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# USE OF POLYMERS AS PROTECTING GROUPS IN ORGANIC SYNTHESIS IV
# APPLICATIONS OF A POLYSTYRYLBORONIC ACID RESIN TO THE SELECTIVE FUNCTIONALIZATION OF SOME GLYCOSIDES

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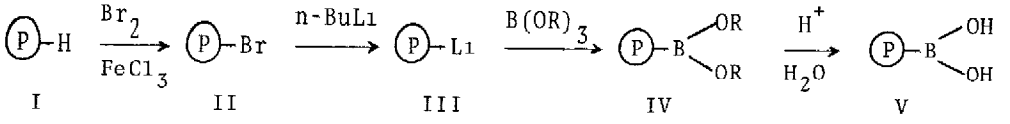
Several polymers have been developed recently for the protection of hydroxyl groups in polymer assisted syntheses Thus, a polymeric trityl chloride reagent was used for the protection of the C-6 hydroxyl group of a glycoside[1] and in the selective functionalization of several polyols[2] Earlier, a polymer containing acid chloride functional groups[3] was used in the monoprotection of several diols, and vinylbenzaldehyde resins[4,5] were utilized in the solid phase synthesis of 2 and 2,3-disubstituted derivatives of methyl α-D-glucopyranoside

The application of phenylboronic acid to the protection of diol functional groups has been studied extensively and has been most successful in the field of carbohydrate chemistry[6-8] Although cyclic boronate esters are formed very readily and are stable to a number of reaction conditions, many are also quite sensitive to humidity[9] and take up water with loss of the phenyl boronic acid These properties of boronate esters coupled to the advantages inherent to solid phase syntheses[10] make a polystyryl boronic acid resin particularly attractive, since it should provide a useful and easily removed diol protecting group

We report here the synthesis of a polystyryl boronic acid resin which can be used efficiently for the protection of polyols and can be removed under exceedingly mild reaction conditions The resin is fully regenerated during the cleavage step and can be used again without loss of activity

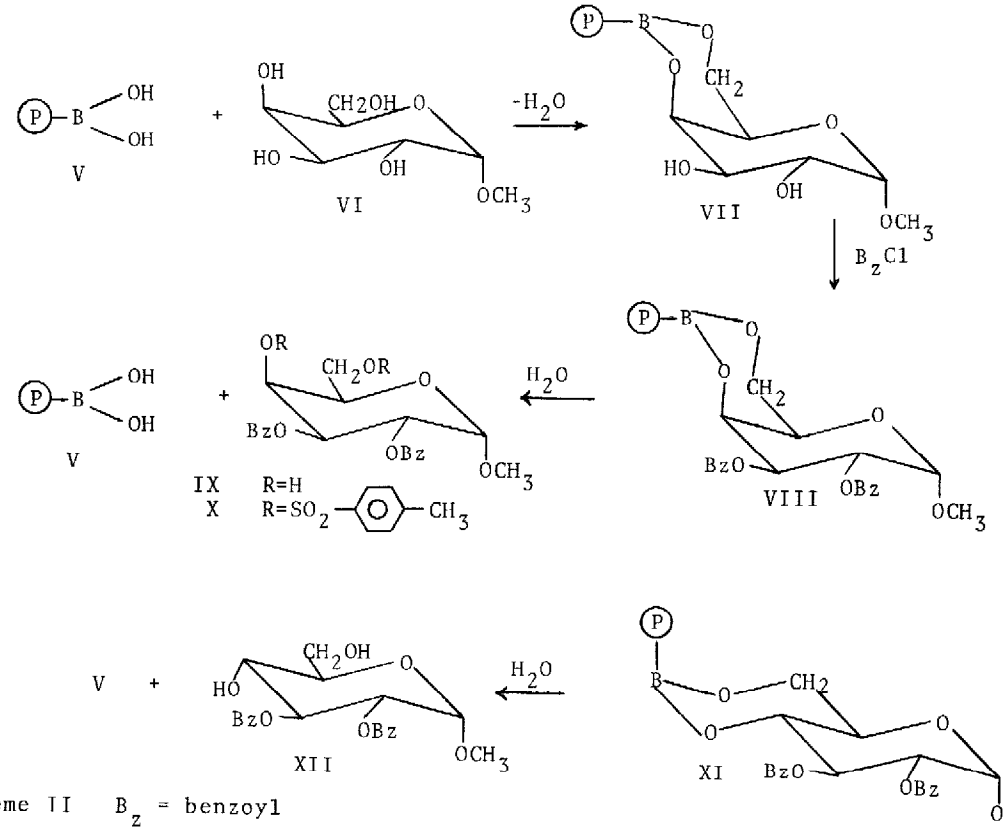
In recent years several polymers containing dihydroboroxyl functional groups have been prepared for use as adsorbents in the chromatographic separation of nucleic acids by complex formation The polymers were prepared by chemical modification of cellulose[11], of an acrylamide gel[12,13], or of Chromosorb 102[14]. In all cases however, the polymers had a low capacity, from 0 2 to 0 6 mmole of functional group per gram, and were not suitable for use in solid phase synthesis Since we anticipated that a polystyrylboronic acid having a higher capacity might prove useful as a dual purpose support for applications in solid phase synthesis as well as in chromatographic separations, we chose to use a macroreticular resin (Amberlite XE 305) which possesses a fairly rigid but porous structure, is easy to filter, and can be used efficiently in both aqueous and organic solvents

The preparation of the polystyrylboronic acid resin is outlined in Scheme I below




Scheme I R = n-butyl or methyl

The macroporous resin I was brominated with bromine in carbon tetrachloride[15] and in the presence of a catalytic amount of ferric chloride[16]. Resin II contained from 1 to 5 milliequivalents of bromine per gram, depending on the reaction conditions Reaction of II with n-butyllithium at room temperature and under nitrogen gave III, which was then allowed to react at -78° with a slight excess of a trialkylborate. Hydrolysis of the two alkyl groups of IV by reaction with aqueous hydrochloric acid gave the desired product V which contained 1-2 mmoles of functional group per gram[17] The i r spectrum of V included a large hydroxyl absorption centered at 3450 $cm^{-1}$ The application of V to the solid phase synthesis of glycosides such as methyl 2-3-di-0-benzoyl-α-D-galactopyranoside (IX) and the corresponding glucoside (XII) is shown in Scheme II




Scheme II $B_z$ = benzoyl

The coupling reaction was carried out in dry pyridine containing methyl α-D-galactopyranoside VI or methyl α-D-glucopyranoside, with azeotropic removal of the water produced in the reaction After benzoylation, the solvent and all soluble by-products were removed, and the resin was washed with dry benzene The intermediate products, VII, VIII and XI were not isolated Cleavage of the desired product IX or XII from the polymer support was effected by adding a 4 1 mixture of acetone and water After filtration the glycosides were obtained by concentration of the filtrate while resin V, which had been regenerated by the cleavage step, could be reused after drying. In typical experiments the coupling yields were of the order of 50 - 70% (e g., 1 054 g of IX were obtained from 2.5 g or 4 4 mequiv of V) Methyl 2,3-di-O-benzoyl-α-D-galactopyranoside was obtained as an amorphous solid which had an n.m.r. spectrum consistent with that expected for IX and had $[\alpha]_D$ +200 (C 1.2, chloroform) Since IX had not been characterized previously, its 4,6-di-O-(p-tolylsulfonyl) derivative was prepared and obtained as a crystalline material with physical properties in agreement with those given in the literature[18] Methyl 2,3-di-O-benzoyl-α-D-glucopyranoside XII was also obtained as an amorphous solid which had an n m r spectrum and an optical rotation in agreement with data previously recorded[4,19]

The synthesis of IX and XII demonstates the usefulness of the polystyrylboronic acid resin as a diol protecting group. Resin V should prove particularly useful in cases where the protection and deprotection steps have to be carried out under neutral conditions We are presently investigating the applications of V to the selective functionalization of several triols and other polyols, and to the chromatographic separation of diols

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References and Footnotes

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