

solution left at room temperature for 72 hr. The dark brown crystalline deposit was collected and recrystallized from water-ethanol (charcoal decolorization) yielding light tan monoclinic needles. The infrared spectrum was similar to that of the sulfonate II, N-H at 2.65 and 2.80 μ , weak C-H at 3.30 μ , no carbonyl absorption, weak nitrile at 4.4 μ , and strong singlet sulfonate (S=O) bands at 7.80 and 9.30 μ .

Anal. Calcd. for $C_2H_3KN_2O_3S$: C, 13.8; H, 1.73; K, 22.5; N, 16.1; S, 18.4. Found: C, 13.9; H, 1.60; K, 22.7; N, 15.5; S, 18.6.

This product is postulated to be an hydrolysis product of potassium aminocarbamoylcyanomethanesulfonate (II) and is assigned the structure of potassium aminocyanomethanesulfonate (XIII).

Sample B was treated with acetone until cloudy and the filtered

solution was left at room temperature for 72 hr. A small yield of straw-colored needles was obtained which exhibited a much simpler infrared spectrum than that of salt II; N-H absorption appeared at 2.80 and 2.90 μ , no carbonyl absorption was present, a weak unconjugated nitrile at 4.4 μ , and multiple sulfonate (S=O) absorption at *ca.* 8.0 and 9.4 μ .

Anal. Calcd. for $C_2H_2K_2N_2O_3S_2$: C, 8.21; H, 0.69; N, 9.58; S, 21.9. Found: C, 7.86; H, 0.91; N, 9.60; S, 22.4.

On the basis of analytical and spectroscopic data, particularly by comparison with the spectrum of potassium aminocarbamoylmethionate, the compound is postulated to be the partial hydrolysis product dipotassium aminocyanomethionate (XIV).

When the above procedures were repeated and the period of time before work-up was extended to 9 weeks, the sole product isolated was potassium sulfate.

[CONTRIBUTION FROM THE ADVANCED ORGANIC CHEMICALS RESEARCH LABORATORY, ORGANIC CHEMICALS DIVISION, MONSANTO CHEMICAL CO., SAINT LOUIS, MO.]

The Mechanism of the Base-Catalyzed Addition of Thiols to Maleic Anhydride¹

BY BASIL DMUCHOVSKY, BILLY D. VINEYARD, AND FERDINAND B. ZIENTY

RECEIVED FEBRUARY 10, 1964

Rate data are presented for the base-catalyzed addition of thiols to maleic anhydride in xylene. Third-order kinetics have been observed, first order each in thiol, maleic anhydride, and triethylenediamine. Added product and radical inhibitor have no effect on the rate of thiol disappearance, which has no apparent activation energy. Spectroscopic studies show interaction between thiol and base, but not between thiol and maleic anhydride; the xylene solutions, however, are nonconducting. An inverse hydrogen isotope effect has been observed. The results are discussed in terms of an equilibrium between thiol and base to form an ion pair followed by the rate-limiting attack of thiolate anion on maleic anhydride.

Introduction

A previous report from this laboratory² was concerned with preparation of alkylthio and arylthio anhydrides achieved by the addition of thiols to anhydrides in the presence of basic catalysts under anhydrous conditions. The purpose of the present paper is to establish the mechanism of the addition reaction and to determine the relative nucleophilicities of thiols or thiolate anions for addition to an α,β -unsaturated anhydride.

No side reactions occur under preferred preparative conditions. The data obtained indicate that the reaction appears to involve dissociation of the thiol and addition of the thiolate to a polarized double bond. Qualitative experiments demonstrated that the addition of thiol is kinetically controlled and that the rates of thiol additions are proportional to the acid strengths of the thiols. Base strength and steric effects in the amines used influence the rate of the addition reaction as does the nature of the solvent.

Iwakura and Okada³ studied the kinetics of the tertiary amine catalyzed addition of thiols to isocyanates and found the reaction to be first order in each reactant. Clearly their system is similar to ours. The catalytic activity of the bases paralleled that of the pK values except for the unusually active, sterically unhindered triethylenediamine. They were unable to explain their finding that an aromatic thiol adds less readily than an aliphatic thiol. The latter result does not agree with observations made in our previous study. The rate of reaction was found to be generally

dependent upon the dielectric constant of the solvent but no definite relationship was established.

Results

Table I lists data obtained for the addition of 1-butanethiol to maleic anhydride in the presence of triethylenediamine in xylene solution. The second-order nature of the reaction is shown by the calculated rate constants and the satisfactory plot in Fig. 1. The effects of the initial concentrations of reactants on the rate of thiol disappearance are collected in Table II and reveal that the addition is first order in each reactant, but each run is pseudo second order since the concentration of amine remains essentially constant throughout the course of reaction.

TABLE I
SAMPLE DATA FOR THE ADDITION OF 1-BUTANETHIOL TO MALEIC ANHYDRIDE AT EQUAL CONCENTRATION IN THE PRESENCE OF $3.17 \times 10^{-3} M C_6H_{12}N_2$ AT 25°

Time, sec.	$n-C_4H_9SH$, $M \times 10^3$	k , $M^{-1} \text{ sec.}^{-1} \times 10^3$	Time, sec.	$n-C_4H_9SH$, $M \times 10^3$	k , $M^{-1} \text{ sec.}^{-1} \times 10^3$
0	3.96	..	1920	2.78	5.61
600	3.48	5.68	2010	2.78	5.38
690	3.42	5.68	2700	2.46	5.71
1200	3.27	4.45	2790	2.43	5.71
1290	3.07	5.68			

TABLE II
EFFECTS OF INITIAL CONCENTRATIONS ON THE RATE OF ADDITION

$n-C_4H_9SH$, $M \times 10^3$	$H_2C_4O_3$, $M \times 10^3$	$C_6H_{12}N_2$, $M \times 10^3$	$-d[RSH]/dt$, $M \text{ sec.}^{-1} \times 10^3$	k , $M^{-2} \text{ sec.}^{-1} \times 10^{-3}$
3.96	3.96	3.17	5.45	1.8
7.92	3.96	3.17	10.2	1.7
3.96	7.92	3.17	11.2	1.7
3.96	3.96	6.34	11.2	1.9

(1) Presented at the 146th National Meeting of the American Chemical Society, Denver, Colo., Jan. 20, 1964.

(2) F. B. Zienty, B. D. Vineyard, and A. A. Schlepplnik, *J. Org. Chem.*, **27**, 3140 (1962).

(3) (a) Y. Iwakura and H. Okada, *Can. J. Chem.*, **38**, 2418 (1960); (b) *ibid.*, **41**, 1846 (1963); (c) A. Farkas and G. A. Mills, *Advan. Catalysis*, **13**, 393 (1962).

Table III shows the kinetic data for the addition of 1-butanethiol as a function of several variables.

TABLE III
RATE DATA FOR THE ADDITION OF 1-BUTANETHIOL TO
MALEIC ANHYDRIDE

No.	Temp., °C.	$10^{-2}k, M^{-2} \text{ sec.}^{-1}$	Remarks
9	25	1.8 ± 0.1	
4	25	2.0 ± 0.2	$7.92 \times 10^{-6} M$ 2,6-di- <i>t</i> -butyl- <i>p</i> -cresol added
1	25	2.1	$1.98 \times 10^{-3} M$ <i>n</i> -butylthiosuccinic anhydride added
3	25	3.0 ± 0.5	<i>n</i> -C ₄ H ₉ SD used
2	15	$1.9 \pm .1$	
3	35	$1.5 \pm .5$	
1	45	1.8	

Added *n*-butylthiosuccinic anhydride and added 2,6-di-*t*-butyl-*p*-cresol do not affect the rate of thiol disappearance. The observed third-order rate constant undergoes little change from 15 to 45°. The apparent activation energy, -0.6 ± 0.9 kcal./mole, is consistent with third-order reactions and is usually explicable by an exothermic equilibrium prior to the rate-limiting step where $\Delta H_{\text{eq}} = E_a$.⁴ The entropy of activation is about -45 Gibbs/mole using an average value of $1.9 \times 10^2 M^{-2} \text{ sec.}^{-1}$ for k_3 and $E_a = 0$.

The three hydrogen isotope experiments show poor agreement ($2.3, 3.0, 3.8 \times 10^2 M^{-2} \text{ sec.}^{-1}$), but the average value of $3.0 \times 10^2 M^{-2} \text{ sec.}^{-1}$ for k_D is significantly different⁵ from the value for k_H . The ratio of k_H/k_D is 0.65 ± 0.11 and shows that hydrogen-bond cleavage is not important in the transition state.⁶

Solutions of any one or any pair of reactants in xylene show no conductivity. The same is true for the reaction solution; therefore, very few ions free to move independently exist in this medium of low dielectric constant.⁷

Spectroscopic studies reveal that there is interaction between thiol and base. A solution of 20% by weight of 1-butanethiol in xylene displays the typical⁸ S-H stretching frequency at 2566 cm.^{-1} . A solution containing 20% by weight of both 1-butanethiol and triethylenediamine shows a decrease in the relative intensity of the S-H band of about 10%. Simultaneously a new band appears at 3253 cm.^{-1} and is attributed⁹ to an N-H stretching mode in a protonated tertiary amine where hydrogen bonding is not important. The corresponding bands for the deuterated analogs are 1850 cm.^{-1} for the S-D stretch and 2380 cm.^{-1} for $\equiv \text{N}^+ - \text{D}$. No other interactions are observed. Further confirmation of thiol-base interaction is provided by qualitative n.m.r. evidence.¹⁰

(4) S. W. Benson, "The Foundations of Chemical Kinetics," McGraw-Hill Book Co., Inc., New York, N. Y., 1960, pp. 305-312.

(5) H. S. Mickley, T. K. Sherwood, and C. E. Reed, "Applied Mathematics in Chemical Engineering," 2nd Ed., McGraw-Hill Book Co., Inc., New York, N. Y., 1957, Chapter 2.

(6) J. Bigeleisen and M. Wolfsberg, "Advances in Chemical Physics," Vol. I, I. Prigogine, Ed., Interscience Publishers, Inc., New York, N. Y., 1958, pp. 15-77.

(7) H. S. Harned and B. B. Owen, "The Physical Chemistry of Electrolyte Solutions," 3rd Ed., Reinhold Publishing Corp., New York, N. Y., 1958, Chapter 7.

(8) A range of $2550-2600 \text{ cm.}^{-1}$ is given in L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1958, Chapter 22.

(9) R. H. Nuttall, D. W. A. Sharp, and T. C. Waddington, *J. Chem. Soc.*, 4965 (1960).

(10) Unpublished results of M. L. Oftedahl and M. W. Dietrich, but a much smaller shift was observed when triethylenediamine was used.

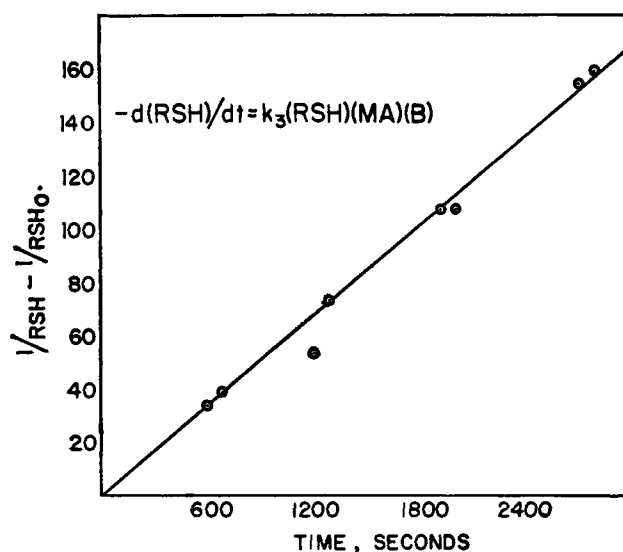


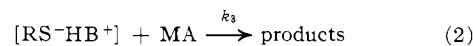
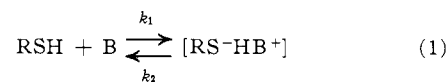
Fig. 1.—Second-order plot of 1-butanethiol disappearance at 25°.

A solution of 4-chlorobenzenethiol in deuteriochloroform has a chemical shift of 3.23 p.p.m. When equal parts of 4-chlorobenzenethiol and triethylamine are mixed in deuteriochloroform a chemical shift of 8.40 p.p.m. is observed. When triethylenediamine is used in large excess with 4-chlorobenzenethiol a shift of 5.24 p.p.m. results.

A third-order rate constant of $1.5 \times 10^4 M^{-2} \text{ sec.}^{-1}$ was found for the addition of 4-chlorobenzenethiol to maleic anhydride at 25°. The addition of 2-methyl-2-propanethiol gives a third-order rate constant of $18 M^{-2} \text{ sec.}^{-1}$ at 50° and $31 M^{-2} \text{ sec.}^{-1}$ at 25°. The highest value found for the aromatic thiol supports our previous information.²

Discussion

The third-order rate law and the physical evidence for interaction between thiol and base suggest the sequence of steps indicated by eq. 1 and 2; B denotes triethylenediamine, MA is maleic anhydride, and RSH is thiol. The complex $[\text{RS}^-\text{HB}^+]$ is visualized as an

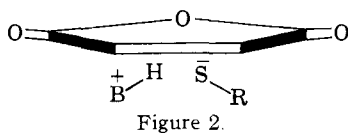


ion pair with no hydrogen bonding, as deduced from the infrared evidence.⁹ The lack of conductivity is consistent with the expected behavior of ion pairs in such a solvent system.⁷

Using the model represented by eq. 1 and 2 and the stationary-state hypothesis we can derive the observed third-order rate equation with the assumption that $k_2 \gg k_3[\text{MA}]$, with k (experimental) = $k_1k_3/k_2 = k_3K$ where $K = k_1/k_2$. The observed inverse isotope effect is unusual. Normally inverse ratios are secondary isotope effects,¹¹ but such a situation hardly seems likely in this case. Interpretation of this inverse isotope effect is complicated by the existence of one or more equilibria preceding the rate-limiting step. Recently, however, Bell and Crooks¹² studied the effect of deuterium substitution on equilibrium constants in

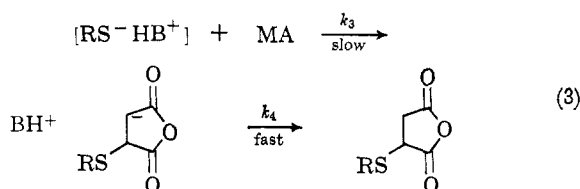
(11) For examples see S. I. Miller, *J. Phys. Chem.*, **66**, 978 (1962); T. J. Katz and R. Dessau, *J. Am. Chem. Soc.*, **85**, 2172 (1963).

(12) R. P. Bell and J. E. Crooks, *J. Chem. Soc.*, 3513 (1962).



nonexchanging media using substituted phenols and amines in toluene. The results, $K_H/K_D > 1$, were confirmed by theoretical calculations. The same sort of calculations for our system, using the equations of Bigeleisen and Mayer¹³ in the form written by Kaplan and Wilzbach¹⁴ revealed that $K_H/K_D = 0.68$ for the thiol-base equilibrium. The infrared stretching frequencies used are given under Results. The close agreement between the observed kinetic isotope ratio of 0.65 and the calculated equilibrium isotope ratio of 0.68 indicates that there is no difference in the rate constants for the rate-controlling step.

It can, therefore, be concluded that the rate-limiting step does not involve the cleavage of a hydrogen bond. The most likely rate-limiting step is the addition of the thiolate portion of the ion pair to maleic anhydride followed by the rapid transfer of a proton from the protonated amine to the adduct anion. The sequence is shown by eq. 3.



The approach of the ion pair to maleic anhydride is shown in an idealized way in Fig. 2. In order for addition to the π -orbital to occur, the ion pair must be perpendicular to the plane of the anhydride ring. This required geometry, together with the lack of conductivity, intimates that preferential *cis* addition of the thiol is followed in contrast to the *trans* addition of thiols to olefins found in more polar media.¹⁵ This possibility is currently being investigated. The close proximity of the reactants and the precise geometry indicated account for the high negative entropy of activation which is common to third-order reactions in solution.¹⁶

This addition reaction provides a direct method for determining nucleophilicities of various thiolate anions provided that relative measures of the prior equilibria can be obtained. Acid dissociation constants are convenient for this purpose if they are taken in a consistent solvent system. This necessarily assumes that the behavior of the thiols in the pK measurement system parallels the behavior in xylene. Table IV shows the nucleophilicities derived in this way for three thiolate anions. The trend of k_3 is in the expected direction; greater nucleophilicity is shown by the aliphatic thiolates. The results are in agreement with displacements at bivalent sulfur and saturated carbon.¹⁷ The aromatic thiolate ion dissipates the negative charge by

(13) J. Bigeleisen and M. G. Mayer, *J. Chem. Phys.*, **15**, 261 (1947).

(14) I. Kaplan and K. E. Wilzbach, *J. Am. Chem. Soc.*, **77**, 1297 (1955).

(15) W. A. Pryor, "Mechanisms of Sulfur Reactions," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p. 71.

(16) C. G. Swain, *J. Am. Chem. Soc.*, **70**, 1119 (1948), records a value of -49 e.u. for the methanolysis of trityl chloride in benzene.

(17) J. O. Edwards and R. G. Pearson, *ibid.*, **84**, 16 (1962).



conjugation with the benzene ring. This means of distributing the negative charge in the ion pair is, of course, not available to aliphatic thiolates. Steric effects cause 2-methyl-2-propanethiolate to be less nucleophilic than 1-butanethiolate.

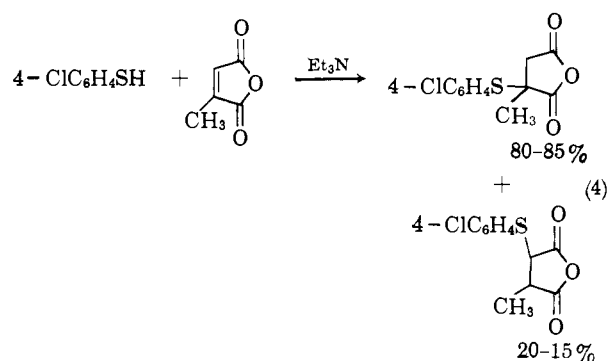
TABLE IV
RELATIVE RATE CONSTANTS AT 25°

	k_{exptl}	pK_a	k_3
<i>n</i> -C ₄ H ₉ SH	11	12.4 ^a	3300
<i>t</i> -C ₄ H ₉ SH	1	12.7 ^a	600
4-ClC ₆ H ₄ SH	830	6.96 ^b	1

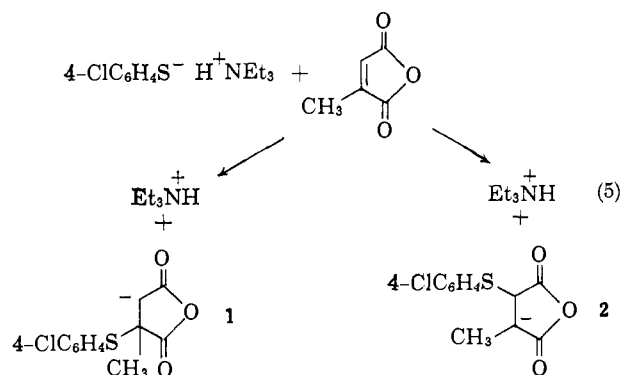
^a J. Maurin and R. Paris, *Compt. rend.*, **232**, 2428 (1951).

^b T. G. Bordwell and H. M. Andersen, *J. Am. Chem. Soc.*, **75**, 6019 (1953).

The possible importance of steric effects in this addition is demonstrated by the addition of 4-chlorobenzethiol to citraconic anhydride in the presence of triethylamine. Equation 4 shows that two products are obtained in the ratio of 5 to 1. Since the reaction is



subject to kinetic control it is necessary to account for the results in terms of the differences in free energy between the two paths shown in eq. 5. For convenience it will be assumed that the transition states resemble



the intermediates 1 and 2. Structure 1 should be of lower energy because secondary carbanions are thought to be more stable than tertiary carbanions.

Figure 3 shows steric effects to be more pronounced in structure 2 because of the interaction between the ring methyl and protonated triethylamine. Both electronic and steric factors raise the energy of structure 2 rela-

tive to structure 1 and explain the product distribution found. The result is the same whether the transition state resembles the intermediates 1 and 2 or the close approach of the ion pair to the anhydride. The energy difference between the common ground state and transition state 1 is smaller and therefore the rate is greater.

The extension of this interpretation to the additions of thiols and alcohols to isocyanates^{3a} is obvious and may prove helpful.

Experimental

Materials.—Untreated analytical reagent grade xylene (boiling range 137–140°) obtained from Mallinckrodt was used as the reaction solvent. Because of the high dilution of reactants it was felt that traces of water might affect the rate of reaction. Freshly distilled sodium-treated solvent was used for a kinetic run to test the influence of water. The results were no different from those observed with untreated xylene. The commercially available thiols used were distilled prior to use and made up as 2% stock solutions. The uncorrected boiling points are: 1-butanethiol, 96–97°; 2-methyl-2-propanethiol, 63–64°; 4-chlorobenzenethiol, 117° (48 mm.). Stock solutions of maleic anhydride were made by dissolution in warm xylene and filtration to remove the insoluble maleic acid; very little acid was recovered. Triethylenediamine obtained from the Houdry Process Co. was used as received. Denatured 95% ethanol and analytical reagent grade silver nitrate were used without purification.

Preparation of S-Deuterio-1-butanethiol.—This thiol was prepared in 12% yield by the method of Hobden and co-workers.¹⁸ The purity, 95–100% RSD, was established by infrared analysis; the S–H stretching frequency was shifted from 2566 to 1850 cm.⁻¹ with deuterium substitution. The corresponding shift found by Hobden for S-deuterio-1-ethanethiol was 2566 to 1863 cm.⁻¹.

Sample Kinetic Procedure and Analysis.—The reaction vessel was a 500-ml., three-necked, round-bottomed flask fitted with a mechanical stirrer, condenser, and a gas inlet tube for the introduction of nitrogen to prevent thiol oxidation, all immersed in a 30-l. water bath. The temperature was controlled to ±0.2° by a Thermo-o-watch regulator attached to a thermometer dipping into the reaction solution. To the reaction flask there was charged 3.0 g. of a 3% stock solution of maleic anhydride in xylene and

(18) F. W. Hobden, E. F. Johnston, L. H. P. Weldon, and C. L. Wilson, *J. Chem. Soc.*, 61 (1939).

4.14 g. of a 2% stock solution of 1-butanethiol in xylene was added. To this solution 192.3 g. of xylene was added and the resulting solution was stirred rapidly under a nitrogen atmosphere for 30–60 min. to ensure temperature equilibration. The reaction was initiated by the addition of 0.2 ml. of a stock solution containing 5% triethylenediamine in xylene; prior to the addition of base to the reaction two 10-ml. aliquots of the stock solution were withdrawn for the zero time titers. Aliquots of the reaction solution were withdrawn at measured times for the thiol titer, and immediately quenched with an excess of concentrated sulfuric acid in 25 ml. of alcohol. Larger initial concentrations of reactants led to undesirably fast rates and to the development of color due to the competing maleic anhydride polymerization reaction.

The samples of the reaction solution (5 to 10 ml.) were transferred to 150-ml. beakers and diluted to 100 ml. with 95% alcohol; the extent of the reaction was determined by amperometric titration with standard silver nitrate solution.¹⁹ The titration assembly consisted of a saturated calomel reference electrode and a rotating platinum indicator electrode (driven by a synchronous motor) connected in series to a galvanometer having a sensitivity of 0.22 ma. per millimeter. Accuracies of about 3% were achieved.

Data Treatment.—The initial rates of reaction with different initial concentrations of reactants dictated eq. 6 for the case of equal initial thiol and anhydride concentrations and eq. 7 for the

$$k = \frac{1}{(B)t} \left[\frac{1}{(RSH)} - \frac{1}{(RSH)_0} \right] \quad (6)$$

case where $(RSH)_0 > (MA)_0$. MA refers to maleic anhydride,

$$k = \frac{2.3}{(B)t \{ (RSH)_0 - (MA)_0 \}} \log \frac{(MA)_0 (RSH)}{(RSH)_0 (MA)} \quad (7)$$

B to triethylenediamine, and RSH to thiol. The average deviation in k was usually about 8% for any given run with 9 points, but the data for 16 runs showed a mean value of k_3 of $1.9 \times 10^2 M^{-2} \text{sec.}^{-1}$ with a standard deviation of the mean of ±0.05 and a value of 1.9 ± 0.1 with 95% confidence limits.

Acknowledgments.—Many of the titrations were performed by Mr. H. Yepez, the infrared measurements were done by Mr. O. Kinast and Dr. B. Katlafsky, and n.m.r. analyses were done by Dr. M. W. Dietrich.

(19) I. M. Kolthoff and W. E. Harris, *Anal. Chem.*, **18**, 161 (1946).

[CONTRIBUTION FROM THE CENTRAL BASIC RESEARCH LABORATORY, ESSO RESEARCH AND ENGINEERING CO., LINDEN, N. J.]

Organic Sulfur Compounds. XIII.¹ Free-Radical Addition of Thiols to Phenylacetylene²

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RECEIVED AUGUST 20, 1963

Nucleophilic addition of thiols to acetylenes is well understood but little is known about the stereochemistry of the free-radical addition. In the present study, therefore, aromatic and aliphatic thiols and thiolacetic acid were added to phenylacetylene by a chain mechanism both in the absence and in the presence of ultraviolet light or hydroperoxide initiation. When equimolar amounts of reactants were mixed at ambient temperatures, mainly *trans* monoaddition occurred, yielding *cis*-1-substituted mercapto-2-phenylethenes. The apparent stereoselectivity of the reaction increased when an excess of phenylacetylene was used. The resulting *cis* adducts were readily isomerized by thiyl radicals to equilibrium mixtures consisting mainly of the *trans* isomer. The various *cis*-*trans* isomer mixtures were analyzed by a combination of the g.c. and n.m.r. techniques; n.m.r. and infrared spectra of the *cis* and *trans* adducts and their mixtures were systematically studied and led to general rules for the identification of the configuration of these adducts.

Introduction

As an extension of our studies of radical addition of thiols to mono-⁴ and diolefins,^{5–7} this paper describes

the addition of thiols to phenylacetylene (phenylethyne). The work was undertaken primarily to elucidate the stereochemistry of the *cis* and/or *trans* monoadducts of such reactions.

(1) The previous paper of this series: *J. Org. Chem.*, **28**, 2355 (1963).

(2) Presented before the Organic Chemistry Division, 145th National Meeting of the American Chemical Society, New York, N. Y., Sept., 1963.

(3) To whom inquiries should be sent.

(4) A. A. Oswald, *J. Org. Chem.*, **25**, 467 (1960).

(5) A. A. Oswald and F. Noel, *ibid.*, **26**, 3948 (1961).

(6) A. A. Oswald, B. E. Hudson, Jr., G. Rodgers, and F. Noel, *ibid.*, **27**, 2439 (1962).

(7) A. A. Oswald, K. Griesbaum, W. Thaler, and B. E. Hudson, Jr., *J. Am. Chem. Soc.*, **84**, 3897 (1962).