Synthesis and Polymerization of Chiral Acrylamidosulfonic Acids

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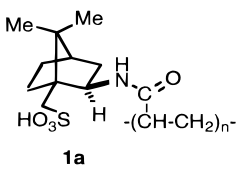
ABSTRACT: Reductive amination of (*1S*)-(+)-10-camphorsulfonic acid with $NaCNBH_3/NH_4OAc$ has afforded diastereomeric *exo*- and *endo*-aminosulfonic acids, that can be separated by crystallization from methanol. Treatment of these diastereomers with acryloyl chloride gave high yields of novel, chiral acrylamides that incorporate both a sulfonic acid substituent and a chiral auxiliary. The free radical (AIBN) polymerization of these acrylamides gave high yields (84−90%) of novel, water-soluble polyacrylamides (M_w = 5500−7800). ^{1}H NMR studies showed these to be essentially atactic. Their circular dichroism spectra were similar to their corresponding acrylamide monomers. This indicates that the sulfonic acid chiral auxiliary in the monomer precursors does not induce and/or maintain macroasymmetry in the resulting polyacrylamide chains. Hydrogels with equilibrium water contents as high as 99.96% could be obtained by copolymerizing {$(NH_4)_2S_2O_8$ initiator} these chiral acrylamides with equimolar acrylamide and varying ratios of *N,N′*-methylenebisacrylamide as cross-linker.

Introduction

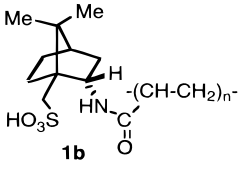
The synthesis of water-soluble polyelectrolytes has been an area of active recent interest.[1−3] In particular, the polymerization of vinyl monomers containing ionic pendant groups has led to both anionic and cationic polyelectrolytes, with uses in areas as diverse as water treatment and biomaterials. Such monomers have also been used to form hydrogels with cross-linked, interpenetrated networks. These have a number of potential applications in the pharmaceutical, food, and environmental industries.[4−6]

There has also been considerable recent activity in the incorporation of such polyelectrolytes and hydrogels into conducting polymers based on polypyrrole and polyaniline, to generate composites that combine favorable structural and processability features with good conductivity.[7−10] Optically active synthetic polymers, including gels and chiral conducting polymers are also of current interest because of their chiral recognition properties and their potential applications for asymmetric synthesis, as chiral stationary phases in HPLC and as chiral membranes for the separation of mixtures of enantiomers.[11−13]

We wish to report here the synthesis of novel chiral acrylamides that incorporate both a sulfonic acid group and a chiral auxiliary. The free radical polymerization of these monomers has provided new polyacrylamides **1a** and **1b** which are unusual in that they possess both optical activity and polyelectrolyte behavior, as well as the potential to act as chiral dopants in conducting polymers. The preparation of a hydrogel from the polyacrylamide **1b** is also reported and its chiroptical and mechanical properties described.



1a



1b

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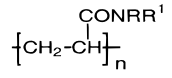
The only previously reported optically active polyacrylamides are a series of *N,N*-disubstituted acrylamides **2** (R, R^1 = aryl). These were obtained[14] via the asymmetric polymerization of the appropriate acrylamide monomers using chiral anionic initiators consisting of (−)-sparteine and organolithium reagents. The optical activity of the polymers **2** was believed to arise from preferential one-handed helicity of the polymer chain, induced during polymerization by the chiral initiator and maintained by the bulky *N,N*-diarylamino group preventing stereomutation of the helix. In the present study, the possibility that both these roles (i.e. preferential formation of a one-handed helix and its maintenance by steric constraints) could be performed by the one agent (the chiral auxiliary) is explored.



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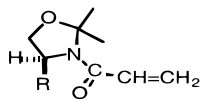

3 (R = Ph, Bu^t, Pr^i)

Our studies are also of relevance to the question of control of stereoregularity during the free radical polymerization of acyclic alkenes.[15−18] Until recently, little stereocontrol had been observed in the free radical polymerization of vinyl monomers. However, it has been recently reported[17] that the free radical (AIBN) polymerization of acrylamides **3**, containing chiral oxazolidine auxiliaries, produced polyacrylamides with high tacticity (up to 92% isotactic polymer). The tacticity of the novel polyacrylamides **1** was therefore also examined in the present study using ^{1}H NMR spectroscopy.

Experimental Section

Chemicals and Materials. (1*S*)-(+)-10-camphorsulfonic acid, sodium cyanoborohydride, ammonium acetate (99%), sodium hydroxide, ammonium persulfate, acryloyl chloride, acrylamide, *N,N,N′,N′*-tetramethylethylenediamine (TMEDA), *N,N′*-Methylenebisacrylamide and atactic poly(acrylic acid) were purchased from Aldrich Chemical Co. and used as supplied. 2,2′-Azobisisobutyronitrile (AIBN), from TCI Chemical Co., Japan, was recrystallized from ethanol and kept in a freezer prior to use. Dowex cation-exchange resin (50-X8) and

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Milli-Q deionized water were used for ion-exchange chromatography. Methanol was dried by distillation from magnesium turnings, and dimethylformamide (DMF) was dried by distillation from calcium hydride under reduced pressure. A Selby Anex type 453105 dialysis membrane was used for purification of polymers.

Spectroscopic Studies. UV−visible spectra were measured on a Shimadzu UV-1601 spectrophotometer. Solution and gel circular dichroism (CD) spectra were recorded using a Jobin Yvon Dichrograph 6. Optical rotations at 589 nm were measured in aqueous solution at room temperature using a JASCO DIP-370 digital polarimeter.

Solution ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra were recorded on a Varian Unity 400 MHz NMR spectrophotometer. Solid state ^{13}C NMR spectra were measured using a Bruker MSL 300 NMR spectrophotometer with cross polarization magic angle spinning (5 kHz). The hydrogel **6** (see synthesis below) was also grown in an NMR tube using D_2O as solvent. To remove unreacted reagents and catalyst, the NMR tube was filled with D_2O, left overnight and then decanted. This washing procedure was repeated for several days and the ^{1}H and ^{13}C NMR spectra recorded each day. Electrospray mass spectra were determined on a VG Quattro triple quadrupole spectrometer. The analytes (100 pmol μL^{-1}) were dissolved in water and the solvent stream was water/methanol (1/1). A skimmer voltage of 50 V was generally employed. Infrared spectra (as Nujol mulls on NaCl plates) were recorded on a Bomem MB 154 Fourier transform spectrophotometer.

Elemental analyses were carried out by the Australian National University and Queensland University Analytical Services.

Preparation of Acrylamidosulfonic Acid Monomers. (1*S*,2*R*,4*S*)- and (1*S*,2*S*,4*S*)-α-[2-Amino-7,7-dimethylbicyclo[2.2.1]-1-heptyl]methanesulfonic Acids, 4a and 4b. Method 1. A solution of (1*S*)-(+)-10-camphorsulfonic acid (23.3 g, 0.1 mol), sodium cyanoborohydride (4.4 g, 0.07 mol), and ammonium acetate (75 g, 0.97 mol) in dry methanol (300 mL) was refluxed for 3 days under a dinitrogen atmosphere. The methanol was then evaporated on a rotary evaporator. The colorless residue was dissolved in distilled water (100 mL) and chromatographed on a Dowex cation-exchange resin (50−X8) that had been conditioned with 2 mol dm^{-3} HCl, using water as eluent. The first two fractions were evaporated to give a mixture of the diastereoisomers **4a** and **4b** in a ratio of ca. 60:40, respectively. These were then dissolved in methanol for crystallization. The minor diastereoisomer crystallized out first, was filtered off and washed with methanol to afford pure **4b** (5.4 g). Further crystallization of the mother liquor gave more **4b** (3.8 g), while prolonged cooling afforded the major diastereoisomer **4a** (200 mg). The majority of **4a** remained in the mother liquor as a mixture with **4b**. The later fractions from the above column afforded more **4a** (180 mg) after evaporation of water. Repeated crystallization of the mixture of diastereoisomers from methanol afforded further pure **4a** (3.2 g). Total isolated yield of pure **4a** and **4b** was 54%.

4a: ^{1}H NMR (D_2O) δ 0.79 (s, 3H, Me), 0.88 (s, 3H, Me), 1.16 (m, 1H), 1.51 (m, 1H), 1.85−171 (m, 5H), 2.93 (d, 1H, H^{10}diast, J = 15 Hz), 3.14 (d, 1H, H^{10} diast, J = 15 Hz) 3.42 (t, 1H, J = 7.8 Hz); ^{13}C NMR (D_2O) δ 37.9, 44.9, 51.0, 57.5, 62.5, 66.5, 67.2, 67.9, 73.9, 75.5; ESMS (+ve) m/z 234 ([M + H]$^+$, 100%); (−ve) m/z 232 ([M − H]$^-$, 100%); $[\alpha]^{23}_D = -57°$ (0.5 g/100 mL, H_2O). Anal. Calcd for $C_{10}H_{19}NO_3S$: C, 51.5; H, 8.2; N, 6.0; S, 13.7. Found: C, 51.3; H, 7.9; N, 5.9; S, 13.2.

4b: ^{1}H NMR (D_2O) δ 0.77 (s, 3H, Me), 0.79 (s, 3H, Me), 1.02 (dd, 1H, J = 3.5, 13.8 Hz), 1.19 (m, 1H), 1.67 (m, 4H), 2.27 (m, 1H), 2.89 (d, 1H, J = 14.7 Hz), 3.02 (d, 1H, J = 14.7 Hz), 3.60 (dd, 1H, J = 2.9, 10.8 Hz); ^{13}C NMR (D_2O) δ 17.2, 18.5, 23.7, 26.7, 34.2, 42.8, 48.2, 51.2, 52.8, 55.3; ESMS (+ve) m/z 234 ([M + H]$^+$, 100%); (−ve) m/z 232 ([M − H]$^-$, 100%); $[\alpha]^{23}_D$ = +23° (0.5 g/100 mL, H_2O). Anal. Calcd for $C_{10}H_{19}NO_3S$: C, 51.5; H, 8.2; N, 6.0; S, 13.7 Found: C, 51.5; H, 8.1; N, 5.9; S, 13.5.

Method 2. Method 1 was repeated, but without the ion exchange chromatography step. The colorless material from the initial rotary evaporation was cooled overnight and collected on a sintered glass funnel using vacuum filtration. It was then dissolved in methanol for crystallization. The pure diastereoisomer **4b** was recovered in good yield (7.9 g) after filtration and washing with methanol. Further crystallization of the mother liquor afforded starting material (5 g) and subsequently the major diastereoisomer **4a** in low yield (800 mg). Addition of acetone and diethyl ether to the mother liquor and further crystallization gave a mixture of diastereoisomers as a white powder, that was recrystallized from methanol to give **4a** (2.7 g) and **4b** (1.2 g) as pure white solids.

(1*S*,2*R*,4*S*)- and (1*S*,2*S*,4*S*)-α-[2-Acrylamido-7,7-dimethylbicyclo[2,2,1]-1-heptyl]methanesulfonic Acids, 5a and 5b. The diastereomerically pure aminosulfonic acid **4b** (3.5 g, 0.015 mol) was dissolved in 20% aqueous NaOH (88 mL). Acryloyl chloride (25 mL, 0.28 mol) was added slowly (0.5 mL at a time), while the reaction mixture was being swirled vigorously in an ice bath (the reaction being exothermic). After the addition was complete, the reaction mixture was left stirring for 1 h. The reaction mixture was then acidified with dilute aqueous HCl and extracted with chloroform (3 × 50 mL). The solvent was evaporated and the residue dissolved in water (50 mL) and extracted with diethyl ether (3 × 50 mL). Evaporation of the water layer afforded **5b** as a white, crystalline solid (3.9 g, 90%). This was stored under vacuum in the presence of phosphorus pentoxide prior to use.^{1}H NMR (D_2O): δ 0.81 (s, 3H, Me), 0.84, (s, 3H, Me), 0.89 (dd, 1H, J = 4.5 Hz, 13.5 Hz), 1.16 (m, 1H), 1.59 (t, 1H), 1.87−1.63 (m, 3H) 2.30 (m, 1H), 2.88 (d, 1H, H^{10} dist, J = 15 Hz), 2.95 (d, 1H, H^{10} dist, J = 15 Hz), 4.06 (dd, 1H, J = 1.5, 5.4 Hz), 5.59 (dd, 1H, J = ca. 1, 10.2 Hz), 6.02 (dd, 1H, J = ca. 1, 17 Hz), 6.14 (dd, 1H, J = 10.2, 17 Hz). ^{13}C NMR (D_2O): δ 17.5 (Me), 18.7 (Me), 23.9, 27.1, 36.7, 43.4, 48.7, 49.7, 53.0, 54.7, 126.3 (vinyl), 130.0 (vinyl), 168.2 (CO). ESMS: (+ve) m/z 288 ([M + H]$^+$, 100%); (-ve) m/z 286 ([M − H]$^-$, 100%). $[\alpha]^{23}_D = +3.4°$ (0.5 g/100 mL, H_2O). Anal. Calcd for $C_{13}H_{21}NO_4S$: C, 54.3; H, 7.4; N, 4.9; S, 11.2. Found: C, 53.7; H, 7.3; N, 4.7; S, 11.0.

A similar procedure was employed to prepare the acrylamide **5a,** starting from **4a.** ^{1}H NMR (D_2O): δ 0.74 (s, 3H, Me), 0.82 (s, 3H, Me), 1.05, (m, 1H), 1.22 (m, 1H), 1.89−1.50 (m, 5H), 2.74 (d, 1H, H^{10} diast, J = 15 Hz), 3.23 (d, 1H, H^{10} dist, J = 15 Hz), 3.88, (dd, 1H, J = 4.5 Hz, 8.7 Hz), 5.55 (dd, 1H, vinyl CH_2, J = 1.2, 10.2 Hz), 5.99 (dd, 1H, vinyl CH_2, J = 1.2, 17 Hz), 6.20 (dd, 1H, vinyl CH_2, J = 10.2, 17 Hz). ^{13}C NMR (D_2O): δ 39 (Me), 44.5 (Me), 51, 55, 58, 62, 67, 67.5, 68.5, 74.5, 145 (vinyl), 149 (vinyl), 186 (CO). ESMS: (+ve) m/z 288 ([M + H]$^+$, 100%); (-ve) m/z 286 ([M − H]$^-$, 100%). $[\alpha]^{23}_D = -66.6°$-(0.5 g/100 mL, H_2O).

Synthesis of Chiral Polyacrylamides 1a and 1b. Method 1. A solution of the monomer **5a** or **5b** (150 mg) in dry DMF (2 mL) was placed in a thick-walled glass tube that was purged with dinitrogen for 20 min. AIBN (5 mol %) was added and the tube sealed and then heated at 70−80 °C for 3 days. The solution was then cooled and diluted with acetone and the precipitate collected on a sintered glass funnel under vacuum filtration. It was washed several times with acetone and then dried. The polymers **1a** (126 mg, 84% yield) and **1b** (135 mg, 90% yield) were obtained as colorless, hygroscopic solids that were best kept in a desiccator.

1a: CPMAS ^{13}C NMR (solid state, 75.5 MHz) δ 176.2 (CO), 56.2, 49.0, 44.5, 40.8, 35.2, 27.6, 20.5 (Me). $[\alpha]^{21}_D = -49°$ (0.5 g/100 mL, H_2O).

1b: CPMAS ^{13} C NMR (solid state, 75.5 MHz) δ 176.3 (CO), ca. 56, 49.2, 44.2, 28.2, 18.8 (Me). ^{13}C NMR (D_2O, 125 MHz) δ 176.5(CO), 55.7, 53.0, 49.1, 43.5, 36.9, 27.4, 24.4, 19.6(Me), 18.3(Me). $[\alpha]^{21}_D = +15°$ (0.5 g/100 mL, H_2O). Anal. Calcd for $C_{13}H_{21}NO_4S$: C, 54.3; H, 7.4; N, 4.9; S, 11.2. Found: C, 53.6; H, 6.9; N, 4.5; S, 9.7.

Method 2. A solution of the monomer **5a** or **5b** (150 mg) and ammonium persulfate (15 mg) in water (2.5 mL) was placed in a thick-walled glass tube that was purged with dinitrogen for 20 min. TMEDA (4 mL from a solution of 160 mL of TMEDA in water (100 mL)) was added and the tube sealed and heated at 45−50 °C for 2 days. The water was then evaporated and the crude polymer (186 mg of **1a** and 210 mg

of **1b**) purified by dissolution in water (10 mL) and dialyzing for 72 h (Selby Anax dialysis membrane, type 453105). Evaporation of the sealed membrane contents gave pure **1a** (98 mg, 65% yield) or **1b** (120 mg, 80% yield).

The polymers **1a** and **1b** obtained from method 2 had essentially identical ^{13}C NMR spectra to those obtained above via method 1. **1b**: $[\alpha]_d^{21} = +10°$ (0.2 g/100 mL, H_2O). $\Delta\epsilon =$ 0.01 M^{-1} cm^{-1} at 290 nm in water. An identical CD spectrum was obtained at pH 1 (addition of HCl) and pH 14 (addition of NaOH).

Hydrolysis of Polyacrylamide 1b to Poly(acrylic acid). Hydrolysis of the polyacrylamide **1b** made via method 2, to release the aminosulfonic acid chiral auxiliary and poly(acrylic acid) (PAA), was achieved using the following procedure: polyacrylamide **1b** (400 mg, 1.4 mmol) was dissolved in 15 mL of 2 mol dm^{-3} HCl and the solution refluxed for 48 h. During this period, the poly (acrylic acid) product separated from the aqueous solution as an oil. After being cooled to room temperature, the aqueous fraction was removed by pipet and rotary evaporated to dryness to give recovered aminosulfonic acid **4b** (confirmed by ^1H NMR). The oily fraction was dried under vacuum and its ^1H NMR spectrum recorded in D_2O, confirming it to be the expected PAA, together with **4b** impurity. Washing the crude PAA product twice with a little D_2O removed some **4b** (at this low pH the PAA was insoluble). Complete removal of the **4b** inpurity was achieved by dialysis with a molecular weight 2000 cutoff membrane for 20 h. The remaining PAA residue was then dissolved in D_2O and its tacticity determined by ^1H NMR spectroscopy.

Attempted Preparation of a Hydrogel from 5a. (1*S*,-2*R*,4*S*)-α-[2-Acrylamido-7,7-dimethylbicyclo[2.2.1]-1-heptyl]-methanesulfonic acid, **5a** (100 mg, 0.35 mmol), together with *N*,*N*′-methylenebisacrylamide cross-linker (1.2 mg 0.007 mmol) were dissolved in 2 mL of water. The solution was purged with dinitrogen for 20 min and then ammonium persulfate initiator (2 mg, 0.008 mmol) and *N*,*N*,*N*′,*N*′-tetramethylenediamine accelerator (TMEDA, ca. 3 μL) were added. The solution was quickly transferred to and sealed in a dinitrogen-filled tube for gelation. However, prolonged standing (even with warming) did not give a gel.

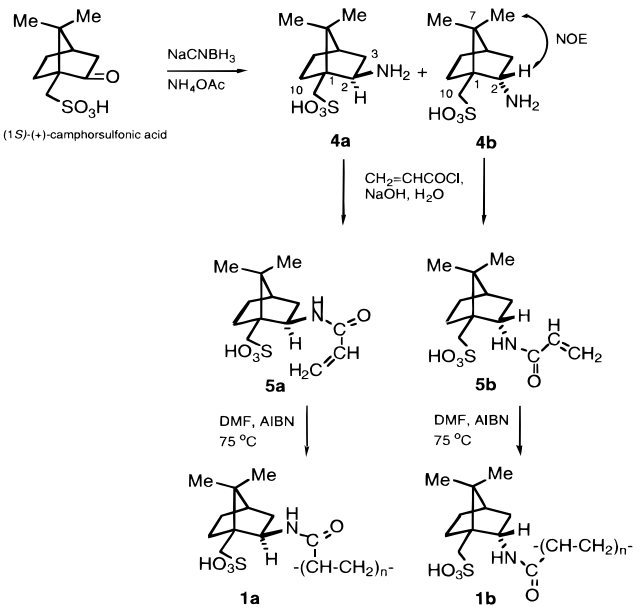
Preparation of Copolymer Chiral Hydrogel 6. (1*S*,-2*R*,4*S*)-α-[2-Acrylamido-7,7-dimethylbicyclo[2.2.1]-1-heptyl]-methanesulfonic acid **5b** (100 mg, 0.35 mmol) and acrylamide (comonomer, 25 mg, 0.35 mmol), together with *N*,*N*′-methylene bisacrylamide cross-linker (1.2 mg, 0.007 mmol) were dissolved in 2 mL of water. The solution was purged with dinitrogen for 20 min, and then ammonium persulfate initiator (2 mg, 0.008 mmol) and *N*,*N*,*N*′,*N*′-tetramethylenediamine accelerator (TMEDA ca. 3 μL) were added. The solution was quickly transferred to and sealed in a dinitrogen-filled tube, where gelation occurred within a few minutes at room temperature (ranging from 15 to 20 °C). After a few hours, the gel **6** was removed carefully and immersed in a beaker containing 200 mL of water for several days to remove unreacted monomer, initiator and catalyst. During this process the gel absorbed a very large amount of water (EWC = 99.96%).

A sample of the hydrogel was evaporated in an oven at 60 °C for 2 days. It was then further dried under vacuum in the presence of phosphorus pentoxide at 40 °C for 3 days. Anal. Calcd (assuming same monomer ratio in gel as in feed solution): S, 8.7. Found: S, 6.2.

Related gels were also prepared by using different proportions of the cross-linker (e.g. 8, 10, 16 and 40 mg of cross-linker with a constant 140 mg of chiral amide) in order to enhance the gel's mechanical properties.

Molecular Weight Measurements of Polymers. The molecular weights of the polymers **1a** and **1b** from method 1 and polymer **1b** from method 2 were determined by gel permeation chromatography (GPC). The polymer solutions in 0.25 mol dm^{-3} $NaNO_3$ were buffered with 0.01 mol dm^{-3} NaH_2PO_4 and eluted at pH 7 on a TSK gel G2500PWXL column at 20 °C. The detector was a differential refractive index detector using poly(ethylene glycol) (PEG) standards in the range 21000−1500 g mol^{-1}.

Scheme 1



Equilibrium Water Content (EWC) of Hydrogel 6. A portion of the fully swollen gel **6** was carefully wiped with blotting paper and then weighed and transferred to an oven and maintained for 2 days at 60 °C. The dried gel was quickly transferred to a desiccator containing silica gel for 30 min to cool and was weighed in a sealed vessel. The equilibrium water content (EWC) was calculated using eq 1, where W_h is the mass of hydrated gel and W_d is the mass of dehydrated gel.

$$\mathrm{EWC} = \frac{W_h - W_d}{W_h} \times 100 \qquad (1)$$

Results and Discussion

Preparation and Characterization of Chiral Monomers. Aminosulfonic acids 4a and 4b. Reductive amination[19] of (1*S*)-(+)-10-camphorsulfonic acid with sodium cyanoborohydride and ammonium acetate in methanol solution at reflux for 3 days gave a 60:40 mixture of the novel *exo*-aminosulfonic acid **4a** and the *endo*-aminosulfonic acid **4b**, respectively (Scheme 1). The two diastereoisomers could be conveniently separated by ion-exchange chromatography and selective crystallization from MeOH. Diastereomer **4b** was less soluble than **4a** in methanol and could be readily isolated diastereomerically pure in higher yield than **4a**, despite being the minor diastereomer in the crude reaction product (as established by ^1H NMR).

The stereochemical outcome and diastereoselectivity of this reductive alkylation was that expected from studies on the reduction of (1*S*)-(+)-10-camphorsulfonic acid itself.[20] The stereochemistry of the minor diastereoisomer **4b** was unequivocally determined by NOESY ^1H NMR experiments that showed a strong cross-peak between one C-7 methyl group and H-2; while a similar study on **4a** showed a cross-peak between H-2 and the H-10 proton.

The infrared spectra of **4a** and **4b** confirmed the formation of amine products {υ(NH stretch) (Nujol) at ca. 3300 cm^{-1} and υ(NH bend) at ca. 1618 cm^{-1}}. A strong $\upsilon(SO_3)$ band at 1157 cm^{-1} also supported the presence of the sulfonic acid substituent, as did the $[M - H]^-$ ion observed as the base peak at *m*/*z* 232 in the negative ion ESMS of the two diastereomers. Interestingly, their positive ion ESMS showed not only the

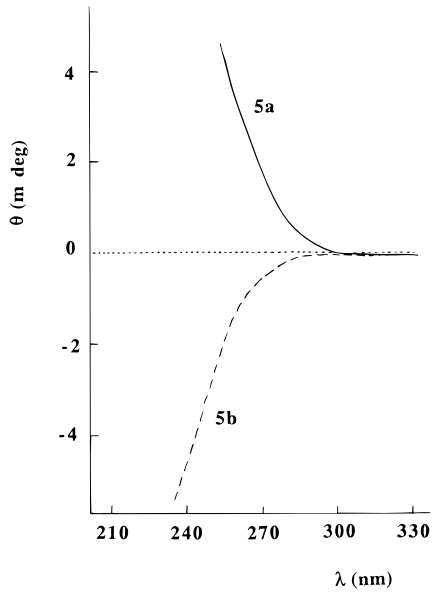


Figure 1. Circular dichroism spectra of acrylamides **5a** (—) and **5b** (- - -) in water (7.0×10^{-3} and 4.9×10^{-3} mol dm^{-3}, respectively).

expected $[M + H]^+$ ion as the base peak (*m*/*z* 234) but also a moderately intense ion at *m*/*z* 467, presumably arising from the presence of a self-protonated dimeric cluster.

Acrylamide Monomers 5a and 5b. Treatment of a basic solution of **4a** or **4b** with an excess of acryloyl chloride at 0 °C, followed by acidification of the reaction mixture, gave the acrylamides **5a** and **5b** in 90% yields (Scheme 1). These novel acrylamides incorporate both a sulfonic acid group and a chiral auxiliary. Their ^{1}H and ^{13}C NMR spectra and elemental analyses (see Experimental Section) were fully consistent with the proposed structures. Conversion to the amides was also confirmed by the appearance in the infrared spectra of a ν(NH) stretch at 3300−3400 cm^{-1} and ν(NH) and ν(CO) bands at 1544 and 1652 cm^{-1}, respectively. The negative ion ESMS of diastereomers **5a** and **5b** again exhibited $[M - H]^-$ ions (*m*/*z* 286) as the base peaks, consistent with the presence of the sulfonic acid substituent.

Chiroptical Properties of Sulfonic Acid Monomers 4a, 4b, 5a, and 5b. The UV−visible spectra of the novel acrylamide monomers **5a** and **5b** each showed an expected weak shoulder at 230 nm for the amide (CONH) chromophore. Intense absorption below 240 nm prevented meaningful CD data being obtained at lower wavelengths, even for highly diluted aqueous solutions. However, the two diasteromers **5a** and **5b** exhibited positive and negative CD ellipticities, respectively, at wavelengths below 280 nm, consistent with their amide chromophore (Figure 1). Their $[\alpha]_D$ values of −66 and +3°also indicated that the sign of the optical rotation in the two diastereomers is dominated by the opposite configurations of the C-2 atoms (to which the amide substituent is attached). The absence of mirror symmetry in the CD spectra and optical rotations of **5a** and **5b** arises from the presence in each case of fixed configurations at the C-1 and C-4 atoms of the chiral auxiliary.

The aminosulfonic acids **4a** and **4b** exhibited no absorption bands in their aqueous UV−visible spectra between 200 and 600 nm. No circular dichroism bands were therefore observed in this region. However, their $[\alpha]_D$ values (see Experimental Section) were consistent with their diastereomeric formulations.

Table 1. Molecular Weights of Chiral Polyacrylamides

polymer	method	M_n	M_w	peak M_p	γ
1a	1	3450	5470	7010	1.28
1b	1	5150	7840	9520	1.52
1b	2	45900	52000	53900	1.13

Chiral Polyacrylamides. Synthesis. Free radical polymerization of **5a** or **5b** with AIBN initiator (5 mol %) in DMF solvent at 75 °C for 70 h gave high yields (84−90%) of the polymer **1a** or **1b**, respectively (Scheme 1). The polymerization reactions could be conveniently monitored by ^{1}H NMR (D_2O) analysis of reaction aliquots, by observing the disappearance of the olefinic protons of the monomer precursors near 6 ppm. After polymerization was complete, the DMF solution was cooled and the polymer product precipitated by the addition of acetone and collected by vacuum filtration.

Alternatively, the polymer **1a** or **1b** could be prepared in somewhat lower yield (65−80%) by heating an aqueous solution of **5a** or **5b** in the presence of ammonium persulfate as initiator and TMEDA as accelerator at 45−50 °C for 2 days. The polymers **1a** and **1b** were further purified from smaller molecular weight oligomers by dialysis. These purified polymers had spectral properties very similar to those of the respective polymers prepared above using AIBN as initiator.

Gel permeation chromatography studies showed that for the polyacrylamides obtained via method 1 (AIBN initiator), polymer **1b** had a somewhat higher molecular weight (M_n ca. 5200) than the diastereomeric **1a** (M_n ca. 3500) (Table 1). The polydispersivity (1.52) was also higher for diastereomer **1b**. These molecular weights were lower than those obtained for polyacrylamides prepared under similar conditions by Porter *et al.*[17] from related oxazolidine acrylamides (M_n ca. 30 000). However, they are similar to those (M_n = 3200−4100) reported by Okamoto *et al.*[14] for chiral poly(*N*,*N*-disubstituted acrylamides) **2** prepared by an alternative route using a chiral anionic initiator {(−)-sparteine/organolithium} for polymerization. Significantly, a much higher molecular weight (M_n ca. 50 000) was determined for polymer **1b** (obtained via method 2) using persulfate as initiator (Table 1). The latter polymerization was significantly faster than that using AIBN as initiator (see Experimental Section). Presumably, a similar enhancement does not occur for the termination step, resulting in the higher molecular weight product observed.

The novel polyacrylamides **1a** and **1b** were readily soluble in water and were characterized by solution (D_2O) and solid-state ^{1}H and ^{13}C NMR spectroscopy. The solution ^{1}H NMR spectrum of each polymer confirmed that the olefinic proton resonances for the respective acrylamide monomers (e.g. at 6.02−5.47 ppm for **5b**) were absent. Olefinic carbon resonances were also absent in the ^{13}C NMR spectra of the polymers (Figure 2). Furthermore, there was a characteristic downfield shift of the amide carbonyl resonance upon converting the monomer to the polymer {e.g., for **5bT1b**, 168.2 ppm (unsaturated CONHR) shifts to 176.5 ppm (saturated CONHR)}.

The new polyacrylamides were also soluble in DMF but insoluble in acetone, chloroform, and diethyl ether.

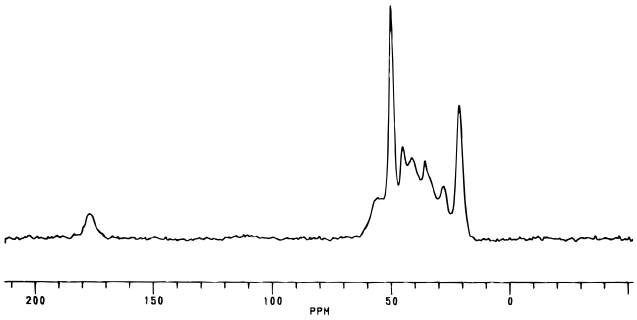
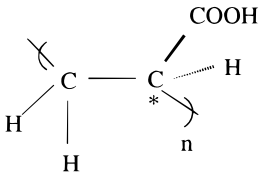


Figure 2. CPMAS ^{13}C NMR spectrum of polyacrylamide **1b** in D_2O.

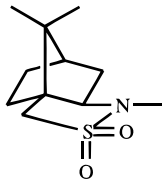
Tacticity of the Polymers. The broadness of the solution- and solid-state ^1H and ^{13}C NMR spectra of the polyacrylamides (e.g., Figure 2—CPMAS ^{13}C NMR spectrum of **1a**) precluded the direct estimation of their tacticity. The polymers **1b** obtained via methods 1 and 2 were therefore converted via mild acid hydrolysis (2 mol dm^{-3} HCl) to poly(acrylic acid) (PAA), to determine its tacticity by ^1H NMR spectroscopy using the method described by Matsuzaki *et al.*[21] and Monjol *et al.*[22] This approach has been applied successfully by Porter *et al.*[17] to establish the tacticity of polyacrylamides prepared via the free radical (AIBN) polymerization of the related chiral polyacrylamides **3**. Tests revealed that only partial hydrolysis of **1b** to PAA and **4b** occurred after refluxing for 3 h in 2 mol dm^{-3} HCl. Hydrolysis was therefore carried out at reflux for a further 45 h, at which stage ^1H NMR spectroscopy showed complete hydrolysis.

After purification of the PAA product (see Experimental Section), assignment of the poly(acrylic acid) resonances was made on the basis of earlier stereochemical studies[17,22,23] on PAA and by comparison with the ^1H NMR spectrum (D_2O, pH 1) of a sample of commercially available atactic poly(acrylic acid). The two diastereotopic methylene protons that are *m* (isotactic) diad peaks were observed at 1.77 and 1.48 ppm, while the diastereotopic methylene protons that are in an *t* (syndiotacic) triad resonated at 1.60 ppm. Comparison with the ^1H NMR spectrum of atactic PAA clearly showed that the PAA products from the hydrolyses of polymers **1b** were essentially atactic.



PAA

Examples of stereocontrol in the free radical polymerization of vinyl monomers are rare. Apart from the recent report of up to 90% isotacticity by Porter *et al.*[17] for polymerizations carried out under similar conditions using a related oxazolidine chiral auxiliary, there are only a few reports[24,25] in which free radical vinyl polymerization has led to predominantly isotactic or syndiotactic polymers. The lack of steroselectivity observed here with the aminosulfonic acid chiral auxiliary mirrors the poor stereoselectivity recently reported for the related Oppolzer's sultan **7**.[18] It may similarly arise from a mismatch between auxiliary and 1,3-control elements.



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Chiroptical Properties of the Chiral Polyacrylamides. Aqueous solutions of the new polyacrylamides **1a** and **1b** showed no strong CD maxima in the wavelength range 500−220 nm, as expected from the absence of significant absorption peaks in this region. Nevertheless, the diastereomeric polymers revealed positive and negative CD ellipticities, respectively, at wavelengths below 270 nm, consistent with optical activity associated with their amide chromophore. (Unfortunately CD spectra could not be recorded at lower wavelengths than 220 nm, even for dilute solutions, due to intense absorption). Significantly, the intensity of the CD signals for the polymers below 270 nm were similar to those measured for their respective acrylamide monomer precursors. The absence of enhanced CD signals for the polymers therefore indicates that they have not selectivity adopted stable one-sense helical conformations. This conclusion is also supported by the similar magnitudes of the $[\alpha]_D$ values for the monomer acrylamides **5** and their resultant polyacrylamides **1.**

In contrast, Okamoto *et al.*[14] have reported that the polymerization of *N*,*N*-disubstituted acrylamides (**2**; R, R^1 = aryl) using chiral anionic initiators gave polyacrylamides whose intense circular dichroism spectra (e.g. $\Delta\epsilon_{l-r} = -2.5$ mol^{-1} dm^3 cm^{-1} at 245 nm for R = R^1 = phenyl) suggested that the polymer chains adopted one-handed helicity. These $\Delta\epsilon_{l-r}$ values were ca. 50 times larger than the CD intensities observed for our polymers **1a** and **1b**.

Interestingly, concentrated aqueous solutions (>2.8 $\times 10^{-2}$ mol dm^{-3}) of polymers **1a** and **1b** exhibited weak CD bands of opposite sign at 290 nm ($\Delta\epsilon_{l-r}$ ca. − 0.01 and + 0.01 mol^{-1} dm^3 cm^{-1}, respectively; Figure 3). The origin of this weak band, which is not observed for dilute solutions, is uncertain.

Chiral Hydrogels. An attempt to prepare an hydrogel from the acrylamide **5** using $(NH_4)_2S_2O_8$ as initiator, *N*,*N*′-methylenebisacrylamide as cross-linker, and TMEDA as accelerator was unsuccessful, even after prolonged standing and warming. However, using a 1/1 mixture of monomer **5a** and acrylamide and the same initiator/cross-linker/and accelerator ratios as above, a gel was obtained within a few minutes at room temperature (Scheme 2). Unreacted reagents were removed from the gel by immersing the gel in a large volume of water for several days (the water being changed daily). The gel was observed to swell markedly during this process, due to the absorption of a large volume of water. The equilibrium water content (EWC) of the hydrogel was estimated to be 99.96%.

The progress of polymer gel formation could be monitored by ^1H NMR spectroscopy for samples prepared in an NMR tube. Consumption of each of the monomers was confirmed by the near disappearance within an hour of the vinyl proton signals at 5.5−6.2 ppm. Further confirmation of polymer formation was the observation of amide carbonyl resonances at 176−178 ppm in the ^{13}C NMR spectrum of the hydrogel **6**,

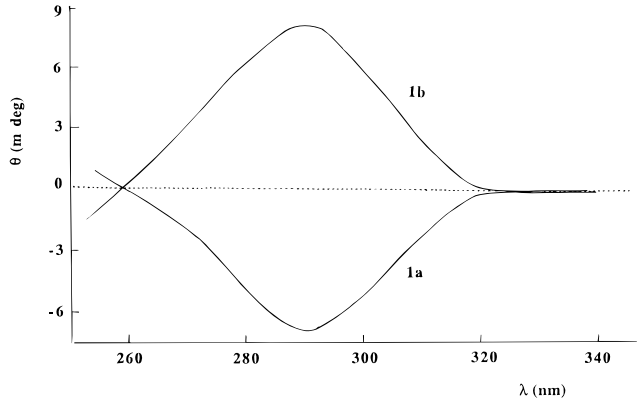
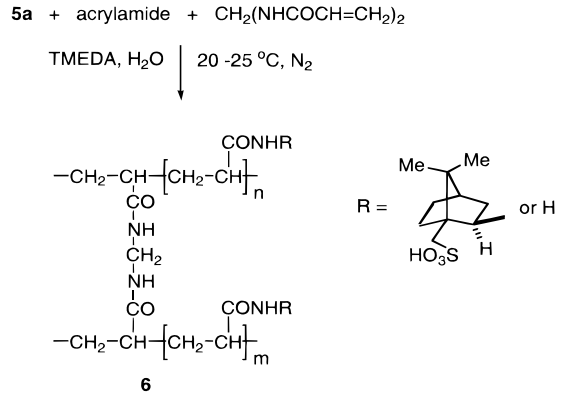


Figure 3. Circular dichroism spectra of polyacrylamides **1a** (0.03 mol dm^{-3}) and **1b** (0.04 mol dm^{-3}) in water.

Scheme 2



which are considerably downfield from the amide carbonyl signals for the monomer substrates.

The presence of a substantial fraction of chiral acrylamide **5a** repeat units in the hydrogel **6** was confirmed by the sulfur content of 6.2% (see Experimental Section). This value is somewhat lower than that estimated from the monomer feed solution (8.7%), indicating that the polymerization of this more bulky monomer is slower than that of acrylamide itself.

A sample of the copolymer hydrogel **6** was also prepared in a 1 cm cell (volume = 3 mL) using 140 mg of monomer **5b**, an equimolar amount of acrylamide, and the standard molar ratios of $(NH_4)_2S_2O_8$ initiator, cross-linker, and accelerator. The gel rapidly filled the cell. Its CD spectrum showed a positive band at 290 nm (Figure 4), which was very similar in position and intensity ($\Delta\epsilon_{l-r} = 0.02$ mol^{-1} dm^3 cm^{-1}) to that observed for the analogous un-cross-linked polyacrylamide **1b**. The absence of intense CD bands for this hydrogel therefore argues against the presence of a preferred one-handed helical conformation for the polymer chain.

There has been considerable recent interest[26] in the swelling properties of hydrogels, due to emerging applications in areas such as the pharmaceutical and environmental industries.[4−6] Hydrogel **6** exhibited exceptional swelling characteristics in water, with a measured equilibrium water content (EWC) of 99.96%. However, because of its high water content, the mechanical strength of hydrogel **6** was not very high. Preliminary experiments using higher cross-linker/monomer ratios have produced gels with considerably reduced water uptake behavior and qualitatively enhanced mechanical strength.

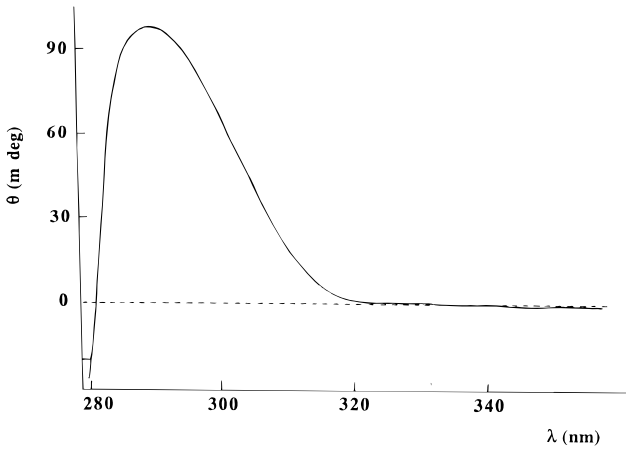
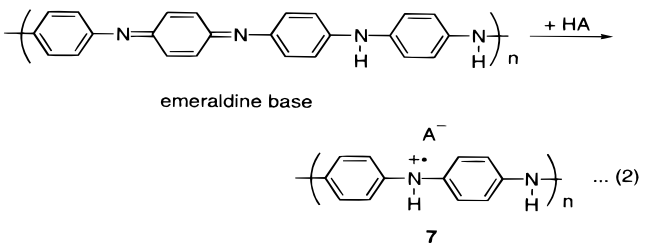


Figure 4. Circular dichroism spectrum of hydrogel **6**.

Novel chiral acrylamides incorporating both a sulfonic acid substituent and a chiral auxiliary can be readily prepared via two high-yield steps from (1*S*)-(+)-10-camphorsulfonic acid. Free radical (AIBN) polymerization of these acrylamides provides high yields (84−90%) of novel, water-soluble polyacrylamides. The presence of the chiral auxiliary in the monomer precursors does not lead to significant isotacticity in the resultant polyacrylamides. Circular dichroism studies also indicate that the chiral auxiliary does not induce and/or maintain macroasymmetry in the polyacrylamide chains. Copolymerization of the chiral acrylamides with acrylamide and *N*,*N*′-methylenebisacrylamide as cross-linker provides novel chiral hydrogels with very high EWC (99.96%).

Studies are now underway in our laboratories investigating the applications of these new chiral polyacrylamides and associated hydrogels. For example, preliminary studies of the electropolymerization of pyrrole in the presence of aqueous **5a** or **1a** confirmed the formation of electroactive polypyrrole salts incorporating the conjugate bases of these acrylamidosulfonic acid as monomeric and polymeric dopant anions.[27] We have also recently reported[28] that the emeraldine base form of polyaniline can be doped with **5a** (HA) in DMF solution to generate optically active polyaniline salts of the type **7** (eq 2). Studies have also begun exploring the use of the chiral hydrogel **6** for the separation of enantiomeric anions.



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