

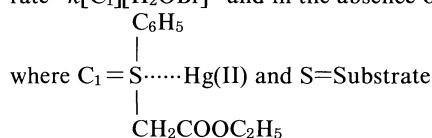
Kinetics and Mechanism of Oxidation of Ethyl Phenylthioacetates by Bromamine-B

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The kinetics of oxidation of several substituted ethyl phenylthioacetates by bromamine-B (sodium salt of *N*-bromobenzenesulfonamide) has been studied in 50% (v/v) aqueous ethanol medium. Disodium hydrogenphosphate and sodium dihydrogenphosphate buffer has been used. The reaction is of a total second order, first order each with respect to the reactants. A catalytic effect of mercury has been observed and the order with respect to Hg(II) is one. Electron-releasing substituents generally accelerate the rate while electron-withdrawing groups retard the rate. A good correlation is found to exist between $\log k_2$ and Hammett σ constants. Two mechanisms have been proposed, one in presence of Hg(II) and the other in the absence of Hg(II). In presence of Hg(II), $\text{rate} = k[C_1][H_2OBr]^+$ and in the absence of Hg(II), $\text{rate} = k[S][H_2OBr]^+$



Susceptibility of the reaction to the steric effect of ortho substituents, has been analyzed in the light of application of Taft's steric energy relationships.

During the investigation into the reactions of insulated systems (containing groups or atoms between the reaction site and bulk of the molecule), we have reported^{1–6)} the preparation of a number of meta, para, and ortho-substituted phenoxyacetic, phenylthioacetic and phenylsulfonylacetic acids and their ethyl esters. Kinetics of esterification, ester hydrolysis, and oxidation with Mn(VII) and Ce(IV) were described (i) to test the applicability of LFER to these reactions, (ii) to seek evidence for the expansion of valency shells of chlorine, bromine and iodine, (iii) to study the effect of substituents and (iv) to compare the difference in the behavior of the insulated groups viz., –O–, –S–, and –SO₂– under similar conditions of the reactions.

Correlation analysis of the rate data of these reactions of ortho-substituted derivatives was also sought in the light of free energy–steric energy relationships.

Study of interaction of the above insulated systems with *N*-halo compounds is rare. Hence it was thought of interest to follow the kinetics of some substituted ethyl phenylthioacetates by bromamine-B (sodium salt of *N*-bromobenzenesulfonamide, BAB) to calculate the composition of localized, delocalized, and steric components operating in this reaction.

Oxidation studies of a few phenylthioacetic acids by potassium peroxodisulfate,⁷⁾ chloramine-T,⁸⁾ Ce(IV),⁹⁾ peroxodiphosphate,¹⁰⁾ and peroxomonophosphoric acid¹¹⁾ have already been reported in the literature.

Results and Discussion

The first-order dependence of the reaction on BAB is obvious from the linearity of the plot of $\log [\text{BAB}]$ vs. time. The second order rate constants at different $[\text{substrate}]$ and $[\text{BAB}]$ are listed in Table I. The plot of $\log k_{\text{obsd}}$ vs. $\log [\text{substrate}]$ is linear with a slope of unity

(Fig. 1). This shows that the reaction is first-order with respect to substrate. Addition of benzenesulfonamide, one of the products, retards the rate of the reaction considerably.

Mercury(II) acetate introduced to trap the bromide ion, catalyzes the reaction (Table I). Further investigation showed that Hg(II) formed intermediate (C_1) with the substrate and the order with respect to Hg(II) was found to be unity. The formation of the intermediate

Table I. Pseudo First-Order and Second-Order Rate Constants for the Oxidation of Ethyl Phenylthioacetate with BAB in 50% (v/v) Aqueous Ethanol at 30 °C^{a)}

[substrate]	[BAB]	[Hg(II)]	pH	k_{obsd}	k_2
10 ^{–2} M	10 ^{–4} M	10 ^{–4} M		10 ^{–4} s ^{–1}	10 ^{–2} M ^{–1} s ^{–1}
1.00	10.00	—	6.51	1.99	1.99
1.50	10.00	—	6.51	3.01	2.01
2.00	10.00	—	6.51	4.17	2.09
3.00	10.00	—	6.51	6.11	2.04
4.00	10.00	—	6.51	8.45	2.11
2.00	5.00	—	6.51	4.56	2.28
2.00	7.50	—	6.51	4.41	2.20
2.00	10.00	—	6.51	4.18	2.09
2.00	12.50	—	6.51	4.03	2.02
2.00	10.00	1.00	6.51	5.64	2.82
2.00	10.00	2.00	6.51	8.24	4.12
2.00	10.00	3.00	6.51	15.54	7.77
2.00	10.00	4.00	6.51	20.06	10.03
2.00	10.00	5.00	6.51	25.85	12.92
2.00	10.00	—	5.96	4.66	2.33
2.00	10.00	—	6.27	4.47	2.24
2.00	10.00	—	6.51	4.18	2.09
2.00	10.00	—	7.23	3.68	1.84
2.00	10.00	—	7.54	3.24	1.62

M = mol dm^{–3}.

(C₁) has been well established by previous workers in a similar kinetic study. Hence it was thought, the necessity of identifying and isolating such an intermediate is not warranted.

As pH decreases the rate increases showing that H⁺ ion accelerates the rate of the reaction (Table 1). The

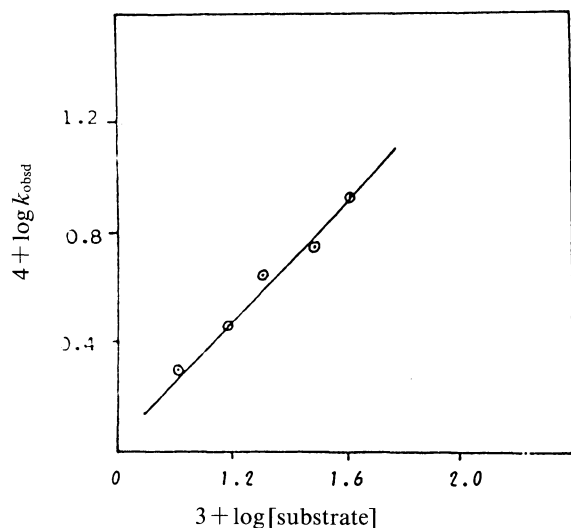


Fig. 1. Plot of $3 + \log [\text{substrate}]$ vs. $4 + \log k_{\text{obsd}}$. Correlation coefficient (r)=0.999; Slope=1.037, [Substrate]=0.01 M to 0.04 M, [Oxidant]=0.001 M. Solvent=50% aqueous ethanol (v/v), pH=6.51, Buffer=Sodium dihydrogenphosphate-Disodium hydrogenphosphate buffer.

Table 2. Effect of Solvent Composition and Ionic Strength on Reaction Rate

Ethanol-water (v/v)%	$10^4 k_{\text{obsd}}$	Ionic strength $\times 10^2$	$10^4 k_{\text{obsd}}$
70-30	1.92	1	5.64
60-40	3.05	2	8.17
50-50	4.18	3	9.60
40-60	5.34	4	17.19
30-70	7.96	5	19.94

[substrate]: 2×10^{-2} M, [BAB]: 1×10^{-3} M, pH: 6.51.

order with respect to H⁺ is fractional (0.1).

The rate data at different solvent compositions (Table 2) showed that the reaction is facilitated by an increase in the polarity and/or nucleophilicity of the medium, suggesting a polar rate limiting transition state. The reaction shows a positive salt effect as evident from the rate constants (Table 2) at different ionic strength (maintained by adding NaClO₄).

The rate constants for the oxidation of substituted ethyl phenylthioacetates by BAB at different temperatures and the activation parameters computed from the slope and intercept of Eyring's plot¹³) are listed in Table 3. The negative entropy of activation ($\Delta S^\ddagger$) values indicate that the rate determining transition state is less disorderly relative to the reactants. The data in Table 3 reveal that the electron-releasing substituents enhance the rate while electron-withdrawing substituents retard it.

The plot of $\log k_2$ (30 °C) vs. σ (Hammett's substituent

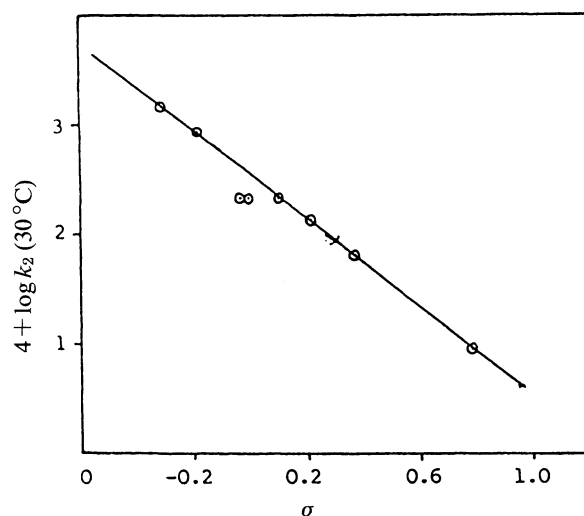


Fig. 2. Plot of σ (Hammett constants) vs. $4 + \log k_2$ (30 °C). Correlation coefficient (r)=0.918, Reaction constant=-1.754, [Substrate]=0.02 M, [Oxidant]=0.001 M. Solvent=50% aqueous ethanol (v/v), pH=6.51, Buffer=Sodium dihydrogenphosphate-Disodium hydrogenphosphate buffer.

Table 3. Second-Order Rate Constants and Activation Parameters for the Oxidation of para- and meta-Substituted Ethyl Phenylthioacetates^{a)}

No.	Substituent	$10^4 k_2 / \text{M}^{-1} \text{s}^{-1}$					$\Delta H^\ddagger$	$-\Delta S^\ddagger$
		25 °C	30 °C	35 °C	40 °C	45 °C	kJ mol ⁻¹	J K ⁻¹ mol ⁻¹
1.	-H	123.79	208.83	249.34	301.61	395.49	40.0	147.6
2.	<i>p</i> -OCH ₃	913.51	1384.59	1722.00	1910.50	2127.95	29.4	166.6
3.	<i>p</i> -CH ₃	551.80	793.76	1116.79	1773.70	2804.33	61.3	64.4
4.	<i>p</i> -Cl	93.46	139.35	197.35	242.65	254.46	38.0	156.8
5.	<i>p</i> -NO ₂	6.76	9.33	15.91	32.31	38.32	66.5	83.6
6.	<i>m</i> -OCH ₃	143.46	234.24	329.75	356.81	411.18	37.5	154.4
7.	<i>m</i> -CH ₃	135.07	209.97	274.01	310.13	397.92	37.8	154.4
8.	<i>m</i> -Cl	42.13	70.24	94.69	115.80	125.05	39.9	156.7
9.	<i>m</i> -Br	37.43	68.06	92.43	93.30	105.52	35.9	170.5

a) Solvent=ethanol-water 50% (v/v), pH 6.51, [sub]= 2×10^{-2} M, [oxi]= 1×10^{-3} M.

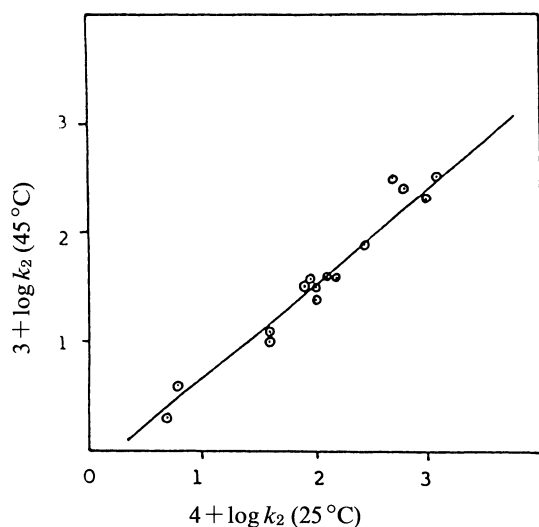


Fig. 3. Plot of $4 + \log k_2$ (25 °C) vs. $3 + \log k_2$ (45 °C). Correlation coefficient (r) = 0.989, [Substrate] = 0.02 M, [Oxidant] = 0.001 M, Solvent = 50% aqueous ethanol (v/v), pH = 6.51, Buffer = Sodium dihydrogenphosphate–Disodium hydrogenphosphate buffer.

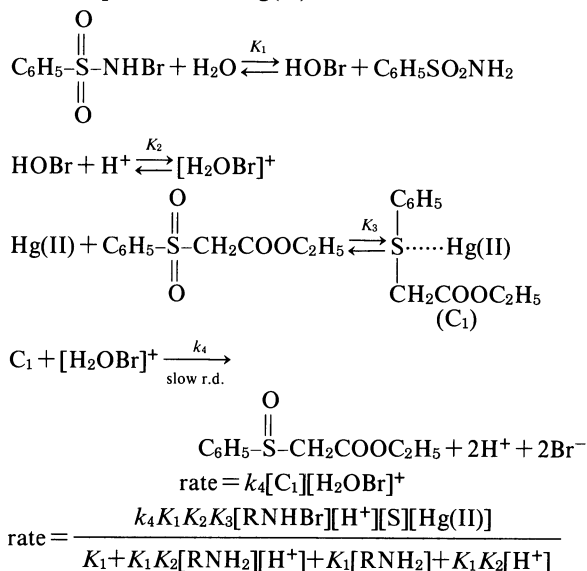
constants) is linear (correlation coefficient $r = 0.918$) affording a (reaction constant) value of -1.754 (Fig. 2), in consonance with the proposed mechanism.

The reaction series generally obey the isokinetic relationship as shown by a typical linearity of the plot of $\log k_2$ (25 °C) vs. $\log k_2$ (45 °C)¹⁴ (Fig. 3). Such a correlation indicates that all the esters undergo oxidation through the same mechanism.¹⁵ The plot of $\Delta S^\ddagger$ and $\Delta H^\ddagger$ gives a straight line (correlation coefficient $r = 0.957$) and from the slope, the isokinetic temperature is found to be 294.1 K.

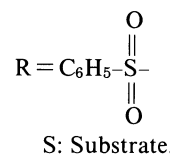
Mechanism and Rate Law

From the above observations, two probable mechanisms have been proposed, in the presence and in the absence of Hg(II).

1. In the presence of Hg(II).

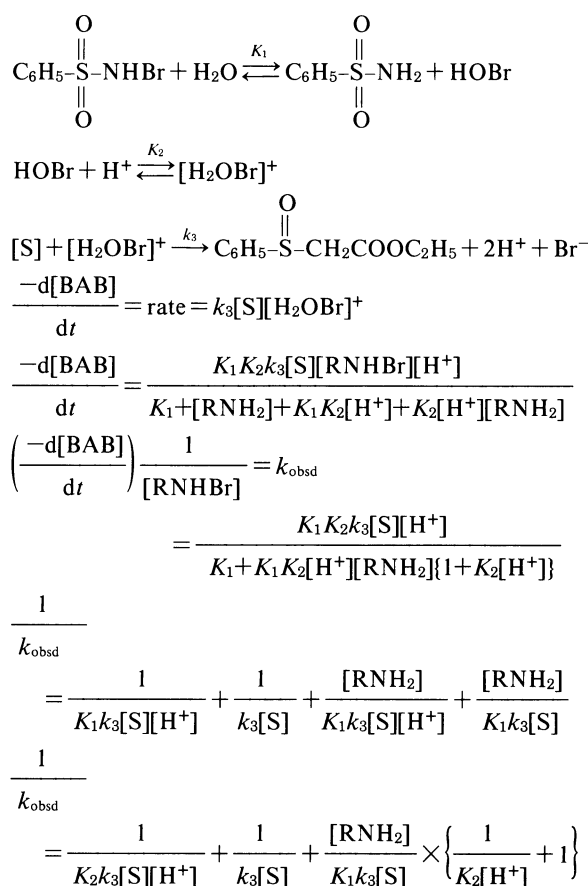


$$\begin{aligned}
 \left(\frac{-d[\text{BAB}]}{dt} \right) \frac{1}{[\text{RNHBr}]} &= k_{\text{obsd}} \\
 &= \frac{k_4 K_1 K_2 K_3 [\text{H}^+][\text{S}][\text{Hg(II)}]}{K_1 + K_1 K_2 [\text{RNH}_2][\text{H}^+] + K_1 [\text{RNH}_2] + K_1 K_2 [\text{H}^+]}
 \end{aligned}$$



The occurrence of [S] and [RNHBr] in the numerator of the rate expression is clearly supported by the observed fact that the overall reaction is first order each in [BAB] and [Ester]

2. In the absence of Hg(II).



The rate law and the proposed mechanism find support from the dependence of rate on solvent polarity, negative entropy of activation, and the negative (reaction constant) value of the reaction.

The kinetic data and the activation parameters of a few ortho-substituted compounds are given in Table 4.

Regression analysis of the data has been carried out with Taft's¹⁶ linear free energy–polar energy relationship (Eqs. 1 and 3) and linear free energy–steric energy relationship (Eqs. 2 and 4).

$$\log k_{(\text{ortho})} = \sigma_o^* \rho_o^* + h \quad (1)$$

$$\log k_{(\text{ortho})} = \delta E_s + h \quad (2)$$

In the above equations σ_o^* (polar) and E_s (steric) are

Table 4. Ortho Effect-Separation of Polar and Steric Effects

No.	Substituent	$10^4 k_2 / \text{M}^{-1} \text{s}^{-1}$					$\Delta H^\ddagger$	$-\Delta S^\ddagger$
		25 °C	30 °C	35 °C	40 °C	45 °C	kJ mol^{-1}	$\text{J K}^{-1} \text{mol}^{-1}$
1.	<i>o</i> -OCH ₃	1194.69	1626.20	2166.30	2652.50	2863.26	32.9	153.0
2.	<i>o</i> -CH ₃	675.80	863.20	1175.70	1649.30	2361.46	47.0	110.9
3.	<i>o</i> -F	173.86	255.61	373.83	522.55	712.43	53.2	100.7
4.	<i>o</i> -Cl	90.62	139.53	193.72	258.36	307.29	45.8	130.9
5.	<i>o</i> -Br	86.34	130.21	194.47	265.14	339.18	51.9	110.9
6.	<i>o</i> -NO ₂	4.66	9.17	14.36	20.15	21.30	58.1	113.3

substituent constants, ρ^* is a reaction constant analogous to ρ and is a susceptibility constant.

At 35 °C

$$\log k_{(\text{ortho})} = -1.83 \sigma_o^* - 0.96 \quad (3)$$

$$(r=0.99, \text{SD}=0.16, n=6)$$

r =correlation coefficient, SD=standard deviation, n =number of data points.

$$\log k_{(\text{ortho})} = -0.6077 E_s - 1.23 \quad (4)$$

$$(r=0.3082, \text{SD}=0.81, n=6).$$

To understand the composition of localized (L), delocalized (D), and steric (S) components operating in these reactions the rate data are analyzed with LD and LDS Eqs. 5 and 6.^{17,18)}

$$\log k_{(\text{ortho})} = L\sigma_1 + D\sigma_R + h \quad (5)$$

$$\log k_{(\text{ortho})} = L\sigma_1 + D\sigma_R + S\gamma + h \quad (6)$$

Where σ_1 , σ_R , and γ are inductive, resonance, and steric substituent constants respectively. The γ scale has been developed by Aslam et al.¹⁹⁾

Following are the results of correlation at 35 °C.

$$\log k_{(\text{ortho})} = L\sigma_1 + D\sigma_R + h$$

$$\log k_{(\text{ortho})} = -1.7894 \sigma_1 - 2.2257 \sigma_R - 1.4504$$

$$(\pm 1.7810 \times 10^{-1}) (\pm 1.9292 \times 10^{-1})$$

(Unsubstituted compound included; NO₂ group planar)

$$\log k_{(\text{ortho})} = -2.0529 \sigma_1 - 2.0320 \sigma_R - 1.2652$$

$$(\pm 4.269 \times 10^{-2}) (\pm 4.152 \times 10^{-2})$$

$$(R=0.999, n=6, \text{SE}=0.0128, \text{CL}=99\%)$$

(Unsubstituted compound excluded; NO₂ group planar)

$$\log k_{(\text{ortho})} = -1.9966 \sigma_1 - 2.4635 \sigma_R - 1.4688$$

$$(\pm 1.8218 \times 10^{-1}) (\pm 2.1549 \times 10^{-1})$$

$$(R=0.990, n=6, \text{SE}=0.0581, \text{CL}=99\%)$$

(Unsubstituted compound included; NO₂ group orthogonal)

$$\log k_{(\text{ortho})} = -2.2166 \sigma_1 - 2.2628 \sigma_R - 1.2992$$

$$(\pm 1.2641 \times 10^{-1}) (\pm 1.3942 \times 10^{-1})$$

$$(R=0.997, n=6, \text{SE}=0.038, \text{CL}=99\%)$$

(Unsubstituted compound excluded; NO₂ group orthogonal)

$$\log k_{(\text{ortho})} = L\sigma_1 + D\sigma_R + S\gamma + h \quad (6)$$

$$\log k_{(\text{ortho})} = -2.0860 \sigma_1 - 2.1198 \sigma_R - 6.5138 \times 10^{-2} \gamma - 1.3162$$

$$(\pm 5.55781 \times 10^{-2}) (\pm 1.021 \times 10^{-1}) (\pm 6.898 \times 10^{-2})$$

$$(R=0.999, n=6, \text{SE}=0.016, \text{CL}=99\%)$$

(Unsubstituted compound included; NO₂ group planar)

$$\log k_{(\text{ortho})} = -2.1359 \sigma_1 - 2.3615 \sigma_R - 3.7522 \times 10^{-1} \gamma - 1.5291$$

$$(\pm 6.24 \times 10^{-2}) (\pm 6.996 \times 10^{-2}) (\pm 1.073 \times 10^{-1})$$

$$(R=0.999, n=6, \text{SE}=0.2152, \text{CL}=99\%)$$

(Unsubstituted compound included; NO₂ group orthogonal)

Furthermore, correlations obtained with LD and LDS equations are justified by F-test significance (95% in CL in many cases). For the oxidation of ortho-substituted ethyl phenylthioacetates, either by including the unsubstituted ester or by considering the NO₂ group (either planar or orthogonal) the conclusion remains the same.

The better description of the composition of the electrical effect is given by the percent localized factor P_L where

$$P_L = \frac{L \times 100}{L + D}$$

The P_L values are 44.57 and 50.26 for including and excluding the unsubstituted compound, when the NO₂ group is planar and the corresponding values are 54.5 and 49.5, if the NO₂ group is considered orthogonal. These values show that the orientation of NO₂ group is orthogonal, and such an orientation in space does not affect the reaction rate. In the LDS equation, L , D , S and h terms are significant of 85, 85, 40, and 75% CL of t -test respectively, if the NO₂ group is planar. But they are significant of 90, 90, 20, and 80% CL of t -tests respectively, if the NO₂ group is orthogonal. These results also clearly demonstrate the operation of significant localized effect, thus dissuading the contribution of delocalized and steric effects.

A better description of the composition of the electrical effect and steric effect is given by the 'percent steric factor', P_s where

$$P_s = \frac{S \times 100}{L + D + S}$$

The P_s values are 1.57 and 9.10 when the NO₂ group is planar and orthogonal respectively.

A plot of $\log k_{(\text{ortho})}$ (observed) vs. $\log k_{(\text{ortho})}$ (calculated) gave a good correlation.

The following conclusions emerge from the foregoing analysis

i. the localized effect is a major component in many cases.

ii. steric effect plays a minor role.

iii. the negative signs of electronic effect terms viz. I and R indicate that the reaction is accelerated by electron-releasing substituents.

Experimental

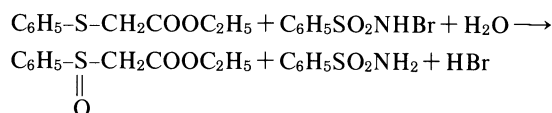
Reagents: Bromamine-B was prepared from benzenesulfonamide, bromine, and aqueous sodium hydroxide by the standard procedure.²⁰ Ethyl esters of phenylthioacetic acids were prepared by refluxing the acids with ethanol in the presence of sulfuric acid for 2 h followed by neutralization with sodium carbonate and ether extraction. The phenylthioacetic acids were prepared by the method of Gabriel.²¹

A modified procedure was adopted for obtaining *p*-nitrophenylthioacetic acid from chloronitrobenzene and thio glycollic acid.

Kinetic Measurements: The kinetic studies were carried out in 50% (v/v) aqueous ethanol medium under pseudo first-order conditions with ethyl phenylthioacetate and bromamine-B in the ratio, 20 : 1. The rate of the reaction was followed by estimating the unreacted bromamine-B, iodometrically up to 70% of the reaction. The pH was maintained from 6.51 to 9.5 with a phosphate buffer.

Stoichiometry: The stoichiometry of the reaction was determined by carrying out several sets of experiments with varying amounts of [BAB] largely in excess over [substrate]. The estimation of unreacted [BAB] showed that one mole of each ester reacts with one mole of BAB.

Product Analysis: Analysis by Co-TLC showed that sulfoxides were the products formed in the reaction, leading to the following stoichiometric equation.



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