Poly(α-aminoacrylic acid)

{Poly[1-(1-ammonio-1-carboxylato)ethylene]}

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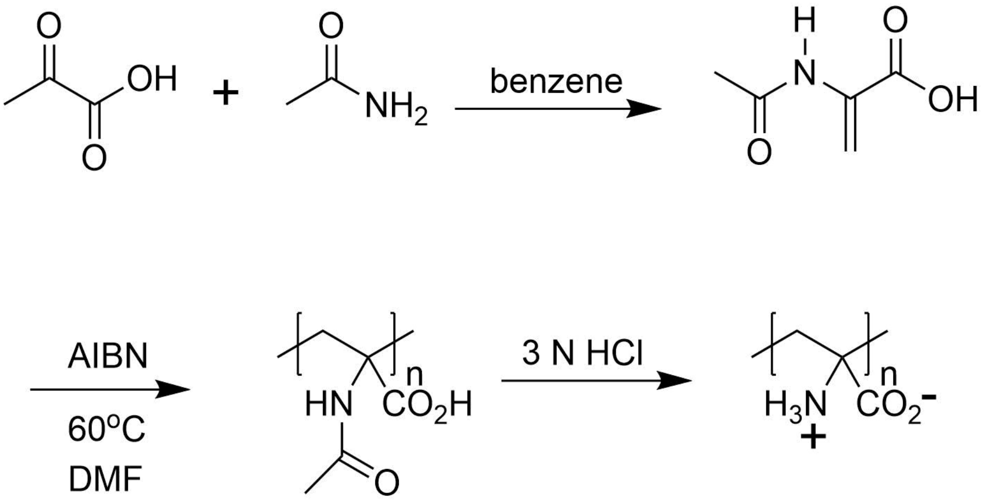

1. Procedure

Acetamide, 44.3 g (0.75 mil), and pyruvic acid (Note 1), 132.1 g (1.5 mol), are added to a 2L, three-necked, round-bottomed flask containing benzene (**Caution! Toxic Solvent!**), 1000 mL, and equipped with a mechanical stirrer, a water separator with a stopcock, a condenser, and a nitrogen-inlet tube (Note 2). The system is purged for 30 min with N_2 and then heated to reflux. The water produced in the reaction is removed by azeotropic distillation. The product, 2-acetamidoacrylic acid, precipitates as it forms. After the reaction is complete [3-6 h is required for evolution of the theoretical amount of H_2O (Note 3)] and the reaction mixture has cooled to room temperature, the product is collected by suction filtration. The crude product is then suspended in acetone, stirred for a short time, and recovered by filtration. The acetone wash is repeated and the product finally dried in a vacuum oven at 60° to give 70.1 g (78% yield) of pure 2-acetamidoacrylic acid, mp 198-199° (Note 4).

2-Acetamidoacrylic acid, 30 g, and azobisisobutyronitrile (AIBN), 1.9 g, are dissolved in *N,N*-dimethylformamide (DMF), 130 mL, in a 250 mL round-bottomed flask. The flask, sealed with a syringe cap, is purged with N_2 for 1 h. The monomer is polymerized at 60° over a 20 h period. The resulting viscous solution is added to 10 times its volume overnight at room temperature to give poly(2-acetamidoacrylic acid) is quantitative yield, η_{sp} (1 g/dL, DMF) = 0.37 dL/g at 25° (Note 5).

The hydrolysis of poly(2-acetamidoacrylic acid) is accomplished by heating the polymer in 3 *N* HCl. The polymer, 25 g , is dissolved in water, 500 mL, in a 1 L, three-necked, round-bottomed flask equipped with a mechanical stirrer, condenser, and gas-inlet tube. Concentrated HCl, 165 mL, is added slowly to the water solution of polymer. The system is purged with N_2, heated to reflux, and maintained at this temperature for about 12 h. Poly(α-aminoacrylic acid), which precipitates during the course of hydrolysis, is collected by suction filtration after the reaction mixture has cooled to room temperature. It is then washed with acetone, and dried under oil-pump vacuum at room temperature to yield 11 g (65% yield, Note 6) of a white powder.

2. Characterization

2-Acetamidoacrylic acid, mp 198-199° [literature value 198-199°[4]], is characterized by IR spectroscopy (KBr) as having peaks at 3320 (s), 2900/2500 (m), 1700 (s), 1625/1600 (s), 1520 (s), 1450 (w), and 1360 (s) cm^{-1}, as well as 10 additional well-defined peaks down to 600 cm^{-1}. The 90 MHz NMR spectrum (10% NaOD in D_2O) of the monomer is characterized by three peaks at δ 5.86 (s, 1, ==CH), 5.78 (s, 1, ==CH), and 2.12 (s, 3, CH_3) ppm.

Poly(2-acetamidoacrylic acid) is a white solid that is soluble in water, aqueous base, DMSO, and DMF, and insoluble in acetic acid, acetonitrile, acetone, and ethanol. The salient features of teh IR spectrum (nujol) are peaks at 3550/3400 (w), 2950 (w), 2600 (w), 1725 (s), 1650 (s), 1520 (s), 1450 (m), and 1380 (m) cm^{-1}. The 90 mHz NMR spectrum (D_2O) of he intermediate polymer is characterized by two peaks, one at 1.94 (CH_3) and one at 2.7 (β, CH_2) ppm (Note 7). The ratio between the areas of the two peaks is 3:2 (CH_3/CH_2). The specific viscosity (1 g/dL, DMF) is 0.37 dL/g at 25°. Anal. Calcd. for $(C_5H_7NO_3)_x$: C, 46.51%; H, 5.46%; N, 10.84%. Found: C, 39.77%; H, 6.28%; N, 9.28%. Based on this analysis the C/N ratio is 5.0, the same as calculated for the fully acetylated polymer. The calculated analysis for the polymer with 1.25 mol of H_2O/repeat unit is C, 39.60%; H, 6.27%; N, 9.24%, which is in good agreement with the actual analysis.

Poly(α-aminoacrylic acid) is a white solid that is soluble in aqueous base (Note 6) and insoluble in acetone, acetonitrile, ethanol, dioxane, methylene chloride, toluene, and hexane. The IR spectrum (film cast from aqueous base on a mercury pool) is characterized by absorptions at 3250 (s), 2950 (w), 1660 (s), 1550 (s), 1420 (m/s) cm^{-1}. the 90 MHz NMR spectrum (10% NaOD in D_2O) consists of a single broad peak at 2.45 ppm (CH_2) sometimes contaminated with a small superimposed peak at 1.95 ppm from residual acetyl groups. Anal. Calcd. for $(C_3H_5NO_2)_x$ (Note 6): C, 41.32%; H, 5.79%; N, 16.09%. Found: C, 41.32%; H, 5.89%; N, 15.70%. The polymer also contained a small amount (3.04%) of chlorine (Note 8).

3. Notes

1. Pyruvic acid (mp 13°, bp 65°, 10 torr) should be distilled twice at reduced pressure (10 - 20 torr) and then fractionally crystallized by partial freezing. Use of the crude acid produces low yields of 2-acetamidoacrylic acid.
2. The reactants are not completely soluble even in refluxing benzene and the product precipitates during the course of reaction. For these reasons magnetic stirring is not adequate.
3. Complete reaction is indicated by formation of two clear layers, water and benzene, in the water trap. The water separated out during he course of reaction is usually more than the theoretical amount, presumably because the benzene is not predried.
4. Recrystallization from ethanol, recommended by Asquith et at[4], gave poor yields and melting points and an impurity, evidenced by IR peaks at 1140 and 3400 cm^{-1}, that was insoluble in DMF, the polymerization solvent. Recrystallizaiton from DMF gave pure product, but in low lields. Our procedure produces monomer in good yields with a consistently high melting point and with no evidence of the impurity mentioned above.
5. The specific viscosity of the intermediate polymer depends on the monomer/initiator ratio. As this ratio increases, so does the viscosity. At this point the polymer may be contaminated with DMF, as evidenced by NMR (D_2) peaks at 8.45 and 2.3 ppm. For purposes of elemental and NMR analysis the polymer should be dialyzed against water and isolated by lyophilization.
6. The yield and the analysis are calculated assuming 37% premature hydrolysis and the zwitterionic repeat unit $C_3H_5NO_2$ instead of the hydrochloridesalt repeat unit $C_3H_6ClNO_2$, which was

originally expected. Under dehydrating conditions, such as drying in a heated vacuum oven or standing in a desiccator, the polymer will lose water in intramolecular (nearest-neighbor) lactam formation or intermolecular amide formation. This result will be apparent from an elemental analysis that can be accommodated only by postulating a negative mole fraction of H_2O (i.E., dehydration), and eventually from a loss of solubility, which in some cases may be reversed by heating in aqueous base. Such dehydration can be prevented by isolating the polymer as the sodium salt.

7. The methylene peak is very broad and results from the overlap of three peaks that are resolved at 300 MHz.

8. This polymer is not described accurately by the zwitterionic repeat unit ($C_3H_5NO_2$). In addition to this unit there are the hydrochloride salt ($C_3H_6ClNO_2$) and the residual unhydrolyzed polymer ($C_5H_7NO_3$). Based on the C/N and Cl/N ratios, the mole fractions of these repeat units are 0.885, 0.08, and 0.035%, respectively. Considering 0.24 mol of H_2O/repeat unit completes the interpretation of the elemental analysis.

4. Methods of Preparation

The synthesis of 2-acetamidoacrylic acid by the method employed here has been described in the literature.[4,5,6,7,8,9] The procedure reported here is a modification of the method of reference[4], and produces monomer in higher yield and purity, as well as complete hydrolysis on the intermediate poly(2-acetamidoacrylic acid). The syntheses of other suitable blocked α-aminoacrylic acids have been reported.[9,10,11,12,13,14] Of these, the α-carbobenzyloxyaminoacrylic acid[11], the *N*-formyl methyl ester[11,12], the *N*-carboxydehydralanine anhydride[13], the *N*-phthaloyldehydroalanine[13], and the 5-methylenehydantoin[14] have been converted to the corresponding polymers and subsequently deblocked to give poly(α-aminoacrylic acid).[12-14] Some of these reports also mention the complications described here regarding amide and lactam formation.

5. References

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