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Kinetics of the Reactions of [*p*-Nitrophenoxy(phenyl)carbene]pentacarbonylchromium(0) with Aryloxide Ions, Hydroxide Ion, and Water in Aqueous Acetonitrile. Concerted or Stepwise?[†]

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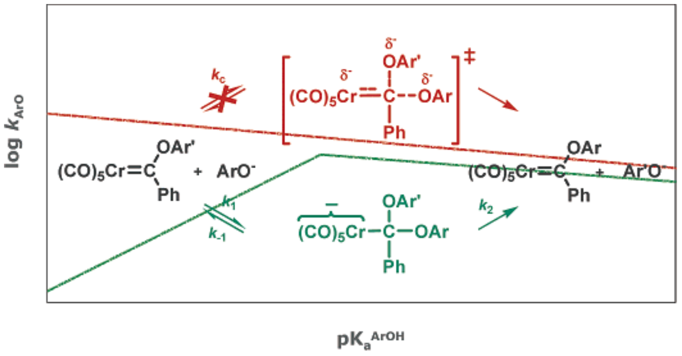

The main question addressed in this paper is whether the nucleophilic substitution of the *p*-nitrophenoxy group in $(CO)_5Cr{=}C(OC_6H_4\text{-}4\text{-}NO_2)Ph$ (**1-NO₂**) by a series of substituted phenoxide ions is concerted or stepwise. Rate constants, k_{ArO}, for these substitution reactions were determined in 50% MeCN−50% water (v/v) at 25 °C. A Brønsted plot of log k_{ArO} versus pK_a^{ArOH} is consistent with a stepwise mechanism. This contrasts with reactions of aryl oxide ions with *p*-nitrophenyl acetate and with similar acyl transfers which are concerted. The reason for the contrast is that the tetrahedral intermediates formed in the reactions of **1-NO₂** are much more stable than those in acyl transfers and the intrinsic barriers to their decomposition are higher than for the ester reactions. The points on the Brønsted plots for which $pK_a^{ArOH} \geq pK_a^{PNP}$ define a straight line with $\beta_{nuc} = -0.39$, suggesting that bond formation has made very little progress at the transition state and that partial desolvation of the nucleophile is part of the activation process. The hydrolysis of **1-NO₂** and of the unsubstituted analogue (**1-H**) has also been studied over a wide pH range, providing rate constants for nucleophilic attack by hydroxide ion (k_{OH}), by water (k_{H_2O}), and by general base-catalyzed reaction with water (k_B). Furthermore, k_{H_2O} values were obtained for the hydrolysis of $(CO)_5Cr{=}C(OC_6H_4X)Ph$ (**1-X**) as a byproduct of the reactions of **1-NO₂** with aryl oxide ions. Structure−reactivity relationships for these reactions are discussed in terms of inductive, π-donor, and steric effects.

Introduction

A major characteristic of transition-metal carbene complexes of the Fischer type is the electrophilic nature of the carbene carbon.[1] Hence, Fischer carbenes undergo facile addition and/or substitutions by a variety of nucleophiles. Such reactions have been well documented with OH^-,[2] water,[2] methoxide ion,[3] amines,[3e,4] thiolate ions,[5] carbanions,[6] and other nucleophiles.[7] There is ample evidence that these reactions are stepwise

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[†] Physical Organic Chemistry of Transition Metal Carbene Complexes. 34. Part 33: Bernasconi, C. F.; Bhattacharya, S.; Wenzel, P. J.; Olmstead, M. M. *Organometallics* **2006**, *25*, 4322.

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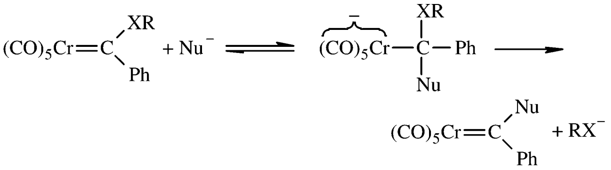
10.1021/jo062138r CCC: $37.00

involving tetrahedral intermediates, analogous to those that occur for the reactions of carboxylic esters.[9,10] This is shown in the generalized eq 1 for a phenyl pentacarbonyl chromium carbene reacting with an anionic nucleophile; RX^- is typically an alkoxide, aryloxide or alkanethiolate ion. Some of the most compelling evidence for the stepwise nature of the reaction has come from the study of systems where the intermediate was directly detectable,[3,5b,d] including cases where the reaction is intramolecular.[11]


(1)

Regarding nucleophilic substitutions on esters and other acyl compounds, not all of them are stepwise. As first shown by Williams et al.,[12] the reaction of *p*-nitrophenyl acetate with aryl oxide ions is most likely a concerted one-step process. This conclusion was based on the fact that the Brønsted plot for a series of aryl oxide ions spanning a wide pK_a range, including pK_a values higher as well as lower than the pK_a of the *p*-nitrophenoxide ion (PNP) leaving group was linear, i.e., did not have a break. If the reaction were stepwise as shown in eq 2, the second-order rate constant derived from the steady-state approximation would be given by eq 3. If one makes the

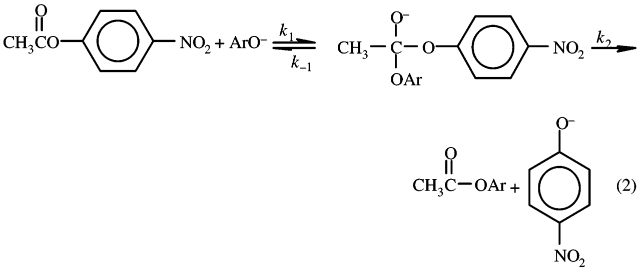
$$k_{ArO} = \frac{k_1 k_2}{k_{-1} + k_2} \tag{3}$$

reasonable assumption that the leaving group ability of aryl oxide ions is linearly correlated with their basicity, the relationship $k_{-1} > (\gg)\ k_2$ should hold for ArO^- less basic than *p*-nitrophenoxide ion which reduces eq 3 to eq 4, while for ArO^- more basic than *p*-nitrophenoxide ion one expects $k_{-1} < (\ll)$

$$k_{ArO} = K_1 k_2 \tag{4}$$

k_2, and hence, eq 3 becomes eq 5. This would result in a Brønsted plot for k_{ArO} that has an initial slope (when $pK_a^{ArOH} < pK_a^{PNP}$) that is relatively large, a break at $pK_a^{ArOH} \approx pK_a^{PNP}$, and a much more shallow slope for $pK_a^{ArOH} > pK_a^{PNP}$.

$$k_{ArO} = k_1 \tag{5}$$


(2)

Subsequent studies by Williams et al.[13] and others[14] have confirmed that reactions of esters with good leaving groups such as aryl oxide ions undergo nucleophilic substitutions by a concerted mechanism that bypasses the tetrahedral intermediate.[15]

In view of their similarities with esters, one needs to ask whether Fischer carbenes with particularly good leaving groups might also undergo nucleophilic substitutions by a concerted mechanism. We have therefore undertaken a kinetic study of the reaction of [*p*-nitrophenoxy(phenyl)carbene]pentacarbonylchromium(0), **1-NO$_2$**, with a series of aryl oxide ions (X = 4-CH_3, 4-OMe, H, 4-Cl, 4-Br, 3-Cl, 3-CF_3, 4-CF_3, 3-CN, 4-CN, 3,5-$(CF_3)_2$, 4-CHO, 2,4,5-Cl_3); Scheme 1 shows the two mechanistic possibilities (upper pathway: stepwise; lower pathway: concerted).

Our results indicate that, in contrast to the corresponding reaction with *p*-nitrophenyl acetate, the reaction with **1-NO$_2$** still appears to be stepwise. However, the reaction showed some unusual behavior in that for most aryl oxide ions the nucleophilic reactivity *decreases* with increasing basicity. We also report a detailed kinetic study of the hydrolysis of **1-NO$_2$** and **1-H** and a limited study of the hydrolysis of **1-X** (for X, see above).

Results

General Features. The reactions were conducted in 50% MeCN−50% water (v/v) at 25 °C and an ionic strength of 0.1

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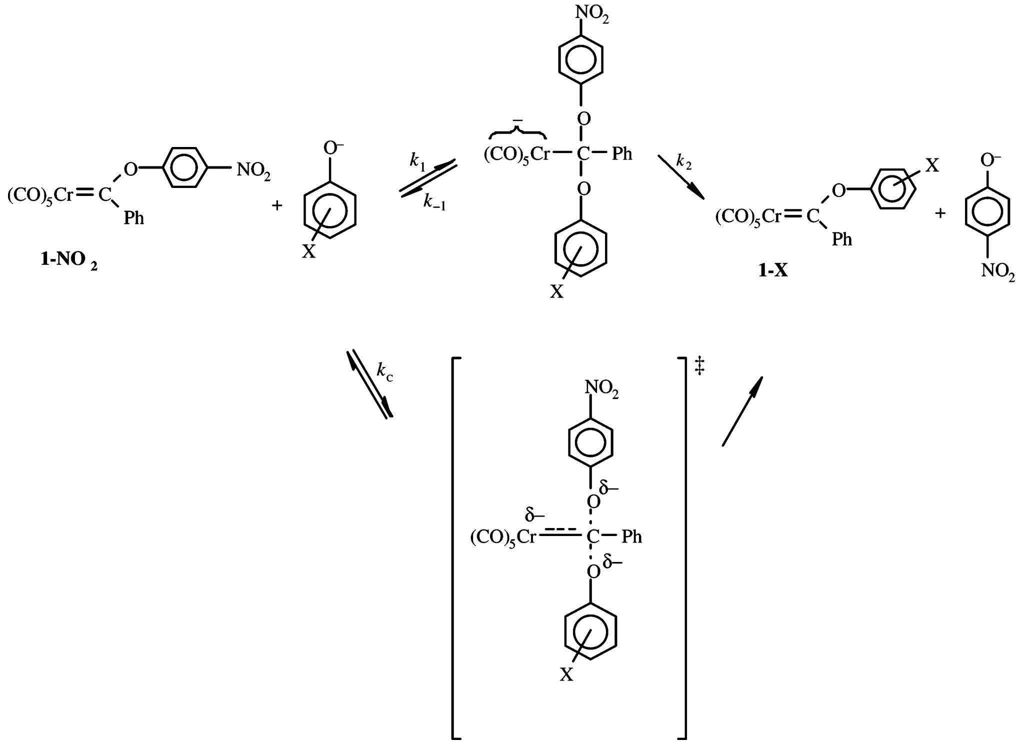
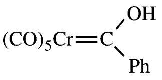
(15) Even though this view has been challenged,[16] it has been upheld in subsequent studies.[14]

SCHEME 1



M maintained with KCl. All kinetic runs were performed under pseudo-first-order conditions with the carbene complexes as the minor component. Most rate measurements were carried out in a stopped-flow spectrophotometer except for the hydrolysis of **1-H** at pH ≤ 11.20, which was slow enough to be monitored in a conventional spectrophotometer.

Hydrolysis of 1-NO$_2$ and 1-H. The hydrolysis of **1-NO$_2$** showed strictly first-order kinetics over the entire pH range. The same was true for the hydrolysis of **1-H** except for the runs in HCl solution where biphasic kinetics was observed. In these cases, the fast phase refers to the hydrolysis while the slow phase represents the decomposition of the hydrolysis product **2H**; this latter process was not investigated further.



2H

Rate−pH profiles for the hydrolysis of **1-NO$_2$** and **1-H** are shown in Figure 1. For **1-NO$_2$**, rates were determined in KOH and HCl solutions and in triethylamine, *N*-morpholine, and acetate buffers. In KOH solutions, rates were measured at 10 concentrations ranging from 0.001 to 0.1 M by monitoring the increase in absorbance at 400 nm due to formation of *p*-nitrophenoxide ion. A plot of the observed pseudo-first-order rate constant versus [KOH] was linear (Figure S1 in the Supporting Information)[17] with a slope of 15.9 ± 0.2 M^{-1} s^{-1} corresponding to k_{OH} for the reaction with OH^- and an intercept of 0.316 ± 0.009 s^{-1} corresponding to k_{H_2O} for the water reaction.

In HCl solutions, rates were measured at six concentrations ranging from 0.001 to 0.01 M by monitoring the decrease in absorbance at 420 nm due to loss of **1-NO$_2$**. The k_{obsd} values were independent of [HCl] and yielded an average value of 0.291 ± 0.006 s^{-1}, which corresponds to k_{H_2O}.

In the triethylamine buffer, rates were determined at pH 11.20, 10.90, 10.20, 9.96, 9.55, and 9.22, in the *N*-methylmorpholine buffers at pH 8.46, 7.99, 7.50, and 7.06 and in the acetate buffers at pH 6.49, 5.91, 5.52, and 5.03. The reactions in the triethylamine buffers were monitored at 400 nm (formation of the *p*-nitrophenoxide ion), the ones in the other buffers at 420 nm (loss of **1-NO$_2$**). For some selected pH values, the reaction was tested for general base catalysis. Weak catalysis was observed with triethylamine tested at pH 11.20, 10.90, and 10.20. Plots of k_{obsd} versus [B] were linear with slopes, k_B, averaging 0.75 ± 0.15 M^{-1} s^{-1}. With *N*-methylmorpholine a k_B value of 0.43 ± 0.02 M^{-1} s^{-1} was determined at pH 7.50. The points on the rate−pH profile that refer to runs in triethylamine and *N*-morpholine buffers represent values that are extrapolated to zero buffer concentration. No catalysis could be detected in acetate buffers.

The data for the hydrolysis of **1-H** were obtained in a similar way as for **1-NO$_2$** except that all runs were monitored at 420 nm, since the phenoxide ion has no convenient chromophore. The plot of k_{obsd} versus [KOH] (Figure S2, Supporting Information)[17] yielded $k_{OH} = 2.39 \pm 0.03$ M^{-1} s^{-1} and $k_{H_2O} = (2.48 \pm 0.18) \times 10^{-2}$ s^{-1}, while the results with HCl solutions afforded an average $k_{H_2O} = (1.76 \pm 0.12) \times 10^{-2}$ s^{-1}. General base catalysis was again observed with triethylamine ($k_B = (0.429 \pm 0.022)$ M^{-1} s^{-1}) but no catalysis by acetate ion could be detected.

Reaction of 1-NO$_2$ with Aryl Oxide Ions. The reactions of **1-NO$_2$** with the aryloxide ions were carried out at pH values that were close to the pK_a of the respective phenol. They showed the presence of two kinetic processes. The faster of the two

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[17] See the Supporting Information paragraph at the end of this paper.

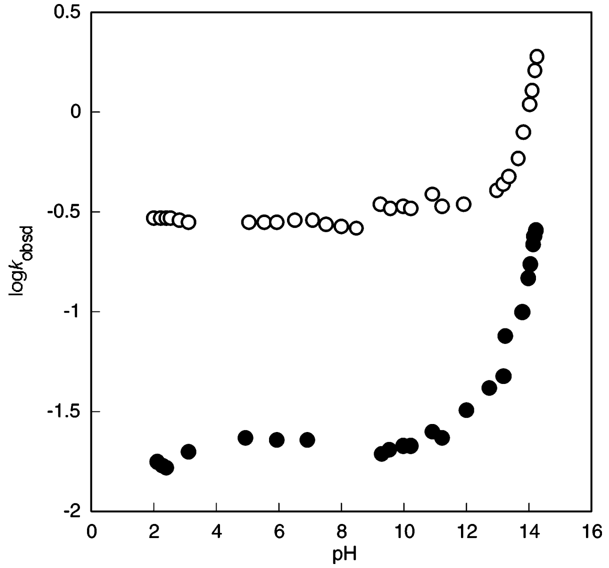


FIGURE 1. Rate−pH profile for the hydrolysis of **1-NO$_2$** (○) and **1-H** (●).

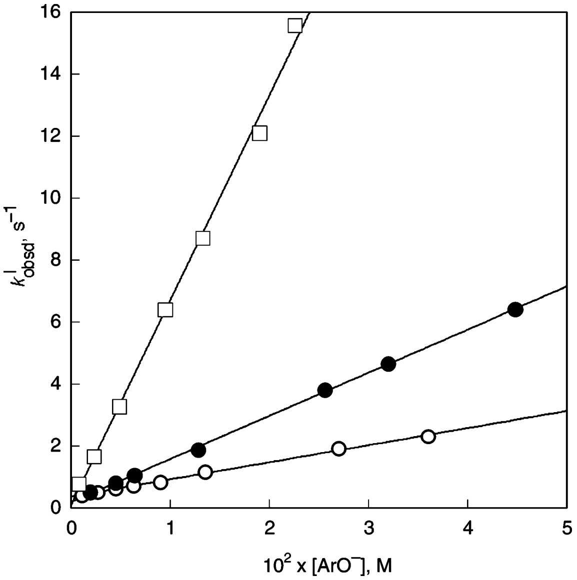


FIGURE 2. Reaction of **1-NO$_2$** with aryl oxide ions: ○, X = 4-Me; ●, X = 4-Br; □, X = (CF$_3$)$_2$.

manifested itself by an increase in absorbance at 400 nm resulting from the release of *p*-nitrophenoxide ion while the slow process led to a decrease of absorbance at the same wavelength. The observed pseudo-first-order rate constants of the first process were linearly dependent on the aryloxide ion concentration and are given by eq 6 where k_h refers to hydrolysis. Figure 2 shows three representative plots while Figures S3−S5[17] summarize the data for the other aryloxide ions. The absorbance changes and the dependence on [ArO$^-$] indicate that this process refers to the conversion of **1-NO$_2$** to **1-X**.

$$k^{I}_{obsd} = k_{ArO}[ArO^-] + k_h \qquad (6)$$

The rate constant for the second, slower process (k^{II}_{obsd}) did not depend on aryl oxide ion concentration. It is attributed to the hydrolysis of **1-X** which is the product of the fast process. This was confirmed in the case of X = H by comparing k^{II}_{obsd} to k_{obsd} for the hydrolysis of **1-H** measured directly as described in the previous section: $k^{II}_{obsd} = (2.50 \pm 0.28) \times 10^{-2}$ s^{-1} at pH 11.59 versus $k_{obsd} = 2.42 \times 10^{-2}$ s^{-1} extrapolated from the rate−pH profile in Figure 1 to pH 11.59.

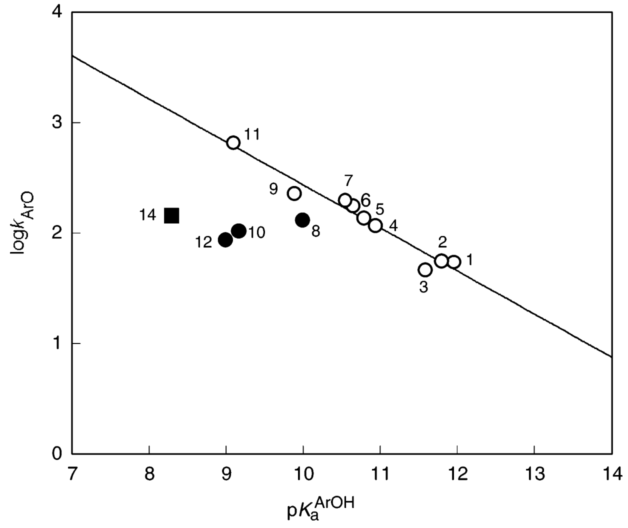


FIGURE 3. Brønsted plot for the reaction of **1-NO$_2$** with aryl oxide ions. The numbers refer to those in Table 1.

TABLE 1. Rate Constants, k_{ArO}, for the Reaction of 1-NO$_2$ with ArO$^-$ and Rate Constants, k^{II}_{obsd}, for the Hydrolysis of 1-X in 50% MeCN−50% Water (v/v) at 25 °C^a

no.	X	$pK_a^{ArOH\,b}$	$\sigma_X{}^c$	k_{ArO} (M^{-1} s^{-1})	$10^2 \times k^{II}_{obsd}{}^{d,e}$ (s^{-1})
1	4-CH$_3$	11.95	−0.17	55.0 ± 1.1	1.39
2	4-OCH$_3$	11.79	−0.27	56.9 ± 0.9	1.97
3	H	11.58	0.00	45.1 ± 0.8	2.50
4	4-Cl	10.93	0.23	117 ± 8	6.24
5	4-Br	10.78	0.23	139 ± 1	5.56
6	3-Cl	10.64	0.37	176 ± 2	6.66
7	3-CF$_3$	10.54	0.43	199 ± 3	8.79
8	4-CF$_3$	9.99	0.54	133 ± 4	11.0
9	3-CN	9.88	0.56	231 ± 6	17.6
10	4-CN	9.16	0.66	107 ± 4	20.4
11	3,5-(CF$_3$)$_2$	9.09	0.86	660 ± 18	41.0
12	CHO	8.99	0.42	86.8 ± 1	14.4
13	4-NO$_2$	8.30	0.78	−	34.2
14	2,4,5-Cl$_3$	8.29		144 ± 3	29.9

[a] μ = 0.1 M (KCl). [b] In 50% MeCN−50% water. [c] Values taken from Reference 28. [d] k^{II}_{obsd} refers to the hydrolysis of **1-X**; $k^{II}_{obsd} = k_{H_2O}$; see text. [e] Estimated error ± 5% or less.

Attempts at measuring rates of the reaction of **1-NO$_2$** with 2,3,5-trichlorophenoxide ion (pK_a^{ArOH} = 8.07) and pentafluorophenoxide ion (pK_a^{ArOH}= 6.46) were unsuccessful because hydrolysis of **1-NO$_2$** was faster than the reaction with the aryl oxide ions.

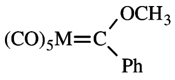
Discussion

Reaction of 1-NO$_2$ with Aryl Oxide Ions. A. Mechanism. The rate constants, k_{ArO}, for the reaction of **1-NO$_2$** with ArO$^-$ are summarized in Table 1. The table also includes the rate constants, k^{II}_{obsd}, for the hydrolysis of the corresponding products, **1-X**, to be discussed later.

A Brønsted plot of $\log k_{ArO}$ versus pK_a^{ArOH} is shown in Figure 3. The points for X = 4-CH$_3$, 4-OCH$_3$, H, 4-Cl, 4-Br, 3-Cl, 3-CF$_3$, 3-CN, and 3,5-(CF$_3$)$_2$ define a straight line with a β_{nuc} = −0.39 ± 0.03. There are four points that show a significant negative deviation from the line: 4-CF_3 (−0.31 log units), 4-CN (−0.73 log units), 4-CHO (−0.88 log units), and 2,4,5-Cl_3 (−0.94 log units). As the following analysis will show, our findings are consistent with a stepwise mechanism (top pathway in Scheme 1) but not with a concerted one-step mechanism (lower pathway in Scheme 1).

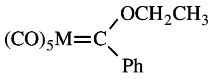
(1) The straight line in Figure 3 is based on points for which $\mathrm{p}K_a^{\mathrm{ArOH}} \geq \mathrm{p}K_a^{\mathrm{PNP}}$. Applying Williams et al.'s[12,13] argument regarding eq 2 to our reactions, we conclude that these points refer to reactions where nucleophilic attack (k_1) is rate limiting, i.e., $k_2 > (\gg)\ k_{-1}$ and thus $k_{\mathrm{ArO}} = k_1$.

(2) The negative β_{nuc} value is unusual but not without precedent. For example, in the reaction of the Fischer carbene complexes **3-M**,[18] **4-M**,[18] and **5-M**[19] with thiolate ions the β_{nuc} values for the nucleophilic attack step were found to range from −0.24 to −0.30. Negative β_{nuc} values have also been reported for some phosphoryl transfer reactions to amines,[20] for reactions of highly reactive carbocations with amines,[21,22] and for the reactions of oximate ions with electrophilic phosphorus centers;[23] β_{nuc} values close to zero have been found in the reaction of diphenylketene with amines.[24] According to Jencks et al.,[20] negative β_{nuc} values result from a combination of minimal progress of bond formation at the transition state and the requirement for partial desolvation of the nucleophile before it enters the transition state. In a first approximation, β_{nuc} may be expressed by eq 7 where β_{d} and β'_{nuc} are defined by eqs 8 and 9, respectively; K_{d} represents the equilibrium constant for partial desolvation of the nucleophile, while k'_1 is the rate constant for nucleophilic attack by the partially desolvated aryl oxide ion. Since desolvation becomes more difficult with increasing basicity of the nucleophile, $\beta_{\mathrm{d}} < 0$ which, along with a small β'_{nuc} value can lead to $\beta_{\mathrm{nuc}} < 0$. A more elaborate treatment of this problem has been presented elsewhere.[18]



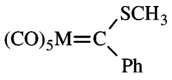
$\mathrm{(CO)_5M{=}C(OCH_3)Ph}$

3-Cr (M = Cr)
3-W (M = W)



$\mathrm{(CO)_5M{=}C(OCH_2CH_3)Ph}$

4-Cr (M = Cr)
4-W (M = W)



$\mathrm{(CO)_5M{=}C(SCH_3)Ph}$

5-Cr (M = Cr)
5-W (M = W)

$$\beta_{\mathrm{nuc}} = \beta_{\mathrm{d}} + \beta'_{\mathrm{nuc}} \tag{7}$$

$$\beta_{\mathrm{d}} = \mathrm{d}\log K_{\mathrm{d}}/\mathrm{d}\,\mathrm{p}K_a^{\mathrm{ArOH}} \tag{8}$$

$$\beta'_{\mathrm{nuc}} = \mathrm{d}\log k'_1/\mathrm{d}\,\mathrm{p}K_a^{\mathrm{ArOH}} \tag{9}$$

(3) The negative deviation of the point for X = 2,4,5-Cl_3 is related to the $\mathrm{p}K_a^{\mathrm{ArOH}}$ value of 8.29, which is lower than that for all of the other aryl oxide ions but virtually the same as that of *p*-nitrophenol (8.30). This implies that k_{-1} and k_2 are similar, which means that k_{ArO} is now given by eq 3, i.e., $k_{\mathrm{ArO}} < k_1$; if k_{-1} and k_2 were exactly equal, k_{ArO} would be $0.5k_1$, which would correspond to the breakpoint on the Brønsted plot.

The fact that the point for X = 2,4,5-Cl_3 deviates by as much as 0.94 log units rather than just 0.3 log units suggests that the situation is more complex. One possibility is that the chlorine in the ortho position introduces a steric effect that lowers k_{ArO}. Even though a steric contribution cannot be ruled out altogether, the absence of a negative deviation from the Brønsted plot for the reaction of aryloxide ions with *p*-nitrophenyl acetate[12] where no change in rate-limiting step occurs argues against it.[25] The fact that, as shown above, bond formation between the aryloxide ions and the carbene carbon of **1-NO₂** has made minimal progress at the transition state further reduces the likelihood of a significant steric effect.

A more plausible explanation for the larger than expected negative deviation is that the break point on the Brønsted plot is shifted to $\mathrm{p}K_a^{\mathrm{ArOH}}$ values that are higher than $\mathrm{p}K_a^{\mathrm{PNP}}$. Such a shift would occur if k_2 were lower than k_{-1} for an aryl oxide ion that has the same basicity as the *p*-nitrophenoxide ion. In this case, k_{ArO} for 2,4,5-trichlorophenoxide ion would be approximated by K_1k_2 (eq 4).[26]

(4) The reason why k_2 is lower than expected based on the $\mathrm{p}K_a$ of *p*-nitrophenol is related to the reason why the points for X = 4-CF_3, 4-CN, and 4-CHO deviate negatively from the Brønsted plot. Both are the result of charge delocalization into the 4-X substituent which is particularly strong for NO_2 and CHO, intermediate for CN, and weak for CF_3.[27] This charge delocalization provides extra resonance stabilization to the respective aryl oxide ions, which leads to a higher Marcus *intrinsic* barrier[29] for the nucleophilic attack as well as for leaving group departure. Specifically, the increase in the intrinsic barrier for the k_2 step comes about because, at the transition state, resonance development in the departing *p*-nitrophenoxide ion lags behind bond cleavage, while for the k_1 step the enhanced intrinsic barrier is the result of the loss of resonance stabilization of the nucleophile running ahead of bond formation. These types of transition-state imbalances and their effect on intrinsic barriers are well established and always occur when resonance effects are involved.[31]

B. Why Is the Reaction Not Concerted? What makes the reaction of **1-NO₂** with aryl oxide ions stepwise while the reaction of *p*-nitrophenyl acetate with the same nucleophiles is concerted? As Jencks has pointed out, the change from a stepwise to a concerted mechanism occurs when the respective intermediate becomes so unstable and the barrier for its

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(18) Bernasconi, C. F.; Kittredge, K. W.; Flores, F. X. *J. Am. Chem. Soc.* **1999**, *121*, 6630.

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

(20) Jencks, W. P.; Haber, M. T.; Herschlag, D.; Nazaretian, K. L. *J. Am. Chem. Soc.* **1986**, *108*, 479.

(21) Richard, J. P. *J. Chem. Commun.* **1987**, 1768.

(22) McClelland, R. A.; Kanagasabapathy, V. M.; Banait, N. S.; Steenken, S. *J. Am. Chem. Soc.* **1992**, *114*, 1816.

(23) (a) Terrier, F.; Le Guével, E.; Chatrousse, A. P.; Moutier, G.; Buncel, E. *Chem. Comm.* **2003**, 600. (b) Terrier, F.; Rodriguez-Dafonte, P.; Le, Guével, E.; Montiers, G. *Org. Biomol. Chem.* **2006**, *4*, 4352.

(24) Andraos, J.; Kresge, A. J. *J. Am. Chem. Soc.* **1992**, *114*, 5643.

(25) However, two chlorine substituents in ortho positions lead to a strong steric effect.[12]

(26) If more points were available at $\mathrm{p}K_a^{\mathrm{ArOH}} < \mathrm{p}K_a^{\mathrm{PNP}}$, the Brønsted plot would have a positive slope in the region where $k_{\mathrm{ArO}} = K_1k_2$ because K_1 would increase with increasing $\mathrm{p}K_a^{\mathrm{ArOH}}$ while k_2 would also show a slight increase due to an enhanced electronic push by the electron pairs on the aryloxy group oxygen.

(27) The σ_{P} values for 4-CF_3, 4-CN, 4-CHO, and 4-NO_2 are 0.54, 0.66, 0.42, and 0.78, respectively, while the σ_{P}^- values are 0.56, 0.99, 0.98, and 1.28, respectively.[28] Hence, the $\Delta\sigma = \sigma_{\mathrm{P}}^- - \sigma_{\mathrm{P}}$ values for 4-CF_3, 4-CN, 4-CHO, and 4-NO_2 are 0.02, 0.33, 0.56, and 0.49, respectively. σ_{R} values, another measure of π-acceptor strength, yield the same qualitative order: 0.09 (4-CF_3), 0.18 (4-CN), 0.23 (4-CHO), and 0.16 (4-NO_2).[28]

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

(29) The Marcus intrinsic barrier of a reaction is the barrier in the absence of a thermodynamic driving force, i.e., when $\Delta G° = 0$.[30]

(30) Marcus, R. A. *J. Phys. Chem.* **1968**, *72*, 891.

(31) Bernasconi, C. F. *Acc. Chem. Res.* **1987**, *20*, 301. (b) Bernasconi, C. F. *Adv. Phys. Org. Chem.* **1992**, *27*, 119. (c) Bernasconi, C. F. *Acc. Chem. Res.* **1992**, *25*, 9.

SCHEME 2

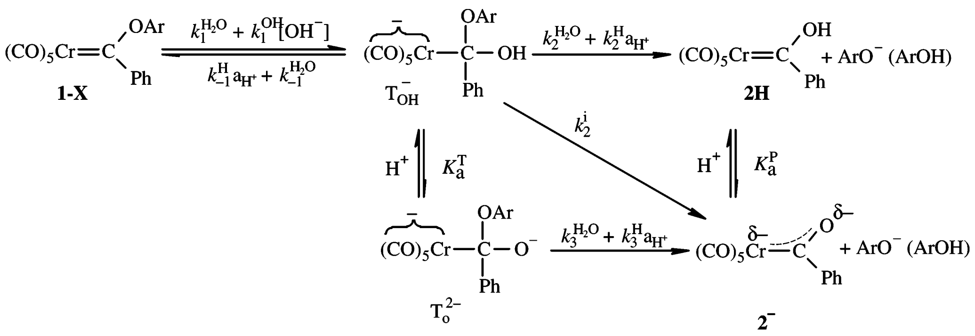
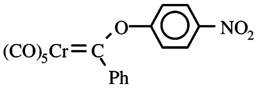
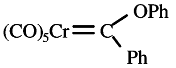
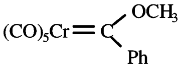
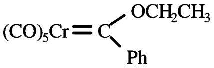
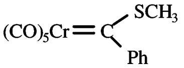
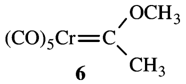


TABLE 2. Rate Constants for the Hydrolysis of 1-H and $1\text{-}NO_2$ in 50% MeCN−50% Water (v/v) at 25 °C

		k_{H_2O} s^{-1}	k_{OH} M^{-1} s^{-1}	k_{OH}/k_{H_2O} M^{-1}	$k_B(Et_3N)$ M^{-1} s^{-1}	$k_B(NMM)$[b] M^{-1} s^{-1}	k_{PhO}[c] M^{-1} s^{-1}
	**($1\text{-}NO_2$)**	0.30	15.9	53	0.90	0.43	45.1
	**(1-H)**	0.025[a]	2.39	95.6	0.44		
	**(3-Cr)**[d]	2.9×10^{-3}	26.6	9.17×10^{3}	0.16	2.5×10^{-2}	
	**(4-Cr)**[d]	4.5×10^{-4}	10.5	2.33×10^{4}	3.00×10^{2}	4.64×10^{-3}	
	**(5-Cr)**[e]	1.30×10^{-3}	0.127	123			

[a] Value obtained in KOH and buffer solutions; see text. [b] NMM = *N*-methylmorpholine. [c] Reaction of **$1\text{-}NO_2$** with PhO^-. [d] Reference 2b. [e] Reference 2c.

decomposition so small that it cannot exist.[14a,32] This is apparently the case for the tetrahedral intermediate in eq 2 but not for the tetrahedral intermediate in Scheme 2. There are two reasons why the intermediate in the reactions of **$1\text{-}NO_2$** does exist. (1) It is thermodynamically much more stable than the intermediate in the ester reactions because the $(CO)_5Cr$ moiety is much more effective than the carbonyl oxygen in stabilizing the negative charge.[1,8] One measure for the difference in the stabilizing power is the much higher acidity of **6** ($pK_a^{CH} = 12.3$)[33] compared to that of ethylacetate ($pK_a = 25.6$).[34] (2) It is kinetically more stable because the intrinsic barriers for the k_{-1} and k_2 steps are higher than for the ester reactions due to the delocalization of the negative charge into the CO ligands.[8,35]



6

Hydrolysis of 1-X. A. Mechanism. The hydrolysis of **1-H** and **$1\text{-}NO_2$** was examined in detail over a wide pH range (Figure 1) which provided rate constants for the reactions with OH^-, water, and general base catalysis by triethylamine and *N*-methylmorpholine. These rate constants are summarized in Table 2 along with corresponding parameters for the hydrolysis of the previously investigated carbene complexes **3-Cr**, **4-Cr**, and **5-Cr**. Regarding k_{H_2O} for **1-H**, the value obtained in KOH solutions and buffers is deemed more reliable than that determined in HCl solution. This is because the precision in rate measurements in the latter medium is probably adversely affected by the interference of the decomposition of **2H**.

A more limited set of data for the hydrolysis of **1-X** (X = 4-CH_3, 4-OCH_3, H, 4-Cl, 4-Br, 4-Cl, 3-CF_3, 3-CN, 4-CF_3, 3,5-$(CF_3)_2$, 4-CHO, and 2,4,5-Cl_3) was also obtained as a byproduct of the study of the reaction of **$1\text{-}NO_2$** with the various aryloxide ions. The respective rate constants, k_{obsd}^{II}, are included in Table 1. These rate constants were determined at a pH value low enough that the contribution by the hydroxide ion reaction is negligible so that one may equate them with k_{H_2O}.

The mechanism of the hydrolysis of **3-Cr** and **4-Cr** was shown to involve rate-limiting formation of a tetrahedral

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(32) (a) Jencks, W. P. *Acc. Chem. Res.* **1980**, *13*, 161. (b) Jencks, W. P. *Chem. Soc. Rev.* **1981**, *10*, 345.

(33) Gandler, J. R.; Bernasconi, C. F. *Organometallics* **1989**, *8*, 2282.

(34) Amyes, T. L.; Richard, J. P. *J. Am. Chem. Soc.* **1996**, *118*, 3129.

(35) Bernasconi, C. F.; Stronach, M. W. *J. Am. Chem. Soc.* **1993**, *115*, 1341.

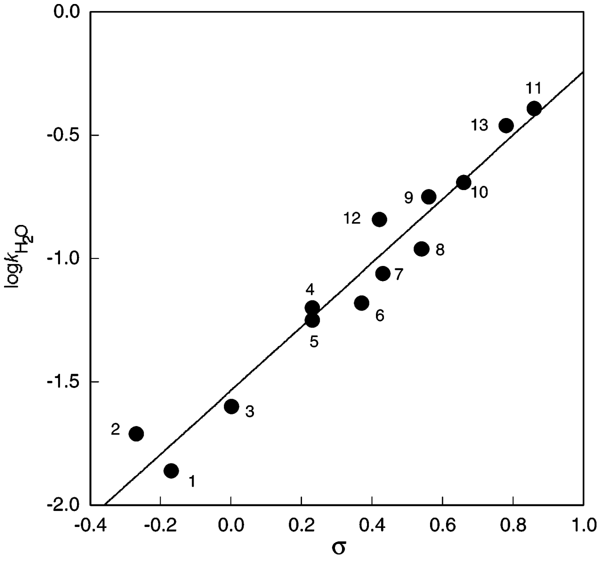
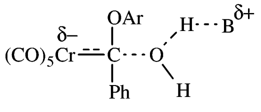


FIGURE 4. Rate constants for the hydrolysis of **1-X** by water. The numbers refer to those in Table 1.

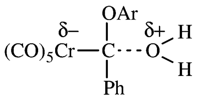
intermediate from nucleophilic attack by OH^- or water, followed by rapid conversion of the intermediate to products involving three concurrent pathways.[2b] Scheme 2 shows this mechanism applied to the hydrolysis of **1-X**. Note that general base and general acid catalysis steps (k_1^{B} [B], k_{-1}^{BH} [BH], k_2^{BH} [BH] and k_3^{BH} [BH]) are also involved but have been omitted to avoid clutter. The inclusion of a pathway through a dianionic intermediate (T_{O}^{2-}) and of a pathway involving intramolecular acid catalysis (k_{2i}) was required to explain why the intermediate T_{OH}^- was not detectable despite a favorable equilibrium of the first step.[2b]

Just as replacing the methoxy or ethoxy leaving groups with the much better *p*-nitrophenoxy nucleofuge is not sufficient to change the mechanism from stepwise to concerted in the reaction of aryl oxide ions with **1-NO₂**, it is very unlikely that the hydrolysis mechanism would change from stepwise for **3-Cr** or **4-Cr** to concerted for **1-X**. Hence, we conclude Scheme 2 is the correct mechanism and the nucleophilic attack steps are rate limiting, i.e., $k_{\text{OH}} = k_1^{\text{OH}}$ at high pH and $k_{\text{H}_2\text{O}} = k_1^{\text{H}_2\text{O}}$ at low pH.

Regarding the mechanism of general base catalysis (k_1^{B}), it most likely represents a class *n* mechanism[36] with a transition state such as **7**.

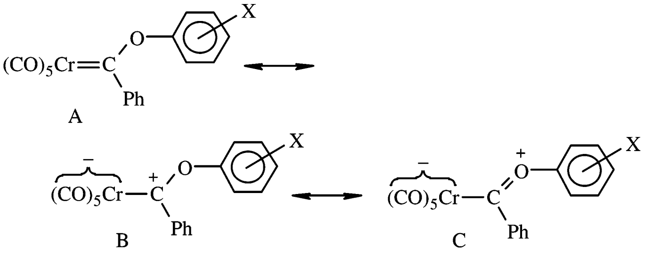


7



8

B. Structure−Reactivity Relationships. A plot of log $k_1^{\text{H}_2\text{O}}$ versus Hammett σ values is shown in Figure 4; it yields $\rho = 1.29 \pm 0.08$. There are three factors that may contribute to the rate acceleration by electron-withdrawing substituents. The first is enhanced electrophilicity of the carbene carbon (resonance structure B).[1] The second one is the decrease in reactant stabilization by the π-donor effect of the oxygen (resonance structure C). The third one is stabilization of the developing negative charge at the transition state (**8**). However, the latter effect is expected to be weak because the stabilizing effect on the developing negative charge is partially offset by the *de*stabilization of the partial positive charge on the approaching nucleophile. This is reminiscent of the situation with other neutral nucleophiles such as amines where a similar compensation between stabilization and destabilization of the transition state occurs.[4g,4h]



Further insights into the factors that affect reactivity can be gained from comparisons of **1-H** and **1-NO₂** on the one hand with **3-Cr**, **4-Cr**, and **5-Cr** on the other (Table 2). The k_1^{OH} value for **3-Cr** is about 11 fold higher than for **1-H** despite the stronger electron-withdrawing effect of the phenoxy group, which should enhance the reactivity of **1-H**, and the stronger π-donor effect of the methoxy group, which should lower the reactivity of **3-Cr**. This implies that the steric effect of the larger phenoxy group more than offsets the electronic effects and is responsible for the lower rate constants for **1-H**. Similar arguments apply to the comparison between **1-H** and **4-Cr**. Even the strong electron-withdrawing effect of the *p*-nitrophenoxy group is not enough to make **1-NO₂** more reactive than **3-Cr**. That steric effects on the reaction of nucleophiles with carbene complexes are important has also been shown by Zoloff Michoff et al.[2d]

In contrast, the $k_1^{\text{H}_2\text{O}}$ values for **3-Cr** and **4-Cr** are 8.6-fold and 55.5-fold, respectively, *lower* than for **1-H**, suggesting that for the water reaction the electronic effects are dominant. This contrast may be attributed to a change from a relatively early transition state for the hydroxide ion reaction to a relatively late transition state for the water reaction, as one would expect based on the Hammond−Leffler[37,38] postulate. In a late transition state the loss of the resonance stabilization arising from the π-donor effect is more advanced and hence has a greater effect on the reaction barrier. On the other hand, the steric effect may not necessarily be greater than for an earlier transition state because, despite a less advanced bond formation, the carbene carbon is still essentially trigonal, and thus, crowding may be as severe as in a more tetrahedral but tighter transition state.[39]

Another manifestation of the patterns described above is that for the carbene complexes with the weaker π-donor effects (**1-NO₂**, **1-H**) the $k_1^{\text{OH}}/k_1^{\text{H}_2\text{O}}$ ratios are on the order of 50 to 100 M^{-1} while for the carbene complexes with strong π-donor effects (**3-Cr**, **4-Cr**) these ratios are on the order of $1-2 \times 10^4$ M^{-1} (Table 2). Not surprisingly, the $k_1^{\text{OH}}/k_1^{\text{H}_2\text{O}}$ ratio for **5-Cr** (133) is similar to that for **1-NO₂** and **1-H** since the methylthio group is also a weak π-donor.[41] The fact that the absolute value

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[36] Jencks, W. P. *Acc. Chem. Res.* **1976**, *9*, 425.

[37] Hammond, G. S. *J. Am. Chem. Soc.* **1955**, *77*, 334.

[38] Leffler, J. E.; Grunwald, E. *Rates and Equilibria of Organic Reactions*; Wiley: New York, 1963.

[39] A similar situation exists in the hydrolysis of α-alkyl-α-(methylthio)-methylene Meldrum's acids.[40]

[40] Bernasconi, C. F.; Brown, S. D.; Ali, M.; Rappoport, Z.; Yamataka, H.; Salim, H. *J. Org. Chem.* **2006**, *71*, 4795.

[41] $\sigma_{\text{R}} = -0.43$ and -0.15 for MeO and MeS, respectively.[28]

of k_1^{OH} for **5-Cr** is much lower than for any other carbene complex is the result of the larger size of the sulfur atom which leads to a larger steric effect.[42]

C. Relative Reactivities of PhO$^-$ and OH$^-$. The nucleophilic reactivity of hydroxide ion is known to be much lower than one might expect on the basis of its basicity. For example, the rate of nucleophilic attack on *p*-nitrophenyl acetate by OH$^-$ in water is only 15.3-fold higher than for nucleophilic attack by phenoxide ion,[43] even though the pK_a of water is 5.9 units higher than that of phenol. The depressed reactivity of OH$^-$ is the result of the unusually strong solvation of the hydroxide ion coupled with the requirement of partial desolvation as it enters the transition state.[44] For the reaction of **1-NO$_2$** the situation is even more dramatic: here it is the reaction with PhO$^-$ that is faster with a k_{PhO}/k_{OH} ratio of 2.84. This result ties in with the negative β_{nuc} value found for the reaction of **1-NO$_2$** with aryloxide ions: the fact that in this reaction the requirement for partial desolvation has such a great influence even on the reactivity of the aryloxide ions implies that this requirement has an unusually large effect on the hydroxide ion reaction.

Conclusions

(1) The reaction of **1-NO$_2$** with aryl oxide ions is stepwise and occurs via a tetrahedral intermediate as shown in the upper part of Scheme 1. This conclusion is mainly based on the characteristics of the Brønsted plot (Figure 3) which is linear for $pK_a^{ArOH} \geq pK_a^{PNP}$ but shows a break when $pK_a^{ArOH} \leq pK_a^{PNP}$. It is also consistent with the higher thermodynamic stability of such intermediates compared to the corresponding putative tetrahedral intermediates in comparable acyl transfer reactions, and with the higher intrinsic barriers for the decomposition of the intermediate in the reaction of **1-NO$_2$** compared to that for the ester reactions.

(2) The Brønsted plot for k_{ArO} has a negative slope (β_{nuc}). This results from a combination of minimal progress of bond formation at the transition state and the requirement of partial desolvation of the nucleophile before it enters the transition state.

(3) The points on the Brønsted plot for aryloxide ions with a π-acceptor in the para position deviate negatively from the line defined by the other aryloxide ions. This is the result of charge delocalization into the substituent which increases the intrinsic barrier.

(4) The hydrolysis of **1-X** is also stepwise (Scheme 2), with nucleophilic attack by OH$^-$ ($k_{OH} = k_1^{OH}$) being rate limiting at high pH and attack by water ($k_{H_2O} = k_1^{H_2O}$) being rate limiting at intermediate and low pH. There is also a general base-catalyzed pathway via an *n* class mechanism (**7**).

(5) The Hammett ρ value for the hydrolysis of **1-X** by water is 1.29. The main factors responsible for the positive ρ value are enhancement of the electrophilicity of the carbene carbon and reduction of the π-donor effect of the oxygen by electron withdrawing substituents.

(6) In the reactions **1-NO$_2$**, **1-H**, **3-Cr**, **4-Cr**, and **5-Cr** with OH$^-$ steric effects dominate reactivity as seen in the relatively high k_{OH} values for **3-Cr** and **4-Cr**. On the other hand, for the reactions with water, π-donor stabilization of the carbene complex is the main factor determining relative reactivities. These observations are consistent with an early transition state for the OH$^-$ reactions and a late transition state for the water reactions.

(7) The k_{PhO}/k_{OH} ratio is particularly large for **1-NO$_2$**. This is attributed to an unusually large rate depression in the hydroxide ion reaction which results from the requirement for partial desolvation of the nucleophile before it enters the transition state.

Experimental Section

Instrumentation. ^{1}H and ^{13}C NMR spectra were recorded in CDCl$_3$ on a 500 MHz Varian Unity instrument. Kinetic experiments were performed on an Applied Photophysics DX.17MV stopped-flow apparatus (fast reactions) or an Agilent 8453 diode-array spectrophotometer (slow reactions).

Materials. Schlenk techniques were used in synthesizing and handling the carbene complexes, with argon as protecting gas. Carbene complexes were prepared according to Pulley et al.[45] The compounds were identified by NMR as follows: For **1-H**: ^{1}H NMR δ 7.16−7.50 (m, 9H, pH and OPh); ^{13}C NMR δ 121.57, 124.70, 127.49, 127.94, 130.36, 131.02, 154.57, 159.63 (Ph and OPh), 215.22 (CO, cis), 224.87 (CO, trans), 351.61 (C=). For **1-NO$_2$**: ^{1}H NMR δ 7.34 (d, 2H, OC$_6$H$_4$-4-NO$_2$), 7.44−7.49 (m, 5H, Ph), 8.39 (d, 2H, OC$_6$H$_4$-4-NO$_2$); ^{13}C NMR δ 122.91, 125.09, 126.14, 128.32, 131.83, 146.34, 153.99, 163.16 (Ph and OC$_6$H$_4$-4-NO$_2$), 215.08 (CO, cis), 224.41 (CO, trans), 351.58 (C=).

Acetonitrile was reagent grade and was used without further purification. Water was taken from a Milli-Q water purification system. *N*-Methylmorpholine and triethylamine were refluxed over Na and freshly distilled prior to use. Reagent-grade sodium acetate and KCl were used as received. HCl and KOH solutions were prepared using "dilut-it" from Baker Analytical. The phenols were recrystallized or distilled prior to use according to literature methodologies.[46]

Kinetic Runs. Most stopped-flow reactions were performed by mixing equal volumes of an acetonitrile solution of the substrate with an aqueous solution of the buffer. For the reactions measured by conventional spectrophotometry, reaction solutions were freshly prepared by injecting a small amount of a stock solution of the carbene complex in pure acetonitrile into the 50% acetonitrile−50% water solution containing all the other ingredients. All reactions were run under pseudo-first-order conditions with the substrate as the minor component. For **1-H**, reactions were monitored by following the decrease in absorbance at the λ_{max} of the substrate (415 nm). For **1-NO$_2$**, at low pH, reactions were monitored following the decrease in absorbance at the λ_{max} of the substrate (420 nm). At high pH, reactions were followed at the λ_{max} of the *p*-nitrophenoxide ion (400 nm). Due to solubility problems, for 2,4,5-trichlorophenol and *p*-trifluoromethylphenol, the phenol was dissolved in acetonitrile with the substrate (tests were run to ensure that no reaction takes place under these conditions during a reasonable period of time). These solutions were mixed with aqueous solutions containing KOH in the appropriate quantities to deprotonate the phenol and form the buffer. For the reactions with phenols, most reactions were run at a pH close to the pK_a of the phenol. For 2,4,5-trichlorophenol, reactions were run at pH 11.10 with KOH as buffer.

pH and pK_a Measurements. The pH in 50% acetonitrile−50% water was determined according to Allen and Tidwell.[47] The pH

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[42] Other factors such as the smaller electron withdrawing inductive effect of the MeS group compared to MeO and PhO groups contribute to differences in the k_1^{OH} values.[2c]

[43] Jencks, W. P.; Gilchrist, M. *J. Am. Chem. Soc.* **1962**, *84*, 2910.

[44] Hupe, D. J.; Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 451.

[45] Pulley, S. R.; Sen, S.; Vogorushin, A.; Swanson, E. *Org. Lett.* **1999**, *1*, 1721.

[46] Perrin, D. D.; Armarego, L. F. *Purification of Laboratory Chemicals*, 3rd ed.; Pergamon Press: New York, 1989.

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

of the reaction solutions for the stopped-flow runs was measured in mock-mixing experiments that simulated the stopped-flow runs. The pK_a values of the phenols were determined by measuring the pH of 1:1 buffer solutions under the reaction conditions.

Acknowledgment. This research was supported by Grant No. CHE-046622 from the National Science Foundation. The fellowship to M.E.Z.M. from CONICET (Argentina) is also gratefully acknowledged.

Supporting Information Available: Figures S1−S4 and Tables S1−S3 (kinetic data). This material is available free of charge via the Internet at http://pubs.acs.org.

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