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Reactivity of Substituted Phenyldimethylsulfonium Ions with Common Nucleophiles. A Test of p$K_{\mathrm{lg}}^{\mathrm{Me}}$ for Phenyldimethylsulfonium Salts and a Comparison with Methyl Arenesulfonates

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The correlations of nucleophilic rate data for phenyldimethylsulfonium ions with common nucleophiles with p$K_{\mathrm{lg}}^{\mathrm{Me}}$ values shows that the slopes of the line, $\beta_{\mathrm{lg}}^{\mathrm{Me}}$, correlate qualitatively with Edwards hardness parameter for the nucleophile, and not with the Swain−Scott n_{o} parameter. Comparison with substituted methyl arenesulfonates shows different leaving group behavior in the two systems. These results support Shaik's hypothesis that leaving group behavior consists of some SET character.

Introduction

Quantitative expressions of leaving group behavior are useful for mapping transition states for nucleophilic reactivity.[1,2] A particularly useful parameter[1] is p$K_{\mathrm{lg}}^{\mathrm{Me}}$ which is defined using equilibrium data provided by Lewis[3] et al. for exchange of methyl groups between arenesulfonate ions in sulfolane−dimethylsulfone eutectic, eq 1. The slopes of plots of p$K_{\mathrm{lg}}^{\mathrm{Me}}$ vs log k_{nuc} ($\beta_{\mathrm{lg}}^{\mathrm{Me}}$)

$$\mathrm{Ar^1SO_3Me + Ar^2SO_3^- \rightleftharpoons Ar^1SO_3^- + Ar^2SO_3Me} \tag{1}$$

are limited to values[1] between 0.0 and 1.0. They thus form a counterpart to β_{nuc} values of the nucleophile side of nucleophilic reactivity.

Our group has recently reported[4] on p$K_{\mathrm{lg}}^{\mathrm{Me}}$ values for methyl group transfer between methyl phenyl thioethers, defined analogously to p$K_{\mathrm{lg}}^{\mathrm{Me}}$ for methyl arenesulfonates, from Lewis data on these compounds.[3] These p$K_{\mathrm{lg}}^{\mathrm{Me}}$ values in both the methyl arenesulfonates and the phenyldimethylsulfonium salt series correlate well with their reduction potentials and with the energies of lowest unoccupied molecular orbitals (ELUMO).[4] The present paper reports on the quantitative use of the p$K_{\mathrm{lg}}^{\mathrm{Me}}$ from phenylmethyl thioethers, eq 2, in measuring nucleophilic activity.

$$\mathrm{Ar^1S^+Me_2 + Ar^2SMe \rightleftharpoons Ar^1SMe + Ar^2S^+Me_2} \tag{2}$$

Experimental Results

Nucleophiles from the Swain−Scott[5] list of nucleophiles in methanol were used to represent typical nucleophilic attack from known cases in the same solvent that we previously used, methanol-$d_{4.}$ We can make a claim that these reactions are not reversible at least in the cases of the phenolate ions. Mixtures of the corresponding substituted methyl phenyl ethers, sodium fluoroborate, and methylphenyl thioethers in methanol-d_4 gave no ^{1}H NMR spectra corresponding to the phenyldimethylsulfonium fluoroborate substrates. The correlations, shown below, indicate that a good case can be made that all of the reactions, under our experimental conditions, are not readily reversible on the time scale of our reactions (1−2 days). The expected small solvent kinetic isotope effects are ignored. The kinetics for reaction 3 (where Ar = $C_6H_5^-$) were followed by our published ^{1}H NMR method,[2] where the disappearance of the S^+Me_2 signals is measured. The internal standard in this case was 1,1,1-trichloromethane. The temperature control was held at 30° (±0.3) by the variable temperature probe of the Varian XL200 NMR. The rate constants were determined in at least duplicate, many times triplicate or more.

$$\mathrm{G{-}ArS^+Me_2 + Nu{:}^- \rightarrow G{-}ArSMe + NuMe} \tag{3}$$

The F^-, N_3^-, and SCN^- nucleophiles were from reagent grade sodium and potassium salts, and the kinetics runs were pseudo-first-order with a 10-fold excess of the anion. Pyridine was Fisher Reagent grade and was used as received in pseudo-first-order reactions. Second-order rate constants were obtained by division of the pseudo-first-order rate constants by the known concentrations of the excess nucleophiles.

Phenoxide salts were made by treating a known amount of the substituted phenol with a stoichiometric amount of a standardized 0.5 M solution of methoxide in methanol. Evaporation gave the crude salts, which were recrystallized from acetone-methyl *tert*-butyl ether. The methyl arenesulfonates have all previously been reported.[2]

The substituted phenyldimethylsulfonium salts have all been previously characterized.[6] The physical properties of the salts were all consistent with the literature

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Table 1. Nucleophilic Reactivity of Substituted Phenyldimethylsulfonium Fluoroborates, Eq 3 in CD_3OD at 30 °C

		k(SD) × 10^5 M^{-1} s^{-1}				k(SD) × 10^3 M^{-1} s^{-1}	
G	$pK_{lg}^{Me\ a}$	SCN^-	N_3^-	F^-	Py	$3\text{-}NO_2C_6H_4O^-$	PhO^-
4-CN	−2.479	6.75(0.75)	7.0(1.4)	3.1(0.3)	0.46(0.08)	4.5 (1.0)	849(10)
H	0.00	4.20(0.003)	0.75(0.03)	1.07(0.5)	0.25(0.09)	0.80(0.1)	139(5.5)
4-Me	0.712	3.7(0.9)	0.53(0.12)	0.29(0.9)	0.18(0.08)	0.13(0.05)	35 (5)
4-NO_2	−3.532	7.3(1.5)	9.21(0.4)	3.1(0.8)	0.84(0.14)	10.0(0.9)	3320(35)

[a] Defined in sulfolane.

Table 2. Rate Data for Eq 3 (Nu:$^-$ = G−$C_6H_4O^-$, Ar = Ph) in CD_3OD at 30 °C

G	pK_{AH}[a]	k × 10^3 M^{-1} s^{-1}(SD)
3-CN	13.02[b]	30(4)
3-Br	13.4	19(1)
4-Me	13.9	85(15)
4-MeO	15	310(11)
4-NO_2		15(3)
Nu = MeO^-	16.7[c]	630(20)

[a] In MeOH. [b] From a Hammett plot reported in ref 2a. [c] From Coetzee; Ritchie. *Solute−Solvent* Interactions; Dekker: New York, 1969; Vol. 1.

Table 3. Reactivity Data for Nucleophiles with Methyl Arenesulfonates in Methanol-d_4 at 30 °C (±0.3), Reaction 4

	nucleophile k × 10^4(SD)(L/mol)		
G	N_3^-	SCN^-	PhO^-
4-NO_2	5.2(0.0)	5.6(0.1)	59(19)
4-Me,3-NO_2	4.5(0.2)	3.4(0.0)	29(0.0)
H	1.4(0.7)	0.67(0.02)	3.9(0.8)
4-MeO	0.65(0.5)	0.586(0.003)	2.5(0.3)
4-Br			38(4.4)

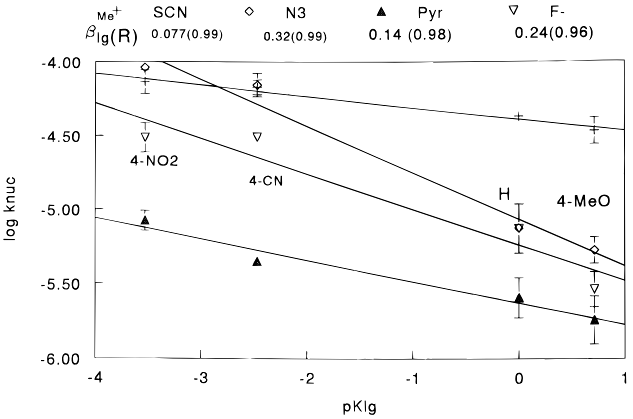

Figure 1. Brönsted−Lewis plots for G−$ArS^+Me_2BF_4^-$ vs simple nucleophiles in methanol-d_4 at 30 °C.

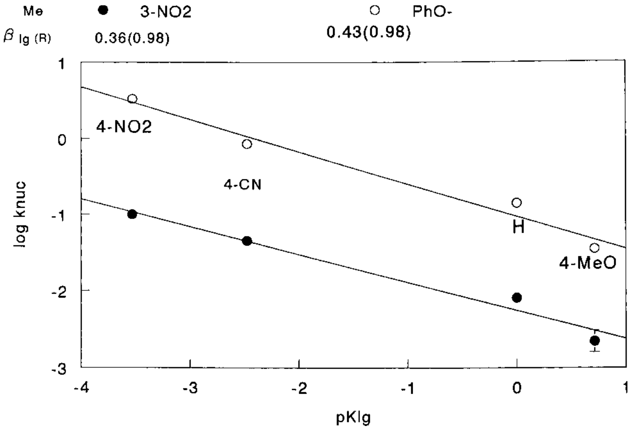

Figure 2. Brönsted−Lewis plots for G−$ArS^+Me_2BF_4^-$ vs G−phenolates in methanol-d_4 at 30 °C.

values, and the new salts, i.e., G = 4-CN, had microanalysis consistent with the assigned structure (±0.4).

The rate laws for all the reactions of the phenolates were cleanly second order, showing straight lines through at least three half-lives. The rate law was the simplified version of a second-order expression where starting materials are each of 0.025 M concentration. The ^1H NMR spectra of the products contained nothing but the spectra of the products at the ends of the reactions. Table 1 summarizes the rate data.

An additional study that varied the substitution on the phenolate ion was done using phenyldimethylsulfonium fluoroborate. Table 2 summarizes the data. The rate for methoxide ion is also in this table.

The rates for reactions of these nucleophiles with methyl arenesulfonates, reaction 4, were obtained by our

$$G{-}ArSO_3Me + Nu:^- \rightarrow G{-}ArSO_3^- + NuMe \quad (4)$$

published method,[2a] using pseudo-first-order conditions for the inorganic ions, and second-order conditions for the phenolate anions, where the concentrations of both the phenolate and the aryldimethylsulfonium salts were equal. The results are summarized in Table 3.

Correlations of Data

The data in Table 1 and 2 are correlated in Figures 1−3. Data in Table 3 are correlated in Figure 5. Figures 1 and 2 show Brönsted−Lewis plots where the pK_{lg}^{Me}, based on phenyldimethylsulfonium ions transferring methyl groups to phenylmethyl thioethers, eq 2, correlate with log k_{nuc}. Figure 3 is a Brönsted plot using the pK_{NuH^+} values for phenols in methanol, which are based on a Hammett plot (not shown, 7 points, R = 0.994) of literature data.[7] The pK_{NuH^+} values that were not in the data set of ref 7 were calculated from the equation of the plot. The 4-nitrophenol was fitted to the plot by σ^-.

In the Brönsted plot in Figure 3 the 4-nitrophenolate points plot significantly off the line, reducing the goodness of fit. The rate constant for this nucleophile was repeatedly larger than for the 3-nitrophenolate with all of the phenyldimethylsulfonium ions. This problem may be due to the difference in the ability of methanol-d_4 and methanol to aid in resonance stabilization of the 4-nitrophenolate anion. Such solvent assisted resonance (SSAR) has been extensively discussed by Taft[8] et al. The pK_a for 4-nitrophenol in methanol-d_4 may be greater than it is in methanol, due to the reduced ability of the NO_2 group to bond to DO, vs HO. Bonner, for example, has shown the degree of association of CH_3OD to be about 32% less than for CH_3OH at 2.47 M concentration in carbon tetrachloride,[9] and Bell discusses this also.[10]

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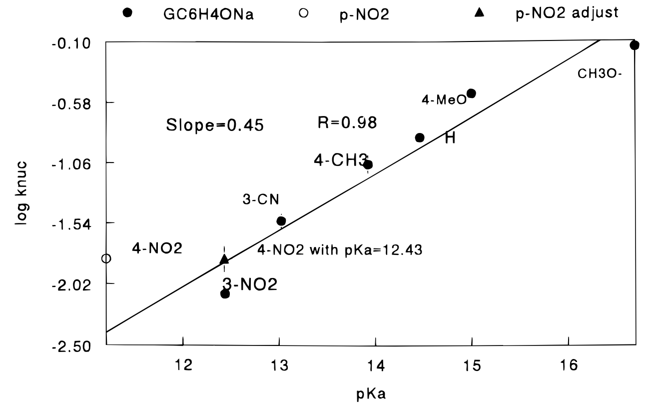

Figure 3. Brönsted plot for G−phenolates vs $PhS^{+}Me_2BF_4^{-}$ in methanol-d_4 at 30 °C.

When the Hammett plot for the substituted phenols was used to compute the pK_a for 4-nitrophenol using $\sigma = 0.78$ (instead of $\sigma^{-} = 1.25$ showing through resonance) the pK_a value was 12.43. This value and the log k_{nuc} plot exactly on the line, as shown in Figure 3, thus lending some credence to the argument for less resonance. The Brönsted β_{nuc} in Figure 3 is 0.45, excluding the 4-nitro point. This Brönsted plot covers 2.4 powers of ten in reactivity and 4.3 powers of ten in basicity.

Figure 5 correlates the data in Table 3 with the pK_{lg}^{Me} values used by us[2] and Hoffman.[1] The phenoxide value of β_{lg}^{Me} is very close to that of a normal nucleophile and compares well with other values of this parameter in the literature for normal nucleophilic behavior.

Discussion

There is an apparent large difference in the leaving group behavior of substituted phenylmethyl thioethers induced by various nucleophiles. A comparison of the nucleophilic order predicted by the Swain−Scott parameters indicates that nucleophiles with large n_o values, such as N_3^- and SCN^- ($n_o = 5.78$ and 6.70, respectively), achieve the transition state with less S−C bond rupture than do phenolates and pyridine. Yet, these "better" nucleophiles have the slowest reactions. Interpreting the β_{lg}^{Me} to give the bond order (BO) between S and C as BO $= 1.0 - \beta_{lg}^{Me}$ give a BO value of 0.913 for SCN^-. The weaker nucleophiles on this scale, such as SCN^- and N_3^- produce larger bond orders for the S−C bond in the TS, corresponding to early transition states, at least from the leaving group side. The substituted phenoxy anions show the greatest β_{lg}^{Me} values, thus indicating the greatest S−C bond cleavage at the TS.

The N_3^- ion and the phenolate ion have nearly the same n_o value, yet in the phenyldimethylsulfonium ion system the measured value of k_{nuc} is much smaller (k_{rel} = ca 1.7×10^4) than the values for the phenolate in Figure 2. This comparison indicates that a relationship different from the nucleophilicity defined by displacing Br^- in methanol is necessary to explain the β_{lg}^{Me} values for these phenyldimethylsulfonium ions. The two substituted phenolates show that the nominally better nucleophile in methanol-d_4 produces the largest β_{lg}^{Me} value. Clearly the β_{lg}^{Me} values indicate that something other than nucleophilicity derived by the Swain−Scott scale governs reactivity here.

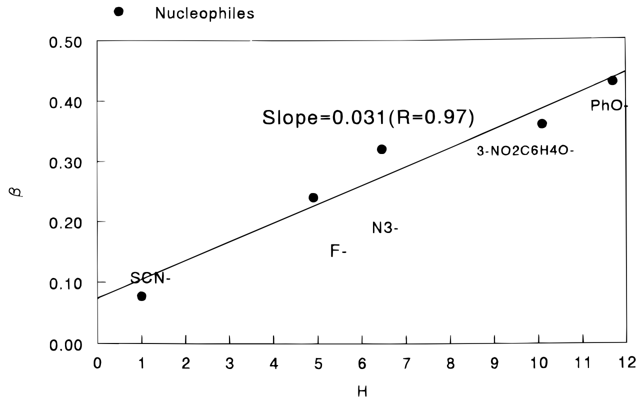

Figure 4. Plot of β_{lg}^{Me} vs hardness parameter, *H*.

The charged nucleophiles, N_3^-,F^-, SCN^-, and PhO^-, follow roughly the Edwards hardness parameter, H[6]. The definition of H (pK_a + 1.70) when applied to 3-nitrophenolate gives $H = 10.1$. Of course this definition applies strictly to water, so a direct quantitative application to methanol is not warranted. Figure 4 shows the correlation of *H* with log k_{nuc}, and indicates qualitatively ($R = 0.97$, 5 points) that these nucleophiles with phenyldimethylsulfonium ions follow the water defined hardness parameter. We do not yet have the Edwards *H* hardness values for these anions in methanol, so Figure 4 indicates no quantitative conclusion, but indicates a qualitative order. A quantitative expression is being explored at present, but involves new analytical chemistry to find the pK_a values of HSCN, HF, and HN_3 in methanol, thus new experimentation. Tentatively, and qualitatively we may conclude that the Edward hardness of the nucleophile controls the degree of S−C bond cleavage in the TS.

The Brönsted plot in Figure 3 for the substituted phenolates shows a very ordinary β_{nuc} value. It is clear that with these much higher *H* nucleophiles, the β_{lg}^{Me} values, along with β_{nuc}, are useful for mapping transition states. The sums of the bond orders, measured by β_{nuc} and $1.0 - \beta_{lg}^{Me}$ sum to less than 1.0. The better nucleophile shows more bond cleavage at the TS. This "looser" transition state for these higher *H* bases is interesting because in the theory of hard and soft acids and bases normally hard nucleophile−hard electrophile combination imply early transition states, with electrostatic attraction contributing more than bond formation.[11] With these salts the lowest *H* nucleophile (SCN^-) gives apparently the earliest transition state, at least from the leaving group side. These facts might suggest, if *H* values have anything to do with hardness−softness, that when charge neutralization occurs between the incoming nucleophile and the alkylating agent the degree of looseness or tightness is dictated by factors other than the usual considerations of hardness−softness. (Note: ref 5 seems to use *H* values as indicators of hardness.)

Within the series of nucleophiles, N_3^-, F^-, SCN^-, 3-nitrophenolate, phenolate, and pyridine, there is no correlation between the energy of the highest occupied molecular orbital (EHOMO) and the β_{lg}^{Me}. However, the EHOMO values for 3-nitrophenolate and phenolate are in the correct order. The enhanced degree of solvation of the small charged nucleophiles N_3^-, F^-, and SCN^- may account for lack of correlation of β_{lg}^{Me} values with this

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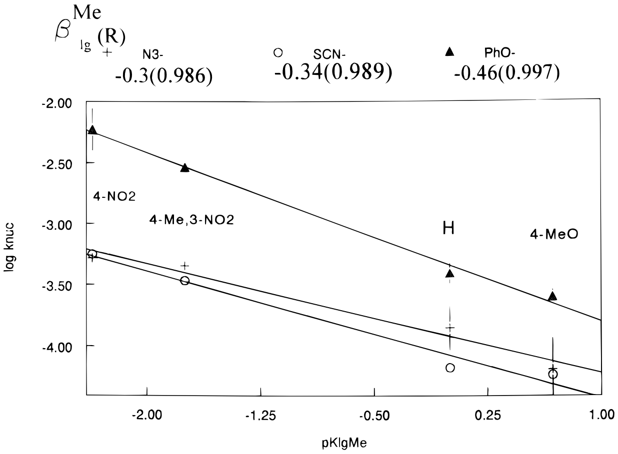

Figure 5. Brönsted−Lewis plots of various nucleophiles vs methyl arenesulfonates in methanol-d_4 at 30 °C.

gas phase calculation of ionization potential. We have already reported that the $\beta_{\mathrm{lg}}{}^{\mathrm{Me}}$ of the phenyldimethylsulfonium ions do correlate with their ELUMO and their E(red) potential from electrochemical experiments.[4]

Comparison of $\beta_{\mathrm{lg}}{}^{\mathrm{Me}}$ Values for Phenyldimethylsulfonium Salts with Methyl Arenesulfonates. Table 3 and Figure 5 present and summarize the nucleophilic reactivity data for transfer of methyl groups from substituted arenesulfonate anions, reaction 4. The corresponding $\beta_{\mathrm{lg}}{}^{\mathrm{Me}}$ values are quite similar to those of the phenyldimethylsulfonium series, except for the SCN^- ion, which behaves differently with phenyldimethylsulfonium ions than with methyl arenesulfonates, showing $\beta_{\mathrm{lg}}{}^{\mathrm{Me}}$ values of 0.077 and 0.42, respectively. The $\beta_{\mathrm{lg}}{}^{\mathrm{Me}}$ of the N_3^- and the PhO^- ions are similar and of the same magnitude in both the cases of methylating agents.

The Edwards hardness of the nucleophiles does not correlate the $\beta_{\mathrm{lg}}{}^{\mathrm{Me}}$ values for methyl arenesulfonates. The soft ($H = 1.0$) SCN^- gives a very different value of $\beta_{\mathrm{lg}}{}^{\mathrm{Me}}$ with methyl arenesulfonates (0.42) than with phenyldimethylsulfonium ions. The lack of correlation of the H parameter defined in water in the methyl arenesulfonate case, but correlation in the phenyldimethylsulfonium case with the water-defined H values, shows significant differences in the effects of nucleophilic factors on the leaving group behavior, regardless of the potential differences of H values in water and in methanol.

The reported correlation[4] of the $pK_{\mathrm{lg}}{}^{\mathrm{Me}}$ values with the experimental $E_{1/2}$ values for reduction (a single electron transfer parameter) and correlation with the ELUMO of both sets of methylating agents[4] indicate that a degree of single electron transfer (SET) character attends the departure of these leaving groups from C atoms. This conclusion supports the Shaik model, the state correlation diagram (SCD) model of the S_N2 transition state. However, the ELUMO of the methyl arenesulfonates correlated less well with the $pK_{\mathrm{lg}}{}^{\mathrm{Me}}$ than with the phenyldimethylsulfonium salts, indicating that other factors, such as the exact behavior of a captured electron in the SO_3 portion, play a role also.

The neutral nucleophile, pyridine, is moderately hard ($H = 7.04$) yet makes little S−C bond cleavage at the TS in phenyldimethylsulfonium salts ($\beta_{\mathrm{lg}}{}^{\mathrm{Me}} = 0.14$). This fact correlates with a lack of excess negative charge to transfer to the leaving group. The charge type for this reaction is transfer of positive charge from S^+ to N and is different from all other TSs where charge is neutralized or dispersed in the TS.

Conclusion

The correlations of the nucleophilic reactivity of moderately hard to hard nucleophiles, as measured by the Edwards hardness parameter, H, with $\beta_{\mathrm{lg}}{}^{\mathrm{Me}}$ values for phenyldimethylsulfonium ions and methyl arenesulfonates are similar. Because the derivations of these two $pK_{\mathrm{lg}}{}^{\mathrm{Me}}$ scales stem from the same concepts and the same types of data, they should serve as good quantitative indicators of leaving group behavior, particularly with these types of nucleophiles.

The behavior of the nucleophiles with smaller H values with these substrates is not yet clear. From just the leaving group behavior data, it may be that current quantitative relationships for the nucleophilic side of the reaction will need revison.

The limited data available at present support the Shaik suggestion that SET behavior is important in leaving groups. Further work along these lines is underway.

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