591. *Dealkylation and Deacylation of Carbohydrate Derivatives with Boron Trichloride and Boron Tribromide.*

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The use of boron trichloride and boron tribromide is described for the deacylation and demethylation of mono-, di-, and poly-saccharide derivatives, the last two types being converted into the monosaccharide constituents.

All the monosaccharides investigated are stable to the reagent, except fructose and sorbose which are both degraded to 5-hydroxymethylfurfuraldehyde.

THE oxygen atoms of ethers, esters, and many other derivatives of carbohydrates provide sites for co-ordination with electron-deficient molecules such as Lewis acids. Since some diversity of co-ordinating power can arise in a molecule through variation in polar character and steric environment of these basic oxygen centres there are clearly possibilities for effecting particular reactions at selected sites. Some initial studies with aluminium chloride were only partially successful because this reagent is difficult to separate from the products of reaction. Boron trichloride does not have this disadvantage and has proved to be a versatile reagent in carbohydrate chemistry, as has already been reported briefly.[1] Although it is a gas at room temperature (b. p. 12°), boron trichloride is strongly reactive at temperatures well below its boiling point and can easily be handled in a medium such as a mixture of solid carbon dioxide and acetone (*ca.* −80°).[2] One of its valuable uses is for removal of *O*-methyl groups from methylated sugars which provides a rapid and

[1] Allen, Bonner, Bourne, and Saville, *Chem. and Ind.*, 1958, 630.
[2] Gerrard and Lappert, *J.*, 1951, 2545.

convenient method of identifying the monosaccharide units in a methylated polysaccharide, or in the methylated monosaccharides derived therefrom. The polysaccharide requires only partial methylation, sufficient to effect dissolution in the reagent, and partial acetylation is equally effective. A survey of this method of converting carbohydrate derivatives into the monosaccharide units present has been carried out for over 60 compounds and forms the main subject of this paper. Cyclic *O*-methylenedioxy-, *O*-ethylidene-dioxy-, and *O*-benzylidenedioxy-derivatives of hexitols also react with boron trichloride, giving the unsubstituted hexitol as the main product; the mechanism of this ring opening is the subject of a separate report.[3]

All the monosaccharides so far investigated are unchanged by prolonged contact with boron trichloride, except fructose which, whether free or part of a higher saccharide, is always substantially converted into 5-hydroxymethylfurfuraldehyde; only traces of fructose itself survive.

The formation of oligosaccharides in some reactions indicated that boron trichloride can initiate syntheses in some cases; *e.g.*, with methyl α-D-glucoside co-ordination at the glycosidic oxygen could lead to the formation of a glucosyl cation, the hemiacetal character of a glucoside providing resonance stabilisation through the ring oxygen atom adjacent
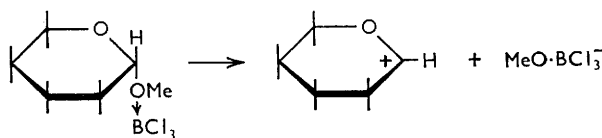
to $C_{(1)}$. The ionic complex may undergo conversion into glucosyl chloride and methoxy-boron dichloride but under suitable conditions either form should behave as a glucosylating agent. This possibility has been investigated by removing the excess of boron trichloride from the product of its reaction with methyl α-D-glucoside and adding an excess of a suitable substrate. The expected products have been obtained with benzene, phenols, and glucose, the last forming a number of disaccharides. This synthetic use of boron trichloride is being investigated further.

Reactions with boron trichloride are conveniently carried out in dichloromethane which is inert and easily removed. Few solvents are suitable since the reagent co-ordinates readily with any electronegative centre in the solvent molecule and even if there is no subsequent decomposition the complex formed is usually non-volatile. The only other solvents which appear to have found use are n-pentane [2] and tetrahydropyran.[4] Reaction of a substrate with boron trichloride requires a homogeneous environment. This is sometimes achieved without the addition of a solvent, dissolution gradually occurring in the boron trichloride as the temperature rises from *ca.* −80° to room temperature. Where dissolution did not occur, boron tribromide (b. p. 92°) often provided an alternative. Disaccharides, in particular, which were recovered unchanged from prolonged contact with boron trichloride underwent partial dissolution in boron tribromide with the expected scission at the glycosidic linkage. Boron tribromide was also more effective in the reaction with tri-*O*- and tetra-*O*-methyl-D-glucose, almost complete demethylation being effected in a single treatment in both cases, in contrast to the formation of some partly methylated derivatives in the reaction with boron trichloride.

In the general procedure, the reactants and solvent were mixed at *ca.* −80°, allowed to attain room temperature, and left overnight. After removal of excess of boron trichloride and dichloromethane, and treatment of the residue with methanol or silver carbonate, the product was isolated and examined by paper chromatography in several different solvents; where desirable, separation by ionophoresis in a borate buffer was also

[3] Bonner and Saville, *J.*, 1960, 2851.
[4] Brown and Tierney, *J. Amer. Chem. Soc.*, 1958, **80**, 1552.

used. The results reported in detail in the Table are based on a qualitative examination only of 1—10 mg. amounts of substrate.

Methylated monosaccharides form the monosaccharide as the chief product (see Table),

Substance	Principal product	Other products *
Methylated sugars		
2,3,5-Tri-O-methyl-L-arabinose	Arabinose	Oligosaccharides, 2·7 † ‡, 3·8 † ‡
2,4-Di-O-methyl-L-arabinose	Arabinose	1·4 † ‡
Me 2,3,4-tri-O-methyl-α-L-fucoside	Fucose	0·9 † ($R_{\rm F}$)
2-O-Methyl-L-fucose	Fucose	Oligosaccharides, 2-O-methyl-fucose †
2,3,4,6-Tetra-O-methyl-D-galactose and 3,4-di-O-methyl-L-rhamnose	Galactose, rhamnose	0·88 † ($R_{\rm F}$)
2,3,4,6-Tetra-O-methyl-D-glucose	Glucose	Mono-, di-, and tri-O-methyl-glucoses
2,3,6-Tri-O-methyl-D-glucose	Glucose	Mono- and di-O-methyl-glucoses, 0·77 † ($R_{\rm G}$)
Me 2,3-di-O-methyl-α-D-glucoside	Glucose	Mono-O-methylglucoses †
3-O-Methyl-D-glucose	Glucose	3-O-Methyl-D-glucose †
2,3,4,6-Tetra-O-methyl-D-mannose	Mannose	0·37, 0·52, 0·61 †, 0·74, 0·93 ($R_{\rm G}$) ‡
3,4-Di-O-methyl-D-mannose monohydrate	Mannose	0·40, 0·56 ($R_{\rm G}$) ‡
Di-O-methylsucroses	Glucose, 5-hydroxymethyl-furfuraldehyde	Fructose,† di-O-methyl-sucroses †
3-O-Methyl-D-xylose	Xylose	—
Methylated amylopectin	Glucose	Mono- and di-O-methyl-glucoses
Methylated cellulose	Glucose	Mono- and di-O-methyl-glucoses
Glycosides		
Me β-D-arabinoside	Arabinose	Me β-D-arabinoside †
Me α-D-fructofuranoside	Fructose, 5-hydroxymethyl-furfuraldehyde	—
Me α-D-galactoside	Galactose	—
Me β-D-galactoside	Galactose	—
Me α-D-glucoside	Glucose	Oligosaccharides †
Me β-D-glucoside	Glucose	—
Ph α-D-glucoside	Glucose, phenol	—
Ph β-D-glucoside	Glucose, phenol	—
Quinol β-D-glucoside (arbutin)	Glucose, quinol	—
o-Hydroxymethylphenyl β-D-glucoside (salicin)	Glucose, saligenin	—
Me α-D-mannoside	Mannose	Oligosaccharides †
Me α-L-rhamnoside	Rhamnose	—
Me β-D-riboside	Ribose	—
Me α-D-xylofuranoside	Xylose	—
Acetals and ketals		
4,6-O-Benzylidene-D-glucose	Glucose	—
Me 4,6-O-benzylidene-α-D-glucoside	Glucose	—
1,2:5,6-Di-O-isopropylidene-D-glucose	Glucose	—
1,2-O-Isopropylidene-D-glucose	Glucose	—
2,3:4,5-Di-O-isopropylidene-D-fructose	5-Hydroxymethylfurfur-aldehyde	Fructose †
Acetylated sugars		
Octa-O-acetylgentiobiose	Glucose	Gentiobiose, 1·15, 1·5 ᵃ
Penta-O-acetyl-β-D-glucose	Glucose	2·7, 5·0 †
Octa-O-acetylsucrose	Glucose, 5-hydroxymethyl-furfuraldehyde	2·4 †
Acetylated amylopectin	Glucose	Oligosaccharides, 1·9, 2·2
Acetylated cellulose	Glucose	Oligosaccharides, 1·9, 2·2
Anhydro-sugars		
1,6-Anhydro-β-D-galactopyranose	Galactose	Oligosaccharides
1,6-Anhydro-α-D-galactofuranose	Galactose	Oligosaccharides
1,6-Anhydro-β-D-glucopyranose	Glucose	Oligosaccharides
1,6-Anhydro-β-D-gulopyranose	Gulose	Oligosaccharides
1,6-Anhydro-β-D-mannopyranose	Mannose	Oligosaccharides
Me 2,3-anhydro-4,6-O-benzylidene-α-D-mannoside	2·3, 2·5 ($R_{\rm mannose}$)	4·7 † ($R_{\rm mannose}$)
Me 2,3-anhydro-β-L-riboside	0·7, 1·7 ($R_{\rm ribose}$)	

TABLE. (*Continued.*)

Substance	Principal product	Other products *
Monosaccharides		
L-Arabinose	Arabinose	Oligosaccharide †, 2·4 † ($R_{glucose}$)
D-Galactose	Galactose	
D-Glucose	Glucose	
D-Lyxose	Lyxose	
D-Mannose	Mannose	
L-Rhamnose	Rhamnose	
D-Xylose	Xylose	
D-Fructose	5-Hydroxymethylfurfur-aldehyde	0·90 † (R_F)
L-Sorbose	5-Hydroxymethylfurfur-aldehyde	Sorbose
Disaccharides		
Lactose	Galactose, glucose	Lactose
Maltose	Glucose	Maltose
Melibiose	Galactose, glucose	Melibiose †, 1·6 † ($R_{glucose}$)
Sucrose	Glucose, 5-hydroxymethyl-furfuraldehyde	Sucrose †
Turanose	Glucose, 5-hydroxymethyl-furfuraldehyde	Fructose †
Miscellaneous		
Raffinose	Galactose, glucose, 5-hydr-oxymethylfurfuraldehyde	Fructose †
Inulin	5-Hydroxymethylfurfur-aldehyde	
Nitrocellulose	Glucose	0·38, 2·1, 3·6 †
Me 4,6-*O*-benzylidene-2,3-di-*O*-methyl-α-D-glucoside	Glucose	Mono- and di-*O*-methyl-glucoses, 0·70 † (R_G)
Me 4,6-*O*-benzylidene-2-*O*-*p*-toluene sulphonyl-α-D-glucoside	5·7 ($R_{glucose}$)	Glucose †

* Unless otherwise stated, unidentified products are indicated by R_x values in butanol–ethanol–water (4 : 1 : 5), where *x* refers to the principal product in each case. R_G indicates that 2,3,4,6-tetra-*O*-methyl-D-glucose is the reference compound.

† Traces only present. ‡ Probably partially methylated products. ᵃ Solvent propan-1-ol–ethyl acetate–water (7 : 1 : 2).

and frequently any other formed is only present in traces. Highly methylated sugars that are not completely demethylated in a single treatment with boron trichloride give the expected partially methylated derivatives which in some cases were identified chromato-graphically; when authentic compounds were not available for comparison, the R_F values of the products clearly indicated this type of derivative. In the case of the monomethyl product from 2,3,4,6-tetra-*O*-methyl-D-glucose, elution from the paper on which it was separated and examination of the eluted product by ionophoresis established that no selective demethylation had occurred. The M_G values of 0·21 and 0·81 (with values of 0·26 and 0·82 in a duplicate determination) indicate the presence of either or both 2- (M_G 0·23) and 4-*O*-methylglucose (M_G 0·24), and of either or both the 3- (M_G 0·82) and 6-*O*-methylglucose (M_G 0·82).[5] The two methylated polysaccharides gave mainly glucose as expected, with some mono- and di-*O*-methylglucose. Di-*O*-methylsucrose is converted into glucose and 5-hydroxymethylfurfuraldehyde; the latter showed the same chromato-graphic behaviour as the product obtained on a preparative scale directly from the same treatment of fructose. The structure of this product was established by comparison of its ultraviolet absorption spectrum with that of an authentic specimen and by conversion by mild oxidation into 5-hydroxymethyl-2-furoic acid. Stoicheiometrically, the reaction involves loss of three molecules of water from fructose. Mechanisms have been proposed for this dehydration when brought about by acids[6] and by iodine in dry dimethyl-formamide.[7] In the latter reaction, the presence of the furanoside ring and of the attached hydroxy- and hydroxymethyl groups at the tertiary carbon atom at position 2 provide

[5] Foster, *J.*, 1953, 982.
[6] Haworth and Jones, *J.*, 1944, 667.
[7] Bonner, Bourne, and Ruszkiewicz, *J.*, 1960, 787.

a plausible route for the progressive elimination of three molecules of water. A similar scheme for the interaction with boron trichloride could be formulated based on the formation of a carbonium ion at $C_{(2)}$ similar to that of the glucosyl ion (above), followed by elimination of a proton at $C_{(1)}$ to give an aldehyde group; the aldehyde group would assist the elimination of the second and third molecules of water from positions 2,3 and 4,5 by resonance stabilisation through conjugation with the olefinic bonds so formed, as in the iodine reaction.

Glycosides, acetals, and ketals are converted almost exclusively into the parent sugar (accompanied on chromatograms by the corresponding aglycone in the case of the phenyl glucosides), except when a fructose unit is present. Acetylated sugars behave similarly, but small amounts of subsidiary products are formed which appear to be incompletely deacetylated derivatives; oligosaccharides appear in addition with cellulose and amylopectin acetates. Nitrocellulose also gives glucose as the main product, with smaller amounts of other derivatives. The behaviour of 1,6-anhydro-sugars contrasts with that of 2,3-anhydro-compounds. The former react normally with boron trichloride, but neither of the 2,3-anhydro-sugars examined gave detectable quantities of the parent sugar, the chief products in both cases having R_F values well removed from the expected values. Chloro-sugars may be formed with these substrates and this possibility is being examined. No evidence has been obtained that any monosaccharide formed as the principal product in the reaction of boron trichloride with its derivatives itself undergoes detectable degradation with this reagent under the experimental conditions reported in the Table. The effect of boron tribromide was examined when no dissolution in boron trichloride was apparent, but no differences in the type of reactivity of the two reagents were observed. D-Fructose forms 5-hydroxymethylfurfuraldehyde with both reagents; this product is also obtained by the action of boron tribromide on L-sorbose, which is not soluble in boron trichloride.

The disaccharides investigated, together with raffinose, did not dissolve in or react with boron trichloride, but reaction occurred with boron tribromide in all cases, with fission into the expected monosaccharide units; as expected, 5-hydroxymethylfurfuraldehyde appears in the products from sucrose, turanose, and raffinose with only traces of fructose. This was the only product from inulin which, in contrast to the other three substrates, reacts with boron trichloride.

One type of sugar derivative which is being investigated further is that containing the toluene-*p*-sulphonyl group. Only a trace of glucose was obtained from methyl 4,6-*O*-benzylidene-2-*O*-toluene-*p*-sulphonyl-α-D-glucoside, the main product having a high R_F value. Unless there is some particular effect exerted by the toluene-*p*-sulphonyl group, the α-methyl and benzylidene groups should be completely removed by the reagent; the product might then be the monotoluene-*p*-sulphonyl ester. If this is the case, it should be possible to demethylate methylated toluene-*p*-sulphonic esters of sugars with retention of the ester group.

EXPERIMENTAL

Materials.—Commercial methanol was used without purification.

Boron trichloride was handled as described elsewhere.[3] Boron tribromide (b. p. 92°) was distilled before use. Dichloromethane was washed with 5% aqueous sodium carbonate and water, dried (CaCl$_2$), and distilled, the fraction boiling at 39·5—41° being collected.

Paper Chromatography and Paper Ionophoresis.—Paper chromatography was carried out on Whatman No. 1 filter paper, with the following solvents (the organic phase being used where two phases form): (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 (4 : 1 : 5). The sprays most commonly used to detect the sugars and their derivatives were: (1) silver nitrate and ethanolic sodium hydroxide; (2) *p*-anisidine hydrochloride; (3) aniline hydrogen phthalate; (4) urea hydrochloride; (5) diphenylamine, aniline, and phosphoric acid; (6) 2,4-dinitrophenylhydrazine and

hydrochloric acid; (7) α-naphthol and phosphoric acid; (8) phloroglucinol and trichloroacetic acid; (9) potassium periodatocuprate.[8]

Paper ionophoresis was carried out on Whatman No. 3 paper in borate buffer (0·2M) at pH 10·0.

Interaction of Sugar Derivatives and Boron Trichloride.—The sugar derivative (1—10 mg.) was dissolved or suspended in dry dichloromethane (1—2 ml.) and cooled in acetone–solid carbon dioxide. Boron trichloride (1—2 g.), cooled to −80°, was then added. The mixture was kept at −80° for 30 min., then allowed to warm to room temperature and kept for 16 hr. under anhydrous conditions. Substances which were insoluble in dichloromethane initially frequently became soluble as the mixture attained room temperature. Any solvent or boron trichloride remaining was removed under diminished pressure at room temperature. The glassy residue was treated by adding either (*a*) methanol (3 × 3 ml.) and evaporating to dryness under diminished pressure after each addition or (*b*) an aqueous suspension of silver carbonate to neutralise the solution, filtering from the insoluble silver salts, and freeze-drying the aqueous filtrate. The residue in either case was dissolved in a small amount of methanol or water and examined by paper chromatography and paper ionophoresis.

Interaction of D-Fructose and Boron Trichloride.—Boron trichloride (10 g.) was added to a suspension of D-fructose (1·6 g.) in dichloromethane at −80°. After 30 min. at −80° and 16 hr. at room temperature excess of boron trichloride and of dichloromethane was removed and the product treated by the silver carbonate method. On examination by paper chromatography (with solvents 1, 2, 3, and 5) and by paper ionophoresis, the principal product could not be distinguished from authentic 5-hydroxymethylfurfuraldehyde. This product was purified by chromatography on several sheets of thick paper (Whatman No. 3) in solvent 1. The papers were viewed under ultraviolet light, which rendered 5-hydroxymethylfurfuraldehyde visible. The appropriate sections were cut into thin strips and extracted with ether (Soxhlet). Concentration of the extract gave a syrup (0·4 g.) which was shown to be pure 5-hydroxymethyl-furfuraldehyde by chromatography and by oxidation with silver oxide (1 g.) and sodium hydroxide (1·6 g.) in water to 5-hydroxymethyl-2-furoic acid (0·37 g.), m. p. and mixed m. p. 165°. A solution of the sample in water had the same ultraviolet absorption spectrum as a pure sample of 5-hydroxymethylfurfuraldehyde.[9]

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[8] Bonner, *Chem. and Ind.*, 1960, 345.
[9] Wolfrom, Schuetz, and Cavalieri, *J. Amer. Chem. Soc.*, 1948, **70**, 514.