New Polymeric Acids Containing Potentially Hydrolyzable Bonds

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ABSTRACT: A new family of polymeric acids containing, besides carboxylic groups, biodegradable functions in their main chain have been prepared by Michael-type polyaddition of bis(thiols) to 2,2-bis(acrylamido)-acetic acid. The ability of the same polymers to enter into coupling reactions with model compounds, as well as the possibility of using them as macromonomers, has been verified.

Introduction

Considerable interest is being focused on polymeric acids containing chemical bonds cleavable in aqueous media, especially in relation with their potential usefulness in the pharmaceutical field as promoieties for preparing polymeric and oligomeric prodrugs.[1-13] On this subject, we thought it interesting to relate here the synthesis and properties of a new family of carboxylated polymers containing hydrolyzable bonds in their main chain.

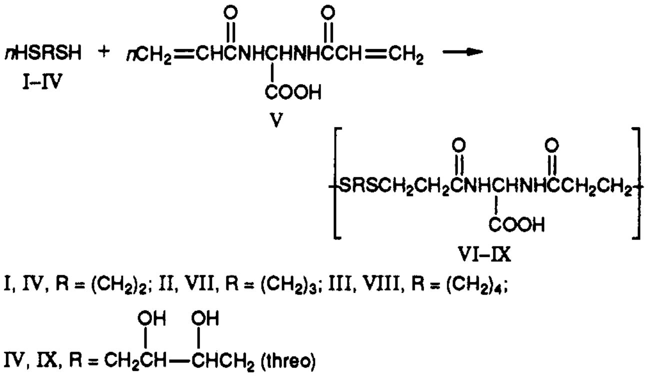
The polymeric acids described in this paper have been prepared by Michael-type polyaddition of bis(thiols) to 2,2-bis(acrylamido)acetic acid. It may be observed that a related polymerization technique was used in the past to synthesize polymeric products containing no additional functions besides the thioether and amidic functions, starting from bis(thiols) and unfunctionalized bis(acrylamides).[4] On the other hand, several new families of multifunctional polymers containing tertiary amino groups in their main chain were prepared by polyaddition of 2,2′-alkylenediiminodiethanethiols to compounds bearing activated double bonds.[5-8] However, 2,2-bis(acrylamido)-acetic acid has not been considered so far as a monomer for stepwise polyadditions.

It may be noted that Michael-type polyadditions may allow, in principle, the preparation of vinyl-terminated polymeric products, acting as macromonomers. According to some results already obtained with a different family of polyaddition polymers, poly(amidoamines),[9] such macromonomers can be used, inter alia, for preparing cross-linked resins, and for surface grafting on various materials, thus dramatically modifying their surface properties. To our knowledge, vinyl-terminated carboxylic acid macromonomers of well-defined structure are barely to be found in the literature.

In the present study, we have prepared carboxylic acid macromonomers, and we have demonstrated the possibility of using them for obtaining cross-linked, potentially hydrolyzable carboxylated resins. Furthermore, since the new polymeric acids described in this paper may be interesting as constituents of drug delivery systems, we have studied their ability to enter into coupling reactions with an alcohol, an amine, and an aldehyde as model compounds.

Results and Discussion

Synthesis and Properties. Polymers VI-IX were prepared by Michael-type polyaddition of bis(thiols) I-IV to 2,2-bis(acrylamido)acetic acid V.



$$n\mathrm{HSRSH} + n\mathrm{CH_2{=}CH\overset{\overset{\displaystyle O}{\|}}{C}NH\underset{\underset{\displaystyle COOH}{|}}{C}HNH\overset{\overset{\displaystyle O}{\|}}{C}CH{=}CH_2} \longrightarrow \left[\mathrm{SRSCH_2CH_2\overset{\overset{\displaystyle O}{\|}}{C}NH\underset{\underset{\displaystyle COOH}{|}}{C}HNH\overset{\overset{\displaystyle O}{\|}}{C}CH_2CH_2}\right]$$

I–IV; V; VI–IX

I, IV, R = $(CH_2)_2$; II, VII, R = $(CH_2)_3$; III, VIII, R = $(CH_2)_4$;

IV, IX, R = $\mathrm{CH_2\overset{\overset{\displaystyle OH}{|}}{C}H{-}\overset{\overset{\displaystyle OH}{|}}{C}HCH_2}$ (threo)

The same polymerization technique has been recently employed for preparing other families of multifunctional polymers containing aminic functions in their main chain.[5-7] In the present case, the polymerization took place easily in lower alcohols, or aqueous alcoholic mixtures, and in the presence of 1.2 mol of triethylamine/mol of acid, with the excess base acting as catalyst. Pure water is a poor solvent for higher bis(thiols). Aprotic solvents were not considered, since they proved to be unsuitable for Michael-type polyadditions, with the reaction becoming very slow at high conversions.[10] Under the conditions we chose, at room temperature (20 °C) the reaction went to completion in about 5 days. We did not consider higher reaction temperatures, which may favor solvolysis of amidic bonds.[11]

The free polymeric acids were recovered by diluting the reaction mixtures with water and ice and strongly acidifying with hydrochloric acid. While polymers VI-VIII precipitated in a "dry" form and could be easily recovered by filtration after washing with distilled water, IX precipitated in a highly swollen form and, after washing with water, was isolated by decantation.

After drying, all polymers VI-IX are white powders, stable on storage. In some cases, however, they became partly insoluble on standing for several weeks at room temperature. This was probably due to the presence of some residual double bonds, and we found that the addition to the reacting mixture of a monofunctional thiol, such as, for instance, 2-mercaptoethanol, a few hours before isolating the products was indeed effective in stabilizing them.

Absolute molecular weight determinations were not performed because of the poor solubility of the polymers in most suitable solvents, coupled with the fact that they tenaciously retain water (see the results of the elemental

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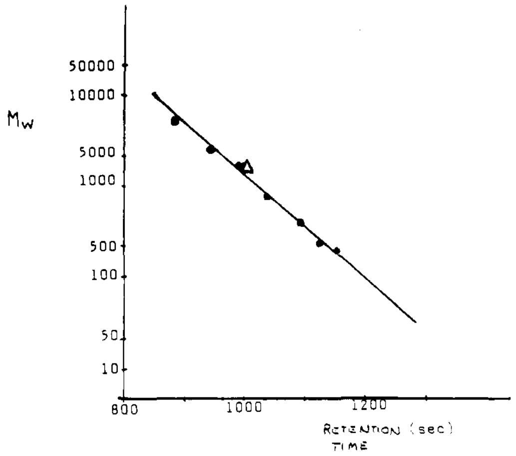


Figure 1. GPC retention times of polymers VI–IX (△) and PEG standard calibration curve (●). Experimental conditions: mobile phase = phosphate buffer pH 8.0, flow rate = 1 mL/min.

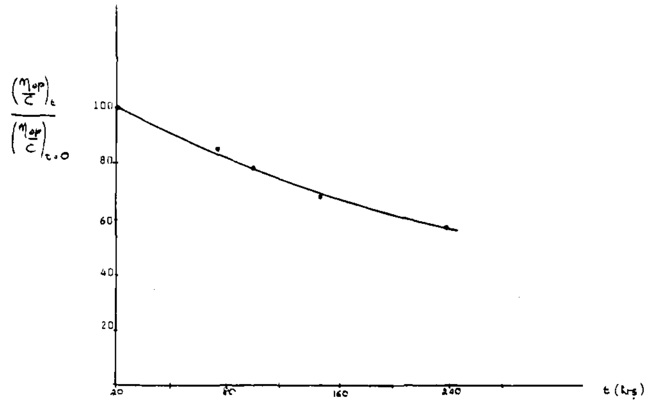


Figure 2. Decrease of the reduced viscosity of polymer VI in 0.1 M aqueous sodium carbonate over time. Experimental conditions: pH = 9.65, temperature = 40 °C, c = 1.99 g/dL.

analyses), making it difficult to obtain reliable osmometric measurements. GPC chromatograms were run in phosphate buffer, pH 8.0. For comparison purposes, retention times of all polymers were reported in Figure 1 together with a standard PEG calibration curve, obtained in the same experimental conditions. Though this calibration method is not absolute, it indicates that hydrodynamic volumes of polymers VI–IX lie in the range of those of PEG650 and PEG23700.

Intrinsic viscosities and solubility properties of polymers VI–IX are reported in Table I. From viscometric measurements, the molecular weights of all polymers seem to be rather low. We cannot exclude that some cleavage of the main chain by hydrolysis or alcoholysis of the amidic bonds occurs even at room temperature, by analogy to what already was observed in the polyaddition of amines to bis(acrylamides).[10] On the other hand, as pointed out above, aprotic solvents are not recommended for Michael-type polyadditions.

It may be observed that a hydrolyzable backbone is obviously an advantage in many medical applications, avoiding the risk of a perpetual permanence within the body. To this point, we have performed experiments to demonstrate that the new polymeric acids are indeed degradable in aqueous media. The degradation at basic pH was studied by viscometric measurements. An example of the curve obtained with polymer VI is reported in Figure 2.

Regarding the solubility properties of VI–IX, it may be observed that they are insoluble in most common solvents and water. However, they are all soluble in aqueous media at pH's > 4.5.

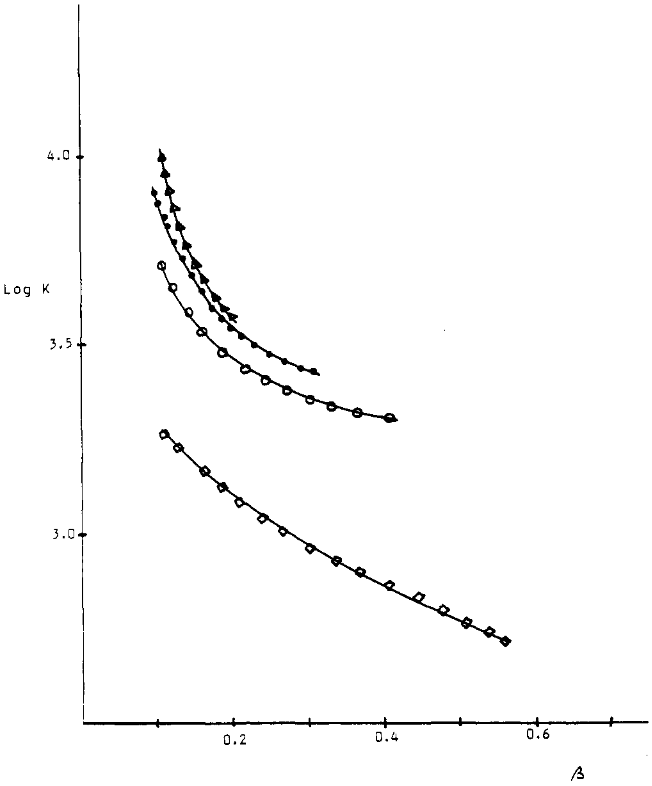


Figure 3. Basicity constants (log K) versus the degree of protonation β for polymers VI (○), VII (●), VIII (▲), and IX (◇) in 0.1 M sodium chloride at 25 °C.

The protonation behavior of the polymeric acids has been studied at 25 °C in 0.1 M sodium chloride aqueous solution, by potentiometric titration. Some preliminary results are reported below.

This new family of polymers has a limited range of pH solubility, in which the protonation reaction of the COO^- group is strongly limited by the solubility of the whole macromolecule. Polymer IX, having hydroxyl groups, is soluble over a wider pH range.

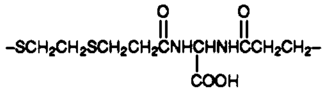
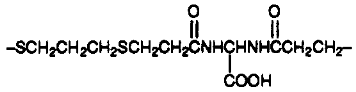
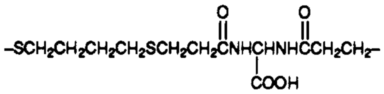
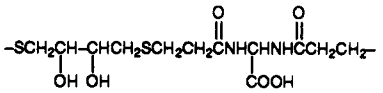
Figure 3 shows the protonation constant plots for all studied polymers. The protonation constants of all polymers have been evaluated down to critical β values, because beyond these values the pH remains constant even if further protons are added, while the polymer solution becomes cloudy. Regarding the protonation process $COO^- + H^+ \rightarrow COOH$, the polymers show a high polyelectrolyte effect, because the log K values strongly decrease with the degree of protonation β, at least in the narrow range of their solubility. The behaviors within the series VI–VIII seem to be similar to each other, with the only limitation being their hydrophobic character, due to the different length of the methylene chains. Any increase of the latter, in fact, narrows the α solubility range of the polymer. The highest β value at which the polymer remains in solution decreases from 0.4 to 0.2 on passing from VI to VIII, with intermediate behavior for VII.

The basicity constants of the polymeric acids are low and compatible with that of many fairly simple carboxylic acids.[12] The calculated log K values for VIII are higher than that of the more soluble analogue IX. The latter obeys the modified Henderson–Hasselbalch equation

$$\mathrm{pH} = \log K^\circ + n \log (1 - \beta)/\beta$$

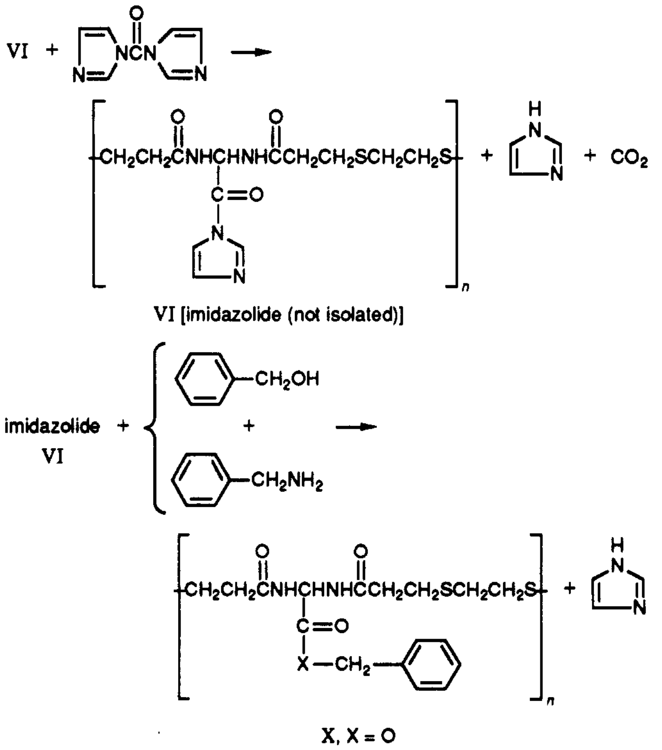
(log K° = 2.85; n = 1.59), in a way followed by many poly(amido acids) that were studied by us.[13,14]

Table I
Structure and Properties of Polymers from Michael-Type Polyaddition of Bis(thiols) to 2,2-Bis(acrylamido)acetic Acid

no.	structure of repeating unit	$[\eta]$[a]	solubility tests[b]
VI	 $-SCH_2CH_2SCH_2CH_2\overset{O}{C}NH\underset{COOH}{CH}NH\overset{O}{C}CH_2CH_2-$	0.19	sol:[c] C, D, O, P ins:[c] A, B, E–I, L–N
VII	 $-SCH_2CH_2CH_2SCH_2CH_2\overset{O}{C}NH\underset{COOH}{CH}NH\overset{O}{C}CH_2CH_2-$	0.20	sol:[c] C, D, O, P ins:[c] A, B, E–I, L–N
VIII	 $-SCH_2CH_2CH_2CH_2SCH_2CH_2\overset{O}{C}NH\underset{COOH}{CH}NH\overset{O}{C}CH_2CH_2-$	0.24	sol:[c] C, D, O, P ins:[c] A, B, E–H, L–N
IX	 $-SCH_2\underset{OH}{CH}-\underset{OH}{CH}CH_2SCH_2CH_2\overset{O}{C}NH\underset{COOH}{CH}NH\overset{O}{C}CH_2CH_2-$	0.23	sol:[c] C, D, O ins:[c] B, E–I, L–N sw:[c] A sh:[c] P

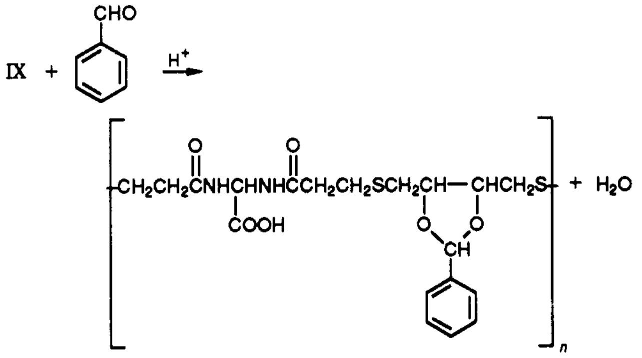
[a] Intrinsic viscosity in DMSO at 30 °C (dL/g). [b] Solvents tried: water (A); 0.1 M HCl (B); acetate buffer pH 4.68 (C); phosphate buffer pH 6.88 (D); chloroform (E); methanol (F); isopropyl alcohol (G); ethyl ether (H); acetone (I); ethyl acetate (L); *n*-heptane (M); toluene (N); DMSO (O); DMF (P). [c] sol = soluble; ins = insoluble, sw = swellable; sh = soluble near boiling point.

Coupling Reactions. In order to investigate the ability of the new polymeric acids to enter into coupling reactions with alcohols and amines, we have chosen as model molecules benzyl alcohol and benzylamine, and, as coupling reagent, *N,N'*-carbonyldiimidazole, which is known to give good results with poly(acrylic acids).[15] We have performed this reaction with polymer VI as a representative of the family, keeping in mind that polymer IX, bearing hydroxyl groups, is probably not suitable for this kind of coupling. The coupling reactions were quantitative. Some characterizations of the resulting polymers are given in Table II.


VI [imidazolide (not isolated)]

X, X = O
XI, X = NH

Polymer IX was tested for its coupling ability with carbonyl compounds, choosing benzaldehyde as the model:

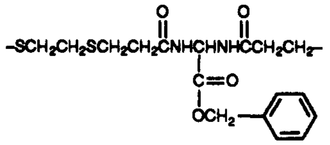
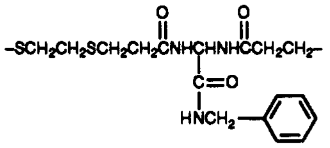
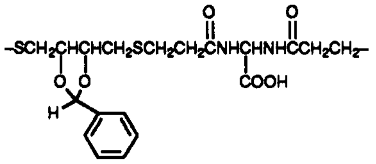

XII

The above reaction went to about 50% yield. Some characterizations of the resulting polymer XII are reported in Table II.

Cross-Linked Resins. It is apparent that polymers VI–IX, obtained by Michael-type polyaddition of bis(thiols) to a substituted bis(acrylamide), are in fact macromonomers, since their end groups, in the absence of side reactions, are either SH or NHC(O)CH=CH$_2$. When the polymerization reaction is performed with a nonstoichiometric ratio of the two monomers, polymers totally or predominantly end capped with one or the other of the above groups may be obtained. In particular, an excess of V in the monomeric mixture leads to polymers predominantly end capped with acrylamido groups. These, in turn, can be used for preparing cross-linked resins, by curing with radical initiators with or without the addition of a vinyl comonomer. The same technique has been used to prepare heparin-adsorbing poly(amidoamine) resins, starting from acrylamido-terminated poly(amidoamine)s obtained by polyaddition of bis(amines) to bis(acrylamides) in excess.[16]

By choosing polymer VI as representative of the whole family, we prepared a sample starting from a monomer mixture with a bis(thiol)/bis(acrylamide) ratio equal to 0.8. Without isolation, this sample was mixed with *N*-vinyl-2-pyrrolidinone and warmed in the presence of a radical initiator. A cross-linked resin XIII was obtained. The same treatment performed without the addition of

Table II
Structure and Properties of Polymers from Coupling of VI and IX with Low Molecular Weight Model Compounds

no.	structure of repeating unit when coupled with model molecule	$[\eta]^a$	solubility tests^b
X		0.36	sol: O, P ins: A–I, L–N
XI		0.21	sol: O, P ins: A–I, L–N
XII		0.25	sol: O, P ins: A–I, L–N

^{a} Intrinsic viscosity in DMSO at 30 °C (dL/g). ^{b} Solvents tried: water (A); 0.1 M HCl (B); acetate buffer pH 4.68 (C); phosphate buffer pH 6.88 (D); chloroform (E); methanol (F); isopropyl alcohol (G); ethyl ether (H); acetone (I); ethyl acetate (L); *n*-heptane (M); toluene (N); DMSO (O); DMF (P).

Table III
Ion-Exchange Capacity and Water Uptake of Resins XIII and XIV

no.	ion-exchange capacity,^{a} mol/g of resin	water uptake, g/g of dry resin	
		free acid	sodium salt
XIII	1.68×10^{-3}	1.69	11.31
XIV	3.65×10^{-3}	1.41	9.60

^{a} The ion-exchange capacity of the linear polymer is 3.76×10^{-3} mol/g.

N-vinyl-2-pyrrolidinone also gave a cross-linked resin XIV. After careful extraction with a media solvent for the linear polymers, the resins were characterized for their ion-exchange capacity and their water uptake in aqueous media either as free acids or as sodium salts. The results are given in Table III.

It may be observed that XIII has an ion-exchange capacity higher than what could be expected on the basis of the monomer composition of the starting polymerization mixture, probably because either *N*-vinyl-2-pyrrolidinone did not polymerize completely or it polymerized, in part, to soluble homopolymer. On the other hand, resin XIV has the expected ion-exchange capacity. It may be also interesting to note that the water uptake of both resins changes markedly by passing from the free acids to their dissociated forms.

Experimental Section

Measurements. Intrinsic viscosities were measured in DMSO at 30 °C, with an Ubbelohde viscometer, and determined according to the method of Solomon and Ciuta.[17] ^{1}H NMR spectra were run at 60 MHz on a EM 360A Varian spectrometer in DMSO-d_6, using TMS as the internal reference. ^{13}C NMR spectra were run at 50.3 MHz using a Varian UXR-200 spectrometer in DMSO-d_6, using TMS as the internal reference.

GPC chromatograms were obtained by using BIO RAD TSK40 and TSK30 columns in series with a phosphate pH 8.0 buffer as eluent, flow rate 0.1 mL/min (ERMA Model ERC 2020 instrument), with both a Knauer RI detector and a Knauer UV detector operating at 240 nm. The retention times reported are those corresponding to the peak maximum.

Elemental analyses were performed by the Redox Co. (Cologno Monzese, Italy). The potentiometric titrations were carried out with a digital Radiometer PHM-84 potentiometer, equipped with a Ross glass electrode (Orion Model 80-01) and a Ross reference electrode (Orion Model 80-05), and a Metrohm Multidosimate piston buret connected to an Olivetti M20 computer.

Materials. 1,2-Ethanediol (I), 1,3-propanedithiol (II), 1,4-butanedithiol (III), and *threo*-1,4-dimercapto-2,3-butanediol (IV) were purchased from the Fluka Co. and used without further purification. Benzyl alcohol, benzylamine, benzaldehyde, *N,N'*-carbonyldiimidazole, and 2,2'-azobis(isobutyronitrile) were purchased from the Aldrich Chemical Co. and used without further purification. *N*-Vinyl-2-pyrrolidinone, purchased from the Fluka Co., was distilled under reduced pressure just before use. 2,2-Bis(acrylamido)acetic acid (V) was purchased from the Aldrich Chemical Co. It invariably contained some amount of insoluble matter. It was purified just before use by recrystallization from isopropyl alcohol and in the presence of a small amount of *p*-methoxyphenol as radical inhibitor.

Polymer VI. A mixture of I (1.561 g, 16.56 mmol), V (3.281 g, 16.56 mmol), and 95% ethanol (10 mL) was carefully purged with nitrogen. Degassed triethylamine (2.8 mL, 19.87 mmol) was then added under a stream of nitrogen, and the reaction mixture was maintained at room temperature (about 18 °C) for 6 days with occasional shaking. The resulting viscous solution was then treated with 2-mercaptoethanol (1 mL) and allowed to stand at room temperature for a further 6 h. The reaction mixture was finally diluted with water (100 mL) and acidified with hydrochloric acid. The polymer precipitated at once as a white powder. It was separated by filtration, thoroughly washed with water, and dried to a constant weight at room temperature and 0.1 mmHg: yield 3.583 g (74.0%).

^{1}H NMR (DMSO-d_6): δ 2.1–3.1 (m, 12 H, CH_2S and CH_2CO), 5.5–5.9 (m, 1H, NCHN), 8.7–8.9 (m, 2 H, NH). ^{13}C NMR (DMSO-d_6): δ 28 ($SCCH_2CO$), 30 ($SCCH_2S$), 37 (COC), 57 (NHCNH), 171 (C=OOH), 172 (C=O).

Anal. Calcd for ($C_{10}H_{16}N_{24}O_2S_2 \cdot {}^1/_2H_2O$): C, 39.85; H, 5.68; N, 9.30. Found: C, 39.87; H, 5.74; N, 9.28.

Polymers VII and VIII were prepared in exactly the same way, by substituting II (1.793 g, 16.56 mmol) and III (2.020 g, 16.56 mmol) for I, respectively. Yields were similar.

Polymer VIII. ^{1}H NMR (DMSO-d_6): δ 1.7 (q, 2 H, CCH_2C), 2.1–3.1 (m, 12 H, CH_2S and CH_2CO), 5.5–5.9 (m, 1 H, NCHN), 8.7–9.0 (m, 2 H, NH). ^{13}C NMR (DMSO-d_6): δ 27 ($SCCH_2CO$), 29 (CH_2CCH_2), 30 ($SCCH_2S$), 38 (COC), 56 (NHCNH), 171 (C=OOH), 172 (C=O).

Anal. Calcd for ($C_{11}H_{18}N_2O_4S_2 \cdot {}^1/_4H_2O$): C, 42.50; H, 6.00; N, 9.01. Found: C, 42.18; H, 5.93; N, 8.98.

Polymer VIII. ^{1}H NMR (DMSO-d_6): δ 1.4–1.9 (m, 4 H, CCH_2C), 2.1–2.9 (m, 12 H, CH_2S and CH_2CO), 5.5–5.9 (m, 1 H, NCHN), 8.7–8.9 (m, 2 H, NH). ^{13}C NMR (DMSO-d_6): δ 27 ($SCCH_2CO$), 28 ($(CH_2CCH)_2$), 31 ($SCCH_2CH_2S$), 37 (COC), 56 (NHCNH), 170 (C=OOH), 171 (C=O).

Anal. Calcd for $(C_{12}H_{20}N_2O_4S_2 \cdot {}^1/_2H_2O)_x$: C, 43.75; H, 6.42; N, 8.50. Found: C, 43.79; H, 6.30; N, 8.35.

Polymer IX was prepared exactly as VI, by substituting IV (2.554 g, 16.56 mmol) for I. The product was isolated in the same way, but the temperature was always maintained below 10 °C. Even so, some losses could not be avoided, since IX separated on acidification in a highly swollen state and was washed by decantation. The yield was considerably lower, 42%.

^{1}H NMR: δ 2.1–2.8 (m, 12 H, CH_2S and CH_2CO), 3.1–3.5 (m, 2 H, CHO), 4.5–5.1 (br m, 2 H, OH), 5.5–5.9 (m, 1 H, NCHN), 8.7–8.9 (m, 2 H, NH). ^{13}C NMR (DMSO-d_6): δ 28 ($SCCH_2CO$), 36 (CHOHCS), 37 ($COCCH_2$), 56 (NHCNH), 73 (COH), 170 (COOH), 171 (C=O).

Anal. Calcd for ($C_{12}H_{20}N_2O_6S_2 \cdot {}^1/_2H_2O$): C, 39.98; H, 5.86; N, 7.75. Found: C, 39.95; H, 5.60; N, 8.04.

Coupling Product X. A solution of VI (0.195 g) in anhydrous DMSO (15 mL) was dried by evaporating under reduced pressure to $^1/_3$ of the solvent, and then it was treated with *N,N'*-carbonyldiimidazole (0.107 g, 30% excess on the acid). Much carbon dioxide was evolved. After the solution was left at room temperature for 30 min, benzyl alcohol (0.090 g, 30% excess on the acid) was added, and the reaction mixture was maintained at 60 °C for 12 h. The product was then isolated by pouring the reaction mixture in water (50 mL). The product precipitated at once. It was repeatedly washed with water, dilute hydrochloric acid, water, methanol, and ether. It was finally dried to constant weight as above. The degree of substitution, as determined by ^{1}H NMR, was about 100%: yield 0.126 g (90%).

^{1}H NMR: δ 2.1–3.1 (m, 12 H, CH_2S and CH_2CO), 4.3–4.8 (s, 2 H, CH_2Bz), 5.5–5.9 (m, 1 H, NCHN), 7.2–7.7 (m, 5 H, aromatic CH), 8.7–8.9 (m, 2 H, NH).

Coupling product XI was prepared exactly in the same way, by substituting benzylamine (0.0942 g, 30% excess on the acid) for benzyl alcohol. The reaction mixture was not warmed but was allowed to stand at room temperature overnight before isolating the product. The degree of substitution, as determined by ^{1}H NMR, was about 100%: yield 0.211 g (90%).

^{1}H NMR (DMSO-d_6): δ 2.1–3.1 (m, 12 H, CH_2S and CH_2CO), 4.3–4.8 (s, 2 H, CH_2Bz), 5.5–5.9 (m, 1 H, NCHN), 7.2–7.7 (m, 5 H, aromatic CH), 8.7–8.9 (m, 3 H, NH).

Coupling Product XII. A solution of IX (0.500 g) in anhydrous DMSO (5 mL) was treated with benzaldehyde (0.430 g, 10% excess on the diol). *p*-Toluenesulfonic acid (0.2 g) was added, and the reaction mixture was maintained at room temperature for 24 h.

The product was then isolated by pouring the reaction mixture in water (50 mL). The product precipitated at once. It was repeatedly washed with water, dried, extracted repeatedly with ether, and dried as above. The degree of substitution, as determined by ^{1}H NMR, was about 50%: yield 0.615 g (68%).

^{1}H NMR (DMSO-d_6): δ 2.1–2.8 (m, 12 H, CH_2S and CH_2CO), 3.1–3.5 (m, 3 H, CHO), 5.5–5.9 (m, 1 H, NCHN), 7.2–7.0 (m, 0.5 × 5 H, aromatic CH), 8.7–8.9 (m, 2 H, NH).

Cross-Linked Resin XIII. A solution of VI in 95% ethanol was prepared exactly as described above, but using only 1.249 g (13.24 mmol) of I. After the solution stood for 2 days at room temperature, acetic acid (0.168 g, 2.81 mmol), *N*-vinyl-2-pyrrolidinone (9.06 g, 98.5 mmol), and 2,2′-azobis(isobutyronitrile) (0.080 g, 0.49 mmol) were added to the viscous reacting mixture, which was then maintained at 60 °C under nitrogen atmosphere for a further 24 h. The resulting gel was then triturated, washed with water, treated with dilute hydrochloric acid, and then extracted with water until no traces of hydrochloric acid could be detected in the mother liquors. The product was finally dried to constant weight as in the previous cases: yield 6.101 g (44.9%).

Cross-linked resin XIV was prepared in the same way, but the addition of *N*-vinyl-2-pyrrolidinone was omitted: yield 57.9%.

The ion-exchange capacities of the resins were determined by treating a weighed amount of finely subdivided dry resin with a measured excess of 0.1 M sodium hydroxide, allowing it to stand at room temperature for 15 min, and titrating the excess base with 0.1 M hydrochloric acid.

The water uptake of the resins was determined as follows. The resin in the form of course particles was equilibrated for 12 h with either water or 0.1 M sodium hydroxide. It was then carefully soaked with water, recovered by filtration, and dried over filter paper. Weighed amounts were then dried to a constant weight at 40 °C and 0.1 Torr. The loss of weight was assumed as a measure of the water content of the swollen resin and related to the weight of the residue as corresponding to the dry resin or its sodium salt, respectively.

The protonation equilibria of polymers were studied with potentiometric techniques using a previously described method.[18] The potentiometric titrations were carried out in a glass cell kept at constant temperature of 25 °C and at a constant ionic strength of 0.1 M sodium chloride. For each titration experiment, the cell was filled with about 100 mL of 0.1 M sodium chloride solution, in which a known amount of solid polymer was dispersed by magnetic stirring. An excess of a measured volume of standardized sodium hydroxide was then added to the aqueous dispersion. The polymer completely dissolved within few a hours. During all operations a nitrogen stream was maintained over the surface of the polymer solution, to avoid carbon dioxide contamination. The polymer solution was then titrated with standardized hydrochloric acid. The end point of the potentiometric titration curve was taken to calculate the excess of sodium hydroxide equivalents. The differences between the initial amount of OH^- and the OH^- equivalents gave the polymer proton equivalents. The results always agreed with the amount of polymer initially weighed. The basicity constants for the polymers were computed by a APPARK program on the Olivetti M20 computer, as previously reported.[18]

Conclusions

From the above experimental data it may be reasonably concluded that 2,2-bis(acrylamido)acetic acid can be used as the monomer in Michael-type polyadditions involving bis(thiols). The reaction allows the preparation of polymeric acids under very smooth and easy conditions. The resulting polymeric acids are fairly strong, stronger than poly(acrylic acid). Additional functions can be introduced by using as comonomers suitably functionalized bis(thiols) furthermore, moieties of model amines, alcohols, and, in the case of polymers containing *vic*-diol groups, aldehydes can be grafted onto the polymers by polymer analogous reactions.

The new polymeric acids obtained deserve attention in two respects. First, they contain hydrolyzable bonds in their main chain. Second, they can be easily obtained in the form of vinyl-terminated macromonomers, which, in turn, can be useful for a variety of purposes. As an example, cross-linked homo- and copolymeric resins have been obtained by radical postpolymerization. By analogy with other functional vinyl macromonomers,[9] they are also being considered by our group for surface grafting on various functional matrices in order to modify their surface properties by introducing ionic charges.

References and Notes

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Registry No. (I)(V) (copolymer), 134111-41-4; (I)(V) (SRU), 134111-47-0; (II)(V) (copolymer), 134111-43-6; (II)(V) (SRU), 134111-49-2; (III)(V) (copolymer), 134111-44-7; (III)(V) (SRU), 134111-50-5; (IV)(V) (copolymer), 134111-42-5; (IV)(V) (SRU), 134111-48-1; (I)(V)(*N*-vinyl-2-pyrrolidinone) (copolymer), 134111-45-8; water, 7732-18-5.