salts do not undergo thermodynamic equilibration as readily as do retinals in the presence of acids.[14] However, an enzyme-catalyzed route is possible. At any rate, care must be exercised in the preparation and handling of these compounds.

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Reactivity in Methyl Transfer Reactions. 3. Equilibria and Rates in Transfers between Substituted Thiophenoxides

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Abstract: Methyl phenyl sulfide methylates substituted thiophenoxide ions reversibly at elevated temperatures. Using a GC analysis, the rates and equilibria for five substituted cases have been measured at several temperatures in the range ca. 110–210 °C, and the identity reaction with unsubstituted thiophenoxide has also been measured using a ^{35}S tracer. The Hammett ρ for the forward reaction is close to half that for the equilibrium, suggesting a transition state with a half-transferred methyl group. This represents the first measurement of substituent effect on both rate and equilibrium for a simple organic substitution reaction.

In the first two papers of this series,[1,2] substituent effects in an attacking nucleophile were compared for leaving groups of greatly differing reactivity in some virtually quantitative reactions. Surprisingly, substituent effects were large and remarkably similar over a wide range of rate, although the reactivity–selectivity principle[3] leads to an expectation of reduced substituent effects with the most reactive leaving groups, such as trifluoromethanesulfonate. The term "large" substituent effect implies, however, a standard of comparison, and the only ones available were those of one leaving group with another. A more reasonable comparison is between the substituent effect on the reaction rate and that on the equilibrium position in the same reaction, perhaps expressable as ρ_+ and ρ_{eq}, the Hammett reaction constants for the forward rate constants and the equilibrium constants, respectively (similarly ρ_- for the reverse reaction can be defined, but it is not independent, for $\rho_{\mathrm{eq}} = \rho_+ - \rho_-$). The ratio $\rho_+/\rho_{\mathrm{eq}}$ can then be used to measure the extent of proton transfer with the same utility and limitations as using the Brønsted α or β (which are also comparisons of effect of structural changes on rate and equilibrium) to measure the extent of proton transfer.[4]

Equilibria have been measured for very few organic reactions, except acidities and oxidation–reduction processes. One, of complex mechanism, is listed in Hammett's tabulation,[5] Jaffe[6] lists six more, and most of these do not have rates measured also. More recently, both rates and equilibria have been measured for some diazonium[7] and carbonium[8] ion reactions with nucleophiles. There appears to be only one published report of equilibria in methyl transfers,[9] and rates were not reported. A very relevant study of methyl iodide with pyridine is not yet published.[10]

We report the study of the reaction

$$\mathrm{ArS^- + CH_3SPh} \underset{k_-}{\overset{k_+}{\rightleftharpoons}} \mathrm{ArSCH_3 + {}^-SPh} \qquad (1)$$

This reaction is, of course, too slow to study near room temperature, but is fast enough to measure between about 110 and 210 °C in ethanol. Rate constants, measured as initial rates by a gas chromatographic procedure comparing $\mathrm{PhSCH_3}$ and $\mathrm{ArSCH_3}$ peak areas, fit the Arrhenius equation with the results expressed as $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$, presented in Table I. The case of Ar = Ph was followed using ^{35}S-labeled $\mathrm{PhS^-}$. The kinetic law, assumed to be first order in each reagent, was essentially confirmed in one case illustrated in Figure 1, in which experimental points of mole fraction of $\mathrm{ArSCH_3}$ as a function of time in experiments at 144 °C are shown together with the curve calculated from the equation

$$\frac{K}{2A_0}\ln\left[\frac{C\sqrt{K} - C + A_0}{C\sqrt{K} + C - A_0}\right] = k_+t \qquad (2)$$

for a reversible second-order reaction with equal starting concentrations, A_0 of the two reagents. In this equation C is the product concentration, and values were $k_+ = 8.0 \times 10^{-7}$ $\mathrm{M^{-1}\,s^{-1}}$, $K = 2.0$, and $A_0 = 0.90$ M. The plot also shows experimental points for the reverse reaction, starting with $\mathrm{PhS^-}$ and $\mathrm{CH_3SC_6H_4CH_3}$; the calculated curve uses $k_- = 4 \times 10^{-7}$ $\mathrm{M^{-1}\,s^{-1}}$ and an initial concentration of 0.80 M. The time scale on Figure 1 shows why this was not done routinely. A further demonstration of the kinetic law is that no reaction was detected when thiol was used instead of the salt.

Equilibrium constants in Table I are calculated as k_+/k_-, but several were measured directly after long time periods.

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Table I. Temperature Dependence of Rates and Equilibria for Reaction 1

substituent	*p*-*t*-Bu	*p*-CH$_3$	H[a]	*p*-Cl	*m*-Cl	3,4-Cl$_2$
temp range, °C	126-212	109-212	126-167	109-213	126-214	125-212
k_+,[b] $M^{-1}\,s^{-1}$ 150 °C	1.5×10^{-6}	1.4×10^{-6}	1.2×10^{-6}	2.6×10^{-7}	1.5×10^{-7}	4.2×10^{-8}
$\Delta H^{\ddagger}{}_+$, kcal/mol[c]	25.4 ± 0.5	26.0 ± 0.4	27.5 ± 0.6	29.5 ± 0.8	31.0 ± 1.0	32.8 ± 0.7
$\Delta S^{\ddagger}{}_+$, Gibbs/mol[d]	−25.9 ± 1.2	−24.6 ± 0.9	−21.4 ± 1.4	−19.7 ± 1.9	−17.2 ± 2.4	−15.5 ± 1.7
k_-,[b] 150 °C	5.7×10^{-7}	7.1×10^{-7}	1.2×10^{-6}	3.2×10^{-6}	6.4×10^{-6}	1.4×10^{-5}
$\Delta H^{\ddagger}{}_-$[c]	28.1 ± 0.9	27.9 ± 0.9	27.5 [illegible] 0.6	26.7 ± 1.2	25.3 ± 0.8	24.5 ± 0.9
$\Delta S^{\ddagger}{}_-$[d]	−21.5 ± 2.1	−21.5 ± 2.1	−21.4 ± 1.4	−21.3 ± 2.8	−23.3 ± 1.9	−23.6 ± 2.1
K,[e] 150 °C	2.6	2.0	1.0	8.2×10^{-2}	2.3×10^{-2}	3.0×10^{-3}
ΔH, kcal/mol[f]	−2.7 ± 1.0	−1.9 ± 1.3	0.0	2.8 ± 1.4	5.7 ± 1.3	8.3 ± 1.1
ΔS, Gibbs/mol[g]	−4.4 ± 2.5	−3.1 ± 2.4	0.0	1.6 ± 3.1	6.1 ± 2.4	8.1 ± 2.4

[a] This "identity" reaction was measured in only one direction, the equilibrium constant was taken as unity, and the precision is not as great as the other reactions. [b] Calculated from Arrhenius equation fit. [c] Rate data were fitted to the Arrhenius equation, and $H^{\ddagger}$ taken as $E_a - 0.8$. [d] Calculated using eq 8.72 of J. F. Bunnett in "Technique of Chemistry", Vol. VI, Part I, E. S. Lewis, Ed., Wiley-Interscience, New York, N.Y., 1974, p 404. [e] $K = k_+/k_-$. [f] $\Delta H = \Delta H^{\ddagger}{}_+ - \Delta H^{\ddagger}{}_-$. [g] $\Delta S = \Delta S^{\ddagger}{}_+ - \Delta S^{\ddagger}{}_-$.

Table II. Temperature Dependence of Equilibria

substituent	temp, °C	K_{obsd}, $M^{-1}\,s^{-1}$	K_{calcd}, $M^{-1}\,s^{-1}$
p-CH$_3$	144	2.0	2.08
p-CH$_3$	174	1.7	1.78
p-CH$_3$	190	1.6	1.65
p-CH$_3$	212	1.5	1.51
p-Cl	145	0.071	0.078
p-Cl	174	0.084	0.091
p-Cl	190	0.10	0.11
p-Cl	213	0.13	0.13

These are presented in Table II, together with the values calculated from the temperature dependencies in Table I. The agreement is satisfactory.

The quality of fit to the Arrhenius equation for two of the cases is illustrated in Table III, where experimental rates are compared with those calculated from the Arrhenius fit of Table I. The deviations for the *p*-CH$_3$ substituent are almost all within 10%; some of the data on the *p*-Cl compound are farther off, although the average deviation from the observed points is only 12% over a range of over 2000 in rate. The level of agreement in the other cases is shown by the standard errors in $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ in Table I.

The rate constants fit the Hammett equation adequately, yielding $\rho_+ = -2.05$, $\rho_- = +1.75$, and $\rho_{\text{eq}} = -3.80$. Extrapolating the equilibrium constants to 25 °C gives $\rho_{\text{eq}} = -6.6$. This seems very large, compared, for example, to ρ_{eq} for ionization of thiophenols in 95% ethanol of +2.85.[11] Part of the discrepancy is attributable to incipient ionization of the thiols by hydrogen bonding, which makes the change in charge on sulfur smaller in thiol ionization than in the conversion of methyl thioethers to thiolates; part may be due to extrapolation errors. The ratio ρ_+/ρ_{eq} is 0.54, and is not particularly temperature sensitive.

The value of ρ_{eq} has potentially a further value. In the reaction $ArS^- + CH_3X \rightleftharpoons ArSCH_3 + X^-$, it can be shown that, although the equilibrium constant is very sensitive to X, the value of ρ_{eq} is independent of X. We had originally hoped to get a value of ρ_{eq} applicable to our earlier measurements with various other X, but the difference in solvent and the extreme range of temperature extrapolation make the objective still out of reach.

The reaction series is not isoentropic; the differences in $\Delta S^{\ddagger}{}_+$ and ΔS are far outside of random experimental error or any systematic error we have been able to think of. It is interesting that in the reverse reaction $\Delta S^{\ddagger}{}_-$ is almost constant, within experimental error, and this leads to the conclusion that the variation in entropy is attributable primarily to structural variation in ArS^-, not on the sulfides or the transition states, since the ionic species in the reverse reaction is the same in every case. We tentatively relate this sensitivity of the salt entropy to structure to ion-pairing effects and the probable release of solvent molecules on pair formation, for the solutions are quite concentrated (ca. 1 M). Experiments in more dilute solution to check on this are possible, but the reactions become very slow in much more dilute solution.

There is a correlation between $\Delta H^{\ddagger}{}_+$ and $\Delta S^{\ddagger}{}_+$, corresponding to an isokinetic temperature[12] of about 800 K. The source of variation in $\Delta S^{\ddagger}$, being obscure as described above, makes it not worthwhile to explore the significance of this correlation further.

An alternative to the Hammett equation presentation of the data is a plot of log k_+ vs. log K; this is shown in Figure 2. The slope (0.54) should be identical with ρ_+/ρ_{eq} if the fit to the Hammett equation is perfect, but is more useful since it can be applied to structural changes not covered by the Hammett (or Taft) equation or where the choice of substituent constant is uncertain (as here: should σ or σ^- be used?). We may conclude that the methyl group is about half transferred in the transition state for this nearly symmetrical reaction. This apparently trivial result has not been demonstrated before for a substitution on carbon.

A related treatment, a plot of $\Delta H^{\ddagger}{}_+$ vs. ΔH, following Polanyi,[13] is also linear with a slope of 0.65. Perhaps these different potential methods to measure the product-like character of the transition state do not differ fundamentally, especially in view of the suggestion that most of the entropy

Table III. Temperature Dependence of Rate Constants ($M^{-1}\,s^{-1} \times 10^7$) for Reaction 1 with Ar = *p*-YC$_6$H$_4$

Y	*t*, °C	$k_{+\text{obsd}}$	$k_{+\text{calcd}}$	$k_{-\text{obsd}}$	$k_{-\text{calcd}}$
CH$_3$	109	0.46	0.46	0.19	0.18
CH$_3$	144	8.0	8.9	4.0	4.3
CH$_3$	174	80.	78.	51.	45.
CH$_3$	190	210.	220.	130.	130.
Cl	109	0.053	0.055	0.94	0.96
Cl	145	1.6	1.7	22.	22.
Cl	174	23.	18.	300.	190.
Cl	190	64.	60.	590.	540.
Cl	213	240.	280.	1900.	2200.

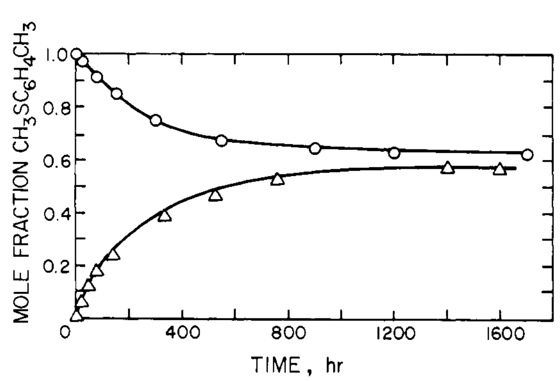

Figure 1. Time dependence of approach to equilibrium of reaction 1 with Ar = p-$CH_3C_6H_4$. Points are experimental, triangles for forward reaction, circles for the reverse; curves are calculated as described in text.

effect might disappear on dilution. It is interesting to compare these measures based on the substituent effects with another proposed measure, the function $p = E_a/(2E_a - \Delta H)$.[14] This is different for each substituent, varying from 0.48 (for p-t-Bu) to 0.58 (for 3,4-dichloro), and averages 0.52. The value is not exactly 0.5 only because of the choice of substituents, with more $\sigma > 0$ than < 0.

Experimental Section

Materials. The substituted benzenethiols were commercial materials, except *p-tert*-butylthiophenol, kindly supplied by Mr. T. H. Colle, and all were redistilled. They were converted to the methyl aryl sulfides (thioanisoles) by neutralization with sodium hydroxide and treatment with methyl iodide, and the products were purified by distillation. Absolute ethanol was used as the solvent, but the thiophenoxide solutions were made by adding the calculated amount of sodium hydroxide to the ethanolic solution of the thiol; thus the solvent contained about 1.5% water, thus avoiding special effects of traces of water sometimes found with rigorously dried solvents. Forward rates were measured by sealing, after degassing and evacuation to $<10^{-2}$ Torr, a solution of the substituted thiophenoxide and thioanisole (but with 5% excess of the salt) into 7-mm Pyrex glass tubes. Larger tubing did not survive the pressure at high temperatures. These tubes were then placed in short lengths of capped steel pipe to contain possible explosions, and immersed in an oil thermostat at the desired temperature. Some earlier results using an oven instead of the thermostat are included, although the temperature control is not as good. After the desired time, a tube was removed, allowed to cool, and analyzed for extent of reaction. The analysis consisted in partitioning the reaction mixture between pentane and water, again extracting the water extracts with pentane and the pentane extracts several times with water, then concentrating and injecting the solution into a gas chromatograph, and comparing the areas of the peak due to thioanisole with that due to the substituted thioanisole, as measured by a Vidar Auto lab digital integrator. Peak areas were corrected for differences in sensitivity of the two sulfides in the flame ionization detector before being converted to extents of reaction. Rate constants were calculated assuming pseudo-zero-order kinetics, and only points less than 10% of the equilibrium amount of product were used, except as illustrated in Figure 1. The 5% excess of thiophenoxide was ignored in these calculations, on the grounds that thiols and their salts are likely to be lost by adventitious oxidation and acidification and the thiols are not as easily purified as the thioanisoles. The error from this neglect is always in the same direction and is less than 5%. Reverse reactions were followed in the same way except that the substituted thioanisole was mixed with sodium thiophenoxide. Total salt concentrations varied from 0.5 to 1.3 M, and no evidence of a salt effect was seen over this concentration range. At the higher temperatures some samples were allowed to reach equilibrium, and equilibrium constants calculated

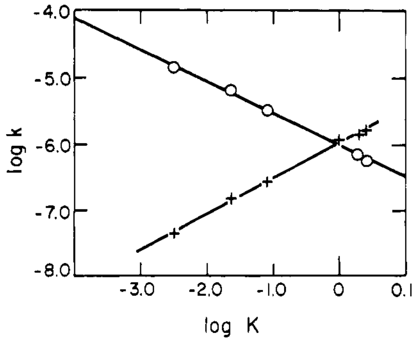

Figure 2. Logarithmic plot of rate constants vs. equilibrium constants for reaction 1 with phenyl substituents from right to left p-$(CH_3)_3C$, p-CH_3, H, p-Cl, m-Cl, 3,4-dichloro. Crosses are forward reaction points with the least-squares line of slope + 0.54 shown. The plot for the reverse reaction, circles, is not independent. The point for H is common to both curves.

were generally in agreement with those calculated as k_+/k_-.

Experiments in other solvents gave results unsatisfactory for various reasons. In diglyme the product was formed at a rate about the same as in ethanol, but the source of the methyl group was not identified. In some, dark colorations formed more rapidly than the substituted thioanisole; in others, including diglyme, extra unidentified peaks appeared on the gas chromatograph. p-Methoxythiophenoxide was an unsuitable reagent even in ethanol; it turned dark before significant reaction occurred. In times longer than required for the kinetics, 3,4-dichlorothioanisole and m-chlorothioanisole with thiophenoxide also developed perceptible but not intense color.

The identity reaction between thiophenoxide and thioanisole was followed using ^{35}S-labeled thiophenol, kindly supplied by Dr. M. Yoshihara. The thioanisole was separated from the alcohol and salts by the same method used in the other reactions, solvent was removed, and the total residue was then counted in toluene solution by solution scintillation counting. The activity of the thioanisole was compared with that of the thiophenoxide, counted after acidification and extraction. This separation leaves the thioanisole contaminated with accidental traces of radioactive diphenyl disulfide, and thus the count rate is a little too high. Some samples were washed with sodium dithionite solution to reduce the disulfide contaminant before counting, which reduced the rate by 10%, and this correction was applied throughout. The reaction was only followed in the one direction.

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