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A precursor to the β-pyranosides of 3-amino-3,6-dideoxy-D-mannose (mycosamine)

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ABSTRACT

S_N2-type reaction of 3-*O*-(1-imidazyl)sulfonyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose with benzoate gave the 3-*O*-benzoyl-α-D-*allo* derivative **2**, which was hydrolysed to give the 5,6-diol **3**. Compound **3** was converted into the 6-deoxy-6-iodo derivative **4** which was reduced with tributylstannane, and then position 5 was protected by benzyloxymethylation, to give 3-*O*-benzoyl-5-*O*-benzyloxymethyl-6-deoxy-1,2-*O*-isopropylidene-α-D-allofuranose (**6**). Debenzoylation of **6** gave **7**, (1-imidazyl)sulfonylation gave **8**, and azide displacement gave 3-azido-5-*O*-benzyloxymethyl-3,6-dideoxy-1,2-*O*-isopropylidene-α-D-glucofuranose (**9**, 85%). Acetolysis of **9** gave 1,2,4-tri-*O*-acetyl-3-azido-3,6-dideoxy-α,β-D-glucopyranose (**10** and **11**). Selective hydrolysis of AcO-1 in the mixture of **10** and **11** with hydrazine acetate (→ **12**), followed by conversion into the pyranosyl chloride **13**, treatment with *N*,*N*-dimethylformamide dimethyl acetal in the presence of tetrabutylammonium bromide, and benzylation gave 3-azido-4-*O*-benzyl-3,6-dideoxy-1,2-*O*-(1-methoxyethylidene)-α-D-glucopyranose (**15**). Treatment of **15** with dry acetic acid gave 1,2-di-*O*-acetyl-3-azido-4-*O*-benzyl-3,6-dideoxy-β-D-glucopyranose (**16**, 86% yield) that was an excellent glycosyl donor in the presence of trimethylsilyl triflate, allowing the synthesis of cyclohexyl 2-*O*-acetyl-3-azido-4-*O*-benzyl-3,6-dideoxy-β-D-glucopyranoside (**17**, 90%). *O*-Deacetylation of **17**, conversion of the product into the (1-imidazyl)sulfonic ester, and S_N2 substitution with benzoate gave cyclohexyl 3-azido-2-*O*-benzoyl-4-*O*-benzyl-3,6-dideoxy-β-D-mannopyranoside (**18**), which was reduced and *N*-acetylated to give cyclohexyl 3-acetamido-2-*O*-benzoyl-4-*O*-benzyl-3,6-dideoxy-β-D-mannopyranoside (**19**).

INTRODUCTION

The total synthesis of amphotericin B, or related synthesis work in this field, requires the construction of a 1,2-*cis* linkage between a suitable derivative of 3-amino-3,6-dideoxy-D-mannopyranose (mycosamine) and an aglycon. β-D-Mannosides can be synthesised from β-D-glucosides in excellent yield by an oxidation–reduction sequence involving position 2, or by nucleophilic displacement[1–5] of such leaving groups as triflate or (1-imidazyl)sulfonate[1–5].

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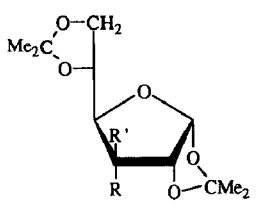
Thus, suitable D-glucopyranoside derivatives are required and a range of alkyl 2,4-di-*O*-acetyl-3-azido-3,6-dideoxy-α-D-glucopyranosides has been prepared by Redlich and Roy[6]. 1,2-*O*-Isopropylidene-3,6-di-*O*-tosyl-α-D-allofuranose was treated[6] with $LiAlH_4$ to give the 6-deoxy derivative which was reacted with azide, followed by hydrolysis and acetylation, to give 1,2,4-tri-*O*-acetyl-3-azido-3,6-dideoxy-α,β-D-glucopyranoside (**10** and **11**). The pyranosyl bromide was prepared by treatment of this mixture with $TiBr_4$ and used in Koenigs–Knorr syntheses. In this sequence, the glycosyl donor is not suitable for inversion at C-2 after glycosylation. Nicolaou et al.[7], in 16 steps from D-glucose, prepared the trichloroacetimidate[8] of 2-*O*-acetyl-3-azido-4-*O*-*tert*-butyldimethylsilyl-3,6-dideoxy-α-D-glucopyranose as a glycosyl donor. Inversion of configuration at position 2 was achieved by an oxidation–reduction sequence.

We now report the synthesis of an alternative donor **16**, its behaviour in a model glycosylation reaction, and processing of the glycoside into a protected β-mycosaminide. Imidazylates[9] were preferred over triflate as leaving groups, because of their cheapness.

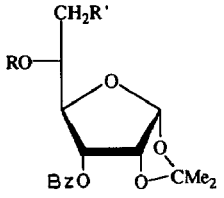
DISCUSSION

1,2-*O*-Isopropylidene-3,6-di-*O*-tosyl-α-D-allofuranose was obtained[10] in a yield of only 28% from 1,2-*O*-isopropylidene-3-*O*-tosyl-α-D-allofuranose. Our scheme involves the 6-deoxy-6-iodo derivative **4** as the reducible intermediate. Thus, treatment of 3-*O*-(1-imidazyl)sulfonyl-1,2 : 5,6-di-*O*-isopropylidene-α-D-glucofuranose (**1**) with benzoate gave the 3-*O*-benzoyl-α-D-*allo* derivative **2**. Selective, acid hydrolysis of **2** gave the 5,6-diol **3** (93%), which, with iodine–triphenylphosphine–imidazole[11], gave the 6-deoxy-6-iodo derivative **4** (88%). Treatment of **4** with tributylstannane gave the 6-deoxy derivative **5** in practically quantitative yield. Protection of HO-5 in **5** as the acid-labile benzyloxymethyl ether (96%) gave **6**, and then alkaline methanolysis gave the alcohol **7** which was converted via the imidazylate **8** into the 3-azido-3-deoxy-α-D-*gluco* derivative **9**. Acid hydrolysis of **9** removed all the protecting groups. The resulting free sugar was not isolated but treated with pyridine and acetic anhydride to give a 3:2 α,β-mixture (**10** and **11**; 74% from **9**). The α,β-mixture **10** and **11** was reported[6] to have mp 97.1°, intermediate of those for **10** (81°) and **11** (141°).

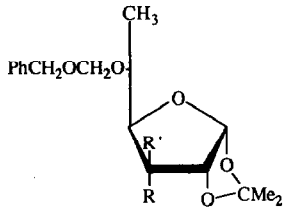
Differentiation of positions 2 and 4 was achieved by the preparation of the ortho ester **14**. Hydrolysis of AcO-1 in the mixture of **10** and **11** with hydrazine acetate[12] gave **12** which, with oxalyl chloride in the presence of *N*,*N*-dimethylformamide[13], yielded the α-pyranosyl chloride **13**. Treatment of **13** with *N*,*N*-dimethylformamide dimethyl acetal and tetrabutylammonium bromide[14] finally yielded **14** (81% overall yield). Alkaline methanolysis of **14** followed by conventional benzylation gave the benzyl ether **15** (82%). Opening of the dioxolane ring in **15** with dry acetic acid[15] then gave the β-acetate **16** (86%).



1 R = H, R' = imidazylate
2 R = OBz, R' = H



3 R = H, R' = OH
4 R = H, R' = I
5 R = R' = H
6 R = CH_2OCH_2Ph, R' = H



7 R = OH, R' = H
8 R = imidazylate, R' = H
9 R = H, R' = N_3

Compound **16** proved to be an excellent glycosylating agent in the presence of trimethylsilyl triflate[16] and reacted with cyclohexanol to give the β-D-glucoside derivative **17** (90%). This result contrasts with the low yield obtained in the glycosylation of a derivative of amphoteronolide B by the trichloroacetamidate procedure[7]. Alkaline methanolysis of **17** followed by substitution at position 2 by the imidazylate procedure gave the 2-*O*-benzoyl-β-D-*manno* derivative **18** (84%). This reaction may be unusually favourable since the 1,2-*cis*-glycoside was obtained as a single isomer in 73% overall yield.

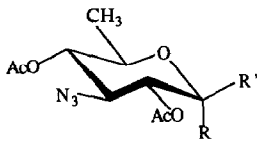
Reduction of **18** by the 1,3-propanedithiol procedure[17] gave an amine, which was acetylated to give cyclohexyl 3-acetamido-2-*O*-benzoyl-4-*O*-benzyl-3,6-dideoxy-β-D-mannopyranoside (**19**, 75%).

EXPERIMENTAL

General methods.—Chromatography was performed on silica gel (Chromagel 6–35 μm). ^{1}H-NMR spectra (250 MHz) (see Tables I–III) were recorded for solutions in $CDCl_3$ (internal Me_4Si). Optical rotations were determinated for solutions in chloroform.

3-O-Benzoyl-1,2;5,6-di-O-isopropylidene-α-D-allofuranose (**2**).—A mixture of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (10.4 g, 40 mmol) and NaH (60% dispersion in oil; 2.4 g, 60 mmol) in dry *N*,*N*-dimethylformamide (200 mL) was stirred for 0.5 h at room temperature, then cooled to −40°. 1.1′-Sulfuryldi-imidazole (11.88 g, 60 mmol) was added, the mixture was kept for 2 h at −40°, methanol (2 mL) was added, and stirring was continued for 15 min at −40°. The mixture was poured into water and extracted with ether, the extract was washed with water, and the solvent was evaporated, to give crude 3-*O*-(1-imidazolylsulfonyl)-1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose (**1**).

A solution of crude **1** (7.8 g, 20 mmol) and tetrabutylammonium benzoate (21.72 g, 60 mmol) in dry toluene was heated at 100° for 2 h, then diluted with CH_2Cl_2,

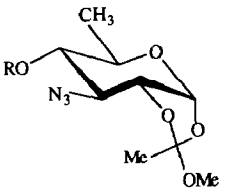


10 R = OAc, R' = H

11 R = H, R' = OAc

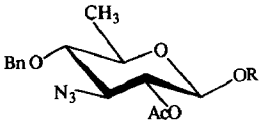
12 R , R' = H, OH

13 R = Cl, R' = H



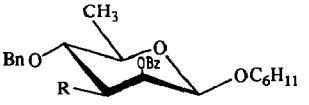
14 R = Ac

15 R = Bn



16 R = Ac

17 R = cyclohexyl



18 R = N_3

19 R = NHAc

and washed with water, and the solvent was evaporated. Chromatography (hexane–ether, 5:1) of the residue gave **2** (4.95 g, 68%), mp 72–73° (from CH_2Cl_2–hexane); lit.[18] mp 75.6°.

3-O-Benzoyl-1,2-O-isopropylidene-α-D-allofuranose (**3**).—A solution of **2** (7.28 g, 20 mmol) in aq 60% acetic acid was kept for 1 h at 50°, then concentrated. The residue was extracted with CH_2Cl_2, the extract was washed with water, and the solvent was evaporated to give **3** (6.02 g, 93%), mp 106–107° (from CH_2Cl_2–hexane); lit.[18] mp 107–109°.

3-O-Benzoyl-6-deoxy-6-iodo-1,2-O-isopropylidene-α-D allofuranose (**4**).—A stirred mixture of **3** (3.24 g, 10 mmol), triphenylphosphine (3.93 g, 15 mmol), imidazole (2.04 g, 30 mmol), and iodine (3.8 g, 15 mmol) was heated at 60° for 2 h, then cooled to room temperature, diluted with ether (200 mL), washed with water, aq 10% $Na_2S_2O_3$, and satd aq NaCl. The solvent was evaporated and chromatography (hexane–EtOAc, 4:1) of the residue gave **4** (3.82 g, 88%), mp 81–82° (from EtOH–hexane), $[\alpha]_D$ +15° (*c* 0.22).

Anal. Calcd for $C_{16}H_{19}IO_6$: C, 44.26; H, 4.41; O, 22.11. Found: C, 44.38; H, 4.45; O, 21.83.

3-O-Benzoyl-6-deoxy-1,2-O-isopropylidene-α-D-allofuranose (**5**).—A solution of **4** (4.34 g, 10 mmol), tributylstannane (5.38 mL, 20 mmol), and azoisobutyronitrile (30 mg) in dry toluene (100 mL) was boiled under reflux for 10 min, then concentrated. A solution of the residue in hexane was extracted with MeCN, and the extract was

TABLE I

^{1}H-NMR data (δ in ppm, J in Hz) for furanose derivatives [a]

Proton	**4** [b]	**5**	**6**	**7**	**9**
H-1	5.88	5.88	5.88	5.79	5.89
	(4)	(4)	(4)	(4)	(4)
H-2	5.0	5.0	4.97	4.57	4.65
	(5)	(5)	(5)	(5)	(4)
H-3	5.11	5.11	5.15	3.99–4.11 [c]	3.92–4.07 [d]
	(8)	(8.5)	(8)	(8)	
H-4	4.45	4.28	4.35	3.78	3.92–4.07 [d]
	(5)	(3)	(3)	(4)	
H-5	4.0	4.18	4.15	3.99–4.11 [c]	3.92–4.07 [d]
	(8)(5)	(6.5)	(6.5)	(6.5)	(6)
Me [e]		1.24	1.38	1.30	1.39
OH	2.68	2.48		2.50	
Me_2C	1.35, 1.57	1.33, 1.55	1.32, 1.53	1.37, 1.56	1.32, 1.52
OCH_2O			4.81	4.80, 4.86	4.83, 4.89
				(7) (7)	(7) (7)
$PhCH_2$			4.56, 4.63	4.60, 4.67	4.61, 4.70
			(12) (12)	(12) (12)	(12) (12)

[a] The J values given in brackets are for J_{n_a,n_b} (if any) $J_{n,n+1}$, or $J_{n_a,(n+1)_b}$. Signals for Ph are not reported. [b] δ 3.25 (dd, $J_{5,6a}$ 8, $J_{6a,6b}$ 10.5 Hz, H-6a), 3.39 (dd, $J_{5,6b}$ 5 Hz, H-6b). [c] The signals of H-3,5 overlap. [d] The signals of H-3,4,5 overlap. [e] These signals are doublets with J 6.5 Hz.

concentrated. Chromatography (hexane–EtOAc, 4 : 1) of the residue gave **5** (3.01 g, 98%), mp 98–99° (from EtOH), $[\alpha]_D$ +13° (c 0.535).

Anal. Calcd for $C_{16}H_{20}O_6$: C, 62.32; H, 6.54; O, 31.14. Found: C, 62.40; H, 6.45; O, 31.11.

TABLE II

^{1}H-NMR data (δ in ppm, J in Hz) for pyranose derivatives [a]

Proton	**10**	**11**	**13**	**14** [d]	**15** [e]	**16** [f]
H-1	6.24	5.65	6.25	5.66	5.53	5.61
	(4)	(8)	(4)	(5.5)	(5)	(8)
H-2	4.92	5.05	4.82	4.26	4.24	4.95
	(10.5)	(10)	(10)	(4.5)	(5)	(10)
H-3	3.88–4.01 [b]	3.59–3.74 [b]	4.03	3.80	3.87–3.72 [b]	3.64
	(10.5)	(10)	(10)	(4.5)		(10)
H-4	4.75	4.77	4.75	4.67	3.16	3.14
	(10.5)	(10)	(10)	(9)	(9)	(10)
H-5	3.88–4.01 [b]	3.59–3.74 [b]	4.14	3.87	3.87–3.72 [b]	3.61
	(6.5)	(6.5)	(6.5)	(6.5)	(6)	(6.5)
Me [c]	1.19	1.23	1.21	1.27	1.27	1.32
OAc	2.09	2.05	2.16	2.15		2.12
OAc	2.16	2.11	2.16			2.08
OAc	2.18	2.15				

[a] See Foonote *a* in Table I. [b] The signals of H-3,5 overlap. [c] The signals are doublets, $J_{5,6}$ 6.5 Hz. [d] δ 1.71 (s, $MeCO_3$), 3.30 (s, MeO). [e] δ 1.68 (s, $MeCO_3$), 3.29 (s, MeO), 4.57 and 4.78 (2 d, J 12 Hz, $PhCH_2$). [f] δ 4.66 and 4.86 (2 d, J 12 Hz, $PhCH_2$).

TABLE III

^{1}H-NMR data (δ in ppm, J in Hz) for cyclohexyl β-D-glycosides [a]

Proton	17 [b]	18	19 [e]
H-1	4.45	4.74	4.91
	(8)	(1)	1.5
H-2	4.80	5.63	5.42
	(10)	(3)	(3.5)
H-3	3.56 [c]	3.0–3.75 [c]	4.59
	(10)		
H-4	3.11	3.45–3.55 [d]	3.49
	(10)		(8)
H-5	3.42	3.45–3.55 [d]	3.70
	(6.5)		
Me [f]	1.33	1.48	1.44
CH_2Ph	4.85, 4.62	4.87, 4.68	4.70, 4.60
	(12) (12)	(12) (12)	(12) (12)
Cyclohexyl			
H-1′	3.56	3.0–3.75 [c]	3.70
H-2′–H-6′	1.38–1.85	1.2–1.95	1.25–1.9

[a] See Foonote *a* in Table I. [b] δ 2.11 (s, Ac). [c] The signals of H-3 and H-1′ overlap. [d] The signals of H-4 and H-5 overlap. [e] δ 2.12 (s, NAc), 6.29 (d, J 8 Hz, NH). [f] The signals are doublets, $J_{5,6}$ 6.5 Hz.

3-O-Benzoyl-5-O-benzyloxymethyl-6-deoxy-1,2-O-isopropylidene-α-D-allofuranose (**6**).—A mixture of **5** (2.5 g, 8.12 mmol), benzyloxymethyl chloride (3.4 mL, 24.4 mmol), collidine (4.3 mL, 32.5 mmol), Drierite (2 g), and CH_2Cl_2 (100 mL) was boiled under reflux for 48 h. Methanol was added, boiling under reflux was continued for 2 h, and then the mixture was washed with water and concentrated. Chromatography (hexane–EtOAc, 4:1) of the residue gave **6** (3.34 g, 96%), $[\alpha]_D$ +10° (*c* 1.05).

Anal. Calcd for $C_{24}H_{28}O_7$: C, 67.28; H, 6.59; O, 26.13. Found: C, 67.39; H, 6.71; O, 26.17.

5-O-Benzyloxymethyl-6-deoxy-1,2-O-isopropylidene-α-D-allofuranose (**7**).—A solution of **6** (4.28 g, 10 mmol) and NaOMe (540 mg) in MeOH (100 mL) was kept for 12 h at room temperature, then neutralised with Dowex-50 (H^+) resin, filtered, and concentrated to give **7**, mp 57–58° (from hexane), $[\alpha]_D$ +4° (*c* 0.55).

Anal. Calcd for $C_{21}H_{24}O_6$: C, 62.95; H, 7.46; O, 29.60. Found: C, 62.72; H, 7.32; O, 29.35.

3-Azido-5-benzyloxymethyl-6-deoxy-1,2-O-isopropylidene-α-D-glucofuranose (**9**).—Sodium hydride (60% in oil; 420 mg, 10.5 mmol) was added to a solution of **7** (2.26 g, 7 mmol) in dry *N*,*N*-dimethylformamide (35 mL). The mixture was stirred for 30 min at room temperature, then cooled to −40°. 1,1′-Sulfuryldi-imidazole (2.08 g, 10.5 mmol) was added, the mixture was kept for 1 h at −40°, and MeOH was added (1.4 mL). The mixture was kept at −40° for 15 min, then extracted with ether, and the extract was washed and concentrated to give **8**.

A solution of crude **8** and tetrabutylammonium azide (5.95 g, 21 mmol) in toluene (50 mL) was kept for 1 h at 80°, then cooled, diluted with CH_2Cl_2, washed

with water, and concentrated. Chromatography (hexane–ether, 19:1) of the residue gave **9** (2.08 g, 85%), $[\alpha]_D$ +2° (*c* 0.32).

Anal. Calcd for $C_{17}H_{23}N_3O_5$: C, 58.44; H, 6.63; N, 12.03; O, 22.90. Found: C, 58.16; H, 6.82; N, 12.17; O, 22.65.

1,2,4-Tri-O-acetyl-3-azido-3,6-dideoxy-α,β-D-glucopyranoside (**10** *and* **11**).—A solution of **9** (2.09 g, 6 mmol) in dioxane (10 mL) and M HCl (10 mL) was boiled under reflux for 12 h, then cooled, neutralised with IRA-45 (HO^-) resin, filtered, and concentrated. Acetylation (acetic anhydride–pyridine, 1:1) of the residue gave a mixture of **10** and **11**, which was resolved by chromatography (hexane–EtOAc, 4:1) to give, first, **10** (1 g, 60%), mp 81–83° (from EtOH), $[\alpha]_D$ +11° (*c* 0.68).

Anal. Calcd for $C_{12}H_{17}N_3O_7$: C, 45.71; H, 5.44; N, 13.35; O, 35.52. Found: C, 45.85; H, 5.25; N, 13.51; O, 35.54.

Eluted second was **11** (620 mg, 40%), mp 141–142° (from EtOH), $[\alpha]_D$ +6° (*c* 0.37).

Anal. Found: C, 46.28; H, 5.33; N, 14.01; O, 35.73.

4-O-Acetyl-3-azido-3,6-dideoxy-1,2-O-(1-methoxyethylidene)-α-D-glucopyranose (**14**).—A solution of the mixture of **10** and **11** (2.4 g, 7.6 mmol) and hydrazine acetate (840 mg, 8.4 mmol) in *N*,*N*-dimethylformamide (30 mL) was kept for 2 h at room temperature, then diluted with CH_2Cl_2. The organic layer was washed with water and satd aq NaCl, and the solvent was evaporated to give crude **12**.

A solution of oxalyl chloride (2 mL) in CH_2Cl_2 (10 mL) was added dropwise to a solution of **12** in CH_2Cl_2 (50 mL) containing *N*,*N*-dimethylformamide (0.2 mL). The mixture was stirred for 24 h at room temperature, then washed with aq $NaHCO_3$ and ice–water. The solvent was evaporated and chromatography (hexane–EtOAc, 4:1) of the residue gave the chloride **13** (1.99 g, 90%).

A solution of **13** (1.54 g, 5.28 mmol), tetrabutylammonium bromide (1.79 g, 5.28 mmol), and *N*,*N*-dimethylformamide dimethyl acetal (0.84 mL, 6.4 mmol) in $(CH_2Cl)_2$ was boiled under reflux for 24 h, then cooled, washed with water, and concentrated. Chromatography (hexane–EtOAc, 4:1) of the residue gave **14** (1.23 g, 81%), $[\alpha]_D$ +15° (*c* 0.83).

Anal. Calcd for $C_{11}H_{17}N_3O_6$: C, 45.99; H, 5.97; N, 14.63; O, 33.42. Found: C, 45.71; H, 5.82; N, 14.42; O, 33.64.

3-Azido-4-O-benzyl-3,6-dideoxy-1,2-O-(1-methoxyethylidene)-α-D-glucopyranose (**15**).—A solution of **14** (1.435 g, 5 mmol) and NaOMe (135 mg) in MeOH (50 mL) was kept for 1 h at room temperature, then concentrated, and toluene was evaporated several times from the residue. To a solution of the residue in *N*,*N*-dimethylformamide (20 mL) was added sodium hydride (60% dispersion in oil; 400 mg, 10 mmol), the mixture was stirred for 30 min, benzyl bromide (0.9 mL) was added, and stirring was continued for 2 h at room temperature. Methanol was added and the product was extracted with CH_2Cl_2. Chromatography (hexane–EtOAc, 4:1) gave **15** (1.37 g, 82%), mp 50–51° (from EtOH–H_2O), $[\alpha]_D$ +11° (*c* 1.36).

Anal. Calcd for $C_{16}H_{21}N_3O_5$: C, 57.30; H, 6.31; N, 12.53; O, 23.86. Found: C, 57.15; H, 6.15; N, 12.27; O, 23.95.

1,2-Di-O-acetyl-3-azido-4-O-benzyl-3,6-dideoxy-β-D-glucopyranose (**16**).—A solution of **15** (1 g, 3 mmol) in dry acetic acid (10 mL) was kept for 30 min at room temperature, then concentrated, and toluene was evaporated several times from the residue. Chromatography (hexane–EtOAc, 5:1) then gave **16** (940 mg, 86%), mp 117–118° (from EtOH), $[\alpha]_D$ +1.5° (*c* 0.32).

Anal. Calcd for $C_{17}H_{21}N_3O_6$: C, 56.19; H, 5.83; N, 11.57; O, 26.42. Found: C, 56.01; H, 5.79; N, 11.27; O, 26.59.

Cyclohexyl 2-O-acetyl-3-azido-4-O-benzyl-3,6-dideoxy-β-D-glucopyranoside (**17**). —A mixture of **16** (146 mg, 0.4 mmol), cyclohexanol (80 μL, 0.8 mmol), and Drierite in dry CH_2Cl_2 (5 mL) was stirred for 30 min at room temperature, then cooled to −20°. Trimethylsilyl triflate (1.2 mmol, 0.23 mL) was added, the mixture was stirred for 1 h at −20°, neutralised at this temperature with triethylamine, filtered, and washed with water, and the solvent was evaporated. Chromatography (hexane–EtOAc, 9:1) of the residue gave **20** (148 mg, 90%), mp 74–76° (from EtOH), $[\alpha]_D$ +33° (*c* 0.68).

Anal. Calcd for $C_{21}H_{29}N_3O_5$: C, 62.51; H, 7.25; N, 10.42; O, 19.83. Found: C, 62.76; H, 7.33; N, 10.29; O, 19.96.

Cyclohexyl 3-azido-2-O-benzoyl-4-O-benzyl-3,6-dideoxy-β-D-mannopyranoside (**18**).—A solution of acetate **17** (108 mg, 0.3 mmol) and NaOMe (54 mg) in MeOH (10 mL) was kept for 2 h at room temperature, then neutralised with Dowex-50 (H^+) resin, filtered, and concentrated. To a solution of the residue in dry *N*,*N*-dimethylformamide (5 mL) was added NaH (60% in oil; 18 mg, 0.45 mmol). The mixture was stirred for 30 min at room temperature, then cooled to −40°, and 1,1′-sulfuryldi-imidazole (90 mg, 0.45 mmol) was added. Stirring was continued for 1 h at −40°, MeOH (0.2 mL) was added, the mixture was kept for 15 min at −40°, and the crude imidazylate was extracted with ether and dissolved in dry toluene (10 mL). Tetrabutylammonium benzoate (325 mg, 0.9 mmol) was added to the solution which was kept for 2 h at 80°. Chromatography (hexane–EtOAc, 9:1) of the product in CH_2Cl_2 extract gave **18** (117 mg, 84%), $[\alpha]_D$ −10° (*c* 0.45).

Anal. Calcd for $C_{26}H_{31}N_3O_5$: C, 67.08; H, 6.71; N, 9.03; O, 17.18. Found: C, 67.32; H, 6.78; N, 8.91; O, 17.34.

Cyclohexyl 3-acetamido-2-O-benzoyl-4-O-benzyl-3,6-dideoxy-β-D-mannopyranoside (**19**).—A solution of **18** (33 mg, 70 μmol) in dry MeOH (2 mL) containing 1,3-propanedithiol (0.1 mL, 1 mmol) and triethylamine (140 μL; 1 mmol) was kept for 24 h at room temperature, then concentrated. Chromatography (hexane–EtOAc, 2:1) of the residue gave the amine, to a solution of which in dry CH_2Cl_2 (5 mL) at 0° were added 4-dimethylaminopyridine (60 mg, 0.5 mmol) and acetic anhydride (50 μL, 0.5 mmol), and the mixture was stirred for 1 h between 0° and room temperature. The usual extraction followed by chromatography (hexane–EtOAc) gave **19** (25 mg, 75%), mp 179–180° (from EtOH), $[\alpha]_D$ −12° (*c* 0.60).

Anal. Calcd for $C_{28}H_{35}NO_6$: C, 68.83; H, 7.33; N, 2.91; O, 18.93. Found: C, 69.17; H, 7.36; N, 2.65; O, 19.71.

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