

The Reactivity of *N*-Chloro- and *N*-Methylbenzenesulfonamide Anions with Methyl Methanesulfonate in Methanol¹

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A comparison of the reactivity of *N*-chlorobenzenesulfonamide anion (pK_a of the conjugate acid in methanol = 9.5) and *N*-methylbenzenesulfonamide anion ($pK_a = 15.5$) with methyl methanesulfonate in methanol has shown that the weakly basic anion exhibits a second-order rate constant about five times larger than its *N*-methyl counterpart. On the basis of an extended Brønsted plot, a deceleration of 1000-fold would be expected. This finding represents a dramatic example of the α effect in displacement at saturated carbon.

The rate coefficient for the quantitative alkylation of *N*-chlorobenzenesulfonamide by methyl methanesulfonate is about five times larger than the rate coefficient for the alkylation of *N*-methylbenzenesulfonamide by methyl methanesulfonate. The Brønsted equation for general base catalysis, an often used correlation for reactivity, indicates that the *N*-chloro compound exhibits a 1500-fold increase in reactivity from expectations based on the basicity of the anion.¹ Clearly, the reason for enhanced reactivity must lie elsewhere.

It is the purpose of this paper to demonstrate that this finding is an example of the α effect in operation at saturated carbon.

The α effect which is the enhanced reactivity of certain nucleophiles and its importance in displacements on saturated carbon substrates remains an area of considerable interest. The common structural feature of these nucleophiles is "an electronegative atom containing one or more pairs of unsaturated electrons adjacent and attached to the nucleophilic site," in the description of Edwards and Pearson.³

There is, as yet, no thorough explanation of this effect; it appears to be separate from factors linking reactivity to polarizability, basicity, or solvation changes.⁴

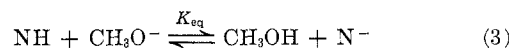
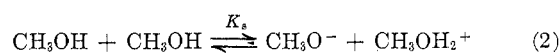
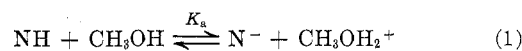
Large, positive deviations from the extended Brønsted relation have been reported for α nucleophiles in reaction series where a high response to the basicity of the nucleophile (*i.e.*, nucleophilic attack at carbonyl carbon) is a recognized factor. The slope of the plot of the second-order rate constants *vs.* pK_a 's of the nucleophile conjugate acids approaches 1. To a lesser extent, these departures from expected behavior have been observed in nucleophilic displacements where polarizability of the nucleophile has been correlated with nucleophilicity (*i.e.*, displacements at saturated carbon).⁵⁻⁷ The slope of the extended Brønsted plot here is about 0.5 for many reaction series.

Solvation changes have been ruled out as an explanation of the α effect by a study of Bruice and Gregory⁴ of aminolysis of *p*-nitrophenyl acetate in acetonitrile.

The magnitude of the effect in the present study is a 1500-fold increase in the expected second-order rate constant at 25°. The Brønsted plot for the present report was developed in a previous paper.⁸

The kinetics of the alkylation reactions of some nitrogen nucleophiles with saturated carbon centers in methanol solution have been previously reported by Bunnett and Beale.⁸ A technique for quantitatively coping with the complication of nucleophilic competition with methoxide ion was described.

The pK_a of *N*-methylbenzenesulfonamide was determined by conductimetric studies¹ in methanol utilizing the high mobility of methoxide ion. Letting NH represent the free sulfonamide and N⁻ its conjugate base, we may write



It is easily shown that $K_a = K_s \cdot K_{eq}$. The K_{eq} value was determined at 25° by perturbing the equilibrium 3 by additions of nitrogen acid, NH. The extent of the lowering of equivalent conductance was used to calculate K_{eq} and derive K_a . Details are given in ref 1, pp 44-55. The pK_a value of *N*-methylbenzenesulfonamide reckoned in this way is 15.5.

The pK_a value of *N*-chlorobenzenesulfonamide was estimated to be 9.5 in absolute methanol. It was determined by titration to a glass electrode⁹ of the stable salt in base¹⁰ with acid in 50% aqueous methanol and then converted to absolute methanol by accepted relations.

pK_a Values of NH compounds determined by titration in aqueous methanol and also by an independent conductivity measurement in absolute methanol are in good agreement.¹

The slope of the extended Brønsted plot is taken to indicate the degree of bond formation in the transition state. In the study cited⁸ it is 0.4.

The reactivities of *N*-methyl- and *N*-chloro-substituted benzenesulfonamides were compared to determine the magnitude of the effect in displacements at saturated carbon. The sizes and polarizabilities of methyl and chloro substituents are essentially equal.¹¹ One then expects that differences in reactivity will be solely electronic in nature.

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A comparison of the alkylation of *N*-methylbenzenesulfonamide and *N*-chlorobenzenesulfonamide by methyl iodide was attempted¹ to relate to the series previously reported.⁸ The initial rate of alkylation of *N*-chlorobenzenesulfonamide anion by methyl iodide was rapid compared to methoxide reactivity. However, satisfactory rate data for the complete reaction were not obtained due to the consumption of chloramine in oxidizing iodide ion and other complicating reactions. Reduction of the iodine back to iodide before titration did not yield satisfactory kinetic results.

Attempted alkylations of *N*-hydroxy- and *N,N*-dimethylaminobenzenesulfonamides were studied briefly. The initial rates of formation of alkylation products seemed much faster than competitive alkylation of methoxide, but the main course of reaction led to decomposition products of the arylsulfonamide anions.¹

Experimental Section

Pseudo-first-order kinetic studies of the reaction of *N*-chlorobenzenesulfonamide with methyl methanesulfonate were conducted by following the formation of methylation product in the ultraviolet spectrum at 249 and 266 nm. An excess of methoxide ion (transparent in the uv) was present. Chloramine is stable in the presence of base. Since the compound is strongly acidic, no unconverted free acid was present and the concentration of nucleophile was exactly known.

The rate constants for the methylation of *N*-methylbenzenesulfonamide by methyl methanesulfonate (Tables I and II)

TABLE I

RATE DATA FOR REACTION OF *N*-METHYLBENZENESULFONAMIDE ANION WITH METHYL METHANESULFONATE IN METHANOL

[CH ₃ O], <i>M</i>	[CH ₃ OSO ₂ -CH ₃], <i>M</i>	[CH ₃ NH-SO ₂ Ph], <i>M</i>	<i>k</i> ₂ , <i>M</i> ⁻¹ sec ⁻¹	Temp, °C
0.0183	0.0500	0.132	1.43 × 10 ⁻²	50.0
0.0183	0.0500	0.0764	1.47 × 10 ⁻²	50.0
0.0183	0.0500	0.0419	1.31 × 10 ⁻²	50.0
0.0183	0.0604	0.119	5.93 × 10 ⁻³	39.8
0.0183	0.0604	0.092	5.5 × 10 ⁻³	39.8
0.0183	0.0604	0.060	5.3 × 10 ⁻³	39.8
0.0138	0.0572	0.120	9.55 × 10 ⁻⁴	25.0
0.0130	0.0572	0.0805	9.50 × 10 ⁻⁴	25.0

TABLE II

REACTION OF *N*-CHLORO- AND *N*-METHYLBENZENESULFONAMIDE ANIONS WITH METHYL METHANESULFONATE IN METHANOL

Nucleophile	Temp, °C	<i>k</i> ₂ , ^c <i>M</i> ⁻¹ sec ⁻¹	Δ <i>H</i> [‡] , kcal mol ⁻¹	Δ <i>S</i> [‡] , cal deg ⁻¹ mol ⁻¹
<i>N</i> -Methylbenzenesulfonamide	25	1.05 × 10 ^{-3 b}	20.8	-4.9
	25	9.55 × 10 ⁻⁴		
	39.8	5.68 × 10 ⁻³		
	50.0	1.44 × 10 ⁻²		
<i>N</i> -Chlorobenzenesulfonamide ^a	22.0	4.7 × 10 ⁻³	15.2	-19.7
	22.7	5.0 × 10 ⁻³		
	22.0	5.8 × 10 ⁻³		
	22.7	5.3 × 10 ⁻³		
	25.0	6.4 × 10 ^{-3 b}		
	30.3	9.4 × 10 ⁻³		
	30.3	9.9 × 10 ⁻³		
	33.0	1.2 × 10 ⁻²		
	33.6	1.4 × 10 ⁻²		

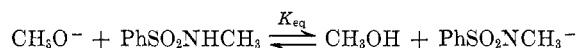
^a Derived from pseudo-first-order kinetic rate constant, methyl methanesulfonate concentration, 0.15 *M*. ^b Extrapolated value. ^c *k*₂ Values corrected for volume expansion of methanol.

were determined at several temperatures by two independent methods. The small values of absorbance change noted¹ by following this reaction in the uv (at 249 or 266 nm) and the un-

certainty of the concentration of the nitrogen nucleophile owing to incomplete conversion of the weak acid to its anion made it desirable to determine the reactivity by another method. Thus, the reaction was followed in a separate series of second-order kinetic studies by analyzing for the disappearance of base. The true nucleophilic rate constant was obtained by adding controlled excesses of conjugate acid (NH) to methoxide solutions and determination of *k*_N values as reported earlier.⁸

Results and Discussion

These data show that the stoichiometric excess of NH suppresses the reaction of methoxide (the slower competitive reaction). The equilibrium constant for the reaction



has been previously determined¹ and found to be rather small (*ca.* 10). For this reason, rather large molar ratios of the nucleophile conjugate acid (*N*-methylbenzenesulfonamide) to methoxide ion were employed in the second-order kinetic study followed by acid-base titration. This technique gives nearly constant *k*₂ values and the iteration required to find *k*_N values as reported in ref 1 was not required. Within experimental error *k*₂ = *k*_N in this work.

A plot of log *k*_N vs. p*K*_a(NH) for the more extensive study of methyl iodide alkylations has a slope of 0.4. The rate constants for *N*-methylbenzenesulfonamide anion toward methyl iodide and methyl methanesulfonate, respectively, at 25° are 1.01 × 10⁻³ and 1.05 × 10⁻³ *M*⁻¹ sec⁻¹. By simple proportion, the reactivity of *N*-chlorobenzenesulfonamide toward methyl iodide is expected to be 6.1 × 10⁻³ *M*⁻¹ sec⁻¹. Placement of this value on the extended Brønsted plot indicates a rate acceleration in alkylation of *N*-chlorobenzenesulfonamide of some 1500-fold.

This acceleration effect is one to two orders of magnitude larger than previous examples.⁵

The lower energy of activation of the *N*-chlorobenzenesulfonamide may be a general feature of α nucleophiles.^{3,12} It indicates either that the energy of the reactant nucleophile is higher or the transition state is stabilized by partial bonding of the lone pair of electrons on the α atom. Both these explanations have been advanced,^{4,7,13,14} but the data here do not allow a decision on the cause of the effect. The observations to date by others and this work are consistent with the notion of participation of α electrons to lower the energy of the transition state.

This work gives a positive demonstration that the effect operates not only in displacement reactions highly dependent on the basicity of the nucleophile (large Brønsted slope), but also in reactions where little bond formation may have occurred in the transition state (Brønsted slope 0.4).

Registry No.—*N*-Chlorobenzenesulfonamide, 80-16-0; *N*-methylbenzenesulfonamide, 5183-78-8; methyl methanesulfonate, 66-27-3.

(12) J. O. Edwards, 1967, private communication.

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