Lower Critical Solubility Temperature Study of Alkyl Ether Based Polyphosphazenes

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ABSTRACT: A series of poly[(alkyl ether)phosphazenes] was synthesized and their lower critical solution temperatures (LCST) were examined in water at concentrations from 0.1 to 30.0 wt %. The polymers synthesized were poly[bis(2,3-dimethoxypropanoxy)phosphazene], poly[bis(2,3-bis(2-methoxyethoxy)propanoxy)phosphazene], poly[bis(2,3-bis(2-(2′-methoxyethoxy)ethoxy)propanoxy)phosphazene], poly[bis(2,3-bis(2-(2′-(2″-dimethoxyethoxy)ethoxy)ethoxy)phosphazene], and poly[bis(2-(2′-methoxyethoxy)ethoxy)phosphazene]. All the polymers examined showed LCST behavior. The LCST values were approximately 44.0, 38.0, 49.5, 61.5, and 65.0 °C, respectively. Cross-linked polymer films were examined as hydrogels in water at various temperatures and showed a rapid decrease in volume and weight as the temperature was raised through the LCST. The change in LCST was also examined as a function of increasing ionic strength in the presence of NaCl. A linear decrease in LCST was detected as a function of increasing ionic strength. The enthalpies of phase separation for 5 wt % solutions of the polymers were determined by DSC analysis and were found to be directly related to the LCST for each polymer.

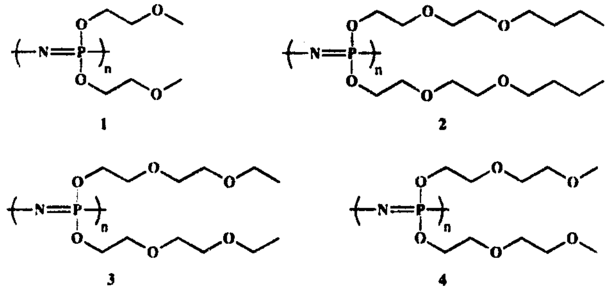
Introduction

Certain water-soluble polymers exhibit a phase transition known as the lower critical solution temperature (LCST) when the temperature of a polymer solution is raised. Specifically, this phase transition is characterized by a polymer that is soluble below its LCST, but precipitates from solution as the temperature is raised above the LCST. This transition is attributed to a change in balance between the hydrophilic and hydrophobic components of the polymer with respect to its interaction with a hydrogen-bonding solvent such as water.[1] Below the LCST, hydrogen-bonding interactions between the polymer and the water predominate over hydrophobic interactions and this favors polymer solubility. As the temperature of the solution is raised, the hydrogen-bonding interactions weaken and the hydrophobic characteristics of the polymer begin to predominate.[2] Once, the hydrophobic interactions reach a critical level at the LCST, the polymer precipitates from solution. Thus, this phenomenon is a result of the increase in hydrophobic interactions between the polymer chains and solvent, and the resultant increase in entropy of the system.

The unique characteristics of water-soluble LCST polymers make them ideal for a number of different uses, for example in fields such as membranes, drug delivery,[3] solute separation,[4] and enzyme activity control.[5] One of the advantages in the use of these types of polymers is that they can be processed in water without the use of organic solvents. Three well-known organic polymers with LCST's are poly(ethylene glycol),[6] poly(propylene glycol),[7] and poly(*N*-isopropylacrylamide).[8] The last polymer and its various derivatives have been studied in particular detail.

The LCST phenomenon has also been detected for inorganic backbone polymers such as polyphosphazenes.[9] These macromolecules have a backbone comprised of alternating phosphorus–nitrogen atoms with two organic side groups attached to each phosphorus. Earlier research in our program identified a number of water-soluble polyphosphazenes that showed LCST behavior.[9] These polymers are poly[bis(methoxyethoxy)phosphazene] (**1**), poly[bis((butyloxy)ethoxy)ethoxy)phosphazene] (**2**), poly[bis((ethoxyethoxy)ethoxy)phosphazene] (**3**), and poly[bis(2-(2′-methoxyethoxy)phosphazene] (4) (Chart 1). The behavior of these macromolecules in buffered solutions resulted in LCST's at 30, 51, 38, and 80 °C, respectively. It has now been found that a related groups of phosphazene polymers with branched alkyl ether side groups also show LCST behavior when dissolved in water. The alkyl ether side group phosphazene polymers synthesized in this work are poly[bis(2,3-dimethoxypropanoxy)phosphazene] (**5**), poly[bis(2,3-bis(2-methoxyethoxy)propanoxy)phosphazene] (**6**), poly[bis(2,3-bis(2-(2′-methoxyethoxy)ethoxy)propanoxy)phosphazene] (**7**), poly[bis(2,3-bis(2-(2′-(2″-dimethoxyethoxy)ethoxy)ethoxy)phosphazene] (**8**), and poly[bis(2-(2′-methoxyethoxy)ethoxy)phosphazene] (**4**). The structures are shown in Chart 2.

Chart 1



1 2 3 4

The new polymers were found to have properties related to those of the alkyl ether phosphazene polymer **4** which was studied earlier with respect to its LCST behavior.[9] For example, polymer **4** is a good solid solvent for salts and these solid salt solutions have high solid-state ionic conductivities, which makes them appropriate for use in rechargeable lithium batteries.[10,11] Polymer **4** also forms hydrogels,[12] which can be utilized in membranes,[13] and has been used for the immobilization of enzymes.[14] These applications and the similarity of polymers **5**–**8** to polymer **4** provide a strong incentive for understanding their behavior in aqueous media. For

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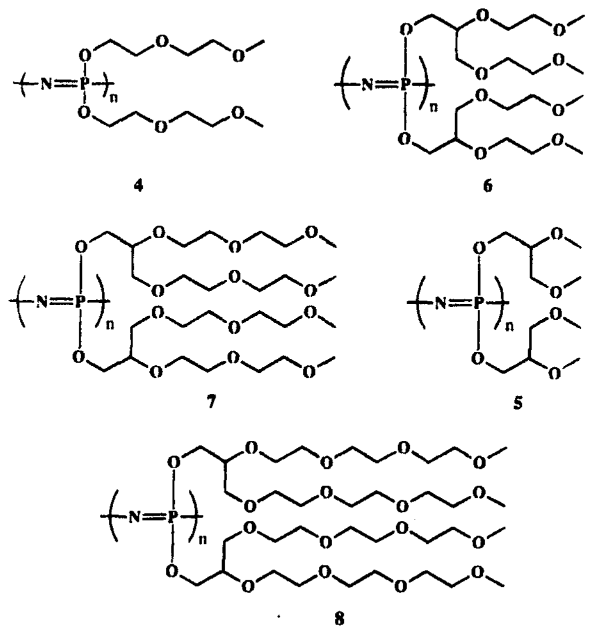
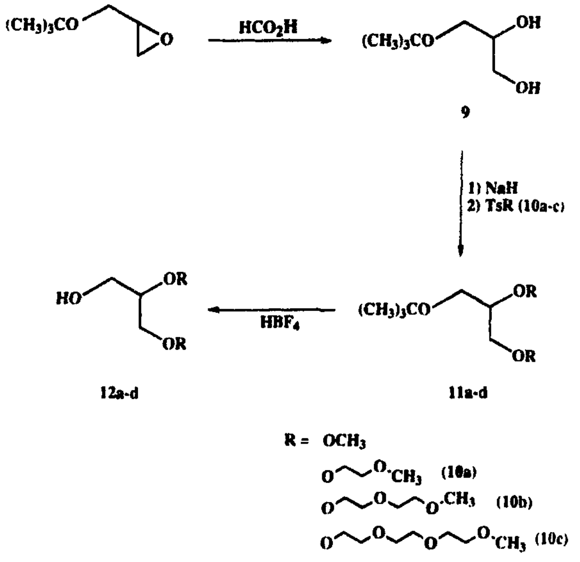
Chart 2



Scheme 1

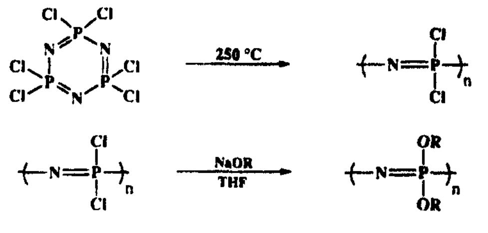


example, their LCST characteristics may lead to a better understanding of the hydration and precipitation of polymers from solution.

The methods used for the synthesis of the polymer side groups (podands) are shown in Scheme 1 and are described in the Experimental Section, together with their characterization. Synthesis of the polymers involved the thermal ring opening, melt polymerization of hexachlorocyclotriphosphazene to poly(dichlorophosphazene), followed by nucleophilic replacement of the chlorine atoms by the organic side groups (Scheme 2).[15] The characterization and purification of the polymers are described in the Experimental Section.

The focus of this study was to examine the LCST behavior of polymers **4–8** as a function of their concentration in water. Films of the polymers were also cross-linked by γ radiation and the resultant materials were allowed to swell in water to form hydrogels. The hydrogels were then examined over a range of temperatures with an emphasis on the effect of temperature on the hydrogel swellability. The influence of dissolved NaCl on the LCST of 5 wt % polymer solutions was also examined as a function of ionic strength. The enthalpy associated with the phase separation of each polymer solution was measured by DSC analysis and was correlated to the measured LCST.

Scheme 2



R = podand or methoxyethoxyethoxy

Experimental Section

Reagents. Hexachlorocyclotriphosphazene (Ethyl Corp./Nippon Fine Chemical Co.) was recrystallized from heptane and was sublimed at 40 °C (0.002 mmHg). Water was distilled and passed through ion exchangers (Cole Parmer). Sodium chloride (Aldrich), potassium carbonate (Aldrich), HBF_4 54% in diethyl ether (Fluka), activated carbon (Aldrich), magnesium sulfate (Aldrich), tosyl chloride (Aldrich), NaH 60% dispersion (Aldrich), methyl *p*-toluenesulfonate (Aldrich), and formic acid (Aldrich) were used as received. Pyridine (Baker) and methylene chloride (Baker) were stored over CaH and were distilled as needed. Tetrahydrofuran (Baker) was dried and distilled from sodium benzophenone. Methoxyethanol, 2-(2′-methoxyethoxy)ethanol, and triethylene glycol monomethyl ether (Aldrich) were vacuum distilled before use. Poly(dichlorophosphazene) was prepared by the thermal polymerization of $(NPCl_2)_3$ using a procedure describe by us previously.[9]

Equipment. ^1H, ^{13}C, and ^{31}P NMR spectra were recorded using a Bruker WM-360 spectrometer operated at 360, 90, and 146 MHz, respectively. The solvent used for all the spectra was $CDCl_3$ and the chemical shifts were referenced internally to $CDCl_3$. Infrared spectra were obtained using a Perkin-Elmer 1600 series FTIR spectrometer. DSC analyses were recorded using a Perkin-Elmer Series 7 thermal analysis system with a PE 7500 computer. Electron impact spectra were obtained using an AEI MS 950 unit. Polymer molecular weights were estimated using an HP 1090 LC instrument coupled to a 1047A RI detector using Phenomenex columns at a flow rate of 1.0 mL/min. Calibration was carried out using narrow molecular weight polystyrene standards. Data manipulation made use of Polymer Laboratories Software HP 2.0.

3-(*tert*-Butyloxy)-1,2-propanediol (9). Compound **9** was prepared by following a procedure described previously.[16] Into a 500 mL round-bottom flask containing 83 mL (2.2 mol) of formic acid was added dropwise *tert*-butyl glycidyl ether (141 mL, 1.0 mol). The temperature of the mixture was maintained below 30 °C and the reaction mixture was stirred overnight under argon. A solution of sodium hydroxide (100 g in 150 mL of H_2O) was added dropwise to the reaction mixture with the temperature maintained below 40 °C. The mixture was stirred for an additional 2 h. The organic layer was separated, extracted with methylene chloride, and dried ($MgSO_4$), and the solvent was removed. The oil was distilled (63 °C at 20 μmHg) to yield 77.2 g (52.2%). ^1H NMR ($CDCl_3$) δ 1.2 (s, 6H), 2.4 (s, 1H), 2.8 (s, 1H), 2.4–3.8 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 27.3, 63.5, 64.3, 70.9, 73.4; IR (NaCl) 3397, 2932, 1474, 1389, 1363, 1196, 1082, 883 cm^{-1}; *m/e* 149 MH^+.

2-Methoxyethyl *p*-Toluenesulfonate (10a). Into a round-bottom flask containing pyridine (200 mL) and tosyl chloride (137.0 g, 0.72 mol) cooled in an ice bath was added dropwise 2-methoxyethanol (50.0 g, 0.66 mol). The cooling was maintained for an additional 0.5 h before the mixture was allowed to warm slowly to room temperature. The reaction mixture was poured into ice water (500 mL) and was extracted with methylene chloride. The organic layer was washed with dilute HCl and dried ($MgSO_4$), and the solvent was removed. The resultant oil was vacuum distilled (110 °C at 20 μmHg) to give a colorless oil, yield 124.1 g (81.9%). ^{1}H NMR ($CDCl_3$) δ 2.4 (s, 3H), 3.3 (s, 3H), 3.5 (t, 2H), 4.1 (t, 2H), 7.3 (d, 2H), 7.7 (d, 2H); ^{13}C NMR ($CDCl_3$) δ 21.5, 58.7, 69.1, 69.8, 127.8, 129.8, 132.9, 144.9; IR (NaCl) 2891, 1598, 1451, 1354, 1174 cm^{-1}; *m/e* 231 MH^{+}.

2-(2′-Methoxyethoxy)ethyl *p*-Toluenesulfonate (10b). Compound **10b** was synthesized using a similar procedure to that described for compound **10a**. Specific reagents used for the reaction were tosyl chloride (94.9 g, 0.498 mol), 2-(2′-methoxyethoxy)ethanol (59.8 g, 0.498 mol), and pyridine (200 mL). Before removal of the solvent, the solution was treated with activated carbon and dried ($MgSO_4$), and the solvent was removed to give a pale yellow oil, yield 136.5 g (88.3%). ^{1}H NMR ($CDCl_3$) δ 2.4 (s, 3H), 3.3 (s, 3H), 3.4 (t, 2H), 3.5 (t, 2H), 3.6 (t, 2H), 4.1 (t, 2H), 7.3 (d, 2H), 7.7 (d, 2H); ^{13}C NMR ($CDCl_3$) δ 21.5, 58.9, 68.6, 69.2, 70.6, 71.7, 127.9, 129.8, 132.9, 144.8; IR (NaCl) 2880, 1598, 1452, 1358, 1177 cm^{-1}; *m/e* 275 MH^{+}.

2-(2′-(2″-Methoxyethoxy)ethoxy)ethyl *p*-Toluenesulfonate (10c). Compound **10c** was synthesized using the procedure developed for compound **10b**. The amounts of reagents used for the synthesis were as follows: tosyl chloride (85.2 g, 0.447 mol), 2-(2′-(2″-methoxyethoxy)ethoxy)ethanol (73.4 g, 0.447 mol), and pyridine (200 mL). Isolation of the product yielded a pale yellow oil, yield 124.1 g (87.3%). ^{1}H NMR ($CDCl_3$) δ 2.4 (s, 3H), 3.4 (s, 3H), 3.5 (t, 2H), 3.6 (t, 2H), 3.7 (t, 2H), 4.2 (t, 2H), 7.3 (d, 2H), 7.8 (d, 2H); ^{13}C NMR ($CDCl_3$) δ 21.6, 59.0, 68.6, 69.2, 70.5, 70.7, 71.9, 127.9, 129.8, 133.0, 144.7; IR (NaCl) 2878, 1598, 1452, 1357, 1177 cm^{-1}; *m/e* 319 MH^{+}.

1-(*tert*-Butyloxy)-2,3-dimethoxypropane (11a). To a solution of NaH (18.4 g) in THF (500 mL) was added **9** (32.6 g, 0.220 mol) dropwise in THF (100 mL) with mechanical stirring. After the addition, the reaction mixture was heated at reflux for 1 h. A solution of methyl *p*-toluenesulfonate (85.6 g, 0.460 mol) in THF (50 mL) was added dropwise to the refluxing reaction mixture. Refluxing was continued for 24 h, after which time the mixture was cooled to room temperature and filtered and the solvent removed. The dark colored oil was dissolved in methylene chloride and washed with water. The organic layer was dried ($MgSO_4$) and the solvent was removed. The oil was vacuum distilled (25 °C at 2 μmHg) to give a clear colorless oil, yield 38.2 g (98.7%). ^{1}H NMR ($CDCl_3$) δ 1.2 (s), 3.3 (s), 3.4 (s), 3.5 (s); ^{13}C NMR ($CDCl_3$) δ 27.4, 57.9, 59.2, 61.0, 72.6, 73.0, 79.8; IR (NaCl) 2928, 1462, 1363, 1198, 1100 cm^{-1}; *m/e* 265 MH^{+}.

1-(*tert*-Butyloxy)-2,3-bis(methoxyethoxy)propane (11b). The same procedure outlined for the synthesis of compound **11a** was employed. The amounts of reagents used were as follows: compound **9** (20.0 g, 0.135 mol), **10a** (65.6 g, 0.285 mol), and NaH (11.4 g). The oil was vacuum distilled (70 °C at 50 μmHg) to give 35.6 g (99.0%). ^{1}H NMR ($CDCl_3$) δ 1.1 (s, 9H), 3.2 (s, 6H), 3.4 (d, 2H), 3.4–3.7 (m, 9H), 3.8 (t, 2H); ^{13}C NMR ($CDCl_3$) δ 27.4, 58.7, 58.8, 61.7, 69.7, 70.6, 71.7, 71.9, 72.1, 72.8, 78.9; IR (NaCl) 2974, 1458, 1363, 1199, 1108 cm^{-1}; *m/e* 265 MH^{+}.

1-(*tert*-Butyloxy)-2,3-bis(2-(2′-methoxyethoxy)ethoxy)propane (11c). Compound **11c** was also prepared using the same procedure outline for compound **11a**. The quantities of reagents were as follows: **9** (27.9 g, 0.189 mol), **10b** (104.1 g, 0.380 mol), and NaH (15.2 g). The oil was vacuum distilled (130 °C at 2 μmHg) to give 52.1 g (78.3%). ^{1}H NMR ($CDCl_3$) δ 1.1 (s, 9H), 3.3 (s, 6H), 3.4 (d, 2H), 3.5–3.7 (m, 17H), 3.8 (t, 2H); ^{13}C NMR ($CDCl_3$) δ 27.4, 58.9, 61.7, 69.8, 70.4, 70.5, 70.6, 70.7, 71.6, 71.9, 72.8, 78.9; IR (NaCl) 2880, 1457, 1363, 1199, 1100 cm^{-1}; *m/e* 353 MH^{+}.

1-(*tert*-Butyloxy)-2,3-bis(2-(2′-(2″-methoxyethoxy)ethoxy)ethoxy)propane (11d). Product **11d** was synthesized using the same procedure as for compound **11a**. The amount of reagents were as follows: **9** (36.7 g, 0.244 mol), NaH (20.0 g), and **10c** (159.0 g, 0.500 mol). An attempted distillation of the oil resulted in deprotection of the alcohol and in its subsequent distillation. The analysis values listed are for the crude compound **11d**. ^{1}H NMR ($CDCl_3$) δ 1.2 (s, 9H), 3.4–3.8 (m, 35H); ^{13}C NMR ($CDCl_3$) δ 27.5, 59.0, 61.7, 69.8, 70.5, 70.6, 70.7, 70.8, 71.6, 71.9, 72.9, 78.9; IR (NaCl) 2878, 1457, 1364, 1198, 1097 cm^{-1}; *m/e* 441 MH^{+}.

2,3-Dimethoxypropanol (12a). Deprotection of the alcohol was carried out by the dropwise treatment of compound **11a** (38.2 g, 0.217 mol) dissolved in methylene chloride (150 mL) with a solution of fluoboric acid 54% in diethyl ether (43.0 mL, 0.315 mol). After the addition, the reaction mixture was stirred for 0.5 h, before the introduction of a large excess of potassium carbonate (powder). The mixture was then stirred overnight. The yellow solution was filtered and the solvent removed. The oil was vacuum distilled (25 °C at 2 μmHg) to give a colorless oil, yield 10.4 g (39.9%). ^{1}H NMR ($CDCl_3$) δ 2.2 (s, 1H), 3.4 (s, 3H), 3.4 (m, 2H), 3.5 (s, 3H), 3.5 (d, 2H), 3.7 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 57.7, 59.3, 62.3, 72.3, 79.9; IR (NaCl) 3450, 2952, 1464, 1363, 1193, 1111, 1071 cm^{-1}; *m/e* 121 MH^{+}.

2,3-Bis(2-methoxyethoxy)propanol (12b). The synthesis of compound **12b** was carried out using the procedure described for **12a**. Reactants used were as follows: **11b** (50.2 g, 0.190 mol) and HBF_4 54% in diethyl ether (37.7 mL, 0.276 mol). The oil was vacuum distilled (90 °C at 2 μmHg) to give 35.0 g (88.6%). ^{1}H NMR ($CDCl_3$) δ 2.8 (s, 1H), 3.3 (s, 3H), 3.3 (s, 3H), 3.5–3.8 (m, 13H); ^{13}C NMR ($CDCl_3$) δ 58.9, 59.0, 62.7, 69.5, 70.8, 71.4, 71.8, 72.2, 79.6; IR (NaCl) 3454, 2919, 1455, 1362, 1200, 1109 cm^{-1}; *m/e* 209 MH^{+}.

2,3-Bis(2-(2′-methoxyethoxy)ethoxy)propanol (12c). The procedure for compound **12c** was the same as that used for compound **12a**. The quantities of reagents were as follows: **11c** (52.1 g, 0.148 mol) and HBF_4 54% in diethyl ether (29.3 mL, 0.215 mol). The resultant oil was then vacuum distilled (140 °C at 2 μmHg) to give 35.13 g (80.2%). ^{1}H NMR ($CDCl_3$) δ 2.8 (s, 1H), 3.4 (s, 6H), 3.5–3.9 (m, 21H); ^{13}C NMR ($CDCl_3$) δ 59.0, 62.6, 69.5, 70.4, 70.5, 70.7, 70.8, 71.3, 71.8, 71.9, 79.6; IR (NaCl) 3470, 2923, 1457, 1376, 1200, 1112 cm^{-1}; *m/e* 297 MH^{+}.

2,3-Bis(2-(2′-(2″-methoxyethoxy)ethoxy)ethoxy)propanol (12d). The alcohol was deprotected as was described previously during distillation of compound **11c**. The oil collected at 225 °C at 2 μmHg was found to be compound **12d**, yield 52.5 g (56.0%). ^{1}H NMR ($CDCl_3$) δ 2.9 (s, 1H), 3.4 (s, 6H), 3.5–3.8 (m, 29H); ^{13}C NMR ($CDCl_3$) δ 58.8, 62.4, 69.4, 70.3, 70.4, 70.7, 71.1, 71.8, 79.5; IR (NaCl) 3472, 2871, 1459, 1351, 1200, 1109 cm^{-1}; *m/e* 385 MH^{+}.

Poly[bis(2,3-dimethoxypropanoxy)phosphazene] (5). To a mixture of NaH (2.4 g) in THF (100 mL) was added dropwise compound **12a** (7.66 g, 0.0638 mol) dissolved in THF (100 mL). This was then followed by 24 h of stirring. To the reaction mixture was added poly(dichlorophosphazene) (2.1 g, 0.0181 mol) in THF (250 mL) dropwise. The mixture was then heated at reflux for 48 h. The polymer was purified by dialysis against water (6 days) and methanol (5 days) and was then precipitated into hexane, yield 3.05 g (63%). ^{1}H NMR ($CDCl_3$) δ 3.3 (3H), 3.4 (3H), 3.5 (1H), 3.6 (2H), 4.0 (2H); ^{13}C NMR ($CDCl_3$) δ 57.8, 59.0, 64.9, 72.4, 79.0; ^{31}P NMR ($CDCl_3$) δ −8.1.

Poly[bis(2,3-bis(2-methoxyethoxy)propanoxy)phosphazene] (6). To a suspension of NaH (2.8 g) in THF (100 mL) was added compound **12b** (14.5 g, 0.0695 mol) in THF (100 mL) followed by stirring for 24 h. To this mixture was added dropwise poly(dichlorophosphazene) (4.0 g, 0.0345 mol) in 500 mL of THF. The reaction mixture was stirred at reflux for 24 h. The polymer was purified by dialysis against water (6 days) and methanol (5 days) and was then precipitated into hexane, yield 13.1 g (82.7%). ^{1}H NMR ($CDCl_3$) δ 3.3 (6H), 3.5 (4H), 3.6 (2H), 3.7 (1H), 3.8 (4H), 3.9 (2H); ^{13}C NMR ($CDCl_3$) δ 58.6, 58.8, 65.5, 69.7, 70.7, 71.9, 72.0, 72.2, 78.4; ^{31}P NMR ($CDCl_3$) δ −8.9.

Poly[bis(2,3-bis(2-(2′-methoxyethoxy)ethoxy)propanoxy)phosphazene] (7). To a stirred mixture of NaH (2.99 g) in THF (200 mL) was added dropwise a solution of compound **12c** (21.7 g, 0.0734 mol) in THF (100 mL) followed by 24 h of stirring. Poly(dichlorophosphazene) in THF (500 mL) was added dropwise to the mixture, which was then refluxed for 24 h. Purification involved dialysis of the polymer against water (6 days) and methanol (5 days) and precipitation into hexane, yield 18.05 g (82.4%). ^{1}H NMR ($CDCl_3$) δ 3.4 (6H), 3.5 (6H), 3.6 (10H), 3.7 (3H), 3.9 (2H); ^{13}C NMR ($CDCl_3$) δ 58.6,

Table 1. Polymer Characterization and Properties

polymer	T_g (°C)	solubility[a]	LCST 5% wt (°C)	M_w	PDI
5	−81	soluble	44.0	1.5×10^6	1.4
6	−81	soluble	38.0	1.0×10^6	1.4
7	−81	soluble	49.5	1.7×10^6	1.2
8	−80	soluble	61.5	1.2×10^6	1.4
4	−84	soluble	65.0	1.0×10^6	1.5

[a] Solubility in water at 25 °C.

58.7, 65.3, 69.8, 70.2, 70.3, 70.4, 70.5, 70.7, 71.7, 71.9, 78.4; ^{31}P NMR (CDCl$_3$) δ −9.3.

Poly[bis(2,3-bis(2-(2′-(2″-dimethoxyethoxy)ethoxy)ethoxy)propanoxy)phosphazene] (8). To a mixture of NaH (2.08 g) in THF (100 mL) was added dropwise a solution of compound **12d** (22.7 g, 0.0517 mol) in THF (100 mL). The reaction mixture was stirred for 24 h. Poly(dichlorophosphazene) in THF (250 mL) was then added dropwise to the mixture and then refluxed for 24 h. The polymer was purified by dialysis against water (6 days) and methanol (5 days) and precipitated into hexane, yield 8.9 g (63.8%). ^{1}H NMR (CDCl$_3$) δ 3.4 (6H), 3.5 (8H), 3.6 (16H), 3.7 (3H), 3.8 (2H); ^{13}C NMR (CDCl$_3$) δ 58.9, 58.9, 69.8, 70.3, 70.4, 70.5, 70.7, 71.7, 71.9, 78.4; ^{31}P NMR (CDCl$_3$) δ −9.3.

Poly[bis(2-(2′-methoxyethoxy)ethoxy)phosphazene] (4). To a mixture of NaH (2.6 g) in THF (100 mL) was added dropwise 2-(2′-methoxyethoxy)ethanol (7.4 mL, 0.0621 mol) in THF (100 mL). The reaction mixture was stirred for 24 h. Poly(dichlorophosphazene) in THF (300 mL) was added dropwise and refluxed for a total of 24 h. The phosphazene polymer was purified by dialysis against water (6 days) and methanol (5 days) and precipitated into hexane, yield 6.3 g (86.0%). ^{1}H NMR (CDCl$_3$) δ 3.4 (3H), 3.5 (2H), 3.6 (4H), 4.0 (2H); ^{13}C NMR (CDCl$_3$) δ 58.8, 65.2, 70.3, 70.4, 72.0; ^{31}P NMR (CDCl$_3$) δ −7.7.

LCST Measurements. Approximately 2 mL samples of the polymer solutions were placed in glass vials which were capped. The vials were partially immersed in a silicone oil bath with the level of the polymer solution in the vial maintained below that of the silicone oil. The oil bath was then heated at a rate of approximately 10 °C/h. The LCST was identified at the point at which the solution became turbid (white) and a fine polymer precipitate formed in the vial. The same method was used to determine the LCST of the polymers based on the ionic strength of NaCl.

Preparation of Cross-Linked Films. The polymer films were prepared by dissolving 2 g of polymer in THF (50 mL) followed by casting into 9.5 cm × 9.5 cm aluminum frames sealed to glass plates. The cast solutions were covered and the solvent was allowed to evaporate slowly over a period of 4 days. The polymer films were then removed from the glass plates and dried further under vacuum. The films were then submitted to the Breazeale Nuclear Reactor at The Pennsylvania State University for exposure to 10 Mrads of ^{60}Co γ-radiation.

DSC Measurements. The DSC measurements were performed using aluminum sample pans containing 5 wt % polymer solutions. The samples were scanned at a rate of 5 °C/min and referenced against an empty aluminum sample pan. Calibration of the instrument was carried out against a known weight of indium.

Polymer Hydrogels. Cross-linked polymer films were placed in glass vials of water and stored at 25 °C. The hydrogels were found to reach an equilibrated weight after approximately 48 hr at 25 °C. Heating of the hydrogels was carried out by placing the vials in an oven at predetermined temperatures.

Results and Discussion

Polymer Solution LCST's. The macromolecules synthesized in this study consisted of polyphosphazenes with either linear or branched ethyleneoxy side group units, as shown in Chart 2. Examination of the physical properties showed them to be very similar to each other in texture, solubility, and T_g's (Table 1). All the polymers synthesized had similar dimensional stabilities except for polymer **4**, which showed a tendency to flow under ambient conditions. The improved dimensional stability of polymers **5**−**8** over that of polymer **4** is believed to be a result of greater chain entanglement brought about by the branched nature of the side groups, since the T_g's of the polymers differed by only approximately 3−4 °C. All the polymers studied were found to be readily soluble in water at room temperature and all showed LCST behavior.

As discussed previously, the LCST occurs as a result of the change in the hydrophilic and hydrophobic balance between the polymer and the hydrogen-bonding solvent as the temperature is raised. Polymers **4**−**8** were examined for this LCST phase transition over a range of concentrations from 0.1 to 30.0 wt % in water. All the polymer solutions showed an LCST phase transition for the entire range of concentrations when dissolved in water and heated. The LCST of the 5 wt % solutions for each polymer was chosen as the temperature for comparison of the different polymer systems to each other. The LCST's of the different polymers varied over a range of 38.0 to 65.0 °C. The only observable trend occurred with polymers **6**−**8** in which an increase in the LCST was directly related to an increase in the length of the side groups. Thus, successive extensions of the number of ethyleneoxy segments on each side group resulted in an increase in the measured LCST for each polymer. The LCST's increased from 38.0 °C for polymer **6**, to 49.5 °C for polymer **7**, to 61.5 °C for polymer **8**. The relationship between the increasing LCST and increasing side group length appears to be related to the larger number of oxygen atoms offered by the longer side group structures and the increased opportunities for hydration. This results in a system that has stronger tendency to remain in solution at higher temperatures. The other two polymers **4** and **5** could not be compared directly in these terms due to the slight differences in side group structure. However, these polymers gave LCST's of 44.0 and 65.0 °C, respectively.

The polymers were examined over the range of weight percentages 0.1−30.0 wt % in water to determine the possibility that the LCST's might be concentration dependent. Analysis of the LCST values for each polymer showed them to be essentially independent of the concentration in water. A plot of the LCST's for the different polymers at various concentrations is shown in Figure 1. Precipitation of each polymer from solution occurred at an almost constant temperature for the entire range of concentrations examined, without any major changes in the measured LCST. However, a slight increase in the LCST was detected at low polymer concentrations and was found for all the polymers studied. A similar trend has been reported previously in studies of poly(*N*,*N*-diethylacrylamides) at low concentrations in water and is not considered to be unique.[17] The similar line shape for each of the polymer LCST's suggests that the polymers have a similar LCST effect when they dissolve and precipitate from solution.

Influence of Dissolved Salt on the LCST. The presence of a third component in a polymer solution can cause significant changes in the LCST of a polymer. To examine this possibility, sodium chloride was added to 5 wt % solutions of each of the five polymers **4**−**8**. The concentration of NaCl was then varied from ionic strengths of 0.1−1.0 in each of the solutions. The LCST's of the solutions were then examined by the

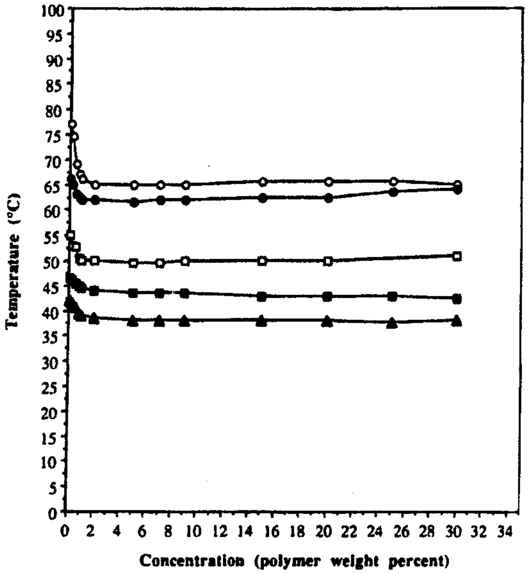


Figure 1. Graph showing the LCST's of the polymers as a function of polymer concentration for poly[bis(2,3-dimethoxypropanoxy)phosphazene] (■), poly[bis(2,3-bis(2-methoxyethoxy)propanoxy)phosphazene] (▲), poly[bis(2,3-bis(2-(2′-methoxyethoxy)ethoxy)propanoxy)phosphazene] (□), poly[bis(2,3-bis(2-(2′-(2″-dimethoxyethoxy)ethoxy)ethoxy)phosphazene] (●), and poly[bis(2,3-bis(2-(2′-methoxyethoxy)ethoxy)phosphazene] (○).

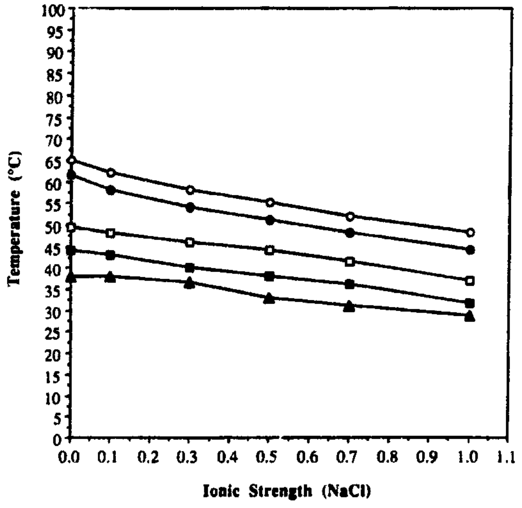


Figure 2. LCST's of the polymers as a function of increasing ionic strength of NaCl for poly[bis(2,3-dimethoxypropanoxy)phosphazene] (■), poly[bis(2,3-bis(2-methoxyethoxy)propanoxy)phosphazene] (▲), poly[bis(2,3-bis(2-(2′-methoxyethoxy)ethoxy)propanoxy)phosphazene] (□), poly[bis(2,3-bis(2-(2′-(2″-dimethoxyethoxy)ethoxy)ethoxy)phosphazene] (●), and poly[bis(2,3-bis(2-(2′-methoxyethoxy)ethoxy)phosphazene] (○).

previously described procedure. The addition of NaCl to the solutions was found to influence the LCST significantly for each of the polymers studied. As the ionic strength of the solution was gradually increased, it resulted in a corresponding decrease in the polymer LCST's (Figure 2). The rate of decrease in LCST for each polymer was also consistent from polymer to polymer as the ionic strength of the solution was raised. This suggests that the hydration of the different polymers in water is very similar. If the hydration were different, each polymer should show a different variation in slope for the LCST with an increase in ionic strength. The detection of decreasing LCST with increasing ionic strength of NaCl also agrees with previous observations from the study of poly(*N*-isopropylacrylamide).[8]

The general explanation for the decrease in the LCST's at the higher salt concentrations is that the increase in NaCl electrolyte concentration causes a "salting out" effect.[18] The ions in solution disrupt the hydrophilic and hydrophobic balance between the polymer and water molecules.[2] Therefore, the more salt present, the greater is the salting out effect and the lower is the LCST. However, these trends are both salt- and polymer-dependent, with possible variations from system to system.[19]

Polymer Hydrogels. Water-soluble polymers that are cross-linked and then placed in aqueous media absorb water to form hydrogels. A hydrogel is a three-dimensional matrix of lightly cross-linked polymer chains that can imbibe significant amounts of water. Hydrogels derived from polymers with an LCST can undergo a phase transition called "thermodeswelling" when heated above the LCST of the polymer.[20] The thermodeswelling is characterized by a decrease in hydrogel weight and volume as the temperature is raised above the LCST. As discussed previously, at temperatures above the LCST the hydrophobic characteristics of the polymer begins to predominate and the polymer chains undergo association with each other. It is this hydrophobic association above the LCST that results in the expulsion of water and the concurrent loss of hydrogel weight and volume.

The hydrogels were generated by immersion of cross-linked polymer films in water at 25 °C and allowing the materials to swell to an equilibrated volume and weight. The temperature was then raised in approximately 5 °C increments and held at a given temperature for a minimum of 3 h. After this time, the hydrogels were removed and weighed to determine any change in weight. Excess water adhering to the hydrogels was allowed to drain off before weighing. The five polymers **4**–**8** were studied from 25 to 100 °C in water and their change in weight was compared to those of their respective unswelled polymer films. The average percentage change in weight vs temperature for each polymer is shown graphically in Figure 3. At temperatures near their LCST's, all five polymers **4**–**8**, showed the characteristic thermodeswelling of the LCST hydrogels. The transitions of the hydrogels were characterized by a change in appearance, from clear to opaque. The change in appearance also coincided with the point at which the hydrogel weight and volume began to decrease. The hydrogels also became rigid and could support their own weight at temperatures above their LCST's.

The decrease in hydrogel weight occurred rapidly near their LCST's and did not a require long exposure to the new temperature. The films also reached an equilibrium weight only a few degrees above their respective LCST's. The main advantage of this rapid response is that a solvent can be extruded rapidly from the hydrogel without a need for long-term exposure to heat. This rapid response is similar to that emphasized in a recent publication involving comb-type grafted poly(*N*-isopropylacrylamide), in which rapid thermodeswelling was observed.[21] The main disadvantage of grafted systems is that no guarantee exists that the same sites will be grafted from one experiment to the next, and the size of grafted segment is difficult to determine. The advantage of polymers **4**–**8** is that the structure of the macromolecules are known before cross-linking, and

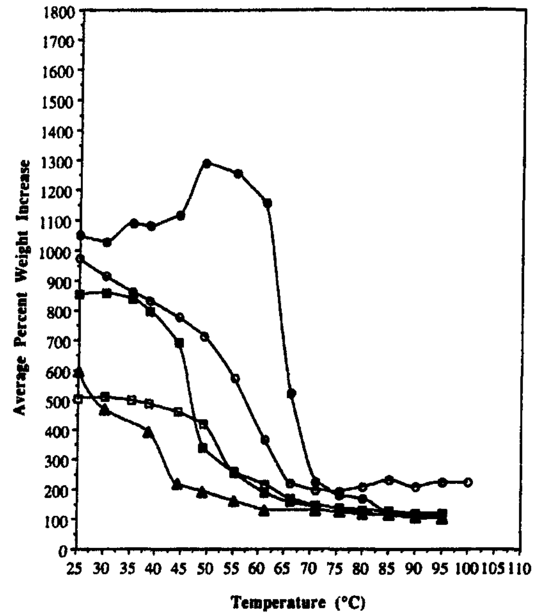


Figure 3. Changes in hydrogel swellability as a function of temperature for poly[bis(2,3-dimethoxypropanoxy)phosphazene] (■), poly[bis(2,3-bis(2-methoxyethoxy)propanoxy)phosphazene] (▲), poly[bis(2,3-bis(2-(2′-methoxyethoxy)ethoxy)propanoxy)-phosphazene] (□), poly[bis(2,3-bis(2-(2′-(2″-dimethoxy)ethoxy)-ethoxy)phosphazene] (●), and poly[bis(2,3-bis(2-(2′-methoxy-ethoxy)ethoxy)phosphazene] (○).

therefore the hydrogel structure and behavior can be duplicated readily.

A comparison of the initial hydrogel weights equilibrated in water at 25 °C emphasized the wide range of swelling ratios. Hydrogels of polymers **4** and **8** at 25 °C both underwent an approximately 10-fold increase in weight compared to their respective unswelled polymer films. Hydrogels prepared from polymers **5**, **6**, and **7** showed weight increases that were significantly less, with average weight increases of approximately 8.5-, 6-, and 5-fold, respectively, compared to their unswelled counterparts. These differences did not fit any obvious trends based on side group structure or measured LCST.

Analysis of the hydrogels at the various temperatures showed that the hydrogel formed from polymer **8** underwent a slight thermoswelling at ~50 °C; i.e., the hydrogels underwent an increase weight as the temperature of the solution was increased. A possible explanation for this behavior is that an increase in thermal motion of the polymer side groups at the higher temperatures results in greater dimensional freedom, and this could allow more water to be included within the polymer film. The other four polymers **4**–**7** did not show any noticeable thermoswelling and maintained a constant hydrogel weight or began to decrease in weight as the temperature was raised. As the temperature was raised above the point at which a rapid weight loss occurred, the rate of weight loss leveled off. This leveling off effect was permanent and indicates that the polymers had reached their equilibrium volume quickly. Comparisons of the equilibrium weights showed that the four branched polymers, **5**–**8**, at temperatures higher than 85 °C, contained approximately twice as much water as their respective unswelled polymer films. The linear ethyleneoxy side group polymer, **4** at the higher temperatures reached an equilibrated weight that was approximately triple its initial unswelled counterpart. The difference in equilibrated weights is believed to be related to the different structure of the polymer side groups and possibly different cross-link densities. The lower equilibrated weights of polymers **5**–**8** over that of polymer **4** is attributed to the more branched structures of the polymer side groups. The greater branching of the side groups allows for an increased probability that the side groups interact with each other as the polymer becomes more hydrophobic in character as the temperature increases. This increase in side group aggregation would, in turn, extrude more water due to the reduced free volume present in the film. Polymer **4**, which has no side group branching, would have less side group interactions and greater film free volume and should give a higher equilibrium hydrogel weight.

The dimensional stability of the hydrogels was also found to depend on film thickness at higher temperatures. Films prepared from polymer concentrations in THF that were lower than that described in the Experimental Section yielded films that were too thin to be studied as useful hydrogels. Hydrogels prepared from these thin films lost their dimensional stability at high temperatures in the range of 90–100 °C. The films did not dissolve, but formed fine dispersions in water. Thicker films could be recycled repeatedly between temperatures without any noticeable changes in the hydrogel dimensional stability.

Enthalpy of Separation. The LCST phase change that occurs with the precipitation of a polymer from solution has a measurable energy change associated with the precipitation. Guillet[8] found that the energy required for the phase separation of LCST polymers could be measured by DSC analysis in the study of poly(*N*-isopropylacrylamide) in water. The phase transition was found to occur near the LCST of poly(*N*-isopropylacrylamide) and manifested itself as an endothermic transition associated with the phase separation. The endothermic transition is related to the energy needed to disrupt the hydration of the polymer and cause it to precipitate from solution. In the present study, 5 wt % polymer solutions in water were prepared using polymers **4**–**8**. These were then examined by DSC analysis to determine the energy associated with the phase separation of each polymer. The DSC analyses showed each solution to have an endothermic transition close to the LCST's of each respective polymer. The shape of the endotherm transitions was similar to those of previously measured LCST polymers.[1,8,19,22,23] The samples were scanned only once, since it could not be guaranteed that the polymers would redissolve completely.

The energies measured for the phase separations were averaged and correlated to the measured LCST of each individual polymer. A direct relationship was found between the measured enthalpies and the polymer LCST's. This relationship is shown graphically in Figure 4, in which the LCST of the polymer solutions at 5 wt % concentration in water are plotted vs their measured enthalpy. As is shown in Figure 4, the LCST's of the polymers show a linear relationship to the measured enthalpy, with an *R* value of 0.98. This means that the higher an LCST value, the more it will experience a concurrent and predictable decrease in the enthalpy of phase separation. A similar trend was observed by Kim and co-workers in their study of copolymers of poly(*N*-isopropylacrylamide), in which they noted a direct relationship between the LCST and the enthalpy of phase separation for a variety of different copolymers.[1] Therefore, our results support

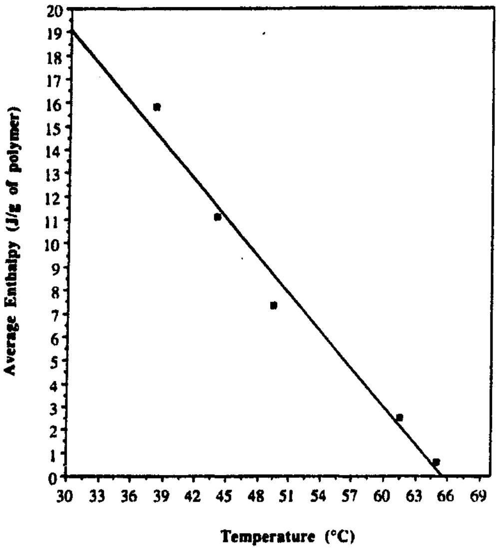


Figure 4. Enthalpy of phase separation as related to LCST of the polymers poly[bis(2,3-dimethoxypropanoxy)phosphazene] (■), poly[bis(2,3-bis(2-methoxyethoxy)propanoxy)phosphazene] (▲), poly[bis(2,3-bis(2-(2′-methoxyethoxy)ethoxy)propanoxy)-phosphazene] (box), poly[bis(2,3-bis(2-(2′-(2″-dimethoxyethoxy-)ethoxy)ethoxy)phosphazene] (●), and poly[bis(2,3-bis(2-(2′-methoxyethoxy)ethoxy)phosphazene] (○) at 5 wt % concentration.

the theory proposed Kim in which the enthalpy of phase separation is directly related to the LCST of the polymer.[1] These results indicate that theories associated with organic based polymer LCST phenomena can be extended to the study of ethyleneoxy side group polyphosphazenes.

Conclusions

A series of alkyl ether based polyphosphazenes has been synthesized and their LCST behavior in water examined. The LCST's of the polymers were found to be essentially independent of their concentration in water and showed only slight fluctuations from linearity at low concentrations. The hydrogels derived from the cross-linked polymers underwent rapid extrusion of water, together with concurrent loss of weight, near the LCST of the respective un-cross-linked polymers, followed by a rapid leveling off effect as the temperature was raised further. This rapid leveling off effect indicates that an equilibrium state is reached quickly for the hydrogels at higher temperatures. Analysis of the LCST's in the presence of NaCl showed a gradual decrease in the LCST of the solutions as the ionic strength of the solution was increased. This decrease was related to the salting-out effect by the NaCl and its effect on the hydrophilicity of the polymer system in water. DSC measurements of the phase separation of the polymers showed a direct correlation between the LCST of the polymers and the enthalpy of phase separation. The higher the LCST, the lower the enthalpy required for phase separation. Data for the enthalpy of phase separation vs LCST gave a straight line. The results of this study indicate that all the polymers discussed here behave similarly when they are dissolved in water and precipitated by an increase in temperature. The physical characteristics of the hydrogels appear to be appropriate for a number of technological and biomedical uses, including controlled drug delivery, enzyme reactors, and membrane applications.

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