is interesting to note that not only is the chemical shift difference between the methyl pairs large (up to 74 Hz) but one methyl group pair is shifted to such high field so as to be upfield of $Me_4Si$ (see Figure 4). This led to the suggestion that rotation of the isopropyl groups is restricted not only by opposition between 9 and 10 positions but also due to the 1 and 4 substituents, and this results in one pair of the methyl groups being positioned in the shielding region of the unsubstituted outer ring. Similar effects were noted for the analogous 9,10-diethyl and 9,10-dibenzyl derivatives, where the result could be confirmed by the significant differences in coupling constants between $H_9$ (and $H_{10}$) and each of the protons in the adjacent $CH_2R$ group.

## Conclusions

In retrospect, it is not difficult to understand why the 1,4-cyclohexadiene ring system has provided so many problems with regard to its conformational analysis. Although it now appears that 1,4-dihydrobenzenes, 1,4-dihydronaphthalenes, and 9,10-dihydroanthracenes prefer planar, flattened boat and boat-shaped conformations, respectively, when bearing a single small substituent (or presumably no substituent), it is evident that appropriate substitution can lead to wide variation in geometry. For example, the usually planar 1,4-dihydrobenzene adopts a boat conformation with cis-1,4-disubstitution, the nearly flattened 1,4-dihydronaphthalene becomes highly puckered with a single large substituent, and the normally boat-shaped 9,10-dihydroanthracene becomes flattened with two large cis substituents in the 9 and 10 positions. It is obvious that such diversity in structure cannot be approached without the firm establishment of characteristic parameters which, in this case, appear to be the homoallylic coupling constants. In fact, it has been primarily the delay in establishing theoretical predictions and empirical values for these relationships that has withheld the key to understanding the stereochemistry of this system.

Future studies will no doubt provide additional information concerning the effect of substitution (particularly multiple substitution) in these systems, especially in 1,4-cyclohexadienes and 1,4-dihydronaphthalenes where relatively little work has been done. We are also very interested in the possible application of $^{13}C$ NMR to the dynamic processes such as ring inversion in dialkyl-9,10-dihydroanthracenes which cannot be observed within the range of $^1H$ NMR. In any event, it is hoped that these studies on the cyclohexadiene ring systems may provide another pillar on which our general information about the conformational analysis of carbocyclic rings will rest.

*I thank my co-workers, many of whom have been undergraduates, and also the following for financial support: Lilly Research Laboratories, Indianapolis, Ind., and the Donors of the Petroleum Research Fund, administered by the American Chemical Society.*

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(46) P. W. Rabideau and J. W. Paschal, *J. Am. Chem. Soc.*, **94**, 5801 (1972).

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# Kinetic Behavior of Short-Lived Anionic σ Complexes

CLAUDE F. BERNASCONI

*Thimann Laboratories of the University of California, Santa Cruz, California 95064*

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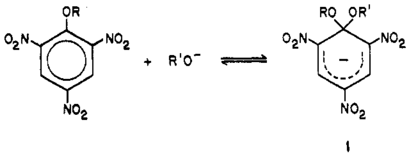
The interest in anionic σ complexes goes back to the beginning of the century when Jackson and Gazzolo[1] proposed structure 1 for the strongly colored species



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which form when potassium alkoxides interact with picryl ethers. Experiments by Meisenheimer,[2] in which the same complex was isolated by treating either 2,4,6-trinitroanisole with ethanolic KOH or 2,4,6-trinitrophenetole with methanolic KOH, lent strong support to structure 1; such complexes are therefore often referred to as "Meisenheimer complexes".

The advent of NMR spectroscopy led to a significant breakthrough in the structural identification of anionic σ complexes; after the publication of the first spectrum (1 with $R = R' = CH_3$) by Crampton and Gold,[3] NMR quickly became the main tool in the structure determination of numerous such complexes.[4]

Rate studies were not reported before 1955 when Caldin and Long[5] investigated the reaction of ethoxide ion with 1,3,5-trinitrobenzene and some other nitroaromatics. The main reason for the absence of earlier reports appears to be the high rates associated with most of these reactions and thus the necessity of using

Claude F. Bernasconi was born in Zürich, Switzerland. He obtained his Ph.D. in 1965 (with Heinrich Zollinger) from the Swiss Federal Institute of Technology (ETH). Following a year of postdoctoral work with Manfred Eigen at the Max Planck Institute for Biophysical Chemistry in Göttingen, he joined the faculty of the University of California at Santa Cruz, where he is now Professor of Chemistry and Chairman of the Board of Studies in Chemistry. His research interests center around problems of mechanism, reactivity, and catalysis in organic reactions. His major contributions have been in the area of nucleophilic aromatic substitution reactions, anionic σ complexes, and more recently, nucleophilic additions and substitutions in vinylic systems and electron transfer reactions. Dr. Bernasconi is the author of a recent book on relaxation techniques.

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(1) C. J. Jackson and F. H. Gazzolo, *J. Am. Chem. Soc.*, **23**, 376 (1900).

(2) J. Meisenheimer, *Justus Liebigs Ann. Chem.*, **323**, 205 (1902).

(3) M. R. Crampton and V. Gold, *J. Chem. Soc.*, 4293 (1964).

(4) For reviews see (a) M. J. Strauss, *Chem. Rev.*, **70**, 667 (1970); (b) T. N. Hall and C. F. Poranski, Jr., in "The Chemistry of the Nitro and Nitroso Groups", Part 2, H. Feuer, Ed., Interscience, New York, N.Y., 1970, p 329; (c) M. R. Crampton, *Adv. Phys. Org. Chem.*, **7**, 211 (1969).

(5) E. F. Caldin and G. Long, *Proc. R. Soc. London, Ser. A*, **226**, 263 (1955).

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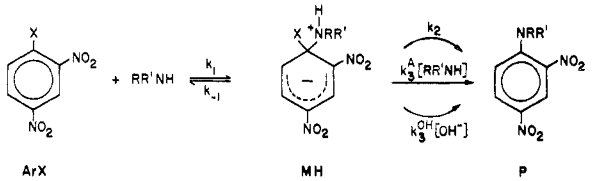
fast reaction techniques.[6] During the past 10 years, as more laboratories have acquired stopped-flow and temperature-jump equipment, the number of reports of kinetic studies has greatly increased. A significant portion of these investigations were carried out in my laboratory. These studies have not only enhanced our understanding of Meisenheimer complex chemistry proper, but have led to insights which are of wider scope and which have implications in other areas of physical organic chemistry. In this Account I shall discuss four areas in which we have either gained new insights or uncovered some unresolved problems. They are (a) the mechanism of base catalysis of $S_NAr$ reactions involving amine nucleophiles; (b) solvent and steric effects on proton transfer reactions; (c) the transition state of concerted acid-base catalyzed reactions; (d) leaving group abilities of amines, alkoxide, and aryloxide ions.

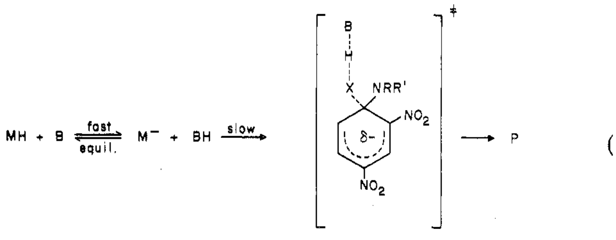
## The Mechanism of Base Catalysis in $S_NAr$ Reactions

Equation 1 shows a familiar example of the well-established intermediate complex mechanism of $S_NAr$ reactions involving an amine nucleophile.[7] We shall only deal with the base-catalyzed pathways; in aqueous or partly aqueous solution there is most commonly a term for hydroxide ion catalysis and a term for catalysis by the amine which is used as the nucleophile. Addition of other bases may contribute additional rate terms.



(1)

In the "early days" (1958) catalysis was assumed to be a consequence of rate-limiting deprotonation of MH, followed by rapid leaving group departure.[8] However, when it became generally known that proton transfers between "normal" acids and bases are very fast,[9] this mechanism lost favor and was replaced by the SB-GA (specific base-general acid) mechanism shown in eq 2



(2)

for the case of a general base B; it involves rapid equilibrium deprotonation of MH followed by rate-limiting, concerted general acid (BH) catalyzed leaving-group departure.[10]

The SB-GA mechanism became generally accepted after Orvik and Bunnett[11] presented direct evidence that in the reaction of 1-ethoxy-2,4-dinitronaphthalene with *n*-butylamine in $Me_2SO$ leaving-group departure is in fact rate limiting and general acid catalyzed. To this date there is little doubt that this is the correct mechanism in *aprotic* solvents.

In *protic* solvents the situation is quite different. In the course of investigating the kinetics of various Meisenheimer complex systems we made four observations which all indicated that the SB-GA mechanism does not operate and that general base catalysis is a consequence of rate-limiting deprotonation of MH. For a better understanding of the significance of these observations, let us first discuss how the relative rates of the various steps in the reaction (rewritten as eq 3)

$$\mathrm{ArX} + \mathrm{RR'NH} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{MH} \underset{k_{-3p}}{\overset{k_{3p}}{\rightleftharpoons}} \mathrm{M}^- \xrightarrow{k_4} \mathrm{P} \qquad (3)$$

determine which mechanism prevails; $k_{3p}$ and $k_{-3p}$ are defined by eq 4 and 5 where $k_{3p}^{B_i}$ and $k_{3p}^{OH}$ refer to the

$$k_{3p} = \sum_i k_{3p}^{B_i}[B_i] + k_{3p}^{OH}[OH^-] \qquad (4)$$

$$k_{-3p} = \sum_i k_{-3p}^{B_i}[BH_i] + k_{-3p}^{OH} \qquad (5)$$

deprotonation of MH by general bases $B_i$ (notably RR'NH) and by $OH^-$, respectively, while $k_{-3p}^{B_i}$ and $k_{-3p}^{OH}$ refer to the protonation of $M^-$ by general acids $BH_i$ (notably $RR'NH_2^+$) and by the solvent; $k_4$ is defined by eq 6 where $k_4^{B_i}$ refers to catalysis of leaving-group departure by general acids (notably $RR'NH_2^+$) while $k_4^{OH}$ refers to the unassisted or solvent-assisted leaving-group departure.[12]

$$k_4 = \sum_i k_4^{B_i}[BH_i] + k_4^{OH} \qquad (6)$$

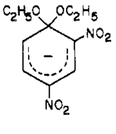
The two main limiting situations of interest are:

*Case 1*: $k_4 \gg k_{-3p}$ and $k_{3p} <(\ll)\ k_{-1}$. Here the $k_{3p}$ step is overall rate limiting, i.e., base catalysis is a consequence of rate limiting proton transfer.

*Case 2*: $k_4 \ll k_{-3p}$ and $k_{3p}k_4/k_{-3p} <(\ll)\ k_{-1}$. Here the $k_4$ step is rate limiting. Inasmuch as the general acid catalysis terms ($\sum k_4^{B_i}[BH_i]$, eq 6) are significant, this corresponds to the SB-GA mechanism. If $\sum k_4^{B_i}[BH_i] = 0$ or very small, the overall reaction should show specific rather than general base catalysis.

The four observations referred to above allow us to estimate the rates of the various steps of eq 3; they are now discussed.

**Observation One.** General acid catalysis of alkoxide ion departure from complexes such as **1** (R = R' = $CH_3CH_2$, $CH_3$, $CH_3OCH_2CH_2$, $ClCH_2CH_2$, $HC{\equiv}CCH_2$)[13] and **2**,[13] and of spiro ring opening in **3**,[14] **4**[15]



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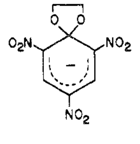

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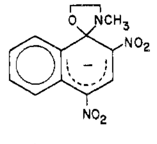

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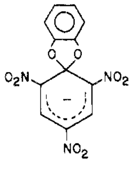

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[6] In the case of the reaction of ethoxide ion with 1,3,5-trinitrobenzene two approaches were used:[5] (a) measurements at very low temperatures (-80 °C) by conventional kinetic methods; (b) use of the stopped-flow technique at room temperature.

[7] For reviews see (a) C. F. Bernasconi, *MTP Int. Rev. Sci., Org. Chem. Ser. One, 1973*, **3**, 33 (1973); (b) F. Pietra, *Q. Rev. Chem. Soc.*, **23**, 504 (1969); (c) J. Miller, "Aromatic Nucleophilic Substitution", American Elsevier, New York, N.Y., 1968.

[8] J. F. Bunnett and J. J. Randall, *J. Am. Chem. Soc.*, **80**, 6020 (1958).

[9] M. Eigen, *Angew. Chem., Int. Engl. Ed.*, **3**, 1 (1964).

[10] (a) J. F. Bunnett and G. T. Davis, *J. Am. Chem. Soc.*, **82**, 665 (1960), footnote 27; (b) J. F. Bunnett and R. H. Garst, *ibid.*, **87**, 3879 (1965); (c) J. F. Bunnett and C. F. Bernasconi, *ibid.*, **87**, 5209 (1965); (d) A. J. Kirby and W. P. Jencks, *ibid.*, **87**, 3217 (1965).

[11] J. A. Orvik and J. F. Bunnett, *J. Am. Chem. Soc.*, **92**, 2417 (1970).

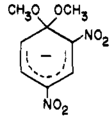
[12] Under typical conditions pathways involving $H^+$ contribute negligibly to $k_{-3p}$ and $k_4$, and the solvent pathway contributes little to $k_{3p}$; equally, the $k_2$ pathway (eq 1) contributes little to the overall rate under typical conditions.

[13] C. F. Bernasconi and J. R. Gandler, in preparation.

(C–O bond breaking), and 5,[16] is weak or undetectable (e.g., for 5). By this we mean that, e.g., in aqueous solution, catalysis only becomes detectable with acids whose $pK_a$ values are $\sim$6 or lower and when these acids are present at relatively high concentrations. Catalysis by $RR'NH_2^+$ of typical amines used as nucleophiles in eq 1 (e.g., piperidine, *n*-butylamine) is usually too weak to be detected in aqueous solution, although there is some definite catalytic activity in 60% dioxane–40% water.[13]

The SB–GA mechanism, on the other hand, requires that general acid catalyzed leaving-group departure is very effective. For example, if the data of the piperidine-catalyzed reaction of 2,4-dinitrophenyl phenyl ether in 10% dioxane–90% water[10c] were analyzed under the assumption that the SB–GA mechanism prevailed, they would imply that a 1 M solution of piperidinium ion accelerates phenoxide ion departure from $M^-$ 65-fold over the unassisted pathway.[17] This contrasts with our findings that the same concentration of piperidinium ion increases the rate of ethoxide ion departure from 1 ($R = R' = C_2H_5$) by less than 50%[13] in aqueous solution. For the same reaction in 60% dioxane–40% water[10b] the SB–GA mechanism would imply that a 1 M solution of piperidinium ion enhances the rate of phenoxide ion departure $\sim 10^5$-fold, whereas the acceleration for the model reaction (1, $R = R' = C_2H_5$) is only 80-fold in this solvent.[13] Considering that the model reaction should be even more sensitive to acid catalysis due to the higher basicity of the leaving group (ethoxide vs. phenoxide), the above comparisons actually understate the case. Thus we conclude that one of the conditions for the SB–GA mechanism, namely that $\sum k_4^{B_i}[BH_i]$ is large, is not met.

**Observation Two.** Suitable extrapolation of the rates of alkoxide and phenoxide ion departure from complexes such as 1 ($R = R' = CH_3$),[18] 6,[19] and 7,[20] and



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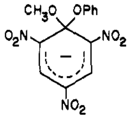

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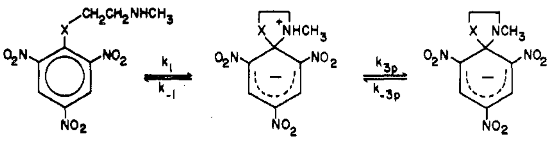
of spiro ring opening in 3[14] and 5[16] have allowed us to estimate the order of magnitude of $k_4$ ($\approx k_4^{OH}$) for typical leaving groups in reaction 3.[17] For example, using two independent extrapolation procedures, based on different model reactions, we estimated $k_4$ to be as high as $4–8 \times 10^7\ s^{-1}$ in the reaction of piperidine with 2,4-dinitrophenyl phenyl ether (phenoxide ion departure) in 10% dioxane–90% water.[17] As will be shown under observation four, $k_{-3p}$ can never reach such high values; for example, for the reactions of piperidine with 2,4-dinitrobenzene derivatives in 10% dioxane–90% water we have estimated $k_{-3p} = k_{-3p}^{OH} + k_{-3p}^{RR'NH}[RR'NH_2^+] \approx 500 + 2 \times 10^4[RR'NH_2^+]\ s^{-1}$.[17] This means that with a good leaving group such as phenoxy we have $k_4 \gg k_{-3p}$ by a large margin, which is inconsistent with case 2 but consistent with case 1.

On the other hand, for the much more sluggish methoxy leaving group our estimate for $k_4$ is $10^2$–$10^3\ s^{-1}$ in 10% dioxane–90% water, 20–200 $s^{-1}$ in 60% dioxane–40% water; these estimates are low enough to make $k_4 \ll k_{-3p}$, at least under certain conditions.[17] When $k_4 \ll k_{-3p}$ one would, based on observation one, predict that reaction 3 should show *specific* rather than *general* base catalysis. This is in fact the case, e.g., for the reaction of piperidine with 2,4-dinitroanisole and with 1-methoxy-4,7-dinitronaphthalene in 60% dioxane–40% water.[17]

**Observation Three.** Temperature-jump studies on model systems such as eq 7[15,21] and similar systems[15,22]

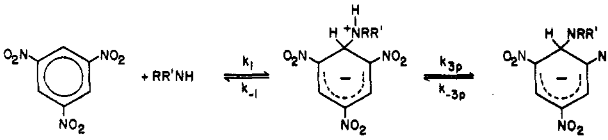


(7)

8 ($X = O$ or $N\text{-}CH_3$) 9 10

revealed that amine departure from complexes such as 9 is remarkably fast; for example, $k_{-1} = 1.9 \times 10^5\ s^{-1}$ when $X = NCH_3$,[21] $1.2 \times 10^5\ s^{-1}$ when $X = O$.[15] As a consequence deprotonation of 9, even though thermodynamically favored (see observation four) and thus essentially diffusion controlled (more on this under "Solvent and Steric Effects on Proton Transfer Rates"), becomes rate limiting ($k_{3p}$[23] $\ll k_{-1}$), or partially so ($k_{3p}$[23] $< k_{-1}$) at low pH and low buffer concentration.

Extrapolation of these $k_{-1}$ values to typical $S_NAr$ substrates such as 2,4-dinitrobenzene derivatives (eq 1) leads to estimated $k_{-1}$ values in the order of $10^7$ to $10^8$ $s^{-1}$.[17,21] More recent studies on reaction 8 with RR′NH



11 12

(8)

= methylamine, dimethylamine, *n*-butylamine, piperidine, and pyrrolidine have confirmed these conclusions.[24] Hence for the 2,4-dinitrobenzene derivatives the relationship $k_{3p} <(\ll) k_{-1}$ can be expected to hold up to the rather high base concentrations which were used in typical studies of base catalysis of $S_NAr$ reactions.[10b–d,25] In other words there is nothing "unreasonable" about diffusion-controlled deprotonation of MH being rate limiting under typical $S_NAr$ conditions.

**Observation Four.** Another result from the studies of reactions 7 and 8 is that the basicity of complexes

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(14) M. R. Crampton and M. J. Willison, *J. Chem. Soc., Perkin Trans. 2*, 1686 (1974).

(15) C. F. Bernasconi, C. L. Gehriger, and R. H. de Rossi, *J. Am. Chem. Soc.*, **98**, 8451 (1976).

(16) C. F. Bernasconi and H.-C. Wang, *J. Am. Chem. Soc.*, **98**, 6265 (1976).

(17) C. F. Bernasconi, R. H. de Rossi, and P. Schmid, *J. Am. Chem. Soc.*, **99**, 4090 (1977).

(18) J. H. Fendler, E. J. Fendler, and C. E. Griffin, *J. Org. Chem.*, **34**, 689 (1969).

(19) C. F. Bernasconi, *J. Am. Chem. Soc.*, **90**, 4982 (1968).

(20) C. F. Bernasconi and M. C. Muller, in preparation.

(21) C. F. Bernasconi and C. L. Gehriger, *J. Am. Chem. Soc.*, **96**, 1092 (1974).

(22) C. F. Bernasconi and F. Terrier, *J. Am. Chem. Soc.*, **97**, 7458 (1975).

(23) $k_{3p}$ and $k_{-3p}$ are defined by eq 4 and 5, respectively, as for reaction 3.

(24) C. F. Bernasconi, M. C. Muller, and P. Schmid, in preparation; this study supersedes some of the conclusions of an earlier report: C. F. Bernasconi, *J. Am. Chem. Soc.*, **92**, 129 (1970).

(25) (a) C. F. Bernasconi, *J. Org. Chem.*, **32**, 2947 (1967); (b) C. F. Bernasconi and P. Schmid, *ibid.*, **32**, 2953 (1967); (c) J. F. Bunnett and C. F. Bernasconi, *ibid.*, **35**, 70 (1970).

such as **10** and **12** is considerably less than the basicity of the parent amine (**8** and RR′NH, respectively). Based on these results we have estimated that the $pK_a$ of MH (eq 3) is approximately three units lower than the $pK_a$ of the parent $RR'NH_2^+$ in 10% dioxane–90% water, about 2 units lower in 60% dioxane–40% water.[17] As a consequence the $k_{-3p}$ step refers to a thermodynamically disfavored proton transfer under all typical conditions, with a correspondingly low rate. This implies that $k_4 \gg k_{-3p}$ for good leaving groups, as shown under observation two.

## Solvent and Steric Effects on Proton Transfer Rates

The study of reactions such as eq 7 and 8 provided us with rate constants for the proton transfer between **9** or **11** and various bases ($OH^-$, $H_2O$, phosphate, aryloxides, amines).[15,21,22,24] Furthermore, a large number of old data on base catalysis of $S_NAr$ reactions which had permitted the evaluation of $k_3^A/k_3^{OH}$ ratios[26] (eq 1) can now be used to calculate the relative rates of the deprotonation of MH (eq 3) by amines and $OH^-$. This is possible because the establishment of the mechanism of base catalysis being a rate-limiting proton transfer means that $k_3^A$ and $k_3^{OH}$ in eq 1 simply refer to deprotonation rate constants.

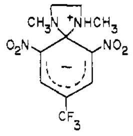
Some of our major findings can be summarized as follows. (1) In aqueous solution deprotonation of complexes such as **9** by $OH^-$, and protonation of complexes such as **10** by $H_3O^+$, occurs at rates expected for diffusion-controlled reactions;[9] typical values for $k_{3p}^{OH}$ are $\sim 5 \times 10^9$ $M^{-1}$ $s^{-1}$,[15,21] while rate constants for the protonation of **10** by $H_3O^+$ are $\sim 2\text{–}5 \times 10^{10}$ $M^{-1}$ $s^{-1}$.[15,21]

(2) In $Me_2SO$–water mixtures deprotonation of complexes such as **9** or **11** by $OH^-$ becomes slower with increasing $Me_2SO$ content. Typically $k_{3p}^{OH} \approx 5 \times 10^8$ $M^{-1}$ $s^{-1}$ in 30% $Me_2SO$,[24] $k_{3p}^{OH} \approx 2 \times 10^7$ $M^{-1}$ $s^{-1}$ in 70% $Me_2SO$.[22] An earlier interpretation of this rate reduction was that in the $Me_2SO$-containing solvents there is an internal hydrogen bond between the ammonio proton and an *o*-nitro group of **9** or **11**.[22,27] Based on our recent findings that there is a significant rate reduction even in a solvent containing as little as 30% $Me_2SO$[24] (which has about the same dielectric constant as pure water) we believe that an alternative interpretation of these rate reductions in terms of hydrogen bonding to $Me_2SO$ is an attractive possibility; $Me_2SO$ is known to be a much stronger hydrogen bond acceptor than water.[28] According to this interpretation the rate reductions would result from the necessity of breaking the hydrogen bond to $Me_2SO$ prior to the proton transfer.[24] We are currently testing these ideas in systems which cannot form *internal* hydrogen bonds.

In contrast to the deprotonation reactions by $OH^-$, the rates of proton transfer from complexes such as **9** and **11** to bases other than $OH^-$ change little with the solvent; $k_{3p}^B$ is typically around $10^7$ $M^{-1}$ $s^{-1}$ for bases whose $pK_a$ is such as to make the proton transfer thermodynamically favored by at least two $pK$ units.[22,24,27] The reasons why general bases behave differently from $OH^-$ are not clear at this time. Studies aimed at a better understanding of this phenomenon are in progress in my laboratory.

(3) In aqueous solution or in 10% dioxane–90% water proton transfer from complexes such as **9** and **11** to bases other than $OH^-$, particularly amines, is 50–500-fold slower than deprotonation by $OH^-$.[15,21,24] Normally, proton transfer from NH acids to N or O bases are only about 2–5 times slower than proton transfer to $OH^-$.[9,29] The large rate reductions in our systems appear to be due to a steric effect; the reactive site in **9** or **11** is rather crowded and cannot easily be approached by bases which are much larger than $OH^-$. This explanation is supported by the fact that for the sterically less crowded MH in eq 1 (only one *o*-nitro group) comparable rate reductions are only in the range of 20–100-fold.[17]

The above rate reductions which can be expressed as $k_{3p}^{OH}/k_{3p}^B$ ratios become smaller when $Me_2SO$ is added to the solution. Thus for the deprotonation of **11** by RR′NH the $k_{3p}^{OH}/k_{3p}^B$ (B = RR′NH) is ~400 in 10% dioxane–90% water[24] but only ~30 in 30% $Me_2SO$–70% water.[24] In 70% $Me_2SO$–30% water the $k_{3p}^{OH}/k_{3p}^B$ ratios for the deprotonation of **13** are only ~4–8, for **14** only ~3–4,[30] where the bases are aryloxide ions, indazole, and imidazole ion.[22,27] In view of our observations discussed under (2) the decrease in the $k_{3p}^{OH}/k_{3p}^B$ ratios cannot be due to a decrease in the importance of the steric effect on $k_{3p}^B$, but is a consequence of the reduction of $k_{3p}^{OH}$ with increasing $Me_2SO$ content.



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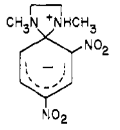

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## The Transition State of Concerted Acid Catalyzed C–O Bond-Breaking

In the first part of this Account we have emphasized that in aqueous solution general acid catalysis of alkoxide ion departure from Meisenheimer complexes is weak or undetectable (observation one) with very weak acids such as protonated aliphatic amines. However, with increasing acidity of the catalyst, catalysis becomes easily detectable and, e.g., with substituted pyridinium ions, obeys the Brønsted relation quite well.[13] We have determined the Brønsted $\alpha$ exponent for reaction 9 as a function of R; for reaction 10, as a function of X.

Our results relate to the current interest in how the transition state of concerted reactions changes with the structure of the reactants and to the discussion of this problem in terms of the free-energy contour diagrams made popular by More O'Ferrall[31] and Jencks.[32] If one makes the idealized assumption that the reaction coordinate of the concerted process lies on the diagonal of the diagram, with the transition state in the center

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[26] All literature data known at the time which permit calculation of $k_3^A/k_3^{OH}$ ratios have been summarized in ref 7a. For additional and more recent data see ref 17.

[27] C. F. Bernasconi and F. Terrier, in "Chemical and Biological Applications of Relaxation Spectrometry", E. Wyn-Jones, Ed., D. Reidel, Dordrecht, Holland, 1975, p 379.

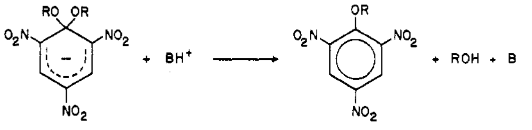
[28] (a) M. J. Kamlet and R. W. Taft, *J. Am. Chem. Soc.*, 98, 377 (1976); (b) H. H. Szmant, in "Dimethylsulfoxide", S. W. Jacob, E. E. Rosenbaum and D. C. Woods, Ed., Vol. 1, Marcel Dekker, New York, N.Y., 1971, Chapter 1.

[29] M.-L. Ahrens and G. Maass, *Angew. Chem., Int. Eng. Ed.*, 7, 818 (1968).

[30] The smaller ratios for **14** compared to **13** are again best explained in terms of a steric effect.

[31] R. A. More O'Ferrall, *J. Chem. Soc. B*, 274 (1970).

[32] W. P. Jencks, *Chem. Rev.*, **72**, 705 (1972).



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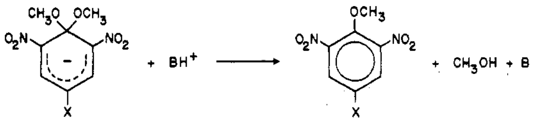
(9)

$R = CH_3CH_2, CH_3, CH_3OCH_2CH_2, ClCH_2CH_2, HC{\equiv}CCH_2$

$\alpha = \approx 0.65, 0.61, 0.53, 0.47, 0.35$



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(10)

$X = CN, SO_2CH_3, NO_2, SO_2CF_3$

$\alpha = 0.58, 0.59, 0.61, 0.63$

(Figures 1 and 2), one comes up with the following predictions.

(1) The effect of making R more electron withdrawing (eq 9) is to stabilize $RO^-$ (corner C) and to destabilize the zwitterionic complex in corner B. This raises the energy of corner B over that of corner C and causes the transition state to shift toward corner C ("perpendicular effect", Thornton rule[33]), as shown in Figure 1. On the other hand, since there is no charge on the oxygen in ROH (corner A) or the complex in corner D, the relative energies of corners A and D do not change much and hence there is no significant effect on the transition state along the reaction coordinate ("parallel effect", Hammond postulate[34]). Thus the overall change in transition-state structure is practically solely determined by the perpendicular effect whose horizontal component indicates that there must be a decrease in $\alpha$ for reaction 9. This is what we in fact observe. Similar observations have been reported for other systems and interpreted along similar lines,[35-38] although this kind of interpretation has been questioned by Johnson[39] on grounds that there is a "drastic variation of structure in R adjacent to the reaction site" which could, for example, lead to steric effects. The fact that the same trend in $\alpha$ is observed for aryloxide ion departure from benzaldehyde methyl aryl acetals[36] (structural changes far from reaction site) argues against Johnson's objections.

(2) The effect of making X more electron withdrawing (eq 10) is to stabilize the complexes in the corners B and D. As a result, the lowering of the energy of D relative to A shifts the transition state toward A ("parallel effect", Hammond postulate[34]), the lowering of B relative to C shifts it toward B ("perpendicular effect", Thornton rule[33]), as indicated in Figure 2 for the diagonal reaction coordinate. The perpendicular effect is assumed to be smaller than the parallel effect because the stabilization of corner B is less than that of D, owing to the positive charge in the complex of B. The net result of the two effects is to shift the transition state in the direction of more proton transfer (larger $\alpha$) for reaction 10. Even though there is indeed a slight increasing trend in our experimental $\alpha$ values, it is very small and hardly distinguishable from experimental error. It is noteworthy that for phenoxide ion departure from substituted benzaldehyde methyl phenyl acetals, a reaction which is very similar to ours, $\alpha$ changes strongly with the substituent, in the direction predicted by the diagram;[36] at present it is unclear why there is this discrepancy in the behavior of the two reactions. However, we note that a relative insensitivity of $\alpha$ to changes in the electrophile has been reported for other, related reactions.[39] This suggests that our results for

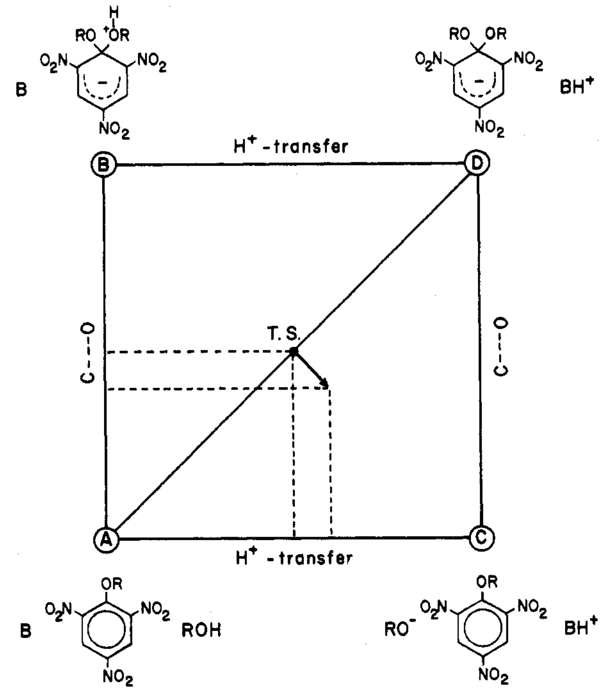

**Figure 1.** Effect of making R more electron withdrawing on the transition state of reaction 9, assuming a diagonal reaction coordinate.

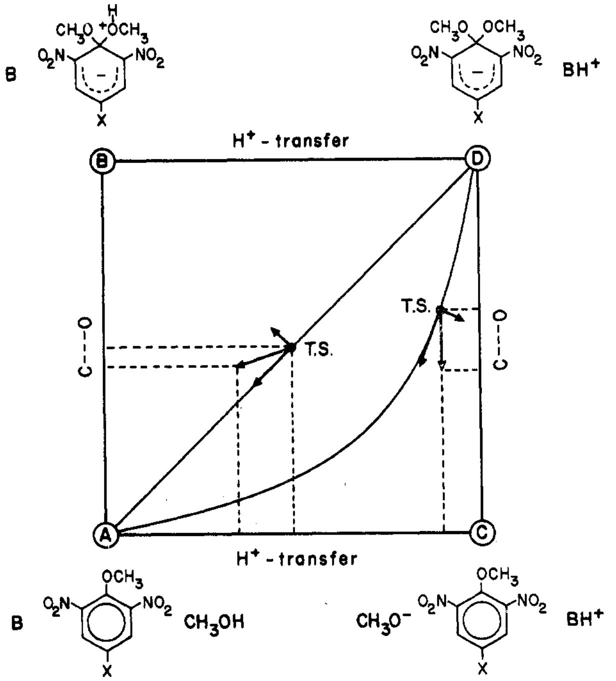

**Figure 2.** Effect of making X more electron withdrawing on the transition state of reaction 10, assuming (a) a diagonal, (b) a curved reaction coordinate.

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[33] E. R. Thornton, *J. Am. Chem. Soc.*, **89**, 2915 (1967).

[34] G. S. Hammond, *J. Am. Chem. Soc.*, **77**, 334 (1955).

[35] N. Gravitz and W. P. Jencks, *J. Am. Chem. Soc.*, **96**, 507 (1974).

[36] B. Capon and K. Nimmo, *J. Chem. Soc., Perkin Trans. 2*, 1113 (1975).

[37] R. G. Bergstrom, M. J. Cashen, and A. J. Kresge, personal communication.

[38] J. M. Sayer and M. De Pecol, *J. Am. Chem. Soc.*, **99**, 2665 (1977).

[39] C. D. Johnson, *Chem. Rev.*, **75**, 755 (1975).

reaction 10, even though contrary to the predictions based on the above model, may in fact be more typical than those reported for the substituted benzaldehyde methyl phenyl acetals.

A possible interpretation of this insensitivity of $\alpha$ is that the reaction coordinate is curved as shown in Figure 2. This implies that C–O bond breaking is ahead of proton transfer in the transition state, with some net negative charge on oxygen; this would be consistent with our observation that reaction 9 is faster with more electron withdrawing R groups[13] (stabilization of negative charge). If the transition state is located at the point indicated in Figure 2 a more electron-withdrawing X substituent has the following effects: the strong stabilization of corner D relative to C and A exerts a strong parallel effect and shifts the transition state toward the A–C edge. The perpendicular effect is mainly governed by the relative energy change between corners B and D (rather than between B and C as for the diagonal reaction coordinate); thus the relatively stronger stabilization of D induces a shift toward the D–C edge. The vector resulting from the combination of the parallel and perpendicular effects has no significant component in the proton-transfer axis and hence no significant change in $\alpha$ is expected. This interpretation, even though still consistent with the observed effect of changing R on $\alpha$, is not without its own problems. It can be shown[13] that a change in the acid strength of the catalyst might, under certain circumstances, induce the transition state to be displaced along the proton transfer axis, the consequences of which would be a change in $\alpha$ values (curved Brønsted plots) with changing catalyst. No such curvature in the Brønsted plots was observed. The problem will be discussed in greater detail in a forthcoming paper.[13]

## Leaving-Group Abilities of Alkoxide (Aryloxide) Ions and Amines

The most noteworthy results on leaving-group abilities which we have obtained so far can be summarized as follows.

(1) A plot of the log of the rate constants of uncatalyzed alkoxide ion departure from complexes such as **15** in aqueous solution vs. the p$K_a$ of ROH gives a straight line with a slope $\beta_{lg} = -0.98$;[13] phenoxide ion departure from **7** is about $10^7$ times faster than methoxide ion departure from **16** ($X = NO_2$);[20] spiro ring opening in **5** is $\geq 10^5$ faster than in **3**.[14,16] These results all indicate a high sensitivity of leaving group ability to the p$K_a$ of the leaving group. Similarly high or even higher sensitivities to the p$K_a$ of the leaving group have been found in other systems, e.g., in the alkoxide ion departure from tetrahedral addition compounds of *N,O*-trimethylenephthalimidium ion ($\beta_{lg} = -0.9$),[35] aryloxide ion departure from 2-aryloxytetrahydrofurans[40] ($\beta_{lg} = -1.08$),[41] alkoxide ion departure from alkyl monocarbonates ($\beta_{lg} = -1.1$, also $k^{PhO}/k^{MeO} \approx 10^6$),[42] and aryloxide ion departure from aryl acetoacetate anions ($\beta_{lg} = -1.29$).[43]

On the other hand, there exist some reports of much lower sensitivity to the p$K_a$ of the leaving group, e.g., for the aryloxide ion departure from aryl carbamate anions ($\beta_{lg} = -0.65$)[44] or phenoxide vs. methoxide ion departure from sulfone anions of the type $PhSO_2CH^-CH_2OR$ ($k^{PhO}/k^{MeO} \approx 10^3$).[45] At present it is not very clear what factors determine whether the reaction has a high or a low sensitivity to the leaving group p$K_a$.

(2) A question of considerable chemical and biochemical importance is whether the generally much faster leaving group departure of (protonated) amines[46] compared to alkoxide ions is mainly a consequence of the usually much lower basicity of the amine or whether amines are intrinsically better leaving groups. Gravitz and Jencks[47] came to the conclusion that the latter is the case; it was based on a rate comparison of the breakdown of tetrahedral addition compounds of *N,O*-trimethylenephthalimidium ion with amines and alkoxide ions, respectively, where the expulsion of secondary amines is about $10^5$ times faster than that of alkoxide ions of *comparable* p$K_a$.

In contrast, our own data on leaving group departure from Meisenheimer complexes between 1,3,5-trinitrobenzene and amines or alkoxide ions, respectively, indicate that for comparable p$K_a$ values leaving group abilities of alkoxide ions are similar to, or even slightly greater than, those of amines.[24] These results suggest that relative leaving group abilities may greatly depend on the nature of the electrophile; there is a clear need for more work in this area.

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(40) H. Lönnberg and V. Pohjola, *Acta Chem. Scand., Ser. A*, **30**, 669 (1976).

(41) $\beta_{lg}$ was not given in the paper but is calculated from Lönnberg and Pohjola's[40] data.

(42) C. K. Sauers, W. P. Jencks, and S. Groh, *J. Am. Chem. Soc.*, **97**, 5546 (1975).

(43) R. F. Pratt and T. C. Bruice, *J. Am. Chem. Soc.*, **92**, 5956 (1970).

(44) H. Al-Rawi and A. Williams, *J. Am. Chem. Soc.*, **99**, 2671 (1977).

(45) P. J. Thomas and C. J. M. Stirling, *J. Chem. Soc., Chem. Commun.*, 829 (1976).

(46) E.g., $k_{-1}$ step in eq 1.

(47) N. Gravitz and W. P. Jencks, *J. Am. Chem. Soc.*, **96**, 499 (1974).