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Synthesis and polymerization of new pyrrolidone-containing methacrylate monomers

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Seven new pyrrolidone-containing methacrylate monomers have been synthesised and characterised via n.m.r. and *FT*i.r. These monomers were polymerized using azobisisobutyronitrile as a thermal initiator at 60°C. Basic solubility tests were performed at room temperature and two of the polymers were found to be water soluble, namely poly(2-pyrrolidone-1-isopropenyl ketone) (PPIK) and poly(2-ethyl-2-pyrrolidone methacrylate) (PEPMA). The lower critical solution (LCST) behaviour of these two polymers was investigated and found to be in a temperature range similar to that reported for poly(N-isopropylacrylamide) (PNIPAAM) with onset LCST values (on heating) between 29 and 34°C. The effect was found to be reversible on cooling the solution. A comparison was made with PNIPAAM which seemed to indicate a slightly broader LCST transition for the two new polymers, however no conclusions could be firmly established on this as the molecular weights of the polymers were not measured.

(Keywords: pyrrolidone; lower critical solution temperature; thermotropic)

Introduction

N-vinyl pyrrolidone (NVP) monomer has been widely used for a range of commercial applications, especially as a monomeric component in contact lenses. However, there are some problems associated with the use of NVP, namely its poor reactivity in copolymerization reactions[1] and an incompatibility with fluorine containing monomers. To overcome the latter problem researchers have synthesised hydroxylated fluorine containing monomers to improve solubility in NVP[2]. An alternative approach is to modify the pyrrolidone monomer itself, with the aim of improving the following:

(1) monomer reactivity, to minimise compositional drift in the reaction;
(2) polymer compatibility and miscibility with fluorinated polymers, allowing flexibility in copolymer composition;
(3) hydrophilicity, allowing some control over the equilibrium swelling of hydrogels based on the monomers.

Previous work has been conducted in this area by Molock *et al.*[3] who synthesised a range of modified pyrrolidones, and by Iskander *et al.*[4] who modified α-methylene pyrrolidones with different alkyl substitution on the N-atom. In addition, there has been substantial interest in utilising the LCST behaviour of water soluble polymers, especially poly(N-isopropyl acrylamide) (PNIPAAM) for a diverse range of applications (see Ref. [5] and references cited therein). Whilst other polymers have been investigated, PNIPAAM has remained the polymer of choice because of its strong transition behaviour at 30–35°C. One area of development in controlling the LCST and enhancing the acuity of the transition has been to control the architecture of the polymer chains. In this respect, PNIPAAM has some disadvantages as acrylamides are not amenable to many polymerization control strategies, therefore a methacrylate based monomer would be advantageous. This paper contains a description of the syntheses of seven new pyrrolidone monomers with methacrylate-type functionality and provides some preliminary information on the properties of their corresponding homopolymers.

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Experimental

Materials. Diethyl ether, THF and toluene were refluxed over Na-*p*-benzoquinone and distilled prior to use. Other solvents (Aldrich) were dried over CaH_2, distilled and stored over a molecular sieve (4 Å). Other reagents were used without purification. 1-(2-hydroxyethyl)-2-pyrrolidone was also obtained from commercial sources (Aldrich).

Analyses. The i.r. spectra were recorded as liquid films between salt plates on a Perkin Elmer (2000 FTIR) instrument. ^{1}H n.m.r. spectra were recorded on a Bruker AC 300F n.m.r. using $CDCl_3$ as solvent. Reaction mixtures were examined by t.l.c. on Kieselguhr PF 254 plates with ethyl acetate:methanol, 3:1 (v:v) as eluent. All vacuum distillations were done using Kugelrhor apparatus (Buchi GKR-51).

Syntheses. The structures of the seven pyrrolidone products are given in *Figure 1*. The synthetic routes to these products and the supporting spectroscopic data are listed below.

Preparation of 1-(hydroxyalkyl)-2-pyrrolidones. The following 1-(hydroxyalkyl)-2-pyrrolidones were prepared by related procedures as follows.

1[(3-Hydroxy-1-propyl)-2-pyrrolidone. 2-Pyrrolidone (Aldrich) (3.4 g, 0.04 mol) was added dropwise to a stirred mixture of finely powdered potassium hydroxide (4.48 g,

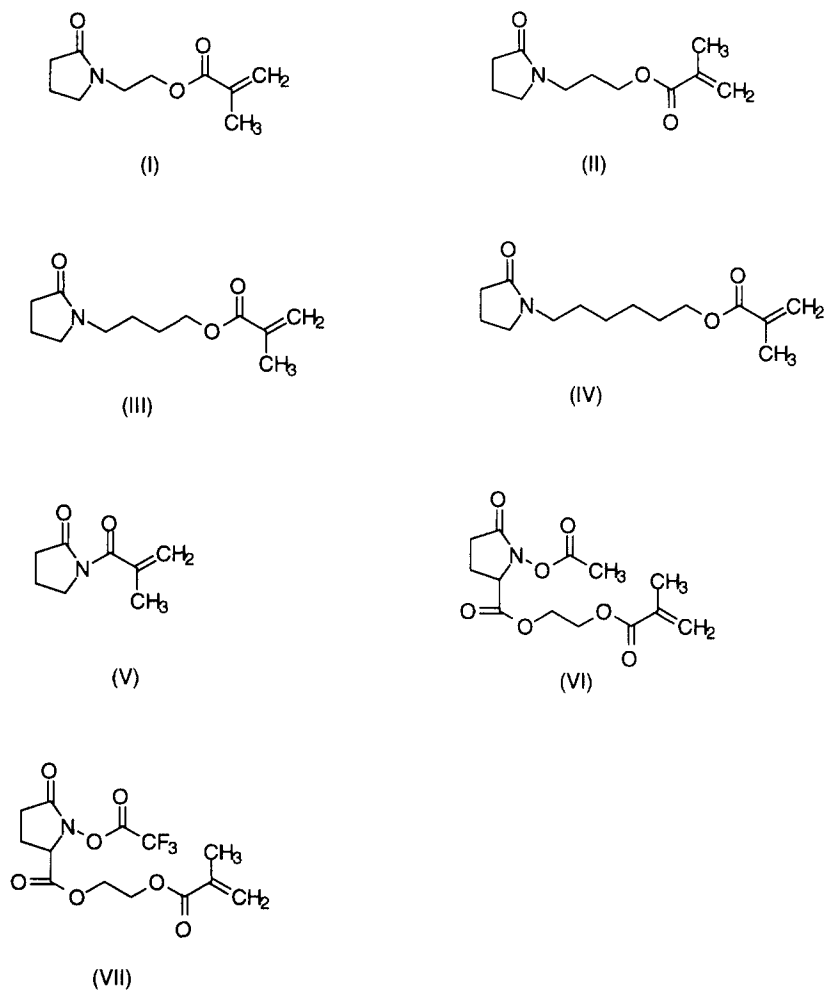

Figure 1 Structures of the seven pyrrolidone containing monomers

0.08 mol) and dry dimethyl sulphoxide (5 ml) with cooling (*ca.* 15°C). 3-Chloropropanol (4.25 g, 0.045 mol) was added, and the mixture stirred under N_2 for 48 h. The reaction mixture was poured into water (30 ml) saturated with NaCl, and the product was extracted with dichloroethane, dried over anhydrous sodium sulphate, and distilled under reduced pressure, leaving a colourless liquid (84% theor.), bath temperature 190°/0.01 torr; R_F 0.39; i.r.:ν_{max} 3391 (OH str.), 1687 (C=O), 1470, 1438, 1295, 1116, 1037 and 959 cm^{-1}; ^1H n.m.r.: δ 4.0 (brs, 1H, –OH), 3.30 (m, 2H, C_5–H,s), 3.20 (m, 2H, C_3–H,s), 3.0–3.25 (4H, > NCH_2– and –OCH_2–), 2.05 (m, 2H, C_4–H,s) and 1.35–1.95 (m, 2H, chain-alkyl-H,s).

1(6-Hydroxy-1-hexyl)-2-pyrrolidone. Colourless liquid (98% theor.); bath temperature 190°/0.01 torr; R_F 0.39; i.r.:ν_{max} 3409 (OH str.), 1682 (C=O), 1470, 1438, 1378, 1295, 1116, 1056, 957 and 757 cm^{-1}. ^1H n.m.r.: δ3.60 (1H, brs, OH), 3.40 (4H, m, > NCH_2 and –OCH_2–), 3.36 (m, 2H, C_5–H,s), 2.38 (m, 2H, C_3–H,s), 1.92 (m, 2H, C_4–H,s) and 1.35-1.60 (8H, m, chain-alkyl-H,s).

1(4-Hydroxy-1-butyl)-2-pyrrolidone from 1[4(2-tetrahydropyranyloxy)-1-butyl]-2-pyrrolidone. Potassium hydroxide (2.46 g, 0.044 mol) and 4-chlorobutyltetrahydropyranyl ether[6] (4.0 g, 0.022 mol) were added to a solution of 2-pyrrolidone (1.7 g, 0.02 mol) in dimethyl sulphoxide (5 ml) at ambient temperature. The mixture was stirred for 72 h. After aqueous work-up and extraction with diethyl ether, the product (50%) was distilled, bath temperature 180°/0.01 torr, R_F 0.69; i.r.:ν_{max} 1691 (C=O), 1502, 1447, 1364, 1295, 1212, 1134, 1078, 1042, 996, 913 and 876 cm^{-1}; ^1H n.m.r: δ 4.50 (m, 1H, > CHO, pyran), 3.50 (m, 2H, > NH_2), 3.35 (m, 2H, C_5–H,s), 3.23 (m, 2H, CH_2O–, chain), 2.30 (m, 2H, C_3–H,s), 1.96 (m, 2H, C_4–H,s) and 1.42–1.84 (m, 12H, Pyran-H,s and side chain alkyl-H,s).

The pyranyl ether was hydrolysed with methanol, containing a few drops of concentrated HCl at ambient temperature. The product mixture was subjected to an aqueous work-up and extraction with diethyl ether, which after evaporation, left a colourless liquid of the title compound (90% theor.), bath temperature 175°/0.01 torr; R_F 0.44; i.r.:ν_{max} 3400 (OH str), 1668 (C=O), 1502, 1442, 1295, 1069 and 1037 cm – 1. ^1H n.m.r.: δ 3.70 (brs, 1H, OH), 3.62 (m, 2H, C_5–H,s), 3.25–3.40 (4H, > NCH_2– and –OCH_2–), 2.35 (m, 2H, C_3–H,s), 2.0 (2H, m. C_4–H,s) and 1.43–1.70 (4H, m, chain alkyl-H,s).

Preparation of 1-(n-alkyl-2-pyrrolidone) methacrylates. These are prepared in a similar fashion as follows.

1(2-Ethyl-2-pyrrolidone)methacrylate (I). Triethylamine (7.6 g, 0.75 mol) was added to an ice-cooled and stirred

solution of 1 (2-hydroxyethyl)-2-pyrrolidone (12.9 g, 0.1 mol) in dichloroethane (30 ml), followed by the slow addition (over 0.5 h) of methacroyl chloride (11.50 g, 0.05 mol). The mixture was allowed to reach room temperature with stirring overnight before being poured into water (20 ml) saturated with NaCl. The aqueous phase was extracted twice with dichloroethane (40 ml total). The combined extracts were washed once with water before being dried over anhydrous sodium sulphate. The pale yellow oil was redissolved in diethyl ether (50 ml) and percolated through a short column of silica. The solvent was removed giving a colourless liquid (80% theor.), bath temperature 130°/0.01 torr, n_D^{26} 1.475, R_F 0.2 (EtOAc, n-Hex.; 4:1, v:v); i.r.:ν_{max} 1726 (C=O), 1696 (C=O, ring), 1498, 1447, 1323, 1300, 1171, 1120, 1042, 954 and 825 cm^{-1}. ^1H n.m.r.: δ 5.97 (m, 1H, $=CH_2$), 5.44 (m, 1H, $=CH_2$), 4.40 (2H, $-OCH_2-$, chain), 3.45 (m, 2H, $>NCH_2$), 3.33 (m, 2H, C_5–H,s), 2.33 (m, 2H, C_3–H,s), 1.90 (m, 2H, C_4–H,s) and 1.80 (d, 3H, CH_3).

1(3-Propyl-2-pyrrolidone)methacrylate (II). Colourless liquid (60% theor.), bath temperature 155–160°C/1.6 × 10^{-2} torr; n_D^{26} 1.464; R_F 0.30; i.r.:ν_{max} 1724 (C=O), 1691 (C=O, ring), 1645, 1457, 1429, 1300, 1176, 1120, 1047, 941 and 821 cm^{-1}. ^1H n.m.r.: δ 6.0 (m, 1H, $=CH_2$), 5.50 (m, 1H, $=CH_2$), 4.16 (m, 2H, $-CH_2O-$, chain), 3.90 (m, 2H, $>NCH_2$), 3.30–3.60 (m, 4H, C_3 and C_5–H,s), 2.25 (m, 2H, C_4–H,s), 2.0 (m, 2H, CH_2-chain) and 1.90 (d, 3H, CH_3).

1(4-Butyl-2-pyrrolidone)methacrylate (III). Pale yellow oil (95.6% theor), bath temperature 175°/0.01 torr; n_D^{26} 1.475; R_F 0.29; i.r.:ν_{max} 1723 (C=O) 1696 (C=O, ring), 1503, 1457, 1387, 1332, 1304, 1176, 1125, 1061, 950 and 821 cm^{-1}. ^1H n.m.r.: δ 5.98(m, 1H, $=CH_2$), 5.45 (m, 1H, $=CH_2$), 4.08 (2H, $-CH_2O-$, chain), 3.12–3.60 (4H, C_5 and $>NCH_2$), 2.30 (m, 2H, C_3–H,s), 1.90 (m, 2H, C_428–H,s), 1.80 (d, 3H, CH_3) and 1.35–2.0 (two CH_2, chain).

1(6-Hexyl-2-pyrrolidone)methacrylate (IV). Pale yellow oil (86.5% theor.), bath temperature 185°/0.01 torr; n_D^{26} 1.471; R_F 0.41; i.r.:ν_{max} 1729 (C=O), 1691 (C=O, ring), 1502, 1457, 1300, 1176, 1120, 1042 and 945 cm^{-1}. ^1H n.m.r.: δ 6.05 (m, 1H, $=CH_2$), 5.50 (m, 1H, $=CH_2$), 4.08 (m, 2H, $-CH_2O-$, chain), 3.43 (m, 2H, C_5H,s), 3.42 (m, 2H, $>NCH_2$), 3.2 (m, 2H, C_3–H,s), 1.90 (d, 3H, CH_3), 1.20–2.10 (m, 10H, C_4 and side chain alkyl H,s).

Preparation of 2-pyrrolidone-1-isopropenyl ketone (V). 2-Pyrrolidone (8.5 g., 0.1 mol) was added dropwise to a suspension of sodium hydride (2.64 g, 0.11 mol) in a mixture of n-hexane (100 ml) and diethyl ether (50 ml). The mixture was briefly heated to 60°C for 0.5 h with stirring, and after cooling in an ice bath, methacroyl chloride (11.5 g, 0.11 mol) was added dropwise (1 h). The reaction mixture was stirred at room temperature overnight, then poured into water (75 ml) to isolate the organic phase. The organic phase was then washed with $NaHCO_3$ solution (10%) and dried over anhydrous sodium sulphate. The solvent was evaporated leaving a colourless liquid (8.08 g, 70% theor.), bath temperature 150°C/0.01 torr, n_D^{26} 1.469; i.r.:ν_{max} 1755 (C=O), 1686 (C=O, ring), 1535, 1461, 1336, 1258, 1162, 1037 and 780 cm^{-1}. ^1H n.m.r.: δ 5.30 (d, 2H, $=CH_2$), 3.79 (m, 2H, C_5–H,s), 2.57 (m, 2H, C_3–H,s), 2.05 (2H, C_4–H,s) and 1.97 (d, 3H, CH_3).

Preparation of methacroyl 2'-ethyl(1-acetyl-2-pyrrolidone)-5-carboxylate (VI). Pyrrolidone-5-carboxylic acid (Aldrich) (1.29 g, 0.01 mol) was acylated by dissolving in acetic anhydride (20 ml) at 80°C for 1 h. The clear solution was left to stand overnight at room temperature. Methanol (50 ml) was added and the mixture was stirred for 4 h to ensure the destruction of excess acetic anhydride. The solution was evaporated under reduced pressure leaving a viscous colourless liquid of the 1-acetyl derivative (0.85 g, 50%) which was converted to the acid chloride by reacting with an excess of thionyl chloride.

2-Hydroxyethylmethacrylate (HEMA) (1.32 g, 0.01 mol) was added dropwise (1 h, 0°C) to a solution of the acid chloride (1.90 g, mol) in dichloroethane (25 ml). Triethylamine (1.21 g, 0.011 mol) was subsequently added and the mixture was stirred for a further 1 h at 0–5°C, before standing at room temperature overnight. The reaction mixture was partitioned with water (30 ml) and the organic phase isolated. The aqueous phase was extracted twice with dichloroethane (50 ml total), and the combined extracts were dried over anhydrous sodium sulphate. The product was percolated through a short silica gel column with ethyl acetate:methanol (1:1, v:v). The solvent was removed leaving a yellow oil (80% theor.); bath temperature 190°C/1.6 × 10^{-2} torr; n_D^{26} 1.455; i.r.: ν_{max} 1756 (C=O), 1723 (C=O, ring), 1645, 1461, 1378, 1327, 1305, 1185, 1088 and 1047 cm^{-1}. ^1H n.m.r.: δ 6.09 (m, 1H, $=CH_2$), 5.55 (m, 1H, $=CH_2$), 4.20–4.33 (4H, two $-OCH_2-$, chain), 3.80 (m, 1H, C_2–H), 3.55–3.70 (4H, C_3– and C_4–H,s), 1.90 (s, 3H, $-COCH_3$) and 1.23 (d, 3H, CH_3 chain).

Preparation of methacroyl-2'-ethyl(1-trifluoroacetyl-2-pyrrolidone)-5-carboxylate (VII). 1-Trifluoroacetyl-2-pyrrolidone-5-carboxylic acid (TFPCA) was prepared in an analogous manner to the acetyl derivative using trifluroacetic anhydride. The product is a colourless solid (70% theor.), m.p. 185° (from MeOH-EtOAc). i.r.:ν_{max} (Nujol) 3308 (OH), 1719 (CO), 1650, 1466, 1240, 1116 and 710 cm^{-1}. ^1H n.m.r.: δ (D_2O) δ 2.56 (m, 4H, C_3 and C_4–H,s) and 4.42 (m, 1H, C_5–H).

HEMA (1.08 g, 0.011 mol) was added slowly to a solution of the acid chloride of TFPCA (2.44 g, 0.01 mol) in dichloroethane (30 ml) at *ca.* 5°C, followed by the addition of triethylamine (1.21 g, 0.011 mol). The mixture was maintained at this temperature for 3 h, then allowed to stand at room temperature overnight before being partitioned with water. The organic phase, was dried over anhydrous sodium sulphate and isolated from the solvent to yield a yellow oil (82% theor.); bath temperature 170°/1.6 × 10^{-2} torr; n_D^{26} 1.426; i.r.:ν_{max} 1746 (CO), 1732 (CO, ring), 1645, 1457, 1355, 1309, 1226, 1176, 1065, 1042 and 955 cm^{-1}. ^1H n.m.r.:δ 6.10 (m, 1H, $=CH_2$), 5.6 (m, 1H, $=CH_2$), 4.38 (m, 4H, two $-OCH_2-$), 3.80 (m, 1H, C_2–H), 3.60–3.75 (m, 4H, C_3 and C_4–H,s) and 1.90 (d, 3H, CH_3)

Polymerization. The monomers were polymerized in bulk under nitrogen using azobisisobutyronitrile (AIBN) as the initiator (1% wt:wt) at 60°C. Polymers were precipitated in either tetrahydrofuran (THF) or diethyl ether.

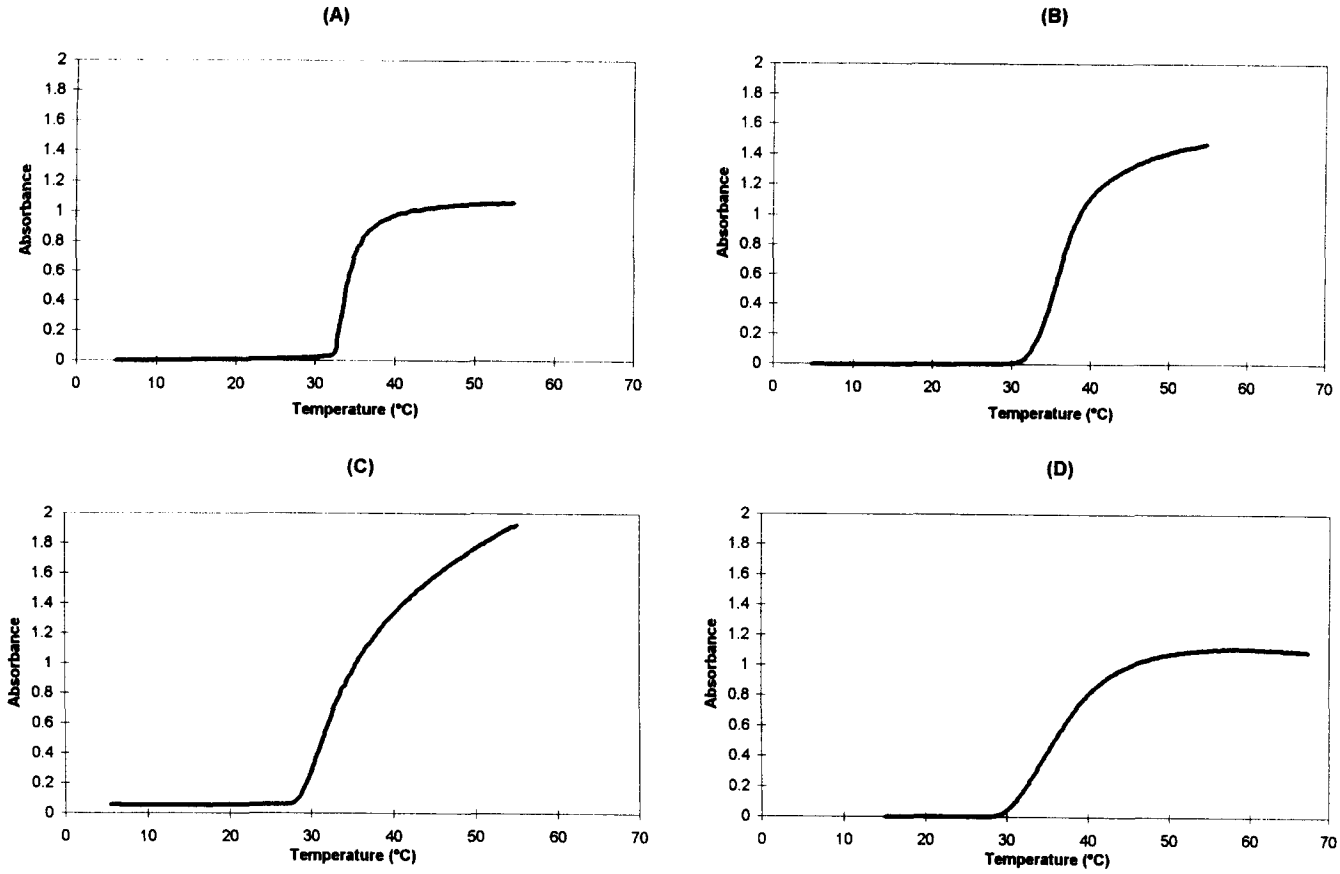

Figure 2 LCST behaviour for: (a) PNIPAAM aqueous solution heating at 1°C/min; (b) PEPMA aqueous solution heating at 1°C/min; (c) PEPMA aqueous solution cooling at 1°C/min; (d) PPIK aqueous solution heating at 1°C/min

Table 1 Solubility data for homopolymers based on the seven monomers (I–VII)

Sample no.	Water	THF	Diethyl ether	Methanol	Chloro-form	DMSO
I	✓	x	x	✓	✓	✓
II	x	x	x	✓	✓	✓
III	x	x	x	x	✓	✓
IV	x	✓	x	✓	✓	✓
V	✓	✓	x	✓	✓	✓
VI	x	x	x	x	x	✓
VII	x	✓	x	✓	✓	✓

LCST determinations. The LCSTs of the homopolymers of monomers (I) and (V) in water (0.7 wt%) were measured using a Jasco ETC-505S V-530 u.v./VIS spectrometer at a fixed wavelength of 550 nm. The absorbance of the solution was monitored on heating from 5 to 55°C at 1°C/min. The reversibility of the LCST transition was monitored for PEPMA by cooling the solution from 55 to 5°C.

Results and discussion

Basic solubility tests were conducted on all the polymers; the results are given in *Table 1*. Two of the polymers, PEPMA and PPIK, proved to be water soluble at room temperature, and further studies revealed that aqueous solutions of these polymers exhibit a LCST in the range 29–33°C. The cloud-point traces from u.v.-vis spectrometry are given in *Figure 2b* and *d*, together with a trace for PNIPAAM, *Figure 2a* for comparison. The trace for PEPMA is similar in form to the PNIPAAM result, although the transition appears to be slightly broader. It is generally accepted that LCST data obtained from cloud point measurements are relatively independent of the polymer concentration[7], however there is evidence that the molecular weight distribution does exert an influence[8]. Therefore, no conclusions can be drawn on the relative breadth or strength of the LCST transitions without further information on the respective molecular weights of the polymer samples studied here. The LCST for PEPMA was found to be reversible, as shown in *Figure 2c* where the solution was cooled from 55 to 5°C. The main advantage of PEPMA over the widely-studied PNIPAAM in the investigation of LCST behaviour is the relative ease with which poly(methacrylate) derivatives can be synthesised with controlled molecular weight distributions[9]. As pointed out by Schild[5], NIPAAM is extremely difficult to polymerize with any 'living' method thus restricting the effectiveness of fundamental studies (on PNIPAAM) into LCST behaviour.

Conclusions

Seven new pyrrolidone containing monomers have been synthesised and polymerized. Two of the resultant polymers, PEPMA and PPIK, exhibit strong LCST behaviour in water over the temperature range 29–34°C.

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