Thiobenzoyl Chloride.—Dithiobenzoic acid (37.5 g.) was dissolved in ether (50 ml.) and the solution was treated with thionyl chloride (*ca.* 40 ml.) under conditions defined by earlier workers[5,6] to give thiobenzoyl chloride (23.1 g., 61%) as a violet-red, lachrymatory liquid, b.p. 88° (3.75 mm.).

1,5-Anhydro-2,3,4-tri-O-benzoyl-D-arabinitol.—α-D-Arabinopyranose tetrabenzoate[16] (22.64 g.) was warmed gently with 40 ml. of a 30% solution of hydrogen bromide in glacial acetic acid until 2,3,4-tri-O-benzoyl-β-D-arabinopyranosyl bromide began to crystallize from the clear solution. The mixture was then stirred at room temperature for 2.5 hr., and the solution was decanted from the crystalline halide which was washed three times (by decantation) with petroleum ether b.p. (60–70°). Dissolved in 250 ml. of ethyl acetate, the halide was treated with 2.0 g. of 10% palladium on charcoal (presaturated with hydrogen) and 10.0 g. of triethylamine; on shaking with hydrogen, the solution absorbed the theoretical amount of hydrogen in 5.8 hr.; after removal of the catalyst by filtration, the solution was washed with aqueous sodium bicarbonate and concentrated to give 15.29 g. (86%) of 1,5-anhydro-2,3,4-tri-O-benzoyl-D-arabinitol, m.p. 119°. Recrystallization from methanol afforded pure material: m.p. 119–120°, $[\alpha]^{20}D$ −219° (*c* 0.11, $CHCl_3$). Fletcher and Hudson[9] reported m.p. 120–121° and $[\alpha]^{20}D$ −220° ($CHCl_3$) for 1,5-anhydro-2,3,4-tri-O-benzoyl-D-arabinitol.

1,5-Anhydro-2-O-benzoyl-3,4-O-isopropylidene-D-arabinitol.—1,5-Anhydro-2,3,4-tri-O-benzoyl-D-arabinitol was debenzoylated in conventional fashion using ammonia in methanol to give 1,5-anhydro-D-arabinitol as a sirup which crystallized on seeding. Without further purification, the anhydride (15.6 g.) was suspended in 200 ml. of anhydrous acetone containing 0.2 g. of *p*-toluenesulfonic acid. The solution was boiled for 16 hr. under a Soxhlet extractor holding Molecular Sieve, type 5A, and then neutralized with ammonia. After filtration, the solution was concentrated and the residue was distilled *in vacuo* to give 1,5-anhydro-3,4-O-isopropylidene-D-arabinitol as a yellow oil: b.p. 78–80°, (0.1–0.05 mm.), 19.05 g. (94%) A sample of the product was benzoylated with benzoyl chloride in pyridine to give 1,5-anhydro-2-O-benzoyl-3,4-O-isopropylidene-D-arabinitol as fine needles from ethanol: m.p. 102–103°, $[\alpha]^{20}D$ −111° (*c* 0.50, CH_2Cl_2).

Anal. Calcd. for $C_{15}H_{18}O_5$ (278.31): C, 64.76; H, 6.52. Found: C, 64.62; H, 6.76.

1,5-Anhydro-2-O-benzyl-3,4-O-isopropylidene-D-arabinitol.—1,5-Anhydro-3,4-O-isopropylidene-D-arabinitol (3.36 g.) was mixed with 50 ml. of anhydrous tetrahydrofuran, 2.2 g. of powdered potassium hydroxide,[17] and 3.65 g. of benzyl chloride, and the suspension was boiled under reflux for 12 hr. Solid carbon dioxide was added, the solution was concentrated to dryness, and the residue was extracted with acetone. The sirup obtained on concentrating the extract was distilled to give a mobile yellow oil: b.p. 110–120° (0.1 mm.), 4.5 g. (88%). A benzene solution of the crude product was passed through a short column of neutral alumina and then concentrated, the sirupy residue being distilled as before: 3.91 g., $[\alpha]^{20}D$ −57° (*c* 1.19, ethanol), $n^{20}D$ 1.5125. Attempts to obtain the product in crystalline form were unsuccessful.

Anal. Calcd. for $C_{15}H_{20}O_4$ (264.33): C, 68.16; H, 7.63. Found: C, 68.28; H, 7.50.

1,5-Anhydro-2-O-benzyl-D-arabinitol.—1,5-Anhydro-2-O-benzyl-3,4-O-isopropylidene-D-arabinitol (22.4 g.) was dissolved in 300 ml. of 50% aqueous ethanol. Amberlite IR-120(H) (5.0 g.) was added, and the solution was refluxed and stirred for 3 hr. After filtration and removal of the solvent, the product was dried by azeotroping with benzene. Crystallization was spontaneous: 18.8 g. (99%), m.p. 99–100°. After two recrystallizations from benzene, the product was obtained as fine needles: m.p. 101–102°, $[\alpha]^{20}D$ −35° (*c* 1.19, ethanol).

Anal. Calcd. for $C_{12}H_{16}O_4$ (224.25): C, 64.27; H, 7.19. Found: C, 64.44; H, 7.21.

1,5-Anhydro-3,4-di-O-benzoyl-2-O-benzyl-D-arabinitol.—1,5-Anhydro-2-O-benzyl-D-arabinitol (18.80 g.) was benzoylated with benzoyl chloride in pyridine to give a sirup which solidified to a crystalline mass: 34.83 g. (96%). Recrystallized twice from petroleum ether (60–80°), the ester was obtained as needles: m.p. 62–63°, $[\alpha]^{20}D$ −155° (*c* 0.95, ethanol).

Anal. Calcd. for $C_{26}H_{24}O_6$ (432.45): C, 72.21; H, 5.59. Found: C, 72.28; H, 5.78.

1,5-Anhydro-3,4-di-O-benzoyl-D-arabinitol.—Palladium chloride (1 g.) was suspended in ethanol (15 ml.) and reduced with hydrogen at room pressure. 1,5-Anhydro-3,4-di-O-benzoyl-2-O-benzyl-D-arabinitol (2.16 g.), dissolved in 100 ml. of ethanol, was added to the suspended catalyst and the mixture was agitated with hydrogen until no more gas was absorbed. The catalyst was removed by filtration and the solution was concentrated *in vacuo*, finally at 80° (bath) to give 1.68 g. (98%) of crude crystalline product, m.p. 134–136°. Recrystallized from ethanol–hexane and sublimed at 135° and 0.01 mm., the ester melted at 134–135° and showed $[\alpha]^{20}D$ −212° (*c* 0.85, ethanol).

Anal. Calcd. for $C_{19}H_{18}O_6$ (342.33): C, 66.66; H, 5.30. Found: C, 66.39; H, 5.52.

1,5-Anhydro-3,4-di-O-benzoyl-2-O-thiobenzoyl-D-arabinitol.—To a solution of 3.4 g. of 1,5-anhydro-3,4-di-O-benzoyl-D-arabinitol in 15 ml. of dry pyridine (5.4 g., 3.5 molar equiv.) of thiobenzoyl chloride was added in one portion without cooling. A viscous sirup separated and the medium assumed a red-brown coloration distinct from the violet-red color of the reagent. After 12 hr., water (1 ml.) was added, then, after a further 30 min., the pyridine was removed by evaporation at 80°. The residue was dissolved in dichloromethane and the solution washed successively with dilute hydrochloric acid, water, and saturated aqueous sodium bicarbonate. After removal of moisture with sodium sulfate, the solution was concentrated to a red, viscous oil (7.1 g.). With benzene as a solvent, thin-layer chromatography on silica gel resolved the product into four components, a fast moving red fraction (R_f ~0.9), two closely associated orange and yellow fractions (R_f ~0.5), and one fraction which failed to migrate. Chromatography of 1.0 g. of the mixture on a short column of silica gel (10 g., packed as a slurry in benzene) effected an excellent resolution of the orange (0.03 g.) and yellow (0.40 g.) components. The characteristic color, optical activity, and infrared spectrum of the latter identified it as the required thionobenzoate; yield was equivalent to 62%, based on the 1,5-anhydro-3,4-di-O-benzoyl-D-arabinitol. Thin layer chromatography of the product thus isolated revealed a trace of a contaminant which fluoresced under ultraviolet light. Final purification by rapid distillation at 0.03 mm. and 220° (bath) afforded chromatographically pure material which rotated $[\alpha]^{20}D$ −140.2 ± 3.0° in ethanol (*c* 0.5): ultraviolet absorption data, λ_{max}^{EtOH} 282 mμ (ε 9680), 292 mμ (ε 9400).

Anal. Calcd. for $C_{26}H_{22}O_6S$ (462.53): C, 67.52; H, 4.79. Found: C, 67.81; H, 4.81.

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An Improved Method for the Preparation of Methyl 6-Chloro-6-deoxy-α-D-glucopyranoside

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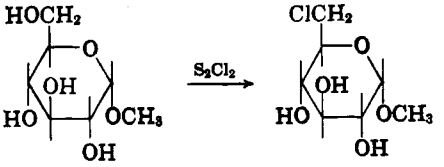
The only reference found in the literature to the preparation of methyl 6-chloro-6-deoxy-α-D-glucopyranoside is by Helferich, Klein, and Schaefer,[2] who report an over-all 8% yield[3] of methyl 6-chloro-6-deoxy-α-D-glu-

(1) This is a laboratory of the Northern Utilization Research and Development Division, Agricultural Research Service, U. S. Department of Agriculture.

(2) B. Helferich, W. Klein, and W. Schaefer, *Ber.*, **59B**, 79 (1926).

(3) The yield reported in ref. 2 is much lower than 8%, but subsequent work by B. Helferich and H. Bredereck [*Ber.*, **60B**, 2002 (1927)] on methyl β-D-glucopyranoside improved the chlorination step, and this improvement was used in the calculation.

copyranoside from methyl α-D-glucopyranoside. Their procedure probably discouraged further investigation of chlorinated hexoses for it not only resulted in a low yield, but also involved successively, tritylation with trityl chloride, acetylation with acetic anhydride, chlorination with phosphorus pentachloride, and hydrolysis with barium hydroxide. In contrast, a convenient procedure has been devised, namely, reaction of methyl α-D-glucopyranoside with sulfur monochloride (S_2Cl_2) and separation of the reaction products on a Darco G-60–Celite 535[4] column. This improved procedure results in a 30–35% yield of methyl 6-chloro-6-deoxy-α-D-glucopyranoside.



When sulfur monochloride is mixed with methyl α-D-glucopyranoside in N,N-dimethylformamide, a slightly exothermic reaction occurs accompanied by the separation of sulfur. After the destruction of unreacted sulfur monochloride with water and removal of the sulfur by filtration, the filtrate is rapidly adjusted with sodium carbonate to pH 8. Following its concentration to a convenient volume, the solution is applied to a Darco G-60–Celite 535 column.[5]

Surprisingly, the chlorinated glucoside is strongly held on the Darco G-60; after elution with water to remove inorganic salts and with 5% ethanol to remove methyl α-D-glucopyranoside,[6] at least 12% ethanol is required to elute the chloroglucoside. The yield of purified methyl 6-chloro-6-deoxy-α-D-glucopyranoside, m.p. 110–112°, is 30–35%.

Experimental

Methyl 6-Chloro-6-deoxy-α-D-glucopyranoside.—To a solution of methyl α-D-glucopyranoside (10 g., m.p. 164–166°) in N,N-dimethylformamide (250 ml., reagent grade used directly from the bottle) was added in one portion sulfur monochloride (15 ml., Eastman Kodak practical grade). Immediately, a canary yellow milkiness developed and the solution warmed slightly. The stoppered flask was cooled in flowing tap water for 0.5 hr. and allowed to stand at room temperature overnight (*ca.* 17 hr.) during which time the milkiness was replaced by crystalline sulfur. Water was then added with cooling in tap water as follows:

Water, ml.	2	2	2	44	50	50
Time, min.	0	35	45	60	105	115

After standing at room temperature for 0.5 hr., the solution was filtered through a small pad of Celite 535 to remove sulfur; the filtrate was diluted with 750 ml. of water and adjusted to pH 8 (paper) with solid sodium carbonate. This solution was concentrated under vacuum (bath temperature <65°) to approximately 750 ml. and, after filtration to remove a trace of insoluble material, placed on a Darco G-60–Celite 535 column (6 × 34 cm., 1-l. bed volume). The column was eluted with 4 l. of water, 4 l. of 5% ethanol, and finally 4 l. of 12% ethanol. The final eluate was collected separately and concentrated on a steam bath to give 4.57 g. of an oil that crystallized on standing (2–4 hr.). To eliminate the majority of contaminating Celite, the crystalline solid was dissolved in boiling absolute ethanol (*ca.* 20 ml.) and filtered while hot. After concentrating the filtrate to dryness at room temperature, a crystalline solid resulted containing a trace of Celite; this trace was easily removed by dissolving the crystals in boiling absolute ethanol (*ca.* 10 ml.), adding slowly ethyl acetate (*ca.* 50 ml.) to the boiling solution until a light tan floc separated, and then filtering the hot solution. From this filtrate, concentrated at room temperature, separated crystalline[7] methyl 6-chloro-6-deoxy-α-D-glucopyranoside, 3.50 g. (32%), m.p. 110–112°. An analytical sample was prepared by recrystallization twice from ethanol–ethyl acetate, m.p. 111.2–112.0°, $[\alpha]^{25}D$ +141° (*c* 0.658, H_2O) (lit.[2] m.p. 110–112°, $[\alpha]^{21}D$ +139°).

Anal. Calcd. for $C_7H_{13}ClO_5$: C, 39.54; H, 6.16; Cl, 16.67. Found: C, 39.75; H, 6.10; Cl, 16.31.

Linear horizontal chromatography[8] revealed only one spot with an R_f of 0.61 (methyl α-D-glucopyranoside R_f 0.29) when the $AgNO_3$–NaOH dipping reagent of Smith was used.[9]

(4) The mention of trade products does not imply that they are endorsed by the Department of Agriculture over similar but unmentioned products.

(5) R. L. Whistler and J. N. BeMiller, *Methods Carbohydrate Chem.*, **1**, 42 (1962).

(6) W. J. Whelan and K. Morgan, *Chem. Ind.* (London), 78 (1954).

(7) Occasionally an oil separates that readily crystallizes.

(8) Paper was S and S 2043b; solvent was *n*-BuOH–*i*-PrOH–H_2O, 3:1:1 (v./v.). For horizontal technique refer to R. G. Strobel and J. Holme, *Cereal Chem.*, **40**, 361 (1963).

(9) I. Smith, "Chromatographic Techniques," Interscience Publishers, Inc., New York, N. Y., 1958, p. 169.

Synthesis of D-*lyxo*-Hexulose (D-Tagatose) and 1-Deoxy-D-*lyxo*-hexulose[1]

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In continuation of our work on the general method for the preparation of ketoses from the acetylated sugar acids with one less carbon atom,[3] we report herein the application of this method to the synthesis of D-*lyxo*-hexulose (D-tagatose) and 1-deoxy-D-*lyxo*-hexulose (1-deoxy-D-tagatose). D-Tagatose has been synthesized: by the action of potassium hydroxide on D-galactose,[4] by the pyridine-catalyzed epimerization of D-galactose,[5-9] by oxidation of D-talitol with *Acetobacter suboxydans*,[7] and by a series of reactions from D-galacturonic acid.[10] D-Tagatose has been obtained in crystalline condition as a hydrolytic product from a gum exudate of the tropical tree *Sterculia setigera*[11] and has been reported to be present in the lichens *Rocella linearis* and *Rocella fucoformis*.[12] The chemistry of D-tagatose has been reviewed.[13]

(1) Paper No. 22 in the series entitled "The Action of Diazomethane upon Acyclic Sugar Derivatives"; previous communication: M. L. Wolfrom and R. B. Bennett, *J. Org. Chem.*, **30**, 458 (1965); preliminary communication: Abstracts of Papers, 147th National Meeting of the American Chemical Society, Philadelphia, Pa., April 1964, p. 15C.

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