

The oily residue was covered with water and the mixture was neutralized by addition of solid sodium carbonate and filtered, giving aqueous extract B. The residue (C) was a mixture of black metallic selenium and a yellow solid.

The ether extract A was dried over magnesium sulfate, filtered, and evaporated.⁸ On the assumption that the yield of Teague and Roe² was realized in the oxidation step (*i.e.*, 30 g. of 3-isoquinolinecarboxaldehyde) the crude mixture of 3-isoquinolinecarboxaldehyde and 3-methylisoquinoline was dissolved in 300 ml. of acetone and 30 ml. of 30% hydrogen peroxide was added to the solution. The temperature rose to 45° and remained there for several hours. An additional 40 ml. of 30% hydrogen peroxide was added and the mixture was allowed to stand overnight. The fluffy white precipitate was collected by filtration, air-dried, and suspended in 350 ml. of water. The suspension was boiled for one hour, but the solids did not dissolve.⁹ The mixture was filtered. Evaporation of the filtrate gave 0.3 g. of 3-isoquinolinecarboxylic acid, m.p. 164–166° (lit.¹⁰ m.p. 167–168°). The solid was dissolved in dilute sodium hydroxide solution; the solution was treated with charcoal, filtered, acidified with acetic acid, and the resultant mixture was filtered. The pale cream colored solid remaining after air drying (14 g., m.p. 210–211°) was recrystallized from acetone, giving 12 g. of 3-isoquinolinecarboxylic acid-2-oxide, m.p. 211–211.5° dec.

Anal. Calcd. for $C_{16}H_{17}NO_3$: C, 63.49; H, 3.73; N, 7.40. Found: 63.97; H, 3.98; N, 7.25.

Extract B was treated with charcoal, filtered, and acidified with acetic acid. The resultant solid was recrystallized from water, giving 0.6 g. of 3-isoquinolinecarboxylic acid, m.p. 166–167°.

Residue C was extracted in a Soxhlet apparatus with pyridine. On chilling the pyridine in ice and filtering 2.0 g. of bright yellow needles, m.p. 320–321° dec. was obtained. A small sample (sufficient to form a saturated solution) was recrystallized twice from 25 ml. of pyridine giving 0.08 g. of di(3-isoquinolinyl)glyoxal, m.p. 322–323° dec.

Anal. Calcd. for $C_{20}H_{12}N_2O_2$: C, 76.91; H, 3.87; N, 8.97. Found: C, 77.19; H, 3.33; N, 8.65.

3-Isoquinolinecarboxylic acid-2-oxide. To a solution of 1.0 g. of 3-isoquinolinecarboxylic acid in 20 ml. of glacial acetic acid, 10 ml. of 30% hydrogen peroxide was added and the solution was heated for 2 hr. on the steam bath. On cooling and diluting with water pale tan needles precipitated and were collected and recrystallized from acetone, giving 0.4 g. of 3-isoquinolinecarboxylic acid-2-oxide, m.p. 211–211.5° dec., mixed melting point with product described above the same.

3-Isoquinolinecarboxamide. To 17.5 g. (0.093 mole) of 3-isoquinolinecarboxylic acid-2-oxide suspended in 150 ml. of chloroform, 26 ml. (*ca.* 0.3 mole) of phosphorus trichloride was added, and the mixture was heated for one hour under reflux on the steam bath (protected from moisture). The solid did not appear to dissolve, but did change in appearance. The solid was filtered off and added quickly to 200 ml. of concentrated ammonium hydroxide containing some crushed ice. A vigorous reaction took place and a pale cream colored solid deposited, which was collected by filtration and recrystallized (without drying) from dilute methanol, giving 6.0 g. (38%) of 3-isoquinolinecarboxamide, melting point and mixed melting point with an authentic sample² 212–213° (lit.² m.p. 213°).

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(8) Fractional distillation of the residue under reduced pressure in other experiments gave 9–13 g. (25–37%, based on 3-methylisoquinoline consumed in the reaction) of 3-isoquinolinecarboxaldehyde, b.p. 140–160° (10 mm.), m.p. 48.5–50.5° (lit.² m.p. 47°).

(9) This quantity of hot water will dissolve at least 25 g. of 3-isoquinolinecarboxylic acid.

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Rates of Reaction of *m*- and *p*-Substituted-1,2-Epoxyethylbenzenes with Thiosulfate in Aqueous Ethanol

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The observation¹ that β -halogen and other electron-withdrawing groups increase the rates of reaction of 1,2-epoxyalkanes with thiosulfate is in marked contrast to the effect of β -halogen in displacement reactions on haloalkanes by thiosulfate² and thiophenolate,³ although alkyl substituents decrease the rates of both epoxides and halides.

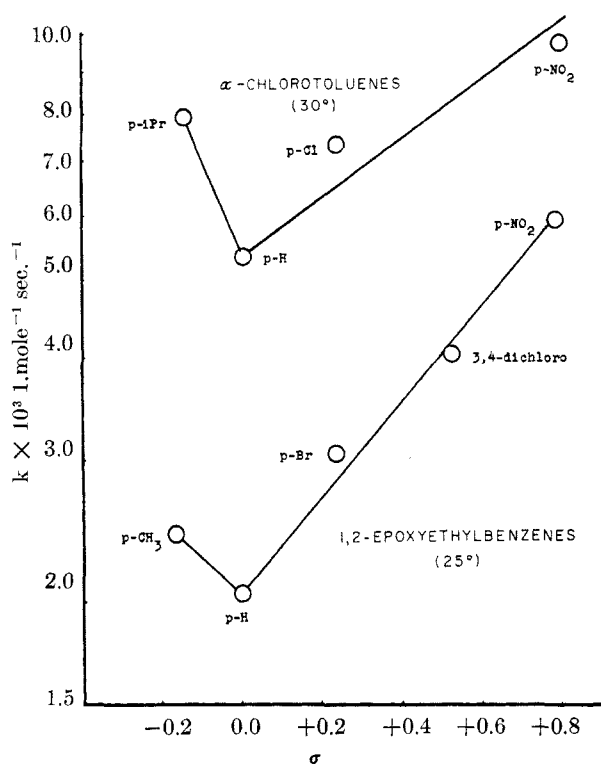


Fig. 1. Rates of reaction of 1,2-epoxyethylbenzenes and of α -chlorotoluenes with thiosulfate in 60% ethanol-40% water.

It was, therefore, of interest to compare the effect of substituents on rates of reaction of 1,2-epoxyethylbenzenes with that of *m*- and *p*-substituted- α -chlorotoluenes, in which substituents act predominantly by electronic effects. It has been generally observed that both electron-withdrawing and electron-donating substituents increase the rate of reaction of α -chlorotoluenes with anions such iodide in

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acetone,⁴ bromide in glycol diacetate,⁵ alkoxides,^{6,7} hydroxide in aqueous ethanol,⁶ and thiosulfate in various solvents.⁸ Comparison of the substituted 1,2-epoxyethylbenzenes with α -chlorotoluenes may raise the objection that attack by a nucleophile with a large steric requirement, such as thiosulfate, may take place considerably or even predominantly at the primary carbon atom of the epoxide ring.⁹ However, the rates of reaction of (2-chloroethyl)benzene¹⁰ and of α -chlorotoluene are similarly affected by substituents.

The rates of reaction of 4-methyl-, unsubstituted, 4-bromo, 3,4-dichloro-, and 4-nitro(1,2-epoxyethyl)benzene with sodium thiosulfate in 60% ethanol-40% water at 25° have now been measured, by titration of the base liberated as a result of ring opening (Table I). The rates parallel those of the α -chlorotoluenes,⁸ and are of the same magnitude if the temperature difference is taken into account.

TABLE I

RATES OF REACTION OF 3- AND 4-SUBSTITUTED (1,2-EPOXYETHYL)BENZENES WITH THIOSULFATE IN 60% ETHANOL-40% WATER AT 25°

Y =	$k \times 10^3 \text{ l. Mole}^{-1} \text{ Sec.}^{-1}$		Average
4-Methyl	2.40 (2.68) (2.03)	2.40 (2.73) (2.03)	2.40 (2.71) ^b (2.03) ^c
4-Hydrogen	2.00	2.08	2.04
4-Bromo	3.06	3.07	3.07
3,4-Dichloro	4.27	4.10	4.19
4-Nitro	5.93	5.95	5.94

^a (Oxide) = 0.033M, ($\text{S}_2\text{O}_3^{2-}$) = 0.05M. ^b ($\text{S}_2\text{O}_3^{2-}$) = 0.025M. ^c ($\text{S}_2\text{O}_3^{2-}$) = 0.025M, (NaNO_2) = 0.087 molal; ionic strength of this solution equals that of 0.05M $\text{S}_2\text{O}_3^{2-}$.

The procedure used was essentially that of Ross,¹ but the base was titrated continuously with 1M

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acetic acid using a Beckman Model K automatic titrator, which added increments of approximately 0.02 ml. of acid. The reference end point was slightly more basic than the ethanolic thiosulfate solution, but insufficiently basic to change the color of phenolphthalein. Although the solution was thus maintained faintly basic, the hydroxide ion concentration was too low to cause any appreciable amount of the competing reaction of glycol formation.

Consistent second-order rate constants were obtained over at least 60–65% completion. The specific rate of the 4-methyl compound depends on the thiosulfate concentration. Reduction of the thiosulfate concentration by one-half increases the rate constant slightly, which is consistent with the expected ionic strength effect. If the ionic strength of the diluted thiosulfate is brought up to the original value by the addition of sodium nitrate, the rate constant is decreased to slightly below the original value.

EXPERIMENTAL

Materials. The preparation of the epoxides has been previously described.¹¹ Each compound was redistilled before use. Commercial absolute ethanol was used directly to make the 60% ethanol-40% water (by volume) solvent mixture.

Rate measurements. A 100-ml. portion of 0.075M thiosulfate solution in 60% ethanol was pipetted into a 400-ml. beaker, brought to 25.0° and maintained at $25.0 \pm 0.3^\circ$ throughout the run. After adjusting the reference pH, a sample containing 0.005 mole of the epoxide in 50 ml. of solvent at 25° was added (time = 0). The volume of 1.09N acetic acid added from a microburet was periodically recorded. The amount of acid was in the range of 1.3–2.7 ml. at 60–65% completion, and this small dilution was neglected in subsequent calculations. Second-order rate constants were calculated from the equation $k = \frac{2.303}{t(a-b)}$

$\log \frac{b(a-x)}{a(b-x)}$. The results of a typical run are shown in Table II.

TABLE II

RATE OF REACTION OF 4-BROMO(1,2-EPOXYETHYL)BENZENE WITH THIOSULFATE IN 60% ETHANOL-40% WATER AT 25°

Elapsed Time, Sec.	Vol. 1.09N Acid, ml.	(RCI) ^a	$k \times 10^3 \text{ l. Mole}^{-1} \text{ Sec.}^{-1}$
0	0.000	0.0333	
720	0.451	0.0300	3.02
1260	0.764	0.0277	3.00
1980	1.120	0.0251	3.03
2940	1.550	0.0220	3.12
3900	1.885	0.0196	3.10
5220	2.251	0.0169	3.08
6960	2.621	0.0142	3.05
			Av. 3.06 \pm 0.04 ^b

^a Initial ($\text{S}_2\text{O}_3^{2-}$) 0.0518. Concentrations in mole l.⁻¹

^b Average deviation.

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