# KINETICS AND MECHANISM OF THE INTERACTION OF AMINES WITH ARYL β-HALOETHYL SULPHONES

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The influence of a number of factors, i.e. amine basicity, substrate structure, temperature and deuterium isotope effect, on the rate of phenyl  $\beta$ -bromoethyl sulphone and aryl  $\beta$ -chloroethyl sulphone 1,2-elimination by reaction with amines in acetonitrile was investigated. On the basis of a comparative analysis of the  $\rho^0$ ,  $\beta$ ,  $k_{\rm H}/k_{\rm D}$ ,  $\Delta {\rm H}^{\ddagger}$  and  $\Delta S_{15}^{\ddagger}$ values obtained with those for the reaction of  $\beta$ -halopropiophenone 1,2-elimination, the conclusion was drawn that the E2 mechanism with an anion-like transition state occurs for the given substrates under the conditions studied.

# INTRODUCTION

Current views on 1,2-elimination reactions induced by bases to yield alkenes involve consideration of two alternative reaction mechanisms, i.e. concerted E2 and stepwise E1cB mechanisms (Scheme 1).<sup>1-10</sup>

The concerted E2 mechanism is usually realized for non-activated compounds (Z = H, Alk, Ar).<sup>1a,3</sup> In the case of electron-withdrawing substituents Z the stability of the carbanion 3 increases and the reaction may proceed via a stepwise E1cB mechanism. 1b,c,4-9

Application of the steady-state hypothesis to the stepwise E1cB process gives the following expression for the observed first-order rate constant:

$$k_{\rm obs} = k_1 k_2 [\mathbf{B}] / (k_{-1} [\mathbf{BH}^+] + k_2)$$
(1)

In the framework of the E1cB mechanism, two limiting cases are possible:

(i) when  $k_2 \gg k_{-1}[BH^+]$ , the irreversible formation

of carbanion 3 takes place and the reaction rate is determined by the proton abstraction step, i.e.  $k_{obs} = k_1$ ,  $(E1cB)_{I}$  mechanism;

(ii) when  $k_2 \ll k_{-1}[BH^+]$ , the reversible formation of carbanion 3 occurs and the reaction rate is limited by the leaving group expulsion step, i.e.  $k_{obs} = k_1 k_2 [B]/k_{-1} [BH^+]$ ,  $(E1cB)_R$  mechanism.<sup>4-7</sup>

The above applies to steady-state conditions. When  $k_1 \ge k_{-1}, k_2$  the carbanion 3 is generated in a concentration greater than the steady-state concentration and an E1cB anionic mechanism is realized.<sup>4</sup>

In some cases the reaction intermediate exists in the form of an ion pair of type 4,  $(E1cB)_{ip}$  mechanism.<sup>8,9</sup>



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Received 25 May 1993 Revised 27 April 1994 It should be noted that the presence of an electronwithdrawing substituent by itself in molecule 1 does not guarantee that the reaction proceeds through the E1cBmechanism. The lifetime of the carbanion intermediate is also very important.<sup>3a,6b</sup> For example, if X is a good leaving group, the reaction can also proceed through the E2 mechanism.<sup>5,7e</sup>

It was shown earlier<sup>10</sup> that the interaction of  $\beta$ -halopropiophenones (5, X = Cl, Br, I) with amines resulting in aryl vinyl ketones (6) proceeds through the E2 mechanism via an anion-like transition state:

ArCOCH<sub>2</sub>CH<sub>2</sub>X + R<sup>1</sup>R<sup>2</sup>R<sup>3</sup>N 
$$\rightarrow$$
  
5  
ArCOCH=CH<sub>2</sub> + R<sup>1</sup>R<sup>2</sup>R<sup>3</sup>N<sup>+</sup>H + X<sup>-</sup> (2)

When proton-containing amines are used, the subsequent reaction of amine addition to an aryl vinyl ketone proceeds, resulting in  $\beta$ -aminopropiophenones.<sup>11</sup>

It is known<sup>5,12</sup> that the interaction of aryl  $\beta$ haloethyl sulphones (7) with tertiary amines results in the formation of aryl vinyl sulphones (8) [equation (3)]. Aryl vinyl sulphones, similarly to aryl vinyl ketones, may interact with proton-containing amines giving aryl  $\beta$ -aminoethyl sulphones (9) [equation (4)].

ArSO<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>X + R<sup>1</sup>R<sup>2</sup>R<sup>3</sup>N 
$$\rightarrow$$
  
(7)  
ArSO<sub>2</sub>CH=CH<sub>2</sub> + R<sup>1</sup>R<sup>2</sup>R<sup>3</sup>N<sup>+</sup>HX<sup>-</sup> (3)  
(8)  
ArSO<sub>2</sub>CH=CH<sub>2</sub> + R<sup>1</sup>R<sup>2</sup>NH  $\rightarrow$   
(8)

$$ArSO_2CH_2CH_2NR^{1}R^{2} \quad (4)$$

The mechanism of the addition of proton-containing amines to aryl vinyl sulphones [equation (4)] has been reported in literature and discussed by several workers.<sup>13</sup> Aryl vinyl sulphone formation reactions with 1,2-elimination of aryl  $\beta$ -X-ethyl sulphones were investigated under the action of a number of charged bases, e.g. MeO<sup>-</sup>, <sup>5a,7a</sup> EtO<sup>-</sup>, <sup>7</sup> *t*-BuO<sup>-</sup> and PhO<sup>-</sup>.<sup>14</sup> From neutral bases only the tertiary amines were studied, <sup>5,9</sup> probably owing to experimental difficulties and the intention to simplify the process concerned. The kinetic, stereochemical and other data show that a variety of mechanisms [*E*2, (*E*1*cB*)<sub>R</sub>, (*E*1*cB*)<sub>ip</sub>, (*E*1*cB*)<sub>1</sub>] can be realized in the 1,2-elimination reaction of sulphonyl-activated ethanes depending on the nature of the leaving group base, solvent and other factors. <sup>5,7,9</sup>

The aim of this work was to investigate the kinetic relationships and the mechanism of aryl vinyl sulphone formation in the reaction of aryl  $\beta$ -haloethyl sulphones with the several groups (primary, secondary, tertiary) of amines and to compare the data obtained with those

for the previously studied reaction of  $\beta$ -halopropiophenones with amines [equation (2)].

# **RESULTS AND DISCUSSION**

## Kinetics

Reaction (3) of aryl  $\beta$ -haloethyl sulphones (7, X = Cl, Br) with amines was studied in acetonitrile with the amine in large excess. In all cases the rate of reaction (3) was described by a second-order (first order in each of the reactants) rate equation, which was testified by the invariability of the observed rate constants ( $k_{obs}$ ,  $s^{-1}$ ) in the course of the reaction (Table 1) and by the linear dependence of  $k_{obs}$  on the amine concentration (Figure 1).

#### **Deuterium isotope effect**

We studied the elimination of HBr and DBr from phenyl  $\beta$ -bromoethyl sulphone and its  $\alpha, \alpha$ -dideuterated analogue (Table 2). The observed deuterium isotope effect,  $k_{\rm H}/k_{\rm D} = 3 \cdot 2 - 4 \cdot 3$ , shows a slight dependence on the amine's  $pK_{\rm a}$  (in the range  $12 \cdot 33 - 18 \cdot 75$ ). The values of this effect are lower than the maximum possible and the largest value (for isobutylamine) is lower than that for the reaction of  $\beta$ -halobpropiophenones  $(k_{\rm H}/k_{\rm D} = 7 - 10^{10c})$ . Nevertheless, the effect can be identified as a primary kinetic isotope effect (cleavage of the  $C_{\alpha}$ —H bond in the rate-limiting step).

This can be possible when a reaction proceeds through an E2 or  $(E1cB)_I$  mechanism  $(k_1$  is the ratelimiting step in Scheme 1). However, a large 'element effect' (see below) in the transition from X = Br to X = CI rules out the possibility of the reaction proceeding through the  $(E1cB)_I$  mechanism.

The calculated values for  $k_{\rm H}/k_{\rm D}$  include also a secondary deuterium isotope effect, since we used  $\alpha, \alpha$ dideutero derivatives. In the reaction of diastereomeric phenyl  $\beta$ -fluoro- $\beta$ -phenylthio- $\alpha$ -deuteroethyl sulphones (10) having a similar structure with triethylamine in benzene (50 °C), for which the  $(E1cB)_{\rm ip}$  mechanism has been postulated, <sup>9</sup> an inverse thermodynamic deuterium isotope effect,  $k_{\rm H}/k_{\rm D} = 0.8$ , is observed in the case of sulphone 10a (syn-elimination of DF); for sulphone 10b (syn-elimination of HF) the secondary deuterium isotope effect was  $k_{\rm H}/k_{\rm D} = 1.1$ .<sup>9</sup>



Reaction	Reaction	R	Conversion	$k_{obs} \times 10^3$	$k \times 10^3$ (1 mol <sup>-1</sup> s <sup>-1</sup> )
	(3)		(,v)		(11101 3 )
$PhSO_2CH_2CH_2Cl + PhCH_2NH_2, 25 °C,$	0	220			
$[PhCH_2NH_2] = 0.207 \text{ mol } 1^{-1}$	25	200	1.5	0.609	2.94
	76	170	4.4	0.596	2.88
	120	150	7.0	0.609	2.94
	222	120	12.5	0.604	2.92
	330	100	18.1	0.604	2.92
	407	90	21.7	0.604	2.92
	507	80	26.4	0.604	2.92
	648	70	32.3	0.602	2.91
	856	60	40.3	0.600	2.90
	1200	50	51.2	0.600	2.90
	1890	40	67.8	0.600	2.90
		28.8			
				A	Av.: $2 \cdot 92 \pm 0 \cdot 02$
$PhSO_2CH_2CH_2Br + Et_3N, 35 \degree C,$	0	300			
$[Et_3N] = 0.093 \text{ mol } 1^{-1}$	7.5	200	11.9	0.0168	0.181
	16	150	23.7	0.0169	0.182
	22	130	31.0	0.0169	0.181
	38	100	47.4	0.0169	0.182
	49	90	55.3	0.0164	0.177
	65	80	65.2	0.0162	0.175
	77	75	71 · 1	0.0161	0.174
	93	70	77.9	0.0162	0.175
	121	65	85.7	0.0160	0.173
	185	60	94.8	0.0160	0.172
		57.5			
				Av	$0.177 \pm 0.003$





Figure 1. Plot of  $k_{obs}$  versus amine concentration for the reaction between phenyl  $\beta$ -chloroethyl sulphone and triethylamine in acetonitrile at 25 °C

Therefore, we rule out the possibility of an  $(E1cB)_R$ mechanism and the observed values of  $k_H/k_D$  as a result of the high values of both the thermodynamic and secondary isotope effects in the reaction. Such an assumption also contradicts to the fact that H–D exchange does not occur when proton-containing amines are used.

It has also been noted that for an  $(E1cB)_R$ mechanism the accumulation of ammonium salt during the reaction should decrease  $k_{obs}$  with time, since  $k_{obs} = k_1k_2[B]/k_{-1}[BH^+]$ ; however, we failed to observe this (Table 1).

#### 'Element effects'

In all cases, the change from Br to Cl in the sulphone 7 decreases the reaction rate substantially (by factors of  $7 \cdot 5 - 13 \cdot 5$ ) (Tables 2–4). It is indicative of the fact that a cleavage of the  $C_{\beta}$ —X bond in sulphone 7 (and also cleavage of the  $C_{\alpha}$ —H bond) takes place in the rate-limiting step. The earlier studied reactions of aryl  $\beta$ -haloethyl sulphone elimination, for which an E2 mechanism was proposed, also display high values of the  $k_{\rm Br}/k_{\rm Cl}$  ratio (7, <sup>5a</sup> 4–36<sup>5b</sup>).

Amine $pK_a^{a} = \begin{pmatrix} k_H \times 10^2 & k_D \times 10^2 \\ (  mol^{-1} s^{-1}) & (  mol^{-1} s^{-1}) \end{pmatrix}$	<i>k</i> н/ <i>k</i> d
Pyridine $12 \cdot 33$ $(5 \cdot 0 \pm 0 \cdot 3) \times 10^{-3}$ $(1 \cdot 22 \pm 0 \cdot 10) \times 10^{-3}$ 4	$\cdot 1 \pm 0.6$
<i>N</i> -Methylimidazole $14.99^{\text{b}}$ $0.092 \pm 0.003$ $0.0247 \pm 0.0022$ 3	$\cdot 7 \pm 0.5$
Benzylamine $16.76$ $2.37 \pm 0.08$ $0.750 \pm 0.042$ 3	$\cdot 2 \pm 0.3$
Isobutylamine $17.92$ $12.0 \pm 0.7$ $2.77 \pm 0.29$ 4	$\cdot 3 \pm 0.7$
Triethylamine $18.46$ $76 \pm 5^{\circ}$ $20.5 \pm 1.7$ 3	$.7 \pm 0.6^{\circ}$
Diethylamine $18.75$ $126 \pm 9$ $36.0 \pm 2.3$ $3$	$\cdot 5 \pm 0.5$

Table 2. Rate constants for the reactions of phenyl  $\beta$ -bromoethyl sulphone ( $k_{\rm H}$ , C<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>Br) and phenyl  $\alpha, \alpha$ -dideutero- $\beta$ -bromoethyl sulphone ( $k_D$ , C<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>CD<sub>2</sub>CH<sub>2</sub>Br) with amines in acetonitrile at 25 °C

<sup>a</sup> Data from Ref. 15.

<sup>b</sup> The value of  $pK_a$  is taken as equal to the  $pK_a$  of imidazole. <sup>16</sup> <sup>c</sup> The values  $k_{\rm H} = 0.681 \, \rm l \, mol^{-1} \, s^{-1}$  (UV spectrophotometry) and  $k_{\rm H}/k_{\rm D} = 3.6$  have been reported. <sup>5b</sup>

As follows from the data in Table 4, an approximately similar sensitivity to the leaving group nature is observed for reaction (2) of  $\beta$ -halopropiophenones (5) with amines for which a concerted E2 mechanism has been established.<sup>10</sup>

On the basis of the foregoing, one may conclude that the hydrogen halide elimination in the sulphone 7 (X = Br, Cl) proceeds via an E2 mechanism.

## **Brønsted** correlations

The rate of reaction of phenyl  $\beta$ -bromoethyl sulphone with the analysed amines (Table 2) depends substantially on the amine basicity. Thus, for instance, the transition from diethylamine ( $pK_a = 18.75$ ) to pyridine  $(pK_a = 12.33)$  is accompanied by a 25 200-fold decrease in reaction rate. Quantitatively the dependence of rate constants for the reaction of phenyl  $\beta$ -bromoethyl sulphone with amines is well described by the Brønsted equation:

$$\log k = \log k_0 + \beta p K_a \tag{5}$$

which gives the following equations for non-deuterated and deuterated substrates,\* respectively:

$$\log k_{\rm H} = -(13.0 \pm 0.9) + (0.69 \pm 0.05) pK_{\rm a} \quad (6)$$
  
s = 0.28, n = 6, r = 0.989

$$\log k_{\rm D} = -(13.7 \pm 0.9) + (0.69 \pm 0.05) pK_a \quad (7)$$
  
s = 0.29, n = 6, r = 0.989

 $\log k_{\rm H} = -(15 \cdot 4 \pm 0 \cdot 9)$ +  $(0.82 \pm 0.05)$  pK<sub>a</sub>, s = 0.17, r = 0.993;  $\log k_{\rm D} = -(15 \cdot 9 \pm 1 \cdot 2)$ 

 $+(0.82 \pm 0.07)pK_{a}, s = 0.21, r = 0.990.$ 

A few higher Brønsted coefficients  $\beta$  are observed for aryl  $\beta$ -chloroethyl sulphones (Table 3).

We failed to measure the rate of reaction of aryl  $\beta$ chloroethyl sulphones with pyridine owing to the very · low reaction rate (for the method used). The calculation using Brønsted dependences may also yield erroneous rate constants since the constant for the reaction of phenyl  $\beta$ -bromoethyl sulphone with pyridine has a positive deviation from a straight line. Accordingly, we determined the ratio  $k_{\rm Br}/k_{\rm Cl}$  for the reaction of phenyl  $\beta$ -haloethyl sulphones with pyridine by extrapolation of the dependence of log  $(k_{\rm Br}/k_{\rm Cl})$  on amine pK<sub>a</sub> (Figure 2). On the basis of the value obtained  $(k_{\rm Br}/k_{\rm Cl} \approx 14)$ , the rate constant for the reaction of phenyl  $\beta$ chloroethyl sulphone with pyridine was estimated (Table 4). As is seen from the data in Table 4 (columns 5 and 8) and Figure 2, the nature of the relationships between log  $(k_{\rm Br}/k_{\rm Cl})$  and amine pK<sub>a</sub> for the sulphones 7 and the ketones 5 is, in general, of a similar type (increasing ratio  $k_{\rm Br}/k_{\rm Cl}$  with decrease in the amine basicity).

High coefficients  $\beta$  for reaction (3) prove substantial proton transfer in the transition state of the reaction under consideration.<sup>17</sup>

For reaction (2) of  $\beta$ -halopropiophenones (5) with  $\beta_{\rm Br} = 0.74 \pm 0.05$ .  $^{10a}$ amines we obtained similar values of the Brønsted and

It should also be noted that all the amines studied (i.e. primary, secondary and tertiary) are subordinated to the common correlation relationship (5) that corroborates the unity of mechanism of their interaction with the sulphones 7.

## Hammett-Taft correlations

To establish the charge sign on the  $\alpha$ -carbon atom in transition state 2 of the reaction under study, the influence of substituents in the substrate benzene ring on the

<sup>\*</sup> Deleting the point for pyridine (the most deviant value) gives the following relationships:

Table 3. Rate const	ants, $k \times 10^2$ (1 mol <sup>-1</sup> s <sup>-1</sup>	), and parameters	s of equations (4) amines in acet	and (7) for the r onitrile at 25 °C	eactions of aryl f	3-chloroethyl sul	phones (ArSO <sub>2</sub> (	CH2CH2	CI) with
Ar	N-Methylimidazole	Benzylamine	Isobutylamine	Triethylamine	Diethylamine	Log ko	β	S <sup>a</sup>	٢٩
Phenyl 3-Nitrophenyl 3.5-Dinitrophenyl	(9-2 ± 0-5) × 10 <sup>− 3</sup> 0-17 ± 0-03 2-65 ± 0-07	$0.29 \pm 0.01$ $5.92 \pm 0.08$ $107 \pm 6$	$1 \cdot 60 \pm 0 \cdot 09$ $39 \cdot 8 \pm 1 \cdot 0$ $587 \pm 9$	10·0 ± 0·6 <sup>b</sup> 260 ± 15 —	14·0 ± 0·5 360 ± 20	$-17 \cdot 0 \pm 0 \cdot 2$ -16 \cdot 3 \pm 0 \cdot 3 -13 \cdot 7 \pm 1 \cdot 1	$\begin{array}{c} 0.86 \pm 0.05 \\ 0.90 \pm 0.05 \\ 0.81 \pm 0.07 \end{array}$	0-05 0-06 0-14	966-0 9666-0
bog ko s r	$-4.03 \pm 0.03$ $1.76 \pm 0.03$ $0.03$ $0.9998$	$\begin{array}{c} 2\cdot 53 \pm 0\cdot 02 \\ 1\cdot 83 \pm 0\cdot 03 \\ 0\cdot 03 \\ 0\cdot 9999 \end{array}$	$-1.76 \pm 0.09$ $1.84 \pm 0.09$ $0.09$ $0.999$	$(-1 \cdot 00)^{c}$ (1 · 99) <sup>c,d</sup>	(– 0. 85)° (1 - 99)°				
<sup>a</sup> s = Standard devia <sup>b</sup> The values $k = 0^{-1}$ <sup>c</sup> Estimated by two <sup>d</sup> The value $\rho = 1.8$ of 2 $\cdot 08 \pm 0.14$ .	tion; <i>r</i> = correlation coeff 7/12 (spectrophotometry) points. I has been reported by Y	ficient. and 0·0708 l mol ano and Oae <sup>5a</sup> foi	<sup>-1</sup> s <sup>-1</sup> (acid-base r the same reactio	titration) have b n at 5 °C; using t	een reported. <sup>3b</sup> their data we obt	ained a Hamme	tt ø value (not f	o <sup>0</sup> as in <sup>7</sup>	[able 3]
Table 4. Compariso	on of rate constants for t	he reactions of ph	nenyl $eta$ -haloethyl :	sulphones (7) and	d β-halopropiopt	tenones (5) with	amines in acete	onitrile a	t 25 °C
		PhSO <sub>2</sub> CH <sub>2</sub> C	H <sub>2</sub> X		PhCOCH <sub>2</sub>	CH <sub>2</sub> X			

		d	hSO2CH2CH2X		PhCC	DCH <sub>2</sub> CH <sub>2</sub> X		-	4
		1 ~ 102	L ~ 102	k <sub>Br</sub>	E ~ 10 <sup>2</sup>	L ~ 102	k <sub>Br</sub>	KCO	Kso <sub>2</sub>
Amine	pKa <sup>a</sup>	$(1 \text{ mol}^{-1} \text{ s}^{-1})$	$(1 \text{ mol}^{-1} \text{ s}^{-1})$	<u>kcı</u>	$(1 \text{ mol}^{-1} \text{ s}^{-1})^b$	$(1 \text{ mol}^{-1} \text{ s}^{-1})^c$	<u>kcı</u>	$\mathbf{X} = \mathbf{Br}$	X = Cl
Pyridine	12.33	$5.0 \times 10^{-3}$	$(3\cdot6\times10^{-4})^{d}$	(14·0) <sup>d</sup>	$1.63 \times 10^{-3}$	$6.52 \times 10^{-5}$	25	0.33	(0.18)
N-Methylimidazole	14.99	0.092	$9.2 \times 10^{-3}$	10.0	0.104	$5.7 \times 10^{-3}$	18-2	1.13	0-62
Benzylamine	16.76	2.37	0-29	8.2	2-32	0.216	10.7	0.98	0.74
Isobutylamine	17.92	12.0	1.60	7.5	12.9	1.90	6.8	$1 \cdot 08$	1.19
Triethylamine	18.46	76	10.0	7.6	74-4	7.42	10.0	0.98	0.74
Diethylamine	18.75	126	14-0	0.6	112	15.0	7-5	0.89	$1 \cdot 07$
<sup>a</sup> Data from Ref. 15.									

 $^b$  Data from Ref. 10a.  $^c$  Data from Ref. 10b.  $^c$  Data from Ref. 10b.  $^d$  Calculated by extrapolation of the plot of log(ka/kcı) versus pKa from Figure 2.



Figure 2. Plots of  $\log(k_{Br}/k_{Cl})$  versus  $pK_a$  of amines in acetonitrile for the ( $\bigcirc$ ) phenyl  $\beta$ -haloethyl sulphone and ( $\textcircled{\bullet}$ )  $\beta$ -halopropiophenone reactions at 25 °C

reaction rate was analysed. This effect (Table 3) is well described by the Hammett-Taft equation:

$$\log k = \log k_0 + \rho^0 \sigma^0 \tag{8}$$

High positive values of  $\rho^0$  (Table 3) allow the conclusion that cleavage of both the  $C_{\alpha}$ —H and  $C_{\beta}$ —X bonds in transition state 2 is asynchronous (with the cleavage of  $C_{\alpha}$ —H bond predominating, i.e.  $\Delta n_{C_{\alpha}}$ —H >  $\Delta n_{C_{\beta}}$ —X, where  $\Delta n$  is the change in the corresponding bond order). In other words, the reaction under investigation occurs by an E2 mechanism via an anion-like transition state of type 11.<sup>18</sup>



As is seen from Table 3, the  $\beta$  values in equation (5) are not sensitive to the introduction of substituents into the substrate benzene ring and the  $\rho^0$  values display very little (not more than the standard deviation)

increase with increase in amine basicity. This corroborates the stability (or at least insufficient variation) of the transition state in the reaction under examination within the interval of changing the base and the substrate structure examined. The same conclusion can be drawn from the data on deuterium isotope effects for various amines (Table 2).

### Activation parameters for reactions (2) and (3)

We investigated the rate dependences of the reactions of phenyl  $\beta$ -bromoethyl sulphone and  $\beta$ -bromopropiophenone with isobutylamine and triethylamine on temperature and carried out a comparative analysis of their activation parameters. The results are summarized in Table 5. For the same amines the activation parameters for phenyl  $\beta$ -bromoethyl sulphone and  $\beta$ -bromopropiophenone are very close, which corroborates the above conclusion on the identity of the mechanisms for the given processes (*E*2 mechanism with an anion-like transition state).

## Mechanism. Comparison with $\beta$ -halopropiophenones

In the above conclusion about  $C_{\beta}$ —X bond cleavage in the rate-limiting step of reaction (3), which is based on



Figure 3. Plots of  $\log(k_{\rm CO}/k_{\rm SO_2})$  versus  $pK_{\rm a}$  of amines in acetonitrile for the reactions of  $\beta$ -halopropiophenones and phenyl  $\beta$ -haloethyl sulphones at 25 °C.

- O, Log(kPhCOCH2CH2Br/kPhSO2CH2CH2Br);
- •,  $\log(k_{PhCOCH_2CH_2Cl}/k_{PhSO_2CH_2CH_2Cl})$

	PhSO <sub>2</sub> CI	H <sub>2</sub> CH <sub>2</sub> Br	PhCOCH	H <sub>2</sub> CH <sub>2</sub> Br
Parameter	<sup>i</sup> BuNH <sub>2</sub>	Et <sub>3</sub> N	<sup>i</sup> BuNH <sub>2</sub>	Et <sub>3</sub> N
10 °C			_	$44 \cdot 1 \pm 0 \cdot 7$
12 °C	$5.63 \pm 0.09$	$41 \pm 3$		_
15 °C	_	_	$7.83 \pm 0.09$	$57 \cdot 2 \pm 4 \cdot 0$
25 °C	$12.0 \pm 0.7$	$76 \pm 5^{a}$	$12.9 \pm 0.2^{b}$	$74 \cdot 4 \pm 0 \cdot 8^{b}$
35 °C	$16.8 \pm 0.8$	$116 \pm 9^{a}$	$16.7 \pm 0.2$	$151 \pm 4$
45 °C	$27 \pm 3$	$178 \pm 3$	$32.5 \pm 0.6$	$233 \pm 6$
55 °C	$42 \pm 4$	$258 \pm 10$	$41 \cdot 2 \pm 0 \cdot 5$	$310 \pm 2$
Log A	$5 \cdot 27 \pm 0 \cdot 23$	$5.71 \pm 0.03$	$4.94 \pm 0.46$	$6.04 \pm 0.37$
$E_{\rm A}$ (kJ mol <sup>-1</sup> )	$35 \cdot 6 \pm 1 \cdot 3$	$33 \cdot 3 \pm 0 \cdot 2$ $31 \cdot 8^{\circ}$ $34 \cdot 7^{\circ}$	$33 \cdot 4 \pm 2 \cdot 7$	$34 \cdot 8 \pm 2 \cdot 2$
\$	0.025	0.0037	0.047	0.048
r	- 0 • 998	- 0.9999	-0.990	- 0.992
$\Delta H^{\ddagger}$ (kJ mol <sup>-1</sup> )	$33 \cdot 1 \pm 1 \cdot 2$	$   \begin{array}{r}     30 \cdot 8 \pm 0 \cdot 2 \\     29 \cdot 3^{c} \\     32 \cdot 2^{d}   \end{array} $	$30.9 \pm 2.5$	$32 \cdot 3 \pm 2 \cdot 0$
$\Delta S_{25}^{\ddagger}$ (J mol <sup>-1</sup> K <sup>-1</sup> )	- 152 ± 7	$-144 \pm 1$ -151 <sup>c,e</sup> -160 <sup>d,e</sup>	159 ± 15	$-138 \pm 9$

Table 5. Rate constants,  $k \times 10^2$  (I mol<sup>-1</sup> s<sup>-1</sup>), at various temperatures and activation parameters for the reactions of phenyl  $\beta$ -bromoethyl sulphone and  $\beta$ -bromopropiophenone with amines in acetonitrile

<sup>a</sup> The values  $k_{25} = 0.681 \text{ I mol}^{-1} \text{ s}^{-1}$  and  $k_{35} = 1.06 \text{ I mol}^{-1} \text{ s}^{-1}$  have been reported. <sup>5b</sup>

<sup>b</sup>Data from Ref. 10a.

<sup>c</sup> Data from Ref. 5b.

<sup>d</sup> Data from Ref. 5b for the reaction between PhSO<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>Cl and Et<sub>3</sub>N. Yano and Oae<sup>5a</sup> have reported values of  $\Delta H^4 = 39 \cdot 3 \text{ kJ mol}^{-1}$  and  $\Delta S_{50}^4 = 92 \cdot 1 \text{ J mol}^{-1} \text{ K}^{-1}$  for this reaction; but using their data Fiandanese *et al.* <sup>5b</sup> obtained a value of  $\Delta S_{50}^4 = 141 \text{ J mol}^{-1} \text{ K}^{-1}$ . <sup>c</sup> At 50 °C.

high values of the rate ratio  $k_{\rm Br}/k_{\rm Cl}$  (Table 4), there is one aspect which requires an individual discussion. If on changing the leaving group in the sulphones 7 from X = Br to Cl the mechanism is changed from E2 to  $(E1cB)_{\rm I}$ , we may also have high values of  $k_{\rm BI}/k_{\rm CI}$ . Thus, Stirling and co-workers<sup>7b,e</sup> showed that sulphone 7 1,2-elimination induced by sodium ethylate in ethanol proceeds through an E2 mechanism for X = I and, possibly, for X = Br, and through an  $(E1cB)_I$ mechanism for X = Cl, OAc, OTs and OMes. They drew such a conclusion on the basis of the correlation relationship between logarithms of the reaction rate constants and Taft constants  $\sigma^*$  for groups CH<sub>2</sub>X (as a measure of CH-acids ionization<sup>7c</sup>) with X = F, OAc, OTs, OMes and Cl and positive deviations from this relationship for X = I, Br. It should be noted that the value for X = Cl has some positive deviation from the relationship log k vs  $\sigma^*(CH_2X)$  and the deuterium isotope effect  $k_{\rm H}/k_{\rm D}$  for X = I (5.6), Br (5.0) and Cl (3.6) differs substantially from that for X = F(2.0), OAc (1.9) and OTs (2.0).  $^{10b,e}$ . Moreover, in earlier papers Yano and Oae<sup>5a</sup> and Fiandanese *et al.*<sup>5b</sup> proposed the E2 mechanism for sulphone 7 1,2-elimination under the action of tertiary amines. Hence for sulphones 7 with X = Cl complementary arguments in favour of either mechanism would be of use.

We think that in this respect it would be useful to compare the rates for 1,2-elimination reactions of haloethanes activated by phenacyl and phenylsulphonyl groups  $(k_{CO}/k_{SO_2})$  for chloro and bromo derivatives. If one considers acetophenone and methyl phenyl sulphone, one should expect that for the stepwise carbanionic  $(E1cB)_1$  process ketones 5 will react far faster than sulphones 7  $(k_{CO}/k_{SO_2} \ge 1)$ , as acetophenone is approximately a 4–5 orders of magnitude stronger CH-acid than methyl phenyl sulphone (in DMSO):  $pK_a(PhSO_2Me) = 29.04$ , <sup>20</sup> 27, <sup>21</sup> 26.75, <sup>22</sup> 29.0; <sup>23</sup>  $pK_a(PhCOMe) = 24.7$ , <sup>20</sup> 22.5, <sup>22</sup> 24.6, <sup>23</sup> 24.4, <sup>24</sup> 21.5. <sup>25</sup> In fact it is not observed and  $k_{CO}/k_{SO_2} \approx 1$  for chloro and bromo derivatives (Table 4).

However, the analogy with acetophenone and methyl phenyl sulphone may be considered fairly successful. As Stirling and co-workers<sup>7c</sup> showed, the sensitivity of the ionization rate for sulphonyl-activated CH-acids (PhSO<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>X,  $\rho^* = 4.9$ ) to a change in the CH<sub>2</sub>X group structure (Taft constants  $\sigma^*$  were used) is higher than that for phenacyl-activated acids

(PhCOCH<sub>2</sub>CH<sub>2</sub>X,  $\rho^* = 3 \cdot 2$ ). The crossing point for these relationships is at  $\sigma^*$  (CH<sub>2</sub>X)  $\approx 1.05$ , which approximately coincides with the  $\sigma^*$  value for the CH<sub>2</sub>C1 group. Rate constants for the chloroethane 5 and 7 1,2-elimination under the action of sodium ethylate are close ( $k_{CO} = 761 \text{ I mol}^{-1} \text{ s}^{-1}$ ,  $k_{SO_2} =$ 798 l mol<sup>-1</sup> s<sup>-1</sup>,  $k_{CO}/k_{SO_2} \approx 1$ ) and on the basis of this it was concluded<sup>7c</sup> that during transition from ketones to sulphones the mechanism of reaction is not changed and the reaction proceeds as and (*E1cB*)<sub>1</sub> process.

As shown above for phenyl  $\beta$ -bromoethyl sulphone and earlier for  $\beta$ -halopropiophenones,<sup>10</sup> the reaction with tertiary amines proceeds via an E2 mechanism. If phenyl  $\beta$ -chloroethyl sulphone reacts by an  $(E1cB)_{\rm I}$ mechanism, it should result in anomalous  $k_{\rm CO}/k_{\rm SO_2}$ ratios for X = Cl. In fact, as is seen from Table 4 and Figure 3, the  $k_{\rm CO}/k_{\rm SO_2}$  ratios for X = Cl and X = Br are close in general and they are reduced with decrease in the amine basicity. It is interesting that the nature of the  $k_{\rm CO}/k_{\rm SO_2}$  dependence for bromo derivatives on amine  $pK_a$  (Figure 3) reproduces well the dependence of  $k_{\rm H}/k_{\rm D}$ on amine  $pK_a$  for  $\beta$ -bromopropiophenone<sup>10c</sup> (bell-like dependence predicted by theory<sup>19</sup>).

## **EXPERIMENTAL**

<sup>1</sup>H NMR spectra were recorded on a Gemini-200 spectrometer operating at 200 MHz, using TMS as internal standard and acetone- $d_6$  as solvent. Melting points were measured in a Koefler hot-stage apparatus and are uncorrected.

A laboratory-made conductimeter for kinetic measurements was assembled according to the differential-transformator scheme from commercial instruments;<sup>26</sup> platinum electrodes were used.

*Materials.* Acetonitrile,<sup>27</sup> benzylamine,<sup>27</sup> isobutylamine,<sup>27</sup> diethylamine,<sup>27</sup> triethylamine,<sup>27</sup> pyridine<sup>28</sup> and *N*-metylimidazole<sup>29</sup> were purified by the usual methods.  $\beta$ -Bromopropiophenone was obtained and purified as described earlier.<sup>7e</sup> Phenyl  $\beta$ chloroethyl sulphone was obtained by the earlier described<sup>12b</sup> method and was twice recrystallized from ethanol; m.p. 53·5–54·0 °C; lit.<sup>12</sup> m.p. 53–54 °C.

3-Nitrophenyl  $\beta$ -chloroethyl sulphone. Phenyl  $\beta$ chloroethyl sulphone (1.00 g) was added slowly with stirring to a mixture of fuming nitric acid (10 ml, d = 1.51 g ml<sup>-1</sup>) and 60% oleum (10 ml). The mixture was heated at  $80 \pm 5$  °C for 2 h and poured into ice-water (150 ml). The solid was collected by filtration, washed with water and dried to yield the sulphone (1.06 g, 87%), m.p. 83–84 °C (from ethanol); lit.<sup>12</sup> m.p 84–84.5 °C. Found: C, 38.8; H, 3.5; Cl, 14.4; N, 5.6; S, 13.0. Calculated for C<sub>8</sub>H<sub>8</sub>ClNO<sub>4</sub>S: C, 38.5; H, 3.2; Cl, 14.2; N, 5.6; S, 12.85%. <sup>1</sup>H NMR,  $\delta$ : 8.73 (1H, dd,  $J_{2,4} = 2 \cdot 3$  Hz,  $J_{2,6} = 1 \cdot 75$  Hz, H-2),  $8 \cdot 63$  (1H, ddd,  $J_{4,5} = 8 \cdot 2$  Hz,  $J_{4,6} = 1 \cdot 05$  Hz, H-4),  $8 \cdot 41$  (1H, ddd,  $J_{6,5} = 7 \cdot 85$  Hz, H-6),  $8 \cdot 03$  (1H, dd, H-5),  $3 \cdot 91$  (4H, m, CH<sub>2</sub>CH<sub>2</sub>).

3,5-Dinitrophenyl  $\beta$ -chloroethyl sulphone. Phenyl  $\beta$ -chloroethyl sulphone (1.00 g) was added with stirring to a mixture of fuming nitric acid (15 ml, d = 1.51 g ml<sup>-1</sup>) and 60% oleum (20 ml). The mixture was boiled under reflux for 4 h and poured into ice-water (250 ml). The solid was collected by filtration, washed with water and dried to yield the sulphone (0.58 g, 40%), m.p. 124.5-125.5 °C (from ethanol). Found C, 32.5 · H, 2.4; Cl, 11.8; N, 9.5, S, 10.7. Calculated for C<sub>8</sub>H<sub>7</sub>ClN<sub>2</sub>O<sub>6</sub>S: C, 32.6; H, 2.4; Cl, 12.0; N, 9.5; S, 10.9%. <sup>1</sup>H NMR,  $\delta$ : 9.26 [1H, t,  $J_{4,2(4,6)} = 2.05$  Hz, H-4], 9.11 (2H, d, H-2, H-6), 4.10 (2H, m, SO<sub>2</sub>CH<sub>2</sub>—, A<sub>2</sub>B<sub>2</sub>), 3.97 (2H, m, -CH<sub>2</sub>Cl, A<sub>2</sub>B<sub>2</sub>).

Phenyl β-bromoethyl sulphone. A saturated solution of HBr in acetic acid was prepared by adding acetyl bromide  $(15 \cdot 8 \text{ ml})$  to water (4 ml). Phenyl vinyl sulphone <sup>12b</sup> (0 · 50 g) was added to this solution and the mixture was sealed into a thick-walled ampoule and heated at 100 °C for 7 days. The mixture was evaporated under reduced pressure and the residue was crystallized from hexane (50 ml) to yield the sulphone (0 · 62 g, 77%); after recrystallization from hexane m.p. 79–80 °C. Found: C, 38 · 5; H, 3 · 6; Br, 32 · 0; S, 12 · 8. Calculated for C<sub>8</sub>H<sub>9</sub>BrO<sub>2</sub>S: C, 38 · 6; H, 3 · 6; Br, 32 · 1, S, 12 · 9%. <sup>1</sup>H NMR, δ: 7 · 95 (2H, m, H-2, H-6), 7 · 75 (3H, m, H-3, H-4, H-5), 3 · 80 (2H, m, SO<sub>2</sub>CH<sub>2</sub>—, A<sub>2</sub>B<sub>2</sub>), 3 · 58 (2H, m, —CH<sub>2</sub>Br, A<sub>2</sub>B<sub>2</sub>).

Phenyl  $\alpha, \alpha$ -dideutero- $\beta$ -bromoethyl sulphone. A saturated solution of DBr in CH<sub>3</sub>COOD was prepared by adding acetyl bromide  $(31 \cdot 1 \text{ ml})$  to D<sub>2</sub>O  $(8 \cdot 7 \text{ ml})$ . Phenyl vinyl sulphone  $(1 \cdot 0 g)$  was added to this solution and the reaction was carried out as described above for phenyl  $\beta$ -bromoethyl sulphone. The phenyl  $\alpha$ -deutero- $\beta$ -bromoethyl sulphone (1 · 2 g) obtained was added to a solution of triethylamine (0.86 ml, 1.1)equiv.) in diethyl ether (40 ml). After standing at room temperature for 2 h, triethylamine hydrobromide was removed by filtration and the filtrate evaporated to give the partly deuterated phenyl vinyl sulphone, which was recrystallized from hexane. A saturated solution (30 ml) of DBr in CH<sub>3</sub>COOD was added to this product and the above procedure was carried out once more. After three stages of H–D exchange, the sulphone (0.10-0.15 g)with a degree of deuteration >90% was obtained, m.p. 79-80 °C (from hexane).

*Kinetics*. Kinetic measurements were carried out under pseudo-first-order reaction conditions (excess of amine) with up to 70-90% substrate conversion.

Reactions were followed conductimetrically by the appearance of ammonium salts.

The observed first-order rate constants  $(k_{obs}, s^{-1})$  were calculated by the equation

$$k_{\rm obs} = \frac{1}{\tau} \ln \left( \frac{R_{\tau}^{-1} - R_{\infty}^{-1}}{R_{0}^{-1} - R_{\infty}^{-1}} \right)$$
(8)

where  $R_0$ ,  $R_\tau$  and  $R_\infty$  are the initial, present and final resistances of the solution;  $\tau$  is the time from the start of the reaction.

The second-order rate constants  $(k, 1 \text{ mol}^{-1} \text{ s}^{-1})$  were calculated as  $k = k_{obs} / [R^{1}R^{2}R^{3}N]$ .

Between 10 and 30 measurement of  $R_{\tau}$  were made during the reaction and rate constants were evaluated as the arithmetic mean of all the measurements. When  $\delta,\delta$ -dideutero- $\beta$ -bromoethyl sulphone was used in kinetic experiments, slightly increased value of  $k_{obs}$ were observed at the beginning of the reaction owing to impurities of non-deuterated and partly deuterated sulphones. These points were ignored when the mean value of  $k_{obs}$  were calculated.

The estimation of the accuracy of the results obtained and calculations of correlation parameters were made by mathematical statistical methods (the root-meansquare deviations are given).

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