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THE SYNTHESIS OF 3-AMINO-3-DEOXY-α-D-GLUCOPYRANOSYL α-D-GLUCOPYRANOSIDE (3-AMINO-3-DEOXY-α,α-TREHALOSE)

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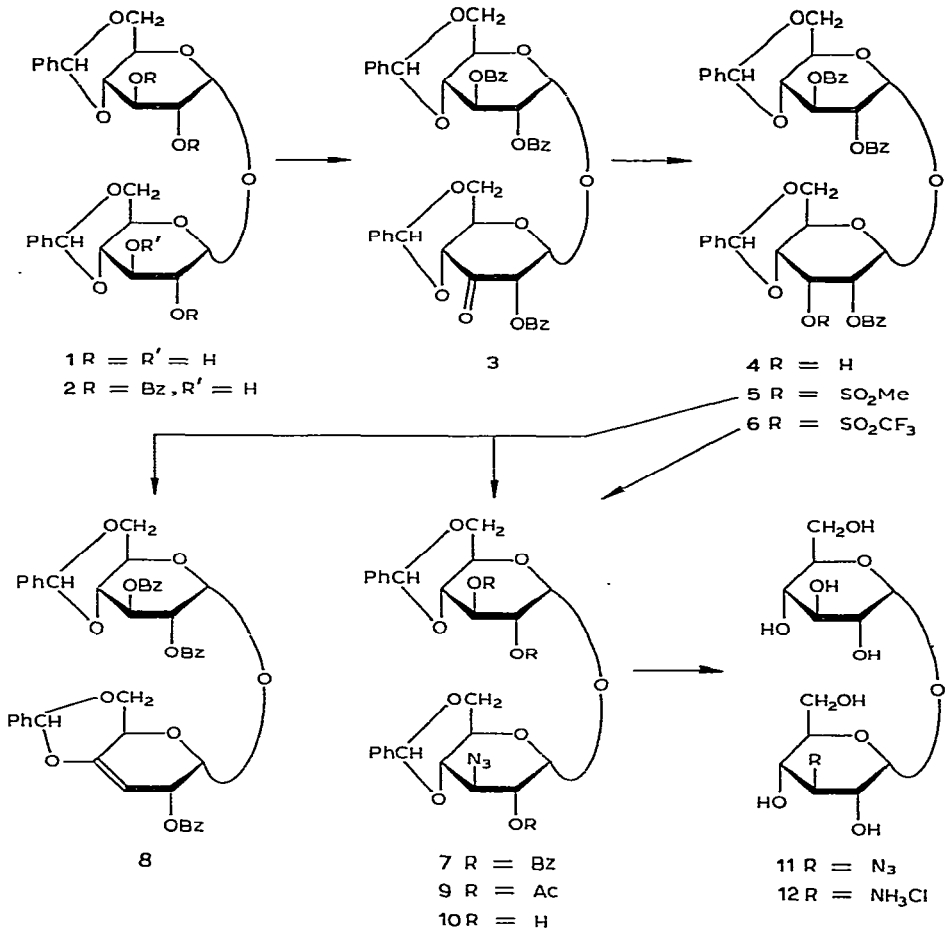
ABSTRACT

The preparation of 2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-α-D-glucopyranosyl 2-*O*-benzoyl-4,6-*O*-benzylidene-α-D-*ribo*-hexopyranosid-3-ulose (**3**) from 4,6:4′,6′-di-*O*-benzylidene-α,α-trehalose (**1**) via the 2,3,2′-tribenzoate **2** has been improved. Reduction of **3** with sodium borohydride gave 2-*O*-benzoyl-4,6-*O*-benzylidene-α-D-allopyranosyl 2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-α-D-glucopyranoside (**4**), which was converted into the methanesulfonate **5** and trifluoromethanesulfonate **6**. Displacement of the sulfonic ester group in **6** with lithium azide was very facile and afforded a high yield of 3-azido-2-*O*-benzoyl-4,6-*O*-benzylidene-3-deoxy-α-D-glucopyranosyl 2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-α-D-glycopyranoside (**7**), whereas similar displacement in **5** proceeded sluggishly, giving a lower yield of **7** together with an unsaturated disaccharide (**8**). The azido sugar **7** was converted by conventional reactions into the analogous 2,3,2′-triacetate **9**, the corresponding 2,3,2′-triol **10**, and deprotected 3-azido-3-deoxy-α-D-glucopyranosyl α-D-glucopyranoside (**11**). Hydrogenation of **11** over Adams' catalyst furnished crystalline 3-amino-3-deoxy-α,α-trehalose hydrochloride (**12**), the overall yield from **3** being 35%.

INTRODUCTION

For biochemical investigations of the metabolism and the functions of α,α-trehalose, a domain of research attracting much current interest[1–4], a large assortment of modified derivatives of this disaccharide is required. As a contribution in this direction, we have recently synthesized[5] the 3,3′-dideoxy-3,3′-dinitro and 3,3′-diamino-3,3′-dideoxy derivatives of α,α-trehalose, as well as the corresponding D-*gluco*,D-*manno* and D-*manno*,D-*manno* epimers. None of these nitrogenous analogs exhibited affinity to cockchafer trehalase in assays kindly arranged by Dr. J. Defaye (Grenoble). This result was in line with the high specificity known to be associated with that enzyme, and corroborated the finding[4a] that, for a modified trehalose molecule to be recognized as a substrate, one unmodified α-D-glucopyranosyl moiety is a minimum structural requirement. We now report the synthesis of a new, monomodified amino analog, namely, the title compound (**12**). This derivative should be of interest, not only for studies concerning the action of trehalases, but also by



reason of the divergent bioactivity of the three known, positional isomers with which it may be compared; the naturally occurring 2-amino-2-deoxy (trehalosamine)[6a] and 4-amino-4-deoxy isomers display antibiotic activity, whereas the synthetic 6-amino-6-deoxy isomer[7] is inactive[8].

RESULTS

The aforementioned, symmetrically disubstituted, nitrogenous disaccharides had been obtained[5] by the nitromethane method, but attempts to modify the procedure appropriately for the preparation of monosubstituted analogs met with difficulties. A first prerequisite for a short and economical application, namely, the selective periodate oxidation of only one of the D-glucopyranosyl moieties in unprotected α,α-trehalose, could not be achieved in a satisfactory way*. We therefore took an

alternative approach to **12**, following the lines of syntheses of monomodified trehaloses previously elaborated by French[2] and British[3] teams. The key intermediate was to be 3-azido-2-*O*-benzoyl-4,6-*O*-benzylidene-3-deoxy-α-D-glucopyranosyl 2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-α-D-glucopyranoside (**7**), whose synthesis from the known[3] glycosid-3-ulose **3** via suitable α-D-allopyranosyl α-D-glucopyranoside derivatives amenable to azide displacement provided a challenge. Difficulties could be anticipated in view of the statement[3] that attempted azide displacements of sulfonyloxy groups at C-3 and C-3′ in symmetrically disubstituted, analogously protected α-D-allopyranosyl α-D-allopyranosides had been unsuccessful.

4,6:4′,6′-Di-*O*-benzylidene-α,α-trehalose (**1**) was partially benzoylated with *N*-benzoylimidazole essentially as described[3], except for the use of three molar equivalents of the reagent and a longer reaction-time (3–4 days). Chromatographic separation of the products furnished the desired 2,3,2′-tribenzoate (**2**) crystalline in 43% yield, together with 28% of the 2,3,2′,3′-tetrabenzoate and 8% of what, presumably, was the 2,2′-dibenzoate**. Compound **2** was oxidized by use of dimethyl sulfoxide–acetic anhydride[2,9] to give, in nearly quantitative yield, the glycos-3-ulose **3**, previously prepared[3] in 72% yield by a similar oxidation of **2** with dimethyl sulfoxide–phosphorus pentaoxide. Reduction of **3** with sodium borohydride, performed in an acetate-buffered medium as recorded[3] for the analogous glycosid-3,3′-diulose but at −60° rather than at room temperature, proceeded quantitatively and stereospecifically to afford crystalline 2-*O*-benzoyl-4,6-*O*-benzylidene-α-D-allopyranosyl 2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-α-D-glucopyranoside (**4**).

At this point, we decided first to explore the feasibility of sequential *O*-mesylation and azide displacement as a route to **7**. Conventional methanesulfonylation of **4** furnished the 3-sulfonate **5** readily enough (74% yield), but difficulties in the displacement step did indeed occur. After various trials, a procedure involving treatment of **5** with lithium azide in 1:3 dimethyl sulfoxide–hexamethylphosphoric triamide for 12 h at 105–108° was adopted. Monitoring of the reaction by t.l.c. (6:1 toluene–ethyl acetate) revealed that **5** was replaced by a fast-moving, main product and several minor, more-slowly moving products. Column chromatography on silica gel permitted the separation, in 34% yield, of crystalline material (presumed to be **7**) that gave a single spot corresponding to the main product, in t.l.c. with the solvent-system just mentioned. It displayed a sharp azide band in the i.r. spectrum and, in the n.m.r. spectrum, showed substituent resonances expected for **7**. However, elemental analysis indicated too high a content of carbon, and a low nitrogen value suggested the

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*Trial experiments were also performed with α-D-allopyranosyl α-D-glucopyranoside[2], kindly donated by Drs. J. Defaye and H. Driguez, in the hope that the *allo* ring would be preferentially cleaved, but insufficient selectivity was noted.

**Birch and coworkers[3], whose target was the 2,2′-dibenzoate, employed two equivalents of the acylating agent and reaction times of 8–12 h; they isolated the dibenzoate in 75% yield, and mono-, tri-, and tetra-benzoates in 2–5% yields. Defaye and his associates[2] obtained, with *N*-acetylimidazole (3 equiv., 24 h), the corresponding di-, tri-, and tetra-acetates in yields of 16, 40, and 23%, respectively.

presence of a substantial proportion (approximately 25%) of a non-nitrogenous contaminant. Fitting microanalytical data were obtained only after several, uneconomical recrystallizations. When the crude **7** (as eluted from the column) was inspected by t.l.c. with multiple irrigation by a different solvent-system (3:1 petroleum ether–ether), the accompanying by-product became detectable as a slightly faster-moving spot. The two components could be separated, laboriously, by preparative t.l.c. to give **7** and the by-product in 3:1 ratio. The overall yield of pure **7** from **5** was 20%. For further characterization, the compound was converted into the 2,3,2′-triacetate **9** by sequential debenzoylation and acetylation.

The crystalline by-product proved to be free from nitrogen, methylsulfonyl, and hydroxyl groups, according to microanalytical and spectral evidence. In the aromatic-proton region of the n.m.r. spectrum, it showed two groups of signals in the intensity ratio of 6:19 (lower:higher field), indicating the presence of three benzoyl and two benzylidene groups. Further upfield were two groups of signals in the regions δ 6.5–5 and 4.5–3, integrating to 8 and 7 protons, respectively. The former set was judged to comprise two anomeric and two benzylidene methine protons, three ring-protons at benzoylated positions, and one alkenic proton, and the latter set accounted for the protons at C-6, -6′, -5, -5′, and -4. When the compound was debenzoylated (Zemplén) and then rebenzoylated, the n.m.r. and i.r. spectra were unchanged. We assign it the constitution of 2-*O*-benzoyl-4,6-*O*-benzylidene-3-deoxy-α-D-*erythro*-hex-3-enopyranosyl 2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-α-D-glucopyranoside (**8**). Elimination reactions attending azide displacements of sulfonic esters of sugars have been observed and discussed before[10,11].

A much superior way of generating the azido sugar **7** was subsequently found in azide displacement of the 3-trifluoromethanesulfonate **6**. Although the latter was obtained, from **4**, in somewhat lower yield (61%) than the methanesulfonate **5**, its reaction with lithium azide in 1:1 *N*,*N*-dimethylformamide–dimethyl sulfoxide was extremely facile, proceeding almost instantaneously at room temperature. It was completed by warming for 1 h at 60° and gave **7** in 80% yield (purified); there was no evidence for formation of the unsaturated product **8**. Zemplén debenzoylation then gave the triol **10**, and subsequently, mild acid-hydrolysis gave the unprotected azido disaccharide **11**, as microcrystalline solids in yields of 90 and 88%, respectively. Catalytic hydrogenation of **11** over Adams' catalyst in the presence of dilute hydrochloric acid was almost quantitative and furnished the highly crystalline 3-amino-3-deoxy-α,α-trehalose hydrochloride (**12**); see also note added in proof, p. 184.

The ^{1}H-n.m.r. data for compounds **2**–**10** are listed in Tables I and II. They are in agreement with the postulated structures.

EXPERIMENTAL

General methods. — These were the same as those previously reported[5]. Optical rotations were measured at approximately 25°. Unless otherwise indicated, t.l.c. plates were developed with 6:1 toluene–ethyl acetate (solvent *A*), 10:1 toluene–

TABLE I

PROTON CHEMICAL-SHIFT DATA FOR COMPOUNDS **2–10**.

Compd.	*Solvent*	*Chemical shifts*[a] *(δ)*									
		H-1	*H-1′*	*H-2*	*H-2′*	*H-3*	*H-3′*	*H-4*	*H-4′*	*H-5,5′,6,6′*	*PhCH*
2[b]	$CDCl_3$	5.56d	5.47d	5.30dd	5.13dd	6.09t	4.43sx[c]	3.81t	←——— 4.2–3.3m ———→		5.37, 5.34
3[d]	$CDCl_3$	5.64d	5.74s	5.37dd	5.74s	6.08t	—	3.91t	4.34d	~4.3–3.5m	5.49, 5.37
4	$CDCl_3$	5.61d	5.42[e]	5.37dd	5.16	6.10t	4.54sx[f]	←———— 4.3–3.4m ————→			5.43, 5.39
5	$CDCl_3$	5.58d	5.5[g]	5.29dd	5.26t	6.22t	5.5[g]	←———— 4.4–3.4m ————→			5.45, 5.44
	$(CD_3)_2CO$	5.6[h]	5.68d	5.41dd	5.39t	6.23t	5.6[h]	4.13t	4.05dd	4.4–4.2, 3.8–3.5m	5.62(2)
6	$CDCl_3$	5.64d	5.43d	5.36dd	5.35t	6.22t	5.55nm	3.88t	3.75dd	4.22o, 3.73–3.3m	5.46, 5.39
	$(CD_3)_2CO$	5.71d	5.67d	5.47dd	5.59t	6.23t	5.79nm	←———— 4.4–4.1, 3.9–3.5m ————→			5.62(2)
7	$CDCl_3$	5.55d	5.48d	5.32dd	5.04dd	6.09t	4.36t	←———— 4.1–3.4m ————→			5.39, 5.36
8	$CDCl_3$	5.60d(2)		5.4m[h]	5.80m[f]	6.06t	5.4m[h]	3.81t	—	~4.5–3.4m	5.45, 5.35
	C_6D_6	5.8(2)[j]		5.62dd	5.8m[f,j]	6.42t	5.35nm	3.60t	—	~4.7–3.2m	5.26, 5.15
9	$CDCl_3$	5.34d	5.31d	5.00dd	4.80dd	5.67dd	4.19t	←———— 4.3–3.4m ————→			5.55, 5.49
10	$CDCl_3$	4.91d	4.75d	←———— 4.6–3.0m ————→							5.49, 5.32

[a]From 100-MHz spectra (lock signal: tetramethylsilane) recorded at 250- or 500-Hz sweep-width. The non-primed hydrogen atoms refer to the 2,3-di-*O*-benzoylated (**2–8**), 2,3-di-*O*-acetylated (**9**), or 2,3-unsubstituted (**10**) glucopyranosyl moieties. Signal multiplicities: d, doublet; m, multiplet; nm, narrow multiplet; o, octet; s, singlet; sx, sextet; and t, triplet. Numbers in parentheses indicate number of protons (by integration). In addition to the signals listed, all compounds showed at low field the patterns of aromatic-proton resonances as required by the respective structures. The $MeSO_3$ signal (s, 3H) of **5** occurred at δ 3.24 (in $CDCl_3$) and 3.23 [in $(CD_3)_2CO$], and the AcO signals (s, 3H each) of **9** occurred at δ 2.18, 2.12, and 2.06. [b]These data are in essential agreement with those reported[3], although, among the latter, the chemical-shift values for H-1′ and H-2 appear to have been inadvertently interchanged and the value given for H-4 probably is a typographical error. [c]Collapsing to t upon addition of D_2O to the solution, with concomitant disappearance of the OH-3′ signal at δ 2.60 (d, $J_{3',OH}$ 3Hz). [d]The interpretation of some of the signals differs from that proposed in the literature[3]. The C-3′ carbonyl group evidently deshields the vicinal protons H-2′ and H-4′ by 0.4–0.5 p.p.m., and H-1′ by ~0.15 p.p.m., relative to their positions[15] in the 2,3,2′,3′-tetrabenzoate corresponding to **2**; as a result, the H-1′ and H-2′ signals coincide, fortuitously, to give a 2-proton singlet and no coupling is observed. [e]Presumably a doublet overlapped by PhCH and the downfield part of H-2 signals. [f]As for *c*, with the OH-3′ signal at δ 2.83 (d, $J_{3',OH}$ ~3Hz). [g]Unresolved, because of partial overlap with PhCH signals. [h]Signal partially obscured by PhCH signal. [i]Complex multiplet containing 2-Hz splittings that are presumably due to long-range coupling with H-5. [j]Signals for H-1, H-1′, and H-2′ form an unresolved group.

TABLE II

PROTON–PROTON, SPIN-COUPLING DATA FOR COMPOUNDS 2–10

Compd.	*Solvent*	*Splittings*[a] *(Hz)*							
		$J_{1,2}$	$J_{1',2'}$	$J_{2,3}$	$J_{2',3'}$	$J_{3,4}$	$J_{3',4'}$	$J_{4,5}$	$J_{4',5'}$
2	$CDCl_3$	4	3.7	9.5	9.5	9.5	9.5	9.5	
3	$CDCl_3$	3.7	0	9.8		10		10	9.7
4	$CDCl_3$	4	~3.5	9.5	~3.5	9.5	~3.5	9.5	
5	$CDCl_3$	4	3.5	9.8	3.5	9.8			
	$(CD_3)_2CO$	4	3.5	9.5	3.5	9.5	2.5	9.5	10
6	$CDCl_3$	3.7	~4.5	9.3	~4.5	9.3	2	9.5	10
	$(CD_3)_2CO$	4	~4	9.5	4.5	9.5	~2		
7	$CDCl_3$	4	3.5	10	10	9.5	10		
8	$CDCl_3$	4	4.5	9.5	~2	9.5		9.5	
	C_6D_6	3.8		9.8	[b]	9.8			
9	$CDCl_3$	4	3.7	10	10.3	9.5	9.5		
10	$CDCl_3$	3.8	3.8						

[a]See footnote *a* in Table I. [b]Not directly measurable, but estimated to be small, because of the narrowness (width at half-height, ~4.5 Hz) of the H-3′ signal, which also exhibited a small splitting, arising from $J_{1',3'}$ coupling.

ethyl acetate (solvent *B*), or 3:1 petroleum ether–ether (solvent *C*). Petroleum ether refers to the fraction boiling at 30–60°.

2,3-Di-O-benzoyl-4,6-benzylidene-α-D-glucopyranosyl 2-O-benzoyl-4,6-O-benzylidene-α-D-glucopyranoside (**2**). — Partial benzoylation[12] by *N*-benzoylimidazole[13] was applied to 4,6:4′,6′-di-*O*-benzylidene-α,α-trehalose[14] (**1**) as described by Birch *et al.*[3], with the following changes in details. A solution of **1** (9.1 g, 17.5 mmol) in dry *N*,*N*-dimethylformamide (30 mL) was mixed with purified[3] chloroform (200 mL), and a solution of *N*-benzoylimidazole (75 mmol, made from 7.8 g of imidazole and 8.0 g of benzoyl chloride) in purified chloroform (50 mL) was added. The mixture, which was initially turbid but which cleared shortly on boiling, was boiled for 80 h under reflux, after which time t.l.c. (solvent *A*) showed two major spots and one or two trace spots. The mixture was evaporated and the residue dissolved in dichloromethane. The solution was washed once with aqueous, saturated sodium hydrogencarbonate and twice with water, dried (magnesium sulfate), concentrated, and applied to a column of silica gel (400 g). Elution with solvent *B* gave, in turn: (*a*) 2,3,2′,3′-tetra-*O*-benzoyl-4,6:4′,6′-di-*O*-benzylidene-α,α-trehalose (4.5 g, 27.5%), m.p. 240° (lit.[3] m.p. 237–239°) having 100-MHz n.m.r. data in excellent agreement with those reported[15]; (*b*) the desired tribenzoate **2** (6.3 g, 43%), m.p. 253–256° (dec.) after crystallization from ethanol, $[\alpha]_D$ +195° (*c* 0.4, chloroform); ν_{max}^{KBr} 3550 (OH) and 1725 cm^{-1} (BzO), lit.[3] m.p. 250–253° (dec.) and $[\alpha]_D$ +202.5°; and (*c*) a slow-moving product (1.0 g) having an R_F value similar to that of the corresponding 2,2′-dibenzoate. Fractions *a* and *c* were combined for regeneration of **1** by Zemplén debenzoylation.

2,3-Di-O-benzoyl-4,6-O-benzylidene-α-D-glucopyranosyl 2-O-benzoyl-4,6-O-benzylidene-α-D-ribo-hexopyranosid-3-ulose (**3**). — The tribenzoate **2** (4.0 g) was oxidized, as described[2] for the analogous triacetate, by dissolving it in dimethyl sulfoxide (80 mL) and adding acetic anhydride (40 mL). The mixture was kept for 24 h at room temperature and then chilled and poured into ice–water (1 L). The copious precipitate formed was washed well with water and then dissolved in dichloromethane. The solution was washed with water, concentrated to low volume, and carefully diluted with ethanol to effect crystallization of **3**. The product was recrystallized from ethanol; yield 3.8 g (95%); m.p. 243–244.5° (dec.), $[\alpha]_D$ +162° (*c* 0.4, chloroform); ν_{max}^{KBr} 1760 (CO) and 1730 cm^{-1} (PhCO); lit.[3] m.p. 233–236° dec., $[\alpha]_D$ +155°.

2-O-Benzoyl-4,6-O-benzylidene-α-D-allopyranosyl 2,3-di-O-benzoyl-4,6-O-benzylidene-α-D-glucopyranoside (**4**). — A solution of the glycosulose **3** (1.0 g) in dichloromethane (15 mL) was mixed with a solution (10 mL) of anhydrous sodium acetate in methanol, which had been adjusted to pH 6.5 by addition of acetic acid. The mixture was cooled to −60° and sodium borohydride (0.15 g) was added portionwise during 2 h, with continued cooling and dropwise addition of 20% acetic acid in dichloromethane so as to maintain pH 7. The mixture then showed a single spot in t.l.c. (solvent *A*) and was deionized with Dowex-1 X8 (HCO_3^- form); the resin was then filtered off and washed with dichloromethane (10 mL) and ethanol (10 mL). The filtrate was concentrated under diminished pressure until the first crystals formed. The product then crystallized completely on being kept and was recrystallized from dichloromethane–ethanol; yield, 0.98 g (97%), m.p. 215–217°, $[\alpha]_D$ +159° (*c* 0.3, chloroform); ν_{max}^{KBr} 3630 (OH) and 1725 cm^{-1} (PhCO).

Anal. Calc. for $C_{47}H_{42}O_{14}$ (830.8): C, 67.94; H, 5.10. Found: C, 67.88; H, 5.14.

2-O-Benzoyl-4,6-O-benzylidene-3-O-methylsulfonyl-α-D-allopyranosyl 2,3-di-O-benzoyl-4,6-O-benzylidene-α-D-glucopyranoside (**5**). — Compound **4** (1.3 g) in dry pyridine (15 mL) was treated with methanesulfonyl chloride (1.3 mL) under initial ice cooling. After 24 h at room temperature, the mixture was processed conventionally. The crude, solid product obtained (1.5 g) was purified by passage through a small column of silica gel, with solvent *A* as eluant, and was subsequently recrystallized from ether–ethanol to give 1.05 g (74%) of the sulfonate **5**, m.p. 144–146°, $[\alpha]_D$ +147° (*c* 0.4, chloroform); ν_{max}^{KBr} 1730 cm^{-1} (PhCO).

Anal. Calc. for $C_{48}H_{44}O_{16}S$ (908.9): C, 63.43; H, 4.88; S, 3.53. Found: C, 63.26; H, 4.89; S, 3.43.

2-O-Benzoyl-4,6-O-benzylidene-3-O-trifluoromethylsulfonyl-α-D-allopyranosyl 2,3-di-O-benzoyl-4,6-O-benzylidene-α-D-glucopyranoside (**6**). — Compound **4** (0.84 g) was trifluoromethanesulfonylated[16] by adding a solution of triflic anhydride (1 mL) in pyridine (5 mL) to its solution in pyridine (10 mL). The temperature was maintained at −15° during the addition, and the mixture was then kept overnight at 0°. T.l.c. (solvent *C*) then showed one major product and traces of (faster-moving) by-products. The mixture was poured into ice–water (300 mL) to give a precipitate that was washed with water, dried, dissolved in a small amount of dichloromethane, and passed through a small column of silica gel (11 g) by means of solvent *C*. Crystalliza-

tion of the main-product fraction from ether–ethanol–hexanes afforded the triflate **6** (0.60 g, 61%) as white needles, m.p. 177–178° (dec.), $[\alpha]_D$ +138° (*c* 0.5, chloroform); ν_{max}^{KBr} 1738, 1730, and 1708 cm^{-1}.

Anal. Calc. for $C_{48}H_{41}F_3O_{16}S$ (962.5): C, 59.89; H, 4.26; S, 3.33. Found: C, 60.17; H, 4.30; S, 3.51.

3-Azido-2-O-benzoyl-4,6-O-benzylidene-3-deoxy-α-D-glucopyranosyl 2,3-di-O-benzoyl-4,6-O-benzylidene-α-D-glucopyranoside (**7**). *A. From* **6**. — To a solution of the triflate **6** (0.58 g) in dry *N,N*-dimethylformamide (5 mL) was added a saturated solution of lithium azide (0.40 g) in dimethyl sulfoxide (5 mL). Inspection by t.l.c. (solvent *C*) suggested that the reaction was half complete within a few min. The mixture was then warmed for 1 h at 60°, poured into ice–water (300 mL), and processed further by washing the precipitate with water, dissolving it in dichloromethane, and washing the dichloromethane solution with water. After drying (magnesium sulfate) and concentration to low volume, the solution was applied to a small column of silica gel (18 g), which was eluted with 12:1 toluene–ethyl acetate. Recrystallization of the product so obtained, from dichloromethane–ethanol, afforded **7** as white needles (0.41 g, 80%), m.p. 184–186°, $[\alpha]_D$ +255° (*c* 0.3, chloroform). The i.r. and n.m.r. spectra were identical with those of **7** described under *B*.

B. From **5**. — A mixture of the methanesulfonate **5** (0.5 g), lithium azide (0.5 g), dimethyl sulfoxide (5 mL), and hexamethylphosphoric triamide (15 mL) was maintained for 12 h at 105–108°, whereupon t.l.c. (solvent *A*) showed that **5** was completely consumed and a fast-moving, major product was formed. (There were also several minor spots, presumably due to decomposition products.) The solvents were evaporated from the mixture (60°, 0.1 torr), and the residue was extracted with dichloromethane. The extract was washed with water, dried (magnesium sulfate), and evaporated to a syrup that was passed over a column of silica gel (20 g) by means of solvent *A*. The fractions that contained solely the fast-moving, chief product (homogeneous in t.l.c. with this solvent) gave, upon evaporation, a semi-crystalline material (0.16 g, 34%); ν_{max}^{KBr} 2105 (N_3) and 1730 cm^{-1} (PhCO); substituent resonances in the n.m.r. spectrum were in agreement with structure **7**. However, the material (found: C, 66.58; H, 4.78; N, 3.52) contained a contaminant that was detected by t.l.c., when several irrigations with solvent *C* were employed, as a marginally faster-moving spot. After multiple recrystallizations from ether–ethanol, the product melted at 182–184° and gave the n.m.r. data listed in Tables I and II.

Anal. Calc. for $C_{47}H_{41}N_3O_{13}$ (855.8): C, 65.96; H, 4.83; N, 4.91. Found: C, 66.20; H, 4.87; N, 4.63.

Several combined batches of crude **7** (obtained from columns of silica gel) were subjected to preparative t.l.c. The plates (40 × 18 cm) were coated with MN Kieselgel G/UV_{254} (thickness, 1.5 mm), and the substance (30 mg per run) was applied in ethyl acetate solution. The separations were performed by seven consecutive irrigations with solvent *C*, after which stage the band-positions were marked under u.v. light. Zone elution with ethyl acetate furnished, from a total of 0.60 g of crude product, 0.12 g of by-product **8** (front zone) and 0.36 g of pure **7** (rear zone). A border zone of

incomplete separation was discarded. Compound **7** thus purified was converted into the triacetate **9**.

2-O-Acetyl-3-azido-4,6-O-benzylidene-3-deoxy-α-D-glucopyranosyl 2,3-di-O-acetyl-4,6-O-benzylidene-α-D-glucopyranoside (**9**). — The tribenzoate **7** (0.35 g) was catalytically debenzoylated with sodium methoxide in methanol and chloroform, and the product was immediately acetylated[2] with *N*-acetylimidazole, to give 0.24 g (88%) of crystalline **9**; m.p. 249–250° dec., $[\alpha]_D$ +92.6° (*c* 0.3, chloroform); ν_{max}^{KBr} 2100 (N_3) and 1740 cm^{-1} (OAc).

Anal. Calc. for $C_{32}H_{35}N_3O_{13}$ (669.6): C, 57.39; H, 5.27; N, 6.28. Found: C, 57.44; H, 5.36; N, 6.14.

*2-O-Benzoyl-4,6-O-benzylidene-3-deoxy-α-D-*erythro*-hex-3-enopyranosyl 2,3-di-O-benzyl-4,6-O-benzylidene-α-D-glucopyranoside* (**8**). — The unsaturated disaccharide **8**, separated from **7** by t.l.c. as just described, had m.p. 199–201° (dec.) (after recrystallization from dichloromethane–ether), $[\alpha]_D$ +145° (*c* 0.3, chloroform); ν_{max}^{KBr} 1725, 1710, and 1685 cm^{-1}.

Anal. Calc. for $C_{47}H_{40}O_{13}$ (812.8): C, 69.45; H, 4.96. Found: C, 69.94; H, 4.73; N, 0.0.

3-Azido-4,6-O-benzylidene-3-deoxy-α-D-glucopyranosyl 4,6-O-benzylidene-α-D-glucopyranoside (**10**). — Conventional debenzoylation of **7** (0.35 g) with methanolic sodium methoxide, followed by deionization with Amberlite IR-120 (H^+) resin, gave **10** (0.20 g, 90%) as a microcrystalline powder (from ether–hexanes), m.p. 140–143° (dec.), that displayed an apparent change in crystal form at 125°, $[\alpha]_D$ +87° (*c* 0.5, methanol); ν_{max}^{KBr} 3510 (OH) and 2107 cm^{-1} (N_3).

Anal. Calc. for $C_{26}H_{29}N_3O_{10}$ (543.5): C, 57.45; H, 5.38; N, 7.73. Found: C, 57.47; H, 5.37; N, 7.55.

3-Azido-3-deoxy-α-D-glucopyranosyl α-D-glucopyranoside (**11**). — To a solution of the benzylidene acetal **10** (0.15 g) in aqueous, 80% ethanol (2 mL) was added 1 drop of concentrated hydrochloric acid. The mixture was kept for 3 h at 50° and then made neutral with silver carbonate, filtered, and the filtrate evaporated to dryness. The residue was dissolved in abs. ethanol, and careful addition of ethyl acetate followed by hexanes produced **11** as a white powder (115 mg, 88%), which, on heating, showed evolution of gas at 117–119° followed by gradual decomposition with browning from 123–165°, $[\alpha]_D$ +195.5° (*c* 0.5, methanol); ν_{max}^{KBr} 3480 (OH) and 2107 cm^{-1} (N_3).

Anal. Calc. for $C_{12}H_{21}N_3O_{10}$ (367.3): C, 39.24; H, 5.76; N, 11.44. Found: C, 38.93; H, 5.99; N, 11.12.

3-Amino-3-deoxy-α-D-glucopyranosyl α-D-glucopyranoside hydrochloride (**12**). — Platinum dioxide catalyst (50 mg) was prehydrogenated and subsequently washed with water until it was neutral. The azide **11** (80 mg) in water (2 mL) and M hydrochloric acid (0.21 mL) were added, and hydrogenation was conducted for 1 h at room temperature and pressure. The catalyst was filtered off and washed exhaustively with water, and the filtrate was concentrated *in vacuo* to a colorless oil that, upon trituration with abs. ethanol, yielded **12** (78.5 mg, 95%) as hexagonal

platelets. Recrystallized from water–ethanol, they showed $[\alpha]_D$ +178° (*c* 0.5, water) and decomposed at 200–215°.

Anal. Calc. for $C_{12}H_{24}ClNO_{10}$ (377.8): C, 38.15; H, 6.40; N, 3.71. Found: C, 38.45; H, 6.47; N, 3.52. (The sample was dried at 110°/1 torr.).

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NOTE ADDED IN PROOF

E. Bar-Guilloux and J. Defaye (private communication) have determined that **12** is a substitute for cockshafer trehalose[2,4a,4b]. They found K_m 10mM and a V_{max} value which is 8% of that for α,α-trehalose.

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