was cooled to 45–50° and 2.26 g. (0.02 mole) of chlorobenzene in 15.0 ml. of thiophene-free benzene was added over an hour with high speed stirring; the mixture was then stirred for an additional 2 hr. At the end of this time the mixture was jet black. To the mixture containing phenylsodium was added a solution of 2.20 g. (0.012 mole) of isopropyl phenyl sulfone in 15.0 ml. of pure benzene, and the mixture was stirred for 14 hr. At the end of this time 4.0 ml. of 98% deuterium oxide was added with external cooling to avoid a temperature rise. Stirring was continued for one minute after the addition, and the mixture was then poured into 300 ml. of ether. The ether solution was washed to neutrality with water, dried over sodium sulfate and concentrated *in vacuo*, affording 1.8 g. of product which on infrared analysis was found to be 99.6% deuterated.

Reaction of Cyclopropyl Phenyl Sulfone with Phenylsodium Followed by Deuterium Oxide Quenching.—With the same apparatus described in the preceding experiment a dispersion was prepared from 2.76 g. (0.12 mole) of sodium and 80.0 ml. of isoöctane. To this was added at 35° a solution of 6.76 g. (0.06 mole) of chlorobenzene in 30.0 ml. of isoöctane. The addition was made over 1 hr. and stirring was continued for an additional 2 hr. To the bluish-black dispersion was added a solution of 4.36 g. (0.024 mole) of cyclopropyl phenyl sulfone in 30 ml. of anhydrous thiophene-free benzene. The mixture was stirred for 7.5 hr. At the end of this period the mixture was quenched by adding 4.00 ml. of 98% deuterium oxide with careful cooling to prevent a temperature rise; the product, weighing 3.96 g., was obtained as in the previous experiment. Quantitative infrared analysis indicated this to be 87.1% deuterated.

Competitive Ionization of Cyclopropyl Phenyl Sulfone and Isopropyl Phenyl Sulfone to Afford Sodium Conjugate Bases under Equilibrium Conditions.—Using the same apparatus as in the preceding two experiments 0.23 g. (0.01 mole) of sodium was dispersed in 10.0 ml. of isoöctane. The first 7 drops of a solution of 0.56 g. (0.005 mole) of chlorobenzene in 10.0 ml. of dry benzene were added at 70–75° and the remainder at 35–40° during 15 min. The mixture was then stirred for an additional 2 hr., and then a solution of 0.50 g. each of cyclopropyl phenyl sulfone and isopropyl phenyl sulfone and 10.0 ml. of dry benzene was added to the jet black phenylsodium dispersion. The mixture was then stirred for 3 hr. Following this, 1.0 ml. of 98% deuterium oxide was added with cooling and worked up as before. Quantitative infrared analysis indicated $q_a = 0.435$, $q_b = 0.550$, $q_c = 0.0899$ and $q_d = 0.0238$.

In a second run the same procedure was followed except that 0.276 g. (0.012 mole) of sodium, 0.678 g. (0.006 mole) of chlorobenzene and 0.0027 mole of each of the sulfones was used; also, in this run the time of stirring between addition of the sulfones and quenching with deuterium oxide was extended to 6 hr. Quantitative infrared analysis indicated $q_a = 0.326$, $q_b = 0.348$, $q_c = 0.201$ and $q_d = 0.107$.

The procedure of run two was followed in run three except that the time before quenching was extended to 16 hr. Here $q_a = 0.315$, $q_b = 0.233$, $q_c = 0.0122$ and $q_d = 0.0222$.

Competitive Ionization with Phenylsodium Generated from Diphenylmercury.—A dispersion of 0.138 g. (0.006 mole) of sodium in 10.0 ml. of isoöctane prepared as before was treated hot with the first few drops of a solution of 1.06 g. (0.003 mole) of diphenylmercury in 20.0 ml. of dry benzene. The rest of the diphenylmercury solution was added over 20 min. at room temperature. The mixture was then stirred for 6 hr. Following this a solution containing 0.50 g. each of cyclopropyl phenyl sulfone and isopropyl phenyl sulfone in 10.0 ml. of dry benzene was added and stirring was continued for 13 hr. After quenching with 1.00 ml. of deuterium oxide, the mixture was worked up as usual to afford 0.56 g. of material subjected to quantitative infrared analysis: $q_a = 0.546$, $q_b = 0.101$, $q_c = 0.230$ and $q_d = 0.0528$.

Competitive Ionization with Phenylpotassium.—To 0.24 g. (0.006 mole) of potassium dispersed in 10.0 ml. of isoöctane was added during 20 min. 1.06 g. (0.003 mole) of diphenylmercury dissolved in 20.0 ml. of anhydrous benzene. The mixture turned jet black, and stirring was continued for 2 hr. To the phenylpotassium thus produced was added a solution of 0.50 g. each of cyclopropyl phenyl sulfone and isopropyl phenyl sulfone in 10.0 ml. of dry benzene, and stirring was continued for 3 hr. more. Quenching with 1.00 ml. of deuterium oxide with external cooling and the usual workup afforded 0.72 g. of product analyzing as $q_a = 0.464$, $q_b = 0.629$, $q_c = 0.481$ and $q_d = 0.243$.

Acknowledgment.—The authors wish to express their appreciation of the support of this research by the Alfred P. Sloan Foundation.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF NOTRE DAME]

The Relative Nucleophilic Character of Several Mercaptans toward Ethylene Oxide[1]

BY JAMES P. DANEHY AND CHARLES J. NOEL[2]

RECEIVED AUGUST 17, 1959

Pseudo-first order rate constants have been determined for the reactions in buffered aqueous solutions of ethylene oxide with twelve different mercaptans. Values for the rate constants increase with increasing *p*H over a *p*H range characteristic for each mercaptan. With the single exception of thiophenol, plots of k *vs.* $[RS^-]/[RSH]$ are linear. Thus, the mercaptide ion is the reactive species, and the slopes of the straight lines afford a relative measure of the intrinsic reactivities of the various mercaptide ions with respect to ethylene oxide. Values for the dissociation constants of thirteen mercaptans have been determined at 20° and, in five cases, at 30 and 40° as well. In general, the higher the value for pK_a for the mercaptan, the greater the intrinsic reactivity toward ethylene oxide. However, *o*-aminothiophenol has a uniquely high intrinsic reactivity and constitutes the major exception to this generalization.

Introduction

There are several references, mostly preparative in nature, to the formation of hydroxyalkyl thioethers by the reactions of mercaptans with epoxides.[3] Searles[4] studied the reactions of thiophenol and of several aliphatic mercaptans with trimethylene oxide and found that the reactions proceeded smoothly in alkaline solution to give good yields of 3-hydroxypropyl sulfides while poor yields were obtained in acidic solution. Berbe[5] made a kinetic study of the reactions of hydrogen sulfide and of 2-mercaptoethanol with ethylene oxide and with propylene oxide. He claimed that the expected product is a catalyst for

(1) Presented at the 135th Meeting of the American Chemical Society, Boston, Mass., April 10, 1959.

(2) Du Pont Fellow, 1957–1958.

(3) C. D. Nenitzescu and N. Scarlatescu, *Ber.*, **68B**, 587 (1935); N. Hellström, *Svensk Kem. Tid.*, **49**, 201 (1937); B. Sjöberg, *ibid.*, **50**, 250 (1938); D. F. Othmer and D. Q. Kern, *Ind. Eng. Chem.*, **32**, 160 (1940); B. Sjöberg, *Ber.*, **74B**, 64 (1941); **75B**, 13 (1942); M. S. Malinovskiĭ and B. N. Moryganov, *Zhur. Priklad. Khim.*, **21**, 995 (1948); Yu. K. Yurev and K. Yu. Novitskiĭ, *Doklady Akad. Nauk S.S.S.R.*, **63**, 285 (1948); F. N. Woodward, *J. Chem. Soc.*, 1892 (1948); H. Gilman and L. Fullhart, THIS JOURNAL, **71**, 1478 (1949); C. C. J. Culvenor, W. Davies and N. S. Heath, *J. Chem. Soc.*, 278 (1949); L. N. Owen and P. N. Smith, *ibid.*, 2973 (1951).

(4) S. Searles, THIS JOURNAL, **73**, 4515 (1951).

(5) F. Berbe, *Bull. soc. chim. Belg.*, **59**, 448 (1950).

TABLE I

RATE CONSTANTS FOR THE REACTIONS OF ETHYLENE OXIDE WITH MERCAPTANS AS A FUNCTION OF TEMPERATURE AND *p*H

Temp., °C.	*p*H	$[RS^-]/[RSH] \times 10^5$	$k \times 10^5$, l. m.$^{-1}$ sec.$^{-1}$
		Thioglycolic acid	
20.0	2.58	0.0015	0.619 ± 0.019
	3.55	0.0141	0.802 ± .020
	5.44	1.10	5.24 ± .25
	6.90	31.6	34.6 ± .78
	7.15	56.1	56.0 ± 1.8
30.0	5.57	2.24	3.75 ± 0.04
	6.22	10.0	19.2 ± 0.48
	6.62	25.2	50.7 ± 1.02
	6.92	50.0	99.1 ± 0.72
	7.10	75.8	147 ± 1.3
40.0	5.45	2.51	9.91 ± 0.05
	6.01	9.11	32.1 ± .24
	6.33	19.1	71.1 ± .67
	6.51	28.1	105 ± 1.83
	6.67	41.6	150 ± 1.5
		Ethyl mercaptan	
20.0	6.15	4.46	3.48 ± 0.08
	7.00	31.6	21.0 ± 0.29
	7.09	38.9	27.4 ± 1.47
	7.40	79.5	54.0 ± 0.80
	7.59	124	87.3 ± 0.40
		β-Mercaptopropionic acid	
20.0	4.05	0.071	0.585 ± 0.007
	4.71	.324	.640 ± .013
	4.89	.490	.913 ± .11
	5.42	1.66	5.45 ± .30
	5.86	4.56	3.60 ± .39
	6.09	7.75	6.26 ± .42
	6.50	20.0	12.7 ± 1.2
	6.82	41.6	28.6 ± 1.7
30.0	5.73	5.00	8.02 ± 0.05
	6.37	21.9	26.9 ± .48
	6.60	37.1	49.0 ± .65
	6.81	60.2	79.9 ± 1.1
	6.95	83.0	108 ± 1.8
40.0	5.33	3.02	6.58 ± 0.03
	5.93	12.0	29.1 ± .45
	6.19	21.9	50.9 ± .40
	6.37	33.1	79.9 ± .93
	6.50	44.6	110 ± 2.1
		2-Mercaptoethanol	
20.0	3.07	0.039	0.734 ± 0.035
	3.70	.166	1.09 ± .05
	4.15	.467	1.75 ± .07
	4.95	2.95	2.09 ± .35
	5.34	7.25	3.84 ± .22
	6.05	37.2	12.8 ± .12
	6.26	60.3	26.1 ± .12
	6.42	87.0	23.1 ± .50
	6.52	110	46.1 ± .10
	6.60	132	55.2 ± 1.2
30.0	5.26	8.70	7.03 ± 0.10
	5.58	18.2	5.81 ± .01
	5.75	26.9	19.5 ± .60
	6.11	61.6	47.0 ± .80
	6.28	91.3	79.4 ± .74
	6.45	135	104 ± 1.7
40.0	4.95	6.04	8.13 ± 0.06
	5.35	15.1	20.1 ± .54
	5.65	30.2	41.6 ± .52
	5.88	51.2	73.0 ± .68
	5.98	64.5	94.5 ± .68
		2-Mercaptoethanesulfonic acid	
20.0	2.94	0.072	0.204 ± 0.009
	3.56	.302	.517 ± .007
	3.97	.775	.996 ± .010
	4.89	6.45	2.50 ± .21
	5.23	14.1	5.53 ± .18
	6.19	129	46.9 ± 1.1
	6.51	269	84.2 ± 0.85
		1-Thio-D-sorbitol	
20.0	4.80	2.00	0.887 ± 0.023
	5.40	7.95	3.02 ± .05
	6.03	33.9	7.06 ± .05
	6.40	79.5	13.5 ± .22
	6.77	186	28.5 ± .26
	7.00	316	53.0 ± .35
30.0	5.42	11.5	4.02 ± .06
	6.05	50.0	14.7 ± .36
	6.31	91.2	28.2 ± .48
	6.62	186	56.0 ± .75
	6.85	316	97.5 ± .83
40.0	5.20	10.0	6.09 ± .12
	5.52	20.9	11.0 ± .23
	6.20	100	54.2 ± 1.00
	6.44	174	94.3 ± 0.85
		2-Mercaptoethylamine	
20.0	3.02	0.468	0.328 ± 0.014
	3.70	2.24	0.517 ± .040
	4.98	44.6	5.04 ± .18
	5.50	141	14.4 ± .40
	5.84	309	36.7 ± 1.40
30.0	3.75	3.55	0.951 ± 0.008
	4.28	12.0	2.99 ± .04
	5.08	75.8	15.1 ± .39
	5.40	158	35.9 ± .33
	5.75	355	79.1 ± .87
40.0	3.90	7.07	3.06 ± .03
	4.35	20.0	8.01 ± .04
	5.20	141	56.0 ± .70
	5.40	224	87.0 ± .85
	5.52	295	115 ± 2.00
		Thioglycolic acid methyl ester	
20.0	2.97	1.95	0.624 ± 0.009
	3.57	7.85	1.28 ± .05
	4.40	52.5	6.07 ± .06
	5.38	501	49.8 ± 1.5
	5.89	1620	154 ± 4.5
		L-Cysteine	
20.0	3.61	1.95	1.80 ± 0.22
	4.93	40.8	3.08 ± .25
	5.23	81.2	7.84 ± .02
	5.67	224	16.4 ± .58
	5.92	396	40.2 ± 3.2
		L-Cysteine methyl ester	
20.0	3.03	34.9	0.699 ± 0.014
	3.76	182	1.97 ± .02
	4.13	536	7.83 ± .13
	4.53	1070	15.2 ± .18
	4.77	1860	27.5 ± .43
	4.95	2820	40.1 ± .29

Temp., °C.	pH	$[RS^-]/[RSH] \times 10^5$	$k \times 10^6$, l. m.$^{-1}$ sec.$^{-1}$
		Thiophenol	
20.0	3.08	2.00	0.892 ± 0.027
	3.86	12.0	2.39 ± .38
	4.18	25.2	5.27 ± .10
	4.40	42.7	18.5 ± .10
	4.66	75.8	64.8 ± 2.0
		o-Aminothiophenol	
20.0	1.12	0.339	162 ± 6.7
	1.66	1.18	195 ± 2.4
	1.73	1.38	206 ± 4.2
	1.86	1.86	232 ± 3.8
	2.03	2.76	261 ± 11.5

the reaction and he failed to recognize the extreme sensitivity of the reactions to variations in *p*H values. Several years ago, while using aqueous ethylene oxide as a "blocking" reagent for sulfhydryl groups in partially reduced keratin fibers, one of us obtained anomalous results.[6] The anomaly was resolved when the overriding importance of *p*H was recognized.

In the presently reported investigation the rates of reaction of several mercaptans with ethylene oxide have been determined as a function of *p*H and temperature. In each case, at constant temperature, the values for pseudo-first order rate constants (k) increase exponentially with increasing *p*H values. But the plots of k *vs.* $[RS^-]/[RSH]$, with the single exception of thiophenol, are rectilinear.

Since, in order to determine the ratio of mercaptide ion to mercaptan at any given *p*H value it was necessary to know the dissociation constant (pK_a) of the mercaptan, these have been determined in each case because of the discrepancies in the literature.

Finally, a comparison of the true second-order rate constants for the different systems affords a measure of the relative nucleophilicity of the different mercaptide ions toward a single reactant: ethylene oxide.

Experimental

Materials.—The sources of the mercaptans, and their purities as determined by iodimetric titration, were as follows. Thioglycolic acid (85% aqueous solution), β-mercaptopropionic acid (98.7%), cysteine hydrochloride (101.7%), cysteine hydrochloride methyl ester (99.4%), 2-mercaptoethanesulfonic acid sodium salt (aqueous solution, *p*H 3.04), and 1-thio-D-sorbitol (84.2%) were received as gifts from the research laboratories of the Toni Co., Chicago 54, Ill. 2-Mercaptoethylammonium chloride (93.7%) was obtained as a gift from Evans Chemetics, Inc., New York 17, N. Y. *o*-Aminothiophenol (99.5%) was obtained as a gift from American Cyanamid, New York 20, N. Y. Ethyl mercaptan, 2-mercaptoethanol (99.5%), thiophenol (101.7%) and thioglycolic acid methyl ester (100.0%) were purchased from Distillation Products Industries, Rochester, N. Y.

Ethylene oxide was purchased from the Matheson Co., E. Rutherford, N. J. Aqueous solution (25–30% by weight) were prepared and the concentrations determined at the beginning of each kinetic run by the method of Swan.[7]

Procedure for Kinetic Measurements.—A buffer solution (150 ml.) of the desired *p*H value was pipetted into each of two 500-ml. round-bottom flasks equipped with ground glass stoppers and the flasks placed in a constant temperature bath. Two 100-ml. volumetric flasks, one containing aqueous ethylene oxide solution and the other containing distilled water, were also placed in the bath. After temperature equilibration had proceeded for about one hour a suitable volume (2.00 to 20.0 ml.) of mercaptan solution was pipetted into each of the buffer solutions. The ethylene oxide solution was quickly poured into one of the flasks, the solutions mixed thoroughly, a 25.0-ml. aliquot immediately withdrawn, and the latter acidified to quench the reaction. The iodine titer of this first aliquot was assigned to zero time. A second aliquot was withdrawn for *p*H determination. The distilled water in the second volumetric flask was added to the second buffered mercaptan solution, the solutions mixed thoroughly, a 25.0-ml. aliquot withdrawn, the latter acidified, and titrated with iodine. The initial titer of the kinetic sample was adjusted to equal the initial titer of the blank (the adjustment rarely exceeded 0.10 ml. in a total volume of ~12.5 ml. iodine solution added) and the same correction was applied to each subsequent determination. Since the value of the iodine titer of the blank diminishes slowly with time by reason of aerial oxidation, the value of the blank titer at time t was taken as a and the value of the titer of the reaction mixture was taken as $(a - x)$, thus automatically correcting for loss of mercaptan not due to reaction with ethylene oxide. Values of k for the rate of disappearance of mercaptan were calculated from the expression, $k = 2.303 \log (a/a - x)/t[C_2H_4O]$. The results of the kinetic runs are summarized in Table I.

Determination of the Dissociation Constants of the Mercaptans. Titrimetic Method.—A solution of mercaptan, approximately tenth molar, was prepared and standardized by titration with standard iodine solution. A 10-ml. aliquot of the mercaptan solution was diluted with 100 ml. of distilled water and this solution was titrated electrometrically with 0.1 *N* sodium hydroxide solution using a Beckman *p*H meter, model G, equipped with a type E glass electrode. A titration curve was drawn and the value for pK_a was considered to be the *p*H value at the half-equivalence point taken from the curve. In the case of *o*-aminothiophenol, because of its insolubility in water, a sample (0.4000 to 0.5000 g.) was transferred to a beaker containing 200 ml. of distilled water, the volume of standard alkali corresponding to exactly one-half the equivalence of the mercaptan was added rapidly, and sufficient ethanol added to give a homogeneous solution. The value for the pK_a of the thiol group of *o*-aminothiophenol was taken to be the *p*H value for this solution. For the determination of the dissociation constant or the substituted ammonium ion (amino group) in *o*-aminothiophenol the same procedure was used but with standard hydrochloric acid. Three successive determinations of both constants gave virtually identical results.

Spectrophotometric Method.—The procedure employed was essentially that of Benesch and Benesch.[8] Spectrophotometric measurements were made with a Beckman spectrophotometer, model DU, equipped with thermospacers for measurements at constant temperature. All *p*H measurements were made at the same temperature as the corresponding spectrophotometric readings. A phosphate buffer system was used: aqueous phosphoric acid was brought to the desired *p*H value with sodium hydroxide and the solution diluted to a final volume in which the phosphate concentration was 0.05 *M*.

A sample of mercaptan, 0.10 ml. of 1.0 to 2.0 *M*, was pipetted into 10.0 ml. of buffer solution. The absorption spectrum was determined immediately after mixing, using the corresponding buffer as blank, and the maximum in the range of 235–250 mμ noted. Oddly enough, thioglycolic acid methyl ester did not give a maximum in the appropriate range so that the method could not be used.

For the five mercaptans for which dissociation constants were measured at three temperatures, the values for heats of dissociation were determined graphically from the slopes of the rectilinear plots of log pK_a *vs.* reciprocal of the absolute temperature. The values obtained, in kcal. per mole, are: thioglycolic acid, 7.39; β-mercaptopropionic acid, 7.31; 2-mercaptoethanol, 6.49; 1-thio-D-sorbitol, 6.32; 2-mercaptoethylamine, 6.08.

Discussion

While plots of pseudo-first order rate constants *vs.* *p*H at constant temperature (data of Table I) give characteristically exponential curves, plots of

(6) J. P. Danehy, *Proc. Indiana Acad. Sci.*, **68**, 128 (1958).

(7) J. D. Swan, *Anal. Chem.*, **26**, 878 (1954).

(8) R. Benesch and R. Benesch, THIS JOURNAL, **77**, 5877 (1955).

TABLE II

ACID DISSOCIATION CONSTANTS FOR SEVERAL MERCAPTANS

Mercaptan	Titrimetric method 20°	Spectrophotometric method 20°	30°	40°	Previously obtained values
Ethyl mercaptan	10.50				
Thioglycolic acid	10.06	10.40	10.22	10.05	10.4[a]
β-Mercaptopropionic acid	10.27	10.20	10.03	9.85	10.2[a]
2-Mercaptoethanol	9.58	9.48	9.32	9.17	9.6,[a] 9.5[b]
1-Thio-D-sorbitol		9.50	9.35	9.20	
2-Mercaptoethylamine	8.10	8.35	8.20	8.05	8.6,[b] 8.35[c]
Thioglycolic acid methyl ester	7.68				7.8[b]
Thiophenol	7.78				6.5,[a] 7.8[b]
Cysteine	8.70	8.32			10.4,[a] 8.3,[b] 8.53[c]
Cysteine methyl ester	6.50				7.45[c]
2-Mercaptoethanesulfonate	9.53	9.08			
p-Chlorothiophenol	7.50				
o-Aminothiophenol[d]	6.59				

[a] R. H. DeDeken, J. Broekhuysen, J. Bechet and A. Mortier, *Biochim. Biophys. Acta*, 19, 45 (1956). [b] M. Calvin, "Glutathione Symposium," Academic Press, Inc., New York, N. Y., 1954, p. 9. [c] Benesch and Benesch, ref. 8. [d] pK_a ($-NH_3^+$) 3.00.

the rate constants *vs.* the ratio of mercaptide ion to mercaptan are excellent approximations to straight lines. The data for thiophenol constitute the single exception to this generalization: in this case the plot suggests two intersecting straight lines, the first over the range of 0 to 30 ($[RS^-]/[RSH] \times 10^5$), and the second, with much steeper slope, over the range of 35 to 80.

Whatever may be the reason for the unexpected behavior of thiophenol the data indicate clearly the direct dependence of speeds of reaction on the proportion of the mercaptan present in ionic form. The mechanism proposed for these reactions, consonant with the data, is given by the sequence

$$RSH \rightleftharpoons RS^- + H^+ \quad (1)$$

$$RS^- + H_2C\text{—}CH_2 \longrightarrow RSCH_2CH_2O^- \quad (2)$$
$$\qquad\qquad \diagdown\ \diagup \quad O$$

$$RSCH_2CH_2O^- + H^+ \longrightarrow RSCH_2CH_2OH \quad (3)$$

Reaction 1 is the instantaneous ionization of the mercaptan for which the ratio of mercaptide ion to mercaptan is controlled by the hydrogen ion concentration according to the expression for the dissociation constant

$$K_a = [RS^-][H^+]/[RSH]$$

Reaction 2 is the rate-determining step since the final reaction, the capture of a proton by the substituted ethoxide ion, is doubtless also instantaneous. Thus, in the presence of a large excess of ethylene oxide the experimentally determined decrease in mercaptan concentration with time depends on the ratio of mercaptide ion to mercaptan, and the calculated values for the pseudo-first order rate constants at different *p*H values should be directly proportional to the ratios of mercaptide ion to mercaptan at those *p*H values. The proportionality constant for this relationship should be k_2, the true second-order rate constant for reaction 2. That is, k_2 should be independent of *p*H; it should be represented by the slope of the rectilinear plot of k *vs.* $[RS^-]/[RSH]$.

The calculated values for k_2 furnish a quantitative measure of the relative reactivities of the different mercaptans (strictly speaking, the mercaptide ions) toward a single reactant: ethylene oxide. In Table III values of k_2 are listed in order of decreasing magnitude for eleven mercaptans. For the twelfth mercaptan, thiophenol, the value for k_2 is that corresponding to the initial slope. The observed order of reactivity is interpreted as a measure of the nucleophilic character of the mercaptide ions involved.

TABLE III

RELATIVE REACTIVITIES[a] TOWARD ETHYLENE OXIDE OF TWELVE MERCAPTANS AT 20.0°

Mercaptan	k_2	pK_a
o-Aminothiophenol	13	6.59
Thioglycolic acid	0.1024	10.40
Ethyl mercaptan	.0705	10.50
β-Mercaptopropionic acid	.0698	10.20
2-Mercaptoethanol	.0410	9.48
2-Mercaptoethanesulfonic acid	.0328	9.08
Thiophenol	.0211	7.78
1-Thio-D-sorbitol	.0166	9.50
2-Mercaptoethylamine	.0118	8.35
Thioglycolic acid methyl ester	.0096	7.68
L-Cysteine	.0092	8.32
L-Cysteine methyl ester	.0015	6.50

[a] Relative reactivities are considered to be in the same proportion to each other as the values for $k_2 = k/([RS^-]/[RSH])$.

The corresponding values for the dissociation constants of the mercaptans have also been included in Table III since there is an interesting empirical relationship between them and the relative reactivities. While there are evident exceptions there is a definite trend that seems to go beyond the possibilities of chance coincidence: the higher the value for the pK_a of the mercaptan, the higher the relative reactivity of the corresponding mercaptide ion.

The most remarkable exception to the generalization just stated is furnished by *o*-aminothiophenol which, though it has next to the lowest pK_a value, has a relative reactivity 130 times greater than the next most reactive compound. A number of other substituted thiophenols are being investigated in an effort to furnish a basis for understanding this anomaly.

With five of the mercaptans the reactions with ethylene oxide were studied at three temperatures: 20, 30 and 40°. From the slopes of the strictly linear plots of log k_2 *vs.* reciprocal of the absolute temperature the activation energies for each of these reactions were determined (Table IV). While the differences are small, they are considered to be significant, and they raise a rather interesting question, for the activation energies are in completely reversed order from what might have been expected from the observed rates of reaction. The thioglycolate ion, which reacts the most rapidly, has the highest activation energy, while the mercaptoethylammonium ion, which reacts least rapidly, has the lowest activation energy. However, when values for entropy of activation and frequency factors are calculated from the data it is seen that for both terms the order of the values favors the order of reaction rates actually observed. A consideration of the two extreme cases gives us some basis for accounting for the fact that the rates of reaction are so highly dependent on entropy effects.

Over the whole *p*H range in which thioglycolate was studied the carboxyl group is completely dissociated so that the mercaptide which attacks the ethylene oxide is a doubly charged anion with the two negative charges separated only by a short distance. This should be a highly solvated species with water dipoles attracted to the negative charges. The product of reaction, however, is a singly charged anion and should be much less solvated.

TABLE IV

ACTIVATION ENERGIES, ENTROPIES OF ACTIVATION AND FREQUENCY FACTORS FOR THE REACTIONS OF FIVE MERCAPTANS WITH ETHYLENE OXIDE

Mercaptan	ΔE_a, kcal./mole	ΔS_c*, u.u.	A, l. m.$^{-1}$ sec.$^{-1}$
Thioglycolic acid	11.65	−25.32	5.0×10^7
β-Mercaptopropionic acid	11.53	−26.53	2.7×10^7
2-Mercaptoethanol	11.48	−27.74	1.4×10^7
1-Thio-D-sorbitol	10.87	−31.62	0.2×10^7
2-Mercaptoethylamine	10.78	−32.57	0.13×10^7

The reaction can be considered then as consuming a highly solvated species to form a less solvated species with the release of a considerable number of solvent molecules.

Over the *p*H range in which the mercaptoethyl ammonium ion was studied the substituted ammonium group is undissociated so that the species which attacks the ethylene oxide is a dipolar ion with electrostatic attraction holding the two charged groups relatively close together. Because of the partial neutralization of the opposing charges this species is probably not too highly solvated. The product of reaction, however, is singly charged cation which should be appreciably more solvated. In this reaction, then, the consumption of a slightly solvated species to form a more highly solvated species brings about the restriction of position of a large number of solvent molecules.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

Stereochemistry of Allylic Rearrangements. X. The Isomeric Rearrangement and Solvolysis of *trans*-α,γ-Dimethylallyl *p*-Nitrobenzoate in Aqueous Acetone[1]

BY HARLAN L. GOERING AND MELVIN M. POMBO[2]

RECEIVED SEPTEMBER 8, 1959

The first-order solvolysis of optically active *trans*-α,γ-dimethylallyl *p*-nitrobenzoate (I) in 90% aqueous acetone is accompanied by a first-order intramolecular (SNi′) rearrangement of the ester—in this system rearrangement results in the interconversion of enantiomers, *i.e.*, racemization. The first-order rate constant for racemization (k_{rac}) is over four times larger than that for solvolysis (k_t). Thus during solvolysis the remaining ester becomes progressively racemic and at 50% reaction is about 95% racemic. The racemization of carbonyl-O^{18} labeled I in the presence of unlabeled *p*-nitrobenzoic acid and lithium *p*-nitrobenzoate does not result in exchange. From this and from the kinetic behavior it is clear that the rearrangement (racemization) is completely intramolecular. The relative positions of the oxygen atoms in the reactant (*d*-ester) and product (*dl*-ester) have been determined using carbonyl-O^{18} labeled optically pure *d*-ester. Isolation of the unsolvolyzed but racemized (rearranged) ester followed by reresolution showed the label to be distributed between the two positions in each enantiomer. The rate of O^{18} equilibration in the two enantiomers is 1/2.9 times that of racemization. The kinetic and O^{18} experiments are consistent with the idea that the intramolecular rearrangement involves internal return from an internal ion-pair intermediate. According to this interpretation, the data show that in the present case there is one chance in 2.9 that the oxygen atoms will become equivalent on passing through the intermediate.

Introduction

Evidence was presented in earlier papers in this series[3-5] that an internal ion-pair[6] intermediate is involved in carbonium-ion reactions of allylic esters and chlorides. This intermediate can (a) return to the original allylic compound or its allylic isomer (internal return[6])—this is an intramolecular isomeric (SNi′) rearrangement—or (b) dissociate to the carbonium ion and the accompanying anion. As was pointed out in the previous paper in this series[5] in hydroxylic solvents the carbonium ion formed by dissociation of the intermediate is completely intercepted by the solvent

(1) This work was supported by (a) The Office of Ordnance Research and (b) The Research Committee of the Graduate School with funds given by the Wisconsin Alumni Research Foundation.

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(3) H. L. Goering and E. F. Silversmith, THIS JOURNAL, **77**, 1129 (1955); **77**, 6249 (1955); **79**, 348 (1957).

(4) H. L. Goering, T. D. Nevitt and E. F. Silversmith, *ibid.*, **77**, 5026 (1955).

(5) H. L. Goering and R. W. Greiner, *ibid.*, **79**, 3464 (1957).

(6) S. Winstein, E. Clippinger, A. Fainberg, R. Heck and G. Robinson, *ibid.*, **78**, 328 (1956).