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Synthesis and solution properties of a new ionic polymer and its behavior in aqueous two-phase polymer systems

Hasan A. Al-Muallem, Mohamed I.M. Wazeer, Sk. Asrof Ali*

Department of Chemistry, King Fahd University of Petroleum and Minerals, Dhahran 31261, Saudi Arabia

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Abstract

The amine salt, *N*,*N*-diallyl-*N*-carboethoxymethylammonium chloride was copolymerized in dimethyl sulfoxide using ammonium persulfate or azo-bis-isobutyronitrile (AIBN) to afford the cationic polyelectrolyte (CPE) having five-membered cyclic structure on the polymeric backbone. The CPE on acidic (HCl) hydrolysis of the pendent ester groups gave the corresponding cationic acid salt (CAS) having the equivalent of chloride salt of *N*,*N*-diallylammonio ethanoic acid as monomeric unit. The CAS was converted into an anionic polyelectrolyte (APE) and polybetaine (PB) [having the monomeric unit equivalent of sodium *N*,*N*-diallylaminoethanoate and *N*,*N*-diallylammonioethanoate] by treatment with two and one equivalent of base, respectively. The solution properties of APE were investigated by potentiometric and viscometric techniques. Basicity constant of the amine functionality in APE is found to be 'apparent' and as such follow the modified Henderson–Hasselbalch equation; the protonation of the APE becomes more and more difficult as the degree of protonation (α) of the whole macromolecule increases. The composition and phase diagram of the aqueous two-phase systems of APE and poly(ethyelene glycol) (PEG) has been studied for the first time for this class of ionic polymers. The CAS and PB were found to be virtually insoluble in water. © 2001 Elsevier Science Ltd. All rights reserved.

Keywords: Polyelectrolyte; Polybetaine; Ionic polymer

1. Introduction

Butler's pioneering work [1] led to the discovery of cyclopolymerization of *N*,*N*-diallyl quaternary ammonium salts **1**, and provided an efficient access [2,3] to an array of water-soluble cationic polyelectrolytes **2**. The ammonium salts have also been successfully copolymerized [4–6] with sulfur dioxide to give the copolymers **3** (Scheme 1). These cationic polyelectrolytes have found extensive industrial and commercial applications [2,3,7–9] as paper additives, de-emulsifier of dispersed oil, paint thickeners, flocculants and coagulant aid in potable water and waste water treatment, biocides in water, in coal floatation and metal electroplating. Poly(diallyldimethylammonium chloride) alone accounts for over 1000 patents and publications. There are quite a few reports [10–19] in the literature of homo-and co-polymerization of zwitterionic monomers **1** (R^2 being an anionic pendent) leading to polyzwitterions. Amphoteric polymers containing zwitterions on the same monomer (i.e. betaines) or along the same backbone (i.e. ampholytes) have found applications in drag reduction [20], in electrophoresis as amphoteric buffers [21] and can be used as a simple model [22–24] for understanding the complex behavior of proteins. Amphoteric polymers, unlike polyelectrolytes, can exhibit 'anti-polyelectrolyte behavior' [11,25–27] i.e. enhancement in viscosity and solubility in the presence of added electrolytes (e.g. NaCl) due to the neutralization of the ionically cross-linked network in a collapsed coil [27,28] conformation of the polyampholytes.

In our endeavor to synthesize special polymers containing two pH-triggerable funtionalities (*N* and CO_2^-) which are expected to exhibit pH responsive solution behavior, we have directed our attention to cyclocopolymerize a diallylamine salt (**1**, $R^1 = H$) (Scheme 2) having a pendent ester functionality (instead of usual diallyl quaternary ammonium salts) with sulfur dioxide. To our knowledge, this work utilizes Butler's cyclopolymerization technique for the first time to synthesize efficiently and cheaply novel amino acid–sulfur dioxide copolymers **7–10**. We also report the study of aqueous two-phase system of polymer **9** and poly(ethylene glycol).

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* Corresponding author. Tel.: +966-3-860-3830; fax: +966-3-860-4277.
E-mail address: shaikh@kfupm.edu.sa (Sk. Asrof Ali).

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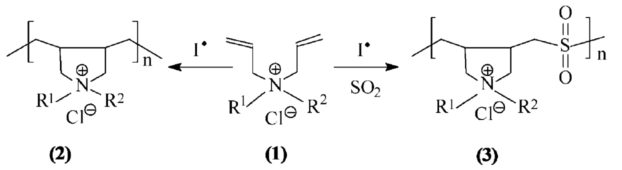


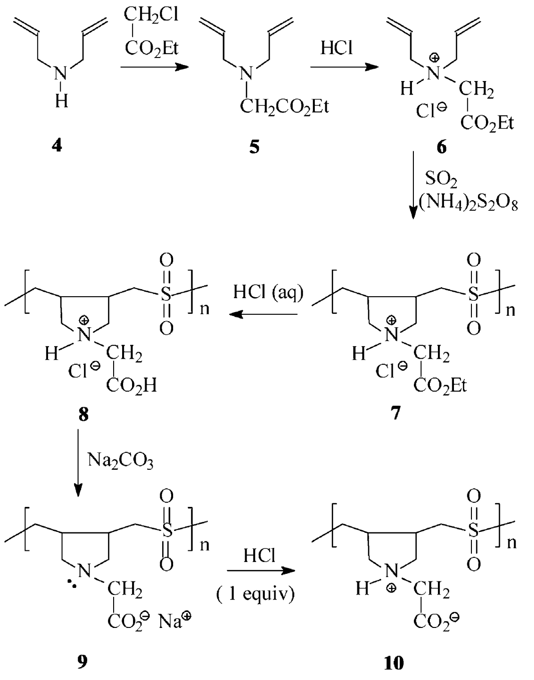
Scheme 1.

2. Experimental

2.1. Physical methods

Melting points are recorded in a calibrated Electrothermal-IA9100-Digital Melting Point Apparatus using heating rates of 1 °C/min in the vicinity of the melting points. Elemental analyses were carried out in a Carlo-Erba elemental analyzer Model 1102. IR spectra were recorded on a Perkin Elmer 16F PC FTIR spectrometer (Spectral resolution, 4 cm^{-1}; Number of scans, 19). ^{1}H and ^{13}C NMR spectra of the polymers were measured in D_2O using dioxane as internal standard on a JEOL LA 500 MHz spectrometer. Viscosity measurements were made by an Ubbelohde viscometer (having Viscometer Constant of 0.005718 centistokes/s at all temperatures) using pure water under N_2 in order to avoid CO_2 absorption which may affect the viscosity data.

The equipment used for thermal analysis was a Simultaneous Thermal Analyzer (STA 429) manufactured by Netzsch, Germany. The polymer sample to be tested (usually 30 mg) was placed in an alumina crucible. The aluminum oxide (Al_2O_3, 100 mg) was placed in an identical alumina crucible as a reference sample. Using the sample carrier system, which has two sets of 10% Pt–Pt/Rh thermocouples, the sample carrier was placed in the middle of the vertical furnace, which was programmed and controlled by a microprocessor temperature controller. The temperature was raised at a uniform rate of 10 °C/min. The analyses were made over a temperature range of 20–1000 °C in an atmosphere of N_2 flowing at a rate of 100 ml/min.



Scheme 2.

2.2. Materials

Ammonium persulfate (APS) from BDH Chemical Co. (Poole, UK), ethyl chloroacetate and diallylamine from Fluka Chemie AG (Buchs, Switzerland) were used as received. AIBN from Fluka was purified by recrystallization from a chloroform–ethanol mixture. PEG of molecular weight of 35 000 was purchased from Merck-Schuchardt. All glassware were cleaned using deionized water. Dimethylsulfoxide (DMSO) was dried over calcium hydride overnight and then distilled under reduced pressure at a bp of 64–65 °C (4 mmHg). For dialysis, Spectra/Por membrane with MWCO of 6–8000 was purchased from Spectrum Laboratories Inc.

2.3. *N,N-diallyl-N-carboethoxymethylamine* (**5**)

To a magnetically stirred mixture of diallyl amine (48.6 g, 0.50 mol), water (75 cm^3) containing K_2CO_3 (0.25 mol) at 60 °C was added with ethyl chloroacetate (55.2 g, 0.45 mol) dropwise over a period of 1 h. The mixture was then stirred under N_2 at 60 °C for an additional 5 h. An additional 0.25 mol of K_2CO_3 was added to the reaction mixture and was extracted with ether (3 × 50 cm^3). The combined organic layers was dried ($MgSO_4$), concentrated and the residual liquid upon distillation afforded the diallyl derivative as a colorless liquid (65 g, 78.9%). Bp$_{8\ \mathrm{mbarHg}}$, 93 °C; (Found: C, 65.3; H, 9.25; N, 7.6. $C_{10}H_{17}NO_2$ requires C, 65.54; H, 9.35; N, 7.64%); $\upsilon_{\max}$ (neat) 3852, 3744, 3648, 3078, 2980, 2924, 2838, 2360, 1844, 1740, 1642, 1540, 1450, 1418, 1370, 1264, 1188, 1118, 1030, 992, 850, 724 cm^{-1}. δ_H ($CDCl_3$) 1.26 (3H, t, $J = 7.0$ Hz), 3.25 (4H, d, $J = 6.8$ Hz), 3.31 (2H, s), 4.16 (2H, q, $J = 7.0$ Hz), 5.17 (4H, m), 5.86 (2H, m); δ_C ($CDCl_3$) 14.27, 53.91, 57.23, 60.30, 118.11, 135.33, and 171.35.

2.4. *N,N-diallyl-N-carboethoxymethylammonium chloride* (**6**)

To a magnetically stirred, salt–ice cooled, solution of *N*,*N*-diallyl-*N*-carboethoxymethylamine (**5**) (50 g, 0.273 mol) in diethyl ether (500 cm^3), was bubbled moisture-free gaseous HCl. Upon its formation, the ether-insoluble hydrochloride salt (**6**) separated as a liquid, and the HCl-bubbling was continued until the supernatant liquid became clear and no further precipitation was observed. The supernatant ether layer was removed by decantation. The chloride salt was

Table 1
Effect of concentration of monomer and initiator on polymerization of the monomer 6/SO_2 copolymerization (polymerization reactions were carried out in DMSO using 20 mmol of each of the monomer and SO_2)

Entry number	DMSO (g)	Initiator[a] (mg)	Temperature (°C)	Time (h)	Yield[b] (%)	Intrinsic viscosity[c] (dl g^{-1})
1	4.0	A 50	40	20	7	–
2	4.0	A 80	50	20	14 (11)	–
3	4.0	A 130	50	4	24	
				20	23 (21)	0.902
4	4.0	A 130	55	3	32	
				5	37 (33)	0.892
5	5.0	A 130	55	3	52	
				5	62	
				7	64 (60)	0.843
6	6.5	A 130	55	5	50	
				20	48 (45)	0.448
7	4.0	B 80	55	15	81 (73)	1.11
8	4.0	B 100	55	15	88 (80)	1.32
9	4.0	B 120	55	15	93 (84)	1.25

[a] A is Ammonium persulfate; B is Azobisisobutyronitrile.

[b] Yield as determined by ^1H NMR analysis; isolated yields are written in parentheses.

[c] Viscosity of 1–0.125% polymer solution on 0.1 N NaCl at 30 °C was measured with a Ubbelohde Viscometer ($K = 0.005718$).

crystallized from acetone–ether mixture to provide (**6**) very hygroscopic white crystals (52.8 g, 88%) and the salt was dried under vacuum at 40 °C until no further decrease in weight was observed. Mp 59–60 °C closed capillary). The elemental analysis was not so precise because of the highly hygroscopic nature of the monomer (Found: C, 53.9; H, 8.6; N, 6.2. $C_{10}H_{18}NO_2Cl$ requires C, 54.67; H, 8.26; N, 6.38%); υ_{max} (KBr) 3418, 3084, 2982, 2494 (broad), 1746, 1642, 1426, 1216, 1164, 1072, 1004, 948 cm^{-1}. δ_H (D_2O) 1.16 (3H, t, $J = 7.1$ Hz), 3.63 (4H, d, $J = 7.0$ Hz), 3.84 (2H, s), 4.16 (2H, q, $J = 7.1$ Hz), 5.44 (4H, m), 5.81 (2H, m). δ_C (D_2O) 14.09, 53.05, 57.73, 64.57, 126.10, 128.43, and 167.61.

*2.5. General procedure for the copolymerization of the monomer **6** with SO_2*

All the polymerizations were carried out using conditions as described in Table 1. The experiment under entry no. 5 was repeated in large scale as described below. In a typical experiment, SO_2 (4.676 g, 73 mmol) was absorbed in a solution of the monomer **6** (16.04 g, 73 mmol) in DMSO (18.3 g). The required amount of the initiator (APS) (as listed in Table 2, 0.475 g) was then added under N_2 and the closed flask was magnetically stirred at 55 °C for 7 h. The reaction mixture which remained transparent throughout the polymerization process, was precipitated in acetone.

Table 2
Experimental details for protonation of polymers at 25 °C in salt-free water and 0.1 M NaCl using 0.1015 M HCl

Run	$Z^{\pm}$ (mmol)	α-range	pH-range	Points[a]	log K^0 [b]	n[b]	R^2 [c]
*Polymer APE **9** in salt-free water*							
1	0.3302	0.17–0.73	9.88–7.85	15	8.72	1.81	0.9966
2	0.4193	0.14–0.75	10.12–7.89	18	8.77	1.84	0.9991
3	0.4519	0.15–0.76	9.93–7.73	18	8.68	1.82	0.9957
4	0.4832	0.15–0.74	9.89–7.99	19	8.75	1.76	0.9972
	Average				8.73 (4)	1.81 (3)	
	log K[d] $= 8.73 + 0.81 \log[(1-\alpha)/\alpha]$						
*Polymer APE **9** in* 0.1 M *NaCl*							
1	0.3251	0.13–0.81	8.73–7.11	16	7.84	1.15	0.9984
2	0.4039	0.20–0.84	8.60–7.13	17	7.90	1.17	0.9974
3	0.4717	0.18–0.82	8.64–7.19	17	7.91	1.15	0.9966
4	0.5764	0.14–0.82	8.72–7.10	21	7.86	1.16	0.9973
	Average				7.88 (3)	1.16 (1)	
	log K[d] $= 7.88 + 0.16 \log[(1-\alpha)/\alpha]$						

[a] Number of data points from titration curve.

[b] Values in the parentheses are standard deviations in the last digit.

[c] R is the correlation coefficient.

[d] $\log K = \log K^0 + (n-1)\log[(1-\alpha)/\alpha]$.

The white polymer was dissolved in minimum amount of water and reprecipitated in acetone. This process was repeated four times in order to ensure the complete removal of the unreacted monomer. The copolymer was then dried to a constant weight (13.3 g, 60.4%) at 50 °C under vacuum. The hygroscopic white polymer, CPE **7**, was stored in a desiccator. The onset of thermal decomposition (Closed capillary) 232 − 250 °C (decomposed, turned brown) (Found: C, 39.9; H,6.5; N, 4.80; S, 10.3. $C_{10}H_{18}NO_4SCl{\cdot}H_2O$ requires C, 39.80; H, 6.68; N, 4.64; S, 10.62%); υ_{max} (KBr) 3422, 2982, 2936, 2610 (broad), 1744, 1634, 1426, 1382, 1297, 1222, 1122, 1071, 1021, 954, and 850 cm^{-1}.

2.6. Acidic hydrolysis of the copolymer 7

A solution of the CPE **7** (from entry no. 5) (9.9 g, 32.8 mmol) in 6 M HCl (100 cm^3) was stirred in a sealed flask at 50 °C for 96 h (or until the hydrolysis of the ester group was complete as indicated by the absence of the ethoxy proton signals in the ^1H NMR spectrum). During hydrolysis, the product gradually precipitated in the reaction mixture. The insoluble polymer was separated from the reaction mixture and then soaked in deionized water (20 cm^3) overnight, after that it was dried under vacuum at 50 °C for 6 h. The polymer, CAS **8** was then crushed into powder and redried under vacuum to a constant weight (8.70 g, 96.9%) at 50 °C. The onset of thermal decomposition (Closed capillary) 235–250 °C (decomposed, turned brown, charred at 290 °C) (Found: C, 35.4; H, 6.1; N, 5.2; S, 11.5. $C_8H_{14}NO_4SCl{\cdot}H_2O$ requires C, 35.10; H, 5.89; N, 5.12; S,11.71 %); υ_{max} (KBr) 3430, 2922, 2600 (broad), 1738, 1636, 1416, 1306, 1258, 1219, 1122 and 856 cm^{-1}.

2.7. Basification of the CAS 8

To a solution of Na_2CO_3 (5 g, 47 mmol) in water (50 cm^3) was added polymer **8** (6.00 g, 21.9 mmol). The mixture was stirred until the polymer dissolved completely to give a clear solution. The solution was dialized against deionized water to remove excess Na_2CO_3, $NaHCO_3$ and NaCl (monitored by $AgNO_3$ test). The resulting solution of the anionic APE **9** was freeze dried and subsequently dried under vacuum to a constant weight (5.49 g, 90%) at 50 °C. ^1H NMR spectrum revealed the presence of minor amount of the PB **10** in addition to the major APE **9**. During dialysis a minor portion of the APE is equilibrated to the PB.

In order to make APE free of the PB, a sample of the APE as prepared (~3.33 g, ~12 mmol) was dissolved in a minimum quantity of water (~10 cm^3) and then treated with a solution (5 cm^3) of 1.0 N NaOH. The polymer was immediately precipitated in methanol (50 cm^3) and filtered. The polymer was redissolved in methanol–water mixture and reprecipitated in acetone. The process was repeated three times. Finally the polymer was filtered and dried to a constant weight (2.8 g) under vacuum at 55 °C. The onset of thermal decomposition (Closed capillary) 240–250 °C (decomposed, turned brown, charred at 280 °C) (Found: C, 34.4; H, 5.75; N, 5.15, S, 11.2. $C_8H_{12}NO_4SNa{\cdot}2H_2O$ requires C, 34.66; H, 5.82; N, 5.05; S 11.56%); υ_{max} (KBr) 3444, 2924, 1588, 1412, 1304, and 1124 cm^{-1}.

2.8. Acidification of APE 9 with 1 equiv. HCl

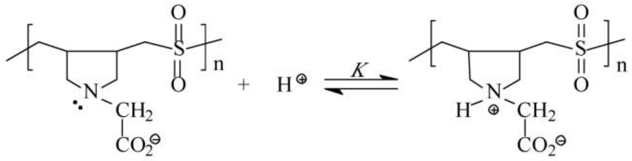
To a 0.1015 N HCl solution (6.00 cm^3, 0.61 mmol) the polymer **9** (170 mg, 0.61 mmol) was added. The resultant insoluble PB **10** was kept in the mixture for 48 h. The mixture was centrifuged and the residue was soaked in acetone for overnight. The polymer was then dried under vacuum to a constant weight (142 mg, 98.1%) at 55 °C. The onset of thermal decomposition (Closed capillary) 240–250 °C (decomposed, turned brown, charred at 250 °C) (Found: C, 40.8; H, 6.3; N, 5.7, S, 13.45. $C_8H_{13}NO_4S{\cdot}H_2O$ requires C, 40.50; H, 6.37; N, 5.90; S 13.51%); υ_{max} (KBr) 3440, 2951, 1628, 1399, 1296, 1114, and 640 cm^{-1}.

2.9. Potentiometric titrations

The potentiometric titrations were carried out at 25 °C on a Corning pH Meter 220. A gentle stream of N_2 was passed through distilled deionized water at 90 °C for 15 min in order to remove dissolved gases. This water was used in the titration in salt-free and salt (NaCl, 99.9% purity) solutions and for viscosity measurements. For each titration 200 cm^3 of salt-free or 0.1 N NaCl solution containing a weighed amount (usually around 0.5 mmol) of the APE **9** was used. The solution was titrated with 0.1015 M HCl delivered by a buret under N_2. After each addition of the titrant (in the range 0.10–0.25 cm^3) the solution was stirred briefly, using a magnetic stir bar, under N_2. The pH of the solution was recorded using a Corning pH Meter 220. Under the conditions (containing large volume of 0.1 N NaCl) the small amount of polymers or the small volume of the titrant used do not contribute much to the ionic strength and as such the data were not corrected to zero ionic strength and activity coefficient corrections were not applied.

2.10. Method of calculation

$\log K$ is calculated at each pH value by the well-known Henderson–Hasselbalch Eq. (1) (Scheme 3) where degree of protonation (α) is the ratio $[ZH^{\pm}]_{eq}/[Z^-]_i$. The $[Z^-]_i$ is the initial analytical concentration of the monomeric units in the APE **9** and $[ZH^{\pm}]_{eq}$ is the concentration of the protonated species at the equilibrium given by Ref. [29] $[ZH^{\pm}]_{eq} = C_H^+ - [H^+] + [OH^-]$, where C_H^+ is the concentration of the added HCl; $[H^+]$ and $[OH^-]$ at equilibrium was calculated from the pH value. The typical electrolytes having apparent basicity constants could be described by Eq. (2) (Scheme 3) where $\log K^0 = \text{pH}$ at $\alpha = 0.5$ and $n = 1$ in the case of sharp basicity constants. The linear regression fit of pH vs. $\log[(1-\alpha)/\alpha)]$ gave $\log K^0$ and n as the intercept and slope, respectively. Only values of α in the range 0.13–0.84 were accounted in order to minimize the effect of simultaneous protonation of COO^- base.



9 10

$$Z^- + H^+ \rightleftharpoons ZH^\pm$$
$$(1-\alpha) \qquad (\alpha)$$

$$\log K = \mathrm{pH} - \log[(1-\alpha)/\alpha] \qquad \text{(Eq 1)}$$

$$\mathrm{pH} = \log K^o + n\log[(1-\alpha)/\alpha] \qquad \text{(Eq 2)}$$

$$\log K = \log K^o + (n-1)\log[(1-\alpha)/\alpha] \qquad \text{(Eq 3)}$$

Scheme 3.

Simultaneous protonation of the two basic sites is least likely since the basicity constant for the COO^- group is less than that of the amine group by at least five orders of magnitude.

The experimental details of the potentiometric titrations are summarized in Table 2. Inserting the value of pH from Eq. (2) into Eq. (1) leads to modified Henderson–Hasselbalch equation (Eq. (3)) [30,31] (Scheme 3) where $(n-1)$ gives a measure of the deviation of the studied polymers from the behavior of small molecules showing sharp basicity constants (for molecules having sharp basicity constants, n becomes 1).

2.11. Phase compositions and phase diagram

2.11.1. The NMR method

Several systems of known compositions as described in Table 3 were made. The phase separation happened within minutes after thorough shaking and the mixture was kept at 23 °C for 24 h. The volume and the density of the top (~1.04 g/cm^3) and bottom layers (~1.09 g/cm^3) were measured. The ^{1}H NMR spectra of the top and bottom layers were measured in D_2O (after removal of H_2O by a gentle stream of nitrogen). The top and bottom layers were found to be overwhelmingly rich in PEG and APE, respectively.

The ^{1}H NMR signals for the polymers were well separated in the absence of HCl and the mole ratios of the repeating units of the polymers were easily calculated using the integration of the four-proton singlet at δ 3.58 for PEG and the 12-proton complex signals in the range δ 2.4–3.50 for the polymer APE. In presence of HCl, the determination of the mole ratios were difficult since the singlet for PEG overlapped with the signals for the APE protons which were shifted downfield (δ 2.6–3.70). However, basification (K_2CO_3) followed by ^{1}H NMR measurements allowed us to determine the mole ratios. The tie lines *A–D* were constructed using the systems 4–7 in Table 3. Weight percent of each polymer is determined by using Eqs. (4) and (5) as described in our earlier work [6]

$$[\mathrm{APE_b}] = \frac{\mathrm{PEG_0}/44.03 - (\mathrm{APE_0}/277.27)([\mathrm{PEG}]/[\mathrm{APE}])_\mathrm{t}}{V_\mathrm{b}\{([\mathrm{PEG}]/[\mathrm{APE}])_\mathrm{b} - ([\mathrm{PEG}]/[\mathrm{APE}])_\mathrm{t}\}} \tag{4}$$

where, subscript t and b represent top and bottom phase, respectively. [APE] and [PEG] represent concentration of the anionic polyelectrolyte and poly(ethylene glycol) in mmol of repeat unit cm^{-3}. APE_0 and PEG_0 represent total mass in mg of the polymers and V represent the volume in cm^3. Molar masses of the repeat units of the $APE \cdot 2H_2O$ and PEG were taken as 277.27 and 44.03, respectively. [PEG]/[APE] represents molar ratio of the polymers as determined by ^{1}H NMR integration. The mass of polymer APE in the bottom phase is then calculated using

$$\mathrm{APE_b} = [\mathrm{APE_b}]V_\mathrm{b} \times 277.27\ \mathrm{mg} \tag{5}$$

Once one of the polymer concentration is known in a phase, then the rest of the concentrations and weight percents of the polymers in the two phases are easily calculated from the known volume, density and mass of the two phases.

2.11.2. The turbidity method

About 5 g of a concentrated solution (~10% w/w) of APE (treated with 0.70 equiv. HCl) in 0.1 N KCl was taken in a flask and a known weight of a concentrated solution (~25% w/w) of the PEG (in 0.1 N KCl) of molecular weight

Table 3
Phase composition of the APE **9**–PEG–H_2O system at 23 °C

	Total system				Top phase		Bottom phase		
System	APE (% w/w)	PEG (% w/w)	KCl (N)	HCl (Equiv.)	APE (% w/w)	PEG (% w/w)	APE (% w/w)	PEG (% w/w)	Volume ratio[a]
1	5.227	2.690	1.5	0.70	0.135	5.19	9.95	0.364	1:1
2	5.227	2.690	1.0	0.70	0.409	5.05	10.4	0.150	1.14:1
3	5.215	2.69	0.5	0.70	0.425	4.94	10.6	0.158	1.21:1
4	5.468	5.468	0.1	0.70	0.175	7.99	16.6	0.172	2:1
5	2.8115	5.629	0.1	0.70	0.775	6.85	11.8	0.270	4.7:1
6	7.676	1.584	0.1	0.70	1.38	4.92	10.0	0.353	0.432:1
7	5.204	2.69	0.1	0.70	1.57	4.61	9.15	0.647	1.308:1
8	11.14	8.28	0.5	0	~0	21.2	18.1	0.212	0.67:1
9	5.934	10.205	0.5	0	~0	16.9	14.8	0.240	1.57:1
10	6.22	10.34	0.5	0	~0	15.8	15.9	0.180	1.67:1

[a] Volume ratio of top and bottom phase.

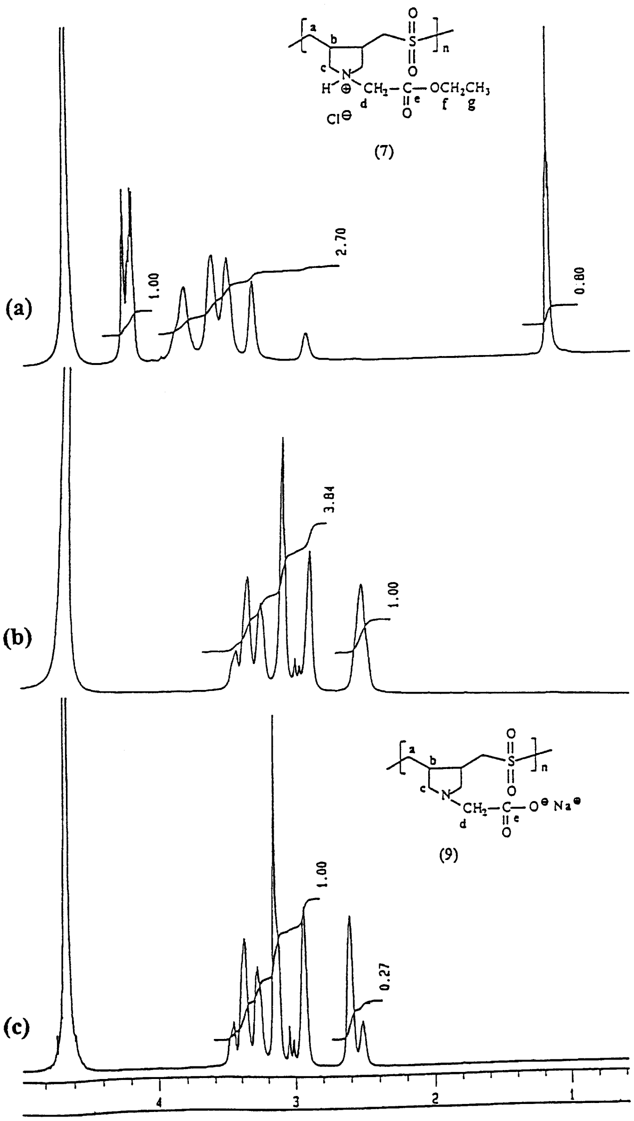


Fig. 1. ^{1}H NMR spectrum of (a) CPE **7**, (b) APE **9** and (c) APE **9** containing a minor portion of the polybetaine **10** in D_2O.

of 35 000 was added to the flask and stirred with a magnetic stir bar until the transparent system turned turbid. Then a known weight of 0.1 N KCl solution was added dropwise until the system became transparent again. At this point, the final composition of the two polymers calculated corresponds to a point on the binodial curve. After obtaining the first point, a concentrated solution of PEG was added again to obtain a turbid suspension, and dilution with water (0.1 N KCl) was repeated to obtain a second point on the binodial. This procedure was continued until a sufficient number of points for the construction of the binodial curve were obtained. In order to obtain points on the other end of the binodial, the concentrated solution of the PEG was titrated with the APE (+0.70 equiv. HCl) with PEG solution using same way as described above. Points obtained by turbidity method are joined together in Fig. 6. The experiments were carried out at 23 °C.

3. Results and discussion

Diallyl amine (**4**) on treatment with one equivalent of ethyl chloroacetate afforded tertiary amine **5** which upon reaction with hydrogen chloride gas gave the hydrochoride salt **6** (Scheme 2). Our earlier work [17,18] on quaternary ammonium salts with ethoxycarbonymethyl pendant indicated that the homopolymerization did not give polymer in appreciable yields, hence we decided to carry out copolymerization with sulfurdioxide. The monomer **6**–SO_2 mixture was subjected to polymerization in DMSO using APS as the initiator and the copolymer **7** was obtained in low to moderate yields (7–60%). However, the polymerization reaction went smoothly using AIBN as the initiator to give the CPE **7** in excellent yields. The results of the polymerization under various conditions and the intrinsic viscosities of the resultant polymers are given in Table 1. The CPE **7** was hydrolyzed in 6 M HCl to produce water-insoluble CAS **8** in excellent yield (73–84%). The addition of an excess of Na_2CO_3 followed by dialysis against deionized water afforded APE **9** which, on addition of 1 equiv. HCl, gave the water-insoluble PB **10**. During dialysis it was observed that a minor amount of the APE equilibrated to PB **10** as revealed by ^{1}H NMR data (*vide infra*). The APE free of polybetaine was prepared by treating a mixture of **9** and **10** with NaOH and precipitating the resultant APE in methanol–acetone. While the CPE **7** and APE **9** are soluble in water, PB **10** and the CAS **8** were found to be practically insoluble in every common solvent including methanol and water in presence or absence of common salts (e.g. KCl). In a typical experiment, a mixture of the polymer **8** (150 mg) in deionized water (5 cm^3) was stirred under N_2 at 25 °C for 96 h. After centrifugation, the supernatant aqueous phase was removed and the polymer was dried under vacuum at 55 °C to a constant weight of 149 mg. This ensured the virtual insolubility of the polymer. Similar experiments were carried out in 0.5 and 0.1 N KCl solutions and solubility of the polymer **8** was again found to be almost zero. The PB **10** was also found to have almost zero solubility in 0.5 N KCl solution.

The IR spectrum of the copolymers **7**–**10** indicates the presence of the SO_2 unit into the polymeric backbone. The two strong bands at ~1300 and ~1120 cm^{-1} were assigned to the asymmetric and symmetric vibrations of SO_2 unit. Absorption at 1744 cm^{-1} in the IR spectrum of CPE **7** indicates the presence of an ester group and the absorption at 1738 was attributed to C=O stretch of COOH in the polymer **8**. While the symmetric stretching of COO^- in the dipolar form of **10** and anionic form of **9** appeared at 1399 and 1412 cm^{-1}, respectively, their corresponding antisymmetric stretching appeared at 1628 and 1588 cm^{-1}, respectively. The absorption peaks are in agreement with those observed for simple amino acids [32].

^{1}H and ^{13}C NMR spectra of the polymers **7** and **9** are displayed in Figs. 1 and 2, respectively. It is evident, after comparing the proton spectra of the polymers (Fig. 1), that

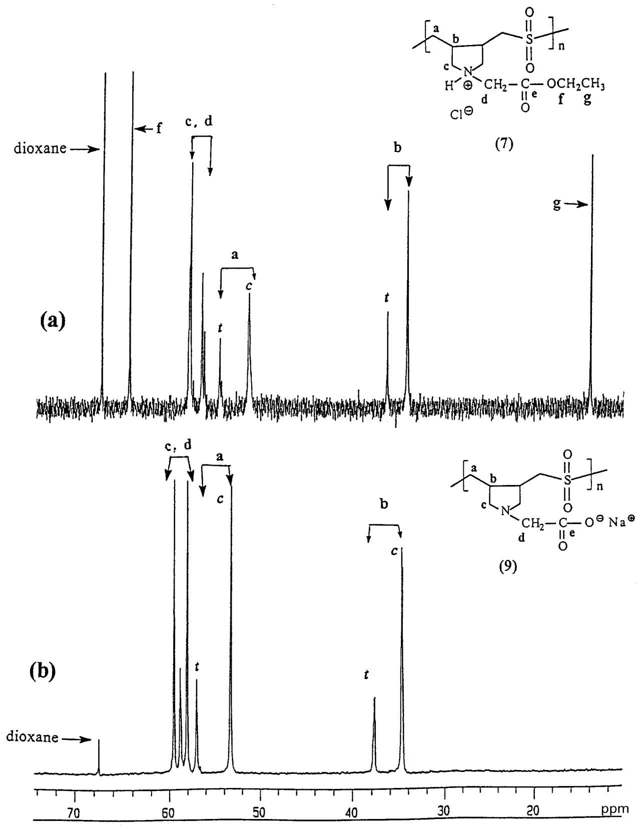


Fig. 2. ^{13}C NMR spectrum of (a) CPE **7** and (b) APE **9** in D_2O. The letter *c* and *t* indicate signals for the *cis* and *trans* isomers.

the CH_3–CH_2OC and the CH_3CH_2–OC protons, which appeared at δ 1.18 (t) and 4.21 ppm, respectively, for the CPE **7**, are absent in the spectrum of the APE (**9**). A similar observation is made from the ^{13}C NMR spectra; the carbons of the ethyl group (Fig. 2) are absent from the spectrum of **9**, thus indicating the complete removal of the ester groups by hydrolysis. Integration of the relevant peaks in the ^{13}C spectrum yields the *cis*/*trans* ratio of the ring substituents to be 75/25 which is similar to that observed for the polymers derived from the corresponding quaternary ammonium salts [17,18]. Carbonyl carbon resonances observed at 167.32 ppm for CPE **7** and 178.17 for APE **9**, are not shown in Fig. 2. The spectrum in Fig. 1c belongs to a sample derived via dialysis and thus indicates the presence of certain portion of the polymer as polybetaine **10**. The broad signal at δ 2.55 ppm (Fig. 1b) is split into two signals and shifted downfield. It was observed during phase study (vide supra) in the presence of 0.70 equiv. HCl that these signals were shifted downfield to around δ 2.7 and 3.2 ppm. The NCH_2CO_2 signal at $\sim\delta$ 3.1 ppm was also shifted downfield indicating contribution of the positively charged nitrogen center in shifting the signal downfield.

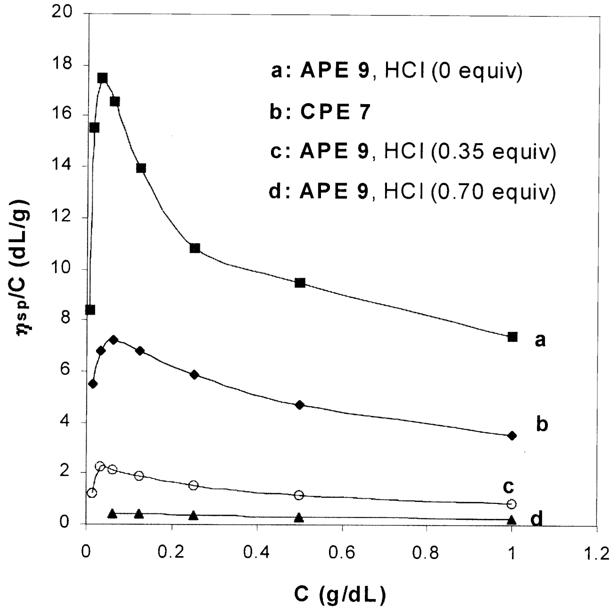


Fig. 3. Effect of added HCl on the viscosity behavior of the APE **9** (obtained via hydrolysis of the CPE **7** from entry 5, Table 1) in water at 30 °C using an Ubbelohde Viscometer.

The differential thermal analysis and thermogravimetric analysis of the polymers have been carried out. The polymers showed some predecomposition weight loss (5–10%), which was attributed to the loss of moisture. The polymers were stable up to 220 °C since no further weight loss was observed. Thermal degradation appeared to happen at around 230–250 °C for all the polymers and is attributed to the loss of sulfur dioxide.

The simple conversion of the CPE **7** to APE **9** thus provided us an opportunity for the direct comparison of the solution properties of a cationic, anionic and zwitterionic polymer having the same degree of polymerization. Viscosity data for CPE **7** (entry 5, Table 1) and its corresponding APE **9** is presented in Figs. 3 and 4. In the absence of added salt (NaCl), the plots are typical for polyelectrolyte i.e concave upwards. However, at higher dilution, the reduced viscosities of both the APE and CPE tend to fall off and this could be attributed to the formation of the zwitterionic species **10** and neutral species **11** (Scheme 4) by partial protonation and deprotonation, respectively, of APE **9** and CPE **7**. The relative concentration of these species is expected to increase with dilution. The CPE **7** was expected to have higher viscosity values than that of the APE **9** for the following reason. The distance between the neighboring positive charges in CPE is much smaller than that of the negative charges in APE and as such the former is expected to have more extended polymer backbone to relieve repulsion between positive charges. However, contrary to our expectation, the APE **9** is found to have much higher reduced viscosities than the CPE **7** even though they both have similar degree of polymerization and charge (albeit of opposite sign). Upon the addition of strong electrolytes (such as NaCl) the viscosity behavior of polymer **7** and **9** becomes normal (Fig. 4) and with the same viscosity trend i.e. the viscosity of APE is higher than CPE. It is tempting to believe that the protonated nitrogen is H-bonded to the

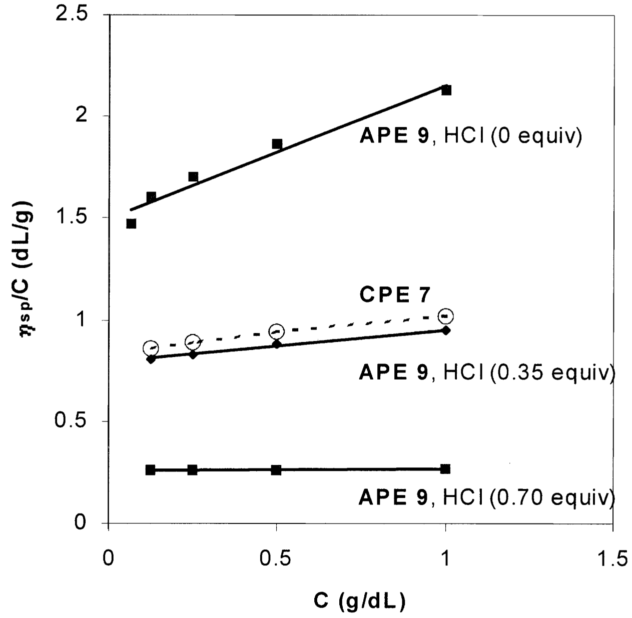
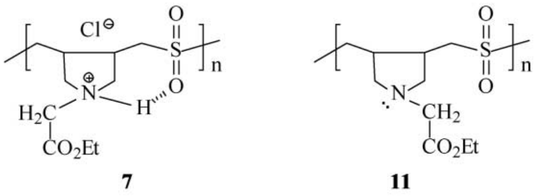


Fig. 4. Effect of added salt (0.1 N NaCl) and HCl (*x* equiv.) on the viscosity behavior of the APE **9** (obtained via hydrolysis of the CPE **7** from entry 5, Table 1) in water at 30 °C using an Ubbelohde Viscometer.

oxygen of the sulfone moiety thus resulting in dispersion of the positive charges, and reduction of the electrostatic repulsion between the positive nitrogens in the CPE (Scheme 4). The liberation of the protonated nitrogen in the APE **9** provokes an extension of the polyanion because of the presence of charged COO^- groups. The viscosity of APE decreases upon addition of HCl as shown in Figs. 3 and 4. While the intrinsic viscosities of the APE in presence of 0, 0.35, and 0.70 equiv. HCl in 0.1 N NaCl were determined to be 1.50, 0.792 and 0.257 dl/g, respectively (Fig. 4), the corresponding reduced viscosities for a 0.0625% APE solution in salt-free water was found to be 16.6, 2.12, 0.438 dl/g (Fig. 3). On addition of HCl, the concentration of the zwitterionic species **10** increases and the polymer tends to move toward a compact coil due to the internal neutralization of charges. The APE **9** starts to precipitate in 0.1 N NaCl and salt-free water after the addition of around 0.85 and 0.80 equiv. HCl, respectively.

In order to gain further information on the conformational transitions, we have determined the basicity constant, K^0, and corresponding *n* values relative to the protonation of the tertiary amine in salt-free water and 0.1 N NaCl solution. The basicity constant for the protonation of the COO^- group was not determined because of the insoluble nature of the PB **10** and the CAS **8**. The experimental details of the potentiometric titrations, basicity constants and the corresponding *n* values are reported in Table 2.



Scheme 4.

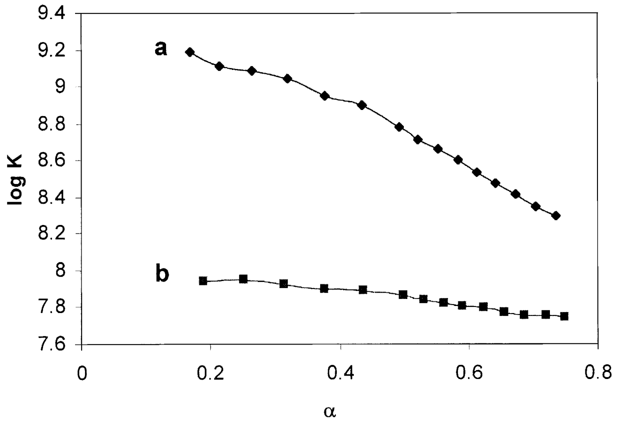


Fig. 5. Plot for the apparent log *K* vs. α for APE **9** (a) in salt-free water and (b) in 0.1 N NaCl.

The basicity constants in this polymer are found to be 'apparent' [30,31,33,34] since the *n* values are not equal to 1 and as such they vary with the degree of protonation (α). This behavior i.e. variation of *K* with α, is known as polyelectrolyte effect; polymer exhibiting a strong polyelectrolyte effect shows a large change in log *K* in going from one end to the other end of the titration. The magnitude of the *n* reflects the polyelectrolye effect and can be regarded as an index of accessibility of the proton to the amine nitrogen during the protonation reaction.

The apparent basicity constants (log *K*) of the amine group is lesser by almost an unit in 0.1 N NaCl when compared to salt-free water (Fig. 5). The presence of the Na^+ may neutralize part of the negative charges on the COO^- pendant thus diminishing overall the electron density on the nitrogen, hence making it less basic. The *n* values for the protonation of the APE **9** in 0.1 N NaCl and salt-free water were found to be 1.16 and 1.81, respectively (Table 2). The *n* values greater than 1 indicate that the approach of the incoming protons to the amine nitrogen groups becomes more and more difficult as the degree of protonation (α) of the whole macromolecule increases. The basicity constant (log *K*) thus decreases progressively due to a decrease in the electrostatic field force as a result of decreasing overall negative charge density in the macromolecule (Fig. 5). Calorimetric studies [35] on the protonation of the amine nitrogen in some polyamino acids have amply demonstrated that as the degree of protonation, α increases, the exothermic enthalpy changes (ΔH^0) remained constant but the positive entropy changes (ΔS^0) decreases thus making the ΔG^0 less and less negative and protonation increasingly difficult. The change in basicity constant with α is attributed to the entropy effect which is affected by conformational and solvation effects of the whole macromolecule. The polymer **9** in salt-free water is highly extended and more hydrated

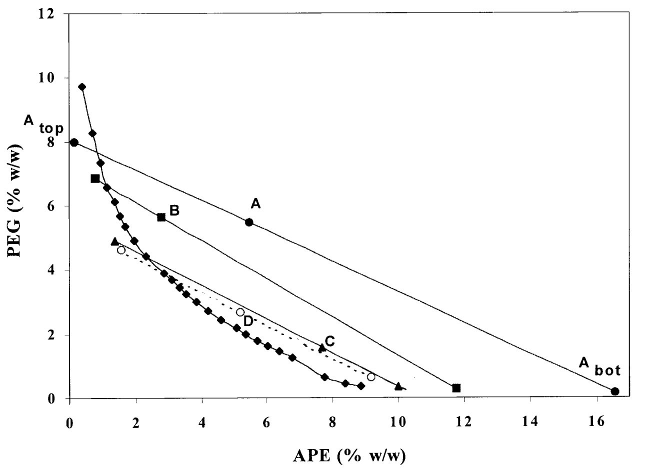


Fig. 6. Phase diagram of the system containing APE **9** (treated with 0.70 equiv. HCl) and PEG-35000 in 0.1 N KCl at 23 °C.

than in salt solution (0.1 N NaCl) where the polymer chain adapts a compact conformation due to screening of the negative charges by the sodium ions. It could be assumed that the polyelectrolytic effect, i.e. variation of basicity constant with α in our study is also due only to entropy effects.

Greater n value in salt-free water is attributed to a increasingly more compact structure that brings the positive ions closer and closer, resulting in more difficult protonation of the uncharged groups. The observations presented above are supported by the viscometric studies (vide supra). The measurement of the basicity constants was carried out in solution in the concentration range of 0.045–0.080 g/dl and indeed the relative changes of reduced viscisities during progressive protonation is much more drastic in salt-free water than in 0.1 N NaCl solution (Figs. 3 and 4).

The study of phase diagram is an important step in this work. The binodial curve distinguishes between single-and two-phase regions and provides information about the concentration of both polymers required for protein separation work. Fig. 6 shows the phase diagram for a system composed of PEG-35000 and APE 9 (+0.70 equiv. HCl) at 0.1 N KCl. The phase diagram and the tie lines are constructed by turbidity method and ^{1}H NMR technique [6], respectively. The polymers displayed segregative phase separation behavior. The binodial was found to be fairly symmetrical and thus the two polymers may have very similar hydrodynamic volumes [36]. The phase separation takes place at relatively low total polymer concentrations, typically below 10%; phase separation in a low concentration could be useful from an industrial point of view. The PEG and APE displayed overwhelming preference to remain in the top and bottom phase, respectively. Several tie lines (*A–D*), which connect the phases in equilibrium, are constructed by NMR technique [6]. The tie lines are helpful in constructing two-phases with suitable volume ratio of the top and bottom phases. For instance the total system represented by the point A will have the top and bottom phase compositions represented by A_{top} and A_{bot}, respectively, but the volume or the mass ratio of the top and bottom phases will be determined by the ratio of length $A - A_{\mathrm{bot}}$ and $A - A_{\mathrm{top}}$, respectively. As is evident from Table 3, phase inversion does not happen with higher salinity (entries 1–3) of the medium; the PEG-rich phase always remains on the top. The pH of the medium has a large effect on the phase composition; it is to be noted that in absence of added HCl (entries 8–10) the top layers revealed the exclusive presence of the PEG. Aqueous two-phase polymer systems as constructed above may offer a friendly environment for the separation [36–39] of labile proteins. Purified dextran, used in the most common dextran-poly(ethylene glycol) system for protein separation, is quite expensive and biodegradable [40]. The pH dependent solubility behavior of the new polymer described in this work may allow its effective removal and recycling.

4. Conclusions

A very convenient synthetic route for obtaining the new ionic polymers **7–10** using inexpensive starting materials is described. The work has also demonstrated the simple way to convert a cationic polyelectrolyte into a polybetaine and anionic polyelectrolyte and thus has provided the opportunity to compare the solution properties of the different type of ionic polymers having identical degree of polymerization. Conformational behavior of the polymers is strongly influenced by the nature and the net charge on the chain. These new ionic polymers may have applications in protein purification. One of the most gratifying aspect of the polymer is its almost zero solubility in water below pH ~ 7 in the presence or absence of salt thus, making it a suitable candidate for industrial applications since it will permit its effective removal from solution by precipitation. At this stage, however, we cannot offer any rationale for this interesting solubility behavior of the PB **10** and CSA **8**. Further studies on the hydrophobic modification of this polymer as well as its potential in protein separation are currently under investigation in our laboratory.

Acknowledgements

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