583. *Some Reactions of Sugars catalysed by a Cation-exchange Resin.*

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The cation-exchange resin, Amberlite I.R.-120, has been shown to be effective as a catalyst for the formation and hydrolysis of certain sugar glycosides and *iso*propylidene derivatives. Its catalytic activity has been compared with that of sulphuric acid in the hydrolysis of maltose, methyl-α-D-glucoside, sucrose, and starch (cf. Cadolte, Smith, and Spriestersbach, *J. Amer. Chem. Soc.*, 1952, **74**, 1501).

SUSMAN (*Ind. Eng. Chem.*, 1946, **38**, 1228) observed that acid-regenerated cation-exchange resins may sometimes advantageously replace free mineral or organic acid as catalysts for the formation of esters and for the inversion of sucrose. Bodamer and Kunin (*Amer. Chem. Soc.*, 118th Meeting, Sept., 1950) and Mariani (*Ann. Chim. appl.*, 1950, **40**, 500) studied quantitatively the rate of inversion of sucrose, and Haskell and Hammett (*J. Amer. Chem. Soc.*, 1949, **71**, 1284) studied the kinetics of hydrolysis of esters in the presence of a cation-exchange resin. They showed that reactions may be catalysed in both aqueous and non-aqueous solution, the rates being proportional to the weight of catalyst employed.

Furthermore, reduction of the particle size increased the catalytic activity, but below a certain minimum size the rate was limited by the chemical reaction rather than by the diffusion of the reactants into the body of the resin; for a maximum rate of reaction efficient agitation must be provided.

It has been observed that a number of reactions involving sugars may be satisfactorily catalysed by the solid-phase resin, providing that both the initial reactants are soluble in the liquid phase. The relative efficiency of the resin, compared with a free acid, varies with the nature of the reaction. Amberlite I.R.-120 was used for all the experiments detailed here. This resin is a strongly acidic sulphonated polystyrene of high exchange capacity, possessing excellent thermal stability, and insoluble in most solvents.

Catalysts of reactions by cation-exchange resins in place of soluble acids can greatly simplify manipulative procedure, since the catalyst may be readily removed by filtration. The removal of free acid catalysts at the end of the reaction, by means of anion-exchange resins, is sometimes impracticable since the sugars which contain potentially free aldehyde groupings may be absorbed or modified on the alkaline resin.

Hydrolyses of methyl-α-D-glucoside, maltose, and starch to glucose, inversion of sucrose, and formation of methylglucosides from glucose have been followed polarimetrically. In each case, parallel experiments, with either I.R.-120 or free sulphuric acid as catalyst, were carried out. The rate of reaction when the resin was used was, in each case, slower than when its equivalent of free sulphuric acid was used (for the determination of the equivalent weight of the resin, see the Experimental section). In contrast, Thomas and Davies (*Nature*, 1947, **159**, 372) observed enhanced catalytic activity in the hydrolysis of certain esters by sulphonic acid type cation-exchange resins in comparison with sulphuric acid.

In the presence of a cation-exchange resin, neutral salts present in the reactants may give rise to free acids by absorption of the cations. Thus, it is necessary to be cautious in attributing catalytic activity to the resin unless one can be quite certain of the absence of all anions from the reactants. In all the reactions studied here the possibility that the presence of free acid had made a significant contribution to the rate of reaction has been eliminated by checking, after the reaction was complete, that only a negligible quantity of free acid was present.

The rate of hydrolysis of a soluble starch, with a resin as catalyst, is exceedingly slow if the solution is first de-ionised by shaking it with mixed anion- and cation-exchange resins (Fig. 4, curve *B*). However, the use of a trace of free mineral acid in conjunction with the resin gives a rate of hydrolysis greater than the sum of the rates obtained when each is used separately (Fig. 4). Nevertheless, even in this case, the efficiency of the resin as a hydrolytic agent is only approximately one-twentieth of the value calculated from its equivalent weight. The addition of dry Amberlite I.R.-120 to an aqueous solution of glucose, maltose, or starch increases the optical rotation of the solution, suggesting that, while the solvent penetrates the body of the resin, the larger solute molecules do not penetrate the matrix so readily.

It therefore, appears that the inefficiency of the resin as a catalyst for the hydrolysis of starch may be due to the inability of the large molecules to penetrate the resin, but that the presence of a trace of free mineral acid degrades the starch to dextrins which may then diffuse into the body of the resin and undergo further hydrolysis by hydrogen ions associated with the resin.

A methylated starch was subjected to methanolysis and then hydrolysis in the presence of the resin, and the resultant methylated sugars obtained in high yield. The average chain length was determined by colorimetric estimation (Bartlett, Hough, and Jones, *Chem. and Ind.*, 1951, 76,) of the proportions of tetramethyl and trimethyl D-glucose and gave a value in good agreement with that obtained by hydrolysis of the same material in the presence of hydrochloric acid.

A further application of resin catalysis is in the isolation of " a reaction intermediate." Thus, when acetone is refluxed through an intimate mixture of mannitol and resin, contained in a Soxhlet thimble, a high yield of a mixture of mono- and di-*iso*propylidene mannitols was obtained, the former predominating. The reaction is largely prevented from giving

the fully substituted tri*iso*propylidene mannitol by the rapid removal, from the presence of the catalyst, of the soluble, partly substituted derivatives.

It has also been observed that the resin will catalyse the formation of methyl-α- and -β-L-arabofuranosides from L-arabinose and methyl alcohol, and of di*iso*propylidene D-glucose from glucose and acetone. 6-Methyl D-glucose has been obtained by the hydrolysis of a 6-methyl dimethylene D-glucose. A number of polysaccharides have been hydrolysed, but the possibility exists that hydrolysis was initiated by traces of acid derived from ash, present in the materials. Nevertheless, the practical utility of the method remains unimpaired, since, in each case, the amount of such free acid present was small enough to allow the solution to be evaporated to a syrup at 100° with no visible decomposition. The sugars produced on hydrolysis could then be separated and identified on the paper chromatogram in the usual manner (Partridge, *Biochem. J.*, 1947, **42**, 238).

An intimate mixture of an anion- and cation-exchange resin has been found to provide an efficient and rapid method for the removal of ash from neutral polysaccharides in both aqueous and non-aqueous solution, and no difficulty has been experienced in recovering the polysaccharides in high yield.

Experimental

Preparation of Resin.—The resin used throughout these experiments was Amberlite I.R.-120, analytical grade, 40—50 mesh. The resin was washed with 0·5N-sulphuric acid (3 l. per/l. of wet resin) on a sintered-glass filter, and then with distilled water until the washings were neutral. It was then washed with alcohol, and the excess of alcohol removed under reduced pressure at 30°.

Equivalent Weight of Resin.—A weighed quantity of resin was shaken with a known volume of 0·1N-sodium hydroxide for 1 hour, and the excess of alkali then determined with standard acid. The equivalent weight of the resin was **344**.

Experimental Procedure.—Reactions, unless otherwise stated, were carried out in sealed T-shaped Pyrex-glass tubes with optically flat end-plates. Agitation of the resin was accomplished by slowly rotating the tubes, which were immersed in a water-bath at the required temperature.

Effect of Addition of Resin on Rotation of Solutions.—An aqueous solution of glucose (5·59 c.c.; *c*, 9·95), containing a trace of ammonia, was placed in a T-shaped polarimeter tube and had α +3·19°. Dry Amberlite I.R.-120 (1·23 g.) was then added and the tube sealed and shaken for 3 hours, α was then +3·38°; this represents an absorption of 0·31 c.c. of water by the resin or 0·26 c.c. of water per g. of dry resin.

In the same manner, the resin was found to effect a change in rotation, equivalent to the absorption of 0·25 c.c. of water per/g. of dry resin from aqueous maltose, and 0·29 c.c. of water per g. of dry resin from aqueous starch.

No allowance has been made for this change in optical rotation in any of the following experiments.

Comparative Rates of Catalysis.—Maltose (0·273 g.), resin (1·03 g.), and water (4·5 c.c.) were sealed in the polarimeter tube and rotated in a water-bath at 100°, the optical rotation being observed at intervals. A parallel experiment was conducted with a known concentration of maltose in standard sulphuric acid. From the observed optical rotation and the known equilbrium rotations of maltose and glucose, the percentage of unhydrolysed maltose may be calculated. Fig. 1 shows the graph obtained by plotting the logarithm of the percentage of unhydrolysed maltose against time. It is linear, indicating that the reaction is of the first order. From the slope and the known concentrations of sulphuric acid and resin (with allowance for their respective equivalent weights), the resin is found to be 13% as efficient as sulphuric acid as a catalyst for this reaction.

In a similar manner, the relative efficiency of the resin as a catalyst for the hydrolysis of methyl-α-D-glucoside has been found to be 49% (Fig. 2), and in the inversion of sucrose at 25° 74% (Fig. 3).

Hydrolysis of Starch.—" AnalaR " soluble starch (20 g.) in water (100 c.c.) was heated at 40° for 1 hour and then de-ionised by shaking it with mixed I.R.-120–I.R.-400 resins, and all insoluble material removed on the centrifuge. The concentration of this solution (9·63% w/v) was determined by evaporating a known volume to dryness and weighing the residue. Four portions of solution were then placed in polarimeter tubes: (i) control, (ii) made N/50 with respect to sulphuric acid, (iii) containing I.R.-120 (25% w/v), and (iv) made N/50 with respect to sul-

phuric acid, I.R.-120 resin (25% w/v) being then added. Each tube was sealed and heated in a boiling-water bath. The course of the hydrolysis was followed by observing, at intervals, the change in optical rotation. The percentage hydrolysis was then calculated as for the hydrolysis of maltose. In Fig. 4 the logarithm of the percentage of starch dextrins remaining unhydrolysed is plotted against time.

Chain-length of a Methylated Starch.—Methylated waxy maize starch (0·3682 g.), methanol (6 c.c.), and resin (0·5 g.) were heated with shaking at 100° for 18 hours. Methanol was then removed by evaporation, and water (6 c.c.) added, and the tube resealed and heated at 100° for a further 30 hours. The resin was filtered off and the filtrate evaporated to a syrup (0·384 g.;

FIG. 1.

A, 0·416N *to I.R.*-120 *resin.*
B, 0·045N *to* H_2SO_4.

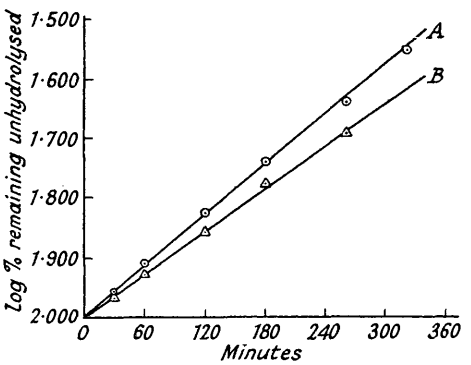


FIG. 2.

A, 0·312N *to I.R.*-120 *resin.*
B, 0·100N *to* H_2SO_4.

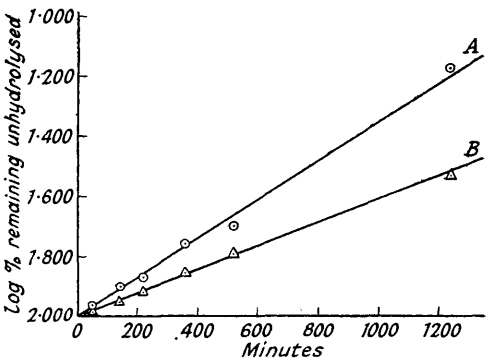


FIG. 3.

A, 0·46N *to I.R.*-120 *resin.*
B, 1·00N *to* H_2SO_4.

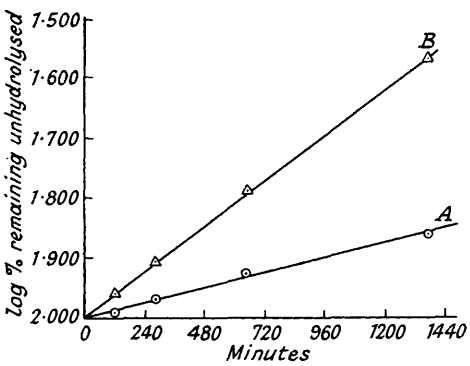
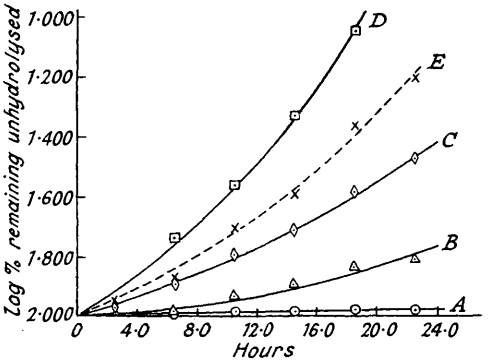


FIG. 4.

A, *Neutral control.*
B, 0·68N *to I.R.*-120 *resin.*
C, 0·02N *to* H_2SO_4.
D, 0·02N *to* H_2SO_4 *and* 0·88N *to I.R.*-120 *resin.*
E, *The sum of curves B and C.*



96%). End-group assay, by the colorimetric procedure, gave a chain length of 27, while a parallel experiment with hydrochloric acid gave a chain length of 25.

iso*Propylidene Mannitols.*—Mannitol (12 g.) and resin (16 g.) were intimately mixed in an extraction thimble and continuously extracted in a Soxhlet apparatus with boiling acetone for 18 hours. After cooling of the acetone extract, unchanged mannitol (0·60 g.) was removed by filtration and the filtrate evaporated to a syrup (19·43 g.), which was shaken with water (500 c.c.); crude tri*iso*propylidene mannitol was removed on the filter (4·3 g.; m. p. 68·5° on recrystallisation from light petroleum). Examination of the filtrate on the paper chromatogram, with benzene–ethanol–water (84 : 23 : 7, top layer) as the mobile phase and ammonical silver nitrate as the developer, indicated the presence of a preponderance of mono*iso*propylidenemannitol (R_F 0·11), a small amount of a di*iso*propylidene derivative (R_F 0·83), and a trace of mannitol (R_F 0·00).

Methylarabinosides.—L-Arabinose (0·1 g.), methanol (2 c.c.), and resin (0·1 g.) were shaken at 20° for 24 hours. The resin and a little undissolved arabinose were removed by filtration and the filtrate was concentrated to a syrup. Examination on the paper chromatogram, with ammoniacal silver nitrate as the developer, showed the presence of methyl-α- and -β-L-arabofuranosides contaminated with small quantities of methyl-α- and β-L-arabopyranosides and -L-arabinose.

*Di*iso*propylidene Glucose.*—D-Glucose (0·1 g.) and resin (0·1 g.) were suspended in acetone (2 c.c.) in a sealed tube and shaken at 20° for 5 days. The resin was removed by filtration, the filtrate concentrated to a syrup, and light petroleum (5 c.c.) added. Di*iso*propylidene D-glucose crystallised, and after one recrystallisation had m. p. 109° (70 mg.).

Di*iso*propylidene D-glucose was also prepared in 60% yield by the procedure used for the *iso*propylidene mannitol derivatives.

6-*Methyl* D-*Glucose.*—A 6-methyl dimethylene D-glucose (0·1 g.), resin (0·1 g.), and methanol (2 c.c.) were heated at 100° for 18 hours. The methanol was then removed by evaporation. Water (2 c.c.) was added to the residue and the tube was resealed and heated at 100° for a further 18 hours. The resin was removed by filtration and the filtrate on concentration crystallised, to yield chromatographically pure 6-methyl D-glucose, m. p. 140°.

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