excess boron fluoride. The organic layer was dried, the solvent removed, and the residue distilled to give a small amount of dithianaphthenylmethane and 6.6 g. of material, b.p. 290–315° (0.2 mm.). The product was redistilled to remove traces of di(3-thianaphthenyl)methane. The infrared spectrum potassium bromide of the final product was identical with the spectrum potassium bromide of fraction B.

Reaction of thianaphthene and trioxane with aluminum chloride as catalyst. A mixture of 134 g. (1 mole) of thianaphthene and 18 g. 0.5 mole) of trioxane was dissolved in a mixture of 100 ml. of chloroform and 100 ml. of carbon disulfide. The temperature was kept at 0–10° and 42. g. of powdered anhydrous aluminum chloride was added with stirring over the course of 10 hr. The temperature was then maintained at about 10° and stirring was continued for 4 days. The reaction mixture became very black and nearly solid. After the addition of ice water to decompose excess aluminum chloride, the mixture was filtered to remove the tarry solids. The filtrate was washed with dilute sodium hydroxide and water and dried over magnesium sulfate. The solvent was removed and the residue was distilled to give 3 g. of thianaphthene and 71 g. (50%) of di(3-thianaphthenyl)methane, b.p. 200–220° (1 mm.). The melting point for and the analysis of the dibromide were the same as for those of the dibromide obtained in the analogous boron trifluoride catalyzed reaction. When the impure di(3-thianaphthenyl)methane was allowed to stand for a time, a small amount of crystals appeared in the viscous sirup. A little ether was added to make the mass more fluid, and the crystals were collected. Recrystallization from dioxane yielded pearly leaflets, m.p. 300–302°.

Anal. Calcd. for compound I, $C_{18}H_{10}S_2$: C, 74.47; H, 3.48; S, 22.04. Found: C, 75.19; H, 3.11; S, 22.00.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF DELAWARE]

The Kinetics of the Reactions of Phenyl Isocyanate with Thiols[1]

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The base-catalyzed reactions of phenyl isocyanate with 1-butanethiol, 2-butanethiol, and 2-octanethiol in various solvents at 25° were studied to elucidate the mechanism. The slight catalytic effect of the product on the initial second-order reaction was shown to require the amide hydrogen, since *n*-butyl-*N*,*N*-diphenyl thiolcarbamate had no effect. The rate of reaction depended primarily upon the concentration and type of amine catalyst and the polarity of the solvent. The catalytic ability of an amine was generally proportional to its base strength; however, a steric requirement was also apparent. A mechanism is proposed which includes a spontaneous reaction, a base-catalyzed reaction, a product-catalyzed reaction, and a product-base-catalyzed reaction. From kinetic equations based on this mechanism rate constants were calculated, which compare favorably with experimental data.

It has been shown previously[2] that the reactions of phenyl isocyanate with thiols in the presence of triethylamine follow approximate second order kinetics during the early stages. As the reactions progress there is an increase in the rate, which was attributed to catalysis by the thiolcarbamate produced during the reaction. It was the purpose of this work to continue the study of the base-catalyzed reaction of phenyl isocyanate with thiols in order to propose a mechanism and to derive a rate equation. Many studies have been made on the kinetics of the reactions of isocyanate with alcohols[3–5] and with amines,[6] but the thiol reaction has not been thoroughly investigated.

The major portion of this work was done with phenyl isocyanate and 1-butanethiol in various solvents with several base catalysts. The study also included the reaction of the isocyanate with the secondary thiols, 2-butanethiol and 2-octanethiol. The triethylamine-catalyzed reaction between phenyl isocyanate and 1-butanethiol at 25° was shown[2] to produce a single product, *n*-butyl thiolcarbanilate. This product was found to be inactive toward phenyl isocyanate under these conditions. Similarly, the reaction between phenyl isocyanate and 2-butanethiol produced only the secondary butyl thiolcarbanilate.

The kinetic results obtained from the reactions of phenyl isocyanate with 1-butanethiol, 2-butanethiol, and 2-octanethiol at various isocyanate to thiol ratios and at various concentrations of triethylamine in toluene are summarized in Table I. The second order rate curves (Fig. 1) for several reactions of phenyl isocyanate with 1-butanethiol

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[1] From the Ph.D. Thesis of John F. Glenn and the M.S. Thesis of Edward G. Lendrat, University of Delaware, 1960. Presented at the 138th meeting of the American Chemical Society, New York, N. Y., September 1960. Received by the *J. Am. Chem. Soc.*, July 13, 1960.

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[3] (a) J. W. Baker and J. B. Holdsworth, *J. Chem. Soc.*, 713 (1947); (b) J. W. Baker and J. Gaunt, *J. Chem. Soc.*, 9 (1949); (c) J. Burkus and C. F. Eckert, *J. Am. Chem. Soc.*, **80**, 5948 (1958); (d) L. L. Ferstandig and R. H. Scherrer, *J. Am. Chem. Soc.*, **81**, 4838 (1959).

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TABLE I

RATES OF TRIETHYLAMINE CATALYZED REACTION OF PHENYL ISOCYANATE WITH THIOLS IN TOLUENE AT 25°

RSH	$\frac{[RSH]}{[C_6H_5NCO]}$	$10^4[(C_2H_5)_3N]$ M	$10^4 k_e$, L. Mole^{-1} Sec.$^{-1}$
1-C_4H_9SH[a]	1.6[b]	4.04	4.48
		10.1	11.2
	2.0[b]	3.76	4.14
		3.96	4.24
		5.77	5.87
		6.62	6.48
		6.85	6.58
		8.34	8.92
		8.65	9.16
		9.63	9.72
		9.89	10.4
		18.5	19.2
	3.0[b]	5.49	5.98
		9.65	10.2
		11.2	12.7
	4.0[b]	5.26	5.41
2-C_4H_9SH[c]	1.0[e]	32.3	4.48[d]
		42.2	5.75[d]
		73.5	9.92[d]
		73.6	9.53
		96.2	11.9
	2.0[f]	20.4	2.90
		40.8	4.59
		48.4	6.09
		48.5	6.14
	3.0[f]	21.2	2.18
		35.4	4.69
		35.6	4.63
		42.6	4.48
2-$C_8H_{17}SH$[c]	1.0[f]	74.0	7.30
		147.	15.1
		167.	15.9

[a] Per cent of reaction used in calculating k_e was less than 15. [b] $[C_6H_5NCO]$ approx. 0.0750M. [c] $[C_6H_5NCO]$ approx. 0.200M, except as noted. [d] Determined by chemical method, $[C_6H_5NCO]$ 0.100M. [e] Per cent of reaction used in calculating k_e was 38–78. [f] Per cent of reaction used for k_e was 9–36.

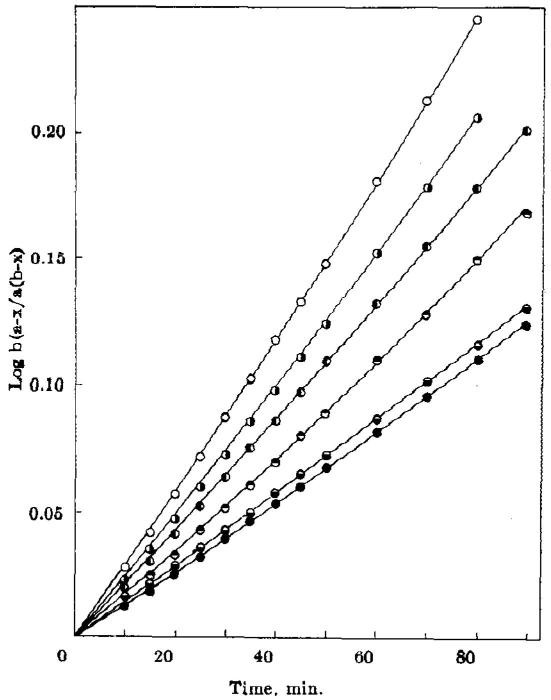


Fig. 1. Second order rate curves for reactions of phenyl isocyanate with 1-butanethiol and 2-butanethiol at 25° with triethylamine catalyst: ○, C_6H_5NCO 0.073M, 1-C_4H_9SH 0.27M, $(C_2H_5)_3N$ 5.2 × $10^{-4}M$; ,◑ C_6H_5NCO 0.075M, 1-C_4H_9SH 0.22M, $(C_2H_5)_3N$ 5.5 × $10^{-4}M$; ◐, C_6H_5NCO 0.076M, 1-C_4H_9SH 0.16M, $(C_2H_5)_3N$ 8.6 × $10^{-4}M$; ◓ C_6H_5NCO 0.196M, 2-C_4H_9SH 0.4114M, $(C_2H_5)_3N$ 24.0 × $10^{-4}M$; ◒ C_6H_5NCO 0.075M, 1-C_4H_9SH 0.15M, $(C_2H_5)_3N$ 6.6 × $10^{-4}M$; ● C_6H_5NCO 0.077M, 1-C_4H_9SH 0.12M, $(C_2H_5)_3N$ 10.1 × $10^{-4}M$

and 2-butanethiol are based on dilatometric data (except as noted).

A conclusion previously stated[2] that the isocyanate/thiol ratio affected the rate constant is withdrawn on the basis of (a) new data (Table I) obtained at lower concentrations (more nearly ideal solutions) and (b) the constancy of the slope of the graph of initial rate constant *vs.* amine concentration for small ratios. Pseudo first order kinetics were observed for large isocyanate/thiol ratios.

All the rate curves for the triethylamine catalyzed reaction of phenyl isocyanate with 1-butanethiol showed a slight upward curvature. To test whether this curvature was produced by product catalysis, the carbamate product, *n*-butyl thiolcarbamate, was added at the beginning of the reaction in varying ratios. The results of these runs are summarized in Table II and typical plots (at varying amine concentrations) are given in Fig. 2. In each case the plots of the rate data by the usual second order function gave a straight line. When the data of Table II were plotted as initial rate constant *vs.* amine concentration, the slope of the resultant straight line varied directly with the amount of product added at the beginning of the reaction. These slopes varied from 1.35 for reaction mixtures that were 0.075M in product to 1.84 for mixtures that were 0.225M in product.

The catalytic action of the product, *n*-butyl thiolcarbanilate is apparently due to the amide hydrogen, since the fully substituted compound, *n*-butyl-*N*,*N*-diphenyl thiolcarbamate has no catalytic effect.

If no triethylamine was used as catalyst for reaction mixtures containing phenyl isocyanate, 1-butanethiol and the thiol carbanilate product, a very slow reaction was noted. The rate constant for these reactions was approximately 8 × 10^{-6} l. mole^{-1} sec.$^{-1}$

Energies and entropies of activation for the triethylamine-catalyzed reaction of phenyl isocyanate with 1-butanethiol and 2-butanethiol in toluene are listed in Table III. These values are very similar to those obtained for the catalyzed reaction of phenyl isocyanate with 1-butanol.[3c]

Solvent effects for the amine-catalyzed reaction of 1-butanethiol with phenyl isocyanate are indicated by the data of Table IV. The ratio $k_{CH_3CO_2C_4H_9}/k_{toluene}$ is 3, while $k_{NO_2C_6H_5}/k_{toluene}$ is

TABLE II

RATES[a] OF TRIETHYLAMINE CATALYZED REACTION OF PHENYL ISOCYANATE WITH THIOLS IN PRESENCE OF ADDED THIOLCARBAMATES IN TOLUENE AT 25°

RSH and Product	Ratio RSH: Product: C_6H_5NCO	10^4 $[(C_2H_5)_3N]$ M	10^4 k_e, L. Mole^{-1} Sec.$^{-1}$
1-C_4H_9SH[b] and $C_6H_5NHCOSC_4H_9(n)$	2:1:1	0	0.032
		3.25	4.61
		5.46	8.83
		9.46	12.5
		9.68	12.9
	2:1.5:1	5.33	7.21
		9.27	14.0
	2:2:1	0	0.080
		3.67	5.83
		5.25	6.47
		7.87	13.7
		8.61	14.3
	2:3:1	5.62	10.1
		8.35	16.0
1-C_4H_9SH[b] and p-$CH_3OC_6H_4NHCOS$-$C_4H_9(n)$	2:2:1	4.50	7.21
		7.04	10.8
		9.12	17.4
		13.5	20.0
1-C_4H_9SH[b] and $(C_6H_5)_2NCOSC_4H_9(n)$	2:2:1	6.43	7.27
		7.90	8.62
		10.2	11.1
2-C_4H_9SH[c] and $C_6H_5NHCOSC_4H_9(sec)$	1:1:1	15.0	2.19
		30.2	6.99
		44.6	8.08
		55.4	10.00

[a] Per cent of reaction used in calculating initial k_e was less than 15. [b] $[C_6H_5NCO]$ approx. 0.0750M. [c] $[C_6H_5NCO]$ approx. 0.200M.

TABLE III

ENERGIES AND ENTROPIES OF ACTIVATION FOR REACTIONS OF PHENYL ISOCYANATE WITH THIOLS IN TOLUENE WITH TRIETHYLAMINE AS CATALYST

		10^4 k_e in l. mole^{-1} sec.$^{-1}$			
Thiol	10^4 $[(C_2H_5)_3N]$	At 20.00°	At 25.00°	ΔE, K.Cal.	ΔS, E.U.
1-C_4H_9-SH[a]	6.26	7.0[b]	7.9[c]	3.9	−64
2-C_4H_9-SH[a]	62.6	7.6[b]	8.7[c]	4.6	−58

[a] Concn. of thiol and of isocyanate each 0.20M. [b] Average of two runs. [c] Average from graph of k_e vs. $(C_2H_5)_3N$.

200. The ionizing effect of the solvent is not necessarily the determining factor; reactions in acetonitrile are very slow. The nitrile group may possibly compete with the isocyanate for the electrons of the amine, thereby depressing the rate by removal of the amine catalyst.

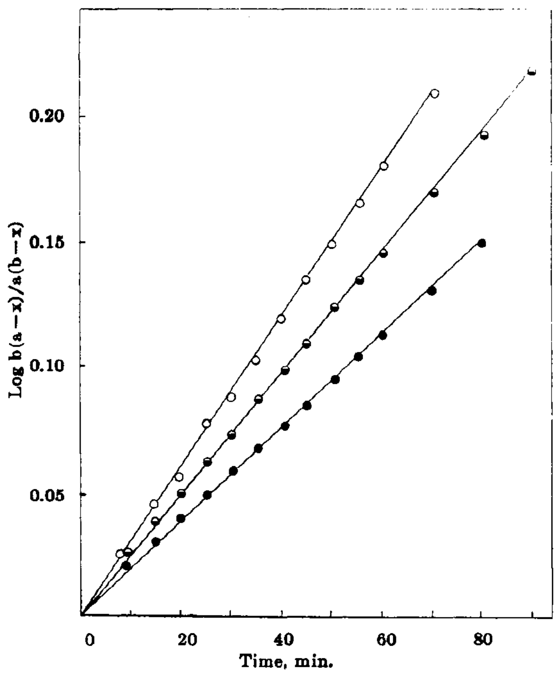


Fig. 2. Second order rate curves for reaction of phenyl isocyanate with 1-butanethiol in the presence of 1-butyl thiolcarbanilate at 25° with triethylamine catalyst; ○, C_6H_5NCO 0.077M, 1-C_4H_9SH 0.159M, $(C_2H_5)_3N$ 0.00787M, $C_6H_5NHCOSC_4H_9$ 0.157M; ◒, C_6H_5NCO 0.075M, 1-C_4H_9SH 0.152M, $(C_2H_5)_3N$ 0.00056M, $C_6H_5NHCOSC_4H_9$ 0.215M; ●, C_6H_5NCO 0.075M, 1-C_4H_9SH 0.163M, $(C_2H_5)_3N$ 0.00054 M, $C_6H_5NHCOSC_4H_9$ 0.082M

TABLE IV

TRIETHYLAMINE CATALYZED RATES OF REACTION OF PHENYL ISOCYANATE WITH 1-BUTANETHIOL IN SOLVENTS OTHER THAN TOLUENE

$[C_6H_5NCO]$ = 0.0750M; $[1\text{-}C_4H_9SH]$ = 0.1600M

Solvent	10^4 $[(C_2H_5)_3N]$ M	10^4 k_e, L. Mole^{-1} Sec.$^{-1}$	%[a]
$CH_3CO_2C_4H_9$	2.40	Too slow	
	4.80	4.02	7
	9.62	17.6	15
	10.9	22.0	16
	17.5	40.5	20
	18.1	44.3	18
	23.3	62.9	23
$C_6H_5NO_2$	0.0506	Too slow	
	0.152	31.1	15
	0.173	30.4	14
	0.196	32.0	25
	0.389	78.3	38
	1.04	216.	68
	2.58	Too rapid	
CH_3CN	4.76	Too slow	
	22.9	0.05	5
	35.0	0.04	7

[a] Per cent of reaction used in calculating k_e.

When dimethylformamide and dimethyl sulfoxide were used as solvents, the rates became too fast to measure, either with or without the triethylamine catalyst. It is probable that these solvents also act as basic catalysts and, when present in large excess, become efficient catalysts, although in small amounts their catalytic effect is slight (Table V).

It was noted throughout this study that the concentration of the basic catalyst was the major factor determining the rate. The graph of the initial rate constant against the amine concentration in a

TABLE V

RATES OF REACTION OF PHENYL ISOCYANATE WITH THIOLS IN TOLUENE AT 25° WITH CATALYSTS OTHER THAN TRIETHYLAMINE

Base	10^3 [Cat] M	10^4 k_c, L. Mole^{-1} Sec.$^{-1}$	10^3 [Cat] M	10^4 k_c L. Mole^{-1} Sec.$^{-1}$
	1-BUTANETHIOL[a]			
Benzyldimethylamine	1.25	3.81	3.79	14.5
	2.54	8.96	4.46	14.6
	3.21	11.3	5.12	18.3
1,4-Diazabicyclo[2.2.2]octane (DABCO)	0.180	4.09	0.594	12.6
	0.349	7.94	0.699	14.9
	0.524	11.0	0.795	17.5
Diethylaniline	82.1	Too slow	507	Too slow
Dimethylformamide[b]	5.75	0.0003	502	0.213
	133.	0.0560		
Dimethyl sulfoxide	21.7	Too slow	560	1.37
	277.	0.383		
Pyridine	102.	Too slow	537	0.92
	365.	0.39		
Tri-n-butylamine	2.10	3.77	4.01	9.40
	2.54	6.55	5.33	10.9
	3.73	7.10	7.33	16.6
Tri-n-propylamine	1.97	4.02	5.86	11.6
	3.87	6.75	7.50	13.6
	4.84	9.49	8.78	16.4
1-Ethylmorpholine	3.47	0.550	65.9	9.63
	13.7	1.86	73.9	10.7
	32.4	4.52	131.	19.1
1-Ethylpiperidine	1.04	7.35	1.81	12.5
	1.39	8.33	2.07	13.0
	1.49	8.84	2.41	16.0
1-Methylpiperidine	0.700	4.11	1.71	10.5
	0.985	5.72	2.10	12.4
	1.40	8.62	2.47	15.2
1,2,2,6,6-Pentamethylpiperidine	0.947	4.34	2.30	8.48
	1.34	5.09	2.81	9.90
	1.87	6.42	3.20	12.6
	2-BUTANETHIOL[c]			
Tri-n-butylamine	21.1	5.74	26.6	7.68
	24.4	6.44	43.3	9.37
	25.8	5.20		
Pyridine	298	0.157	500	0.280
	483	0.223		

[a] Determinations with all bases except dimethylformamide were made at 0.0750M isocyanate and 0.1600M thiol concentrations. [b] Concentration isocyanate 0.2500M; thiol 0.5000M. [c] Concentration isocyanate 0.2000M; thiol 0.2000M.

given solvent produced a straight line, as shown in Fig. 3. The slope of this line, k_B, is a measure of the catalytic efficiency of the amine. The effects of variations in the structure of the amine on the k_B values are given in Tables V and VI, and a graph of the log of the k_B value against base strength is shown in Fig. 4.

In general the catalytic rate constant (k_B) is directly influenced by the base strength of the amine, as illustrated by the amines that are directly on the line. However, a second important factor is the amount of steric hindrance around the nitrogen atom, as shown by the lower catalytic efficiency of the highly hindered amines like pentamethyl piperidine and the very great catalytic efficiency of the unhindered amine 14-diazabicyclo[2.2.2]-octane (DABCO).

The very low catalytic effect of pyridine is in accord with its low base strength. Diethylaniline was found to be inactive as a catalyst, even at 0.5M concentration. Its inactivity in catalyzing

TABLE VI

CATALYTIC RATE CONSTANT AND BASE STRENGTH OF AMINE

Amine	k_B (1-C_4H_9SH)	k_B (2-C_4H_9SH)	pK_b
1,2,2,6,6-Pentamethylpiperidine	0.37		2.75
Tri-n-butylamine	0.22	0.028	3.11
Triethylamine	1.03	0.13	3.26
Tri-n-propylamine	0.19		3.35
1-Ethylpiperidine	0.65		3.60
1-Methylpiperidine	0.55		3.87
Benzyldimethylamine	0.37		5.07
1,4-Diazabicyclo[2.2.2]-octane	2.17		5.80
N-Ethylmorpholine	0.0147		6.30
Diethylaniline	0		7.44
Pyridine	0.00016	0.000051	8.85

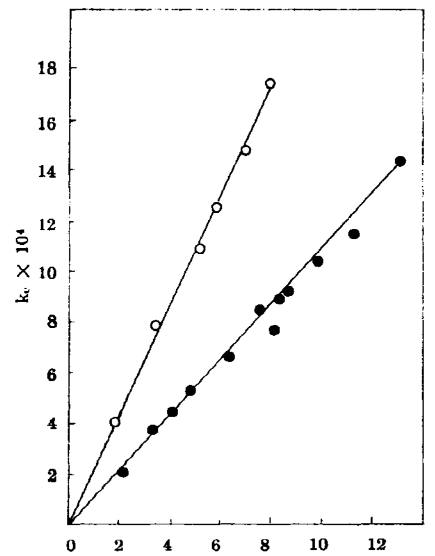


Fig. 3. Second order rate constants plotted against catalyst concentration for reaction of phenyl isocyanate (0.075*M*) with 1-butanethiol (0.15*M*); ○, 1,4-diazabicyclo[2.2.2]octane; ●, triethylamine

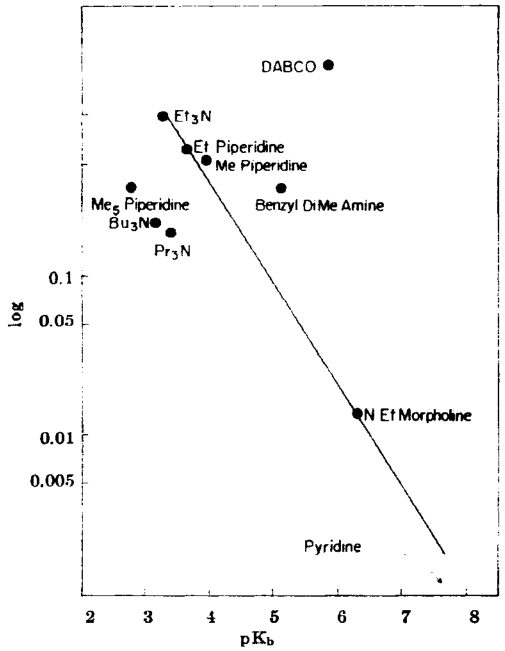


Fig. 4. Plot of log catalytic rate constant against base strength of various catalysts

reactions of phenyl isocyanate with alcohols[3] and with amines[6] was reported by Baker and coworkers.

The fact that a true Brönsted plot is not observed in the base-catalyzed reaction of phenyl isocyanate with 1-butanethiol indicates that the function of the amine does not depend on proton transfer and argues strongly for the isocyanate amine complex proposed by Baker and Holdsworth[3] and by the present authors.

The following series of equations explain the present observations.

$$C_6H_5NCO + C_4H_9SH \xrightarrow[k_0]{} C_6H_5NHCOSC_4H_9 \quad (1)$$

$$C_6H_5NCO + (C_2H_5)_3N \rightleftarrows \text{Complex 1} \xrightarrow[k_B]{C_4H_9SH} C_6H_5NHCOSC_4H_9 + (C_2H_5)_3N \quad (2)$$

$$C_6H_5NCO + C_6H_5NHCOSC_4H_9 \rightleftarrows \text{Complex 2} \xrightarrow[k_P]{C_4H_9SH} 2\ C_6H_5NHCOSC_4H_9 \quad (3)$$

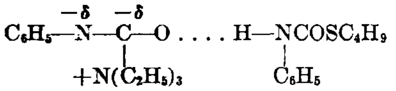
$$\text{Complex 1} + C_6H_5NHCOSC_4H_9 \rightleftarrows \text{Complex 3} \xrightarrow[k_{BP}]{C_4H_9SH} 2\ C_6H_5NHCOSC_4H_9 + (C_2H_5)_3N \quad (4)$$

The spontaneous reaction (Equation 1) is considerably slower with the thiols than with the alcohols, probably due to the fact that thiols are less basic than alcohols and therefore less able to attack the carbonyl group of the isocyanate.

The pronounced effect of bases as catalysts is indicated by Equation 2. Presumably the addition of the tertiary amine to the isocyanate makes the carbonyl carbon more electrophilic, thus more susceptible to attack by the thiol or thiolate ion. The fact that the thiolate ion is a stronger nucleophile than the alcoholate ion may explain the higher sensitivity of the reactions of the thiols to catalysis by bases; smaller increases in base concentration give greater changes in reaction rates.

Catalysis by the product in the absence of the amine is shown in Equation 3. This is actually a small effect; the addition of product to a reaction mixture containing no amine gave a rate constant only 3 to 4 times as great as that for the spontaneous reaction.

The combined catalytic effect of the product and of the base is represented by Equation 4. The ter-



$$C_6H_5{-}\overset{-\delta}{N}{-}\underset{+N(C_2H_5)_3}{\overset{-\delta}{\underset{|}{C}}}{-}O \ldots\ldots H{-}\underset{C_6H_5}{\underset{|}{N}}COSC_4H_9$$

nary complex (Complex 3) involves the amide hydrogen atom, as shown by the inactivity of the disubstituted carbamate. Further evidence is the retardation of rate obtained on addition of a thiolcarbamate having a less acidic amide hydrogen. For example, when *n*-butyl-*N*-*p*-methoxyphenyl thiolcarbamate was added to a reaction mixture of phenyl isocyanate, 1-butanethiol and triethylamine, the catalytic rate constant was 1.57, but with addition of the normal product, the constant was 1.77.

From the mechanism given above, the following summary rate equation was derived:

$$k_e = k_0 + k_B[\text{Base}] + k_P\,[\text{Product}] + k_{BP}\,[\text{Base}]\,[\text{Product}] \quad (5)$$

In this equation k_e is the experimental second order rate constant, k_B the catalytic rate constant for the base catalyzed reaction, k_P the catalytic rate constant for the product-catalyzed reaction, and k_{BP} the catalytic rate constant for the base-product-catalyzed reaction. The catalytic rate constants can be expressed in terms of the rates for each of the steps in the reaction series by the usual stationary state treatment.

The value for k_B was determined from the slope of the graph of initial rate constant plotted against the amine concentration. For the triethylamine catalyzed reaction of 1-butanethiol with phenyl isocyanate in toluene, its value was found to be 1.04. The catalytic rate constant for the product-catalyzed reaction, k_P, was determined from the slope of the plot of the experimental rate constant *vs.* product concentration. The experimental rate constants were determined from the instantaneous slope of the rate curve at a predetermined product concentration. The value of k_P was found to be approximately $10.^{-3}$ It is not possible to determine k_P accurately by this method, since the slope tends to increase with increasing base concentration. This is the influence of the base-product-catalyzed reaction rate on the value of k_P.

The catalytic rate constant, k_{BP} for the base-product-catalyzed reaction was determined by graphical methods from the data of eight runs. This was done by selecting a constant value for product concentration and determining the experimental second order rate constant from the rate curve. Since the base concentration did not vary during any given run, the rate equation (5) was then solved for k_{BP}. The value of k_{BP} was 2.2.

The values of these catalytic rate constants were tested in the rate equation by calculating the second order rate constant from the summary equation and comparing it to the observed values for the initial second order rate constant on twenty-eight determinations selected at random. These were chosen to give a variety of base concentrations and a range of isocyanate to thiol ratios as well as runs which had product added at the beginning of the reaction. The average deviation of the calculated from the observed rate constants, of which the values ranged from 3.5×10^{-4} to 16.1×10^{-4} l. moles^{-1} sec.,$^{-1}$ was only 0.3 unit. These results substantiate the proposed mechanism, at least as far as the major steps are concerned.

EXPERIMENTAL

Procedure. Multitubed dilatometers of approximately 50-ml. capacity were prepared from tubing of 7 mm. inside diameter and with capillaries with a uniform bore of 0.5 mm. A standard taper joint at the top of each capillary permitted filling of the dilatometers from a flask containing a stopcock at its base. Tubes containing silica gel were attached to the capillaries after filling the latter with the mixed reagents. The dilatometers were mounted in a water bath controlled at 25 ± 0.002°. The exposed capillaries of the dilatometers were protected from air currents within the area of the water bath by means of a Lucite shield around the capillary tubes. All small glassware was rinsed with dry acetone and dried in the vacuum oven for at least 2 hr. at 120° and then cooled and stored in a desiccator over Drierite. The dilatometers were rinsed with dry acetone and dried by passing a stream of dry nitrogen through the tubes for about 2 hr. prior to making a run. All reactants were stored and all solutions of the reactants were prepared in a Lucite dry box containing phosphorus pentoxide which was changed as necessary. Weights of isocyanate, thiols, and amines were known to a precision of at least 1 part in 2500. During a run, readings of the scale were made every half minute for the first 8 min. after equilibration, and every minute thereafter for the next 7 min., and at 5-min. intervals for about 2 hr. The final readings were generally determined after the reaction had been allowed to run overnight. Total shrinkage in volume was at least 100 mm., read to 0.1 mm. Using the multitube dilatometer the temperature rise during the initial period was negligible; equilibration was obtained within 5 min. from the start of the reaction. The method of calculation of the rate constants was that used previously. Duplicate runs showed coincident points when the rate curves were plotted on the same graph and indicated that any curvature produced was outside of experimental error.

Determination of rate constants by the chemical method was carried on as previously described.[2]

Materials. Eastman phenyl isocyanate was distilled from phosphorus pentoxide; the fraction boiling at 45–47° at 10 mm. pressure was used. 1-Butanethiol and 2-butanethiol were stored over calcium oxide and distilled through a Vigreux column. Toluene was stored over sodium and distilled from the sodium through a saddle-packed column. Nitrobenzene and butyl acetate were purified by the method of Ephraim *et al.*[6] Acetonitrile was distilled from phosphorus pentoxide. Dimethyl sulfoxide was distilled at 80° at 10 mm. pressure, the first 20% being discarded. Triethylamine, benzyldimethylamine, diethylaniline, and pyridine were stored for several days over solid sodium hydroxide and fractionated from the sodium hydroxide. Tri-*n*-propylamine, tri-*n*-butylamine, 1-methylpiperidine, 1-ethylpiperidine, 1,2,2,6,6-pentamethylpiperidine, and *N*-ethylmorpholine were fractionated from lithium aluminum hydride through a Vigreux column. 1,4-Diazabicyclo[2.2.2]octane[7] was recrystallized from petroleum ether (b.p. 35–75°). Acetone which was used for washing and drying glassware and the dilatometers was dried and purified by storage over and distillation from Linde Molecular Sieve 4A.

n-Butyl thiolcarbanilate was prepared as described previously.[2] For this study it was recystallized from petroleum ether. The micromelting point was 69.5–70°.

sec-Butyl thiolcarbanilate. A solution of 3.18 g. (0.35 mole) of 2-butanethiol and 0.49 g. (0.0048 mole) of triethylamine in 50 ml. of dry toluene was added to a solution of 3.47 g. (0.29 mole) of phenyl isocyanate in 50 ml. of dry toluene. After 7 days at approximately 25°, the excess reactant and solvent were evaporated and the product crystallized as long needles, 5.27 g. (87% yield). After recrystallization from 1:3 alcohol-water, the product melted at 91–92° (corr.).

Anal. Calcd. for $C_{11}H_{15}NOS$: C, 63.45; H, 7.24. Found: C, 63.25; H, 7.17.

n-Butyl N,N-diphenylthiocarbamate. This new compound was prepared by a modification of the procedure used by Weijlard and Tishler[8] for the preparation of quaternary derivatives of disubstituted thiolcarbamates. A solution of 92.7 g. (0.4 mole) of diphenylcarbamyl chloride (Eastman) dissolved in 150 ml. of dry toluene was added dropwise to a stirred solution of 40.5 g. (0.45 mole) of 1-butanethiol in 47.4 g. (0.4 mole) of pyridine. The temperature was raised to 85° and maintained for 6 hr. The contents of the flask were cooled and added to 300 ml. of water. The water, toluene, and pyridine were removed in a flash evaporator. The

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(7) Sample kindly furnished by the Houdry Process Corporation.

(8) J. Weijlard and M. Tishler, *J. Am. Chem. Soc.*, **73**, 1497 (1951).

resulting semisolid was dissolved in water containing a small quantity of hydrochloric acid and extracted 3 times with ether. Evaporation of the ether extract gave 100 g. of a heavy oil (60% yield). A benzene solution of the oil was chromatographed twice on alumina and the solution evaporated to an oil to a constant micro melting point of 62.7 to 63.5°. The over-all yield of purified material was 44 g. (29%). The ultraviolet spectrum showed a λ_{max} of 245 and an ϵ_{max} of 11,680.

Anal. Calcd. for $C_{17}H_{19}NOS$: C, 71.57; H, 6.66; N, 4.91. Found: C, 71.73; H, 6.52; N, 5.10.

n-Butyl-N-p-methoxyphenyl thiolcarbamate. This compound was prepared by the same procedure as that used for *n*-butyl thiolcarbanilate.[9] The product, micro melting point 62.5–63°, was obtained in a yield of 100%. After recrystallization from petroleum ether the micro melting point was 64.0°.

Anal. Calcd. for $C_{12}H_{17}NO_2S$: C, 60.25; H, 7.11; N, 5.86. Found: 59.98; H, 7.29; N, 5.90.

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Peroxide Desulfurization of Thioureas

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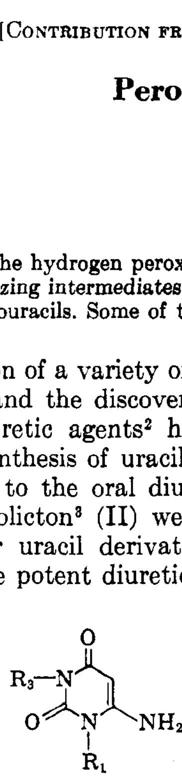
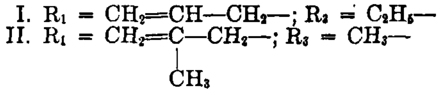
Investigation of the hydrogen peroxide desulfurization of thioureas to the corresponding ureas has led to a convenient method for synthesizing intermediates which lead to physiologically active uracils. The method has been extended to the synthesis of 5-ureidouracils. Some of the limitations of the reaction are discussed.

The preparation of a variety of 1,3-disubstituted 6-aminouracils[1] and the discovery of their usefulness as oral diuretic agents[2] has led to further studies in the synthesis of uracil derivatives. New synthetic routes to the oral diuretic agents Mincard[3] (I) and Rolicton[3] (II) were investigated as well as to other uracil derivatives which might prove to be more potent diuretic agents.



I. $R_1 = CH_2{=}CH{-}CH_2{-}$; $R_3 = C_2H_5{-}$



II. $R_1 = CH_2{=}\underset{\displaystyle CH_3}{\underset{|}{C}}{-}CH_2{-}$; $R_3 = CH_3{-}$

The syntheses of Mincard[3] and Rolicton[3] from urea and cyanoacetic acid followed by alkaline cyclization has been described in detail[1] and these steps give good yields of the desired products. The preparation of the starting ureas was reinvestigated because the starting material in the preparation of Rolicton,[3] *N*-2-methylallyl-*N*′-methylurea, is most readily prepared from 2-methylallylamine, a substance which is not readily available in commercial quantities.

As the corresponding thiourea can be readily prepared by reaction of 2-methyallyl chloride with an alkali thiocyanate followed by condensation of the resultant isothiocyanate with an amine,[4] the conversion of thioureas to ureas was now thoroughly investigated.

There are several methods in the literature for the conversion of thioureas to the correspondig urea. Oxidizing agents which have been employed successfully are alkali bromates and iodates,[5] benzoperoxide,[6] and sodium peroxide,[7] or alkaline hydrogen peroxide.[8] The last two reagents seemed to give the best yields and their use involved mild conditions. It seemed most logical therefore to investigate the peroxide desulfurization of 2-methylallylthiourea and *N*-2-methylallyl-*N*′-methylthiourea.

Although it has been reported that the alkali peroxides are not as good reagents as alkaline hydrogen peroxide for the conversion of thioureas to ureas,[8] it was shown in the case of the above thioureas that both reagents gave about the same yield of comparable quality urea. The alkaline hydrogen peroxide method was found preferable only because the handling of large quantities of

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(3) Registered trademark.

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