

Phase Transfer Catalysis

Synthesis of Polymers Containing Acetamide Structure and Their Use as Phase Transfer Catalyst

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Summary

N-Methyl-N-(p-vinylbenzyl)acetamide was synthesized by the reaction of p-chloromethylstyrene with N-methylacetamide in the presence of sodium hydride. This monomer was readily polymerized or copolymerized with styrene by AIBN. The resulting polymers served as effective phase transfer catalysts for several nucleophilic substitution reactions under liquid-liquid biphasic conditions. The catalytic activity was discussed on the terms of cation binding ability of the polymers and activation of anions caused by the desolvation on hydrophobic region of the polymers.

Introduction

Polymeric phase transfer catalysts present a big advantage for the simplification of work-up procedure in organic synthesis(1-4). Most of these polymers were synthesized by merely attaching classical phase transfer catalysts such as ammonium salts, phosphonium salts, crown ethers, and cryptands to insoluble polymeric supports. Meanwhile, polymeric phosphoramides (5,6), and sulfoxides(7-10) were found to have similar catalytic activity to the above compounds, although monomeric analogs do not serve as phase transfer catalyst. However, the relationship between structure and activity has not been investigated in detail.

Recently, we reported that polymeric sulfoxide(8,10), sulfones(11), and formamides(12) prepared by the copolymerization of corresponding vinyl monomers with styrene possess extraordinary catalytic activity for several nucleophilic substitutions in two phase system. Furthermore, we suggested that hydrophobic environment around the active site is an important factor for catalytic activity.

These polymers are regarded as the polymers containing active sites of typical dipolar aprotic solvents such as dimethylsulfoxides, hexamethylphosphoramide, sulfolane, and dimethylformamide. N,N-Diethylacetamide has been shown to have similar properties to dipolar aprotic solvents(2). Actually, Regen et al.(13) recently showed that even the cross-linked poly(acrylamide)s having several alkyl chains could work as co-solvent for substitution reaction of phenoxide.

On the basis of these findings, we hoped that polymers containing acetamide structure might exhibit the ability of phase transfer catalyst. In this article, we describe the

synthesis of a new monomer containing acetamide structure, its polymerization, and further discuss the relationship between the structure and the catalytic activity of resulting polymers for biphasic reactions.

Experimental

A. Materials

Styrene was purified by the ordinary method and distilled under nitrogen just before use. 2,2'-Azobisisobutyronitrile (AIBN) used as an initiator was recrystallized from methanol. Octyl bromide, benzyl bromide, phenol, thiophenol and solvents were used after distillation. Other reagents were obtained commercially and used without further purification.

B. Preparation of N-methyl-N-(p-vinylbenzyl)acetamide (MVAA)

To a slurry of 0.40 g (60 mmol) of sodium hydride and 80 ml of DMF was added 2.96 g (40 mmol) of N-methylacetamide. The mixture was stirred under nitrogen at room temperature for 1 h. To this mixture 3.04 g (20 mmol) of p-chloromethylstyrene was added slowly over a 30 min. period. After the reaction mixture was heated at 50°C for 4 h, it was filtered and the solids were washed with DMF. The residue obtained after solvent removal was dissolved in 30 ml of water and the mixture was extracted three times with 20 ml of chloroform. The organic layer was washed with a 2 % hydrochloric acid, followed by washing with water, and dried over sodium sulfate. After solvent removal, the product was separated by column chromatography (Wakogel-200, eluent; CHCl₃) to give oily product in 2.68 g (71 %) yield.

NMR (CDCl₃) δ = 2.17 (s, 3H), 2.45 (s, 3H), 4.60 (t, 2H), 5.26 (dd, 1H), 5.74 (dd, 1H), 6.60 (dd, 1H), 7.1-7.6 ppm (m, 4H).
IR: 910, 990, 1050, 1260, 1350, 1400, 1510, 1630, 2910, 3410 cm⁻¹.
Anal.: Calcd. for C₁₂H₁₅NO: C, 76.16; H, 7.99; N, 7.40 %
Found: C, 75.89, H, 7.74; N, 7.47 %

C. Polymerization procedure

Polymerization was carried out in a sealed glass tube with shaking in a water bath maintained at 60°C by a thermostat. The charge of the reagents into a tube and its seal were undertaken according to a similar method reported previously(14).

After polymerization for a given time, the tube was opened and its content was poured into a large amount of methanol to precipitate the polymer formed. The resulting polymer was purified by the reprecipitation from benzene into a mixture of ether and petroleum ether (1:1). The conversion was calculated from the weight of the dry polymer obtained.

Copolymerization was carried out by the same method as mentioned previously(14). The composition of the copolymers was calculated from their elementary analysis of nitrogen.

D. Extraction of potassium picrate

To a 20 ml of benzene solution of the polymer containing 6×10^{-3} mmol of amide group was added 5 ml of an aqueous picric acid solution (5×10^{-5} mol/l) containing excess potassium hydroxide (1×10^{-2} mol/l). The mixture was stirred magnetically for 1 h at 20°C. After separation, the aqueous solution was analyzed on the picrate absorption at 355 nm ($\epsilon = 14400$) by spectrophotometry.

E. Substitution reaction

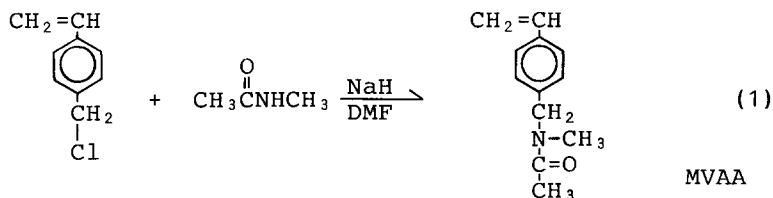
The two-phase reactions were carried out under standard phase transfer condition(15). In a typical run, a toluene solution (3 ml) of n-octyl bromide (0.32 g), a solution of potassium iodide (6.64 g) in water (5 ml), and polymer 1 (57 mg) were charged in a test tube, which was degassed and sealed under vacuum. The tube was heated without shaking in an oil bath at 100°C for 20 h. Thus, the reaction mixture was poured into petroleum ether to precipitate solids. The solid was filtered and the filtrate was analyzed by gas chromatography. The yield of octyl iodide was 21 %. The precipitated solid was washed with diluted hydrochloric acid. Its IR spectrum was in good agreement with that of polymer 2. The polymer was recovered in 96 % yield.

F. Measurement

IR spectra were recorded on a JASCO-2 spectrometer. The separation of product was performed by gas chromatography (HITA-CHI-063) and the internal standard method was adopted for yield determinations. The column used included 20 % Carbowax 20 M (1m x 6 mm) on Celite 545. NMR spectra were recorded by HITA-CHI R-20B spectrometer with tetramethylsilane as an internal standard. UV spectra were taken by HITACHI 124 spectrometer.

Results and Discussion

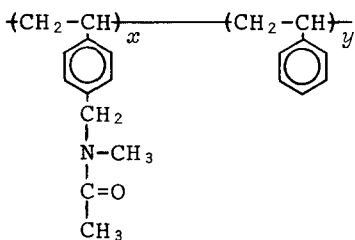
In order to obtain the relationship between the catalytic activity and microenvironment of active site, polymers with well-defined structure are desired. For this purpose, copolymerization methods are superior to the polymer reaction methods which have been employed in most cases. Thus, we designed N-methyl-N-(p-vinylbenzyl)acetamide (MVAA) as a monomer carrying acetamide structure. MVAA has high polymerizability and no other functional groups except for amide group. This monomer was readily prepared in moderate yield from the reaction of p-chloromethylstyrene and N-methylacetamide in the presence of sodium hydride. The structure was confirmed by spectroscopic data and elemental analysis.



MVAA was successfully polymerized in benzene by AIBN at 60°C to yield a white solid with an intrinsic viscosity of 0.10 dl/l. It was soluble in chloroform, benzene, DMSO and DMF, but insoluble in n-hexane, methanol, and water. In order to clarify the reactivity of MVAA in radical copolymerization, copolymerization with styrene was carried out. The results are summarized in Table 1. The monomer reactivity ratio is obtained by Fineman-Ross method as $r_{\text{MVAA}} = 0.66$, $r_{\text{St}} = 0.66$. From these values, the resonance stabilized factor Q and electrical factor e were calculated as $Q = 0.83$, $e = 0.22$. The values are very similar to those of p-chloromethylstyrene(16).

The catalytic activity of polymeric acetamides prepared by the method mentioned above was examined. Catalysts 1-4 em-

ployed here are as follows:



Cat.	$x/x+y$	η (dl/l)
1	1.00	0.10
2	0.56	0.50
3	0.39	0.26
4	0.32	0.17

Table 1. Copolymerization of MVAA (M_1) and styrene (M_2)^{a)}

M_1 ^{b)}	Conversions (%)	N (%)	m_1 ^{c)}
0.85	2.9	5.92	0.69
0.70	2.2	5.86	0.68
0.60	3.0	5.26	0.57
0.50	3.8	4.95	0.53
0.40	3.6	4.28	0.43
0.30	3.4	3.65	0.35
0.15	1.8	2.22	0.19

a) Copolymerizations were carried out in benzene at 60°C for 1 h.

$[M_1] + [M_2] = 1$ mol/l.

$[AIBN] = 6 \times 10^{-3}$ mol/l.

b) Mole fraction of M_1 in monomers.

c) Mole fraction of M_1 in copolymer.

The reaction of n-octyl bromide and potassium iodide was undertaken to test the catalytic activity. The reaction was carried out in toluene-water two phase system, and the results were summarized in Table 2.

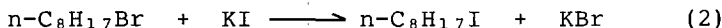


Table 2. Phase transfer reaction of n-octyl bromide with potassium iodide at 100°C for 20 hr

Entries	Catalysts	Yields of products (%)
1	$\text{CH}_3\text{CON}(\text{CH}_3)_2$	trace
2	$\text{CH}_3\text{CON} \begin{matrix} \text{CH}_3 \\ \text{CH}_2\text{Ph} \end{matrix}$	trace
3	polystyrene	trace
4	$\frac{1}{4}$	21
5	$\frac{4}{4}$	92

$[\text{Cat.}] = 3 \times 10^{-4}$ mol

$[\text{C}_8\text{H}_{17}\text{Br}] = 0.55$ M (in toluene), 3 ml

$[\text{KI}] = 8$ M (in H_2O), 5 ml

As can be seen from Table 2, this reaction proceeded in the presence of 1 or 4, but is not catalyzed by monomeric acetamide such as acetamide and N-benzylacetamide. It is noticeable that the catalytic activity is enhanced by introducing the active site to polystyrene.

The polymers employed here are soluble in toluene, but insoluble in water in spite of having an amide group which strongly interacts with water. Therefore, we believe that amide group in polymer interacts with potassium cation at the interface and transfers the cation to organic phase accompanying with thiocyanate anion as a result.

In order to examine this possibility, the extraction of potassium cation by polymeric acetamides was investigated by the Smid's method (17). The results are shown in Table 3.

All polymeric amides can extract potassium picrate, but monomeric acetamides can not extract it to any detectable

degree. This extraction ability increases with increasing the concentration of active site in polymer. This result suggests the cumulative chelation of metal ion with several amide groups.

Next, in order to investigate the effect of microenvironment around the active site, halogen exchange reaction was carried out by using the polymers which have four different composition ratios; the results are provided in Figure 1.

Interestingly, there is a maximum at certain composition ratio of amide to styrene unit. From 0 to approximately 1 of composition ratio, the yield is inversely related to the extraction ability mentioned above. This finding strongly implies the importance of hydrophobic region around the active site, and further suggests the activation of nucleophile by desolvation. Beyond 1, the yield follows the extraction ability.

From these results, the catalytic activity of polymeric acetamides was found to depend strongly on extraction ability and hydrophobicity around active site.

Finally, we would like to demonstrate the feasibility of those polymeric acetamide catalysts for several displacement reaction. As can be seen from Table 4, these polymers serve as phase transfer catalyst in several S_N2 type reactions such as the reaction of alkyl bromide with potassium thiocyanate, sodium thiocyanate, lithium iodide, sodium iodide and sodium phenoxide.

In addition, these soluble polymeric acetamides are recovered readily by reprecipitation and following treatment of a weak acid for the removal of alkali metal cations and reagents.

Table 3. Extraction of potassium picrate by polymeric amides

Entries	Amides	potassium picrate extracted in %
1	DMF	0
2	N-benzyl-N-methyl acetamide	0
3	$\frac{1}{2}$	4.5
4	$\frac{2}{3}$	2
5	$\frac{3}{4}$	>1
6	$\frac{4}{4}$	>1

Solvent: H₂O/benzene (5 ml/20 ml)
 [Picric acid] = 5.0×10^{-5} mol/l
 [KOH] = 1.0×10^{-2} mol/l
 [Amide] = 6×10^{-3} mmol

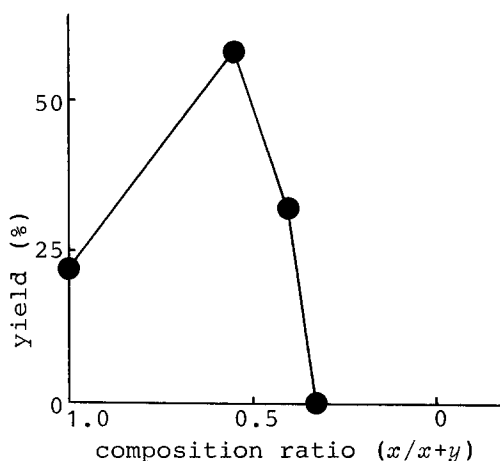


Figure 1. Dependence of product yield on composition ratio (x/x+y) in copolymer

[n-C₈H₁₇Br]=0.55 M in toluene, 5 ml
 [KI] = 4.0 M in H₂O, 15 ml
 [Cat.] = 0.3 mmol based on amide group

Table 4. Phase transfer reactions catalyzed by polymeric acetamide^{a)}

Entries	Substrates ^{b)}	Reagents ^{c)}	Catalysts ^{d)}	Yields	Products
1	n-C ₈ H ₁₇ Br	KSCN	3	92 %	n-C ₈ H ₁₇ SCN
2	"	NaSCN	3	92	"
3	"	LiI	2	63	n-C ₈ H ₁₇ I
4	"	NaI	2	97	"
5	"	KI	2	58	"
6	C ₆ H ₅ CH ₂ Br	C ₆ H ₅ ONa	2	85	C ₆ H ₅ CH ₂ OC ₆ H ₅

a) Reaction condition: temp. = 100°C, time = 20 h

b) [Substrate] = 0.55 mol/l (in toluene), 3 ml

c) [Reagent] = 8.0 mol/l (in H₂O), 5 ml

d) 0.3 mmol based on amide group

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