Amination of Poly(vinylbenzyl chloride) with *N*,*N*-Dimethylformamide

Spiro D. Alexandratos* and Xiaoping Zhu

Department of Chemistry, Hunter College of the City University of New York, 695 Park Avenue, New York, New York 10021

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Introduction

Poly(vinylbenzyl chloride) [polyVBC], both linear and prepared by suspension polymerization to form cross-linked beads, is widely used in the synthesis of polymer-supported reagents.[1] Its usefulness stems from the propensity of the pendant $-CH_2Cl$ groups to undergo reaction with nucleophiles. In numerous organic syntheses, *N*,*N*-dimethylformamide (DMF) is used as the solvent because of its ability to dissolve compounds with a range of polarity differences.[2−6] This property can be important when reactions are conducted between nucleophilic reagents and polyVBC: the DMF compatibilizes the two and allows the reaction to occur within the polymer network.[7−9] The success of these reactions is predicated on the inertness of DMF as a reagent.

When synthesizing polymer-supported reagents, it is important that the resulting structure be well-defined. If the polymer is to be used in ionic recognition studies, the presence of unidentified ligands will give misleading metal ion affinities. If the polymer is to be used as a reagent, the unidentified ligands can interact with the substrate to give unpredictable results. In the current research, DMF was used as the solvent in the reaction between the sodium salt of 1,2-ethanediol and polyVBC. The resulting polymer, however, was found by titrimetric analysis to have a significant acid capacity where none was possible from the immobilized ligand that was expected. This report details findings that DMF reacts with polyVBC to form ion-complexing ligands.

Experimental Section

The preparation of polyVBC beads cross-linked with 2% divinylbenzene (DVB) has been described.[10] Poly(glycidyl methacrylate) [polyGMA] beads were prepared by suspension polymerization.[11] Aqueous solutions of 2.671 g of poly(vinyl alcohol) [PVA] (Aldrich Chemical Co., 98% hydrolyzed, 13 000−23 000 MW) in 450 mL of water (heated until the PVA dissolved) and 59.34 g of $CaCl_2$ in 50 mL of water were combined in a 1 L round-bottom flask fitted with a condenser, N_2 inlet, thermometer, and overhead stirrer and sparged for 10 min. An organic solution of 126.84 g of GMA, 21.66 g of DVB (technical grade, 55.4% meta and para isomers), 1.50 g of benzoyl peroxide, and 225 g of isobutyl acetate in a 500 mL flask was sparged for 5 min with nitrogen and combined with the aqueous solution. The stir speed was adjusted to 190 rpm, the flask heated to 80 °C over a 2 h period, and the temperature maintained at 80 °C for 17 h. The isobutyl acetate was then removed by steam distillation. The beads were washed with 500 mL of 10^{-4} M HCl and water, followed by Soxhlet extraction with toluene and air-drying in the fume hood. All beads used were 250−425 μm in diameter.

In a typical reaction with DMF, 2.0 g of polyVBC was contacted with 100 mL of DMF at a given temperature for 24 h. The DMF was then removed, and the beads were washed with dioxane and water, placed in a glass frit funnel, and conditioned with 1 L each of H_2O, 1 M NaOH, H_2O, 1 M HCl, and H_2O. The polymers were analyzed by FTIR (Bomem (MB Series); Hartmann-Braun), chlorine and nitrogen elemental analyses, and acid capacity determinations (0.5 g of Buchner-dried resin was added to 50 mL of 0.1000 M NaOH containing 5% NaCl in a 250 mL Erlenmeyer flask; the flask was stoppered and shaken at room temperature for 17 h; 10 mL aliquots of the solution were titrated with standardized 0.1000 M HCl to give the acid capacity).[12] For the FTIR spectra, KBr pellets were prepared with 0.01 g of resin and 0.100 g of KBr followed by grinding and compression into pellets. Solid-state NMR spectra were accumulated on a Varian UnityPlus 300 MHz spectrometer operating at 75.44 MHz for carbon, employing a 7 mm Varian probe and the standard Varian CP-MAS sequence, i.e., Xpolar 1. A spinning speed of 7 kHz was used to accumulate 1024 transients at a 90° pulse of 5 μs, a contact time of 500 μs, an acquisition time of 30 μs, and a relaxation delay of 3 s.

Table 1. Modification of PolyVBC by DMF at Reflux Temperature

contact time (h)	$tot(Cl)_{acid}$[a]	$tot(Cl)_{base}$[b]	$tot(N)_{base}$[c]
2	4.83	4.49	0.53
4	3.07	2.69	1.28
8	2.87	0.19	2.74
24	3.18	0.00	2.87
48	3.14	0.00	2.93

[a] Total chlorine elemental analysis after HCl/H_2O elution, mmol/g. [b] Total chlorine elemental analysis after $NaOH/H_2O$ elution, mmol/g. [c] Total nitrogen elemental analysis after $NaOH/H_2O$ elution, mmol/g.

Table 2. Effect of Temperature on Functionalization[a]

temperature (°C)	$tot(Cl)_{base}$[b]	$tot(N)_{base}$[c]
25	6.40	
40	6.34	
60	4.78	0.71
100	4.63	0.84
120	2.50	1.18
140	0.33	2.98

[a] 17 h contact time. [b] Total chlorine elemental analysis after $NaOH/H_2O$ elution, mmol/g. [c] Total nitrogen elemental analysis after $NaOH/H_2O$ elution, mmol/g.

Results

PolyVBC beads were first refluxed with DMF from 2 to 48 h (Table 1). The copolymer had an initial chlorine capacity of 6.40 mmol/g (and an initial acid capacity of 0.00). Elemental analyses indicate that a reaction is occurring: after a 48 h reflux and elution of the beads with water/NaOH/water/HCl/water, the chlorine capacity decreased from 6.40 to 3.14 mmol/g, and the nitrogen capacity increased from 0.00 to 3.09 mmol/g. Furthermore, an acid capacity determination gave a value of 2.16 mmol/g. Subsequent elution of the polymer with 1 M NaOH and water gave values for the chlorine, nitrogen, and acid capacities of 0.00, 2.93, and 0.31 mmol/g, respectively. Loss of chlorine after $NaOH/H_2O$ elution indicates that it is ionically, rather than covalently, bound. Similar results were obtained at a 24 h reflux period, as shown in Table 1; additionally, the acid capacity decreased from 2.25 mmol/g after HCl/H_2O elution to 0.00 after $NaOH/H_2O$ elution. There was complete reaction at the $-CH_2Cl$ groups and total loss of chloride after an 8 h reflux period. The nitrogen elemental analysis indicates that the reaction is evident even at a 2 h reaction time.

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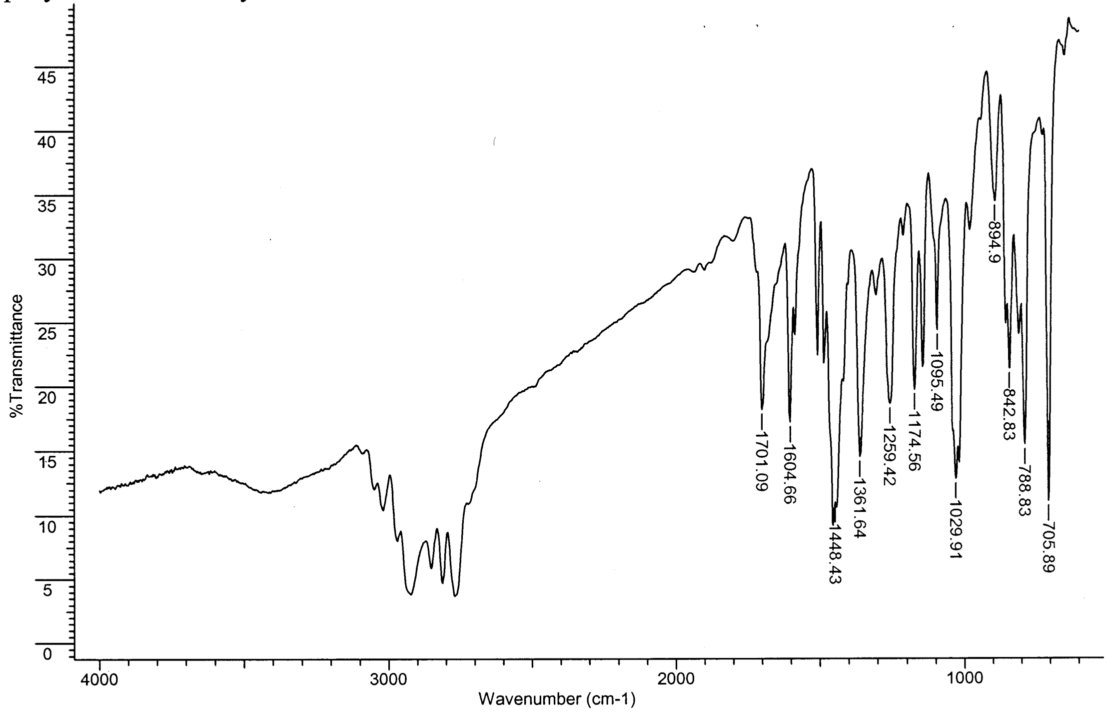
polyVBC + dimethylamine



polyVBC + DMF(8h)

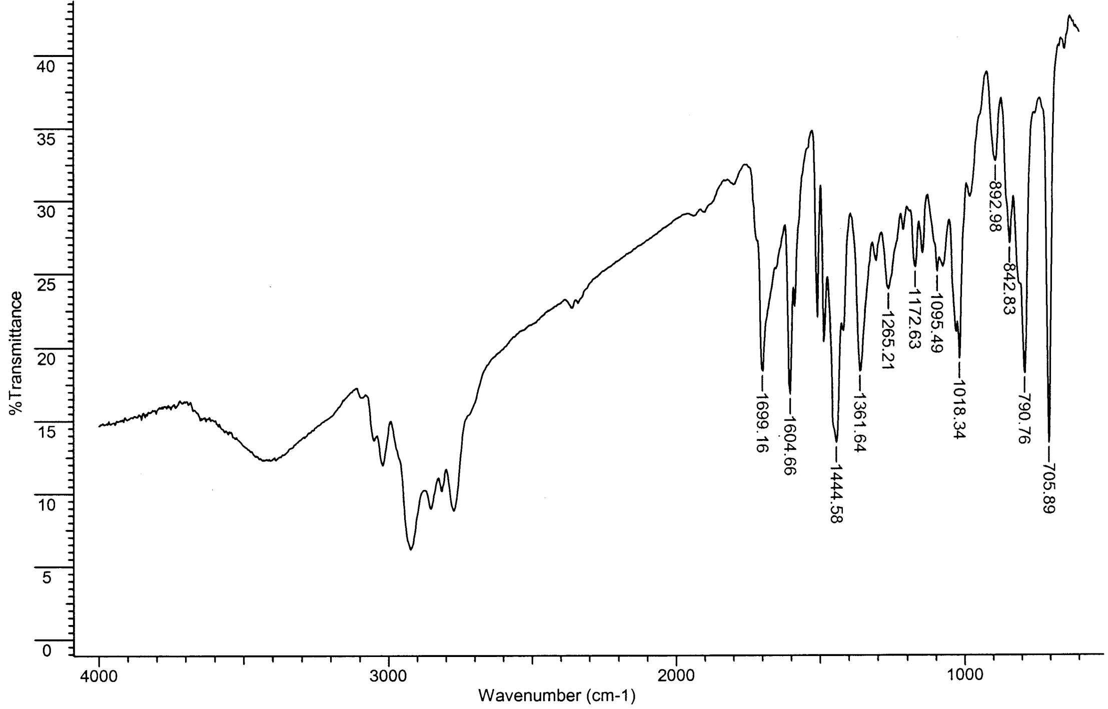


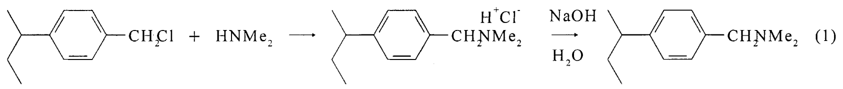
Figure 1. FTIR spectra of polyVBC reacted with dimethylamine (top) and DMF (bottom).

The effect of reaction temperature was quantified at a 17 h contact time (Table 2). Reaction begins at approximately 60 °C and is complete by 140 °C. The loss of covalently bound chlorine parallels the increase in nitrogen.

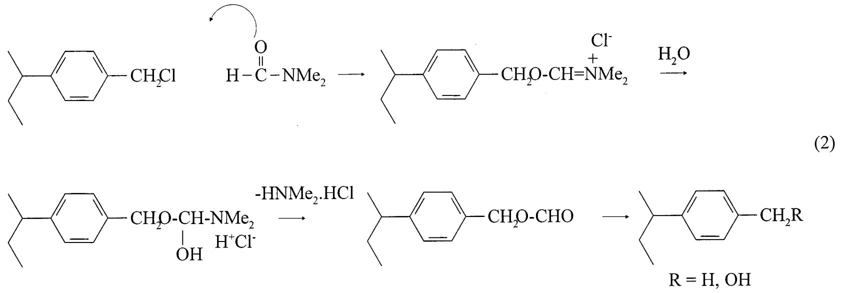
Discussion

The presence of an acid capacity in the product of the reaction between polyVBC and DMF indicated the formation of a ligand with an exchangeable proton. However, that it was tied to an exchangeable chloride ion pointed to something other than a carboxylic acid ligand. The presence of a tertiary amine group would be consistent with the nitrogen capacity and the exchangeable ions as H^+Cl^- on the polymer. A tertiary amine polymer was then synthesized by the reaction of dimethylamine with polyVBC (Scheme 1). After washing and elution with 1 M HCl and then H_2O, the polymer had an acid capacity of 3.55 mmol/g, a chlorine capacity of 4.91 mmol/g, and a nitrogen capacity of 4.70 mmol/g; after elution with 1 M NaOH and then H_2O, the acid, chlorine, and nitrogen capacities were 0.00, 0.00, and 4.66 mmol/g, respectively—behavior identical to that observed after reaction of the polyVBC with DMF.

Scheme 1



Scheme 2



Additionally, the FTIR spectra of the tertiary amine polymer with the polyVBC/DMF product after an 8 h reaction time are almost identical (Figure 1).

Formation of a $-CH_2NMe_2$ ligand by reaction of the polyVBC with DMF is consistent with decomposition of the DMF to carbon monoxide and dimethylamine[13] followed by amination of the polymer. Since the theoretical nitrogen capacity is 4.85 mmol/g at complete reaction of the $-CH_2Cl$ groups and the values determined do not exceed 3 mmol/g, then there must be an additional reaction that removes chloride but does not add nitrogen. Nucleophilic attack by the carbonyl oxygen on the polyVBC would be consistent with the results (Scheme 2). The reaction follows a pathway suggested by the Vilsmeier reaction.[14] Mechanistic studies under Vilsmeier conditions have focused on phosphoryl chloride, thionyl chloride, and phosgene as the active chloride reagent;[15] however, that benzyl chloride is prone to nucleophilic attack is well-known.[16] The parallel to the Vilsmeier reaction includes a formate ester as an intermediate—compounds that have been prepared under these conditions from alcohols.[17] Subsequent decomposition of the formate ester on the polymer in the presence of water can give a $-CH_2OH$ group while decomposition without the intervention of water will give a methyl group. Comparison of the FTIR spectra (Figure 1) shows a difference in the −OH region that is consistent with this. Solid-state ^{13}C NMR spectra of the polymers prepared by direct reaction with dimethylamine and with DMF provided further support. Both spectra have identical aromatic peaks at 120−150 ppm, a large peak at 40−50 ppm (the $-CH_3$ groups), and a peak at 60 ppm (the $-CH_2$ moiety adjacent to the nitrogen). The DMF polymer, however, has a peak at 70 ppm that is much more pronounced than a similar and much smaller peak in the dimethylamine polymer. The peak at 70 ppm is consistent with a $-CH_2-$ adjacent to an oxygen. (Experiments were run that eliminated the possibility of this being a spinning sideband.) We thus propose the formation of $-CH_2OH$ groups, and the possibility of some methyl group formation, along with an approximately equal amount of dimethylamine ligands when polyVBC is heated with DMF above a threshold temperature of 60 °C. While the polymer consists of a 60:40 mix of meta and para isomers, this is not expected to play a role in the mechanism or final reaction: the reaction with dimethylamine is representative of nucleophilic reactions on this polymer, and there is no differentiation between the positional isomers.[18,19]

Supporting the proposed mechanism is the report by Knunyants et al., that acyl chlorides undergo reaction with DMF to form aldehydes and amines.[20] The common feature with the current reaction is the presence of a carbon with a displaceable chloride capable of undergoing nucleophilic attack and both reactions following the same mechanism. The reaction does not occur on epoxides: poly(glycidyl methacrylate), when refluxed with DMF for 24 h, shows no nitrogen capacity and gives an IR spectrum that is identical to the starting polymer. The $-CH_2Cl$ moiety in polyVBC or chloromethylated polystyrene is thus of sufficient reactivity for nucleophilic reaction by DMF at elevated temperatures.

Conclusions

The use of DMF as a solvent in reactions with polyVBC or chloromethylated polystyrene is not recommended at temperatures exceeding 60 °C due to attack by the DMF at the $-CH_2Cl$ moieties to form tertiary amine, hydroxymethyl, and methyl groups. The amine groups will interfere in metal ion affinity studies, and the methyl groups will make the polymer more hydrophobic than expected. Moreover, the targeted ligand capacity can be significantly less than theoretical. The nucleophilicity of the amine group and the hydrophobicity of the methyl group can also interfere when the resulting polymers are used as reagents or catalysts.

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