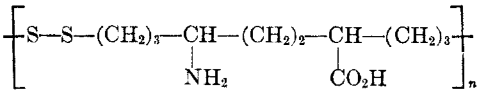
[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

The Synthesis of a Regular Polyampholyte[1]

C. S. MARVEL AND G. L. DETOMMASO

Received May 18, 1960

A regular polyampholyte of the structure



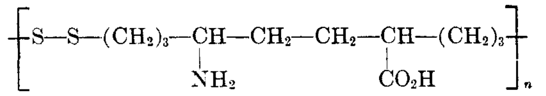
$$\left[-S-S-(CH_2)_3-\underset{NH_2}{CH}-(CH_2)_2-\underset{CO_2H}{CH}-(CH_2)_3-\right]_n$$

has been synthesized.

The polyampholytes synthesized thus far generally possess a random distribution of the acidic and basic groups which often are not attached directly to the polymer skeletal chain. Such polyampholytes have been prepared by copolymerization techniques using acidic and basic monomers, *e.g.*, 2-vinylpyridine and methacrylic acid.[2] Reactions of polymers such as polystyrene[3] have also been employed to incorporate amino acid groups into the polymer. The only regular polyampholyte reported from the use of either technique is that by Vrancken and Smets[4] who prepared a polyampholyte in which the free amino and acid functions were directly attached to the skeletal backbone of the chain with approximately 63% alternation.

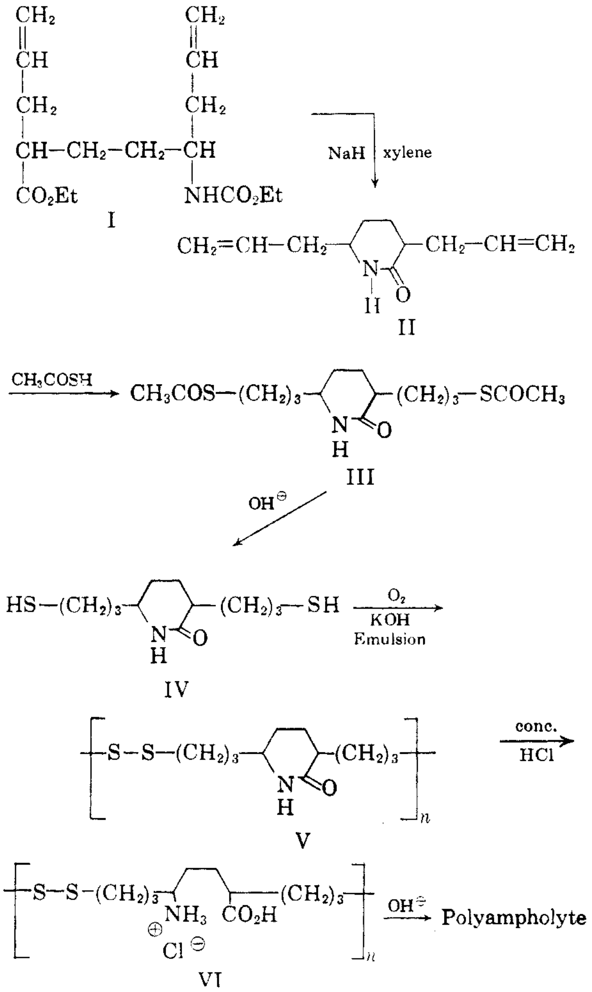
The synthesis of a true polyampholyte with an unequivocally alternating structure has been realized by Marvel and Moyer.[5] However, the low molecular weight polymer obtained did not have solubility properties that made it suitable for a study of the polyampholyte properties, which were expected to be of interest.

This paper describes the synthesis of another polyampholyte which possesses regular amphoteric units



$$\left[-S-S-(CH_2)_3-\underset{NH_2}{CH}-CH_2-CH_2-\underset{CO_2H}{CH}-(CH_2)_3-\right]_n$$

The synthesis was accomplished by the following series of reactions



4-Carbethoxy-7-aminocarbethoxy-1,9-decadiene (I) was prepared according to the procedure of Marvel and Moyer.[5] Ring closure of I to 3,6-diallyl-2-piperidone (II) was effected with sodium hydride in refluxing xylene in 65% yield. 3,6-Bis-(3-mercaptopropyl)-2-piperidone (III) was obtained in 80% yield from the reaction of II with twice distilled thiolacetic acid and either benzoyl peroxide or ultraviolet light as catalyst. Basic hydrolysis of III yielded the crude dithiol (IV) in 98% yield. Purification of IV by normal re-

---

(1) The work discussed herein was sponsored by a grant (NSF-G-2626) from the National Science Foundation. This paper is based on portions of a thesis submitted by G. L. DeTommaso to the Graduate College of the University of Illinois in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(2) T. Alfrey, Jr., H. Morawetz, E. B. Fitzgerald, and R. M. Fuoss, *J. Am. Chem. Soc.*, **72**, 1864 (1950).

(3) K. Schloegl and H. Fabitschowitz, *Monatsh. Chem.*, **85**, 1223 (1954).

(4) M. Vrancken and G. Smets, *J. Polymer Sci.*, **14**, 521 (1954).

(5) C. S. Marvel and W. W. Moyer, Jr., *J. Am. Chem. Soc.*, **79**, 4990 (1957).

crystallization techniques was unsuccessful; however, the formation of the polymeric lead mercaptide from the crude IV and lead diacetate followed by recrystallization of the regenerated dithiol afforded an analytically pure sample.

The oxidative polymerization of IV in emulsion employing the techniques[6] developed in this laboratory yielded the polydisulfide (V) in approximately 60–70% conversions; precoagulation of the polymer occurred in all polymerizations and therefore prevented an accurate record of the yield. It is believed that precoagulation occurred as a consequence of the solubility of 3,6-bis(3-mercaptopropyl)-2-piperidone (IV) in water which prevented total incorporation of the monomer into the emulsion micelles and thereby caused solution polymerization to occur. Use of lower polymerization temperatures and additional emulsifying agent did not increase the molecular weight.

Hydrolysis of the polydisulfide (V) was effected by heating with concentrated hydrochloric acid for twenty-four hours and this yielded the water-soluble hydrochloride of the polyampholyte plus a water-insoluble residue whose infrared spectrum indicated it to be V containing several isolated amino acid hydrochloride units. The hydrochloride (VI) had an inherent viscosity of 0.784 (in water) which did not change upon dilution.

The polyampholyte was obtained by neutralization of the hydrochloride (VI) with an equivalent amount of sodium hydroxide. The polyampholyte was insoluble in water and both wet and dry tetrahydrofuran and dioxane.

Some other routes to the final polyampholyte were investigated and some of the intermediates obtained in these reactions are described.

EXPERIMENTAL

2,5-Diallyladipic acid (VII). This compound was prepared according to the procedure of Marvel and Moyer.[5] Distillation of the crude acid yielded a white solid, m.p. 97–100°, b.p. 150–155° (0.05 mm.), from which an analytically pure sample was obtained after two recrystallizations from very dilute ethanol, m.p. 102.5–103.5°. The yield was 89.9%.

2,5-Bis(3-mercaptopropyl)adipic acid diacetate (VIII). The procedure employed is similar to that of Marvel and Cripps[7] for the preparation of bisthiolacetates. A mixture of 32.6 g. (0.144 mole) of α,α'-diallyladipic acid, a pinch of benzoyl peroxide, and 250 ml. of dry benzene was warmed to complete the solution of the acid in benzene. Freshly distilled thiolacetic acid (53.3 g., 0.7 mole) was added in a dropwise manner at such a rate as to maintain the temperature of the reaction mixture near reflux. The reaction mixture was refluxed overnight and cooled whereupon a white solid precipitated. Recrystallization of the crude solid from dilute ethanol yielded 39.7 g. (73%), m.p. 148–149°. The ultraviolet spectrum showed a single absorption, λ_{max} 228 mμ (ϵ 6136) in absolute ethanol. The infrared spectrum showed absorption maxima for carboxylic acid (2550–2650 and 1705 cm.$^{-1}$) and thiolacetate (1690 and 950 cm.$^{-1}$). No trace of terminal olefin absorption was detectable.

Anal. Calcd. for $C_{16}H_{26}O_8S_2$: C, 50.8; H, 6.88; S, 16.92. Found: C, 51.06; H, 7.08; S, 16.50.

Polymeric anhydride (IX) *of 2,5-bis(3-mercaptopropyl) adipic acid diacetate.* The procedure used was similar to that of Fieser and Martin.[8] A mixture of 200 ml. of dry cyclohexane, 11.3 g. (0.03 mole) of 2,5-bis(3-mercaptopropyl)-adipic acid diacetate, and 7.5 g. (0.09 mole) of freshly distilled acetyl chloride was refluxed for 6 hr. The cyclohexane and excess acetyl chloride were removed leaving a colorless viscous liquid whose infrared spectrum showed strong absorption maxima assignable to acid anhydride (1742 and 1785–1815 cm.$^{-1}$), thiolacetate (1690 and 950 cm.$^{-1}$), and weak absorption for acid (1710 cm.$^{-1}$). Treatment of the viscous oil in dry chloroform with gaseous ammonia at ice-salt bath temperatures yielded 2,5-bis(3-mercaptopropyl)-adipic acid, 2,5-bis(3-mercaptopropyl)adipamic acid, m.p. 145–146° (from dilute ethanol), and 2,5-bis(3-mercaptopropyl)adipamide diacetate, m.p. 247° (from dimethylformamide) in a ratio of 1:2:1.

Distillation of the polymeric anhydride according to the procedure of Hill[9] yielded a yellow oil, b.p. 181–186° (0.15 mm.) which solidified upon standing. Recrystallization from dilute ethanol yielded a white solid, m.p. 66–67°, whose infrared spectrum showed major absorption maxima for cyclopentanone (1730 cm.$^{-1}$) and thiolacetate (1690 and 950 cm.$^{-1}$). These data are consistent with the structure of 2,5-bis(3-mercaptopropyl)cyclopentanone diacetate.

Anal. Calcd. for $C_{15}H_{24}O_3S_2$: C, 56.96; H, 7.61; O, 15.18; S, 20.25. Found: C, 56.85; H, 7.42; O, 15.24; S, 20.90.

4-Carbethoxy-7-aminocarbethoxy-1,9-decadiene (I). This compound was prepared according to the procedure of Marvel and Moyer.[5] A colorless liquid, b.p. 135–140° (0.1 mm.), n_D^{25} 1.4650 was obtained.

3,6-Diallyl-2-piperidone (II). A mixture of 56.00 g. (0.19 mole) of 4-carbethoxy-7-aminocarbethoxy-1,9-decadiene, 1 l. of dry xylene, and 4.8 g. (0.2 mole) of finely divided sodium hydride was refluxed for 6 hr. The resultant reddish solution was cooled and poured into 1 l. of ice-cold water acidified with hydrochloric acid. The aqueous layer was separated and washed with two 150-ml. portions of benzene, and the combined benzene-xylene extracts were evaporated under reduced pressure to yield a crude reddish semisolid. Distillation of the crude semisolid *in vacuo* yielded 22.1 g. (65.4%) of a white solid, b.p. 102–105° (0.25 mm.), m.p. 86.5–87.5° (from very dilute ethanol).

The infrared spectrum showed absorption for a δ-lactam (3380, 1640, 975, and 947 cm.$^{-1}$) and terminal olefin (1650, 995, and 918 cm.$^{-1}$).

Anal. Calcd. for $C_{11}H_{17}ON$: C, 73.74; H, 9.49; N, 7.81. Found: C, 73.80; H, 9.51; N, 7.70.

3,6-Bis(3-mercaptopropyl)-2-piperidone diacetate (III). A method similar to that of Marvel and Cripps[7] was employed. Ten milliliters of freshly distilled thiolacetic acid was added to a mixture of 3.0 g. (0.017 mole) of 3,6-diallyl-2-piperidone, 30 ml. of dry cyclohexane, and a pinch of benzoyl peroxide. After 4 hr. at reflux temperature, a white solid was collected and washed with ether. Recrystallization of the crude solid first from cyclohexane and then dilute ethanol yielded 4.5 g. (81.2%) of product, m.p. 120–121°. The infrared spectrum contained absorption maxima for a δ-lactam (3400, 3080, and 1645 cm.$^{-1}$) and thiolacetate (1683 and 955 cm.$^{-1}$). The ultraviolet spectrum contained a single absorption maximum, λ_{max} 232 mμ (8856) in absolute ethanol.

Anal. Calcd. for $C_{15}H_{25}O_3NS_2$: C, 54.38; H, 7.55; N, 4.23; S, 19.33. Found: C, 54.31; H, 7.62; N, 4.24; S, 19.41.

3,6-Bis(3-mercaptopropyl)-2-piperidone (IV). The hydrolysis of 3.0 g. (0.009 mole) of 3,6-bis(3-mercaptopropyl)-2-

---

(6) C. S. Marvel and L. E. Olson, *J. Am. Chem. Soc.*, **79**, 3089 (1957); C. S. Marvel, P. V. Bonsignore, and S. Banerjee, *J. Org. Chem.*, **25**, 237 (1960).

(7) C. S. Marvel and H. N. Cripps, *J. Polymer Sci.*, **9**, 53 (1952).

(8) L. F. Fieser and E. L. Martin, *Org. Syntheses*, **Coll. Vol. II**, 560 (1943).

(9) J. W. Hill, *J. Am. Chem. Soc.*, **52**, 4110 (1930).

piperidone diacetate was effected with 2.4 g. (0.036 mole) of potassium hydroxide in 25 ml. of 85% ethanol. After stirring at room temperature for 10 hr., the mixture was cooled and acidified with concd. hydrochloric acid to the Congo red paper end point. Evaporation of the solution to one fourth the original volume yielded a white solid which could not be purified by recrystallization.

The polymeric lead mercaptide was prepared from lead diacetate and the dithiol in ethanol. The dithiol was regenerated by bubbling hydrogen sulfide into an ether suspension of the yellow mercaptide, filtration of the lead sulfide, and evaporation of the ether. Recrystallization of the crude solid from cyclohexane yielded 2.0 g. (91%) of the product, m.p. 83.5–85°. The infrared spectrum showed absorption maxima assignable to a δ-lactam (3380, 3080, and 1645 cm.$^{-1}$) and thiol (2550 cm.$^{-1}$).

Anal. Calcd. for $C_{11}H_{21}ONS_2$: C, 53.44; H, 8.50; N, 5.67; S, 25.87. Found: C, 53.17; H, 8.39; N, 5.45; S, 25.98.

Polymerization of 3,6-bis(3-mercaptopropyl)-2-piperidone to the polydisulfide (V). A method similar to that employed by Marvel and Olson[6] and the apparatus and temperature modification reported by Marvel, Bonsignore and Banerjee were utilized. The following procedure was employed in all the oxidative emulsion polymerizations conducted at 77°: 3,6-Bis-(3-mercaptopropyl)-2-piperidone, 2.0 g.; potassium hydroxide, 2.0 g.; lauric acid, C.P., 1.5 g.; distilled water, 25 ml.; selenious acid, 15 mg.; Antifoam A (Dow-Corning), 1 drop.

During all polymerization runs some polymer precoagulated which prevented an accurate recording of the yield. After a 7-day polymerization period, the polymer latices were coagulated by pouring slowly into 600 ml. of 50% aqueous methanol containing approximately 5 ml. of concd. hydrochloric acid. A yellow to pink powdery solid was obtained which was soluble in hot formic acid, hot tetrachloroethane, and a hot 1:1 mixture of chloroform and glacial acetic acid. The polymer was purified by dissolution in hot tetrachloroethane, filtration of the hot solution and reprecipitation into 80% aqueous methanol. A white solid polymer was obtained, m.p. 212–259°. The infrared spectrum showed absorption maxima for a δ-lactam (3380, 3140, 1650, and 960 cm.$^{-1}$).

Anal. Calcd. for $C_{11}H_{19}ONS_2$: C, 53.87; H, 7.75. Found: C, 50.48; H, 7.13.

Upon correction for a water-soluble residue obtained upon combustion of the polymer sample, the analytical values were:

Found: C, 53.58; H, 7.56.

Hydrolysis of polymer to polyampholyte. The method of Marvel and Schniepp[10] for the hydrolysis of 2-piperidone was employed. One-half gram of the polymer was refluxed in 25 ml. of concd. hydrochloric acid for 24 hr. The finely divided polymer remained suspended in part in the acid and with heating changed color to dark brown. The residue was filtered and dried and showed absorption maxima in the infrared which indicated hydrolysis of several isolated lactam functions.

The acid filtrate was evaporated to dryness, and the yellow residue was dissolved in water, decolorized with charcoal, and filtered. Lyophilization of the aqueous solution yielded a white rubbery polymer, m.p. 247–264° (83%) with an inherent viscosity of 0.784 in water. The infrared spectrum showed major absorption maxima for acid (2500–2700, 1705, and 950 cm.$^{-1}$) and amine hydrochloride (3100–3500, 2400–2500, 2050, 1615, 935, and 965 cm.$^{-1}$).

Anal. Calcd. for $C_{11}H_{26}O_4NS_2Cl \cdot 2H_2O$: C, 39.34; H, 7.14. Found: C, 39.82; H, 7.77.

Neutralization of the amine hydrochloride with potassium hydroxide yielded a white rubbery solid which was insoluble in hot water and wet and dry tetrahydrofuran and dioxane.

URBANA, ILL.

---

[10] C. S. Marvel and L. E. Schniepp, *J. Am. Chem. Soc.*, **57**, 1557 (1935).

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Cationic Copolymerization of Some α-Methylstyrenes with Vinyl 2-Chloroethyl Ether. Solvent Effects[1]

C. S. MARVEL AND JAMES F. DUNPHY

Received May 26, 1960

Reactivity ratios for vinyl 2-chloroethyl ether with α-methylstyrene, α,*p*-dimethylstyrene and *p*-methoxy-α-methylstyrene in a cationic system in the solvents benzene and nitrobenzene have been determined. No solvent effect was apparent.

Although it is well known that the rates of cationic homopolymerization of styrene and α-methylstyrene are markedly enhanced by an increase in the dielectric constant of the medium,[2] the relative reactivity ratios of monomer pairs in cationic copolymerization had been shown not to vary with the dielectric constant of the medium. Thus, Overberger, Arond, and Taylor[3] have shown that the composition of the initial copolymer formed in the stannic chloride–initiated copolymerization of styrene and *p*-chlorostyrene is independent of the dielectric constant of the medium. Similar results were obtained using titanium tetrachloride and aluminum bromide.[4] It was suggested that the lack of solvent effects was due to the similarity in structure of the monomers studied. The concept

---

[1] This is a partial report of work done under contract with three Utilization Research and Development Divisions, Agricultural Research Service, U. S. Department of Agriculture, and authorized by the Research and Marketing Act. The contract was supervised by Dr. J. C. Cowan of the Northern Division. This paper is based on portions of a thesis submitted by James F. Dunphy to the Graduate College of the University of Illinois in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

[2] D. C. Pepper, *Nature*, **158**, 789 (1940); D. C. Pepper, *Trans. Faraday Soc.*, **45**, 397 (1949).

[3] C. G. Overberger, L. H. Arond, and J. J. Taylor, *J. Am. Chem. Soc.*, **73**, 5541 (1951).

[4] C. G. Overberger, R. J. Ehrig, and D. Tanner, *J. Am. Chem. Soc.*, **76**, 772 (1954).