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## **61.** *Some* N-*Substituted Derivatives of Poly-α-aminoacrylic Acid.*

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Poly-α-carbobenzyloxyaminoacrylic acid, poly-α-formamidoacrylic acid and its methyl ester, and poly-α-carbethoxyaminoacrylic acid have been prepared by polymerisation of suitable monomers. Removal of the protecting group attached to the α-amino-group of these polymers has not yet been realised.

IN an attempt to synthesise polyelectrolytes containing in each unit both the amino- and the carboxy-group, the polymerisation of certain derivatives of α-aminoacrylic acid has been studied. As starting materials the following derivatives were used: α-carbobenzyloxyamino- (I) and α-formamidoacrylic acid (II) [and its methyl ester], and αα-di(carbethoxyamino)propionic acid (III).

The acid (I) was prepared from αα-di(carbobenzyloxyamino)propionic acid (Martell and Herbst, *J. Org. Chem.*, 1941, **6**, 878) by treatment with hot glacial acetic acid (cf. Bergmann and Grafe, *Z. physiol. Chem.*, 1930, **187**, 187). The acid (III) was obtained by condensation of urethane with pyruvic acid. Preparation of (II) from α-formamidolactic acid was reported by Shive and Shive (*J. Amer. Chem. Soc.*, 1946, **68**, 117); we prepared (II) by condensation of formamide and pyruvic acid under conditions set out in the Experimental section, isolation of the lactic acid being unnecessary; the yields in our method are lower but the procedure is more convenient. Esterification of (II) was carried out with methyl sulphate as described by Rothstein (*J.*, 1949, 1968) for the corresponding *N*-acetyl compound.

$CH_2{:}C(CO_2H){\cdot}NH{\cdot}CO{\cdot}O{\cdot}CH_2{\cdot}C_6H_5$ (I) $CH_2{:}C(CO_2H){\cdot}NH{\cdot}CHO$ (II) $CH_3{\cdot}C(CO_2H)(NH{\cdot}CO_2Et)_2$ (III)

Polymerisation experiments with (I) and (II) were carried out in *NN*-dimethylformamide at 60° with benzoyl peroxide as catalyst, and at 0° with toluene-*p*-sulphinic acid as catalyst (Hagger, *Helv. Chim. Acta*, 1948, **31**, 1624). The products constituted white hard materials, insoluble in water and the usual organic solvents. The molecular weight of a polymer obtained from (I) (benzoyl peroxide as catalyst) was found to be about 30,000 by light scattering (solution in *NN*-dimethylformamide). The intrinsic viscosity in this solution was 0·13 (concn. in g./100 ml.). Toluene-*p*-sulphinic acid gave a polymer of (I) having in *NN*-dimethylformamide an intrinsic viscosity of 0·51. When (III) was heated above its melting point, a polymer was obtained, the analysis of which was in agreement with the formula of poly-α-carbethoxyaminoacrylic acid. Apparently the monomer formed under these conditions by elimination of one mole of urethane immediately polymerised. The monomer could not be isolated by treating (III) with hot glacial acetic acid. The poly-α-carbethoxyaminoacrylic acid was dissolved in methanol and precipitated with ether. It is soluble in methyl, as well as in ethyl, alcohol and slightly soluble in water. The intrinsic viscosity in methanol solution of this polymer was 0·58. Potentiometric titration in aqueous solution gave the form of curve characteristic for hysteresis, indicating strong aggregation in which the functional carboxylic groups were involved. In conformity with this, addition of alkali beyond the equivalent point caused a drop in relative viscosity as a consequence of the breakdown of aggregates.

With the polymer obtained from (I) with benzoyl peroxide as catalyst, experiments were carried out to remove the carbobenzyloxy-group by catalytic hydrogenolysis, by reduction with phosphonium iodide, and by acid or alkaline hydrolysis. None of these methods has so far been successful. Difficulties in the removal of this group from polymeric peptides were encountered also by other workers (Frankel and Katchalski, Sci. Papers pres. to Ch. Weizmann, 1944, 24, 74; Katchalski, Grossfeld, and Frankel, *J. Amer. Chem. Soc.*, 1947, **69**, 2564; 1948, **70**, 2094; Hanby, Waley, and Watson, *J.*, 1950, 3239). Poly-α-formamido- and poly-α-carbethoxyamino-acrylic acid were not hydrolysed by acid or alkali. Similar difficulties are reported by Adams and his co-workers (*J. Amer. Chem. Soc.*, 1950, **72**, 5080) in a paper which appeared after the experiments presented here were concluded ; these authors failed to remove the acetyl groups from poly-α-acetamido-acrylic acid and ascribe the resistance to hydrolysis of the polymer to lactam formation.

## EXPERIMENTAL

(Analyses are by Drs. Weiler and Strauss, Oxford. M. p.s are uncorrected.)

*α-Carbobenzyloxyaminoacrylic Acid.*—αα-Di(carbobenzyloxyamino)propionic acid (50 g.) (Martel and Herbst, *loc. cit.*) in glacial acetic acid (250 ml.) was boiled under reflux for 3 minutes and then cooled as quickly as possible. The cooled solution was poured into ice-water (1·5 l.) with vigorous stirring. A yellow oil separated which solidified after 10—20 minutes. The mixture was left in the ice-box overnight, then filtered, and the solid material extracted repeatedly with four 20-ml. portions of ice-cold sodium hydroxide solution (3%). The combined filtrates were acidified with concentrated hydrochloric acid with cooling and stirring. The slightly yellow oil which separated upon acidification solidified at once. It was left overnight in the ice-box and then filtered off. The white powder was dried in a desiccator over concentrated sulphuric acid (yield, 53%) and recrystallised twice from toluene. The *α-carbobenzyloxyaminoacrylic acid* was insoluble in water, slightly soluble in benzene and toluene, and soluble in alcohol, ethyl acetate, ether, acetone and dioxan. It melts at 105° with decomp. (Found : C, 60·1; H, 5·3; N, 6·4. $C_{11}H_{11}O_4N$ requires C, 59·7; H, 5·0; N, 6·3%).

*Polymerisation.* The acid (5 g.) and benzoyl peroxide (150 mg.) were dissolved in *NN*-dimethylformamide (15 ml.), and nitrogen was passed through the solution for 20 minutes. The vessel was sealed and left for 12 hours in a thermostat at 60°. The *poly-α-carbobenzyloxyaminoacrylic acid* was precipitated from the highly viscous solution by addition of ether and filtered off. It was a white, hornlike material, soluble in glacial acetic acid and *NN*-dimethylformamide, insoluble in water and the common organic solvents. It was dissolved in *NN*-dimethylformamide and reprecipitated with ether, then dried in a vacuum (yield, 4·4 g.) (Found : C, 60·1; H, 5·2; N, 6·7%).

The monomer (0·5 g.) and toluene-*p*-sulphinic acid (15 mg.) were dissolved in *NN*-dimethylformamide (1·5 ml.), and nitrogen was passed through the solution for 10 minutes. The vessel was sealed and kept in an ice-bath for 12 hours. The polymer was precipitated and washed as in the foregoing experiment.

*α-Formamidoacrylic Acid.*—Anhydrous formamide (10 g.) and freshly redistilled pyruvic acid (20 g.) were heated at 70° under an air condenser at 30 mm. After about 2 hours white crystals were precipitated. The heating was continued for an additional hour. The flask was then cooled and left overnight in the ice-box. The solidified mixture was washed with small quantities of cold water and filtered with suction. The crystalline material obtained (2·6 g.), recrystallised from ethanol, decomposed at 170° (Found : C, 41·9; H, 4·3; N, 12·0. Calc. for $C_4H_5O_3N$ : C, 41·7; H, 4·4; N, 12·2%).

Unsaturation was determined with Dam's reagent; 96% and 95% of the theoretical value were obtained.

*Polymerisation.* A mixture of the monomer (0·5 g.), benzoyl peroxide (15 mg.), and *NN*-dimethylformamide (1·5 ml.) was deaerated and sealed under nitrogen. After 2 hours at 60° a slight turbidity was perceptible. Within 12 hours at 60° the *polymer* was precipitated; it was washed with *NN*-dimethylformamide and ether (Found : C, 41·4; H, 4·2; N, 12·0%).

*Methyl α-Formamidoacrylate.*—Formamidoacrylic acid (2 g.) was suspended in methanol (35 ml.), and a 6% sodium methoxide solution in methanol was added drop by drop until all the acid had dissolved. Quinol (0·3 g.), sodium carbonate (1 g.), methyl sulphate (3 g.), and one drop of methyl-orange were added and the mixture was heated on the water-bath for 2 hours, during which a small quantity of sodium carbonate was added from time to time to maintain alkalinity. The solution was then cooled, dry ether was added, and the precipitated sodium salts were filtered off. The ether was evaporated *in vacuo*. The remaining viscous oil was distilled under reduced pressure, giving *methyl α-formamidoacrylate* (60—70%), m. p. 53° b. p. 87°/5 mm. (Found : C, 46·5; H, 5·5; N, 10·9. $C_5H_7O_3N$ requires C, 46·5; H, 5·4; N, 10·9%).

*Polymerisation.* (i) This was carried out in *NN*-dimethylformamide as for the acid. The polymer was precipitated from the viscous solution by water and the hornlike substance was filtered off, dried, and powdered. It was insoluble in the usual organic solvents.

(ii) A mixture of the ester (1 g.) and benzoyl peroxide (10 mg.) in a test-tube was heated at 60° for 12 hours. A yellow brittle glass was obtained.

*αα-Di(carbethoxyamino)propionic Acid.*—Urethane (25 g.) and freshly distilled pyruvic acid (13 g.) were heated under an air-condenser at 80°/25—30 mm. for 3 hours. Then it was cooled in ice–salt, and cold water (10 ml.) was added. After vigorous stirring, the oil solidified. It was left overnight in the ice-box, then filtered off and washed with a small quantity of cold water. The white crystalline material (55%) was dried over concentrated sulphuric acid in a desiccator.

*αα-Di(carbethoxyamino)propionic acid*, recrystallised from ethyl acetate, had m. p. 120° (Found : C, 43·7; H, 6·5; N, 11·0. $C_9H_{16}O_6N_2$ requires C, 43·6; H, 6·5; N, 11·3%).

*Poly-α-carbethoxyaminoacrylic Acid.*—The foregoing acid (2 g.) was heated at 125° for 1 hour, giving a yellow gel which was dissolved in methanol (5 ml.) and precipitated by ether (25 ml.). The white amorphous precipitate was centrifuged, redissolved in methanol, and reprecipitated with ether. After centrifugation, the *poly-α-carbethoxyaminoacrylic acid* was powdered and dried *in vacuo* (yield, 30%). It is soluble in alcohol and acetone, slightly soluble in water [Found : C, 44·9; H, 5·8; N, 8·9. $(C_6H_9O_4N)_n$ requires C, 45·3; H, 5·7; N, 8·8%].

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