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# Intermediates in Nucleophilic Aromatic Substitution. XII.[1] Kinetic and Equilibrium Study of the Spiro Meisenheimer Complex of 1-(β-Hydroxyethoxy)-2,4-dinitrobenzene

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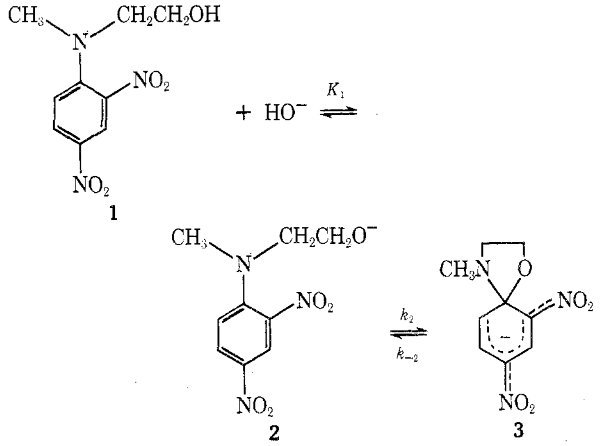
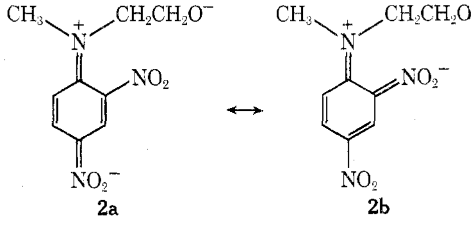
The spiro Meisenheimer complex formed from 1-(β-hydroxyethoxy)-2,4-dinitrobenzene (**4**) in the presence of strong base in aqueous DMSO is considerably more stable than the analogous complex from *N*-β-hydroxyethyl-*N*-methyl-2,4-dinitroaniline (**1**). This difference in stabilities, which becomes more pronounced in DMSO-rich mixtures, is attributed mainly to greater ground-state resonance stabilization in **1**. In water-rich mixtures the rates at which the two spiro Meisenheimer complexes revert to starting materials are almost identical, indicating that the higher stability of the complex derived from the title compound is entirely due to a higher rate of formation. This is shown to be consistent with a complex-like transition state. In DMSO-rich solvents the results indicate a shift toward a more reactant-like transition state in agreement with the Hammond postulate.

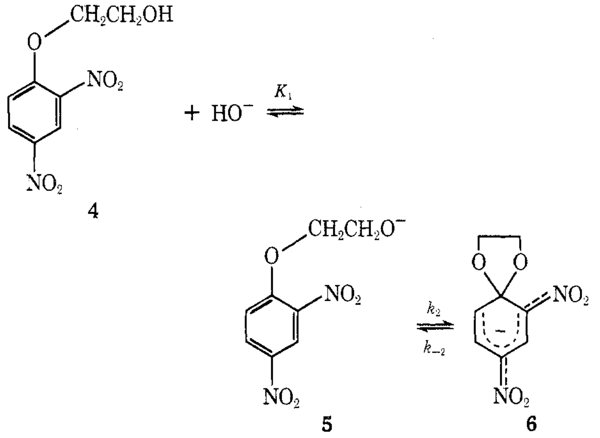
We recently published a kinetic study on the formation of the cyclic Meisenheimer complex (**3**) derived from *N*-β-hydroxyethyl-*N*-methyl-2,4-dinitroaniline (**1**) in various mixtures of dimethyl sulfoxide (DMSO) and water.[3] We were particularly concerned with the rate coefficient $k_{-2}$ since it provides a point of reference for the expected rates of leaving-group departure in typical nucleophilic aromatic substitution reactions of amines with 1-X-2,4-dinitrobenzene compounds.[4]



(1)

In trying to understand better the factors on which leaving group reactivities depend, we have now investigated the reaction of eq 2. One point of special interest is whether resonance stabilization in **2** (**2a**, **2b**) has a major influence on the rate constants $k_2$ and $k_{-2}$ of eq 1. Inasmuch as resonance stabilization of this type is expected to be less important in **5**, a comparison between the two systems should be revealing.[5]





(2)

## Results

Upon addition of base to a solution of **4** in aqueous DMSO, **6**[6] is formed according to eq 2; the stability of **6** relative to the starting materials increases with increasing DMSO content, a well-known phenomenon in Meisenheimer complex chemistry[7] as well as in many other nucleophilic additions or substitutions.[8]

Absorption spectra in 54% DMSO (v/v) at various base concentrations are shown in Figure 1. Owing to hydrolysis the solutions were not very stable; the spectra shown represent extrapolations to zero time.

If we assume that at [KOH] ≥ 0.5 *M* conversion to **6** is quantitative, one calculates an extinction coefficient of 21,000 at $\lambda_{max}$ 495 nm. This extinction coefficient is the same as the one determined indirectly (see below) in 50% DMSO (v/v). Spectra taken in 80% DMSO in the presence of tetramethylammonium hydroxide indicate $\epsilon_6$ 32,200 at $\lambda_{max}$ 500 nm; *i.e.*, $\epsilon_6$ is significantly solvent dependent.

**Kinetics.** The kinetics of the equilibrium formation of **6** were monitored spectrophotometrically in the stopped-flow (SF) or the temperature-jump (TJ) apparatus. In all runs the base was in a large excess over the substrate concentration, assuring pseudo-first-order kinetics throughout. Thus the reciprocal relaxation time is given by eq 3,

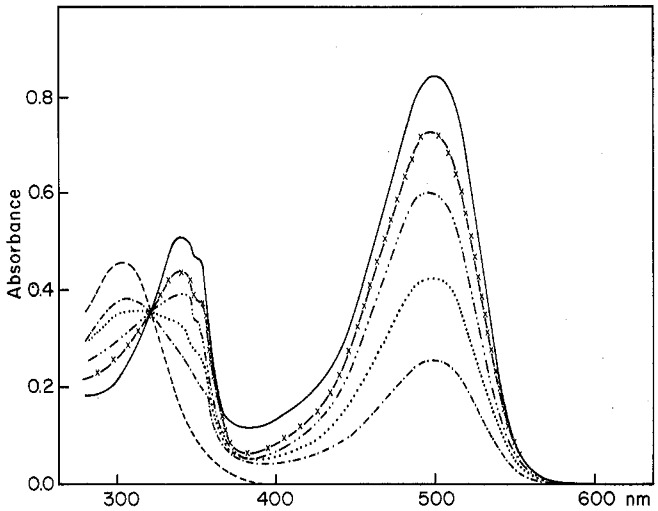


**Figure 1.** Uv-visible spectra of 4 at various KOH concentrations in 54% DMSO (v/v) ($\mu$ = 0.5 $M$, $[4]_0$ = 4.0 × $10^{-5}$ $M$): — — —, without base; — · —, 0.006 $M$; . . . ., 0.0125 $M$; — · · —, 0.025 $M$; — x —, 0.05 $M$; ———, 0.5 $M$.

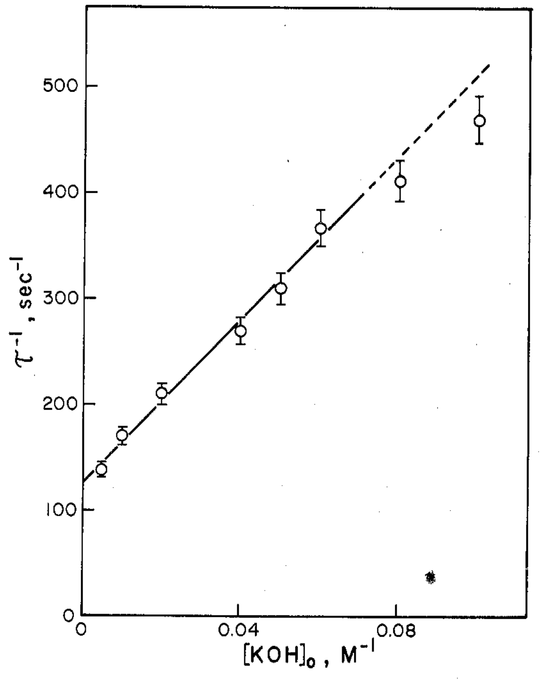


**Figure 2.** Reaction in 50% DMSO (v/v), $\mu$ = 0.5 $M$, $\tau^{-1}$ as function of $[KOH]_0$.

since the acid-base equilibrium $4 \rightleftharpoons 5$ is always rapidly established with respect to the time scale of $\tau$; $[HO^-]_0$ refers to the stoichiometric base concentration.

$$\frac{1}{\tau} = k_2\frac{K_1[HO^-]_0}{1 + K_1[HO^-]_0} + k_{-2} \qquad (3)$$

In any given solvent the ionic strength was kept constant by adding KCl as necessary. Our results are summarized in Table I.

As confirmed by equilibrium measurements reported below, complex formation is disfavored in 2% DMSO (v/v). Thus $\tau^{-1}$, which is independent of base concentration in this solvent, is equivalent to $k_{-2}$.

In 20% DMSO (v/v) $\tau^{-1}$ increases slightly with base concentration. A plot of $\tau^{-1}$ *vs.* $[HO^-]_0$ (not shown) is linear, indicating that $K_1[HO^-]_0 \ll 1$; thus eq 3 simplifies to eq 4 with $k_2K_1$ = 144 $M^{-1}$ sec$^{-1}$ and $k_{-2}$ = 719 sec$^{-1}$.

$$\frac{1}{\tau} = k_2K_1[HO^-]_0 + k_{-2} \qquad (4)$$

**Table I**
**Reciprocal Relaxation Times in Various Solvent Mixtures at 25°**

| % DMSO (v/v) | $[KOH]_0$, $M$ | $\mu$, $M$ | $[4]_0$, $M$ | $\tau^{-1}$, sec$^{-1}$ | Method |
|---|---|---|---|---|---|
| 2 | 0.2 | 1.0 | 2 × $10^{-3}$ | 1460 ± 70 | TJ |
| 2 | 0.5 | 1.0 | 2 × $10^{-3}$ | 1460 ± 70 | TJ |
| 2 | 1.0 | 1.0 | 2 × $10^{-3}$ | 1440 ± 70 | TJ |
| 20 | 0.2 | 1.0 | 2 × $10^{-3}$ | 751 ± 35 | TJ |
| 20 | 0.5 | 1.0 | $10^{-3}$ | 786 ± 39 | TJ |
| 20 | 1.0 | 1.0 | 5 × $10^{-4}$ | 865 ± 43 | TJ |
| 50 | 0.005 | 0.5 | 8 × $10^{-5}$ | 139 ± 7 | SF |
| 50 | 0.01 | 0.5 | 8 × $10^{-5}$ | 169 ± 9 | SF |
| 50 | 0.02 | 0.5 | 2 × $10^{-5}$ | 210 ± 11 | SF |
| 50 | 0.04 | 0.5 | 2 × $10^{-5}$ | 266 ± 13 | SF |
| 50 | 0.05 | 0.5 | 2 × $10^{-5}$ | 310 ± 15 | SF |
| 50 | 0.06 | 0.5 | 2 × $10^{-5}$ | 367 ± 18 | SF |
| 50 | 0.08 | 0.5 | 2 × $10^{-5}$ | 412 ± 21 | SF |
| 50 | 0.10 | 0.5 | 2 × $10^{-5}$ | 471 ± 23 | SF |
| 65 | ~0.0003 | 0.46 | 4 × $10^{-4}$ | 53 ± 3 | TJ |
| 65 | 0.0015 | 0.46 | 2 × $10^{-5}$ | 97 ± 5 | SF |
| 65 | 0.0025 | 0.46 | 2 × $10^{-5}$ | 139 ± 7 | SF |
| 65 | 0.005 | 0.46 | 2 × $10^{-5}$ | 221 ± 11 | SF |
| 65 | 0.0075 | 0.46 | 2 × $10^{-5}$ | 313 ± 15 | SF |
| 65 | 0.01 | 0.46 | 2 × $10^{-5}$ | 396 ± 20 | SF |

In 50% DMSO (v/v) the dependence of $\tau^{-1}$ on base concentration is much stronger; a plot of $\tau^{-1}$ *vs.* $[HO^-]_0$ is shown in Figure 2. The plot is linear at low base concentrations ($K_1[HO^-]_0 \ll 1$) with $k_2K_1$ = 4020 $M^{-1}$ sec$^{-1}$ and $k_{-2}$ = 124 sec$^{-1}$, but shows a tendency to curve down at the highest concentrations. Determinations of $\tau^{-1}$ at still higher concentrations would have been desirable for purposes of evaluating $k_2$ and $K_1$ separately; this was not possible with our equipment for the following reasons. (1) The rates become too fast for the stopped-flow technique. (2) There is no suitable wavelength where the relaxation amplitude in a temperature-jump experiment was satisfactory at $[KOH]_0$ >0.1 $M$.[9]

In 65% DMSO (v/v) $\tau^{-1}$ increases about ten times more strongly with base concentration than it does in 50% DMSO. For the same reasons as in 50% DMSO it was not possible to determine $\tau^{-1}$ at $[KOH]_0$ >0.01 $M$; up to this concentration the dependence is linear (plot not shown) with $k_2K_1$ = 3.53 × $10^4$ $M^{-1}$ sec$^{-1}$ and $k_{-2}$ = 50 sec$^{-1}$.

**Equilibrium Measurements.** In 2% DMSO $k_2K_1$ cannot be determined from kinetics, whereas in 20% DMSO the kinetically determined value of $k_2K_1$ is not very accurate since it is the small slope of a plot of $\tau^{-1}$ *vs.* $[KOH]_0$. One can, however, obtain $k_2K_1$ indirectly from equilibrium measurements.

We carried out such measurements by the spectrophotometric method. At the absorption maximum of 6 there is no other species in the equilibrium which absorbs a significant amount of light. Thus in a 1-cm cuvette Beer's law is given by eq 5.

$$A = \epsilon_6[6] \qquad (5)$$

The equilibrium concentration of 6 in the presence of an excess of base is given by eq 6, where $[4]_0$ is the stoichiometric concentration of 4 and $K_2 = k_2/k_{-2}$. Combining eq 5 with eq 6 affords eq 7.

$$[6] = \frac{K_1K_2[HO^-]_0}{1 + (K_1 + K_1K_2)[HO^-]_0}[4]_0 \qquad (6)$$

$$\frac{A}{\epsilon_6[4]_0} = \frac{K_1K_2[HO^-]_0}{1 + (K_1 + K_1K_2)[HO^-]_0} \qquad (7)$$

Absorption readings in 2, 20, and 50% DMSO (v/v) are summarized in Table II. In 2 and 20% DMSO absorption increases linearly with base concentration (plots not shown), indicating $(K_1 + K_1K_2)[\mathrm{HO^-}]_0 \ll 1$ up to $[\mathrm{KOH}]_0 = 1\ M$. Thus eq 7 simplifies to eq 8. Assuming that $\epsilon_6$ at the respective absorption maxima in 2 and in 20% DMSO is the same (21,000) as the one determined in 50% DMSO, one obtains $K_1K_2 = 4.1 \times 10^{-2}\ M^{-1}$ and thus $k_2K_1$ (= $K_1K_2k_{-2}$) = 59.5 $M^{-1}$ sec$^{-1}$ in 2% DMSO, $K_1K_2$ = 0.24 $M^{-1}$ and thus $k_2K_1$ = 173 $M^{-1}$ sec$^{-1}$ in 20% DMSO.

$$\frac{A}{\epsilon_6[\mathbf{4}]_0} = K_1K_2[\mathrm{HO^-}]_0 \qquad (8)$$

In 50% DMSO a plot (not shown) of $A$ *vs.* $[\mathrm{KOH}]_0$ is curved. For evaluation we invert and rearrange eq 7 and obtain eq 9. A plot of the left-hand side of eq 9 *vs.* $[\mathrm{HO^-}]_0^{-1}$ is shown in Figure 3. By again choosing $\epsilon_6$ = 21,000 we obtain the same value for $K_1K_2$ of 32.1 $M^{-1}$ (reciprocal slope of Figure 3) as from kinetics ($K_1k_2/k_{-2}$).[10]

$$\frac{\epsilon_6[\mathbf{4}]_0}{A} = 1 + \frac{1}{K_2} + \frac{A}{K_1K_2[\mathrm{HO^-}]_0} \qquad (9)$$

In 65% DMSO (v/v) the equilibrium favors **6** over **4** to such an extent that a spectrophotometric equilibrium determination was not attempted since most measurements would have to be made at base concentrations $<10^{-3}\ M$, which are difficult to maintain without buffers.

**Table II**
**Absorbance at $\lambda_{max}$ in Various Solvent Mixtures at 25°**

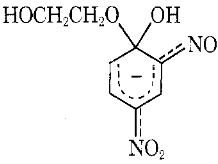
| % DMSO (v/v) | $[\mathrm{KOH}]_0$, $M$ | $\mu$, $M$ | $[\mathbf{4}]_0$, $M$ | $A^a$ at $\lambda_{max}$ | $\frac{A \text{ at } \lambda_{max}{}^b}{\epsilon_6[\mathbf{4}]_0}$ |
|---|---|---|---|---|---|
| 2 | 0.2 | 1.0 | $10^{-3}$ | 0.185 | 0.0088 |
| 2 | 0.4 | 1.0 | $10^{-3}$ | 0.370 | 0.0176 |
| 2 | 0.5 | 1.0 | $10^{-3}$ | 0.448 | 0.0213 |
| 2 | 0.6 | 1.0 | $10^{-3}$ | 0.535 | 0.0255 |
| 2 | 0.8 | 1.0 | $10^{-3}$ | 0.703 | 0.0335 |
| 2 | 1.0 | 1.0 | $10^{-3}$ | 0.888 | 0.0423 |
| 20 | 0.1 | 1.0 | $10^{-3}$ | 0.570 | 0.0271 |
| 20 | 0.3 | 1.0 | $5 \times 10^{-4}$ | 0.815 | 0.0776 |
| 20 | 0.4 | 1.0 | $5 \times 10^{-4}$ | 1.037 | 0.0988 |
| 20 | 0.6 | 1.0 | $5 \times 10^{-4}$ | 1.530 | 0.146 |
| 20 | 0.7 | 1.0 | $2 \times 10^{-4}$ | 0.706 | 0.168 |
| 20 | 0.9 | 1.0 | $2 \times 10^{-4}$ | 0.872 | 0.208 |
| 20 | 1.0 | 1.0 | $2 \times 10^{-4}$ | 1.037 | 0.247 |
| 50 | 0.01 | 0.5 | $10^{-4}$ | 0.444 | 0.212 |
| 50 | 0.02 | 0.5 | $10^{-4}$ | 0.871 | 0.415 |
| 50 | 0.03 | 0.5 | $10^{-4}$ | 1.014 | 0.484 |
| 50 | 0.04 | 0.5 | $5 \times 10^{-5}$ | 0.618 | 0.589 |
| 50 | 0.05 | 0.5 | $5 \times 10^{-5}$ | 0.651 | 0.620 |
| 50 | 0.06 | 0.5 | $5 \times 10^{-5}$ | 0.746 | 0.711 |
| 50 | 0.08 | 0.5 | $5 \times 10^{-5}$ | 0.795 | 0.757 |
| 50 | 0.10 | 0.5 | $5 \times 10^{-5}$ | 0.826 | 0.786 |

[a] $\lambda_{max}$ 480 nm in 2 and 20% DMSO, 494 nm in 50% DMSO. [b] $\epsilon_6$ assumed to be 21,000 throughout as determined in 54% DMSO.

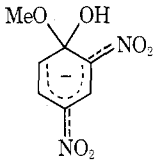
## Discussion

Table III summarizes all kinetics and equilibrium parameters of this study along with those of the system of eq 1. Note that the values for $k_{-2}$ and $K_1K_2$ referring to the system of eq 2 have been statistically corrected (experimental $k_{-2}$ divided by 2, experimental $K_1K_2$ multiplied by 2).

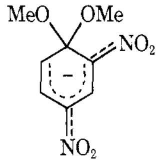
In treating our data we have implicitly assumed that **6** is the only species contributing significantly to the absorption of visible light. In response to a comment by a referee we shall briefly discuss the possibility that formation of **7** might compete with the formation of **6**. This is a real possibility, since Hasegawa and Abe[11] have found that complex **8** is formed in solutions of 2,4-dinitroanisole in aqueous DMSO in the presence of hydroxide ion, preceded by the *transient appearance of a 1,3 complex* (attack of $\mathrm{HO^-}$ on the 3 position).



**7**



**8**



**9**

The stability constant for **9** in methanol is $K \approx 5 \times 10^{-5}\ M^{-1}$.[12] Based on findings with $\sigma$ complexes formed between 1,3,5-trinitrobenzene and $\mathrm{HO^-}$ or $\mathrm{MeO^-}$, respectively,[13] the stability constant in water of **8**—and by analogy that of **7** as well—is expected to be no greater than that of **9** in methanol, and probably smaller.

Let us now make the hypothesis that the colored species in our study is **7** instead of **6**; the quantity $K_1K_2$ in Table III would thus take on the meaning of the stability constant, $K$, of **7**. In 2% DMSO this quantity is $8.2 \times 10^{-2}\ M^{-1}$, which is more than $10^3$-fold greater than the upper limit ($5 \times 10^{-5}\ M^{-1}$) expected for the stability constant of **7**. Further, if we were dealing with **7** instead of **6**, the high rate of complex dissociation (*e.g.*, in 2% DMSO $k_{-2}$ = 725 sec$^{-1}$) would be difficult to rationalize since expulsion of $\mathrm{HO^-}$ from **7** in 2% DMSO is expected to be no greater and probably slower than expulsion of $\mathrm{MeO^-}$ from **9** in methanol[13] (42 sec$^{-1}$).[12] We conclude that the color in our system is virtually exclusively due to **6**. This conclusion is further supported by the fact that we observe only one relaxation process and that $K_1K_2$ determined from kinetics in 20% DMSO agrees with $K_2K_2$ determined spectrophotometrically within the experimental error.

Let us now turn our attention to a comparison of the systems of eq 1 and 2. There are striking differences be-

**Table III**
**Kinetic and Equilibrium Parameters for the Reactions of Equations 1 and 2**

| DMSO (v/v) | 2% | 20% | 50% | 65% |
|---|---|---|---|---|
| | | $\mathbf{4} \rightleftharpoons \mathbf{5} \rightleftharpoons \mathbf{6}$ | | |
| $k_{-2}$,$^a$ sec$^{-1}$ | 725 ± 35 | 360 ± 18 | 62 ± 3 | 25 ± 5 |
| $K_1k_2$, $M^{-1}$ sec$^{-1}$ | 59.5 ± 5$^b$ | 173 ± 15$^b$ | $4.01 \pm 0.2 \times 10^3$ | $3.53 \pm 0.14 \times 10^4$ |
| $K_1K_2$,$^a$ $M^{-1}$ (kinetic) | | 0.40 ± 0.08 | 64.2 ± 6 | 1410 ± 200 |
| $K_1K_2$,$^a$ $M^{-1}$ (spectr) | $8.20 \pm 0.3 \times 10^{-2}$ | 0.48 ± 0.02 | 64.2 ± 6$^c$ | |
| | | $\mathbf{1} \rightleftharpoons \mathbf{2} \rightleftharpoons \mathbf{3}$ | | |
| $k_{-2}$, sec$^{-1}$ | 929 | 650 | 332 | 166 |
| $K_1k_2$, $M^{-1}$ sec$^{-1}$ | 4.56$^b$ | 4.95$^b$ | 19.9$^b$ | 156$^b$ |
| $K_1K_2$, $M^{-1}$ (spectr) | $4.92 \times 10^{-3}$ | $7.60 \times 10^{-3}$ | $5.98 \times 10^{-2}$ | 0.94 |
| $(k_{-2})_6/(k_{-2})_3$ | 0.78 | 0.55 | 0.187 | 0.150 |
| $(K_1k_2)_6/(K_1k_2)_3$ | 13.1 | 35 | 202 | 226 |
| $(K_1K_2)_6/(K_1K_2)_3$ | 16.7 | 63.2 | 1075 | 1500 |

[a] Statistically corrected. [b] From $K_1K_2$ (spectr) × $k_{-2}$. [c] $\epsilon_6$ chosen such as to give $K_1K_2$ (spectr) = $K_1K_2$ (kinetic); see text.

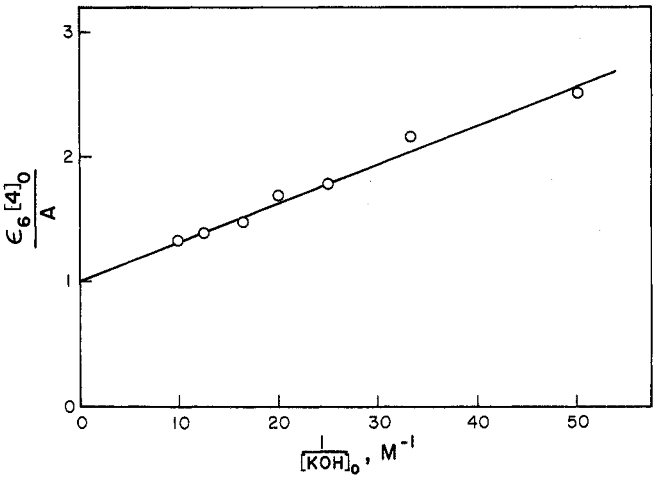


**Figure 3.** Reaction in 50% DMSO (v/v), $\mu$ = 0.5 *M*, inversion plot according to eq 9.

tween the two systems, both in the absolute values of the kinetic and equilibrium parameters as well as in their solvent dependence. For example, for **6** the effect on $k_{-2}$ of increasing the DMSO content is comparable in magnitude to similar solvent effects on the rate of decomposition of $\sigma$ complexes between $HO^-$ and 3,5-dinitropyridine[14] or 3,5-dinitrobenzonitrile;[15] for **3** this solvent effect on $k_{-2}$ is much smaller. This suggests that **6** behaves "normally," **3** "abnormally."

Comparing the $K_1K_2$ values in the two systems, we note that **3** is considerably less stable than **6**. Since $K_1$, the acid dissociation constant of **1** and **4**, respectively, can be expected to be very similar for both compounds, the higher $K_1K_2$ value for **6** must mainly reflect a higher $K_2$ value.[16]

Possible factors accounting for the lower stability of **3** include ground-state resonance stabilization in **2** (**2a**, **2b**), a larger steric strain (eclipsing effects) in the five-membered ring of **3**, and the stabilizing effect of two alkoxy substituents on the $sp^3$ carbon[18] of **6**.

We believe that the first factor may very well be the most important of the three for the following reasons. When the DMSO content of the solvent is increased, the ratio $(K_1K_2)_6/(K_1K_2)_3$ increases from 16.7 in 2% to 63.2 in 20% to 1075 in 50% to 1500 in 65% DMSO. Assuming that the solvent effect on $K_1$ is comparable in both systems, these data indicate that the stability of **6** increases more than does the stability of **3**. In other words, the factor responsible for the higher stability of **6** over **3** becomes more important in DMSO-rich mixtures.

Since DMSO is well known to be more effective than water in solvating large dipoles,[8] resonance forms such as **2a** and **2b** may in fact become more important in DMSO-rich mixtures and with it ground-state stabilization of **2**, thus accounting for the solvent effect on $(K_1K_2')_6/(K_1K_2)_3$. It would be more difficult to rationalize the solvent effect on the basis of the two other possible factors (steric strain or $sp^3$ carbon stabilization).

This interpretation is also consistent with the idea that **6** is the "normal," **3** the "abnormal" compound as suggested earlier.

An interesting question regards the extent to which the transition state is affected by the resonance stabilization. In **2** and in 20% DMSO both **6** and **3** revert to their starting materials at essentially the same rates. This means that it is the forward rate coefficient ($k_2$) which is entirely responsible for the difference in complex stability between **3** and **6**. We conclude from this that the transition state for the reaction $2 \rightleftharpoons 3$ does not benefit from resonance stabilization and thus must closely resemble the complex.

As the DMSO content is increased $k_{-2}$ becomes coresponsible for the lower stability of **3**; in 65% DMSO $k_{-2}$ for **3** is almost seven-fold larger than for **6**. This suggests that in DMSO-rich mixtures there is some resonance stabilization in the transition state; *i.e.*, the transition state must move closer to **2** as the DMSO content increases. Since complex stability increases at the same time, such an effect would be consistent with Hammond's postulate.[19]

Though more data of a similar kind are needed for definite conclusions, this study suggests that developing resonance stabilization in the transition state of the product-forming step in nucleophilic aromatic substitution reactions by amines probably only plays an important role when the intermediate complex is very stable.

## Experimental Section

**Materials.** 1-($\beta$-Hydroxyethoxy)-2,4-dinitrobenzene was prepared according to Blanksma and Fohr,[20] mp 111° after recrystallization from ethanol. DMSO (Baker Analyzed Reagent Grade) and KCl (Mallinckrodt) were used without further purification. Tetramethylammonium hydroxide (Matheson Coleman and Bell) was recrystallized from anhydrous ethanol. KOH solutions were prepared from Titrisol (Merck). Reaction solutions were prepared by dispensing the appropriate amount of DMSO into a volumetric flask, then adding an aqueous solution of the other ingredients, and finally filling to the mark with distilled water.

**Rate and Equilibrium Measurements.** Kinetic determinations were made on a temperature-jump transient spectrophotometer of Messanlagen Studiengesellschaft, Göttingen, and on a stopped-flow spectrophotometer of Durrum Instruments Corp. Chemical relaxation was monitored between 490 and 530 nm. Spectrophotometric equilibrium measurements were carried out in a modified thermostatted Bechman DU spectrophotometer. Owing to hydrolysis, absorbance readings decreased slowly with time. The values reported in Table II are extrapolated to time zero.

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**Registry No.**—**1**, 37580-86-2; **3**, 37541-32-5; **4**, 2831-60-9; **6**, 12128-27-7.

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(5) Steric repulsion between the *o*-nitro group and the *N*-methyl substituent is not expected to diminish resonance stabilization of **2** to such an extent as to make it comparable or less important than in **5**. A comparison of the p$K_a$ values of various aniline and *N,N*-dimethylaniline derivatives with nitro groups in the 2 and/or 4 and/or 6 position show that the resonance effect, though decreased by steric hindrance, is still substantial.

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(9) Apart from an apparently rather small enthalpy of reaction, it was not possible to optimize the amplitude by monitoring the relaxation at a wavelength of strong absorption of the disfavored species **4** because of interference with the spectrum of **6** (see Figure 1). There was no such problem with the reaction of eq 1, since **1** has a maximum at 390 nm where the complex **3** has a minimal absorption.[3]

(10) An "inversion plot" according to eq 9 offers the interesting possibility of determining $K_2$ and $K_1$ separately provided that $K_2$ is quite small ($K_2$ <1) so that the intercept ($1 + K_2^{-1}$) is significantly larger than 1. With $\epsilon_6$ = 21,000 this intercept is, however, 1.02 ±

0.05, *i.e.*, indistinguishable from 1. For the system of eq 1 a similar inversion plot in 65% DMSO had afforded an intercept of 1.35 from which $K_2$ was calculated.[3] We now have serious reservations about this value because of a possibly erroneous extinction coefficient ($\epsilon_3$). For lack of any better value we were forced to use $\epsilon_3$ determined in 85% DMSO. Our present study indicates that $\epsilon_6$ decreases from 32,200 in 80% DMSO to 21,000 in 50% DMSO. If $\epsilon_3$ depends in a similar way on the solvent as does $\epsilon_6$, the true intercept of said inversion plot would become indistinguishable from 1.

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(16) *Though the* p$K_a$ *values of compounds like* RN(CH$_3$)CH$_2$CH$_2$OH (R = alkyl) have to the best of our knowledge not been reported, we expect such compounds to be slightly less acidic than compounds like ROCH$_2$CH$_2$OH (p$K_a$ = 14.8 for R = methyl[17]) on the basis of a somewhat higher inductive effect in the latter. With R = 2,4-dinitrophenyl, resonance which is more important for the nitrogen analog (**2a, 2b**) *would tend to counteract the inductive effect. If the* $K_1$ values were still substantially different, the more weakly basic anion (higher $K_1$) would also be a weaker nucleophile (lower $K_2$); thus even in this worst case $K_1K_2$ would still be a reasonably good comparative measure for the stabilities of the two $\sigma$ complexes.

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# Equilibrium Additions of Nucleophiles to Carbon-Nitrogen Double Bonds in Nonaqueous Solutions. Addition of Alcohols to Substituted Benzylideneanilines

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Rate and equilibrium constants for the base-catalyzed addition of methanol to benzylideneanilines in methanol–acetonitrile (90:10 v/v) were determined by means of spectrophotometry. The equilibrium constant increases by electron-withdrawing substituents in the aniline ring as well as in the benzylidene ring, showing a correlation with the $\sigma^+$ constants. Also the rate constant increases by electron-withdrawing groups, showing a correlation with $\sigma$ in this case. The solvent deuterium isotope effects are 0.98 for $K_0^{\mathrm{MeOH}}/K_0^{\mathrm{MeOD}}$ and 0.60 for $k_f^{\mathrm{MeOH}}/k_f^{\mathrm{MeOD}}$. The structural change of alcohol leads to the Taft equation for equilibrium constant, $K_0$: log $(K_0^{\mathrm{X}}/K_0^{\mathrm{Me}}) = -8.2\sigma^* + 0.48E_s$. The rate decreases in the order *n*-BuOH > EtOH > MeOH > *sec*-BuOH > *t*-BuOH > *i*-PrOH, showing no simple correlation. The observed base catalysis, substituent effect, and solvent isotope effect are best explained by a mechanism involving a rate-determining attack by the alkoxide ions on the imino carbon atom. Thermodynamic parameters are calculated.

Equilibrium additions of nucleophiles to C=O bonds have been extensively studied[1] but the studies on the additions to C=N bonds are few except for the hydrolysis of Schiff bases[2-5] and for the additions of amines[5] and of hydrogen cyanide.[6,7] Only a few reports have paid attention to the addition of alcohols to C=N.[2,8,9] Because of the higher basicities[2-4] and lower electrophilicity of C=N than those of C=O,[1] these reactions involve the protonated Schiff bases, where negative $\rho$ values have been observed.[2-7]

The present report describes the base-catalyzed equilibrium addition of alcohols to benzylideneanilines **1–11** in which no subsequent reactions such as C—N cleavage in hydrolysis occur.

$R^1C_6H_4CH{=}NC_6H_4R^2$

| Compd | R$^1$ | R$^2$ | Compd | R$^1$ | R$^2$ |
|---|---|---|---|---|---|
| **1** | *p*-NO$_2$ | *m*-NO$_2$ | **7** | H | *m*-NO$_2$ |
| **2** | *p*-NO$_2$ | *m*-Cl | **8** | H | *m*-Cl |
| **3** | *p*-NO$_2$ | *p*-Cl | **9** | H | *p*-Cl |
| **4** | *p*-NO$_2$ | H | **10** | H | H |
| **5** | *p*-NO$_2$ | *p*-Me | **11** | *p*-Cl | H |
| **6** | *p*-NO$_2$ | *p*-OMe | | | |

## Results

**Base-Catalyzed Addition of Methanol.** The stoichiometry of equilibrium addition of methanol to benzylideneanilines was confirmed by the decrease in extinction at 340 nm in the uv spectrum and appearance of the CH proton at *ca.* $\tau$ 4.5 with a decrease in the CH= proton at $\tau$ 1.7 in the nmr spectrum. The addition in neutral methanol solution requires several days to reach an equilibrium, while in the presence of a basic catalyst it is much more rapid. Addition of acetonitrile to the basic equilibrium solution causes the extinction at 340 nm to increase until a new equilibrium position is established, because of the decrease in methanol concentration. Moreover, the value of equilibrium constant, $K_0$, evaluated in terms of a following stoichiometry from the decrease in extinction of a Schiff base, is consistent with that evaluated from the relative strengths of the CH proton signal *vs.* the -CH= proton signal in the nmr spectrum of the solution. Hence

$$R^1C_6H_4CH{=}NC_6H_4R^2 + MeOH \overset{K_0}{\rightleftharpoons} R^1C_6H_4CH(OMe)\text{-}NHC_6H_4R^2$$

Although rapid solvolysis of Schiff bases occurs in acidic methanol to afford the corresponding benzaldehyde dimethyl acetals and anilines, no solvolysis occurs in alkaline methanol.

**Effect of Substituent in Benzylideneanilines.** The equilibrium and rate constants for addition of methanol to benzylideneanilines are shown in Table I. *N*-Benzylideneanilines with a single electron-releasing group such as methyl or methoxy have very small equilibrium constants showing only poor addition of the alcohol ($K_0 \leq 10^{-3}\ M^{-1}$ based on ≤1% conversion of Schiff base).

The equilibrium constants show a good correlation with the Brown–Okamoto's $\sigma^+$ constant,[10] giving a $\rho^+$ value of 1.42 ($r$ = 0.993) at 15°, 1.41 ($r$ = 0.994) at 25°, and 1.43 ($r$ = 0.995) at 30° for *N*-(*p*-nitrobenzylidene)(substituted anilines), 1.58 for *N*-benzylidene(substituted anilines), and