Meisenheimer Complexes. 1,1 and 1,3 Adducts from 2,6-Dinitro-4-trifluoromethylsulfonyl- and 4-Methylsulfonylanisoles. Kinetics in Methanolic Dimethyl Sulfoxide

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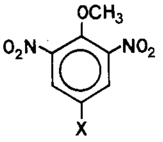
In methanolic solution, 2,6-dinitro-4-trifluoromethylsulfonylanisole (**4a**) gives a Meisenheimer 1,1-dimethoxy adduct **6a** which is completely formed in a solution with methoxide ion concentration as low as 5×10^{-4} M. The kinetics of formation and decomposition of **6a** have been studied between pH 4 and 13.5 by using buffer solutions. Whereas the reaction **4a** + $CH_3O^- \rightarrow$ **6a** is the only one observed above pH 12, the formation of **6a** arises partly from the attack of a methanol molecule on the parent ether **4a** between pH 10 and 11. Ths is apparently the first report of this kind in the field of benzenic Meisenheimer complexes. At pH >14.2, i.e., in methanolic solutions of potassium methoxide $3 \times 10^{-3} - 0.2$ M, the formation of the transient 1,3-dimethoxy adduct **5a** precedes that of **6a**. The kinetic and thermodynamic parameters for formation and decomposition of **5a** and **6a** are compared with data obtained in this work for the analogous 1,3 and 1,1 adducts **5b** and **6b** derived from 2,6-dinitro-4-methylsulfonylanisole **4b** as well as with data previously reported for the trinitro 1,3 and 1,1 adducts **9** and **8**. The results emphasize the much greater stabilizing effect exerted by the SO_2CF_3 group on the Meisenheimer adducts as compared with that of the nitro and methylsulfonyl groups. The adducts **5a** and **6a** are in fact the most stable benzenic 1,3 and 1,1 adducts yet observed in methanol. The dimethyl sulfoxide influence on the reactions is also discussed.

NMR studies have shown that the reaction of various substituted 4-X-2,6-dinitroanisoles **1** with methoxide ion in Me_2SO initially yields the 1,3 complex **2** which is subsequently converted into the thermodynamically more stable 1,1 complex **3**.[2-5] Kinetic studies of this interaction in methanol–Me_2SO mixtures allowed a better understanding of its mechanism.[6,7] Decreasing the Me_2SO content in the mixtures results in a dramatic decrease in the stability and the lifetime of 1,3 complexes which are thus less easily observed in mixtures rich in methanol.[6-8] As could be expected, the minimum Me_2SO amount necessary to their detection is, however, dependent to a large extent on the electron-withdrawing power of the X substituent. Whereas 1,3 complexes formed from 4-fluoro- and 4-chloro-2,6-dinitroanisoles[6a] are only observable in mixtures with >70% Me_2SO by weight, those formed from 2,4,6-trinitroanisole[7] and 3,5-dinitro-4-methoxypyridine[6c] (considered to be a 4-aza-2,6-dinitroanisole) can be seen in pure methanol despite very short half-lives of about 0.10 and 0.40 s, respectively, at 25 °C.



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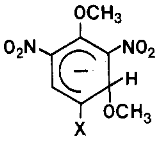

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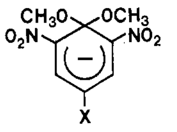

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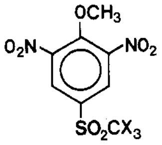
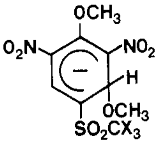
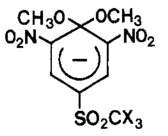
The Hammett σ parameters determined for the SO_2CF_3 group from pK_a measurements on anilines, phenols, and benzoic acids containing this substituent indicate that it is the strongest neutral electron-withdrawing group which has ever been studied.[9] This is clearly reflected in nucleophilic aromatic substitution reactions. Both 1-chloro-2-nitro-4-trifluoromethylsulfonyl- and 1-chloro-4-nitro-2-trifluoromethylsulfonylbenzenes react faster than does 1-chloro-2,4-dinitrobenzene with nucleophiles such as methoxide ion or amines.[10] In view of these findings, we could reasonably expect the reaction of methoxide ion with 2,6-dinitro-4-trifluoromethylsulfonylanisole to give a 1,3 complex as well as a 1,1 complex which are more stable than the respective complexes of less activated substrates. This is, of course, of interest with respect to general implications of the formaton of such species in nucleophilic aromatic substitution reactions.[11] As a continuation of our work in this area, we have therefore carried out a comprehensive kinetic and thermodynamic analysis of the formation and decomposition of **5a** and **6a** in methanol and methanol–Me_2SO mixtures. Following a preliminary communication,[12] we now report detailed results and additional data for this study. For the purpose of comparison, we report also rate and equilibrium data for the reaction of methoxide ion with 2,6-dinitro-4-methylsulfonylanisole (**4b**) in the same mixtures.







X = F 4a 5a 6a

X = H 4b 5b 6b

Results

2,6-Dinitro-4-trifluoromethylsulfonylanisole (4a). A. 1,1-Complex Formation in Methanol. The reaction of methoxide ion with **4a** in methanol results in the immediate formation of the yellow-colored 1,1 adduct **6a**, the absorption spectrum of which is shown in Figure 1 (λ_{max} 465 nm, ϵ 15 300 M^{-1} cm^{-1}). At this wavelength, the parent molecule has negligible absorption. The formation of **6a**, which was identified by NMR spectroscopy,[5] appears, in fact, to be complete in a solution with methoxide ion concentration as low as 5×10^{-4} M. We had, therefore, to use buffer solutions in the range pH 4–13.5 to carry out a comprehensive study of the formation and decomposition of **6a**. The buffer solutions were prepared from various carboxylic acids and phenols AH and made up so as to give a total ionic strength of 0.01 M from the buffer species A^- alone without any added neutral salt. As we have shown previously,[13] the mean activity coefficient $\gamma_\pm$ could then be calculated by using a simplified Debye–Hückel type equation ($\log \gamma_\pm = -Bz^2 \sqrt{\mu}$), thus allowing the hydrogen ion concentration $[H^+]$ of the methanolic solutions to be deduced from the measured activity a_{H^+} of the solvated proton ($[H^+] = a_{H^+}/\gamma_\pm$). The pH values are relative to the standard state in methanol.

A plot (not shown) of the variations at 465 nm of the optical density obtained at equilibrium as a function of pH shows that

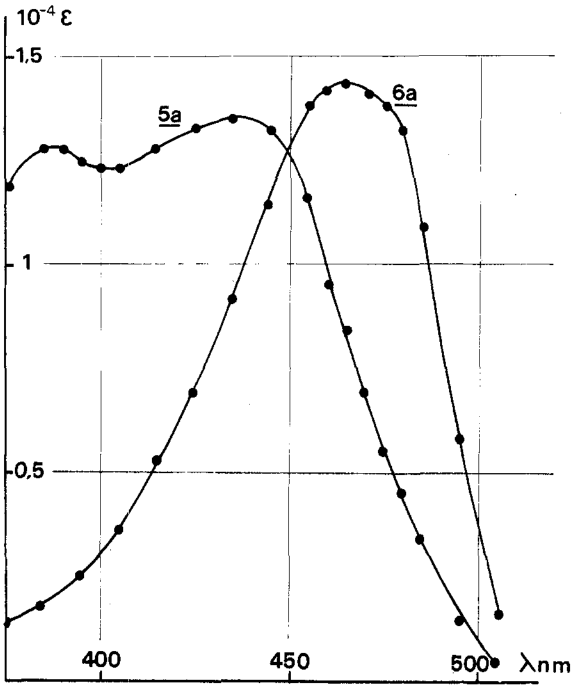


Figure 1. Absorption spectra of complexes **5a** and **6a** in methanol.

the 1,1 complex **6a** is half formed at pH 10.68. In view of the relatively high value of the coefficient B in methanol[13] (B = 1.80), this $\mathrm{pH}_{1/2}$ value corresponds to the $\mathrm{p}K_\mathrm{a}$ value for the formation of **6a** (eq 1) at $\mu = 0.01$ M. Assuming $\gamma_{4a} \simeq 1$ in eq 2, which is here a reasonable assumption, the thermodynamic $\mathrm{p}K_\mathrm{a}$ value at zero ionic strength was determined by a Debye–Hückel extrapolation from similar $\mathrm{pH}_{1/2}$ measurements at $\mu = 2.5 \times 10^{-3}$, 5×10^{-3}, and 2×10^{-2} M: $\mathrm{p}K_\mathrm{a}{}^{4a} = 10.90 \pm 0.03$.

$$\mathbf{4a} + \mathrm{CH_3OH} \rightleftarrows \mathbf{6a} + \mathrm{H^+} \qquad K_\mathrm{a} = \frac{a_{6a}a_{\mathrm{H^+}}}{a_{4a}} \tag{1}$$

$$\mathrm{p}K_\mathrm{a} = \mathrm{pH}_{1/2} - \log\frac{\gamma_{6a}}{\gamma_{4a}} \tag{2}$$

Employing the stopped-flow method as well as conventional methods, we have investigated the kinetics of the formation and decomposition of **6a** at 465 nm. In all cases, the appearance or disappearance of **6a** was a clear first-order process. The pH dependence of the observed first-order rate constant k_obsd for the combined formation and decomposition of **6a** is shown in Figure 2. Variation of buffer concentration at constant pH did not significantly change the value of k_obsd with experimental error, indicating the absence of catalysis by buffer, at least at the low concentrations used. In addition, a smooth pH–rate profile was obtained despite the fact that buffers of varying chemical types were used, showing as expected in methanol that buffer species (particularly phenoxide anions) do not react with **4a**. We have observed essentially similar behavior in the case of 2,4,6-trinitroanisole (**7**),[14] and 2,4-dinitro-5-methoxythiophene and -selenophene (**10** and **12**)[15] (see structures in discussion).

The rate constant k_obsd reflects the rate of approach to equilibrium between **4a** and **6a** and is the sum of the individual pseudo-first-order rate constants k_f and k_d, respectively, for the formation and decomposition of **6a**. As shown previously,[15,16] k_f and k_d for such a system may be calculated from eq 3 and 4 where $a_{\mathrm{H^+}_{1/2}} = 10^{-\mathrm{pH}_{1/2}}$.

$$k_\mathrm{f} = \frac{k_\mathrm{obsd}}{1 + \dfrac{a_{\mathrm{H^+}}}{a_{\mathrm{H^+}_{1/2}}}} \tag{3}$$

$$k_\mathrm{d} = \frac{k_\mathrm{obsd}}{1 + \dfrac{a_{\mathrm{H^+}_{1/2}}}{a_{\mathrm{H^+}}}} \tag{4}$$

Complete data are graphically represented in Figure 3, which shows the pH dependence of k_f and k_d.

As those observed for **7**, **10**, and **12**[14,15] as well as for 4,6-dinitro-7-methoxybenzofurazan (**14**)[1c] (see structure in discussion), these pH–rate profiles fit very well to equations of the form

$$k_\mathrm{f} = k_1{}^{\mathrm{CH_3OH}} + k_2[\mathrm{CH_3O^-}] = k_1{}^{\mathrm{CH_3OH}} + \frac{k_2K_\mathrm{s}}{a_{\mathrm{H^+}}\gamma_\pm} \tag{5}$$

$$k_\mathrm{d} = k_{-1}[\mathrm{H^+}] + k_{-2} = \frac{k_{-1}a_{\mathrm{H^+}}}{\gamma_\pm} + k_{-2} \tag{6}$$

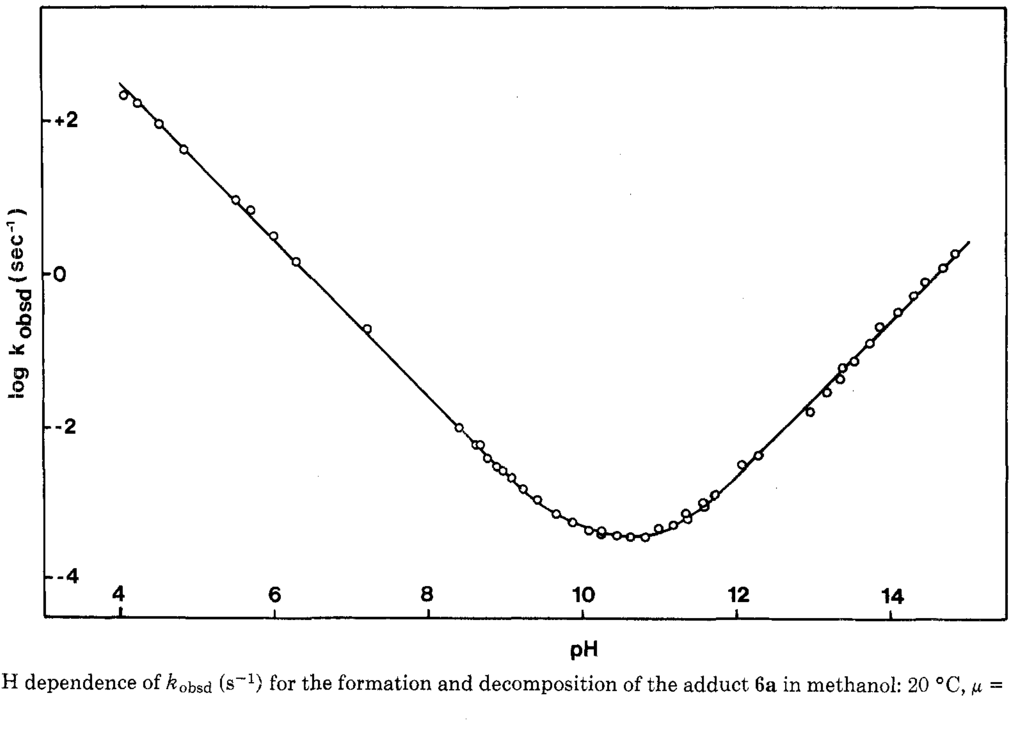


Figure 2. The pH dependence of k_obsd ($\mathrm{s^{-1}}$) for the formation and decomposition of the adduct **6a** in methanol: 20 °C, $\mu = 0.01$ M.

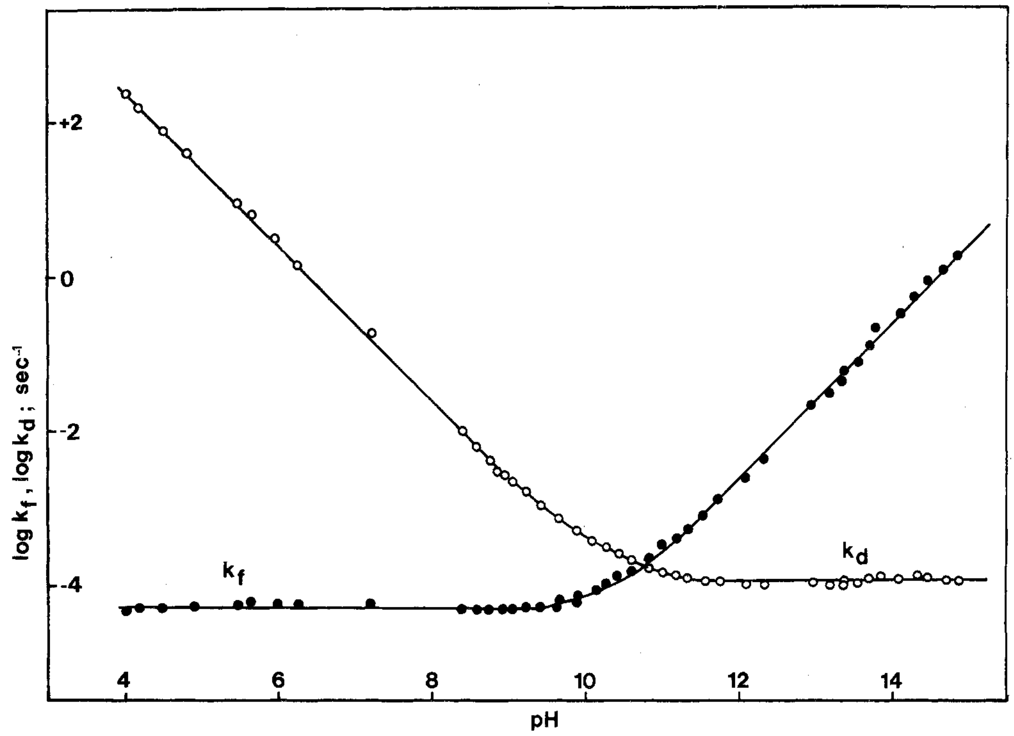


Figure 3. The pH dependence of k_f (s^{-1}) and k_d (s^{-1}) for the formation and decomposition of the adduct **6a** in methanol: 20 °C, μ = 0.01 M.

Scheme A shows the reactions to which the various constants refer, viz., $k_1^{CH_3OH}$ and k_2 represent attack of **4a** by methanol and methoxide ion, respectively, while k_{-1} and k_{-2} refer to H^+-catalyzed and spontaneous decomposition of **6a,** respectively. The various rate coefficients have been easily determined from the two linear portions of each of k_f and k_d pH–rate profiles (high and low pH regions of each, respectively). We thus obtain $k_1^{CH_3OH} = 5 \times 10^{-5}\ s^{-1}$, $k_{-1} = 1.66 \times 10^6\ M^{-1}\ s^{-1}$, $k_2 = 141\ M^{-1}\ s^{-1}$, $k_{-2} = 1.17 \times 10^{-4}\ s^{-1}$ ($K_s = 10^{-16.86}$ at 20 °C[13]).

Scheme A

$$4a + CH_3OH \underset{k_{-1}}{\overset{k_1^{CH_3OH}}{\rightleftharpoons}} 6a + H^+ \qquad (7)$$

$$4a + CH_3O^- \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} 6a \qquad (8)$$

Inserting these values into the expression given by eq 9 for k_{obsd}, we see that at low pH (pH <9), $k_{obsd} = k_d$, i.e., only the reverse reaction $6a + H^+ \rightarrow 4a + CH_3OH$ is important while above pH 12 $k_{obsd} = k_f$, i.e., only the reaction $4a + CH_3O^- \rightarrow 6a$ is important. This is in agreement with our experimental results. In the intermediate pH range, values of the terms $k_2K_s/a_{H^+}\gamma_\pm$ and/or $k_{-1}a_{H^+}/\gamma_\pm$ cannot be neglected relative to the sum $k_{-2} + k_1^{CH_3OH}$ so that no plateau appears in the experimental pH profile (see Figure 2).

$$k_{obsd} = \frac{k_{-1}a_{H^+}}{\gamma_\pm} + k_{-2} + k_1^{CH_3OH} + \frac{k_2K_s}{a_{H^+}\gamma_\pm} \qquad (9)$$

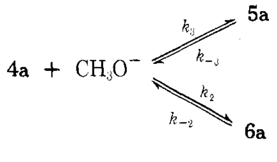
The formation of the adduct **6a** has also been studied in dilute solutions of potassium methoxide 5×10^{-4}–3×10^{-3} M, keeping the ionic strength μ constant at 0.01 M by adding NaBr as necessary. In this case, only the reaction 8 occurs and the observed first-order rate constant k_{obsd} is given by the reduced equation

$$k_{obsd} = k_{-2} + k_2[CH_3O^-] \qquad (10)$$

A plot of k_{obsd} against the methoxide ion concentration afforded a good straight line with a slope equal to k_2 and an intercept equal to k_{-2}. As expected from the data obtained in buffer solutions, the intercept was, in fact, not distinguishable from zero and did not allow a new estimation of k_{-2}. In contrast, a nice agreement was observed between the value of 150 $M^{-1}\ s^{-1}$ so obtained for k_2 and that determined (141 $M^{-1}\ s^{-1}$) from the pH profile of Figure 3 (see Table I).

B. 1,3-Complex Formation in Methanol. When the methoxide ion concentration was greater than 3×10^{-3} M, the oscilloscope pictures revealed that the appearance of **6a** is preceded by the much faster formation of a thermodynamically less stable species which is completely formed in a solution of potassium methoxide 0.20 M. In view of previous results in analogous systems,[2-4] there was little doubt that this species, which shows an absorption band at 430 nm (ϵ 14 000 $M^{-1}\ cm^{-1}$), was the 1,3 adduct **5a** (Figure 1). We have, in fact, recently confirmed the structure of this transient 1,3 adduct by NMR spectroscopy in Me_2SO-d_6.[5]

Scheme B



Scheme B describes the interaction which consists of two separated steps. The first step is the fast equilibration between **4a** and **5a.** Assuring pseudo-first-order conditions with an excess of the methoxide reagent (concentration range of 5×10^{-3}–0.2 M) the observed first-order rate constant k'_{obsd} for this process is given by eq 11.

$$k'_{obsd} = k_{-3} + k_3[CH_3O^-] \qquad (11)$$

Values of k_3 and k_{-3} were easily obtained from a plot of k'_{obsd} vs. $[CH_3O^-]$, which is linear: $k_3 = 750\ M^{-1}\ s^{-1}$, $k_{-3} = 25\ s^{-1}$. We calculated the equilibrium constant $K_3 = 30\ M^{-1}$ from $K_3 = k_3/k_{-3}$.

Table I. Rate and Equilibrium Constants for the Formation and Decomposition of Benzenic or Heterocyclic *gem*-Dimethoxyl Complexes 6a, 6b, 8, 11, 13, and 15 in Methanol at 20 °C

	6a[a]	**6b**[a]	8	11[d]	13[d]	15[e]
k_2, M^{-1} s^{-1}	141	1.75	11.8[b]	28.2	71	2.52×10^5
k_{-2}, s^{-1}	1.17×10^{-4}	1.68×10^{-2}	6.05×10^{-4} [b]	7.8×10^{-5}	1.04×10^{-5}	4.9×10^{-6}
$k_1^{CH_3OH}$, s^{-1}	5×10^{-5}	1.50×10^{-7}	1.80×10^{-6} [c]	10^{-7}	5.75×10^{-7}	4.46×10^{-3}
$k_{-1}^{H^+}$, M^{-1} s^{-1}	1.66×10^6	4.7×10^7	2.9×10^6 [c]	1.05×10^4	2.65×10^3	1.7×10^3
pK_a	10.68	14.86	12.58[b]	11.16	9.86	5.93

[a] This work. [b] Calculated at 20 °C from data in ref 4b. [c] Reference 14. [d] Reference 15. [e] Reference 16.

The second step is the slow equilibrium formation of the stable 1,1 adduct **6a** from the molecule which is considered to be in instantaneous equilibrium with **5a**. As previously shown,[6,7] the pertinent expression for the corresponding observed first-order rate constant k''_{obsd} is given by

$$k''_{obsd} = k_{-2} + \frac{k_2[CH_3O^-]}{1 + K_3[CH_3O^-]} \qquad (12)$$

Neglecting k_{-2}, which is small compared with the second term at these base concentrations, eq 12 reduces to

$$k''_{obsd} = \frac{k_2[CH_3O^-]}{1 + K_3[CH_3O^-]} \qquad (13)$$

Whereas a plot of k''_{obsd} vs. $[CH_3O^-]$ is curved (Figure 4), an inversion plot according to

$$\frac{1}{k''_{obsd}} = \frac{1}{k_2[CH_3O^-]} + \frac{K_3}{k_2} \qquad (14)$$

is linear. The intercept and the reciprocal of the slope provide $K_3/k_2 = 0.182$ s and $k_2 = 174$ M^{-1} s^{-1}, respectively, leading to a value of 31.7 M^{-1} for K_3. In view of the differences in the ionic strength of the solutions, the results compare well with our earlier determinations. On the other hand, and as expected, k''_{obsd} reaches a plateau at the highest base concentrations where we have a complete initial formation of **5a** (Figure 4). Since this latter complex undergoes a complete conversion into **6a**, the maximum value of k''_{obsd}, which is given by

$$k''_{obsd}{}^{max} = \frac{k_2}{K_3} = k_{-2}\frac{K_2}{K_3} \qquad (15)$$

can be used as a reference for its lifetime. A half-life of about 0.14 s is thus calculated for **5a** in pure methanol ($t_{1/2} = 0.693/k''_{obsd}{}^{max}$).

C. 1,1- and 1,3-Complex Formation in Solutions of Potassium Methoxide in Methanol–Me_2SO Mixtures. In methanol–Me_2SO mixtures with a Me_2SO content equal to or greater than 13.35% Me_2SO by weight, the formation of **5a** was found always to precede that of **6a**, even at the lowest methoxide ion concentrations used. Scheme B was therefore analyzed as just described in methanol. In mixtures containing 13.35 and 25.3% Me_2SO by weight, both k_3 and k_{-3} could be determined from the linear plots of k'_{obsd} vs. $[CH_3O^-]$ and consequently K_3 from the ratio k_3/k_{-3}. Measuring k''_{obsd} for the appearance of **6a** also allowed the determination of k_2 and K_3. At higher Me_2SO concentrations, k_{-3} was too small for an accurate determination and plots of k'_{obsd} vs. $[CH_3O^-]$ afforded only k_3 values. On the other hand, the plots of k''_{obsd} vs. $[CH_3O^-]$ are limited to the plateau corresponding to the maximum value of k''_{obsd}, preventing also a determination of k_2 and K_3 from eq 14.

The rate and equilibrium parameters for the formation and decomposition of **6a** in methanol are compared in Table I with analogous data reported for the most stable *gem*-dimethoxyl complexes **8, 11, 13,** and **15** previously studied. Table II summarizes the various kinetic and equilibrium parameters associated with the formation and decomposition of **5a** and **6a** in the methanol–Me_2SO mixtures.

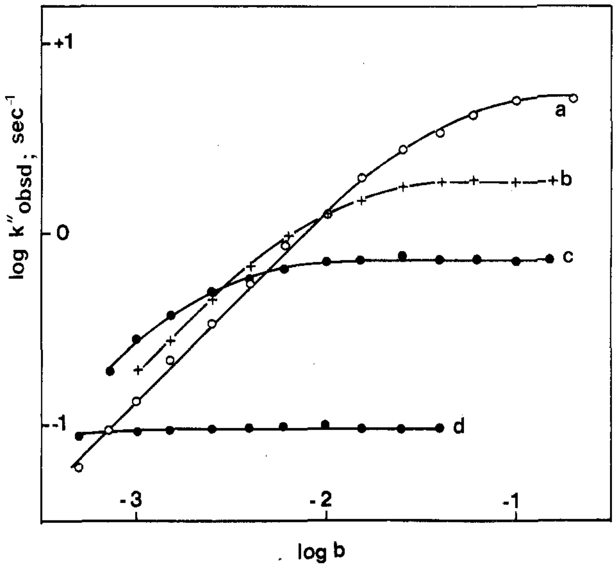


Figure 4. Plots of k''_{obsd} against methoxide ion concentration b for the appearance of **6a** in methanol (a), 13.35% (b), 25.3% (c), and 47.5% (d) Me_2SO.

2,6-Dinitro-4-methylsulfonylanisole (4b). In the concentration range of 5×10^{-4}–10^{-1} M, the reaction of methoxide ion with **4b** in methanol and methanol–Me_2SO mixtures with less than about 35% Me_2SO by weight gives directly the pink-colored 1,1 complex **6b** [λ_{max} (CH_3OH) 512 nm (ϵ 19 000 M^{-1} cm^{-1})]. The observed first-order rate constant k_{obsd} for the equilibrium attainment of **4b** is therefore given by eq 10. Plotting k_{obsd} vs. $[CH_3O^-]$ easily yields values of k_2 and k_{-2} for formation and decomposition of **6b**. The equilibrium constant K_2 was calculated from $K_2 = k_2/k_{-2}$.

In the mixtures with higher Me_2SO concentrations, the formation of the 1,3 adduct **5b** [λ_{max} 455 nm (ϵ 20 600 M^{-1} cm^{-1})] occurs first followed by the much slower appearance of **6b**. A kinetic analysis of the interaction according to scheme B leads to the rate and equilibrium parameters for the formation and decomposition of **5b** and **6b** which are listed in Table III.

Discussion

General Features. As can be seen in Tables I and IV, the stability of the trifluoromethylsulfonyl 1,1 and 1,3 complexes **6a** and **5a** is respectively 70- and 12-fold higher than that of the trinitro analogues **8** and **9** which are usually considered to be the references for this type of complex. Replacing the 4-SO_2CF_3 group of **4a** by a 4-SO_2CH_3 group still causes a more dramatic decrease in the K values for complex formation. Whereas the 1,1 complex **6b** is about 10^4-fold less stable than **6a**, the 1,3 complex **5b** is not observable in pure methanol as opposed to **5a**. Using an estimated value of 0.08 for $K_3{}^{5b}$ in

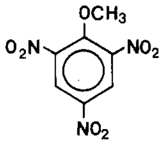
Table II. Kinetic and Equilibrium Parameters for the Reaction of Methoxide Ion with 4a in Methanol and Various Methanol–Me$_2$SO Mixtures at 20 °C

Solvent composition % Me$_2$SO by weight	1,3 complex **5a** k_3, M^{-1} s^{-1}	k_{-3}, s^{-1}	K_3, M^{-1}	1,1 complex **6a** k_2, M^{-1} s^{-1}	k_{-2}, s^{-1}	K_2, M^{-1}	$k_{\text{obsd}}{''}^{\text{max}}$, s^{-1}	$t_{1/2}$, s
0	750	25	30	141, 150	1.17×10^{-4}	1.2×10^6	≃5	≃0.14
13.35	1 530	8.3	185	350			1.9	0.365
25.3	2 300	3.7	620	450			0.73	0.95
47.5	7 750						9.8×10^{-2}	7.05
57.5	20 000						2.7×10^{-2}	25.6
67	44 000						7.4×10^{-3}	93.5
76	100 000						1.86×10^{-3}	372
84.8							4.1×10^{-4}	1690
92.6							6.3×10^{-5}	11 000

Table III. Kinetic and Equilibrium Parameters for the Reaction of Methoxide Ion with 4b in Methanol and Various Methanol–Me$_2$SO Mixtures at 20 °C

Solvent composition % Me$_2$SO by weight	1,3 complex **5b** k_3, M^{-1} s^{-1}	k_{-3}, s^{-1}	K_3, M^{-1}	1,1 complex **6b** k_2, M^{-1} s^{-1}	k_{-2}, s^{-1}	K_2, M^{-1}	$k_{\text{obsd}}{''}^{\text{max}}$, s^{-1}	$t_{1/2}$, s
0				1.75	1.68×10^{-2}	101		
13.35				2.74	1.12×10^{-2}	245		
25.3				5.8	8×10^{-3}	720		
47.5	362	30	12	17			1.4	0.5
57.5	1 150	14.7	78	37			0.59	1.17
67	3 160	5.5	575	117			0.204	3.4
76	10 000						0.06	11.5
84.8	33 000						0.017	40.8
92.6	≃140 000						2.75×10^{-3}	2.5×10^2

methanol (see further in discussion) a ratio $K_3{}^{5a}/K_3{}^{5b}$ of about 375 is obtained. These results clearly emphasize the much stronger electron-withdrawing character of the SO$_2$CF$_3$ group as compared with that of the NO$_2$ and SO$_2$CH$_3$ groups.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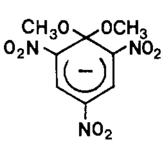
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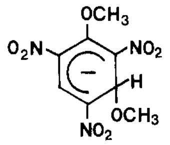
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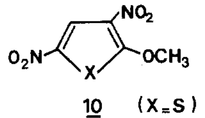
It is of interest to note that complexes **5a** and **6a** are the most stable benzenic 1,3 and 1,1 complexes which have ever been observed to form in methanol.

The differences in the ratios $K_2{}^{6a}/K_2{}^{8}$ and $K_3{}^{5a}/K_3{}^{9}$ reveal that the effect of the SO$_2$CF$_3$ group on the complex stability is greater when it is located in the para rather than in the ortho position of the sp^3 carbon. This behavior is essentially the same as that observed for the nitro group and therefore suggests a higher capacity of resonance stabilization by a para SO$_2$CF$_3$ group than by an ortho SO$_2$CF$_3$ group. This also confirms previous conclusions[9,17] that the SO$_2$CF$_3$ group exerts a large conjugative effect, presumably involving the d orbitals of the sulfur atoms,[18] in addition to an expected large inductive effect. In the present case, this would allow an extensive delocalization of the negative charge of the 1,1 complex **6a**, thus enhancing its stability.

The higher stability of **6a** and **5a** compared with that of trinitro analogues **8** and **9** or methylsulfonyl analogues **6b** and **5b** derives both from an increase in the rate of formation and a decrease in the rate of decomposition. For methoxide ion attack on the methoxyl-bearing carbon of the parent ethers, the second-order rate constant is 141 M^{-1} s^{-1} for **4a** compared with 11.8 M^{-1} s^{-1} for **7** and 1.75 M^{-1} s^{-1} for **4b**. For attack on the unsubstituted 3 carbon, the second-order rate constants are 750 M^{-1} s^{-1} for **4a**, 690 M^{-1} s^{-1} for **7**, and 35 M^{-1} s^{-1} for **4b**. This dependence of the rates on the substituent are of the same order of magnitude than those observed by Shein et al. in comparing the nucleophilic attack of methoxide ion on 2,4-dinitrochlorobenzene with that on related 4- (or 2-) trifluoromethylsulfonyl or methylsulfonyl 2- (or 4-) nitrochlorobenzenes.[10] A more noteworthy feature is the occurrence of methanol attack on the methoxyl-bearing carbon of **4a**. As shown by the simple calculation of each term of eq 9, the methanol attack contributes for about 10–15% to the rate of appearance of **6a** between pH 10 and 11. This is really a striking result since such a process appeared to be negligible in the pH range where the adducts **8** and **6b** are formed and was found to contribute only to a very small extent to the formation of the roughly similarly stable five-membered ring adducts **11** and **13**[15] (about 2–3% in the most favorable conditions for **13**). As can be seen in Table I, the methanol attack on **4a** is, however, much less significant than that which occurs on the methoxyl carbon of 4,6-dinitro-7-methoxybenzofuran (**14**) to give the more stable adduct **15**.[16]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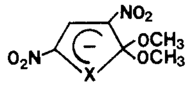
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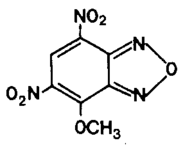
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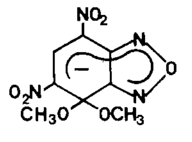
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Table IV. Effect of Substituent on the Rate and Equilibrium Constants for Formation and Decomposition of 1,1 and 1,3 Complexes in Pure Methanol

X	SO_2CF_3	NO_2	-N-	CN	SO_2CH_3	CF_3	Cl	F	H
k_2, M^{-1} s^{-1}	141[a]	11.8[b]	16.5[d]	2.82[e]	1.75[a]	0.4[h]	1.2×10^{-2}[h]	2.5×10^{-3}[h]	1.5×10^{-3}[h]
k_{-2}, s^{-1}	1.17×10^{-4}[a]	6.05×10^{-4}[b]	5.75×10^{-3}[d]	1.68×10^{-2}[a]	1.68×10^{-2}[a]	8×10^{-2}[h]	5[h]	30[h]	20[h]
K_2; M^{-1}	1.2×10^{6}[a]	19 500[b]	2870[d]	168[e]	101[a]	5[h] (2)[i,j]	2.5×10^{-3}[h] (4.3×10^{-3})[j]	8.5×10^{-5}[h]	7.5×10^{-5}[h] (9×10^{-5})[j]
$k_2^{SO_2CF_3}/k_2^{X}$	1	11.9	8.5	50	80	350	1.17×10^{4}	5.65×10^{4}	9.4×10^{4}
$k_{-2}^{X}/k_{-2}^{SO_2CF_3}$	1	5.2	49	144	144	585	4.3×10^{4}	2.56×10^{5}	1.7×10^{5}
$K_{2-}^{SO_2CF_3}/K_2^{x}$	1	61.5	418	7.15×10^{3}	1.19×10^{4}	2.4×10^{5}	5×10^{8}	1.41×10^{10}	1.6×10^{10}
k_3, M^{-1} s^{-1}	750[a]	690[c]	275[d]	60[f]	35[g]	2.5[h]	2[h]	1[h]	
k_{-3}, s^{-1}	25[a]	270[c]	25[d]	420[f]	440[g]	1400[h]	2000[h]	5000[h]	
K_3, M^{-1}	30[a]	2.56[c]	11[d]	0.143[f]	0.08[g]	1.8×10^{-3}[h]	10^{-3}[h]	2×10^{-4}[h]	
$k_3^{SO_2CF_3}/k_3^{X}$	1	1.09	2.72	12.5	21.4	300	375	750	
$k_{-3}^{X}/k_{-3}^{SO_2CF_3}$	1	10.8	1	16.8	18	56	80	200	
$K_3^{SO_2CF_3}/K_3^{X}$	1	11.7	2.73	210	375	1.67×10^{4}	3×10^{4}	1.5×10^{5}	

[a] This work at 20 °C. [b] Calculated at 20 °C from ref 4b. [c] Calculated at 20 °C from ref 7. [d] Reference 6c. [e] Reference 6b. [f] Extrapolated from data in ref 6b. [g] Extrapolated from data of this work. [h] Extrapolated from data in ref 6a. [i] Reference 22. [j] Reference 21.

As pointed out by the following ratios, **6a** and **5a** decompose spontaneously more slowly than their nitro or methylsulfonyl analogues: $k_{-2}^{8}/k_{-2}^{6a} = 5$, $k_{-2}^{6b}/k_{-2}^{6a} = 144$, $k_{-3}^{9}/k_{-3}^{5a} = 10.8$, $k_{-3}^{5b}/k_{-3}^{5a} = 18$. The H^+-catalyzed decomposition of **6a** is similarly slower than that of **8** and **6b**: the ratios k_{-1}^{8}/k_{-1}^{6a} and k_{-1}^{6b}/k_{-1}^{6a} are equal to 1.7 and 28.3, respectively. Also, the high value of k_{-1} for **6a** should be noted with respect to those found for the similarly stable five-membered ring 1,1 adducts **11** and **13**. Whereas these latter decompose spontaneously 1.5- and 11-fold slower than **6a**, respectively, they have a much lower susceptibility to the H^+-catalyzed decomposition than **6a**: the ratios k_{-1}^{6a}/k_{-1}^{11} and k_{-1}^{6a}/k_{-1}^{13} are equal to 158 and 630, respectively. Unfortunately, the available data do not warrant an extensive discussion of possible reasons for this interesting contrast at this time.

Effect of Solvent. Adding Me_2SO to the methanolic solutions causes a strong increase in the equilibrium constants K_2 and K_3 for the formation of 1,1 complexes **6a** and **6b** and 1,3 complexes **5a** and **5b**. This reflects both an increase in the rate constants of formation k_2 and k_3 and a decrease in the rate constants of decomposition k_{-2} and k_{-3}, respectively. Rather than emphasizing these findings, which are quite similar to those previously found for other Meisenheimer complexes,[6,8,19] it is more interesting to point out some other striking features.

Let us turn our attention to Figure 5, where the available data for formation and decomposition of 1,1 and 1,3 complexes derived from all the substituted 4-X-2,6-dinitroanisoles studied to date are summarized. As can be seen, good parallel straight lines are obtained on plotting log k_2, log k_3 as well as $-\log k_{-2}$, $-\log k_{-3}$ vs. the molar fraction of Me_2SO, implying that the effect of solvent composition is approximately independent of the nature of the substituent and of the type of complex which is formed. This is in agreement with previous observations of the existence of such linear relationships between the specific rate or equilibrium constants of various Meisenheimer adducts and the amount of Me_2SO cosolvent.[6b,8,19,20] As a consequence, the *relative* thermodynamic stability of 1,1 and 1,3 complexes is practically unaffected by a change in the Me_2SO concentration, which is an interesting result with respect to the lifetime of transient 1,3 complexes. As mentioned before, the maximum value of the observed first-order rate constant k''_{obsd} can be used as a measure for this lifetime. In view of the independence of the ratio K_2/K_3, eq 15 thus shows that the influence of Me_2SO on $k_{obsd}''^{max}$ is similar to that observed on the rate constant k_{-3} for the decomposition of 1,3 complexes. Increasing the Me_2SO con-

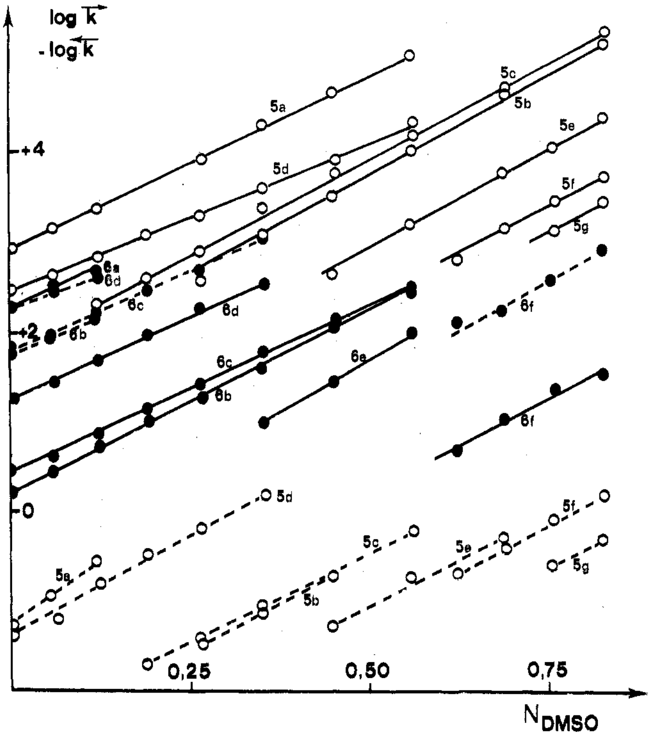

Figure 5. Plots of the rate constants for the formation $\overrightarrow{k}$ (—) and decomposition $\overleftarrow{k}$ (- - -) of 1,3 and 1,1 complexes against molar fraction of Me_2SO: **5a**, **6a** (X = SO_2CF_3); **5b**, **6b** (X = SO_2CH_3); **5c**, **6c** (X = CN); **5d**, **6d** (X = -N-); **5e**, **6e** (X = CF_3); **5f**, **6f** (X = Cl); **5g**, **6g** (X = F).

centration therefore results in a strong decrease in $k_{\mathrm{obsd}}''^{\mathrm{max}}$ which is paralleled by a strong increase in the lifetime of these transient species. Whereas the half-life of **6a** is about 0.14 s in methanol, it is almost 11 000 s in a mixture containing 92.6% Me_2SO, i.e., 10^5-fold greater than in the absence of Me_2SO cosolvent. Similarly, the half-life of **6b** is changing from 0.5 s in 47.5% Me_2SO to 250 s in 92.6% Me_2SO. These results, which are best appreciated on inspection of Tables II and III which list the $t_{1/2}$ values in the various mixtures, allow us to account for the possible NMR observation of such transient species in Me_2SO.[4b,5,21]

The linear correlations of Figure 5 are also useful to safely estimate rate and equilibrium constants not directly measurable in a given solvent. This is in particular the case in methanol where the values of k_2, k_{-2}, and K_2 for formation and decomposition of 1,1 complexes with X = CF_3, Cl, F, H as well as values of k_3, k_{-3}, and K_3 for formation and decomposition of 1,3 complexes with X = CN, SO_2CH_3, CF_3, Cl, F have thus been obtained by extrapolation of the data available in methanol–Me_2SO mixtures. In the case of X = CF_3, Cl, H the values so calculated for K_2 are equal to 5, 2.5×10^{-3}, and 7.5×10^{-5}, respectively, which compares fairly well with the values of 2, 4.3×10^{-3}, and 9×10^{-5} previously determined by using the acidity function method.[22,23] This agreement between these two sets of values further supports the reliability of the extrapolation procedure. All the calculated parameters, together with those of the complexes which could be directly studied in methanol, are summarized in Table IV. They allow a general analysis of the effect on the X substituent on the stabilities of 1,1 and 1,3 complexes in the 4-X-2,6-dinitroanisole series. First, we note that going from X = SO_3CF_3 to X = F results in a much larger decrease in the equilibrium constant K_2 for 1,1 complex formation than in the equilibrium constant K_3 for 1,3 complex formation: the ratios $K_2^{SO_2CF_3}/K_2^{F}$ and $K_3^{SO_2CF_3}/K_3^{F}$ are respectively equal to 1.6×10^{10} and 1.5×10^5. This difference in the effect of the substituent X on the equilibrium constants of 1,1 and 1,3 complexes, respectively, mainly reflects the well-known fact that complex stability is more sensitive to changes in the substituent para to the site of nucleophilic attack than ortho to it.[4,6,24] On the other hand, it appears from the ratios $k_2^{SO_2CF_3}/k_2^{X}$ and $k_{-2}^{X}/k_{-2}^{SO_2CF_3}$ that changes in the equilibrium constant K_2 for 1,1 complex formation are more dependent on changes in the rates of decomposition than of those in the rates of formation, suggesting a somewhat reactant-like transition state. When going from X = SO_2CF_3 to X = H, we note, however, *that the changes in k_2 become more and more coresponsible* for the changes in K_2, indicating that the transition state must progressively move closer to the complex as the electron-withdrawing power of the X substituent is decreased. Since complex stability is decreasing at the same time, such an effect would be consistent with Hammond's postulate.[25] Table IV shows also that the changes in the K_3 values for 1,3 complex formation are more dependent on the changes in k_3 than of those in k_{-3}, the difference between the two factors increasing with decreasing electron-withdrawing power of X. Again in agreement with Hammond's postulate, this now suggests a transition state which is more and more complex-like.

A rigorous discussion of the origin of the observed solvent effects on the rate parameters for formation and decomposition of complexes has to be made in terms of the changes in the activity coefficients of the reactants, transition states, and products.[19b,26,27] The rate constants k_2, k_3 and k_{-2}, k_{-3} in MeOH–Me_2SO mixtures are in fact related to those in pure *methanol* by the equations[19b,26]

$$k_2^{\mathrm{MeOH-Me_2SO}} = k_2^{\mathrm{MeOH}} \frac{\gamma'_{\mathrm{ether}}\gamma'_{\mathrm{CH_3OK}}}{\gamma'_2{}^{\ddagger}}$$

$$k_3^{\mathrm{MeOH-Me_2SO}} = k_3^{\mathrm{MeOH}} \frac{\gamma'_{\mathrm{ether}}\gamma'_{\mathrm{CH_3OK}}}{\gamma'_3{}^{\ddagger}}$$

$$k_{-2}^{\mathrm{MeOH-Me_2SO}} = k_{-2}^{\mathrm{MeOH}} \frac{\gamma'_{\mathrm{1,1\ complex}}}{\gamma'_2{}^{\ddagger}}$$

$$k_{-3}^{\mathrm{MeOH-Me_2SO}} = k_{-3}^{\mathrm{MeOH}} \frac{\gamma'_{\mathrm{1,3\ complex}}}{\gamma'_3{}^{\ddagger}}$$

where the γ''s represent the transfer activity coefficients for the various species, i.e., the activity coefficients in the mixed solvent compared to pure methanol as the standard state ($\gamma' = \gamma^{\mathrm{MeOH-Me_2SO}}/\gamma^{\mathrm{MeOH}}$). The fact that the solvent effects on the rate constants are independent of the substrates and of the type of complex thus suggests that the ratios $\gamma'_{\mathrm{ether}}/\gamma'^{\ddagger}$ and $\gamma'_{\mathrm{complex}}/\gamma'^{\ddagger}$ are themselves independent of these factors. Since Fendler et al.[25] have shown that the stabilizing effect of Me_2SO is in the order complex > transition state > parent ether and increases with increasing the Me_2SO concentration, one possibility would be that the relative changes in γ'_{ether}, $\gamma'^{\ddagger}$, and $\gamma'_{\mathrm{complex}}$ are the same in a given mixture whatever the substrate and the formed complex may be. This is not unreasonable in the case of γ'_{ether} and $\gamma'_{\mathrm{complex}}$ but this further supposes in the case of $\gamma'^{\ddagger}$ that the transition state would keep the same structure when changing the substituent in a given series (1,1 complex or 1,3 complex) or changing the series (1,1 complex and 1,3 complex). Such a conclusion is then inconsistent with those derived on the basis of a comparison of the contributions of changes in $\vec{k}$ and $\overset{\leftarrow}{k}$ values to the variations in the K values, and therefore with the application of Hammond's postulate to our results. Another possibility would be that the changes in γ'_{ether}, $\gamma'^{\ddagger}$, and $\gamma'_{\mathrm{complex}}$ are dependent on the substrates and of the type of complex but that the ratios $\gamma'_{\mathrm{ether}}/\gamma'^{\ddagger}$ and $\gamma'_{\mathrm{complex}}/\gamma'^{\ddagger}$ are fortuitously the same. This would rule out, of course, any physical meaning to the correlations observed between log k values and the Me_2SO concentration but would not be inconsistent with changes in the structures of the transition states. Evidently, the experimental data do not permit us to choose between these two conflicting situations which point out that due care must therefore be taken in interpreting solvent effects observed on rate and equilibrium constants for formation and decomposition of Meisenheimer complexes.

Experimental Section

Materials. 2,6-Dinitro-4-trifluoromethylsulfonyl- and 4-methylsulfonylanisoles (**4a** and **4b**) were prepared as previously described:[5] **4a**, mp 59 °C; **4b**, mp 206 °C. Methanol and methanolic potassium methoxide solutions were prepared as previously described.[13a] The various buffers used for the rate measurements were purified according to classical methods. Buffers used were trichloroacetate (pH 4–5), dichloroacetate (pH 5–6.5), salicylate (pH 6.8–8.1), succinate (pH 8.3–9), benzoate (pH 8.6–9.7), 2,4,6-trichlorophenoxide (pH 9.8–10.6), 2,6-dichlorophenoxide (pH 10.7–11.5), 4-cyanophenoxide (pH 11.4–12.4), and 4-chlorophenoxide (pH 12.9–13.5).

Rate and pH Measurements. Stopped-flow determinations were performed on a Durrum stopped-flow spectrophotometer, the cell compartment of which was maintained to ±0.5 °C. Other kinetic measurements were made using a Beckman DB-G spectrophotometer. All kinetic runs were carried out under pseudo-first-order conditions with a substrate concentration of about 3×10^{-5} M. Rate constants are accurate to ±3%.

The pH was measured on a Radiometer Model pH meter according to a method previously reported.[13] The pH values are relative to the standard state in pure methanol.

Registry No.—**4a**, 19822-29-8; **4b**, 39880-50-7; **5a**, 35344-09-3; **5b**, 40203-33-6; **6a**, 35298-04-5; **6b**, 40203-26-7; methoxide ion, 3315-60-4.

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Conformational Analysis. 32. Conformational Energies of Methyl Sulfide, Methyl Sulfoxide, and Methyl Sulfone Groups[1]

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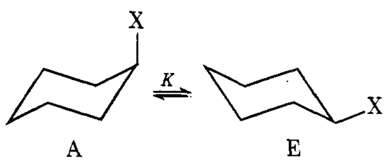
Conformational energy ($-\Delta G$) values for the title groups have been determined by low-temperature ^{13}C NMR signal area measurements. The values for CH_3SO_2, 2.5 kcal/mol, and CH_3SO, 1.2 kcal/mol, were determined by a "counterpoise" method, taking the ratio of the areas of the decoalesced spectra (at -95 ± 5 °C) of *cis*-4-methylcyclohexyl methyl sulfone and *cis*-4-methylcyclohexyl methyl sulfoxide and allowing for -1.7 kcal/mol as the ΔG value of the methyl group. The value for CH_3S, 1.0 kcal/mol, was determined both by an analogous method and by direct low-temperature ^{13}C NMR analysis of cyclohexyl methyl sulfide; it is in good agreement with the value in the literature.

Recently we reported[1] that the CH_3S group attached at C(5) in a 1,3-dioxane has a stronger preference for the equatorial conformation than it does when attached to a cyclohexyl ring.[2,3] In contrast, similarly placed methylsulfinyl (CH_3SO) and methylsulfonyl (CH_3SO_2) groups prefer the axial conformation. In the latter two cases, unfortunately, comparison with cyclohexyl methyl sulfoxide and sulfone was tenuous; in the case of the sulfone function, only a rather inaccurate value (2.5 kcal/mol) for phenylsulfonyl ($C_6H_5SO_2$) derived by NMR from an extremely one-sided equilibrium[4] was available; and the sulfoxide value[5] (1.9 kcal/mol) rested on the now discredited kinetic method. It is clear, however, even from the crude data, that cyclohexyl methyl sulfide, sulfoxide, and sulfone all exist with the sulfur function quite predominantly in the equatorial conformation.

The availability of ^{13}C NMR spectroscopy now makes it possible to determine, by signal area measurement at low temperature, conformational equilibria for a variety of substituents in a number of systems which were heretofore difficult to study.[6] However, measurement of signal areas[7] is difficult for conformations constituting less than 5% of the total. This difficulty can be obviated through use of a "counterpoise" method.[8] Thus, for cyclohexyl methyl sufide (**1**), it is adequate to measure the equilibrium shown in Scheme I, since the minor isomer constitutes about 6% of the total at −90 °C. But for cyclohexyl methyl sulfoxide (**2**), this value drops to 3.5% and for the sulfone **3** to much less than 1%; for the sulfoxide and sulfone functions it is desirable to measure the equilibrium shown in Scheme II, and this is preferable even for CH_3S. Here the equilibrium constants correspond to 12% of the minor isomer for **4**, 19% for **5**, and 10% for **6**, values

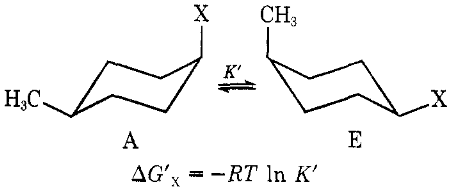
Scheme I



$\Delta G_X = -RT \ln K$

1, $X = CH_3S$
2, $X = CH_3SO$
3, $X = CH_3SO_2$

Scheme II



$\Delta G'_X = -RT \ln K'$

4, $X = CH_3S$
5, $X = CH_3SO$
6, $X = CH_3SO_2$