The product can be recrystallized from 2-propanol–water (2:1) with very little loss, but is already very pure as shown by the following analysis.

Anal. Calcd. for $C_{34}H_{44}N_3NaS_2$: acidic methylene group, 1.48 mequiv./g. Found (by titration with $KOCH_3$ in dimethylformamide): acidic methylene group, 1.48 mequiv./g.

This procedure was used for the compounds containing a long aliphatic chain. Recrystallization from a suitable solvent (acetic acid or Methyl Cellosolve) produced the sulfonates with a purity of 98.5–100% in yields between 85 and 93%. The lower molecular weight sulfonates are highly soluble in water. Therefore, after acidifying the reaction mixture with acetic acid, they had to be salted out by the addition of sodium acetate or chloride.

Acknowledgment.—We wish to thank Professor Dr. A. Van Dormael, Director of the Chemical Research Department, for his kind interest in this work. We are indebted to Dr. Moelants, Head of the Analytical Department, for the analyses.

Reactions of Thiols with Sulfoxides. III. Catalysis by Acids and Bases

THOMAS J. WALLACE AND JOHN J. MAHON

The Esso Research and Engineering Company, Process Research Division, Exploratory Research Section, Linden, New Jersey

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The oxidation of 1-dodecanethiol by tetramethylene sulfoxide was studied in the presence of four amines at 100 ± 0.1°. The disappearance of thiol adhered to good pseudo-first-order kinetics in the presence of excess sulfoxide and a catalytic amount of the amine. In the presence of N,N-dimethylaniline and 2,6-lutidine (thiol–amine = 10) the rate of oxidation of 1-dodecanethiol was increased by a factor of only 2 to 3. In the presence of 1-dodecylamine and tri(*n*-butyl)amine a rate increase of 84 to 269 was observed. The catalytic nature of the amine was also established. A plot of the log of the observed rate constant for oxidation *vs.* the concentration of amine at various thiol–amine ratios resulted in a linear relationship. It is proposed that the amine, thiol, and sulfoxide form a more favorable transition state for the production of an unstable thiol–sulfoxide adduct during the rate-determining step in these reactions. The effect of pyrrole, phosphoric acid, and acetic acid on these reactions was also determined. A mild catalysis, rather than inhibition, was observed in the presence of these acids. This is apparently due to a more favorable transition state for protonation of the sulfoxide. The general acid–base catalysis of these reactions was confirmed by kinetic studies in the presence of 2-hydroxypyridine. The implications of these results with respect to the mechanism of thiol–sulfoxide reactions are discussed.

Previous publications from these laboratories[1-3] have described in detail the oxidation of thiols to disulfides by tetramethylene sulfoxide (TMSO) and dimethyl sulfoxide (DMSO). Variation of the reaction temperature indicated that the order of thiol reactivity was aryl > aralkyl ≫ alkyl. Subsequent kinetic studies[3] established that the rate of thiol–sulfoxide reactions was markedly dependent on the acidity of the thiol. For example, benzenethiol was oxidized about 10^5 times faster than 1-dodecanethiol in the presence of TMSO at 100°. Further, the reactions were first order in thiol and sulfoxide indicating that the reactions were over-all second order in nature. Thus, it was concluded that the rate-determining step in these reactions was initial reaction of the thiol with a sulfoxide molecule to form an unstable thiol–sulfoxide adduct that is rapidly destroyed by reaction with another molecule of thiol.

$$RSH + R_2SO \xrightarrow{\text{slow}} [R_2\ddot{S}(OH)SR] \quad (1)$$

$$[R_2\ddot{S}(OH)SR] + RSH \xrightarrow{\text{fast}} RSSR + R_2S + H_2O \quad (2)$$

The present paper is an extension of our previous studies in this area. Kinetic studies in the presence of acidic and basic catalysts have been carried out in an effort to uncover suitable methods of accelerating aliphatic thiol–sulfoxide reactions and to gain more definitive knowledge on the nature of the transition state in these reactions. Specifically, the effect of acidic and basic nitrogen compounds on the oxidation of 1-dodecanethiol by TMSO, the effect of acetic acid on the oxidation of α-toluenethiol by TMSO, and the effect of phosphoric acid on the oxidation of 1-dodecanethiol by TMSO have been determined. An attempt to establish that these reactions are subject to general acid and base catalysis has also been made.

(1) T. J. Wallace, *Chem. Ind.* (London), 501 (1964).
(2) T. J. Wallace, *J. Am. Chem. Soc.*, **86**, 2018 (1964).
(3) T. J. Wallace and J. J. Mahon, *ibid.*, **86**, 4099 (1964).

Results

Kinetic studies on the oxidation of 1-dodecanethiol by TMSO have been carried out in the presence of four basic amines and the acidic amine, pyrrole. All reactions were conducted under nitrogen in sealed vials. Rate measurements were obtained by sampling the reaction mixture with a syringe and subsequently analyzing the aliquot by gas chromatography according to the procedure outlined in the Experimental section. Quantitative data were obtained by measuring the area of the thiol peak using an internal hydrocarbon standard as a reference. Initially, the oxidation of 1-dodecanethiol by TMSO at 100 ± 0.1° was investigated in the presence of N,N-dimethylaniline, 2,6-lutidine, 1-dodecylamine, and tri(*n*-butyl)amine. A 4 *M* excess of sulfoxide to thiol was employed and the molar ratio of thiol to amine catalyst was 10. In all cases, good pseudo-first-order kinetics for thiol disappearance was observed. This point is demonstrated in Figure 1 which contains two first-order rate plots for the disappearance of 1-dodecanethiol at two different molar ratios of the thiol to 1-dodecylamine. The observed first-order rate constants in the presence of each amine are summarized in Table I. Each rate constant has been calculated relative to the rate observed for the uncatalyzed reaction of 1-dodecanethiol with TMSO. As indicated, N,N-dimethylaniline and 2,6-lutidine increased the rate by a factor of only 2 to 3. The two

TABLE I

EFFECT OF AMINE BASICITY ON THE RATE OF OXIDATION OF 1-DODECANETHIOL BY TMSO AT 100°[a]

Amine	k, sec.$^{-1}$	Rel. rate
None	7.58×10^{-6}	1.0
N,N-Dimethylaniline	1.15×10^{-5}	1.5
2,6-Lutidine	1.64×10^{-5}	2.2
1-Dodecylamine	6.42×10^{-4}	84.4
Tri(n-butyl)amine	2.04×10^{-3}	269

[a] 6.25 mmoles of 1-$C_{12}H_{25}SH$, TMSO–1-$C_{12}H_{25}SH$ = 4, 1-$C_{12}H_{25}SH$–amine = 10, mesitylene internal standard.

aliphatic amines, 1-dodecylamine and tri(n-butyl)-amine, increased the rate by a factor of 84 to 269.

The catalytic nature of the aliphatic amines was further substantiated by varying the molar ratio of 1-dodecanethiol to 1-dodecylamine from 10 to 40 in the presence of excess TMSO. The observed rate constants at three different thiol to amine ratios are summarized in Table II. As anticipated, the rate of oxidation increased as the concentration of amine increased. Further, a plot of the log of the observed rate constants for oxidation *vs.* the concentration of 1-dodecylamine gave an excellent linear relationship (see Figure 2). Thus, it can be concluded that aliphatic amines function primarily as catalysts for thiol–sulfoxide reactions.

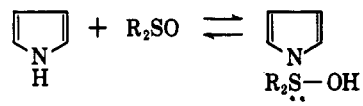
TABLE II

EFFECT OF THIOL–AMINE RATIO ON THE OXIDATION OF 1-DODECANETHIOL BY TMSO[a]

1-$C_{12}H_{25}SH$–1-$C_{12}H_{25}NH_2$ ratio	1-$C_{12}H_{25}NH_2$ M	1-$C_{12}H_{25}NH_2$ mmole	k, sec.$^{-1}$	log k
No amine	...	...	7.58×10^{-6}	−5.12
40	0.0438	0.1525	3.16×10^{-5}	−4.50
20	0.0855	0.3150	6.37×10^{-5}	−4.20
10	0.1690	0.6250	6.42×10^{-4}	−3.19

[a] 6.25 mmoles of thiol, R_2SO–thiol = 4, 100 ± 0 1°.

The effect of the acidic amine, pyrrole, on thiol–sulfoxide reactions was next investigated. Since pyrroles are susceptible to autoxidation[4] and oxidation by chemical oxidizing agents[5] the possibility of pyrrole–sulfoxide reactions was first investigated. In the presence of excess TMSO and DMSO, no reaction with pyrrole was observed at 100°. Gas chromatographic analyses indicated that essentially all of the pyrrole was unreacted after 20 hr. Thus, the possibility of the formation of either a pyrrole–sulfoxide adduct or a pyrrole dimer was discounted. The oxidation of



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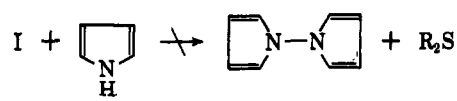


(4)

(4) See for example (a) R. H. Linnel and S. Umar, *Arch. Biochem. Biophys.*, **57**, 264 (1955); (b) M. Clerc-Bory, *Bull. soc. chim. France*, 88 (1955); (c) R. J. S. Beer, T. Broadhurst, and A. Robertson, *J. Chem. Soc.*, 4496 (1952), and references therein.

(5) For a review see R. M. Acheson, "Introduction to the Chemistry of Heterocyclic Compounds," Interscience Publishers, Inc., New York, N. Y., 1960, Chapter 3.

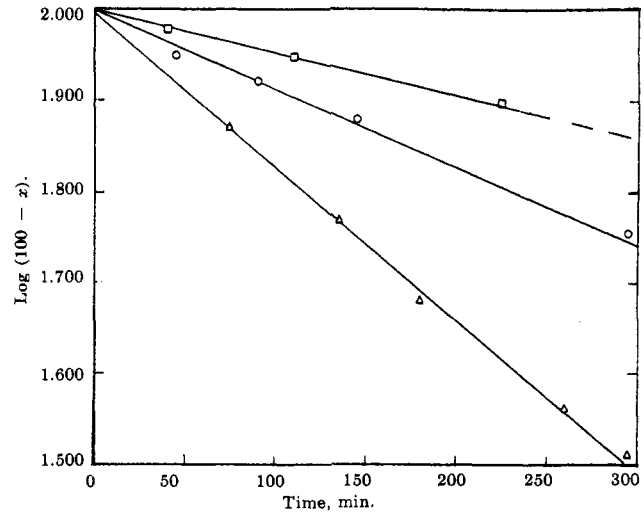


Figure 1.—Typical first-order rate plots for the oxidation of 1-$C_{12}H_{25}SH$ by TMSO at 100° in the presence of amines: ○, 1-$C_{12}H_{25}SH$–1-$C_{12}H_{25}NH_2$ = 20; △, 1-$C_{12}H_{25}SH$–1-$C_{12}H_{25}NH_2$ = 10; □, 1-$C_{12}H_{25}SH$–pyrrole = 5.

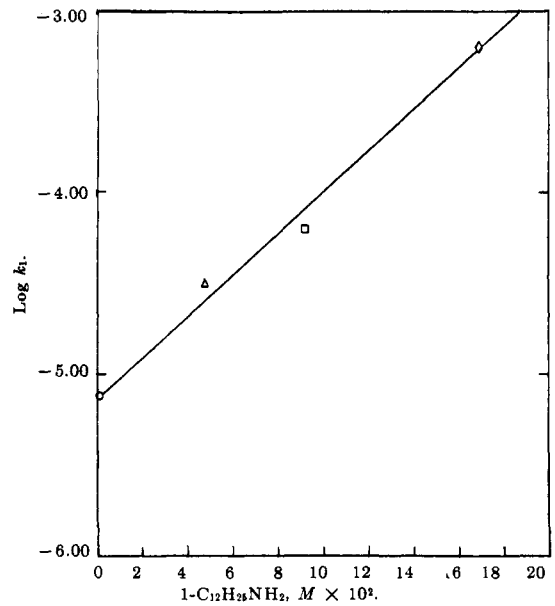


Figure 2.—Catalysis of the oxidation of 1-dodecanethiol by TMSO in the presence of 1-$C_{12}H_{25}NH_2$ at 100°; 1-$C_{12}H_{25}SH$–1-$C_{12}H_{25}NH_2$: ◊, 10; □, 20; △, 40; ○, no amine.

1-dodecanethiol by TMSO at 100° in the presence of pyrrole was next investigated. The results of this study are shown in Table III. As indicated, an inhibition of the thiol–sulfoxide reaction did not occur. Rather, a mild catalysis of the reaction was observed. For example, at a thiol–pyrrole ratio of 5 the rate of oxidation was increased by a factor of 2.5. A plot of the log of the observed rate constants *vs.* the con-

TABLE III

EFFECT OF PYRROLE ON THE OXIDATION OF 1-DODECANETHIOL BY TMSO[a]

1-$C_{12}H_{25}SH$–pyrrole ratio	Pyrrole M	Pyrrole mmoles	k, sec.$^{-1}$	log k
No amine	...	...	7.58×10^{-6}	−5.12
20	0.0750	0.3125	8.93×10^{-6}	−5.07
10	0.1875	0.625	1.33×10^{-5}	−4.89
5	0.3375	1.250	1.78×10^{-5}	−4.76

[a] 6.25 mmoles of 1-$C_{12}H_{25}SH$, R_2SO–RSH = 4, 100 ± 0.1°.

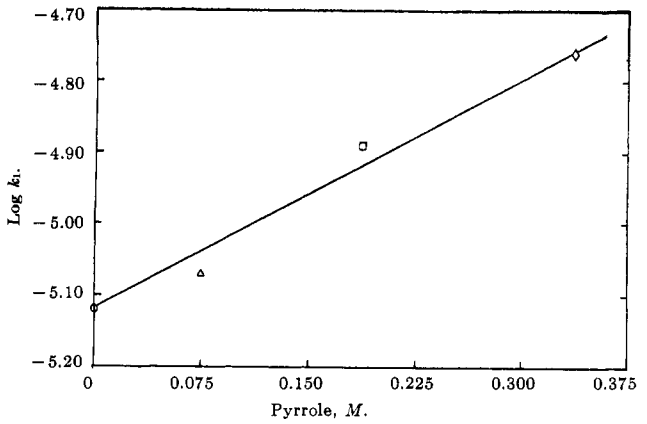


Figure 3.—Catalysis of the oxidation of 1-dodecanethiol by TMSO in the presence of pyrrole at 100°; 1-$C_{12}H_{25}SH$–pyrrole: ◊, 5; □, 10; △, 20; ○, no amine.

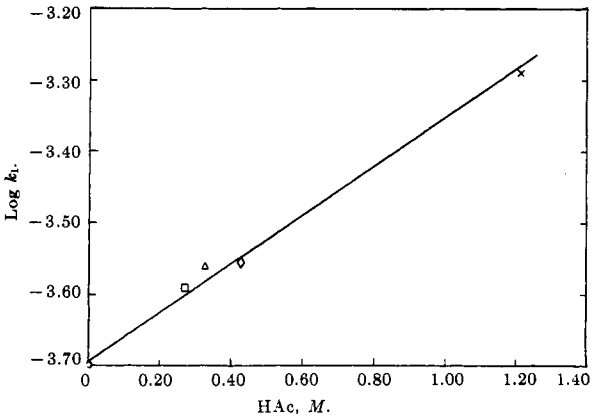


Figure 4.—Catalysis of the oxidation of α-toluenethiol by TMSO in the presence of acetic acid at 100°; $C_6H_5CH_2SH$–HAc: ×, 2.1; ◊, 6.3; △, 8.2; □, 10; ○, no acid.

centration of pyrrole is shown in Figure 3. A linear relationship was obtained for the concentration range employed. Thus, pyrrole functions as a mild catalyst and not as a coreactant or inhibitor under these conditions.

The above results with pyrrole prompted us to determine the effect of a stronger acid on these reactions. The oxidation of a more acidic thiol, α-toluenethiol, by TMSO was investigated in the presence of acetic acid at 100°. Since this thiol is oxidized more readily than 1-dodecanethiol, any significant inhibition would be more easily observed. Details of this study are summarized in Table IV. As indicated, the rate of oxidation was not inhibited by acetic acid. Actually, mild catalysis of the reaction was observed as the concentration of acetic acid was increased. The catalytic nature of the acid is also apparent from Figure 4. A plot of the log of each rate constant *vs.* the concentration of acid was linear for the concentration range investigated. Similar data for the oxidation of 1-dodecanethiol by TMSO in mesitylene using phosphoric acid as a catalyst are summarized in Table V and Figure 5. As indicated, the rate of oxidation of the aliphatic thiol was increased by a factor of 4.

The above results suggested that these reactions are general acid and general base catalyzed. This conclusion has been substantiated by studying the oxidation of 1-dodecanethiol by TMSO in the presence of 2-hydroxypyridine, which is both a weak acid and a weak base.[6] The results of this study are summarized in Table VI. As the thiol–2-hydroxypyridine ratio was varied from 50 to 10, the rate of oxidation increased by a factor of 7.5. Further, as shown in Figure 6, 2-hydroxypyridine is also a true catalyst for these reactions.

TABLE IV

EFFECT OF ACETIC ACID ON THE RATE OF OXIDATION OF α-TOLUENETHIOL BY TMSO[a]

Thiol–acetic acid ratio	Acetic acid, M	Acetic acid, mmoles	k, sec.$^{-1}$	log k
No acid	...	...	1.92×10^{-4}	−3.70
10	0.269	0.630	2.57×10^{-4}	−3.59
8.2	0.325	0.760	2.72×10^{-4}	−3.56
6.3	0.424	1.000	2.77×10^{-4}	−3.55
2.1	1.208	3.00	5.13×10^{-4}	−3.29

[a] 6.25 mmoles of $C_6H_5CH_2SH$, R_2SO–RSH = 4, 100 ± 0.1°.

TABLE V

EFFECT OF PHOSPHORIC ACID ON THE RATE OF OXIDATION OF 1-DODECANETHIOL BY TMSO IN MESITYLENE[a]

RSH–H_3PO_4 ratio	H_3PO_4, M	H_3PO_4, mmoles	k, sec.$^{-1}$	log k
No catalyst	...	...	9.78×10^{-7}	−6.10
9.8	8.97×10^{-2}	6.35	3.40×10^{-7}	−5.47
13.4	5.93×10^{-2}	4.68	1.90×10^{-6}	−5.72
30.5	2.65×10^{-2}	2.05	1.29×10^{-6}	−5.96

[a] 6.25 mmoles of 1-$C_{12}H_{25}SH$, R_2SO–RSH = 4, 100°.

TABLE VI

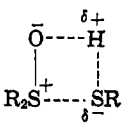
EFFECT OF 2-HYDROXYPYRIDINE ON THE RATE OF OXIDATION OF 1-DODECANETHIOL BY TMSO IN MESITYLENE[a]

1-$C_{12}H_{25}SH$–2-hydroxypyridine ratio	2-Hydroxypyridine, M[b]	2-Hydroxypyridine, mmoles	k, sec.$^{-1}$[c]	log k
No catalyst	...	...	9.12×10^{-7}	−6.04
50	0.0129	0.1250	1.16×10^{-6}	−5.94
20	0.0324	0.3125	2.89×10^{-6}	−5.54
10	0.0648	0.6250	6.87×10^{-6}	−5.16

[a] 6.25 mmoles of 1-$C_{12}H_{25}SH$, R_2SO–RSH = 4, 100 ± 0.1°. [b] In mesitylene (total volume of 9.36 ml.). [c] Cetane was used as an internal standard for quantitative data.

Discussion

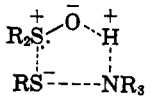
Our previous kinetic studies[3] established that the rate-determining step in thiol–sulfoxide reactions is initial reaction of the thiol with the sulfoxide to form an unstable adduct. The most probable transition state for such a reaction is a four-centered intermediate which involves a formal charge separation in the sulf-



oxide linkage and some partial ionic character in the sulfur–hydrogen bond of the thiol. Such a transition state would account for the fact that aromatic thiols are about 10^4 times more reactive than aliphatic thiols in the presence of a sulfoxide. This is a direct consequence of thiol acidity since the ΔpK_a between ben-

(6) C. G. Swain and J. F. Brown, *J. Am. Chem. Soc.*, **74**, 2534, 2538 (1952).

zenethiol and 1-dodecanethiol is about 6 to 7. The results in Table I indicate that aliphatic amines accelerate the rate of oxidation of aliphatic thiols by a factor of 84 to 269. It seems reasonable to conclude that the observed catalysis is due to increased ionic character of the sulfur–hydrogen bond in the transition state. In the presence of the amine, the transition state most likely consists of a five-membered intermediate that involves sulfoxide, thiol, and amine.



Such a transition state implies that there is a fair degree of ionic character in the presence of the amine catalyst. This would seem reasonable since, in the presence of tri(*n*-butyl)amine, 1-dodecanethiol is oxidized at a rate which is not significantly less than that observed for benzenethiol. This point can be seen more clearly in Table VII which contains a comparison of the pseudo-first-order rate constants for oxidation of the two thiols by TMSO at 100°. Benzenethiol is oxidized only 20 times faster than 1-dodecanethiol when the amine catalyst is employed.

TABLE VII

COMPARISON OF THE RATE OF OXIDATION OF BENZENETHIOL AND 1-DODECANETHIOL IN THE PRESENCE OF TMSO AT 100°

Thiol	k, sec.$^{-1}$	Rel. rate
1-$C_{12}H_{25}SH$	7.58×10^{-6}	1.0
1-$C_{12}H_{25}SH$ + $(C_4H_9)_3N$	2.04×10^{-3}	2.7×10^{2}
C_6H_5SH[a]	3.95×10^{-2}	5.2×10^{3}

[a] Taken from ref. 3.

The low catalytic activity of N,N-dimethylaniline and 2,6-lutidine is probably due to their decreased basicity in comparison to aliphatic amines.[5] This is not surprising since it is known that aliphatic amines are much more efficient catalysts for the autoxidation of thiols than aromatic amines and that aliphatic aminothiols are autoxidized more readily than their corresponding aliphatic thiol analogs.[7,8] Since the amine is a true catalyst, other advantages become apparent. From a synthetic standpoint, the oxidation of aliphatic thiols by sulfoxides can be accomplished at lower temperatures and in shorter reaction times. Further, thiols containing an amino functional group can be oxidized selectively at the thiol group without any attack on the amino group.

The observed effect of acids on these reactions was not entirely expected since halogen acids are oxidized by sulfoxides.[9] Thus, it was anticipated that pyrrole and acetic acid could function as inhibitors for thiol–sulfoxide reactions by complexing with the sulfoxide linkage. The data shown in Tables III–V and Figures 3–5 clearly show that this is not the case. A rate increase of two- to threefold was observed for the oxidation of 1-dodecanethiol in the presence of pyrrole

(7) A. A. Oswald, F. Noel, and A. J. Stephenson, *J. Org. Chem.*, **26**, 3969 (1961).

(8) For a review see A. A. Oswald and T. J. Wallace in "Organic Sulfur Compounds," Vol. II, N. Kharasch, Ed., Pergamon Press, New York, N. Y., 1965, Chapter 8.

(9) For a summary see W. O. Ranky and D. C. Nelson, "Organic Sulfur Compounds," Vol. I, N. Kharasch, Ed., Pergamon Press, New York, N. Y., 1961, Chapter 17.

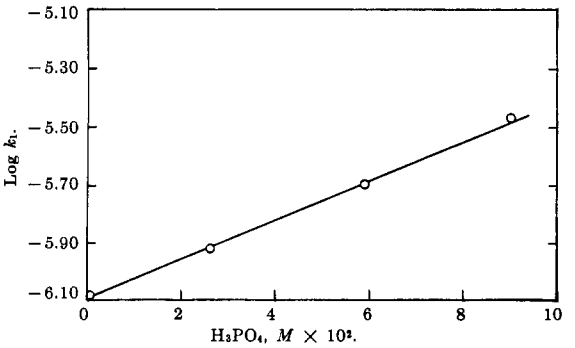


Figure 5.—Catalysis of the oxidation of 1-dodecanethiol by TMSO in the presence of phosphoric acid.

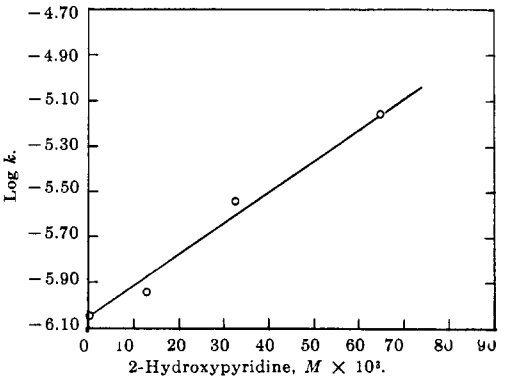
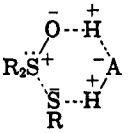


Figure 6.—Catalysis of the oxidation of 1-dodecanethiol by TMSO in the presence of 2-hydroxypyridine.

and for the oxidation of α-toluenethiol in the presence of acetic acid. Since the catalytic nature of both acids was established, it is obvious that their presence results in a slightly more favorable transition state for reaction. This can be pictured as one which involves thiol–sulfoxide–acid pseudo-six-membered, or possibly eight-membered, ring formation. Such a transition state favors initial protonation of the sulfoxide. The above



conclusions are consistent with our results from 2-hydroxypyridine. Since the catalytic efficiency of this compound lies between the pyrrole–aliphatic amine systems it must function by both modes of catalysis.

Finally, some comments on an alternative mechanism for these reactions should be made. Prior to our catalysis studies, the possible intermediacy of sulfenate ions (RSO^-) in these reactions could not be ruled out.[10] Such intermediates could form by the following reaction sequence. Such a sequence would certainly

$$RSH \rightleftharpoons RS^- + H^+ \quad (5)$$

$$RS^- + R_2SO \rightleftharpoons RSO^- + R_2S \quad (6)$$

$$RSO^- + H^+ \rightleftharpoons RSOH \quad (7)$$

$$RSOH + RSH \rightleftharpoons RSSR + H_2O \quad (8)$$

depend on thiol acidity. However, lack of inhibition by acetic acid and phosphoric acid and effective

(10) We are grateful to Professor H. C. Brown who first called this possibility to our attention.

catalysis by 2-hydroxypyridine would indicate that reactions 5 and 6 are improbable under these conditions.

Experimental

Reagents.—1-Dodecanethiol (Columbia Organic Chemicals) and α-toluenethiol (Evans Chemetics) were obtained as reagent grade materials. Gas chromatographic analysis indicated that each thiol was at least 98% pure. Tetramethylene sulfoxide (K and K Laboratories) was purified by distillation over Linde-13X Molecular Sieves to remove any adsorbed water. The sieves were previously conditioned by calcination under nitrogen at 400° for 4 hr. The sulfoxide gave only one peak when analyzed by gas chromatography on a 3-ft., 20 wt. % Carbowax (20 MM) on Chromosorb-W column. 2,6-Lutidine, N,N-dimethylaniline, 1-dodecylamine, tri(*n*-butyl)amine, and pyrrole, which were used in catalysis studies, were purified by distillation through a 16-in. column equipped with a tantalum-wire spiral. The physical properties of each amine agreed with the known literature values.

General Procedure for Kinetic Studies.—A general procedure was employed in all kinetic studies. The sulfoxide, an equimolar amount of internal hydrocarbon standard, and catalyst were weighed into a vial in a nitrogen drybox with the aid of an analytical balance. The vial was capped (under nitrogen) with a self-sealing Neoprene stopper. The stopper extended down from the mouth of the vial and further sealing was accomplished by wrapping a piece of heavy copper wire around this portion of the stopper. Thus, the contents of the vial were doubly protected against moisture and oxygen. Upon sealing, the vial was placed in a Primoil-D constant-temperature bath (±0.1°). After the vial had reached thermal equilibrium, the desired quantity of prethermostated thiol was injected into the vial by a syringe, the vial was immediately shaken to obtain a homogeneous solution, and an initial sample was withdrawn by another syringe. When perfected, this operation can be performed in about 3 sec. Sampling was also accomplished with the aid of a syringe. At the desired time, an aliquot was withdrawn (5 to 10 μl.) and immediately injected into a sealed vial containing a small quantity (0.25-to 0.50 ml.) of cold acetone (0° or below). The last step stopped the reaction. A portion of the acetone solution was withdrawn by a syringe and subsequently analyzed by gas–liquid chromatography. Quantitative data was obtained from the areas of the internal standard and reactant in question using predetermined molar response factors.

Gas–Liquid Chromatographic Techniques.—The g.l.c. unit employed was an F and M Model 609 flame ionization gas chromatograph equipped with a Minneapolis Honeywell recorder and a disk integrator (Model 201). The injection port of the unit was maintained at 305° and the inlet pressure of helium was 36 p.s.i.g. The block of the detector was maintained at a constant temperature of 245°. The helium flow through the column was 100 cc./min. when measured by a flow meter. Quantitative data for each thiol was obtained on a 3-ft., 20% Carbowax (20 MM) on Chromosorb-W column (0.25-in. stainless steel tubing). This column gave excellent separation of all the thiol–hydrocarbon–sulfoxide mixtures investigated. No interference by sulfide or disulfide was encountered.[11]

Diphenylmethane and mesitylene were employed as the internal standards for measuring the rate of α-toluenethiol and 1-dodecanethiol disappearance. The column temperatures ranged from 200–225°. The response factor between α-toluenethiol and diphenylmethane was 1.87 and that between 1-dodecanethiol and mesitylene was 1.54[12] (see Table VII). Usually, the sulfoxide was eluted from the column before the thiol and its internal standard.

In the catalysis studies with 2-hydroxypyridine reactions were conducted in mesitylene since the catalyst was not completely soluble under the above conditions. Mesitylene (5 ml.) was used and the total volume of each solution was 9.63 ml. The kinetic analyses of these solutions were performed on a 2-ft. silicone rubber column at 185°. Cetane (6.25 mmoles) was employed as the internal standard and the predetermined molar response factor for 1-dodecanethiol was 1.61 at 185°.

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(11) T. J. Wallace and J. J. Mahon, *Nature*, **201**, 817 (1964), contains a detailed description of these techniques.

(12) For a detailed discussion on the significance of molar response factors, see A. E. Messner, D. M. Rosie, and P. A. Argabright, *Anal. Chem.*, **31**, 230 (1959).

Azomethine Chemistry. IV. Chemistry of Fused Thiazolidines[1,2]

RICHARD G. HISKEY AND SAMUEL J. DOMINIANNI[3]

The Venable Chemical Laboratory, University of North Carolina, Chapel Hill, North Carolina

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Several fused thiazolidines have been prepared by standard methods. Bromination, reduction, oxidation, and hydrolysis of these compounds have been studied. The n.m.r. spectra are rationalized in terms of the molecular geometry.

In connection with another study concerned with nucleophilic additions to azomethines,[4] the reaction of several β-aminoethylmercaptans with various keto acids were of interest. Reactions of this type are well known and have been shown to provide saturated thiazolo[2,3-*a*]isoindoles,[5] thiazolo[3,2-*a*]pyridines,[6] and thiazolo[2,1-*b*]pyrroles.[7] The present report concerns the preparation of several hexahydropyrrolo[2,1-*b*]-thiazoles[8] and a study of their chemical reactions and n.m.r. spectra.

When β-benzoylpropionic acid (**1**) was refluxed with 2-mercaptoethylamine in methanol, the fused thiazolidine (**2a**) was obtained in 60–65% yield. Azeotropic distillation of a benzene solution of **1** and 2-mercapto-2-methylpropylamine provided **2b**[4] in 50% yield. A similar reaction involving γ-benzoylbutyric acid and the

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(2) Part III of this series: R. G. Hiskey and R. C. Northrop, *J. Am. Chem. Soc.*, **87**, 1753 (1965).

(3) Abstracted in part from the Ph.D. Dissertation of S. J. Dominianni, University of North Carolina, Aug. 1964.

(4) R. G. Hiskey and J. M. Jung, *J. Am. Chem. Soc.*, **85**, 578 (1963).

(5) G. L. Oliver, J. R. Dann, and J. W. Gates, *ibid.*, **80**, 702 (1958).

(6) D. Todd and S. Teick, *ibid.*, **75**, 1895 (1953).

(7) H. H. Wasserman, F. M. Precopio, and T. C. Liv, *ibid.*, **74**, 4093 (1952).

(8) The numbering system for hexahydropyrrolo[2,1-*b*]thiazoles follows.