

Thermodynamics of Formation of the Meisenheimer Complex from Thiophenoxide and 1,3,5-Trinitrobenzene and Heats of Transfer in Methanolic Dimethyl Sulfoxide

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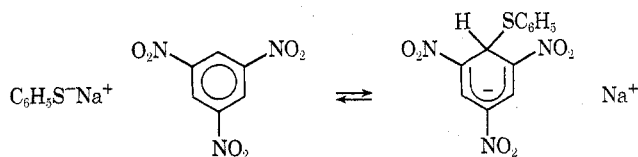
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Received May 15, 1972

The heat of formation of the Meisenheimer complex formed from sodium thiophenoxide and 1,3,5-trinitrobenzene has been measured in methanol-DMSO mixtures. These data were combined with free energies from the literature to calculate ΔS for this reaction. Except at very high DMSO concentrations, this reaction is isoentropic across the methanol-DMSO solvent continuum. The heats of transfer of the starting materials and product from methanol to methanol-DMSO mixtures have been measured. The heat of reaction between thiophenoxide and 1,3,5-trinitrobenzene becomes more exothermic as the concentration of DMSO increases. This is due to the fact that the heat of transfer of the Meisenheimer complex from methanol becomes more exothermic as the DMSO concentration increases. The heat of transfer of sodium thiophenoxide also decreases (becomes more exothermic) as the DMSO concentration increases, but it does not change so rapidly as does the heat of transfer of the complex.

Recently the formation of Meisenheimer complexes and related species has been under investigation by a number of groups. The area has been thoroughly reviewed.²⁻⁸ In spite of the intense activity in this area, a good thermodynamic picture has not been developed. Since the complexes are readily prepared and are subject to large solvent effects, an understanding of the solution thermodynamics of these complexes should add significantly to our understanding of solvent effects on complex organic systems. A number of groups have reported equilibrium constants for formation of a variety of Meisenheimer complexes in a number of solvents. However, few enthalpies and entropies of complex formation are available. We have undertaken calorimetric measurements designed to fill this gap.

Since we are interested in solvent effects, we needed a reaction for which both equilibrium constants and heats could be measured in a variety of solvents. Such a reaction is the one between sodium thiophenoxide and 1,3,5-trinitrobenzene (TNB) in methanolic dimethyl sulfoxide.



Crampton⁹ has recently published a reliable set of equilibrium constants for this reaction in methanol-DMSO mixtures. We have measured the heat of this reaction calorimetrically and combined these heats of reaction with Crampton's free energies to obtain the entropies of this reaction in a number of methanol-DMSO mixtures. In the course of this work, heats of transfer of the reactants, sodium thiophenoxide and 1,3,5-trinitrobenzene, and a number of related molecules were measured. These data are useful in dissecting the thermodynamics of the complex-form-

ing reaction and also provide a frame of reference for the consideration of solvent effects in this system.

Experimental Section

The calorimeter¹⁰ and solvent purification¹¹ have been described previously. Insofar as possible, Crampton's⁹ experimental conditions were duplicated. Both thiophenol and 1,3,5-trinitrobenzene were purified commercial samples. Thiophenoxide was prepared in the calorimeter by adding a slight excess of thiophenol to a solution containing sodium methoxide. The heat of solution of the last bit of thiophenol added was always the same as the heat of solution of thiophenol in the solvent being used, indicating that all the methoxide had reacted. All solutions were used immediately after preparation. The heat of reaction between 1,3,5-trinitrobenzene and thiophenoxide was measured at $20 \pm 1^\circ$.

Results

The heats of solution of thiophenol, 1,3,5-trinitrobenzene, and methanol in methanol-DMSO mixtures are given in Table I. In all cases, the heats of solution

TABLE I

HEATS OF SOLUTION ($\Delta \bar{H}_s$) OF THIOPHENOL, METHANOL, AND 1,3,5-TRINITROBENZENE (TNB) IN METHANOL-DMSO MIXTURES

Vol % DMSO in MEOH	$\Delta \bar{H}_s, \text{C}_6\text{H}_5\text{SH}^a$ kcal/mol	$\Delta \bar{H}_s, \text{TNB}^b$ kcal/mol	$\Delta \bar{H}_s, \text{CH}_3\text{OH}^b$ kcal/mol
0	-0.08 ± 0.02	3.20 ± 0.34	0
10	-0.24 ± 0.04	2.56 ± 0.14	0.02 ^c
20	-0.34 ± 0.07	2.38 ± 0.16	0.02 ^c -0.00 ± 0.02
30	-0.39 ± 0.04	2.28 ± 0.09	0.0 ^c
40	-0.53 ± 0.04	2.44 ± 0.26	-0.01^c
50	-0.56 ± 0.03	2.25 ± 0.17	-0.02^c -0.02 ± 0.04
60	-0.62 ± 0.03	2.44 ± 0.08	-0.07^c
70	-0.73 ± 0.01	2.41 ± 0.02	-0.12^c
80	-0.81 ± 0.04	2.48 ± 0.11	-0.18^c
90			-0.27^c -0.25 ± 0.01
95	-0.94 ± 0.03	2.29 ± 0.22	-0.30^c -0.31 ± 0.01
100	-0.94 ± 0.12	2.45 ± 0.07	-0.32^c -0.34 ± 0.01^d

^a At $20 \pm 1^\circ$. ^b At $25 \pm 1^\circ$. ^c Data from ref 12. ^d Reference 13, -0.34 kcal/mol.

were measured by dissolving at least six 50-100-mg samples of the solute in 200 ml of the appropriate sol-

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vent. The temperature was either 20 ± 1 or $25 \pm 1^\circ$ (see Table I). Since no dependence of the heat of solution on the concentration of the solute was observed, all heats are effectively at infinite dilution. The reported errors are the standard deviation from the average value. Good agreement was found between literature values^{12,13} for the heat of solution of methanol in methanolic DMSO and the results reported here.

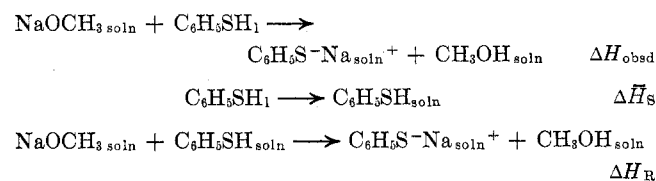
Table II contains the heats of reaction between 1,3,5-

TABLE II
HEATS OF REACTION BETWEEN 1,3,5-TRINITROBENZENE AND SODIUM THIOPHENOXIDE AND BETWEEN THIOPHENOL AND SODIUM METHOXIDE AT $20 \pm 1^\circ$

Vol % DMSO in MeOH	$\Delta H_{R, \text{TNB} + \text{C}_6\text{H}_5\text{S}^- \text{Na}^+}$, kcal/mol	$\Delta H_{R, \text{C}_6\text{H}_5\text{SH} + \text{NaOCH}_3}$, kcal/mol
0		-5.15 ± 0.25
10	-3.69 ± 0.86^a	-6.59 ± 0.25
20	-4.21 ± 0.10	-6.74 ± 0.08
30	-4.11 ± 0.17	-7.61 ± 0.26
40	-5.11 ± 0.27	-7.72 ± 0.19
50	-5.48 ± 0.07	
60	-6.62 ± 0.05	-8.24 ± 0.29
70	-7.10 ± 0.05	-9.21 ± 0.20
80	-7.52 ± 0.15	-10.17 ± 0.24
95	-8.95 ± 0.72	-11.97 ± 0.09
100	-9.93 ± 0.41	

^a Uncertain value. No value was obtained in another attempt in this solvent.

trinitrobenzene and sodium thiophenoxide and also the heats of reaction between thiophenol and sodium methoxide. The reported heats of reaction between thiophenol and sodium methoxide were obtained by measuring the heat of solution of thiophenol in the requisite solvent ($\Delta \bar{H}_s$) and in the same solvent containing an excess of sodium methoxide (ΔH_{obsd}). As shown below, subtraction gives the heat of reaction directly; *i.e.*, $\Delta H_R = \Delta H_{\text{obsd}} - \Delta \bar{H}_s$. This technique



was also used for the reaction between 1,3,5-trinitrobenzene and thiophenol when the equilibrium constant was larger than 10^3 . That is, when the equilibrium constant is large and an excess of thiophenoxide is used, essentially all the 1,3,5-trinitrobenzene injected reacts. However, when the equilibrium constant is less than *ca.* 10^3 , the fact that the reaction does not go to completion must be considered. As before,¹⁰ $\Delta H_R = \Delta H_{\text{obsd}}/[C]V$, where ΔH_{obsd} is the observed heat in calories, $[C]$ is the concentration of the complex formed, and V is the volume of the solution. The observed heat, ΔH_{obsd} , is the difference between the heat measured during complex formation and the heat which would have resulted if the 1,3,5-trinitrobenzene had dissolved without reacting. It is the heat due to formation of $[C]V$ moles of complex. The concentration

of C formed can be determined easily from the known equilibrium constant K and the concentrations of 1,3,5-trinitrobenzene and sodium thiophenoxide as shown below. The heats of reaction between 1,3,5-

$$[C] = \frac{\{[\text{TNB}] + [\text{C}_6\text{H}_5\text{S}^- \text{Na}^+] + 1/K \pm \sqrt{([\text{TNB}] + [\text{C}_6\text{H}_5\text{S}^- \text{Na}^+] + 1/K)^2 - 4[\text{TNB}][\text{C}_6\text{H}_5\text{S}^- \text{Na}^+]}\}}{2}$$

trinitrobenzene and thiophenoxide reported here for solutions containing less than 60% (v/v) DMSO are dependent on the values of K used, and are no more accurate than these values. There are two independent checks on the equilibrium constants measured by Crampton⁹ that were used here. It is possible to calculate K using enthalpies of reaction measured at different ratios of $[\text{TNB}]/[\text{C}_6\text{H}_5\text{S}^- \text{Na}^+]$ using a method developed by Bolles and Drago.¹⁴ This method was applied to the calorimetric data and equilibrium constants in agreement with Crampton's were obtained. Feeling that it is better to use independently measured values for K and ΔH whenever possible, we have utilized Crampton's equilibrium constants throughout. A second less rigorous check is the fact that the ΔH values which are independent of K form a continuous series with those whose magnitude is dependent on K . Reliable data could not be obtained in pure methanol. A number of attempts resulted in calorimetric data which were not consistent with a single equilibrium. The equilibrium constant in this solvent is quite low ($K = 1.5$) and requires quite precise calorimetric data.¹⁵ It is quite possible that we were unable to obtain the precision necessary to obtain meaningful data. From Crampton's equilibrium constants and the enthalpy values in Table II, ΔG , ΔH , and ΔS can be calculated for the reaction between sodium thiophenoxide and 1,3,5-trinitrobenzene. These data are contained in Table III.

TABLE III
THERMODYNAMICS OF THE REACTION BETWEEN 1,3,5-TRINITROBENZENE AND SODIUM THIOPHENOXIDE IN METHANOLIC DMSO AT 20°

Vol % DMSO in MeOH	ΔG , kcal/mol	ΔH , kcal/mol	ΔS , eu
0	-0.37		
10	-0.97	-3.69 ± 0.86	-9.29
20	-1.42	-4.21 ± 0.17	-9.54
30	-2.01	-4.11 ± 0.17	-7.16
40	-2.50	-5.11 ± 0.27	-8.90
50	-3.05	-5.48 ± 0.07	-8.30
60	-3.73	-6.62 ± 0.05	-9.88
70	-4.47	-7.10 ± 0.05	-8.98
80	-4.92	-7.52 ± 0.15	-8.88
95	-6.41	-8.95 ± 0.72	-8.67
100	-6.63	-9.93 ± 0.41	-11.27

Using the data from Tables I and II together with the heats of solution of sodium methoxide reported in ref 11, it is possible to calculate the heat of transfer of sodium thiophenoxide from methanol to methanol-DMSO mixtures and of the Meisenheimer complex from 10% DMSO (v/v) to solvents richer in DMSO. This

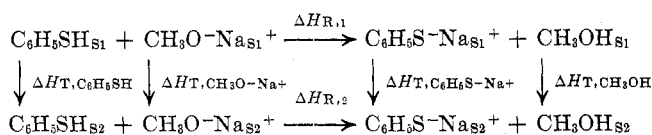
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is done for sodium thiophenoxide using the enthalpy cycle shown below.



In the above scheme, solvents 1 and 2 are indicated by subscripts S1 and S2, ΔH_{R} is the heat of reaction, and ΔH_{T} is a heat of transfer from solvent 1 to solvent 2. Thus $\Delta H_{\text{T},\text{C}_6\text{H}_5\text{S}^-\text{Na}^+} = \Delta H_{\text{R},1} + \Delta H_{\text{T},\text{CH}_3\text{OH}} - \Delta H_{\text{R},2} - \Delta H_{\text{T},\text{CH}_3\text{O}^-\text{Na}^+} - \Delta H_{\text{T},\text{C}_6\text{H}_5\text{SH}}$. A similar cycle can be written for the heat of transfer of the thiophenoxide-1,3,5-trinitrobenzene complex ($\Delta H_{\text{T,comp}}$): $\Delta H_{\text{T,comp}} = \Delta H_{\text{T,TNB}} + \Delta H_{\text{T,C}_6\text{H}_5\text{S}^-\text{Na}^+} + \Delta H_{\text{R},2} - \Delta H_{\text{R},1}$. These data are shown in Figure 1. Notice that the heats of transfer were measured at 25° while the heats of reaction were measured at 20° to conform to Cramp-ton's data. We feel that the heat capacities are small enough so that heats of transfer at 25° will not be significantly different from heats of transfer measured at 20°.

Discussion

The thermodynamics of formation of the Meisenheimer complex (Table III) will be considered first. The standard state for the data in Table III is dilute solution in the solvent used. This means that only the difference in ΔG , ΔH , and ΔS between the starting compounds and the complex in that particular solvent is known. For example, how a change in solvent affects the free energy of the starting materials or product is unknown. However, the effect of a change in solvent on the difference in free energy between the starting materials and product is a known quantity.

The most outstanding feature of the data in Table III is the fact that, except in 100% DMSO, the reaction is isoentropic. Changes in ΔH are exactly followed by changes in ΔG while $\Delta S \cong -9$ eu. In the following discussion, the sodium ion will be ignored. No indications of ion pairing were observed; so it seems reasonable that the sodium ion is not taking part in the reaction and its solvation remains the same throughout the reaction. Whenever two molecules combine to form one, there is a large loss of translational entropy. Using the Sakur-Tetrode equation, it can be estimated that the entropy loss occasioned by the formation of this complex in the gas phase is *ca.* -45 eu. To discuss the entropy of Meisenheimer complex formation in solution, the translational entropy loss *in solution* must be known. Unfortunately, it cannot be calculated at present with any accuracy in this system, although attempts in other systems have been made.^{16,17} Values of *ca.* -20 have been suggested as reasonable¹⁸ and Jencks has suggested that much lower values (*ca.* -30 to -40 eu) are possible. However, the situation is complicated by the structure of the solvent (unknown) and the interaction of the solvent molecules with the solvent.¹⁷ To the extent that the solute exists in a

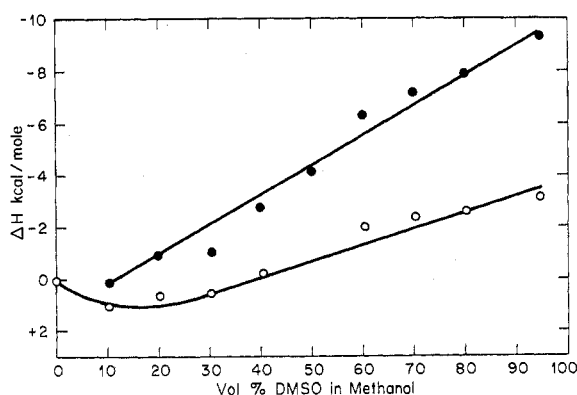
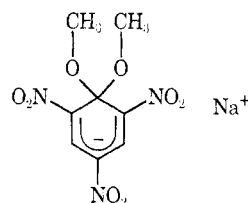


Figure 1.—Heat of transfer of the Meisenheimer complex (●) from 10% DMSO-90% methanol and of sodium thiophenoxide (○) from methanol to methanolic dimethyl sulfoxide at 20°.

“cage” formed by the solvent, the translational motion will be replaced by a vibration within the cage. The loss of these vibrations on combination will not be so large a factor as the loss of translational freedom. If a large negative value for the loss of translational entropy is adopted, then the observed values can be explained as arising from the imposition of a positive entropy term resulting when solvating solvent molecules are freed during the reaction. This means that the resulting Meisenheimer complex does not require so many complexed solvent molecules as do the reactants. Conversely, it can be argued that the observed negative entropy arises from the increased solvation of the complex, compared to the starting materials. It is quite obvious that our knowledge of solvent structure and solvent effects in such systems as this is minuscule and does not allow a decision to be made between the alternative explanations.

The enthalpy of this reaction is somewhat easier to deal with. The heat of transfer of the Meisenheimer complex is nearly identical with that of the related complex 3.¹¹ Since the two are quite similar in structure,



this is to be expected. It was suggested earlier¹¹ that this negative heat of transfer arose from stabilization of the highly colored, polarizable complex by DMSO-rich solvents due to London force interactions. Though the heats of transfer for the two complexes are the same, the heat of reaction between thiophenoxide and 1,3,5-trinitrobenzene decreases much less on going from methanol to DMSO than does the heat of reaction between methoxide and 2,4,6-trinitroanisole. The reason for this is obvious from the data in Figure 1. The heat of transfer of sodium thiophenoxide is exothermic, while that for sodium methoxide is quite endothermic.¹¹ In the reaction involving thiophenoxide, both products and reactants are becoming more stable as the DMSO concentration increases, but the increase in the stabilization of the product is greater.

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The thermodynamic data for the reaction between thiophenoxide and 1,3,5-trinitrobenzene can be compared with the few other Meisenheimer complex forming reactions which have been studied in detail. For the reaction of sodium methoxide with 2,4,6-trinitroanisole, ΔG , ΔH , and ΔS are available from pure methanol to 30% DMSO-methanol (v/v).¹⁹ As mentioned earlier, ΔH for this reaction decreases quite rapidly, as does ΔS , dropping from +3.05 eu in methanol to -2.45 eu in 30% DMSO-methanol. In general the entropies of reaction of alkoxide ions in alcohols with picrate esters²⁰ are negative. However, the entropies of their reaction with 1,3,5-trinitrobenzene²⁰ or cyanonitroanisoles¹⁰ are positive. A thorough study of the reactions of lyate ions in alcohols with 1,3,5-trinitrobenzene exists. Except for hydroxide ion in water (-30.5 eu) and isopropoxide ion in isopropyl alcohol (-9.7 eu), all of the values are between 7.6 and 13.3 eu.²¹ Norris has also published a thermodynamic study of the interaction of cyanide ion with 1,3,5-trinitrobenzene in a series of alcohols.²² Here both ΔH and ΔS become more negative as the alcohol becomes less polar. This was interpreted as indicating decreasing solvation of the cyanide ion as the alcohol was varied from methanol to *tert*-butyl alcohol. It seems that specific effects are quite important and there is not yet enough data available to arrive at any general conclusions about solvent effects in these systems.

It is interesting to compare the heats of transfer from methanol to methanol-DMSO for the several compounds for which data are available. The anions will be considered first. In all cases, the cation is sodium and its contribution will be the same in each case; so the observed differences must be due to the anions. For the highly colored, highly polarizable Meisenheimer complexes (sodium salt), the heats of transfer are quite negative (exothermic). For the less polarizable, less delocalized thiophenoxide, the heats of transfer are still negative, but significantly smaller in absolute magnitude than those of the Meisenheimer complexes. For the small, much less polarizable sodium methoxide,

the heats of transfer are positive. Thus, as the anion becomes "harder," less polarizable and with a smaller π system, it is solvated better by methanol and worse by DMSO. This is as expected.²³ Data are also available for several neutral molecules. The heat of transfer from methanol to 95% DMSO-5% methanol (v/v) of 2,4,6-trinitroanisole and 1,3,5-trinitrobenzene are -1.8 and -0.91 kcal/mol, respectively. The two molecules are similar. Apparently, the loss of hydrogen bonding by the methanol is compensated by the interactions of the π system with the dipolar DMSO. The heat of transfer from methanol to DMSO for methanol (-0.34 kcal/mol) and thiophenol (-0.94 kcal/mol) are again consistent with the polarizability of the molecules. However, since these molecules are undoubtedly extensively hydrogen bonded in both solvents, an interpretation in terms of polarizabilities alone is untenable. In Figure 1, the break in the plot of ΔH_{trans} vs. solvent composition for sodium thiophenoxide is unmistakable. Similar breaks are observed for similar plots of the heat of solution of both methanol and DMSO in methanolic DMSO.¹² Such behavior is quite common in aqueous systems and is often interpreted in terms of increased water structure being induced by the organic solute.²⁴ The reason for this behavior in this system is not clear.

The formation of Meisenheimer complexes is a reaction which is quite easy to study thermodynamically and one which is quite sensitive to solvent changes. As such, it is a good probe of solvent-solute interactions in complex organic systems. Work in this area is continuing.

Registry No.—Title Meisenheimer complex, 35886-34-1; sodium thiophenoxide, 930-69-8; 1,3,5-trinitrobenzene, 99-35-4; thiophenol, 108-98-5; methanol, 67-56-1; sodium methoxide, 124-41-4.

Acknowledgment.—We are grateful to the Research Corporation for partial support of this work. Support by the National Science Foundation through a predoctoral fellowship (L. L. M.) and undergraduate research support (S. E.) is gratefully acknowledged.

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