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Note

Sucrochemistry
Part XI[1]. Synthesis of 1′,6,6′-triamino-1′6,6′-trideoxy derivatives of sucrose

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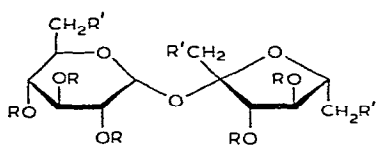
Amino sugars are components of antibiotics[2] and bacterial polysaccharides[3], and interest was therefore stimulated in the synthesis of amino derivatives of sucrose. Syntheses of 1′,6,6′-triamino-1′,6,6′-trideoxysucrose[4], 6-amino-6-deoxysucrose hepta-acetate[5], and 3-acetamido-3-deoxy-α-D-allopyranosyl β-D-fructofuranoside[6] have been reported. Ambiguity in the proof of structure of the first compound[4] has been pointed out by Hough *et al.*[7,8], and we now report an unambiguous synthesis of 1′,6,6′-triamino-1′,6,6′-trideoxysucrose.

1′,6,6′-Tri-*O*-tosylsucrose pentabenzoate[9] underwent nucleophilic substitution by azide in hexamethylphosphoric triamide at 105° to give the 1′,6,6′-triazide **1**. The structure of **1** was supported by the n.m.r. data, which showed an *eq,ax,ax,ax* arrangement for H-1, H-2, H-3, and H-4, respectively. The 1′,6,6′-triazide **1** was de-esterified with methanolic sodium methoxide to give 1′,6,6′-triazido-1′,6,6′-trideoxy-sucrose (**2**), which had physical properties different from those reported[4] for 1′,6,6′-triazido-1′,6,6′-trideoxysucrose. Umezawa *et al.*[4] detritylated 2,3,3′,4,4′-penta-*O*-acetyl-1′,6,6′-tri-*O*-tritylsucrose by the method of Mckeown *et al.*[10] to give a product considered to be 2,3,3′,4,4′-penta-*O*-acetylsucrose. It has been well established[11–14] that this detritylation procedure causes a 4→6 acetyl migration to give 2,3,3′,4′,6-penta-*O*-acetylsucrose. Thus, the structure of the compounds reported by Umezawa *et al.* must be reassigned accordingly.



1 R = Bz, R′ = N_3 5 R = H, R′ = NH_2
2 R = H, R′ = N_3 6 R = H, R′ = NHAc
3 R = Ac, R′ = N_3 7 R = Ac, R′ = NHAc
4 R = Ms, R′ = N_3

With acetic anhydride–pyridine, the 1′,6,6′-triazide **2** gave a syrupy penta-acetate **3**, for which the first-order coupling constants ($J_{1,2}$ 3.7, $J_{2,3}$ 10.0, $J_{3,4}$ 9.5, $J_{4,5}$ 10.0 Hz) established the α-D-*gluco* configuration. Similarly, treatment of **2** with methanesulphonyl chloride in pyridine at 0° gave 1′,6,6′-triazido-1′,6,6′-trideoxy-sucrose pentamethanesulphonate (**4**), the physical properties of which differed from those of 1′,6′-diazido-1′,6′-dideoxy-3′,4′-di-*O*-mesyl-β-D-fructofuranosyl 4-azido-4-deoxy-2,3,6-tri-*O*-mesyl-α-D-galactopyranoside[7,8]. The structure of **4** was confirmed by its 100-MHz n.m.r. spectrum.

Hydrogenation of **2** over palladium-on-charcoal gave the corresponding 1′,6,6′-triamine **5**, which was *N*-acetylated with acetic anhydride in methanol to afford 1′,6,6′-triacetamido-1′,6,6′-trideoxysucrose (**6**). With acetic anhydride in pyridine, **6** gave 1′,6,6′-triacetamido-1′,6,6′-trideoxysucrose penta-acetate (**7**), the first-order coupling constants ($J_{1,2}$ 3.5, $J_{2,3}$ 10.0, $J_{3,4}$ 10.0, $J_{4,5}$ 10.0 Hz) of which confirmed the *gluco* configuration and the $^4C_1$ conformation.

EXPERIMENTAL

The general experimental data are as described in Part VI.

1′,6,6′-Triazido-1′,6,6′-trideoxysucrose pentabenzoate (**1**). — (*a*) A solution 1′,6,6′-tri-*O*-tosylsucrose pentabenzoate[9] (3.5 g) in hexamethylphosphoric triamide (60 ml) was stirred with sodium azide (3.5 g) for 60 h at 105–110°. The reaction mixture was poured on to ice–water, and the precipitate was collected and washed thoroughly with water. T.l.c. (chloroform–light petroleum, 7:1) showed a mixture of several products. The solid residue was dried, and re-benzoylated using benzoyl chloride (2 ml) in pyridine (100 ml) for 24 h at room temperature. T.l.c. then showed a fast-moving, major product. Elution from a column of silica gel (25 g), using chloroform–light petroleum (1:1), afforded a syrup which, on crystallisation from ethanol, gave **1** (1.7 g, 66.2%), m.p. 58–60°, $[\alpha]_D$ +31° (*c* 1.06, chloroform); ν_{max} 2100 (azide), 1750 cm^{-1} (ester). N.m.r. (100 MHz) data: 3.99 (*d*, 1 proton, $J_{1,2}$ 3.5 Hz, H-1), 4.62 (*q*, 1 proton, $J_{2,3}$ 10.0 Hz, H-2), 3.95 (*t*, 1 proton, $J_{3,4}$ 10.0 Hz, H-3), 4.44 (*t*, 1 proton, $J_{4,5}$ 10.0 Hz, H-4), 4.05 (*d*, 1 proton, $J_{3',4'}$ 6.0 Hz, H-3′), 4.06 (*t*, 1 proton, $J_{4',5'}$ 6.0 Hz, H-4′), 1.8–2.84 (*m*, 25 protons, 5Bz).

Anal. Calc. for $C_{47}H_{39}N_9O_{13}$: C, 60.2; H, 4.2. Found: C, 60.3; H, 4.2.

(*b*) A mixture of 1′,6,6′-tri-*O*-mesylsucrose pentabenzoate[9] (2 g) and sodium azide (2 g) in hexamethylphosphoric triamide (40 ml) was stirred for 60 h at 105–110°. The reaction was worked up as described in (*a*) to give **1** (1 g, 68%), m.p. and mixed m.p. 57–60°.

1′,6,6′-Triazido-1′,6,6′-trideoxysucrose (**2**). — A cooled (3°) solution of **1** (500 mg) in dry methanol (50 ml) was treated with sodium methoxide to pH 10 and then stored for 20 h at room temperature. T.l.c. (chloroform–methanol, 4:1) showed a slow-moving, major product. The solution was deionised with Amberlyst 15 and concentrated, and the residue was eluted from a column of silica gel (30 g), using dichloromethane–acetone (2:1), to give **2** as a syrup (150 mg, 67.4%), $[\alpha]_D$ +64° (*c* 0.58, acetone); ν_{max} 3350 (OH), 2100 cm^{-1} (azide).

Anal. Calc. for $C_{12}H_{19}N_9O_8 \cdot C_3H_6O$: C, 37.8; H, 5.2; N, 27.0. Found: C, 37.0; H, 4.8; N.27.1.

Conventional treatment of **2** (500 mg) with acetic anhydride (2 ml) in pyridine (50 ml) for 24 h at room temperature gave the syrupy penta-acetate **3** (670 mg, 90%), $[\alpha]_D$ +101° (*c* 0.57, chloroform); ν_{max} 2100 (azide), 1750 cm^{-1} (ester).

Anal. Calc. for $C_{22}H_{29}N_9O_{13}$: C, 42.1; H, 4.6. Found: C, 43.0; H, 4.9.

1',6,6'-Triazido-1',6,6'-trideoxysucrose pentamethanesulphonate (**4**). — A solution of **2** (600 mg) in pyridine (50 ml) was treated with methanesulphonyl chloride (5 ml) at 0°. The reaction mixture was stored for 24 h at room temperature. T.l.c. (chloroform–acetone, 5:1) then showed a fast-moving product. Water (0.5 ml) was added to the cooled (0°) reaction mixture, which was kept for 0.5 h at room temperature and then poured on to ice–water. The precipitate was collected, washed well with water, dried, and crystallised from methanol to give **4** (970 mg, 84%), m.p. 72–74°, $[\alpha]_D$ +55° (*c* 0.72, chloroform), ν_{max} 2110 cm^{-1} (azide).

Anal. Calc. for $C_{17}H_{29}N_9O_{18}S_5$: C, 25.3; H, 3.6; N, 19.8. Found: C, 25.7; H, 3.6; N, 19.3.

1',6,6'-Triamino-1,6,6'-trideoxysucrose (**5**). — A solution of the triazide **2** (500 mg) in ethyl acetate–methanol–triethylamine (100 ml, 3:6.8:0.2) was hydrogenated in the presence of palladium-on-charcoal (50 mg) at 45 p.s.i. for 24 h at 35°. T.l.c. (chloroform–methanol, 2:1) then revealed a slow-moving, major product, which gave a positive reaction with ninhydrin. The catalyst was removed, the filtrate was concentrated, and the residue was partitioned between ethyl acetate and water. The aqueous layer was decolourised with charcoal and concentrated to a syrup; trituration with acetone then gave **5** (270 mg, 67%), m.p. 121–125°, $[\alpha]_D$ +68.5° (*c* 0.85, water); ν_{max} 3400–3100 (OH, NH_2), 1630 cm^{-1}.

Anal. Calc. for $C_{12}H_{25}N_3O_8 \cdot H_2O$: C, 40.3; H, 7.6. Found: C, 39.7; H, 7.3.

1',6,6'-Triacetamido-1',6,6'-trideoxysucrose (**6**). — (*a*) A solution of **2** (500 mg) was hydrogenated as described above. The product was dried, and treated with acetic anhydride (2 ml) in dry methanol for 24 h at room temperature. T.l.c. (chloroform–methanol, 2:1) then showed a fast-moving, major product. The solution was concentrated and the residue was triturated with ether to give **6** (440 mg, 79%), m.p. 107–110°, $[\alpha]_D$ +36° (*c* 1, methanol); ν_{max} 3300 (NH), 1650 and 1550 cm^{-1} (amide).

Anal. Calc. for $C_{18}H_{31}N_3O_{11}$: C, 46.45; H, 6.7. Found: C, 46.8; H, 7.0.

1',6,6'-Triacetamido-1',6,6'-trideoxysucrose penta-acetate (*7*). — (*a*) The triazide **2** (200 mg) was hydrogenated, as described above, and the product was treated with acetic anhydride (1 ml) in pyridine (10 ml) for 24 h at room temperature. T.l.c. (chloroform–methanol, 8:0.5) then showed a fast-moving, major product. The solution was concentrated by codistillation with toluene to give a syrup, which was eluted from a column of silica gel (25 g), using dichloromethane–acetone (4:1), to give **7** (220 mg, 68%), m.p. 99–101° (from methanol), $[\alpha]_D$ +37° (*c* 0.98, chloroform); ν_{max} 3300 (NH), 1750 (ester), 1650 and 1550 cm^{-1} (amide). N.m.r. (100 MHz) data: 4.37 (*d*, 1 proton, $J_{1,2}$ 3.5 Hz, H-1), 5.25 (*q*, 1 proton, $J_{2,3}$ 10.0 Hz, H-2), 4.55 (*t*, 1 proton, $J_{3,4}$ 10.0 Hz, H-3), 5.13 (*t*, 1 proton, $J_{4,5}$ 10.0 Hz, H-4), 4.77–4.9 (2 protons,

H-3′ and H-4′), 3.48 (broad *t*, 3 protons, $J_{NH,?}$ 6.0 Hz, 3 H-N), 7.82–8.01 (24 protons, 8 Ac).

Anal. Calc. for $C_{28}H_{41}N_3O_{16}$: C, 49.8; H, 6.1; N, 6.2. Found: C, 49.1; H, 6.3; N, 5.8.

(*b*) The triacetamide **6** (200 mg), on acetylation using acetic anhydride (2 ml) and pyridine (10 ml) for 24 h at room temperature, gave **7** (239 mg, 82%).

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