Organometallics **2001,** *20,* 3383−3389

Physical Organic Chemistry of Transition Metal Carbene Complexes. 22.[1] Substituent Effects on the Reversible Cyclization of Fischer Carbene Complexes $(CO)_5W{=}C(SCH_2CH_2OH)C_6H_4Z$ in Aqueous Acetonitrile

Claude F. Bernasconi* and Mahammad Ali†

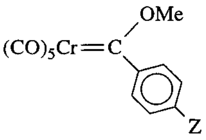
Department of Chemistry and Biochemistry, University of California,
Santa Cruz, California 95064

Received May 4, 2001

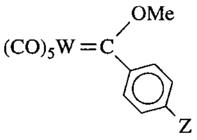
A kinetic study of the reversible cyclization of (((2-hydroxyethyl)thio)arylcarbene)-pentacarbonyltungsten(0) complexes, **2-SR(Z)**, in 50% MeCN−50% water (v/v) at 25 °C is reported. The results are consistent with Scheme 1, which shows a pathway in basic solution that involves rapid deprotonation of the OH group followed by rate-limiting cyclization and a pathway in acidic solution that involves direct nucleophilic attack by the OH group. Rate and equilibrium constants for the various elementary steps were determined as a function of the phenyl substituent. They were found to correlate well with the Hammett equation. The ρ values provide insights into (a) the reasons that the equilibrium constants are highly sensitive to substituent effects despite the fact that the negative charge of the adducts is strongly dispersed, (b) the mechanistic details of the cyclization pathway in acidic solution, and (c) the extra stabilizing effect of soft−soft interactions in previously studied adducts between a soft thiolate ion and the extra-soft carbene complex (**2-SR(Z)**).

Introduction

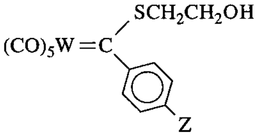
The study of substituent effects on rates and equilibria is one of the classic tools used by physical organic chemists to investigate structure−reactivity relationships and probing transition state structure. In our ongoing attempts at developing the physical organic chemistry of Fischer carbene complexes,[2] we have recently started to make use of this tool in reactions of some selected carbene complexes with nucleophiles. Specifically, we have investigated the effect of changing the phenyl substituent of carbene complexes such as **1-OMe(Z)**, **2-OMe(Z)**, and **2-SR(Z)** in the reactions of



1-OMe(Z)

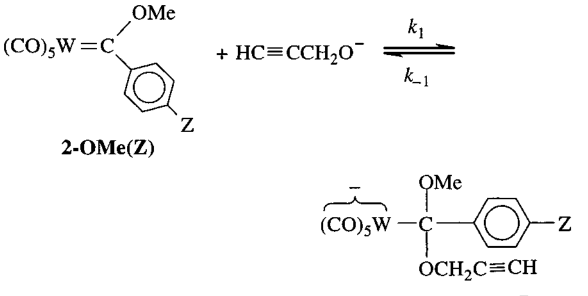


2-OMe(Z)



2-SR(Z)

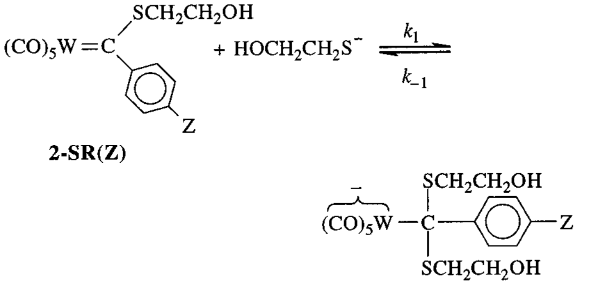
1-OMe(Z) and **2-OMe(Z)** with OH^-,[3] alkoxide ions,[3] and *n*-butylamine[4] and the reactions of **2-SR(Z)** with $HOCH_2CH_2S^-$ and $HOCH_2CH_2SH$.[5] In general, the data were found to obey the Hammett relationship very well but relatively large differences in the ρ values for what would appear to be similar reactions indicate that our understanding of electronic effects governing these processes is incomplete. For example, for the reversible addition of $HC{\equiv}CCH_2O^-$ to **2-OMe(Z)** in 50% MeCN−50% water (eq 1) $\rho(k_1) = 1.73$ and $\rho(K_1) = 3.11$.[3] This is



2-OMe(Z)

2-(OMe,OR)(Z) $^-$ (1)

in contrast with $\rho(k_1) = 0.78$ and $\rho(K_1) = 1.45$ for the reaction shown in eq 2 in the same solvent;[5] it indicates



2-SR(Z)

2-(SR)$_2$(Z)$^-$ (2)

---

† Current address: Department of Inorganic Chemistry, IACS, Jadavpur University, Calcutta 700 032, India.

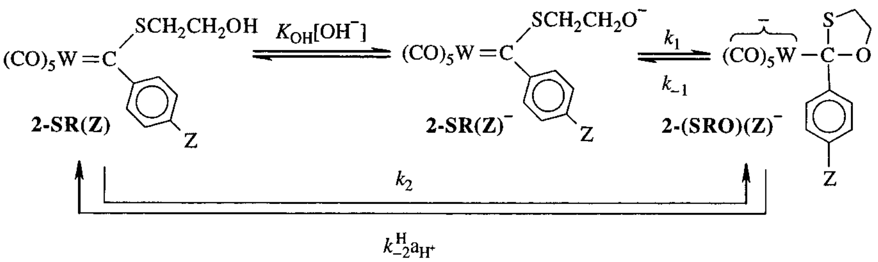
[1] Part 21: Bernasconi, C. F.; Perez, G. S. *J. Am. Chem. Soc.* **2000**, *122*, 12441.

[2] For a recent review, see: Bernasconi, C. F. *Chem. Soc. Rev.* **1997**, *26*, 299.

[3] Bernasconi, C. F.; García-Rio, L. *J. Am. Chem. Soc.* **2000**, *122*, 3821.

10.1021/om010364f CCC: $20.00
Publication on Web 06/30/2001

Scheme 1



that the rate and equilibrium constants of eq 2 are much less sensitive to substituent effects than those of eq 1.

One easily identifiable difference between the two reactions is that the first one involves an oxyanion nucleophile and alkoxycarbene complex while in the second there is a thiolate ion nucleophile adding to a (alkylthio)carbene complex. Some insight as to why these changes lead to such a strong reduction in the ρ values may come from the study of the reactions of (alkylthio)carbene complexes with an oxyanion nucleophile or of an alkoxycarbene complex with a thiolate ion nucleophile. A reaction of the former type is the cyclization process shown in Scheme 1; a recent study of this reaction with Z = H[6] has shown that clean kinetic data are more easily obtained for this process than for an *inter*molecular reaction of alkoxide ions with a (alkylthio)carbene complex. Herein we report results of a kinetic study of Scheme 1 with Z = F, Cl, CF$_3$, Me, MeO, Me$_2$N.

Results

General Features. The synthesis of the substituted carbene complexes **2-SR(Z)** was based on the reaction of NaSCH$_2$CH$_2$OH with the corresponding **2-OMe(Z)**. The general methodology for determination of rate and equilibrium constants was quite similar to that described before,[6] and hence, only a brief account is given here. All data were obtained in 50% MeCN–50% water (v/v) at 25 °C.

Two types of kinetic experiments were performed, which were mostly carried out in a stopped-flow spectrophotometer. In the first, **2-SR(Z)** was mixed with a KOH or triethylamine buffer solution. Under these conditions the reaction favors the cyclic adduct **2-(SRO)(Z)**$^-$. In the second experiment, **2-(SRO)(Z)**$^-$ was first generated in a dilute KOH solution and then immediately[7] mixed with HCl, chloroacetate, methoxyacetate, acetate, or *N*-methylmorpholine buffer solution. Under these conditions the reaction favors **2-SR(Z)**. No significant buffer catalysis by any of the buffers could be detected at total buffer concentrations of up to 0.05 or 0.1 M.

Rate–pH profiles, with k_{obsd} referring to the observed pseudo-first-order rate constant, are shown in Figure 1 for X = F, Cl, CF$_3$, and MeO, and the profile for Z = Me$_2$N is given in Figure 2; that for Z = H has been reported before,[6] while that for Z = Me has been omitted to reduce clutter in Figure 1. For all carbene complexes except **2-SR(Me$_2$N)** (see below) k_{obsd} is given by eq 3.

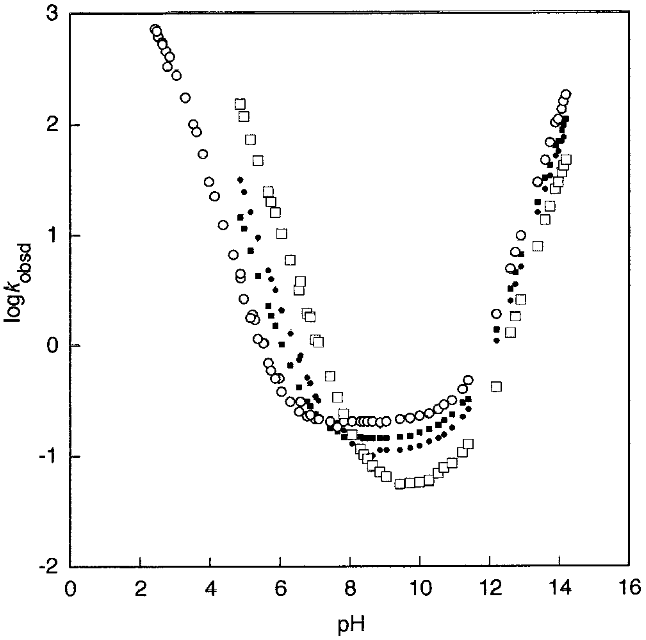


Figure 1. Rate–pH profiles for the cyclization of **2-SR(Z)** with Z = CF$_3$ (○), Cl (■), F (●), OMe (□). The profile for Z = Me is very similar to that for Z = MeO and has been omitted to reduce clutter in the figure.

$$k_{obsd} = K_{OH}k_1[OH^-] + k_{-1} + k_2 + k_{-2}a_{H^+} \qquad (3)$$

The evaluation of $K_{OH}k_1$ and k_{-2}^{H} from the pH-dependent portions of the rate–pH profiles was straightforward and yielded the results summarized in Table 1.

The k_2 and k_{-1} values were obtained by two independent methods. One, the "kinetic method," is based on the plateaus in Figure 1. As shown previously,[6] $k_2 \gg k_{-1}$ and, hence, the plateau can be approximated by k_2. In conjunction with k_{-2}^{H} one obtains $K_2 = k_2/k_{-2}^{H}$ for the equilibrium constant that refers to eq 4. From this one

$$\textbf{2-SR(Z)} \overset{K_2}{\rightleftharpoons} \textbf{2-(SRO)(Z)}^- + H^+ \qquad (4)$$

calculates $K_{OH}K_1 = K_2/K_w$, with K_w being the ionic product of the solvent;[8] thus, k_{-1} is obtained as $K_{OH}k_1/K_{OH}K_1$. In the second method, k_2 was determined as $k_2 = K_2k_{-2}^{H}$, with K_2 being measured spectrophotometrically (see Experimental Section); in this case $K_{OH}K_1 = K_2/K_w$ was calculated using the spectrophoto-

---

(4) Bernasconi, C. F.; Whitesell, C.; Johnson, R. A. *Tetrahedron* **2000**, *56*, 4917.

(5) Bernasconi, C. F.; Ali, M. *J. Am. Chem. Soc.* **1999**, *121*, 11384.

(6) Bernasconi, C. F.; Ali, M.; Lu, F. *J. Am. Chem. Soc.* **2000**, *122*, 1352.

(7) On standing, solutions of **2-(SRO)(Z)**$^-$ decomposed to form unidentified products with half-lives of several minutes to hours. For more details on this problem see ref 6.

(8) K_w (pK_w) = 6.46 × 10^{-16} (15.19) in 50% MeCN–50% water (v/v) at 25 °C and μ = 0.1 M (KCl).[9]

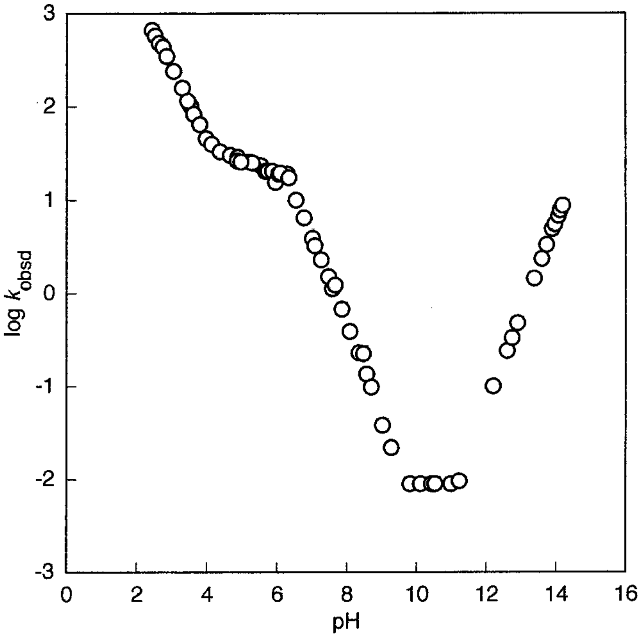


Figure 2. Rate–pH profile for the cyclization of **2-SR(Me$_2$N)**.

metric value of K_2. The various $K_{OH}K_1$, k_{-1}, k_2, and K_2 values obtained as described above are included in Table 1.

The rate–pH profile for **2-SR(Me$_2$N)** exhibits two additional breaks in the acidic region. They can be attributed to the protonation of the Me$_2$N group, which leads to Scheme 2; note that in this pH range the equilibrium favors the reactants and only the breakdown steps are shown in the scheme. The expression for k_{obsd} is given by eq 5. Between pH ~9.5 and ~6.2

$$k_{obsd} = (k_{-1} + k^{H}_{-2}\, a_{H^+})\frac{K^{NH}_{a}}{K^{NH}_{a} + a_{H^+}} + (k'_{-1} + k'^{H}_{-2})\frac{a_{H^+}}{K^{NH}_{a} + a_{H^+}} \qquad (5)$$

the situation is analogous to that for all the other **2-SR(Z)** species; i.e., k_{obsd} is given by eq 6 ($k^{H}_{-2}\, a_{H^+} \gg$

$$k_{obsd} = k^{H}_{-2}\, a_{H^+} \qquad (6)$$

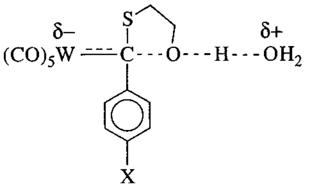
k_{-1}, $k^{H}_{-2}\, a_{H^+} \gg k'_{-1} + k'^{H}_{-2} a_{H^+}$, and $K^{NH}_{a} \gg a_{H^+}$). The break at pH ~6.2 corresponds to the pK^{NH}_{a} value of the N-protonated adduct **(2-SRO(Me$_2$NH$^+$)$^-$**; hence, at pH <(≪)6.2 eq 5 simplifies to eq 7, with the second term becoming dominant at pH <4.1.

$$k_{obsd} = k^{H}_{-2}\, K^{NH}_{a} + k'^{H}_{-2} a_{H^+} \qquad (7)$$

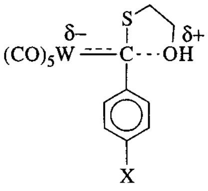
Discussion

Mechanism. In our earlier paper[6] several lines of evidence were presented in support of the mechanism shown in Scheme 1 and against some plausible alternatives. Hence, Scheme 1 will form the basis of the discussion to follow.

With respect to the k_2–k^{H}_{-2} pathway, there exists a potential ambiguity as to the nature of the transition state. One possibility is that the reaction is a one-step concerted process where water acts as a general base catalyst in the k_2 step and H_3O^+ as a general acid catalyst in the k^{H}_{-2} step, with the transition state **3**.

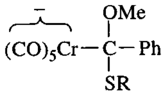


3

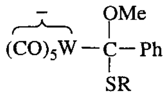


4

The failure to observe general acid–base catalysis by acetate, *N*-morpholine, and triethylamine buffers renders this mechanism unattractive, although one cannot rigorously exclude it. For the reactions of **1-OMe(H)** and **2-OMe(H)** with water,[10] and for the acid-catalyzed MeO$^-$ loss from **5** and **6**,[11] general acid–base catalysis by various buffers *was* observed and interpreted as an indication that a concerted mechanism is operative.

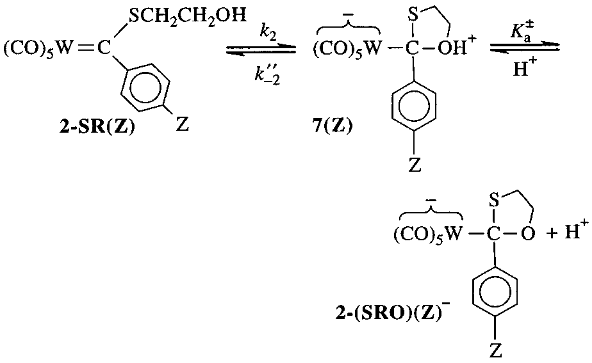


5



6

The second possibility is that the reaction is stepwise, as shown in eq 8, with the transition state **4**. For this



(8)

mechanism the observed k^{H}_{-2} is given by $k''_{-2}/K^{\pm}_{a}$ with $K^{\pm}_{a}$ being the acidity constant of the zwitterionic intermediate **7(Z)**. Apart from the fact that the absence of buffer catalysis is more easily accounted for by this mechanism than by the concerted one, the Hammett ρ values discussed below also support it. A potential problem with eq 8 would occur if the $pK^{\pm}_{a}$ value of **7(Z)** were below −5.3. Since $k''_{-2} = k^{H}_{-2}\, K^{\pm}_{a}$ and the highest measured k^{H}_{-2} value is $\sim 5 \times 10^{7}$ M^{-1} s^{-1} (Table 1, Z = Me$_2$N), $pK^{\pm}_{a} = -5.3$ would require $k''_{-2} \approx 10^{13}$ s^{-1}, which corresponds to the rate of a molecular vibration.[12] If this were the case, **7(Z)** could not exist as an intermediate and the concerted mechanism would be enforced.[12] However, it is unlikely that the $pK^{\pm}_{a}$ value

---

[9] Bernasconi, C. F.; Sun, W. *J. Am. Chem. Soc.* **1993**, *115*, 12526.

[10] Bernasconi, C. F.; Flores, F. X.; Kittredge, K. W. *J. Am. Chem. Soc.* **1997**, *119*, 2103.

[11] Bernasconi, C. F.; Kittredge, K. W.; Flores, F. X. *J. Am. Chem. Soc.* **1999**, *121*, 6630.

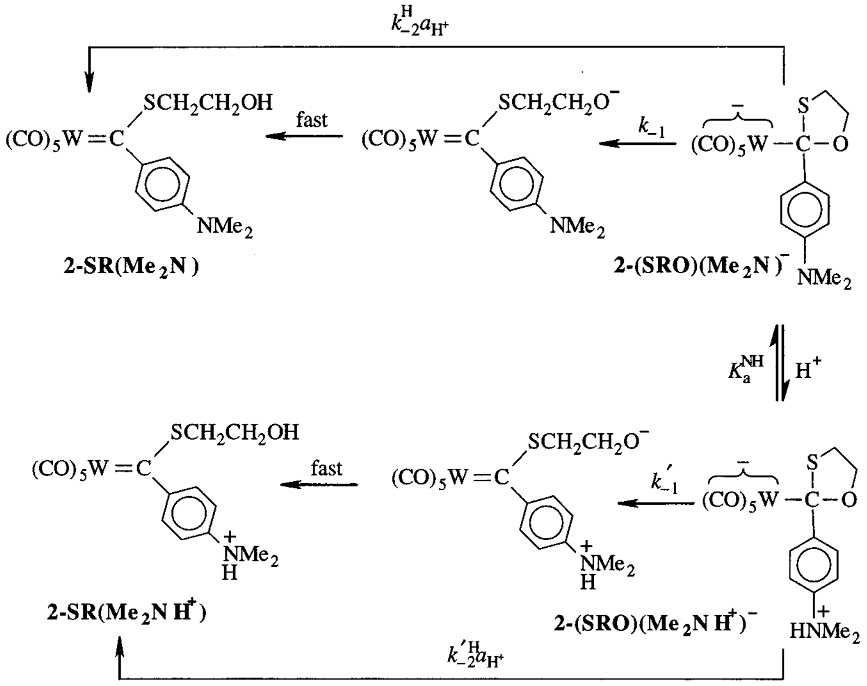
[12] (a) Jencks, W. P. *Acc. Chem. Res.* **1976**, *9*, 425. (b) Jencks, W. P. *Acc. Chem. Res.* **1980**, *13*, 161. (c) Jencks, W. P. *Chem. Soc. Rev.* **1981**, *10*, 345.

Table 1. Rate and Equilibrium Constants for the Reactions of Scheme 1 in 50% MeCN−50% Water (v/v) at 25 °C and μ = 0.1 M (KCl)

Z	$K_{OH}k_1$, M^{-1} s^{-1}	k_{-2}^{H}, M^{-1} s^{-1}	k_{-1},[a] s^{-1}	K_2,[a] M	$K_{OH}K_1$,[a] M^{-1}	k_2,[a] s^{-1}
CF_3	$(1.83 \pm 0.03) \times 10^{3}$	$(3.14 \pm 0.02) \times 10^{5}$	$(1.38 \pm 0.07) \times 10^{-6}$ *$(1.39 \pm 0.11) \times 10^{-6}$*	$(8.50) \pm 0.20) \times 10^{-7}$ *$(8.49 \pm 0.45) \times 10^{-7}$*	$(1.32 \pm 0.03) \times 10^{9}$ *$(1.31 \pm 0.07) \times 10^{9}$*	$(2.67 \pm 0.08) \times 10^{-1}$ *$(2.67 \pm 0.12) \times 10^{-1}$*
Cl	$(1.12 \pm 0.02) \times 10^{3}$	$(1.01 \pm 0.01) \times 10^{6}$	$(5.10 \pm 0.15) \times 10^{-6}$ *$(5.13 \pm 0.23) \times 10^{-6}$*	$(1.42 \pm 0.02) \times 10^{-7}$ *$(1.42 \pm 0.04) \times 10^{-7}$*	$(2.20 \pm 0.03) \times 10^{8}$ *$(2.20 \pm 0.06) \times 10^{8}$*	$(1.43 \pm 0.03) \times 10^{-1}$ *$(1.43 \pm 0.05) \times 10^{-1}$*
F	$(9.07 \pm 0.15) \times 10^{2}$	$(2.26 \pm 0.01) \times 10^{6}$	$(1.32 \pm 0.04) \times 10^{-5}$ *$(1.20 \pm 0.08) \times 10^{-5}$*	$(4.47 \pm 0.05) \times 10^{-8}$ *$(4.88 \pm 0.26) \times 10^{-8}$*	$(6.92 \pm 0.08) \times 10^{7}$ *$(7.55 \pm 0.40) \times 10^{7}$*	$(1.01 \pm 0.02) \times 10^{-1}$ *$(1.10 \pm 0.06) \times 10^{-1}$*
H[b]	$(4.26 \pm 0.11) \times 10^{2}$	$(4.74 \pm 0.08) \times 10^{6}$	$(1.55 \pm 0.11) \times 10^{-5}$ *$(1.84 \pm 0.12) \times 10^{-5}$*	$(1.77 \pm 0.08) \times 10^{-8}$ *$(1.50 \pm 0.06) \times 10^{-8}$*	$(2.74 \pm 0.12) \times 10^{7}$ *$(2.32 \pm 0.09) \times 10^{7}$*	$(8.40 \pm 0.52) \times 10^{-2}$ *$(7.17 \pm 0.41) \times 10^{-2}$*
Me	$(3.67 \pm 0.08) \times 10^{2}$	$(7.70 \pm 0.05) \times 10^{6}$	$(3.26\pm 0.10) \times 10^{-5}$ *$(3.81 \pm 0.30) \times 10^{-5}$*	$(7.27 \pm 0.06) \times 10^{-9}$ *$(6.22 \pm 0.35) \times 10^{-9}$*	$(1.13 \pm 0.01) \times 10^{7}$ *$(9.63 \pm 0.54) \times 10^{6}$*	$(5.60 \pm 0.10) \times 10^{-2}$ *$(4.79 \pm 0.29) \times 10^{-2}$*
MeO	$(4.76 \pm 0.06) \times 10^{2}$	$(1.07 \pm 0.10) \times 10^{7}$	$(5.88 \pm 0.13) \times 10^{-5}$ *$(6.69 \pm 0.47) \times 10^{-5}$*	$(5.23 \pm 0.05) \times 10^{-9}$ *$(4.60 \pm 0.27) \times 10^{-9}$*	$(8.10 \pm 0.08) \times 10^{6}$ *$(7.12 \pm 0.42) \times 10^{6}$*	$(5.60 \pm 0.56) \times 10^{-2}$ *$(4.92 \pm 0.74) \times 10^{-2}$*
Me_2N	$(8.90 \pm 0.10) \times 10^{1}$	$(4.43 \pm 0.07) \times 10^{7}$	$(2.83 \pm 0.30) \times 10^{-4}$ *$(1.78 \pm 0.53) \times 10^{-4}$*	$(2.03 \pm 0.20) \times 10^{-10}$ *$(2.49 \pm 0.72) \times 10^{-10}$*	$(3.14 \pm 0.31) \times 10^{5}$ *$(3.86 \pm 1.11) \times 10^{5}$*	$(9.00 \pm 1.04) \times 10^{-3}$ *$(1.43 \pm 0.26) \times 10^{-2}$*
Me_2N^+H		$(2.34 \pm 0.03) \times 10^{5}$				

[a] The first number given is from the kinetic method, and the second number given (in italics) is from the spectrophotometric method. [b] Reference 6.

Scheme 2



of **7-Z** is below −5.3. Protonated ethers have pK_a values ∼−3.5;[13] the potentially acidifying effect of the sulfur in **7-Z** is expected to be largely offset by the negative charge on the $(CO)_5W$ moiety.

Rate and Equilibrium Constants. All rate and equilibrium constants extracted from our kinetic and equilibrium measurements are summarized in Table 1. For k_{-1}, K_2, $K_{OH}K_1$, and k_2 there are two sets; the first set relies on rate measurements only, while the second set (numbers in italics in Table 1) is based on a combination of kinetic data (k_{-2}^{H}) with a spectrophotometric determination of K_2. The agreement between the two sets is excellent and lends confidence to our results. In view of the mostly lower standard deviations for the purely kinetic set and its slightly better correlation by the Hammett equation (see below), we will focus our discussion on these parameters; note, however, that none of the conclusions to be drawn depend on which set is chosen.

The K_{OH} values for the deprotonation of **2-SR(Z)** by OH^- could not be determined experimentally, because no appreciable ionization occurs within the pH range accessible to our measurements. However, a K_{OH} value of ∼7.7 M^{-1} was previously estimated for **2-SR(H)**[6] on the basis of the measured K_{OH} value of the oxygen analogue of **2-SR(H)**. Since the influence of Z on K_{OH} should be minimal due to the large distance between the phenyl ring and the OH group, we shall assume that K_{OH} = 7.7 M^{-1} for **2-SR(H)** is applicable to all **2-SR(Z)** species. The K_1 and k_1 values calculated on the basis of K_{OH} = 7.7 M^{-1} are summarized in Table 2 along with the "kinetic" k_{-1} values. Also included in Table 2 are the k_{-2}^{H} values and the "kinetic" k_2 and K_2 values.

Hammett plots are shown in Figures 3 and 4. The ρ values, including normalized ρ values obtained directly from plots (not shown) of log k_1 vs log K_1, log k_2 vs log

---

[13] Streitwieser, A.; Heathcock, C. H.; Kosower, E. M. *Introduction to Organic Chemistry*, 4th ed.; Macmillan: New York, 1992; Appendix IV.

Table 2. Rate and Equilibrium Constants for the Cyclization/Ring-Opening Steps and Hammett ρ Values

Z	σ	k_1 (s^{-1})	k_{-1} (s^{-1})	K_1	k_2 (s^{-1})	k_{-2}^{H} (M^{-1} s^{-1})	K_2 (M)
Me_2N^+H	0.74[a]					2.34×10^5	
CF_3	0.54	ca. 2.38×10^2	1.83×10^{-6}	1.72×10^8	2.67×10^{-1}	3.14×10^5	8.50×10^{-7}
Cl	0.23	ca. 1.45×10^2	5.10×10^{-6}	2.84×10^7	1.43×10^{-1}	1.01×10^6	1.42×10^{-7}
F	0.06	ca. 1.18×10^2	1.32×10^{-5}	8.93×10^6	1.01×10^{-1}	2.26×10^6	4.47×10^{-8}
H	0.00	ca. 5.53×10^1	1.55×10^{-5}	3.57×10^6	8.40×10^{-2}	4.74×10^6	1.77×10^{-8}
Me	−0.17	ca. 4.77×10^1	3.26×10^{-5}	1.46×10^6	5.60×10^{-2}	7.70×10^6	7.27×10^{-9}
MeO	−0.27	ca. 6.18×10^1	5.88×10^{-5}	1.05×10^6	5.60×10^{-2}	1.07×10^7	5.23×10^{-9}
Me_2N	−0.83	ca. 1.16×10^1	2.83×10^{-4}	4.10×10^4	9.00×10^{-3}	4.43×10^7	2.03×10^{-10}
ρ[b]		ca. 0.96 ± 0.11	−1.65 ± 0.09 *−1.67 ± 0.15*	ca. 2.67 ± 0.11 ca. *2.55 ± 0.19*	1.06 ± 0.07 *0.95 ± 0.08*	−1.59 ± 0.11	2.67 ± 0.11 *2.55 ± 0.19*

[a] Estimated on the basis of $\sigma = 0.60$ for $Z = NH_3^+$ and $\sigma = 0.82$ for $Z = NMe_3^+$.[17] [b] The first number given is from the kinetic method, and the second number given (in italics) is from the spectrophotometric method.

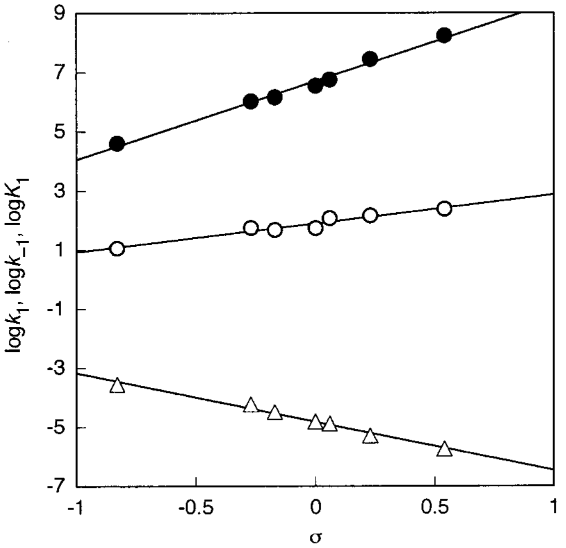


Figure 3. Hammett plots for k_1 (○), k_{-1} (△), and K_1 (●) (Scheme 1).

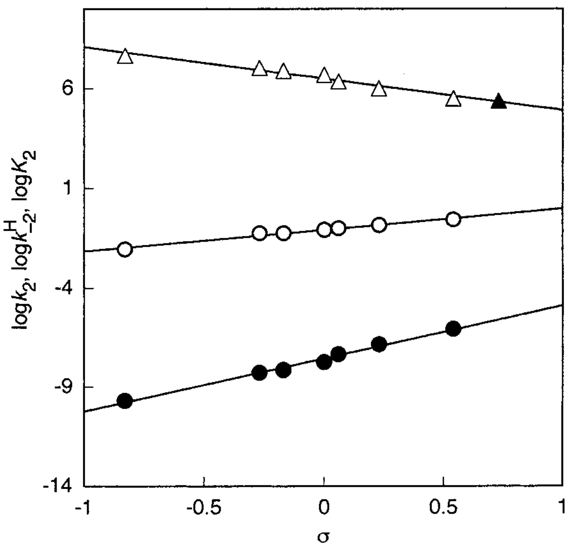


Figure 4. Hammett plots for k_2 (○), k_{-2}^{H} (△), and K_2 (●) (Scheme 1). The ▲ symbol refers to k_{-2}^{H} for **2-SR-(Me$_2$N$^+$H)**.

K_2, etc., are summarized in Table 3. Also included in Table 3 are ρ values for the reactions of eqs 1 and 2.

Reaction through the k_1-k_{-1} Pathway. The systems listed in Table 3 include a reaction of a thioalkyl complex with an oxyanion nucleophile (entry 1), a reaction of an (alkylthio)carbene complex with a thiolate ion nucleophile (entry 3), and a reaction of a methoxycarbene complex with an oxyanion (entry 2). With respect to the issue raised in the Introduction, i.e., the much lower $\rho(k_1)$ and $\rho(K_1)$ values for eq 2 (entry 3) compared to eq 1 (entry 2), a comparison with $\rho(K_1)$ for the cyclization reaction (entry 1) is revealing. It shows that it is the nature of the nucleophile rather than the identity of the group attached to the carbene carbon that dramatically changes the response to substituent effects. In other words, $\rho(K_1)$ is only modestly affected by the change from a methoxy (entry 2) to a thioalkyl group (entry 1) in the reactions with an oxyanion, but $\rho(K_1)$ is much smaller in the reaction of a thiolate ion (entry 3) than in the reaction of oxyanions with the same carbene complex.

These results may be understood in the context of soft−hard acid−base theory.[14] The Fischer carbene complexes can be regarded as soft electrophiles, especially the alkylthio complexes (**2-SR(Z)** and **2-SR$^-$(Z)**). Hence, the adducts **2-(SR)$_2$(Z)$^-$** formed by the reaction of **2-SR(Z)** with a thiolate ion nucleophile enjoy enhanced stability due to the symbiotic effect[14] of adding a soft nucleophile. This extra stability is reflected in the K_1 values for eq 2, e.g., $K_1 = 3.87 \times 10^5$ M^{-1} (Z = H),[5] which is significantly larger than $K_1 = 4.33 \times 10^3$ M^{-1} for the reaction of $HOCH_2CH_2S^-$ with **2-OMe(H)**.[11,15] The stabilization from the multiple soft−soft interactions apparently reduces the need for additional stabilization by the phenyl substituent, which translates into a reduced $\rho(K_1)$ value.

Before discussing the $\rho(k_1)$ and $\rho(k_{-1})$ values, a comment about the absolute magnitude of the $\rho(K_1)$ values is in order. In view of the strong stabilization of the adducts by the $(CO)_5M$ moiety which allows dispersion of the negative charge into the CO ligands, the $\rho(K_1)$ values for entries 1 and 2 seem unusually large,

---

[14] Pearson, R. G.; Songstad, J. *J. Am. Chem. Soc.* **1967**, *89*, 1827.

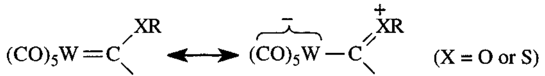
[15] There are additional factors that affect the relative K_1 values for the addition of $HOCH_2CH_2S^-$ to **2-SR(H)** (eq 2) and **2-OMe(H)**. One is the stronger reactant stabilizing π-donor effect of the MeO group compared to the $HOCH_2CH_2S$ group,[16] which reduces K_1 for **2-OMe(H)** relative to K_1 for **2-SR(H)**. This effect is counteracted by the greater steric crowding in the adduct derived from **2-SR(H)**,[18] which lowers K_1 for **2-SR(H)** relative to that for **2-OMe(H)**, and also by the larger electron-withdrawing inductive effect of the MeO group,[20] which enhances K_1 for **2-OMe(H)** relative to K_1 for **2-SR(H)**. In an earlier paper[5] the symbiotic effect of adding a soft nucleophile to the soft **2-SR(H)** was not taken into consideration, and hence it was concluded that the larger K_1 value for **2-SR(H)** is the result of the π-donor effect being the dominant factor. In light of our present results this conclusion is no longer tenable; i.e., the symbiotic effect is likely to contribute significantly to the enhanced K_1 value for **2-SR(H)** relative to **2-OMe(H)**. This implies that the steric factor is more important than previously[5] assumed, in agreement with its large effect on the intrinsic barrier of the reaction. [5.]

Table 3. Hammett ρ Values[a]

entry no.	reacn		$\rho(\vec{k})$	$\rho(\overleftarrow{k})$	$\rho(\vec{K})$	$\rho_n(\vec{k})$	$\rho_n(\overleftarrow{k})$
1	**2-SR(Z)**$^-$ $\underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}}$ **2-(SRO)(Z)**$^-$	(Scheme 1)	ca. 0.96	−1.65	ca. 2.67	0.36	−0.64
2	**2-OMe(Z)** + HC≡CCH$_2$O$^-$ $\underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}}$ **2-(OMe,OR)(Z)**$^-$	(eq 1)	1.73	−1.38	3.11	0.56	−0.44
3	**2-SR(Z)** + HOCH$_2$CH$_2$S$^-$ $\underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}}$ **2-(SR)$_2$(Z)**$^-$	(eq 2)	0.78	−0.67	1.45	0.54	−0.46
4	**2-SR(Z)** $\underset{k^{H}_{-2}}{\overset{k_2}{\rightleftharpoons}}$ **2-(SRO)(Z)**$^-$ + H$^+$	(Scheme 1)	1.06	−1.59	2.67	0.39	−0.61

[a] $\vec{k} = k_1$ or k_2; $\overleftarrow{k} = k_{-1}$ or k^{H}_{-2}; $\vec{K} = K_1$ or K_2. All ρ values were determined in 50% MeCN−50% water, at 25 °C.

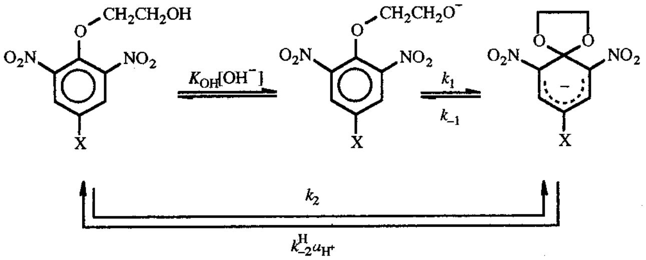
i.e., about as large as $\rho(K_1) = 2.7$ for OH$^-$ addition to substituted benzaldehydes,[21] even though there is no charge dispersion in the aldehyde adducts. This comparison suggests that the large $\rho(K_1)$ values for the carbene complexes reflect not only the stabilization of the anionic charge of the adducts by electron-withdrawing substituents but also a significant *de*stabilization of the carbene complex itself. This destabilization is related to the strong π-donor effect of the RX groups (**8b**). Since the negative charge in **8b** is more dispersed than its positive charge, the net effect of an electron-withdrawing substituent is a destabilization of **8b**. The still larger $\rho(K_1)$ value for the reaction of **2-OMe(Z)** with HC≡CCH$_2$O$^-$ (3.11) than for the cyclization of **2-SR(Z)**$^-$ (2.67) is consistent with the stronger π-donor effect of RO compared to RS.[16] Similar conclusions regarding the destabilization of **8b** by electron-withdrawing substituents were reached on the basis of a recent study of the rates of reactions of amines with **1-OMe** and **2-OMe**.[22]



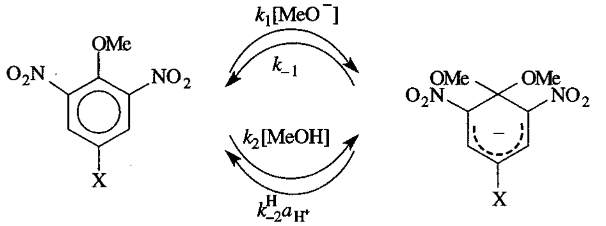
8a **8b**

Turning to $\rho(k_1)$ and $\rho(k_{-1})$, we note that the *normalized* values for entries 2 and 3 are very similar, because $\rho(k_1)$ for entry 3 is reduced by a factor similar to that for $\rho(K_1)$ relative to entry 2. This suggests that bond formation at the transition state has made similar progress in the two reactions. This is in contrast with entry 1, where $\rho_n(k_1)$ is much smaller and $\rho_n(k_{-1})$ much larger than for the other reactions. Since entry 1 is an *intra*molecular process, one would not necessarily expect equal progress of bond formation at the cyclic transition state as in *inter*molecular reactions. We therefore refrain from offering an explanation. Nevertheless, we note that the intramolecular reaction is thermodynamically much more favorable ($K_1 = 3.57 \times 10^6$ for **2-SR(H)**$^-$) than the reaction of **2-OMe(H)** with HC≡CCH$_2$O$^-$ ($K_1 = 3.40 \times 10^2$ M^{-1}),[3] and hence a transition state with less bond formation is consistent with the Hammond[23]−Leffler[24] postulate.

Scheme 3



Scheme 4



Reaction through the k_2−k^{H}_{-2} Pathway. In comparing the substituent dependence of the k_2−k^{H}_{-2} pathway with that of the k_1−k_{-1} pathway, we note that the $\rho(k_2)$ and $\rho(k^{H}_{-2})$ values are quite similar to the corresponding values for the k_1−k_{-1} pathway (Table 3). Since $\rho(K_2) = \rho(K_1)$, this means that we also have $\rho_n(k_2) \approx \rho_n(k_1)$ and $\rho_n(k^{H}_{-2}) \approx \rho_n(k_{-1})$, suggesting that the transition states of both pathways are about equally advanced. This seems surprising because, on the basis of the Hammond[23]−Leffler[24] postulate, the reaction with the weaker nucleophile (OH group) should have a more advanced transition state (larger $\rho_n(k_2)$) than the reaction with the much stronger oxyanion nucleophile. Examples of reactions that are similar to the ones discussed here and where this expectation, i.e., $\rho_n(k_2) > (\gg)\ \rho_n(k_1)$, *is* met are shown in Schemes 3 and 4. Both systems were studied in water at 25 °C and yielded the following normalized ρ values: Scheme 3,[25] $\rho_n(k_1) = 0.58$, $\rho_n(k_2) = 0.70$; Scheme 4,[26] $\rho_n(k_1) = 0.47$, $\rho_n(k_2) = 0.63$. In both systems $\rho_n(k_2)$ is significantly larger than $\rho_n(k_1)$, consistent with the Hammond−Leffler postulate.

The key to the understanding of the differences between the reactions of Scheme 1 and those of Schemes

---

(16) $\sigma_R = -0.43$ and -0.15 for MeO and MeS, respectively.[17]

(17) Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165.

(18) Taft's[19] steric substituent constants E_S are −0.55 for MeO and −1.07 for MeS, respectively.

(19) Unger, S. H.; Hansch, C. *Prog. Phys. Org. Chem.* **1976**, *12*, 9.

(20) $\sigma_F = 0.30$ and 0.20 for MeO and MeS, respectively.[17]

(21) (a) Bover, W. J.; Zuman, P. *J. Chem. Soc., Perkin Trans. 2* **1973**, 786. (b) Bover, W. J.; Zuman, P. *J. Am. Chem. Soc.* **1973**, *95*, 2531.

(22) The $\rho(k_1)$ values for nucleophilic attack of *n*-butylamine on **1-OMe** and **2-OMe** are 2.25 and 1.79, respectively:[4] i.e., similar to the $\rho(k_1)$ values for the reactions with anionic nucleophiles. If only substituent effects on the transition state were important, much smaller (possibly negative) $\rho(k_1)$ values would be expected for the amine reaction because, besides the partial negative charge on the (CO)$_5$M moiety, there is a partial *positive* charge on the nitrogen.

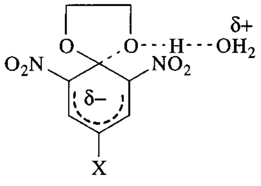
(23) Hammond, G. S. *J. Am. Chem. Soc.* **1955**, *77*, 334.

(24) Leffler, J. F.; Grunwald, E. *Rates and Equilibria of Organic Reactions*; Wiley: New York, 1963; p 128.

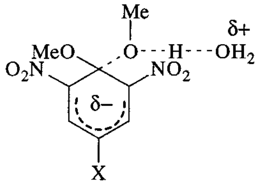
(25) Bernasconi, C. F.; Howard, K. A. *J. Am. Chem. Soc.* **1983**, *105*, 4690.

(26) Bernasconi, C. F.; Gandler, J. R. *J. Am. Chem. Soc.* **1978**, *100*, 8117.

3 and 4 is that the latter show significant buffer catalysis while the former does not. This implies that the $k_2 - k_{-2}^{H}$ pathway in Schemes 3 and 4 involves general base catalysis by water/general acid catalysis by H_3O^+, suggesting transition states such as **9** and **10**,



9



10

while for the $k_2 - k_{-2}^{H}$ pathway in Scheme 1 it was concluded above that the transition state is best represented by **4**. The important difference between **4** and **9** or **10** is that in **4** the partial positive charge is on the attacking oxygen, i.e., much closer to the X substituent than in **9** or **10**. Hence, the rate-enhancing effect of electron-withdrawing substituents—due to stabilization of the negative charge at the transition state combined with the destabilization of the reactant state (see above)—is partially offset by the destabilization of the positive charge on the oxygen at the transition state. This results in a reduction in $\rho_n(k_2)$ and is probably the principal reason $\rho_n(k_2)$ is not substantially larger than $\rho_n(k_1)$.

Conclusions

(1) The rate−pH profiles are consistent with Scheme 1. As to the details of the $k_2 - k_{-2}^{H}$ pathway, the absence of buffer catalysis and the fact that $\rho_n(k_2)$ does not substantially exceed $\rho_n(k_1)$ are more easily accounted for by the stepwise process of eq 8, with transition state **4**, than by a concerted reaction with transition state **3**.

(2) The $\rho(K_1)$ values for the reactions summarized in Table 3 show that K_1 for addition of the soft $HOCH_2CH_2S^-$ nucleophile to the soft **2-SR(Z)** is much less sensitive to substituent effects than K_1 for addition of the hard oxyanion nucleophiles to the soft **2-SR(Z)** or to the somewhat less soft **2-OMe(Z)**. These results indicate that the extra stabilization of the **2-(SR)$_2$(Z)$^-$** adduct by multiple soft−soft interactions reduces the need for additional stabilization by the phenyl substituents.

(3) The fact that $\rho(K_1)$ for the cyclization as well as for the reaction of **2-OMe(Z)** with $H{\equiv}CCH_2O^-$ is about as large as $\rho(K_1)$ for OH^- addition to substituted benzaldehydes indicates that a major source of the substituent effect on K_1 is the destabilization of the carbene complex by electron-withdrawing substituents due to the partial positive charge on X (**8b**).

(4) Despite the much weaker substituent effect on K_1 for the reaction of $HOCH_2CH_2S^-$ with **2-SR(Z)** than for the reaction of $HC{\equiv}CCH_2O^-$ with **2-OMe(Z)**, the *normalized* ρ values are about the same, indicating that bond formation at the transition state has made similar progress in both reactions. On the other hand, the normalized ρ values for the cyclization reaction are significantly lower than for the other oxyanion reaction (eq 2); this is consistent with the Hammond−Leffler postulate, although the fact that the comparison is between an intramolecular and intermolecular reaction may render this a fortuitous result.

Experimental Section

Materials. The carbene complexes **2-SR(Z)** were available from a previous study.[5] Triethylamine and *N*-methylmorpholine were refluxed and distilled over Na/CaH_2 prior to use. Reagent grade acetic acid was used without further purification. Acetonitrile was purchased from Fisher Scientific and used as received. KOH and HCl solutions were prepared using "Dilut it" from Baker Analytical. Water was taken from a Milli-Q purification system.

Instrumentation. UV−vis spectra were obtained on a Hewlett-Packard 8452A diode array spectrophotometer. Kinetic experiments were performed on an Applied Photophysics DX.17MV stopped-flow apparatus (fast reactions) or a Hewlett-Packard 8452A spectrophotometer (slow reactions).

Kinetic Measurements. All kinetic runs were conducted under pseudo-first-order conditions ensured by a large excess of KOH, HCl, or buffer over the substrate. The reactions were monitored at or near λ_{max} of the neutral carbene complex (**2-SR(H)**, 452 nm; **2-SR(F)**, **2-SR(Cl)**, **2-SR(CF$_3$)**, and **2-SR(Me)**, 454 nm; **2-SR(MeO)**, 458 nm; **2-SR(Me$_2$N)**, 504 nm); at these wavelengths there is no significant absorption by the cyclic adducts.[6]

Equilibrium Measurements. The pseudo-acidity constants (K_2 in eq 4) were determined spectrophotometrically. The K_2 values were obtained by a nonlinear least-squares fit of A vs a_{H^+} according to eq 9 with A being the absorbance in

$$A = \frac{A_{max}a_{H^+} + A_{min}K_2}{K_2 + a_{H^+}} \tag{9}$$

N-methylmorpholine buffers, A_{max} the absorbance in 0.1 M HCl (100% **2-SR(Z)**), and A_{min} the absorbance in 0.1 KOH (100% **2-(SRO)(Z)$^-$**). A was measured after equilibrium between **2-SR(Z)** and **2-(SRO)(Z)$^-$** was complete but before significant decomposition of **2-(SRO)(Z)$^-$** could occur. Since some small degree of decomposition could not be avoided, A was determined by extrapolation to "zero time."

pH Measurements. The pH in 50% MeCN−50% water was determined according to eq 10[27] with pH_{meas} referring to the reading of the pH meter calibrated with standard buffers. All

$$pH = pH_{measd} + 0.18 \tag{10}$$

pH measurements were done on an Orion 611 pH meter equipped with a glass electrode and a "Sure Flow" (Corning) reference electrode. The pH of reaction solutions for stopped-flow experiments was adjusted in mock-mixing experiments that mimicked the stopped-flow runs.

Acknowledgment. This research has been supported by Grants No. CHE-9734822 and CHE-0098553 from the National Science Foundation.

OM010364F

---

[27] Allen, A. D.; Tidwell, T. T. *J. Am. Chem. Soc.* **1987**, *109*, 2774.