was not depressed and the infrared spectra were superimposable. The data are summarized in Table III.

2-Hydroxybenzothiazole.—A stirred solution of 42.4 g. (0.25 mole) of 2-chlorobenzothiazole in 90.1 g. (2.0 moles) of formamide was heated at 180–190° for 5 hr. During this heating period hydrocyanic acid was liberated. After cooling to 10°, 200 g. of ice–water was added and stirring was continued at 0–10° for 1 hr. The resulting precipitate was collected by filtration, washed with 100 ml. of cold water, and air dried at 45°. The product, m.p. 118–121°, was obtained in 90% yield. After recrystallization from dilute ethyl alcohol it melted at 138–139°. A mixture melting point with an authentic sample was not depressed and the infrared spectra of the two were superimposable.

Anal. Calcd. for C_7H_5NOS: N, 9.27; S, 21.21. Found: N, 9.44; S, 21.27.

Acknowledgment.—The authors wish to acknowledge their indebtedness to Dr. M. J. S. Dewar, Dr. W. H. Urry, Dr. N. J. Leonard, and Mr. R. O. Zerbe for their helpful suggestions during the course of this investigation.

2-Substituted Thiobenzothiazole and Related Compounds. II.[1,2] A Kinetic Study of the Reaction of 2-Chlorobenzothiazole with the Sodium Salt of 2-Mercaptobenzothiazole

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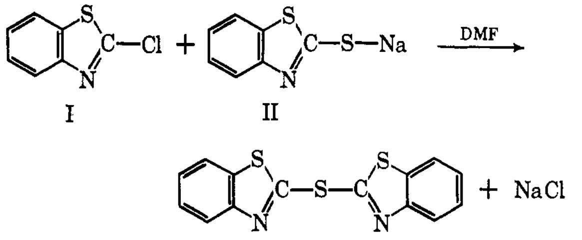
The kinetics of the reaction of 2-chlorobenzothiazole (I) with the sodium salt of 2-mercaptobenzothiazole (II) in dimethylformamide to yield 2,2'-thiobis(benzothiazole) (III) were studied. Rate constants for the reaction were determined at various temperatures. The reaction was found to be second order with an activation energy of 20.9 ± 1.6 kcal. and an activation entropy of −18.0 e.u. An analytical scheme for the determination of I, II, and III was developed and applied to the measurement of the rate constants. The rate constants obtained from the concentrations of I, II, and III were in good agreement and eliminated the presence of possible competitive and consecutive reactions under the cited conditions.

In order to propose a plausible mechanism for the reaction of 2-chlorobenzothiazole (I) with the sodium salt of 2-mercaptobenzothiazole (II) to yield 2,2'-thiobis(benzothiazole) (III) and sodium chloride in part I[2] of this series of publications, a knowledge of the reaction order of reaction 1 was essential.



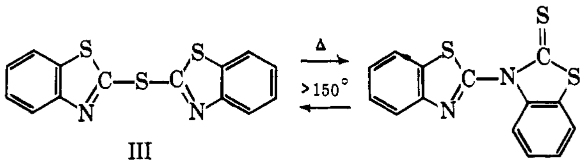
(1)

Brower and co-workers[3] reported the reaction of I with piperidine to be a second-order reaction and Lemons and co-workers[4] indicated that the reaction of I with ammonia is also a second-order reaction.

Gilman and co-workers[5] prepared 2-ethoxybenzothiazole by the reaction of I with sodium ethoxide, but no kinetic data for the reaction were reported.

The knowledge of several possible competitive and consecutive reactions made it highly desirable to follow initially all concentrations of I, II, and III at higher temperatures, and to determine the extent of such interfering reactions. Evidence was given in part I[2] of this series for the existence of the competitive reaction where I reacts with DMF at 150–160° to give 2-(N,N-dimethylamino)benzothiazole in 89.5% yield.

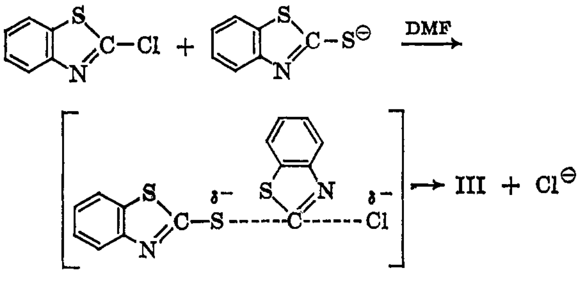
A consecutive reaction discussed in part III[6] of this series involving the rearrangement of III to 3-(2-benzothiazolyl)-2-benzothiazolinethione (reaction 2) could exist and cause erroneous conclusions.



(2)

In view of these possible sources of error, it was deemed essential that any study made must be sufficiently comprehensive to detect and correct for any of these interfering reactions, if present, under the conditions selected. Therefore, specific analytical methods based on ultraviolet spectroscopy and vapor phase chromatography (v.p.c.) were developed and applied to the determination of I, II, and III in DMF as described in the Experimental Section.

The reaction of I with II was thought to involve a nucleophilic displacement of chloride ion of I (S_N2) by II anion (reaction 3). On the other hand, there was the



(3)

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[1] Presented at the 16th Pittsburgh Conference on Analytical Chemistry and Applied Spectroscopy, Pittsburgh, Pa., March 2, 1965.

[2] Paper I: J. J. D'Amico, S. T. Webster, R. H. Campbell, and C. E. Twine, *J. Org. Chem.*, **30**, 2618 (1965).

[3] K. R. Brower, J. W. Way, W. P. Samuels, and E. D. Amstutz, *ibid.*, **19**, 1830 (1954).

[4] J. F. Lemons, R. C. Anderson, and G. W. Watt, *J. Am. Chem. Soc.*, **63**, 1953 (1941).

[5] H. Gilman, K. E. Lantz, and J. A. Beel, *ibid.*, **74**, 1081 (1952).

[6] J. J. D'Amico, S. T. Webster, R. H. Campbell, and C. E. Twine, *J. Org. Chem.*, **30**, 2628 (1965).

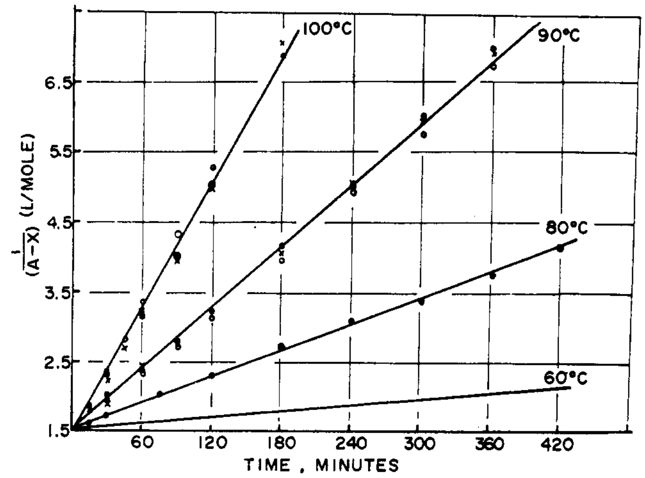

Figure 1.—Determination of rate constants at various temperatures: ×, II; ●, II; and ○, III.

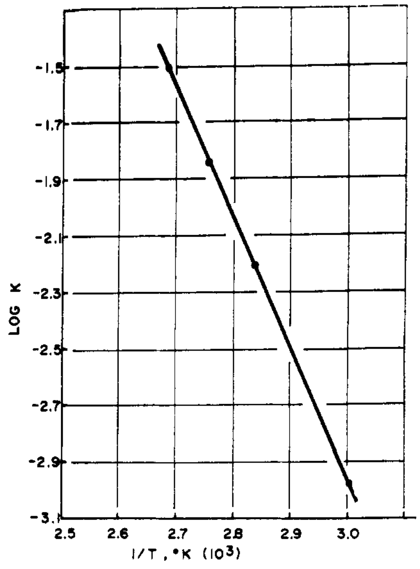

Figure 2.—Determination of energy of activation for the reaction of I with II.

possibility of a solvolysis mechanism (SN1) involving two stages where ionization of I to form the benzothiazolyl carbonium ion and chloride would be the rate-controlling step followed by the combination of benzothiazolyl carbonium ion with the benzothiazolylthio anion.

The rates of the reaction in DMF were determined at temperatures of 60, 80, 90, and 100°. A treatment of these rate data indicated the reaction was second order, and thus supported the mechanism shown in reaction 3. The rate data based on the analyses of I, II, and III are presented in Figure 1. Owing to the increase in reaction time, the rate data for 60° was extrapolated back to zero time. Since equimolar amounts (0.5 mole) of I and II in 600 ml. of DMF were used as starting concentrations at all temperatures, the reciprocal of a reactant concentration *vs.* time should give a linear relationship for a second-order reaction.

The rate constants of the reaction at various temperatures based on the concentration of I, II, and III are given in Table I. The fairly close agreement of these constants at 100 and 90° indicated no significant occurrence of the interfering reactions. Furthermore, 2-(N,N-dimethylamino)benzothiazole and 2-(2-benzothiazolyl)-2-benzothiazolinethione would have been detected during the v.p.c. analyses, but neither was found in the reaction samples at 100 and 90°. In addition, as reported in part I[2] of this series, the reaction of I with II in DMF at temperatures of 140–150° yielded III exclusively in 99% yield.

TABLE I

SECOND-ORDER RATE CONSTANTS

Temp., °C.	*K*, l./mole min.			
	I	II	III	Mean
60	...	1.10×10^{-3}	1.02×10^{-3}	1.06×10^{-3}
80	...	6.19×10^{-3}	...	6.19×10^{-3}
90	1.44×10^{-2}	1.46×10^{-2}	1.41×10^{-2}	1.44×10^{-2}
100	3.18×10^{-2}	3.06×10^{-2}	3.22×10^{-2}	3.15×10^{-2}

The energy of activation, ΔE_a, for the reaction was found to be 20.9 kcal. from the slope of the log of the mean *k* values *vs.* $1/T$ relationship as shown in Figure 2. A ΔE_a of 20.9 ± 1.6 kcal. (based on ±2 standard deviations) was determined by least-squares regression analyses.

It has been theoretically calculated[7] and experimentally shown[3] that the fusion of a benzene ring to another nucleus bearing a halogen substituent and other activating group would lower the activation energy required for halogen displacement. Brower and co-workers[3] found the ΔE_a of the piperidine reaction with I and with 2-chlorothiazole to be 11.0 ± 1.0 and 13.8 ± 1.0 kcal., respectively. Therefore, by analogy, it is predicted that the energy of activation for the reaction of 2-chlorothiazole with II will be higher than that of I with II and in the order of 26 kcal.

The entropy of activation, ΔS_a of -18.0 e.u. was calculated[8] using the average rate constant of 2.04×10^{-4} l./mole sec. at 90° and ΔE_a of 20.9 kcal. Since this value was not excessively large, it is likely that no great distortion of the ring systems occurred during the transition state.

Experimental Section

Preparation of Reagents.—The sodium salt of 2-mercaptobenzothiazole was prepared by dissolving 169 g. (1.0 mole) of 99% 2-mercaptobenzothiazole in 1 l. of ethanol and adding 1.0 mole of A.R. grade sodium hydroxide. The mixture was stirred for 4 hr. and the ethanol was stripped off under vacuum. The residue was dried further at 100–110° for 3 days. Since the reagent showed some tendency to be hygroscopic, it was stored in a sealed bottle until used. An analysis of this reagent by titration indicated no free base and assayed 97.3% sodium salt of 2-mercaptobenzothiazole. The 2-chlorobenzothiazole (Eastman White Label) showed no detectable impurity upon the v.p.c. analysis; therefore, it was used without further purification.

The 2,2′-thiobis(benzothiazole) was prepared as described in part I[2] of this series. Upon recrystallization from ethanol a melting point of 101–102° was obtained.

All other reagents—bibenzyl, dimethylformamide, chloroform, and methanol—were A.R. grade.

Apparatus.—An insulated ethylene glycol constant-temperature bath was heated with an immersion heating element coupled to an F & M 220 power proportioning temperature controller that afforded a temperature control of ±0.3°. All spectrophotometric measurements were made using a Cary Model 11 spectrophotometer with matched 1-cm. quartz cells. The v.p.c. meas-

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(7) M. J. S. Dewar, *J. Am. Chem. Soc.*, **74**, 3357 (1952).

(8) S. Glasstone, K. J. Laidler, and H. Eyring, "The Theory of Rate Processes," McGraw-Hill Book Co., Inc., New York, N. Y., 1941, p. 196.

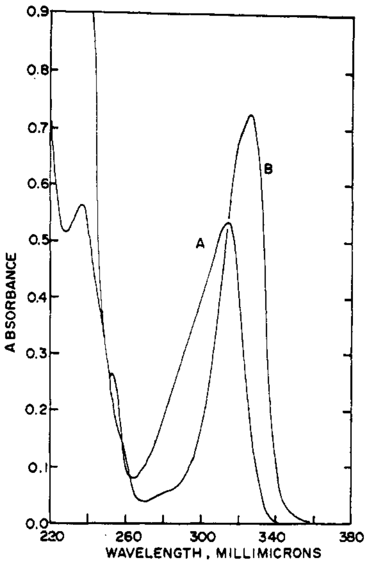

Figure 3.—The ultraviolet spectra of 2-mercaptobenzothiazole and II: concentration, 4.26 × 10^{-3} g./l. in methanol; A, II; B, 2-mercaptobenzothiazole.

urements were made using a F & M Model 720 dual-column programmed-temperature gas chromatograph.

Analytical Methods.—The analytical scheme is based on the separation of water-soluble II from I and III followed by subsequent dilutions, ultraviolet measurement of II and III, and v.p.c. measurement of I.

A. **Sample Preparation.**—Periodically, 10-ml. aliquots of the reaction mixture were taken and transferred to a separatory flask containing 25 ml. of chloroform. A 50-ml. aliquot of 0.2 *N* NaOH (containing 2% sodium chloride) was added to the separatory flask. The mixture was extracted and the chloroform layer was transferred to a 50-ml. volumetric flask. The aqueous layer was extracted with an additional 10 ml. of $CHCl_3$, the $CHCl_3$ layer was separated, and added to the first $CHCl_3$ aliquot. The aqueous layer was transferred to a 100-ml. volumetric flask and diluted to volume with water.

B. **Measurement and Calculation of Concentration of I.**—A measured aliquot of bibenzyl (internal standard) was added to an aliquot of the $CHCl_3$ extract containing I and III. The resulting solution was chromatographed on a 4-ft. 15% SE-30 silicone gum rubber on Gas Chrom CL (45–60 mesh) column at 160° with a helium flow rate of 100 cc./min. The compound I and the internal standard had retention times of 2.5 and 5.5 min., respectively. The amount of I in the $CHCl_3$ aliquot was calculated by use of eq. 4 in which A is the area, S is internal standard,

$$\text{grams of I} = \frac{(\text{grams of S})(A_{\text{I}})f}{(A_{\text{S}})} \qquad (4)$$

and f is the response factor (1.16) obtained from v.p.c. of standard mixtures of I and bibenzyl in $CHCl_3$.

C. **Measurement and Calculation of II Concentration.**—An aliquot of the aqueous solution was diluted with methanol as required and the last solution of the series was made acid to a concentration of 2.0% acetic acid. As shown in curves A and B of Figure 3, the presence of acid converts II to 2-mercaptobenzothiazole which has a stronger absorption maximum at 326 mμ (a_M 28,200 l./mole cm.) than II at 312 mμ (a_M 20,900 l./mole cm.). Including the acid in the last diluted sample provided a constant acidity which prevented errors that could have arisen from II if small changes in pH occurred in the unbuffered system. The absorbance of the diluted sample was measured. The concentration was calculated using the Beer–Bouger equation (5),

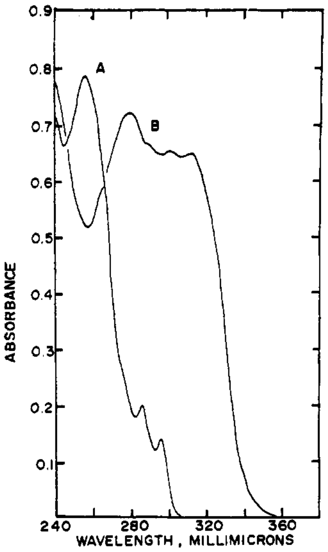

Figure 4.—The ultraviolet spectra of I and III: A, I in chloroform, 0.01601 g./l.; B, III in chloroform, 0.01335 g./l.

$$A = a_M bc \qquad (5)$$

where A is the absorbance, b is the cell thickness in centimeters, c is the concentration in moles per liter, and a_M is the molar absorptivity constant in liters per mole centimeter.

D. **Measurement and Calculation of Concentration of III.**—An aliquot of the $CHCl_3$ extract was diluted with $CHCl_3$ as required to measure the ultraviolet absorbance at 312 mμ. This solution contained III and I, but as shown in curves A and B of Figure 4, the ultraviolet spectra of I did not interfere with the absorption maximum of III (a_M 14,900 l./mole cm.) at 312 mμ. Therefore, the concentration of III could be determined from the ultraviolet absorbance in the presence of I. The concentration of III was calculated in the same manner as in the preceding measurement of II.

The weight of I per aliquot was corrected for dilutions and converted to concentration in moles per liter.

Testing of Methods.—The following analytical scheme was tested by analyzing known mixtures of I, II, and III in varying concentrations. The mixtures were made to simulate actual samples and analyzed immediately to prevent significant reaction between the reactants. Known weights of II and III were added to a separatory flask followed by a known weight of I in 10 ml. of DMF. The mixture was shaken and the analyses were performed immediately according to the described procedures. In all cases recoveries were better than 97%. The fact that the average recoveries of I and II were slightly low, 98.1 and 97.7%, respectively, and that of III was high, 100.2%, may indicate that some reaction occurred during the mixing of the standards prior to analyses.

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