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# Water swelling, brine soluble imidazole based zwitterionic polymers – synthesis, studies of reversible UCST behaviour and gel-sol transitions

Vivek Arjunan Vasantha,<br/>\*" Satyasankar Jana," Anbanandam Parthiban<br/>\*" and Julius G. Vancso $^{\mathbf{a},b}$ 

<sup>a</sup>Institute of Chemical and Engineering Sciences (ICES), Agency for Science, Technology and Research (A\*STAR), 1 Pesek Road, Jurong Island, Singapore 627833.

<sup>b</sup>MESA+ Research Institute for Nanotechnology, Faculty of Science and Technology, University of Twente, P. O. Box 217, 7500 AE Enschede, The Netherlands.

E-mail: vivek\_vasantha@ices.a-star.edu.sg; aparthiban@ices.a-star.edu.sg

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#### 1. Experimental

#### Materials

All reactions and polymerizations were performed with Schlenk techniques under Argon atmosphere. Vinlybenzyl chloride, 1, 3 propane sultone, imidazole, benzimidazole, and 4, 4'-azobis(4-cyanovaleric acid) (ACVA) were purchased from Aldrich and used as received. Solvents like acetonitrile (ACN), N, N-dimethylformamide (DMF), toluene, tetrahydrafuron were freshly dispensed from Glass Contour - Solvent Purification System. All other solvents used were of analytical grade. Deionized water is used for swelling and other aqueous studied. Other chemicals for this study were analytic reagents obtained from Aldrich.

#### Synthesis of monomers

#### 3-(1-(4-vinylbenzyl)-1H-imidazol-3-ium-3-yl)propane-1-sulfonate (ZIM-1)

The synthesis of vinylbenzylimidazole has been previously reported<sup>1</sup>. In a 500 ml two-necked round-bottomed flask equipped with a condenser and a magnetic stirrer were introduced 19.82 g (0.3 mol) of imidazole, 21.66 g (0.14 mol) of vinylbenzyl chloride, and 250 mL of chloroform. The solution was heated 50 °C for 8 h, cooled to room temperature, and filtered. The solvent was removed by evaporation; the reaction mixture was diluted with 500 mL diethyl ether, washed with water, dried over anhydrous magnesium sulfate. The crude product was purified by column chromatography using SiO<sub>2</sub> gel and diethyl ether as eluent. Finally diethyl ether was evaporated off. The desired product was obtained as oily liquid. The compound was directly used in the next step for ring opening, nucleophilic addition reaction. A solution of vinylbenzylimidazole (11.28 g, 61.3 mmol) and 1, 3 propane sultone (7.49 g, 61.3 mmol) in 250ml of dry acetonitrile was heated at 50 °C for 48 h. A white precipitate was obtained. The reaction mixture was concentrated in vacuo and the reaction product was Recrystallized from washed with acetone and dried in vacuum (13.85g, 73.77 %). water/ethanol mixture. The hygroscopic crystal with melting point of 206.24°C (DSC). <sup>1</sup>H NMR (D<sub>2</sub>O) : 8.84 (s, 1H) N-CH=N; 7.3-7.5 (m, 6H) CH<sub>aromatic</sub> and CH<sub>imidazole</sub>; 6.68-6.75 (dd, 1H) CH<sub>olefine</sub>; 5.8 and 5.3 (d, 2H) CH<sub>cis and trans</sub>; 5.32 (s, 2H) CH<sub>2 benzvl</sub>; 4.33 (t, 2H) -N-CH<sub>2</sub>; 2.88 (t, 2 H) S-CH<sub>2</sub>; 2.2-2.3 (m, 2 H) C-CH<sub>2</sub>-C. MS signal at  $m/z = 307.11 [M-H]^+$ 

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#### 3-(1-(4-vinylbenzyl)-1H-benzo[d]imidazol-3-ium-3-yl)propane-1-sulfonate (ZIM 2)

ZIM 2 was prepared in the same manner as reported for ZIM 1. A solution of vinylbenzylbenzoimidazole (8.3 g, 34.1 mmol) and 1, 3 propane sultone (4.6 g, 37.5 mmol) in 100 ml of dry acetonitrile was heated at 50 °C for 48 h. The reaction mixture was concentrated in vacuo and the reaction product was washed with acetonitrile, followed by acetone and then dried in vacuum. Yield = 7.94 g, (65.37 %). Recrystallized from water/methanol mixture. The melting point is 245.02°C (DSC). <sup>1</sup>H NMR (D<sub>2</sub>O) : 9.01 (s, 1H) N-CH=N; 7.21-6.59 (m, 6H) CH<sub>aromatic</sub> and CH<sub>imidazole</sub>; 5.85-5.77 (dd, 1H) CH<sub>olefine</sub>; 4.9 and 4.3 (d, 2H) CH<sub>cis and trans</sub>; 4.84 (s, 2H) CH<sub>2 benzyl</sub>; 3.79 (t, 2H) –N-CH2; 1.65 (t, 2 H) S-CH<sub>2</sub>; 1.32-1.36 (m, 2 H) C-CH2-C. MS signal at m/z =379.11 [MNa]<sup>+</sup>

#### General procedure for the preparation of polyzwitterions (PZI 1 and 2)

In a dried Schlenk tube (50 mL), ZIM (3.29 mmol) was introduced and dissolved in 0.5 M NaBr solution (25% w/v, 3 mL). The solution was purged with Argon gas for 45 min. The initiator ACVA (0.0165 mmol) was added all at once. The system was degassed by three consecutive vacuum-argon sweeping cycles and sealed-off under Ar atmosphere at room temperature. The reaction flask placed in a constant temperature bath at 90 °C for 24 h. The resulting viscous polymer solution was cooled and diluted with 5mL of 0.5 M NaBr. The solution was then dialysized against deionized water for 3 days (MWCO = 3500). The resulting water-insoluble polymer was lyophilized and dried *in vacuo* at 50 °C for 48 h.

#### Poly-[3-(1-(4-vinylbenzyl)-1H-imidazol-3-ium-3-yl)propane-1-sulfonate] (PZI 1)

PZI **1** was synthesized from ZIM **1** (1.01g, 3.29 mmol) and ACVA (4.8mg, 0.0165 mmol) in 0.5 M NaBr solutions (3mL) for 1.5 h at 90 °C. <sup>1</sup>H NMR (2 % NaCl/D<sub>2</sub>O): 9.28 (1H) N-CH=N; 6.6-7.5 (6H) CH<sub>aromatic</sub> and CH<sub>imidazole</sub>; 5.5 (2H) CH<sub>2</sub> benzyl; 4.59 (2H) –N-CH<sub>2</sub>; 3.01 (2 H) S-CH<sub>2</sub>; 2.4-2.3 (2 H) C-CH<sub>2</sub>-C; 2.3 (1H) CH<sub>backone</sub>; 1.72 (2H) CH<sub>2</sub> backbone. GPC analysis:  $M_n = 6500$  (PDI 2.02).UV-Vis (22.6 wt % NaCl): 232 and 261 nm

### Poly-[3-(1-(4-vinylbenzyl)-1H-benzo[d]imidazol-3-ium-3-yl)propane-1-sulfonate] (PZI 2)

PZI **2** was synthesized from ZIM **2** (1.00 g, 2.81 mmol) and ACVA (5.3mg, 0.0189 mmol) in 0.5 M NaBr solutions (5 mL) for 24 h at 90 °C. <sup>1</sup>H NMR (2 % NaCl/D<sub>2</sub>O): 7.21-6.59 (m, 6H) CH<sub>aromatic</sub> and CH<sub>imidazole</sub>; 4.84 (2H) CH<sub>2 benzyl</sub>; 3.79 (2H) –N-CH2; 1.65 (2 H) S-CH<sub>2</sub>; 1.32-1.36 (2 H) C-CH<sub>2</sub>-C. GPC analysis:  $M_n = 10600$  (PDI 1.40). UV-Vis (22.6 wt % NaCl): 232, 26, 271 and 278 nm

#### 2 Characterization methods

#### Instrumentation

<sup>1</sup>H nuclear magnetic resonance (NMR) spectra were recorded at room temperature on 400 MHz Bruker UltraShield AVANCE 400SB spectrometer. The zwitterionic polymers showed limited solubility in most common deterated solvents, but were soluble in 2% NaCl/D<sub>2</sub>O solution. Residual solvent peaks were used as internal standard. The aqueous GPC system

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was equipped with a Delta 600 HPLC pump, a 600 controller, a 717 plus autosampler, a 2487 dual absorbance detector and a 2414 refractive-index detector, all from Waters. The following GPC columns were arranged in series: Ultrahydragel guard, and Ultrahydragel 120 (7.8 mm ID  $\times$  300 mm) and an Ultrahydragel Linear (7.8 mm ID  $\times$  300 mm). The eluant (0.1 M NaNO<sub>3</sub> in deionized water) flow rate was 0.7 mL/min and the columns were maintained at 30 °C. The results were obtained using poly(ethylene oxide) (PEO) calibrations. Infrared spectra were run as KBr pellets for solids using Digilab Excalibur FTIR. High resolution mass spectra were recorded using electrospray ionisation (ESI) techniques in positive and negative ion modes by Thermo Finnigan MAT 95 XP. Mass spectral data is reported as the mass-to-charge ratio (m/z). UV absorption spectra were measured on a Shimadzu UV-VIS UV 2550 spectrometer. The solution samples were measured in 1 cm length cell and measured in the 200-600 nm regions. The transmittance studies for critical salt concentration or cloud point measurements were recorded at 600 nm.

#### Solubility

Solubility of PZI **1** and **2** in organic solvents at room temperature was determined by dispersing 1 wt % of polymer in various solvent and heating the mixture at 70 °C for 1h.

#### **Hydration Studies**

The samples in triplicate of known weight of PZIs were immersed in excess of DI water and kept in sealed containers which were placed in water bath at 23 °C and equilibrated for 48 h. The samples were removed and blotted dry. The swelling ratio of the polymer gel was determined gravimetrically. The swelling ratios were calculated from the ratio of the weight of the equilibrated gel to the dry weight. For each polymer, the average value was calculated. The swelling of PZI **1** was carried out in a polyester tea bag. The dry PZI **2** was studied in the form of disc.

#### Critical salt concentration or cloud point measurement

The cloud point titration was carried out using 0.9 wt % PZIs dissolved in 22.62 wt % aq. NaCl solution at 25 °C. The CSC values obtained by visual determination of the cloud point (clear solution became turbid) with error value  $\pm$  0.2 %. The CSC values are reported in Table 2.

#### Phase behaviour measurements

UCST of diluted PZI solutions was determined with respect to temperature with varying NaCl concentration. The polymer solution (2 ml) was poured into a glass vial, and placed directly into temperature controlled bath (Lauda Alpha RA 8) (temperature variation  $\pm 0.1$  °C). The solutions, which were turbid at room temperature, turned clear (transparent) upon heating. The transition point (UCST) was taken as the temperature at which the solution turned from cloudy to transparent.

#### **Aggregation Studies**

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Dynamic light scattering (DLS) was performed by using a Zetasizer NanoZS Instrument (Malvern Instruments, UK) equipped with a He–Ne laser (633 nm) and with non invasive backscattering (NIBS) detection at a scattering angle of  $173^{\circ}$ . The autocorrelation function was converted in a volume-weighted particle size distribution with Dispersion Technology Software from Malvern Instruments. Each measurement was repeated at least three times, and the average result was reported as the final Z average diameter (nm). The measurements were performed in the temperature range of  $10-60^{\circ}$ C with a temperature interval of 5 °C and an equilibration time of 10 min. Polymer solutions with various concentrations were prepared in NaCl solution at 50 °C and filtered using a 0.45 µm disposable membrane filter to remove any dust in solution.

#### **Viscosity measurements**

Viscosity of the zwitterionic polymers was measured on an Anton Paar MCR 501 rheometer. The viscosity was determined by a rotary viscometer at UCST concentration. The polymers were dissolved in salt solution at 40 °C. The measure geometry used was a spindle with cyclinder, equipped with a size 19 cylindrical spindle set for constant shear rate at 1000 s<sup>-1</sup>. The temperature dependence of the viscosity is fitted by Stettin analysis method. For temperature dependence studies, the samples were heated at 40 °C and cooled to 15 °C at the rate of 1 °C /min until the phase transition. The effect of shear rate with respect to viscosity was studied by placing the samples into the sample cup, equilibrating for 10 min at the required temperature and then subjecting to linearly increasing shear rate from 1 to 2000 s<sup>-1</sup> as a function of viscosity at constant temperature, 40 °C using 5 ml of PZI solutions. The flow curve of the material with shear thickening behaviour was fitted by Herschel-Bulkley analysis method.

#### **Gel-Sol transition measurement**

The gel (non-flow)-sol (flow) phase transition ( $T_{c, gel}$ ) of the PZI **1** and **2** in an aqueous/salt solution was determined using the tube inverting method. Briefly, the polymer was dissolved in 22.62 wt % NaCl solution at a concentration of 9.36 wt %. The sample vials were placed in a water-bath and heated slowly from 0 to 50 °C. The samples were equilibrated for 30 min at temperature intervals of 2 °C. The gel–sol transition was determined by inverting the vial. The error was  $\pm 0.5$  °C.



Scheme S2. Synthesis of zwitterionic monomers ZIM 1 and 2



Fig. S1 <sup>1</sup>H NMR spectra of new zwitterionic monomers ZIM 1and 2

 Table S1. Characterization of non-hydrolyzable zwitterionic monomers

Zwitterionic Monomers	Cation	Anion	Yield (%)	ESI-MS [M-H] <sup>+</sup>	Mol. wt g/mol	m.p (°C, DSC)
ZIM 1	Imidazole	- $CH_2SO^{-}_3$	73.77	307.11	306.38	206.24
ZIM 2	Benzoimidazole	- $CH_2SO^{-}_3$	65.37	379.11*	356.44	257.19
*[M-Na] +						



**Fig. S2.** GPC of zwitterionic polymer PZI1 (Mn=6500; PDI=2.02) and PZI 2 (Mn= 10600; PDI =1.40)



Fig. S3. <sup>1</sup>H NMR of zwitterionic polymer PZI 1



Fig. S4. FTIR of zwitterionic polymer PZI 1 and 2  $\,$ 



Fig. S5. UV-Vis of zwitterionic polymer PZI 1 and 2

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Solvents	PZI 1	PZI 2
Water	-	-
Methanol	-	-
Chloroform	-	-
Acetic acid	-	-
DMF	-	-
DMSO	-	-
DCA	-	-
Formic acid	+	+
Trifluoroethanol	+	+
Hexafluoroisopropanol	+	+
Brine (Sat. NaCl)	+	+
Formamide	+	+
Hexamethyl phosphoramide	±	-
Glycerol	-	±
Trichloroacetic acid	+	+
Trifluoroacetic acid	±	+

Tabel S2. Solubility of zwitterionic polymers in protic and aprotic solvents

1 w/w % of polymer solution was made after preheating at 70 °C for 1h. b'+' indicates soluble; '-' indicates insoluble; ' $\pm$ ' indicates partially soluble.

## **Table S3.** Potentiometric titration of polymer PZI **1** and **2** Vs 1.0091 M HCl in 22.62 wt % NaCl solutions.

Physical Properties	PZI 1	PZI <b>2</b>
$pK_{a}$	-1.189±0.84	$-1.4957 \pm 1.06$



**Fig. S6.** (a) Schematic representation of swelling behaviour and photography of swollen polymers. (b) Equilibrium swelling ratio (48 h) of polyzwitterions in DI water.



**Fig. S7.** Effect of salt concentration with respect to UV- transmittance (a) and DLS (b) using 0.9 wt % of PZIs in 22.6 wt % of NaCl and titrated with deionised water at 25  $^{\circ}$ C



**Fig. S8**. Temperature dependence of the Z average diameter of PZI **1** and **2** in NaCl solution during heating and cooling cycle. (a) PZI **1** (0.07 wt% of PZI **1** in 1.62 wt% NaCl), PZI **1**: 39.14±0.097 nm at 40 °C; 3986±559 nm at 20 °C; (b) PZI **2** (0.31 wt % of PZI **2** in 7.89 wt% NaCl), PZI **2**: 63.39±2.44 nm at 40 °C; 514±38.2 nm at 20 °C; (c) UCST of PZIs in NaCl solutions during heating and cooling process.



**Fig. S9.** Temperature dependence of PZIs in NaCl solution. ● (red): PZI **1** (0.07 wt % of PZI **1** in 1.62 wt % NaCl); ■ (black): PZI **2** (0.31 wt % of PZI **2** in 7.89 wt % NaCl)



Figure S10. Viscosity and shear stress of PZI 1 and 2 salt solutions as a function of shear rate. ■ (blue): PZI 1 (0.07 wt % of PZI 1 in 1.62 wt % NaCl); ■ (red): PZI 2 (0.31 wt % of PZI 2 in 7.89 wt % NaCl).

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Figure S11. Change of viscosity of zwitterionic polymers PZI 1 and 2 with temperature. ● (red): PZI 1 (0.07 wt % of PZI 1(a) in 1.62 wt % NaCl); ◆ (black): PZI 2 (0.31 wt % of PZI 2(b) in 7.89 wt % NaCl).

1. M. D. Green, J. H. Choi, K. I. Winey and T. E. Long, *Macromolecules*, 2012, **45**, 4749-4757.