Intermediates in Nucleophilic Aromatic Substitution. XI.[1,2] Kinetic and Proton Magnetic Investigations of the Interaction of Lyate Ions with 1-Substituted 2,4,6-Tricyanobenzenes

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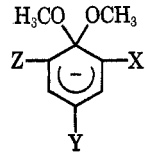
Rate constants for the formation, k_1, and those for the decomposition, k_{-1}, of the methoxyl complex of 2,4,6-tricyanoanisole (6) have been determined in DMSO-rich methanolic solutions. The equilibrium constant for the formation of 6 in methanol, determined from linear Benesi–Hildebrand plots, is 42,500-fold smaller than that for the formation of the 1,1-dimethoxy-2,4,6-trinitrocyclohexadienylide ion. No accumulation of complexes analogous to 6 have been observed in the interaction of hydroxide ion in aqueous solutions with 1-bromo-2,4,6-tricyanobenzene or with 2,4,6-tricyanoanisole in which case the rate-determining step is the formation of the complex. The structure of 6 has been established from its pmr spectrum. A linear relationship between the H-3,5 chemical shifts of the methoxyl Meisenheimer complexes of trinitro-, tricyano-, and the isomeric cyanodinitro- and dicyanonitroanisole in DMSO-d_6 and the equilibrium constants for their formation in methanol at 25.0° has been found.

In the previous parts of this series we have examined the stabilities of Meisenheimer complexes **1–5** quantitatively.[4,5] The obtained equilibrium constants for the formation of these complexes in methanol at 25.00°, $K_1 = 17{,}000$, $K_2 = 2600$, $K_3 = 280$, $K_4 = 34$, $K_5 = 10$ l. mol^{-1}, parallel the extent of the electron-withdrawing power of the substituents. More importantly, replacement of a para nitro group by a cyano group causes a considerably more dramatic effect than the corresponding replacement in the ortho position. In order to assess the relative importance of steric and resonance effects on these nucleophilic aromatic substitutions, we have investigated the interaction of methoxide ions with 2,4,6-tricyanoanisole (7) in methanol and methanolic dimethyl sulfoxide. The structure of the methoxyl complex of 7 (6) which results from this interaction has been established from the pmr parameters of the isolated and *in situ* generated complex. In addition, kinetic and thermodynamic investigations of the reaction of hydroxide ion with 1-bromo-2,4,6-tricyanobenzene (8) and 2,4,6-tricyanoanisole (7) in water afford additional comparisons between the nucleophilic reactivities of tricyano- and trinitro-substituted arenes.



1, X = Y = Z = NO_2
2, X = CN; Y = Z = NO_2
3, Y = CN; X = Z = NO_2
4, X = Z = CN; Y = NO_2
5, X = Y = CN; Z = NO_2
6, X = Y = Z = CN

Experimental Section

The solvents and reagents were prepared, purified, and standardized as previously described.[4-6]

1-Bromo-2,4,6-tricyanobenzene (8) was prepared from 2-bromomesitylene according to a modified procedure of Wallenfels, *et al.*[7] 2-Bromomesitylene (40 g, 0.201 mol) (Aldrich Chemical Co.) in a solution of 10 g of sodium hydroxide in 1 l. of water was heated to boiling and *ca.* one-half of 210 g of potassium permanganate was added. After refluxing the mixture for 15 hr, the remainder of the potassium permanganate was added and the mixture was refluxed for 24 hr. The hot reaction mixture was filtered, the manganese dioxide was washed three or four times with 150 ml of hot water, and the filtrate was concentrated to *ca.* 300 ml by distillation. The warm pot residue was acidified with concentrated nitric acid until the first thick white precipitate redissolved. After being cooled and allowed to stand, filtration yielded 2-bromomesitylenic acid (9), mp 275–278° (lit.[7] mp 260–275°), after drying *in vacuo*. Additional product was recovered by extracting the filtrate with isopropyl ether four or five times followed by rotary evaporation of the combined extracts with 100 ml of water added to decompose peroxides. 2-Bromomesitylenic triamide (10) was prepared by refluxing 17.0 g (58.8 mmol) of crude 9 in 48.1 ml of thionyl chloride for 22 hr, followed by vacuum rotary evaporation of the clear reaction solution to dryness. The residue was dissolved in 450 ml of dry benzene and ammonia was bubbled through the stirred reaction mixture for *ca.* 4 hr. The white precipitate of ammonium chloride and 10 was filtered, dried at 105–110°, and suspended in 200 ml of water. Filtration gave white crystalline 10, which was washed with water and dried at 105–110°, mp >300°. 1-Bromo-2,4,6-tricyanobenzene (8) was prepared by refluxing a mixture of 10.69 g (37.2 mmol) of 10, 7.5 g of sodium chloride, and 75 ml of phosphorus oxychloride for 6 hr. The excess phosphorus oxychloride was removed by rotary evaporation at 0.1 mm and the residue was pulverized and poured into 113 ml of ice water. The precipitate was filtered, washed with water, and dried *in vacuo* over phosphorus pentoxide. After recrystallization from benzene and drying *in vacuo*, the white crystals of 8 melted at 214–215° (lit.[7] 212–215°).

2,4,6-Tricyanoanisole (7) was prepared by the addition of 1.00 ml (6 mmol) of 5.95 *M* potassium methoxide in methanol to a warm solution of 1.09 g (5 mmol) of 8 in 10 ml of methanol. The reaction mixture was refluxed for 30 min, cooled, and poured onto *ca.* 25 g of ice. The white, crystalline precipitate was filtered, washed with distilled water, and dried *in vacuo* over phosphorus pentoxide, mp 147–148°.

Anal.[8] Calcd for $C_{10}H_5N_3O$: C, 65.7; H, 2.75; N, 23.0. Found: C, 65.4; H, 2.90; N, 22.7.

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(2) For recent reviews on Meisenheimer complexes and their relevance in nucleophilic aromatic substitution, see (a) R. Foster and C. A. Fyfe, *Rev. Pure Appl. Chem.*, **16**, 61 (1966); (b) E. Buncel, A. R. Norris, and K. E. Russell, *Quart. Rev., Chem. Soc.*, **22**, 123 (1968); (c) P. Buck, *Angew. Chem., Int. Ed. Engl.*, **8**, 120 (1969); (d) J. Miller, "Aromatic Nucleophilic Substitutions," Elsevier, Amsterdam, 1968; (e) M. R. Crampton, *Advan. Phys. Org. Chem.*, **7**, 211 (1969); (f) F. Pietra, *Quart. Rev., Chem. Soc.*, **23**, 504 (1969); (g) M. J. Strauss, *Chem. Rev.*, **70**, 667 (1970).

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(5) E. J. Fendler, J. H. Fendler, C. E. Griffin, and J. W. Larsen, *ibid.*, **35**, 287 (1970).

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(7) K. Wallenfels, F. Witzler, and K. Friedrich, *Tetrahedron*, **23**, 1353 (1967).

(8) The analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn.

2,4,6-Tricyanoanisole ($O^{14}CH_3$) was prepared by the addition of 1.09 g (5 mmol) of **8** to a solution containing 1 ml of methanol-^{14}C (200 μCi), 1 ml of methanol, and 1.00 ml (6 mmol) of 5.95 M potassium methoxide in methanol. Dry dioxane (3 ml) was added, and the reaction mixture was refluxed for *ca.* 10 min followed by stirring at room temperature for 5 hr. After cooling to *ca.* 0°, the reaction mixture was poured into 25 ml of ice water, filtered, washed with ice water, and dried *in vacuo* over phosphorus pentoxide. After recrystallization from aqueous methanol using decolorizing charcoal, the white needles melted at 146–147°. The pmr spectrum in DMSO-d_6 was identical with that of the unlabeled ether **7**.

Potassium 1,1-dimethoxy-2,4,6-tricyanocyclohexadienylide (**6**) was prepared by the addition of 0.192 ml (0.972 mmol) of 5.05 M potassium methoxide in methanol to a solution of 0.1668 g (0.985 mmol) of **7** in 0.60 ml of dry dioxane. The yellow crystals, which formed upon evaporation of a small amount of the solvents with dry nitrogen, were filtered and washed with dry benzene and anhydrous ether in an atmosphere of dry nitrogen. The yellow crystals were pulverized and dried *in vacuo* over phosphorus pentoxide.

Anal.[8] Calcd for $C_{11}H_3N_3O_2K$: C, 52.2; H, 3.18; N, 16.6; K, 15.4. Found: C, 50.3; H, 2.70; N, 16.3; K, 15.6.

Absorption spectra of **7** and **8** in several media were recorded on a Cary 14 spectrophotometer. Absolute absorbance measurements were obtained using a Beckman DU-2 spectrophotometer. The attainment of the equilibrium for the formation of **6** was followed at 400 nm in the thermostated cell compartment of the latter instrument. The temperature was measured inside the cells and was maintained within ±0.02°. The mixing techniques for the fast reactions have been described previously.[4] Since the concentration of **7** was at least 50-fold smaller than that of the methoxide ion, good pseudo-first-order kinetics were observed for the equilbrium formation of **6**. The rate constants, k_ψ, for the reaction of the hydroxide ion with **7** and **8** in aqueous solution were obtained by monitoring the increase in the absorbance at 360 nm. Good first-order plots for these reactions were obtained.

The 60-MHz pmr spectra were obtained with a Varian Associates A-60 spectrometer at ambient probe temperature or at 25° (probe temperature maintained with a V6040 variable-temperature controller). Unless otherwise noted, all spectra were determined on solutions in DMSO-d_6 using tetramethylsilane (TMS) as an internal standard; chemical shifts are given on the τ scale in parts per million relative to TMS (τ 10.00 ppm) and are accurate to ±0.03 ppm. Chemical shift data were taken from spectra determined at sweep widths of 500 Hz.

Results

The addition of nucleophiles to **7** and **8** results in the development of new absorption bands (Table I). When sodium methoxide (up to 2.1 M) is added to a methanolic solution of **7**, a fairly sharp new absorption band develops at 280 nm. At higher methoxide ion concentrations, or alternatively in DMSO–methanol solutions, a second band, with a maximum at 400 nm, appears (Figure 1). These two absorption bands are due to the formation of the methoxyl complex of 2,4,6-tricyanoanisole (**6**) since the isolated complex **6** shows the same absorption bands and since the equilibrium constants for the formation of **6** obtained from Benesi–Hildebrand plots at 280 and 400 nm agree within exerimental error (Table II).

The addition of sodium hydroxide to aqueous solutions of **7** and **8** results in the development of a new band at 360 nm, while absorption bands at 280 and 400 nm, characteristic of **6** and its possible hydroxyl analog, are absent (Table I). In aqueous sodium hydroxide solutions (up to 2.0 M) of **7** and **8** no evidence can be adduced, therefore, for the formation of σ-type addition complexes. The absorption at 360 nm is due to the formation of the 2,4,6-tricyanophenoxide ion. Supporting this interpretation is the fact that the absolute absorbances of **7** and **8** in alkaline solutions did not diminish upon neutralization to pH 3.[9]

In the absence of alkoxide ions, **7** is quite stable in methanol or in methanolic dimethyl sulfoxide solutions. Toluene–water extracted samples[11] of carbon-14 labeled

TABLE I
ABSORPTION SPECTRA OF 1-SUBSTITUTED 2,4,6-TRICYANOBENZENES

Substituent	Condition[a]	λ_1 (ϵ_1), nm (cm^{-1} l. mol^{-1})	λ_2 (ϵ_2), nm (cm^{-1} l. mol^{-1})
Br	Methanol	250 (12,400)	310 (6250)
Br	2.00 M NaOH		360 (2250), 400 (50)
OCH_3	Methanol	225 (32,900)	310 (2060)
OCH_3	2.11 M $NaOCH_3$, methanol	280 (18,000)	
OCH_3	5.73 M $KOCH_3$, methanol	280 (17,600)	400 (14,800)
OCH_3	DMSO–methanol, 70:30 (v/v)	260 (7000)	320 (2000)
OCH_3	0.024 M $NaOCH_3$, DMSO–methanol, 70:30 (v/v)	280 (17,300)	400 (18,900)
OCH_3	2.00 M NaOH		360 (2600), 400 (40)

[a] At 25.00°, [1-(X)-2,4,6-tricyanobenzene] $\simeq 5.0 \times 10^{-5}$ M, using a pair of 1.0-cm matched cells and blanks identical in composition with the samples with the exception of the aromatic compound.

TABLE II
INTERACTION OF 2,4,6-TRICYANOANISOLE (5.0×10^{-5} M) WITH SODIUM METHOXIDE IN METHANOLIC DIMETHYL SULFOXIDE AT 25.00°

[DMSO], M	$10^3 \times$ [$NaOCH_3$], M	$10^3 k_{obsd}$, sec^{-1}	k_1, l. mol^{-1} sec^{-1}	$10^4 k_{-1}$, sec^{-1}	K, l. mol^{-1}
0					0.4[a]
4.23					280,[a] 320[b]
7.03	5.24	2.30	0.33	6.0	550
	7.86	3.13			
	10.48	4.00			
	13.10	4.80			
	15.75	5.90			
	22.00	7.65			
8.44	2.00	1.45	0.57	3.0	1890
	4.15	2.57			
	5.20	3.15			
	8.30	4.80			
	10.4	6.16			
	14.00	8.20			
10.55	1.3	2.69	1.75	2.0	8000
	2.6	5.52			
	4.12	7.56			
	5.20	9.77			
	8.24	14.7			
11.25	1.04	4.90	4.00		
	1.30	5.92			
	2.08	8.50			
	2.60	11.0			
	4.16	16.9			
	8.32	32.4			
	10.4	42.0			

[a] From Benesi–Hildebrand plots at 280 nm (eq 1). [b] From Benesi–Hildebrand plots at 400 nm (eq 1).

(9) The pK of 2,4,6-tricyanophenol is *ca.* 1[10] and hence would be completely ionized, whereas a σ complex would unquestionably decompose in acidic solution.

(10) K. Dimroth and K. J. Kraft, *Angew. Chem., Int. Ed., Engl.*, **3**, 384 (1964).

(11) J. H. Fendler, *J. Amer. Chem. Soc.*, **88**, 1237 (1966).

7 ($O^{14}CH_3$) in methanol did not show any loss of activity at 45.00° over a period of 1 week and no absorbance changes were observed for the methanol solutions over the same time period. However, subsequent to the formation of 6, especially under pmr conditions, a slow decomposition was observed (*vida supra*).

Rate constants for the formation, k_1, and the decomposition, k_{-1}, of 6 in methanol are too high to be kinetically determined by our techniques.[4,5] The equilibrium constant, K, for the formation of 6 in methanol has been obtained, however, from the slope and intercept of linear Benesi–Hildebrand[12] plot (eq 1) where A

$$\frac{[7]}{A} = \frac{1}{\epsilon} + \frac{1}{K\epsilon}\left(\frac{1}{[CH_3O^-]}\right) \quad (1)$$

is the absorbance in a 1.0-cm cell and ϵ is the molar extinction coefficient (Figure 2). The stability of complex 6 increases in DMSO-rich methanolic solutions to such an extent that pseudo-first-order rate constants for its equilibrium attainment, k_{obsd}, could be determined at 400 nm. Since the absorbance remains essentially constant over a large range of methoxide ion concentration, the equilibrium (eq 2) is complete. The ob-

$$7 + CH_3O^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} 6 \quad (2)$$

served rate constants, k_{obsd}, for solutions of (1.0–22.0) · 10^{-3} M sodium methoxide in 7.03, 8.44, 10.55, and 11.25 M DMSO in methanol are given as shown in eq 3 where

$$k_{obsd} = k_1[OCH_3^-] + k_{-1} \quad (3)$$

k_1 is the second-order rate constant for the formation of 6 and k_{-1} is the first-order rate constant for its decomposition. Table II contains the data for k_{obsd}, k_1, and k_{-1} in methanol at 25.00° and in several dimethyl sulfoxide–methanol solutions. Errors in k are ±4% and those in k_{-1} are ±10%.

Tables III and IV summarize the kinetic and thermodynamic parameters for the reactions of 7 and 8 with

TABLE III

INTERACTION OF 2,4,6-TRICYANOANISOLE (3×10^{-4} M) WITH HYDROXIDE ION IN WATER[a]

[NaOH], M	10^3k_ψ, sec^{-1}, at 25.00°	10^3k_ψ, sec^{-1}, at 45.00°
0.010		4.50
0.015		6.90
0.020		9.20
0.025		11.3
0.030	2.73	13.8
0.050	3.97	
0.10	8.05	
0.15	11.9	
0.20	15.2	
0.25	17.3	

[a] k_{OH} = 6.71 × 10^{-2} and 4.33 × 10^{-1} l. mol^{-1} sec^{-1} at 25.00 and 45.00°, respectively; E = 17.6 ± 0.8 kcal mol^{-1}; $\Delta S^{\pm}$ at 25.00° = −7.0 ± 2.0 eu.

hydroxide ion in aqueous solution. Errors in k_{OH} are ±5%.

The pmr data for 7 and 8 and for isolated and *in situ* generated 6 in DMSO-d_6 solutions are collected in Table V.

(12) H. A. Benesi and J. H. Hildebrand, *J. Amer. Chem. Soc.*, **71**, 2703 (1949).

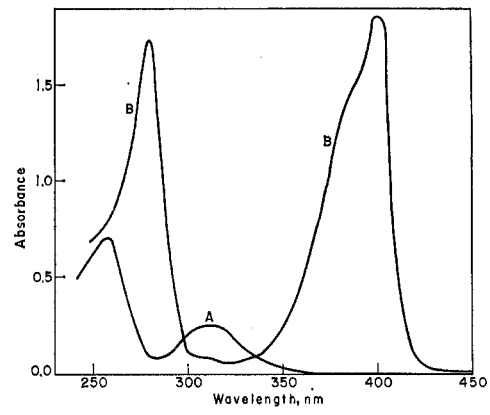


Figure 1.—Absorption spectra of 2,4,6-tricyanoanisole in 75:25 DMSO–MeOH (v/v) at 25.00°, using a pair of matched 1.00-cm cells. [$NaOCH_3$] = 0 M (A) and 0.024 M (B).

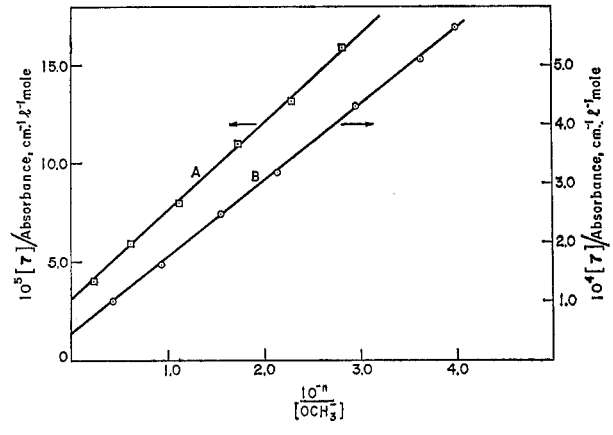


Figure 2.—Benesi-Hildebrand plots for the formation of 6: A, in 4.23 M DMSO, n = 3, determined at 400 nm; B, in MeOH. n = 0, determined at 280 nm.

TABLE IV

INTERACTION OF 1-BROMO-2,4,6-TRICYANOBENZENE (3×10^{-4} M) WITH HYDROXIDE ION IN WATER[a]

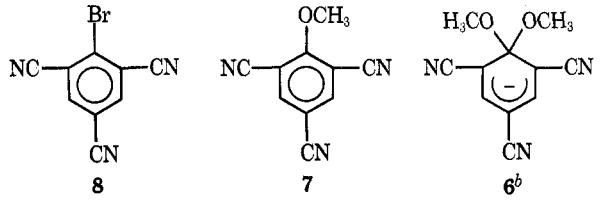
[NaOH], M	10^3k_ψ, sec^{-1}, at 25.00°	10^3k_ψ, sec^{-1}, at 45.00°
0.01	2.49	5.43
0.02	3.81	11.1
0.04		20.5
0.05	5.45	26.7
0.10	8.54	
0.15	13.5	
0.20	16.8	

[a] k_{OH} = 7.30 × 10^{-2} and 5.00 × 10^{-1} l. mol^{-1} sec^{-1} at 25.00 and 45.00°, respectively; E = 18.1 ± 0.6 kcal mol^{-1}; $\Delta S^{\pm}$ at 25.00° = −8.7 ± 2.0 eu.

Discussion

The stability of the methoxyl complex of 2,4,6-tricyanoanisole (6) in methanol is 42,500-fold smaller than that of its trinitro-substituted analog 1. Significantly, the presence of one and two nitro groups in the isomeric 2,4,6-dicyanonitroanisole (5 and 6) and cyanodinitroanisole (2 and 3) Meisenheimer complexes results in 25- to 85-fold and 700- to 6500-fold, respectively, greater equilibrium constants for complex formation than that for 6. These results are in agreement with quantum mechanical calculations which have demonstrated that

TABLE V
PMR SPECTRA OF 1-SUBSTITUTED 2,4,6-TRICYANOBENZENES AND THE POTASSIUM 1,1-DIMETHOXYCYCLOHEXADIENYLIDE[a]



	8	7	6[b]
τ_{OCH_3}		5.68,[c] 5.86	7.12 (7.08),[c] (7.23)
$\tau_{H-3,5}$	1.00,[c] 1.50	1.52,[c] 1.88	2.82 (2.83),[c] (3.15)

[a] At 25° unless specified otherwise. [b] Values in parentheses have been obtained for the complex generated *in situ* by the dropwise addition of 5.95 *M* potassium methoxide in methanol to a *ca.* 2 *M* solution of **7** in DMSO-d_6. [c] At 42°.

the negative charge resides largely on the nitro groups.[13] The equilibrium constants for the formation of complexes **1**–**6** are manifestations of the extent of electron delocalization at the site of nucleophilic attack by the substituents.

Increasing the concentration of dimethyl sulfoxide as the cosolvent in methanol considerably enhances the stability of **6**. The equilibrium constant for its formation in 30% DMSO (4.23 *M*) is greater by a factor of 750 than that in pure methanol (Table II). A similar, although somewhat less significant, rate enhancement by dipolar aprotic dimethyl sulfoxide has been observed for the formation of **1**[14] and **4**.[5] In all these cases, the increase in the equilibrium constant with increasing dimethyl sulfoxide concentration is a composite effect of an increase in k_1 and a decrease in k_{-1}. Furthermore, the magnitude of the rate-constant enhancement by DMSO is greater for the forward reaction, k_1, than for the retardation of the reverse reaction, k_{-1}. In the case of **4** a linear relationship has been obtained between log k_1 and log k_{-1} *vs.* molar dimethyl sulfoxide concentration. Similarly, log k_1 values for the formation of **6** increase linearly with increasing molar concentrations of DMSO in the 7.03 to 11.25 *M* range (not shown). If this linear plot is extrapolated to zero dimethyl sulfoxide concentration, a value of $k_1 = 4.7 \times 10^{-3}$ l. mol^{-1} is obtained for the formation of **6**. Combining this value with that for the equilibrium constant for the formation of **6** in methanol, 0.4 l. mol^{-1}, the rate constant for the decomposition of **6** in methanol is found to be $k_{-1} = 1 \times 10^{-3}$ sec^{-1}. However, due to the possible invalidity of a linear extrapolation, this value should only be considered to be accurate within an order of magnitude. Indeed, the linear relationship between the rate enhancement of k_1 and the DMSO concentration may be fortuitous. Rate constants for the formation of complex **6** in DMSO–MeOH solutions, $k_1^{\text{DMSO-MeOH}}$, are related to that in pure methanol, k_1^{MeOH}, and to the activity coefficents of **7** and of sodium methoxide in the DMSO–MeOH solutions as shown in eq 4. Similarly, the rate

$$k_1^{\text{DMSO-MeOH}} = k_1^{\text{MeOH}} \frac{f'_7 f'_{\text{NaOCH}_3}}{f'^{\ddagger}} \quad (4)$$

constants for the decomposition of **6** in DMSO–MeOH solutions, $k_{-1}^{\text{DMSO-MeOH}}$, are expressed as shown in eq 5

$$k_{-1}^{\text{DMSO-MeOH}} = k_{-1}^{\text{MeOH}} \frac{f'_6}{f''^{\ddagger}} \quad (5)$$

where $f'^{\ddagger}$ and $f''^{\ddagger}$ in eq 4 and 5 represent the activity coefficients for the transition states of the forward and reverse reactions relative to methanol, respectively. From determinations of the rate constants for the formation and decomposition of **1** in DMSO–MeOH mixtures and the relative solubilities of **1** and 2,4,6-trinitroanisole (**11**) in these solvents, we demonstrated recently[14] that DMSO stabilized both the initial and transition states for the *formation* of complex **1** and that the stabilization is greater for the transition state than for the ether **11**. DMSO also stabilizes both the initial and transition states for the *decomposition* of the complex. Conversely, complex **1** is stabilized to a greater extent than the transition state through which the ether **11** is reformed.[14] These results, of course, substantiate the accepted mechanism for bimolecular nucleophilic aromatic substitution[2] and imply that due care should be taken in interpreting solvent effects.

Since no detectable intermediates are observed in the interaction of hydroxide ion with **7** or **8** in aqueous solutions and by analogy with the interaction of hydroxide ion with **11**,[15] the rate-determining step in these reactions is the formation of the hydroxyl Meisenheimer complexes. The rate constant for the formation of the hydroxyl Meisenheimer complex of **7** in water is roughly 15 times greater than that for the formation of **6** in methanol. Differences in the media as well as the uncertainties in the k_1 value in methanol do not allow, however, meaningful comparisons of the reactivities of hydroxide and methoxide ions toward **7**. The greater activating power of the nitro group as compared to the cyano group is, once again, manifested in the twofold smaller value of k_{OH} for the formation of the hydroxyl adduct of **7** than that of **11**. The corresponding difference in the reactivity of methoxide ion in methanol toward **7** and **11** (k_1 for **1** = 17 l. mol^{-1} sec^{-1},[15] k_1 for **6** $\simeq$ 4.7×10^{-3} l. mol^{-1} sec^{-1}) is considerably greater. These relative reactivity differences are due to the solvation requirements of the respective initial and transition states. The determined enthalpies and entropies of activation for the interaction of hydroxide ion with **7** and **8** correspond to those available for the hydroxydehalogenation of nitro-substituted arenes.[2] Lack of data for **11** prohibits a more direct comparison of the enthalpy and entropy values for trinitro- and tricyano-substituted benzenes.

We have again used proton magnetic resonance spectroscopy to substantiate the postulated structure of complex **6** and to investigate the possible existence of other intermediates or transients. No pmr data has been reported previously for tricyano-substituted benzenes. The spectrum of complex **6** consists of a singlet at τ 7.08 ppm (relative intensity 6) and a singlet at τ 2.83 ppm (relative intensity 2) attributable to the methoxyl and ring proton resonances, respectively. This spectrum is completely consistent with a 1:1 σ complex and eliminates the possibility of a charge-transfer or π complex. In addition, the strong shielding of the complex protons relative to those of the parent ether **7** (see Table V) is characteristic of Meisenheimer complexes[1,2,4-6] and is the consequence of the rehybridization of C-1 from sp^2 to sp^3 and the increased electron

(13) P. Caveng, P. B. Fischer, E. Heilbronner, A. L. Miller, and H. Zollinger, *Helv. Chim. Acta*, **50**, 848 (1967).
(14) J. H. Fendler, and J. W. Larsen, unpublished results.
(15) V. Gold and C. H. Rochester, *J. Chem. Soc.*, 1710 (1964).

density in the ring. Not unexpectedly both the chemical shifts of the methoxyl resonances of complexes **1–6** (τ 6.92–7.08 ppm) and the magnitude of the upfield shifts ($\Delta\delta$ 1.00–1.49 ppm)[4,5] are relatively insensitive to the position or nature of the aromatic substituents. However, the chemical shift of the H-3,5 resonances and the difference in the chemical shifts ($\Delta\delta$)[4,5] increase as a function of increasing substitution of cyano groups in the ring. HMO calculations have shown that the negative charge of Meisenheimer complexes is primarily delocalized over the nitro groups.[13] Since charge delocalization by cyano groups should be less than that by nitro groups, an increase in π-electron density, and hence in the upfield shifts, as a function of increasing cyano substitution is quite reasonable. Indeed, we have found a linear relationship between the H-3,5 chemical shifts of complexes **1–6** and the respective equilibrium constants for complex formation, K (Figure 3). No linear relationship exists, however, between the H-3,5 chemical shifts of the anisoles and K and thus the corresponding plot for $\Delta\delta$ and K exhibits a poor linear relationship. These results suggest that contributions other than electron density to the H-3,5 chemical shifts of complexes **1–6**, such as anisotropy, are either constant or relatively small and that approximate equilibrium constants for complexes containing other substituents at C-2, -4, and -6, *e.g.*, CF_3, could be predicted from the pmr spectra of the complex.

In the case of 2,4,6-trinitroanisole,[4,16] 2-cyano-4,6-dinitro- and 4-cyano-2,6-dinitroanisole,[4] and 2,4-dicyano-6-nitroanisole,[5] initial attack of methoxide ion

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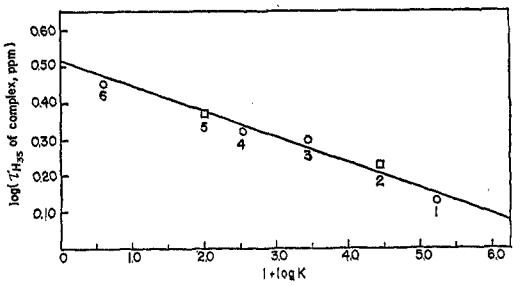

Figure 3.—Plot of log ($\tau_{H_{35}}$, ppm) for complexes **1–6** in DMSO-d_6 *vs.* log K for complex formation in methanol at 25.00°: ○, $\tau_{H_{35}}$; □, $(\tau_{H_3} + \tau_{H_5})/2$.

was found to occur at C-3, an unsubstituted aromatic carbon atom para to a nitro group. In order to investigate this possibility and the existence of any other fairly stable transients involved in the interaction of methoxide ions with **7**, we examined the formation of **6** *in situ* in DMSO-d_6 using pmr spectroscopy. On the time scale necessitated by this technique,[4,5] no transients could be detected prior to or concurrent with the formation of **6**. On a much longer time scale (>24 hr at 42°), partial decomposition of **6** was found to occur.

Registry No.—**6**, 29826-25-3; **7**, 29897-71-0; **7** $O^{14}CH_3$, 29897-72-1; **8**, 13520-05-3.

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Kinetics and Mechanism of Methyl Transfer from Sulfonium Compounds to Various Nucleophiles

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A series of substituted phenyldimethylsulfonium perchlorates has been prepared and the reaction of these compounds with various nucleophiles has been investigated. With oxygen nucleophiles in water, elevated temperatures are required to effect methylation, whereas a slow reaction is observed with amines in water at 25°. A large solvent effect associated with these reactions permits the convenient study of the methylation of amine nucleophilies in acetonitrile at 25°. The values of ρ obtained from Hammett plots of the kinetic data are quite similar, using either hydroxide ion, pyrrolidine, or *n*-butylamine as the added nucleophile. Activation parameters and data derived from various linear free-energy relationships for the reaction of methylsulfonium compounds with nucleophiles are compared with data for the analogous reactions in which methyl iodide acts as the methylating agent. These data are discussed in relation to enzyme-catalyzed transmethylations which use the sulfonium compound *S*-adenosylmethionine as the methyl donor.

The process of transferring one-carbon moieties is ubiquitous in biological systems.[1] A considerable amount of information has been accumulated concerning the mechanism by which the folate enzymes activate formaldehyde and effect one-carbon transfer.[2] Equally important and even more widespread in their distribution in metabolic pathways are the reactions involving transfer of intact methyl or methylene groups.[3] Acceptors of these one-carbon moieties include such diverse molecules as catecholamines,[4] nucleic acids,[5] histones,[6] quinones and fatty acids,[7] to name but a few. The remarkable feature of biological transmethylations, involving such a wide variety of acceptor molecules, is that the donor of the "activated" methyl group is universally (−)-*S*-adenosyl-L-methionine[1] (**1**), hereafter referred to as SAM. The reaction of SAM with a nucleophilic acceptor results in the formation of *S*-adeno-

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