Nucleophilic Displacements on Halogen Atoms. II. Kinetic Study of the Reactions of α-Halo Sulfones with Triphenylphosphine[1]

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Abstract: A series of α-halo sulfones, $ArCHXSO_2Ph$ (where X = Cl, Br, I, or Ar is meta and para substituted with a variety of groups: NO_2, CN, Cl, CO_2H, CO_2Et, $COCH_3$, and H), was treated with triphenylphosphine (TPP) in aqueous DMF to give the reduced sulfones, $ArCH_2SO_2Ph$, in quantitative yield. A $\sigma\rho$ (using σ^- constants) correlation gave the following ρ's: $(Cl)\rho = +2.23$; $(Br)\rho = +5.97$; $(I)\rho = +6.29$. The relative rates for the reduction of $ArCHXSO_2Ph$ with TPP in 90% aqueous DMF at 25° are $k_{Br}/k_{Cl} \approx 10^2$–$10^6$ and $k_{Br}/k_I \approx$ 2–40. The observation that the α-iodo sulfones are less easily reduced than the corresponding α-bromo sulfones can be explained in terms of the relative bond strengths of the carbon–halogen and phosphorus–halogen bonds being made and broken in the transition state. Ion-pair return also might account for the relative slowness of the α-iodo sulfones; however, evidence is presented which indicates that ion-pair return is only of small importance with respect to the overall rate of reaction.

One of the most widely studied reactions in chemistry is the nucleophilic displacement reaction. In organic chemistry, the alkyl halides have served as typical compounds for study in which the nucleophile attacks the central carbon atom with concomitant cleavage of the carbon–halogen bond: the classical S$_N$2 reaction. This type of reaction is so ingrained in our thinking that the mention of an S$_N$2 mechanism nearly always evokes thoughts of nucleophiles displacing leaving groups (*e.g.*, halide ions) from the corresponding alkyl compounds. However, S$_N$2 reactions are ubiquitous, and by no means are nucleophiles confined to attacking only carbon atoms; many atoms are capable of suffering nucleophilic attack. Our interest is focused on reactions which occur *via* nucleophilic attack on halogen atoms. Although such S$_N$2 reactions are well known for positive halogen compounds (*e.g.*, halogens, hypohalites, *N*-haloamines, and *N*-haloamides), nucleophiles usually react with alkyl halides *via* displacement of halide ion from the carbon atom. However, if the normal S$_N$2 reaction on carbon is made difficult (as with aryl halides[2] and bridgehead halides[3]), displacement on the halogen atom may occur to release a carbanion. The more common occurrence, however, is where the incipient carbanion is stabilized by one or more carbanion stabilizing groups. Displacement on the halogen atoms in alkyl halides also is made more likely if the central carbon atom is made less accessible through steric effects. In addition to the steric and electronic properties of the alkyl halides, soft nucleophiles[4] encourage attack at the halogen atoms particularly for the bromides and iodides. α-Halo sulfones appeared to be well suited for our study since the effect of the sulfonyl group is such that it not only stabilizes the incipient carbanion, but it also blocks normal S$_N$2 reactions at the α-carbon atom.[5] The nucleophile chosen was triphenylphosphine (TPP) which has been used in a number of studies in similar systems.[6,7]

Results and Discussion

When this study was initiated, there were no reports in the literature on the absolute rate differences for displacements by nucleophiles on chlorine atoms *vs.* bromine atoms *vs.* iodine atoms involving breakage of the carbon–halogen bond.[9] Since then, a paper has appeared which determined that in the reactions of sulfide ion in methanol–water with 2-(2-thienyl)-1-haloacetylenes to give the corresponding 1-protioacetylenes,[11]

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[1] For a preliminary account of this work, see B. B. Jarvis and J. C. Saukaitis, *Tetrahedron Lett.*, 709 (1973); presented in part at the 8th Middle Atlantic Regional Meeting of the American Chemical Society, Washington, D. C., Jan 1973, and at the 163rd National Meeting of the American Chemical Society, Boston, Mass., April 1972.

[2] J. F. Bunnett, *Accounts Chem. Res.*, **5**, 139 (1972).

[3] C. W. Jefford, D. Kirkpatrick, and F. Delay, *J. Amer. Chem. Soc.*, **94**, 8905 (1972).

[4] See (a) R. G. Pearson and J. Söngstad, *ibid.*, **89**, 1827 (1967); (b) R. F. Hudson, "Structure and Mechanism in Organo-Phosphorus Chemistry," Academic Press, New York, N. Y., 1965, Chapters 4 and 5.

[5] F. G. Bordwell and B. B. Jarvis, *J. Org. Chem.*, **33**, 1182 (1968).

[6] For general references on the use of trivalent phosphorus as a halogen nucleophile, see (a) H. Hoffmann and N. J. Diehr, *Angew. Chem., Int. Ed. Engl.*, **3**, 737 (1964); (b) ref 4b; (c) G. Miller, *Top. Phosphorus Chem.*, **2**, 133 (1965); (d) P. A. Chopard, *Chimia*, **20**, 429 (1966). For recent references, see (e) I. J. Borowitz, K. C. Kirby, Jr., P. E. Rusek, and E. W. R. Casper, *J. Org. Chem.*, **36**, 88 (1971); (f) I. J. Borowitz, D. Weiss, and R. K. Crouch, *ibid.*, **36**, 2377 (1971); (g) A. Fujii and S. I. Miller, *J. Amer. Chem. Soc.*, **93**, 3694 (1971); (h) I. J. Borowitz, H. Parnes, E. Lord, and K. C. Yee, *ibid.*, **94**, 6817 (1972); (i) R. Filler and F. P. Avonda, *J. Chem. Soc., Chem. Commun.*, 943 (1972); (j) C. J. Devlin and B. J. Walker, *J. Chem. Soc., Perkin Trans. 1*, 1249 (1972); (k) M.-F. Chasle and A. Foucaud, *Bull. Soc. Chim. Fr.*, 1535 (1972); (l) M. Svilarich-Soemen and A. Foucaud, *Tetrahedron*, **28**, 5149 (1972).

[7] Detailed kinetic studies have been performed for the reactions of 1-haloalkynes[6g] and α-halo ketones[6h] with trivalent phosphorus nucleophiles. However, both systems prove to be complicated by reactions other than simple nucleophilic displacements on halogen atoms. The α-halo ketones are particularly rich in varied reactions with nucleophiles.[6h,8]

[8] I. J. Borowitz, S. Firstenberg, G. B. Borowitz, and D. Schuessler, *J. Amer. Chem. Soc.*, **94**, 1623 (1972).

[9] However, there are a number of quantitative studies of radical displacement reactions (S$_H$2 reactions) on halogen atoms which have established that iodides react *ca.* 10^3–10^4 times faster than bromides which react *ca.* 10^3–10^4 times faster than the chlorides.[10]

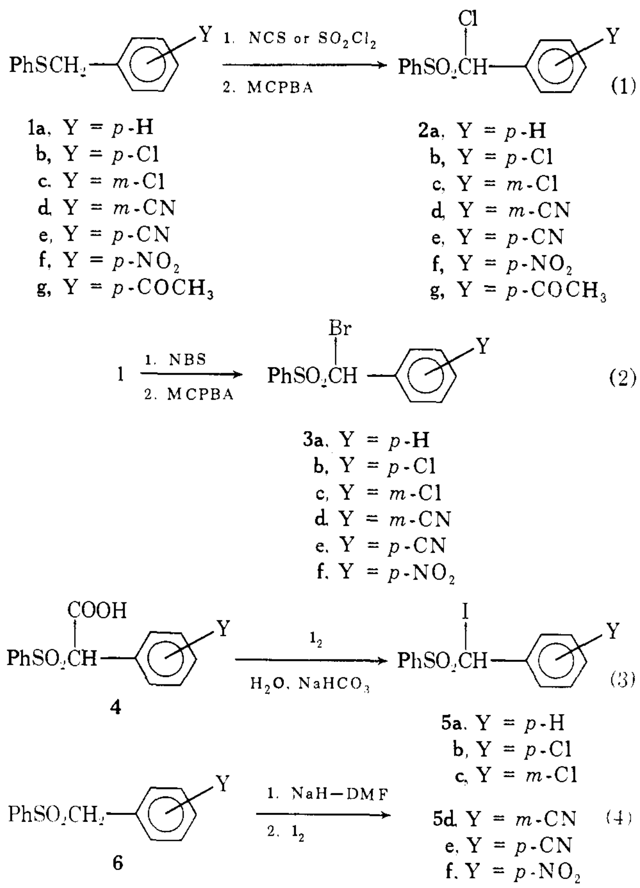
[10] (a) R. J. Fox, F. W. Evans, and M. Szwarc, *Trans. Faraday Soc.*, **57**, 1915 (1961); (b) E. Warhurst, *Quart. Rev., Chem. Soc.*, **5**, 44 (1951); (c) J. W. Hodgins and R. L. Haines, *Can. J. Chem.*, **30**, 473 (1952); (d) L. W. Menapace and H. G. Kuivila, *J. Amer. Chem. Soc.*, **86**, 3047 (1964); (e) M. Mohammad and E. M. Kosower, *ibid.*, **93**, 2709, 2713 (1971); (f) F. S. D'yachkovskii and A. E. Shilov, *Kinet. Katal.*, 919 (1963); *Chem. Abstr.*, 60, 4846g (1964).

[11] M. C. Verploegh, L. Donk, H. J. T. Bos, and W. Drenth, *Recl. Trav. Chim. Pays-Bas*, **90**, 765 (1971).

the iodide reacts *ca.* 10^3 times faster than the bromide which reacts *ca.* 10^5 times faster than the chloride. This result is in agreement with the general observation that in reductions of organo–halogen compounds $\mathrm{RI} > \mathrm{RBr} > \mathrm{RCl}$ is the order observed.

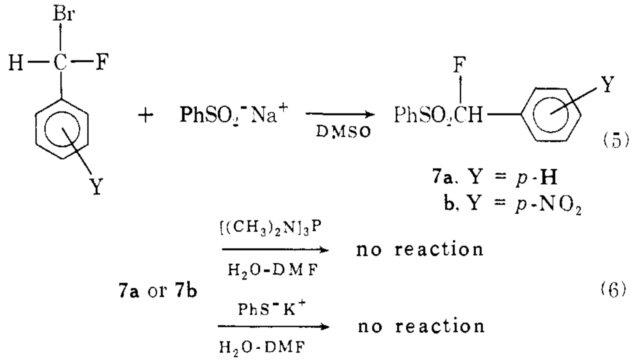
We have studied the rates of reaction of TPP with α-halobenzyl phenyl sulfones in 90% aqueous dimethylformamide (DMF) in order to determine the relative rates for nucleophilic displacement on the various halogen atoms and also to measure the Hammet ρ values for these reactions. The syntheses of the α-halo sulfones are outlined in Scheme I.

Scheme I



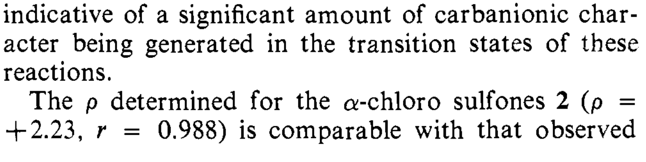
Conversion of sulfides **1** to the α-chloro and α-bromo sulfones **2** and **3** followed procedures previously used.[12] In general, we found sulfuryl chloride a more satisfactory chlorinating agent then *N*-chlorosuccinimide (NCS). These chlorinations followed by oxidation with *m*-chloroperbenzoic acid (MCPBA) gave **2** in higher yields than the corresponding bromination with *N*-bromosuccinimide (NBS) followed by oxidation with MCPBA to give the bromides **3**. The iodinative decarboxylation, eq 3, is analogous to the reactions of bromine and chlorine with α-carboxy sulfones[13,14] which give α-bromo and α-chloro sulfones, respectively. The presence of electron-stabilizing groups ($-\mathrm{CN}$ and $-\mathrm{NO_2}$) on the benzyl ring allows for easy removal of the benzylic proton in the sulfone **6** by strong base, NaH. Iodination of the resulting carbanion gives **5d–f**.[15] The iodides **5a–f** were obtained in *ca.* 50% yield by these methods. The parent sulfones **6** were synthesized either by oxidation of the sulfides **1** or by the reaction of sodium benzenesulfinate in dimethyl sulfoxide (DMSO) with the appropriate α-chloro- or α-bromotoluene derivative (see Experimental Section).

Two α-fluorobenzyl phenyl sulfones, **7a** and **7b**, were synthesized, eq 5, in order to examine the feasibility of studying nucleophilic displacements on fluorine atoms. Both fluorides proved to be very unreactive toward these reduction reactions. Even powerful nucleophiles such as thiophenoxide ion and hexamethylphosphorous triamide failed to react with **7a** or **7b**.



The rates of reaction of TPP with the α-halo sulfones **2**, **3**, and **5** in 90% aqueous DMF (v/v) were investigated at a number of temperatures and the data are recorded in Tables I–IV. The Hammett σρ plots of the data in Table IV are shown in Figures 1–3.

The reactions, which quantitatively yield reduced sulfones **10**, obey good second-order kinetics, first order each in TPP and sulfone.[16,17] The large negative $\Delta S^{\ddagger}$'s associated with these reactions (see Table IV) are typical for reactions involving the conversion of neutral molecules to ions.[19] Our data as well as others[6a–d] are consistent with the following mechanism (7).



$$\underset{\mathbf{8}}{\mathrm{Ar}\overset{\mathrm{X}}{\mathrm{C}}\mathrm{HSO_2Ph}} + \mathrm{Ph_3P{:}} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \underset{\mathbf{9}}{[\mathrm{Ar\ddot{C}HSO_2Ph}]^- [\mathrm{XPPh_3}]^+} \xrightarrow[\mathrm{H_2O}]{k_2} \underset{\mathbf{10}}{\mathrm{ArCH_2SO_2Ph}} + \mathrm{Ph_3P{=}O} + \mathrm{HX} \quad (7)$$

The Hammett σρ plots (Figures 1–3) show a better correlation with σ^- constants (determined from the acidity of phenols) than with normal σ constants. Such behavior (as well as the large positive ρ's observed) is indicative of a significant amount of carbanionic character being generated in the transition states of these reactions.

The ρ determined for the α-chloro sulfones **2** ($\rho = +2.23$, $r = 0.988$) is comparable with that observed

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(12) (a) D. L. Tuleen and V. C. Marcum, *J. Org. Chem.*, **32**, 204 (1967); (b) G. E. Wilson, Jr., and M. G. Huang, *ibid.*, **35**, 3002 (1970).

(13) L. A. Carpino, L. V. McAdams, III, R. H. Rynbrandt, and J. W. Spiewak, *J. Amer. Chem. Soc.*, **93**, 476 (1971).

(14) For an example of iodinative decarboxylation, see T. Ammo, *et al.*, Japanese Patent 6,806,609 (1968); *Chem. Abstr.*, **69**, 96242d (1968).

(15) Other α-iodo sulfones have been made by a similar procedure: N. P. Neureiter, *J. Org. Chem.*, **30**, 1313 (1965).

(16) Under anhydrous conditions, **3f** reacts with TPP to give a phosphonium salt.[18] However, this product is not the result of a normal SN2 reaction at the α-carbon atom but arises by displacement by the α-sulfonyl carbanion on the phosphorus atom in the intermediate ion pair **9**.[6a]

(17) Unlike the analogous reductions of α-halo ketones, the rates of reduction for these α-halo sulfones by TPP remain unchanged, except for a slight salt effect, when run in the presence of 0.1–0.5 *M* acid (HX).

(18) H. Hoffmann and H. Förster, *Tetrahedron Lett.*, 1547 (1963).

(19) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," 2nd ed, Wiley, New York, N. Y., 1961, p 138.

Table I. Rate Constants for the Reaction of α-Chlorobenzyl Phenyl Sulfones, $YC_6H_4CHClSO_2Ph$, with TPP in 90% Aqueous DMF

Y	Temp, °C	10^4k_2, M^{-1} sec^{-1}
p-H	110.07	0.821 ± 0.015
	120.20	1.73 ± 0.08
	130.42	3.07 ± 0.11
p-Cl	120.20	7.35 ± 0.07
	130.42	13.9 ± 0.10
	140.74	24.5 ± 0.25
m-Cl	100.05	4.33 ± 0.16
	110.07	8.55 ± 0.02
	120.20	17.8 ± 0.14
p-$COCH_3$	80.60	3.37 ± 0.07
	90.80	6.40 ± 0.10
	100.05	11.2 ± 0.35
m-CN	80.60	3.10 ± 0.08
	90.80	6.33 ± 0.22
	100.05	11.6 ± 0.28
p-CN	70.44	4.24 ± 0.08
	80.60	9.39 ± 0.01
	90.80	17.4 ± 0.57
p-NO_2	55.24	3.53 ± 0.10
	65.38	7.77 ± 0.10
	75.53	15.2 ± 0.57

Table II. Rate Constants for the Reaction of α-Bromobenzyl Phenyl Sulfones, $YC_6H_4CHBrSO_2Ph$, with TTP in 90% Aqueous DMF

Y	Temp, °C	10^3k_2, M^{-1} sec^{-1}
p-H	90.70	0.278 ± 0.001
	100.05	0.538 ± 0.005
	110.07	0.998 ± 0.010
p-Cl	60.30	0.384 ± 0.026
	70.42	1.09 ± 0.03
	80.56	2.52 ± 0.05
m-Cl	45.18	0.878 ± 0.032
	55.25	1.75 ± 0.04
	65.36	3.62 ± 0.13
m-CN	40.10	6.15 ± 0.38
	50.19	11.4 ± 0.9
	60.30	22.4 ± 0.5
p-CN	14.97	82.4 ± 1.4
	25.00	160 ± 5.4
	35.06	300 ± 3.5
p-NO_2	9.96	10,800 ± 890
	19.98	19,170 ± 1080
	30.03	29,200 ± 570

Table III. Rate Constants for the Reaction of α-Iodobenzyl Phenyl Sulfones, $YC_8H_4CHISO_2Ph$, with TPP in 90% Aqueous DMF

Y	Temp, °C	10^3k_2, M^{-1} sec^{-1}
p-H	100.00	0.143 ± 0.012
	110.30	0.256 ± 0.010
	120.20	0.473 ± 0.024
p-Cl	80.70	0.205 ± 0.013
	90.80	0.385 ± 0.004
	100.05	0.678 ± 0.005
m-Cl	70.44	0.372 ± 0.006
	80.60	0.872 ± 0.026
	90.80	1.92 ± 0.05
m-CN	40.10	0.350 ± 0.008
	50.19	0.930 ± 0.011
	60.30	2.16 ± 0.006
p-CN	25.00	9.90 ± 0.56
	35.06	20.5 ± 0.1
	45.14	42.4 ± 0.3
p-NO_2	25.00	4,360 ± 70
	35.06	7,610 ± 260
	45.14	13,400 ± 240

Table IV. Rate Constants and Activation Parameters for the Reaction of α-Halobenzyl Phenyl Sulfones, $YC_8H_4CHXSO_2Ph$, with TPP in 90% Aqueous DMF at 25°

X	Y	k_2, M^{-1} sec^{-1}	$\Delta H^{\ddagger}$	$\Delta S^{\ddagger}$
Cl	*p*-H	4.79×10^{-8}	19.3	−27
	p-Cl	3.19×10^{-7}	18.3	−27
	m-Cl	4.14×10^{-7}	19.8	−21
	m-CN	2.75×10^{-6}	17.2	−26
	p-$COCH_3$	4.59×10^{-6}	15.5	−30
	p-CN	9.20×10^{-6}	16.6	−25
	p-NO_2	2.80×10^{-5}	15.7	−26
Br	*p*-H	1.07×10^{-6}	17.7	−26
	p-Cl	8.06×10^{-8}	21.2	−11
	m-Cl	1.75×10^{-4}	14.4	−27
	m-CN	2.07×10^{-3}	12.7	−28
	p-CN	1.61×10^{-1}	10.7	−26
	p-NO_2	2.35×10^{1}	7.9	−26
I	*p*-H	4.09×10^{-7}	16.6	−32
	p-Cl	2.76×10^{-8}	15.6	−32
	m-Cl	4.30×10^{-8}	19.4	−18
	m-CN	7.76×10^{-5}	18.1	−17
	p-CN	9.90×10^{-3}	13.0	−24
	p-NO_2	4.36	9.9	−18

in the reaction of TPP with substituted α,α-dichloro-α-phenylamides in acetonitrile ($\rho \simeq +2.6$).[20]

The value of ρ increases markedly for the α-bromo sulfones **3**, $\rho = +5.97$ ($r = 0.998$). A smaller increase in ρ is observed going from **2** to the α-iodo sulfones **5**, $\rho = +6.29$ ($r = 0.993$).[21] These large ρ values are comparable with ρ's obtained from other reactions involving formation of carbanions: base-catalyzed polymerization of substituted styrenes ($\rho = +5.0$)[25] and nucleophilic aromatic substitution reactions ($\rho = +3.5$–8.5).[26]

The increase in ρ going from chlorides to bromides to iodides appears to indicate an increasing degree of ionic character (carbon–halogen bond breaking) in the transition states for these reactions. This conclusion also is supported by a solvent effect study which shows that increasing the water content of the reaction mixtures

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(20) A. J. Speziale and L. J. Taylor, *J. Org. Chem.*, **31**, 2450 (1966).

(21) The point for the less reactive iodo sulfone **5a** fell considerably above the line in Figure 3 and has been omitted. Inclusion of **5a** in the series leads to a much poorer fit of the data: $\rho = +5.74$, $r = 0.986$. We feel that exclusion of this point gives a more meaningful ρ value for the iodo series. We have observed that these iodides are heat and particularly light sensitive which indicates alternate (presumably free radical[22]) reaction pathways available. At lower temperatures, in the absence of light, we obtained good kinetic results free from interference by free-radical reactions. However, when the rates were measured at higher temperatures (>90°), the rate data became much less reliable due to irreproducibility. Therefore, the data given for **5a** and **5b** (Tables III and IV) are somewhat suspect. Often, extrapolation of rate data gathered at high temperatures to give *k* at 25° leads to rate constants ($k_{25°}$) which are too large.[24] Although a correction of our data for this effect might improve the line fit, it would not change the basic arguments presented.

(22) Benzyl iodides are known to be quite sensitive to free-radical decomposition.[23] Furthermore, since α-bromo sulfones are susceptible to free-radical rearrangements [see J. C. Philips and M. Oku, *J. Amer. Chem. Soc.*, **94**, 1012 (1972)], it is not surprising that the α-iodo sulfones are unstable.

(23) (a) M. D. Bentley and M. J. S. Dewar, *J. Amer. Chem. Soc.*, **92**, 3991 (1970); (b) J. A. Hemmingson and R. M. Noyes, *ibid.*, **94**, 9148 (1972).

(24) S. A. Sherrod, R. G. Bergman, G. J. Gleicher, and D. G. Morris, *ibid.*, **94**, 4615 (1972).

(25) M. Shima, D. N. Bhattacharyya, J. Smid, and M. Swarc, *ibid.*, **85**, 1306 (1963).

(26) J. Miller, "Aromatic Nucleophilic Substitution," Elsevier, New York, N. Y., 1968, p 69.

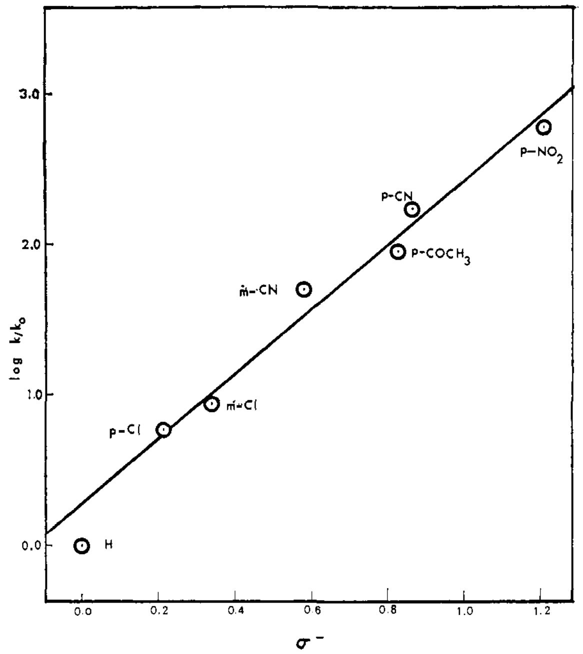

Figure 1. Plot of log k/k_0 *vs.* σ^- constants (from acidity of phenols) for the reaction of substituted α-chlorobenzyl phenyl sulfones, $YC_6H_4CHClSO_2Ph$ (**2**), wth TPP in 90% aqueous DMF at 25° (see Table IV).

increases the reaction rates (Figure 4).[27] The sensitivity of the reaction rates to solvent polarity parallels the Hammett ρ values, *i.e.*, I > Br ≫ Cl in both ρ's and sensitivity to change in solvent polarity.[29]

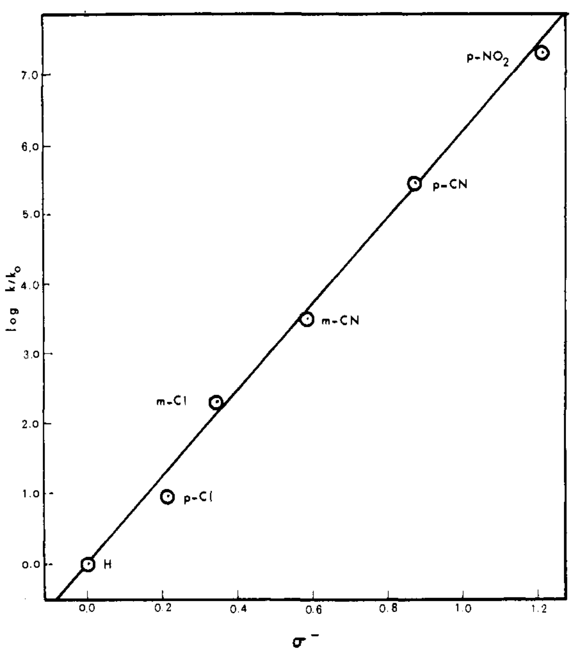

Figure 2. Plot of log k/k_0 *vs.* σ^- constants (from acidity of phenols) for the reaction of substituted α-bromobenzyl phenyl sulfones, $YC_6H_4CHBrSO_2Ph$ (**3**), with TPP in 90% aqueous DMF at 25° (see Table IV).

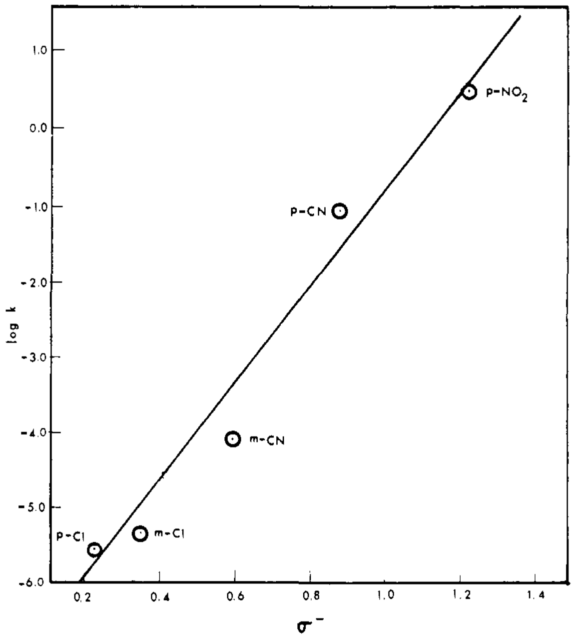

Figure 3. Plot of log k *vs.* σ^- constants (from acidity of phenols) for the reaction of substituted α-iodobenzyl phenyl sulfones, $YC_6H_4CHISO_2Ph$ (**5**), with TPP on 90% aqueous DMF at 25° (see Table IV).

Interestingly, the bromides **3** react with TPP 2–40 times faster than the corresponding iodides **5** (Table IV). Although iodides usually are more reactive than bromides in normal solvolysis reactions,[35] exceptions are often noted in highly protic solvents (*e.g.*, water) where hydrogen bonding plays a major role.[23a,36] This

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(27) A similar effect was noted in the reactions of TTP with α-bromo- and α-iodo-*p*-nitrobenzyl phenyl sulfones (**3f** and **5f**, respectively) upon the addition of $LiClO_4$ (0.0025–4.000 *M*). In 80% aqueous DMF at 25°, a linear relationship between ionic strength (μ) and log k was observed which fit the expression $\log k = \log k_0 + b\mu$.[28] The slopes (b) of the lines were 0.323 (r = 0.996) for **3f** and 0.466 (r = 0.997) for **5f**. Since the rates of reactions of the α-iodo-*p*-nitrobenzyl phenyl sulfone (**5f**) with TTP were more sensitive to solvent polarity than the rates for **3f**, it is not surprising that at some point the iodide **5f** reacts faster than the bromide **3f**. In 70% aqueous DMF at −10° which was 4.0 *M* in $LiClO_4$, $k_I/k_{Br} \cong 4$.

(28) K. J. Laidler, "Reaction Kinetics," Vol. 2, Pergamon Press, Long Island City, N. Y., 1966, p 25.

(29) Care must be exercised in the interpretation of ρ constants.[30] For those reactions in which the overall rate is determined by a composite of several steps, the value of ρ will have a less clear-cut meaning. Such may be the case in studies of H–D exchange reactions of substituted toluenes[31] where ρ = 4.0, a value perhaps low for carbanion generating reactions.[32] The lower values of ρ determined for H–D exchange reactions of substituted toluenes may be due in part to internal return. Of particular relevance to our work is the ρ (+3.5) observed for the base-catalyzed exchange reaction of $ArCH_2SO_2CH_3$, despite the fact that the anion, $[Ar\ddot{C}HSO_2CH_3]^-$, is *ca.* 2 pK_a units less stable than the anion, $[Ar\ddot{C}HSO_2Ph]^-$, we are observing.[33] The low value of ρ (+3.5) for the reaction above is due in part to internal return, a well-known phenomenon in H–D exchange reactions of sulfones.[34] We feel that internal return is relatively unimportant in our system (*vide infra*).

(30) C. D. Johnson and K. Schofield, *J. Amer. Chem. Soc.*, **95**, 270 (1973).

(31) A. Streitwieser, Jr., and H. F. Koch, *ibid.*, **86**, 404 (1964); see also K. J. Klabunde and D. J. Burton, *ibid.*, **94**, 820 (1972), who found for H–D exchange of $ArCH(CF_3)_2$ that ρ = 4.0, but the correlation was best for σ rather than σ^- constants. They concluded that internal return was unimportant and the intermediate carbanion was pyramidal rather than planar.

(32) A ρ value of 5 found for the anionic polymerization of aryl-substituted styrenes[25] has been suggested as a guide for reactions involving carbanions: C. H. DePuy, G. F. Morris, J. S. Smith, and R. J. Smat, *ibid.*, **87**, 2421 (1965).

(33) R. H. Imes, Ph.D. Dissertation, Northwestern University, 1969.

(34) (a) F. G. Bordwell and M. D. Wolfinger, *J. Amer. Chem. Soc.*, **93**, 6303 (1971); (b) D. J. Cram, D. A. Scott, and W. D. Nielsen, *ibid.*, **83**, 3696 (1961); (c) J. Hine, J. C. Philips, and J. I. Maxwell, *J. Org. Chem.*, **35**, 3943 (1970).

(35) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," 2nd ed, Cornell University Press, Ithaca, N. Y., 1969, p 453.

(36) (a) R. E. Robertson, *Suom. Kemistilehti A*, **33**, 3 (1960); (b) E. A. Moelywyn-Hughes, "The Chemical Statics and Kinetics of Solutions," Academic Press, New York, N. Y., 1971, p 234.

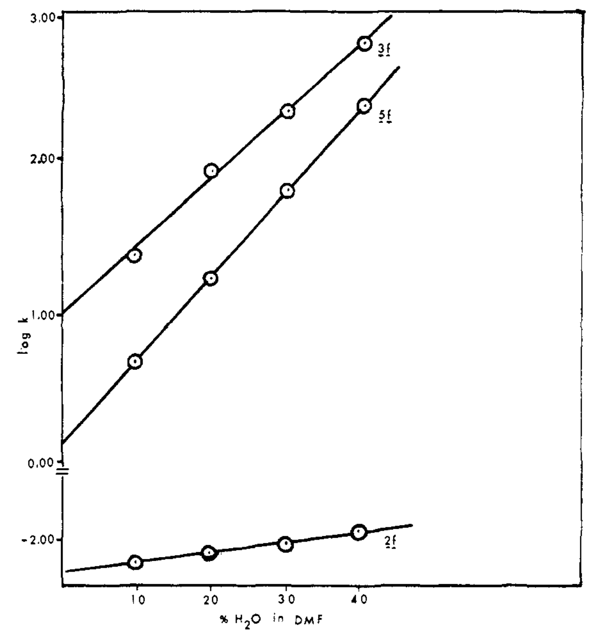


Figure 4. Plots of log *k vs.* % water in DMF for the reactions of *p*-nitro-α-bromobenzyl phenyl sulfone (**3f**) (at 25°), *p*-nitro-α-iodobenzyl phenyl sulfone (**5f**) (at 25°), and *p*-nitro-α-chlorobenzyl phenyl sulfone (2f) (at 90°) with TPP.

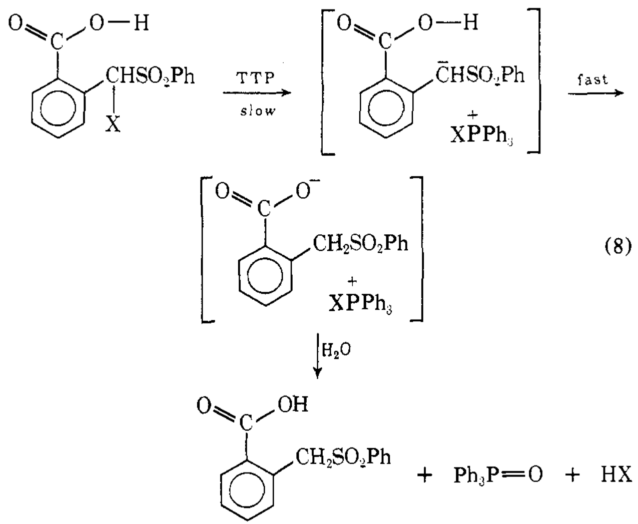
clearly does not account for the relative rates ($k_{Br} > k_I$) observed in our study since the halogen atom is not leaving as a halide ion.

The reaction mechanism presented (eq 7) suggests that internal return (k_{-1}) may play a role in these reactions. Indeed, if ion-pair return (**9** → **8**) is more important for the iodo sulfones compared with the bromo sulfones, then the overall rates of reduction might be slower for the iodides even though $k_1{}^I > k_1{}^{Br}$. From our data, internal return appears unimportant since our rate plots exhibited good linearity through several half-lives. Since the acidity of the media increases with increasing reaction time, the rates of these reactions might have been expected to show an upward drift from linearity if k_{-1} was important.

We sought further evidence on this point and attempted to trap the intermediate carbanion (eq 8).[37] As the data show, the iodide reacts *ca.* three times slower than the bromide indicating that the neighboring carboxylic acid group has no appreciable effect on the k_{Br}/k_I ratio.[38]

We also have determined k_H/k_D for the reactions of TPP with **3** and **5** in 10% D_2O–90% DMF solutions at 25° and find that k_H/k_D is 1.34 and 1.43 for **3e** and **5e**, respectively. This low value suggests that the proton-transfer step to the carbanion occurs after the rate-determining step. The 35–45% rate increase with H_2O (*cf.* D_2O) can be attributed to solvation effects.[39]

In light of the previously observed "normal" order of reactivity of sulfide ion toward the alkynyl halides,[11] a



(8)

11a, X = Br ($k_{60°} = 3.46 \times 10^{-3}\ M^{-1}\ \mathrm{sec}^{-1}$)
b, X = I ($k_{60°} = 1.18 \times 10^{-3}\ M^{-1}\ \mathrm{sec}^{-1}$)

possible explanation for our results can be based on the relevant bond dissociation energies. These values decrease going from chlorides to bromides to iodides, but the drop is particularly large going from P–Br to P–I.[40] Since in the transition states for these reactions a P–X bond is being made as well as the C–X bond being broken, the stronger P–Br bond (*cf.* P–I) being made offsets the effect of the stronger C–Br bond (*cf.* C–I) being broken. It will be interesting to examine the k_{Br}/k_I ratio for various nucleophiles.[41]

Experimental Section

Melting points were taken on a Fisher-Johns apparatus and are uncorrected. The nmr spectra were recorded on a Varian Associates A-60D nmr spectrometer operating at ambient temperature. Spectra were taken in carbon tetrachloride or deuteriochloroform with tetramethylsilane (δ = 0.00) as an internal standard. Distilled deionized water was used. Reagent grade DMF was twice distilled from P_2O_5 and stored under nitrogen. When the spectrophotometric technique was used (*vide infra*), the DMF was distilled from P_2O_6 repeatedly until the concentration of dimethylamine was in the range of 10^{-4}–10^{-8} M[42] and the solvent was used immediately. Elemental analyses were performed by Dr. Franz Kasler and Mrs. Shelesa Brew, of the University of Maryland.

***p*-Bromomethylacetophenone.** To a solution containing 53.6 g (0.40 mol) of *p*-methylacetophenone dissolved in 350 ml of carbon tetrachloride, 71.2 g (0.40 mol) of NBS and a few milligrams of benzoyl peroxide were added. The solution was held at reflux and irradiated with a 275-W sun lamp until the NBS appeared to be converted entirely to succinimide. The solution was filtered and the solvent removed on a rotary evaporator. The liquid was distilled under reduced pressure to yield 47 g of *p*-bromomethylacetophenone (55%), bp 105–107° (1.8 mm), mp 38–39°, from hexane–methylene chloride: nmr 7.3–7.9 (m, 4 H), 4.47 (s, 2 H), 2.50 (s, 3 H).

Anal. Calcd for C_9H_9BrO: C, 50.73; H, 4.26. Found: C, 50.72; H, 4.29.

Preparations of Benzyl Phenyl Sulfides (1). The substituted benzyl phenyl sulfides were all prepared in the same manner, an example of which is given below. The starting benzyl chlorides and bromides were commercially available (Aldrich) with the exception of *p*-bromomethylacetophenone (*vide supra*). The sulfides were purified by distillation or recrystallization (Table V).

***p*-Acetobenzyl Phenyl Sulfide (1g).** To 4.9 g (0.088 mol) of potassium hydroxide dissolved in 50 ml of 95% ethanol was added

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(37) A similar experiment involving intramolecular trapping of the intermediate carbanion in a related system was successful: G. Stavtz, C. Charrier, and H. Normant, *Bull. Soc. Chim. Fr.*, 1707 (1966).

(38) Since the results of this experiment are negative, one cannot conclude ion-pair return must be of little importance. Conceivably, the carbanion was not effectively trapped by the internal proton source even though the carboxylic acid and the benzyl sulfone differ in acidity by well over 15 pK_a units.

(39) R. P. Bell, "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y., 1959, p 199.

(40) F. L. Cottrell, "The Strengths of Chemical Bonds," Academic Press, New York, N. Y., 1958, pp 270–284.

(41) Results from these laboratories [W. Tong, unpublished results] show in the reactions of **3** and **5** with sodium benzenesulfinate to give the reduced sulfones, that $k_{Br} > k_I$ and that the ρ's are even larger than those observed with TPP.

(42) H. E. Zaugg and A. D. Schaefer, *Anal. Chem.*, **36**, 2121 (1964).

Table V.[a] Benzyl Phenyl Sulfides and Sulfones

Compd	Mp (lit. mp), °C	% yield	^{1}H nmr, δ
1a	40–41 (42.0–43.4)[b]	78	7.0–7.3 (m, 10 H), 4.00 (s, 2 H)
1b	74–75 (78–78.5)[c]	90	7.2–7.4 (m, 9 H), 4.00 (s, 2 H)
1c	bp 138–140 (20 mm)	65	7.0–7.3 (m, 9 H), 3.93 (s, 2 H)
1d	bp 148–150 (20 mm)	68	7.16–7.55 (m, 9 H), 4.00 (s, 2 H)
1e	69–70 (73–74)[d]	82	7.17–7.65 (m, 9 H), 4.07 (s, 2 H)
1f	76–77 (75–76)[e]	93	7.2–8.2 (m, 9 H), 4.10 (s, 2 H)
1g	93–94	85	7.1–7.9 (m, 9 H), 4.00 (s, 2 H), 2.43 (s, 3 H)
6a	147–148 (147–148)[f]	90	6.8–7.8 (m, 10 H), 4.30 (s, 2 H)
6b	189–191 (180–181)[g]	95	6.9–7.9 (m, 9 H), 4.27 (s, 2 H)
6c	110–111 (100–101)[g]	85	7.0–7.75 (m, 9 H), 4.23 (s, 2 H)
6d	157–159	82	7.3–7.8 (m, 9 H), 4.33 (s, 2 H)
6e	208–210 (204.5)[h]	85	7.1–7.9 (m, 9 H), 4.35 (s, 2 H)
6f	209.5–210.5 (209.5)[e]	87	7.2–8.3 (m, 9 H), 4.40 (s, 2 H)
6g	215–216	87	7.1–8.0 (m, 9 H), 4.35 (s, 2 H), 2.58 (s, 3 H)
2a	186–188 (185–186)[i]	50	7.28–7.9 (m, 10 H), 5.71 (s, 1 H)
2b	149–150 (148–149)[j]	55	7.2–8.0 (m, 9 H), 5.75 (s, 1 H)
2c	120–121	84	7.2–8.0 (m, 9 H), 5.68 (s, 1 H)
2d	166–167	80	7.4–8.0 (m, 9 H), 5.73 (s, 1 H)
2e	159.5–160.5 (162.5–163.5)[k]	75	7.4–8.0 (m, 9 H), 5.75 (s, 1 H)
2f	170–171 (168–169)[j]	76	7.3–8.4 (m, 9 H), 5.87 (s, 1 H)
2g	139–141	80	7.2–8.0 (m, 9 H), 5.75 (s, 1 H), 2.43 (s, 1 H)
3a	193–194 (193–194)[l]	32	7.3–7.9 (m, 10 H), 5.73 (s, 1 H)
3b	128–129	65	7.2–8.0 (m, 9 H), 5.72 (s, 1 H)
3c	115–116	45	7.2–8.0 (m, 9 H), 5.67 (s, 1H)
3d	178–179	40	7.4–8.0 (m, 9 H), 5.76 (s, 1 H)
3e	173–174	63	7.4–8.0 (m, 9 H), 5.77 (s, 1 H)
3f	153–154.5	69	7.3–8.4 (m, 9 H), 5.83 (s, 1 H)
5a	198–199	46	7.1–7.9 (m, 10 H), 5.90 (s, 1 H)
5b	132.5–133.5	55	7.1–7.8 (m, 9 H), 5.90 (s, 1 H)
5c	122–123	45	7.1–7.8 (m, 9 H), 5.85 (s, 1 H)
5d	157–158	40	7.3–7.8 (m, 9 H), 5.97 (s, 1 H)
5e	167–169	40	7.4–7.8 (m, 9 H), 6.00 (s, 1 H)
5f	114–115	21	7.2–8.4 (m, 9 H), 6.10 (s, 1 H)

[a] All new compounds gave satisfactory elemental analyses. [b] "Handbook of Chemistry and Physics," 49th ed, The Chemical Rubber Co., Cleveland, Ohio, 1968, p C-552. [c] A. Jamar and W. Schulze, *J. Prakt. Chem.*, **5**, 83 (1957). [d] R. F. Brooks, *et al.*, *J. Sci. Food Agr.*, **9**, 141 (1958); *Chem. Abstr.*, **52**, 11772 (1958). [e] W. R. Waldron and E. E. Reid, *J. Amer. Chem. Soc.*, **45**, 2399 (1923). [f] M. N. Shio and T. Ito, *Chem. Pharm. Bull.*, **13**, 1392 (1965); *Chem. Abstr.*, **64**, 9553 (1966). [g] R. S. Asthana and G. S. Misra, *J. Indian Chem. Soc.*, **31**, 459 (1954); *Chem. Abstr.*, **49**, 13144 (1955). [h] J. Troger and O. Beck, *J. Prakt. Chem.*, [2] **87**, 289 (1912). [i] Y. Shivota, T. Nagai, and N. Tokura, *Bull. Chem. Soc. Jap.*, **39**, 405 (1966). [j] Reference 12a. [k] J. Troger and W. Muller, *Arch. Pharm.*, **252**, 32 (1914); *Chem. Abstr.*, **8**, 3778 (1914). [l] Reference 5.

9.6 g (0.088 mol) of thiophenol. In another flask containing 60 ml of 95% ethanol was added 18.5 g (0.087 mol) of *p*-bromomethylacetophenone. The former solution was added to the stirring solution of *p*-bromomethylacetophenone. After 10 min, *ca.* 300 ml of water was added to the reaction mixture. Upon cooling of this solution to 0°, a solid precipitated. Recrystallization of this solid from 95% ethanol–water yielded 18 g (85%) of *p*-acetobenzyl phenyl sulfide (**1g**). Those sulfides which were low melting solids or liquids at room temperature were extracted with ether from the aqueous solution. The ether extract was dried ($MgSO_4$) and the solvent removed by rotary evaporation. The resulting oil was distilled under reduced pressure (Table V).

α-Thiophenoxy-*p*-chlorophenylacetic Acid. A solution of 10.5 g (0.065 mol) of *p*-chlorophenylacetic acid (Aldrich) was held at reflux in 50 ml of dry benzene and 50 ml of thionyl chloride for *ca.* 3 hr. The thionyl chloride was removed by distillation. Dry benzene (50 ml) was added followed by 10.45 g (0.065 mol) of bromine in 50 ml of dry benzene (dropwise over the next 2–3 hr). The solution was held at reflux and irradiated with a 275-W sun lamp during the addition. The course of the reaction was followed by nmr spectroscopy. The solution was washed with a 10% sodium thiosulfate solution and dried ($MgSO_4$), and the solvent was removed by rotary evaporation. The liquid obtained was used without further purification or characterization. The above liquid (7.8 g) was dissolved in 30 ml of 95% ethanol. This solution was added dropwise to a solution containing 3.8 g (0.067 mol) of potassium hydroxide and 7.4 g (0.067 mol) of thiophenol. After addition, the solution was allowed to stir for 10 min and then poured into 500 ml of water, acidified, and extracted with two 300-ml portions of ether. The ether solution was dried ($MgSO_4$) and the solvent removed by rotary evaporation to yield an oil which was crystallized from hexane–methylene chloride to yield 5.5 g (65%) of α-thiophenoxy-*p*-chlorophenylacetic acid: mp 92.5–93.5°; nmr 11.80 (s, 1 H), 7.1–7.5 (m, 9 H), 4.68 (s, 1 H).

Anal. Calcd for $C_{14}H_{11}ClO_2S$: C, 60.32; H, 3.98. Found: C, 60.65; H, 3.95.

α-Thiophenoxy-*m*-chlorophenylacetic Acid. This acid was prepared by the same procedure as described for the *p*-chloro isomer to give the acid in 65%: mp 57–58° (from hexane–methylene chloride); nmr 11.55 (s, 1 H), 7.1–7.5 (m, 9 H), 4.68 (s, 1 H).

Anal. Calcd for $C_{14}H_{11}ClO_2S$: C, 60.32; H, 3.98. Found: C, 60.05; H, 3.85.

α-Phenylsulfonyl-*p*-chlorophenylacetic Acid (4b). One gram (0.004 mol) of α-thiophenoxy-*p*-chlorophenylacetic acid was dissolved in 10 ml of glacial acetic acid. To this solution was added 8.5 ml (0.08 mol) of 30% hydrogen peroxide. The reaction was allowed to stir for 12–16 hr and then the solvent was removed by rotary evaporation to give a solid which on recrystallization from hexane–methylene chloride yielded 0.88 g (77%) of α-phenylsulfonyl-*p*-chlorophenylacetic acid (**4b**): mp 143–145° dec; nmr 8.68 (s, 1 H), 6.8–7.8 (m, 9 H), 5.12 (s, 1 H).

Anal. Calcd for $C_{14}H_{11}ClO_4S$: C, 54.11; H, 3.56. Found: C, 53.90; H, 3.65.

α-Phenylsulfonyl-*m*-chlorophenylacetic Acid (4c). This acid was prepared by the same procedure as described for the *p*-chloro isomer to give **4c** in 70% yield after recrystallization from hexane–methylene chloride: mp 140–145° dec; nmr 8.80 (s, 1 H), 7.1–7.8 (m, 9 H), 5.10 (s, 1 H).

Anal. Calcd for $C_{14}H_{11}ClO_4S$: C, 54.11; H, 3.56. Found: C, 53.89; H, 3.57.

α-Bromo-α-fluoro-*p*-nitrotoluene. Five grams (0.032 mol) of *p*-nitrobenzyl fluoride[43] was dissolved in 100 ml of carbon tetrachloride. To this solution was added 7.0 g of NBS (40% excess). The solution was held at reflux and irradiated with a 275-W sun lamp until the NBS was consumed. The solution was filtered and the solvent removed by rotary evaporation to give an oil which after distillation under reduced pressure gave 3.35 g (50%) of α-bromo-α-fluoro-*p*-nitrotoluene: bp 92° (0.7 mm); nmr 8.11 (d, 2 H, J = 9.6 Hz), 7.60 (d, 2 H, J = 9.6 Hz), 7.47 (d, 1 H, J_{HF} = 50 Hz).

Anal. Calcd for $C_7H_5BrFO_2$: C, 35.92; H, 2.14. Found: C, 36.02; H, 2.22.

α-Fluorobenzyl Phenyl Sulfone (7a). A solution containing 5.0 g (0.0264 mol) of α-bromo-α-fluorotoluene[44] in 10 ml of DMSO at 50° was added dropwise to a solution containing 6.5 g (0.0396 mol) of sodium benzenesulfinate (Aldrich) in 70 ml of DMSO at 50°. The solution was poured into 400 ml of water and stored in the refrigerator overnight to allow the precipitate to form. The solution was filtered and recrystallization of the solid from ether–pentane yielded 3.3 g (50%) of α-fluorobenzyl phenyl sulfone (**7a**): mp 154–155.5°; nmr 7.3–8.0 (m, 10 H), 6.11 (d, 1 H, J_{HF} = 50 Hz).

Anal. Calcd for $C_{13}H_{11}FO_2S$: C, 62.38; H, 4.43. Found: C, 62.15; H, 4.57.

α-Fluoro-*p*-nitrobenzyl Phenyl Sulfone (7b). A solution containing 5.0 g (0.024 mol) of α-bromo-α-nitrotoluene in 10 ml of DMSO was added dropwise to a solution containing 5.26 g (0.032 mol) of

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(43) J. Bernstein, J. S. Roth, and W. T. Miller, Jr., *J. Amer. Chem. Soc.*, 70, 2310 (1948).

(44) R. A. Moss, *Tetrahedron Lett.*, 1961 (1968).

sodium benzenesulfinate in 70 ml of DMSO at 50°. The solution was allowed to stir for 45 min, after addition was complete. The solution was poured into 400 ml of water and stored in the refrigerator overnight to allow the precipitate to form. The solution was filtered, and recrystallization of the solid from ether–pentane yielded 4.8 g (78%) of α-fluoro-*p*-nitrobenzyl phenyl sulfone (**7b**): mp 171.5–172.5°; nmr 7.5–8.4 (m, 9 H), 6.20 (d, 1 H, J_{HF} = 50 Hz).

Anal. Calcd for $C_{13}H_{10}FO_4NS$: C, 52.87; H, 3.41. Found: C, 52.61; H, 3.52.

Preparation of Substituted Benzyl Phenyl Sulfones (6). These sulfones were synthesized by treating the appropriately substituted benzyl bromides or chlorides with sodium benzenesulfinate in dimethyl sulfoxide (DMSO) (*vide infra*).

***p*-Chlorobenzyl Phenyl Sulfone.** To a solution containing 16.4 g (0.10 mol) of sodium benzenesulfinate dissolved in 140 ml of DMSO at 60° was added 12.9 g (0.080 mol) of *p*-chlorobenzyl chloride. The reaction was allowed to stir for an additional 30 min. The mixture was poured into 1000 ml of water and the solid collected, and recrystallization from ethanol gave 20.3 g (95%) of *p*-chlorobenzyl phenyl sulfone. In a similar manner were prepared the other parent sulfones (Table V).

Preparation of the α-Halobenzyl Phenyl Sulfones. The same procedures were followed with all the α-halo sulfones. Typical syntheses for each of the classes of α-halo sulfones are given below and the physical data for the compounds may be found in Table V.

α-Chloro-*m*-cyanobenzyl Phenyl Sulfone (2d). Dry *m*-cyanobenzyl phenyl sulfide (12 g, 0.053 mol) was dissolved in 200 ml of freshly distilled carbon tetrachloride (from P_2O_5) in a 500-ml, three-necked round-bottom flask equipped with a magnetic stirring bar, reflux consenser, and a drying tube (Drierite). A solution containing 7.20 g (0.053 mol) of sulfuryl chloride dissolved in 60 ml of dry carbon tetrachloride was added dropwise over a period of 100 min to the refluxing solution of the sulfide. The solution was allowed to reflux for another hour and then cool to room temperature. The solution was cooled in an ice bath and oxidized to the sulfone by the dropwise addition of a solution of 100 ml of dry methylene chloride containing 20 g (0.12 mol) of 90% *m*-chloroperbenzoic acid (MCPBA). The addition was carried out over a 30-min period. The solution was allowed to stir overnight. The mixture was washed with saturated sodium carbonate solution, then sodium thiosulfate solution, and again with saturated sodium carbonate solution, dried ($MgSO_4$), and evaporated on a rotary evaporator to give a solid which after recrystallization from hexane–methylene chloride yielded 12.44 g (80%) of α-chloro-*m*-cyanobenzyl phenyl sulfone (see Table V).

α-Bromo-*m*-chlorobenzyl Phenyl Sulfone. Dry *m*-chlorobenzyl phenyl sulfide (10 g, 0.043 mol) was dissolved in 200 ml of freshly distilled carbon tetrachloride (from P_2O_5) in a 500-ml, three-necked round-bottom flask equipped with a magnetic stirring bar, reflux condenser, and a drying tube (Drierite). The solution was brought to reflux and 8.4 g (0.047 mol) of NBS and a few milligrams of benzoyl peroxide were added all at once. The solution was irradiated with a 275-W sun lamp for *ca.* 30 min. The succinimide was filtered off under dry nitrogen and the solution was cooled in an ice bath and oxidized to the sulfone by the dropwise addition of a solution of 250 ml of dry methylene chloride containing 18.6 g (0.094 mol) of 90% MCPBA. The addition was carried out over a 30-min period. The solution was allowed to stir overnight. The mixture was washed with saturated sodium carbonate solution, then with sodium thiosulfate solution, and again with saturated sodium carbonate solution, dried ($MgSO_4$), and evaporated on a rotary evaporator to give a solid which after recrystallization from hexane–methylene chloride yielded 7.92 g (54%) of α-bromo-*m*-chlorobenzyl phenyl sulfone (see Table V).

α-Iodobenzyl Phenyl Sulfone (5a). To a solution of 2.0 g (0.007 mol) of α-phenylsulfonyl phenylacetic acid[45] in 25 ml of water containing 5.0 g (0.018 mol) of potassium carbonate in a 300-ml, two-necked flask equipped with an addition funnel and an air-cooled condenser was added dropwise 2.3 g (0.009 mol) of iodine in 20 ml of a 20% potassium iodide solution. When the rate of disappearance of the iodine color slowed, the iodine addition was stopped until the color had faded. The tan precipitate was collected by filtration and washed with water; the filtrate was returned to the flask and the iodine addition was continued until the color again began to fade (much more slowly). The above procedure of filtration was repeated; the filtrate was returned to the flask and the remainder of the iodine solution was added slowly. The mixture was stirred for an additional hour and the precipitate was collected by filtration. The three precipitates were combined and air dried to give a crude yield of 2.5 g. Recrystallization from ethanol–acetone gave 1.2 g (46%) of white crystals, mp 198–199°. In a like manner were prepared *m*-chloro- and *p*-chloro-α-iodobenzyl phenyl sulfones (Table V).

α-Iodo-*p*-cyanobenzyl Phenyl Sulfone. In a three-necked, 50-ml flask, 1.0 g (0.004 mol) of *p*-cyanobenzyl phenyl sulfone was dissolved in 15 ml of dry DMF at 50–60° under dry nitrogen. To this solution was added 230 mg of sodium hydride (50% dispersion in oil). The temperature 50–60° was maintained while the solution stirred (color changed from yellow to orange). After 10 min the solution was transferred *via* syringe to a solution of 1.0 g of iodine in 5 ml of dry DMF. The resulting mixture was poured into 400 ml of water and the precipitate was collected and recrystallized from acetone to yield 0.50 g (40%) of α-iodo-*p*-cyanobenzyl phenyl sulfone, mp 167–169°. In a like manner were prepared *m*-cyano- and *p*-nitro-α-iodobenzyl phenyl sulfones (see Table V).

Ethyl *o*-Phenylsulfonylmethylbenzoate. To a solution of 5.97 g (0.030 mol) of ethyl *o*-chloromethylbenzoate[46] in 10 ml of DMSO was added 5.1 g (0.031 mol) of sodium benzenesulfinate in 70 ml of DMSO. The solution was heated at 40° for 1 hr and poured into 300 ml of water. The mixture was extracted with ether. The ether was dried ($MgSO_4$) and removed by rotary evaporation to give 6.8 g (75%) of ethyl *o*-phenylsulfonylmethylbenzoate: mp 91–92° (from hexane–methylene chloride); nmr ($CDCl_3$) 7.2–8.0 (m, 9 H), 5.07 (s, 2 H), 4.20 (q, 2 H, *J* = 7.0 Hz), 1.30 (t, 3 H, *J* = 7.0 Hz).

Anal. Calcd for $C_{16}H_{16}O_4S$: C, 63.14; H, 5.30. Found: C, 63.23; H, 5.22.

***o*-Carboethoxy-α-bromobenzyl Phenyl Sulfone.** To a solution of 2.1 g (0.007 mol) of ethyl *o*-phenylsulfonylmethylbenzoate in 12 ml of dry DMF was added 0.50 g of sodium hydride (50% oil dispersion) under nitrogen. This solution was stirred at room temperature for 15 min and then transferred *via* syringe to a solution of 0.5 ml of bromine in dry DMF at 0°. This solution was poured immediately into 100 ml of water. The aqueous solution was extracted with ether, and the ether extract was washed with a 10% solution of sodium thiosulfate and dried ($MgSO_4$), and the ether removed by rotary evaporation. The resulting solid was recrystallized from hexane–ether to give 1.2 g (45%) of the α-bromo sulfone: mp 70–71°; nmr ($CDCl_3$) 7.2–8.2 (m, 10 H),[47] 4.26 (q, 2 H, *J* = 7.0 Hz), 1.32 (t, 3 H, *J* = 7.0 Hz).

Anal. Calcd for $C_{16}H_{15}BrO_4S$: C, 50.14; H, 3.95. Found: C, 50.04; H, 3.92.

***o*-Carboethoxy-α-iodobenzyl Phenyl Sulfone.** The synthesis for this α-iodo sulfone was done in the same manner as for the corresponding α-bromo sulfone (*vide supra*) except that the carbanion solution was added to a solution of 2.0 g of iodine in 5 ml of dry DMF at room temperature. The reaction gave the α-iodo sulfone in 40% yield: mp 96–97° (from hexane–ether); nmr ($CDCl_3$) 8.25–8.45 (m, 2 H), 8.17 (s, 1 H), 7.3–8.0 (m, 7 H), 4.25 (q, 2 H, *J* = 7.0 Hz), 1.29 (t, 3 H, *J* = 7.0 Hz).

Anal. Calcd for $C_{16}H_{15}IO_4S$: C, 44.66; H, 3.51. Found: C, 44.67; H, 3.44.

***o*-Carboxyl-α-bromobenzyl Phenyl Sulfone (11a).** To a solution of 1.0 g (0.0026 mol) of *o*-carboethoxy-α-bromobenzyl phenyl sulfone dissolved in 10 ml of THF, 40 ml of ethanol, and 40 ml of water was added 1.0 g of potassium hydroxide dissolved in 10 ml of water. This mixture stood at room temperature for 2.5 hr (reaction can be monitored conveniently by tlc) and was then poured into 200 ml of 5% hydrochloric acid. The mixture was extracted with ether. The ether extract was extracted with a 10% sodium bicarbonate solution; the bicarbonate extract was acidified to pH 2 (HCl) and then extracted into ether. The ether was dried ($MgSO_4$) and removed by rotary evaporation to give 0.85 g (92%) of **11a**: mp 212–213° (from acetone); nmr (CD_3SOCD_3) 7.4–8.2 (m, 10 H),[47] 5.1–5.8 (broad singlet, 1 H).

Anal. Calcd for $C_{14}H_{11}BrO_4S$: C, 47.34; H, 3.12. Found: C, 47.58; H, 3.07.

***o*-Carboxyl-α-iodobenzyl Phenyl Sulfone (11b).** In the same manner **11b** was prepared from the corresponding ester in 85% yield: mp 206–208° (from acetone; nmr (CD_3SOCD_3) 8.0–8.2 (m, 2 H), 7.92 (s, 1 H), 7.4–7.9 (m, 7 H)), 4.4–5.1 (broad singlet, 1 H).

Anal. Calcd for $C_{14}H_{11}IO_4S$: C, 41.81; H, 2.76. Found: C, 41.76; H, 2.67.

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(45) K. Fuchs and T. Breuer, *Monatsh. Chem.*, **53**, 438 (1929).

(46) F. Gadient, E. Jucker, A. Lindenmann, and M. Taeschler, *Helv. Chim. Acta*, **45**, 1860 (1962).

(47) A sharp spike at *ca.* δ 7.8 appears to be the signal for the benzylic proton.

Kinetic Methods. (a) **Potentiometric Titration.** Solutions (90% aqueous DMF, v/v) of TPP and the sulfone were made such that addition of 10 ml of sulfone solution to the TPP solution gave solutions that were 0.100 *M* in TPP and 0.0100 *M* in sulfone. The solutions were mixed at the appropriate reaction temperature and the time at mixing was taken as time zero. Samples (*ca.* 5 ml) were withdrawn with a 5-ml pipet fitted with a three-way stopcock. For reactions run at $\geq$60° and for all the α-iodo sulfones, individual aliquots were placed in sealed ampoules. The ampoules for the α-iodo sulfones were wrapped with aluminum foil. The aliquots were quenched with 40 ml of distilled deionized water and the solution filtered through Johns–Manville Celite, analytical filter aid. The filtrate was titrated against silver nitrate solution on a Sargent-Welch Recording Titrator Model D. Rate constants were determined from plots of log $(D_\infty - D_t)$ *vs.* time, where *D* is the distance to the point of inflection. The second-order rate constants were determined by dividing the pseudo-first-order rate constants by the concentration of TPP. The TPP concentration was varied from 0.10 to 0.40 *M*, and the sulfone concentration was varied from 0.010 to 0.001 *M*, and in each case the rate plots exhibited a first-order pattern.

(b) **Conductiometric Technique.** Separate solutions of TPP and sulfone were placed in a constant-temperature bath and allowed to equilibrate for 30 min. The solutions were mixed and placed into a Freas conductivity cell which was thermostated in the same constant-temperature bath. The timer was started and conductance readings were taken at various intervals with a Barnstead Conductivity Bridge, Model PM-70CB. The rate constants were obtained by plotting log $(C_\infty - C_t)$ *vs.* time, where *C* is the conductance reading in mhos. The second-order rate constants were obtained by dividing the pseudo-first-order rate constants by the concentration of TPP. The TPP concentrations were 0.10–0.20 *M*, and the sulfone concentration was 0.0010 *M*.

(c) **Spectrophotometric Technique.** A solution of TPP containing chlorophenol red indicator (Eastman) was made such that the absorbance at 599.4 nm was *ca.* 0.8. Three milliliters of this solution in a cuvet was thermostated in the cell holder of a Cary 15 ultraviolet–visible spectrophotometer. To this solution was added 10 μl of sulfone solution and absorption as a function of time was recorded. The TPP concentration varied from 0.00010 to 0.200 *M* and the sulfone concentration varied from 1.50×10^{-5} to 7.50×10^{-6} *M*. The rate constants were obtained by dividing the pseudo-first-order rate constants by the concentration of TPP.

Comparison of Kinetic Methods. The second-order rate constants were determined for α-bromo-*m*-cyanobenzyl phenyl sulfone (**3d**) by all three techniques which gave the following data.

Method	Temp, °C	10^3k, M^{-1} sec^{-1}
a	19.98	1.65 ± 0.10
c	19.98	1.50 ± 0.06
b	50.19	12.2 ± 0.82
c	50.19	11.4 ± 0.65

Product Analysis. Preparative runs for these reactions were made with **2f**, **3b**, and **5a** at temperatures of 70–80° for a reaction time of 1 half-life. Upon work-up, each reaction mixture yielded a solution which was shown by nmr spectroscopy to be a 50:50 mixture of starting α-halo sulfone and reduced sulfone (**6**). The sulfones were isolated by preparative tlc (silica gel, methylene chloride) and identified by ir, melting point, and mixture melting point.

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Interpretation of the Charge and Energy Changes in Two Nucleophilic Displacement Reactions

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Abstract: By means of the virial partitioning method the energies of activation for two SN2 displacement reactions (F^- and $CN^- + CH_3F$) are divided into contributions from spatially defined fragments of the total system. In this way, the course of a reaction may be followed for each fragment individually, by monitoring the change in its charge distribution and kinetic energy from reactants to transition state to products. The bound (F) fragment of CH_3F, for example, is more stable than an isolated F^- ion by −199 kcal/mol. In the FCH_3CN^- transition state the net charge on the (leaving) fluorine fragment has developed to −0.954 e and its energy increased to within 36 kcal/mol of F^-. The process of bond breaking with the leaving group thus contributes 163 kcal/mol to a total activation energy of 22 kcal/mol. In general, it is found that the nucleophilic fragments (F) and (CN) and the (C) fragment of CH_3F are stabilized in the formation of the transition state, while the leaving (F) fragment is considerably destabilized. The (H) fragments are raised in energy (by ~15 kcal/mol) because of the compression of these fragments in both transition states. This compression of the (H) fragments results in a transfer of electronic charge density from (H) to (C). The (C) fragment bears a net positive charge in both transition states (+0.463 e in FCH_3F^- and +0.316 e in FCH_3CN^-).

This paper presents a detailed study of the redistribution of the charge density and the associated energy changes for two gas-phase nucleophilic displacement reactions. The reactions considered are the displacement of fluoride ion from methyl fluoride by fluoride ion and by cyanide ion. The changes in the charge distribution and energy during the course of each reaction are related to one another *via* the virial partitioning method. This is a procedure for spatially subdividing a system into fragments wherein the kinetic and potential energies of each fragment obey the virial relationship.[1,2] The partitioning surfaces

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