

perature was centrifuged at 8000 g. for 0.5 hour. The rotations on the supernatant were observed. This solution was maintained at room temperature for a period of 9 days and the dispersion curve was repeated. This was again centrifuged and a dispersion curve made. The results are summarized in Table I.

TABLE I

RESULTS OF TIME DEPENDENCE IN FORMATION OF AGGREGATES AT ROOM TEMPERATURE

Solution	$[\alpha]_{589.6}^{25}$	Dispersion
1 2% Solubilized at room temp. and centrifuged	46.2°	Linear
2 Soln. 1 standing 9 days	33.6	Complex
3 Soln. 2 centrifuged	44	Linear

^a Not corrected for loss of Methocel MC due to aggregation.

2. A 2% solution of Methocel MC solubilized at 0° in a period of two weeks slowly became aggregated. This was evidenced by the slow drift in the dispersion curve of the aged solution back to the original base line. It was not as aggregated as the room temperature material, but it did indicate that given a sufficient length of time the two solutions would undoubtedly have identical equilibrium states.

Conclusions

In order to obtain a true randomly dispersed solution of partially methylated cellulose, the temperature must be lowered to at least 10° and preferably colder. The results with the 5% solution of methylcellulose also indicated that as the concentration of the polymer increases, a greater length of time is required for complete hydration. At this low temperature, the molecule becomes enveloped with a bound water layer which prevents any aggregation. As the temperature is raised, part of the water envelope is disrupted. Such a situation provides an opportunity for the Methocel MC molecules to become associated in a sheet-like structure. This aggregate slowly settles to the bottom of the solution. As the temperature continues to increase the polysaccharide becomes completely dehydrated and falls out of solution.

Yang and Doty^{3b} were able to show a similar type association for low molecular weight polypeptides. They also demonstrated^{3b} that the formation of these intermolecular bonded structures was concentration dependent. A similar situation was found to be true for solutions of methylcellulose. As the concentration becomes greater, more opportunity for aggregation is provided and the reverse situation occurs as the concentration is decreased.

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Preparation of Polymeric Condensation Products Containing Functional Thiol Side Chains. Polyurethans¹

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The purpose of this study was to develop a general method of synthesis for a polyurethan and a polyester containing free sulfhydryl groups. Addition of benzyl mercaptan to dimethylitaconate followed by reduction to the glycol II gave a useful monomer. A polyester was prepared from this glycol and adipoyl chloride, but the benzyl group could not be removed without degradation of the polymer. A series of polyurethans was prepared and characterized by reaction of the glycol II with available diisocyanates. The benzyl group was successfully removed from the polyurethan made with the glycol and tolylene 2,4-diisocyanate with sodium in a mixed solvent of liquid ammonia and *n*-propylamine.

Polymers containing sulfhydryl groups are compounds of considerable interest for a variety of reasons. The effect of environment on the oxidation-reduction potentials of the sulfhydryl-disulfide system is of biochemical significance.³ Thiols combine with heavy metals to form mercaptides, a property which has been used for the detection of thiol groups in biological systems as well as for the preparation of exchange resins for the removal of heavy metal ions.⁴

The sulfhydryl group is essential to the activity of a number of enzymes in biological processes.⁵

(1) This is the 19th in a series of papers on new monomers and polymers; for this previous paper in this series, see C. G. Overberger and J. E. Mulvaney, *THIS JOURNAL*, **81**, 4697 (1959).

(2) This paper comprises part of the thesis presented by Herbert Aschkenasy in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the graduate school of the Polytechnic Institute of Brooklyn.

(3) E. S. G. Barron, Vol. XI, "Advances in Enzymology," Interscience Publishers Inc., N. Y., 1951, pp. 219 et seq.

(4) J. R. Parrish, *Chemistry & Industry*, 137 (1956); H. P. Gregor, D. Dallas and G. K. Hoeschele, *THIS JOURNAL*, **77**, 3675 (1955).

Oxidation of the sulfhydryl group in many cases inactivates the enzyme. Synthetic polymers containing thiol groups might be of considerable usefulness as reducing agents in the thiol-disulfide system as Overberger and Lebovits⁶ have demonstrated by reactivating urease, inactivated by chemical oxidation, with a sulfhydryl-containing vinyl polymer.

In addition, it has been established empirically that compounds having a sulfhydryl group are the most efficient protectors of living organisms against ionizing radiation,⁷ and a great variety of compounds, preponderantly monomeric in nature, have been prepared for testing in this connection. A

(5) L. Hellerman, M. C. Perkins and W. M. Clark, *Proc. Natl. Acad. Sci. U. S.*, **19**, 855 (1933); E. S. G. Barron and T. B. Singer, *Science*, **97**, 358 (1943).

(6) C. G. Overberger and A. Lebovits, *THIS JOURNAL*, **78**, 4792 (1956).

(7) Proposed Anti-Radiation Drug Program. Part II, Dept. of Nuclear Medicine, Walter Reed Army Institute of Research, Walter Reed Medical Center, Washington, D. C.

limited number of synthetic sulfhydryl polymers have previously been prepared by addition polymerization as well as condensation polymerization. Brubaker⁸ has reported the preparation, polymerization and copolymerization of vinyl thioacetate. Copolymers of vinyl thioacetate and vinylene carbonate and their saponification products have also been reported.⁹ Overberger and Lebovits⁶ have prepared *p*-vinylthioacetate and its homopolymer. Saponification of the resultant polymer gave an alkali-soluble polymer. Several other preparations of sulfhydryl-containing addition polymers have been reported.¹⁰ In the area of condensation polymers, Cairns¹¹ and co-workers introduced the mercaptomethyl fragment into nylon, and several methods for the introduction of thiol residues "*de novo*" into proteins have been reported.¹² The thiol content in these instances is not homogeneous, however, because of the statistical nature of functional group introduction into preformed polymer chains.

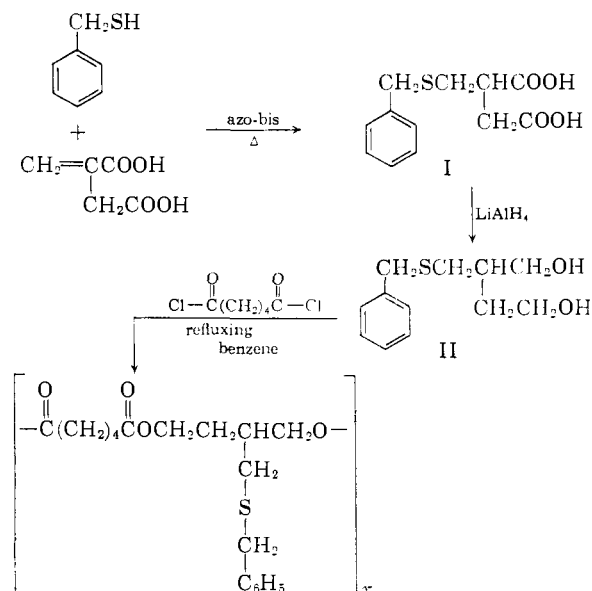
This and subsequent papers describe general synthetic methods for the preparation of condensation polymers containing functional thiol side chains homogeneously distributed along the chain and of known environment.

Initial attempts were directed at the synthesis of a polyester containing the desired free sulfhydryl group. The addition of benzyl mercaptan to dimethyl itaconate by the method of Knuth, *et al.*,¹³ yielded dimethyl benzylthiomethylsuccinate. Several attempts at effecting polycondensation reactions with ethylene glycol did not yield characterizable polymers because of elimination and/or decomposition, ascribable to the sensitivity of the monomer to both acidic and basic catalysts at the elevated temperatures required. It was thought that benzylthiomethylsuccinic anhydride might be suitable for use under milder reaction conditions. This material was prepared by dehydration of the corresponding acid I, which was obtained by a free radical-catalyzed addition of benzyl mercaptan to itaconic acid. Attempted polycondensation of the anhydride with ethylene glycol also led to considerable decomposition.

An attempt to use 1,6-bis-diazohexane as a mild reagent for the polyesterification by the procedure of Samour and Mason¹⁴ did not give the desired product. In our hands the product with adipic acid, although exhibiting ester absorption in the infrared, had an inherent viscosity below even low polymer range and could be molecularly distilled. A possible cyclic ester structure is suggested.

Reduction of dimethyl benzylthiomethylsuccinate as well as benzylthiomethylsuccinic acid, by

means of lithium aluminum hydride, yielded the expected glycol II. The glycol could be satisfactorily converted to a polyester (III) by treatment with adipoyl chloride in refluxing benzene using nitrogen to flush the gaseous hydrogen chloride formed out of the reaction mixture.



Attempts at reductive cleavage of the blocking benzyl group to generate the sulfhydryl functions failed to give the desired product. Of the methods tried, only sodium in liquid ammonia-tetrahydrofuran gave debenzylation, but with extensive degradation of the polymer. It could be demonstrated, by using a less than theoretical quantity of sodium, that degradation, presumably in the backbone of the chain, was at least as rapid as debenzylation.

The availability of the glycol II opened a route to another class of polymers, namely polyurethans. Reaction of the glycol with a variety of diisocyanates at room temperature gave three new polyurethans (Table I).

TABLE I
POLYURETHANS DERIVED FROM 2-BENZYLTHIOMETHYL-1,4-BUTANEDIOL

Diisocyanate	Softening point range, ¹⁷ °C.	$[\eta]$ at 29.8°
Hexamethylene 1,6-	90-95	0.30 ^a
Toluene 2,4-	110-115	.10 ^b
Diphenylmethane 4,4'-	110-117	.19 ^a

^a In dimethylformamide. ^b In acetone.

All these materials were prepared in benzene, in which the monomers are soluble and the polymer insoluble. It appeared that when the polymer achieved a certain degree of polymerization it precipitated from solution. In support of this, it was observed that the polyurethan derived from diphenylmethane 4,4'-diisocyanate when prepared in benzene gave a softening range of 110-117° (Table I) after one day at room temperature, whereas the same procedure using a better solvent for the polymer, namely dioxane, gave a precipitate only after four days at room temperature, and exhibited a

(8) M. M. Brubaker, U. S. Patents 2,378,535 and 2,378,536 (1945).

(9) C. G. Overberger, H. Bilech and R. G. Nickerson, *J. Polymer Sci.*, **27**, 381 (1958).

(10) Y. Nakamura, *J. Chem. Soc., Japan, Ind. Chem. Sect.*, **58**, 269 (1955); M. Okarawa, T. Nagakawa and E. Imoto, *ibid.*, **60**, 73 (1957).

(11) T. L. Cairns, H. W. Gray, A. K. Schneider and R. S. Schreiber, *THIS JOURNAL*, **71**, 655 (1949).

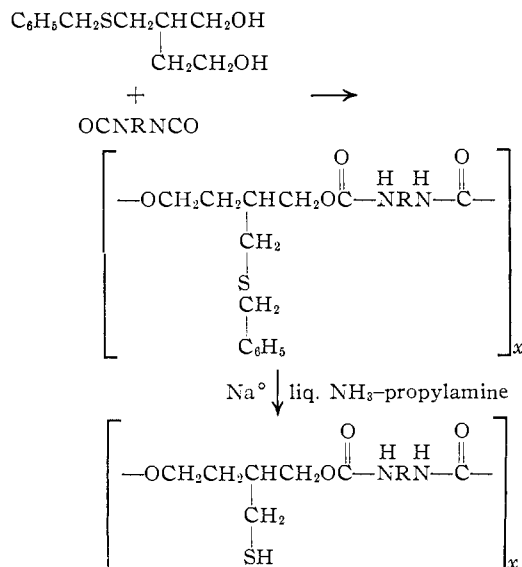
(12) A. Schöberl, *Angew. Chem.*, **60**, 7 (1948); R. Benesch and R. F. Benesch, *Proc. Natl. Acad. Sci.*, **44**, 848 (1958); R. Benesch and R. F. Benesch, *THIS JOURNAL*, **78**, 1597 (1956).

(13) C. Knuth, A. Bavley and W. A. Lazier, *J. Org. Chem.*, **19**, 845 (1954).

(14) C. M. Samour and J. P. Mason, *THIS JOURNAL*, **76**, 441 (1954).

softening range which extended beyond 250°. This polymer was soluble in dimethylformamide and insoluble in acetone.

The polyurethan derived from 2,4-tolylene diisocyanate was used as a model for the attempted removal of the benzyl blocking group. The polymer was not soluble in liquid ammonia but was soluble in low molecular weight amines. A modification of the procedure of Benkeser, *et al.*¹⁵ using a mixed solvent system of liquid ammonia-propylamine and metallic sodium gave the desired product.



Elemental analysis indicated complete removal of the benzyl blocking group from the polymer which, it was estimated, contained at least ten such residues.¹⁶ The product was slightly base soluble, gave a strongly positive nitroprusside test in alkaline media and showed a weak absorption, characteristic of the sulfhydryl group at 2550 cm^{-1} , as well as a strong absorption at 1700 cm^{-1} indicating retention of the urethan linkage. It is indeed remarkable that in a polymeric system the debenzilation reaction proceeded quantitatively.

Experimental¹⁷

Dimethyl β -Benzylthiomethylsuccinate.—To a stirred mixture of 5 g. of anhydrous potassium carbonate in 89 g. (0.5 mole) of dimethyl itaconate was added dropwise, with ice-bath cooling, 62 g. (0.5 mole) of benzyl mercaptan, using the general method of Knuth, *et al.*¹³ The hydroquinone present as a polymerization inhibitor in the ester was not removed. After addition was completed the reaction mixture was stirred for 18 hours, filtered, and the filtrate distilled under reduced pressure, yielding 121 g. (86%), b.p. 166–167° (1.0 mm.), n_D^{20} 1.5292, d_4^{20} 1.1630. Infrared analysis gave normal ester and phenyl absorptions.

Anal. Calcd. for $\text{C}_{14}\text{H}_{18}\text{O}_4\text{S}$: C, 59.55; H, 6.42; S, 11.35. Found: C, 59.38; H, 6.31; S, 11.40.

(15) R. A. Benkeser, C. Arnold, R. F. Lambert and O. H. Thomas, *THIS JOURNAL*, **77**, 6042 (1955).

(16) A model compound prepared by adding a small excess of the glycol to 2,4-tolylene diisocyanate was shown to be primarily trimer by end group titration using the method of L. E. St. Pierre and C. C. Price, *ibid.*, **78**, 3432 (1956), and had a softening point 30° below its higher chain length analog.

(17) Elemental analyses were done by Schwarzkopf Microanalytical Laboratories, Woodside, N. Y. All melting points are uncorrected and were determined by the capillary method except for polymers for which the Fisher-Johns block was employed.

Benzylthiomethylsuccinic Acid.—A solution of 65 g. (0.5 mole) of itaconic acid and 74.4 g. (0.6 mole) of benzyl mercaptan in 200 ml. of dioxane was heated to 65° under a nitrogen atmosphere and 3.2 g. (2 mole %) of azobisisobutyronitrile was added in small portions over a 60-hour period. The dioxane was removed under reduced pressure and the syrupy residue dissolved in 1 liter of water containing 53 g. (0.5 mole) of sodium carbonate. The aqueous solution was extracted twice with 200 ml. portions of ether and acidified with concentrated hydrochloric acid to a pH of 1. The mixture was cooled until the oily bottom layer solidified (2–3 days). The solid was removed by filtration and recrystallized from 800 ml. of hot water giving a white crystalline solid, 50.8 g. (40%), m.p. 111–112°. Infrared analysis gave normal carboxylic acid and phenyl absorptions.

Anal. Calcd. for $\text{C}_{12}\text{H}_{14}\text{O}_4\text{S}$: C, 56.67; H, 5.55; S, 12.60; neut. equiv., 126. Found: C, 56.82; H, 5.77; S, 12.86; neut. equiv., 126.

Benzylthiomethylsuccinic Anhydride. A.—A mixture of 51 g. (0.2 mole) of benzylthiomethylsuccinic acid and 40.8 g. (0.4 mole) of acetic anhydride containing two drops of concentrated sulfuric acid was warmed on a steam-bath with shaking until solution took place, and then for an additional 15 minutes. The reaction mixture, after being allowed to come to room temperature, was shaken with 100 ml. of pentane and cooled. The precipitate was removed by filtration, taken up in methylene chloride, washed with 200 ml. of 1 *N* aqueous sodium bicarbonate, then 200 ml. of water and the methylene chloride solution dried over anhydrous magnesium sulfate. The product was recrystallized from a boiling methylene chloride-pentane solution, yielding 35 g. (75%), m.p. 66–68°. Infrared analysis gave the characteristic anhydride frequencies at 1800 and at 1870 cm^{-1} as well as phenyl absorption.

Anal. Calcd. for $\text{C}_{12}\text{H}_{12}\text{O}_5\text{S}$: C, 60.99; H, 5.12; S, 13.51. Found: C, 60.93; H, 5.35; S, 13.41.

B.—An alternative procedure employed phosphorus trichloride. A mixture of 5.08 g. (0.02 mole) of β -benzylthiomethylsuccinic acid and 2.75 g. (0.02 mole) of phosphorus trichloride was warmed to 60° for 0.5 hr. The mixture was allowed to cool to room temperature, shaken with 50 ml. of carbon tetrachloride and recrystallized from a boiling methylene chloride-pentane solution, giving 4.02 g. (85%), identical with the product from procedure A.

Benzylthiomethyl-1,4-butanediol. A.—A solution of 22.8 g. (0.604 mole) of lithium aluminum hydride in 1 liter of anhydrous ether was refluxed for 3 hours, after which a solution of 90 g. (0.355 mole) of β -benzylthiomethylsuccinic acid in 100 ml. of tetrahydrofuran was added dropwise with stirring. The resulting mixture was refluxed for 72 hours, the white salt was decomposed by dropwise addition of water, and solids were removed by filtration. The filtrate was washed several times with water until the wash water was neutral and dried over anhydrous magnesium sulfate. The ether was evaporated and the oily residue distilled through an 8-inch, heated, center-tube column, yielding 49 g. (63%).

Anal. Calcd. for $\text{C}_{12}\text{H}_{18}\text{O}_2\text{S}$: C, 63.68; H, 8.02; S, 14.16. Found: C, 63.95; H, 8.22; S, 14.24.

B.—An alternative procedure involving reduction of the corresponding dimethyl ester although giving a lower yield may be preferable in some cases because the ester is more readily obtainable.

A solution of 26.2 g. (0.69 mole) of lithium aluminum hydride in 1 liter of anhydrous ether was refluxed for 3 hours, after which a solution of 170 g. (0.60 mole) of dimethyl β -benzylthioitaconate in 200 ml. of anhydrous ether was added dropwise with stirring. The resulting mixture was refluxed for 48 hours, the salt decomposed by dropwise addition of water and all solids removed by filtration. The ether layer was dried over anhydrous magnesium sulfate. The ether was removed by flash distillation and the oily residue distilled, 60.4 g. (44%), b.p. 180° (0.1 mm.), n_D^{20} 1.5643, d_4^{20} 1.1419. Both procedures yielded products with identical infrared spectra, containing strong hydroxyl and phenyl absorptions.

Anal. Calcd. for $\text{C}_{12}\text{H}_{18}\text{O}_2\text{S}$: C, 63.68; H, 8.02; S, 14.16. Found: C, 63.80; H, 8.23; S, 14.31.

Polyurethans.—The polyurethans were prepared by treating equimolar quantities of 2-benzylthiomethyl-1,4-

butanediol with diisocyanates. All the products described gave characteristic urethane absorption in the infrared spectrum, a strong broad absorption at about 1700 cm.^{-1} as well as a N-H stretching frequency at 3400 cm.^{-1} .

A.—A solution of 2.26 g. (0.01 mole) of the diol and 1.74 g. (0.01 mole) of 2,4-tolylene diisocyanate in 30 ml. of benzene and 2 drops of triethylamine was allowed to stand at room temperature for 48 hours. The precipitated polymer was obtained by decantation of the supernatant liquid, dried *in vacuo*, dissolved in acetone and reprecipitated by dropwise addition to a 10-fold excess of benzene. After filtration and drying *in vacuo*, a white solid was obtained, softening range $100\text{--}115^\circ$, $[\eta]$ 0.10 determined in acetone at 29.8° .

Anal. Calcd. for $\text{C}_{21}\text{H}_{24}\text{N}_2\text{O}_4\text{S}$: C, 62.97; H, 6.04; N, 7.00; S, 8.01. Found: C, 63.21; H, 6.09; N, 6.95; S, 8.02.

B.—A solution of 2.26 g. (0.01 mole) of the diol and 1.68 g. (0.01 mole) of hexamethylene 1,6-diisocyanate was prepared as in A and allowed to stand for 48 hours. The resultant precipitate was dissolved in dimethylformamide and precipitated by dropwise addition to a large excess of methanol. The precipitate was filtered and dried *in vacuo*. The product was a white solid, softening range $90\text{--}95^\circ$, $[\eta]$ 0.30 determined in dimethylformamide at 29.8° .

Anal. Calcd. for $\text{C}_{20}\text{H}_{30}\text{N}_2\text{O}_4\text{S}$: C, 60.88; H, 7.66; N, 7.10; S, 8.13. Found: C, 61.13; H, 7.54; N, 6.99; S, 8.35.

C.—A solution of 2.26 g. (0.01 mole) of the diol and 2.50 g. (0.01 mole) of purified diphenylmethane 4,4'-diisocyanate was prepared as in A and allowed to stand for 48 hours. The resultant precipitate was dissolved in dimethyl sulfoxide and precipitated by dropwise addition to a large excess of water. The precipitate was filtered and dried *in vacuo*. The product was a white solid, softening range $110\text{--}117^\circ$ $[\eta]$ 0.19 determined in dimethylformamide at 29.8° .

Anal. Calcd. for $\text{C}_{27}\text{H}_{28}\text{N}_2\text{O}_4\text{S}$: C, 68.04; H, 5.92; N, 5.88; S, 6.73. Found: C, 67.91; H, 6.08; N, 5.90; S, 6.72.

Polymer from Adipic Acid and 2-Benzylthiomethyl-1,4-butanediol.—A solution of 6.79 g. (0.03 mole) of 2-benzylthiomethyl-1,4-butanediol and 5.49 g. (0.03 mole) of redistilled adipoyl chloride was refluxed for 18 hours in 100 ml. of benzene. A stream of prepurified nitrogen was used to flush gaseous hydrochloric acid out of the system. The product was isolated by direct lyophilization from the reaction solvent. The oily residue was dried in a vacuum oven at

100° for 4 hours. It was then dissolved in a minimum volume of benzene and precipitated by dropwise addition to a large excess of Skellysolve A, isolated by decantation and dried in a vacuum oven at 60° for 12 hours. An extremely viscous yellow oil resulted, $[\eta]$ 0.12 determined in benzene at 29.8° . Infrared analysis showed a typical ester peak at 1730 cm.^{-1} .

Anal. Calcd. for $\text{C}_{18}\text{H}_{24}\text{O}_4\text{S}$: C, 64.26; H, 7.19; S, 9.53. Found: C, 64.19; H, 7.24; S, 9.71.

Debenzylation of Polyurethan.—This reduction was carried out by adopting some of the features of the methods of Baddiley and Thain¹⁸ and Benkeser, *et al.*¹⁹ A 5-g. sample of polyurethan derived from 2,4-tolylene diisocyanate and 2-benzylthiomethyl-1,4-butanediol (0.0125 mole of benzyl groups) was dissolved in 25 ml. of propylamine and the system flushed with nitrogen. Liquid ammonia was added until the solution became slightly turbid. Freshly cut pieces of sodium were then added periodically with vigorous stirring and external cooling by a Dry Ice-acetone mixture, until a permanent deep blue color was achieved. Excess ammonia was evaporated in a stream of nitrogen and the excess sodium decomposed by careful addition of ethanol. The addition of 200 ml. of deoxygenated water gave a yellow solution which was filtered by gravity under nitrogen and acidified with concentrated hydrochloric acid to a pH of 10. The resulting precipitate was allowed to settle under nitrogen at refrigerator temperature, the supernatant liquid decanted and the residue dried *in vacuo* over Drierite. The product was a white solid which gave a strong nitroprusside test and a SH stretching frequency at 2550 cm.^{-1} , softening point, $105\text{--}115^\circ$, $[\eta]$ 0.21 determined in dimethylformamide at 29.8° .

A sample was allowed to crosslink in alkaline solution in air and the resulting precipitate was filtered, washed with dimethyl sulfoxide and dried.

Anal. Calcd. for $\text{C}_{11}\text{H}_{17}\text{N}_2\text{O}_4\text{S}$: C, 54.35; H, 5.54; N, 9.06; S, 10.36. Found: C, 54.24; H, 5.78; N, 8.63; S, 10.10.

Acknowledgment.—We wish to acknowledge gratefully the support of this work by a grant from the Charles Pfizer Co., the helpful discussions held with Dr. Richard G. Hiskey and the laboratory assistance of Mr. Robert Liebowitz.

(18) J. Baddiley and E. M. Thain, *J. Chem. Soc.*, 1611 (1953).

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

Reactions of 2*H*,3*H*-Thieno[3,2-*b*]pyrrole-3-one. II.^{1,2} Acetylation and Formylation

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2*H*,3*H*-Thieno[3,2-*b*]pyrrol-3-one (I) reacts with hot acetic anhydride to give 3-acetoxy-4-acetylthieno[3,2-*b*]pyrrole (IV) as the major product, along with a little 3-acetoxy-2,4-diacetylthieno[3,2-*b*]pyrrole (V). The triacetyl derivative V can be obtained from the diacetyl derivative by the action of acetic anhydride in the presence of a little ferric chloride or iodine, but not acetic anhydride alone; acetic acid formed along with IV probably serves as the catalyst for the formation of the triacetyl derivative obtained in the direct acetylation of I. Hot aqueous sodium carbonate removes the O- and N-acetyl groups of V, leading to 2-acetyl-3-hydroxythieno[3,2-*b*]pyrrole, which, like the analogous carbethoxy compound, exists as a dimer. Acylation of the ketone I with ethyl formate and sodium methoxide occurs readily, yielding a nearly colorless monomeric derivative, the structure of which is best represented as the internally hydrogen-bonded hydroxyaldehyde X.

In connection with studies of the chemistry of 2*H*,3*H*-thieno[3,2-*b*]pyrrol-3-one (I),⁴ the acylation of this unique ketone has been investigated. Since I bears a formal resemblance to 2-acetylpyrrole (II), acylation of the two substances might

be expected to proceed similarly. Compound II has been reported to undergo nuclear substitution upon treatment with acetic anhydride, yielding 2,5-diacetylpyrrole (III),⁵ and there is evidence that carbon substitution is the result of a rearrangement of the initially formed N-acetyl derivative.⁶ Therefore, it was anticipated that acylation of I would effect the introduction of an acyl group in the 5-position. Treatment of I with acetic anhy-

(1) For the preceding paper, see W. Carpenter and H. R. Snyder, *This Journal*, **82**, 2592 (1960).

(2) This investigation was supported in part by a grant [C 3969-(C1) Bio] from the National Cancer Institute, Public Health Service.

(3) National Science Foundation Fellow, 1958-1959.

(4) H. R. Snyder and D. S. Matteson, *This Journal*, **79**, 3610 (1957).

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