.80	2.05, 2.05, 2.02 (3s, 9 H, 3 Ac)
14[c,i]	4.27d	3.59dd	3.72d	——3.67–3.42m——		———	3.42, 3.33	7.75, 7.60	6.21d (O*H*-2), 4.86t (O*H*-6)
15[c,d]	4.58d	5.23d	3.92d	——3.51–3.35m——		———	3.47, 3.44	6.50, 6.20	2.11s (6 H, 2 Ac)
17[c,d]	4.65d	5.12d	3.20d	——4.40–4.15m——		———	3.50	7.0, 6.9 6.7, 6.4	2.20, 2.10 (s, 2 Ac), 3.75 *j*

	Coupling constants (Hz)							
	$J_{1,2}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$	$J_{OH,2}$	$J_{OH,4}$	$J_{OH,6}$
5	3.9	~9.8	~9.8	5.0	10.5	9.7		
6	3.6							
8	1.2							
9,18	8.0	~9.5	~9.5	4.3	10.1			
10,19	8.2	~9.3	~9.3	4.4	10.1			
12	7.9	9.6				5.2	6.2	5.6
13	8.0	10.7	4.6	2.6	12.2			
14	8.0	9.8		1.8	12.1	5.3		5.5
15	8.1	9.9	3.9	2.2	12.2			
17	7.8	10.2						

[a] Singlet. [b] Broad singlets. [c] At 300 MHz. [d] In $CDCl_3$. [e] Reduced to d after D_2O exchange. [f] Singlet (PhC*H*); the Ph signals occurred as multiplets at δ 7.45–7.20. [g] At 80 MHz. [h] In acetone-d_6 + D_2O. [i] In dimethylsulfoxide-d_6. [j] *C*-H of $CH(CN)CONH_2$ group.

derivative **17**) were in the range 100.2–102.7, in accord with the presence of equatorial anomeric groups[7]. The position of the methyl ether group in **14** was deduced to be C-4 from the downfield shift incurred by H-2 on acetylation to **15** (δ 3.59→5.23). Similarly, the ring-proton signal at lowest field (δ 5.12) in **17** could be assigned to a proton at an *O*-acetylated position, which must have been C-2 as the proton was coupled with H-1. It follows that the H_2NCO-CH-CN branch was situated at C-4.

From a preparative point of view, the most advantageous procedure for obtaining a 3-carbamoyl-3-cyano-3-deoxy-glucopyranoside is to start from **11** and to use the method of piperidine catalysis, which gave 51% of the β-glycoside **12** in a straightforward manner. The method of methoxide catalysis applied to **11** produced **12** in a

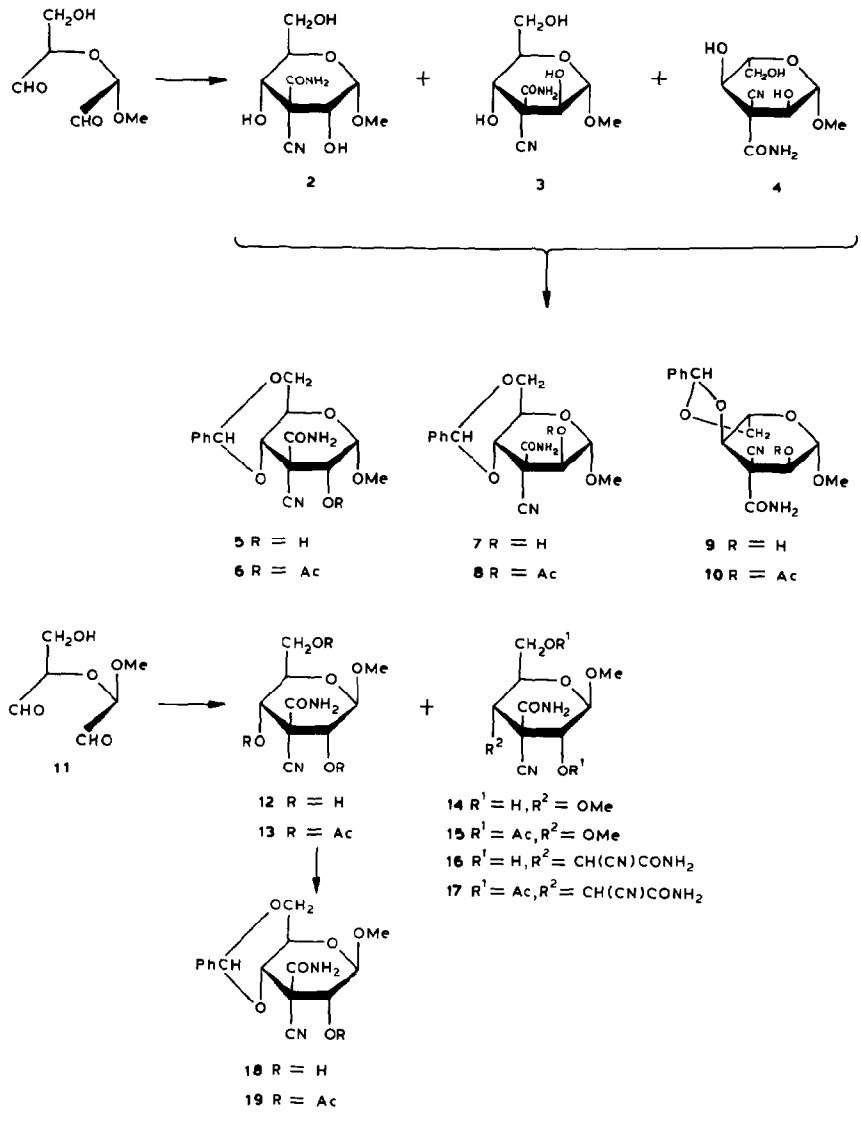
TABLE II

^{13}C-N.m.r. chemical shifts for 3-*C*-carbamoyl-3-*C*-cyano-3-deoxyglycosides

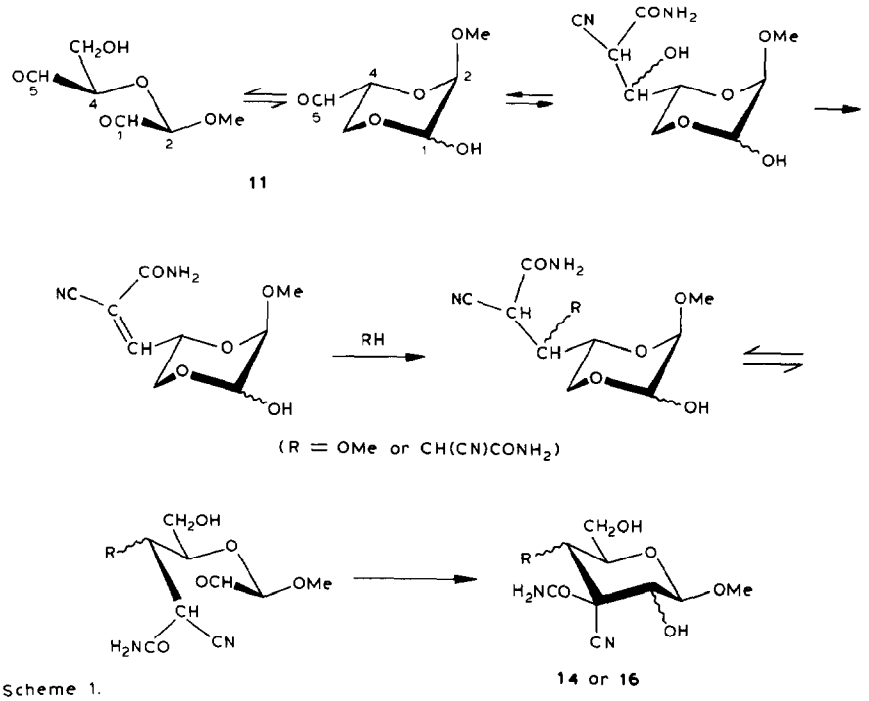
Compound	*Chemical shifts* (δ)									
	C-1	*C-2*	*C-4*	*C-5*	*C-3*	*C-6*	OCH_3	*CN*	$CONH_2$	*Others*[a]
5[a,c]	98.1	70.0	60.4	77.0	54.4	68.7	55.9	116.5	166.2	
6[b,d]	96.1	70.1	60.6	77.6	51.2	68.7	55.8	[e]	165.1	20.5 (*COCH*$_3$)
8[b,c]	98.5	70.1	61.3	74.5	55.6	68.7	55.6	114.6	164.2	168.9 (*MeCO*), 20.7 (*COCH*)
9,18[c,f]	101.6	70.7	65.9	76.7	56.0	68.1	56.8	115.9		
10,19[b,c]	101.4	———	69.3,66.7	———	77.4	54.6	68.5	57.3	115.5	163.7 167.9 (*MeCO*), 20.4 (*COCH*$_3$)
12[c,g]	102.7	70.1	67.8	76.9	60.7	60.4	56.1	117.5	166.8	
13[c,g]	100.2	68.7	67.1	71.8	56.4	61.5	56.6	115.1	163.1	169.9, 168.1, 167.8 (3 *MeCO*), 20.4, 20.14, 20.1 (3 *COCH*$_3$)
14[c,g]	102.7	——	76.8,75.8,70.3	——	59.1	59.7	56.2	117.1	166.7	59.7 (*CH*$_3$*O-4*)
15[b,c]	100.8	——	77.7,73.4,69.2	——	61.1	62.3	56.9	116.3	165.2	170.7, 168.2 (2 *MeCO*), 57.1 (*CH*$_3$*O-4*), 20.9, 20.6 (2 *COCH*$_3$)
17[c,g]	99.8	69.8	[h]	77.3	55.8	63.5	56.1	115.2, 115.0,	164.4 164.1	169.8, 168.3 (2 *MeCO*), 20.4, 20.2 (2 *COCH*$_3$)

[a] All benzylidene derivatives showed 4 signals (Ph) in the range δ 137–126, and a signal for Ph*C*H at δ 102.5 ± 0.5. [b] In $CDCl_3$. [c] At 75.47 MHz. [d] At 20.13 MHz. [e] Signal not discernible. [f] In acetone-d_6 + D_2O. [g] In dimethyl sulfoxide-d_6. [h] One of two signals at δ 38.6 and 35.6, the other one belonging to the C-4 branch carbon atom.

similar yield, but part of the product was isolated only after acetylation to **13**, and 4-substituted byproducts (**14** and **16**) were encountered. The formation of these byproducts is explained as shown in Scheme 1. It is assumed that the primary addition of cyanoacetamide takes place preferentially at C-5 of the 3-oxapentanedial **11**, with the C-1 carbonyl group being "protected" by reversible, cyclic hemiacetal formation with the hydroxymethyl group. Dehydration and subsequent Michael addition of solvent methanol or cyanoacetamide to the unsaturated intermediate, followed by cyclization, leads to **14** or **16**. Similar twofold additions have been observed in related cases[2,3,8,9], and although no similar byproducts were obtained from **1** in the present study, it cannot be ruled out that minor amounts were formed but escaped detection. Compound **1** did give 1:2 adducts in low yields with *tert*-butyl[3] and ethyl[2] cyanoacetate; therefore, no fundamental difference between the anomers **1** and **11** with respect to propensity for double addition is apparent.



On the other hand, the "normal" cyclization of **1** was accompanied by a partial epimerization at C-5 of the product, to give the *β*-L-glucoside **4** (identified as its 4,6-acetal **9**). Whereas epimerization at C-2 and C-4 in pyranosides bearing an activating group on C-3 (*e.g.* **2**⇌**3**) are frequent and mechanistically well-understood[10], especially in the chemistry of 3-deoxy-3-nitro sugars, epimerizations at C-5 are rare. However, instances have been reported in the cyclization[11] of **1** and **11** with nitroethane, and in reactions of **1** with ethyl and *tert*-butyl cyanoacetates[3]. When a methanolic solution of **1** and sodium methoxide was allowed to stand for 1 h prior to addition of cyanoacetamide, the proportion of C-5 epimerized product was not changed signif-



Scheme 1.

icantly, which tends to suggest that the epimerization takes place not in the starting dialdehyde but at some stage during or after the reaction with the active-methylene compound.

EXPERIMENTAL

General methods. — Solutions in nonhydroxylic solvents were dried with anhydrous Na_2SO_4. Column chromatography was performed on silica gel Merck (70–230 mesh, ASTM) with 2:11 (*A*) or 1:10 (*B*) methanol–chloroform or 1:5 ethyl acetate–ether (*C*) as eluents, unless otherwise indicated. Melting points, determined with an electrothermal apparatus, are uncorrected. Optical rotations were measured at room temperature in a Perkin–Elmer 141 instrument. Infrared data (ν_{max}) were recorded using KBr disks. Details of the measurements of ^{1}H- and ^{13}C-n.m.r. spectra are given in Tables I and II.

The dialdehydes **1** and **11** were prepared[12] by oxidation, with sodium metaperiodate, of methyl α-D-glucopyranoside and methyl β-D-glucopyranoside, respectively (2.91 g, 15 mmol, for each experiment).

Cyclization of dialdehyde **1** *catalyzed by sodium methoxide.* — Sodium methoxide solution (freshly prepared from 345 mg of Na in 15 mL of methanol) was added under

stirring to a chilled (−5°) solution of **1** (15 mmol) and cyanoacetamide (1.26 g, 15 mmol) in methanol (75 mL). The mixture was kept for 4 h at −5° in a stoppered flask, then deionized by Amberlite IR-120(H^+) resin. The resin was filtered off and washed exhaustively with methanol, and the filtrate was concentrated to a light-brown syrup. This was passed through a column of silica gel in solvent *B* for separation of the product from unreacted cyanoacetamide and removal of dark-colored impurities. The cyclization products were obtained as a solid (1.88 g, 51%), a solution of which in dry acetonitrile (30 mL) was treated at room temperature with α,α-dimethoxytoluene (1.8 mL) and *p*-toluenesulfonic acid (50 mg) for 2 h and then concentrated at 35° to one-half of its volume to complete the acetalation. Carefully neutralized with triethylamine, the solution was evaporated and the product chromatographed on a column (ether). Eluted first was 0.59 g (12%) of methyl 4,6-*O*-benzylidene-3-*C*-carbamoyl-3-*C*-cyano-3-deoxy-β-L-glucopyranoside (**9**), m.p. 252–253° (from ethyl acetate–hexane), $[\alpha]_D$ +37° (*c* 1, MeOH); ν_{max} 3480, 3440, 3320, 3300, 2250 (CN), 1720, 1700, and 1600 cm^{-1}.

Anal. Calc. for $C_{16}H_{18}N_2O_6$ (334.3): C, 57.50; H, 5.40; N, 8.40. Found: C, 57.27; H, 5.56; N, 8.23.

Subsequent fractions eluted from the column gave 0.80 g (16%) of methyl 4,6-*O*-benzylidene-3-*C*-carbamoyl-3-*C*-cyano-3-deoxy-α-D-glucopyranoside (**5**), m.p. 107–109° (from ethyl acetate–hexane); $[\alpha]_D$ +89.5° (*c* 1, MeOH); ν_{max} 3500–3100, 2200 (CN), 1740, 1690, and 1600 cm^{-1}.

Anal. Calc. as for **9**. Found: C, 57.26; H, 5.67; N, 8.31.

The 300-MHz ^{1}H-n.m.r. spectra of **5** revealed the presence of α-D-*manno* isomer **7** as a minor component (< 10%), recognizable by satellite peaks (δ 5.62 and 3.46) near the PhC*H* (δ 5.52) and OCH_3 (δ 3.51) signals for **5**.

Cyclization of dialdehyde **1** *catalyzed by piperidine.* — A solution of **1** (15 mmol), cyanoacetamide (1.26 g, 15 mmol), and piperidine (0.7 mL) in 1,4-dioxane (50 mL) and water (25 mL) was stored at room temperature for 96 h, then concentrated and coevaporated several times with added ethanol. The crude product was chromatographed (solvent *B*) to give a forefraction of unidentified byproducts, followed by the cyclization products (1.50 g, 41%). The solid material was benzylidenated, processed, and chromatographed as described in the preceding section. The first chromatographic fractions yielded crystalline **9** (0.32 g, 6%). Subsequent fractions gave a mixture (1.17 g, 23%) of **5** and **7**, present in a 2.5:1 ratio as revealed by the ^{1}H-n.m.r. spectrum. To a solution of this mixture (820 mg) in dry chloroform (15 mL) and acetic anhydride (4 mL) was added, at −18°, a solution of pyridine (2 mL) in chloroform (15 mL). The mixture was kept for 4 h at −18° and overnight at 0°, then washed with aq. 5% HCl followed by aq. $NaHCO_3$ and water, dried, and concentrated with coevaporation of added toluene. Column chromatography (1:1 ether–hexane) of the crude material gave, first, 355 mg of methyl 2-*O*-acetyl-4,6-*O*-benzylidene-3-*C*-carbamoyl-3-*C*-cyano-3-deoxy-α-D-glucopyranoside (**6**), m.p. 209–210° (from ethanol), $[\alpha]_D$ +69.9° (*c* 1, $CHCl_3$); υ_{max} 3449, 3250, 3190, 1754, 1712, 1683, 1615, 1222, 1161, and 1062 cm^{-1}.

Anal. Calc. for $C_{18}H_{20}N_2O_7$ (376.4): C, 57.40; H, 5.35; N, 7.44. Found: C, 57.70; H, 5.33; N, 7.11.

Eluted second was 145 mg of methyl 2-*O*-acetyl-4,6-*O*-benzylidene-3-*C*-carbamoyl-3-*C*-cyano-3-deoxy-α-D-mannopyranoside (**8**), m.p. 228–230°, $[\alpha]_D$ +31.5° (*c* 1, $CHCl_3$); ν_{max} 3437, 3335, 1756, 1705, 1606, 1228, 1135, 1079, 1045, and 967 cm^{-1}.

Anal. Calc. as for **6**. Found: C, 57.80; H, 5.49; N, 7.14.

Cyclization of dialdehyde **11** *catalyzed by sodium methoxide.* — Dialdehyde **11** (15 mmol) was cyclized with cyanoacetamide as described for **1**, except that a reaction time of 0.5 h was used. Similar processing and chromatography gave three product fractions. Eluted first was 0.18 g (4.6%) of methyl 3-*C*-carbamoyl-3-*C*-cyano-3-deoxy-4-*O*-methyl-β-D-glucopyranoside (**14**), m.p. 117–120°, $[\alpha]_D$ −13° (*c* 1, MeOH); ν_{max} 3414, 2250, 1720, and 1616 cm^{-1}.

Anal. Calc. for $C_{10}H_{16}N_2O_6$ (260.25): C, 46.15; H, 6.20; N, 10.76. Found: C, 46.30; H, 6.04; N, 10.70.

The intermediate chromatographic fraction yielded 1.50 g (41%) of methyl 3-*C*-carbamoyl-3-*C*-cyano-3-deoxy-β-D-glucopyranoside (**12**), m.p. 296–298°, $[\alpha]_D$ −28° (*c* 1, MeOH); ν_{max} 3530, 3442, 3384, 3241, 1700, 1673, and 1609 cm^{-1}.

Anal. Calc. for $C_9H_{14}N_2O_6$ (246.2); C, 43.90; H, 5.73; N, 11.40. Found: C, 43.87; H, 5.84; N, 11.61.

The slow-moving fraction contained **12** and **16**. It was treated with a mixture of acetic anhydride (3 mL), acetic acid (6 mL), and acetyl chloride (12 mL) for 16 h at room temperature. After concentration to approximately one-half its volume the solution was diluted with chloroform (50 mL), washed several times with aq. $NaHCO_3$ and then water, dried, and evaporated. Column chromatography (solvent *C*) of the crude product gave first 0.60 g (16% based on **1**) of methyl 2,4,6-tri-*O*-acetyl-3-*C*-carbamoyl-3-*C*-cyano-3-deoxy-β-D-glucopyranoside (**13**), m.p. 234°, $[\alpha]_D$ −30.5° (*c* 1, MeOH); ν_{max} 3470, 3243, 3181, 1768, 1740, 1713, and 1686 cm^{-1}.

Anal. Calc. for $C_{15}H_{20}N_2O_9$ (372.3): C, 48.39; H, 5.41; N, 7.52. Found: C, 48.58; H, 5.47; N, 7.63.

Acetylation of pure **12** (1.10 g from the intermediate chromatographic fraction) gave **13** (1.60 g, 96%).

Eluted second from the column was 0.54 g (9.5%) of methyl 2,6-di-*O*-acetyl-3-*C*-carbamoyl-4-*C*-[carbamoyl(cyano)methyl]-3-*C*-cyano-3,4-dideoxy-β-D-glucopyranoside (**17**), m.p. 172–174° (from ethyl acetate–hexane), $[\alpha]_D$ −78° (*c* 1, MeOH); ν_{max} 3400–3200, 2130, 1765, 1706, 1695, 1685, and 1614 cm^{-1}.

Anal. Calc. for $C_{16}H_{20}N_3O_8$ (382.3): C, 50.26; H, 5.27; N, 10.99. Found: C, 50.50; H, 5.29; N, 11.05.

Cyclization of dialdehyde **11** *catalyzed by piperidine.* — A solution of **11** (15 mmol), cyanoacetamide (1.26 g, 15 mmol), and piperidine (0.7 mL) in 1,4-dioxane (50 mL) and water (25 mL) was kept for 46 h at 25°, and concentrated with coevaporation of several additions of ethanol. The residue was chromatographed (solvent *B*) to give a forefraction (0.4 g) of unidentified products, followed by almost pure (n.m.r.) **12** (1.89 g, 51%) usable as such for further reactions. A trace impurity was removed by crystallization from 1:10 methanol–dichloromethane to give pure **12** (1.25 g, 34%).

Benzylidenation of **12** (170 mg) as described for the preparation of **5** and **9** gave

methyl 4,6-O-benzylidene-3-C-carbamoyl-3-C-cyano-3-deoxy-β-D-glucopyranoside (**18**) in 87% yield after chromatography (ether), m.p. 252–253° (from ethyl acetate–hexane), $[\alpha]_D$ −36° (*c* 1, MeOH). The i.r. and n.m.r. spectra were identical with those of **9**.

Anal. Calc. for $C_{16}H_{18}N_2O_6$ (334.3): C, 57.50; H, 5.40; N, 8.40. Found: C, 57.27; H, 5.56; N, 8.23.

Acetylation of **9** *and* **18**. — To a solution of **9** (120 mg) in dry chloroform (15 mL) and acetic anhydride (3 mL) at −18° was added a solution of pyridine (1 mL) in chloroform (10 mL). The mixture was kept for 4 h at −18° and overnight at 0°, washed with aq. 5% HCl followed by aq. $NaHCO_3$ and water, dried, and concentrated with coevaporation of added toluene. The residue was crystallized from ethyl acetate–hexane to give 130 mg (98%) of methyl 2-*O*-acetyl-4,6-*O*-benzylidene-3-*C*-carbamoyl-3-*C*-cyano-3-deoxy-β-L-glucopyranoside (**10**), m.p. 235°, $[\alpha]_D$ +61° (*c* 1, $CHCl_3$); ν_{max} 3420, 3260, 3200, 2250, 1760, 1710, 1690, and 1610 cm^{-1}.

Anal. Calc. for $C_{18}H_{20}N_2O_7$ (376.4): C, 57.40; H, 5.40; N, 7.40. Found: C, 57.26; H, 5.55; N, 7.33.

Compound **18** (120 mg) was acetylated under the same conditions to give an 89% yield of the β-D *enantiomer* **19**, m.p. 232°, $[\alpha]_D$ −63° (*c* 1, $CHCl_3$). The i.r. and n.m.r. spectra were identical to those of **10**.

Anal. Found: C, 57.30; H, 5.41; N, 7.29.

Acetylation of **14**. — Compound **14** (130 mg) was acetylated as described for **12** and **16**. After processing, the product was crystallized from methanol (without prior chromatography) to give 130 mg (76%) of methyl 2,6-di-*O*-acetyl-3-*C*-carbamoyl-3-*C*-cyano-3-deoxy-4-*O*-methyl-β-D-glucopyranoside (**15**), m.p. 294–295°, $[\alpha]_D$ −36.5° (*c* 1, $CHCl_3$); ν_{max} 3458, 3245, 1743, 1705, and 1683 cm^{-1}.

Anal. Calc. for $C_{14}H_{20}N_2O_7$ (328.3): C, 51.21; H, 6.14; N, 8.53. Found: C, 51.10; H, 6.08; N, 8.60.

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