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TWO METHYL ANHYDRO-D-FRUCTOPYRANOSIDES PREPARED FROM D-MANNITOL

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ABSTRACT

D-Mannitol (**1**) was converted into 1,5-anhydro-D-mannitol, which was treated consecutively with *p*-toluenesulfonyl chloride (1 mol. equiv.) and benzoyl chloride (3 mol. equiv.), to produce 1,5-anhydro-2,3,4-tri-*O*-benzoyl-6-*O*-*p*-tolylsulfonyl-D-mannitol. 1,5-Anhydro-2,3,4-tri-*O*-benzoyl-6-deoxy-6-iodo-D-mannitol (**4**) was prepared by displacing the *p*-tolylsulfonyl group by reaction with sodium iodide. 1,5-Diazabicyclo[5.4.0]undec-5-ene eliminated hydrogen iodide from **4**, to yield 1,5-anhydro-2,3,4-tri-*O*-benzoyl-6-deoxy-D-*lyxo*-hex-5-enitol (**5**). Addition of bromine to a methanolic solution in **5** in the presence of potassium carbonate resulted in a separable mixture of methyl 1-bromo-1-deoxy-α-D-fructopyranoside (**6**) and methyl 1-bromo-1-deoxy-β-D-fructopyranoside (**8**). Dilute alkali converted **6** into methyl 1,3-anhydro-α-D-fructopyranoside, identified as its 4,5-diacetate. Dilute alkali converted **8** into methyl 1,4-anhydro-β-D-fructopyranoside.

INTRODUCTION

When treated with concentrated acid, D-fructose undergoes self-condensation to form di-D-fructose dianhydrides[1], occasionally called diheterolevulosans. In 1958, the first anhydro-D-fructose was reported. When treated with nitrogen pentaoxide in the presence of sodium fluoride D-fructose afforded a nonreducing trinitrate of 2,3-anhydro-α-D-fructofuranose, which, on catalytic hydrogenation, yielded free 2,3-anhydro-D-fructofuranose[2]. Hydrogenolysis of sucrose in ethanol at 180° produced[3a] 2,6-anhydro-β-D-fructofuranose in 10% yield; the same anhydride was produced, as its 1-methyl ether, when 1-*O*-methyl-β-D-fructopyranosyl fluoride was treated with alkali[3b].

The difficulty in preparing pure D-fructopyranosides, except for 2-chloroethyl β-D-fructopyranoside[4], the low reactivity of the neopentyl type of 1-carbon group in D-fructopyranosides, and the general lack of suitably blocked D-fructopyranosyl

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derivatives, explain why no anhydro-D-fructopyranosides are described in the literature.

As D-mannitol exhibits end-to-end symmetry, conversion of either C-2 or C-5 into a carbonyl group yields D-fructose. This conversion was elegantly demonstrated when C-5 of styracitol (1,5-anhydro-D-mannitol) was transformed into a carbonyl group, resulting in D-fructose[5]. Similar to the styracitol to D-fructose conversion, we now report the conversion of D-mannitol, through a series of derivatives, into two methyl anhydro-D-fructopyranosides.

RESULTS AND DISCUSSION

When D-mannitol (**1**) is heated for 24 h in concentrated hydrochloric acid, 1,4-anhydro-D-mannitol is produced, but if the reaction time is doubled, 1,5-anhydro-D-mannitol (**2**) results[6]. Reaction of **2** with *p*-toluenesulfonyl chloride (1 mol. equiv.)–pyridine, followed by benzoyl chloride (3 mol. equiv.) produces 1,5-anhydro-2,3,4-tri-*O*-benzoyl-6-*O*-*p*-tolylsulfonyl-D-mannitol[5] (**3**) in 60% yield. Efforts to eliminate *p*-toluenesulfonic acid from **3** with 1,5-diazabicyclo[5.4.0]undec-5-ene (DBU) were unsuccessful. Displacement of the *p*-tolylsulfonyl group was carried out with* sodium iodide–hexamethylphosphoric triamide[7] (HMPA) in toluene (or sodium iodide in butanone), to yield 1,5-anhydro-2,3,4-tri-*O*-benzoyl-6-deoxy-6-iodo-D-mannitol[5] (**4**).

TABLE I

^{1}H-N.M.R.-SPECTRAL DATA

Compound number	*Chemical shift (δ)*								
	H-1	*H-1'*	*H-2*	*H-3*	*H-4*	*H-5*	*H-6*	*H-6'*	*Other*
5	4.38	4.08	5.85	5.66	6.22	—	4.90	4.69	aryl 7.4–8.0
10	4.61	4.44	—	4.74	5.31	5.37	4.02	3.83	methoxy 3.28 acetyl 2.05 2.09
11		4.1				3.7			methoxyl 3.50
12	4.21	4.01	—	5.19	4.53	5.01	4.32	3.75	methoxyl 3.43 acetyl 2.08 2.19

	Coupling constants (Hz)									
5	$J_{1,1'}$ 12.3 $J_{1,2}$ 3.6	$J_{1',2}$ 2.2	$J_{2,3}$ 3.2	$J_{3,4}$ 9.0	$J_{4,6}$ 1.5 $J_{4,6'}$ 1.5	$J_{6,6'}$ 3
10	$J_{1,1'}$ 6.3	$J_{3,4}$ 4.5	$J_{4,5}$ 3.7	$J_{5,6}$ 5.5 $J_{5,6'}$ 3.8	$J_{6,6'}$ 11.9	
12	$J_{1,1'}$ 9.4	$J_{3,4}$ 6.4	$J_{4,5}$ <0.2	$J_{5,6}$ 6.9 $J_{5,6'}$ 1.3	$J_{6,6'}$ 11.1	

*This is a modification of the procedure described in ref. 7a, wherein sodium iodide replaces lithium iodide. Note that it has been reported[7b] that the vapors of hexamethylphosphoric triamide cause cancer in rats.

When **4** was warmed in the presence of DBU, t.l.c. revealed the disappearance of **4** (R_F 0.41) and the appearance of a spot at R_F 0.58. Purification by chromatography resulted in a colorless syrup. ^{1}H-N.m.r. spectroscopy (see Table I) showed fifteen aromatic protons (δ 7.4–8.0), two methylene protons (δ 4.08 and 4.38), and two terminal alkenic protons (δ 4.69 and 4.90), indicating that hydrogen iodide had been eliminated by DBU, to yield 1,5-anhydro-2,3,4-tri-*O*-benzoyl-6-deoxy-D-*lyxo*-hex-5-enitol **5**.

On addition of bromine (1 mol. equiv.) to syrupy **5** in methanol containing potassium carbonate, the bromine color was immediately discharged. T.l.c. immediately following bromine addition revealed 4–6 spots: after 3 h, only two spots, R_F 0.15 and 0.42, remained. Work-up of the mixture resulted in a syrup smelling strongly of methyl benzoate. Chromatography readily separated the spots having R_F 0.15 and 0.42 (and methyl benzoate). The fractions containing the R_F 0.42 spot yielded a syrup, that, on standing, crystallized; similarly, the fractions containing spot having the R_F 0.15 yielded a syrup that crystallized. Analyses agreed with a methyl bromodeoxyglycoside, revealing that the potassium carbonate catalyzed debenzoylation, to produce methyl benzoate. The debenzoylation explained why several spots were observed during the initial phases of the bromomethoxylation of **5**. ^{1}H-N.m.r. spectroscopy confirmed that the compounds having R_F 0.15 and 0.42 contained one methoxyl and one bromomethyl group.

The optical rotation of methyl α-D-fructopyranoside[8] (**7**, depicted in the $^2C_5$ conformation) was $[\alpha]_D$ +44° and the β anomer[9] (**9**) was $[\alpha]_D$ −172°. This data agrees with Hudson's rules of rotation[10] for anomers, where the α anomer is the more dextrorotary in the D-series. Assuming that a 1-bromo-1-deoxy substitution on methyl D-fructopyranoside would result in little conformational change in

TABLE II

^{13}C-N.M.R.-SPECTRAL DATA

Compound number	*Chemical shifts (p.p.m.)*							
	C-1	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*OCH_3*	*Other*
5a	31.21	100.93	65.62	71.47	68.38	62.63	49.11	
7[a]	58.32	101.68	65.17	71.46	68.40	61.20	48.94	
6a	31.76	101.91	69.24	70.37	69.72	65.27	49.01	
9[b]	61.8	101.4	69.3	70.5	70.0	64.7	49.3	
7	79.89	98.08	85.07	69.82[c]	66.34[c]	62.21	50.38	CO 169.8 169.9 CH_3 20.79
8a	69.6	103.6	64.0[c]	80.7	71.6[c]	65.4	54.1	
8b	69.4	102.0	66.7[c]	75.8	72.2[c]	62.4	53.3	CO 169.8 170.1 CH_3 20.88 20.84

[a]Data from ref. 12. [b]Data from ref. 13. [c]Signal assignment is tentative, and may have to be interchanged.

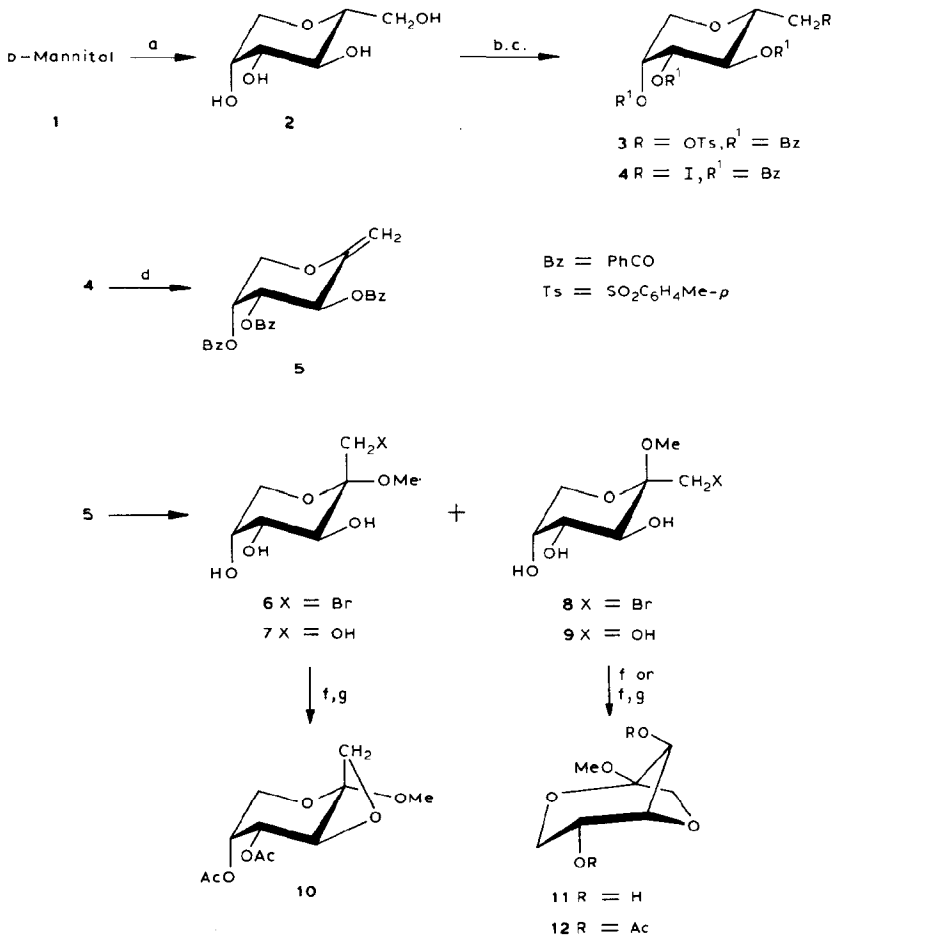
solution, Hudson's rules of rotation would be expected to be valid. As the R_F 0.42 compound shows a more-positive rotation, the structure was assigned as methyl 1-bromo-1-deoxy-α-D-fructopyranoside (**6**), $[\alpha]_D$ −4.3°; thus, the R_F 0.15 compound was the β anomer (**8**), $[\alpha]_D$ −126.9°. Again, assuming that the replacement of a hydroxyl group in methyl D-fructopyranoside by bromine results in little conformational change in solution, the close correspondence in the ^{13}C-n.m.r. spectra (see Table II) between the known fructopyranosides (**7** and **9**) and the bromodeoxyfructopyranosides (**6** and **8**), as assigned by optical rotation, also lends support to the anomeric assignment. Except for C-1, where the bromo for hydroxyl replacement occurs, the small differences in carbon chemical shifts between **6** and **7**, and **8** and **9**, supported the view that the bromine substitution on C-1 resulted in only a small perturbation of conformation in solution from that of the unsubstituted D-fructopyranoside.

On boiling **6** in dilute sodium hydroxide, cooling, neutralizing the base, extracting the solution, and evaporating the extract, a syrup resulted. Acetylation of this syrup with acetic anhydride–pyridine, followed by chromatographic purification, yielded a crystalline compound. In compound **6**, only the 3-hydroxyl group is situated to displace the 1-bromo group, resulting in oxetane (1,3-anhydride) formation. Thus, the compound was assigned the structure methyl 4,5-di-*O*-acetyl-1,3-anhydro-α-D-fructopyranoside (**10**). The downfield signal in the ^{1}H-n.m.r. spectrum for H-4 (δ 5.31) and H-5 (δ 5.37) (see Table I) in **10** showed the location of the acetyl group. As *O*-alkylation causes a large downfield shift[11] of the α-carbon signal, the downfield shift in the ^{13}C-n.m.r. spectrum seen for C-1 and C-3 of **10**, compared to that for **7** is consistent with oxetane formation, an internal *O*-alkylation.

When **8** was boiled in dilute sodium hydroxide, the base neutralized, and the solution exhaustively extracted, a crystalline compound, m.p. 142–143°, was isolated, which was not oxidized by periodate. As **8** could form a 1,4- or 1,5-anhydrofructopyranoside, the failure to be oxidized by periodate suggested a 1,4-anhydro structure or methyl 1,4-anhydro-β-D-fructopyranoside (**11**). However, the suggestion is weak, because 1,6-anhydro-β-D-glucofuranose[14], 2,6-anhydro-β-D-fructofuranose (2,5-anhydro-α-D-fructopyranose)[3a] and 1,6-anhydro-α-D-galactofuranose[15], structures whose vicinal hydroxyl groups exhibit a *trans* orientation similar to that of a 1,5-anhydro-fructopyranoside, failed to react with periodate.

When **11** was acetylated, a crystalline diacetate (**12**) was isolated, the proton spectrum of which was first-order and readily interpreted. The downfield signal of H-5 (δ 5.01) and H-3 (δ 5.19) (see Table I) of **12** established that those positions were acetylated, and that **12** contained a 1,4-anhydro structure. Vicinal coupling between H-4 and H-5 was <0.2 Hz, indicating that the pyranoid ring adopts the $^3C_6$ conformation. In the related boat conformation, $B^{6,3}$, the vicinal coupling would be predicted to be large, as H-4 and H-5 are nearly eclipsed.

From knowledge of the structure of **11** and **12**, the assignment of individual resonances observed in the ^{13}C-n.m.r. spectra was undertaken. The methylene

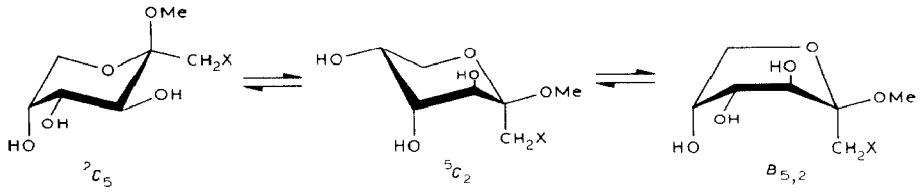


(a) Δ, conc. HCl; (b) 1. TsCl, C_5H_5N; 2. BzCl; (c) NaI, HMPA; (d) DBU, C_5H_5N, 40°; (e) Br_2, MeOH, K_2CO_3; (f) NaOH, H_2O; (g) Ac_2O, C_5H_5N.

carbon atoms, the anomeric carbon atom, and the methoxyl and acetyl carbon atoms were readily assigned, but the signals of the C-3, C-4, and C-5 methine atoms were more difficult to assign. For 1,4-anhydrohexitols, the C-4 signals are observed[11] at 80.9–86.5 p.p.m. On this basis, the C-4 signal for **11** was assigned as 80.7 p.p.m. The shift between the C-4 signal of **11** and that for C-4 of **8** or **9** shows a 10.2–10.3-p..m. downfield shift, agreeing with the observation[11] that *O*-alkylation "leads to a rather large downfield shift of the α-carbon". Using as a guide the information[11] that *O*-acylation causes a small downfield shift in the α-carbon signal and a small upfield shift in the β-carbon signal, further assignments were made among the three methine signals (at 75.8, 72.2, and 66.7 p.p.m.) for **11**. Even though the cumulative effect of multiple acyl groups on the β-carbon signal is

difficult to predict, the 75.8-p.p.m. signal was assigned to C-4 in **11**, as the upfield shift would be relatively small (4.9 p.p.m.) when compared to the other values (8.5 and 14.0 p.p.m.). To account for a small downfield shift for C-3 and C-5 when **11** was acetylated to **12**, the unassigned signals should be matched as listed in Table II.

Between the two chair forms of pyranosides, the more-favored form will minimize non-bonded interactions by placing the hydroxymethyl (or in the case here, bromomethyl) group in an equatorial position. With **8**, the $^2C_5$ conformation would be favored. In the $^5C_2$ conformation, the bromomethyl and OH-4 groups exhibit a 1,3-diaxial relationship and are aligned sterically for bromide displacement to produce a 1,4-anhydro-β-D-fructopyranoside. To produce a 1,5-anhydro-β-D-fructopyranoside would necessitate an energetically disfavored, boat conformation. Presenting a similar conformational and positional relationship as D-fructoside **8**, methyl 6-bromo-6-deoxy-α-D-mannopyranoside, when treated with alkali afforded methyl 3,6-anhydro-α-D-mannopyranoside[16], a 1,4-anhydro structure.



EXPERIMENTAL

General methods. — Melting points are uncorrected. Optical rotations were measured with a Perkin–Elmer Model 241 polarimeter, using the sodium D-line. Microanalyses were performed by Galbraith Laboratories, Knoxville, Tennessee, U.S.A. T.l.c. was performed on Merck, air-equilibrated, precoated plates of 0.25-mm layers of silica gel F-254 with the specified solvents. Spots were rendered visible by spraying with 5% ethanolic sulfuric acid and heating until charring occurred. Column chromatography was performed on ICN silica gel, No. 40265, and, for dry-column chromatography, by dissolving the sample in a small amount of a low-boiling solvent, adding silica gel to obtain a free-flowing powder, placing the powder on the dry column, and developing with a solvent. Each fraction was monitored by t.l.c., and the appropriate fractions were pooled and concentrated. Solutions were concentrated or evaporated under vacuum. N.m.r. spectra (^{1}H- and ^{13}C-) were recorded with a Bruker WM-300WB spectrometer. ^{1}H-Chemical shifts (p.p.m.) were compared against internal Me_4Si. ^{13}C-Chemical shifts (p.p.m.) were compared against chloroform-*d* (77.0 p.p.m.), and, for solutions in D_2O against 1,4-dioxane-d_4 (66.5 p.p.m.).

*1,5-Anhydro-*D*-mannitol* (**2**). — This compound was prepared according to ref. 6. To start crystallization, seeding the ethanolic solution of the crude reaction-product was always needed.

*1,5-Anhydro-2,3,4-tri-*O*-benzoyl-6-*O*-p-tolylsulfonyl-*D*-mannitol* (**3**). — A solution of **2** (10.0 g, 60.9 mmol) in pyridine (200 mL) was cooled to 4–5°. *p*-Toluenesulfonyl chloride (11.8 g, 61.9 mmol) was added, and the solution was swirled until homonogeneous. After keeping the mixture for 24 h at 4–5°, benzoyl chloride (21.6 mL, 185.4 mmol) was added, and the mixture was kept for 24 h at 4–5°. Water (10 mL) was added, and after keeping for 0.5 h, the solution was poured into an ice–water slush (1.2 L). A thick syrup separated that, on stirring, slowly crystallized, 38.5 g (air-dried). The solid was recrystallized from ethanol (1.2 L), to yield **3**, 25.4 g (66%); m.p. 158–159°, $[\alpha]_D^{22}$ −165° (*c* 1.0, chloroform); lit.[5] m.p. 162°, $[\alpha]_D$ −166.5° (*c* 2.0, chloroform).

*1,5-Anhydro-2,3,4-tri-*O*-benzoyl-6-deoxy-6-iodo-*D*-mannitol* (**4**). — (*a*) A well-stirred mixture of **3** (1.0 g, 1.58 mmol), sodium iodide (1.0 g, 6.6 mmol), toluene (40 mL), and hexamethylphosphoric triamide[7] (1 mL) was boiled for 16 h, cooled, and concentrated to a tacky solid. The solid was partitioned between water (50 mL) and dichloromethane (20 mL); the aqueous layer was extracted with two 20-mL portions of dichloromethane. The extracts were combined, successively washed with 50 mL each of water, 5% sodium thiosulfate, and water, dried, and evaporated to a syrup. On dissolving the syrup in warm ethanol (10 mL), crystalline **4** was deposited on cooling, 1.0 g (90%); m.p. 136–138°.

(*b*) A mixture of **3** (8.0 g, 12.6 mmol) and sodium iodide (9.0 g, 60.0 mmol) in butanone (200 mL) was stirred and heated to boiling, and the progress of the reaction was monitored by t.l.c. in 5:1 (v/v) toluene–ethyl acetate. When the reaction was deemed to be complete (~5 h), the mixture was cooled, concentrated, and partitioned between water (150 mL) and dichloromethane (50 mL). The aqueous layer was extracted with three 50-mL portions of dichloromethane. The extacts were combined, washed with 100 mL each of water, 5% sodium thiosulfate, and water, dried, and evaporated, to afford crystalline **4**. Recrystallization from ethanol (70 mL) yielded **4**, 4.75 g (52%); m.p. 137–138.5°, $[\alpha]_D^{22}$ −165° (*c* 1.0, chloroform); lit.[5] m.p. 143–144°, $[\alpha]_D$ −167° (*c* 2.1, chloroform).

*1,5-Anhydro-2,3,4-tri-*O*-benzoyl-6-deoxy-*D*-lyxo-hex-5-enitol* (**5**). — Compound **4** (12.3 g, 17.3 mmol) was dissolved in pyridine (200 mL), 1,5-diazabicyclo[5.4.0]undex-5-ene (DBU; 15 mL, 100 mmol) was added, and the mixture was heated for 18 h at 40°. After evaporation to a reddish-brown syrup, the mixture was partitioned between water (250 mL) and dichloromethane (75 mL). The aqueous layer was extracted with three 75-mL portions of dichloromethane, and the extracts were combined, dried, and evaporated to a brownish syrup. Chromatography of the syrup on a dry column (3.5 × 34 cm) by developing with toluene–ethyl acetate (mL:mL), 600:0; 500:25; and 500:50, pooling the appropriate fractions, and evaporating them, resulted in a viscid, colorless syrup of **5**, 7.0 g (~72%). ^{1}H-N.m.r. spectroscopy (see Table I) supported the structural assignment, and established the presence of a trace of toluene. The syrup was used directly in the next step.

*Methyl 1-bromo-1-deoxy-α-*D*-fructopyranoside* (**6**) *and methyl-1-bromo-1-*

deoxy-β-D-fructopyranoside (**8**). — After dissolving **5** (7.0 g, 12 mmol) in methanol (200 mL), potassium carbonate (1.5 g, 10.8 mmol) was added. To the well-stirred mixture was slowly added a bromine solution, made by dissolving 1.0 mL (19.4 mmol) of bromine in 50 mL of dichloromethane. The addition was continued until the bromine color was not immediately discharged; some 35–39 mL was needed. Monitoring of the reaction by t.l.c. revealed several spots, but, after 3 h only two spots remained, R_F 0.15 and 0.42 (ethyl acetate). On evaporation, a syrup containing solid material resulted; this was covered with methanol (100 mL), stirred briefly, and the suspension filtered to remove insoluble material. The filtrate was evaporated to a syrup having the odor of methyl benzoate. Chromatography of the syrup on a dry column (3.5 × 48 cm) by developing with toluene:ethyl acetate (mL:mL), 250:250; 100:200; ethyl acetate (mL), 300; methanol:ethyl acetate (mL:mL), 15:300; 25:250; 40:200; 75:150; 100:100; methanol:water, 200:0, 200:5, and pooling the appropriate fractions and evaporating, yielded two crystalline solids.

The first compound eluted from the column (R_F 0.42, ethyl acetate) was methyl 1-bromo-1-deoxy-α-D-fructopyranoside (**6**), 1.7 g (43.3%); m.p. 84–85°, $[\alpha]_D^{25}$ −4.3° (*c* 0.159, water); for ^{13}C-n.m.r. data, see Table II.

Anal. Calc. for $C_7H_{13}BrO_5$: C, 32.70; H, 5.09; Br, 31.08. Found: C, 32.82; H, 5.20; Br, 30.81.

The second compound off the column (R_F 0.15, ethyl acetate) was methyl 1-bromo-1-deoxy-β-D-fructopyranoside (**8**), 2.2 g (56.1%); m.p. 86–87°, $[\alpha]_D^{25}$ −126.9° (*c* 0.131, water); for ^{13}C-n.m.r. data, see Table II.

Anal. Calc. for $C_7H_{13}BrO_5$: C, 32.70; H, 5.09; Br, 31.08. Found: C, 32.54; H, 5.00; Br, 31.20.

Methyl 4,5-di-O-acetyl-1,3-anhydro-α-D-fructopyranoside (**10**). — Compound **6** (428.5 mg, 1.66 mmol) was dissolved in water (40 mL); M sodium hydroxide (3.0 mL) was added, and the mixture was boiled for 1 h. After cooling, carbon dioxide was bubbled through the solution, to neutralize the excess of sodium hydroxide, and the solution was placed in a continuous extractor; ethyl acetate was percoated for 16 h. On evaporating the extract, a syrup resulted; this was acetylated by dissolving in pyridine (5 mL)–acetic anhydride (2 mL), and keeping overnight. After adding water (2 mL), the mixture was kept for 2 h, and then evaporated to a syrup. Three 15-mL portion of toluene were added to, and evaporated from, the syrup. Chromatography of the syryp on a dry column (2.5 × 46 cm) developing with 1:1 (v/v) toluene–ethyl acetate, pooling the appropriate fractions, and evaporating resulted in crystalline **10**. Recrystallization from ethanol (5 mL) yielded **10**, 243.2 mg (55%); m.p. 62–63°, $[\alpha]_D^{23}$ −41.9 (*c* 0.105, chloroform); for ^{1}H-n.m.r. data, see Table I; for ^{13}C-n.m.r. data, see Table II.

Anal. Calc. for $C_{11}H_{16}O_7$: C, 50.95; H, 6.17. Found: C, 51.00; H, 6.09.

Methyl 1,4-anhydro-β-D-fructopyranoside (**11**). — To a solution of compound **8** (702.5 mg, 2.72 mmol) in water (50 mL) was added M sodium hydroxide (5 mL), and the solution was boiled 3 h. After cooling, carbon dioxide was bubbled through the solution which was then placed in continuous extractor. Ethyl acetate was

percolated for 66 h, and the extract was evaporated, to afford crystalline **11**, 184.6 mg (38.3%); m.p. 141–143°, $[\alpha]_D^{23}$ +34.3° (*c* 0.46, water); for ^{1}H-n.m.r. data, see Table I; for ^{13}C-n.m.r. data, see Table II. Periodate oxidation was not observed, even after five days.

Anal. Calc. for $C_7H_{12}O_5$: C, 47.72; H, 6.36. Found: C, 48.00; H, 6.66.

*Methyl 3,5-di-*O*-acetyl-1,4-anhydro-β-*D*-fructopyranoside* (**12**). — To a solution of compound **8** (209.7 mg, 0.81 mmol) in water (10 mL) was added M sodium hydroxide (2 mL), and the mixture was heated on a steam bath for 3.5 h. After cooling, carbon dioxide was bubbled through the solution, followed by freeze-drying to afford a fluffy solid which was suspended in pyridine (4 mL), and three 0.2-mL portions of acetic anhydride were added at 4-h intervals. After standing overnight, water (1 mL) was added, followed by stirring for 0.5 h. On evaporation, a syrup remained; this was twice covered with a 10-mL portion of toluene and evaporated. The syrup was partitioned between water (10 mL) and dichloromethane (10 mL). After washing the organic layer with water (10 mL) and evaporating, a brownish syrup remained that crystallized, 161.3 mg. Recrystallization from 95% ethanol (1 mL) produced a light-tan solid, 128.4 mg. Chromatography on a dry column (1.5 × 17 cm), developing with toluene–ethyl acetate (mL:mL), 50:25; 50:50, pooling the appropriate fractions, and evaporating, resulted in colorless, crystalline **12**, 126.0 mg (59.3%); m.p. 123–124°, $[\alpha]_D^{22}$ +38.5° (*c* 0.135, chloroform); for ^{1}H-n.m.r. data, see Table I; for ^{13}C-n.m.r. data, see Table II.

Anal. Calc. for $C_{11}H_{16}O_7$: C, 50.95; H, 6.17. Found: C, 50.80; H, 6.30.

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