(14) Alkyl groups other than methyl show significantly less selectivity in transfer of one particular alkyl group in mixed lithium dialkyl cuprates; cf. W. H. Mandeville and G. M. Whitesides, *J. Org. Chem.*, **39**, 400 (1974).
(15) H. C. Brown, "Organic Syntheses via Boranes", Wiley, New York, N.Y., 1975.
(16) S. C. Watson and J. F. Eastham, *J. Organomet. Chem.*, **9**, 165 (1967).
(17) R. N. Keller and H. D. Wycoff, *Inorg. Synth.*, **2**, 1 (1946).
(18) W. L. Collier and R. S. Macomber, *J. Org. Chem.*, **38**, 1369 (1973).
(19) When excess acid chloride is used, addition of a few pellets of sodium hydroxide helps dissolve the copper salts.
(20) J. R. A. Pollock and R. Stevens, Ed., "Dictionary of Organic Compounds", Oxford University Press, London, 1965.

Methylation of Thioanisoles and Anilines by 1-Methyl-2,5-diphenyl-1,4-dithiinium Tetrafluoroborate. Kinetics and Correlations[1]

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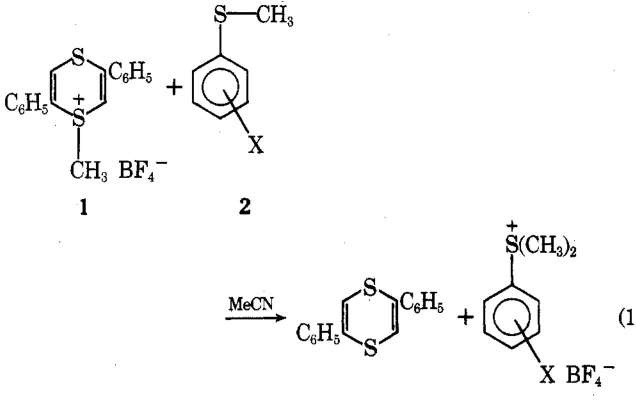
Received March 1, 1976

The kinetics of methyl transfer from 1-methyl-2,5-diphenyl-1,4-dithiinium tetrafluoroborate (1) to a series of thioanisoles (2) and to a comparable series of anilines (5) have been followed spectrophotometrically in acetonitrile under pseudo-first-order conditions at four temperatures for each compound. Derived second-order rate constants, Arrhenius equation constants, and activation thermodynamic parameters have been calculated for intra- and interseries comparison. Both series exhibited well-defined Hammett correlations ($\rho_S = -1.58 \pm 0.04$; corr coeff = 0.999 for the thioanisoles, and $\rho_N = -1.95 \pm 0.05$; corr coeff = 0.998 for the anilines) in which the ρ values were essentially constant over the range 25–80 °C. Specific rate constants for the thioanisole set ($k_S{}^X$) correlated well with those of the aniline set ($k_N{}^X$) via a linear equation: $\log k_S{}^X = m \log k_N{}^X +$ constant, where the slope m is approximated by the ratio of Hammett ρ values (ρ_S/ρ_N). Comparisons with literature data show that dimethyl sulfate is 2.3 times as reactive as 1 toward the thioanisoles, and that 1 is about 10 times as reactive as MeI toward the anilines.

Transmethylation reactions,[3,4] which play a normal role in the cobalamin-dependent biosynthesis of methionine[5] and in the transfer of intact methyl groups from *S*-adenosyl-L-methionine to various receptor substrates,[6] appear to be universally important in biological systems. In addition to the enzyme specificities involved, such reactions apparently depend upon a subtle interplay of relative nucleophilicities of nitrogen, sulfur, oxygen, and cobalt moieties which are not yet well understood. The very concept of nucleophilicity, considered as kinetic basicity, has defied precise quantification and various equations in the literature have been shown to be of limited value for predicting relative nucleophilic reactivity.[7] Some qualitative comparisons of the relative nucleophilicities of S, N, and Co in methyl transfers have been reported by Schrauzer[8] who used simple methylsulfonium, -ammonium, and -cobaloxime models. More recently, Coward and Sweet[9] provided the first detailed kinetic study of methyl transfer from substituted aryldimethylsulfonium perchlorates to various anionic and amine nucleophiles.

In our laboratory we have been particularly interested in the nucleophilicity of bivalent sulfur. Qualitatively, it is well known that simple dialkyl sulfides are easily methylated by methyl iodide, sulfate, or sulfonates to give the corresponding sulfonium salts.[10] Compounds such as thioanisole (2, X = H) or diphenyl sulfide, in which bivalent sulfur is bonded to one or two sp^2 carbons, are alkylated with more difficulty, requiring either methyl sulfate at elevated temperatures or methyl iodide in the presence of equimolar amounts of mercuric iodide,[11] silver tetrafluoroborate,[12] silver perchlorate, or silver 2,4,6-trinitrobenzenesulfonate.[13] These reagents all have limited scope for comparative kinetic studies, and indeed kinetic data in the literature are sparse. Second-order rate constants for the reactions of several dialkyl sulfides with methyl iodide have been reported by Pearson,[7] and a Hammett correlation for methylation of a series of substituted thioanisoles with dimethyl sulfate in benzyl alcohol at 45.2 °C has been published by Gosselck and Barth.[14]

We now wish to report a kinetic study of the methylation of variously substituted thioanisoles (2) and anilines (5) by 1-methyl-2,5-diphenyl-1,4-dithiinium tetrafluoroborate (1),[15] a parallel set of systems (eq 1 and 2, respectively) selected to measure the relative nucleophilicities of bivalent sulfur vis-à-vis trivalent nitrogen of a comparable reference series.



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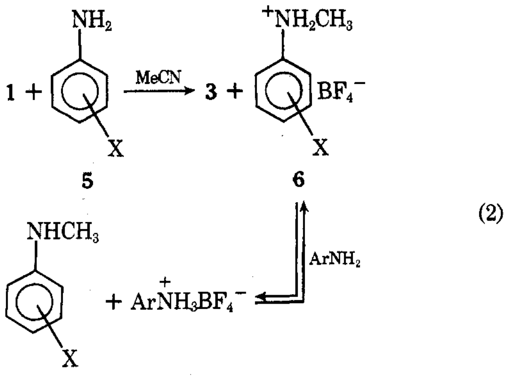

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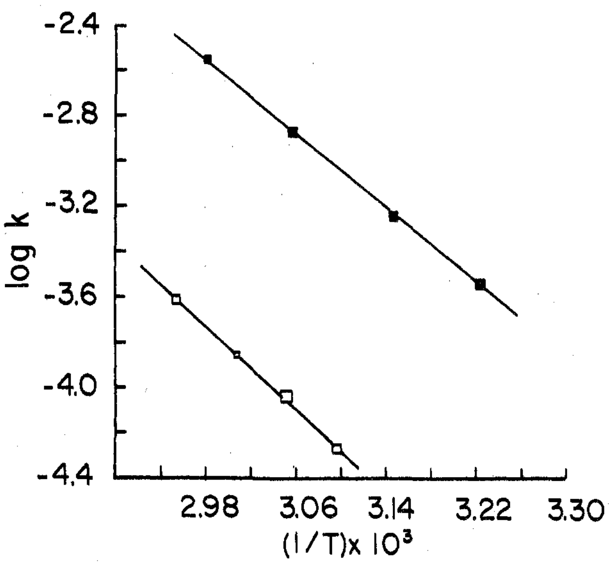


Figure 1. Representative Arrhenius plots for reaction of 1-methyl-2,5-diphenyl-1,4-dithiinium tetrafluoroborate (1) with thioanisole (□) and with aniline (■). Second-order rate constants, k ($M^{-1}\ s^{-1}$), at various temperatures T (K), were determined in acetonitrile.

Table I. Second-Order Rate Constants for Reaction of 1 with Thioanisole at 65.3 ± 0.3 °C

[1], M	24.15×10^{-5}	38.19×10^{-5}	34.68×10^{-5}
[C_6H_5SMe], M	1.014	0.8685	0.5018
$10^4\ k_2$, $M^{-1}\ s^{-1\,a}$	2.35 ± 0.03	2.43 ± 0.02	2.39 ± 0.04

[a] Average of two runs.

Results

A preliminary, preparative scale reaction of the dithiinium salt (1) with thioanisole (**2**, X = H) afforded a high yield (91%) of 2,5-diphenyl-1,4-dithiin (**3**) and dimethylphenylsulfonium tetrafluoroborate (**4**, X = H). Similarly, reaction of **1** with aniline in 16.5-fold excess showed the products to be **3** in 96% yield and N-methylaniline. VPC analysis of these last products showed only a minor trace of dimethylaniline, resulting from secondary alkylation.

Kinetic studies of the reactions of 1-methyl-2,5-diphenyl-1,4-dithiinium tetrafluoroborate (**1**) with thioanisoles and anilines were carried out spectrophotometrically at various temperatures in acetonitrile under pseudo-first-order conditions with the nucleophile present in 10^2- to 10^3-fold excess. The derived second-order rate constants were independent of nucleophile concentration, as illustrated by representative data in Table I, and are completely summarized in the Experimental Section (Table VII). Representative Arrhenius plots for the two series are shown in Figure 1. Rate constants calculated at 330 K and activation thermodynamic parameters at 330 K are summarized in Table II. Hammett plots[16] (Figure 2) gave ρ values of -1.58 ± 0.05 (correlation coefficient 0.999) and -1.92 ± 0.06 (correlation coefficient 0.998) for the thioanisole and aniline series, respectively, at 330 K. The resulting array of data provided a basis for computation of second-order rate constants at selected common temperatures for comparison and correlation.

Discussion

It is well known that the Hammett ρ, defined in eq 3

$$\log \frac{k^{X}}{k^{H}} = \sigma_X \rho \tag{3}$$

provides a measure of the susceptibility of a reaction to variation of substitutents on a reactant.[16,17] According to Jaffe[16] the three main factors which determine this susceptibility are (a) the reaction conditions, including solvent and temperature effects; (b) the transmission of electrical effects of substituent X to the reaction site; and (c) the susceptibility of the reaction to changes in electron density at the reaction site.

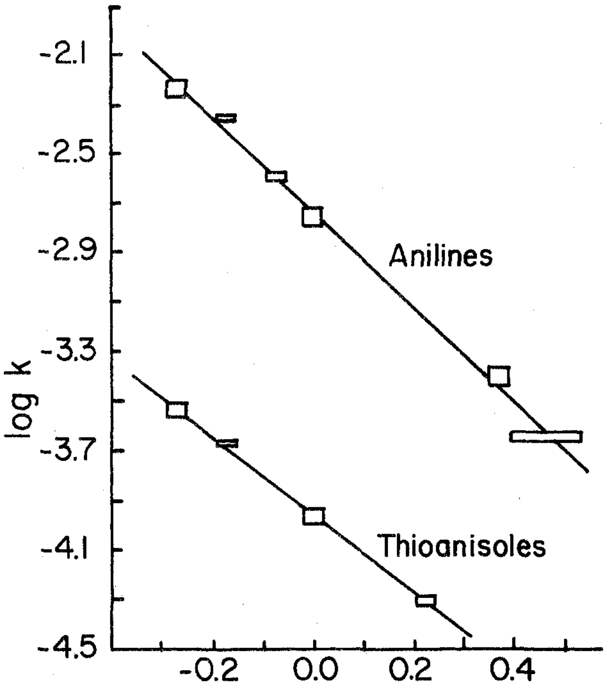


Figure 2. Hammett plots for the reactions of 1-methyl-2,5-diphenyl-1,4-dithiinium tetrafluoroborate (1) with thioanisoles ($\rho_S = -1.58 \pm 0.05$) and with anilines ($\rho_N = -1.92 \pm 0.06$) at 330 K. Error blocks show standard deviations.

In the present study the reaction conditions were essentially identical. However, unlike the thioanisoles (**2**), the anilines (**5**) may be capable of hydrogen bonding with other aniline molecules and possibly with the solvent acetonitrile. The self-association of aniline has been studied by others[18] and does not appear to be significant at the concentrations used in this study. No data for the interaction of anilines with acetonitrile appear to be available. However, reactions of the dithiinium salt (**1**) with N-methylaniline and with N,N-dimethylaniline show second-order rate constants and activation thermodynamic parameters (cf. Table II) very similar to those of aniline itself suggesting that no significant H-bonding interactions occur in the system used.

Variations in the temperature dependence of ρ have been discussed by Wells[17] and others,[16,21] and are given, for the general case, by eq 4[17]

$$\rho = \frac{G_0}{T}\left(\frac{\partial \Delta G^{\ddagger}}{\partial \sigma}\right) \tag{4}$$

in which G_0 is a constant and the partial derivative $[\partial\Delta G^{\ddagger}/\partial\sigma = (\partial\Delta H^{\ddagger}/\partial\sigma) - T(\partial\Delta S^{\ddagger}/\partial\sigma)]$ is also temperature dependent, except for the few known cases where the reaction series are isoentropic. A comparison of the activation parameters in Table II shows that the activation processes for the thioanisole series are isoenthalpic ($\Delta H^{\ddagger}$ = 20.4 kcal/mol) within experimental error, hence ρ should be temperature invariant.[17,21] The aniline series is not so well defined, and a plot of activation enthalpies vs. entropies also shows no isokinetic relationship.[17,21] Values of ρ for both series were calculated at four temperatures in the range 25.0–80.0 °C and found to be constant [$\rho_S = -1.58 \pm 0.04$ (thioanisoles) and $\rho_N = -1.95 \pm 0.05$ (anilines)] within experimental error.

Table II. Activation Parameters and Rate Constants at 330 K[a]

Registry no.	Compd	$10^4 k$,[b] $M^{-1} s^{-1}$	$\Delta H^{\ddagger}$,[c] kcal/mol	$\Delta G^{\ddagger}$,[d] kcal/mol	$\Delta S^{\ddagger}$,[e] eu	σ[f,g]
123-09-1	*p*-Chlorothioanisole	0.488 ± 0.005	20.4 ± 0.2	25.89 ± 0.01	−16.6 ± 0.6	+0.227 ± 0.02
100-68-5	Thioanisole	1.07 ± 0.02	20.4 ± 0.9	25.38 ± 0.02	−15.1 ± 2.9	0
623-13-2	*p*-Methylthioanisole	2.15 ± 0.02	20.0 ± 0.2	24.92 ± 0.01	−14.9 ± 0.5	−0.17 ± 0.02
1879-16-9	*p*-Methoxythioanisole	2.87 ± 0.12	20.8 ± 0.7	24.73 ± 0.03	−11.9 ± 2.1	−0.268 ± 0.02
98-16-8	α,α,α-Trifluoro-*m*-toluidine	2.27 ± 0.06	18.6 ± 0.3	24.89 ± 0.02	−19.4 ± 0.9	+0.467 ± 0.071[g]
108-42-9	*m*-Chloroaniline	3.86 ± 0.06	19.1 ± 0.2	24.54 ± 0.01	−16.5 ± 0.6	+0.373 ± 0.02
62-53-3	Aniline	16.7 ± 0.3	17.8 ± 0.2	23.58 ± 0.02	−17.7 ± 0.7	0
108-44-1	*m*-Toluidine	24.9 ± 0.3	18.9 ± 0.1	23.32 ± 0.01	−13.3 ± 0.4	−0.069 ± 0.02
106-49-0	*p*-Toluidine	44.0 ± 0.9	18.5 ± 0.2	22.94 ± 0.01	−13.5 ± 0.7	−0.170 ± 0.02
104-94-9	*p*-Anisidine	57.9 ± 2.0	16.4 ± 0.4	22.76 ± 0.02	−19.6 ± 1.3	−0.268 ± 0.02
100-61-8	*N*-Methylaniline	31.9 ± 1.3	18.5 ± 0.7	23.15 ± 0.03	−14.4 ± 2.0	
121-69-7	*N*,*N*-Dimethylaniline	27.5 ± 1.3	17.4 ± 0.6	23.25 ± 0.03	−17.7 ± 1.8	

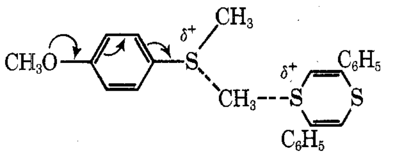
[a] All errors are standard deviations. [b] Calculated by Arrhenius equation: $\log k = (-E_{act}/2.3RT) + \log A$. [c] $\Delta H^{\ddagger} = E_{act} - RT$. [d] $k' = (kT/h)\,e^{-\Delta G^{\ddagger}/RT}$. [e] $\Delta S^{\ddagger} = (\Delta H^{\ddagger} - \Delta G^{\ddagger})/T$. [f] All values except CF_3 were taken from D. McDaniel and H. Brown, *J. Org. Chem.*, **23**, 420 (1958). [g] H. van Bekkum, P. Verkade, and B. Wepster, *Recl. Trav. Chim. Pays-Bas*, **78**, 815 (1959).

Table III. Second-Order Rate Constants ($M^{-1} s^{-1}$) and Differences in Activation Free Energy for Methylation of Thioanisoles (k_S^X) and Anilines (k_N^X) with 1 at 330 K

Substituent X	$10^4 k_S^X$	$10^4 k_N^X$	$\Delta\Delta G^{\ddagger}$, kcal/mol
p-MeO	2.87	57.9	1.97
p-Me	2.15	44.0	1.98
m-Me	(1.38)[a]	24.9	1.89
H	1.07	16.7	1.80
p-Cl	0.488	(6.13)[a]	1.65

[a] Interpolated data calculated from Hammett plots.

As mentioned in item b above, ρ is also determined by the balance of field, inductive, and resonance contributions[19] by which the electrical effect of substituent X is transmitted to the reaction site. In the present study only *p*-methoxythioanisole might have been expected to show unusual stabilization of the transition state via d-orbital conjugation of partially positive sulfur with the methoxy group, as suggested in the following approximation of the transition state structure



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(8). Since all of the substituents, including methoxy, correlated well with primary para (σ_p) and meta (σ_m) substituent constants, the ρ values for both the thioanisole and aniline series reflect parallel differences in their respective susceptibilities to substituent electrical effects.[20] Hence any special conjugation via d-orbital interaction is contraindicated.

Finally, the magnitude of ρ (cf. item c, above) is considered to be a measure of the magnitude of the developing charge at the reaction site.[21] In the present comparison there appears to be no qualitative difference between the behavior of the lone pair of electrons on sulfur or nitrogen, since the ρ values are quite similar. The slightly less negative value of ρ for the thioanisoles with respect to the anilines may simply reflect a more diffuse positive charge on the sulfur than that on the smaller nitrogen atom in their respective transition states.

Rate Correlations. Common Electrophile. A qualitative comparison of the specific rates of methylation of analogous thioanisoles and anilines shows that the ratios k_S^X/k_N^X (substituent X; S and N for the sulfur and nitrogen nucleophiles, respectively) range roughly from 0.02 to 0.04 at 25 °C, tending to increase at higher temperatures. These values are comparable with similar ratios obtained from Pearson's data[7] for reactions of methyl iodide with aliphatic sulfides and amines; e.g. $k_S/k_N = 0.034$ for tetrahydrothiopyran and piperidine at 25 °C.

On the basis of absolute reaction rate theory, for which the familiar equation $k' = (kT/h) \exp(-\Delta G^{\ddagger}/RT)$ applies, such rate ratios are given by

$$k_S^X/k_N^X = \exp(-\Delta\Delta G^{\ddagger}/RT) \qquad (5)$$

where $\Delta\Delta G^{\ddagger}$ is the difference in activation free energy of two series members having given substituent X. This relationship suggested that if $\Delta\Delta G^{\ddagger}$ is approximately constant for all substituents X, a simple linear relationship of the form $k_S^X = mk_N^X + b$ may be applicable, in which the slope (m) should be approximated by the right-hand portion of eq 5 and b is a constant. Table III gives data at 330 K which clearly illustrate the variation in $\Delta\Delta G^{\ddagger}$. Despite this variation a least-squares regression line [$k_S^X = (0.0446 \pm 0.0013)k_N^X + (2.58 \pm 0.48)\ 10^{-5}$] showed an excellent correlation (coefficient $r = 0.998$), and a slope only slightly lower than expected from eq 5 [$\exp(-\Delta\Delta G^{\ddagger}/RT) = 0.059$] using a mean value of $\Delta\Delta G^{\ddagger}$ from Table III. However, similar data from other temperatures showed greater variations in $\Delta\Delta G^{\ddagger}$ and gave lines showing a distinct curvature, thus obviating broad correlation over the whole range of data. We therefore turned to the Hammett equation.

Since both the thioanisoles and anilines separately obey the Hammett relationship (eq 3) using the same primary σ_x values, elimination of σ_x between the two series equations leads to

$$\log k_S^X = \frac{\rho_S}{\rho_N} \log k_N^X + \left(\log k_S^H - \frac{\rho_S}{\rho_N} \log k_N^H\right) \qquad (6)$$

in which the rate constants k^X cover all members of the series including $k^X = k^H$, and the intercept (in parentheses) is defined by the specific rates of the parent thioanisole and aniline. A plot of eq 6 is illustrated in Figure 3 for data at 56.8 °C, which falls within the range of the experimental rate determinations, and shows a correlation coefficient of greater than 0.999. A similar plot at 45.2 °C showed a correlation coefficient of 0.998. Although the slopes of both lines are slightly lower than expected from the ratio $\rho_S/\rho_N = -1.58/-1.95 = 0.81$ (calculated assuming both ρ values to be constant as discussed

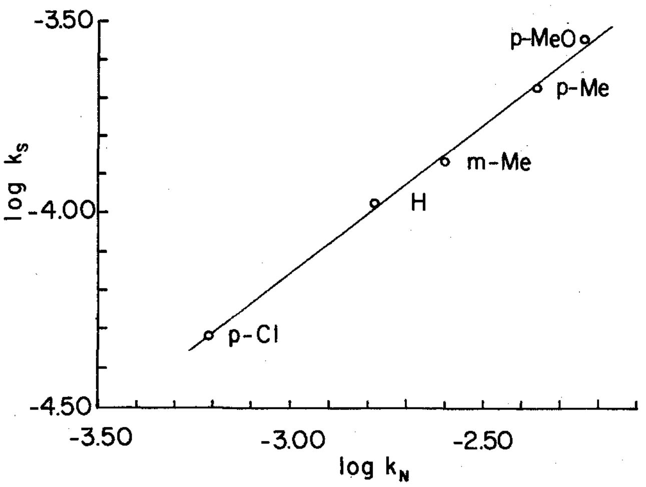


Figure 3. Logarithmic correlation of second-order rates of methylation of thioanisoles (k_S) and anilines (k_N) by 1-methyl-2,5-diphenyl-1,4-dithiinium tetrafluoroborate (1) in MeCN at 330 K, following eq 6. The regression line: $\log k_S = (0.775 \pm 0.019) \log k_N - (1.826 \pm 0.045)$ shows a correlation coefficient >0.999.

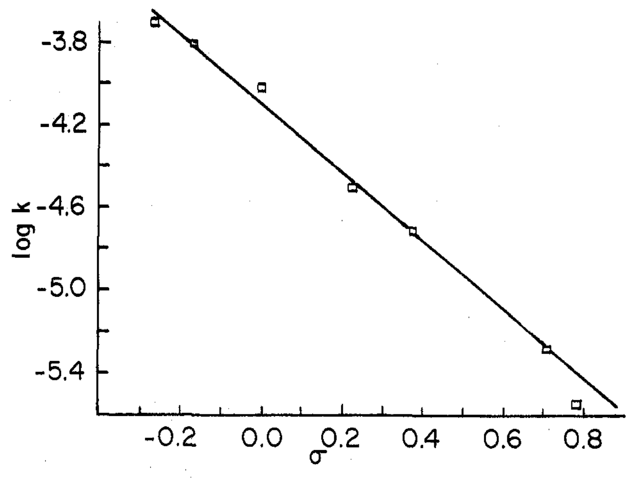


Figure 4. Hammett plot ($\rho = -1.67 \pm 0.06$) for the reaction of dimethyl sulfate with thioanisoles in benzyl alcohol at 45.2 °C. Recalculated from the data of V. Gosselck and H. Barth, *Z. Naturforsch. B*, **16**, 280 (1961). Substituents (reading left to right) are *p*-MeO, *p*-Me, H, *p*-Cl, *m*-Cl, *m*-NO_2, *p*-NO_2.

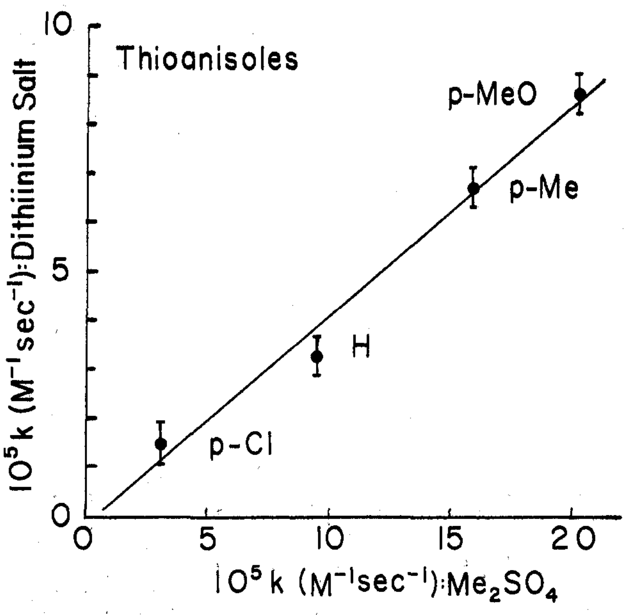


Figure 5. Direct linear relationship: $k_1 = (0.43 \pm 0.03)\, k_{Me_2SO_4} - (0.156 \pm 0.43)\, 10^{-5}$, between the rates of methylation of thioanisoles by 1-methyl-2,5-diphenyl-1,4-dithiinium tetrafluoroborate (1) in MeCN and by dimethyl sulfate in benzyl alcohol at 45.2 °C; correlation coefficient = 0.992; data from Table V.

earlier), the correlation based on eq 6 was quite satisfactory and found to be equally applicable at other temperatures.

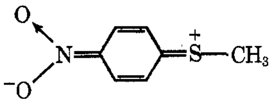
It is of further interest that a parallel application of the Swain–Scott equation[22] to reactions of thioanisoles and anilines with a common electrophile such as compound 1 leads to eq 7, where k_0 is the rate constant of an arbitrary reference nucleophile and n_S^X and n_N^X are nucleophilic reactivity parameters for structurally comparable sets of thioanisoles and anilines, respectively.

$$\log k_S^X = \frac{n_S^X}{n_N^X} \log k_N^X + \left[\left(1 - \frac{n_S^X}{n_N^X}\right) \log k_0\right] \quad (7)$$

The slope (n_S^X/n_N^X) of eq 7 represents the relative nucleophilicity of the thioanisoles with respect to the structurally comparable anilines based on a reference nucleophile defined only numerically by k_0 of the intercept term. Although this reference nucleophile is not chemically defined, it is apparent that, since the slopes of eq 6 and 7 are the same (i.e., $\rho_S/\rho_N = n_S^X/n_N^X$); the ratio of ρ values of the thioanisoles with respect to the analogous anilines represents a measure of the relative nucleophilicities of the two series.

Rate Correlations. Diverse Electrophiles. It was of additional interest to compare the rate behavior of a given series of nucleophiles, such as the thioanisoles or anilines, toward different electrophilic alkylating agents. Substituent effects for reactions 1 and 2 from the present study are compared with related series from the literature in Table IV. All values for literature reactions were recalculated using the σ_p and σ_m values of McDaniel and Brown.[23] Although ρ values are not strictly comparable, since ρ is solvent dependent,[16,24] the values for methylation of thioanisoles with dimethyl sulfate and with the dithinium salt (1) are the same within experimental error.

Specific rate constants for reaction 1 and for the parallel alkylation of thioanisoles (2) with dimethyl sulfate[14] at 45.2 °C are summarized in Table V. A Hammett plot of the literature data is illustrated in Figure 4, which shows a significant deviation only for *p*-nitroanisole. Although Gosselck and Barth[14] made no comments about experimental errors, this deviation can probably be ascribed to enhanced resonance interaction involving simple p–π delocalization of the lone pair on sulfur with the nitro group as suggested by the canonical form (9) shown. In any case, since both σ and ρ are the same for both series, the Hammett relationship is simply $\log (k_1/k_{Me_2SO_4})$ = constant, hence $k_1/k_{Me_2SO_4}$ = constant. Consequently, eq 5 based on transition state theory appeared applicable at constant temperature, with $\Delta\Delta G^{\ddagger}$ = constant. A direct plot of k_1 vs. $k_{Me_2SO_4}$ (Figure 5) showed a correlation coefficient of 0.992, a zero intercept within experimental error, and a constant reactivity ratio $k_1/k_{Me_2SO_4} = 0.43$. Alternately, dimethyl sulfate is 2.3 times as reactive as the dithiinium salt (1) in the alkylation of a given thioanisole.



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A similar comparison of the rates of alkylation of substituted anilines by the dithiinium salt (1) and by methyl iodide is illustrated in Figure 6, based on the data of Table VI. In order to make a comparison with literature data at 80 °C it was necessary in this case to extrapolate our kinetic data about 20

Table IV. Comparison of ρ Values for Methylation of Substituted Anilines and Thioanisoles

Methyl donor	Methyl acceptor	Solvent	Temp, °C	ρ^a	Corr coeff	No. of points
CH_3I	$XC_6H_4NH_2$	$PhNO_2$	80	-2.14 ± 0.13^b	0.993	6
Dithiinium salt (1)	$XC_6H_4NH_2$	CH_3CN	80	-1.83 ± 0.11^c	0.993	6
Dithiinium salt (1)	$XC_6H_4SCH_3$	CH_3CN	80	-1.60 ± 0.03^c	0.9997	4
$(CH_3)_2SO_4$	$XC_6H_4SCH_3$	$PhCH_2OH$	45.2	-1.67 ± 0.06^d	0.998	6
Dithiinium salt (1)	$XC_6H_4SCH_3$	CH_3CN	45.2	-1.57 ± 0.07^c	0.998	4

[a] Error is standard error. [b] Calculated from data of P. Randhakrishnamurti and L. Panigrahi, *J. Indian Chem. Soc.*, **46,** 567 (1969). [c] This work. [d] V. Gosselck and H. Barth, *Z. Naturforsch. B*, **16,** 280 (1961). Does not include p-NO_2. These authors incorrectly reported ρ as −1.14.

Table V. Comparison of Methylation of Substituted Thioanisoles with Dimethyl Sulfate and 1-Methyl-2,5-diphenyl-1,4-dithiinium Tetrafluoroborate (1) at 45.2 °C

Substituent	Dimethyl sulfate[a] $10^5 k$, l./mol·s	1,[b,c] $10^5 k$, l./mol·s	σ^d
p-NO_2	0.283		+0.778
m-NO_2	0.520		+0.710
m-Cl	1.93		+0.373
p-Cl	3.10	1.51	+0.227
H	9.50	3.32	0
p-CH_3	15.9	6.77	−0.170
p-CH_3O	20.3	8.66	−0.268

[a] V. Gosselck and H. Barth, *Z. Naturforsch. B*, **16,** 280 (1961). Solvent: benzyl alcohol. [b] This work. Solvent: acetonitrile. [c] Computed from Arrhenius equation. [d] All values from D. McDaniel and H. Brown, *J. Org. Chem.*, **23,** 420 (1958).

Table VI. Comparison of Methylation of Substituted Anilines with Methyl Iodide and 1-Methyl-2,5-diphenyl-1,4-dithiinium Tetrafluoroborate (1) at 80 °C

Substituent	Methyl iodide[a] $10^4 k$, l./mol·s	1,[b,c] $10^4 k$, l./mol·s	σ^d
m-CF_3		15.4	$+0.467 \pm 0.071^e$
m-Br	1.94		$+0.391 \pm 0.02$
m-Cl	1.57	27.8	$+0.373 \pm 0.02$
p-Cl	3.26		$+0.227 \pm 0.02$
H	9.22	106	0
m-CH_3	16.0	176	-0.069 ± 0.02
p-CH_3	28.0	298	-0.170 ± 0.02
p-CH_3O		318	-0.268 ± 0.02

[a] P. Randhakrishnamurti and G. Panigrahi, *J. Indian Chem. Soc.*, **46,** 567 (1969). Solvent: nitrobenzene. [b] This work. Solvent: acetonitrile. [c] Computed by Arrhenius equation. [d] All values except m-CF_3 from D. McDaniel and H. Brown, *J. Org. Chem.*, **23,** 420 (1958). [e] H. van Bekkum, P. Verkade, and B. Wepster, *Recl. Trav. Chim. Pays-Bas*, **78,** 815 (1959).

°C beyond the range of experimental determinations by using individual Arrhenius equations. Furthermore, since only four substituents among the two sets were directly comparable without still further, and inappropriate, extrapolation based on the Hammett equation, the high correlation coefficient (0.999) probably exaggerates the agreement. Nevertheless, except for the low intercept, which cannot be precisely explained, the rate constants for alkylation of anilines with 1 and with methyl iodide again appear to be a simple linear function. Overall, the dithiinium salt (1) is about ten times as reactive as methyl iodide toward the anilines.

Finally, it is noteworthy that, although the activation energy for the reaction of aniline with methyl iodide (E_{act} = 8.77 kcal/mol) is much smaller than for similar alkylation with the S-methyl dithiinium salt (1) (E_{act} = 18.4 kcal/mol), the activation entropy at 80 °C is vastly more negative for the methyl iodide ($\Delta S^{\ddagger} = -49.9$ eu) reaction than for the reaction of the sulfonium alkylating agent (1: $\Delta S^{\ddagger} = -17.8$ eu). This entropy difference may reflect a greater degree of bonding between the nucleophilic center and the methyl group in methyl iodide, as also implied by the more negative ρ values (cf. Table IV), or alternately may indicate less constraint in the approach route of the nucleophile attacking the carbon of the methylsulfonium system (1).[25]

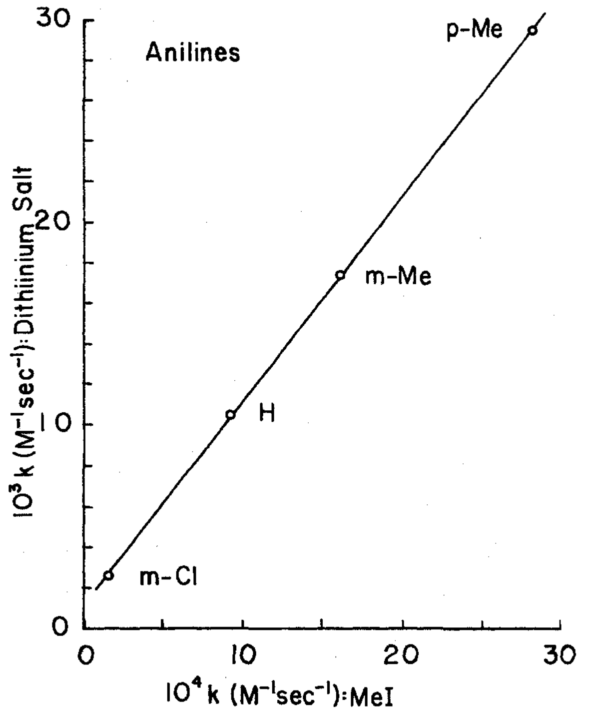

Figure 6. Linear relationship: $k_1 = (10.23 \pm 0.02)\, k_{MeI} + (11.9 \pm 0.3)\ 10^{-4}$; corr coeff >0.999, between the rates of methylation of anilines by 1-methyl-2,5-diphenyl-1,4-dithiinium tetrafluoroborate (1) in MeCN and by methyl iodide in nitrobenzene at 80 °C; data from Table VI.

Experimental Section

Apparatus. Ultraviolet spectra and kinetic data were obtained with a Perkin-Elmer 402 uv–visible spectrophotometer fitted with a cast iron cell block. Constant temperature (±0.03 °C) was maintained by circulating water from a Forma-Temp Jr. constant temperature bath and circulator through a jacketed 1-cm sample cell and the cell block. Reaction temperatures were read (±0.3 °C) from a calibrated thermometer in the cell block. NMR spectra were recorded on a Hitachi Perkin-Elmer R-20A spectrometer. VPC analyses were carried out with a Nester-Faust Anakro IA chromatograph fitted with a silicone SE-30 column. Melting points were determined in capillary tubes using a calibrated Mel-Temp apparatus.

Table VII. Effect of Temperature on the Rate of Methylation of Nucleophiles by 1

Temp, ±0.3 °C	$10^4 k_2$, l./mol·s	Temp, ±0.3 °C	$10^4 k_2$, l./mol·s
	Aniline		*N*-Methylaniline
37.1	2.85 ± 0.06	40.2	6.70 ± 0.13
44.8	5.62 ± 0.10	48.6	15.8 ± 0.7
54.0	13.0 ± 0.4	53.7	23.0 ± 0.8
62.2	26.5 ± 0.5	59.0	39.1 ± 3.5
	m-Chloroaniline		*N,N*-Dimethylaniline
41.1	0.855 ± 0.018	36.8	4.63 ± 0.17
48.9	1.85 ± 0.07	40.0	6.03 ± 0.04
56.7	3.73 ± 0.11	48.6	14.5 ± 0.2
63.4	7.04 ± 0.14	56.6	26.0 ± 0.2
	p-Toluidine		Thioanisole
31.5	3.85 ± 0.02	50.0	0.535 ± 0.014
40.3	9.37 ± 0.02	54.6	0.890 ± 0.054
49.3	22.9 ± 0.6	59.6	1.37 ± 0.06
56.9	43.3 ± 0.6	65.3	2.40 ± 0.05
	p-Anisidine		*p*-Methylthioanisole
39.0	12.7 ± 0.6	48.7	0.964 ± 0.025
44.7	22.5 ± 0.4	54.6	1.72 ± 0.04
47.9	28.2 ± 1.1	60.5	3.07 ± 0.03
56.9	56.3 ± 1.0	67.0	5.45 ± 0.09
59.5	72.0 ± 1.0		*p*-Chlorothioanisole
	α,α,α-Trifluoro-*m*-toluidine	54.5	0.389 ± 0.010
43.8	0.693 ± 0.023	59.6	0.638 ± 0.010
49.8	1.14 ± 0.04	64.3	0.976 ± 0.019
56.7	2.21 ± 0.06	69.9	1.67 ± 0.03
63.4	4.02 ± 0.05		*p*-Methoxythioanisole
65.3	4.71 ± 0.06	49.3	1.28 ± 0.02
	m-Toluidine	54.8	2.46 ± 0.05
37.4	3.81 ± 0.04	60.1	4.00 ± 0.03
44.8	8.01 ± 0.13	67.0	7.44 ± 0.23
51.4	15.3 ± 0.5		
59.2	30.4 ± 0.5		

Materials. 1-Methyl-2,5-diphenyl-1,4-dithiinium tetrafluoroborate (1) was prepared by the method of Young and Lazarus.[15] The amines, which were commercially available, were purified either by distillation under reduced pressure or by recrystallization followed by sublimation. All of the sulfides except *p*-methoxythioanisole were commercial products purified by distillation under reduced pressure. *p*-Methoxythioanisole was prepared according to the procedure of Bordwell and Pitt[26] and was distilled under reduced pressure to give pure product with a boiling point in agreement with literature values. Acetonitrile (Fisher Certified) was distilled three times from phosphorus pentoxide.

Acetonitrile solutions of the dithiinium salt (1) were stable indefinitely at room temperature and for at least 24 h at 66 °C, which represents the upper limit of temperature for these studies. Solutions of 2,5-diphenyl-1,4-dithiin (3) at 66 °C likewise showed no ultraviolet absorbance change for at least the several hours necessary to monitor the aniline reactions. Literature reports of failure of amines to react with acetonitrile[27,28] were confirmed by observing no change in the NMR spectrum of a 1.5 M solution of aniline in acetonitrile at 63 °C overnight. Therefore, competing reactions under the conditions used to study the methylation of anilines are insignificant. In contrast, solutions of the dithiin (3) and thioanisole showed a steady increase in absorbance over a period of hours at 66 °C which would complicate the study of the slower reacting thioanisoles. Apparently this increase was due to oxidation, since careful flushing of the solutions for the thioanisole kinetics with dry nitrogen eliminated the problem.

Identification of Products. Reaction of 1 with Aniline. Six grams (0.0162 mol) of 1-methyl-2,5-diphenyl-1,4-dithiinium tetrafluoroborate (1) and 25.0 g (0.268 mol) of aniline were heated at 78 °C for 3 h. The solution was cooled and the precipitated 2,5-diphenyl-1,4-dithiin (3) was removed by filtration. After it was concentrated on a rotary evaporator, an approximately 0.1 M solution of HCl was added to the filtrate to precipitate the remaining 2,5-diphenyl-1,4-dithiin (3), which was combined with the previous material to give a total yield of 4.15 g (96%). Ammonium hydroxide was then added to separate an amine layer which was extracted into ether and distilled from calcium hydride. VPC analysis showed the mixture to be aniline and *N*-methylaniline with only a trace of *N,N*-dimethylaniline.

Reaction of 1 with Thioanisole. A solution of 0.50 g (0.0014 mol) of 1-methyl-2,5-diphenyl-1,4-dithiinium tetrafluoroborate (1) and 0.25 g (0.002 mol) of thioanisole in 1 ml of acetonitrile was maintained at 65 °C for 18 h. Concentration of the solution led to precipitation of 0.30 g of crude 2,5-diphenyl-1,4-dithiin (3). Addition of ether precipitated 0.24 g (79%) of a white solid with mp 131–132.5 °C. Evaporation of the filtrate to near dryness allowed the collection of another 0.03 g of 3 to give a total crude yield of 0.33 g (91%), which after one recrystallization from absolute ethanol weighed 0.20 g (55%) with mp 114–116 °C (lit.[29] mp 115–117 °C). Recrystallization of the hygroscopic white solid from acetonitrile–ether and drying in vacuo with phosphorus pentoxide gave analytically pure dimethylphenylsulfonium tetrafluoroborate with mp 132.5–133.5 °C; NMR (CD_3CN) δ 3.17 (s, 6, CH_3's), 7.8 ppm (m, 5, ArH).

Anal. Calcd for $C_8H_{11}BF_4S$: C, 42.51; H, 4.91; S, 14.18. Found: C, 42.59; H, 4.95; S, 14.11.

Kinetic Measurements. The progress of the reactions described herein was followed by observing the decrease in ultraviolet absorbance at 340 nm. Beer's law plots of the 2,5-diphenyl-1,4-dithiin (3) and 1-methyl-2,5-diphenyl-1,4-dithiinium tetrafluoroborate (1) were linear and passed through the origin. A least-squares computer procedure gave molar extinction coefficients (ε) of 1.05×10^3 and 4.72×10^3 for the dithiin (3) and the dithiinium salt (1), respectively. Since the reactions were run with an initial dithiinium salt concentration ($S_{t=0}$) of about 20×10^{-5} M and a nucleophile concentration (N) of about 0.01–1.0 M, the integrated rate equation is given by eq 8 following, where S_t = molar concentration of dithiinium salt (1) and D_t = molar concentration of dithiin (3) at time t.

$$\ln \frac{S_{t_1}}{S_{t_2}} = kN(t_2 - t_1) \tag{8}$$

Since

$$A_t = \epsilon_S S_t + \epsilon_D D_t \text{ and } D_t = S_{t=0} - S_t,$$

$$A_t = S_t(\epsilon_S - \epsilon_D) + \epsilon_D S_{t=0} \text{ or } S_t = \frac{(A_t - \epsilon_D S_{t=0})}{\epsilon_S - \epsilon_D}$$

Substitution of this latter equation for S_t into eq 8 gives the final rate equation 9.

$$\ln \frac{A_{t_1} - \epsilon_D S_{t=0}}{A_{t_2} - \epsilon_D S_{t=0}} = kN(t_2 - t_1) \tag{9}$$

Pseudo-first-order plots of ln $(A_t - \epsilon_D S_{t=0})$ vs. time were linear to 2–4 half-lives and both the aniline and thioanisole reactions were found to go essentially to completion. Any absorbance due to the nucleophiles was cancelled by placing in the reference beam a solution of nucleophile of exactly the same concentration as that in the reaction solution. All kinetic determinations were made in triplicate with agreement usually better than ±5%.

Stock solutions of the dithiinium salt (1) and the nucleophile were prepared in the bath. The reaction was started by pipetting a known volume of the dithiinium salt solution into a 10-ml volumetric flask and diluting to the mark with the stock nucleophile solution. In the case of the thioanisole series reactions, dry nitrogen was slowly bubbled through the stock solutions cooled in an ice bath for ca. 20 min and through the reaction solution for about 10 min before placing it in the sample cell. The nucleophile concentrations were typically 0.01–0.20 M for the aniline series reactions and 0.2–1.0 M for the thioanisole series reactions. In the case of the aniline series the fivefold ordinate expansion system of the spectrophotometer was used and the calculated rate constant was usually based on the first 15–30% of the reaction. The normal ordinate plot was used for the thioanisole series and the rate constants were based on approximately the first 75% of the reaction.

Derived rate constants are summarized in Table VII, with errors given as standard deviations. The temperature error (±0.3 °C) represents the outer limits of control as measured at the cell block. A time-averaged standard deviation of temperature in the reaction cuvette could not be determined directly, but was necessarily less than ±0.3 °C.

Registry No.—**1,** 17250-79-2; *p*-chloroaniline, 106-47-8; *m*-methylthioanisole, 4886-77-5; dimethylphenylsulfonium tetrafluoroborate, 33613-52-4.

References and Notes

(1) Based in part on the Ph.D. Dissertation of Alan R. Oyler, Lehigh University, 1973.
(2) National Science Foundation Trainee, 1970–1973.
(3) D. M. Greenberg, *Adv. Enzymol.*, **25**, 395 (1963).
(4) S. K. Shapiro and F. Schlenk, Ed., "Transmethylation and Methionine Biosynthesis", University of Chicago Press, Chicago, Ill., 1965.
(5) L. Jaenicke and H. Rudiger, *Fed. Proc., Fed. Am. Soc. Exp. Biol.*, **30**, 160 (1971).
(6) V. Zappia, C. Zydek-Cwick, and F. Schlenk, *J. Biol. Chem.*, **244**, 4499 (1969).
(7) R. G. Pearson, H. Sobel, and J. Songstad, *J. Am. Chem. Soc.*, **90** 319 (1968).
(8) G. N. Schrauzer and R. J. Windgassen, *J. Am. Chem. Soc.*, **89**, 3607 (1967).
(9) J. K. Coward and W. D. Sweet, *J. Org. Chem.*, **36**, 2337 (1971).
(10) Houben-Weyl, "Methoden der Organischen Chemie", Vol. 9, Georg Thieme Verlag, Stuttgart, 1955.
(11) J. van der Veen, *Recl. Trav. Chim. Pays-Bas*, **84**, 540 (1965).
(12) V. Franzen, H. Schmidt, and C. Mertz, *Chem. Ber.*, **94**, 2942 (1961).
(13) D. J. Petit and G. K. Helmkamp, *J. Org. Chem.*, **29**, 2702 (1964).
(14) V. Gosselck and H. Barth, *Z. Naturforsch. B*, **16**, 280 (1961).
(15) T. E. Young and R. A. Lazarus, *J. Org. Chem.*, **33**, 3770 (1968).
(16) H. Jaffe, *Chem. Rev.*, **53**, 191 (1953).
(17) P. Wells, *Chem. Rev.*, **63**, 171 (1963); P. Wells, "Linear Free Energy Relationships", Academic Press, New York, N.Y., 1968, pp 20–22.
(18) J. Lady and K. Whetsel, *J. Phys. Chem.*, **68**, 1001 (1964).
(19) M. Dewar and P. Grisdale, *J. Am. Chem. Soc.*, **84**, 3539, 3548 (1962).
(20) L. P. Hammett, "Physical Organic Chemistry", 2d ed, McGraw-Hill, New York, N.Y., 1970, p 357.
(21) J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions", Wiley, New York, N.Y., 1963, Chapter 7, p 177.
(22) C. G. Swain and C. B. Scott, *J. Am. Chem. Soc.*, **75**, 141 (1953).
(23) D. McDaniel and H. Brown, *J. Org. Chem.*, **23**, 420 (1958).
(24) Y. Kondo, T. Matsue, and N. Tokura, *Bull. Chem. Soc. Jpn.*, **42**, 1037 (1969).
(25) Reference 21, p 68.
(26) F. Bordwell and B. Pitt, *J. Am. Chem. Soc.*, **77**, 572 (1955).
(27) L. Exner, M. Hurwitz, and P. Denneville, *J. Am. Chem. Soc.*, **77**, 1103 (1955).
(28) G. Reynolds, W. Humphlett, F. Swamer, and C. Hauser, *J. Org. Chem.*, **16**, 165 (1951).
(29) R. H. Barker and C. Barkenbus, *J. Am. Chem. Soc.*, **58**, 262 (1936).

Reactions of Acyl Thiochlorosulfites

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Received March 2, 1976

p-Chlorobenzoyl thiochlorosulfite (**1b**) reacted with thiophenols or potassium xanthates to give acyl aryl dithiosulfites (**3**) or acylalkoxythiocarbonyl dithiosulfites (**4**). The reaction of 1 mol of **1b** with 1.5 mol of aniline gave bis-*p*-chlorobenzoyl dithiosulfite (**2b**) and *N*-sulfinylaniline, whereas 1 mol of **1b** with 2 mol of aniline afforded *p*-chlorobenzanilide. Carboxylic acids with **1b** in the presence of triethylamine gave carboxylic anhydrides and **2b**. Reaction of **1** with potassium thiocyanate gave acyl isothiocyanates.

Previously, one of the authors has reported the preparation of diacyl dithiosulfites RCOSS(O)SCOR′ (**2**) and acyl thiochlorosulfites RCOSS(O)Cl (**1**) by the reaction of thiocarboxylic acids and thionyl chloride.[1] Although chlorosulfites ROS(O)Cl are readily prepared from thionyl chloride and alcohols, thiochlorosulfites RSS(O)Cl have not been isolated and their formation has been only postulated as intermediates in the reaction of thionyl chloride and mercaptans.[2] Accordingly, it appeared of interest to investigate the reactions of **1** with various nucleophilic reagents. Aroyl thiochlorosulfites (**1**, R = Ar) are more stable than acyl thiochlorosulfites (**1**, R = alkyl) and some of the former could be isolated as crystalline solids. Reactions were then examined with *p*-chlorobenzoyl thiochlorosulfite (**1b**, R = *p*-ClC_6H_4) which was especially stable and convenient to handle.

Results and Discussion

Thiobenzoic acid or *p*-chlorothiobenzoic acid was allowed to react with thionyl chloride at low temperature to give benzoyl thiochlorosulfite[1] (**1a**) or *p*-chlorobenzoyl thiochlorosulfite (**1b**) in 60–80% yield (eq 1). Acyl thiochlorosulfites were readily hydrolyzed to give diacyl dithiosulfites[1] (**2**) in