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USE OF POLYMERS AS PROTECTING GROUPS IN ORGANIC SYNTHESIS. II. PROTECTION OF PRIMARY ALCOHOL FUNCTIONAL GROUPS

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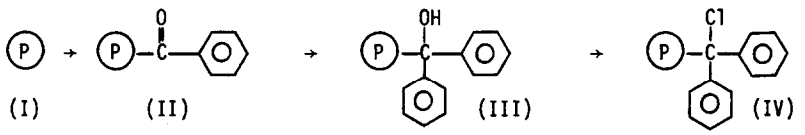
The use of polymers as reagents or protecting groups in organic synthesis has received much attention recently[1]. In a previous paper[2], we reported on the use of a polybenzaldehyde resin for the protection of two hydroxyl groups through the formation of an acetal. We wish to report here the synthesis of a polymer containing trityl chloride functional groups and its application to the synthesis of a selectively acylated derivative of D-glucose.

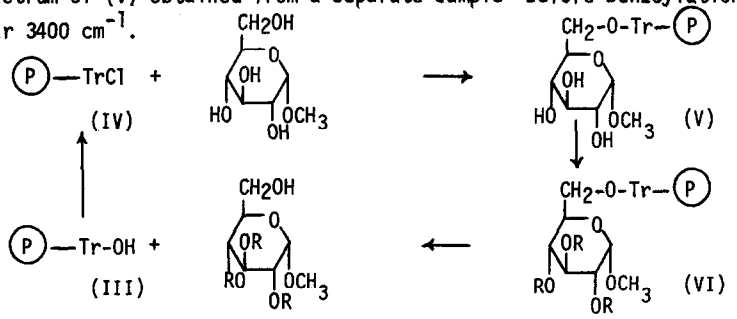
A swellable styrene - 1% divinylbenzene copolymer (P) (I) was chosen as starting material in the synthesis of the polymeric reagent. The polymer swollen in carbon disulfide was benzoylated by reaction with benzoyl chloride in the presence of aluminum chloride. The infrared spectrum of (II) included a large carbonyl absorption centered at 1650 cm^{-1}. Polymer (III) was prepared by reaction of (II) with an excess of phenylmagnesium bromide in dry THF followed by treatment with aqueous HCl in dioxane. The structure of (III) was confirmed by its i.r. spectrum (no band in the carbonyl region, strong absorption near 3580 and 3430 cm^{-1}). As expected, these hydroxyl absorption bands disappeared almost completely when (III) was treated with acetyl chloride in benzene to yield (IV). The capacity of the trityl chloride polymer, estimated by chlorine analysis, was found to be of 0.9 to 2.3 milliequivalent of functional group per gram, indicating that from 12% to 44% of the styrene residues were substituted.



(I) (II) (III) (IV)

The reaction of the polymeric trityl chloride reagent (20.17 g, 26.22 mequiv) with methyl α-D-glucopyranoside (10 g) was carried out in dry pyridine (225 ml) at room temperature. After 5 days of stirring, an excess of benzoyl chloride (27 ml) was added and the mixture was stirred overnight. The excess reagents and by-products were removed by washing the polymer on filter, and the coupling yield was estimated from the gain in weight of the polymer (10.83 g, which corresponds to 11.8 g of resin-bound glycoside, 89% yield based on the resin). The i.r. spectrum of (VI) included a large carbonyl absorption centered at 1720 cm^{-1}, while the i.r.

spectrum of (V) obtained from a separate sample[3] before benzoylation exhibited a broad OH band near 3400 cm^{-1}.



Cleavage of the glycoside from its temporary polymer support was accomplished in nearly quantitative yield by passing a current of dry hydrogen bromide through a suspension of polymer (VI) (24.8 g) in dichloromethane (220 ml) for 15 minutes. After filtration of the reaction mixture and neutralization of the filtrate, 9.06 g (86% yield based on IV) of methyl 2,3,4-tri-O-benzoyl-α-D-glucopyranoside were obtained. The glucoside which crystallized spontaneously was recrystallized from toluene-petroleum ether and had m.p. 140-142° and $[\alpha]_D$ + 54 (C = 1, chloroform) in agreements with earlier data[4]. The resin could be regenerated to (III) easily by washing with dioxane-water on filter.

Although the use of a polymeric protecting group rather than its monomeric counterpart, trityl chloride, did not result in a very significant improvement of the yield, a substantial simplification of the isolation and purification steps was achieved since the work-up, after cleavage of the resin-glucoside bond, consisted only of a filtration followed by the concentration of the soluble phase to yield a crystalline product. The product was therefore free from the usual contaminants, which usually have to be removed by chromatography, and the polymeric reagent was recovered quantitatively and recycled. The applications of (VI) to the synthesis of disaccharides, and of (IV) to the preparation of selectively functionalized derivatives of diols and other polyhydroxy alcohols, are under investigation.

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References and Footnotes.

1. C.C. Leznoff, Chem. Soc. Rev., 3, 65 (1974).

2. J.M.J. Fréchet and G. Pellé, J.C.S., Chem. Commun. 225 (1975).

3. In this case, most of the excess glycoside was recovered after concentration of the filtrate by passing an aqueous solution of the glycoside through a column packed with an ion exchange resin.

4. R.D. Guthrie, A.D. Jenkins and J. Stehlicek, J. Chem. Soc. (C), 2690 (1971).

The glucoside also had an n.m.r. spectrum consistent with that expected for methyl 2,3,4-tri-O-benzoyl-α-D-glucopyranoside.