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NOTE: Synthesis and Characterization of a Poly(acrylamide) with Pendant 1,4-piperazine-2,5-dione Moieties via Post-polymerization Cyclization

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A poly(acrylamide) was synthesized from N^{α}-Boc-N^{ε}-acrolyl-L-lysylglycine methyl ester via radical polymerization. This polymer typically had Mn ~ 100,000 g/mol, Mw ~ 300,000 g/mol, and a T_g of 93°C. Removal of Boc with TFA and cyclization with DABCO™ in DMSO at 65°C afforded a soluble piperazinedione-containing polymer that had a T_g of 157°C and thermal stability up to 300°C. These results demonstrate a viable and efficient synthetic route to piperazinedione-containing polyacrylamides of high molecular weight. Related polymers that incorporate substituted indane moieties could be useful high T_g materials for fabrication of LC and NLO devices.

Keywords: Poly(acrylamide), 1,4-piperazine-2,5-dione, hydrogen bonding, high T_g polymer

1. Introduction

Polyacrylamides are thermally and hydrolytically robust polymers that have many applications (1–3). The versatility of polyacrylamides is due in large part to the structural variability of the amine component. A particularly intriguing set of acrylamide monomers are those derived from natural or unnatural α-amino acids (4, 5). As with proteins, the physical and chemical properties of such polyacrylamides depend on the nature of the amino acid sidechains.

In an effort to develop new compounds that exhibit engineered supramolecular order for the production of materials with useful bulk properties, we have prepared substituted 1,4-piperazine-2,5-diones **1** from the corresponding 2-aminoindane-2-carboxylic acids (6, 7). Crystals of such piperazinediones exhibit very high melting points, due in part to strong reciprocal hydrogen bonding interactions of the amide functional groups. We postulated that polymers such as **2** that incorporate similarly substituted piperazinediones in side chains might exhibit unusually high T_gs, increased thermal stabilities, and useful bulk properties, depending on the indane substituents.

Polymers containing 1,4-piperazine-2,5-dione moieties are not well known in the literature. Imanishi and Kiniwa prepared piperazinedione-containing poly(acrylamide) **3** by radical polymerization of *cyclo*-[N^{ε}-acryloyl-L-Lys-Gly] (8). The yield, polymer molecular weight, and polymer solubility were low and were attributed to the poor solubility of the piperazinedione moiety. Similar problems have been reported when 1,4-piperazine-2,5-dione moieties are components in copolymerizations (9). An alternative synthetic strategy involves cyclization to produce the piperazinedione moiety after polymerization to a high molecular weight. For example, Kim and Jackson reported (10) the synthesis and characterization of polymers with side chain 1,4-piperazine-2,5-dione units related to the Inoue catalyst, *cyclo*-(L-Phe-L-His), which is useful for the enantioselective formation of cyanohydrins (11). However, the numbers of piperazinedione moieties in these constructs were very low.

Our goal was to achieve a high content of 1,4-piperazine-2,5-dione moieties while avoiding solubility problems during and after polymerization. It was therefore decided to prepare an *N*-acrylamide derivative of a protected dipeptide for radical polymerization and to effect cyclization of the piperazinedione in a post-polymerization step to produce model polymer **3** of a high molecular weight. Suitable *N*-acrylamides for preparation of a polyacrylamide precursor to **3** include *N*-Boc-glycyl-N^{ε}-acrolyl-L-lysine methyl ester (**4**) and N^{α}-Boc-N^{ε}-acrolyl-L-lysylglycine methyl ester (**5**). Although both compounds were synthesized in the course of this study, the intermediates in the synthesis of **5** were more easily purified, and so the route to **3** via **5** was preferred and is the subject of this note.

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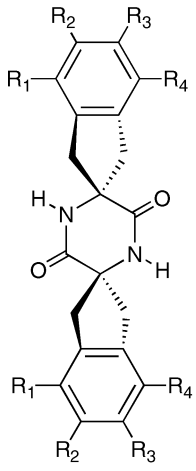

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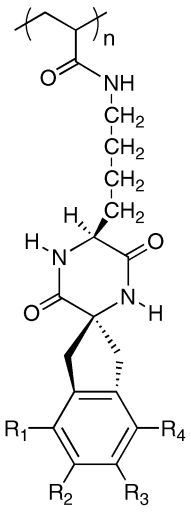

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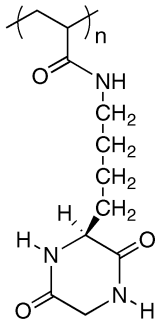

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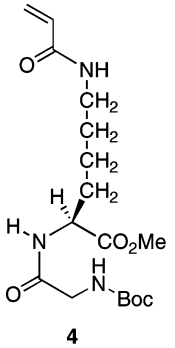
2. Experimental

2.1. *Measurements*

Melting points were taken on a Laboratory Devices MelTemp and are uncorrected. ^{1}H-NMR spectra were acquired at 200 MHz on a Varian Gemini spectrometer, at 250 MHz on a Bruker AM-250 spectrometer, and at 500 MHz on a Bruker AM-500 spectrometer. ^{13}C-NMR spectra were acquired at 50 MHz, 62.5 MHz, and 125 MHz, respectively, on the same instruments. Optical rotations were measured on a Rudolph Research Autopol III polarimeter. Gel permeation chromatography (GPC) was performed on a Waters Ultra Styragel Linear 7.8 × 300 mm column versus PMMA standards using THF as elutant at a flow rate of 1.0 mL/min using a Waters 501 HPLC system with a Waters Differential Refractometer Electronics Unit with a trapped reference as the detector. Differential scanning calorimetry (DSC) was performed on a TA Instruments DSC 2920 Modulated DSC under a nitrogen atmosphere. Thermal gravimetric analysis (TGA) was performed on a TA Instruments SDT 2960 in air. Elemental analyses were performed by Desert Analytics, Tucson, Arizona.



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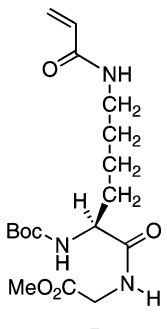

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2.2. *Materials*

N^{α}-Boc-N^{ε}-Cbz-L-lysine and PyBOP® were purchased from Calbiochem/Novabiochem Corporation and were used without further purification. Glycine methyl ester hydrochloride was purchased from Aldrich Chemical Company and was recrystallized from methanol. Diisopropylethylamine (DIEA) was used as obtained. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl under nitrogen. Acetonitrile was pre-dried over $CaCl_2$, then passed through a column of neutral alumina and stored over activated 3Å molecular sieves. Acetonitrile was degassed by bubbling argon through the liquid for 30 min prior to use in polymerizations.

2.3. *Monomer synthesis*

2.3.1. *N^{α}-Boc-N^{ε}-Cbz-L-lysylglycine methyl ester (6)*

To a dry 500 mL, three-neck round-bottom flask fitted with two ground-glass stoppers, a gas inlet adapter, and equipped with a magnetic stir bar under an argon atmosphere were added N^{α}-Boc-N^{ε}-Cbz-L-lysine (**7**, 4.21 g, 11.1 mmol), PyBOP (5.76 g, 11.1 mmol), and dry THF (250 mL). Stirring was commenced, and DIEA (4.82 mL, 3.58 g, 27.7 mmol) and glycine methyl ester hydrochloride (**8**, 1.46 g, 11.6 mmol) were added at room temperature. After 7.5 h, the THF was removed on a rotary evaporator and the resulting oil was dissolved in ethyl acetate (250 mL). The ethyl acetate solution was washed with 2 N HCl (3 × 100 mL), brine (100 mL), sat aq $NaHCO_3$ (100 mL), and brine (100 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated on a rotary evaporator to yield an oil. This oil was purified by column chromatography (70-230 mesh SiO_2, continuous gradient elution from 0.5% MeOH/49.5% EtOAc/50% $CHCl_3$ to 3% MeOH/47% EtOAc/50% $CHCl_3$) to give a colorless, viscous oil. The yield was 5.0 g (100%). The product contained traces of EtOAc, but was pure enough for use in the next step. Solvent-free crystals of **6** could be obtained by crystallization from EtOAc/dry Et_2O, mp 84–85°C, lit. mp 81.5–83.0°C (12). $[\alpha]_D^{20} = -11.1$ (*c* 10, $CHCl_3$); IR (thin film) 3322, 2925, 2840, 1749, 1700, 1674, 1529, 1473 cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1.43 (s, 9H), 1.30–1.90 (m, 6H), 3.10–3.25 (q, 2H, J = 6.0 Hz), 3.67 (s, 3H), 4.01 (d of d, 1H, J = 17.9 Hz, J = 5.2 Hz), 4.05 (d of d, 1H, J = 17.9 Hz, J = 5.1 Hz), 4.05–4.20 (q, 1H, J = 5.6 Hz), 5.00 (br t, 1H), 5.09 (s, 2H), 5.15–5.25 (br d, 1H), 6.70 (br t, 1H), 7.34 (s, 5H); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 22.2, 28.2, 29.2, 31.8, 40.2, 40.9, 52.2, 54.0, 66.4, 79.9, 127.9, 128.2, 128.3, 136.5, 155.6, 156.5, 170.1, 172.5.

2.3.2. *Acrylic anhydride (**10**)*

To a dry 250 mL, three-neck round-bottom flask fitted with rubber septa, a gas inlet adapter, and equipped with a magnetic stir bar under an argon atmosphere were added dry Et_2O (150 mL) and acrylic acid (15.0 mL, 15.8 g, 219 mmol). The solution was stirred and DIEA (38.1 mL, 28.3 g, 219 mmol) was added. The ensuing reaction was slightly exothermic and resulted in a milky white solution. Acrolyl chloride (18.7 mL, 20.8 g, 230 mmol) was then added dropwise via syringe. The ensuing reaction was very exothermic and resulted in formation of a large amount of a white precipitate. After 30 min, the precipitate was removed by filtration and was washed with dry ether. The organic filtrate and washings were combined and concentrated by rotary evaporation to yield an orange oil. This oil was distilled through a Vigreaux column under reduced pressure (ca. 5 mm Hg) to afford **10** as a colorless oil, bp 59.5–60.0°C, lit. bp 68°C at 9.7 mm Hg (13). The yield was 16.2 g (59%). IR (thin film) 3117, 3042, 2923, 2848, 1790, 1727, 1633, 1476 cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$) δ 6.10 (dd, 1H, J = 10.3 Hz, J = 1.8 Hz), 6.22 (dd, 1H, J = 16.5 Hz, J = 10.3 Hz), 6.60 (dd, 1H, J = 16.5 Hz, J = 1.8 Hz); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 127.2, 134.4, 160.9.

2.3.3. *N^{α}-Boc-N^{ε}-acrolyl-L-lysylglycine methyl ester (**5**)*

In a 500 mL round-bottom flask fitted with a three-way stopcock and a stir bar was placed N^{α}-Boc-N^{ε}-Cbz-L-lysylglycine methyl ester (**6**, 3.48 g, 7.71 mmol). Absolute ethanol (250 mL) and acetic acid (0.49 mL, 0.51 g, 8.5 mmol) were added and the solution was stirred vigorously while being placed under vacuum. After 5 min, the flask was back-filled with argon and 10% Pd/C (2 g) was added. The mixture was again vigorously stirred while the flask was placed under vacuum. After 5 min, the flask was backfilled with hydrogen gas from a balloon. The evacuation and filling cycle was repeated two more times. The mixture was then stirred under hydrogen at rt for 30 min at which time TLC indicated that no starting material was present. Dichloromethane (2 mL) was added and the mixture was filtered through a double layer of filter paper. The filtrate was cooled to −78°C and treated with DIEA (3.36 mL, 2.49 g, 19.3 mmol) and acrylic anhydride (1.33 mL, 1.46 g, 11.6 mmol) with stirring under argon. The resulting mixture was allowed to warm to rt over 0.5 h. TLC indicated that none of the intermediate amine **9** was present. The volatile solvents were removed on a rotary evaporator and the residue was dissolved in EtOAc (200 mL). The organic layer was washed with brine (3 × 50 mL), the combined aqueous layers were back-extracted with EtOAc (50 mL), and the combined organic phases dried over $MgSO_4$. The mixture was filtered and concentrated *in vacuo* to give a light yellow oil. This oil was purified by column chromatography (70–230 mesh SiO_2, continuous gradient elution from 2% MeOH/48% EtOAc/50% $CHCl_3$ to 10% MeOH/40% EtOAc/50% $CHCl_3$) to afford a white foam. This foam was dissolved in about 30 mL of EtOAc and dry Et_2O was added to the cloud point. A small amount of EtOAc was added to give a clear solution and the solution was filtered to remove a small amount of a grey precipitate that had formed. This solution was heated to boiling and then allowed to cool to rt. The solution was capped and left to crystallize overnight. The crystals were collected by vacuum filtration and washed with a small amount of dry Et_2O. The mother liquor was concentrated on a rotary evaporator and a second crop of crystals was obtained from EtOAc/hexanes. The total yield was 2.00 g (70%), mp 108–108.5°C. $[\alpha]_D^{20} = -13.3$ (*c* 10, $CHCl_3$); IR (thin film) 3307, 3082, 2976, 2919, 2849, 1754, 1659, 1626, 1538, 1472, 1462 cm^{-1}; ^{1}H-NMR (250 MHz, $CDCl_3$) δ 1.45 (s, 9H), 1.30-1.95 (m, 6H), 3.30–3.42 (dq, 2H, J = 6.2 Hz, J = 2.6 Hz), 3.75 (s, 3H), 4.05-3.95 (dd, 1H, J = 18.3 Hz, J = 5.5 Hz), 4.05-4.15 (dd, 1H, J = 18.3 Hz, J = 5.5 Hz), 4.10–4.20 (m, 1H), 5.15–5.30 (br d, 1H, J = 6.6 Hz), 5.55–5.75 (dd, 1H, J = 10.0 Hz, J = 1.8 Hz), 5.90-6.00 (br s, 1H), 6.05-6.17 (dd, 1H, J = 17.2 Hz, J = 10.0 Hz), 6.25–6.35 (dd, 1H, J = 17.2 Hz, J = 1.8 Hz), 6.75 (br t, 1H); ^{13}C-NMR (50 MHz, $CDCl_3$/1 drop DMSO-d_6) δ 22.1, 28.0, 28.4, 31.7, 38.3, 51.8, 53.8, 79.2, 125.2, 130.8, 155.3, 165.4, 169.8, 172.4. Anal. Calcd for $C_{17}H_{29}N_3O_6$: C, 54.97; H, 7.87: N, 11.31. Found: C, 55.34; H, 8.05; N, 11.10.

2.4. *Polymerization*

2.4.1. *Poly-(N^{α}-Boc-N^{ε}-acrolyl-L-lysylglycine methyl ester) (**11**)*

N^{α}-Boc-N^{ε}-acrolyl-L-lysylglycine methyl ester (**5**, 1.1 g, 3.0 mmol) was placed in a thick-walled Pyrex glass tube and AIBN (4.9 mg, 30 μmol) was added. The tube was capped and placed under high vacuum for 15 min, then backfilled with argon. Dry, argon-purged acetonitrile (3.0 mL) was added to the polymerization tube via syringe. The resulting solution was frozen using a dry ice/acetone bath and placed under vacuum for 30 min. The tube was then sealed, allowed to warm to rt, and was placed in an oil bath at 70°C overnight. The tube was then removed from the oil bath, cooled to rt, frozen using a dry ice/acetone bath, scored with a glass cutter, and opened. The viscous material in the tube was dissolved in THF (5 mL) and the resulting solution added dropwise with vigorous stirring to USP ether (400 mL). The mixture was stirred overnight and the precipitate collected by vacuum filtration. The precipitate was dried in air to give 1.0 g (92%) of the polymer **11** as a fine, white powder, M_n = 127,500 g/mol; M_w = 323,400 g/mol; PDI = 2.54, T_g = 93°C. IR (KBr) 3314, 3082, 2975, 2918, 2849, 1748, 1661, 1530 cm^{-1}; ^{1}H-NMR (500 MHz, DMSO-d_6) δ 0.60–1.80 (br m, 8H), 1.37 (s, 9H), 1.80–2.40 (br s, 1H), 2.60–3.40 (br s, 2H), 3.62 (s, 3H), 3.75–4.30 (br m, 3H), 6.00–6.80 (br s, 1H), 6.80–7.70 (br s, 1H),

7.85–8.35 (br s, 1H); ^{13}C-NMR (125 MHz, DMSO-d_6) δ 22.9, 28.1, 28.8, 31.7, 38.7 (br), 40.6, 42.1 (very br), 51.5, 54.2 (br), 78.1, 155.2, 170.0, 172.7, 174.0 (br). Anal. Calcd for $(C_{17}H_{29}N_3O_6)_n$: C, 54.97; H, 7.87: N, 11.31. Found: C, 54.40; H, 7.90; N, 10.98.

2.5. *Post-polymerization modification*

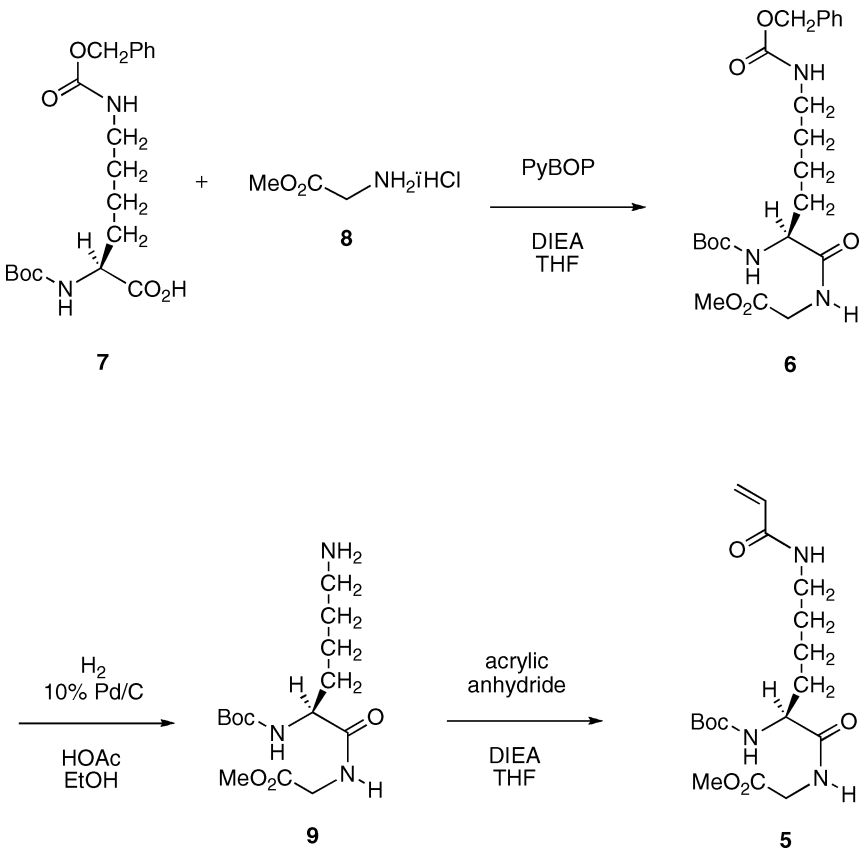
2.5.1. *Poly-[cyclo(N$^{\varepsilon}$-acrolyl-L-lysylglycyl)] (**3**)*

Poly-(N^{α}-Boc-N^{ε}-acrolyl-L-lysylglycine methyl ester) (**11**, 776 mg, 2.1 mmol) was dissolved in trifluoroacetic acid (10 mL) in a 100 mL pear-shaped flask. The flask was capped loosely and allowed to stand at rt overnight. The trifluoroacetic acid was then removed on a rotary evaporator and the residue was dissolved in and recovered from methanol twice using a rotary evaporator. The residue was then placed under high vacuum for 30 min to afford a white foam. To this foam was added DABCO^{TM} (356 mg, 21.0 mmol) and DMSO (20 mL) to give a clear, yellow-brown solution. The flask containing this solution was capped tightly and placed in an oil bath at 65°C overnight. The solution was allowed to cool to rt and added dropwise to methanol (300 mL) with vigorous stirring. The mixture was heated at reflux with stirring for 1 h, then cooled to rt. Most of the liquid phase was removed by careful decantation. Additional methanol (300 mL) was added, the mixture was heated at reflux with stirring for 1 h, then cooled to rt. The precipitate was then collected by vacuum filtration and dried under high vacuum overnight. The product polymer **3** was obtained as an off-white powder, $T_g = 157$°C. Yield 449 mg (90%). IR (KBr) 3280, 3092, 2936, 2873, 1683, 1558, 1458 cm^{-1}; ^{1}H-NMR (500 MHz, TFA-d/CD_3NO_2, 60°C) δ 1.40-1.60 (br s, 2H), 1.60–1.90 (br s, 4H), 1.90-2.20 (br s, 2H), 2.20–2.70 (br m, 1H), 3.10–3.50 (br s, 2H), 3.87 (s, trace, residual Gly-OCH_3), 4.15–4.75 (br m, 6H). Anal. Calcd for $(C_{11}H_{17}N_3O_3)_n nH_2O$: C, 51.31; H, 7.39; N, 16.33. Found: C, 51.53; H, 6.62; N, 15.16.

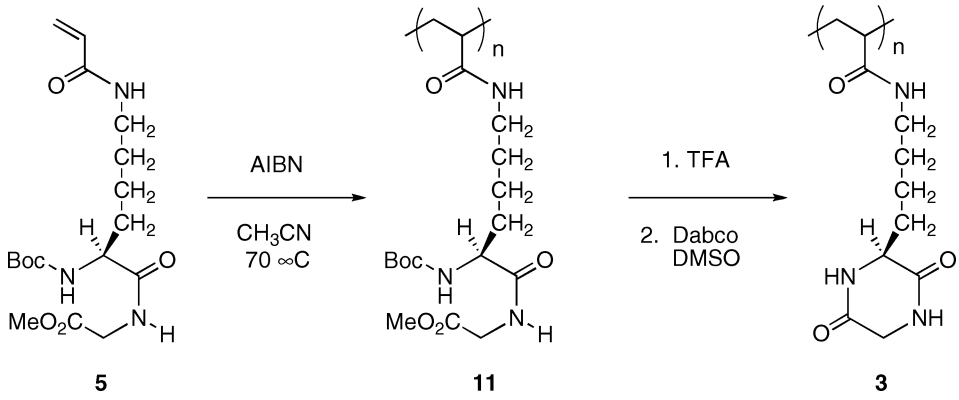
3. Results and discussion

3.1. *Synthesis of monomer*

The synthesis of **5** (Scheme 1) commenced with preparation of the known dipeptide, N^{α}-Boc-N^{ε}-Cbz-L-lysylglycine methyl ester (**6**) (12). This compound was synthesized in high yield by means of a benzotriazolyloxy-tris(pyrrolidino)phosphonium hexafluorophosphate (PyBOP®)-mediated coupling (14) of N^{α}-Boc-N^{ε}-Cbz-L-lysine (**7**) with glycine methyl ester hydrochloride (**8**), both of which are commercially available.



Sch. 1. Synthesis of N^{α}-Boc-N^{ε}-acrolyl-L-lysylglycine methyl ester (**5**).



Sch. 2. Synthesis of Poly-[c*yclo*(N^{ε}-acrolyl-L-lysylglycyl)] (**3**).

Treatment of **6** with hydrogen and 10% Pd/C in ethanol containing 1.1 equivalents of acetic acid cleaved the carbobenzyloxy protecting group selectively to give amine **9**. This compound was not isolated (15), but instead was treated with 2.5 equivalents of *N*, *N*-diisopropylethylamine (DIEA) and 1.5 equivalents of acrylic anhydride (**10**) (13) to provide **5** in 70% yield from **7** after an aqueous work up, chromatography, and recrystallization.

3.2. *Synthesis of poly-[cyclo(N^{ε}-acrolyl-l-lysylglycyl)] (3)*

All polymerizations were carried out in thick-walled Pyrex glass tubes sealed under vacuum. *N*-Hexyl acrylamide was synthesized as a model for monomer **5** and was polymerized in benzene at 60°C using 1% AIBN as the initiator. This led to a good yield of high polymer (Mn = 243,000, Mw = 1,200,000, PDI = 4.95) (16). Polymerization of recrystallized monomer **5** was attempted under similar conditions in several different solvents, including benzene, chlorobenzene, methanol, and THF. Material balances ranged from 50-85%, and SEC confirmed that starting material and/or oligomers were present in the products. Fortunately, argon-purged acetonitrile proved to be a good solvent for polymerization of monomer **5** (Scheme 2). At 70°C, a concentration of 1 mmol of **5** per mL of acetonitrile, and using 1 mol% AIBN as initiator produced polyacrylamide **11** in yields that ranged from 83-92% over five runs (Mn ~ 100,000, Mw ~ 300,000, PDI ~ 3).

The final task in the synthesis of the target polymer **3** was the cyclization of the side-chain protected dipeptide to give the 1,4-piperazine-2,5-dione moiety. A number of methods to affect this transformation were examined. Direct thermolysis of a sample of polymer **11** at 200°C *in vacuo* produced a melt that evolved gas and finally solidified to a hard white foam that could be crushed into a granular state. This material was insoluble in a wide range of solvents, including DMSO, pyridine, TFA, 1,1,1,3,3,3-hexafluoroisopropanol, 1,1,1-trifluoroethanol, tetramethyl guanidine, and water. DMSO and pyridine caused the material to swell, which is an indication of covalent cross-linking.

With the failure of neat thermolysis to provide a soluble (non-crosslinked) polymer, methods in dilute solutions were examined. Nitecki, Halpern, and Westley described a stepwise deprotection and cyclization process for *N*-Boc dipeptide esters that involved cleavage of Boc with formic acid and thermolysis of the resulting dipeptide ester salt in a 4:1 mixture of 2-butanol and toluene (17). This method was applied to polymer **11**, but again an insoluble product was obtained. In an effort to find milder cyclization conditions, the dipeptide ester trifluoroacetate salt derived from polymer **11** was dissolved in DMSO containing 10 equivalents of 1,4-diazabicyclo[2.2.2]octane (DABCO^{TM}). Cyclization proceeded slowly at room temperature, and at a more acceptable rate at 65°C, to produce a polymer that proved to be soluble in mixtures of nitromethane and trifluoroacetic acid. Purification of this polymer presented a challenge. Extraction with boiling methanol appeared to leach DABCO^{TM} and its TFA salt out of the polymer. Repetition of this process led to reasonably pure polymer **3** in yields of up to 90%.

3.3. *Characterization of polymers 11 and 3*

Proton NMR spectra of polymers **11** and **3** appear in Figure 1. The spectrum of polymer **11**, taken in DMSO-d_6, is consistent with the expected structure of this polymer. The spectrum of polymer **3**, taken in a mixture of trifluoroacetic acid-*d* and nitromethane-d_3, supports a cyclized structure for the pendant dipeptide, although the presence of a small signal at 3.88 ppm due to the carboxymethyl moiety indicates that approximately 5% of the dipeptide remains uncyclized in this sample. The weak lines in the spectrum of **3** are due in part to the low solubility of this polymer. Even dilute solutions of **3** are viscous, which contributes to NMR line broadening.

The elemental analysis for polymer **11** was satisfactory, but the elemental analysis for polymer **3** was not within acceptable limits. Although the polymer samples were desiccated under high vacuum at 70°C prior to analysis, this was apparently not sufficient to remove all of the water

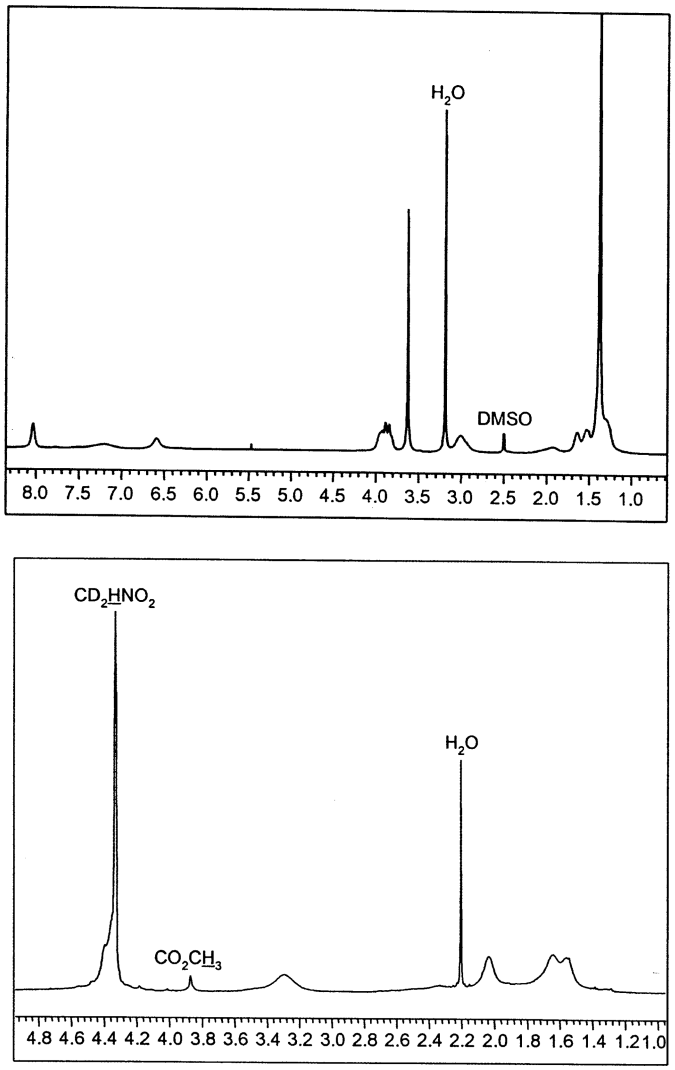


Fig. 1. ^{1}H-NMR spectra of polymer **11** taken in DMSO-d_6 (top) and of polymer **3** taken in a mixture of trifluoroacetic acid-*d* and nitromethane-*d*3 (bottom).

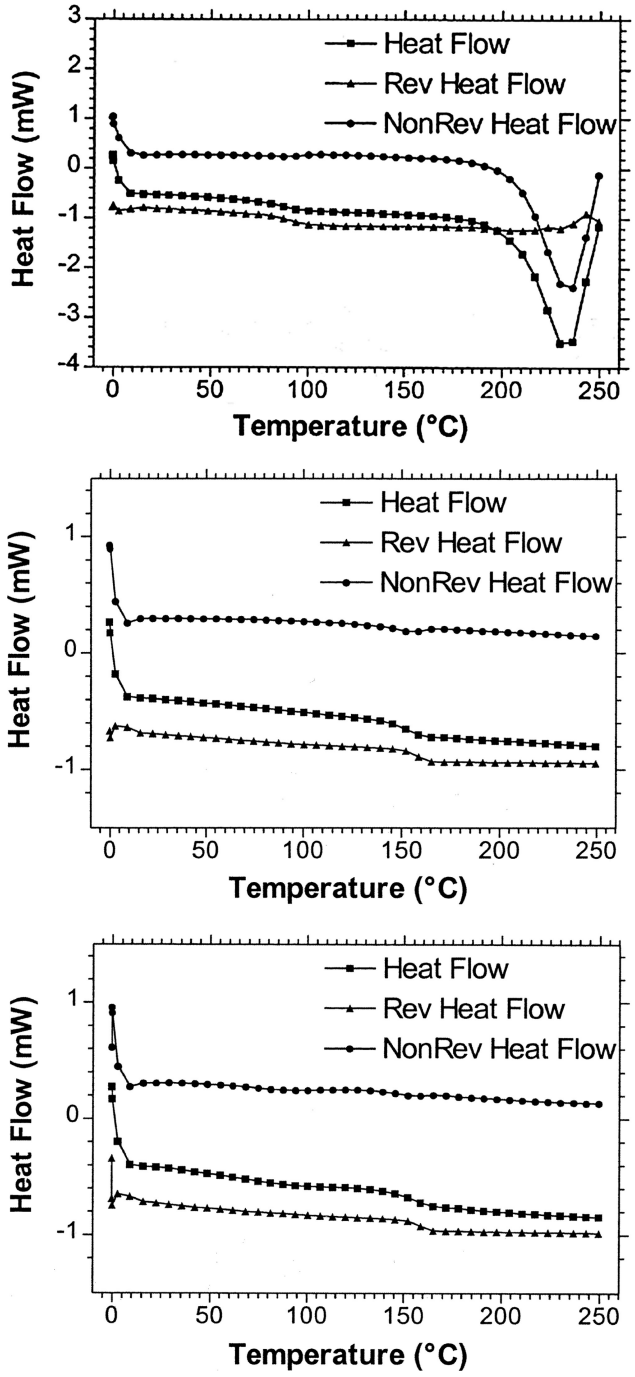


Fig. 2. Modulated differential scanning calorimetry: polymer **11,** first pass (top) and second pass (middle); polymer **3** (bottom).

from polymer **3**. Recalculation of the expected values for the elemental analysis for polymer **3** that assumes one water molecule per 1,4-piperazine-2,5-dione moiety gives much closer agreement with the experimental results, an indication that polymer **3** retains water. However, this polymer did not appear to be deliquescent.

Polymers **11** and **3** were subjected to modulated DSC analysis (Fig. 2). Using modulated DSC, it is possible to separate reversible heat flow from non-reversible heat flow. Reversible heat flow is associated with phase changes, while non-reversible heat flow is normally associated with chemical changes and/or decomposition. Polymer **11** exhibited a glass transition at 93°C and a large, non-reversible endotherm beginning at about 190°C on a first pass (Fig. 2, top). This polymer contained the thermally labile Boc group, and the loss of this group is presumably a contributor to this endotherm. Cyclization of the dipeptide with a loss of methanol would be expected to follow loss of the Boc group and would also contribute to the large endothermic peak in this DSC trace. A second DSC run on the same sample of polymer **11** exhibited one glass transition at 157°C and no other phase or chemical changes (Fig. 2, middle). The first pass DSC of polymer **3** (Fig. 2, bottom) was virtually identical to the second pass DSC run of polymer **11**, suggesting that polymer **11** was converted to polymer **3** on the first DSC pass. Mass loss observed during

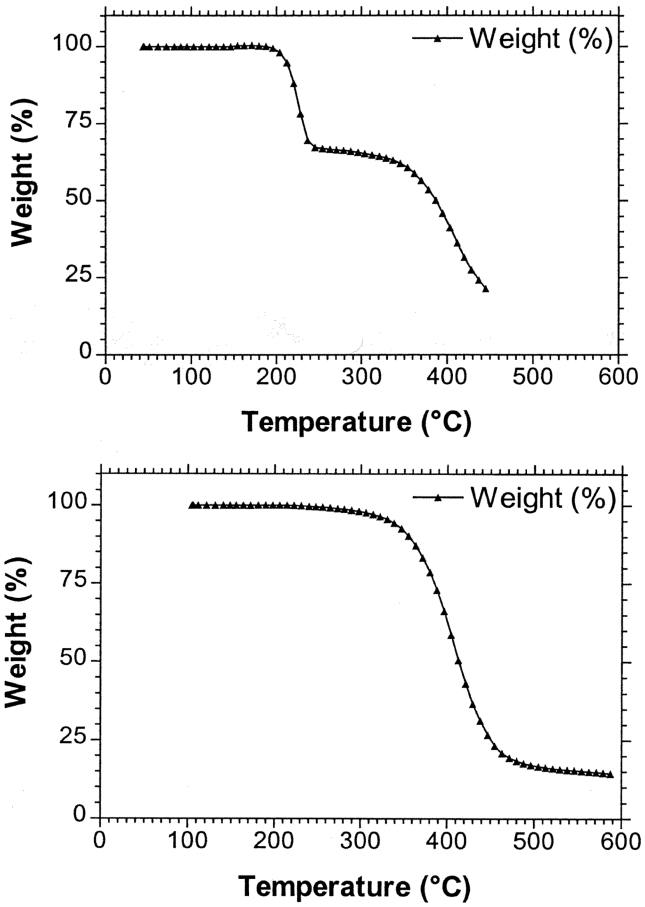


Fig. 3. Thermal gravimetric analysis: polymer **11** (top); polymer **3** (bottom).

TGA of polymer **11** was consistent with this interpretation of the DSC data (*vide infra*).

Polymers **11** and **3** were also subjected to TGA (Fig. 3). Polymer **11** lost approximately 35% of its initial mass from about 190–240°C and was thereafter thermally stable up to about 300°C (Fig. 3, top). The mass lost between 190–240°C corresponds to the loss expected for cleavage of the Boc (loss of methylpropene and CO_2) and loss of methanol following dipeptide cyclization. As might have been expected from these results, polymer **3** showed no loss of mass up to about 300°C (Fig. 3, bottom).

4. Conclusions

The synthesis of a high molecular weight polyacrylamide polymer **3** with a pendant piperazinedione moiety has been demonstrated. Synthesis of the acrylamide monomer **6** was an efficient process, as was polymerization of this monomer to give the uncyclized precursor polymer **11**. Cyclization of **11** was effected thermally to give **3** as a crosslinked foam, or at lower temperatures in solution to give an uncrosslinked polymer that was nevertheless insoluble in most organic solvents and sparingly soluble in strongly polar hydrogen donor solvents, such as trifluoroacetic acid. The cyclized polymer **3** exhibited a glass transition at 157°C and was thermally stable to about 300°C. Incorporation of polar groups and/or long hydrocarbon tails as in substituted polymers **2** may increase the solubility of the resulting polyacrylamide. Preparation of type **2** polymers is presently underway.

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