J. Am. Chem. Soc. 1982, 104, 3491–3497

Cation–Anion Combination Reactions. 21.[1] Reactions of Thiolate Ions, Cyanide Ion, and Amines with Cations and Carbonyl Compounds in Me_2SO Solution

Calvin D. Ritchie,* J. E. VanVerth, and P. O. I. Virtanen

Contribution from the Department of Chemistry, State University of New York at Buffalo, Buffalo, New York 14214. *Received November 2, 1981*

Abstract: The pK_a's of three alkanethiols and of two ammonium ions, and the rates of reactions of the thiolates, amines, and of cyanide ion with Malachite Green, Crystal Violet, 2,4-dinitrophenyl acetate, and 9-acetyl-9-cyanofluorene, all in Me_2SO solution, have been measured. The pK_a's of the thiols in Me_2SO, compared with those in water, indicate important hydrogen bonding of water to the thiolates. The reactions of nucleophiles with both the triarylmethyl cations and 2,4-dinitrophenyl acetate have rate constants that are greater in Me_2SO than in water. The solvent effects on rates are compared with solvent effects on equilibrium constants to arrive at measures of the progress of the transition states toward products as "seen" by solvent. These measures are not in accord with other measures, such as Brønsted slopes, possibly indicating that transition states are not solvated in a manner suggested by stable molecule analogues. The pattern of nucleophilic reactivities toward 9-acetyl-9-cyanofluorene is different from that toward 2,4-dinitrophenyl acetate. A possible rationalization involving concerted reactions of 2,4-dinitrophenyl acetate, but stepwise reactions of the ketone, is discussed.

Although it appears to be generally accepted that both absolute and relative reactivities of nucleophiles are strongly affected by solvent,[2-8] there is surprisingly little data available to allow the development of reasonably detailed theories. Even for the S_N2 reactions of alkyl halides, the most studied in this respect,[2] sufficient data are available only for the reactions of halide ions, azide ion, thiocyanate ion, and acetate ion. Except for azide ion, none of these nucleophiles give measurable equilibria and/or rates for reactions with the relatively stable carbonium ions in which we have been interested.[1]

The major impetus for the present work comes from the above observation. We have chosen Me_2SO, rather than DMF,[2] for the model non-hydrogen-bond-donating solvent for two practical reasons: (1) It is easier to purify Me_2SO to the levels necessary for the study of dilute solutions of basic anions;[9] (2) it is possible to measure pK's of the conjugate acids of nucleophiles in Me_2SO[9] to obtain reliable estimates of the solvent effects on the activities of the nucleophiles.

In the present paper, we report the results of our studies of the reactions of thiolate ions, amines, and cyanide ion with Malachite Green [bis(*p*-dimethylamino)phenyl)phenylmethyl cation], Crystal Violet [tris(*p*-(dimethylamino)phenyl)methyl cation], DNPA (2,4-dinitrophenyl acetate), and ACNF (9-acetyl-9-cyanofluorene), all in Me_2SO solution.

Experimental Section

Materials. Either commercial 99.998% argon of house nitrogen, from liquid nitrogen storage tanks, was used as the inert atmosphere for all of the studies except the pK_a measurements of thiols. These used argon purified by passage through 5-A molecular sieves and Ridox (Fisher Scientific Co.) columns.

Purification of Me_2SO and the preparation of solutions of potassium dimsyl followed Bordwell's procedures.[9] Karl Fischer titration of the purified Me_2SO consistently showed less than 20 ppm water present.

Benzoic acid, *p*-nitrophenol, 2,4-dinitrophenol, and 9-phenylfluorene were commercial materials further purified by recrystallization from ethanol and drying in a vacuum desiccator. Commercial 2,4-dinitrophenyl acetate was recrystallized from heptane and dried in a vacuum desiccator. The potassium salts of *p*-nitrophenol and 2,4-dinitrophenol were prepared by careful neutralization of the phenols with potassium hydroxide in ethanol, evaporation of solvent until crystallization occurred, recrystallization from ethanol, and drying in a vacuum desiccator.

Potassium benzoate was prepared by neutralization of the acid by KOH in ethanol. After evaporation of the solvent, the material was recrystallized from 2-propanol–water and finally dried in an Abderhalden pistol under vacuum at 145 °C (refluxing xylene). The salt was stored and handled under inert atmospheres.

Tetraethylammonium cyanide was obtained from Fluka A.G., recrystallized under nitrogen from 2:1 acetonitrile–ethyl acetate, and dried in a vacuum desiccator. The product was stored and handled under inert atmospheres.

Commercial samples of the alkanethiols were dried over molecular sieves and distilled under nitrogen or vacuum. Purified materials were stored and handled under inert atmospheres. Commercial samples of the amines were dried over solid KOH, distilled under nitrogen, and stored and handled under inert atmospheres.

The preparation of 9-phenylthiofluorene from 9-bromofluorene was carried out as described by Bavin.[10] Fluorenone (*o*-chlorophenyl)hydrazone was a sample kindly supplied by Professor F. G. Bordwell.

Malachite Green and Crystal Violet were used as the fluoborate salts and were available from our earlier work.[8]

9-Acetyl-9-cyanofluorene was prepared from 9-cyanofluorene. The 9-cyanofluorene was obtained as described by Bordwell.[9] In a dry nitrogen atmosphere, 7.3 mmol of sodium hydride in oil dispersion was washed 3 times with pentane; 30 mL of dry, distilled, tetrahydrofuran was added, and then, in portions, 0.90 g (4.7 mmol) of 9-cyanofluorene was added with stirring. The solution was cooled in an ice bath and 0.9 mL (9.5 mmol) of acetic anhydride was slowly added from a syringe over a period of ~0.5 h. The reaction mixture was poured into cold aqueous sodium bicarbonate solution, and after stirring for a few minutes, the precipitated solid was removed by filtration, washed with sodium bicarbonate solution, and dried under vacuum. The crude material was recrystallized twice from cyclohexane to produce 0.42 g of white needles: mp 149.0–149.5 °C; NMR ($CDCl_3$) δ 1.6 (3 H, s), 7.2–7.9 (8 H, m). Anal. Calcd for $C_{16}H_{11}NO$: C, 82.38; H, 4.75; N, 6.01. Found: C, 82.29; H, 4.80; N, 5.98 (Atlantic Microlab, Inc.).

Apparatus. All apparatus used for the prepartion of solutions and pK_a determinations were fitted with three-way stopcocks, allowing inert gas blanketing, as described in detail by Bordwell.[9] The spectrophotometer cell used for the pK_a measurements and slow kinetic studies was similar to one previously described[11] but was modified by the addition of a female glass Luer joint, which accepted a Hamilton Co. three-way Teflon stopcock. In use, a microburet (Gilmont Co.), fitted with a stainless steel needle, was inserted through the stopcock while argon was passed through the third port.

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Table I. pK_a Determinations in Me_2SO Solution[a]

acid	indicator (pK_a)	λ_{max} (log ϵ)[b]	pK_a
CH_3NO_2	9-phenylfluorene (17.9)[c]	408 (4.39)	17.2
$CH_3CH_2CH_2SH$	9-phenylfluorene (17.9)[c]	408 (4.39)	17.0
$HOCH_2CH_2SH$	9-phenylthiofluorene (15.4)[c]	452 (3.28)	15.2
$CH_3O_2CCH_2SH$	fluorenone (*o*-chlorophenyl)hydrazone (12.9)[d]	518 (4.76)	13.0
$CH_3OCH_2CH_2NH_3^+$	*p*-nitrophenol (10.4)[e]	436 (4.55)	9.7

[a] All determinations were at 23 ± 1 °C. [b] Wavelengths are in units of nm and molar absorptivities in units of M^{-1} cm^{-1}. [c] The pK_a's are from ref 9. [d] From ref 16. [e] From ref 15.

The stop-flow spectrophotometers used in the present work are those described in earlier aspects of this series.[12] A Cary Model 14 spectrophotometer was used for the pK_a and slow kinetic studies.

Preparation of Solutions. All solutions were prepared under inert atmospheres by using either glove-bag or gas-tight syringes with three-way stopcock techniques. Thiol solutions were prepared from freshly distilled thiols and were used within 24 h of preparation. Solutions of 2,4-dinitrophenyl acetate in MeSO showed appreciable formation of 2,4-dinitrophenoxide ion within a few hours of preparation; these solutions were used within 1 h after preparation. All other solutions appeared quite stable for at least several days.

pK_a Measurements. The indicator technique described by Bordwell[9] was used, except that amounts of added solutions were measured by volume rather than by weight. Additions of the solutions to the spectrophotometer cell described above were made with a 0.2-mL microburet. The 3–4 mL of Me_2SO for initial filling of the cell was measured with sufficient accuracy with a standard 5-mL gas-tight syringe (Hamilton Co.). A 1.0-cm-pathlength cell was used for the study of hydroxyethanethiol, which employed 9-phenylthiofluorene as the indicator. A 1.0-mm cell pathlength was used for all other measurements. This shorter pathlength cell allowed us to use the wavelengths of maximum absorbance for all of the indicators.

The solutions were initially prepared to contain 3–7 × 10^{-4} M dimsyl ion and a 2- to 4-fold excess of the indicator. These concentrations are low enough to ensure the absence of ion-pairing or homoconjugate formations in the systems studied here.[13]

Kinetic Measurements. The reactions of amines with 9-acetyl-9-cyanofluorene in Me_2SO were slow enough to allow kinetic studies to be carried out by use of the same cell design as that used for the pK_a measurements and the Cary Model 14 spectrophotometer operated at a single wavelength. The reactions were rapid enough, however, to require the use of the rapid-scanning, stop-flow spectrophotometer for complete study of the spectral changes occurring during reactions.

All other reactions were studied by stop-flow spectrophotometry using techniques described in earlier papers.[1,8,12]

Results

pK_a Determinations. The pK_a's determined in the present work, along with pertinent data for the indicators used, are reported in Table I. The pK_a of nitromethane was determined as a check of our techniques; Bordwell[9] has reported a pK_a of 17.2. Our value is in perfect agreement.

The measurements for nitromethane, 2-hydroxyethanethiol, and (methoxycarbonyl)methanethiol showed a precision of a few hundredths of a pK_a unit. For *n*-propanethiol, the precision was ±0.06 unit, the poorest seen for the thiols. We believe that the values reported in Table I are accurate to better than 0.1 unit, relative to the indicators used.

The pK_a determination for 2-methoxyethylammonium ion was carried out by a simple titration of *p*-nitrophenol with the amine in the spectrophotometer cell. The precision observed from 25–60% conversion of the phenol to phenoxide ion was ±0.07 pK_a unit.

Kinetic Studies of Thiolate Ion Reactions. The studies of the thiolate ion reactions required the use of buffered solutions to keep the thiolate ion concentrations low enough to bring rates within a measurable range. We were able to use benzoic acid–potassium benzoate buffers for all of the studies reported here. For the equilibrium measurements on the reaction of Crystal Violet with 2-hydroxyethanethiolate, a more acidic buffer was required. Triethylamine–triethylammonium hydrochloride buffers proved satisfactory.

Neither Crystal Violet nor Malachite Green showed any appreciable reaction with any of the buffer solutions alone over a period of several hours. ACNF in the benzoate buffers showed appreciable formation of the 9-cyanofluorenide ion after several hours, but the reactions were negligibly slow in comparison to those in the presence of thiol. DNPA in the benzoate buffers gave formation of 2,4-dinitrophenoxide ion rapidly enough to require correction of the rates observed for low concentrations of thiolates. This correction was made by measurements of the rates of reactions in the presence and absence of thiol for each of the buffers used in the study. The data obtained in the absence of thiol show that the reaction of DNPA with benzoate ion is first order with respect to both benzoate ion and DNPA concentrations, and is independent of the concentration of benzoic acid and of the buffer ratio. An approximate second-order rate constant of 16 M^{-1} s^{-1} was obtained for the reaction of benzoate ion with DNPA in Me_2SO.

A summary of the experimental conditions used in the thiolate ion reaction studies is given in Table II. For at least the reaction of one thiolate ion with each electrophile, the conditions were varied over sufficient ranges to establish that the reactions are first order with respect to thiolate ion concentration and are independent of buffer ratio, buffer concentration, and thiol concentration. Also for at least one thiolate ion with each electrophile, the reactions were studied using the rapid-scanning, stop-flow spectrophotometer. The entire spectrum of the reaction solution from 260 to 560 nm was obtained 64 times during the reaction. The time intervals were selected so that equally spaced time intervals from less than 10% reaction to more than three half-lives reaction were obtained. The spectra indicated the absence of any intermediates with appreciable absorbances and showed that initial reactants disappeared at the same rate as the appearance of final products. In the case of the DNPA reactions, the spectra show the quantitative production of 2,4-dinitrophenoxide ion, and for the ACNF reactions, there is quantitative formation of the 9-cyanofluorenide ion. The rate constants calculated from absorbances at several different wavelengths were in agreement with each other and with those obtained using the single-wavelength instrument.

The precision of the second-order rate constants calculated from the pseudo-first-order rate constants obtained for at least 5-fold variation of thiolate concentration was generally better than ±10%. We believe that the rate constants reported in Table III are accurate to better than ±20%, which allows for the uncertainties in the pK_a's of the thiols and buffers.

The measurement of the equilibrium constant for the reaction of Crystal Violet with 2-hydroxyethanethiolate gave a value of 1.0 (±0.2) × 10^{11} M^{-1}.

Reactions of Amines. The reactions of the amines were studied in unbuffered solutions. The reaction of at least one amine with each electrophile was studied by the use of the rapid-scanning, stop-flow instrument, as described above for the thiolate reactions. The reactions of DNPA and ACNF give quantitative formation of 2,4-dinitrophenoxide ion and 9-cyanofluorenide ion, respectively. No indications of intermediates were observed. All reactions were accurately first order with respect to amine concentration over at least a 10-fold variation.

For the reaction of ACNF with *n*-butylamine, one critical experiment was performed to rule out the possibility that the reaction proceeds by a rapid and complete formation of carbinolamine followed by a base-catalyzed reaction to final products. In one run, second-order conditions of 2.5 × 10^{-4} M initial concentration of ACNF and 5.06 × 10^{-4} M initial concentration of amine were used, and the reaction was followed by conventional spectrophotometry. Using the same master solutions, pseudo-first-order conditions of 2.5 × 10^{-4} M initial ACNF and 5.06 ×

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Table II. Summary of Experimental Conditions for Thiolate Reactions[a]

electrophile	thiol	thiol, M	thiolate, M	benzoate, M
ACNF	$CH_3O_2CCH_2SH$	$0.46–4.7 \times 10^{-3}$	$0.65–6.7 \times 10^{-6}$	$0.59–1.8 \times 10^{-3}$
	$HOCH_2CH_2SH$	$9.3–9.6 \times 10^{-4}$	$1.2–6.8 \times 10^{-7}$	$1.7–2.1 \times 10^{-3}$
	$CH_3CH_2CH_2SH$	8.6×10^{-3}	4.3×10^{-8}	1.6×10^{-3}
DNPA	$CH_3O_2CCH_2SH$	$0.12–1.2 \times 10^{-2}$	$1.1–9.2 \times 10^{-5}$	$0.68–1.0 \times 10^{-3}$
	$HOCH_2CH_2SH$	1.1×10^{-2}	$0.42–4.3 \times 10^{-6}$	$7.1–8.3 \times 10^{-4}$
MG[b]	$CH_3O_2CCH_2SH$	$0.65–4.4 \times 10^{-4}$	$0.12–1.7 \times 10^{-6}$	1.2×10^{-3}
	$HOCH_2CH_2SH$	$0.23–2.4 \times 10^{-2}$	$0.35–6.6 \times 10^{-7}$	$0.97–1.2 \times 10^{-3}$
CV[b]	$CH_3O_2CCH_2SH$	$0.24–1.6 \times 10^{-3}$	$0.39–7.7 \times 10^{-6}$	$0.11–1.2 \times 10^{-3}$
	$HOCH_2CH_2SH$	$0.11–1.2 \times 10^{-2}$	$0.42–4.4 \times 10^{-7}$	$1.0–4.8 \times 10^{-3}$

[a] All reactions were studied at 23 ± 1 °C. [b] MG is Malachite Green cation; CV is Crystal Violet cation.

Table III. Comparison of Rate Constants in Me_2SO and Water

electrophile	nucleophile	log k_{Me_2SO}[a]	log k_{H_2O}[a]
Malachite Green	$CH_3OCH_2CH_2NH_2$	3.15	0.66
	$CH_3CH_2CH_2NH_2$	3.47	0.87
	CN^-	4.23[b]	-0.29[b]
	$CH_3O_2CCH_2S^-$	8.30	4.48[c]
	$HOCH_2CH_2S^-$	8.30	4.46[c]
Crystal Violet	$CH_3CH_2CH_2NH_2$	2.38	
	CN^-	3.07[b]	−1.27[b]
	$CH_3O_2CCH_2S^-$	7.34	
	$HOCH_2CH_2S^-$[d]	7.46	3.43[c]
DNPA	$CH_3OCH_2CH_2NH_2$	2.30	1.61[e]
	$CH_3CH_2CH_2CH_2NH_2$	2.80	2.07[e]
	CN^-	3.23	−0.26[e]
	$CH_3O_2CCH_2S^-$	5.86	1.97[f]
	$HOCH_2CH_2S^-$	5.80	2.05[f]
ACNF	$CH_3OCH_2CH_2NH_2$	−0.70	
	$CH_3CH_2CH_2CH_2NH_2$	-0.05	
	CN^-	4.70	
	$CH_3O_2CCH_2S^-$	5.54	
	$HOCH_2CH_2S^-$	6.38	
	$CH_3CH_2CH_2S^-$	7.46	

[a] Data are from the present study unless otherwise indicated. Rate constants are in units of $M^{-1}\ s^{-1}$. [b] Reference 14. [c] Reference 8. [d] Association constants (M^{-1}) give log $K_{Me_2SO} = 11.0$; log $k_{H_2O} = 2.88$. [e] Reference 17. [f] Reference 18.

10^{-3} M initial amine were then used in the stop-flow instrument. The reaction under second-order conditions followed accurate second-order kinetics for more than 80% reaction, and the calculated second-order rate constant was within experimental error of that obtained from the run under pseudo-first-order conditions.

Cyanide Ion Reactions. Rate constants for the reactions of cyanide ion with Malachite Green and Crystal Violet were available from our earlier studies.[14]

The reaction of cyanide ion with DNPA, under pseudo-first-order conditions with the concentration of cyanide from 2.1×10^{-5} M to 2.8×10^{-3} M, was accurately first order with respect to both cyanide ion and DNPA concentrations. A rapid-scanning study of the reaction showed the quantitative formation of 2,4-dinitrophenoxide ion, and indicated no intermediates.

Similarly, the reaction of cyanide ion with ACNF, with cyanide ion concentrations from 1.0×10^{-4} to 3.6×10^{-3} M, was first order with respect to both cyanide ion and ACNF concentrations, gave quantitative formation of the 9-cyanofluorenide ion, and gave no indication of intermediates.

The rate constants obtained in the present study are reported together with pertinent rate constants for the same reactions in water in Table III.

Table IV. Acidities in Me_2SO and Water

acid	pK_a (H_2O)[a]	pK_a (Me_2SO)	ΔpK_a[b]
n-propanethiol	10.8[c]	17.0	6.2
2-hydroxyethanethiol	9.5[c]	15.2	5.7
(methoxycarbonyl)methanethiol	8.0[c]	13.0	5.0
thiophenol	6.5	10.3[d]	3.8[d]
2-naphthol	9.6	17.1[d]	7.5[d]
p-nitrophenol	7.1	10.4[e]	3.3
2,4-dinitrophenol	4.1	5.1[f]	1.0
benzoic acid	4.2	11.0[e]	6.8
acetic acid	4.8	11.6[e]	6.8
hydrocyanic acid	9.2	12.9[e]	3.7
hydrazoic acid	4.7	7.9[e]	3.2
n-butylammonium ion	10.6	11.1[q]	0.5
2-methoxyethylammonium ion	9.4	9.6	0.2
triethylammonium ion	10.7	9.0[g]	−1.7

[a] Values are from "Lange's Handbook of Chemistry", 12th ed., J. A. Dean, Ed., McGraw-Hill Book Co., New York, 1979, unless otherwise indicated. [b] pK_a (Me_2SO) − pK_a (H_2O). [c] Reference 8. [d] Reference 16b; ΔpK_a of 3.2 for thiophenol, and of 6.9 for 2-naphthol, reported in ref 19 are apparently in error. [e] Reference 15. [f] Reference 13. [g] Reference 20.

Discussion

Acidities in Me_2SO Solution. The pK_a's in Me_2SO from Table I are compared to pK_a's in water and to pK_a's of other acids in both water and Me_2SO in Table IV.

The only previous study of acidities of alkanethiols in Me_2SO solution appears to be the work of Arnett[21] in which heats of reactions of various acids with dimsyl ion in Me_2SO were measured. From a correlation of these heats with known pK_a's of several of the acids, the pK_a's of all of the acids were estimated. Values of 17.2 and 16.2 for the pK_a's of *n*-butanethiol and ethanethiol, respectively, were obtained. Bordwell has pointed out,[22] however, that Arnett's correlation was based partly on incorrect values for the pK_a's of alcohols. Thus, the close agreement of Arnett's estimates with the value of 17.0 for the pK_a of *n*-propanethiol found in the present work is partly fortuitous.

In a study of solvent isotope effects on the acidities of thiols, Jencks[23] concluded that the thiolate ions are importantly bonded to water. This conclusion is consistent with the data shown in Table IV. The change in pK_a for the solvent change from water to Me_2SO, ΔpK_a, is nearly as large for the alkanethiols as for the comparably acidic 2-naphthol. There is also a clear trend for ΔpK_a to decrease as the pK_a of the thiol decreases. Stated differently, the effect of structure on pK_a of the thiols is larger in Me_2SO than in water. For the three alkanethiols reported here, the effect of structure of pK_a is ~1.4 times greater in Me_2SO than in water.

This factor of 1.4 attenuation of substituent effects on acidity of thiols on going from Me_2SO to water is considerably smaller than the attenuations for other acid types. For benzoic acids, the Hammett ρ value in Me_2SO is 2.6,[24] which is equal to the attenuation factor for the change to water since the ρ value in water

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is unity. For thiophenols, we can use Bordwell's reported[19] pK_a for *m*-(trifluoromethyl)thiophenol of 8.1 in Me_2SO and the Hammett substituent constant of 0.43[25] for the *m*-CF_3 group to estimate a Hammett ρ value of ~5.0 for the ionizations of thiophenols in Me_2SO. The value in water is 1.8.[26] Therefore, the attenuation factor for the change from Me_2SO to water for thiophenols is ~2.8. Bordwell's recent report[13] gives the pK_a of several phenols in *N*-methylpyrrolidone, and data from which the pK_a's in Me_2SO can be calculated. The data for the *p*-acetylphenol, *m*-chlorophenol, and unsubstituted phenols, compared with the pK_a's in water, give an attenuation factor or ~2.2 for phenols. This is similar to the factor of ~2.0 for the attenuation on going from DMF to water, which can be calculated from our study of the acidities of phenols in DMF solution.[27] It should be noted that these attenuation factors are not likely to be very precise since Taft's recent analysis[28] shows the existence of quite important effects arising from specific solvent–substituent interactions.

The attenuations of substituent effects on the acidities of benzoic acids,[29] phenols,[28,29] pyridinium ions,[30] and anilinium ions[31] upon going from the gas phase to aqueous solution and the closely related heats of solutions of ions in water[32,33] are believed to be importantly, perhaps predominantly, determined by substituent-dependent hydrogen bonding of water with the conjugate acids and bases. We had earlier suggested the same concept to account for the solvent dependences of ρ values for the acidities of benzoic acids,[24] phenols,[27] and picolinium ions.[27]

The present finding of a much smaller attenuation for alkanethiols than for other acid types, particularly arenethiols, does not appear to be easily rationalized in terms of hydrogen-bonding effects. Clearly, there is a difference in the solvations of the alkanethiolates and/or alkanethiols from that of other conjugate acid–base systems, but the source of the difference is not obvious.

Mechanisms of the Reactions of Nucleophiles in Me_2SO Solution. We wish to compare the rates of reactions of the nucleophiles in Me_2SO solution to those for the same reactions in water, so it is first necessary to establish, within reason, that the mechanisms in the two solvents are the same.

For the reactions of the triarylmethyl cations, we have simple bond-forming processes where mechanistic problems are expected to be minimal. There are no indications from any of our studies of these systems of any intermediates or side products that might arise from radical paths. The relative reactivities of the two thiolates, and those of the two amines, toward Malachite Green in Me_2SO are the same as in water. It seems most unlikely that these reactions could proceed by different mechanisms in the two solvents.

Reactions of DNPA with nucleophiles in Me_2SO apparently follow the same course as the corresponding reactions in water, giving quantitative formation of the 2,4-dinitrophenoxide. It is worth noting that a study of the reaction of acetate ion with *p*-nitrophenyl acetate in acetonitrile solution[34] identified the expected acetic anhydride product by infrared spectrophotometry. As for the triarylmethyl cation reactions, the relative reactivities of the two thiolates and of the two amines toward DNPA in Me_2SO are the same as in water. For all of the nucleophiles studied, the attacking reagent is more basic than the leaving 2,4-dinitrophenoxide ion, with the smallest difference being 4.1 pK_a units for attack by 2-methoxyethylamine. As in aqueous solutions, there is no evidence for acid or base catalysis of the reactions. All of this information is consistent with the mechanism involving rate-determining attack of nucleophile to form an anionic (or with amines a zwitterionic) tetrahedral intermediate followed by rapid breakdown of the intermediate to products, the same mechanism as postulated for reaction in aqueous solution.[17] The question of the actual existence of the intermediate, in either water or Me_2SO, is unimportant in most contexts,[17] but we will examine it in a later discussion.

The only disturbing feature in our data that pertains to mechanism is the comparison of reaction of nucleophiles with ACNF vs. those with DNPA. The reactions of thiolate ions with ACNF show a Brønsted β of ~0.5, whereas the reactions with DNPA show a zero value. The value of 0.5 is too small to be consistent with a mechanism involving a rate-determining breakdown of a tetrahedral intermediate. Such a mechanism would also be hard to justify with the fact that the pK_a of 9-cyanofluorene (8.3[3,9]) is 4.7 units lower than that of the conjugate acid of the least basic thiolate studied. The Brønsted slope is also much smaller than that of ~1, found by Bordwell[35] for electron-transfer mechanisms in Me_2SO. The information presented under Results shows that the reactions of ACNF do not involve the formation of stable adducts, and are not subject to acid or base catalysis.

Except for the contrast of the patterns of reactivity of the nucleophiles toward ACNF and DNPA, all of the information is consistent with the usual, and expected, rate-determining attack of nucleophiles on ACNF followed by rapid breakdown of the intermediate. We shall return to this problem in the later discussion of the existence of the tetrahedral intermediate in DNPA reactions.

Solvent Effects on Association Equilibria. To provide a basis for the discussion of solvent effects on the rates of the reactions considered here, we wish to know the solvent effects on the equilibria of the same reactions. This will allow us to use solvent effects on rates vs. those on equilibria as measures of transition-state progress toward products, as "seen" by the solvent, in exactly the same way that one uses Brønsted slopes,[18] kinetic vs. equilibrium secondary isotope effects,[7] or rate vs. equilibrium ρ values.[36]

We could adopt the approach, used by Parker,[2] of evaluating single-species activity coefficients. For example, if one naively neglects the activity coefficients of the conjugate acids, the activity coefficients for the anionic bases in Table IV could be obtained from the ΔpK_a values given and the value of -3.3[37,38] for $\log \gamma_{H^+}$ in Me_2SO relative to standard state in water. For these anions, we would obtain $\log \gamma_{A^-} = \Delta pK_a + 3.3$. Similarly, for the ammonium ions, we would obtain $\log \gamma_{BH^+} = -\Delta pK_a - 3.3$.

For the reasonably complex solutes of interest here, we believe that the use of such single-species activity coefficients is unnecessarily complex and easily misleading. It has been recognized implicitly, and sometimes explicitly, for some time that the activity coefficients for complex solutes are determined by approximately additive (in the free-energy sense) contributions from parts of the solute. The entire development of acidity function theory,[39] for example, depends on the cancellation of many of these contributions. Fuchs[40] has shown that group contributions to enthalpies

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(26) P. De Maria, A. Fini, and F. M. Hall, *J. Chem. Soc., Perkin Trans. 2*, 1969 (1973).

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(28) M. Fujio, R. T. McIver, Jr., and R. W. Taft, *J. Am. Chem. Soc.*, **103**, 4017 (1981).

(29) T. B. McMahon and P. Kebarle, *J. Am. Chem. Soc.*, **99**, 2222 (1977).

(30) E. M. Arnett, B. Chawla, L. Bell, M. Taagepera, W. J. Hehre, and R. W. Taft, *J. Am. Chem. Soc.*, **99**, 5729 (1977).

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(33) W. G. Henderson, R. T. C. Brownlee, J. L. Beauchamp, D. Holtz, and R. W. Taft, *J. Am. Chem. Soc.*, **94**, 1369 (1972).

(34) J. Hajdu and G. M. Smith, *J. Am. Chem. Soc.*, **103**, 6192 (1981).

(35) F. G. Bordwell and A. H. Clemens, *J. Org. Chem.*, **46**, 1035 (1981), report β = 1.2, but values of 1.0 are more typical of these reactions.[16b]

(36) For particularly detailed treatments, see: P. R. Young and W. P. Jencks, *J. Am. Chem. Soc.*, **101**, 3288 (1979); P. R. Young and P. E. McMahon, *Ibid.*, **101**, 4678 (1979).

(37) I. M. Kolthoff and M. K. Chantooni, Jr., *Anal. Chem.*, **44** 194 (1972); *J. Phys. Chem.*, **76**, 2026 (1972).

(38) B. G. Cox, G. R. Hedwig, A. J. Parker, and D. W. Watts, *Aust. J. Chem.*, **27**, 477 (1974).

(39) For a good discussion, see: R. H. Boyd, "Solute–Solvent Interactions", Vol. 1, J. F. Coetzee and C. D. Ritchie, Eds., Marcel Dekker, New York, 1969.

(40) R. F. Fuchs and R. F. Rodewald, *J. Am. Chem. Soc.*, **95**, 5897 (1973); R. F. Fuchs, T. M. Young, and R. F. Rodewald, *Ibid.*, **96**, 4705 (1974); P. S. Saluja, L. A. Peacock, and R. F. Fuchs, *Ibid.*, **101**, 1958 (1979).

of transfer can also be obtained. The presence of very polar groups particularly nitro groups,[2] the sheer size of a solute,[41] and many other structural features can give very large effects on activity coefficients, which, however, cancel in the activity coefficient ratios that determine equlibria.

For the reaction of a triarylmethyl cation, R^+, with a nucleophile, Nuc, the change in equilibrium constant (more properly, the change in equilibrium concentration ratios) on going from water to Me_2SO gives the ratio $\gamma_{R^+}\gamma_{Nuc}/\gamma_{RNuc}$, where the activity coefficients are for Me_2SO solution relative to standard state in water. The change in ionization constant for the conjugate acid of the nucleophile for the same solvent change gives $\gamma_{H^+}\gamma_{Nuc}/\gamma_{HNuc}$. Combination of these gives eq 1:

$$\Delta \log K - \Delta pK_a = \log (\gamma_{R^+}\gamma_{HNuc}/\gamma_{H^+}\gamma_{RNuc}) \equiv \log \Pi_- \qquad (1)$$

where K is the association constant for the cation–nucleophile reaction. For the reasons discussed above, the value of the right-hand-side of (1), which we symbolize by $\log \Pi_-$, is expected to be quite insensitive to reasonable variations in the structures of R^+ or Nuc.

We can obtain a value for $\log \Pi_-$ from the measured equilibrium constants for reaction of Crystal Violet with 2-hydroxyethanethiolate in water and Me_2SO. From $\Delta \log K = 8.12$ and $\Delta pK_a = 5.7$ for 2-hydroxyethanethiol, we find $\log \Pi_- = 2.4$. The value for $\log \Pi_-$ can now be used together with the ΔpK_a values from Table IV to estimate $\Delta \log K$ for reactions of triarylmethyl cations with any of the anionic nucleophiles studied. It seems most unlikely that these estimates will be in error by more than ±0.5 unit.

We can use a similar procedure to estimate $\Delta \log K$ for the reactions of the triarylmethyl cations with amines. From the known ΔpK_a values for ammonium ions, however, it does not appear to be reasonable that the right-hand side of (1) will be the same for amine and anion reactions. Specifically, for the reactions studied here HNuc is a primary ammonium ion while RNuc is a secondary ammonium ion. From the limited amount of data available,[20] it appears that the ΔpK_a's of secondary ammonium ions are ~1.3 units more negative than those for correspondingly acidic primary ammonium ions. This indicates that the activity coefficients of the secondary ammonium ions are larger than those for primary ammonium ions, which is in accord with expectations based on the above discussion of acidities in Me_2SO and the greater basicity of Me_2SO than of water. For the reactions of primary amines with the triarylmethyl cations, we expect the right-hand side of (1), rewritten for neutral nucleophile and symbolized by $\log \Pi_0$, to be 1.3 units more *negative* than $\log \Pi_-$. Thus, we estimate $\log \Pi_0 = 1.1$. To the extent that the secondary ammonium ions formed in our reactions are less solvated because of steric hindrance than are the simple secondary ammonium ions, the value of 1.1 will be too positive, leading to estimates of $\Delta \log K$ that are too positive.

It is considerably more difficult to apply the above procedure to the reactions of DNPA with nucleophiles to form the (perhaps hypothetical) tetrahedral intermediates. Certainly, the ratio $\gamma_{DNPA}/\gamma_{T^-}$, where T^- is the anionic tetrahedral intermediate, will be quite different from $\gamma_{R^+}/\gamma_{RNuc}$ due to the localized negative charge on the oxygen of T^-. We will estimate a value for this ratio from an estimate of the pK_a of the tetrahedral intermediate and a comparison of this pK_a with that of other oxygen acids for which ΔpK_a is known.

The pK_a of the hemithioacetal formed from acetaldehyde and 2-methoxyethanethiol in water was estimated by Jencks[42] at 12.7. Using $\rho_I = 8.4$[43] for the ionization of alcohols and an estimated $\sigma_I = 0.46$[44] for replacement of hydrogen by the 2,4-dinitrophenoxy group, we estimate the pK_a of the tetrahedral intermediate from reaction of 2-hydroxyethanethiol with DNPA at 8.8 in water. Comparing this value with that of 9.6 for the pK_a of 2-naphthol in water and allowing for the solvent effect on relative acidities discussed earlier (i.e., the difference in pK_a of the two acids should be ~2.5 times as great in Me_2SO as in water), we estimate $pK_a = 15.1$ in Me_2SO, or $\Delta pK_a = 6.3$. This will be an underestimate of ΔpK_a if the naphthoxide is less solvated by water than is the correspondingly basic alkoxide ion.

Table V. Solvent Effects on Rates and Equilibria

reaction	$\Delta \log K^a$	$\Delta \log k^b$	$\Delta \log k/\Delta \log K$
$MG^c + CH_3OCH_2CH_2NH_2$	1.3	2.6	2.00
$+ CH_3CH_2CH_2NH_2$	1.6	2.6	1.63
$+ CN^-$	6.1	4.5	0.74
$+ CH_3O_2CCH_2S^-$	7.4	3.8	0.51
$+ HOCH_2CH_2S^-$	8.1	3.8	0.47
$CV^c + CN^-$	6.1	4.3	0.70
$+ HOCH_2CH_2S^-$	8.1 (measured)	4.0	0.49
$DNPA + CH_3OCH_2CH_2NH_2$	−7.4	0.7	−0.10
$+ CH_3CH_2CH_2CH_2NH_2$	−7.1	0.7	−0.10
$+ CN^-$	−2.6	3.5	−1.3
$+ CH_3O_2CCH_2S^-$	−1.3	3.9	−3.0
$+ HOCH_2CH_2S^-$	−0.6	3.8	−6.3

[a] K is the association constant for the reaction, and $\Delta \log K = \log K_{Me_2SO}/K_{H_2O}$. Values were estimated as described in the text. [b] $\Delta \log k = \log k_{Me_2SO}/k_{H_2O}$, from data in Table III. [c] MG is Malachite Green and CV is Crystal Violet.

The ΔpK_a is equal to $\log \gamma_{T^-}\gamma_{H^+}/\gamma_{TH})$, and we may reasonably equate this to $\log(\gamma_{T^-}\gamma_{H^+}/\gamma_{DNPA}\gamma_{HNuc})$, which is the negative of the right-hand side of (1) rewritten for the present reaction. We shall use the value of −6.3 plus the ΔpK_a of the conjugate acid of the anionic nucleophiles to estimate $\Delta \log K$ for formation of the anionic intermediates. As for the triarylmethyl cation reactions with amines, those for DNPA reactions require the "correction" of 1.3 units, giving $\Delta \log K = -7.6 + \Delta pK_a$ for the formation of the zwitterionic intermediates.

Before proceeding with the application of these estimates, it is worthwhile to consider the reliability, or lack thereof, of our procedures. The "hard" numbers that have gone into the calculations are the $\Delta \log K$ for reaction of Crystal Violet with 2-hydroxyethanethiol, and the ΔpK_a's shown in Table IV. The assumptions used in the process of going from these numbers to the $\Delta \log K$'s for the reactions of triarylmethyl cations with anions appear reasonable, and it is hard to believe that our estimates for the reactions will be far off. The only additional assumption necessary to arrive at the estimates for the reactions of triarylmethyl cations with amines is that $\log \gamma$ for primary ammonium ions differs from that for secondary ammonium ions of comparable acidity by 1.3 units. As indicated above, this could lead to estimates of $\Delta \log K$ that are too *positive*.

For the DNPA reactions, the procedure is much more questionable. Application of the different procedures used by different authors[43,45,46] for the estimation of the pK_a's of tetrahedral intermediates can frequently give quite different results. For example, the pK_a of the hemithioacetal from acetaldehyde and (methoxycarbonyl)methanethiol is estimated at 12.4 by one procedure[42] and at 14.0 by another.[45] The important conclusion, as will be fully realized below, that we reach by our procedure, however, seems almost inescapable. This conclusion is that $\Delta \log K$ for the formation of anionic or zwitterionic intermediates from DNPA are negative. Since all of the reactions discussed here involve a transfer of charge from either a polarizable anion or a neutral amine to a highly localized nonpolarizable oxide ion center, it would be difficult to understand how $\Delta \log K$ could be other than negative.

Solvent Effects on Rates of Reactions. The solvent effects on rates of reactions, expressed as $\Delta \log k = \log k_{Me_2SO} - \log k_{water}$,

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(41) B. G. Cox and A. J. Parker, *J. Am. Chem. Soc.*, **94**, 3674 (1972).

(42) H. F. Gilbert and W. P. Jencks, *J. Am. Chem. Soc.*, **99**, 7931 (1977).

(43) J. M. Sayer and W. P. Jencks, *J. Am. Chem. Soc.*, **95**, 5637 (1973).

(44) The estimated σ_I for the 2,4-dinitrophenoxy group is obtained from $\sigma_I = 0.38$ for the phenoxy group,[25] a Hammett $\sigma = 0.78$ for the nitro groups,[25] and application of the relationships developed in ref 25 to obtain σ^* or σ_I constants for $ArCH_2$ groups: $\sigma_I(DNPO) = 0.16 \times 0.33 \times (2 \times 0.78) + 0.38$.

(45) J. P. Guthrie, *J. Am. Chem. Soc.*, **100**, 5892 (1978), and earlier papers cited therein.

(46) J. Fastrez, *J. Am. Chem. Soc.*, **99**, 7004 (1977).

together with the estimated solvent effects on the corresponding association equilibria, are summarized in Table V. The last column of Table V contains values of $\Delta \log k/\Delta \log K$, which, in analogy with the usual treatment of structural effects on rates and equilibria, represent the fractional progress of the transition-states of the reactions toward products as "seen" by solvent.

For the reactions of amines with Malachite Green, the solvent effects on rate constants are larger than those estimated on the equilibrium constants, giving greater than 100% progress of the transition states as seen by solvent. The change of solvent from water to Me_2SO increases both the forward and reverse rate constants for these reactions. Measures of transition-state progress, which can be derived from the β_{nuc} values (0.4), or from the effect of changing the triarylmethyl cation reacting with a given amine in water ($\Delta \log k/\Delta pK_R \simeq 0.4$[47]), are quite normal.

For the reactions of thiolate ions with Malachite Green, we can compare the 47–51% progress seen by solvent with several other measures of transition-state progress. In both water and Me_2SO, the rate constants are insensitive to thiolate basicity, showing a Brønsted β_{nuc} of essentially zero; as seen by the thiolate, there is 0% progress of the transition state. (Although the β_{nuc} value in Me_2SO is based on only two points, the two thiolate ions studied show behaviors toward esters and cations in water[18,8] that are typical of other thiolates, and the ΔpK_a values in Table IV give no cause to suspect abnormal behavior in Me_2SO.) It is worth noting also that the near-zero values for β_{nuc} in both water and Me_2SO make it extremely unlikely that the Brønsted slope is the result of compensating desolvation and bond formation. In the reactions of 2-hydroxyethanethiolate with Malachite Green and Crystal Violet, we have found $\log (K_{MG}/K_{CV}) = 2.5$ in water,[8] and from our discussion of (1) we expect the same value in Me_2SO. The rate constants, in both solvents, give $\log (k_{MG}/k_{CV}) \simeq 1$. The ratio of these numbers, 0.4, gives 40% progress of the transition state as seen by the cationic moiety.

Similarly, for the reactions of cyanide ion, we find 74% and 40% progress as seen by the solvent and the cationic moiety, respectively.

Bunton[48] has reported a study of α-secondary-deuterium isotope effects on the reactions of ferrocenylmethyl-type cations with various nucleophiles in aqueous acetonitrile solution. These cations show reactivity patterns with nucleophiles that are quite similar to those of the triarylmethyl cations, indicating quite similar transition states for the two cation types. The isotope effects are nil for the reactions of the anionic nuclephiles, OH^-, BH_4^-, and N_3^-, indicating zero progress of the transition states, and are very small for the reactions of amines, indicating very little progress in these reactions. The effect of cation structure on the rates is large, and essentially the same for both anionic and neutral nucleophiles, indicating substantial progress of the transition states as seen by the cations.

The negative numbers shown in Table V as measures of transition-state progress for the reactions of DNPA underscore discrepancies in measures of progress that have been discussed by others[7,18,36,49] for reactions of nucleophiles with carbonyl compounds. These previous discussions have all called attention to the possibility of complications from solvent effects, and the present measures of negative progress strengthen these suspicions.

If we completely disregard the estimates of $\Delta \log K$ for the DNPA reactions, and simply compare the $\Delta \log k$'s with those for reactions of Malachite Green, we might hope to get some indication of the amount of oxide ion character at the transition states for the DNPA reactions. For the thiolate ion reactions, $\Delta \log k$ is the same for DNPA and Malachite Green, indicating no oxide ion character and, therefore, no progress of the transition states toward intermediate. This interpretation would be in accord with the observation of very small α-deuterium isotope effects in the reactions of thiolates with formyl esters[49] (although the isotope effects can be rationalized in other ways[50]), but is not in accord with the fact that the ρ value for the reaction of cysteine with a series of acyl-substituted *p*-nitrophenyl acetates is essentially equal to that for the equilibrium addition of thiolates to substituted aldehydes.[50] As for the triarylmethyl cation reactions, a near-zero progress of the transition states is also difficult to reconcile with the large values of the $\Delta \log k$'s.

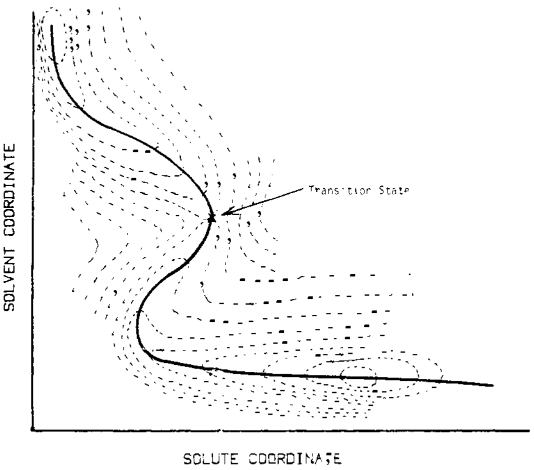

Figure 1. A possible projection of a many-dimensional potential energy surface for a reaction in solution.

Continuing to disregard the $\Delta \log K$'s, the fact that $\Delta \log k$ for the reaction of amines with DNPA is 1.9 units less, and that for reaction of cyanide ion with DNPA is 1.0 units less, than for the corresponding reactions of Malachite Green can be interpreted as indicating some oxide ion character to the transition states for these reactions. For the amine reactions, however, it is extremely difficult to understand how any development of charge at the transition states can be reconciled with the positive values of $\Delta \log k$.

The disregard of the $\Delta \log K$'s for the quantitative estimates of transition-state progress can be reasonably justified. These quantitative estimates have implicitly assumed that developing solvation is synchronous with developing charge or other developing structural features. For example, the $\Delta \log k/\Delta \log K$ value as a measure of the progress of the DNPA reactions implicitly assumes that a given fraction of oxide ion character is solvated by the same fraction of oxide ion solvation. This assumption is probably not correct;[7,18,36,49] it is quite possible, for example, that hydrogen bonding of water to a charged site is an exponential function of the fractional charge.

If one admits the possibility of nonsynchronous solvation processes, the entire problem of understanding structural and solvent effects on rates becomes extremely difficult. Since we have already seen in the discussion of solvent effects on acidities that solvent and structural effects are interdependent, simple interpretations of Brønsted slopes or of ratios of rate–equilibrium ρ values are not possible. The fact that we still run into the difficulties discussed above when the $\Delta \log K$ values are completely disregarded suggests that the problem is more complicated than a simple "lagging" of solvation, which can be visualized by the use of simple 3-D potential-energy surfaces.[18] It seems quite possible that our entire concepts of the solvation of transition states are in error.

In other work, we have pointed out that there is no a priori reason to expect transition states to be solvated in the same way as stable molecule analogues.[51] A representation of a potential-energy surface is shown in Figure 1, where one coordinate represents some aspect of solute geometry, or charge, and the other coordinate represents some measure of solvent location or orientation. The possibility of a convoluted reaction path such as that shown cannot be excluded from consideration, and, in fact, an even more convoluted "path" was found for an electrostatic model

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(47) K. Hillier, J. M. W. Scott, D. J. Barnes, and F. J. P. Steele, *Can. J. Chem.*, **54**, 3312 (1976).

(48) C. A. Bunton, N. Carrasco, and F. Davoudzadeh, *J. Chem. Soc., Perkin Trans. 2*, 1520 (1980).

(49) E. R. Pohl and D. J. Hupe, *J. Am. Chem. Soc.*, **102**, 2763 (1980).

(50) S. L. Shames and L. D. Byers, *J. Am. Chem. Soc.*, **103**, 6170 (1981).

(51) C. D. Ritchie, *Pure Appl. Chem.*, **52**, 153 (1979).

"reaction" in which two counterions, "solvated" by eight dipoles, were brought together.[51] In the many dimensions actually necessary to describe a real system, even a line that intersects itself could correspond to a spiral "path". If the transition state for a reaction lies at the point indicated in Figure 1, or at any other point on the S portion of the curve, there is at least one point on the surface that has the same solute geometry (or charge), a *different* solvation from that of the transition state, and a *lower energy* than the transition state. That is, the transition state is not solvated in the lowest energy manner. It needs to be emphasized that the time required for solvent motion is not, and *can not*, be germane to the discussion of transition states, since transition-state theory is essentially an equilibrium theory (i.e., a Boltzmann distribution is assumed to be maintained).

Further Mechanistic Considerations. There is yet another complication possible in the reactions of nucleophiles with DNPA and ACNF that needs exploration. If the reactions of DNPA followed a concerted mechanism, at least in Me_2SO solution, with negative charge being directly transferred to the leaving 2,4-dinitrophenoxide group, the observed faster rates in Me_2SO than in water might be understandable. The ΔpK_a of 2,4-dinitrophenol is only 1.0, as compared to the 6.1 estimated above for the anionic tetrahedral intermediates.

Such a concerted mechanism might, in fact, be "enforced" by the lifetime of the intermediate.[52] The equilibrium constant for formation of the anionic tetrahedral intermediate from PNPA (*p*-nitrophenyl acetate) and ethanethiolate in water has been estimated[50] at 8×10^{-12} M^{-1}. Allowing for the effect of the second nitro group of DNPA,[44] $K = 3 \times 10^{-11}$ M^{-1} is obtained for the DNPA plus ethanethiolate reaction. Since the rate constant for reaction of ethanethiolate with DNPA in water is[18] 1.7×10^2 M^{-1} s^{-1}, then the rate constant for loss of thiolate from the anionic tetrahedral intermediate is estimated to be $\sim 6 \times 10^{12}$ s^{-1}. Since the rate constant for loss of 2,4-dinitrophenoxide ion is expected to be even greater, the lifetime of the "intermediate" must be less than 10^{-13} s if these estimates are at all realistic. In Me_2SO solution, the rate constant for attack of thiolate increases by nearly 10^4 with, at best, no increase in equilibrium constant. The lifetime of the intermediate in Me_2SO solution, then, is estimated at $\sim 10^{-17}$ s. Equilibrium constants for the formation of zwitterionic intermediates from the reactions of amines with DNPA are expected to be comparable in magnitude to those for the thiolate reactions,[45] while those for formation of the anionic intermediate from cyanide reaction are expected to be $\sim 10^2$ larger,[53] all in aqueous solution. The rate constant for reaction of an alkylamine with DNPA in water is also nearly the same as that for reaction of a thiolate ion, so the intermediate is estimated to have a marginal lifetime in aqueous solution. The expected large decrease in the equilibrium constant in Me_2SO solution (cf. Table V), with no compensating decrease in forward rate constant, again leads to an estimate of an extremely short lifetime of $\sim 10^{-19}$ s for the zwitterionic intermediates in Me_2SO. For the cyanide ion reactions, these estimates allow a reasonable existence of the intermediate in water, but, at best, a marginal existence in Me_2SO.

Jencks[17] has argued reasonably, but not compellingly, that the nonexistence of the tetrahedral intermediates in ester reactions will simply lead to a highly asymmetric reaction coordinate with the single maximum shifting from very "reactant-like" to very "product-like" transition states as the attacking nucleophile is changed from a poorer to a better leaving group than the departing phenoxide ion. Such a situation would leave all of the interpretations of structural effects on reactivity unchanged from those developed for a two-step mechanism. If, however, the negative charge is either not being developed on the carbonyl oxygen, or can easily be polarized onto the phenoxide oxygen in the absence of solvation, the concerted mechanism would lead to different solvent effects than the two-step mechanism, as we stated above.

It is also interesting to note that the tetrahedral intermediates formed from the reactions of nucleophiles with ACNF are expected to be considerably more stable than those for the reactions with DNPA. We can attempt an estimate for the equilibrium constant for formation of the tetrahedral intermediate from reaction of ACNF with (carbomethoxy)methanethiolate as follows: (1) Jencks[42] has estimated the equilibrium constant for formation of the anionic intermediate from acetaldehyde and (carbomethoxy)methanethiolate as $10^{-4.4}$ M^{-1} (we use the smallest of a range of estimates from $10^{-4.4}$ to $10^{-2.2}$).[45] (2) The equilibrium constant for the hydration of acetone is $10^{-2.8}$ times that for the hydration of acetaldehyde.[45] (3) The σ^* value for the 9-cyanofluorenyl group should be roughly equal to twice that for a benzyl group (0.21[25]) plus that for a cyanomethyl group (1.3[25]). (4) The ρ^* value for the addition of anions to aldehydes is $\sim$3.0.[50] We obtain $\log K_{T^-} = -2.1$ for the reaction in aqueous solution. The pK_a of the hemithioacetal can be estimated from the value of 12.4 for that of the corresponding acetaldehyde hemithioacetal, the σ^* value for the 9-cyanofluorenyl group, and the ρ^* = 1.3[45] for the ionization of alcohols, giving $pK_a = 10.2$. Comparing this to the data for 2-naphthol, just as we did earlier for other intermediates, we estimate a pK_a of 18.6 for the tetrahedral intermediate in Me_2SO, or $\Delta pK_a = 8.4$. Again following the earlier procedure, we estimate $\Delta \log K = -3.4$, and, therefore, $\log K_{T^-} = -5.5$ for the formation of the anionic intermediate in Me_2SO. The rate constant for the forward reaction is $10^{5.54}$, so the reverse rate constant for loss of thiolate is $\sim 10^{11.0}$ s^{-1}, allowing a reasonable lifetime for this intermediate.

It appears, therefore, that the mechanisms for the reactions of nucleophiles with ACNF and DNPA could reasonably be different, providing a possible rationalization for the different patterns of nucleophilic reactivities toward these two electrophiles. Such a rationalization, in the specific case of thiolate ion reactions, would, however, require an unlikely, but not inconceivable, coincidence. Rate constants for the reactions of basic thiolate ions with acetaldehyde in water give a nearly zero Brønsted β,[42] as do the basic thiolate ions with DNPA, but unlike the reactions with ACNF. Since the acetaldehyde reactions should be a model for the two-step mechanism, the Brønsted β of $\sim$0.5 for the thiolate reactions with ACNF in Me_2SO appears not to be in accord with the rationalization. It is certainly conceivable, however, that the reactions of acetaldehyde with thiolates in Me_2SO would exhibit a Brønsted slope comparable to that for ACNF. This could easily result from a situation in water where the negative β for desolvation of the thiolates is almost canceled by the positive β for partial bond formation to the aldehyde. Such an explanation, which would require that the behavior of the thiolates toward DNPA in Me_2SO is an unfortunate coincidence, is not so unlikely that it should go unchecked.

Acknowledgment. This work was supported by NSF Grant No. CHE77-24701A. We are greatly indebted to Professor F. G. Bordwell for providing us with data prior to publication, for several samples of indicators used in the pK_a determinations, and for constructive criticisms of the original manuscript. We thank Dr. Joseph Gandler for carrying out some of the preliminary experiments on the reactions of amines with Malachite Green in Me_2SO solution and Dr. R. Brody, who corrected several errors appearing in the first draft of this paper.

Registry No. CH_3NO_2, 75-52-5; $CH_3OCH_2CH_2NH_3^+$, 54005-66-2; $CH_3O_2CCH_2SH$, 2365-48-2; $HOCH_2CH_2SH$, 60-24-2; $CH_3CH_2CH_2SH$, 107-03-9; $CH_3OCH_2CH_2NH_2$, 109-85-3; $CH_3CH_2CH_2NH_2$, 107-10-8; $CH_3O_2CCH_2S^-$, 64743-45-9; $HOCH_2CH_2S^-$, 57966-62-8; $CH_3CH_2CH_2CH_2NH_2$, 109-73-9; $CH_3CH_2CH_2S^-$, 20733-14-6; CN^-, 57-12-5; DNPA, 4232-27-3; ACNF, 81477-52-3; MG, 10309-95-2; CV, 7438-46-2; Malachite Green fluoborate salt, 60885-33-8; Crystal Violet fluoborate salt, 7328-65-6.

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