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REDUCTION OF 1,2;5,6-DI-*O*-ISOPROPYLIDENE-α-D-GLUCOFURANOSE DERIVATIVES WITH LITHIUM ALUMINUM HYDRIDE; A FACILE SYNTHETIC METHOD FOR 3,6-IMINO DERIVATIVES

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ABSTRACT

Treatment of 3-acylamido- or alkylimino-3-deoxy-1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose with lithium aluminum hydride in boiling 1,4-dioxane afforded unusual products, namely, 3,6-*N*-alkylimino-3,6-dideoxy-1,2-*O*-isopropylidene-α-D-glucofuranose or 6-*O*-isopropyl-1,2-*O*-isopropylidene-α-D-glucofuranose derivatives. 3,6-*N*-(Benzyloxy)imino-3,6-dideoxy-1,2-*O*-isopropylidene-β-L-idofuranose, a key intermediate for synthesis of anisomycin, was prepared by use of this reaction.

INTRODUCTION

Reduction of amides with lithium aluminum hydride is widely used for the preparation of secondary amines. Isopropylidene acetals are considered to be stable under conditions of reduction with lithium aluminum hydride, except in the presence of aluminum trichloride[1]. In fact Meyer zu Reckendorf and Bischof prepared 3-deoxy-1,2;5,6-di-*O*-isopropylidene-3-(methylamino)-α-D-glucofuranose from 3-deoxy-3-formamido-1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose by reduction with lithium aluminum hydride[2]. In order to prepare a series of 3-alkylamino derivatives, we reduced 3-acylamido-3-deoxy-1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranoses with lithium aluminum hydride. Unexpectedly, however, 3,6-imino derivatives were obtained, and therefore we examined this reaction in detail.

RESULTS AND DISCUSSION

3-Butanamido-3-deoxy-1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose (**1a**) and lithium aluminum hydride were boiled under reflux for 16 h in oxolane (tetrahydrofuran) to afford two products. One was the expected 3-butylamino-3-deoxy-1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose (**2a**, 33%), and the other was the unexpected

TABLE I

N.M.R. DATA

Compound	*Chemical shifts (δ) ($CDCl_3$–Me_4Si)*							
	H-1	*H-2*	*H-3*	*H-4*	*H-5*	*H-6*	*H-6′*	*Other protons*
2a	5.90 d	4.56 d	3.30 d		← 3.90–4.40 →			2.75 (NCH_2)
2b	5.90 d	4.56 d	3.33 d		← 3.90–4.40 →			2.80 (NCH_2)
2c	5.86 d	4.60 d	3.16 d		← 3.90–4.40 →			2.50 (NCH_3)
2d	5.90 d	4.56 d	3.40 d		← 3.90–4.40 →			3.90 (NCH_2)
3a	5.96 d	4.54 d	3.14 d	4.80 t	4.16 dt	3.20 dd	2.47 dd	2.60 (NCH_2)
3b	6.03 d	4.55 d	3.10 d	4.80 t	4.15 dt	3.30 dd	2.36 dd	2.60 (NCH_2)
3c	6.05 d	4.60 d	3.00 d	4.86 t	4.20 dt	3.05 dd	2.40 dd	2.40 (NCH_3)
3d	6.03 d	4.53 d	3.90 d	4.86 t	4.20 dt	2.95 dd	2.43 dd	4.00 d 3.50 d (CH_2Ph)
4	6.03 d	4.53 d	3.23 d	4.93 t	5.20 dt	3.10 dd	2.66 dd	2.50 (NCH_3) 2.10 s (Ac)
9[a]	6.20 d	4.73 d	4.10 d	4.95 t	4.40 dt	3.35 dd	3.10 dd	
5a	5.88 d	4.56 d	3.35 d		← 3.10–4.40 →			1.17 d (2 CH_3)
5d	5.88 d	4.58 d	3.50 d		← 3.60–4.50 →			4.05 d 3.95 d (CH_2Ph) 1.13 d (2 CH_3)
6	5.95 d	4.66 d	3.23 d	4.40 dd	5.30 m	← 3.50–4.20 →		1.96 s (Ac) 1.13 d (2 CH_3)

Compound	*Coupling constants (Hz)*							
	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$	*Others*
2a	4	0	3					
2b	4	0	3					
2c	4	0	2					
2d	4	0	2					
3a	4	0	6	6	3	6	10	
3b	4	0	6	6	3	6	11	
3c	4	0	5	5	2	5	13	
3d	4	0	5	5	3	6	11	$J_{CH,CH'}$ 14
4	4	0	5	5	4	5	12	
9[a]	4	0	4	4	2	5	10	
5a	4	0	3					J_{CH,CH_3} 6
5d	4	0	3					$J_{CH,CH'}$ 8; J_{CH,CH_3} 6
6	4	0	3	9	2	5		J_{CH,CH_3} 6

[a]Measured in pyridine-d_5.

3,6-*N*-butylimino-3,6-dideoxy-1,2-*O*-isopropylidene-α-D-glucofuranose (**3a**, 54%). The 3,6-imino structure of **3a** was determined on the basis of elemental analysis and n.m.r. spectroscopy (Table I); the H-6 (δ 3.20) and H-6′ (δ 2.47) protons were not equivalent, and the H-4 signal appeared at low field, as in the case of 3,6-anhydro-1,2-*O*-isopropylidene-5-*O*-(methylthio)thiocarbonyl-α-D-glucofuranose[3]. Acetylation of **3a** with acetic anhydride–pyridine afforded the monoacetyl derivative **4**, whose H-5 resonance appeared at considerably lower field than that of **3a**, indicating that the acetyl group had been introduced at the 5-position. When the time of reaction

TABLE II

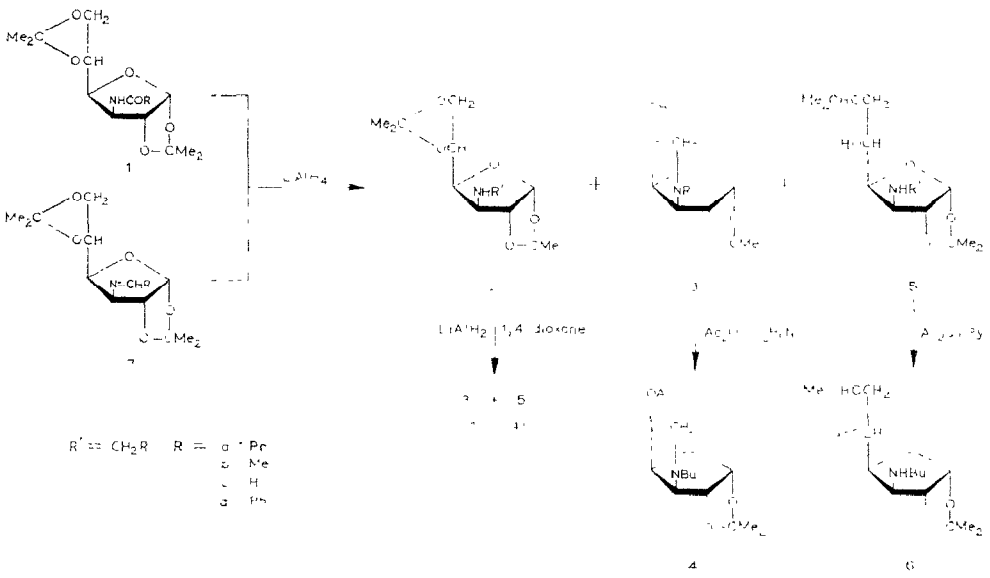
REACTION OF 3-ACYLAMIDO **1** AND *N*-ALKYLIMINO DERIVATIVES (**7**) WITH LITHIUM ALUMINUM HYDRIDE[a]

Starting material	*3-Substituent*	*Solvent*	*Reaction temp.*	*Product ratio*		
				2	**3**	**5**
1a	-NHCOCH$_2$CH$_2$CH$_3$	ether	room temp.[b]	80 (63)	20 (9)	0
		ether	reflux	60 (49)	40 (21)	0
		oxolane	reflux	45 (33)	55 (54)	0
		oxolane	reflux[c]	15 (7)	85 (78)	0
		1,4-dioxane	60°	40 (24)	60 (52)	0
		1,4-dioxane	reflux	0	100 (88)	0
1b	-NHAc	ether	room temp.[b]	80 (62)	20 (14)	0
		ether	reflux	65 (58)	35 (22)	0
		oxolane	reflux	30 (22)	70 (58)	0
		1,4-dioxane	reflux	0	100 (76)	0
1c	-NHCOH	ether	room temp.[b]	85 (68)	15 (8)	0
		ether	reflux	70 (47)	30 (14)	0
		oxolane	reflux	40 (28)	60 (49)	0
		1,4-dioxane	reflux	0	100 (66)	0
1d	-NHBz	oxolane	reflux	100 (75)	0	0
		1,4-dioxane	reflux	0	50 (16)[d]	50 (19)[d]
7a	-N=CHCH$_2$CH$_2$CH$_3$	ether	room temp.[b]	85 (65)	15 (7)	0
		ether	reflux	60 (47)	40 (25)	0
		oxolane	reflux	55 (50)	45 (28)	0
		1,4-dioxane	reflux	0	100 (88)	0
7d	-N=CHPh	oxolane	reflux	100 (76)	0	0
		1,4-dioxane	reflux	0	50 (17)[d]	50 (14)[d]

[a]The starting material (3 mmol) was treated for 16 h with lithium aluminum hydride (13 mmol) in the solvents (20 mL) indicated. The product ratios were determined by n.m.r. spectroscopy; figures in the parentheses showed the isolated yields. [b]The reaction was performed for 2 days because the starting material was detectable in t.l.c. after 16 h. [c]The reaction time was prolonged to 2 days. [d]Complete separation by column chromatography made quantification of the mixture difficult.

was prolonged to 2 days, the ratio of **3a** to **2a** increased to 6:1. Only the 3,6-imino compound **3a** (88%, isolated yield) was detectable by n.m.r. spectroscopy when **1a** was boiled under reflux for 16 h in 1,4-dioxane, whereas the ratio of **3a** to **2a** became 2:3 for reaction in the same solvent for 16 h at 60°. The ratios of **3a** to **2a** were lowered to 2:3 and 1:4, respectively, in boiling diethyl ether or in diethyl ether at room temperature. These results suggest that the product ratios are more sensitive to the temperature of reduction than the solvent employed (Table II).

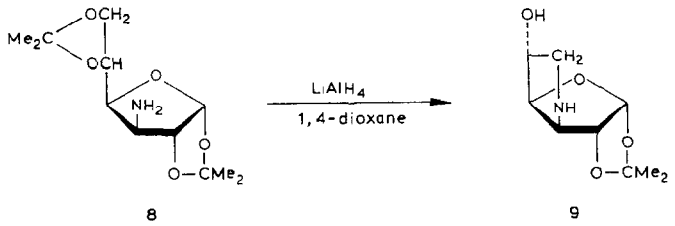
Similar results were obtained in the reactions of 3-acetamido and 3-formamido-3-deoxy-1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose (**1b,c**) with lithium aluminum hydride (Table II). On the other hand, treatment of 3-benzamido-3-deoxy-1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose (**1d**) with lithium aluminum hydride in boiling oxolane provided only the 3-benzylamino derivative **2d**, as judged from n.m.r. spectroscopy (75% isolated yield). When the reaction was conducted in boiling



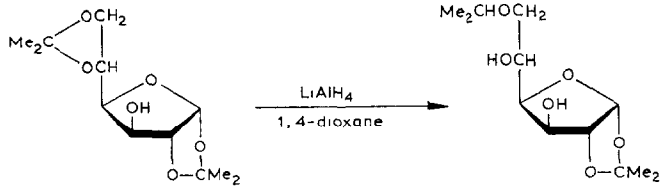
1,4-dioxane, another product (**5d**) was obtained together with the 3,6-imino derivative **3d**. The presence of hydroxyl and amino groups was indicated by i.r. spectroscopy [3550 (OH) and 3330 (NH) cm^{-1} in chloroform]. Acetylation of **5d** with acetic anhydride–pyridine yielded the 5-acetate **6**. As the n.m.r. spectrum of **5d** was complicated, compound **1d** was treated with lithium aluminum deuteride. The signals at δ 1.13 of **5d** and the deuterated derivative of **5d** appeared as a doublet and a singlet, respectively, indicating that compound **5d** was 3-benzylamino-3-deoxy-6-*O*-isopropyl-1,2-*O*-isopropylidene-α-D-glucofuranose. Conversion of the 5,6-*O*-isopropylidene group into the 6-*O*-isopropyl group has been achieved with 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose by treatment with lithium aluminum hydride in the presence of aluminum trichloride[1].

As Gaylord[4] and Hörmann[5] reported that reduction of *N*-monosubstituted amides with lithium aluminum hydride proceeds through an *N*-alkylidenimine intermediate, the 3-butylidenimino and 3-benzylylidenimino derivatives **7a,d** were treated with lithium aluminum hydride. Results similar to those found with the amides **1a** and **1d**, respectively, were observed, including the dependence of the product ratios on the reaction temperature (Table II). The 3-butylamino (**2a**) and 3-benzylamino (**2d**) derivatives were boiled under reflux in 1,4-dioxane in the presence of lithium aluminum hydride to afford the 6-*O*-isopropyl derivatives as major products, and the 3,6-imino derivatives as the minor products (4:1, by n.m.r. spectroscopy), whereas similar treatment of the 3-amino derivative **8** gave only the imino compound **9** (70%). On the other hand, similar treatment of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**10**) did not afford the 3,6-anhydro derivative, but gave instead 6-*O*-isopropyl-1,2-*O*-isopropylidene-α-D-glucofuranose (**11**).

Reduction of the alkylimines **7a** and **7d** gave results the same as those with the

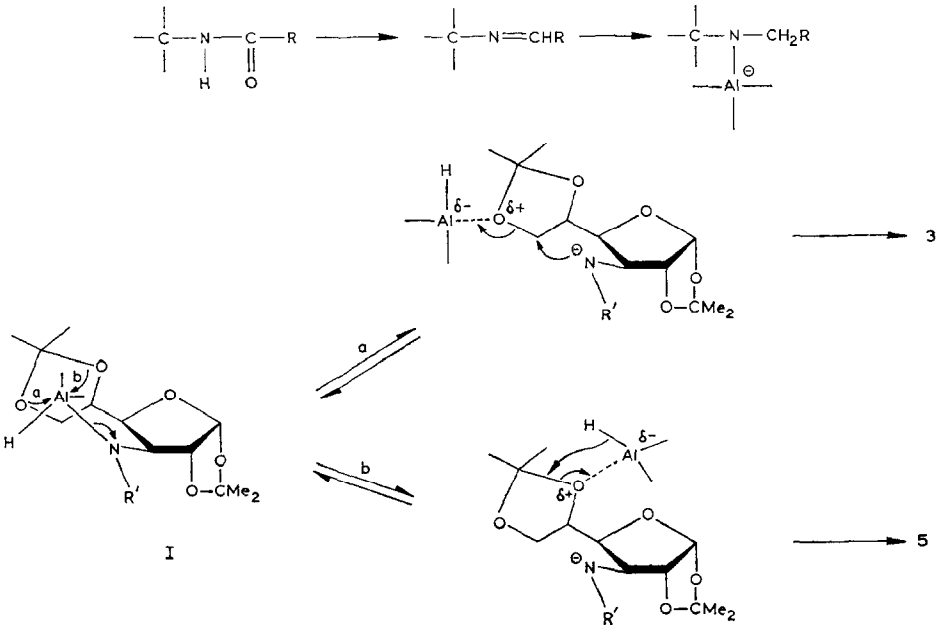


8 9



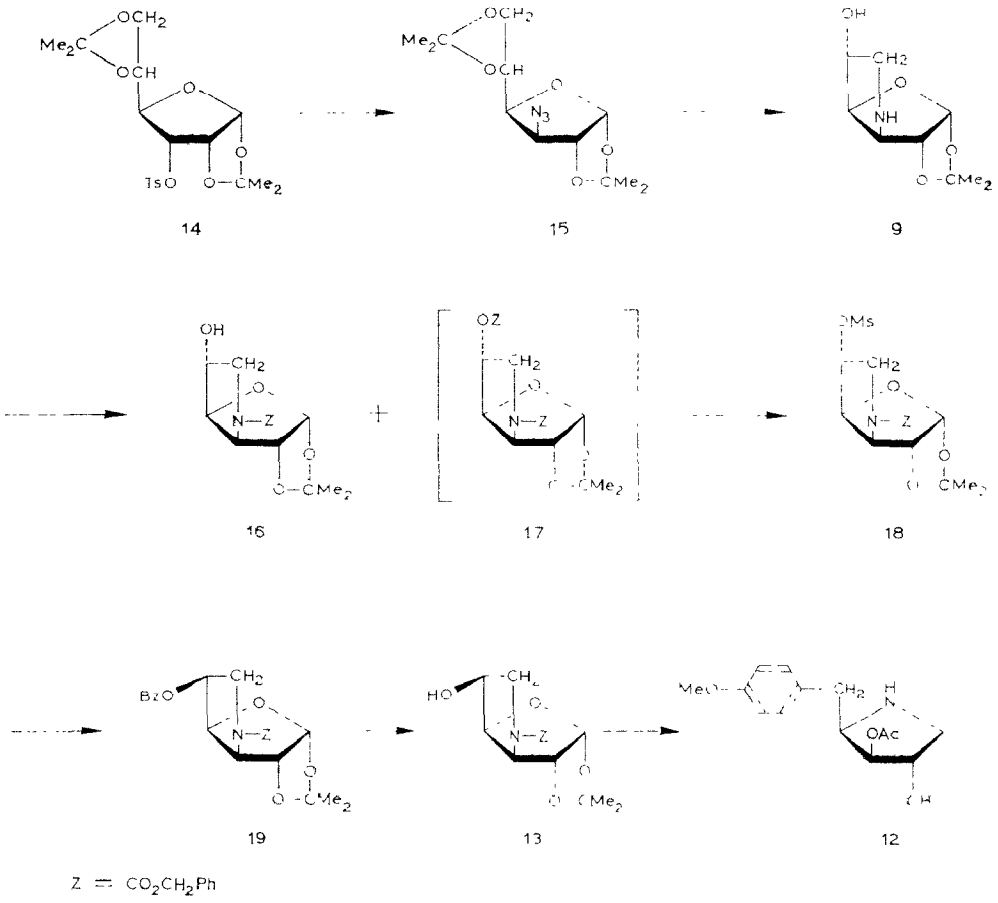
10 11

corresponding acylamido derivatives, supporting the idea that reduction of the acylamido derivative proceeds *via* the imino intermediate, as had been proposed by Gaylord[4] and Hörmann[5]. A reasonable explanation for these results is as follows. Attack of an aluminum hydride anion at the imino carbon atom could give a complex I as the initial intermediate, where aluminum would also coordinate with the oxygen



Scheme I

atoms at either the 5 or 6 position to give an equilibrium mixture, causing weakening of the C–O bond at C-5 and C-6, and thus increasing the nucleophilicity of the amino group (Scheme 1). As a result, the amino group would attack C-6, affording the sterically favorable 3,6-imino derivatives. If the 3-amino group were bulky*, hydride attack at the isopropylidene carbon atom would preponderate over nucleophilic attack of the amino group, giving the 6-isopropyl ethers as the major product. In contrast to the 3-butylamino and 3-benzylamino derivatives, evolution of gas was observed in the reaction of the 3-amino compound **8**, suggesting formation of the aluminum complex I; in fact treatment of **8** with lithium aluminum hydride afforded the 3,6-imine **9** exclusively. Such a difference between the 3-amino and 3-butyl or benzylamino derivatives appears reasonable, because the hydrogen atom of the *N*-alkylamino group should be less acidic than that of the corresponding amino group.



14 15 9

16 17 18

19 13 12

*In contrast to the *N*-butyl-, -ethyl- and -methyl-3,6-imino derivatives (**3a–c**), the benzyl methylene protons of **3d** were nonequivalent, indicating restricted rotation of the *N*-benzyl group[9].

The optically active antibiotic anisomycin (**12**) was synthesized from D-glucose by Moffatt and co-workers[6]. 3,6-*N*-(Benzyloxycarbonyl)imino-3,6-dideoxy-1,2-*O*-isopropylidene-β-L-idofuranose (**13**), the key intermediate, was prepared from 1,2;5,6-di-*O*-isopropylidene-3-*O*-tolylsulfonyl-α-D-allofuranose (**14**) in 9 steps in 41% overall yield. Compound **13** is prepared readily by the present method.

3-Azido-3-deoxy-1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose (**15**), obtained from **14** in 80% yield[7], was treated with lithium aluminum hydride in 1,4-dioxane at room temperature, and then the mixture was boiled under reflux for 1 day. The crude product was treated directly with benzyl chloroformate in the presence of sodium carbonate to afford 3,6-*N*-(benzyloxycarbonyl)imino-3,6-dideoxy-1,2-*O*-isopropylidene-α-D-glucofuranose (**16**, 58% yield from **15**), together with the dibenzyloxy derivative **17** (11%). When 2-propylamine was added to the mixture before processing in the foregoing reaction, the yield of **16** was raised to 67%. Direct epimerization at C-5 with triphenylphosphine–diethyl azocarboxylate–acetic acid[8] allowed the recovery of **16**.

Methanesulfonyl chloride in pyridine converted **16** into the sulfonate **18** in 90% yield. The facile crystallizability of **18** allowed its preparation from **14** without purification of any intermediates (overall yield 58.6%). Conversion of **18** into 5-*O*-benzoyl-3,6-*N*-(benzyloxycarbonyl)imino-3,6-dideoxy-1,2-*O*-isopropylidene-β-L-idofuranose (**19**) by the method of Brimacombe and Mofti[9] gave **19** in 85% yield. Debenzoylation of **19** with sodium methoxide afforded the desired, crystalline **13** in quantitative yield. Thus the present route gave **13** in 51% overall yield from **14** in 6 steps, with the purification of only one intermediate, **18**.

EXPERIMENTAL

General methods. — Melting points are uncorrected. Specific rotations were determined with a JASCO DPI 140 polarimeter. N.m.r. spectra were recorded at 60 MHz with a JNM-PX-60 (JEOL) spectrometer or at 100 MHz with a JNM-PS-100 (JEOL) spectrometer, with tetramethylsilane as the internal standard. I.r. spectra were recorded with a Hitachi 215 spectrometer. T.l.c. was performed with silica gel 5715 (Merck, Darmstadt), with the following solvents: ether (*A*), or (*B*) 7:3 (v/v) benzene–ethyl acetate. Column chromatography was conducted on silica gel (Merck, silica gel 60) with chloroform (*C*) or 49:1 (v/v) chloroform–methanol (*D*) as eluants. Solutions were evaporated under diminished pressure.

Preparation of the amides (**1a–d**). — To an ice-cooled solution of 3-amino-3-deoxy-1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose (**8**, 2.6 g, 10 mmol) in pyridine (10 mL) was gradually added the appropriate acid anhydride (1.2 equiv.). The mixture was kept for 3 h at room temperature, and then poured into crushed ice. 3-Benzamido-3-deoxy-1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose (**1d**) precipitated and was recrystallized from 2-propanol. 3-Butylamido- and -acetamido-3-deoxy-1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose (**1a,b**) were extracted with chloroform, and the extracts were washed successively with 4M hydrochloric acid, M sodium

hydroxide, and water, and evaporated to syrups, which were crystallized from hexane. 3-Deoxy-3-formamido-1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose (**1c**) was prepared according to the method of Meyer zu Reckendorf and Bischof[2].

Compound **1a** had m.p. 100.5–101.5°, $[\alpha]_D^{22}$ −36° (*c* 1.0, chloroform); ν_{max}^{KBr} 3250 (NH), 1650 and 1550 (C=O) cm^{-1}; n.m.r. ($CDCl_3$): δ 7.00 (1-proton doublet, $J_{NH,3}$ 8.0 Hz, NH), 6.00 (1-proton doublet, $J_{1,2}$ 4.0 Hz, H-1), and 4.70 (1-proton doublet, $J_{1,2}$ 4.0 Hz, H-2).

Anal. Calc. for $C_{16}H_{27}NO_6$: C, 58.34; H, 8.26; N, 4.25. Found: C, 58.33; H, 8.11; N, 4.30.

Compound **1b** had m.p. 96–97° (lit.[7] 95–96°).

Compound **1d** had m.p. 155–156°, $[\alpha]_D^{22}$ −77° (*c* 1.0, chloroform); ν_{max}^{KBr} 3320 (NH), 1635 and 1520 (C=O) cm^{-1}; n.m.r. ($CDCl_3$): δ 5.83 (1-proton doublet, $J_{1,2}$ 4.0 Hz, H-1), and 4.60 (1-proton doublet, $J_{1,2}$ 4.0 Hz, H-2).

Anal. Calc. for $C_{19}H_{25}NO_6$: C, 62.79; H, 6.93; N, 3.85. Found: C, 62.54; H, 6.95; N, 3.79.

Preparation of the N-*alkylimines* (**7a–d**). — To a solution of **8** (2.6 g, 10 mmol) and either butanol (0.9 g, 12.5 mmol) or benzaldehyde (1.3 g, 12.3 mmol) in benzene (30 mL) was added solid potassium hydroxide (6 g, 0.11 mol), and the mixture was kept for 5 h with occasional shaking. Potassium hydroxide was removed by filtration, and the filtrate was evaporated. 4-Butylidenimino-3-deoxy-1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose (**7a**) was not completely purified because of its lability on silica gel, but it was sufficiently pure after being dried with a vacuum pump for the next reaction, as judged from its n.m.r. spectrum. 3-Benzylidenimino-3-deoxy-1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose (**7d**) crystallized from hexane.

Compound **7a** had ν_{max}^{NaCl} 1670 (C=N) cm^{-1}; n.m.r. ($CDCl_3$): δ 7.80 (1-proton triplet, J_{CH,CH_2} 5.0 Hz, N=CH), 6.10 (1-proton doublet, $J_{1,2}$ 4.0 Hz, H-1), 4.20 (1-proton doublet, H-2), and 2.26 (2.26 (2-proton multiplet, =CHCH_2).

Compound **7d** had m.p. 86–87.5°, $[\alpha]_D^{22}$ −77° (*c* 1.0, chloroform); ν_{max}^{KBr} 1640 (C=N); n.m.r. ($CDCl_3$): δ 8.40 (1-proton singlet, N=CH), 6.20 (1-proton doublet, $J_{1,2}$ 4.0 Hz, H-1), and 4.56 (1-proton doublet, H-2).

Anal. Calc. for $C_{19}H_{25}NO_5$: C, 65.59; H, 7.25; N, 4.03. Found: C, 65.67; H, 7.18; N, 4.27.

Reduction of the amide, N-*alkylimine, or* N-*alkylamine with lithium aluminum hydride.* — The amide, *N*-alkylimine, or *N*-alkylamine (3 mmol) was added to a stirred suspension of lithium aluminum hydride (13 mmol) in the indicated solvent (25 mL) and the mixture was boiled under reflux, warmed, or kept at room temperature, as indicated in Table II, with stirring until the starting material disappeared (t.l.c.). After cooling the mixture with ice–water, ethyl acetate and subsequently water were carefully added. The inorganic precipitate was removed by filtration and washed well with ether, and the combined filtrates were evaporated to a syrup, which was dissolved in ether, and filtered through a pad of Celite 545 (Johns-Manville). The syrup obtained by evaporation of the filtrate was chromatographed on silica gel.

3-Butylamino-3-deoxy-1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose (**2a**) was eluted with *C*; $[\alpha]_D^{22}$ −37° (*c* 1.6, chloroform); ν_{max}^{NaCl} 3320 (NH) cm^{-1}.

Anal. Calc. for $C_{16}H_{29}NO_5$: C, 60.93; H, 9.27; N, 4.44. Found: C, 60.76; H, 9.10; N, 4.65.

3-Deoxy-3-ethylamino-1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose (**2b**) was eluted with *C*; $[\alpha]_D^{22}$ −38° (*c* 1.0, chloroform); ν_{max}^{NaCl} 3320 (NH) cm^{-1}.

Anal. Calc. for $C_{14}H_{25}NO_5$: C, 58.51; H, 8.77; N, 4.87. Found: C, 58.59; H, 8.74; N, 4.84.

3-Deoxy-1,2;5,6-di-*O*-isopropylidene-3-(methylamino)-α-D-glucofuranose (**2c**) was eluted with *D*; $[\alpha]_D^{22}$ −39° (*c* 1.9, chloroform); ν_{max}^{NaCl} 3320 (NH) cm^{-1}.

Anal. Calc. for $C_{13}H_{23}NO_5$: C, 57.12; H, 8.48; N, 5.13. Found: C, 57.32; H, 8.27; N, 5.06.

3-Benzylamino-3-deoxy-1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose (**2d**) was eluted with *C*; $[\alpha]_D^{22}$ −41° (*c* 3.0, chloroform); ν_{max}^{NaCl} 3310 (NH) cm^{-1}.

Anal. Calc. for $C_{19}H_{27}NO_5$: C, 65.31; H, 7.79; N, 4.01. Found: C, 65.27; H, 7.78; N, 3.78.

3,6-*N*-Butylimino-3,6-dideoxy-1,2-*O*-isopropylidene-α-D-glucofuranose (**3a**) was eluted with *C*; m.p. 26–29°, $[\alpha]_D^{22}$ −26° (*c* 1.64, chloroform); ν_{max}^{KBr} 3470 (OH) cm^{-1}.

Anal. Calc. for $C_{12}H_{23}NO_4$: C, 60.68; H, 9.01; N, 5.44. Found: C, 60.80; H, 9.01; N, 5.39.

3,6-Dideoxy-3,6-*N*-(ethyl)imino-1,2-*O*-isopropylidene-α-D-glucofuranose (**3b**) was eluted with *D*; $[\alpha]_D^{22}$ −21° (*c* 3.3, chloroform); ν_{max}^{NaCl} 3450 (OH) cm^{-1}.

Anal. Calc. for $C_{11}H_{19}NO_4$: C, 57.62; H, 8.35; N, 6.11. Found: C, 57.48; H, 8.13; N, 6.06.

3,6-Dideoxy-1,2-*O*-isopropylidene-3,6-*N*-methylimino-α-D-glucofuranose (**3c**) was eluted with *D*; m.p. 50–51°, $[\alpha]_D^{22}$ −13° (*c* 0.63, chloroform); ν_{max}^{KBr} 3330 (OH cm^{-1}.

Anal. Calc. for $C_{10}H_{17}NO_4$: C, 55.80; H, 7.96; N, 6.51. Found: C, 55.78; H, 7.73; N, 6.51.

3,6-*N*-Benzylimino-3,6-dideoxy-1,2-*O*-isopropylidene-α-D-glucofuranose (**3d**) was eluted with *C*; m.p. 36–37°, $[\alpha]_D^{22}$ −14° (*c* 1.0, chloroform); ν_{max}^{KBr} 3490 (OH) cm^{-1}.

Anal. Calc. for $C_{16}H_{21}NO_4$: C, 65.95; H, 7.27; N, 4.81. Found: C, 65.83; H, 7.21; N, 4.56.

3-Butylamino-3-deoxy-6-*O*-isopropyl-1,2-*O*-isopropylidene-α-D-glucofuranose (**5a**) was eluted with *C*; $[\alpha]_D^{22}$ −41° (*c* 1.9, chloroform); $\nu_{max}^{CHCl_3}$ 3500 (OH) 3300 (NH) cm^{-1}.

Anal. Calc. for $C_{16}H_{31}NO_5$: C, 60.54; H, 9.84; N, 4.41. Found: C, 60.18; H, 9.87; N, 4.32.

3-Benzylamino-3-deoxy-6-*O*-isopropyl-1,2-*O*-isopropylidene-α-D-glucofuranose (**5d**) was eluted with *D*; $[\alpha]_D^{22}$ −36° (*c* 1.9, chloroform); $\nu_{max}^{CHCl_3}$ 3550 (OH) 3330 (NH) cm^{-1}.

Anal. Calc. for $C_{19}H_{27}NO_5$: C, 64.93; H, 8.32; N, 3.99. Found: C, 64.65; H, 8.24; N, 4.01.

3,6-Dideoxy-3,6-imino-1,2-O-isopropylidene-α-D-glucofuranose (**9**). — To a stirred suspension of lithium aluminum hydride (0.5 g, 13 mmol) in 1,4-dioxane (20 mL) was added a solution of **8** (1.0 g, 3.9 mmol) in 1,4-dioxane (5 mL) and the mixture was carefully warmed, as evolution of gas occurred suddenly at ~80 °. The solution was boiled under reflux for one day and then cooled with ice water. Water (10 mL) was carefully added to the solution. Inorganic material that separated was removed by filtration and washed well with methanol (50 mL), and the combined filtrates were evaporated. The syrup was suspended in M aqueous sodium hydroxide (5 mL), and the suspension was chromatographed on Diaion HP-20 (Mitsubishi Chemical Ind. Japan) with water as eluant until the effluent became neutral, and then elution was continued with methanol. The methanolic fraction was collected and evaporated to a powder that crystallized from ethanol to give 550 mg (70%) of **9**: m.p. 154–156°, $[\alpha]_D^{22}$ 50° (*c* 1.0, methanol); ν_{max}^{KBr} 3300–3600 (OH, broad) 3320 (NH) cm^{-1}.

Anal. Calc. for $C_9H_{15}NO_4$: C, 53.72; H, 7.51; N, 6.96. Found: C, 53.77; H, 7.49; N, 6.66.

6-O-Isopropyl-1,2-O-isopropylidene-α-D-glucofuranose (**11**). — A suspension of 1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose[11] (**10**) (1.0 g, 4 mmol) and lithium aluminum hydride (0.5 g, 13 mmol) in 1,4-dioxane was boiled under reflux overnight with stirring, and the solution was cooled with ice–water, and then water (10 mL) was carefully added. Insoluble inorganic material was removed by filtration, and the filtrate was evaporated. The syrup obtained was chromatographed on silica gel with solvent *D* as eluant, and crystallized from hexane to afford 0.7 g (70%) of **11**: m.p. 64–66° (lit.[1] 65–66°).

3,6-(Benzyloxycarbonyl)imino-3,6-dideoxy-1,2-O-isopropylidene-α-D-glucofuranose (**16**). — To a suspension of lithium aluminum hydride (2.5 g, 65 mmol) in 1,4-dioxane (50 mL) was gradually added a solution of 3-azido-3-deoxy-1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose[7] (**15**, 5.0 g, 17.5 mmol) in 1,4-dioxane (10 mL), and the mixture was heated carefully and boiled under reflux for 1 day. The mixture was cooled with ice–water and water (20 mL) was added carefully. Inorganic material that separated was removed by filtration and washed well with methanol (100 mL), and the combined filtrates were evaporated to a powder. The powder was dissolved in water (30 mL) and cooled with ice–water. Benzyl chloroformate (3 g, 17.6 mmol) and aqueous sodium carbonate (2 g, 18.9 mmol, in 5 mL water) were added gradually to the ice-cooled solution at the same time with stirring, and the mixture was kept for 5 h at 5°. 2-Propylamine (0.6 g, 10 mmol) was added, the mixture was stirred for 30 min at room temperature and then extracted with chloroform (50 mL), and the extracts were washed successively with M hydrochloric acid, saturated aqueous sodium hydrogencarbonate, and water. The extracts were dried over sodium sulfate and evaporated to a syrup. The syrup was chromatographed on silica gel with the solvent *D* as eluant to give 3.9 g (67%) of **16** as a syrup that was homogeneous by

t.l.c.; $[\alpha]_D^{22}$ −41° (*c* 1.16, chloroform); ν_{max}^{NaCl} 3450 (OH), 1700 (C=O) cm^{-1}; n.m.r. ($CDCl_3$): δ 5.90 (1-proton doublet, $J_{1,2}$ 4.0 Hz, H-1), 5.20 (2-proton broad singlet, CH_2), and 4.32 (1-proton doublet, $J_{3,4}$ 6.0 Hz, H-3).

3,6-(Benzyloxycarbonyl)imino-3,6-dideoxy-1,2-O-isopropylidene-5-O-(methylsulfonyl)-α-D-glucofuranose (**18**). — To a solution of **16** (3.0 g, 8.9 mmol) in pyridine (20 mL) was added methanesulfonyl chloride (1.2 g, 10.5 mmol) under cooling with ice–water. The mixture was stirred overnight at room temperature, poured into crushed ice, and then extracted with chloroform. The extract was washed with 4M hydrochloric acid, saturated sodium hydrogencarbonate, and water, dried over sodium sulfate and evaporated to a syrup that crystallized from 2-propanol to give 3.3 g(90%) of **18**; m.p. 95–96°, $[\alpha]_D^{22}$ −26° (*c* 1.0, chloroform); ν_{max}^{KBr} 1710 (C=O) cm^{-1}; n.m.r. ($CDCl_3$): δ 5.95 (1-proton doublet, $J_{1,2}$ 4.0 Hz, H-1), 5.20 (2-proton broad singlet, CH_2), 4.30 (1-proton doublet, $J_{3,4}$ 5.0 Hz, H-3), and 3.10 (3-proton singlet, CH_3SO_3).

Anal. Calc. for $C_{18}H_{23}NO_8S$: C, 52.30; H, 5.61; N, 3.39. Found: C, 52.37; H, 5.70; N, 4.05.

5-O-Benzoyl-3,6-(benzyloxycarbonyl)imino-3,6-dideoxy-1,2-O-isopropylidene-β-L-idofuranose (**19**). — A solution of **18** (3.0 g, 7.3 mmol) in *N*,*N*-dimethylformamide (100 mL) containing sodium benzoate (5 g, 34.7 mmol) was boiled under reflux for 5 h. The mixture was cooled and solid material removed by filtration, and then the filtrate was evaporated. The residue was chromatographed on silica gel with solvent *C* as eluant to give 2.7 g (85%) of **19** as a syrup that was homogeneous by t.l.c.; $[\alpha]_D^{22}$ −42° (*c* 2.1, chloroform); ν_{max}^{NaCl} 1710 (C=O) cm^{-1}; n.m.r. ($CDCl_3$): δ 5.82 (1-proton doublet, $J_{1,2}$ 4.0 Hz, H-1), 5.38 (1-proton doublet, *J* 4.0 Hz, H-5), 5.18, and 5.13 (two singlets, integrated ratio ~2:3, 2 H, CH_2).

3,6-(Benzyloxycarbonyl)imino-3,6-dideoxy-1,2-O-isopropylidene-β-L-idofuranose (**13**). — A solution of compound **19** (1.1 g, 2.5 mmol) in M sodium methoxide (10 mL) was stirred overnight at room temperature and then diluted with chloroform (50 mL) and water (50 mL). The organic layer that separated was washed with water and evaporated to a syrup, which crystallized from ethyl acetate–hexane to afford 0.82 g (90%) of **13**; m.p. 105–106°, $[\alpha]_D^{22}$ −57° (*c* 1.0, chloroform); ν_{max}^{KBr} 3450 (OH), 1700 (C=O) cm^{-1}; n.m.r. δ 5.82 (1-proton doublet, $J_{1,2}$ 4.0 Hz, H-1) and 5.20 (2-proton broad singlet, CH_2).

Anal. Calc. for $C_{17}H_{21}NO_6$: C, 60.88; H, 6.31; N, 4.18. Found: C, 60.73; H, 6.42; N, 4.10.

The n.m.r. spectrum of **13** was complicated because of restricted rotation of the *N*-benzyloxycarbonyl group[6,9]. Therefore, compound **13** (0.5 g, 1.5 mmol) was hydrogenated in methanol at atmospheric pressure over 5% palladium-on-carbon to give 3,6-dideoxy-3,6-imino-1,2-*O*-isopropylidene-β-L-idofuranose, which was recrystallized from ethanol–hexane; yield 90% (0.27 g); m.p. 89–90°, $[\alpha]_D^{22}$ +55° (*c* 1.0, methanol); n.m.r. (pyridine-d_5): δ 6.04 (1-proton doublet, $J_{1,2}$ 3.7 Hz, H-1), 5.01 (1-proton doublet, $J_{3,4}$ 4.5 Hz, H-4), 4.75 (1-proton doublet, H-2), 4.53 (1-

proton broad singlet, H-5), 4.30 (1-proton doublet, H-3), and 3.19 (2-proton doublet, $J_{5,6}$ 3.0 Hz, H-6).

Anal. Calc. for $C_9H_{15}NO_4$: C, 53.72; H, 7.51; N, 6.96. Found: C, 53.49; H, 7.40; N, 7.12.

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