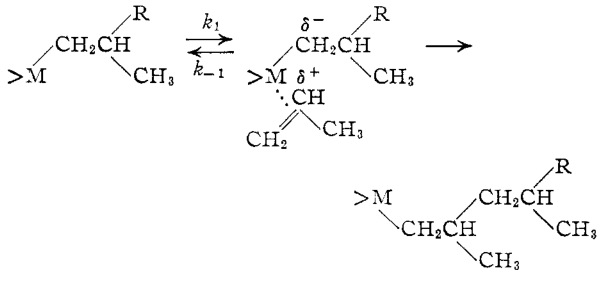
By analogy, one may suggest that the new contribution to olefin polymerization which makes possible "isotactic" polymers of propylene and styrene,[3] is similar utilization of the type of mechanism proposed by Fontana,[15] but at a heterogeneous surface site (or other sterically-restricted center) where the steric requirements are so rigid as to orient the new asymmetric center to the same configuration as its predecessor.[18,19]



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[18] J. C. Bailar, Jr., H. B. Jonassen and A. D. Gott (THIS JOURNAL, **74**, 3132 (1952)), report the partial resolution of a racemate depending on the difference in ease of coördination of enantiomorphs with asymmetric inorganic complexes.

[19] The nomenclature and classification of the course of a polymerization proceeding *via* the mechanism we propose is worthy of some consideration. Viewed from the growing polymer chain, the process would appear to be base-catalyzed or anionic. Viewed from the monomer molecule, a key step is the coördination with a Lewis acid center, suggesting acid-catalyzed or cationic character. Actually, the process as suggested would be coöperative; we suggest it be called "coördinate propagation."

PHILADELPHIA, PA.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, INSTITUTE OF POLYMER RESEARCH, POLYTECHNIC INSTITUTE OF BROOKLYN]

Preparation of *p*-Vinylphenyl Thioacetate,[1] its Polymers, Copolymers and Hydrolysis Products. Water-soluble Copolymers Containing Sulfhydryl Groups[2]

BY C. G. OVERBERGER AND ALEXANDER LEBOVITS

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The preparation of *p*-vinylphenyl thioacetate is described. This monomer was polymerized and copolymerized with methyl methacrylate by free radical catalysis. After hydrolysis, polymers soluble in base were obtained which were precipitated by acids and oxidizing agents. This oxidation could be reversed by thioglycolate ion or cysteine in strong alkaline solution. In addition it was found that the hydrolyzed copolymer could reactivate urease which had been inactivated by iodine oxidation at a similar rate as that determined with thioglycolic acid.

A number of polymers having oxidation–reduction properties have been reported recently in the literature.[3,4] The object of this investigation was the preparation of soluble polymers having oxidation–reduction properties. Such polymers would be expected to be soluble in organic solvents as well as aqueous base and their solubility would decrease on oxidation or acidification. In the former case the decrease in solubility is due to cross-linking of the thiol groups of two polymer chains forming disulfide bridges. If it is remembered that it takes only two thiol groups on a polymer chain to be oxidized—provided that the disulfide link is intermolecular—to form a cross-link, it would be expected that a small degree of oxidation will render the polymer insoluble. It has been reported that polyvinyl mercaptan is insoluble and infusible,[5] and such insolubility has actually been observed by us and by Gregor, *et al.*,[6] who prepared this polymer in a different way. On the other hand the possibility exists that oxidation will lead to some intramolecular disulfide formation which will not decrease the solubility appreciably.

The poly-*p*-thiolstyrene was precipitated from its basic solution on acidification. Introduction of carboxyl groups by copolymerization has been observed to counteract this effect, and thus polymer solutions could be obtained at a suitable *p*H for use in a study of their effect on radiation and reactivation of deactivated urease.

One of the difficulties in preparing monomeric *p*-thiolstyrene was the very likely addition of the sulfhydryl group across a styrene double bond,[7] which would interfere with the synthesis and normal polymerization. To circumvent this difficulty the thiol group was protected by acetylation prior to introduction of the double bond, and liberated by hydrolysis after polymerization.

p-Vinylphenyl thioacetate (I) was prepared by the following scheme. *p*-Aminoacetophenone (II) was diazotized and allowed to react with potassium ethyl xanthate. The intermediate xanthate ester III was not isolated but reduced directly with sodium borohydride in alcohol solution followed by saponification to give *p*-thiol-α-methylbenzyl alcohol (IV) in 66% yield. Although III has been reported previously[8] as an intermediate for *p*-thiolacetophenone (V), the preparation of III and IV is given here in detail, since minor deviation from the procedure has resulted in low yields or in total failure to obtain IV. IV was converted to the

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[1] This is the 12th in a series of articles concerned with the synthesis of monomers and their polymerization; for the previous paper in this series, see C. G. Overberger and L. C. Palmer, THIS JOURNAL, **78**, 666 (1956). For a preliminary report of this work, see C. G. Overberger and A. Lebovits, *ibid.*, **77**, 3675 (1955).

[2] This paper comprises a portion of a thesis presented by Alexander Lebovits in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Graduate School of the Polytechnic Institute of Brooklyn.

[3] H. G. Cassidy, M. Ezrin and I. H. Updegraff, THIS JOURNAL, **75**, 1615 (1953).

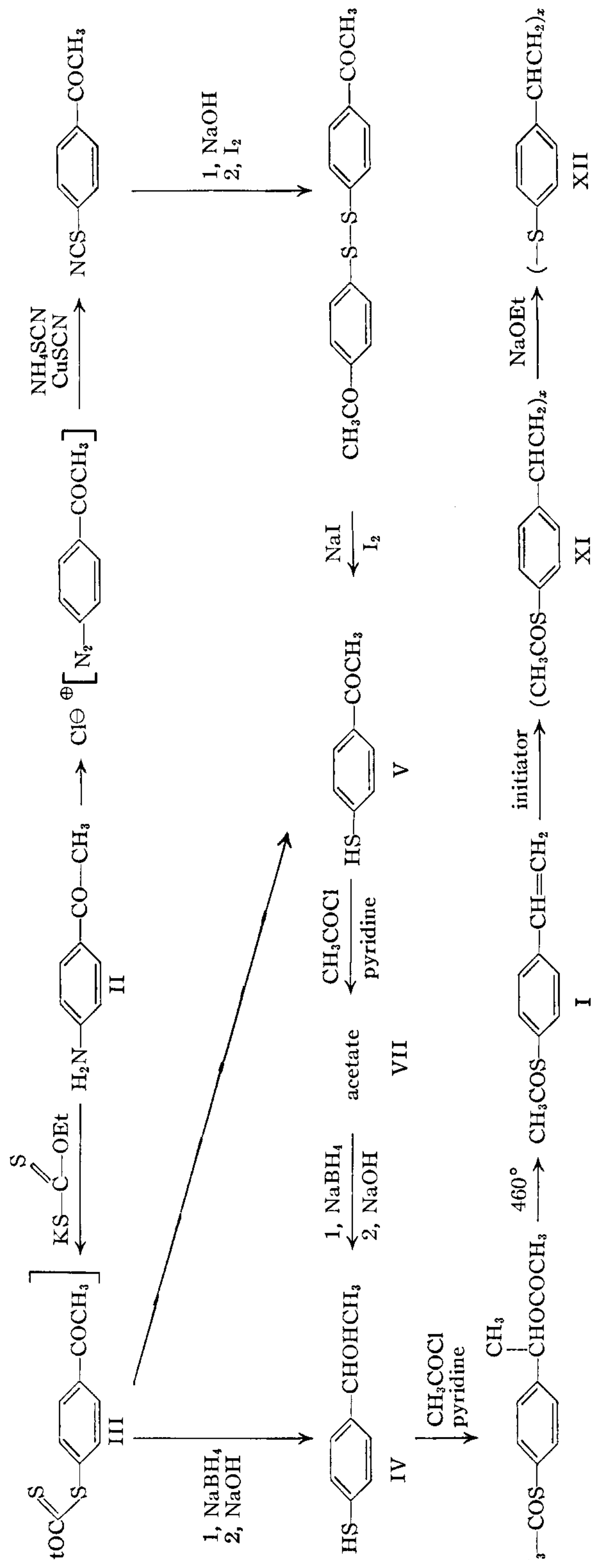
[4] G. Manecke, *Z. Elektrochem.*, **58**, 369 (1954).

[5] M. M. Brubaker, U. S. Patent 2,378,536 (June 19, 1945).

[6] H. P. Gregor, D. Dolar and G. K. Hoeschele, THIS JOURNAL, **77**, 3675 (1955).

[7] F. Ashworth and G. N. Burkhardt, *J. Chem. Soc.*, 1791 (1928); T. Posner, *Ber.*, **38**, 646 (1905).

[8] G. Schwarzenbach and E. Rudin, *Helv. Chim. Acta*, **22**, 360 (1939).



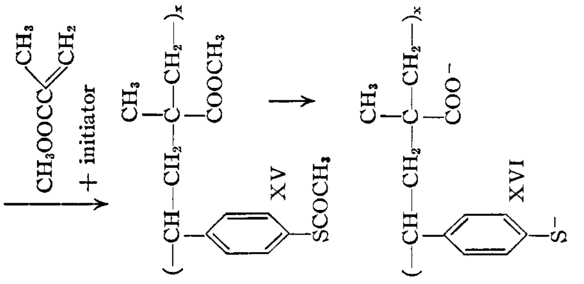
diacetate VI in 90% yield by allowing it to react with acetyl chloride and pyridine in ether solution. VI was converted to I by cracking in a column packed with Raschig rings at 460° in 51% yield, some of VI being recovered and some monomer being lost due to polymerization.

An attempt was made to reduce V to IV with lithium aluminum hydride and with sodium borohydride. In the former case only polymers were obtained and in the latter the reduction was incomplete. The close boiling points of IV and V as well as VI and *p*-acetylphenyl thioacetate (VII) made fractional distillation a poor method for obtaining V or VI pure from an incomplete reduction. It was possible to reduce VII however to give, on hydrolysis, IV in moderate yield and thus the direct reduction of III was attempted and adapted for the large scale preparation of IV.

An unsuccessful attempt to prepare IV was made by allowing *p*-acetylphenyl thiocyanate to react with alcoholic base. Upon oxidation with iodine, 4,4′-diacetyldiphenyl disulfide (IX) was obtained in impure form. Because of the low over-all yield this method was not further investigated. A crude sample of IX has been described previously in the literature.[9] The sample reported here was found to have a considerably higher melting point.

As an alternate route *p*-ethylphenyl thiobenzoate was prepared and bromination at the α-carbon of the side chain attempted. The reaction product, however, could not be obtained pure and an attempted dehydrobromination of the impure material resulted only in polymer formation. Bis-*p*-ethylphenyl disulfide was prepared and characterized in this series of reactions.

The monomer was polymerized using azo-bis-isobutyronitrile (X) as the initiator. Saponification of a polymer sample having the intrinsic viscosity 0.124 in benzene gave poly-*p*-thiolstyrene (XII) which was partially soluble in benzene, cyclohexanone and base, and did not melt when heated to 360°. The chemical properties of the hydrolyzed polymer are described in the Experimental section.



I was copolymerized with methyl methacrylate (XIII) in a 44.6–55.4 mole % mixture using the azo-bis-isobutyronitrile as the initiator to a conversion of about 15%. On hydrolysis of the copolymer a solution was obtained which could be neutralized without formation of a precipitate provided the solution was dilute. In 1.5% solution, a clear solution could only be obtained above a *p*H of 10. Properties of this copolymer are described in the Experimental section.

The thiol group is known to be responsible for the activity of a number of enzymes.[10] Thus, reaction of the thiol group has been demonstrated in urease, an enzyme which acts specifically on urea,

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[9] H. Burton and P. F. Hu, *J. Chem. Soc.*, 178 (1949).

[10] J. B. Sumner and K. Myrbäck, "The Enzymes," Vol. I, Academic Press, Inc., New York, N. Y., 1951, pp. 325, *et seq.*

converting the latter to ammonium carbonate.[11] It has long been known[12] that destruction of the thiol group, *e.g.*, by mild oxidation or combination with heavy metals renders the enzyme inactive and this inactivation can be partially reversed by mild reducing agents such as cysteine, thioglycolate, glutathione, etc.

In our work the capability of the polymer to reactivate oxidized urease was studied and compared to that of thioglycolate ion. The method of determining the urease activity was similar to the colorimetric method of Van Slyke and Archibald.[13] Table I summarizes some results which were characteristic.

TABLE I

INACTIVATION AND REACTIVATION OF UREASE[a]

		Mmole per g. urease					
Urease soln.	Total urease (mg.)	Iodine	Thioglycolate	Polymer SH groups	React. time (sec.)	Sumner units per mg.	Exp.
Ue-1[b]	20	...	...	..	260	0.346	1
Ue-2[c]	14.6	0.05	...	..	>5040	< .0245	2
Ue-2	14.6	.05		*ca.* 0.6[k]	>3420	< .036	3
Ue-3[d]	34	...	...	..	150	.354	4
Ue-3	34	...	...	..	142	.373	5
Ue-4[e]	23	.043	...	..	5400[12]	.00144	6
Ue-4	23	.043	...	..	50000	.00156	7
Ue-5[f]	13.5	.043	3.6[i]	..	2100[l]	.0064	8
Ue-5	11.2	.043	3.6[j]	..	985	.163	9
Ue-5	11.2	.043	3.6[j]	..	107[l]	.15	10
Ue-6[g]	14.2	.043	0.71[j]	..	1740	.073	11
Ue-6	14.2	.043	0.71[j]	..	180[l]	.07	12
Ue-7[h]	10.8	.043		0.6[j]	1530	.109	13
Ue-7	10.8	.043		0.6[j]	115[l]	.145	14

[a] The experiments were carried out at 29.8° and the distilled water used to make solutions coming in contact with urease was redistilled from an all glass apparatus. [b] Ue-1: 42 mg. of $NaH_2PO_4 \cdot H_2O$, 46 mg. of Na_2HPO_4 and 0.4 g. of urease were dissolved in water and diluted to 5.4 g. [c] Ue-2; solution Ue-2: 2.45 g. was combined with 1 ml. 0.00874 *N* iodine. [d] Ue-3; urease, 0.9 g. and 15 mg. of Na_2HPO_4 was dissolved in water and diluted to 9 ml. [e] Ue-4; solution Ue-3, 6.62 g. was combined with 3.2 ml. of 0.00874 *N* iodine. [f] Ue-5; solution Ue-4, 1.36 g. was combined with 0.5 g. of a *ca.* 0.655 *N* sodium thioglycolate solution. [g] Ue-6; solution Ue-4, 1.02 g. was combined with 75 mg. of a *ca.* 0.655 *N* sodium thioglycolate solution. [h] Ue-7; solution Ue-4, 0.7 g. was combined with 0.7 g. of a polymer solution prepared from hydrolysis of 292 mg. copolymer (sample IX) and diluted to 25 ml. [i] The urease activity was determined immediately after adding the sodium thioglycolate. [j] The solutions were allowed to stand overnight after adding the reactivating agent, before the urease activity was determined. [k] Ten drops of a hydrolyzed copolymer solution (from sample IX) equivalent to 1 ml. of 0.00874 *N* iodine were added to the urea buffer and the control buffer before adding the urease solution. [l] The urea buffer used was one-tenth as strong with respect to phosphate buffer as the urea buffer used in the rest of the experiments. In calculating the activity the assumption was made that the color change was ten times as fast.

Table I shows that the activity of urease deactivated with iodine to 0.4% of its original activity (exp. 5–7) can be restored to an appreciable extent with the copolymer and with thioglycolate ion, and that this restoration is of the same order of magnitude provided similar concentrations are used (exp. 11–14). This restoration of activity was not instantaneous and occurred only after standing (exp. 3 and 8 compared to 9, 10, 13 and 14). Even if excess thioglycolate ion was used the degree of activation was dependent on the amount (exp. 9–12).

The partial irreversibility of the inactivation has been observed previously.[12] Our results demonstrate that the copolymer is a strong enough reducing agent to act on the biological system, and that the incorporation of the thiol groups in the polymer chain does not interfere appreciably, if at all, with the accessibility of the deactivated centers to the segments of the polymer chain bearing the thiol groups.

The polymer chain, on acting as a reducing agent, is oxidized and forms disulfide linkages. Since each molecule of urease contains 31 thiol groups[14] a number of these should be expected, from pure statistical reasons, to be attached to polymer chains by disulfide formation, provided that such a disulfide linkage is not energetically unfavored compared to a polymer–polymer disulfide linkage. Such an attachment of polymers and enzyme at the active centers of the latter could interfere with the latter's action. Our data indicate that any such interference is of a minor nature.

One of the toxic effects of X-rays is their capability to deactivate sulfhydryl enzymes. This is believed to occur by oxidation with OH radicals produced from ionizing water.[15] The capability of our polymer to reactivate urease suggests that it might be an effective protecting agent against radiation, as cysteine is known to be. An advantage over cysteine would be the high molecular weight which would not allow excretion by the kidneys making the protection a more permanent one. It is our plan to explore these possibilities. Preliminary results in this direction are positive and will be reported separately.

Experimental

***p*-Thiolacetophenone.**—The general procedure of Leuckart[16] was used although specific details are lacking; these can be obtained by writing the senior author. The reaction between the xanthate solution and the diazonium salt solution was carried out in small portions in order to reduce the explosion hazard.[17]

To a solution of 150 g. of crude ethyl *p*-acetylphenylxanthate (from 270 g. (2 moles) of *p*-aminoacetophenone) in alcohol was added an aqueous solution 70 g. (1.75 moles) of sodium hydroxide and the alcohol distilled off at atmospheric pressure. The clear dark-brown mercaptide solution which resulted was acidified with sulfuric acid and the liberated mercaptan extracted with ether, the ether extract washed with water and dried over anhydrous magnesium sulfate. The residue was distilled through a Vigreux column, 61.8 g. (57% based on *p*-aminoacetophenone), m.p. 27°.[18] On redistillation, 57.8 g. was obtained, b.p. 140.5–141° (11 mm.), $n^{30.7}_D$ 1.6182, m.p. 27.7–29° (b.p. 142° (11 mm.), prepared by a similar method[8]).

Anal.[19] Calcd. for C_8H_8OS: C, 63.13; H, 5.30; S, 21.06. Found: C, 63.06; H, 5.40; S, 21.12.

Acetylation of *p*-Thiolacetophenone.—To an ethereal solution of 12.9 g. (0.085 mole) of *p*-thiolacetophenone and 11 g. (0.14 mole) of acetyl chloride was added with external

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[11] Ref. 10, pp. 873, *et seq.*

[12] L. Hellerman, M. E. Perkins and W. A. Clark, *Proc. Natl. Acad. Sci., U. S.*, **19**, 855 (1933).

[13] D. D. Van Slyke and R. M. Archibald, *J. Biol. Chem.*, **154**, 623 (1944).

[14] J. B. Sumner and L. O. Poland, *Proc. Soc. Exptl. Biol. Med.*, **30**, 553 (1933).

[15] A. Hollaender, "Radiation Biology," Vol. I, McGraw-Hill Book Co., New York, N. Y., 1954, pp. 256, 274.

[16] R. Leuckart, *J. prakt. Chem.*, [2] **41**, 179 (1890).

[17] K. H. Saunders, "The Aromatic Diazo Compounds and their Technical Application," Edward Arnold and Co., London, 1949, p. 326.

[18] All melting points are corrected.

[19] Analyses by Dr. K. Ritter, Basel, Switzerland; Dr. F. Schwarzkopf, New York, N. Y.

cooling in Dry Ice, 12 g. (0.152 mole) of pyridine. After standing 5–10 minutes at 35° the reaction product was cooled, water added and the organic layer washed with dilute alkali until the wash alkali remained alkaline to phenolphthalein and the product was worked-up in the usual manner, to give on distillation 14.8 g. of *p*-acetylphenyl thioacetate, b.p. 165–168° (VII) (89.7%). This solid was recrystallized twice from alcohol; m.p. 62.5–63.5°.

Anal. Calcd. for $C_{10}H_{10}O_2S$: C, 61.83; H, 5.19. Found: C, 61.81; H, 5.09.

Reduction of *p*-Acetylphenyl Thioacetate with Sodium Borohydride.—To an alcoholic solution of 8.7 g. (0.045 mole) of *p*-acetylphenyl thioacetate at 26° was added an alcoholic solution of 1.3 g. (0.034 mole) of sodium borohydride at the same temperature. A temperature rise of 6° was noted within one-half minute. Four more grams of sodium borohydride and 65 ml. of 2 *N* sodium hydroxide were added with cooling, the solution heated for a short time and allowed to stand overnight. Water was added, the alcohol removed at reduced pressure, the solution filtered, acidified and extracted with ether. The ether extract was washed with water and dried. On distillation 4.6 g. of *p*-thiol-α-methylbenzyl alcohol (IV) was obtained, b.p. 136.5–139.5° (9 mm.), $n^{26.7}D$ 1.5885 (66.5%).

The reduction could be carried out directly on the crude xanthate. Crude ethyl 4-acetylphenyl xanthate, 192 g. (420 g. obtained from 270 g. *p*-aminoacetophenone) was dissolved in 146 g. of warm alcohol, and to the slurry forming on cooling, 300 ml. of a solution of 16.1 g. (0.4 mole) of sodium borohydride in 500 ml. of ethanol was added with stirring and cooling below 20°. The solution was heated to 40°, cooled to 10°, the remainder of the sodium borohydride added, followed by a solution of 90 g. (2.25 moles) of sodium hydroxide in 250 ml. of water, followed by 300 ml. of water. The alcohol was removed at reduced pressure until the b.p. reached 45° at 80 mm., the residue washed with ether and added with cooling by Dry Ice to a solution of 130 g. (1.32 moles) of sulfuric acid in 400 ml. of water, at such a rate that the temperature did not rise above 20°. The mercaptan formed was extracted three times with ether, each ether extract washed three times with water, and the combined ethereal solution (1500 ml.) dried over anhydrous magnesium sulfate. The residue was distilled from a modified Claisen flask at a rate of distillation as rapid as possible, to give 92.4 g. (66% based on *p*-aminoacetophenone) of distillate, b.p. 130–180° (1.5–2.5 mm.), $n^{25.8}D$ 1.5911, residue, 15.9 g.

Combination of this distillate with other preparations and fractionation gave pure material which solidified on standing, m.p. 45.2–46.6°, $d^{25.5}{}_4$ of the supercooled liquid 1.1408.

An analytical sample, $n^{25.5}D$ 1.5880, was prepared from a different experiment.

Anal. Calcd. for $C_8H_{10}OS$: C, 62.30; H, 6.54; S, 20.79. Found: C, 62.23; H, 6.68; S, 20.90.

α-Acetoxy-*p*-ethylphenyl Thioacetate.—The acetylation procedure described for *p*-acetylphenyl thioacetate was employed using 26.7 g. (0.174 mole) of *p*-thiol-α-methylbenzyl alcohol, 35.1 g. (0.45 mole) of acetyl chloride and 35 g. (0.44 mole) of pyridine. Fractionation of the 37.3 g. (90%) of crude diacetate gave 22.9 g. (55.5%) of pure product, b.p. 174–175° (9 mm.), $n^{19}D$ 1.5452, $d^{25.1}{}_4$ 1.1460. The infrared spectrum showed strong carbonyl peaks at 5.7 and 5.8 μ and no SH peak in the 3.9 μ area.

Anal. Calcd. for $C_{12}H_{14}O_3S$: C, 60.48; H, 5.92; S, 13.45; sapon. equiv., 238. Found: C, 60.42; H, 5.81; S, 13.56; sapon. equiv., 240, 239.

A special procedure was used to determine the saponification equivalent. A sample of accurately known weight was heated to 110–130° in ethylene glycol with a known amount of base for ten minutes and titrated back with standard acid followed by standard iodine (indicators—phenolphthalein and starch). The difference divided by the weight of the sample was taken as the neutralization equivalent.

***p*-Vinylphenyl Thioacetate.**—A method similar to that of Overberger, *et al.*, was used.[20]

Sixty-five grams (0.27 mole) of α-acetoxy-*p*-ethylphenyl thioacetate was passed through the apparatus[20] in a nitrogen atmosphere at 460° and a dropping rate of 30–50 drops per minute to give 61 g. of pyrolysate which was distilled through a Vigreux column. The second of four fractions, 24.9 g. (51%) boiled at 100–116° (0.9–1.5 mm.), $n^{25}D$ 1.5967.

Redistillation of the second fraction twice, the second time without inhibitor, gave 21.5 g., b.p. 103–110° (0.8 mm.), $n^{25}D$ 1.5985.

An analytical sample obtained by a rapid flash distillation boiled at 103–117° (0.6 mm.), $n^{25.3}D$ 1.5992, $d^{25.5}{}_4$ 1.0953.

The infrared spectrum showed peaks at 5.85 μ (C=O) and at 10.55 and 10.95 μ (vinyl double bond) and no SH peak in the region of 3.9 μ. The ultraviolet spectrum showed a maximum at 265 mμ.

Anal. Calcd. for $C_{10}H_{10}OS$: C, 67.38; H, 5.66; S, 17.99. Found: C, 67.51; H, 5.44; S, 18.28.

***p*-Thiocyanoacetophenone (VIII).**—To an aqueous solution of 3.1 g. (0.023 mole) of *p*-aminoacetophenone and 5 ml. of concd. sulfuric acid was added 1.6 g. (0.023 mole) of sodium nitrite. To the resulting diazo salt solution, 1 g. of urea and 4 g. of ammonium thiocyanate were added, the solution cooled to −5° and 4 g. of cuprous thiocyanate added whereupon a brown cake formed with evolution of nitrogen. After standing overnight the supernatant layer was extracted with ether and discarded and the brown solid extracted with hot ether, benzene and again with ether. The combined organic layer was washed with water and dried to give 3.2 g. of residue. This was extracted with two 12-g. portions of ether, and the residue sublimed to give 1.335 g. Resublimation gave 1.255 g., m.p. 67–80°, and recrystallization from alcohol gave 685 mg. (17%), m.p. 80.5–81.5° (m.p. 82°, 28%, from diazotized *p*-aminoacetophenone, potassium thiocyanate and cobaltous chloride[21]).

4,4′-Diacetyldiphenyl Disulfide. A. From *p*-Thiolacetophenone.—A solution of 3.502 g. (0.023 mole) of *p*-thiolacetophenone in alcoholic base was oxidized with an aqueous iodine solution, and the excess iodine destroyed with sodium bisulfite. On addition of water, removal of the solid by filtration and recrystallization from alcohol, 2.75 g. (79%) of crystals in the form of colorless leaflets were obtained, m.p. 97.1–98.8°; recrystallization from benzene followed by recrystallization from alcohol raised the m.p. to 98.8–99.8° (m.p. 92–93°, diazotized *p*-aminoacetophenone, potassium ethyl xanthate, followed by base and ferric chloride in acetic acid[9]).

Anal. Calcd. for $C_{16}H_{14}O_2S_2$: C, 63.54; H, 4.67. Found: C, 63.62; H, 4.71.

B. From *p*-Acetylphenyl Thiocyanate.—To an alcoholic solution of 786 mg. (0.0045 mole) of *p*-acetylphenyl thiocyanate an aqueous solution 5.6 g. (0.14 mole) of sodium hydroxide was added in the cold, the solution diluted with water, neutralized and oxidized with an iodine solution. The brown precipitate which formed was removed by filtration and recrystallized from alcohol, 320 mg. (47.8%), brown leaflets, m.p. 96.8–98.8°; a mixed melting point with a sample prepared by method A, m.p. 96.3–97.8°, melted at 96.3–97.3°.

***p*-Ethylphenylthiol.**—By a method similar to that employed by "Organic Syntheses"[22] for making thiophenol, *p*-ethylphenylthiol was prepared (63%), b.p. 103–105° (25 mm.) (b.p. 207–209° (730 mm.) from crude ethylbenzenesulfonyl chloride, zinc dust and sulfuric acid).[23]

***p*-Ethylphenyl Thiobenzoate (XVII).**—The procedure of Schiller and Otto[24] for preparing *p*-methylphenyl thiobenzoate was employed. The product, after crystallization from methanol, was obtained in 63.4% yield, and melted at 68.7–71.0°. The m.p. could be raised to 70.5–71° by repeated recrystallization from methanol and ether.

Anal. Calcd. for $C_{15}H_{14}OS$: C, 74.34; H, 5.82. Found: C, 74.46; H, 5.92.

A comparison of the melting point with that of the *ortho*, *meta* and *para* isomers of ethylphenyl benzoate, 38°,[25] 52°,[25] and 59°,[25] *p*-methylphenyl benzoate (71.5°)[26] and *p*-methyl-

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[20] C. G. Overberger, A. Fischman, C. W. Roberts, L. H. Arond and J. Lal, THIS JOURNAL, **73**, 2540 (1951).

[21] E. Schraufstätter and S. Deutsch, *Z. Naturforsch.*, **3B**, 430 (1948).

[22] R. Adams and C. S. Marvel, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1932, p. 504.

[23] C. Hansch and W. A. Blondon, THIS JOURNAL, **70**, 1561 (1948).

[24] R. Schiller and R. Otto, *Ber.*, **9**, 1634 (1876).

[25] A. Behal and E. Choay, *Bull. soc. chim. France*, [3] **11**, 206 (1894).

[26] A. Behal and E. Choay, *ibid.*, [3] **11**, 602 (1894).

phenyl thiobenzoate (76°)[24] suggests strongly that the compound is the *para* isomer.

Bis-*p*-ethylphenyl Disulfide.—To a hot alcoholic solution of 16.8 g. (0.07 mole) of *p*-ethylphenyl thiobenzoate was added a solution of 5.9 g. (0.147 mole) of sodium hydroxide in 10 ml. of water. After dilution and washing with ether to remove unchanged ester an iodine solution containing 8.2 g. (0.032 mole) of iodine was added dropwise, the disulfide extracted with ether, washed with base followed by water and dried over anhydrous magnesium sulfate, 7.9 g. (83%), b.p. 187–195° (1.2–1.4 mm.). The third of four fractions obtained on redistillation, b.p. 157–160° (0.2 mm.), $n^{25.8}_{D}$ 1.6175, m.p. 23.4–24.3, was submitted for analysis.

Anal. Calcd. for $C_{16}H_{18}S_2$: C, 70.02; H, 6.61. Found: C, 69.66; H, 6.68.

Poly-*p*-vinylphenyl Thioacetate.—An evacuated sealed tube containing 1.082 g. of *p*-vinylphenyl thioacetate and 23 mg. of 2,2′-azo-bis-isobutyronitrile, was heated to 73 ± 5° for about two hours. The contents of the tube were dissolved in 30 ml. of benzene and precipitated by dropwise addition of the benzene solution to 300 ml. of methanol. The precipitate formed was filtered, dissolved in benzene and reprecipitated to give 0.9 g. after drying, $[\eta]$, 0.305 (sample I).

Anal. Calcd. for $(C_{10}H_{10}OS)_x$: C, 67.38; H, 5.66. Found: C, 67.16; H, 5.67.

In a similar experiment in which 5.185 g. of monomer and 418 mg. of catalyst were used, 3.5 g., $[\eta]$ 0.124 (benzene), was obtained after two precipitations in methanol (sample II).

Poly-*p*-thiolstyrene.—A benzene solution of 760 mg. of poly-*p*-vinylphenyl thioacetate, sample II, was added dropwise to a boiling lithium ethoxide solution prepared from 89 mg. of lithium metal and 25 ml. of alcohol. The resulting clear yellow mercaptide solution was distilled to remove benzene as the azeotrope, and distilled water which had been boiled to remove dissolved oxygen was added, whereupon a precipitate formed which dissolved on addition of more water. The alcohol was removed and the mercaptide solution was added dropwise with vigorous stirring to dilute hydrochloric acid. The precipitate formed was filtered and dried in a desiccator at 0.2 mm. at room temperature to constant weight, to give 501 mg. (86.5%). This polymer was partially soluble in benzene, cyclohexanone and thiophene, from which solutions it was precipitated by petroleum ether or iodine solution.

A sample consisting of 250 mg. was suspended in 15 ml. of benzene, and after an hour standing the insoluble residue removed by filtration and found to be 10 mg. after drying. The intrinsic viscosity of the soluble 240 mg. was 0.09 (benzene).

An analytical sample was prepared by drying 42 mg. at 180° and 0.35 mm. for three minutes. The sample did not melt when heated to 360°.

Anal. Calcd. for $(C_8H_8S)_x$: C, 70.54; H, 5.92. Found: C, 70.41; H, 6.09.

In a similar experiment a portion of sample I was saponified with sodium ethoxide, and the distilled water used was not boiled to remove oxygen. The poly-*p*-thiolstyrene after drying was insoluble in base and organic solvents, and did not melt on heating to 360°.

Reaction of Poly-*p*-thiolstyrene.—Poly-*p*-vinylphenyl thioacetate, 232 mg., sample II, was saponified as described above with sodium ethoxide containing 104 mg. (0.0045 g. atom) of sodium. To the aqueous sodium polymercaptide solution (*ca.* 40 ml.) resulting from distilling off the organic solvents, Dry Ice was added causing precipitate formation and a *p*H drop to 9. On addition of 1 ml. of 2 *N* base a *p*H of 10 was obtained and solution occurred. The solution was diluted to 50.3 ml. (solution P-1).

Solution P-1, 1 ml., was diluted to 50 ml. which caused a precipitate to form which did not dissolve in bicarbonate, but dissolved on addition of two pellets of sodium hydroxide, which caused a *p*H of 10. Dry Ice addition caused precipitate formation and drop in *p*H to 7.5–8.

Solution P-1, 2 ml., was diluted to 15 ml. and oxidized with 0.1 *N* iodine. The first drop caused only a slight opalescence but no precipitate and oxidation was complete after adding ten drops (0.55 ml.). One additional drop of iodine was added to assure complete oxidation followed by six pellets of sodium hydroxide and two drops (*ca.* 69 mg.) of thioglycolic acid. After refluxing for three minutes the precipitate dissolved.

In a similar experiment the brown precipitate formed on oxidizing 1 ml. was discolored by adding a second milliliter of polymer solution. On oxidation and boiling five minutes with seven pellets of sodium hydroxide no solution occurred, as indicated by the failure of the filtrate to give a precipitate on acidification. A portion of the suspension could be reduced on boiling with two drops of thioglycolic acid.

In a similar experiment 65 mg. of cysteine hydrochloride was substituted for thioglycolic acid. Complete solution occurred only after 20 minutes of refluxing.

Copolymerization of *p*-Vinylphenyl Thioacetate with Methyl Methacrylate.—*p*-Vinylphenyl thioacetate (I) was copolymerized with methyl methacrylate using azo-bis-isobutyronitrile as initiator in the presence or absence of chain transfer agents. The conversion was high except for sample III. Some typical experiments are summarized in Table II.

TABLE II

COPOLYMERIZATION OF *p*-VINYLPHENYL THIOACETATE WITH METHYL METHACRYLATE

Sample	I, g.	Methyl metha-crylate, g.	Cat., mg.	Carbon tetra-chloride, g.	Time of polym. (min.)	Temp. of polym.	$[\eta]$
III[a]	1.135[b]	0.793[c]	11.2	...	5	95	0.25
IV	1.625	.318	20.4	...	26	95	...
V	0.293	.318	3	...	900	85	1.17[d]
VI	.321	.356	3.4	0.142	900	85	0.308[d]
VII	.288	.313	3	0.325	900	85	.119[d]
VIII	3.281	2.348	44	3.575	160	82	.23
IX	1.251	0.730	10.8	Toluene 0.909	60	95	.245

[a] The conversion was only 14.4% and the mole fraction of I in the copolymer was 0.525. *Anal.* Found: S, 11.93. [b] 0.00638 mole. [c] 0.00793 mole. [d] The polymer was not isolated and the value reported is the inherent viscosity based on the total weight of monomers charged.

Hydrolysis of Copolymer.—The copolymer, sample VIII, 4.119 g., was saponified by adding it in powder form (from the methanol precipitation) to a boiling solution of sodium ethoxide prepared from 1.6 g. (0.07 g. atom) of sodium and distilling off the alcohol after adding distilled water. Neutralization with 5 ml. of 5 *N* hydrochloric acid followed by standing overnight in a carbon dioxide atmosphere, resulted in a *p*H drop to 7 and precipitate formation. This precipitate dissolved only on raising the *p*H to 10 (total volume 200–250 ml.). If this solution was diluted tenfold, no precipitate occurred on neutralization with acid to a *p*H 7–8. This solution, containing *ca.* 0.0001 mole of chloride ions, 0.00005 mole of acetate ions, 0.00005 mole of thiol groups, 0.00006 mole of carboxyl groups, 0.000375 mole of sodium ions per milliliter and some carbon dioxide was sent to Dr. Hollaender for investigation as a prophylactic against ionizing radiation. These positive results will be reported elsewhere.

The copolymer, sample IX, 140.8 mg., was saponified by dropping its benzene solution into sodium ethoxide prepared from 60 mg. of sodium. The organic solvents were distilled off and Dry Ice was added, reducing the *p*H to 8.5 and the solution diluted to 25 ml. (solution P-2).

Reactions of the Hydrolyzed Copolymer.—To a 1 ml. solution of P-2 diluted to 5 ml., 0.2 ml. of 0.1 *N* iodine was added. The precipitate formed did not dissolve in the cold in ten minutes on addition of four pellets of sodium hydroxide and 250 mg. of cysteine hydrochloride. Solution occurred on heating to reflux.

In a similar experiment two drops of thioglycolic acid were substituted for cysteine hydrochloride. Solution occurred on warming as the temperature reached 80°.

Cysteine hydrochloride, 240 mg. (0.00152 mole), was oxidized with 13.5 ml. of 0.1 *N* iodine, the resulting blue starch-iodine color discharged with a speck of cysteine hydrochloride, neutralized to phenolphthalein and diluted with water to 16 g. A potassium bicarbonate solution containing 2.3 g. of solution P-2 was divided in two parts to one of which 1 ml. of the above cystine solution was added. On heating, a precipitate formed in the cystine containing portion but not in the control. This precipitate did not dissolve when

0.7 ml. of 2 *N* base was added beyond the point of neutralization with phenolphthalein as the indicator.

The copolymer, sample IX, 185 ml. was added dropwise in benzene solution to alcoholic sodium ethoxide from 120 mg. sodium, water was added, followed by one pellet of sodium hydroxide, and the organic solvents distilled off. After adding 1 ml. of 5 *N* hydrochloric acid the solution was diluted to 25 ml. (solution P-3).

A small part of this solution was used for studies with urease. The remainder of this solution was kept in a closed volumetric flask and gelled after seven days. The gel had a sauce-like consistency after shaking. Addition of one pellet of sodium hydroxide and heating for two hours in boiling water did not cause solution (*p*H 11). After two days standing, ten drops of thioglycolic acid and two pellets of sodium hydroxide were added and solution occurred almost immediately in the cold.

A similar solution was prepared using 189 mg. of copolymer IX, 70 mg. of sodium and 13 drops of 5 *N* hydrochloric acid (solution P-4, 25 ml., *p*H 9–10).

Sixteen drops (0.4 g.) of this solution were diluted and oxidized with 25 drops (*ca.* 1.45 g.) of 0.00874 *N* iodine, of which the first sixteen caused no precipitation, the next three a slight turbidity, and the next three a definite turbidity. The last two drops caused a precipitate and a blue starch–iodine color.

A similar solution was prepared from 292 mg. of copolymer IX and 69 mg. of sodium (solution P-5, 25.5 ml.).

Two milliliters of this solution was oxidized with 5.2 ml. of 0.00874 *N* iodine solution in the presence of bicarbonate. The precipitate formed did not dissolve when boiled for one hour with 28 drops of *ca.* 0.7 *N* sodium thioglycolate and the filtrate gave no precipitate on acidification. A portion of the suspension dissolved on adding six pellets of sodium hydroxide and refluxing.

Reaction of Deactivated Urease with Polymers.—Jack Bean urease employed was obtained in powder form (Type II, Sigma Chem. Corp., St. Louis, Missouri).

The colorimetric method developed by Van Slyke and Archibald[13] was employed with minor modifications. Two 40-ml. vials, one containing a urea phosphate buffer at *p*H 6.7 and the other containing a phosphate buffer at *p*H 7.7, were suspended in a constant temperature bath at 29.8 ± 0.2°, one drop of a mixed indicator (16 mg. brom thymol blue, 17 mg. of phenol red and two drops of 2 *N* base diluted with water to *ca.* 30 ml.) were added followed by a known amount of urease solution (or suspension in the case of urease reactivated by the copolymer), the time necessary for the urea buffer to match the color of the control was determined, and from this and the concentration of the urease the activity in Sumner units (S.U.) per mg. urease were calculated according to equation 1

$$A = \frac{1800}{tU} \qquad (1)$$

where A is activity in S.U. per mg., t the time in seconds and U the urease added in mg. This equation is a modification of the equation given in the original article. The factor 1800 is a combination of the factors 0.6 (correction for temperature) 60 (conversion from minutes to seconds) and 50 (arising from the buffer composition and the definition of the Sumner unit).

The procedure was to prepare a *ca.* 10% urease solution, determine its activity, deactivate the enzyme by adding 0.00874 *N* iodine and determine the activity after reactivation by the addition of neutralized cysteine, sodium thioglycolate, or polymer and redetermine the activity. The solution was then allowed to stand with the reactivating agent overnight and the activity again determined. The results are summarized in Table I.

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[CONTRIBUTION FROM DEPARTMENT OF CHEMISTRY, UNIVERSITY OF FLORIDA]

Preparation and Polymerization of Unsaturated Quaternary Ammonium Compounds. VII. Derivatives of 1,X-Diamino-alkanes[1]

BY GEORGE B. BUTLER AND RUDOLPH J. ANGELO

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As an approach to a study of the effect of distance between active centers in strongly basic ion-exchange polymers on the exchange properties, a number of unsaturated quaternary ammonium salts have been prepared, characterized and polymerized. As intermediates the 1,X-bis-(diallylamino)-alkanes from ethane through decane were prepared. Quaternary ammonium salts studied included the methyl bromide and allyl bromide derivatives of each of the amines.

Polymerization of pure unsaturated quaternary ammonium salts[2] offers an excellent means of producing strongly basic ion-exchange polymers free of other reactive functional groups. It has been shown that the rate of ion-exchange processes is a function of a diffusion factor,[3] and that diffusion rates depend upon the degree of cross-linking of the polymer network. The degree of swelling of an ion-exchange material, also a function of the degree of cross-linking, has an effect on this rate of diffusion of the ions to the exchange centers. Ion-exchange materials having a low degree of swelling, from a practical standpoint, are limited in the fraction of the theoretical capacity of the polymer which can be attained under conditions of practical usage due to this diffusion rate. For example, it has been shown[4] that for a polymer having a coefficient of swelling of 5.08, 88.8% of the theoretical capacity can be attained, while under similar conditions, for a polymer having a coefficient of swelling of 1.17, only 39.4% of the theoretical capacity was attained.

The degree of cross-linking of the polymer network has also been shown to be a factor in the exchange capacity[5] and this capacity decreases as the size of the ion to be exchanged attains a threshold value. This threshold value decreases with increasing degrees of cross-linking, thus supporting the idea that ion-exchange materials are not capable of exchanging ions having an effective diameter larger than the diameter of the opening which permits diffusion to the internal structure of the particle.

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(1) This paper was presented before the Ion Exchange Conference, Gordon Research Conferences, AAAS, New Hampton, N. H., June, 1955, and before the Ion Exchange Symposium, Southeastern Regional Meeting, ACS, Columbia, S. C., November, 1955.

(2) The most recent paper of this series appeared in THIS JOURNAL, **76**, 2418 (1954).

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(4) G. B. Butler and R. L. Goette, *ibid.*, **74**, 1939 (1952).

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