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Application of the Hofmann rearrangement in the synthesis of 3-amino sugar derivatives: preparation of some 3-*tert*-butoxycarbonylamino-3-cyano-3-deoxy and 3-acetamidomethyl-3-*tert*-butoxycarbonylamino-3-deoxy sugars*

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ABSTRACT

The cyclisation of dialdehydes, obtained from sugars, with cyanoacetamide and subsequent Hofmann rearrangement is a convenient and short approach to the synthesis of 3-amino sugar derivatives branched at C-3. Thus, derivatives of 3-carbamoyl-3-cyano-3-deoxy sugars **1–4** were transformed into *N*-protected 3-amino-3-cyano-3-deoxy sugars **5–8** by Hofmann rearrangement (lead tetra-acetate–*N*,*N*-dimethylformamide–*tert*-butyl alcohol). Reduction of the cyano group in these compounds ($NaBH_4$–$CoCl_2$) gave, after acetylation, the corresponding 1,2-diamino derivatives **13–16**.

INTRODUCTION

α-Aminonitriles, the utility of which in organic synthesis is well established[1], can be obtained by the Strecker[2,3] reaction from carbonyl compounds, and by the addition of hydrogen cyanide[3], cyanide ion[3], or trimethylsilyl cyanide[4] to the carbon–nitrogen double bond of azomethines (Schiff bases, oximes, hydrazones).

As part of a programme on the synthesis of modified anthracycline antibiotics, the synthesis of 3-amino-3-cyano-3-deoxy sugars was studied as a first step toward 3-amino-3-aminomethyl-, 3-amino-3-carboxy-, and 3-amino-3-deoxy sugars which, after the appropriate transformations, could be coupled with anthracyclinones.

The Strecker reaction[2,3] and the Bucherer modification[5] have been used only in few instances in order to obtain α-aminonitrile[6] and α-amino acid[7] derivatives of sugars, respectively. The synthesis of such products was envisaged by the use of the Hofmann rearrangement of some 3-carbamoyl-3-cyano-3-deoxy sugar derivatives, and we now report on the synthesis of some 3-*tert*-butoxycarbonylamino-3-*C*-cyano-3-deoxy sugars and their transformation into the corresponding 3-aminomethyl-3-*tert*-butoxycarbonylamino derivatives by reduction of the cyano function by means of the sodium borohydride–cobalt(II) chloride reagent[8].

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RESULTS AND DISCUSSION

Several 3-carbamoyl-3-*C*-cyano-3-deoxy-*C*-glycopyranosylfuran derivatives[9] and 3-carbamoyl-3-*C*-cyano-3-deoxy glycosides[10,11] have been synthesised by the cyclisation of 3-hetero-1,5-dialdehydes with cyanoacetamide, using piperidine or sodium methoxide as catalyst. These compounds are precursors for the synthesis of branched sugars having amino and cyano groups at C-3 by the transformation using the Hofmann rearrangement.

The Hofmann rearrangement usually involves (*a*) aqueous NaOBr or Br_2–NaOMe in methanol[12e], (*b*) iodobenzene diacetate[12f] or [bis(trifluoroacetoxy)iodo]benzene[12g], and (*c*) lead tetra-acetate[12a–d]. Reagent (*c*) was selected for the transformation of the carbamoyl derivatives **1–4** into the *tert*-butyl carbamates **5–8** (70–98%). The reactions were carried out with an excess of lead tetra-acetate, using *tert*-butyl alcohol to trap the intermediate isocyanates.

Zemplén *O*-deacetylation of **5–7** gave the hydroxy compounds **9–11**, respectively. However, when **8** was *O*-deacetylated, **12** was the major product together with < 5% of **17**. Treatment of **12** with sodium methoxide (1.1 equiv.) in methanol gave **17** in quantitative yield, which was transformed into the *N,O*-diacetyl derivative **18** by conventional acetylation. Compound **17** was formed by a selective intramolecular nucleophilic displacement of the *tert*-butoxycarbonyl group by the alkoxide anion formed at C-2 during the reaction. This reaction was not observed with the methyl pyranosides **5–7** probably due to the higher flexibility of the septanoside ring.

Attempts to synthesise 1,2-diamines by hydrogenation of α-aminonitriles were sometimes unsuccesful[13]. The difficulty in obtaining good yields is due to the small differences between the rates of hydrogenation and hydrogenolysis[14]. However, Satoh *et al.*[8a] reported that nitriles can be reduced to primary amines by reaction with transition metal salt–borohydride systems and, in particular, the combination $CoCl_2$ (2 equiv.)/$NaBH_4$ (10 equiv.) was very effective[8b]. The reduction of the cyano group in **5–8** with this reagent afforded **13–16** (63–81%) after acetylation.

Compounds **5–7**, **9–11**, and **13–15** adopt the $^4C_1$ conformation as indicated by the $J_{4,5ax}$ values of 8.6–10.5 Hz (H-4,5*ax trans*-diaxial). The $J_{1,2}$ values were 6.4–10.2 Hz (H-1,2 *trans*-diaxial) for **5**, **7**, **11**, **13**, and **15**, and 4.0 Hz (H-1,2 *cis*) for **6**, **10**, and **14**.

Compounds **8**, **12**, and **16–18** showed $J_{4,5}$ and $J_{1,2}$ values (8.1–10.5 and 6.4–7.6 Hz, respectively) in accordance with a *trans*-diaxial disposition for H-4,5 and a dihedral angle close to 160°[11] for H-1,2 in $a^{0,3}C_6(D)$ conformation. For **17** and **18**, the fused oxazolidinone ring does not change the conformation.

Since the Hofmann[12b,15] and Curtius[16] reactions proceed with retention of configuration, **5–18** should have the configuration at C-3 depicted (NHR equatorial, and the CN or AcNHMe axial).

Instead of the expected doublets and singlet, the signals of H-2 and/or H-4 and of the *tert*-butyl group in **6–7** and **13–15** (see Table I) appeared as broad signals and a broad singlet, respectively. This finding can be ascribed to a restricted rotation about the C–N bond in the carbamate, as was deduced from variable temperature n.m.r. mea-

TABLE I

^{1}H-N.m.r. data for **5–18**

Compound	*Chemical shifts (δ)*									
	H-1	*H-2*	*H-4*	*H-5*eq	*H-5*ax	*H-6*	*H-6'*	CH_2NH	*OMe*	*Others*
5[a,c]	4.65d	5.60d	5.50dd	4.10dd	3.80dd					6.65 (s, 1 H, furan H), 5.10 (bs, 1 H, NH)[d], 4.28 (q, 2 H, *J* 7.2 Hz, CH_3CH_2O), 2.50 (s, 3 H, furan Me), 2.15, 1.98 (2 s, 6 H, 2 Ac), 1.45 (s, 9 H, Me_3C), and 1.30 (t, 3 H, *J* 7.2 Hz, CH_3CH_2O)
6[a]	4.90d	5.60d	5.60d	4.20ddd	4.33dd	4.09dd			3.42s	5.05 (bs, 1 H, NH)[d], 2.17, 2.12, 2.05 (3 s, 9 H, 3 Ac), and 1.40 (bs, 9 H, Me_3C)
7[a]	4.63d	5.28–5.22[e]	5.37–5.32[e]		4.00ddd	4.37dd	4.14dd		3.51s	5.10 (s, 1 H, NH)[d], 2.16, 2.12, 2.05 (3 s, 9 H, 3 Ac), and 1.40 (bs, 9 H, Me_3C)
7[b]	4.59d	5.42bd	5.57[e]		3.94ddd	4.23dd	4.07d		3.41s	7.87 (s, 1 H, NH)[d], 2.08, 2.06, 2.00 (3 s, 9 H, 3 Ac), and 1.35 (bs, 9 H, Me_3C)
8[a]	4.82d	5.38d	5.44d		4.06dd	4.00m			3.40s	7.40–7.30 (m, 5 H, Ph), 5.47 (s, 1 H, PhC*H*), 4.90 (s, 1 H, NH)[d], 4.22 (dd, 1 H, $J_{7ax,7eq}$ 10.9 and $J_{6,7eq}$ 5.4 Hz, H-7*eq*), 3.70 (dd, 1 H, $J_{7ax,7eq}$ 10.9 and $J_{6,7ax}$ 9.4 Hz, H-7*ax*), 2.13, 2.12 (2 s, 6 H, 2 Ac), and 1.41 (s, 9 H, Me_3C)
9[a]	4.45d	3.94dd[f]	4.00m[a]	4.12dd	3.67dd					6.74 (s, 1 H, furan H), 5.85 (bs, 1 H, NH)[d], 5.43 (d, 1 H, $J_{4,OH}$ 3.3 Hz, HO-4)[d], 4.25 (q, 2 H, *J* 7.1 Hz, CH_3CH_2O), 4.10 (d, 1 H, $J_{2,OH}$ 4.3 Hz, HO-2)[d], 2.54 (s, 3 H, furan Me), 1.47 (s, 9 H, Me_3C), and 1.23 (t, 3 H, *J* 7.1 Hz, CH_3CH_2O)
10[b]	4.61d	4.00pseudo-t	3.89dd		3.70–3.40m				3.31s	7.46 (bs, 1 H, NH)[d], 5.92 (d, 1 H, *J* 5.9 Hz, OH)[d], 5.62 (d, 1 H, *J* 5.62 Hz, OH), 4.61 (m, 1 H, CH_2OH)[d], and 1.39 (bs, 9 H, Me_3C)
11[b]	4.24d	3.70dd	3.86dd		3.48m	3.65m	3.31m		3.34s	7.56 (bs, 1 H, NH)[d], 6.05 (d, 1 H, $J_{2,OH}$ 5.2 Hz, HO-2), 5.95 (d, 1 H, $J_{4,OH}$ 7.7 Hz, HO-4), 4.67 (pseudo-t, 1 H, $J_{6,OH} \approx J_{6',OH} \sim 5.9$ Hz, CH_2OH)[d], and 1.37 (s, 3 H, Me_3C)

Table continued overleaf

TABLE I (continued)

^{1}H-N.m.r. data for **5–18**

Compound	*Chemical shifts (δ)*									
	H-1	*H-2*	*H-4*	*H-5*eq	*H-5*ax	*H-6*	*H-6'*	CH_2NH	*OMe*	*Others*
12[a]	4.70d	(h)	4.13dd		——3.94–3.80m——				3.46s	7.50–7.30 (2 m, 5 H, Ph), 5.66 (s, 1 H, NH)[d], 5.52 (s, 1 H, PhC*H*), 4.00 (d, 1 H, $J_{2,OH}$ 5.9 Hz, HO-2)[d], 3.70 (pseudo-t, 1 H, $J_{7ax,7eq} + J_{6,7ax}$ 20.2 Hz, H-7*ax*), 3.70 (d, 1 H, $J_{4,OH}$ 2.2 Hz, HO-4), and 1.44 (s, 9 H, Me_3C)
13[a]	4.58d	5.51[e]	5.16[e]	3.92dd	3.71pseu-do-t			3.97m		6.56 (s, 1 H, furan H), 6.50 (m, 1 H, N*H*Ac), 5.51 (bs, 1 H, N*H*Boc), 4.19 (q, 2 H, *J* 7.0 Hz, CH_3CH_2O), 2.48 (s, 3 H, furan Me), 2.05, 1.97, 1.88 (3 s, 9 H, 3 Ac), 1.38 (bs, 9 H, Me_3C), and 1.27 (t, 3 H, *J* 7.0 Hz, CH_3CH_2O)
14[a]	4.87d	5.82d	5.53[e]		3.92m	4.17dd	4.06dd	[i]	3.37s	6.07 (m, 1 H, N*H*Ac), 6.00 (bs, 1 H, N*H*Boc), 2.08, 2.06, 2.04, 2.00 (4 s, 12 H, 4 Ac), and 1.38 (bs, 9 H, Me_3C)
15[a]	4.67d	5.08–4.98[e]	5.40–5.30[e]		[j]	4.33d	4.00–4.10dd	[j]	3.47s	6.50 (m, 1 H, N*H*Ac), 5.27 (bs, 1 H, N*H*Boc), 2.11, 2.06, 2.05, 1.98 (4 s, 12 H, 4 Ac), and 1.41 (bs, 9 H, Me_3C)
15[b]	4.74d	5.68d	5.80d		————4.20–3.90m————			3.61m	3.35s	7.96 (m, 1 H, NHAc), 6.47 (bs, 1 H, N*H*Boc), 2.01, 2.00, 1.97 (3 s, 12 H, 4 Ac), and 1.30 (bs, 9 H, Me_3C)
16[a]	4.66d	5.28d	5.36d		[k]	3.91pseu-do-t		[k]	3.32s	7.40–7.30 (2 m, 5 H, Ph), 6.52 (bs, 1 H, N*H*Ac), 5.42 (s, 1 H, PhC*H*), 4.92 (bs, 1 H, N*H*Boc), 4.17 (dd, 1 H, $J_{7ax,7eq}$ 10.7, $J_{6,7eq}$ 5.2 Hz, H-7*eq*), 3.66 (pseudo-t, 1 H, $J_{7ax,7eq} + J_{6,7ax}$ 20.3 Hz, H-7*ax*), 2.05, 2.01, 1.98 (3 s, 9 H, 3 Ac), and 1.73 (s, 9 H, Me_3C)

17[b]	4.90d	5.05d	/	3.61pseudo-t	/	3.40s	9.40 (s, 1 H, NH), 7.5–7.3 (2 m, 5 H, Ph), 6.67 (d, 1 H, $J_{4,OH}$ 5.4 Hz, OH), 5.63 (s, 1 H, PhC*H*), 4.16 (dd, 1 H, $J_{7ax,7eq}$ 10.5, $J_{6,7eq}$ 5.3 Hz, H-7*eq*), and 3.70 (pseudo-t, 1 H, $J_{6,7ax} \approx J_{7ax,7eq} \approx$ 10.5 Hz, H-7*ax*)
18[a]	4.97d	4.54d	5.33d	4.11dd	4.03d pseudo-t	3.51s	7.40 (bs, 5 H, Ph), 5.49 (s, 1 H, PhC*H*), 4.24 (dd, 1 H, $J_{7ax,7eq}$ 11.0, $J_{6,7eq}$ 5.1 Hz, H-7e), 3.73 (dd, 1 H, $J_{7ax,7eq}$ 11.0, $J_{6,7ax}$ 9.2 Hz, H-7*ax*), 2.47 (s, 3 H, AcN), and 2.09 (s, 3 H, AcO)

Table continued overleaf

TABLE I (continued)

Compound	*Coupling constants (Hz)*						
	$J_{1,2}$	$J_{4,5ax}$	$J_{4,5eq}$	$J_{5ax,5eq}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$
5	10.2	10.4	5.5	11.3			
6	3.9	8.6			4.3	2.2	12.3
7[a]	7.9	10.0			3.9	2.2	12.4
7[b]	8.0	10.1			4.3	1.2	12.5
8	7.1	8.3			10.0		
9	9.7	10.3	5.0	12.0			
10	4.0	9.6			4.7	[m]	10.2
11	7.9	9.7			[m]	[m]	[m]
12	6.9	8.1			[m]		
13	9.6	9.8	5.2	11.7			
14	3.9	10.5			5.2	2.3	12.1
15[a]	6.4	[m]			[m]	[m]	[m]
15[b]	8.2	9.6			[m]	[m]	[m]
16	6.4	8.8			[m]		
17	7.4	~10.5			~10.5		
18	7.6	8.4			10.0		

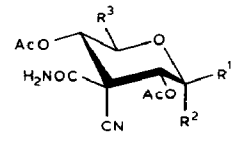
[a] For solutions in $CDCl_3$. [b] For solution in $(CD_3)_2SO$. [c] 80 MHz. [d] Exchangeable with D_2O. [e] Broad signal. [f] d, $J_{1,2}$ 9.7 Hz after isotopic change. [g] dd, $J_{4,5ax}$ 10.3, $J_{4,5eq}$ 5.0 Hz after isotopic change. [h] 4.24–4.20 (m, 2 H, H-2,7*eq*). [i] 4.00 (dd, 1 H, $J_{H,H}$ 15.0, $J_{H,NH}$ 5.1 Hz, CH_2NH), 3.74 (dd, 1 H, J 15.0, and 5.2 Hz, CH_2NH). [j] 4.05–3.85 (m, 3 H, H-5, CH_2NHAc). [k] 4.10–3.98 (m, 3 H, H-5, CH_2NHAc). [l] 4.02–3.90 (m, 2 H, H-4,6). [m] Not accurate from the spectrum.

TABLE II

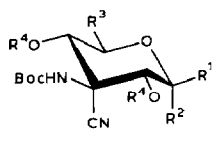
^{13}C-N.m.r. chemical shifts (δ) for **5–18**

Compound	*C-1*	*C-2*	*C-4*	*C-5*	*C-3*	*C-6*	*OMe*	*COMe*	*CONHBoc*	*CN*	*CMe$_3$*	*CMe$_3$*	*MeCO*	*Others*
5[a]	——72.2,69.8,68.5——			65.8	61.4			169.9,169.3	153.1	[d]	82.2	28.1	20.7,20.5	163.5 (*C*OOEt), 160.1 (furan C-2), 146.3 (furan C-5), 111.2 (furan C-4), 60.3 (CH_3CH_2O), and 14.3, 13.8 (furan *Me*, CH_3CH_2O)
6[a]	96.4	——68.8,66.9,66.2——			58.6	61.7	55.7	170.6,169.9, 169.4	152.6	114.5	[e]	28.1	20.7,20.6	
7[b]	100.0	69.3[f]	67.1	70.6[f]	64.2	61.4	56.4	169.8,168.6, 166.3	153.5	114.0	79.6	27.7	20.4,20.3	
8[a]	100.9	72.3	74.7	79.2	57.4	61.1	56.1	170.5,169.1	152.8	113.9	[e]	28.1	20.6	68.9 (C-7)
9[a]	——73.5,73.0,70.5——			66.3	64.4				156.6	[g]	83.4	28.2		163.7 (*C*OOEt), 160.2 (furan C-2), 147.2 (furan C-5), 111.9 (furan C-4), 60.5 (CH_3CH_2O), and 14.4, 13.9 (furan *Me*, CH_3CH_2O)
10[b]	96.5	——70.4,68.9,67.7——			61.9	60.2	54.5		154.7	116.2	79.2	28.0		
11[b]	102.6	——75.8,70.1,67.7——			64.4	60.4	56.2		154.2	116.1	78.8	28.1		
12[a]	103.4	69.1	74.3	81.6	59.9	60.8	56.1		156.0	115.5	*e*	28.2		
13[a]	——71.2,70.5——			64.8	59.9			170.6,169.4, 168.8	154.9		81.0	28.2	23.5,20.8, 20.5	163.7 (*C*OOEt), 159.7 (furan C-2), 147.7 (furan C-5), 114.2 (furan C-4), 60.2 (CH_3CH_2O), 37.6 (CH_2NH), and 14.3, 13.7 (furan *Me*, CH_3CH_2O)
14[a]	97.8	——69.6,67.6,66.6——			59.9	62.9	55.7	171.5,170.8, 169.0,168.7	154.0		80.0	28.2	23.2, 20.8, 20.6	41.3 (CH_2NH)
15[b]	99.1	69.7	67.0	78.1	60.3	62.8	55.8	170.9,170.0, 168.5,168.0	153.0		80.0	28.0	22.4,20.4	38.0 (CH_2NH)
16[a]	100.8 or 100.4	74.5	77.3	78.5	62.8	61.4	55.8	170.2,169.8, 169.2	155.0		80.1	29.7	23.5,20.6	66.9 (C-7), 38.1 (CH_2NH)
17[b]	98.7	——76.8,74.1——		81.8	——61.3,61.1——		55.1			116.5				156.1 (*C*ONH), 68.1 (C-7)
18[a]	98.5	——76.1,75.5——		80.1	58.9	62.1	56.2	171.2		112.4			25.0,20.6	151.1 (*C*ONAc), 69.0 (C-7)

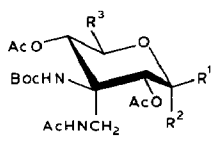
[a] For solution in $CDCl_3$. [b] For solution in $(CD_3)_2SO$. [c] All benzylidene derivatives showed 4 signals for Ph in the range δ 140–126, and a signal for Ph*C*H at δ 101 $\pm$ 1.0. [d] Signals at 114.4 and 113.6 correspond to CN, and furan C-3. [e] Not accurate from the spectrum. [f] Signals that could be interchangeable. [g] Signals at 114.9 and 114.6 correspond to CN, and furan C-3.



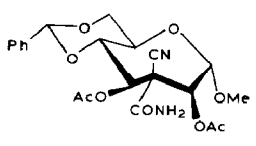
1 $R^1 = X, R^2 = R^3 = H$
2 $R^1 = H, R^2 = OMe, R^3 = CH_2OAc$
3 $R^1 = OMe, R^2 = H, R^3 = CH_2OAc$



5 $R^1 = X, R^2 = R^3 = H, R^4 = Ac$
9 $R^1 = X, R^2 = R^3 = R^4 = H$
6 $R^1 = H, R^2 = OMe, R^3 = CH_2OAc, R^4 = Ac$
10 $R^1 = R^4 = H, R^2 = OMe, R^3 = CH_2OH$
7 $R^1 = OMe, R^2 = H, R^3 = CH_2OAc, R^4 = Ac$
11 $R^1 = OMe, R^2 = R^4 = H, R^3 = CH_2OH$



13 $R^1 = X, R^2 = R^3 = H$
14 $R^1 = H, R^2 = OMe, R^3 = CH_2OAc$
15 $R^1 = OMe, R^2 = H, R^3 = CH_2OAc$



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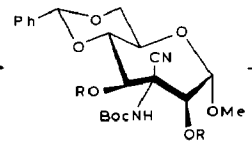
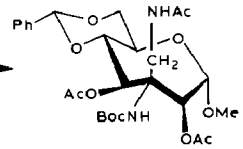


8 R = Ac
12 R = H



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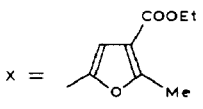

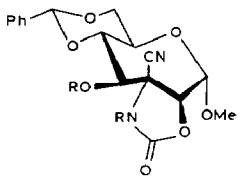

17 R = H
18 R = Ac

surements in **14** (increase of the temperature to 55° sharpened the signals), and is not due to a *through-space* mechanism[17] for spin coupling between H-2*ax*,4*ax* and the *tert*-butyl group because decoupling experiments did not change the shape of the signals. There was a slight improvement in the resolution of the signals when the solvent was changed from $CDCl_3$ to $(CD_3)_2SO$ for **7** and **15**.

The ^{13}C-n.m.r. data of **5**–**18** (see Table II) were in full accordance[18,19] with the assigned structures.

Thus, the cyclisation of dialdehydes obtained from sugars with cyanoacetamide followed by Hofmann rearrangement is a convenient and short way for the synthesis of 3-amino-3-cyano-3-deoxy sugars.

EXPERIMENTAL

General methods. — Melting points were recorded with an Electrothermal apparatus and are uncorrected. Spectral measurements were recorded with Perkin–Elmer 983G (i.r.), Perkin–Elmer 141 ($[\alpha]_D$), and Bruker AM 300 and Varian XL-300 (n.m.r.) instruments. Elemental analyses were obtained with a Perkin–Elmer 240C instrument.

C.i. (ether)-mass spectra were obtained with a Hewlett–Packard 5988A instrument. Optical rotations were measured at room temperature. Column chromatography was performed on silica gel (Merck 70–230 mesh, ASTM).

Hofmann rearrangements. — Lead tetra-acetate was added to a solution of the starting material (**1–4**) in *tert*-butyl alcohol–*N,N*-dimethylformamide. The mixture was stirred and boiled under reflux for 20 min, then cooled, toluene (100 mL) and ether (25 mL) were added, and the solution was filtered, washed with water (2 × 50 mL), dried ($MgSO_4$), and concentrated. The residue was subjected to column chromatography (1:1 ether–hexane). The following conditions were used for the synthesis of **5–8** from **1–4**, respectively:

TABLE III

Starting material (g)	*^tBuOH–$HCONMe_2$ (ratio, mL)*	*$Pb(OAc)_4$ (g)*	*Product (g, %)*
1[a] (1.17)	13:6	5.80	**5** (0.97, 70)
2[b] (1.07)	16:8	7.00	**6** (0.91, 71)
3[b] (1.51)	24:12	10.50	**7** (1.35, 77)
4[c] (0.42)	9:4	2.10	**8** (0.38, 78)

[a] See ref. 9. [b] See ref. 10. [c] See ref. 11.

5-(2,4-Di-*O*-acetyl-3-*tert*-butoxycarbonylamino-3-*C*-cyano-3-deoxy-β-D-xylo-pyranosyl)-3-ethoxycarbonyl-2-methylfuran (**5**) had m.p. 64–66° (from hexane), $[\alpha]_D$ −10° (*c* 1, chloroform); ν_{max}^{KBr} 3353, 1760, 1718, 1618, 1521, 1216, 1162, 1073, 907, 847 cm^{-1}. For the ^1H- and ^{13}C-n.m.r. data, see Tables I and II, respectively.

Anal. Calc. for $C_{23}H_{30}N_2O_{10}$: C, 55.87; H, 6.10; N, 5.66. Found: C, 55.81; H, 5.96; N, 5.90.

Methyl 2,4,6-tri-*O*-acetyl-3-*tert*-butoxycarbonylamino-3-*C*-cyano-3-deoxy-α-D-glucopyranoside (**6**) had m.p. 77–79°, $[\alpha]_D$ +64.5° (*c* 1, chloroform); ν_{max}^{KBr} 3360, 3324, 1749, 1712, 1512, 1454, 1369, 1162, 1037, 950, 913, 855 cm^{-1}. For the ^1H- and ^{13}C-n.m.r. data, see Tables I and II, respectively.

Anal. Calc. for $C_{19}H_{28}N_2O_{10}$: C, 51.35; H, 6.35; N, 6.30. Found: C, 51.50; H, 6.60; N, 6.32.

Methyl 2,4,6-tri-*O*-acetyl-3-*tert*-butoxycarbonylamino-3-*C*-cyano-3-deoxy-β-D-glucopyranoside (**7**) had m.p. 119–121°, $[\alpha]_D$ −27.5° (*c* 1, methanol); ν_{max}^{KBr} 3389, 1757, 1503, 1372, 1228, 1044, 905 cm^{-1}. For the ^1H- and ^{13}C-n.m.r. data, see Tables I and II, respectively.

Anal. Calc. for $C_{19}H_{28}N_2O_{10}$: C, 51.35; H, 6.35; N, 6.30. Found: C, 51.30; H, 6.42; N, 6.37.

Methyl 2,4-di-*O*-acetyl-5,7-*O*-benzylidene-3-*tert*-butoxycarbonylamino-3-*C*-cyano-3-deoxy-D-glycero-α-D-*ido*-heptoseptanoside (**8**) had m.p. 201–202°, $[\alpha]_D$ +44° (*c* 1,

chloroform); ν_{max}^{KBr} 3404, 1758, 1740, 1250, 1219, 1139, 1093, 1068, 1033, 988, 973, 922, 763 cm^{-1}. For the ^1H- and ^{13}C-n.m.r. data, see Tables I and II, respectively.

Anal. Calc. for $C_{25}H_{32}N_2O_{10}$: C, 57.63; H, 6.19; N, 5.38. Found: C, 57.83; H, 6.17; N, 5.70.

Zemplén O-*deacetylation.* — To a solution of the starting material (**5–8**) in dry ethanol or methanol (see Table II) at −15° was added a 10% solution (10 mL) of freshly prepared NaOEt or NaOMe in the corresponding alcohol. After 30 min, the solution was concentrated at room temperature and the residue was subjected to column chromatography. The following amounts and conditions were used to obtain **9–11** from **5–7**, respectively, and **12** and **17** from **8**.

TABLE IV

Starting material (g)	*Solvent (mL)*	*Product (g, %)*
5 (0.23)	EtOH (20)	**9** (0.19, 99)
6 (0.26)	MeOH (20)	**10** (0.14, 76)
7 (1.00)	MeOH (25)	**11** (0.60, 85)
8 (0.50)	MeOH (35)	**12** (0.25, 65)
		17 (<0.02, <5)

5-(3-*tert*-Butoxycarbonylamino-3-*C*-cyano-3-deoxy-β-D-xylopyranosyl)-3-ethoxycarbonyl-2-methylfuran (**9**), isolated by column chromatography (2:1 ether–hexane), had m.p. 59–60° (from ether–hexane), $[\alpha]_D$ −26° (*c* 1, chloroform); ν_{max}^{KBr} 3407, 1693, 1618, 1582, 1521, 1293, 1161, 1092, 852, 779 cm^{-1}. For the ^1H- and ^{13}C-n.m.r. data, see Tables I and II, respectively.

Anal. Calc. for $C_{19}H_{26}N_2O_8$: C, 55.60; H, 6.39; N, 6.82. Found: C, 55.56; H, 6.33; N, 6.79.

Methyl 3-*tert*-butoxycarbonylamino-3-*C*-cyano-3-deoxy-α-D-glucopyranoside (**10**), isolated by column chromatography (ethyl acetate), had m.p. 156–158°, $[\alpha]_D$ +83° (*c* 1, methanol); ν_{max}^{KBr} 3455, 3338, 1687, 1542, 1457, 1363, 1300, 1165, 977, 864 cm^{-1}. For the ^1H- and ^{13}C-n.m.r. data, see Tables I and II, respectively.

Anal. Calc. for $C_{13}H_{22}N_2O_7$: C, 49.05; H, 6.96; N, 8.80. Found: C, 49.12; H, 6.97; N, 8.92.

Methyl 3-*tert*-butoxycarbonylamino-3-*C*-cyano-3-deoxy-β-D-glucopyranoside (**11**), isolated by column chromatography (ether), had m.p. 159–161°, $[\alpha]_D$ −16° (*c* 1, methanol); ν_{max}^{KBr} 3400–3200, 1669, 1543, 1459, 1370, 1300, 1214, 1167, 1086, 1000, 907, 865 cm^{-1}. For the ^1H- and ^{13}C-n.m.r. data, see Tables I and II, respectively.

Anal. Calc. for $C_{13}H_{22}N_2O_7$: C, 49.05; H, 6.96; N, 8.80. Found: C, 49.07; H, 7.03; N, 8.87.

Methyl 5,7-*O*-benzylidene-3-*tert*-butoxycarbonylamino-3-*C*-cyano-3-deoxy-D-*glycero*-α-D-*ido*-heptoseptanoside (**12**), isolated by column chromatography (1:1 ether–hexane), had m.p. 193–195° (from ether–hexane), $[\alpha]_D$ +42° (*c* 1, methanol); ν_{max}^{KBr} 3475, 3260, 1716, 1526, 1277, 1165, 1136, 1074, 1047, 1012 cm^{-1}. For the ^1H- and ^{13}C-n.m.r. data, see Tables I and II, respectively.

Anal. Calc. for $C_{21}H_{28}N_2O_8$: C, 57.77; H, 6.46; N, 6.44. Found: C, 57.57; H, 6.50; N, 6.58.

Eluted second was (methyl 5,7-*O*-benzylidene-3-*C*-cyano-3-deoxy-D-*glycero*-α-D-*ido*-heptoseptano)[3,2-*d*]-oxazolidin-2-one (**17**), m.p. 129–130° (from ether–hexane), $[\alpha]_D$ +14° (*c* 1, methanol); ν_{max}^{KBr} 3385, 1787, 1660, 1452, 1404, 1378, 1288, 1206, 1091, 1060, 1000, 974, 939, 818, 763, 700 cm^{-1}. For the ^1H- and ^{13}C-n.m.r. data, see Tables I and II, respectively.

Anal. Calc. for $C_{17}H_{18}N_2O_7$: C, 56.33; H, 5.00; N, 7.76. Found: C, 56.45; H, 4.98; N, 7.73.

Conventional treatment of **17** (0.1 g) with 2:1 acetic anhydride–pyridine (3 mL) and 4-dimethylaminopyridine (5 mg), with column chromatography (ether–hexane 1:2) of the product, gave the *N,O*-diacetyl derivative **18** (0.111 g, 90%), m.p. 125–126° (from ether–hexane), $[\alpha]_D$ −36° (*c* 1, chloroform); ν_{max}^{KBr} 1810, 1752, 1240, 1105, 1056 cm^{-1}. For the ^1H- and ^{13}C-n.m.r. data, see Tables I and II, respectively.

Anal. Calc. for $C_{21}H_{22}N_2O_9$: C, 56.49; H, 4.97; N, 6.30. Found: C, 56.38; H, 5.00; N, 6.24.

3-C-(Acetamidomethyl)-2,4-di-O-acetyl-3-tert-butoxycarbonylamino-3-deoxy sugars. — $CoCl_2$ was added to a solution of starting compound (**5–8**) in MeOH. $NaBH_4$ was then added in small portions with stirring during 15 min. The mixture was kept at room temperature for 20–45 min, aqueous 30% NH_4Cl (25 mL) was added, and the solution was concentrated. The residue was filtered and extracted with ethyl acetate (3 × 50 mL), and the combined extracts were dried ($MgSO_4$) and concentrated. The residue was acetylated conventionally with 3:2 acetic anhydride–pyridine (5 mL), and the product was subjected to column chromatography (ethyl acetate). The following amounts and conditions were used in the preparation of **13–16** from **5–8**, respectively.

TABLE V

Starting material (g)	*MeOH (mL)*	*$CoCl_2$ (g)*	*$NaBH_4$ (g)*	*Time (min)*	*Product (g, %)*
5 (0.26)	45	0.65	0.65	20	**13** (0.23, 81)
6 (0.20)	25	0.37	0.37	20	**14** (0.18, 82)
7 (0.16)	20	0.30	0.30	20	**15** (0.14, 80)
8 (0.12)	20	0.30	0.30	45	**16** (0.10, 77)

5-(3-*C*-Acetamidomethyl-2,4-di-*O*-acetyl-3-*tert*-butoxycarbonylamino-3-deoxy-β-D-xylopyranosyl)-3-ethoxycarbonyl-2-methylfuran (**13**) was isolated as a syrup, $[\alpha]_D$ −2.7°, $[\alpha]_{436}$ +8.5° (*c* 1, chloroform); ν_{max}^{film} 3329, 1756, 1712, 1661, 1368, 1288, 1222, 1033, 780, 734 cm^{-1}. C.i.-mass spectrum: *m/z* 541 ($M^+ + 1$), 485 ($M^+ + 1 - C_4H_8$). For the ^1H- and ^{13}C-n.m.r. data, see Tables I and II, respectively.

Anal. Calc. for $C_{25}H_{36}N_2O_{11}$: C, 55.55; H, 6.71; N, 5.18. Found: C, 55.21; H, 6.68; N, 4.90.

Methyl 3-*C*-acetamidomethyl-2,4,6-tri-*O*-acetyl-3-*tert*-butoxycarbonylamino-3-

deoxy-α-D-glucopyranoside (**14**) was isolated as a syrup, $[\alpha]_D$ +66° (*c* 1, chloroform); ν_{max}^{film} 3225, 1730, 1650, 1520, 1230, 1050 cm^{-1}. C.i.-mass spectrum: *m/z* 489 ($M^+ - 1$), 431 ($M^+ + 1 - C_2H_4O_2$), 406 ($M^+ + 1 - C_5H_9O$), 399 ($M^+ + 1 - CH_4O - C_2H_4O_2$). For the ^1H- and ^{13}C-n.m.r. data, see Tables I and II, respectively.

Anal. Calc. for $C_{21}H_{34}N_2O_{11}$: C, 51.42; H, 6.99; N, 5.71. Found: C, 51.50; H, 7.15; N, 5.82.

Methyl 3-*C*-acetamidomethyl-2,4,6-tri-*O*-acetyl-3-*tert*-butoxycarbonylamino-3-deoxy-β-D-glucopyranoside (**15**) had m.p. 141–142° (from ethyl acetate), $[\alpha]_D$ −18°, $[\alpha]_{436}$ −38.5° (*c* 1, chloroform); ν_{max}^{KBr} 3365, 1753, 1696, 1663, 1530, 1225, 1042 cm^{-1}. C.i.-mass spectrum: *m/z* 491 ($M^+ + 1$), 435 ($M^+ + 1 - C_4H_8$), 417 ($M^+ + 1 - C_4H_{10}O$), 391 ($M^+ + 1 - C_4H_8 - CO_2$). For the ^1H- and ^{13}C-n.m.r. data, see Tables I and II, respectively.

Anal. Calc. for $C_{21}H_{34}N_2O_{11}$: C, 51.42; H, 6.99; N, 5.71. Found: C, 51.55; H, 7.10; N, 5.78.

Methyl 3-*C*-acetamidomethyl-2,4-di-*O*-acetyl-5,7-*O*-benzylidene-3-*tert*-butoxycarbonylamino-3-deoxy-D-glycero-α-D-ido-heptoseptanoside (**16**) was isolated as a syrup, $[\alpha]_D$ +41° (*c* 1, chloroform); ν_{max}^{film} 3388, 1763, 1666, 1227, 1170, 1141, 1063, 1031, 933, 875, 822 cm^{-1}. C.i.-mass spectrum: *m/z* 567 ($M^+ + 1$), 511 ($M^+ + 1 - C_4H_8$). For the ^1H- and ^{13}C-n.m.r. data, see Tables I and II, respectively.

Anal. Calc. for $C_{27}H_{38}N_2O_{11}$: C, 57.23; H, 6.76; N, 4.94. Found: C, 57.11; H, 6.75; N, 4.85.

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