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### Polymeric Reagents.II. Synthesis and Applications of Crosslinked Poly(vinylpyridinium Hydrobromide Perbromide) Resins

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**Polymeric Reagents. II.\***  
**Synthesis and Applications of Crosslinked**  
**Poly(vinylpyridinium Hydrobromide Perbromide) Resins**

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ABSTRACT

Crosslinked bead polymers containing vinylpyridine units were prepared by pearl copolymerization of monomer mixtures containing various percentages of 4-vinylpyridine, styrene, and divinylbenzene. The polymers were functionalized by reaction with hydrogen bromide and bromine, and the resulting poly-(vinylpyridinium hydrobromide perbromide) resins, which were stable for long periods of time, were used to brominate a number of alkenes and ketones. In most cases, the brominated products were obtained in excellent yields and could be separated from the polymeric by-product by a simple filtration. The polymeric reagent could be fully regenerated after use without loss of activity.

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\*For the previous paper in this series see Fréchet and Haque [ 1].

A number of functional polymers have been prepared recently for use as protecting groups or chemical reagents in organic synthesis. While the polymeric protecting groups [ 2, 3 ] are used as temporary supports in multistep syntheses, polymeric reagents [ 1 ] are generally used in single-step reactions and derive their main advantages from their insolubility. Thus, reactions can often be driven to completion by using an excess of reagent since both the unspent reagent and the polymeric by-product can be separated easily from the desired product of the reaction. In addition, the polymeric reagents can be recovered quantitatively after use, and, in ideal cases, they can be regenerated to their initial activity easily in a single step. Other advantages and properties of polymeric reagents have been reviewed recently [ 4-6 ].

Several halogenated polymers have been prepared for applications as reagents in halogenation or oxidation reactions. Thus, Okawara reported in 1958 and later in 1969 the synthesis of polyimides and their subsequent bromination [ 7, 8 ]. These polymers which contained few N-Br functional groups were not well characterized and gave low yields in oxidation and bromination experiments. More recently, Patchornik and co-workers have also reported [ 9 ] the preparation of an N-bromopolymaleimide and the application of this reagent to brominate substituted styrenes. In our hands, however, N-brominated copolymers of maleimide, styrene, and divinylbenzene were found to have a very low reactivity in bromination reactions and in the oxidation of alcohols or sulfides [ 10 ]. A new N-brominated imine was also prepared recently by Manecke and Stark [ 11 ] on a polystyrene backbone. The polymer was used in the allylic bromination of cyclohexene and in the preparation of benzyl bromide from toluene. In both cases the yields were moderate, and the reaction products required some purification after the reaction. Other halogenated polymeric reagents such as N-chloro nylon 66 have been used successfully in oxidation reactions [ 12, 13 ].

Pyridinium hydrobromide perbromide is a reagent which can be used instead of free bromine for the bromination of alkenes or ketones. The crystalline reagent is easier to handle than liquid bromine and can be handled more accurately in micro quantities; in addition it is often more selective than bromine [ 14 ]. We have prepared a resin containing vinylpyridinium hydrobromide perbromide units and have tested this polymeric reagent in simple halogenation reactions. Our criteria for the acceptability of this polymeric reagent were the following: the reagent must be insoluble, easy to handle, stable for long periods of time, as reactive as the monomeric reagent, and fully regenerable in a simple fashion.

## RESULTS AND DISCUSSION

The resins were prepared by the pearl copolymerization technique by using varying amounts of 4-vinylpyridine, divinylbenzene, and in some cases styrene. The beads obtained had the properties which are required for applications as polymeric reagents: they were insoluble in usual organic solvents, had a good mechanical stability, were easy to filter, and had a large proportion of their functional groups which showed good accessibility.

The poly(vinylpyridinium hydrobromide perbromide) (PVPHP) resins were prepared by reaction of the polyvinylpyridine beads with an excess of hydrogen bromide, followed by reaction with bromine. Elemental analyses indicated that degrees of functionalization of 85-95% could be obtained easily, and thus the reagent has a high capacity and can be used without having to handle a very large amount of resin for a small quantity of substrate. The PVPHP reagent is a remarkably stable odorless solid, made up of free-flowing orange beads which can be stored at room temperature for long periods of time without appreciable loss of bromine. Reactions with PVPHP are easy to follow visually, since the reagent turns yellow as its bromine is being consumed. Typically, the bromination of an alkene in methanol will require 1-2 hr stirring at room temperature; in contrast, PVPHP is completely unreactive in solvents such as chloroform and carbon tetrachloride which are frequently used in brominations involving free bromine.

As can be seen in Table 1, the reaction of PVPHP with simple alkenes generally gave excellent yields of the dibrominated products. In all cases a 10 to 40% excess of the polymeric reagent was used to ensure complete conversion. In the reaction with *cis*-stilbene, a 98% yield of the *dl*-dibromide was obtained, a result which is in contrast with that obtained in the corresponding reaction with bromine since, in that reaction, a mixture of *meso*- and *dl*-dibromides was obtained in lower overall yield [ 15].

In the case of simple ketones ( Table 2), the reaction with PVPHP gave excellent yields of the corresponding  $\alpha$ -bromides and no products resulting from an eventual polybromination were observed.

The spent polymeric reagent was separated easily from the desired product after reaction, and thus the isolation step consisted only of a filtration followed by repeated washing of the resin to extract any product which might have remained in its pores, finally, evaporation of the combined filtrates yielded the product which usually did not require further purification. The polymeric reagent could be regenerated easily after reaction and used again in further bromination reactions. The recycled resin was as active as the original material even after several reaction cycles.

TABLE 1. Bromination of Alkenes with PVPHP<sup>a</sup>

Alkene	Reaction time (hr)	Product	Yield (%)
Cis-stilbene	1	dl-Dibromostilbene	98
Cyclohexene	1.5	1,2-Dibromocyclohexane	88
Styrene	2.3	1-Phenyl-1,2-dibromoethane	99
1,7-Octadiene	1.5	1,2,7,8-Tetrabromooctane	87
Cinnamyl alcohol	0.25	3-Phenyl-2,3-dibromopropanol	55 <sup>b</sup>
Cinnamic acid	1.5 <sup>c</sup>	3-Phenyl-2,3-dibromopropanoic acid	89

<sup>a</sup>Reaction at room temperature unless otherwise noted.

<sup>b</sup>Yield after column chromatography; 17% starting material recovered.

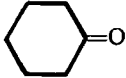
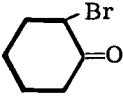
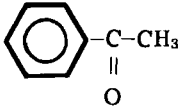
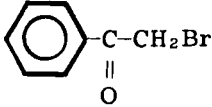
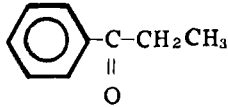
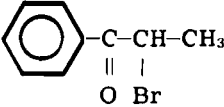
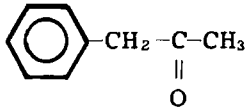
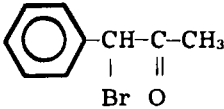
<sup>c</sup>Reaction in refluxing methanol.

We are presently investigating the reaction of PVPHP with various carbohydrate derivatives for the preparation of deoxy bromo sugars. The application of another derivative of the polyvinylpyridine resin, poly(vinylpyridinium chlorochromate), as oxidizing agent in organic synthesis is also under investigation.

## EXPERIMENTAL

4-Vinylpyridine (Polysciences Inc.) and styrene (Fisher Scientific) were purified by distillation immediately before use. Divinylbenzene (Polysciences Inc.) was used without further purification. The poly(vinyl alcohol) used had a molecular weight of 180,000-250,000. All other solvents and chemicals were purified or dried as needed. Bromine analyses were carried out by Chemalytics Inc. or in this laboratory by using the Parr peroxide bomb method. Infrared spectra were recorded on Perkin-Elmer 457 or Beckman IR 20 A spectrophotometers. NMR spectra were recorded by using a Varian HA 100 spectrometer.

TABLE 2. Bromination of Ketones with PVPHP<sup>a</sup>

Ketone	Reaction time (hr)	Product	Yield (%)
	3.5		100
	3.5		99
	0.7 <sup>b</sup>		100
	1		80 <sup>c</sup>

<sup>a</sup>Reaction at room temperature unless otherwise noted.

<sup>b</sup>Reaction in refluxing methanol.

<sup>c</sup>Product contains 20% of starting material.

#### Preparation of the Crosslinked 4-Vinylpyridine-Styrene Copolymer Beads

To a solution of 1 g of poly(vinyl alcohol) in 300 ml of freshly boiled distilled water were added 6.4 g of 4-vinylpyridine, 10.2 g of styrene, 0.4 g of divinylbenzene, and 0.1 g of benzoyl peroxide. The reaction mixture was stirred vigorously and heated to 70-90° C while being kept under inert atmosphere. After 6.5 hr, the cream-colored beads were collected by filtration through cloth and washed several times with water and various organic solvents. After drying, the polymer which weighed 9 g, contained 6.39% of nitrogen (4.56 meq/g), indicating that the resin contained 48% of vinylpyridine residues.

### Preparation of the Poly(vinylpyridinium Hydrobromide Perbromide) Resin (PVPHP)

The resin prepared above (1.49 g) was swollen in dioxane (25 ml) and the suspension was stirred for 1 hr with 2.5 ml of 48% hydrobromic acid. After cooling in ice water, 2 ml bromine was added, and the mixture was stirred for an additional 4 hr. After filtration, the bright orange resin was washed repeatedly with acetic acid and dichloromethane. The resin was then dried under reduced pressure to yield 3.1 g of a product containing 5.6 meq Br/g.

The reaction above was repeated with another batch of cross-linked 4-vinylpyridine copolymer (from 98% 4-vinylpyridine and 2% divinylbenzene). The PVPHP resin which was obtained contained 63% of bromine (7.88 meq Br/g or 2.62 meq functional group/g) which corresponds to a degree of functionalization of more than 90%.

### Bromination of Alkenes with PVPHP

Preliminary experiments on the bromination of cyclohexene showed that the reaction was extremely slow in solvents such as chloroform or carbon tetrachloride, slow in acetic acid, and fast in methanol. Thus, all the bromination reactions were carried out in methanol with a 10 to 40% excess of PVPHP. In a typical reaction, 1 g of *cis*-stilbene was added to a suspension of 2.6 g (6.5 meq) of PVPHP in 25 ml of methanol. The reaction mixture was stirred slowly at room temperature until most of the orange color had disappeared ( $\approx$  30 min). After another 30 min at room temperature, the resin was collected on filter and rinsed three times with chloroform. After evaporation of the solvents 1.85 g (98% yield) of crude *dl*-stilbene dibromide was obtained; after crystallization from methanol the product had mp 111-113°C. In similar reactions, cyclohexene, styrene, and 1,7-octadiene were brominated to the corresponding di- and tetrabromides in good yields (Table 1). The reaction with cinnamic acid did not proceed well at room temperature but was easily performed in refluxing methanol to yield 89% of the desired product. In all cases the products had NMR spectra in agreement with those expected, and no traces of starting materials were found. In the case of cinnamyl alcohol, the reaction gave two products in addition to some starting material. The reaction was stopped after 15 min, since longer reaction times seemed to increase the proportion of side product. Separation on a column of silica gel with the use of benzene-ether mixtures for elution gave a 55% yield

of the desired 3-phenyl-2,3-dibromopropanol, 17% of the starting material, and an unidentified product which contained only one bromine atom.

### Bromination of Ketones with PVPHP

To a solution of 1.4 g of propiophenone in 30 ml of methanol were added 5.71 g of PVPHP (containing approx. 2.5 meq functional group/g). The mixture was stirred slowly and heated to reflux until the bright orange color of the resin had become lighter (40 min). The resin was then collected on filter and washed three times with portions of dichloromethane allowing some time for the solvent to penetrate the beads before each filtration. The combined filtrates were evaporated under reduced pressure to yield 2.22 g (quantitative yield) of phenyl 1-bromoethyl ketone as a yellow oil with an NMR spectrum in agreement with the proposed structure. No trace of starting material could be found in the product.

Similar reactions carried out at room temperature for 3.5 hr with cyclohexanone or acetophenone gave quantitative amounts of the corresponding  $\alpha$ -brominated ketones (see Table 2), while the reaction with benzyl methyl ketone for 1 hr at room temperature gave a mixture of bromobenzyl methyl ketone and starting material in 4:1 ratio. In all cases only one brominated product was obtained.

### Regeneration of the Resin

After each reaction the resin was washed with aqueous sodium hydroxide, then with water. The regeneration was accomplished by reaction with excess 48% hydrogen bromide followed by addition of bromine as described earlier. Alternatively, the resin could be regenerated by the same treatment but without the sodium hydroxide wash. However, the resin regenerated after washing was generally more reactive than that regenerated without prior washing. The regenerated resins which were as reactive as the original material could be used efficiently in similar bromination reactions.

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