

[CONTRIBUTION FROM THE INSTITUTE OF GENERAL CHEMISTRY, INSTITUTE OF ORGANIC CHEMISTRY AND CENTER OF NUCLEAR CHEMISTRY, UNIVERSITY OF PADOVA]

Kinetics of the Thiol-Disulfide Exchange

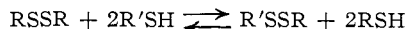
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The kinetics of the reaction between thiols and disulfides, leading to an exchange of radicals, has been studied with the aid of S³⁵. The reaction is first order with respect to disulfide and to mercaptide ion. A number of thiol-disulfide systems have been investigated and the temperature dependence of the rate determined. The temperature dependence of another closely related reaction, namely, the ring opening of a cyclic disulfide (trimethylene disulfide) operated by thiols, has also been studied. Spectrophotometric technique was used here. The rate and the other kinetic parameters are compared and discussed on the basis of a model for the intermediate complex. A slow, heterogeneous exchange is found between thiol and disulfide in the gas phase. The slowness of exchange between aromatic thiol and disulfide is strong evidence against any substantial homolytic dissociation of the disulfide.

A few years ago a preliminary study of the isotopic exchange between organic sulfides or polysulfides and the corresponding thiols was reported.² It was then found that whereas monosulfide does not exchange even in extreme conditions, and the exchange with higher polysulfides is complicated by side reactions which end in the oxidation of the thiol, with disulfide the exchange is measurably fast and free of side reactions. Evidence also was given that the exchange is carried out by the mercaptide ion.

Long before the isotopic exchange between thiol and disulfide had been observed, its existence might have been inferred (though in fact it was not) from the so-called disulfide interchange. The first observation of the reaction



can be found in a paper by Lecher³ in 1920. Later, Goddard and Michaelis⁴ studied the reductive properties of thioglycolic acid on the S-S bond in keratin, and a few years later Bersin and Steudel⁵ did the first quantitative work on the subject following polarimetrically the reaction between L-cysteine and thioglycolic acid. Although these authors rather neglected the kinetic aspect of the problem, they recognized that the exchange of groups is likely to proceed through the RS⁻ ion. Later on, other observations about the disulfide interchange were made⁶ and several patents were also issued⁷ concerning the interchange thiol-disulfide as a method for preparing different disulfides. Recently the significance of the disulfide interchange was indicated clearly by Calvin⁸ who recognized it as an anionic exchange. It seemed to us that a kinetic study was very desirable in view also of the increasing interest given to this system by biochemists.

In the present study the kinetics of the isotopic exchange thiol-disulfide in solution have been studied in some detail for the following systems:

- (1) Istituto di Chimica Generale, Via Loredan 4, Padova, Italy.
- (2) A. Fava and A. Ilceto, *Ricerca Sci.*, **23**, 839 (1953).
- (3) H. Lecher, *Ber.*, **53B**, 591 (1920).
- (4) D. R. Goddard and L. Michaelis, *J. Biol. Chem.*, **106**, 605 (1934).
- (5) T. Bersin and J. Steudel, *Ber.*, **71B**, 1015 (1938).
- (6) G. Gorin, G. Dougherty and A. V. Tobolsky, *THIS JOURNAL*, **71**, 3551 (1949); C. Huggins, D. F. Tapley and E. V. Jensen, *Nature*, **167**, 592 (1951); F. Sanger, *ibid.*, **171**, 1025 (1953); A. P. Ryle and F. Sanger, *Biol. J.*, **60**, 535 (1955).
- (7) See, for instance: C. A., **45**, P636e (1951); **47**, P349h (1953); **49**, P2759c (1955).
- (8) M. Calvin, UCRL report No. 2438 (1954).

n-butyl, *n*-hexyl, *t*-butyl and phenyl. The possibility of gas phase exchange was also investigated. Moreover, the kinetics of the reaction between thiols and a pentatomic cyclic disulfide have been studied.

Experimental

Since disulfides are more stable and less volatile than the corresponding thiols, it was preferable for handling and storage purposes to carry out the exchange with the disulfide initially radioactive. (*n*-C₄H₉S³⁵)₂ was prepared according to the following procedure: BaSO₄ (~100 mg.), having a specific activity of about 2 mc. per millimole, was reduced in a hydrogen atmosphere at 950° yielding BaS quantitatively. This was transferred in a convenient apparatus where H₂S was displaced by means of 10% hydrochloric acid and collected in sodium ethyl alcoholate solution containing a little less than the stoichiometric amount of sodium to form NaHS. A 50*N* solution of the latter was refluxed with *n*-BuBr in slight excess (~20%). The reaction was completed in one-half hour. NaBr was filtered off and lead mercaptide precipitated by adding lead acetate. The precipitate was washed several times with alcohol in order to eliminate small quantities of organic sulfide. Lead mercaptide was oxidized to disulfide with iodine in carbon tetrachloride. For the purification of the tiny amount of product formed, pure non-radioactive disulfide was added (~2 g.) and the mixture distilled at reduced pressure. Before the distillation was completed more disulfide is added and distilled. With this procedure very pure radioactive disulfide is obtained and the over-all yield in the micro preparation is not lower than in an ordinary macro preparation. More pure disulfide was added if necessary to adjust the specific activity to a convenient working level. The same procedure was used to prepare and purify the labeled *n*-hexyl disulfide. (*t*-C₄H₉S³⁵)₂: the preparation was carried out by oxidation of the mercury salt of the corresponding thiol, prepared according to the method of Rheinboldt, Mott and Motzcus⁹ according to which elemental sulfur is made to react with *t*-butylmagnesium chloride in anhydrous ether. The disulfide was purified by distillation under reduced pressure (15 mm. at 81°). In this preparation 6 g. of labeled sulfur was employed. The over-all yield was about 60%. (C₆H₅S³⁵)₂ was prepared according to the method of Clarke, *et al.*,¹⁰ which uses chlorosulfonic acid.¹¹ Benzene was poured slowly on chlorosulfonic acid at room temperature. The liquid was poured on ground ice and the mixture extracted with CCl₄. The solution was washed with water and successively dried with anhydrous Na₂SO₄. The solvent was evaporated and benzenechlorosulfonate reduced with Sn and HCl to thiophenol. This was oxidized

(9) H. Reinboldt, F. Mott and E. Motzcus, *J. prakt. Chem.*, **134**, 257 (1932).

(10) H. Gilman and A. H. Blatt (Editors), "Organic Syntheses," Coll. Vol. I, 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1941, p. 85.

(11) Actually a mixture (about 1:20) of H₂S*O₄ and SO₂HCl, which had been kept at 100° for one hour, was used. This treatment is apparently sufficient to complete isotopic exchange between H₂SO₄ and SO₂HCl, although we have no direct proof of it except that labeled phenyl disulfide ultimately is obtained.

to disulfide which was purified by crystallization from alcohol and successively by sublimation (m.p. 58–59°).

Procedure.—Mixtures of reagent grade *n*-BuOH and water (6%) and MeOH and water (12%) were used as solvents. Since it had been previously recognized² that the exchange (at least in the *n*-butyl system) is very slow with the thiols, whereas it is extremely fast with sodium mercaptide, various attempts were made in order to find intermediate conditions in which this exchange could conveniently be followed. This analysis brought out the fact that the exchange is base catalyzed and the following procedure was henceforth followed: The mixture of thiol and disulfide was made up and properly diluted in order to have predetermined concentrations, put in a thermostat and left there for about 10 minutes. To start the reaction a measured amount of base was introduced quickly and the solution mixed rapidly. To stop the reaction the base was neutralized by introducing an acid and by mixing thoroughly. With this procedure reaction times of less than a minute may be determined with fair accuracy.

After addition of the acid, separation of the reactants was made by precipitation of the thiol as silver salt by addition of alcoholic silver nitrate.¹² This method of separation does not induce appreciable exchange provided the precipitation occurs in dilute solution (at least 5×10^{-3}). In practice before adding AgNO₃ the concentration is reduced to the desired value by adding ethyl alcohol. The silver mercaptide was centrifuged, washed with alcohol and transferred in a small porcelain dish. The alcohol was evaporated and the residue oxidized with nitric acid. The excess acid was evaporated and the residue transferred into a nickel crucible where it was oxidized at red heat with KNO₃-Na₂CO₃ mixture. After cooling, the fused mass was dissolved in water, metallic silver filtered off and finally sulfate precipitated with barium chloride after acidification. Usually only the radioactivity of the thiol (*i.e.*, the reagent initially non-radioactive) was measured. In some control experiments also the activity of disulfide was determined: the solution remaining after precipitation of the thiol was reduced with zinc and acid. Thiol was boiled off and collected in silver nitrate. Silver mercaptide was transformed in BaSO₄ as above.

BaSO₄ was counted for radioactivity with a thin mica window G.M. counter. For counting, samples were mounted in "thick layer." Reproducibility of radioactivity measurement was about 3%.

The reaction between thiols and cyclic disulfide was followed spectrophotometrically taking advantage of the circumstance that whereas open chain disulfides and aliphatic thiols absorb light of about 2500 Å., the cyclic disulfides (five-membered) present an absorption maximum at about 3300 Å.¹³ Since the reaction between thiols and trimethylene disulfide brings about the opening of the ring and the formation of an open chain disulfide, it may be conveniently studied by following the optical density at 3300 Å. It was not possible to study in the same way the analogous reaction with the six-membered cyclic disulfides since the latter absorbs in a region (2800 Å.) which is too close to that characteristic of the open chain disulfides and of mercaptans. A Model 11 Cary recording Spectrophotometer was used. Thermostatic control was attained with a special cell holder.

Gas Phase Exchange—These experiments were performed in a 250-ml. flask to which two vertical arms were attached. The reagents in weighed amounts were contained in vials which were broken with magnetic hammers. The reagents were properly degassed and the vessel sealed under vacuum. Thereafter it was immersed in a constant temperature oil-bath and left there for a suitable time. For separation, the reactants were condensed in one of the arms which was cooled with liquid nitrogen. Air was admitted into the vessel by breaking a thin tip, and the cold arm was cut apart. The condensed mixture was dissolved in alcohol and the separation carried out according to the procedure outlined above for the exchange in solution. NaOH was added to one fraction of the solution and the exchange allowed to attain equilibrium. This experiment gave the equilibrium

(12) In the experiments with the phenyl system, precipitation with silver nitrate induced large and non-reproducible zero-time exchanges. Separation of the thiol as lead salt was found satisfactory.

(13) J. A. Barltrop, P. M. Hayes and M. Calvin, *THIS JOURNAL*, **76**, 4348 (1954).

value of the specific activity. It will be noted at a certain step of this procedure that the reactants become mixed in a condensed phase. It was necessary, therefore, to determine if under these conditions an appreciable exchange occurred. This was done by mixing pure liquid *n*-Bu disulfide and thiol, letting them react for some time and separating them. In an experiment the liquid mixture was left 10 hours at room temperature and then separated. No appreciable exchange had occurred.

Results and Discussion

Mechanism.—As already mentioned, the exchange takes place very slowly in the absence of a base. To give an idea of the order of magnitude of the rate, the half-time for the exchange of *n*-BuSH and the corresponding disulfide in butyl alcohol at room temperature and for concentration of reagents *N*/100 is about 500 hours. Only the base-catalyzed exchange was therefore investigated in some detail. The rate of exchange is given by¹⁴

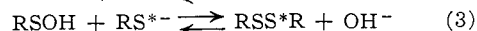
$$R = -\frac{1}{t} \frac{(RSSR) \times (RSH)}{(RSSR) + (RSH)} \ln(1 - F) \quad (1)$$

where (RSSR) and (RSH) are the concentrations of disulfide and thiol, respectively, *t* is the time and *F* the fraction of exchange. Each value of *R* was obtained by measuring the fraction of exchange at five different times and plotting $\log(1 - F)$ against *t*. Orders of reaction were evaluated varying the concentration of the species participating in the reaction one at a time, other conditions being constant. The results obtained for the *n*-butyl exchange using NaOH as catalyst are collected in Table I. The

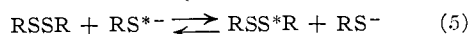
TABLE I
n-BUTYL DISULFIDE-*n*-BUTANETHIOL EXCHANGE
Temp. 25°; solvent *n*-BuOH

(RSSR) × 10 ²	Σ(RSH) × 10 ²	Σ(NaOH) × 10 ³	<i>t</i> _{1/2} , sec.	<i>R</i> × 10 ⁵ , moles l. ⁻¹ sec. ⁻¹	<i>R</i> / (RSSR) (NaOH)	
2.85	2.73	11.7	86	11.2	0.34	
2.93	2.81	8.86	133	7.4	.29	
2.99	2.86	6.04	169	6.0	.33	
2.99	2.86	3.12	316	3.2	.34	
1.50	2.86	6.04	270	2.5	.28	
4.33	2.86	6.04	170	7.0	.27	
5.67	2.86	6.04	150	8.8	.26	
2.68	1.34	5.54	125	4.9	.33	
2.68	8.02	5.68	240	5.8	.38	
					Av.	.31

base catalysis and the first order with respect to disulfide suggest that the slow step involves the cleavage of the S-S bond carried out by a basic species. The mechanisms that may be considered are the following: (A) cleavage of the S-S bond by OH⁻ followed by the fast back reaction which may take place with the labeled mercaptide ion



(B) Sulfication of the thiol, and cleavage of the S-S bond by the mercaptide ion



The following analysis of the results in Table I allows mechanism A to be discarded and shows that

(14) A. C. Wahl and N. A. Bonner (Editors), "Radioactivity Applied to Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1951, p. 11.

the reacting species is mercaptide ion. The calculation of the actual concentration of RS^- ions would involve the knowledge of the hydrolysis constant under the conditions of the experiments. It may be seen, however, that for the sole purpose of calculating the order of reaction, hydrolysis can be neglected. Since in all experiments $\Sigma(RSH) > \Sigma(NaOH)$, there results, neglecting hydrolysis: $(RS^-) \approx \Sigma(NaOH)$. The specific rate calculated from this assumption is shown to remain reasonably constant (last column in Table I). It is therefore concluded that the exchange occurs by mechanism B, the rate being

$$R = k(RSSR)(RS^-) \quad (6)$$

Temperature Dependence.—The rate of exchange and its temperature dependence for various thiol-disulfide systems has been measured. The results are given in Table II.

The Arrhenius plot of the data in Table II gives the experimental energies of activation E_a for the

TABLE II

TEMPERATURE DEPENDENCE OF THE RATE OF ISOTOPIC EXCHANGE FOR VARIOUS THIOL-DISULFIDE SYSTEMS

(a) <i>n</i> -BuSH-(<i>n</i> -BuS) ₂ in BuOH					
$\Sigma(NaOH) = 6.04 \times 10^{-3}$		$\Sigma(RSH) = (RSSR) = 2.86 \times 10^{-2}$			
Temp., °C.	0	15	25	35	
$R \times 10^5$, mole l. ⁻¹ sec. ⁻¹	0.66	2.6	6.0	11.5	
(b) <i>n</i> -BuSH-(<i>n</i> -BuS) ₂ in MeOH					
$\Sigma(NaOH) = 6.25 \times 10^{-3}$		$\Sigma(RSH) = (RSSR) = 3.75 \times 10^{-2}$			
Temp., °C.	0	15	25	35	
$R \times 10^5$, mole l. ⁻¹ sec. ⁻¹	0.68	2.7	6.5	13.5	
(c) C ₆ H ₅ SH-(C ₆ H ₅ S) ₂ in MeOH					
$\Sigma(NaOH) = 2.5 \times 10^{-3}$		$\Sigma(RSH) = (RSSR) = 3.75 \times 10^{-2}$			
Temp., °C.	0	15	25	35	
$R \times 10^5$, mole l. ⁻¹ sec. ⁻¹	0.43	1.9	4.6	12.0	
(d) <i>t</i> -BuSH-(<i>t</i> -BuS) ₂ in MeOH					
$\Sigma(NaOH) = 1.02 \times 10^{-1}$		$\Sigma(RSH) = (RSSR) = 6.1 \times 10^{-2}$			
Temp., °C.	85	95	100	105	
$R \times 10^7$, mole l. ⁻¹ sec. ⁻¹	2.0	4.5	6.7	9.3	
(e) <i>n</i> -HexSH-(<i>n</i> -HexS) ₂ in MeOH					
$\Sigma(NaOH) = 6.25 \times 10^{-3}$		$\Sigma(RSH) = (RSSR) = 3.75 \times 10^{-2}$			
Temp., °C.	25	$R = 6.1 \times 10^{-5}$			

exchanges involved (Table III). A brief discussion about the significance of this quantity in these particular examples seems necessary. From equation 6, taking the logarithm and the derivative with respect to temperature, it results that $d \ln R/dT$ is equal to $d \ln k/dT$ provided that $(RSSR)$ and (RS^-) are constant with respect to temperature. Naturally this is true for $(RSSR)$, but it is not so for (RS^-) if the hydrolysis is not negligible, as it is likely to be in these examples (with the exception of the phenyl systems). If, as normally occurs, the hydrolysis increases with temperature, it is seen that $d \ln R/dT < d \ln k/dT$, *i.e.*, the apparent energy of activation is lower than the true one (by true energy of activation is meant that of

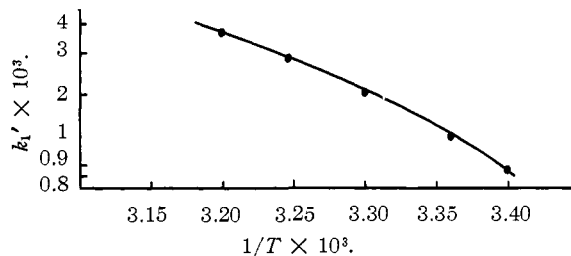




Fig. 1.

the reaction $RSSR + RS^-$). The problem of how much the apparent values differ from the true ones cannot be solved unless some information about the hydrolysis constant is known. On this point the data existing in the literature are extremely scarce. In particular no data have been found concerning

TABLE III

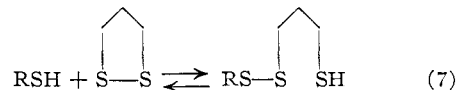
RATE AT 25°, ARRHENIUS ACTIVATION ENERGY (E_a), FREE ENERGY, ENTROPY AND HEATS OF ACTIVATION FOR THE DISULFIDE EXCHANGE

Reaction	k_{250}° , 1. mole ⁻¹ sec. ⁻¹	E_a , kcal.	ΔF^\ddagger	ΔS^\ddagger	ΔH^\ddagger
<i>n</i> -BuS ⁻ + (<i>n</i> -BuS) ₂ ²	0.31 ^b	14.15	18.1		
<i>n</i> -BuS ⁻ + (<i>n</i> -BuS) ₂	.26 ^b	14.45	18.2		
<i>n</i> -HexS ⁻ + (<i>n</i> -HexS) ₂	.26 ^b		18.2		
<i>t</i> -BuS ⁻ + (<i>t</i> -BuS) ₂	1×10^{-7b}	21.75	26.9		
C ₆ H ₅ S ⁻ + (C ₆ H ₅ S) ₂	0.49	15.75	17.9	-9	15.2
<i>n</i> -BuS ⁻ + 	1400	13	13.6		
MeOOC-CH ₂ S ⁻ + 	2.2	11.2	16.9	-21	10.6

^a In BuOH. All other reactions in MeOH. ^b Hydrolysis has not been accounted for.

the heat of ionization of thiols. Nevertheless, a rough calculation was made using the ionization constants given by Maurin and Paris,¹⁵ extrapolating the ionic product of water from data of Kilpi and Warsila,¹⁶ and assuming that the heat of ionization of thiols is negligible with respect to that of water. The energies of activation so obtained for *n*-butyl and *t*-butyl systems were higher than the apparent ones by about 1 and 5 kcal., respectively. The uncertainties of these calculations are such, however, that it is felt much safer for the purpose of comparing the different systems, to compare the rates, *i.e.*, the free energies, rather than the entropies and heats of activation separately.

Reaction with Cyclic Disulfide.—The reaction between thiols and trimethylene disulfide has been studied by Barltrop, Hayes and Calvin¹³ who presented evidence that the over-all reaction is



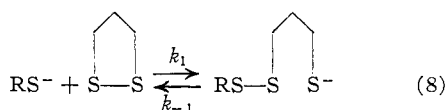
Values of the equilibrium constant at different temperatures and for different thiols were given, but no kinetic work was done in these experiments.

Reaction 7 is quite slow, but it may be accelerated to a very large extent by the presence of a base. For instance a base as weak as acetate ion

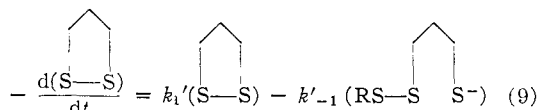
(15) J. Maurin and R. Paris, *J. chim. phys.*, **48**, C30, C37 (1951).

(16) S. Kilpi and H. Warsila, *Z. physik. Chem.*, **A177**, 427 (1936).

was found sufficient to produce a conveniently measurable rate. The reaction was carried out using a large excess of thiol (10 to 30 times); this is necessary if a considerable fraction of the cyclic disulfide is to be transformed. The reaction is considered to be



Under the conditions of the experiments (RS^-) may be considered constant throughout the course of the reaction (RSH being in large excess), so that the reaction may be treated as unimolecular in both directions



k'_1 is related to the specific rate for the forward direction, k_1 , by: $k'_1 = k_1(\text{RS}^-)$. Integrating (9) and introducing the optical densities one obtains

$$\ln \frac{D_0 - D_e}{D - D_e} = k'_1 \frac{X_e}{(\text{S-S})_0} t \quad (10)$$

where D_0 , D and D_e are the optical densities at time zero, time t and at equilibrium, respectively; X_e the equilibrium concentration of open chain

disulfide and $(\text{S-S})_0$ the initial concentration of cyclic disulfide. k'_1 is obtained from plots of $\ln(D_0 - D_e)/D - D_e$ against t . These plots are linear, thereby justifying the assumptions made.

Two series of reactions were carried out using different thiols: *n*-butane thiol and thioglycolic acid methyl ester (TGE). Results are given in Table IV.

TABLE IV
RATE AND EQUILIBRIUM FOR THE REACTIONS BETWEEN
THIOLS AND TRIMETHYLENE DISULFIDE

Temp., °C.	$(\text{S-S})_0 \times 10^3$	$k'_1 \times 10^3$	$X_e \times 10^3$	K
(a) <i>n</i> -BuSH + trimethylene disulfide: $\Sigma(\text{AcONa}) = 8.2 \times 10^{-4}$, $\Sigma(\text{RSH}) = 1.24 \times 10^{-1}$				
20.7	9.8	0.96	5.04	8.9
25	9.8	1.38	4.62	7.5
30	9.65	2.08	4.29	6.65
35.2	9.70	2.90	3.99	5.8
38	9.65	3.70	3.74	5.25
(b) MeOOC-CH ₂ SH + trimethylene disulfide: $\Sigma(\text{NaOH}) = 1.59 \times 10^{-3}$, $\Sigma(\text{RSH}) = 3.37 \times 10^{-1}$				
25	10.1	3.47	5.64	3.79
31	10.2	5.17	5.30	3.27
35.1	10.0	6.34	4.90	2.90
39.5	10.0	8.68	4.76	2.74

These data should be analyzed briefly. It should be noticed that *n*-BuS⁻ reacts much faster than the TGE ion as shown by the fact that in the

presence of sodium acetate as catalyst, *n*-BuSH reacts about as fast as TGE does in presence of sodium hydroxide. Indeed, if NaOH is used with *n*-BuSH, the rate is immeasurably fast. The large difference in rate probably is related to the large difference in basicity exhibited by the two ions: $pK_{n\text{-BuSH}} \approx 13.4^{15}$; $pK_{\text{TGE}} \approx 8$.

The equilibrium constants given in Table IV permit the determination of the heat of reaction. It is found $\Delta H = -5.3$ and -4.2 kcal. for the reaction with *n*-BuSH and TGE, respectively. These figures are of the same order of magnitude as that given by Barltrop, Hayes and Calvin¹³ for the reaction with BzSH (-6.3 kcal.).

Some remarks about the significance of these figures seem necessary. It must be pointed out in fact, that the equilibrium constants measured here concern reaction 7 and are not equal to k_1/k_{-1} . Rather, it is $K = (k_1)(K_{a'})/(k_{-1})(K_a)$ where $K_{a'}$ and K_a are the ionization constants of RSH and RS-S-SH, respectively. Therefore the measured ΔH is equal to that for reaction 8 only if $K_{a'}/K_a$ is constant with temperature. As a consequence the rates and the energies of activation for reaction 8 in the opposite direction cannot be determined unless the ratio $K_{a'}/K_a$ and its variation with temperature are known. However, for the reaction with *n*-BuSH the assumption $K_{a'}/K_a$ constant with temperature would probably be a reasonable one.

Some consideration must also be given to the rates and the experimental activation energies (Table III). For the reaction with TGE, since this is a relatively strong acid and $\Sigma(\text{RSH}) \gg \Sigma(\text{NaOH})$, (RS^-) may be assumed equal to $\Sigma(\text{NaOH})$ at all temperatures. For the reaction with *n*-BuSH, in which acetate ion was used as catalyst, the concentration of mercaptide ion is, neglecting the hydrolysis of acetate ion

$$(\text{RS}^-) = \sqrt{\frac{K_{\text{RSH}}}{K_{\text{AcOH}}}} \times \Sigma(\text{RSH}) \times \Sigma(\text{AcONa}) \quad (11)$$

Clearly (RS^-) is a function of temperature, so that the apparent energy of activation results

$$E_a = E + \frac{1}{2}(\Delta H_{\text{RSH}} - \Delta H_{\text{AcOH}}) \quad (12)$$

E being the true energy of activation and the ΔH 's the heats of ionization of thiol and acetic acid. Since the latter quantities are not known, E cannot be evaluated.

In Table III, the value of E_a is reported to be about 13 kcal. The reason for the uncertainty is that the Arrhenius plot is not linear (Fig. 2). It is difficult to say whether the phenomenon is due to variation of one or more of the terms which combine to give E_a or rather due to some faults of the experiments. It is felt that before drawing any conclusions on this point, the experiments should be checked carefully. In order to evaluate the specific rate, the ratio $K_{\text{RSH}}/K_{\text{AcOH}}$ under the conditions of the experiments is needed. An approximate value can be obtained from the ionization constants determined in hydroalcoholic solution (in 50% alcohol) which are known^{15,16} assuming that the ratio remains constant with respect to variations in the solvent medium. This ratio is

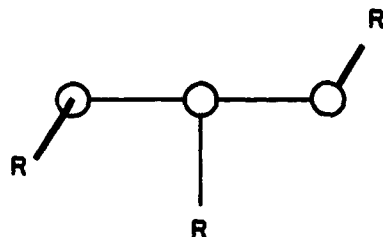


Fig. 2.

$\approx 10^{-8}$, which introduced in equation 11 gives: $(RS^-) \approx 10^{-6}$. The specific rate at 25° is then ≈ 1400 l. mole $^{-1}$ sec. $^{-1}$.

Intermediate Complex.—It is interesting now to compare the rate of all the reactions studied here (Table IV). As mentioned before it is safer to take into consideration only rates and not entropies and energies of activation separately. It is seen that the rate varies very widely from one reaction to another, a variation as large as 10^{10} , corresponding to a free energy difference of about 13 kcal., being observed in the two extreme cases. In order to understand the origin of such wide variations, some considerations have to be made concerning the structure of the intermediate. It is seen easily that the $(RS)_3^-$ complex is electronically similar to the trihalide ions. The structure of compounds of this type has been subject to several studies,¹⁷ from which the linear arrangement of the atoms has been established. The hypothesis is therefore made that in the intermediate $(RS)_3^-$ the three sulfur atoms lie in a straight line, the alkyl radicals being arranged as in Fig. 3. The construction of a scale model has shown that for the *t*-butyl intermediate the steric requirements are such as to make the linear arrangement impossible, without considerable overlapping of the alkyl radicals. Therefore, in the *t*-butyl intermediate either the three sulfur atoms are so arranged as to make an angle $< 180^\circ$ or the distances S-S are sufficiently large to make possible the linear arrangement. In either case the orbital overlapping at the central sulfur decreases and the energy of the intermediate rises.

The high rate for the reaction with cyclic disulfide arises from the strain of the pentatomic ring. In open chain disulfides the dihedral angle between the two C-S bonds is about 90° . In this position the unshared p electrons on the two sulfur atoms offer a minimum overlapping. In the cyclic (pentatomic) disulfide the dihedral angle is $\ll 90^\circ$ ¹⁸ so that a coulombic repulsion arises due to the non-bonding p electron couples. In the formation of the intermediate, while the distance between the two sulfur atoms of the ring increases, the repulsion between the non-bonding electrons decreases. It may be said, in other words, that the energy of the S-S bond decreases with increasing S-S distance less in the cyclic than in the open chain disulfides.

As for the type of bonds involved in the formation of the complexes, *i.e.*, the electronic configura-

(17) R. W. G. Wyckoff, *THIS JOURNAL*, **42**, 1100 (1920); R. C. L. Mooney, *Z. Krist.*, **90**, 324 (1935); **98**, 324 (1938); **100**, 519 (1939); *Phys. Rev.*, **47**, 807 (1935); **53**, 851, 918 (1938).

(18) O. Foss has recently examined the crystal structure of cyclic disulfides. One of them, 3,5-dithiino-1,2,4-dithiazolidine hydroiodide, is exactly planar (private communication).

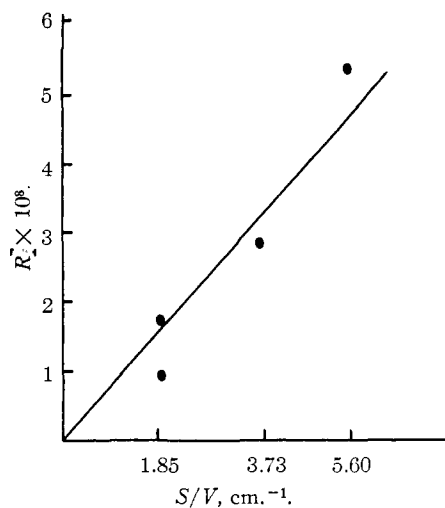
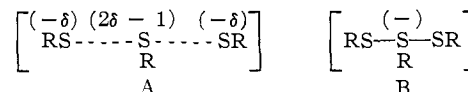


Fig. 3.

tion around the central sulfur atom, our results do not give any clue. The possible electronic configurations of the reaction center in the nucleophilic reactions at the sulfur have been discussed recently.¹⁹ The two possibilities are here represented by



"A" represents a structure in which only p orbitals are involved, one p orbital of the central sulfur being combined with two p orbitals of the incoming and outgoing groups. "B" represents a structure in which the central sulfur uses a d orbital, the hybrid configuration being sdp^3 . The structures differ in the distribution of charge, the central sulfur being somewhat more negative in "B." Since the results presented here do not favor one structure over the other one might use the analogy with the trihalide ions and attribute to the activated complexes the same electronic configuration of the trihalides. Unfortunately the opinions about the trihalides are not unanimous, type "A" structure being favored by some authors and type "B" by some others.²⁰ However, structure "A" seems more probable since it is supported on theoretical calculations.²¹ This is also the type of configuration for which some, though not very strong, evidence was found in the kinetics of the nucleophilic substitution at the sulfur atom. On these bases it could then be concluded that configuration "A" more likely represents the intermediate complex.

Gas Phase Exchange.—Although the scope of these experiments is quite limited, it seems worthwhile to report the results. The reaction between *n*-butyl disulfide and the corresponding thiol was studied. The variation of the vapor pressure of the disulfide with temperature was determined,

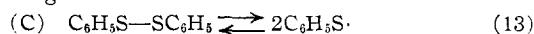
(19) A. Fava and G. Pajaro, *THIS JOURNAL*, **78**, 5203 (1956).

(20) L. Pauling, "The Nature of the Chemical Bond," Cornell Univ. Press, Ithaca, N. Y., 1945, p. 111; N. V. Sidgwick, "The Chemical Elements and their Compounds," Oxford University Press, London, 1950, p. 1190; R. J. Hach and R. E. Rundle, *THIS JOURNAL*, **73**, 4321 (1951); M. Davies and E. Gwynne, *ibid.*, **74**, 2748 (1952).

(21) G. C. Pimentel, *J. Chem. Phys.*, **19**, 446 (1951).

and the temperature of 150°, at which the vapor pressure is 78 mm., was chosen for the experiment. These were carried out at a pressure of 53 mm. of disulfide and twice as much of thiol. Under these conditions the exchange is measurable though very slow, the half-time being about 40 hours. As a test of the homogeneity of the reaction, the surface-volume ratio was varied by partially packing the vessel with Pyrex glass rings. The results are given in Fig. 4. Although the errors involved in these experiments are rather large, and therefore the extrapolation of the rate to zero surface-volume ratio rather arbitrary, the fundamentally heterogeneous character of the reaction is evident.

The Non-base-catalyzed Exchange.—It is often reported in the literature that aromatic disulfides undergo homolytic dissociation at low temperatures (~100°), with the formation of relatively stable sulfenyl radicals. This view is based on optical²¹ and magnetic²² evidence, which is not, however, entirely convincing,²³ so that the matter still seems controversial. It appeared interesting to determine the rate of exchange for diphenyl disulfide under those experimental conditions in which previous workers have proposed that sulfenyl radicals exist in equilibrium with disulfide. In fact, if the disulfide dissociates in free radicals, an alternative path, (C), for the isotopic exchange is offered



Since the hydrogen transfer (14) may be considered very fast, a very high rate of exchange may reasonably be predicted if the concentration of $\text{C}_6\text{H}_5\text{S}\cdot$ radicals is so high as to cause the observed optical anomalies.²⁴

In the preceding sections the possibility of this alternative mechanism was not even mentioned, not because it was overlooked, but because it had

(22) A. Schonberg, E. Rupp and W. Gumlich, *Ber.*, **66B**, 1932 (1933).

(23) H. G. Cutforth and P. W. Selwood, *THIS JOURNAL*, **70**, 278 (1948).

(24) H. Z. Lecher, *Science*, **120**, 220 (1954).

been proved in some preliminary experiments that at low temperature the reaction is base catalyzed and occurs through the intervention of $\text{C}_6\text{H}_5\text{S}^-$ ions. Other experiments were therefore made in which the concentration of $\text{C}_6\text{H}_5\text{S}^-$ was kept as low as possible in order to make the exchange through mechanism (B) a minimum. This was attained by performing the reaction in anhydrous xylene where dissociation of $\text{C}_6\text{H}_5\text{SH}$ may be thought to occur at a very small extent. Experiments at 100° showed a slow rate: for concentration of reagents $7.5 \times 10^{-2} N$ the half-time was 10 hours and $R = 7.2 \times 10^{-7}$ mole l.⁻¹ sec.⁻¹. This figure shows that if mechanism (C) be assumed, the stationary concentration of sulfenyl radicals must be extremely small and could not possibly be responsible for the observed optical anomalies. Rather, the rate is so slow that it can be perhaps accounted for by mechanism (B) since the concentration of $\text{C}_6\text{H}_5\text{S}^-$, though small, cannot be considered zero. This view is supported by the value of the rate of exchange, in the same experimental conditions, between *n*-butyl disulfide and the corresponding thiol. Experiments gave $R = 4.3 \times 10^{-8}$, that is, less than 1/20 as fast. It is then probable that the mechanism is the same in both exchanges and, since there is no evidence whatsoever for thermal homolytic fission of aliphatic disulfides, that mechanism (B) is likely to be operative also in these experimental conditions. It is realized, however, that only a complete kinetic study can unequivocally assign the mechanism.

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PADOVA, ITALY

[CONTRIBUTION FROM THE PYROTECHNICS CHEMICAL RESEARCH LABORATORY, PICATINNY ARSENAL]

The Kinetics of the Thermal Decomposition of Potassium Nitrate and of the Reaction between Potassium Nitrite and Oxygen^{1a}

BY ELI S. FREEMAN^{1b}

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The kinetics of the thermal decomposition of potassium nitrate were studied in oxygen, at a constant pressure of one atmosphere, over the temperature range of 650 to 800°. The rate of reaction was followed by observing changes in volume as a function of time. From 650 to 750° the products of decomposition were found to be potassium nitrite, oxygen and traces of nitrogen dioxide. Equilibrium was also attained between potassium nitrate, potassium nitrite and oxygen. At 800°, decomposition was more extensive, with potassium nitrite decomposing to form nitrogen, oxygen and potassium oxide. The reaction between potassium nitrite and oxygen was investigated from 550 to 790°, by measuring the rate of consumption of oxygen to form potassium nitrate. From 550 to 600°, the reaction goes slowly to completion. From 650 to 750°, equilibrium was attained between the reactants and potassium nitrate. At 790°, decomposition of potassium nitrite was evident. The equilibrium constants of the system were calculated from the data, and on the basis of their temperature dependency, the heats of reaction for decomposition and oxidation were determined. A reaction mechanism is proposed and the kinetics of the reactions as well as the energies of activation were evaluated. In addition, some of the results of this study are compared with those obtained in a previous investigation of sodium nitrate and sodium nitrite.

(1) (a) This paper was presented, in part, before the Division of Physical and Inorganic Chemistry at the North Jersey Meeting in Miniature of the American Chemical Society in Newark, N. J., Janu-

ary 1956, and at the Delaware Valley Regional Meeting in Philadelphia, Pa., February 1956; (b) The Newark Colleges of Rutgers University, Newark 2, N. J.