

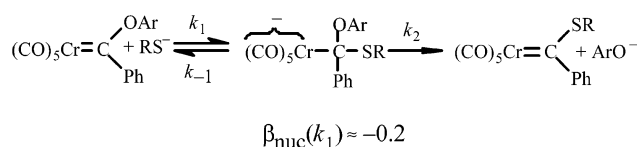
Reactions of [Aryloxy(phenyl)carbene]pentacarbonylchromium(0) Complexes with Thiolate Ions. Decreasing Reactivity with Increasing Basicity of the Nucleophile[†]

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A kinetic study of the reactions of thiolate ions with three Fischer-type [aryloxy(phenyl)carbene]-pentacarbonyl chromium(0) complexes in 50% MeCN–50% water (v/v) is reported. Brønsted plots of the second-order rate constants are biphasic with an initial steep rise for weakly basic thiolate ions ($\beta_{\text{nuc}} \approx 1.0$) followed by a slightly descending leg with a negative slope ($\beta_{\text{nuc}} \approx -0.2$) for strongly basic thiolate ions. This indicates a change from rate-limiting leaving group departure at low $\text{p}K_{\text{a}}^{\text{RSH}}$ to rate-limiting nucleophilic attachment at high $\text{p}K_{\text{a}}^{\text{RSH}}$. The negative β_{nuc} values result from a combination of minimal progress of C–S bond formation at the transition state and the requirement for partial desolvation of the nucleophile before it enters the transition state. Possible factors that may affect the degree of bond formation in reactions of Fischer carbene complexes as well as reactions of other unsaturated electrophiles with thiolate ions are discussed.

Introduction

Nucleophilic reactivity is a subject that has received a great deal of attention over several decades and is discussed in considerable detail in most books on physical organic chemistry and many reviews.^{1–13} The subject is complex because there

are many factors that affect the reactivity of nucleophiles such as its basicity, size, polarizability, charge, solvation, and the nature of the electrophile, just to name the most important ones. The situation becomes much simpler when nucleophiles within the same family, i.e., bases with the same nucleophilic atom and similar structural features, are compared with each other and all the reactions are conducted in the same solvent. In such cases, there is generally a good correlation between rate constants and the basicity of the nucleophile, with the rate constants typically increasing with increasing basicity. This is commonly expressed by the Brønsted eq 1 where $\text{p}K_{\text{a}}^{\text{NucH}}$ is the

$$\log k_{\text{nuc}} = \beta_{\text{nuc}} \text{p}K_{\text{a}}^{\text{NucH}} + c \quad (1)$$

$\text{p}K_{\text{a}}$ of the conjugate acid of the nucleophile and β_{nuc} is equal to the slope of a plot of $\log k_{\text{nuc}}$ versus $\text{p}K_{\text{a}}^{\text{NucH}}$ and represents the sensitivity of the rate to changes in $\text{p}K_{\text{a}}^{\text{NucH}}$; typically $1 > \beta_{\text{nuc}} > 0$.

[†] Physical Organic Chemistry of Transition Metal Carbene Complexes. 35. Part 34: Bernasconi, C. F.; Zoloff Michoff, M. E.; de Rossi, R. H.; Granados, A. M. *J. Org. Chem.* **2007**, *72*, 1285.

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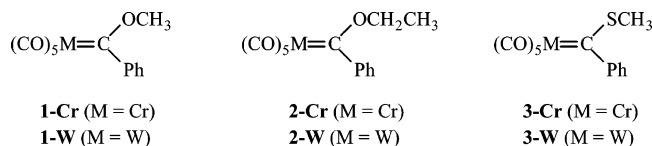
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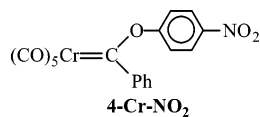
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A common interpretation of the numerical values of β_{nuc} is that they represent an approximate measure of the degree of bond formation between the nucleophile and the electrophilic center of the substrate at the transition state. This interpretation goes back to the seminal contributions by Leffler and Grunwald⁴ and is in keeping with the Hammond postulate.¹⁴

However, a number of cases have been reported where the β_{nuc} value was close to zero or even negative; in such cases this interpretation cannot be correct. Examples where negative β_{nuc} values were found include the reaction of quinuclidines with aryl phosphates,¹⁵ of amines with carbocations,^{16,17} of oximate ions with electrophilic phosphorus centers,¹⁸ of thiolate ions with Fischer carbene complexes such as **1-M**,¹⁹ **2-M**,¹⁹ and **3-M**,²⁰



and of aryloxy ions with [*p*-nitrophenoxy(phenyl)carbene]-pentacarbonylchromium(0) (**4-Cr-NO₂**).^{20,21}



According to Jencks et al.,¹⁵ 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 2 where β_{d} and β'_{nuc} are defined by eqs 3 and 4, respectively;

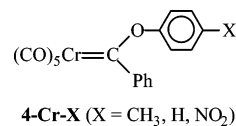
$$\beta_{\text{nuc}} = \beta_{\text{d}} + \beta'_{\text{nuc}} \quad (2)$$

$$\beta_{\text{d}} = \text{d} \log K_{\text{d}} / \text{d} \text{p}K_{\text{a}}^{\text{NucH}} \quad (3)$$

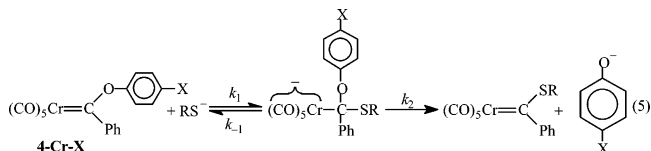
$$\beta'_{\text{nuc}} = \text{d} \log k'_{\text{1}} / \text{d} \text{p}K_{\text{a}}^{\text{NucH}} \quad (4)$$

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 nucleophile. Since desolvation becomes more difficult with increasing basicity of the nucleophile, $\beta_{\text{d}} < 0$ which, along with a small β'_{nuc} value, can lead to a negative β_{nuc} value. A more elaborate treatment of this problem has been presented elsewhere.¹⁹

We now report a kinetic study of the reactions of a series of thiolate ions with the Fischer carbene complexes **4-Cr-CH₃**, **4-Cr-H**,



and **4-Cr-NO₂** in 50% aqueous acetonitrile. The reactions follow the typical two-step mechanism for nucleophilic substitution at the carbene carbon (eq 5).²² Depending on the basicity of the thiolate ion, either the k_1 or the k_2 step is rate limiting. For the reactions where the k_1 step is rate limiting, the β_{nuc} values are again negative but not as strongly negative as for the reaction of **4-Cr-NO₂** with aryloxy ions.²¹



Results

Rates were determined with $\text{CH}_3\text{CH}_2\text{CH}_2\text{S}^-$, $\text{HOCH}_2\text{CH}_2\text{S}^-$, $\text{MeOCOCH}_2\text{CH}_2\text{S}^-$, $\text{MeOCOCH}_2\text{S}^-$, $\text{CF}_3\text{CH}_2\text{S}^-$, PhS^- , $3,4\text{-Cl}_2\text{-C}_6\text{H}_3\text{S}^-$, and $\text{C}_6\text{F}_5\text{S}^-$ as the nucleophiles in 50% MeCN–50% water at 25 °C and an ionic strength of 0.1 M maintained with KCl in most cases. The reactions were conducted under pseudo-first-order conditions, with the carbene complex as the minor component, and at constant pH corresponding to the $\text{p}K_{\text{a}}$ values of the respective thiol ($\text{p}K_{\text{a}}^{\text{RSH}}$). The kinetic runs were monitored in a stopped-flow spectrometer at 390 nm for X = H and CH₃, and at 400 nm for X = NO₂, respectively. Rates were determined at six thiolate ion concentrations ranging from 5×10^{-4} to 5×10^{-3} M in all cases except for $\text{C}_6\text{F}_5\text{S}^-$ where the range was from 0.01 to 0.5 M due to the low reactivity of this thiolate ion.

Representative plots of pseudo-first-order rate constants (k_{obsd}) versus thiolate ion concentration are shown in Figure 1. The slopes of these plots yield k_{RS} , the second-order rate constants for the overall reaction. Table 1 summarizes all k_{RS} values determined in this study.

Discussion

Mechanism. Generally, nucleophilic substitution at the carbene carbon of Fischer carbene complexes involves a two-step mechanism²² as shown in eq 5 for the reactions studied in the present work. Some of the most compelling evidence for the stepwise nature of the mechanism has come from the study of systems where the intermediate is directly detectable,^{19,20,24,25} including cases where the reaction is intramolecular.²⁶ Recently,

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(23) A referee has raised the question as to whether eq 5 might be reversible. We did not find any evidence of reversibility and, in view of the higher nucleophilicity of thiolate ions compared to aryloxy ions and the very low concentrations of $\text{XC}_6\text{H}_4\text{O}^-$ being formed during the reaction, no measurable reversibility is expected.

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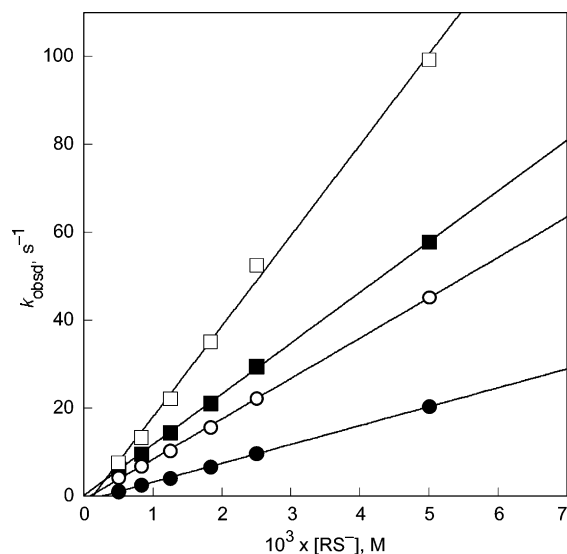


FIGURE 1. Representative plots of k_{obsd} versus thiolate ion concentration for reactions of **4-Cr-H**: (□) $\text{CH}_3\text{CH}_2\text{CH}_2\text{S}^-$; (■) $\text{MeOCOCH}_2\text{CH}_2\text{S}^-$; (○) $\text{MeOCOCH}_2\text{S}^-$; and (●) PhS^- .

it was shown that even with exceptionally good leaving groups such as *p*-nitrophenoxy the reaction of aryloxide ions with **4-Cr-NO₂** is still stepwise.²¹ This contrasts with nucleophilic substitutions on carboxylic acid esters where the reactions become concerted for aryloxy leaving groups.^{27,28} The reason for this contrast is that the intermediates in the reaction of the Fischer carbenes are both thermodynamically and kinetically much more stable than the corresponding tetrahedral intermediates in the ester reactions.^{21,22b}

The results of the present study confirm the stepwise nature of the reaction of **4-Cr-X** with thiolate ions because the data indicate a change in the rate-limiting step as the basicity of the nucleophile changes. This change manifests itself in the biphasic nature of the Brønsted plots for **4-Cr-H** and **4-Cr-Me** (Figure 2A,B). For the reaction of **4-Cr-NO₂** (Figure 2C), the kinetic stopped-flow traces for the reactions with the two least basic thiolate ions were erratic and irreproducible and hence no k_{RS} values could be determined; the reason for the erratic behavior is unclear.

The Brønsted plots in Figure 2A,B show a steep initial rise that is followed by a straight line with a small negative slope. The slope values (β_{nuc}) are summarized in Table 2.

The biphasic nature of the Brønsted plots can be understood based on the rate law for eq 5, which, using the steady state approximation for the intermediate, yields eq 6 for the second-order rate constant k_{RS} . For weakly basic thiolate ions the breakdown of the intermediate back to

$$k_{\text{RS}} = \frac{k_1 k_2}{k_{-1} + k_2} \quad (6)$$

the reactants is faster than its conversion to products ($k_{-1} \gg k_2$) and hence eq 6 simplifies to eq 7.

$$k_{\text{RS}} = K_1 k_2 \quad (7)$$

For strongly basic thiolate ions the opposite is true ($k_{-1} \ll k_2$) and nucleophilic attack becomes rate limiting, eq 8.

$$k_{\text{RS}} = k_1 \quad (8)$$

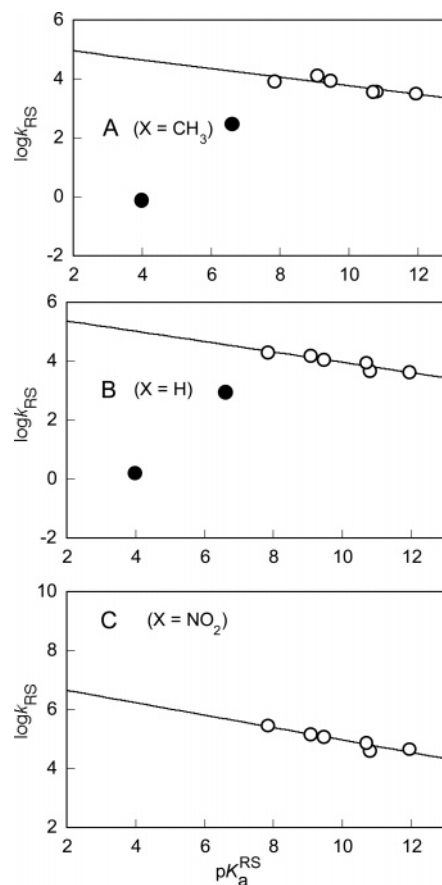
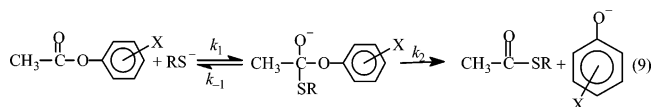


FIGURE 2. Brønsted plot for the reactions of **4-Cr-X** with thiolate ions.

We note that the break in the Brønsted plots of Figure 2A,B which correspond to $k_2 = k_{-1}$ occurs at $\text{p}K_{\text{a}}^{\text{RSH}}$ around 8. This implies that the leaving group abilities of aryloxide ions with $\text{p}K_{\text{a}}^{\text{ArOH}}$ values of 11.6 ($\text{X} = \text{H}$) or 11.9 ($\text{X} = \text{Me}$) are comparable to that of a thiolate ion with $\text{p}K_{\text{a}}^{\text{RSH}} \approx 8.0$. Or, stated differently, aryloxide ions are much better leaving groups than thiolate ions of similar basicities.

A similar conclusion was reached by Douglas and Alborz,²⁹ who showed that aryloxide ions depart from acetoacetate anions 5×10^3 times faster than thiolate ions of the same basicity, and 79 times faster from fluorene-9-carboxylic acid ester anions. On the other hand, in the reactions of thiolate ions with arylacetates, eq 9,



the leaving group ability of the aryloxide ions is comparable or even somewhat less than that of thiolate ions of similar

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TABLE 1. Summary of the Second-Order Rate Constants, k_{RS} , for the Reactions of Thiolate Ions with 4-Cr-X (X = CH₃, H, NO₂) in 50% MeCN–50% Water at 25 °C^a

RS ⁻	pK_a^{RSH}	$10^{-3}k_{RS}(\text{CH}_3)$, M ⁻¹ s ⁻¹	$10^{-3}k_{RS}(\text{H})$, M ⁻¹ s ⁻¹	$10^{-3}k_{RS}(\text{NO}_2)$, M ⁻¹ s ⁻¹
CH ₃ CH ₂ CH ₂ S ⁻	11.94	3.34 ± 0.06	4.30 ± 0.07	46.3 ± 1.8
HOCH ₂ CH ₂ S ⁻	10.79	3.87 ± 0.10	4.90 ± 0.10	38.1 ± 0.2
CH ₃ OCOCH ₂ CH ₂ S ⁻	10.69	7.42 ± 0.14	9.19 ± 0.10	76.8 ± 1.6
CH ₃ OCOCH ₂ S ⁻	9.45	8.97 ± 0.04	11.55 ± 0.09	121 ± 2.1
CF ₃ CH ₂ S ⁻	9.07	13.9 ± 0.04	15.4 ± 0.1	147 ± 3
PhS ⁻	7.84	8.81 ± 0.17	20.6 ± 0.6	294 ± 6
3,4-Cl ₂ -C ₆ H ₃ S ⁻	6.60	0.307 ± 0.013	0.93 ± 0.07	
C ₆ F ₅ S ⁻	3.97	0.00097 ± 0.00004	0.00162 ± 0.0007	

^a $\mu = 0.1$ maintained with KCl except for the reactions with C₆F₅S⁻ where $\mu = 0.5$ M was used due to the higher concentration range of [C₆F₅S⁻].

basicity.³⁰ Specifically, the break in the Brønsted plots ($k_{-1} = k_2$) for these reactions occurs at $pK_a^{RSH} \approx 10.1$ for X = H ($pK_a^{\text{ArOH}} = 9.86$), $pK_a^{RSH} \approx 7.8$ for X = 4-NO₂ ($pK_a^{\text{ArOH}} = 7.14$), and $pK_a^{RSH} \approx 5.0$ for X = 2,4-(NO₂)₂ ($pK_a^{\text{ArOH}} = 5.20$). As discussed in more detail by Douglas and Alborz,²⁹ the relative leaving group abilities of oxyanions and thiolate ions clearly depends strongly on the specific reaction system.

Brønsted Coefficients. The β_{nuc} values determined in the present study as well as those referring to the reactions of other Fischer carbene complexes are summarized in Table 2. As discussed in the Introduction, the negative values for $\beta_{\text{nuc}}(k_1)$ must result from a combination of minimal progress of C–S bond formation at the transition state and the impact of having to partially desolvate the nucleophile as it enters the transition state, i.e., eq 2 applies with $\beta_d < 0$ and $|\beta_d| > \beta'_{\text{nuc}}$.

Regarding the dependence of $\beta_{\text{nuc}}(k_1)$ on the carbene complex the following points are noteworthy.

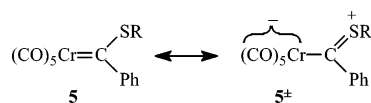
(1) For the three carbene complexes with aryloxy leaving groups (**4-Cr-X** with X = CH₃, H, and NO₂) the $\beta_{\text{nuc}}(k_1)$ values are all around -0.20 , i.e., there is no dependence on the aryl substituent. This implies that either both β_d and β'_{nuc} are constant or that any change in β_d is offset by an equal but opposite change in β'_{nuc} . For example, according to the Hammond¹⁴–Leffler⁴ postulate the increase in reactivity in the order **4-Cr-Me** < **4-Cr-H** << **4-Cr-NO₂** may lead to a decrease in C–S bond formation at the transition state, thereby reducing β'_{nuc} . This would require a corresponding increase in β_d , making it less negative and implying less desolvation of the thiolate ion at the transition state.

(2) For the other carbene complexes with alkoxy and methyl thio leaving groups the $\beta_{\text{nuc}}(k_1)$ values are slightly more negative, i.e., between -0.25 and -0.30 . It is not clear whether the differences within this set or even relative to the set for **4-Cr-X** are significant or just the result of experimental uncertainty. In any case, there is no obvious correlation between the $\beta_{\text{nuc}}(k_1)$ values and the reactivity of the carbene complexes as measured by k_1 for the standard thiolate ion HOCH₂CH₂S⁻ (last column in Table 2). If the $\beta_{\text{nuc}}(k_1)$ values for this second set are truly slightly more negative than for the first, it is not clear whether this is because β'_{nuc} is smaller or β_d is more negative.

(3) For the reaction of **4-Cr-NO₂** with aryloxy ions there is little doubt that the $\beta_{\text{nuc}}(k_1)$ value (-0.39 ± 0.03) should be regarded as significantly more negative than $\beta_{\text{nuc}}(k_1)$ for the reaction of the same carbene complex with thiolate ions (-0.21 ± 0.04). This difference is most plausibly interpreted in terms of differences in solvation energies of thiolate versus oxyanions. Specifically, the stronger hydrogen bonding solvation

of oxyanions implies that their partial desolvation is energetically more demanding, which may translate into a more negative β_d value.

Regarding the $\beta_{\text{nuc}}(K_1k_2)$ values for the reaction of thiolate ions with **4-Cr-Me** (ca. 1.01) and **4-Cr-NO₂** (ca. 1.06), they may be broken down into $\beta_{\text{nuc}}(K_1k_2) = \beta_{\text{eq}} + \beta_{\text{push}}$ where β_{eq} describes the dependence of K_1 on the pK_a^{RSH} and β_{push} refers to the electronic push by the lone pairs of the sulfur atom that arises from the resonance development in the product. These $\beta_{\text{nuc}}(K_1k_2)$ values are quite similar to those reported by Hupe and Jencks³⁰ for eq 9.



Reactivity. The k_1 values for the reaction of **4-Cr-H** with HOCH₂CH₂S⁻ (4.90×10^3 M⁻¹ s⁻¹) are about 4.5-fold lower than for the reaction of **1-Cr** with the same nucleophile. For the reaction with OH⁻ the reactivity difference is a factor of 11 in favor of **1-Cr** relative to **4-Cr-H**.²¹ As pointed out before,²¹ based on electronic effects alone **4-Cr-H** should be more reactive because the PhO group is more electron withdrawing than the MeO group and the methoxy group is a stronger π -donor than the PhO group, which lowers the reactivity of **1-Cr**. The results imply that the steric effect of the larger PhO group more than offsets the electronic effects and is responsible for the lower reactivity of **4-Cr-H**. That steric effects in reactions of nucleophiles with carbene complexes are important has also been shown by Zoloff Michoff et al.³¹ and others.^{20,21}

Hammett Plots. Figure 3 shows Hammett plots for the reactions with CH₃CH₂CH₂S⁻, HOCH₂CH₂S⁻, CH₃OCOCH₂CH₂S⁻, CH₃OCOCH₂S⁻, and CF₃CH₂S⁻. These are the nucleophiles for which k_{RS} is clearly equal to k_1 , so $\rho = \rho(k_1)$. The $\rho(k_1)$ values are 1.24 ± 0.10 , 1.08 ± 0.08 , 1.10 ± 0.09 , 1.22 ± 0.10 , and 1.13 ± 0.15 , respectively, i.e., they are all the same within the experimental uncertainties with an average value of 1.15. The fact that the ρ values are independent of the nucleophile is not only consistent with the observation that the $\beta_{\text{nuc}}(k_1)$ values are independent of the leaving group substituent, they are a required consequence. This is because the dependence of ρ on pK_a^{RSH} and the dependence of $\beta_{\text{nuc}}(k_1)$ on σ are coupled through the cross-correlation coefficient, p_{xy} (eq 10).^{32,33} Our results indicate that $p_{xy} \approx 0$, which is

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(32) $p_{xy} = (d^2 \log k_1)/(d\sigma dpK_a^{RSH}) = (d^2 \log)/(dpK_a^{\text{BH}} d\sigma)$.

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TABLE 2. Brønsted β_{nuc} Values for Reactions of Fischer Carbene Complexes with Thiolate Ions in 50% MeCN–50% Water at 25 °C

Carbene complex		$\beta_{\text{nuc}}(k_1)^a$	$\beta_{\text{nuc}}(K_1k_2)$	$k_1(\text{HOCH}_2\text{CH}_2\text{S}^-)$ $\text{M}^{-1} \text{s}^{-1}$
Reactions with RS^- and ArS^-				
	(4-Cr-Me) ^b	-0.21 ± 0.05	ca. 1.01	3.87×10^3
	(4-Cr-H) ^b	-0.18 ± 0.03	ca. 1.06	4.90×10^3
	(4-Cr-NO ₂) ^b	-0.21 ± 0.04		4.63×10^4
	(1-Cr) ^c	-0.28 ± 0.05		2.25×10^4
	(1-W) ^c	-0.25 ± 0.04		6.52×10^4
	(2-Cr) ^c	-0.28 ± 0.05		1.20×10^4
	(2-W) ^c	-0.26 ± 0.04		4.04×10^4
	(3-Cr) ^d	-0.24 ± 0.07		6.60×10^2
	(3-W) ^d	-0.30 ± 0.04		2.95×10^3
Reaction with ArO^-				
	(4-Cr-NO ₂) ^e	-0.39 ± 0.03		1.39×10^3

^a Errors are standard deviations. ^b This work. ^c Reference 19. ^d Reference 20. ^e Reference 21.

a reasonable result for a reaction where leaving group departure is decoupled from the nucleophilic attachment step.

$$p_{xy} = \frac{d\rho}{d \text{p}K_{\text{a}}^{\text{RSH}}} = \frac{d\beta_{\text{nuc}}(k_1)}{d\sigma} \quad (10)$$

The Hammett plot for the reaction of PhS^- (not shown) has a ρ value of 1.57 ± 0.10 . The somewhat higher value than for the more basic thiolate ions may be attributed to a transition from $k_2 \gg k_{-1}$ to $k_2 > k_{-1}$ so that k_{RS} is no longer strictly equal to k_1 but given by eq 6 where k_2 makes a small contribution to k_{RS} . The fact that the point for PhS^- on the Brønsted plot for **4-Cr-Me** shows a small negative deviation is consistent with this notion. As a consequence of the contribution of k_2 to k_{RS} ,

the ρ value should be enhanced because k_2 is expected to show a much stronger dependence on the leaving group substituent than k_1 .

A comparison of $\rho(k_1)$ for the reactions of thiolate ions with **4-Cr-X** with $\rho(k_1)$ values for nucleophilic attachment to other Fischer carbenes is instructive. These latter are summarized in Table 3. The most obvious interpretation of the positive $\rho(k_1)$ values is that they indicate stabilization of the developing negative charge at the transition state by electron-withdrawing substituents. However, the fact that there are large variations in these $\rho(k_1)$ values suggests that other factors come into play

(34) (a) Bernasconi, C. F.; Ali, M. *Organometallics* **2001**, *20*, 3383. (b) Bernasconi, C. F.; Bhattacharya, S. *Organometallics* **2003**, *22*, 1310.

(35) $\sigma_{\text{R}} = -0.43$ and -0.15 for MeO and MeS, respectively.³⁶

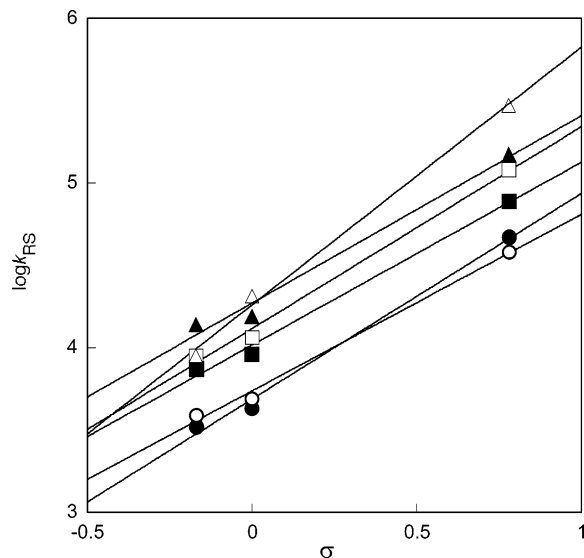


FIGURE 3. Hammett plots for the reactions of **4-Cr-X** with $\text{CH}_3\text{CH}_2\text{CH}_2\text{S}^-$ (Δ), $\text{HOCH}_2\text{CH}_2\text{S}^-$ (\blacktriangle), $\text{MeOCOCH}_2\text{CH}_2\text{S}^-$ (\square), $\text{MeOCOCH}_2\text{S}^-$ (\blacksquare), $\text{CF}_3\text{CH}_2\text{S}^-$ (\circ), and PhS^- (\bullet).

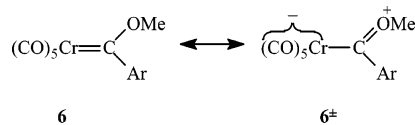
TABLE 3. Representative Hammett $\rho(k_1)$ Values for Reactions of Fischer Carbene Complexes with Nucleophiles in 50% MeCN–50% Water (v/v) at 25 °C

#	Reaction	$\rho(k_1)$	Ref.
1	$(\text{CO})_5\text{Cr}=\text{C}(\text{OAr})\text{Ph} + \text{RS}^-$	1.15 ^a	b
2	$(\text{CO})_5\text{Cr}=\text{C}(\text{OMe})\text{Ar} + \text{OH}^-$	2.20	c
3	$(\text{CO})_5\text{Cr}=\text{C}(\text{OMe})\text{Ar} + \text{OH}^-$	1.78	c
4	$(\text{CO})_5\text{W}=\text{C}(\text{OMe})\text{Ar} + \text{HC}\equiv\text{CCH}_2\text{O}^-$	1.65	c
5	$(\text{CO})_5\text{Cr}=\text{C}(\text{OCH}_2\text{CH}_2\text{OH})\text{Ar}$ intramolecular ^d	2.19	e
6	$(\text{CO})_5\text{Cr}=\text{C}(\text{SCH}_2\text{CH}_2\text{OH})\text{Ar}$ intramolecular ^d	0.96	f
7	$(\text{CO})_5\text{W}=\text{C}(\text{SCH}_2\text{CH}_2\text{OH})\text{Ar} + \text{HOCH}_2\text{CH}_2\text{S}^-$	1.45	g
8	$(\text{CO})_5\text{Cr}=\text{C}(\text{OMe})\text{Ar} + n\text{-BuNH}_2$	2.03	h
9	$(\text{CO})_5\text{Cr}=\text{C}(\text{SMe})\text{Ar} + n\text{-BuNH}_2$	0.59	i

^a Average value for first five thiolate ions in Table 1. ^b This work. ^c Reference 25b. ^d ρ includes dependence of acidity constant of the OH group. ^e Ali, M.; Bernasconi, C. F.; Biswas, S. J. *Organomet. Chem.* **2006**, *691*, 3477. ^f Reference 34a. ^g Reference 20. ^h Bernasconi, C. F.; Whitesell, C.; Johnson, R. A. *Tetrahedron* **2000**, *56*, 4917. ⁱ Reference 34b.

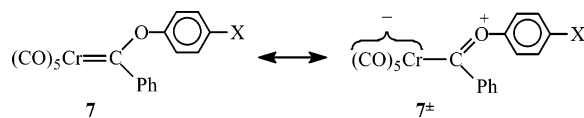
as well. One important factor identified previously is the π -donor effect of the leaving group on the stabilization of the reactant,³⁴

which is particularly strong with alkoxy groups,³⁵ e.g., **6**[±], but weaker for alkylthio groups (**5**[±]).³⁵



Electron-withdrawing substituents destabilize **6**[±], which enhances the reactivity of the carbene complex and hence renders $\rho(k_1)$ more positive. This is believed to be the main reason why $\rho(k_1)$ is larger for alkoxy carbenes (nos. 2–5, 8) than for alkylthio carbenes (nos. 6, 7, 9).

The reactions reported in the current study (no. 1) differ from all the others in that the substituents are on the aryloxy leaving group rather than on the phenyl group directly attached to the carbene carbon. This increases the distance between the substituent and the site of negative charge development at the transition state, thereby strongly reducing the contribution of transition state stabilization to the $\rho(k_1)$ value, assuming a comparable degree of bond formation at the transition state. The fact that the $\rho(k_1)$ value (1.15) is as large as it is and larger than for most reactions where the leaving group is an alkylthio group suggests that here, too, the π -donor effect plays a dominant role. However, the fact that the substituents are on the aryloxy group leads to a somewhat different situation regarding the influence of the π -donor effect. The oxygen in **7**



is less basic than that in **6**, which should reduce its π -donor strength and hence the stabilization of the carbene complex. On the other hand, the closer proximity of the substituents to the π -donor atom in **7** should enhance the *substituent effect* on the π -donor effect. The overall result appears to be a positive contribution to the $\rho(k_1)$ values.

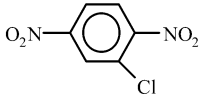
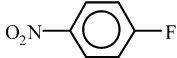
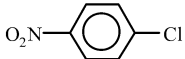
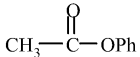
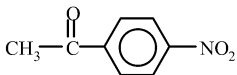
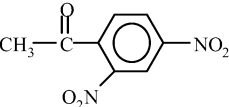
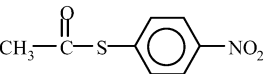
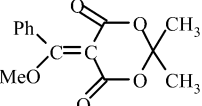
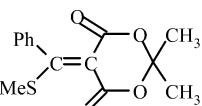
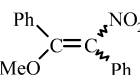
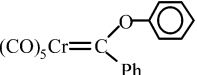
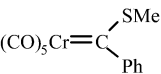
Comparison with Other Reactions. Irrespective of the precise breakdown of $\beta_{\text{nuc}}(k_1)$ into β'_{nuc} and β_{d} , it is reasonable to conclude that C–S bond formation in the reactions of thiolate ions with Fischer carbene complexes has made very little progress at the transition state. How do these $\beta_{\text{nuc}}(k_1)$ values compare with those for the attachment of thiolate ions to other electrophiles such as esters, aromatic compounds, and vinylic substrates? Table 4 summarizes some representative $\beta_{\text{nuc}}(k_1)$ values. The table includes rate constants for the reaction with thiophenoxide ion; these rate constants provide a crude measure of the relative reactivities of the various electrophiles although they do not allow a distinction to be made between cases where k_1 is high mainly because of a large thermodynamic driving force (large K_1) and cases where k_1 is high mainly because of a low Marcus intrinsic barrier or high intrinsic rate constant.³⁷

The range of these $\beta_{\text{nuc}}(k_1)$ values from -0.30 to 0.65 is remarkably large. As is the case for the comparison of $\beta_{\text{nuc}}(k_1)$ values for the reactions within the family of carbene complexes (Table 2), there is no clear correlation between $\beta_{\text{nuc}}(k_1)$ and the reactivity of the electrophiles. For example, within the ester

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(37) The Marcus intrinsic barrier (intrinsic rate constant) is the barrier for a reaction without thermodynamic driving force, i.e., $\Delta G^\circ = 0$ (the rate constant when the equilibrium constant is unity).^{38,39}

TABLE 4. Representative $\beta_{\text{nuc}}(k_1)$ Values for the Attachment of Thiolate Ions to Electrophiles

Electrophile	Solvent (temp.)	$\beta_{\text{nuc}}(k_1)$	$k_1(\text{PhS}^-)$ $\text{M}^{-1} \text{s}^{-1}$	Ref.
	95% EtOH/5% H ₂ O (25°C)	0.65	1.90×10^2	a
	MeOH (50°C)	0.52	2.2×10^{-3}	b
	MeOH (50°C)	0.48	3.3×10^{-4}	b
	H ₂ O (25°C)	0.27	$6.0 \times 10^{-3} \text{ g}$	c
	H ₂ O (25°C)	0.27	3.57×10^{-1}	c
	H ₂ O (25°C)	0.27	ca. 1.7×10^1	c
	H ₂ O (25°C)	0.27	3.60×10^1	c
	50% DMSO-50% H ₂ O (20°C)	0.22	$1.0 \times 10^1 \text{ g}$	d
	50% DMSO-50% H ₂ O (20°C)	0.19	$2.3 \times 10^2 \text{ g}$	e
	50% DMSO-50% H ₂ O (20°C)	0.11	$1.7 \times 10^2 \text{ g}$	f
	50% MeCN-50% H ₂ O (25°C)	-0.18	2.06×10^4	h
	50% MeCN-50% H ₂ O (25°C)	-0.30	$1.0 \times 10^3 \text{ g}$	i

^a Crampton, M. R.; Willison, M. J. *J. Chem. Soc., Perkin Trans. 2* **1974**, 238. ^b Bartoli, G.; Di Nunno, L.; Forlani, L.; Todesco, P. E. *Int. J. Sulfur Chem., C* **1971**, 6, 77. ^c Reference 30. ^d Bernasconi, C. F.; Ketner, R. J.; Chen, X.; Rappoport, Z. *J. Am. Chem. Soc.* **1998**, 120, 7461. ^e Bernasconi, C. F.; Ketner, R. J.; Chen, X.; Rappoport, Z. *Can. J. Chem.* **1999**, 77, 584. ^f Bernasconi, C. F.; Fassberg, J.; Killion, R. B., Jr.; Rappoport, Z. *J. Am. Chem. Soc.* **1990**, 112, 3169. ^g Extrapolated value. ^h This work. ⁱ Reference 20.

family, $\beta_{\text{nuc}}(k_1)$ is constant (0.27) despite a reactivity range of 4 orders of magnitude. Furthermore, the esters as a group are the least reactive electrophiles except for *p*-nitrofluoro and *p*-nitrochlorobenzene yet the $\beta_{\text{nuc}}(k_1)$ values are close to the

midrange. On the other hand, the reactivity of the benzyldiene Meldrum's acid derivatives is quite comparable to that of the respective carbene complexes but the $\beta_{\text{nuc}}(k_1)$ values are much smaller for the latter.

One factor that does seem to play a role in the trend of the $\beta_{\text{nuc}}(k_1)$ values is steric crowding at the transition state. This crowding is particularly severe in the reactions of the carbene complexes due to the large size of the $(\text{CO})_5\text{Cr}$ group;^{20,40} it is also quite considerable in the reactions of the benzyldiene Meldrum's acid derivatives.⁴¹ It appears then that the crowding leads to transition states in which C–S bond formation has made less progress in order to avoid excessive steric strain. However, what is still lacking is a comprehensive theory that encompasses all possible factors that contribute to the degree of bond formation at the transition state of nucleophilic attachment reactions.

Conclusions

(1) The reaction of thiolate ions with the Fischer-type carbene complexes **4-Cr-X** is stepwise (eq 5) as evidenced by the sharp break in the Brønsted plots, indicating a change from rate-limiting leaving group expulsion (k_2) at low $\text{p}K_{\text{a}}^{\text{RSH}}$ to rate-limiting nucleophilic attachment (k_1) at high $\text{p}K_{\text{a}}^{\text{RSH}}$.

(2) The fact that the break in the Brønsted plots where $k_2 = k_{-1}$ occurs at a $\text{p}K_{\text{a}}^{\text{RSH}}$ value (~ 8.0) that is much lower than the $\text{p}K_{\text{a}}^{\text{ArOH}}$ of the aryloxy leaving groups means that the aryloxide ions are much better leaving groups than the thiolate ions of comparable basicities. However, this conclusion does not necessarily apply to other reaction systems such as, e.g., eq 9.

(3) The $\beta_{\text{nuc}}(k_1)$ values for the three carbene complexes are around -0.2 . The negative values result from a combination of minimal progress of bond formation at the transition state and the requirement for partial desolvation of the thiolate ion before it enters the transition state. The $\beta_{\text{nuc}}(k_1)$ values for the reactions of aryloxide ions with **4-Cr-NO₂** are even more negative than those for the reactions of thiolate ions with **4-Cr-X**. This is probably the result of the stronger solvation of the aryloxide ions, which makes their partial desolvation energetically more demanding.

(4) The Hammett $\rho(k_1)$ values are independent of the thiolate ion (average 1.15). This implies a $\text{p}_{\text{xy}} \approx 0$ and is consistent with the $\beta_{\text{nuc}}(k_1)$ values being independent of the X-substituent.

(5) The main factor responsible for the positive ρ values is the increase in the reactivity of **4-Cr-X** with electron-withdrawing substituents, which reduces the stabilization of the carbene complex by the π -donor effect of the oxygen atom. Transition state stabilization plays a minor role due to the large distance of the substituent from the site of negative charge development.

(6) In comparing $\beta_{\text{nuc}}(k_1)$ values for the reaction of thiolate ions with other unsaturated electrophiles no clear correlation with reactivity exists. However, it appears that steric crowding

at the transition state is a factor in retarding the C–S bond formation at the transition state and lowering $\beta_{\text{nuc}}(k_1)$.

Experimental Section

Materials. The carbene complexes **4-Cr-H** and **4-Cr-NO₂** were available from a previous study²¹ while **4-Cr-Me** was prepared as described by Pulley et al.⁴² and identified by NMR (500 MHz, CDCl_3) as follows: ^1H NMR δ 2.44 (3H, s), 7.11–7.44 (9H, Ph and OC_6H_4); ^{13}C NMR δ 121.3, 124.8, 128.0, 130.2, 137.6, 154.7, 157.8 (Ph and OC_6H_4), 215.4 (cis CO), 225.1 (trans CO), 351.7 (C=). Thiols were obtained from commercial vendors in the highest available purity and distilled under argon prior to use. KOH solutions were prepared from DILUT-IT analytical concentrates (J. T. Baker). ACS high-purity HPLC acetonitrile was used without purification. Ultrapure water was obtained from a Millipore MILLI-Q Plus water system.

Kinetic Experiments. All kinetic experiments were conducted in 50% MeCN–50% water (v/v) at 25 °C. The ionic strength was maintained at 0.1 M with KCl except for the reactions with $\text{C}_6\text{F}_5\text{S}^-$ where the ionic strength was 0.5 M because the low reactivity of this thiolate ion required the use of higher concentrations. All rates were measured in a stopped-flow spectrophotometer. In most cases the reactions were initiated by mixing equal volumes of an acetonitrile solution of the carbene complex with an aqueous solution of the thiolate buffer. In this way hydrolysis of the carbene complex prior to its reaction with the thiolate ion could be avoided. For the reactions with $3,4\text{-Cl}_2\text{C}_6\text{H}_3\text{S}^-$ and $\text{C}_6\text{F}_5\text{S}^-$ the reactions were initiated by mixing equal volumes of 50% aqueous acetonitrile solutions of carbene complex and thiolate buffer because of the relatively low solubility of the respective thiols in water. Since these buffer reactions were conducted at low pH hydrolysis was minimal. Special caution was required for the preparation of the aromatic thiolate ion buffers due to their facile oxidation. They were prepared by injecting the freshly distilled thiol into the appropriate KOH solution that had been degassed for 1 h in an ultrasonic bath while under a stream of argon bubbling through the solution. Transfer into the stopped-flow syringe was carried out under argon.

Rates were monitored at 390 nm for **4-Cr-Me** and **4-Cr-H** and at 400 nm for **4-Cr-NO₂**. Typical substrate concentrations were $3\text{--}5 \times 10^{-5}$ M while thiol and thiolate concentrations were always in large excess over the substrate. All pH measurements were carried out on an Orion 611 pH meter equipped with a glass electrode and a Sure-Flow (Corning) reference electrode and calibrated with standard aqueous buffers. The pH in 50% MeCN–50% water (v/v) was determined according to Allen and Tidwell.⁴³ The pH of the reaction solutions for the stopped-flow runs was measured in mock-mixing experiments that simulated the kinetic runs. The $\text{p}K_{\text{a}}$ values of the thiols were determined by measuring the pH of 1:1 or 9:1 buffer solutions under the reaction conditions.

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