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SYNTHESIS OF 6,6'-DISUBSTITUTED SUCROSE DERIVATIVES FROM 1',6,6'-TRI-*O*-TRIPSYLSUCROSE

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ABSTRACT

An improved synthesis of 6,6'-disubstituted derivatives of sucrose is described that uses 1',6,6'-tri-*O*-tripsylsucrose as the starting material. The 6- and 6'-tripsyloxy groups have been selectively displaced, leaving the (more sterically hindered) 1'-tripsyloxy group untouched. Subsequent displacement of the 1'-tripsyloxy group by sodium benzoate, under forcing conditions, effected sulfonate displacement and gave sucrose derivatives substituted at C-6 and C-6'.

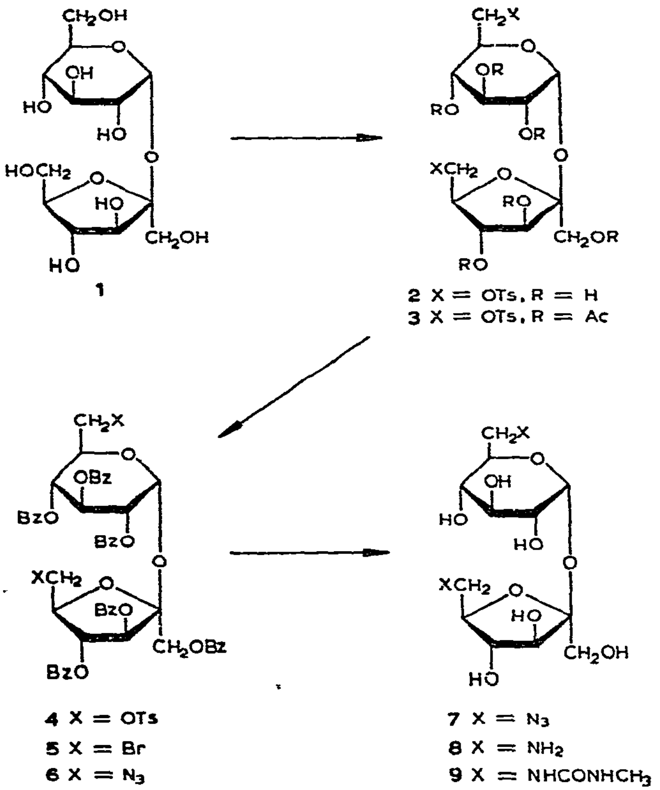
INTRODUCTION

Some 6,6'-disubstituted derivatives of sucrose were required for biological studies. A convenient starting material for the synthesis of these derivatives would be a sulfonylated sucrose derivative. As there are numerous reports in the literature on the synthesis of tosylated sucrose derivatives and their use in preparing 6,6'-disubstituted sucrose derivatives, these synthetic pathways were examined first.

In 1972, Hough and Mufti[1] reported the synthesis of 6,6'-diazido-6,6'-dideoxysucrose (**7**) from 6,6'-di-*O*-tosylsucrose hexaacetate (**3**). Their sequence required 6,6-di-*O*-tosylsucrose (**2**) as an intermediate, which was obtained in only 18% yield from sucrose[2]. This low initial yield, coupled with the need for frequent column-chromatographic purification of intermediates, made their pathway unfavorable.

A major cause for the poor yield of **2** was the difficulty associated with obtaining pure 6,6'-disubstituted sucrose. Lemieux *et al.*[3] reported that selective tosylation of sucrose gave mixtures of 6,6'-di-*O*-tosylsucrose (**2**) together with the isomeric 1',6-di-*O*-tosylsucrose, 1',6'-di-*O*-tosylsucrose and trisulfonates and probably mixed monosulfonates of sucrose. This lack of selectivity for O-6 and O-6' over O-1' is surprising, as O-1' is sterically much more hindered than either O-6 or O-6' and should, as a result, be more difficultly esterified.

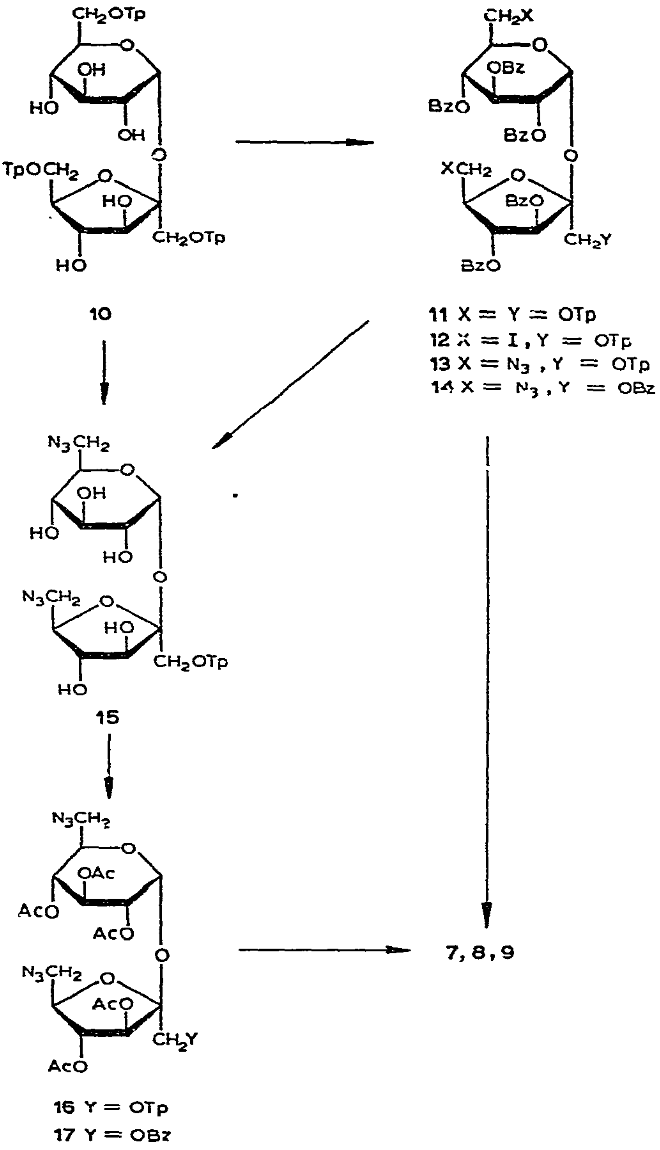
It seemed possible that a sterically more hindered sulfonate might increase the selectivity between the 6,6' and 1' hydroxyl groups and lead to a readily isolated 6,6'-disulfonylated sucrose. For this reason, the reaction of 2,4,6-triisopropylbenzenesulfonyl chloride (tripsyl chloride) with sucrose was investigated. Surprisingly, again



no great selectivity could be obtained and complex mixtures again resulted. However, it was possible to obtain a 54% yield of crystalline 1′,6,6′-tri-*O*-tripsylsucrose (**10**) by simple crystallization[4], as compared to a yield of only 23% for 1′,6,6′-tri-*O*-tosylsucrose after chromatography[5]. A study of the selective displacement of the sulfonate groups of **10** was initiated in an effort to devise a useful procedure for preparing 6,6′-disubstituted sucrose derivatives.

RESULTS AND DISCUSSION

Initially, the approach of Bolton *et al.*[2] using the *p*-toluenesulfonate blocking group was investigated and 6,6′-di-*O*-tosylsucrose (**2**) was benzoylated to give the hexabenzoate **4**. Following the procedure of Hough and Mufti[1], **4** was treated with sodium bromide to give the dibromide **5**, which was then treated with sodium azide in hexamethylphosphoric triamide (HMPA) to give 6,6′-diazido-6,6′-dideoxysucrose hexabenzoate (**6**) in good yield from the sulfonate **2**. Debenzoylation of **6** gave crystalline 6,6′-diazido-6,6′-dideoxysucrose (**7**) in 9% overall yield from sucrose. Hydrogenation of **7** with 10% palladium on carbon gave 6,6′-diamino-6,6′-dideoxysucrose (**8**) as a noncrystallizable syrup that was characterized as the crystalline 6,6′-di-*N*-methyl ureide **9**.



11 X = Y = OTp
12 X = I, Y = OTp
13 X = N_3, Y = OTp
14 X = N_3, Y = OBz

16 Y = OTp
17 Y = OBz

Tp = 2,4,6-triisopropylbenzenesulfonyl

Starting from 1',6,6'-tri-*O*-tripsylsucrose[4] (**10**), two approaches were investigated for the synthesis of 6,6'-diamino-6,6'-dideoxysucrose (**8**). Benzoylation of **10** gave the pentabenzoate **11** in 95% yield. Reaction of **11** with sodium azide directly gave low yields of the desired 6,6'-diazido-6,6'dideoxy-1'-*O*-tripsylsucrose pentabenzoate (**13**). Better overall yields of **13** were obtained by first treating **11** with sodium iodide in acetone to give the 6,6'-diiodide **12** in 98% yield. Carbon-13 n.m.r. studies of **12** (Table I) showed that it was a pure diiodo derivative and not a mixture of isomers. The reaction of **12** with sodium azide in HMPA gave **13** in 93% yield. Carbon-13 n.m.r. spectra confirmed that the two iodo groups had been replaced. Displacement of the 1′-tripsyloxy group of **13** by action of sodium benzoate in HMPA under forcing conditions yielded the crude 1′-benzoate **14**. Debenzoylation of this crude product with sodium methoxide gave **7** in 12% yield, together with 25% of crude, unreacted 6,6′-diazido-6,6′-dideoxy-1′-*O*-tripsylsucrose (**15**). Compound **15** could be acetylated to **16** and treated again with sodium benzoate, with subsequent de-esterification, to give more diazide **7** in 35% yield, and an 18% yield of recovered crude **15**. Continuation of this procedure gave a final yield of 22% of diazide **7**, based on the amount of **13** originally reacted. The overall yield of **7** from sucrose by this route was 11%.

TABLE I

CARBON-13 N.M.R. DATA (δ)

Compound / *Carbon atom*	**10**	**11**	**12**	**13**	**16**	**14**	**5**	**4**	**2**
C-1	92.9	91.4	91.6	91.4	91.1	91.5	91.5	91.1	92.6
C-2	74.2	71.6	73.2	71.3	70.5	71.8	71.8	71.5	74.7
C-3	72.2	71.3	71.2	71.3	70.5	71.2	71.8	71.5	73.1
C-4	71.6	70.3	70.8	70.9	70.1	71.0	71.1	69.6	71.9
C-5	71.0	69.6	70.1	70.2	69.7	70.5	70.8	69.2	71.5
C-6 or C-6′	71.3	69.6	4.8	53.2	53.2	53.5	33.2	70.9	73.3
C-1′	67.0	67.6	68.4	68.3	67.7	65.6	65.5	65.4	64.7
C-2′	103.3	104.7	104.3	104.2	103.9	104.7	104.9	104.8	105.3
C-3′	81.9	80.7	81.5	80.7	80.8	80.8	81.5	79.6	80.8
C-4′	77.5	77.3	78.9	77.3	76.5	78.1	78.6	77.8	79.7
C-5	75.4	76.5	77.9	76.6	75.8	77.3	78.6	76.2	76.4
C-6′ or C-6	69.8	67.6	5.6	51.7	51.6	51.8	32.7	68.6	71.5

During the course of these studies to prepare the diamine **8**, it was discovered that unprotected 6,6′-diazido-6,6′-dideoxy-1′-*O*-tripsylsucrose (**15**) is sufficiently lipophilic because of the tripsyl group to be readily extracted from water by organic solvents. It was therefore unnecessary to esterify the hydroxyl groups of **10** in order to facilitate the processing of the replacement reaction at the 6 and 6′ positions. Thus, **10** reacted with sodium azide in HMPA to yield crude diazide **15** in 84% yield. The diazide **15** did not react with sodium benzoate directly, but required initial acetylation to the hexaacetate **16**. Crude **16** was treated with sodium benzoate in HMPA and then deacetylated to give **7** in 32% yield and a 19% yield of recovered **15**. Continued reaction of **15** as described previously gave a total yield of 40% of **7** from **16**. The overall yield of **7** from sucrose by this synthetic pathway was 17%. This is almost double the yield of **7** obtained when 6,6′-di-*O*-tosylsucrose (**2**) was used as the sulfonylated intermediate, and this pathway required no column-chromatographic purifications. Hydrogenation of the azide **7** prepared from **10** again gave the syrupy amine **8**, characterized as the crystalline diureido derivative (**9**), identical to **9** prepared from the disulfonate **2**.

1′,6,6′-Tri-*O*-tripsylsucrose (**10**) has proved to be a much better intermediate for the preparation of 6,6′-diamino-6,6′-dideoxysucrose (**8**) than 6,6′-di-*O*-tosylsucrose (**2**). The highly lipophilic character of the tripsyl group makes it unnecessary to esterify the sugar hydroxyl groups of **10** prior to treating **10** with sodium azide.

EXPERIMENTAL

General methods. — Melting points were determined on a Thomas–Hoover Uni-Melt apparatus and are corrected. Evaporations were performed *in vacuo*. Optical rotations were measured with a Perkin–Elmer 141 automatic polarimeter. Carbon-13 n.m.r. spectra were recorded with a Varian XL-100-FT (25.17 MHz) n.m.r. spectrometer in acetone-d_6 with tetramethylsilane as an internal standard. I.r. spectra were taken on a Perkin–Elmer 137 spectrometer. P.m.r. spectra were recorded with a Varian T-60 spectrometer. Mass spectra were determined with an LKB Model 9000 gas chromatograph–mass spectrometer. Carbon-13 n.m.r. data for compounds **2**, **4**, **5**, and **10–14**, **16** appear in Table I. The presence of solvents of crystallization was confirmed by p.m.r. spectroscopy.

6,6′-Diazido-6,6′-dideoxysucrose hexabenzoate (**6**). — A mixture of 6,6′-dibromo-6,6′-dideoxysucrose hexabenzoate[1] (**5**) (12.8 g, 11.7 mmoles), sodium azide (7.61 g, 117 mmoles), and dry hexamethylphosphoric triamide (75 ml) was stirred for 3 h at 85°. The mixture was then added with stirring to ice–water (3000 ml), and the resultant, flocculant precipitate was filtered off, washed with water (2000 ml), and dried for 4 h in air. The filter cake was mixed with chloroform (200 ml), and the water layer that formed was separated. The chloroform layer was dried (Drierite) and evaporated to a white, solid foam that solidified on adding hot abs. ethanol (100 ml) to give **6** as a white solid. More **6** was obtained by dissolving the mother liquor in acetone, precipitating the product from water (500 ml), filtering the mixture and solidifying the filter cake with hot abs. ethanol (15 ml). Both portions of product were combined and dried at 60°/1 torr to give **6** as a white solid; yield 11.1 g (93.3%), m.p. 78–80° (softens), melting at 113–125°, $[\alpha]_D^{21}$ +41.5 ±0.52° (*c* 1.6, dichloromethane) [lit.[2] m.p. 75–78°, $[\alpha]_D$ +42.5° (*c* 1.6, dichloromethane)].

Anal. Calc. for $C_{54}H_{44}N_6O_{15}$: C, 63.78; H, 4.36; N, 8.26. Found: C, 63.79; H, 4.13; N, 8.04.

6,6′-Diazido-6,6′-dideoxysucrose (**7**). — *A*. A mixture of 6,6′-diazido-6,6′-dideoxysucrose hexabenzoate (**6**, 11.1 g, 10.9 mmoles) in dry methanol (100 ml) was adjusted to pH 9–11 by adding sodium methoxide. The mixture was slurried until the gummy starting material had dissolved, and then stirred for 16 h at room temperature. Amberlite IRC-50 (H$^+$) resin was added to neutralize the mixture, which was then filtered and the filtrate evaporated to a yellow residue. This residue was mixed with water (75 ml) and chloroform (75 ml) and was continuously extracted with chloroform for 20 h. The water layer was evaporated to a solid, white foam (4.15 g). This foam was crystallized twice from acetone to give white crystalline **7**; yield 2.56 g (59.8%), m.p. 168–169°, $[\alpha]_D^{21}$ +82.0 ±1.0° (*c* 1.0, water) [lit.[1] m.p. 163–164°, $[\alpha]_D$ +78.8° (*c* 0.98, water)].

Anal. Calc. for $C_{12}H_{20}N_6O_9$: C, 36.74; H, 5.14; N, 21.42. Found: C, 36.81; H, 5.24; N, 21.09.

B. A mixture of 6,6′-diazido-6,6′-dideoxy-1′-*O*-tripsylsucrose pentabenzoate (**13**) (27.4 g, 23.2 mmoles), sodium benzoate (33.4 g, 232 mmoles) and dry hexamethylphosphoric triamide (350 ml) was stirred for 17 h at 110°. The mixture was then cooled in an ice bath and water was added to dissolve the excess of sodium benzoate. The reddish-brown solution was poured into 20% aqueous sodium chloride–ice (4000 ml), and the mixture was extracted with ether (1500 ml). The ether layer was washed with ice–water (1000 ml) and saturated sodium chloride solution (300 ml), dried (Drierite) and evaporated to give crude **14** (23.0 g). A solution of crude **14** in dry methanol (250 ml) was adjusted to pH 9–11 by addition of sodium methoxide, stirred for 16 h at room temperature, and then neutralized with IRC-50 (H^+) resin. The mixture was filtered and the filtrate evaporated to an orange syrup. This syrup was mixed with water (150 ml) and chloroform (100 ml) and continuously extracted with chloroform for 20 h. The chloroform layer was evaporated and the resultant orange residue was triturated with petroleum ether (b.p. 30–60°, 300 ml) and the mixture was filtered. The gummy filter-cake was dissolved in acetone and the solution evaporated to a dark-orange, gummy foam. This foam was stirred with water (100 ml) and petroleum ether (100 ml) for 8 h. The petroleum ether layer was separated, and the water layer was stirred with ether for 15 min. The ether layer was separated and evaporated to give crude 6,6′-diazido-6,6′-dideoxy-1′-tripsylate (**15**) as an orange, solid foam (3.77 g, 24.8%). The water layer from the continuous extraction with chloroform was treated with activated charcoal, concentrated to 100 ml, and continuously extracted with 1:1 butanone–ethyl acetate (2 × 200 ml) during two consecutive 20-h periods. The two organic extracts were combined and evaporated to an orange, gummy foam, which was dissolved in water (100 ml) and continuously extracted with chloroform for 40 h. The water layer was evaporated to a yellow, solid foam (5.25 g), which crystallized from acetone (25 ml) to give 6,6′-diazido-6,6′-dideoxysucrose (**7**); yield 1.08 g (11.9%).

C. A solution of 6,6′-diazido-6,6′-dideoxy-1′-*O*-tripsylsucrose pentaacetate (**16**) (2.91 g, 3.35 mmoles) in dry hexamethylphosphoric triamide (50 ml) was stirred with sodium benzoate (4.83 g, 33.5 mmoles) for 16 h at 105–110°. The mixture was then cooled in an ice bath and water was added until the excess of sodium benzoate had dissolved. This reddish solution was poured with stirring into 20% sodium chloride solution (1800 ml) containing ice. This aqueous mixture was extracted with ethyl acetate (1000 ml). The organic layer was washed with 4% sodium chloride solution (2 × 700 ml) and water (700 ml), dried (Drierite), and evaporated to give crude **7** (2.44 g) as an off-white, gummy foam. This foam was dissolved in dry methanol (50 ml), and the solution was adjusted to pH 9–11 by addition of sodium methoxide. This mixture was stirred for 16 h at room temperature, neutralized by addition of IRC-50 (H^+) resin, and was evaporated to an orange syrup. This syrup was mixed with water (40 ml) and chloroform, and continuously extracted with chloroform (150 ml) for 4 h. The chloroform layer was evaporated to an orange syrup. This syrup was stirred with petroleum ether (b.p. 30–60°, 50 ml) for 30 min and then filtered. The filter cake was dissolved in acetone and evaporated to give an orange solid foam, **15**, 0.415 g (18.8%). The water layer was continuously extracted with 2:1 ethyl acetate–butanone (3 x 150 ml) for three continuous 20-h periods. The extracts were evaporated after each 20-h period and the white, solid foams obtained were crystallized from acetone and dried at 60° at 1 torr to give 0.425 g (32.4%) of **7**.

6,6′-Diamino-,6′6-dideoxysucrose (**8**). — A solution of 6,6′-diazido-6,6′-dideoxysucrose (**7**) (4.42 g, 11.3 mmoles) and 10% palladium on carbon (442 mg) in methanol (75 ml), water (22 ml), and triethylamine (1.0 ml) was reduced at 45 lb.in^{-2} of hydrogen gas in a Parr shaker for 20 h. The mixture was then filtered by gravity, and the filtrate evaporated at 50° to give a light-yellow syrup, which was mixed with water (20 ml) and filtered through Celite. The filtrate was evaporated to a white solid foam (**8**, 4.18 g); *m/e* (octa-Me_3Si) 916.

Attempts to crystallize **8** have thus far been unsuccessful. Instead of purifying **8** further it was converted directly into **9**.

6,6′-Di(methylureido)-6,6′-dideoxysucrose (**9**). — Crude 6,6′-diamino-6,6′-dideoxysucrose (**8**) obtained from 4.42 g (11.3 mmoles) of 6,6′-diazido-6,6′-dideoxysucrose (**7**) was dissolved in water (40 ml) and stirred at 0°. Methyl isocyanate (1.75 ml, 28.2 mmoles) was added to the mixture, which was stirred for 1 h at 0°, warmed to room temperature (20 min) and evaporated to a white, solid foam. Crystallization from methanol (18 ml) gave **9**; yield 4.69 g (85.6% based on **7**), m.p. 207–208 dec., $[\alpha]_D^{21}$ $+63.4 \pm 0.8°$ (*c* 0.96, water); p.m.r. (D_2O): δ 5.40 (d, 1, *J* 3.5 Hz, H-1), 3.38 (s, 3, CH_3OH), 2.73 (s, 6, 2 x N-CH_3).

Anal. Calc. for $C_{17}H_{34}N_4O_{12} \cdot CH_3OH$: C, 41.97; H, 7.04; N, 11.52. Found: C, 41.91; H, 6.76; N, 11.68.

1′6,6,′-Tri-O-tripsylsucrose pentabenzoate (**11**). — A solution of 1′,6,6′-tri-*O*-tripsylsucrose[4] (**10**, 29.2 g, 25.5 mmoles) in dry pyridine (200 ml) was stirred at 0° and benzoyl chloride (20.8 ml, 178 mmoles) was added dropwise over a 20-min period. The mixture was stirred for 1.5 h at 0° and for 3 days at room temperature. It was then cooled to 0° and water (7 ml) was added. The mixture was poured into a separatory funnel, and the lower, pink layer was discarded. The upper layer was added dropwise to ice–water (4000 ml) with stirring. The white precipitate that formed was filtered off and washed with water (3000 ml). The dried filter cake was crystallized from abs. ethanol (300 ml) to give a white solid (**11**). The concentrated mother liquor was dissolved in acetone (20 ml) and added dropwise with stirring to ice–water (800 ml). The yellow precipitate that formed was filtered off, and the gummy filter cake was solidified by adding hot abs. ethanol (70 ml) to give more product. Repeating this process with the mother liquor yielded additional product. All product was combined, dried at 60° at 1 torr to give a total of 40.7 g (95.8%) of **11**, m.p. 90–95° (softening), melting at 95–130°, $[\alpha]_D^{21}$ +21.8 ±0.5° (*c* 0.97, chloroform).

Anal. Calc. for $C_{92}H_{108}O_{22}S_3$: C, 66.48; H, 6.55; S, 5.79. Found: C, 66.25; H, 6.43; S, 6.00.

6,6'-Dideoxy-6,6'-diiodo-1'-O-tripsylsucrose pentabenzoate (**12**). — A mixture of the tritripsyl pentabenzoate **11** (40.7 g, 24.5 mmoles), sodium iodide (121 g, 810 mmoles), and acetone (680 ml) was stirred for 5 days at reflux, and then cooled to room temperature and filtered. The filtrate was evaporated to give a yellow solid, which was triturated with chloroform (425 ml) and the mixture filtered. The filter cake was washed with chloroform (425 ml), and the filtrate evaporated to a yellow glass that was slurried with acetone (120 ml) and the mixture filtered. The filter cake was washed with acetone (85 ml) and the filtrate was evaporated. A solution of the resultant residue in chloroform (350 ml) was washed successively with 10% sodium thiosulfate solution (350 ml) and water (350 ml), dried (Drierite), and evaporated to give a white, solid foam (35.7 g). This foam was solidified by adding hot abs. ethanol (125 ml) to give **12** as a white solid. Additional product was obtained from the mother liquor; total yield 32.3 g (98.0%), m.p.98–104°, $[\alpha]_D^{21}$ −1.32 ±0.32° (*c* 0.99, chloroform).

Anal. Calc. for $C_{62}H_{62}I_2O_{16}S$: C, 55.20; H, 4.63; I, 18.81; S, 2.38. Found: C, 55.48; H, 4.65; I, 18.69; S, 2.60.

6',6-Diazido-6,6'-dideoxy-1'-O-tripsylsucrose pentabenzoate (**13**). — A mixture of the diiodide **12** (30.9 g, 22.9 mmoles), sodium azide (14.9 g, 229 mmoles), and dry hexamethylphosphoric triamide (170 ml) was stirred for 1.5 h at 85°. The mixture was then added with stirring to ice–water (7000 ml). The precipitate that formed was filtered off, and the filter cake was washed with water (4000 ml), air-dried for 16 h, and then mixed with chloroform (350 ml). The water layer that formed was separated, and the chloroform layer was dried (Drierite) and evaporated to a white, solid foam. This foam solidified on adding hot abs. ethanol (100 ml) to give **13** as an off-white solid. The mother liquor was concentrated to a yellow syrup, which was dissolved in acetone (20 ml) and added dropwise with stirring to ice–water (500 ml). The yellow precipitate that formed was filtered off, and the dried filter cake solidified on adding hot abs. ethanol (22 ml) to give more product. The two portions of product were combined and dried for 16 h at 40° and 1 mmHg to give **13**; yield 25.3 g (93.8%), m.p. 84–95°, $[\alpha]_D^{21}$ +31.1 ±0.6° (*c* 0.96, chloroform), ν_{max}^{KBr} 2110 cm^{-1} (N_3).

Anal. Calc. for $C_{62}H_{62}N_6O_{16}S$: C, 63.15; H, 5.30; N, 7.13; S, 2.72. Found: C, 63.15; H, 5.20; N, 7.25; S, 2.60.

6,6'-Diazido-6,6'-dideoxy-1'-O-tripsylsucrose (**15**). — A solution of 1',6,6'-tritripsylsucrose (**10**, 5.72 g, 5.01 mmoles) in dry hexamethylphosphoric triamide was stirred with sodium azide (3.26 g, 50.1 mmoles) for 16 h at 85°. The mixture was then poured with stirring into 20% sodium chloride solution (900 ml) containing ice. The aqueous mixture was extracted with ethyl acetate (500 ml) and the extract was evaporated to give a white, solid foam. This foam was slurried in acetone (70 ml), filtered, and the filter cake washed with acetone (40 ml). The filtrate was again evaporated to a white solid foam, which was slurried in acetone (30 ml), cooled and filtered. The filter cake (sodium tripsylate) was washed with cold acetone (20 ml). The filtrate was evaporated to a white solid foam, which was dissolved in ethyl acetate (500 ml), washed with 4% sodium chloride solution (2 × 350 ml) and water (350 ml), dried (sodium sulfate), and evaporated to give crude **15** as an off-white, waxy solid; yield 2.78 g (84.2%), $\nu_{\max}^{\mathrm{KBr}}$ 2110 cm^{-1} (N_3), n.m.r. (acetone-d_6): δ 7.33 (s, 2, H-3 and H-5 of tripsyl), 5.27 (d, 1, J 3.5 Hz, H-1), 1.24 (d, 12, J 7.0 Hz, *o*-CH_3 groups of tripsyl), 1.26 (d, 6, J 7.0 Hz, *p*-CH_3 groups of tripsyl). This material was acetylated without further purification to give the pentaacetate (**16**).

6,6'-Diazido-6,6'-dideoxy-1'-O-tripsylsucrose pentaacetate (**16**). — A solution of crude 6,6'-diazido-6,6'-dideoxy-1'-*O*-tripsylsucrose (**15**, 2.55 g, 3.87 mmoles) in dry pyridine (30 ml) was stirred at 0°, and acetic anhydride (3.65 ml, 38.7 mmoles) was added dropwise. The mixture was stirred for 1 h at 0° and for 16 h at room temperature. The yellow solution was then evaporated at 50° to a yellow oil, which was mixed with methanol (50 ml) and refluxed for 15 min on a steam bath to decompose any excess of acetic anhydride. This mixture was evaporated with toluene to remove pyridine azeotropically and leave an orange syrup. This syrup was dissolved in ether (75 ml) and washed successively with ice-cold, 2M hydrochloric acid (50 ml), saturated sodium hydrogen carbonate solution (50 ml), and water (50 ml). The ether layer was dried (Drierite) and evaporated to give crude **16** as a white, solid foam (3.08 g, 91.7%), $\nu_{\max}^{\mathrm{KBr}}$ 2110 (N_3), 1730 cm^{-1} (OAc); n.m.r. ($CDCl_3$): δ 7.25 (s, 2, H-3 and H-5 of tripsyl), 5.63 (d, 1, J 3.5 Hz, H-1), 1.29 (d, 18, J 7.0 Hz, CH_3 groups of tripsyl). Crude **16** was converted into **17** without further purification.

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