composition of the excess ethyl diazoacetate which produced diethyl fumarate, diethyl maleate, and ethyl norcaranecarboxylate in a ratio of 1.5:0.6:1.0.

Effect of Diphenylpicrylhydrazyl. A solution of diazomethane (0.92 g, 22 mmol) in ether (50 ml) was dropped over a period of 20 min into (a) a solution of nickelocene (92 mg, 0.49 mmol) in ether (50 ml), (b) a solution of nickelocene (92 mg, 0.49 mmol) and diphenylpicrylhydrazyl (190 mg, 0.48 mmol) in ether (50 ml), (c) a solution of nickelocene (92 mg, 0.49 mmol) and diphenylpicrylhydrazyl (385 mg, 0.98 mmol) in ether (50 ml). The gas evolution from the three solutions was (a) 390 ml, (b) 375 ml, and (c) 370 ml and the yield of polymeric precipitate was (a) 275 mg (90%), (b) 292 mg (95%); in (c) only a trace of polymer was formed. Diphenylpicrylhydrazyl alone was also found to effect the decomposition of diazomethane in ether with the generation of only a small trace of polymeric product.

Intermediates in Nucleophilic Aromatic Substitution. I. Temperature-Jump Study of the Decomposition of 1,1-Dimethoxy-2,4-dinitrocyclohexadienate in Methanol[1]

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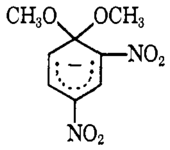
Contribution from the Max-Planck Institut für Physikalische Chemie, Göttingen, Germany. *Received March 1, 1968*

Abstract: The rate of decomposition of 1,1-dimethoxy-2,4-dinitrocyclohexadienate (I) into 2,4-dinitroanisole and methoxide ion has been determined by applying the temperature-jump technique to concentrated solutions of 2,4-dinitroanisole and sodium methoxide in methanol and methanol-o-*d*. An appreciable discrepancy between the equilibrium constant for equilibrium 1 derived from kinetic data and a value reported in the literature is found and discussed. The effect of sodium methoxide concentration on the rates of formation and decomposition of complex I is to increase k_1 and decrease k_{-1}. The activation energy of 11.8 ± 0.5 kcal/mol is found to agree reasonably well with a value of 12.5 kcal/mol predicted by Miller. The present results are discussed with reference to other available kinetic and equilibrium data on related Meisenheimer complexes. The solvent deuterium isotope effect on the equilibrium is $K^H/K^D = 0.38 \pm 0.02$, on the rates is $k_{-1}^H/k_{-1}^D = 1.34 \pm 0.10$ and $k_1^H/k_1^D = 0.51 \pm 0.06$ at 25°. It is interpreted as a secondary solvent isotope effect. Its significance with respect to the mechanism of general base catalyzed nucleophilic aromatic substitutions by amines is discussed.

A large body of evidence has accumulated establishing for nucleophilic aromatic substitution reactions a two-step mechanism involving the formation of an intermediate.[3-10] These intermediates, often referred to as Meisenheimer complexes,[11] aroused considerable interest as to their precise structures, their stabilities, and their rates of formation and decomposition.[12] Depending on the aromatic residue, the attacking nucleophile, the leaving group, and the solvent there is a great variation in the stability of these complexes. Typically the stability increases with any feature in the aromatic residue which brings about a more efficient delocalization of the negative charge, with increasing carbon basicity of nucleophile and leaving group, and with decreasing polarity and hydrogen bond donating ability of the solvent,[13] as long as anionic nucleophiles are involved.[14] The rates of formation and decomposition of these intermediates are expected to correlate with their stabilities.

The three complexes designated by I, II, and III, which are formed by addition of methoxide ion to the respective aryl methyl ethers constitute an interesting series of increasingly stable structures with a stability order I ≪ II < III. Complete equilibrium and kinetic data in methanol solution have recently become available on systems II[15] and III,[16-18] as well as incomplete data on system I.[18,19] In this article a kinetic study of the decomposition of the Meisenheimer complex I in methanol is reported, filling the last gap in our knowledge of the rate–equilibrium relationships in series I–III.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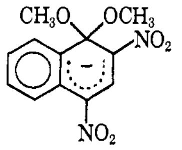
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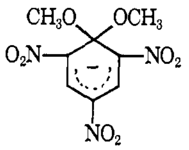
III

The solvent deuterium isotope effect is also reported, and its significance with respect to the mechanistic de-

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[1] Supported, in part, by the "Stiftung für Stipendien auf dem Gebiete der Chemie," Switzerland.

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tails of base-catalyzed nucleophilic aromatic substitutions by amines is discussed.

The temperature-jump method[20] turned out to be a very convenient technique for this type of study.

Experimental Section

Materials. Reagent grade methanol (Merck) was used without further purification. The water content as determined by the Karl Fischer method[21] varied among samples between 0.08 and 0.11%.[22] Methanol-O-*d* (Merck) with >99% deuterium content was used without further purification. 2,4-Dinitroanisole was prepared from 2,4-dinitrochlorobenzene and sodium methoxide by standard methods and recrystallized from methanol, mp 91°. Stock solutions of sodium methoxide in methanol and methanol-O-*d* were prepared by the procedure of Fendler;[18] the alkali content was determined by titration of water-diluted samples with 0.1 *N* hydrochloric acid. Spectra were recorded by means of a Beckman DK spectrophotometer; quantitative evaluations of optical densities for equilibrium measurements were performed on a thermostated Beckman DU spectrophotometer.

Rate Measurements. The temperature-jump apparatus used for the present study has been described.[20] The 2,4-dinitroanisole–sodium methoxide solutions were subjected to temperature jumps of about 3°. Higher jumps were not necessary due to the appreciable temperature dependence of the equilibrium between complex I and the reactants. No cavitation was observed at temperatures ranging from 8 to 34°; the temperatures were determined directly in the cell by means of a thermistor. Relaxation curves were observed at wavelengths between 495 and 525 mμ, depending on the optical density of the solutions. Each rate constant represents the average of at least two experiments with separately prepared solutions; between six and ten relaxation curves per solution were evaluated and averaged for calculating the relaxation time.

Results

Owing to the very low stability of complex I in methanol, relatively high concentrations of 2,4-dinitroanisole and sodium methoxide had to be used in order to build up a concentration of I large enough to allow its detection. With methoxide concentrations of 0.1–1.0 *M* and dinitroanisole concentrations of 0.02–0.1 *M*, an absorption band at 495 mμ, which is typical for Meisenheimer complexes,[12,19] was observed. Optical densities at 495 mμ for a representative set of solutions are set forth in Tables I and II.

Table I. Rate and Equilibrium Data for the Meisenheimer Complex Formed from 2,4-Dinitroanisole and Sodium Methoxide, in Methanol, at 25°

[NaOCH$_3$], *M*	[IV], *M*	OD[a] 495 mμ	$1/\tau = k_{-1}$,[b] sec^{-1}	10^4K_c,[c] M^{-1}	10^2k_1,[d] M^{-1} sec^{-1}
0.1	0.20	0.080	35.3	1.86	0.66
0.2	0.10	0.118	28.7	2.74	0.79
0.3	0.05	0.120	22.1	3.71	0.82
0.5	0.05	0.362	16.8	6.75	1.13
0.7	0.05	0.871	10.6	11.6	1.23
1.0	0.02	1.09	7.63	25.4	1.94
0.5	0.02	0.147	16.0	6.84	1.10
0.5	0.10	0.726	16.5	6.77	1.12

[a] 1-cm path length; estimated limit of error ±2% at lowest [NaOCH$_3$], ±4% at highest [NaOCH$_3$]. [b] Estimated limit of error ±4% at lowest [NaOCH$_3$], ±6% at highest [NaOCH$_3$]. [c] Calculated from eq 4, assuming ϵ_{495} 21,500 for the complex.[19] Same limit of error as OD. [d] Calculated from $k_1 = K_ck_{-1}$. Estimated limit of error ±6% at lowest [NaOCH$_3$], ±10% at highest [NaOCH$_3$].

Table II. Temperature Dependence of K_c and k_{-1} and Solvent Isotope Effect of k_{-1}

Temp, °C	[NaOCH$_3$],[a] *M*	10^4K_c,[b] M^{-1}	$1/\tau = k_{-1}$,[c] CH$_3$OH, sec^{-1}	$1/\tau = k_{-1}$,[c] CH$_3$OD, sec^{-1}	$k_{-1}^{\mathrm{H}}/k_{-1}^{\mathrm{D}}$
13.6	0.2	1.91	12.9	8.9	1.45 ± 0.11
17.8	0.2	2.31	18.3	13.1	1.39 ± 0.11
25.0	0.2	2.79	28.7	21.4	1.34 ± 0.10
28.2	0.2		37.6		
29.8	0.2		38.3	29.2	1.31 ± 0.10
33.0	0.2	3.63	52.5		
12.0	1.0	19.2	2.64		
17.8	1.0	21.5	4.33		
25.0	1.0	23.2	7.63		
29.8	1.0		11.3		
35.0	1.0	28.2	16.6		

[a] [IV] = 0.10 *M* at [NaOCH$_3$] = 0.2 *M*; [IV] = 0.02 *M* at [NaOCH$_3$] = 1.0 *M*. [b] Estimated limit of error ±5% except for the value at 0.2 *M* NaOCH$_3$, where it is ±2%. [c] The estimated limit of error in k_{-1} is ±4% at 0.2 *M* NaOCH$_3$, ±6% at 1.0 *M* NaOCH$_3$.

The concentration of the complex being much too low for a detection by nmr,[23] the evidence that the absorption band at 495 mμ is actually due to formation of I has to be indirect.[24] As a matter of fact, complex I has been isolated from a mixture of approximately 55% dioxane–45% methanol by volume and its structure proven by nmr;[23] dilute solutions of 2,4-dinitroanisole and sodium or potassium methoxide in dioxane–methanol mixtures give rise to the same absorption band at 495 mμ as do more concentrated solutions in pure methanol.[23] Hence the absorption at 495 mμ is definitely attributed to the Meisenheimer complex I.

The initially red solutions were not very stable; upon standing for several hours, the intensity of the absorption at 495 mμ decreased and the solutions turned yellow. The maximum of the new absorption band could not be determined because of overlap with the strong absorption of 2,4-dinitroanisole below 410 mμ. It is very likely that the new band is due to formation of the 2,4-dinitrophenolate ion, either from an S$_\mathrm{N}$2 displacement by methoxide ion at the methyl carbon or from hydroxydemethoxylation at the aromatic carbon, hydroxide ions having been generated by the reaction of methoxide with traces of water present in the solvent. Similar observations have been reported.[25] Addition of small amounts of water up to 5% by volume did increase the rate of destruction of complex I and of formation of the new band, but not very dramatically. If formation of 2,4-dinitrophenolate ion were mainly due to hydroxydemethylation, a very rapid destruction of the complex I and formation of the phenolate ion would have been expected upon addition of water, considering that the usual water content as determined by the Karl Fischer method was only about 0.1%. The S$_\mathrm{N}$2 displacement by methoxide ion clearly turns out to be the more important process, although no kinetic study was attempted to put this conclusion on a more quantitative basis.

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(21) E. Eberius, "Wasserbestimmung mit Karl Fischer Lösungen," Verlag Chemie, Weinheim, 1954.

(22) I am indebted to Mrs. Ruthild Winkler for carrying out these analyses.

(23) W. E. Byrne, E. J. Fendler, J. H. Fendler, and C. E. Griffin, *J. Org. Chem.*, 32, 2506 (1967).

(24) Rochester[19] has reported similar spectra of methanolic solutions of 2,4-dinitroanisole at very high sodium methoxide concentrations and reasonably attributed the absorption at 495 mμ to the complex I, without giving further proof however.

(25) J. F. Bunnett and R. H. Garst, *J. Org. Chem.*, **33**, 2320 (1968).

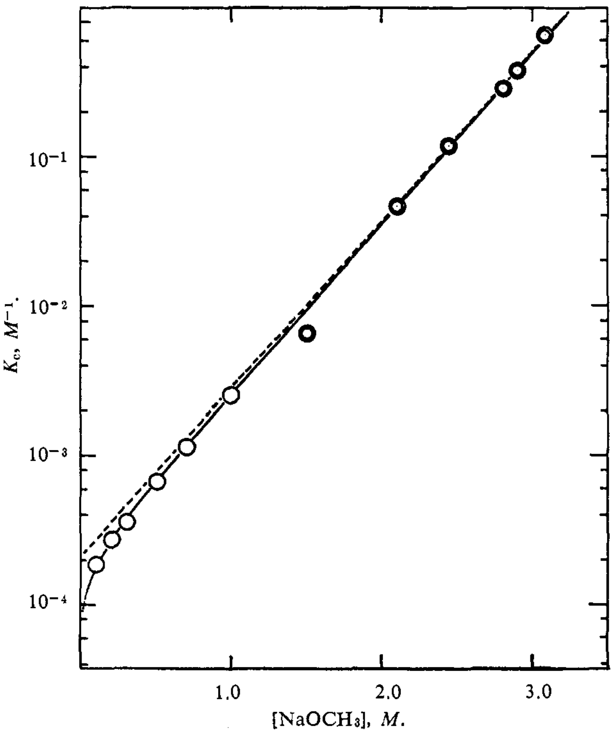


Figure 1. Dependence of K_c on [NaOCH$_3$]; ○, data from Table I; bull's-eyes, data from ref 19.

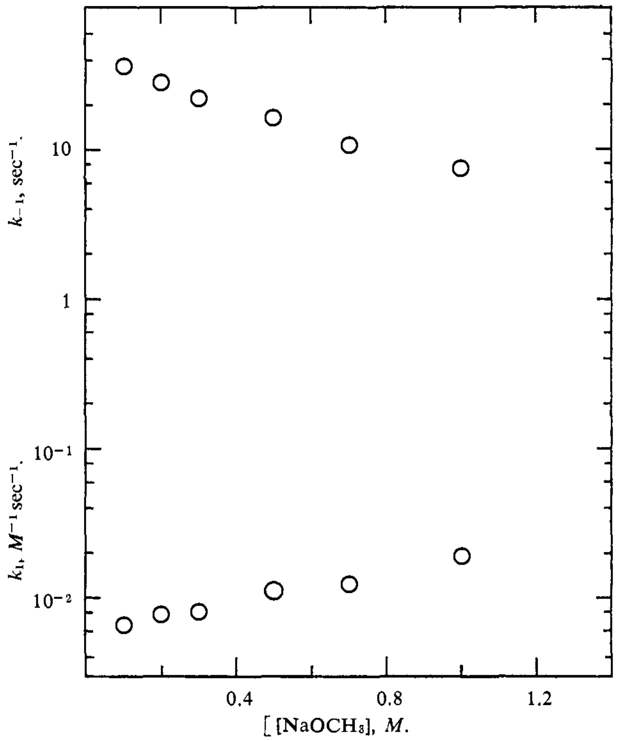
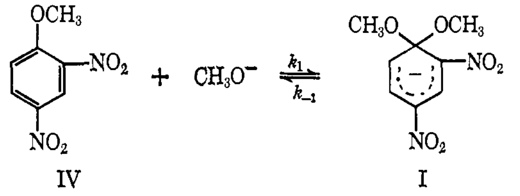


Figure 2. Dependence of k_1 and k_{-1} on [NaOCH$_3$]; data from Table I.

Kinetic Runs. Concentration Dependence of Relaxation Times. The reciprocal relaxation time for equilibrium 1 is given by eq 2. Under all conditions of the present kinetic experiments equilibrium 1 lay strongly on the side of the reactants. Thus $k_{-1} \gg k_1([\text{IV}] + [\text{CH}_3\text{O}^-])$ and eq 2 simplifies to eq 3.



(1)

$$\frac{1}{\tau} = k_1([\text{IV}] + [\text{CH}_3\text{O}^-]) + k_{-1} \qquad (2)$$

Equation 3 predicts $1/\tau$ to be independent of the concentration of any reactant as long as k_{-1} is independent of concentrations. Relaxation times were determined at different concentrations of 2,4-dinitroanisole and sodium methoxide; the results are listed in Table I. They show $1/\tau$ to be independent of dinitroanisole concentration; however, $1/\tau$ decreases considerably with increasing sodium methoxide concentration. A plot of log k_{-1} *vs.* sodium methoxide concentration is shown in Figure 2; a linear extrapolation to infinite dilution gives $k_{-1} = 42 \pm 1.6$ sec^{-1} at 25°.

$$\frac{1}{\tau} = k_{-1} \qquad (3)$$

Besides k_{-1} Table I includes apparent equilibrium constants (K_c) for reaction 1 and rate coefficients for it in the forward direction, k_1. The K_c are calculated from optical densities by use of eq 4, assuming an extinction coefficient of 21,500 for I.[19] The k_1 are reckoned as $k_1 = k_{-1}K_c$. Log K_c and log k_1 as functions of sodium methoxide concentrations are graphically displayed in Figures 1 and 2, respectively.

$$K_c = \frac{\text{OD}}{\epsilon[\text{DNA}][\text{NaOCH}_3]} \qquad (4)$$

Temperature Dependence. The temperature dependence of k_{-1} and K_c has been determined at two different sodium methoxide concentrations. Results are set forth in Table II, Arrhenius plots are shown in Figure 3, and plots of log K_c *vs.* reciprocal temperature in Figure 4.[26] Activation and thermodynamic parameters are listed in Table III.

Solvent Hydrogen Isotope Effect. A few kinetic experiments have been conducted in methanol-O-*d*. A small though significant isotope effect has been found for k_{-1}; it decreases with increasing temperature. Results are summarized in Table II. The activation parameters as derived from the Arrhenius plot in Figure 3 for the reaction in methanol and methanol-O-*d*, respectively, under identical conditions (0.2 *M* NaOCH$_3$), are $\Delta H_\text{H}^{\ddagger} = 11.2 \pm 0.5$ kcal/mol and $\Delta H_\text{D}^{\ddagger} = 12.0 \pm 0.5$ kcal/mol, and $\Delta S_\text{H}^{\ddagger} = -14.3 \pm 1.7$ eu and $\Delta S_\text{D}^{\ddagger} = -12.1 \pm 1.7$ eu, respectively.

The isotope effect on the apparent equilibrium constant K_c has also been determined. At 0.2 *M* sodium methoxide and 25° $K_c^\text{D} = 7.21 \pm 0.25 \times 10^{-4}$ M^{-1} and thus $K_c^\text{H}/K_c^\text{D} = 0.38 \pm 0.02$. From K_c^D and k_{-1}^D one calculates $k_1^\text{D} = 1.54 \pm 0.11 \times 10^{-2}$ M^{-1} sec^{-1} and $k_1^\text{H}/k_1^\text{D} = 0.51 \pm 0.06$ at the same concentration and temperature.

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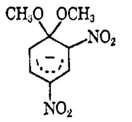
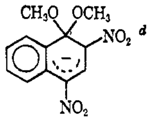
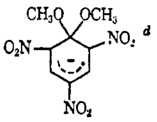
[26] As indicated in Table II, the estimated limit of error for K_c is unexpectedly high. The reason is that the side reaction could make more progress than with the measurements referred to in Table I, due to a longer time allowed for thermal equilibration to take place, thus rendering the optical density readings less certain. On the other hand, these slight changes in optical density upon standing were not critical for the kinetic runs, because the relaxation time does not depend upon the complex concentration.

Table III. Equilibrium and Rate Constants, Thermodynamic and Activation Parameters of Three Meisenheimer Complexes in Methanol at 25°

		 ^{d}	 ^{d}
K_c, M^{-1}	$5.06 \times 10^{-5\,a}$ $2.74 \times 10^{-4\,b}$ $2.54 \times 10^{-3\,c}$	230^{e}	7700^{f} 2260^{g}
k_1, M^{-1} sec^{-1}	$2.12 \times 10^{-3\,h,i}$ $7.90 \times 10^{-3\,b}$ $1.94 \times 10^{-2\,c}$	0.9^{e}	4.0^{f} 4.55^{g}
k_{-1}, sec^{-1}	42.0^{j} 28.7^{b} 7.63^{c}	$3.95 \times 10^{-3\,e}$	$5 \times 10^{-4\,f}$ $2 \times 10^{-3\,g}$ $5 \times 10^{-4\,h,i}$
$\Delta H(K_c)$, kcal M^{-1}	5.6 ± 1.0^{b} 3.1 ± 1.0^{c}	-2.7 ± 1.6^{e}	$-2.8^{g,k}$ $-7.15^{k,l}$
$\Delta S(K_c)$, eu	2.7 ± 3.4^{b} -1.3 ± 3.4^{c}		
$\Delta H^{\ddagger}(k_1)$, kcal M^{-1}	$16.8 \pm 0.5^{h,i}$ $16.8 \pm 1.5^{b,m}$ $16.1 \pm 1.5^{c,m}$	13.2 ± 0.8^{e}	$9.5^{g,k}$
$\Delta S^{\ddagger}(k_1)$, eu	$-17.4 \pm 1.7^{h,i}$ $-9.4 \pm 5.1^{b,n}$ $-15.6 \pm 5.1^{c,n}$	-17.0 ± 2.0^{e}	$-22.9^{g,k}$
$\Delta H^{\ddagger}(k_{-1})$, kcal M^{-1}	11.2 ± 0.5^{b} 13.0 ± 0.5^{c}	15.9 ± 0.8^{e}	$12.3^{g,k}$ $18.8 \pm 1.5^{h,i}$ 16.2 ± 1.5^{o}
$\Delta S^{\ddagger}(k_{-1})$, eu	-12.1 ± 1.7^{b} -14.3 ± 1.7^{c}	-18.0 ± 2.0^{e}	$-29.6^{g,k}$ $-0.9 \pm 4.0^{h,i}$ -19.3 ± 4.0^{o}
Miller's parameters			
$\Delta H(K)$	7.0^{p}	-2.0^{q}	-2.0^{p}
$\Delta H^{\ddagger}(k_1)$	19.5^{p}	14.0^{q}	14.0^{p}
$\Delta H^{\ddagger}(k_{-1})$	12.5^{p}	16.0^{q}	16.0^{p}

[a] Thermodynamic constant derived from kinetics with k_{-1} from this work and k_1 from ref 18. [b] This work, at 0.2 M NaOCH$_3$. [c] This work, at 1.0 M NaOCH$_3$. [d] All data are considered to be thermodynamic values due to the low [NaOCH$_3$] used throughout. [e] See ref 15. [f] See ref 16. [g] See ref 17. [h] See ref 18, at 0.0225 M NaOCH$_3$. [i] See also ref 27. [j] This work, at infinite dilution. [k] Limit of error not known. [l] Calorimetric determination. [m] Calculated as $\Delta H(K_c) + \Delta H^{\ddagger}(k_{-1})$. [n] Calculated as $\Delta S(K_c) + \Delta S^{\ddagger}(k_{-1})$. [o] Calculated using first-order rate coefficients in Table II of ref 18; see ref 39. [p] See ref 37. [q] Personal communication from J. Miller.

Discussion

Equilibrium Constant. Two equilibrium constants for equilibrium 1 are now available, one determined by Rochester,[19] applying the acidity function concept to concentrated sodium methoxide solutions, and one derived from independent kinetic studies of k_1 and k_{-1}. The (thermodynamic) constant of Rochester is 2.88×10^{-4} M^{-1} at 25°.

The rate constant for formation of I has been determined by Fendler:[18,27] $k_1 = 2.12 \times 10^{-3}$ M^{-1} sec^{-1}

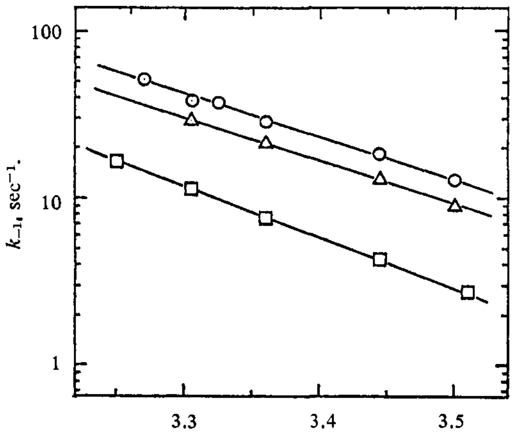


Figure 3. Arrhenius plots for k_{-1}; ○, 0.2 M NaOCH$_3$; □, 1.0 M NaOCH$_3$; △, 0.2 M NaOCH$_3$ in CH$_3$OD; data from Table II.

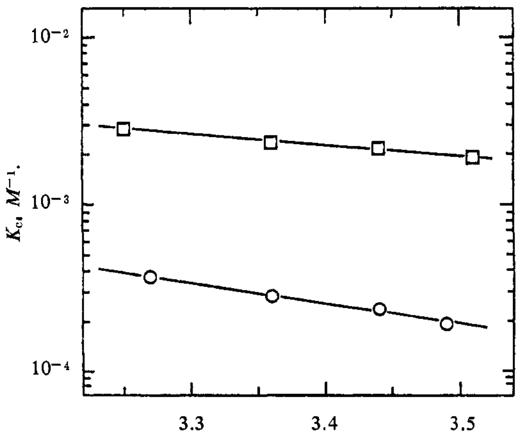


Figure 4. Log K_c vs. reciprocal temperature; ○, 0.2 M NaOCH$_3$; □, 1.0 M NaOCH$_3$.

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[27] A discussion with J. H. Fendler revealed that the value given in ref 18 has to be multiplied by 2 in order to correspond to k_1 of the present work.

at 0.0225 M sodium methoxide at 25°. From this and k_{-1} extrapolated to zero methoxide concentration one calculates a kinetic equilibrium constant, K, of $5.06 \times 10^{-5}\ M^{-1}$.[28] This figure is almost six times smaller than Rochester's value. Part of this large discrepancy may arise from an uncertainty in Rochester's extrapolation procedure; this point is illustrated by Figure 1, where log K_c determined from optical density measurements as well as log K_c values calculated using Rochester's data are plotted *vs.* sodium methoxide concentration. The determination of the thermodynamic equilibrium constant by Rochester was based upon a *linear* extrapolation of log K_c, as measured at relatively high sodium methoxide concentrations, to zero base concentration. Even very small variations in choice of the best straight line through Rochester's experimental points induce an appreciable change in the intercept (logarithmic scale!). As a matter of fact, Rochester has recently pointed out[29] that a value of $K = 9 \times 10^{-5}\ M^{-1}$ is equally or even more consistent with his data.

Furthermore, Figure 1 seems to suggest that at low sodium methoxide concentration log K_c is not quite linearly dependent on this concentration so that the true value at zero base concentration may still be somewhat lower. Although it is difficult to extrapolate the nonlinear portion of the log K_c function to zero base concentration, we do not think that this function quite reaches the value of K as determined from kinetics; the extrapolated constant still seems to be at least 50% higher than the latter. We have no explanation for this remaining discrepancy.

Salt Effects. Salt effects on reactions between an ion and a neutral molecule or on reactions of an ion decomposing to an equally charged ion and a neutral molecule have not received as much attention as salt effects on reactions between two ions. They are less well understood than the latter; it is usually not even possible to predict if a reaction will be accelerated or retarded by an increase in ionic strength.[30,31] The present data therefore constitute a contribution to this field.

A discussion of how k_1 and k_{-1} are influenced by an increase in sodium methoxide concentration has to deal with both a genuine ionic strength effect and the influence of ion pairing. Applying the extended Debye–Hückel equation[32] for expressing the activity coefficients of charged reactants and transition states and the equation of Debye and McAulay[33] for neutral reactants, a linear dependence on the ionic strength μ is predicted for both ln k_1 and ln k_{-1} (eq 5 and 6). The ionic

$$\ln k_1 = \ln k_1^{\circ} + b_1\mu \tag*{(5)[34]}$$

$$\ln k_{-1} = \ln k_{-1}^{\circ} + b_{-1}\mu \tag*{(6)[34]}$$

strength is equal to the sodium methoxide concentration in very dilute solutions but is less than this concentration in more concentrated solutions due to ion-pair formation.[35,36] The ion-pairing association constant of sodium methoxide not being known, one is confined to a qualitative discussion of salt effects.

The present data show that log k_{-1} decreases with ionic strength, indicating $b_{-1} < 0$. If the slope of the best straight line through the points in Figure 2 is taken as an upper limit for b_{-1}, then $b_{-1} < -1.87\ M^{-1}$.

The salt effect on k_1 and thus on K_c is an even more complex function of sodium methoxide concentration, because the ion pairing does not only influence the ionic strength but also reduces the nucleophilic reactivity of the methoxide ions tied up with sodium ions, thus possibly simulating a negative ionic strength effect. k_1 values can be calculated from k_{-1} and K_c as a function of sodium methoxide concentration (Table I); log k_1 as a function of the latter is shown in Figure 2. Appreciable scatter conceals the true character of this function.[37] Nevertheless, there can be no doubt that b_1 is positive; it is estimated to $b_1 \geq 1.3\ M^{-1}$.[3]

The change of the slope of the functions log K_c and log k_1[38] *vs.* sodium methoxide concentration at higher concentrations, if real, may tentatively be attributed to ion pair formation.[35]

Our findings about the salt effect on k_1 have already found an interesting application in clarifying interpretation of the effect of the sodium methoxide concentration on the reactions of piperidine with 2,4-dinitroanisole and its reverse reaction, the methoxydepiperidinylation of N-(2,4-dinitrophenyl)piperidine in methanol.[25]

Meisenheimer Complexes I, II, and III. The relation between structure and stability of Meisenheimer complexes has often been discussed on a qualitative basis.[12] In connection with the present study a comparison of the three complexes I, II, and III as to their stabilities and rates of formation and decomposition is called for, all relevant kinetic and thermodynamic data being now available for the three systems; they are set forth in Table III, together with Miller's[39] calculated activation and thermodynamic parameters.

Equilibrium Constants *K*. As can be inferred from a comparison of I and III, one additional nitro group enhances the stability constant of the Meisenheimer complex by about eight orders of magnitude, or in terms of enthalpies by about 9 kcal.[40] It is interesting to note that extension of the aromatic π system by one benzene nucleus has almost the same stabilizing effect, as well in terms of free enthalpies (equilibrium constants) as in terms of enthalpies.

Miller's[39] calculations predict that both II and III are by 9 kcal more stable than I, in fair to good agreement with the experimental findings, depending on the actual

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(28) Fendler's data at other temperatures suggest that k_1 depends only slightly on sodium methoxide concentration in this highly diluted solution; for the present discussion his value is assumed to be the same as at infinite dilution.

(29) C. H. Rochester, personal communication.

(30) A. A. Frost and R. G. Pearson, "Kinetics and Mechanisms," John Wiley and Sons, Inc., New York, N. Y., 1961, p 152.

(31) K. J. Laidler, "Chemical Kinetics," McGraw-Hill Book Co., Inc., New York, N. Y., 1965, p 219 ff.

(32) E. Hückel, *Phys. Z.*, 26, 93 (1925).

(33) P. Debye and J. McAulay, *ibid.*, 26, 22 (1925).

(34) $b_1 = b_{CH_3O^-} + b_{1V} - b_{\ddagger}$; $b_{-1} = b_{I} - b_{\ddagger}$.[31]

(35) Ion pairing seems to become appreciable above 0.1 M if deviations among the acidity functions for lithium, sodium, and potassium methoxide is taken as an indication thereof.[36]

(36) R. Schaal and G. Lambert, *J. Chem. Phys.*, **59**, 1151, 1164 (1962).

(37) From the dependence of K_c and k_{-1} on concentration one expects a qualitatively similar dependence as for K_c.

(38) Fendler's[18] data already suggested a slight trend to higher k_1 values with increasing methoxide concentration.

(39) J. Miller, *J. Amer. Chem. Soc.*, 85, 1628 (1963).

(40) In the view of the present author $\Delta H = -2.8$ kcal[17] for III as determined from the difference of activation energies for k_1 and k_{-1} is better than the figure determined by calorimetry.[18] ΔH for I at infinite dilution not being known, it is assumed, as a working hypothesis, to be 6.0 ± 1.0 kcal.

figure within the limits set by the experimental uncertainty.

Rate Coefficients and Activation Parameters. In going from the dinitrophenyl to the dinitronaphthyl and then to the picryl system, the rate coefficient k_1 for formation of the complex increases, the coefficient k_{-1} decreases, and the stability of the complex increases; a change in structure affects k_{-1} more than it does k_1. The picture emerging from a comparison of activation parameters is less clear-cut, mainly due to the uncertainty in the activation energy for the decomposition of III. As all three equilibria involve species of the same general structure, it is reasonable to assume relatively small variations in the entropy effects among the three systems. On these grounds, differences in rate constants are expected to reflect mainly differences in activation enthalpies. This expectation is best fulfilled if 16.2 kcal is chosen among the three figures of $\Delta H^{\ddagger}(k_{-1})$ for system III.[41,42] The value of 12.3 kcal,[17] quite apart from entropy considerations, is unsatisfactory because it is lower than for the somewhat less stable complex II; the value of 18.8 kcal,[18] though higher than for complex II, would imply a drastically different entropy of activation compared to the closely related systems I and II and hence would be difficult to account for.

The agreement between the experimental and Miller's[39] predicted parameters is fairly close in some cases, somewhat less satisfactory in others; the activation enthalpy for *decomposition* seems to have been predicted more accurately than that for *formation;* whether this is due to some shortcomings in the theoretical calculations or reflects inaccurate experimental data is difficult to decide at the present time. The author tends to believe, however, that the activation enthalpies for III, determined by Abe, *et al.*,[17] are too low.

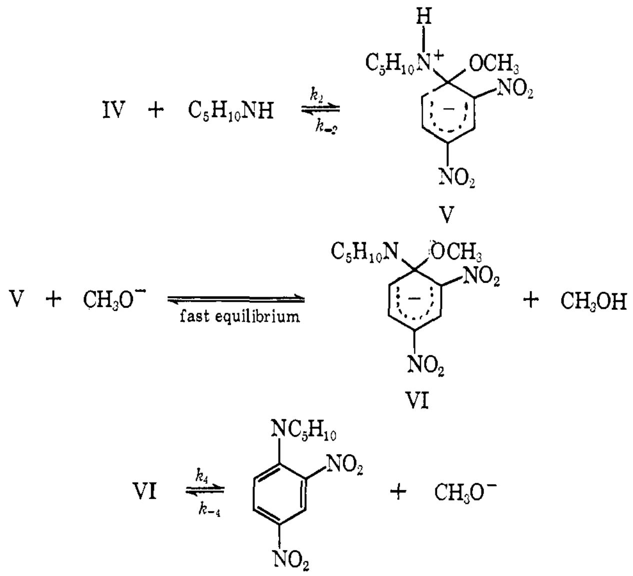
The magnitudes of the activation entropies for k_{-1} call for comment in that they refer to unimolecular reactions and are quite strongly negative. This seems consistent with the idea that part of the negative charge, which was delocalized in the Meisenheimer complex, becomes concentrated on the incipient methoxide ion in the transition state, thus enhancing the solvation requirements of the activated complex and giving rise to a negative entropy of activation. This point is beautifully illustrated by a comparison with the decarboxylation reaction of 2,4,6-trinitrobenzoate yielding the 2,4,6-trinitrophenyl anion and CO_2, for which $\Delta S^{\ddagger}$ is +8.1 eu in ethanol.[43] In this reaction, one deals with the reverse situation, the negative charge being more delocalized on the incipient 2,4,6-trinitrophenyl anion in the transition state than in the reactant. The consequence is a positive entropy of activation.

Solvent Isotope Effects. One can try to predict the equilibrium isotope effect on K_c by applying Bunton and Shiner's[44] procedure. Assuming that the methoxide ion is solvated by three methanol molecules,[45] in analogy to the situation of the hydroxide ion in water,[46] and that the difference in stretching frequency of a methanol hydrogen bonded to methoxide ion and to methanol is about 400 cm^{-1}, as in the case of water–hydroxide ion,[46] one calculates $K_c^H/K_c^D = 0.47$; considering the crudeness of this calculation, this is in excellent agreement with the experimental value of $K_c^H/K_c^D = 0.38 \pm 0.02$.

The calculation of the secondary solvent isotope effect on the rates k_1 and k_{-1} by an analogous procedure[47] is more difficult, because an additional assumption about the degree of solvation of the methoxy group in the transition state and the corresponding stretching frequency of the hydrogen bonds has to be made. Nevertheless the least one can say is that the experimental isotope effects certainly lie in a range where they are to be expected.[47] Their values clearly do not leave room for any appreciable *primary* isotope effect.

This is interesting in connection with the problem of the mechanism of general base catalyzed nucleophilic aromatic substitutions by amines.[5,7,8,48] One mechanistic scheme which has been advocated by a number of workers[7,8,48] is given in Chart I for a specific example taken from a recent and previously mentioned study by Bunnett and Garst.[25] The formal kinetics of the general base catalyzed transformation of V to final products require that the solvent methanol functions as a general acid catalyst in the last step (k_4). This last step is clearly the same process as k_{-1} studied in the present work except for the fact that one methoxy group is changed to a piperidino group in VI, a difference in structure which is not expected to bring any fundamental change in this process. A question arises immediately. Does this reaction involve a transfer of the proton from methanol to the leaving methoxide ion or does the proton lie in a stable potential well so that the methanol merely solvates the incipient methoxide ion, according to the "solvation rule."[49] Following the arguments of Swain, *et al.*,[49] a secondary but no pri-

Chart I



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(41) $\Delta H^{\ddagger}(k_{-1})$ = 16.2 kcal/mol has been calculated using first-order rate coefficients in Table II of ref 18; although the author[42] believes that the uncertainty in his first-order coefficients is greater than in the S values,[18] from which he calculated the activation parameters, this value of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ = −19.3 eu is much more reasonable, perhaps by a fortuitous cancellation of errors.

(42) J. H. Fendler, personal communication.

(43) F. H. Verhoek, *J. Amer. Chem. Soc.*, **61**, 186 (1939).

(44) C. A. Bunton and V. J. Shiner, *ibid.*, **83**, 42 (1961).

(45) C. H. Rochester, *Quart. Rev.* (London), **20**, 511 (1966).

(46) G. Yagil and M. Anbar, *ibid.*, **85**, 2376 (1963).

(47) C. A. Bunton and V. J. Shiner, *ibid.*, **83**, 3207 (1961).

(48) A. J. Kirby and W. P. Jencks, *J. Amer. Chem. Soc.*, **87**, 3217 (1965).

(49) C. G. Swain, D. A. Kuhn, and R. L. Schowen, *ibid.*, **87**, 1553 (1965).

mary solvent isotope effect would be associated with this reaction were the role of the methanol merely to solvate the leaving group. On the other hand, if a proton is being transferred in the rate-determining process of leaving group expulsion, a primary isotope effect might be expected.[50] Our result would seem to be in accord with the first hypothesis. However, one has to be very careful with such a conclusion. (1) It is an open question whether such a concurrent protonation of the departing leaving group would necessarily give rise to a primary isotope effect.[51] (2) It has not been proven that methoxide ion catalysis in the reaction of piperidine with 2,4-dinitroanisole is actually due to *general* base catalysis. If it were due to *specific* lyate ion catalysis, as there are good reasons to believe,[52] no primary isotope effect would be expected. The whole problem of base catalysis in nucleophilic aromatic substitutions will be discussed shortly.[52]

Acknowledgment. I wish to thank the Max-Planck Institut für Physikalische Chemie and particularly Professor M. Eigen for the use of the temperature-jump-equipment and for their great hospitality.

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[50] K. Wiberg, *Chem. Rev.*, **55**, 713 (1955).

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[52] C. F. Bernasconi, to be published.

Thermal and Acid-Catalyzed Reactions of Pulegone Oxide

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Abstract: Pyrolysis of neat liquid samples of pulegone oxide (Ia or Ib) at 200° leads to stereoisomeric 2-acetyl-2,5-dimethylcyclohexanones (IIa and IIb) as the major products. This rearrangement is not catalyzed by acids, bases, or radicals and is insensitive to the Pyrex glass used for the reaction vials. Gas phase pyrolysis at 200° produces 2,2,5-trimethylcycloheptane-1,3-dione (IV) by a surface-catalyzed process. Dilute solutions of pulegone oxide in hydrocarbon solvents react slowly at 200° to give IV, whereas in solvents incorporating oxygen atoms, IIa and IIb are the chief rearrangement products. Reaction of Ia and Ib with boron trifluoride etherate results in stereospecific formation of fluorohydrins Va and Vb, which undergo thermal decomposition to give IV. Reaction of Ia and Ib with *p*-toluenesulfonic acid in benzene leads to isomeric, unsaturated ketols believed to be VIa and VIb. The pyrolysis reactions are discussed.

Our past investigations of high-temperature (>200°) reactions of α,β-epoxy ketones[1,2] have disclosed a radical chain decomposition mode and a surface-catalyzed (Pyrex glass) rearrangement paralleling known Lewis acid catalyzed reactions. We now report that pulegone oxide undergoes a solvent-dependent thermal rearrangement, which is not catalyzed by acids or bases, is not a free-radical chain process, and is not a surface reaction. The mechanism of this rearrangement is not yet apparent, but the transformation is similar to the photochemical rearrangement of this epoxy ketone.[2]

A thermal reaction of pulegone oxide was described by Prileschaev[3] over 40 years ago, and, although Pigulevsky and Mironova[4] have confirmed and elaborated this report, both groups used a crystalline modification of the epoxy ketone which has been shown to be a mixture of diastereoisomers.[5] Pigulevsky, *et al.*,[6] have recently modified their interpretation of the pulegone oxide pyrolysis and propose that isomeric α-diketones are the major products. We are unable to find products of this kind in our experiments with the pure isomers Ia and Ib.

Independent work of several research groups[7] has recently established the configurations of the stereoisomeric pulegone oxides Ia and Ib. Pyrolysis of the pure isomers was effected in sealed Pyrex tubes heated in a furnace (details are given in the Experimental Section). This static system allows a greater control of variables than would be possible by passing the sample through a hot tube. Most of the experiments were conducted at 200°, and, by adjusting the ratio of sample size to container volume and the pressure, essentially liquid phase or gas phase reactions could be effected. The random error in experiments of this kind is rather large (*ca.* ±5%); however, despite the poor reproducibility, numerous duplicate experiments by two independent researchers have confirmed the nature of the rearrangements and have established certain general trends. These results and some related acid-catalyzed reactions are reported in the following paragraphs.

When a neat liquid sample of Ia (or Ib) was heated to 200° for several hours (Scheme I), analysis by glpc revealed epimerization to Ib (or Ia) and rearrangement to a mixture of isomers IIa and IIb (Table I). Isomer Ia proved to be less reactive than Ib with respect to both epimerization and rearrangement. Very little

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[1] W. Reusch, C. K. Johnson, and J. A. Manner, *J. Amer. Chem. Soc.*, **88**, 2803 (1966).

[2] C. K. Johnson, B. Dominy, and W. Reusch, *ibid.*, **85**, 3894 (1963).

[3] M. N. Prileschaev, *Bull. Soc. Chim. Fr.*, **41**, 687 (1927).

[4] G. V. Pigulevsky and I. K. Mironova, *Zh. Obshch. Khim.*, **27**, 1101 (1957).

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[6] S. A. Kozhin, S. I. Yakimovich, and G. V. Pigulevsky, *Zh. Obshch. Khim.*, **32**, 2368 (1962).

[7] (a) G. W. K. Cavill and D. H. Hall, *Tetrahedron*, **23**, 1119 (1967); (b) J. Katsuhara, *J. Org. Chem.*, **32**, 797 (1967); (c) W. Reusch and P. Mattison, *Tetrahedron*, **23**, 1953 (1967).