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Recyclable Polystyrene-Based Polymeric Reagent for the Reduction of Acid Chlorides

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SUMMARY

A polymeric reagent, polystyryldiphenyl-phosphine tetrahydroborate copper, has been prepared by chemical modification of crosslinked polystyrene using a four-step reaction sequence involving a ligand exchange reaction for the binding of cuprous chloride to the phosphine resin. The reagent is very effective in the reduction of acid chlorides to aldehydes and can be regenerated easily without loss of activity.

INTRODUCTION

A major advantage often associated with the use of polymeric reagents is the ease with which soluble reaction products can be isolated from the insoluble polymeric by-products (HODGE and SHERRINGTON 1980, FRECHET 1981). Another interesting feature of many polymeric reagents is their ability to be recovered quantitatively after use for regeneration and recycling; this is an important feature in view of the generally high cost of these custom-made reagents. We have recently prepared a new polymeric reagent containing amine oxide functionalities on a polystyrene backbone (FRECHET et al. 1982) which is useful in the oxidation of alkyl halides into carbonyl compounds. Another interesting polymeric reagent we have described recently is polyvinylpyridinium dichromate (FRECHET et al. 1981), an oxidizing agent based on crosslinked poly(vinylpyridine) which is very effective in the oxidation of alcohols to aldehydes and ketones. This reagent was particularly attractive in view of the commercial availability of suitable vinylpyridine based resins and of its ability to be used safely in mole scale reactions.

Few polymeric reducing agents are available (HODGE and SHERRINGTON 1980 , MENGER et al 1980) and those which have been described are often non-recyclable. We have developed a new polymeric reducing reagent which is effective in the transformation of acid chlorides into

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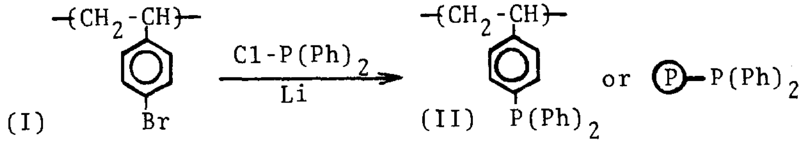
aldehydes and is fully recyclable.

RESULTS AND DISCUSSION

Recent studies have shown that copper tetrahydroborate is a useful reagent to effect the conversion of acid chlorides into aldehydes under mild conditions without production of side products (SORRELL et al. 1978a, 1978b, 1979, FLEET et al. 1978, 1979). Significant problems which remain in these reductions are the difficult isolation of the aldehydes from the reaction media and the fact the spent reagents are not readily recycled. For these reasons it was felt that the use of a polymer as a ligand for copper tetrahydroborate would help alleviate these problems as separation of the spent reagent from the desired product would amount to a simple filtration and regeneration of the polymer should be easily accomplished.

Polystyryldiphenyl phosphine (II) was prepared according to the literature (RELLES and SCHLUENZ 1974, FARRALL and FRECHET 1976) using ring-brominated crosslinked polystyrene beads (I) with a high degree of functionalization (D.F.= 0.8-0.9) and chlorodiphenylphosphine in the presence of lithium metal.



The polymeric phosphine was then used to bind copper (I) chloride. Several different methods were tested to effect this binding, best results being obtained with a ligand exchange reaction involving treatment of the phosphinated polymer (II) with cuprous chloride-tetramethylene diamine complex in acetone (Scheme 1). This reaction can lead to essentially complete functionalization of the phosphine sites on the polymer. The polymer bound copper tetrahydroborate reagent (IV) can then be obtained very easily by treatment of the polymer-CuCl complex (III) with excess sodium borohydride in ethanol, followed by washing of the resin to remove any unbound borohydride. This reaction yields a polymeric reagent with a capacity of up to 1.6 meq of boron per gram, a value which is comparable to that of the monomeric reagent.

Another interesting procedure for the preparation of the polymer bound copper tetrahydroborate reagent involved the use of both polymeric phosphine (II) and monomeric triphenyl phosphine to bind the copper. The advantage of this procedure is that only one of the polymer's active phosphine sites is required for the binding of each molecule of cuprous chloride (Scheme 2).

Polymer (V) is prepared by adding a concentrated solution of triphenylphosphine to (II), removing most of the solvent, then adding an excess of CuCl-TMEDA complex allowing time to equilibrate before filtering and washing the polymer.

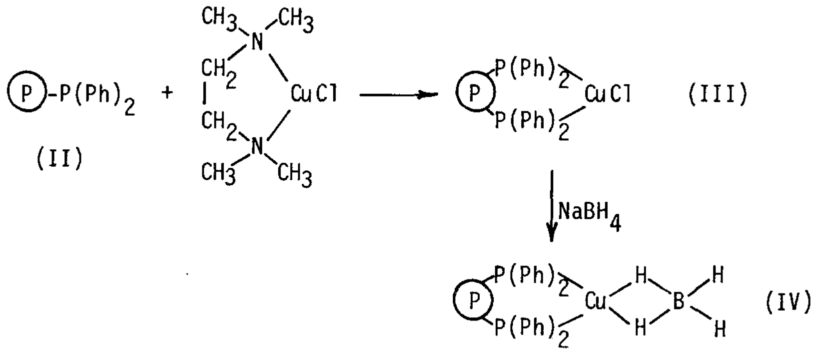
After treatment with borohydride as above, the polymer also had a capacity of 1.5-1.6 meq B/g. The advantage of this procedure is that a larger amount of polymeric reagent can be obtained from a given amount of polymeric phosphine (II); it should be noted however that in the formula of (V), x is always larger than y as confirmed by our gravimetric data. This finding is not unexpected as interaction of the reactive sites in (II) should occur readily during the slow formation of the complex by ligand exchange.

The reduction of acid chlorides to aldehydes is best done in acetone at room temperature. The reaction is very fast, usually complete in 15 minutes or less, affording an aldehyde free from any alcohol. The advantages of using the polymeric reagent are illustrated on Scheme 3: purification of the product is simple as the spent polymeric reagent can be removed from the product by filtration; regeneration of the polymer is also simple as the copper remains firmly bound to the polymer throughout the reaction cycle. When using polymer (IV), care has to be taken to exclude water from the reaction medium as it would react with the acid chloride. Table 1 shows the results which were obtained when 2 mmoles of an acid chloride were treated with 1.5 mmoles of the polymeric reagent. As expected, some acid chloride remained unchanged and, in addition to the major aldehydic product, some side-product was formed. It should be noted that the yield of aldehyde obtained was excellent since the reagent can only supply one hydride ion for the reduction. Thus the capacity of 1.6 mmole/g is the maximum which can be achieved for this reagent, a value which precludes its application to all but small scale reactions. A similar limitation exists for the corresponding monomeric reagent.

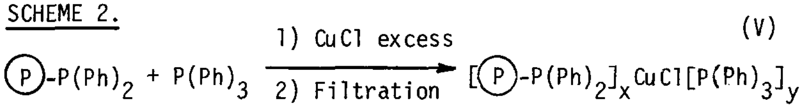
The best solvent for the reduction was found to be acetone, while ether-toluene 1:1 or ether were also satisfactory, but benzene or toluene were not suitable.

Regeneration of the spent polymeric reagent amounted to a new reaction with sodium borohydride, no new addition of CuCl was necessary as no leaching of copper salts from the polymer was observed during a

SCHEME 1.



SCHEME 2.



SCHEME 3.

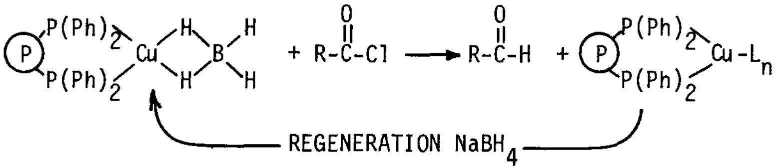


TABLE 1. Reduction of 2 mmoles acid chloride with 1.5mmole (IV)

	Product Analysis %		
Acid Chloride	Starting material	Aldehyde	Other
$CH_3(CH_2)_5COCl$	13	68	19
C_6H_5COCl	7	73	20

TABLE 2. Reductions with a 50% excess of polymeric reagent (IV)

Acid Chloride	*Reaction Cycle (yield of Aldehyde)		
	1st cycle	2nd cycle	3rd cycle
$CH_3(CH_2)_5COCl$	96%	91%	94%
$C_6H_{11}COCl$#	96%	93%	-
C_6H_5COCl	100%	-	-

* Regenerated reagent used in 2nd and 3rd cycles

\# C_6H_{11} = cyclohexyl

typical reaction-regeneration cycle. Table 2 shows the results which were obtained in the reaction of a 50% excess of (IV) with various acid chlorides. The data also inludes results obtained in reactions involving the recycled reagent. It is apparent that the recycled reagent is just as effective as the freshly prepared (IV) and that no loss of activity occurs during regeneration

These results show that (IV) is an effective and fully recyclable polymeric reagent useful in the reduction of acid chlorides to aldehydes. The reagent has a capacity which is essentially as high as that of its low molecular weight counterpart and the two reagents have approximately the same reactivity. The polymeric reagent is somewhat easier to use and to recycle due to the ease with which it can be removed from the reaction medium once the reduction is complete. However, both the polymeric and the monomeric reagents suffer from the fact that large amounts are needed to effect reactions on a preparative scale and it is unlikely that either will find applications outside the research laboratory.

EXPERIMENTAL PROCEDURE

All the reaction were carried using 1 or 2% crosslinked styrene-divinylbenzene resins (Bio-beads SX-1 or SX-2). Resins with lower amounts of crosslinking agent were found to be unsuitable as they tended to dissolve or coalesce during the harsh functionalization steps. The resins were washed thoroughly (FARRALL and FRECHET 1976) before use to remove surface impurities. Chlorodiphenyl phosphine (Aldrich Chem Co) was distilled immediately before use. Tetrahydrofuran was dried over lithium aluminium hydride and distilled. Elemental analyses were performed by Galbraith Laboratories or by MHW laboratories (Phoenix, AZ). Gas chromatographic analyses were performed on aliquots injected in columns of SE-30 or Carbowax on Chromosorb W, detection was by thermal conductivity. NMR spectra were recorded on Varian HA-100, EM-360 or CFT-80 spectrometers.

Preparation of Ⓟ-Br (I).

The bromination of crosslinked polystyrene was carried out as described previously (FARRALL and FRECHET 1976). 50g of washed Bio-beads SX-2 were suspended in 600 mL of carbon tetrachloride in a reactor which was protected from light. After addition of 0.85 g of ferric chloride, the mixture was stirred while 27.5 mL of bromine were added dropwise over a period of 30 min. Stirring was continued at room temperature for 2 hours, then the mixture was refluxed until evolution of HBr ceased. After filtration, the polymer was washed repeatedy with carbon tetrachloride, acetone, THF, dioxane-water 1:1, dioxane, methanol, then dried under vacuum at 40-50°. Analysis: Br, 40.46% (5.1 meq/g).

Preparation of Ⓟ▲P(Ph) (II)

30 g of the brominated polymer were swollen in 600ml of dry THF under inert atmosphere. After stirring at room temperature, 64.5 mL of chlorodiphenyl phosphine were added slowly over a 30 min. period and the mixture was cooled externally while 5.78 g of lithium shot were added. Once the addition was complete, stirring was continued at room temperature for 16 h then at reflux for 3 h. After adding 300 mL of methanol, the mixture was stirred for another 30 min. and the polymer was collected on filter and washed repeatedly with THF, water, dioxane-water (1:1), dioxane, methanol, then dried under vacuum overnight. Analysis: P, 8.80% (2.8 meq/g).

Preparation of polymers (III) and (IV).

The cuprous chloride complex was prepared by reaction of 4.08 g of CuCl with 4.79 g of TMEDA in 400 mL of acetone. To the greenish blue solution were added 22 g of polymer (II) and the mixture was stirred at room temperature for 16 hours. After filtration, the polymer was extracted with various solvents to remove any unbound materials. After drying, a 21 g portion of the polymer was added to a solution of 1.1 g of sodium borohydride and the reaction mixture was stirred overnight at room temperature. After filtration, the polymer was washed with methanol, water, methanol-water, THF-methanol, then dried under vacuum. Analysis: B, 1.78%, P, 8.09%.

Use of polymer (IV) in the reduction of acid chlorides.

A typical reaction was carried out by mixing 1 g of polymer (1.5-1.6 mmole) and 1 mmole of acid chloride in 5 mL of acetone at room temperature. The reaction was ususally complete in less than 5 min. and the aldehyde was obtained by filtration, washing of the polymer and concentration of the organic phase.

Regeneration of (IV).

To a suspension of 5 g of the spent polymer in 10 mL of ethanol containing 0.06 g of triphenylphosphine were added 0.24 g sodium borohydride in 15 mL ethanol. After stirring overnight, the polymer was filtered, washed and dried. The regenerated polymer was as effective a reducing agent as the original material.

ACKNOWLEDGEMENT.

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