A Convenient Synthesis of Macroporous Polymer-Supported Supernucleophilic Reagent and Linear Macromolecules

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ABSTRACT: *N,N′*-Bis(4-pyridinyl)piperazine and *N*-(4-pyridinyl)piperazine have been prepared by treatment of piperazine with 4-chloropyridine. *N,N′*-Bis(4-pyridinyl)piperazine (*bis*-DMAP) is similar to a couple of 4-(*N,N*-dimethylamino)pyridine (DMAP). *N*-(4-Pyridinyl)piperazine as reactive group can be linked onto the macroporous polymeric carrier producing a polymer-bound catalyst. A linear epoxy polymer containing the supernucleophilic functional groups have been synthesized by reaction of epichlorohydrin and 4-aminopyridine. The linear polymeric catalysts have been braced by the macroporous resin to obtain a polymer-supported linear polymeric catalyst. It is found that catalytic activity of *bis*-DMAP approaches that of DMAP. The activity of the polymer-supported linear polymeric catalyst is higher than that of the polymer-bound catalyst in the acetylation of *tert*-butyl alcohol, as monitored by gas–liquid chromatography. © 2000 John Wiley & Sons, Inc. J Appl Polym Sci 75: 593–597, 2000

Key words: polymer-supported catalyst; polymer-bound linear polymeric catalyst; supernucleophilic reagent

INTRODUCTION

4-(*N,N*-Dialkylamino)pyridine derivatives have been used as supernucleophilic reagents in a large number of organic reactions.[1,2] Commercially, the recovery and repeated use of small molecule, or linear polymeric, supernucleophilic species is difficult. It is envisioned that the use of a crosslinked polymeric support for the supernucleophilic species will help negate this problem.

The linking of polystyrene (PS) with pyridinamines has been reported.[3–5] However, the substrates were obstructed by the PS network, leading to poor permeability between the substrates and catalytic species. The PS chains have a low compatibility with the substrates in the acylation system, primarily due to the hydrophobic nature of the PS. Two methods of solving the problems are (a) to use a macroporous polymer and (b) to use a less hydrophobic polymer.

We reported herein the synthesis of macroporous acrylic acid-type polymer that is supported with supernucleophilic reagent. There are a number of carboxyl groups on the macromolecular net. The carboxyl groups were converted to the acid chlorides by reaction with $SOCl_2$. Subsequent reaction of the acid chloride groups with the supernucleophilic reagents (containing hydroxyl or amino groups) linked the polymeric carrier to yield a polymer containing aminopyridine, amide, and ester groups. Polymeric chains containing these groups show good compatibility with the substrates in the system.

In addition, the macroporous polymer has a large specific surface area. The aperture is large enough not to hinder access of the substrates to the catalytic sites. The accessibility of the polymer-supported supernucleophilic catalyst with substrate ranges between that of homogeneous catalysts and heterogeneous catalysts.

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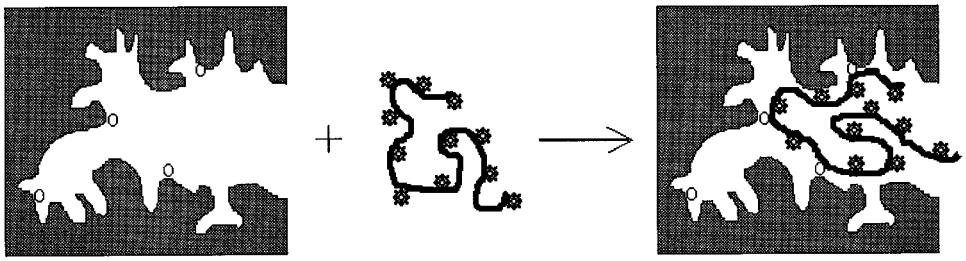


Figure 1 Macroporous resin-supported the linear polymer containing functional groups.

Linear polymeric catalysts can not be used repeatedly because they can dissolve into the system. We also were interested in linking a linear polymeric catalyst with the macroporous polymeric carrier. The density of the catalytic groups of the linear polymer is higher than that of small molecules in the unit volume bore of the macroporous resin because linear chains offer random folding. Because the linear polymers can clog cavities of the network resin, nonbounded linear molecules should be washed out from the carrier. It is possible that the mobility of polymeric chains hinders the approachability between active sites and substrate molecules. However, the effect may be neglected since the pore diameter of carrier cavity is much larger than the length of the molecular chain.

EXPERIMENTAL

4-Chloropyridine and piperazine were supplied by Aldrich Chemical Company (Milwaukee, WI). The macroporous resin D152 (or Amberlite IRC-72) was supplied by Nankai University. FTIR spectra were recorded on a Nicolet 205 spectrometer (Madison, WI). ^{1}H-NMR spectra were recorded on a Bruker AC-P 200 spectrometer (Billerica, MA). Elemental analyses were obtained from PE-2400. Gas–liquid chromatography was carried out on a SP-2305 with a Shimadzu C-RIB system (Columbia, MD).

Macroporous Polyacryloyl Chloride (1)

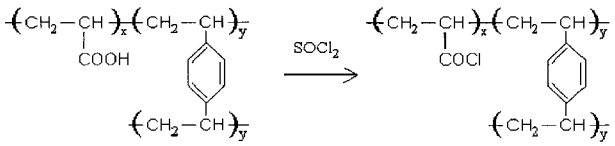
A suspension of 32.0 g (0.35 mol of carboxyl groups) of macroporous acrylic acid type ion exchange resin (D152 or Amberlite IRC-72) in thionyl chloride (100 mL) was refluxed for 5 h. The excess thionyl chloride was evaporated. The residue was washed with absolute ether and dried under vacuum to give 36 g of **1** as a dark yellow bead.

N-(4-Pyridyl)piperazine (2)

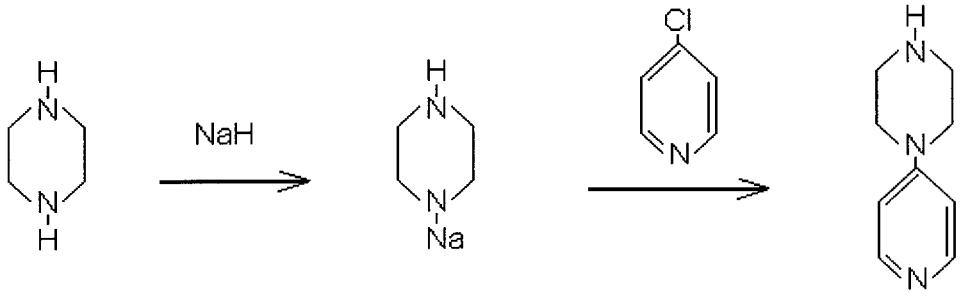
To a solution of 3.44 g (40 mmol) of piperazine in tetrahydrofuran (10 mL) was added 1.10 g (46 mmol) of sodium hydride (washed with heptane). After the suspension was stirred vigorously for 1 h at 60°C, 6.00 g (40 mmol) of 4-chloropyridine hydrochloride was added, and the mixture was stirred for 24 h at 60°C, after which it was filtered and washed three times with acetone. The residue was dissolved in water (10 mL) and chromatographed on silica gel (50 g). Elution of the column with CH_3OH and recrystallization from ether gave 4.2 g of **2** (65% in yield). bp 195–197°C (17 mmHg); mp 135–137°C; IR (KBr): 3250, 1580, 1410, 1360 cm^{-1}. NMR (D_2O) δ: 1.70 (*s,* 1H); 2.70–3.30 (*m,* 8H); 6.55 and 8.15 (2*d*, 4H). ANAL. Calcd. for $C_9H_{13}N_3$: C: 66.23; H: 8.03; N: 25.74. Found C: 66.21; H: 8.00; N: 25.72.

Macroporous Polyacrylate-Supported Supernucleophilic Reagents (3)

To a suspension of 8.0 g (73 mmol —COCl) of **1** in dimethylsulfoxide (20 mL) was added 12.2 g (75 mmol) of **2**, the mixture was stirred for 24 h at 80°C, and the solvent was evaporated to form a dried granula. The beads were marinated in ben-



Scheme 1



Scheme 2

zoyl chloride and then in methanol for 5 h. The product was washed with water and dried under vacuum to give 15.6 g of **3** as a brown bead.

Linear Epoxy Polymer Containing Supernucleophilic Functional Groups (4)

To a solution of 9.40 g (0.1 mol) of 4-aminopyridine and 9.30 g (0.1 mol) of aniline in DMF (20 mL) was added 18.5 g (0.2 mol) of epichlorohydrin. After the mixture was stirred for 3 h, the excess epichlorohydrin was evaporated, and then the concentrated mucilage was precipitated in acetone. The deposited matter was carried out a dissolving/precipitating process with water/acetone for three times and was dried under vacuum to give 23.5 g of **4** as a yellow grume (78% in yield). IR (KBr): 3400, 3140, 1650–1500 cm^{-1}. NMR (200 MHz, D_2O) δ: 8.30 (*d,* 2H); 7.48 (*d,* 2H); 7.20 (*d,* 2H); 4.60 (*m,* 1H); 2.42 (*d,* 2H). ANAL. Calcd. for $C_{17}H_{21}N_3O_2$: C, 68.21; H, 7.07; N, 14.04. Found: C, 68.23; H, 7.10; N, 13.99.

Macroporous Polyacrylic Acid-Supported Linear Epoxy Polymer Containing Supernucleophilic Functional Groups (5)

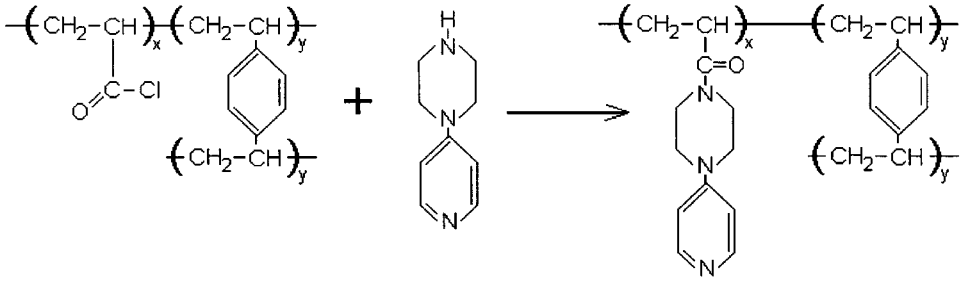
To a solution of 14.3 g (95 mmol —OH) of **4** in dimethyl sulfoxide (20 mL) was added 10.0 g (91 mmol —COCl) of **1**. After the mixture was stirred for 24 h at 80°C, the solvent was evaporated to form a dried granula. The beads were marinated in benzoyl chloride and methanol for 5 h, respectively. The product was washed with water and dried under vacuum to give 19.7 g of **5** as a pale brown bead.

Test of the Catalysts

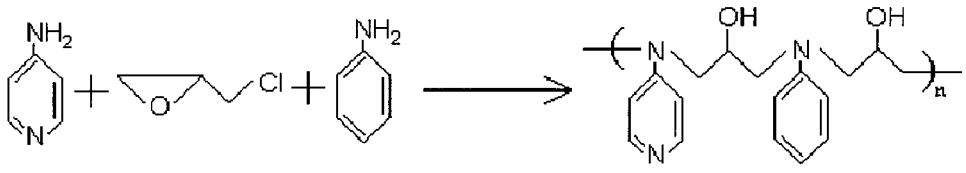
A mixture of 15.78 g (210 mmol) of *tert*-butanol, (5 mol %) of the catalyst and 3 mL (21.6 mmol) of triethylamine, in heptane to total solution (20 mL), was placed in a thermostatically controlled cell at the desired reaction temperature (60°C). After stirring under nitrogen for 15 min, 27.08 mL (260 mmol) of acetic anhydride was added while stirring continued. Progress of the reaction was monitored by timely withdrawal of 10-μL aliquots for gas chromatographic analyses.

RESULTS AND DISCUSSION

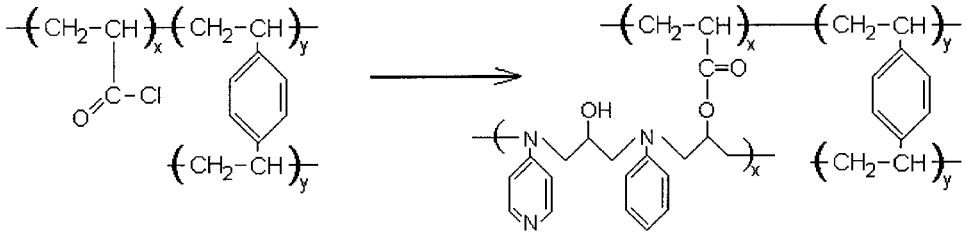
In order to increase reactivity of reactive polymer, a number of carboxyl groups in the macroporous acrylic acid polymer must be changed into acyl chloride. The macroporous resin was marinated into heated thionyl chloride to obtain a macromolecular carrier containing acyl chloride groups (**1**) (Scheme 1).



Scheme 3



Scheme 4



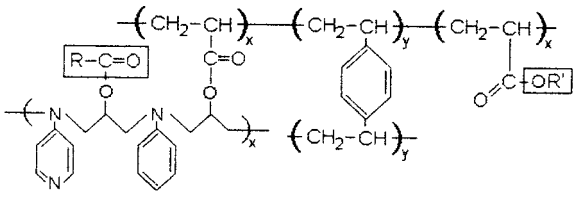
Scheme 5

Piperazine was alkalified by sodium hydride as to improve the nucleophilic capability. *N*-(4-Pyridyl)piperazine (**2**) was produced by alkylation of the excess sodio-piperazine with 4-chloropyridine (Scheme 2).

N—H of **2** is reacted with —COCl of **1** to make an amide bond linking of the low-molecular-weight catalysts with macroporous polymer (**3**) (Scheme 3).

Similarly, 4-aminopyridine was treated with epichlorohydrin and aniline, to yield a linear and a few short-branch of epoxy polymers. Aniline was added to enhance the hydrophobic nature of the macromolecule (Scheme 4). A number of the hydroxyl groups in the epoxy polymer (**4**) are apt to react with the substrate in acylation and **4** can dissolve into the acylation system to lead a catalytic inhibition.

However, the hydroxyl groups of **4** can also react with —COCl of **1** to enclose and immobilize the linear polymers containing catalytic groups into the cavities of the macroporous crosslinked polymer (Scheme 5). A macroporous polymer supported the linear polymer containing higher density catalytic groups (**5**) was synthesized by "sealing of side group" of the polymer, i.e., the residual hydroxyl groups on the linear polymers were sealed by small molecule acyl chlorides (acetyl chloride, benzoyl chloride) and the residual acyl chloride groups on the macroporous polymers were sealed by low-weight alcohols or amines (methanol, methyl amine). Thus, there are no residual reactive group in the polymeric catalyst (Scheme 6).



Scheme 6

A peak descending of *tert*-butanol was recorded in acetylation of *tert*-butanol monitored by gas chromatography. The peak value of the alcohol

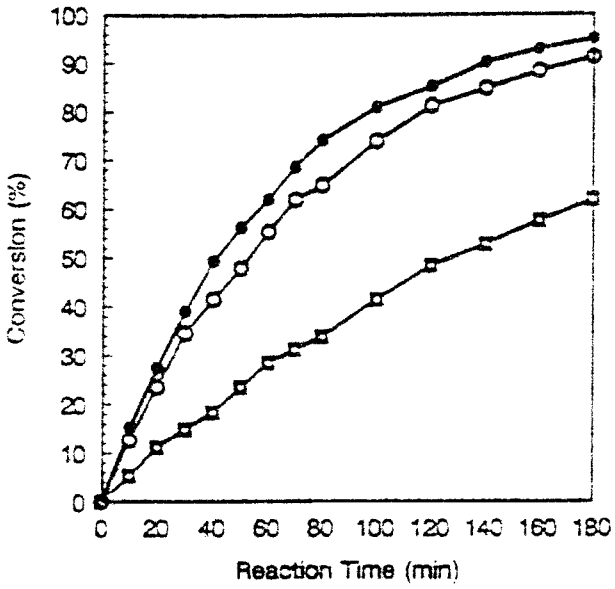


Figure 2 Acetylation of *tert*-butanol catalyzed by (●) DMAP; (○) **5**; and (□) **3**.

was compared with that of internal standard compound (heptane) to give the content of the alcohol. The content at a moment divided the original content to obtain the conversion of *tert*-butanol. A graph of the conversion-reaction time was acquired in the acetylation of the alcohol catalyzed by **3**, **5**, and 4-(*N,N*-dimethylamino)pyridine (DMAP) (Fig. 2).

Figure 2 shows that the macroporous polymer-supported catalysts **3**, **5** have a highly catalytic power closed with DMAP. Catalytic activity of **5** is more effective than that of **3** because the content of **5** is higher than that of **3** in the bore of the macroporous resin. Both **3** and **5** show reduced activity relative to DMAP. This may be due to increased steric hindrance arising from the crosslinked nature of the polymeric support.

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