were filtered and washed with a little methanol. They were stirred for 1 hr. with 10% sodium carbonate solution to remove some unreacted acid and were then crystallized from methanol. The yield of pure methylester of m.p. 155–156° was 13 g.

Anal. Calcd. for $C_{14}H_{11}NO_6S$: C, 52.33; H, 3.45; N, 4.36. Found: C, 52.31; H, 3.27; N, 4.52.

(*18*) *4-(4-Aminophenylsulfonyl)benzoic acid* (XXXI). A. *By catalytic reduction.* 4-(4-Nitrophenylsulfonyl)benzoic acid (10 g.) was suspended in 10 ml. of water and sodium hydroxide was added dropwise to dissolve the acid. The solution was hydrogenated with Raney nickel at 50° and 300 lbs. pressure. The catalyst was filtered and the solution was acidified with acetic acid. The crude amino acid was filtered and recrystallized from 80% acetic acid, yielding 6 g. of pure 4-(4-aminophenylsulfonyl)benzoic acid of m.p. 253–254°. Roblin and Clapp[15] do not report the melting point of the acid.

Anal. Calcd. for $C_{13}H_{11}NO_4S$: C, 56.30; H, 4.00; N, 5.05. Found: C, 56.14; H, 4.02; N, 5.00.

B. *By reduction with ferrous sulfate.* A solution of the sodium salt, prepared from 38 g. of 4-(4-nitrophenylsulfonyl)benzoic acid in 500 ml. of water and a small excess of sodium hydroxide, was added with stirring at 25° to a solution of 210 g. of ferrous sulfate ($FeSO_4 \cdot 7H_2O$) in 1000 ml. of water. To this mixture, 400 g. of 25% sodium hydroxide was slowly added. The mixture was stirred for 8 hr. The undissolved material was filtered and the clear filtrate was acidified, yielding 24 g. of 4-(4-aminobenzylsulfonyl)-benzoic acid of m.p. 253–254°.

(*19*) *4-(4-Aminophenylsulfonyl)benzoic acid methylester* (XXXII). A mixture of 5 g. of 4-(4-aminophenylsulfonyl)-benzoic acid, 100 ml. of methanol, and 20 g. of concd. sulfuric acid was refluxed on the steam bath. After about 3 hr., a homogeneous solution had formed. It was filtered and cooled. The crude methyl ester was filtered and recrystallized from about 100 ml. of methanol, yielding 4 g. of pure ester of m.p. 175–176°.

Anal. Calcd. for $C_{14}H_{13}NO_4S$: C, 57.72; H, 4.50; N, 4.87. Found: C, 58.23; H, 4.38; N, 4.92.

(*20*) *4-(4-Aminophenylsulfonyl)benzoic acid hydrazide* (XXXIII). A mixture of 9 g. of the ester (Experiment 19) and 2.5 ml. of hydrazine hydrate in 60 ml. of methanol was refluxed for 3 hr. On cooling in the refrigerator, 8 g. of 4-(4-aminophenylsulfonyl)benzoic acid hydrazide crystallized. Recrystallization from methanol gave the pure compound of m.p. 199–200°.

Anal. Calcd. for $C_{13}H_{13}N_3O_3S$: C, 53.60; H, 4.50; N, 14.42. Found: C, 53.30; H, 4.35; N, 14.63.

(*21*) *4-[4-(4-Nitrophenylsulfonyl)benzylamino]benzoic acid* (XXXVI). 4-Bromomethyl-4′-nitrodiphenylsulfone (18 g.) and 14 g. of p-aminobenzoic acid were refluxed in 125 ml. of dioxane for 4 hr. The hot solution was filtered from undissolved material and distilled to dryness. The residue was dissolved in 3% sodium hydroxide and the solution was again filtered from undissolved crystals. The clear, yellow filtrate was acidified with acetic acid. After 1 hr. the crystals were filtered and recrystallized from dioxane, yielding 12 g. of 4-[4-(4-nitrophenylsulfonyl)benzylamino]benzoic acid of m.p. 256–258°.

Anal. Calcd. for $C_{20}H_{16}N_2O_6S$: C, 58.24; H, 3.91; N, 6.79. Found: C, 58.07; H, 3.80; N, 6.73.

(*22*) *4-[4-(4-Aminophenylsulfonyl)benzylamino]benzoic acid* (XXXVII). The nitro acid (XXXVI) (5 g.) was hydrogenated catalytically with 2 g. palladium charcoal (3% Pd) in 30 ml. of acetic acid at 40° and 500 lbs. pressure. The resulting mixture contained cyrstals. After addition of 40 ml. of acetic acid, it was refluxed and filtered hot from the catalyst. On cooling, the acid crystallized. Recrystallization from acetic acid yielded 2 g. of pure 4-[4-(4-aminophenylsulfonyl)benzylamino]benzoic acid of m.p. 243–244°.

Anal. Calcd. for $C_{20}H_{18}N_2O_4S$: C, 62.81; H, 4.74; N, 7.34. Found: C, 62.60; H, 5.03; N, 7.14

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Glycosidation with Trimethyl Orthoformate and Boron Trifluoride*

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Methanolic trimethyl orthoformate in the presence of boron trifluoride constitutes a convenient system for glycoside synthesis in the sugar field.

Bergmann[3] applied the Claisen[4] acetalation reaction to the preparation of ethyl 4,6-di-*O*-acetyl-α-D-*erythro*-2-*cis*-hexosenide by heating 4,6-di-*O*-acetyl-D-*erythro*-2-*cis*-hexosene under reflux with ethanolic trimethyl orthoformate in the presence of a small amount of ammonium chloride. This reaction has been repeated by Stacey and co-workers[5] and performed, without ammonium chloride catalysis, with the corresponding D-galactose derivative by Lohaus and Widmaier[6] and with the methyl D-glucose analog by Bergmann and Freudenberg.[7] The corresponding reaction[8] with tetramethyl orthosilicate in the presence of hydrogen chloride was applied by Freudenberg and Jakob[9] to the preparation of

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TABLE I

GLYCOSIDATION WITH TRIMETHYL ORTHOFORMATE AND BORON TRIFLUORIDE[a]

Substance	Product	M.P., °C.	$[\alpha]_D^{20}$ (c 1), Water, Degrees	Yield, %
D-Glucurono-3,6-lactone	Methyl α-D-glucofuranosid-urono-6,3-lactone	147–148	+163[b]	41.5
D-Arabinose	Methyl β-D-arabinopyranoside	168–169	−243	28.0
D-Galactose	Methyl β-D-galactopyranoside	177–178	0	28.0
D-Glucose	Methyl α-D-glucopyranoside	165–166	+158	37.5
D-Mannose	Methyl α-D-mannopyranoside	193.5–194.5	+ 78	47.0
D-Xylose	Methyl β-D-xylopyranoside	156–157	− 65	43.0

[a] See experimental section for details. [b] In ethanol.

methyl 2,3,6-tri-*O*-methyl D-glucopyranoside from 2,3,6-tri-*O*-methyl-D-glucose. The latter workers also utilized trimethyl orthoformate, methanol and hydrogen chloride and, without isolating the reaction products, extended their studies to D-glucose, D-galactose and to a series of methylated D-glucose derivatives. By applying hydrolytic rate studies to the reaction mixtures, they noted that pyranoside formation predominated.

According to Freudenberg and Jakob,[9] Schwarz,[10] and Astle and co-workers,[11] orthoformate esters of certain polyhydroxy compounds are formed by their reaction with ethyl orthoformate in the presence of hydrogen chloride or of an acid exchange resin.

In the work herein reported, D-glucurono-6,3-lactone was shaken for three hours at room temperature with trimethyl orthoformate containing a catalytic amount of boron trifluoride. The nonreducing, wine-red solution yielded a crystalline compound which was found to be methyl α-D-glucofuranosid-urono-6,3-lactone. This synthesis represents a convenient and superior method for the preparation of the α-anomer as previously reported methods[12] result in a mixture of anomers from which the α-glycoside can be isolated only with difficulty and in very low yield.

Application of this boron trifluoride-catalyzed reaction to the common aldohexoses and aldopentoses (Table I) led to a mixture from which one pure anomer crystallized in fair yield. The method is convenient and can be considered as the method of choice for methyl β-D-galactopyranoside. The reaction products were investigated by paper chromatography and were found to consist of a glycoside mixture accompanied by small amounts of unchanged sugar and, save for D-glucose, a fast moving component which may have been an orthoester.

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EXPERIMENTAL

Methyl α-D-glucofuranosidurono-6,3-lactone. Two grams of D-glucurono-6,3-lactone, dried at 50° and 0.01 mm., 50 ml. of trimethyl orthoformate, dried over Drierite (anhydrous calcium sulfate), and 0.2 ml. of a 7% solution of boron trifluoride in methanol, were shaken together for 2 hr. The D-glucurono-6,3-lactone slowly dissolved and the mixture turned initially yellow and finally wine-red in color and became nonreducing toward Fehling solution. The solution was poured into 1 l. of carbon tetrachloride and allowed to stand at 10–12° for 48 hr. Crystals formed and were dissolved in methanol, filtered through activated carbon, and the material obtained on solvent removal was recrystallized from ethyl acetate to give methyl α-D-glucofuranosidurono-6,3-lactone (see Table I).

Anal. Calcd. for $C_8H_{12}O_6(OCH_3)$: C, 44.2; H, 5.26; OCH_3, 16.3. Found: C, 44.44; H, 5.16; OCH_3, 16.28.

Methyl α-D-mannopyranoside. Five grams of D-mannose, dried at 50° and 0.01 mm., 50 ml. of trimethyl orthoformate, dried over Drierite, and 0.5 ml. of a 7% solution of boron trifluoride in methanol, were shaken together for 18 hr. The D-mannose slowly dissolved and the wine-red, nonreducing solution was poured into 1 l. of light petroleum ether (b.p. 30–60°) and allowed to stand at 10–12° for 24 hr. The separated sirup was dissolved in methanol, filtered through activated carbon, and the sirup obtained on solvent removal was crystallized from ethanol to give methyl α-D-mannopyranoside (see Table I).

The above experiment was extended to the other aldoses listed in Table I. In all cases, the initial product was chromatographed on a sheet of Whatman No. 1 filter paper and developed with 1-butanol saturated with water. The spots were detected by spraying with ammoniacal silver nitrate and heating the paper at 100° for a few minutes. There was obtained in all cases evidence for the presence of a small amount of the unreacted sugar, an elongated spot indicating the mixture of glycosides, and a small quantity of a fast-moving unknown component, absent in the case of D-glucose. It is probable that the chromatographic conditions employed would not resolve the glycoside mixture into its components.

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