145. *The Reactivity of the Methyl α-D-Glucoside–Boron Trichloride Reagent.*

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The product formed in dichloromethane from methyl α-D-glucoside and boron trichloride may be a useful glucosylating agent: its reactions with alcohols, phenols, monosaccharides, and benzene have been studied. With the first three types of substrate a mixture of α- and β-isomers is commonly obtained, with one or the other frequently predominating.

The probable mechanism of the formation and reaction of the reagent is discussed.

The formation of oligosaccharides as secondary products in the demethylation of methyl α-D-glucoside with boron trichloride [1] suggested that the two reactants could function as a glucosylating agent towards free hydroxyl groups. Further investigation has shown that glucosylation of alcohols, phenols, monosaccharides, and benzene is possible by means of this reagent.

The most widely used method of glycosylation is that of Koenigs and Knorr [2] employing *O*-acetylglycosyl bromide or chloride. In the normal course of reaction, a glycoside having the opposite configuration at the glycosidic carbon atom to that of the parent glycosyl halide is produced in the presence of silver salts, but with mercuric salts either isomer may be formed.[3] An alternative method of synthesising phenolic glycosides from phenols and polyacetylated sugars shows that the nature of the acid catalyst determines whether the α- or the β-isomer predominates in the product.[4]

As reported below, the methyl α-D-glucoside–boron trichloride reagent usually gives a mixture of α- and β-isomers; the latter isomer might be expected to predominate since reaction probably proceeds by nucleophilic attack at the electron-deficient $C_{(1)}$ atom of the glucose unit (cf. the parallel case of the preferential formation of a 9-β-glucosylpurine by nucleophilic attack of the purine–mercuric chloride reagent on the ortho-ester cation of tetra-*O*-acetylglucosyl chloride [5]). However, only in the case of benzyl glucoside was the β-isomer exclusively formed.

The Synthesis of Glucosides.—The glucosylating reagent was prepared by treating a suspension of methyl α-D-glucoside in dichloromethane with boron trichloride at −80°.

[1] Bonner, Bourne, and McNally, *J.*, 1960, 2929.
[2] Koenigs and Knorr, *Ber.*, 1901, **34**, 957.
[3] Conchie, Levvy, and Marsh, *Adv. Carbohydrate Chem.*, 1957, **12**, 157.
[4] Helferich and Schmitz-Hillebrecht, *Ber.*, 1933, **66**, 378; Montgomery, Richtmyer, and Hudson, *J. Amer. Chem. Soc.*, 1942, **64**, 690; Lemieux and Shyluk, *Canad. J. Chem.*, 1953, **31**, 528.
[5] Blackburn and Johnson, *J.*, 1960, 4347.

On attaining room temperature, the mixture became homogeneous. Removal of the excess of solvent and boron trichloride under diminished pressure provided the solid reagent which was protected from atmospheric moisture. Initially a modified Koenigs and Knorr technique was used to synthesise benzyl glucoside by means of this reagent, the latter being shaken with benzyl alcohol and silver oxide for 24 hr. at room temperature. The two principal products were glucose and benzyl β-D-glucoside (37%); no trace of the α-isomer was obtained. To ensure that no transglucosidation took place in the absence of boron trichloride the reaction was repeated without the latter: the only material isolated was then unchanged methyl α-D-glucoside; the result was also negative when hydrogen chloride was employed in place of boron trichloride.

The above technique, however, was not effective for the synthesis of phenyl glucoside from phenol. Variation of method led to the discovery that phenolic glucosides were readily obtained by heating the methyl glucoside–boron trichloride complex with the phenol in dichloromethane under reflux. By this means, catechol was converted into a mixture of its α- and β-D-glucosides in 57% yield.

Phenyl glucoside prepared by this method was separated as the main fraction on a cellulose column in what at first appeared to be a 91% yield, with small amounts of D-glucose, disaccharides, and 1,6-anhydro-β-D-glucose in the other fractions. The mixture of phenyl α- and β-D-glucoside, with the former anomer predominating, was found to contain a minor constituent of similar but not identical constitution. Removal of the phenyl glucosides from admixture with the unknown constituent was achieved by scission of the glucosidic linkage in the former with an excess of boron trichloride in dichloromethane,[1] followed by chromatographic separation on a cellulose column. The unknown substance was reactive towards reagents which detect a free phenolic group (unlike phenyl glucosides) and its ultraviolet absorption spectrum showed a shift of the absorption band at 275 mμ (due to phenolic OH) to 293 mμ when the aqueous solution was made alkaline (as expected no shift occurred under similar conditions with phenyl glucoside). Oxidation with lead peroxide in alkaline solution gave a product which on examination by paper chromatography and ionophoresis appeared to be principally *p*-hydroxybenzoic acid together with some of the *ortho*-isomer. The evidence strongly suggests that the additional constituent present in the phenyl glucoside fraction was mainly *p*-hydroxyglucosylbenzene, formed by glucosylation of the phenol at its *para*-position, accompanied by a smaller amount of the *ortho*-isomer.

In a similar manner other phenols converted into their glucosides with the methyl α-D-glucoside–boron trichloride reagent included quinol, resorcinol, saligenin (forming 2-hydroxybenzyl glucoside and salicin), and pyrogallol (forming 2,3- and 2,6-dihydroxyphenyl glucoside). Some glucosylation of the aromatic nucleus may have occurred with these substrates also, but a detailed investigation was not carried out; the main product in each case appeared to be the glucoside.

Similar types of reaction were obtained when the reagent was prepared from phenyl α-D-glucoside and boron trichloride; refluxing this reagent with catechol in dichloromethane produced catechol glucoside, and refluxing the reagent with absolute methanol gave methyl glucoside.

The Synthesis of Glucopyranosylbenzene.—The direct glucosylation of benzene has previously been carried out by a Friedel–Crafts reaction with tetra-*O*-acetyl-α-D-glucosyl chloride and a large excess of aluminium chloride.[6] It has been found that a slightly higher yield of glucopyranosylbenzene can be obtained by the present procedure by refluxing the methyl α-D-glucoside–boron trichloride reagent with an excess of benzene and a small amount of aluminium chloride. The yield is considerably less if boron trichloride is omitted, and if the aluminium chloride only is excluded. The greater efficacy of boron trichloride than of aluminium chloride in converting methyl α-D-glucoside into a glucosylating agent corresponds to its greater capacity for demethylation; *e.g.*,

Hurd and Bonner, *J. Amer. Chem. Soc.*, 1945, **67**, 1664.

both 2,3,4,6-tetra-*O*-methyl-D-glucose and methyl α-D-glucoside are demethylated completely by boron trichloride [1] but only partially by aluminium chloride.[7] Both reagents, however, are required to afford glucopyranosylbenzene in optimum yield.

The Synthesis of Disaccharides.—The usual synthesis of a disaccharide, by the Koenigs and Knorr reaction, can provide a particular structure if the acetylated monosaccharide halide is treated with a monosaccharide in which all positions except the one to be substituted are blocked by acetyl groups. Similar specificity may be possible with the methyl α-D-glucoside–boron trichloride reagent by using an appropriately acetylated monosaccharide. The present report, however, is limited to an analysis of the different disaccharides that were obtained when the reagent was treated with a suspension of D-glucose in nitrobenzene in the presence of silver oxide. The products were extracted with water from the nitrobenzene solution and were readily separated on a charcoal–Celite column. In the identification of the disaccharides present by paper chromatography and paper electrophoresis two particularly useful spray reagents were those based on diphenylamine [8] (which gives different colours according to the type of linkage) and triphenyltetrazolium chloride [9] (which reacts with all reducing glucose disaccharides except those with a 1,2-link). By combination of the fractions containing the same disaccharides seven main fractions were found. By assuming that glucose units only were present (subsequently confirmed by showing that glucose was the sole product of acidic hydrolysis of each disaccharide) it was possible to identify tentatively the disaccharides in each fraction. By chromatographic separation of each fraction on thick paper, pure specimens of four disaccharides were obtained—numbers 1a, 3, 5a, and 6 in the Table; number 7,

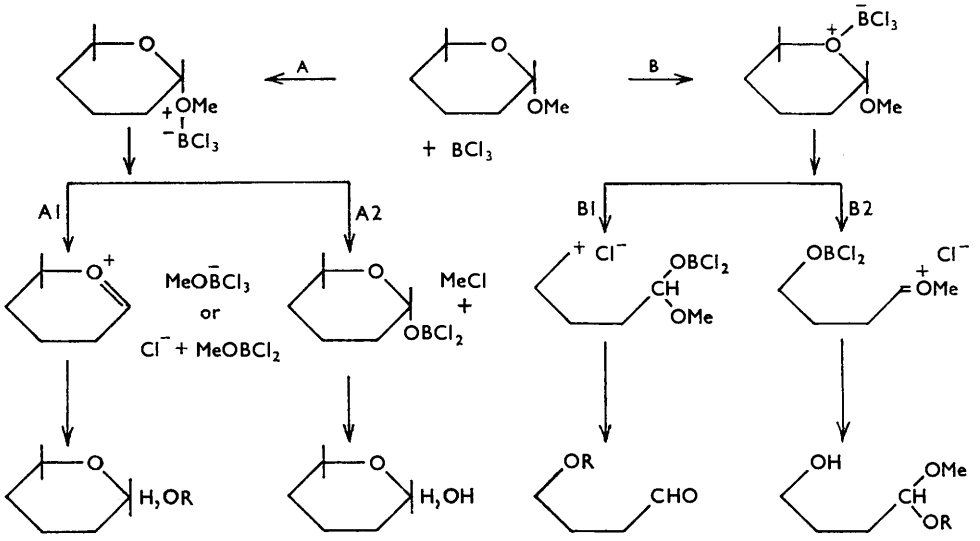
	Link indicated by:					Enzymic hydrolysis by:				
Disaccharide fraction no.	Paper chromatog.	Paper chromatog. of benzylamine derivative	Paper ionophoresis in borate buffer	Reaction with triphenyltetrazolium chloride	Colour with $NHPh_2$	almond β-glucosidase	α-glucosidase	glucamylase	M_s value: disaccharide alcohol	Conclusion
1a	1,6	1,6	1,6 or 1,3	+ve	Grey-green	−ve	+ve	—	0·83	Isomaltose
b	1,2	1,2 or 1,4	1,2	−ve	Yellow	−ve	+ve	—	—	Kojibose
2a	1,4	1,4	1,4	+ve	Blue	—	—	—	—	Maltose
b	1,3 or 1,1 (trace)	—	—	—	—	—	—	—	—	—
3	1,4	1,4	1,4	+ve	Blue	−ve	+ve	+ve	0·50	Maltose
4a	1,4	1,6 and	1,4	+ve	Blue	—	—	—	—	Maltose
b	1,6	1,2 and/or	1,6 or 1,3	+ve	Grey-green	—	—	—	—	Gentiobiose
c	1,2	1,4	—	−ve	Yellow	—	—	—	—	Sophorose
5a	1,6	1,6	1,6 or 1,3	+ve	Grey-green	+ve	−ve	—	0·77	Gentiobiose
b	1,2	—	1,2	−ve	Yellow	+ve	−ve	—	—	Sophorose
6	1,4	1,4	1,4	+ve	Blue	+ve	−ve	−ve	0·40	Cellobiose
7	1,3	1,3	1,6 or 1,3	+ve	Grey-green	+ve *	+ve *	—	0·06	Nigerose and laminaribiose

* Incomplete hydrolysis. M_s = distance migrated by substance/distance migrated by sorbitol.

similarly obtained as a chromatographically pure disaccharide specimen, was shown to be a mixture of nigerose and laminaribiose. The detailed results given in the Table show that eight of the eleven possible glucopyranose disaccharides are formed. Of these, the 1,6-linked products predominated, probably as a result of the greater availability of the primary hydroxyl group at $C_{(6)}$ of the glucose molecule. The preferential formation of 1,6-linked products has been observed in acid reversion, in which water is eliminated between glucose units to form a mixture of di-, tri-, and higher saccharides.[10] The α-isomers were found to predominate in the disaccharide synthesis.

[7] Saville, Ph.D. Thesis, London, 1960.
[8] Schwimmer and Bevenue, *Science*, 1956, **123**, 543.
[9] Wallenfels, *Naturwiss.*, 1950, **37**, 491.
[10] Thompson, Kimiko Anno, Wolfrom, and Inatome, *J. Amer. Chem. Soc.*, 1954, **76**, 1309.

The Mechanism of Glucosylation.—There is almost certainly some reaction between boron trichloride and the hydroxyl groups of methyl α-D-glucoside to form dichloroboronites or chloroboronates, but this reaction is ignored in the following discussion because it has no direct bearing on the mechanism of glucoside synthesis and because the subsequent methods of isolating the required products effectively remove the boron residues. Boron trichloride, in forming a glucosylating agent, could co-ordinate at the oxygen atom of either the methoxyl group (route A) or of the pyranose ring (route B) as shown in the chart. A resonance-stabilised glucosyl cation can be formed only in the first case (A1), the other possibilities (A2, B1, B2) all giving rise to dichloroboronites without any obvious glucosylating capacity. The conclusion that A1 is the most probable mechanism is confirmed by consideration of the probable course of treatment of the complex with an alcohol or phenol followed by water. The predicted reactions with the possible complexes are shown in the chart. In only one case (A1) is formation of a single glucoside stable in the presence of water likely to occur, in accordance with the experimental result. The other complexes would be expected to give a different result the probable products being glucose (A2), an ether of glucose (B1), and a mixed acetal, methyl alkyl (or phenyl) glucoside (B2). In the last case ring closure could occur with formation of either a mixture of methyl glucoside and an alkyl (or phenyl) glucoside or either one of these glucosides exclusively. The latter alternative requires the same product to be obtained whether the methyl glucoside–boron trichloride complex is treated with phenol or phenyl glucoside–boron trichloride with absolute methanol; experimentally the former reaction gives exclusively phenyl glucoside and the latter methyl glucoside, as predicted for mechanism A1. Mechanism A1 is in accord with the mechanism of reaction of boron trichloride with cyclic acetals.[11] The glucosyl cation shown in the A1 pathway has the electrophilic character necessary for direct aromatic substitution (*via* the $C_{(1)}$ atom), the property becoming more marked in the presence of a powerful Friedel–Crafts catalyst such as aluminium chloride.



There is one other possible mechanism affecting the A2 route based on one particular type of decomposition of alkyl dichloroboronites; at atmospheric or higher pressures under reflux or in sealed-tube reactions formation of an alkyl halide can occur. This decomposition in the product obtained in route A2 could lead to glucosyl chloride formation, but it is not likely because the experimental conditions under which the glucosylating

[11] Bonner and Saville, *J.*, 1960, 2851.

complex is obtained include reduced pressure, under which the most likely product from a dichloroboronite is a chloroboronate.[12]

The method of glucosylation described above is particularly useful in glycoside synthesis for the rapid preparation of reference compounds for paper-chromatographic analysis when a specific anomer is not required. As the method gives the free glycoside directly it should be valuable for the synthesis of alkali-labile phenolic glycosides which tend to decompose during deacetylation of the usual product of the Koenigs and Knorr reaction.

Experimental

Materials.—Boron trichloride and dichloromethane were purified as described previously.[1] Phenols and alcohols were recrystallised or redistilled and dried before use.

Paper Chromatography and Paper Ionophoresis.—Paper chromatography was carried out on Whatman No. 1 filter paper by the descending solvent technique. The following solvent systems were used: (1) butan-1-ol–ethanol–water (4 : 1 : 5); (2) propan-1-ol–ethyl acetate–water (7 : 1 : 2); (3) butan-1-ol–benzene–pyridine–water (5 : 1 : 3 : 3); (4) ethyl acetate–acetic acid–water (9 : 2 : 2); (5) butan-1-ol–acetic acid–water (12 : 3 : 5); (6) butan-1-ol–water (1 : 1). The organic phase was used where two phases were formed. In general the following spray reagents were used to detect the carbohydrates and their derivatives: (1) silver nitrate and ethanolic sodium hydroxide; (2) diazotised nitroaniline in hydrochloric acid, followed by sodium hydroxide; (3) triphenyltetrazolium chloride and sodium hydroxide; (4) diphenylamine, aniline, and phosphoric acid; (5) potassium periodatocuprate; (6) aniline hydrogen phthalate; (7) ninhydrin. Paper ionophoresis was carried out on Whatman No. 3 filter paper with the following buffer solutions: (1) borate (pH 10); (2) acetate (pH 5); (3) molybdate (pH 5).

Synthesis of Benzyl Glucoside.—A suspension of methyl α-D-glucoside (0·9 g.) in dichloromethane (5 ml.) was cooled to −80° in acetone–carbon dioxide. Boron trichloride (3·3 g.), cooled to the same temperature, was added, and the mixture was kept at −80° for 30 min., allowed to attain room temperature (the glucoside dissolving completely), and then kept overnight at room temperature. The excess of boron trichloride and solvent was removed by evaporation under diminished pressure, leaving a glass-like residue. Benzyl alcohol (6 ml.; dried over anhydrous magnesium sulphate and redistilled) and silver oxide (4·0 g., dried *in vacuo* at 60° in the dark) were added and the mixture was shaken in a darkened flask for 24 hr. Silver oxide and silver chloride were filtered off and the filtrate was concentrated. Chromatograms of the filtrate in solvent system 1 showed two main components—glucose and benzyl glucoside ($R_{glucose}$ = 5·4). Separation was effected with a Celite column and solvent system 6. Benzyl glucoside appeared in the early fractions and was indistinguishable from the β-isomer on paper chromatography in solvent systems 1, 3, and 4. It gave a positive reaction with the silver nitrate–sodium hydroxide spray but none with aniline hydrogen phthalate, indicating substitution at the reducing positions of glucose. Ionophoretograms in borate buffer at pH 10 showed one product only; this had M_G 0·12 (M_G for benzyl β-D-glucoside = 0·12). Aqueous hydrolysis with an acid resin, Amberlite IR-120 (H^+), showed the presence of D-glucose only in chromatographic tests. Treatment for 7 days at 27° with almond β-glucosidase resulted in almost complete hydrolysis to D-glucose; with α-glucosidase, no hydrolysis was apparent. After several crystallisations of the glucoside from ethyl acetate, a product (0·47 g.), m. p. 121°, was obtained (Found: C, 57·8; H, 6·9. Calc. for $C_{13}H_{18}O_6$: C, 57·8; H, 6·7%). Acetylation with acetic anhydride in dry pyridine gave benzyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucoside, m. p. and mixed m. p. 96°; Fischer and Helferich [13] gave m. p. 96—101°.

Synthesis of Catechol Glucoside.—Methyl α-D-glucoside (3 g.) was treated with boron trichloride (9 g.) as described above. The residue remaining after removal of the excess of boron trichloride and solvent was treated with a solution of catechol (6 g.) in dichloromethane (30 ml.). When the initial evolution of gas had ceased the solution was heated under reflux at 50° for 2 hr. and then cooled. Ether (dried over sodium) was added to this solution until precipitation was complete. The precipitate was filtered off, washed with ether, and made into a slurry with chromatography solvent system 1. A portion of this precipitate remained insoluble and

[12] Gerrard and Lappert, *Chem. Rev.*, 1958, **58**, 1081.
[13] Fischer and Helferich, *Annalen*, 1911, **383**, 68.

was filtered off and neglected as it was shown by paper chromatography to contain no carbohydrates other than a trace of glucose. The filtrate was introduced at the top of a cellulose column (55 × 4·7 cm.) and eluted with solvent system 1; 25-ml. fractions were collected. Analysis of the fractions by paper chromatography showed separation of the three main products: (A) catechol glucoside, (B) glucose, and (C) disaccharides.

Fraction A was indistinguishable from catechol D-glucoside by paper chromatography in solvent systems 1, 3, and 4 and by paper ionophoresis in borate buffer at pH 10. It was partially hydrolysed by both almond β-glucosidase and α-glucosidase. The incubation period was 48 hr. at 37°. Recrystallisation of the product in fraction A from aqueous methanol and light petroleum gave colourless crystals (2·4 g., 57%), $[\alpha]_D^{20}$ +29° (*c* 3 in water) (Found: C, 49·8; H, 6·4. Calc. for $C_{12}H_{16}O_7,H_2O$: C, 49·6; H, 6·2%). Helferich *et al.*[14] gave for catechol β-D-glucoside, $[\alpha]_D^{20}$ −71° in water.

Concentration of fraction B gave D-glucose (0·05 g.), while fraction C yielded a mixture of several disaccharides and was not investigated further.

Synthesis of Phenyl Glucoside.—Methyl α-D-glucoside (5 g.) was treated with boron trichloride (15 g.) as above. The residue remaining after removal of the excess of solvent and boron trichloride was heated under reflux for 1½ hr. with phenol (9 g.) in dichloromethane (25 ml.). Further phenol (4 g.) in dichloromethane was then added and the solution was re-heated for 1 hr. The reaction was completed and the products were separated in the same way as in the previous experiment. Four main fractions were obtained—D (phenyl glucoside), E (1,6-anhydro-β-D-glucose), F (glucose), and G (disaccharides).

Fraction G consisted principally of a mixture of disaccharides. Fraction E was indistinguishable from 1,6-anhydro-β-D-glucose by paper chromatography and, like 1,6-anhydro-β-D-glucose, did not migrate in borate buffer. Concentration of fraction E gave 1,6-anhydro-β-D-glucose (0·012 g.), m. p. and mixed m. p. 178°. D-Glucose (0·04 g.) was obtained on concentration of fraction F.

Fraction D yielded a white solid (6 g.), m. p. 158°, which was found to consist principally of phenyl glucoside but a second component (X) was also present.

The mixture (2·0 g.) was separated by chromatography on charcoal–Celite with aqueous ethanol (0—50%) as the eluent, but only about 15% of the starting material was recovered. Three fractions H, J, and K were obtained. Fractions H and J showed similar chromatographic behaviour but the former reduced the silver nitrate reagent more slowly; a similar difference in this rate may be observed between phenyl α- and β-D-glucoside.

Fraction H yielded phenyl α-D-glucoside (0·2 g.), m. p. and mixed m. p. 170°, $[\alpha]_D^{20}$ +175° (*c* 0·4 in water). Bunton *et al.*[15] gave for phenyl α-D-glucoside, m. p. 169—170°, $[\alpha]_D^{25}$ +181° (*c* 0·65 in water). It was hydrolysed by 0·1N-hydrochloric acid and by α-glucosidase to phenol and glucose, but it was not hydrolysed by almond β-glucosidase. In addition, fraction H was indistinguishable from phenyl α-D-glucoside by paper chromatography and paper ionophoresis.

Similarly fraction J yielded phenyl β-D-glucoside (0·06 g.), m. p. 174—175°, mixed m. p. 174°, $[\alpha]_D^{20}$ −71° (*c* 0·4 in water) [Bunton *et al.*[15] gave for phenyl β-D-glucoside m. p. 173·5—174·5°, $[\alpha]_D^{25}$ −70·7° (*c* 2·0 in water)], indistinguishable from phenyl β-D-glucoside by paper chromatography and paper ionophoresis. Hydrolysis by hydrochloric acid (0·1N) and by almond β-glucosidase yielded phenol and glucose, but it was not hydrolysed by α-glucosidase.

The solid obtained from fraction D (4·0 g.) was dissolved in dichloromethane and cooled to −80°, and boron trichloride (10 g.) was added. The mixture was kept at −80° for 30 min. and at room temperature for 16 hr. under anhydrous conditions. The excess of solvent and boron trichloride was evaporated off at room temperature under diminished pressure. Methanol (3 × 10 ml.) containing a little water was added to the residue and distilled off. The products were separated on a cellulose column, being eluted with solvent system 1. One component (X) (0·1 g.), a colourless oil, gave a positive reaction with the silver nitrate–ethanolic sodium hydroxide and with the diazotised nitroaniline spray (fraction K had reacted similarly).

The ultraviolet spectra of ethanolic solutions of component X and phenyl β-D-glucoside were measured in the range 250—300 mμ. The spectra were measured again after the solutions of component X and phenyl β-D-glucoside had been made alkaline with 0·2% alcoholic potassium hydroxide. Phenyl β-D-glucoside gave absorption bands at 268 and 275 mμ before and after

[14] Helferich, Lang, and Schmitz-Hillebrecht, *J. prakt. Chem.*, 1933, **138**, 276.
[15] Bunton, Lewis, Llewellyn, and Vernon, *J.*, 1955, 4419.

addition of potassium hydroxide, while component X showed a band shift from 268 and 275 mμ to 293 mμ on addition of potassium hydroxide.

Potassium hydroxide (0·25 g.), component X (0·03 g.), and water (0·5 ml.) were heated to 220° and lead peroxide (0·17 g.) was added with continuous stirring. Heating and stirring were continued for 1 hr. and 2N-sulphuric acid was added until the solution was almost neutral. The solution was filtered, acidified, and extracted with ether. Paper chromatography and paper ionophoresis of the resulting solution with acetate and borate buffer solutions showed the presence of *p*-hydroxybenzoic acid with smaller amounts of *o*-hydroxybenzoic acid and phenol.

Synthesis of Glucopyranosylbenzene.—Methyl α-D-glucoside (10·8 g.) was treated with boron trichloride (31 g.) in the usual way. Benzene (300 ml.) and aluminium chloride (5 g.) were added to the solid complex and the mixture was heated under reflux with stirring for 7 hr. After 16 hr. at room temperature the catalyst complex was decomposed with water (500 ml.), and the solution was centrifuged. The benzene layer was separated and washed with water and 10% aqueous sodium hydroxide. The combined aqueous layer and washings were neutralised with sodium hydroxide, and the precipitated aluminium oxide was filtered off. Concentration of the aqueous extract gave an oil which was extracted with boiling pyridine. This solution was in turn evaporated to dryness and extracted with cold chloroform, giving glucopyranosylbenzene (4·3 g., 32%). The product was identified by reaction with acetic anhydride and sodium acetate, to give tetra-*O*-acetyl-β-D-glucopyranosylbenzene, m. p. and mixed m. p. 155—156°, $[\alpha]_D^{25}$ −17° (*c* 0·6 in $CHCl_3$) (Found: C, 58·6; H, 6·05. Calc. for $C_{20}H_{24}O_9$: C, 58·8; H, 5·9%). Hurd and Bonner [6] give m. p. 156·5°, $[\alpha]_D^{25}$ −16·4° (*c* 0·85 in $CHCl_3$). A similar experiment with the boron trichloride omitted gave glucopyranosylbenzene (1·5 g., 11%).

Synthesis of Glucose Disaccharides.—Methyl α-D-glucoside (12 g.) was treated with boron trichloride (50 g.) as described above. The residue remaining after removal of the excess of solvent and boron trichloride was treated with a suspension of D-glucose (12 g.) in dry nitrobenzene (50 ml.). The whole was shaken with silver oxide (25 g.; dried *in vacuo* at 60°) in a darkened flask for 18 hr. The solution was filtered, the residue washed with water, and the nitrobenzene solution extracted with water. The combined aqueous extracts and washings were neutralised with sodium hydrogen carbonate and concentrated at 40°. A charcoal–Celite column eluted with aqueous ethanol was used to separate the products. The fraction containing the same disaccharide or mixture of disaccharides was combined, giving seven main fractions: 1 (0·53 g.), 2 (0·10 g.), 3 (0·50 g.), 4 (0·20 g.), 5 (0·18 g.), 6 (0·10 g.), 7 (0·24 g.).

These fractions were freeze-dried and purified by chromatography on sheets of thick filter paper (Whatman No. 3), eluted with solvent system 1. Guide strips were cut off and the diphenylamine spray reagent was used to locate the disaccharides. By cutting out the appropriate sections and eluting them with water, chromatographically pure specimens of disaccharides 1a, 3, 5a, 6, and 7 (two) were obtained (see Table). The following scheme was used for the identification of the disaccharides: (*a*) Paper chromatography and paper ionophoresis. (*b*) Hydrolysis. (i) Hydrolysis by 1·5N-hydrochloric acid at 100° for 4 hr. (ii) Enzymic hydrolysis by α-glucosidase, almond β-glucosidase, and glucamylase; incubation periods 48 hr. at 37°, 48 hr. at 37°, and 6 hr. at 50°, respectively. (*c*) Reduction followed by paper ionophoresis in molybdate buffer.[16] Each disaccharide (2 mg.) was dissolved in water (0·5 ml.) and reduced with a solution of potassium borohydride (2 mg.) in water (0·5 ml.) at room temperature for 18 hr. Amberlite IR-120 (H^+) resin (0·1 g.) was added and the mixture shaken. The solution was decanted off and concentrated to dryness under diminished pressure at room temperature. Dry methanol (3 × 2 ml.) was added and the whole evaporated to dryness. The resulting disaccharide alcohols were analysed by paper ionophoresis in molybdate buffer solution at pH 5.

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[16] Bourne, Hutson, and Weigel, *Chem. and Ind.*, 1959, 1047.