A Chemical Synthesis of Panose and an Isomeric Trisaccharide[1]

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The direct tritylation of maltose with a 1:1 molar ratio of reagent, and subsequent acetylation, led to the formation of the known di-*O*-tritylmaltose hexaacetate and the two predictable mono-*O*-tritylmaltose heptaacetates. One of the latter could be synthesized from 1,6-anhydro-4-*O*-α-D-glucopyranosyl-β-D-glucopyranose (maltosan) and was therefore the 6-*O*-tritylmaltose heptaacetate (II). Both anomers of this derivative were obtained. The 6′-*O*-tritylmaltose heptaacetate (I), formed in preponderant amount, was shown to be a β-D anomer by nmr spectrometry. Condensation of I with tri-*O*-acetyl-2-*O*-nitro-β-D-glucopyranosyl chloride (III) in the presence of silver perchlorate, with subsequent hydrogenolysis and deacetylation led to the synthesis of crystalline panose (IV, 17%) and its β-D-(1→6) isomer (V, amorphous, 7%). Repetition of the condensation with the detritylated I (6′ = CH_2OH) led to the same products in considerably lower yields [5.7% of panose, 2.5% of β-D-(1→6) isomer] but in essentially the same ratio (2.35:1). Reaction of the nitrated halide (III) with tetra-*O*-acetyl-6-*O*-trityl-β-D-glucopyranose under like conditions led to a somewhat higher total yield of β-isomaltose octaacetate (from VIII) and β-gentiobiose octaacetate (from VII) as had been obtained when the condensation was effected with the trityl group removed. The product ratio was, however, different and about equal amounts of VII and VIII were formed, perhaps indicative of a carbonium ion (VI) intermediate.

The crystalline trisaccharide panose (IV) was first obtained by Pan, Nicholson, and Kolachov[2] by the action of a crude transglycosylase (from *Aspergillus niger*) and its structure was established[3,4] by degradative methods as a linear oligosaccharide containing both an α-D-(1→6) and an α-D-(1→4) linkage. It was later obtained as a product from the acid hydrolysis of amylopectin[5] and glycogen.[6,7] It was considered desirable to establish the structure of panose by synthetic reactions of a type that would confirm the structure assigned by degradative methods. To this end, tetra-*O*-acetyl-4-*O*-(tri-*O*-acetyl-6-*O*-trityl-α-D-glucopyranosyl)-β-D-glucopyranose (I) was synthesized.

Tritylation of maltose in pyridine with a 1 molar equiv of trityl chloride, with subsequent acetylation and isolation by chromatography on a silica gel column, led to the isolation of three crystalline products. One of these was the 6,6′-di-*O*-tritylmaltose hexaacetate described previously by Josephson.[8] The optical rotation of our preparation was in agreement with that obtained by Josephson, but our melting point was very considerably higher. Josephson reported that his preparation contained 1 mole of ethanol per 2 moles of sugar derivative, but a repetition of his procedure yielded our product. It is probable that the Josephson preparation was an unstable addition compound with ethanol not encountered by us. The anomeric nature of this di-*O*-tritylmaltose is not established.

The other products from the tritylation of maltose were two isomeric mono-*O*-tritylmaltose heptaacetates. It was necessary to ascertain which of these was the 6′-*O*-tritylmaltose heptaacetate requisite for the panose synthesis. Asp and Lindberg[9] had synthesized *O*-(tetra-*O*-acetyl-α-D-glucopyranosyl)-(1→4)-1,2,3-tri-*O*-acetyl-D-glucopyranose. That the unacetylated hydroxyl group in this maltose heptaacetate was on C-6 of the reducing portion had been established by its synthesis[9] from 4-*O*-(tetra-*O*-acetyl-α-D-glucopyranosyl)-(1→4)-di-*O*-acetyl-1,6-anhydro-β-D-glucopyranose (maltosan hexaacetate).[9,10] When the maltose heptaacetate of Asp and Lindberg[9] was tritylated, the product was different from either of the two other isomers isolated by us from the tritylation of maltose. The nmr spectrum of this substance showed in the anomeric region of the spectrum an isolated doublet whose properties clearly showed that this third isomer was a β-D anomer (II, 1-β-D-OAc). The isomer obtained by tritylation of the Asp and Lindberg compound was then deacetylated and reacetylated with pyridine and acetic anhydride, giving the α-D anomer (II) identical with one of the products obtained by the direct tritylation of maltose. That it was the α-D anomer was established by nmr spectroscopy and also by its rotatory value, $[\alpha]_D$ +100° (in chloroform), in comparison with that of the β-D anomer, $[\alpha]_D$ +36° (in chloroform). The desired 6′-*O*-tritylmaltose heptaacetate (I) was therefore the remaining isomer, mp 164–165°, $[\alpha]_D$ + 96° (in chloroform), obtained by the tritylation of maltose. It was also desired to remove the trityl group of this substance, and when this was done at 100° with 80% acetic acid,[11] a crystalline product was obtained which was a β-D anomer, as established by nmr spectroscopy. That no anomerization had occurred during the detritylation was determined by reconversion into the original I by retritylation; this I is a β-D anomer, as was also established by nmr spectroscopy.

Compound I was then treated directly with 3,4,6-tri-*O*-acetyl-2-*O*-nitro-β-D-glucopyranosyl chloride[12,13] (III) in nitromethane solution in the presence of silver perchlorate and a drying agent. The reaction was rapid and silver chloride and trityl perchlorate were precipitated. The use of a trityl group in this type of reaction

(1) Preliminary communication: M. L. Wolfrom and K. Koizumi, *Chem. Commun.*, 2 (1966). In this communication, the 6′-*O*-tritylmaltose heptaacetate was designated as an α-D anomer, whereas later work now shows it to be the β-D anomer. The isomeric trisaccharide V was not reported.

(2) S. C. Pan, L. W. Nicholson, and P. Kolachov, *J. Am. Chem. Soc.*, **73**, 2547 (1951).

(3) D. French, *Science*, **113**, 352 (1951).

(4) M. L. Wolfrom, A. Thompson, and T. T. Galkowski, *J. Am. Chem. Soc.*, **73**, 4093 (1951).

(5) A. Thompson and M. L. Wolfrom, *ibid.*, **73**, 5849 (1951).

(6) S. Peat, W. J. Whelan, and T. E. Edwards, *J. Chem. Soc.*, 355 (1955).

(7) M. L. Wolfrom and A. Thompson, *J. Am. Chem. Soc.*, **79**, 4212 (1957).

(8) K. Josephson, *Ann.*, **472**, 230 (1929).

(9) L. Asp and B. Lindberg, *Acta Chem. Scand.*, **6**, 941 (1952).

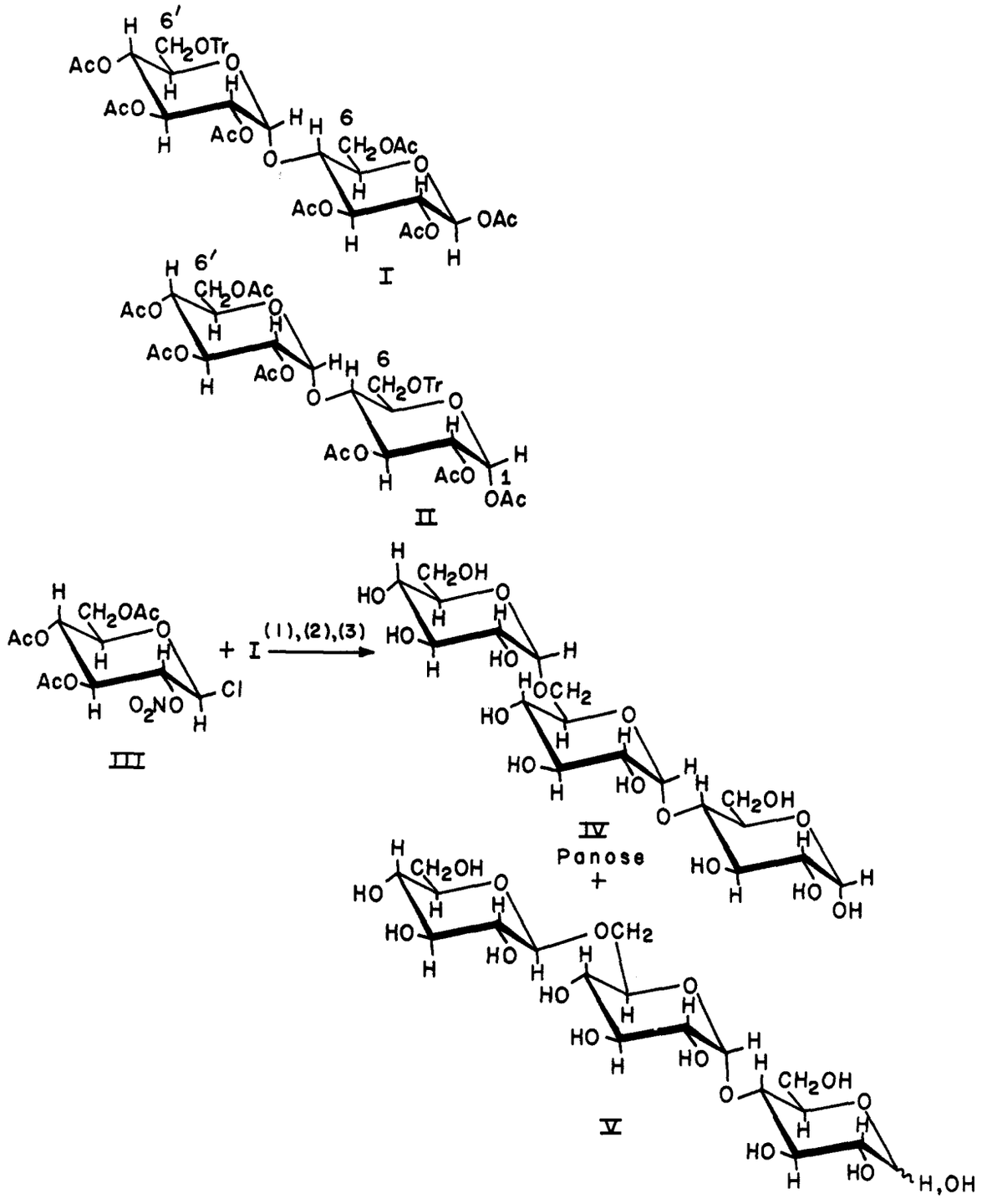
(10) P. Karrer and L. Kamienski, *Helv. Chim. Acta*, **15**, 739 (1932).

(11) R. Kuhn, H. Rudy, and F. Weygand, *Ber.*, **69**, 1546 (1936).

(12) M. L. Wolfrom, A. O. Pittet, and I. C. Gillam, *Proc. Natl. Acad. Sci. U. S.*, **47**, 700 (1961).

(13) M. L. Wolfrom and D. R. Lineback, *Methods Carbohydrate Chem.*, **2**, 341 (1963).

SCHEME I



has been reported by Brederick and co-workers.[14,15] The 2-nitrate derivative prevents neighboring-group participation and results in the formation of an α-D-glucosidic linkage. The product from our condensation was denitrated by hydrogenolysis[16] and deacetylated. The deacetylated product was then chromatographed on a carbon column with aqueous ethanol as the developer, and two isomeric trisaccharides were obtained. One of these was crystalline and was identified by melting point, rotation, and comparative X-ray powder diffraction data as panose (first dimorphous form[7]).

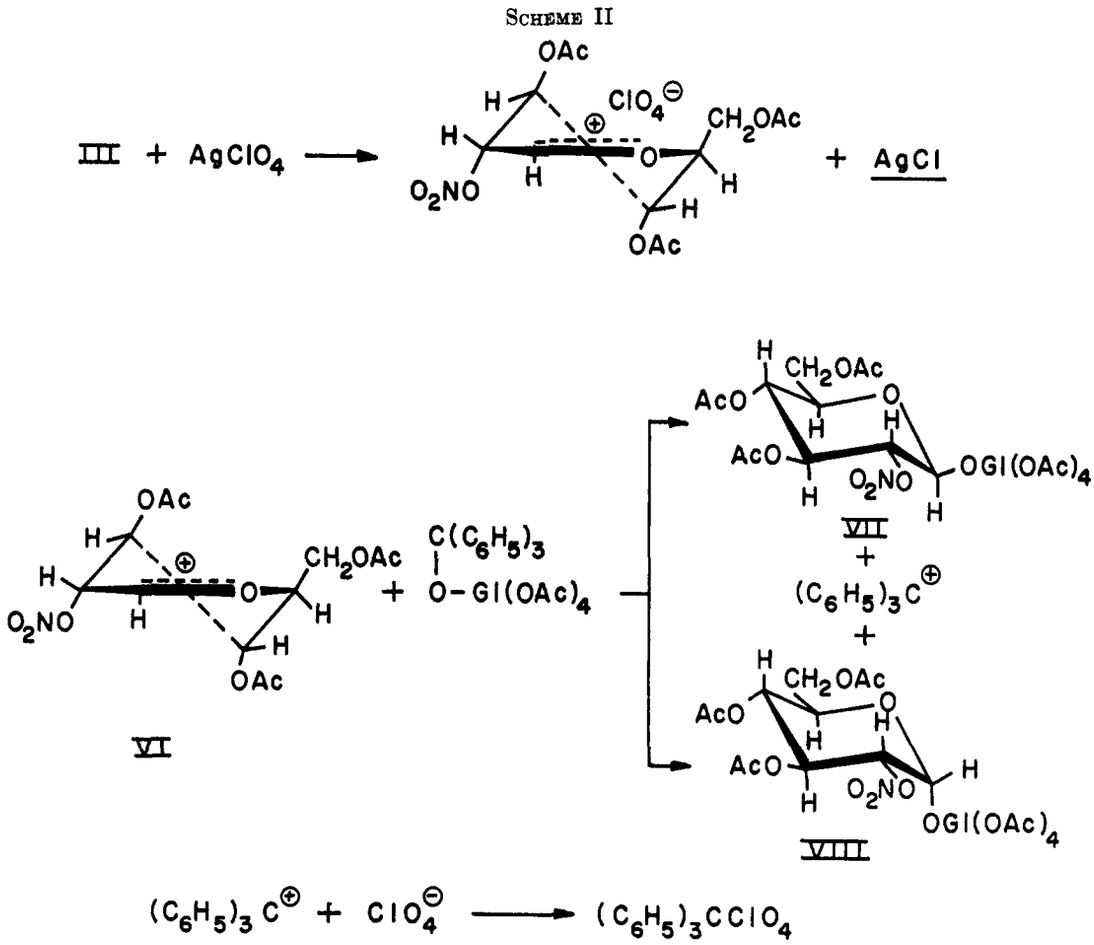
The amorphous trisaccharide, $[\alpha]^{20}D$ +71° (in water), showed the elementary analysis and molecular weight required for such a formulation and was cleaved by β-D-glucosidase to D-glucose and maltose, identified by paper chromatography. These facts and the method of synthesis[12] of this substance establish that it is anomeric with panose at the (1→6)-glycosidic linkage; it is therefore *O*-β-D-glucopyranosyl-(1→6)-*O*-α-D-glucopyranosyl-(1→4)-D-glucopyranose (V). The optical rotatory power of +71° (equilibrated) exhibited by this trisaccharide, in comparison to that of +151°

(14) H. Bredereck, A. Wagner, G. Faver, H. Ott, and J. Rauther, *Ber.*, **92**, 1135 (1959).

(15) H. Bredereck, A. Wagner, D. Geissel, and H. Ott, *ibid.*, **95**, 3064 (1962).

(16) L. P. Kuhn, *J. Am. Chem. Soc.*, **68**, 1761 (1946).

SCHEME II



(equilibrated) for panose, is also in general agreement with such a structure.

The yield of panose was low (17.0%), whereas that of its isomer was 7.0%, resulting in the product ratio 2.4:1. The condensation was repeated with the 6'-trityl group of I removed. The reaction was slower and the yields were somewhat lower, being 5.7% of panose and 2.5% of its β-D-(1→6) isomer, but the product ratio (2.3:1) remained essentially unchanged. The formation of both types of linkage with the α-D preponderant is in accord with previous findings[12] on this type of reaction utilizing III in a reaction with an unsubstituted C-6 hydroxyl group. A carbonium ion, formed from III on C-1, may well be an intermediate in this reaction,[12,15] but even so, the β-D form of the halide must have some directive action favoring the formation, with inversion, of the α-D linkage in preponderant amount, rather than the formation of both the α-D and β-D linkages in the otherwise predictable equal amounts. Obscure steric factors may also be influencing these reactions.

In our previous synthesis of isomaltose,[12,13] the 2-*O*-nitroglycosyl halide (III) was condensed with 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose. This reaction has been repeated employing tetra-*O*-acetyl-6-*O*-trityl-β-D-glucopyranose under conditions utilized for synthesis of panose (IV) and its isomer V (Scheme I). There was so obtained a yield of 16.6% of β-isomaltose octaacetate (VIII) and 18.1% of β-gentiobiose octaacetate (VII): a combined disaccharide yield of 34.7% the amount of each being essentially the same (Scheme II). Wolfrom and Lineback[13] reported a somewhat lower combined disaccharide yield (24.5%), in the reaction where the C-6 hydroxyl is not tritylated, but with a distribution of 20% of β-isomaltose octaacetate and 4.5% of β-gentiobiose octaacetate. Employment of the 6-*O*-trityl group in these monosaccharide derivatives has favored a nearly equal distribution of products, possibly indicating a C-1 carbonium ion (VI) intermediate essentially uninfluenced by the presence of the 2-nitrate group in this rapid and probably essentially ionic reaction.

Experimental Section

Tritylation of Maltose and Acetylation.—β-Maltose monohydrate (5 g, dried over phosphorus pentaoxide under reduced pressure at 100°) was dissolved in dry pyridine (30 ml) and the solvent was distilled at atmospheric pressure until the boiling point of the distillate attained 112–114°. More dry pyridine (100 ml) was added and removed by distillation until bp 114.5–115° was attained for the distillate. The solution was brought to its original volume with more dry pyridine, 4 g of trityl chloride (equimolar) was added, and the stoppered flask was stirred for 64 hr at 37–39°. A further 15 ml of freshly distilled, dry pyridine was added, the flask was cooled to 0°, and 22 ml of acetic anhydride was added. The stoppered flask was maintained for 72 hr at room temperature. The solution was then poured into 300 ml of ice and water and stirred mechanically for 18 hr. The precipitated solid was collected by filtration, washed with water, and dried under reduced pressure over separated compartments of sodium hydroxide pellets and phosphorus pentaoxide.

The dried solid mixture was separated on a silica gel column (5.5 × 66 cm) by development with 3 l. of benzene–ethyl acetate (3:2, v/v) as developer. An automatic fraction collector was utilized and the effluent was collected in 10-ml units. The contents of every tenth tube were chromatographed on silica gel

thin layer plates with the same developer, using anthrone as the indicator. As a result of this examination, the successive eluates containing material were combined into six fractions: first, 310 ml; second, 150 ml; third, 160 ml; fourth, 50 ml; fifth, 700 ml; and sixth, 410 ml. Solvent removal from these fractions led to syrups or crystals which were purified by recrystallization from acetone–methanol. The first fraction contained a ditrityl derivative, R_f 0.76; the third fraction a monotrityl derivative, R_f 0.70; and the fifth fraction a monotrityl derivative, R_f 0.61; the sixth fraction contained mainly maltose octaacetate, R_f 0.45. Fractions 2 and 4 were separable mixtures of the two materials contained in the preceding and succeeding fractions.

Hexa-*O*-acetyl-6,6′-di-*O*-tritylmaltose (I-6-OTr).—This substance was obtained from fractions 1 and 2: yield 1.9 g (13%); mp 222–223° with sintering at 213°; $[\alpha]^{20}D$ +88° (*c* 2.14, chloroform); X-ray powder diffraction data,[17] 11.27 s (2), 8.00 s, 7.16 vs (1), 6.20 s (3), 5.76 w, 5.12 m, 4.53 s, 4.30 m, 4.05 s, and 3.75 m.

Anal. Calcd for $C_{62}H_{62}O_{17}$: C, 69.00; H, 5.79. Found: C, 69.09; H, 6.10.

Josephson[8] reported mp 116–119°, $[\alpha]^{22}D$ +88° (*c* 2.17, chloroform) and stated that his product contained 1 mole of ethanol to 2 moles of the maltose derivative, but a repetition of his procedure yielded our product of mp 222–223° with sintering at 213°.

***O*-(2,3,4-Tri-*O*-acetyl-6-*O*-trityl-α-D-glucosyl)-(1→4)-tetra-*O*-acetyl-β-D-glucopyranose (I).**—This substance was obtained from fractions 2, 3, and 4, and its structure was proved as shown below: yield 3.8 g (31%); mp 164–164.5°; $[\alpha]^{20}D$ +96° (*c* 2.165, chloroform); X-ray powder diffraction data, 12.65 s (1), 9.50 m, 7.62 m, 6.65 s (3), 5.81 w, 4.93 s (2), 4.13 s (3), 3.59 w, and 3.24 m. The H-1 nmr[18] signal was observed at τ 4.20 as a well-isolated doublet, $J_{1,2}$ = 7.8 cps. These data are indicative of an axial H-1 in a β-D-pyranose structure.

Anal. Calcd for $C_{45}H_{50}O_{18}$: C, 61.50; H, 5.73. Found: C, 61.95; H, 6.01.

***O*-(2,3,4-Tri-*O*-acetyl-α,D-glucopyranosyl)-(1→4)-tetra-*O*-acetyl-β-D-glucopyranose (I-6′-OH).**—Compound I (3 g) was dissolved in 300 ml of 80% aqueous acetic acid and heated for 30 min at 100°. The solvent was removed under diminished pressure, and traces of acetic acid were removed from the residue by repeated codistillation with methanol. The residue was dissolved in methanol, and water was added to incipient turbidity. The mixture was cooled to 0° and the precipitated triphenylmethanol was removed by filtration. The crystalline residue obtained on solvent removal from the filtrate was recrystallized from methanol as fine needles: yield 1.42 g (65.4%); mp 177–178°; $[\alpha]^{19}D$ +65° (*c* 1.58 chloroform); X-ray powder diffraction data, 12.21 m, 10.99 s (1), 9.07 s (1), 7.59 w, 6.16 w, 5.51 m, 5.14 s (2), 4.80 m, 4.21 m, 4.18 m, 3.95 w, 3.76 w, and 3.64 w; nmr spectrum τ 3.90 (doublet, $J_{1,2}$ = 8 cps).

Anal. Calcd for $C_{26}H_{36}O_{18}$: C, 49.06; H, 5.70. Found: C, 48.91; H, 5.87.

This substance (160 mg) was dissolved in 2 ml of dry pyridine and 182 mg of trityl chloride was added. The mixture was heated for 3 hr at 100° and was then maintained overnight at room temperature. The reaction product was poured into ice and water and stirred for several hours, and the precipitated solids were collected by filtration and recrystallized from acetone–methanol: yield 151 mg, mp 164–164.5°, $[\alpha]^{20}D$ +95° (*c* 4.18, chloroform). It was therefore identical with I.

***O*-(Tetra-*O*-acetyl-α-D-glucopyranosyl)-(1→4)-1,2,3-tri-*O*-acetyl-6-*O*-trityl-α-D-glucose (II) from Fraction 5.**—This substance was obtained first from fraction 5 and its structure was proved as shown below: yield 0.4 g (3%); mp 189–190°; $[\alpha]^{20}D$ +100° (*c* 1.78, chloroform); X-ray powder diffraction data, 14.40 w, 11.42 m, 9.46 vs (1), 8.46 w, 7.59 s (3), 6.08 w, 5.20 w, 4.81 m, 4.21 w, and 4.05 s (2). The nmr H-1 signal was observed at τ 3.60 as a well-isolated doublet, $J_{1,2}$ = 3.8 cps. These data are indicative of an equatorial H-1 in an α-D-glucopyranose structure.

Anal. Calcd for $C_{45}H_{50}O_{18}$: C, 61.50; H, 5.73. Found: C, 61.97; H, 6.14.

***O*-(Tetra-*O*-acetyl-α-D-glucopyranosyl)-(1→4)-1,2,3-tri-*O*-acetyl-6-*O*-trityl-β-D-glucose (II-1-β-D-OAc).**—O-(Tetra-*O*-acetyl-α-D-glucopyranosyl)-(1→4)-1,2,3-tri-*O*-acetyl-β-D-glucopyranose (II, 1-β-D-OAc, 6-OH, prepared from maltosan,[9] 252 mg) was dissolved in 3 ml of dry pyridine and 279 mg (2.5:1 molar ratio) of trityl chloride was added. The solution was heated for 3 hr at 100° and was then maintained overnight at room temperature, after which the reaction product was subjected to purification by thin layer chromatography on silica gel as before: mp 116–118°, $[\alpha]^{22}D$ +36° (*c* 6.00, chloroform); X-ray powder diffraction data; 10.75 s (2, 2), 9.58 s (2, 2), 8.36 s (1), 7.63 w, 7.17 w, 6.68 m, 6.30 w, 5.94 w, 4.23 m, and 4.02 m. The nmr H-1 signal was observed at τ 4.22 as a well-isolated doublet, $J_{1,2}$ = 7.3 cps. These data are indicative of an axial H-1 in a β-D-glucopyranose structure.

Anal. Calcd for $C_{45}H_{50}O_{18}$: C, 61.50; H, 5.73. Found: C, 61.50; H, 6.08.

Anomerization of *O*-(Tetra-*O*-acetyl-α-D-glucopyranosyl)-(1→4)-1,2,3-tri-*O*-acetyl-6-*O*-trityl-β-D-glucose (II-1-β-D-OAc).—This substance (237 mg) was dissolved in 2.5 ml of 0.05 *M* methanolic sodium methoxide and maintained for 18 hr at 5°, after which time, water was added to the solution and the precipitated solid was collected by filtration, washed with water, and dried over phosphorus pentoxide at 56°.

The dried solid (72 mg) was acetylated with pyridine (0.5 ml) and acetic anhydride (0.5 ml) for 66 hr at room temperature. The crude product obtained on pouring the reaction mixture into an excess of ice and water was crystallized and recrystallized from acetone–methanol: mp 188–190°; $[\alpha]^{20}D$ +98° (*c* 1.00, chloroform); X-ray powder diffraction pattern identical with that described above for II.

Synthesis of Panose (IV) and an Isomeric Trisaccharide (V). A. From the Reaction of III and I.—Silver perchlorate was prepared according to Bredereck and co-workers[14] except that the final solution was concentrated under reduced pressure with occasional filtration. The residue was dried by repeated codistillation with ethanol (reduced pressure) and finally the residue was dissolved in ether, the solvent was evaporated, and the resultant crystalline solid was dried at <1 mm at 56° over phosphorus pentaoxide for 3 days.

Silver perchlorate (0.72 g) was dissolved in 12 ml of absolute nitromethane and 0.7 g of Drierite (anhydrous calcium sulfate) was added to the solution. The solution was allowed to stand for 15 min and then 3 g (3.5 mmoles) of I was added, whereupon the solution became yellow. The solution was cooled to 0° and 1.35 g (3.6 mmoles) of 3,4,6-tri-*O*-acetyl-2-*O*-nitro-β-D-glucopyranosyl chloride[12] (III) was added under vigrous mechanical stirring. The reaction mixture was allowed to warm to room temperature. The solution then became orange, and silver chloride and trityl perchlorate precipitated. After 30 min, the solution was filtered and the filtrate was washed with cold, saturated sodium hydrogen carbonate solution and then with water. Precipitated tritylmethanol was removed by filtration. The nitromethane solution was diluted with chloroform and dried (sodium sulfate). The solution was concentrated under diminished pressure to a syrup which was dissolved in 270 ml of absolute ethanol and hydrogenolized for 3 hr at 35 psi with 150 mg of 10% palladium-on-charcoal catalyst. Filtration and solvent removal gave a syrup, which was deacetylated with 54 ml of 0.05 *M* sodium methoxide in methanol for 18 hr at 5°, deionized by passing through a column of 150 ml of Dowex-50 (H^+), and chromatographed on a column (3 × 40 cm) of Darco G-60–Celite (1:1) using, successively, 1.5 l. each of water with 5, 10, 15, and 30% aqueous ethanol as developer. The eluate obtained with water contained D-glucose, and that obtained with 5% ethanol contained maltose. The eluate from the 10% ethanol solution was concentrated to a syrup which was crystallized from warm methanol: yield 292 mg (17%); mp 221° dec, which was unchanged on admixture with an authentic specimen of panose (first dimorphous form[7]); $[\alpha]^{20}D$ +161 → 151° (*c* 0.3, water); X-ray powder diffraction identical with that of an authentic sample of panose (first form[7]) [lit.[7] mp 220–221° dec, $[\alpha]^{25}D$ +160 → 151° (water)].

The 15% ethanol eluate yielded a colorless, amorphous solid: yield 115 mg (7%), $[\alpha]^{20}D$ +71° (*c* 0.32, water). This substance was chromatographically indistinguishable from panose on paper or Avicel.[19]

(17) Interplanar spacing (A), Cu Kα radiation; relative intensity, estimated visually: s, strong; m, medium; w, weak; v, very. First three strongest lines are numbered (1, strongest). Equal numbers indicate lines of approximately equal intensities.

(18) The nmr spectra were obtained on a Varian A-60 nmr spectrometer in deuteriochloroform solution with tetramethylsilane as an internal reference standard.

(19) M. L. Wolfrom, D. L. Patin, and R. M. de Lederkremer, *J. Chromatog.*, **17**, 488 (1965).

Anal. Calcd for $C_{18}H_{32}O_{16}$: C, 42.86; H, 6.39; mol wt, 504. Found: C, 42.45; H, 6.63; mol wt (by osmometry), 501.

This substance, the isomeric trisaccharide V, was cleaved by β-D-glucosidase[20] to D-glucose and maltose, identified by paper chromatography.

B. From the Reaction of 3,4,6-Tri-*O*-acetyl-2-*O*-nitro-β-D-glucosyl Chloride (III) and *O*-(2,3,4-Tri-*O*-acetyl-α-D-glucopyranosyl)-(1→4)-tetra-*O*-acetyl-β-D-glucopyranose (I-6′-OH).—*O*-(2,3,4-Tri-*O*-acetyl-α-D-glucopyranosyl)-(1→4)-tetra-*O*-acetyl-β-D-glucopyranose (I, 6′-OH; 1.17 g, 1.84 mmoles), Drierite (1.5 g), silver carbonate[12] (1 g), and silver perchlorate (50 mg) were stirred in 50 ml of anhydrous ether for 30 min in the absence of light. To this mixture was then added 0.55 g (1.50 mmoles) of 3,4,6-tri-*O*-acetyl-2-*O*-nitro-β-D-glucopyranosyl chloride[12] (III). The reaction mixture was stirred for 6 hr at room temperature, after which time no chloride ion was detectable. The mixture was filtered through a carbon-precoated filter and washed with 50 ml of ether. The combined filtrate and washings were concentrated to a syrup which was dissolved in 100 ml of absolute ethanol, and the solution was denitrated by hydrogenolysis, deacetylated, and chromatographed on carbon as described above for the previous synthesis of panose, which was isolated and identified in crystalline form: yield 43 mg (5.7%), mp 220–221° dec.

The eluates obtained with 15 and 30% aqueous ethanol were combined. They contained the trisaccharide (V) isomeric with panose (IV) and a small proportion of higher saccharide, separated by chromatography on thick filter paper (Whatman No. 3MM) with 1-butanol–pyridine–water (6:4:3, v/v) as developer; yield of amorphous V was 19 mg (2.5%), $[\alpha]^{20}D$ +70° (*c* 0.6, water).

β-Isomaltose Octaacetate and β-Gentiobiose Octaacetate from Tetra-*O*-acetyl-6-*O*-trityl-β-D-glucopyranose and III.—Tetra-*O*-acetyl-6-*O*-trityl-β-D-glucopyranose[21] (1.69 g) was treated with an equimolar amount (1 g) of III in nitromethane containing silver perchlorate (0.7 g) as described above for the panose synthesis. The syrup obtained after reductive removal of the nitrate group was acetylated for 30 min at 130° with 0.5 g of of sodium acetate and 7 ml of acetic anhydride. The cooled reaction mixture was poured into 30 ml of ice and water and stirred for 18 hr. The resultant solution was extracted with chloroform, and the extract was washed successively with aqueous sodium hydrogen carbonate and water, and concentrated to a syrup. The syrup was dissolved in 24 ml of benzene and chromatographed in two equal parts on Magnesol–Celite as described by Wolfrom and Lineback.[13] The mother liquors from the crystallizations of the material in the two zones obtained were rechromatographed in the same manner, and there was so obtained a total of 304 mg (16.6%) of β-isomaltose octaacetate, mp and mmp 146–147°, and 332 mg (18.1%) of β-gentiobiose octaacetate, mp and mmp 193–194°.

Registry No.—IV, 490-40-4; I-6-OTr, 7482-59-9; I, 7485-48-5; I-6′-OH, 7482-60-2; II, 6748-75-0; II, 1-β-*O*-OAc, 7482-62-4; V, 7485-51-0; β-isomaltose octaacetate, 4627-41-2; β-gentiobiose octaacetate, 4613-78-9.

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(20) "Emulsin" of Worthington Biochemical Co., Freehold, N. J. The preparation hydrolyzed gentiobiose but not isomaltose.

(21) B. Helferich, L. Moog, and A. Jünger, *Ber.*, **58**, 872 (1925).

Confirmation of the Structure of 1,3,5-Tri-*O*-acetyl-2,7-anhydro-β-D-*altro*-heptulopyranose and Its Conversion *via* an Epoxy Intermediate into 2,7-Anhydro-3-*S*-methyl-3-thio-β-D-*gluco*-heptulopyranose

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The structure of 1,3,5-tri-*O*-acetyl-2,7-anhydro-β-D-*altro*-heptulopyranose (II) has been confirmed by the oxidation of the free hydroxyl group at C-4 with dimethyl sulfoxide and acetic anhydride, followed by reduction of the resulting keto group with sodium borohydride and the isolation of 2,7-anhydro-β-D-*manno*-heptulopyranose as one of the products. The tosylate of II slowly reacted with sodium methoxide at room temperature to yield 2,7:3,4-dianhydro-β-D-*manno*-heptulopyranose (VI) isolated as the crystalline diacetate (VII). Epoxide scission of VII by sodium thiomethoxide proceeded in concurrence with the Fürst–Plattner rule yielding 2,7-anhydro-3-*S*-methyl-3-thio-β-D-*gluco*-heptulopyranose (VIII). Desulfurization of VIII with Raney nickel afforded 2,7-anhydro-3-deoxy-β-D-*arabino*-heptulopyranose (X) which was resistant to sodium periodate but not to lead tertaacetate–pyridine. The configurations assigned to these new compounds are based on the fact that any alternative pathway of the reactions described above, including possible epoxide migration, would not produce a deoxyheptulosan which would comply with these specific oxidation results.

Recently in this laboratory during the preparation of the tetraacetate of sedoheptulosan (2,7-anhydro-β-D-*altro*-heptulopyranose, I), known only as a levorotatory syrup,[1] a small amount (4%) of a crystalline triacetate[2] was isolated from the main product. On the basis of its nmr spectrum,[2] this new compound was designated 1,3,5-tri-*O*-acetylsedoheptulosan (II). The presence of an unacetylated, equatorial hydroxyl group at C-4 in compound II seemed rather unusual and is contrary at least to the results of sulfonation reactions[3,4] where preferential tosylation of equatorial hydroxyl groups in locked ring systems has been demonstrated. The selective tosylation[5] of 1,6-anhydro-2-*O*-benzoyl-β-D-altropyranose was of special interest. In this compound, which is structurally analogous to II, Newth[5] successfully tosylated the equatorial hydroxyl group at C-3 in preference to the axial hydroxyl group at C-4. Furthermore, the possibility that the triacetate II resulted from partial hydrolysis of the syrupy tetraacetate seemed very unlikely since the yield of the former compound has now been increased

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