

Physical Organic Chemistry of Transition Metal Carbene Complexes. 16.¹ Reactions of (CO)₅M=C(OR)Ph (M = Cr or W; R = Me or Et) with Thiolate Ions in Aqueous Acetonitrile. Complete Kinetic Dissection of the Two-Step Mechanism

Claude F. Bernasconi,* Kevin W. Kittredge, and Francis X. Flores

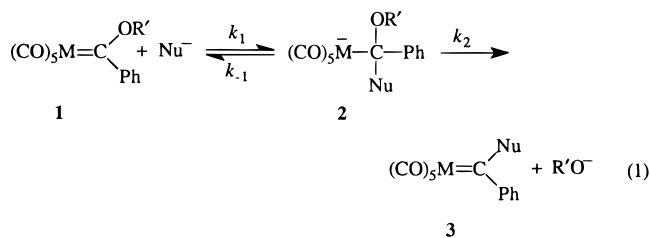
Contribution from the Department of Chemistry and Biochemistry, University of California, Santa Cruz, California 95064

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Abstract: A kinetic study of the reactions of (CO)₅M=C(OR')Ph (**1a**, M = Cr, R' = Me; **1b**, M = W, R' = Me; **1c**, M = Cr, R' = Et; **1d**, M = W, R' = Et) with n-PrS⁻, HOCH₂CH₂S⁻, MeO₂CCH₂CH₂S⁻, and MeO₂CCH₂S⁻ in 50% MeCN–50% water (v/v) at 25 °C is reported. At low [RS⁻] and relatively low pH the reaction leads to the nucleophilic substitution products (CO)₅M=C(SR)Ph without accumulation of any intermediate. At high [RS⁻] and high pH formation of a tetrahedral intermediate, (CO)₅M̄C(OR')(SR)Ph, is observed. Upon addition of acid the intermediate is converted into the substitution product. For the reactions of most thiolate ions a detailed kinetic analysis allowed the determination of the rate constants for nucleophilic attack on the carbene complexes (*k*₁) and its reverse (*k*₋₁), the equilibrium constant for nucleophilic addition (*K*₁ = *k*₁/*k*₋₁), and the rate constants for alkoxide ion departure from the respective intermediates catalyzed by H⁺ (*k*₂^H) and *N*-methylmorpholinium ion (*k*₂^{BH}). The dependence of these rate and equilibrium constants on the metal, the leaving group, and the thiolate ion and comparisons with reactions of thiolate ions with other electrophiles provide insights into the transition state structure, the resonance effect of the (CO)₅M moieties, the requirements for partial desolvation of the nucleophile prior to entering the transition state, and transition state imbalances.

Introduction

In the presence of bases or nucleophiles, transition metal carbene complexes of the Fischer type display reactivity patterns that are similar to those of the isolobal carboxylic esters.^{2,3} A prominent example is the substitution of an alkoxy group by nucleophiles. This process is commonly assumed to involve the two-step mechanism shown in eq 1. Such reactions have been



documented with OH⁻,⁴ water,^{4b} amines,^{2,5} thiolate ions,^{2,6} carbanions,^{2,7} and other nucleophiles.^{2,8}

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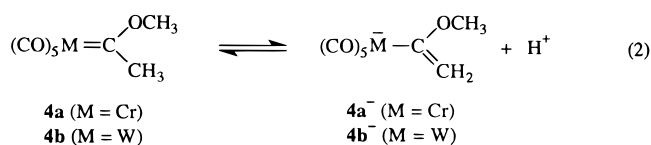
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A major difference between the Fischer carbene complexes and the carboxylic esters is the much higher reactivity of the former. The enhanced reactivity can be mainly attributed to much stronger stabilization of the negative charge in **2** by the (CO)₅M moiety compared to the stabilization of the charge by oxygen in the corresponding ester tetrahedral intermediate. An approximate measure of this increased stabilization can be derived from a comparison of the p*K*_a value of **4a** (12.5)⁹ with



that of ethyl acetate (26.5).¹⁰ Recently it was shown that in the reaction of **1a** and **1b** with MeO⁻ in methanol this enhanced

(6) (a) Fischer, E. O.; Leupold, M.; Kreiter, C. G.; Müller, J. *Chem. Ber.* **1972**, *105*, 150. (b) Lam, C. T.; Senoff, C. V.; Ward, J. E. H. *J. Organomet. Chem.* **1974**, *70*, 273. (c) Aumann, R.; Schröder, J. *Chem. Ber.* **1990**, *123*, 2053.

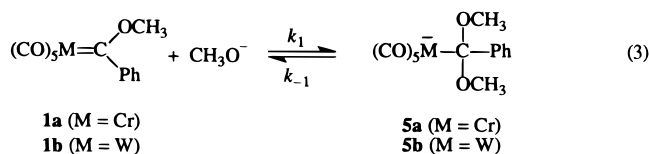
(7) (a) Fischer, E. O.; Riedmüller, S. *Chem. Ber.* **1976**, *109*, 3358. (b) Fischer, E. O.; Held, W.; Kreissl, F. R. *Chem. Ber.* **1977**, *110*, 3842. (c) Burkhardt, T. J.; Casey, C. P. *J. Am. Chem. Soc.* **1973**, *95*, 5833. (d) Fischer, E. O.; Held, F. R.; Kreissl, F. R.; Frank, A.; Hattner, G. *Chem. Ber.* **1977**, *110*, 656. (e) Casey, C. P.; Burkhardt, T. J.; Bunnell, C. A.; Calabrese, J. C. *J. Am. Chem. Soc.* **1977**, *99*, 2127.

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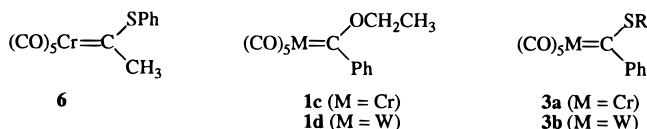
(10) Amyes, T. L.; Richard, J. P. *J. Am. Chem. Soc.* **1996**, *118*, 3129.

stabilization is sufficient to render the equilibrium for intermediate formation (eq 3) favorable at high methoxide ion concentrations.¹¹ This allowed a spectroscopic detection of **5a** and **5b**

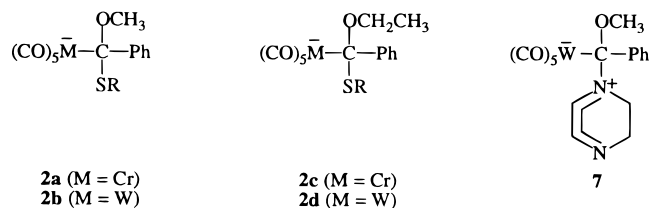


and a determination of the rate constants (k_1 and k_{-1}) for eq 3 as well as the equilibrium constants $K_1 = k_1/k_{-1}$.

Based on these results it seemed likely that in a "real" substitution reaction, i.e., one where the products are different from the reactants, the corresponding intermediate may also be directly observable, provided sufficiently strong nucleophiles are used. Thiolate ions appeared to be among the most promising nucleophiles for two reasons. (1) They are very reactive and have recently led to the successful observation of intermediates in nucleophilic vinylic substitution reactions.¹² (2) Based on a study of the reaction of **4a** with NaSPh in methanol/benzene by Lam *et al.*,^{6b} there is a strong indication that the corresponding intermediate indeed accumulates to detectable levels. Specifically, these authors observed that the reaction leads to an unidentified species that is quite stable but, upon treatment with HCl, yields the substitution product, **6**.



In this paper we report that the reactions of **1a**, **1b**, as well as **1c** and **1d** with a series of alkanethiolate ions ($n\text{-PrS}^-$, $\text{HOCH}_2\text{CH}_2\text{S}^-$, $\text{MeO}_2\text{CCH}_2\text{CH}_2\text{S}^-$, $\text{MeO}_2\text{CCH}_2\text{S}^-$) in 50% MeCN–50% water (v/v) lead to substitution with spectroscopically observable intermediates, **2a–d**. A detailed kinetic analysis is presented that allows the determination of the rate constants of the various steps in eq 1. A preliminary report of some of our results has appeared earlier.¹³



Results

General Features. In the presence of low thiolate ion concentrations at a pH below the $\text{p}K_a^{\text{RSH}}$ of the thiol a clean conversion of **1a**, **1b**, **1c**, and **1d** to the corresponding substitution products **3a** and **3b** is observed. This is illustrated in Figure 1 for the reaction of **1b** with $\text{MeO}_2\text{CCH}_2\text{CH}_2\text{S}^-$ in an *N*-methylmorpholine buffer at pH 7.56 ($\text{p}K_a^{\text{RSH}} = 10.69$, $[\text{RSH}] =$

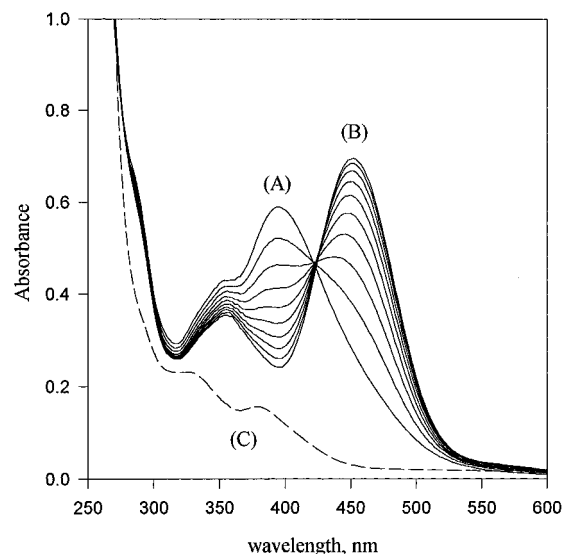


Figure 1. Conversion of 5×10^{-5} M $(\text{CO})_5\text{W}=\text{C}(\text{OMe})\text{Ph}$ (spectrum A, λ_{max} 396 nm) to $(\text{CO})_5\text{W}=\text{C}(\text{SCH}_2\text{CH}_2\text{CO}_2\text{Me})\text{Ph}$ (spectrum B, λ_{max} 452 nm) in the presence of 7.94×10^{-7} M $\text{MeO}_2\text{CCH}_2\text{CH}_2\text{S}^-$ and 10^{-3} M $\text{MeO}_2\text{CCH}_2\text{CH}_2\text{SH}$ in an *N*-methylmorpholine buffer at pH 7.56. Spectra taken every 10 s for 150 s. Spectrum C corresponds to the intermediate (**2b** with $\text{R} = \text{MeO}_2\text{CCH}_2\text{CH}_2$) generated in the presence of 10^{-3} M $\text{MeO}_2\text{CCH}_2\text{CH}_2\text{S}^-$ at pH 10.69.

10^{-3} M, $[\text{RS}^-] = 7.94 \times 10^{-7}$ M). The figure shows a sharp isosbestic point at 422 nm, indicating that there is no accumulation of an intermediate to detectable levels. The behavior seen in Figure 1 is representative for the reactions of all four Fischer carbene complexes **1a–d** with $n\text{-PrS}^-$, $\text{HOCH}_2\text{CH}_2\text{S}^-$, $\text{MeO}_2\text{CCH}_2\text{CH}_2\text{S}^-$, and $\text{MeO}_2\text{CCH}_2\text{S}^-$.¹⁴ For the reactions of **1b** and **1c** with $n\text{-PrS}^-$ the identity of the products was confirmed by comparison with independently synthesized samples.

A different situation arises in the presence of higher thiolate ion concentrations at a pH close to the $\text{p}K_a^{\text{RSH}}$ of the thiol. Here the carbene complex is rapidly converted to a new species whose spectrum (dashed line in Figure 1) resembles neither that of the starting material nor that of **3a** or **3b**, respectively. This species is stable for a few minutes but, upon acidification yields the substitution product. We conclude the new species is the intermediate **2**, specifically **2b** (with $\text{R} = \text{MeO}_2\text{CCH}_2\text{CH}_2$) in Figure 1.¹⁴ Its UV/vis spectrum resembles that of **5b**¹¹ and of **7**.¹¹ IR spectra of **2a** and **2b** ($\text{R} = \text{CH}_3\text{CH}_2\text{CH}_2$) show the characteristic shifts of the CO stretching frequencies compared to those in the starting materials: for **1b** \rightarrow **2b** the bands at 2035 (s), 1911 (w), and 1845 cm^{-1} (m), respectively, while for **1c** \rightarrow **2c** the bands at 2069 (s), 1993 (m), and 1940 cm^{-1} (w) are replaced by bands at 2045 (s), 1905 (s), and 1848 cm^{-1} (m), respectively.

NMR spectra of the intermediates were more difficult to obtain, due to decomposition. The most stable intermediate was **2b** with $\text{R} = n\text{-Pr}$, which yielded relatively clean ^1H and ^{13}C NMR spectra. The most characteristic changes for the conversion of **1b** to **2b** are in the chemical shifts of the MeO groups (^1H NMR: 4.47 ppm in **1b**, 4.04 ppm in **2b**; ^{13}C NMR: 71.4 ppm in **1b**, 49.0 ppm in **2b**) and the carbene carbon (^{13}C NMR: 322.1 ppm in **1b**, 52.4 ppm in **2b**). For more details see the Experimental Section.

Judging from the UV/vis spectra, the reactions of all four carbene complexes with $n\text{-PrS}^-$, $\text{HOCH}_2\text{CH}_2\text{S}^-$, and MeO_2C

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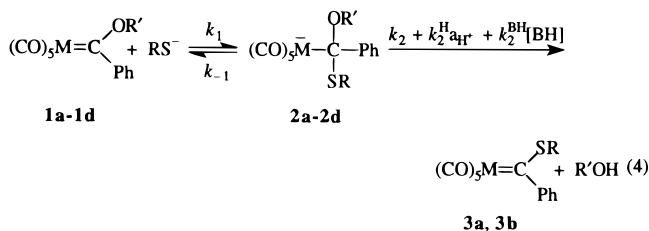
(12) (a) Bernasconi, C. F.; Fassberg, J.; Killion, R. B., Jr.; Rappoport, Z. *J. Am. Chem. Soc.* **1989**, *111*, 6862. (b) Bernasconi, C. F.; Fassberg, J.; Killion, R. B., Jr.; Rappoport, Z. *J. Am. Chem. Soc.* **1990**, *112*, 3169. (c) Bernasconi, C. F.; Ketner, R. J.; Chen, X.; Rappoport, Z. *J. Am. Chem. Soc.* **1998**, *120*, 7461. (d) Bernasconi, C. F.; Ketner, R. J.; Chen, X.; Rappoport, Z. *Can. J. Chem.* **1999**, *77*, 584.

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(14) For spectra of the reaction of **1a** with $\text{MeO}_2\text{CCH}_2\text{CH}_2\text{S}^-$ see ref 13.

CCH₂CH₂S⁻ show similar behavior. However, in the reaction of **1b** with MeO₂CCH₂S⁻ the absorption spectra of intermediate and product suggest contamination by unidentified byproducts while for the reactions of **1a**, **1c**, and **1d** with MeO₂CCH₂S⁻ acidification of the "intermediate" yielded very little if any substitution products, as judged from the absorption spectra of the product solution.

The observations presented above indicate that the reactions of thiolate ions with **1a–d** can be described by eq 4. At high pH and high [RS⁻] the first step is fast and the equilibrium favors the intermediate, while product formation is slow. In fact,



spontaneous conversion of the intermediate to **3a** or **3b** (note that **3a**, the Cr derivative, is the product of both **1a** and **1c**, respectively, while **3b**, the W derivative, is the product of both **1b** and **1d**, respectively) by the k_2 step is so slow that product formation only occurs after addition of acid, indicating hydronium ion and/or buffer acid catalyzed ($k_2^{\text{H}}a_{\text{H}^+}$ and $k_2^{\text{BH}}[\text{BH}]$) alkoxide ion departure. In the absence of acid the intermediate does not lead to **3a** or **3b** but slowly decomposes into unidentified byproducts. For the reactions with MeO₂CCH₂S⁻ decomposition of the intermediate, if it is formed at all (more on this below), occurs quite rapidly and precludes product formation.

At low [RS⁻] and low pH values, **2a–d** turn into steady-state intermediates because the equilibrium of the first step is no longer favorable and a_{H^+} and/or [BH] are high enough to ensure rapid product formation via the $k_2^{\text{H}}a_{\text{H}^+}$ and/or $k_2^{\text{BH}}[\text{BH}]$ pathways. From the fact that product formation is observed even with MeO₂CCH₂S⁻ as nucleophile we conclude that the intermediate is generated under these conditions and that at low pH its acid-catalyzed conversion to products is faster than its decomposition.

Kinetics. All kinetic experiments were run under pseudo-first-order conditions with [RS⁻] held constant either by being present in large excess over the substrate or, at pH $\ll pK_a^{\text{RSH}}$, by having a large excess of RSH over the substrate. The temperature was 25 °C throughout and the ionic strength was maintained at 0.1 M with KCl. Three types of kinetic experiments were performed.

A. Formation of Intermediate. Rates of formation of the intermediate were measured by monitoring the loss of carbene complex in a stopped-flow spectrophotometer. Pseudo-first-order rate constants determined between 5×10^{-4} and 5×10^{-3} M RS⁻ at pH = pK_a^{RSH} showed a linear dependence on [RS⁻] according to eq 5 (Figure 2) from which k_1 (Table 1) could be obtained. The intercepts of the plots of k_{obsd} vs [RS⁻] were too small to yield accurate k_{-1} values.

$$k_{\text{obsd}} = k_1[\text{RS}^-] + k_{-1} \quad (5)$$

Interestingly, the reactions of **1a–d** with MeO₂CCH₂S⁻ showed the same kinetic behavior as those with the other thiolate ions, despite the fact that no clean spectra of the intermediates derived from MeO₂CCH₂S⁻ could be obtained (*vide supra*). This

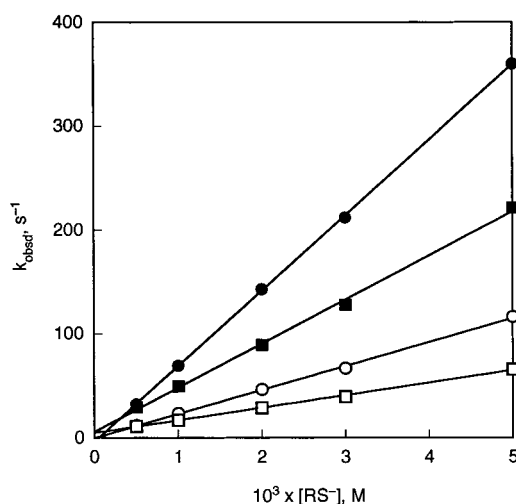


Figure 2. Reactions of **1a–d** with MeO₂CCH₂CH₂S⁻ at pH 10.69 leading to the corresponding intermediates. Plots according to eq 5: (□) **1c**; (■) **1d**; (○) **1a**; and (●) **1b**.

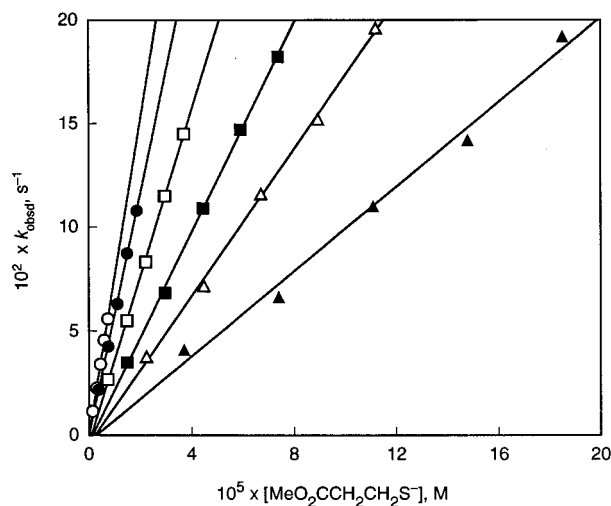


Figure 3. Reaction of **1c** with MeO₂CCH₂CH₂S⁻ in various *N*-methylmorpholine buffers leading to the substitution product **3c** under steady state conditions: (○) pH 6.86; (●) pH 7.26; (□) pH 7.56; (■) pH 7.85; (△) pH 8.04; and (▲) pH 8.26.

suggests that nucleophilic addition *does* occur but that the intermediate decomposes rapidly.

B. Steady-State Kinetics. Rates were determined by monitoring product formation by conventional spectrophotometry. For a reaction with a given thiolate ion k_{obsd} was determined in buffered solutions at 7–9 different pH values. In the reactions with *n*-PrS⁻ the pH range was from 8.56 to 10.56 maintained by triethylamine buffers, in the reactions with HOCH₂CH₂S⁻ and MeO₂CCH₂CH₂S⁻ the pH range was from 6.76 to 8.26 maintained by *N*-methylmorpholine buffers, and in the reactions with MeO₂CCH₂S⁻ the pH range was from 4.93 to 6.93 maintained by acetate buffers. Figure 3 which shows plots of k_{obsd} vs [RS⁻] for the reaction of **1c** with MeO₂CCH₂CH₂S⁻ is representative. All plots are linear with intercepts that are either indistinguishable from zero or quite small; small intercepts on the order of 5×10^{-4} s⁻¹ for **1c** and **1d** and 3×10^{-3} s⁻¹ for **1a** and **1b** are expected due to hydrolysis.¹⁵ The slopes of the plots increase with decreasing pH, demonstrating the effect of

(15) Bernasconi, C. F.; Flores, F. X.; Kittredge, K. W. *J. Am. Chem. Soc.* **1997**, *119*, 2103.

Table 1. Summary of Rate and Equilibrium Constants

| | $\text{CH}_3\text{CH}_2\text{CH}_2\text{S}^-$ $\text{p}K_a^{\text{RSH}} = 11.94 \pm 0.04$ | $\text{HOCH}_2\text{CH}_2\text{S}^-$ $\text{p}K_a^{\text{RSH}} = 10.79 \pm 0.03$ | $\text{MeO}_2\text{CCH}_2\text{CH}_2\text{S}^-$ $\text{p}K_a^{\text{RSH}} = 10.69 \pm 0.02$ | $\text{MeO}_2\text{CCH}_2\text{S}^-$ $\text{p}K_a^{\text{RSH}} = 9.45 \pm 0.03$ | |
|--|--|---|--|--|--|
| | | (CO) ₅ Cr=C(OMe)Ph (1a) | | | |
| $k_1, \text{M}^{-1} \text{s}^{-1}$ (eq 5) | $(1.34 \pm 0.07) \times 10^4$ | $(2.25 \pm 0.10) \times 10^4$ | $(2.30 \pm 0.04) \times 10^4$ | $(6.76 \pm 0.20) \times 10^4$ | |
| $k_1, \text{M}^{-1} \text{s}^{-1}$ (eq 8) | <i>a</i> | $(2.23 \pm 0.29) \times 10^4$ | $(1.72 \pm 0.68) \times 10^4$ | $(7.35 \pm 0.67) \times 10^4$ | |
| $k_2^{\text{H}}/k_{-1}, \text{M}^{-1}$ | $(4.29 \pm 0.62) \times 10^8$ | $(6.98 \pm 0.87) \times 10^8$ | $(3.04 \pm 0.24) \times 10^7$ | $(2.51 \pm 0.32) \times 10^6$ | |
| $k_2^{\text{H}}, \text{M}^{-1} \text{s}^{-1}$ | $(5.39 \pm 0.11) \times 10^8$ | $(3.50 \pm 0.92) \times 10^8$ | $(1.99 \pm 0.02) \times 10^8$ | | |
| k_{-1}, s^{-1} | 1.26 ± 0.21 | 5.01 ± 1.93 | 6.55 ± 0.58 | | |
| K_1, M^{-1} | $(1.06 \pm 0.23) \times 10^4$ | $(4.49 \pm 1.93) \times 10^3$ | $(3.51 \pm 0.35) \times 10^3$ | | |
| $k_2^{\text{BH}}, \text{M}^{-1} \text{s}^{-1 b}$ | | $(1.39 \pm 0.61) \times 10^2$ | $(6.88 \pm 0.80) \times 10^1$ | | |
| | | (CO) ₅ W=C(OMe)Ph (1b) | | | |
| $k_1, \text{M}^{-1} \text{s}^{-1}$ (eq 5) | $(4.21 \pm 0.25) \times 10^4$ | $(6.52 \pm 0.21) \times 10^4$ | $(7.26 \pm 0.05) \times 10^4$ | $(1.73 \pm 0.14) \times 10^5$ | |
| $k_1, \text{M}^{-1} \text{s}^{-1}$ (eq 8) | <i>a</i> | $(6.29 \pm 0.59) \times 10^4$ | $(6.06 \pm 0.59) \times 10^4$ | $(2.39 \pm 0.14) \times 10^5$ | |
| $k_2^{\text{H}}/k_{-1}, \text{M}^{-1}$ | $(1.83 \pm 0.28) \times 10^8$ | $(2.69 \pm 0.45) \times 10^7$ | $(1.26 \pm 0.38) \times 10^7$ | $(1.38 \pm 0.12) \times 10^6$ | |
| $k_2^{\text{H}}, \text{M}^{-1} \text{s}^{-1}$ | $(5.69 \pm 0.25) \times 10^8$ | $(3.76 \pm 0.98) \times 10^8$ | $(2.05 \pm 0.03) \times 10^8$ | | |
| k_{-1}, s^{-1} | 3.11 ± 0.61 | 14.0 ± 5.9 | 16.3 ± 5.8 | | |
| K_1, M^{-1} | $(1.35 \pm 0.35) \times 10^4$ | $(4.66 \pm 2.10) \times 10^3$ | $(4.45 \pm 1.44) \times 10^3$ | | |
| $k_2^{\text{BH}}, \text{M}^{-1} \text{s}^{-1 b}$ | | $(2.17 \pm 1.02) \times 10^2$ | $(1.46 \pm 0.48) \times 10^2$ | | |
| | | (CO) ₅ Cr=C(OEt)Ph (1c) | | | |
| $k_1, \text{M}^{-1} \text{s}^{-1}$ (eq 5) | $(7.05 \pm 0.37) \times 10^3$ | $(1.20 \pm 0.06) \times 10^4$ | $(1.20 \pm 0.02) \times 10^4$ | $(3.43 \pm 0.18) \times 10^4$ | |
| $k_1, \text{M}^{-1} \text{s}^{-1}$ (eq 8) | <i>a</i> | $(1.30 \pm 0.08) \times 10^4$ | $(1.38 \pm 0.04) \times 10^4$ | $(3.74 \pm 0.32) \times 10^4$ | |
| $k_2^{\text{H}}/k_{-1}, \text{M}^{-1}$ | $(3.06 \pm 0.29) \times 10^8$ | $(2.94 \pm 0.42) \times 10^7$ | $(1.70 \pm 0.35) \times 10^7$ | $(1.38 \pm 0.12) \times 10^6$ | |
| $k_2^{\text{H}}, \text{M}^{-1} \text{s}^{-1}$ | $(4.23 \pm 0.09) \times 10^8$ | $(2.67 \pm 0.12) \times 10^8$ | $(1.68 \pm 0.02) \times 10^8$ | | |
| k_{-1}, s^{-1} | 1.38 ± 0.16 | 9.08 ± 1.72 | 9.88 ± 2.15 | | |
| K_1, M^{-1} | $(5.11 \pm 0.86) \times 10^3$ | $(1.32 \pm 0.32) \times 10^3$ | $(1.21 \pm 0.29) \times 10^3$ | | |
| $k_2^{\text{BH}}, \text{M}^{-1} \text{s}^{-1 b}$ | | $(8.40 \pm 2.18) \times 10^1$ | $(4.33 \pm 1.10) \times 10^1$ | | |
| | | (CO) ₅ W=C(OEt)Ph (1d) | | | |
| $k_1, \text{M}^{-1} \text{s}^{-1}$ (eq 5) | $(2.33 \pm 0.11) \times 10^4$ | $(4.04 \pm 0.15) \times 10^4$ | $(4.25 \pm 0.10) \times 10^4$ | $(1.05 \pm 0.07) \times 10^5$ | |
| $k_1, \text{M}^{-1} \text{s}^{-1}$ (eq 8) | <i>a</i> | $(3.62 \pm 0.45) \times 10^4$ | $(2.61 \pm 0.53) \times 10^4$ | $(0.87 \pm 0.01) \times 10^5$ | |
| $k_2^{\text{H}}/k_{-1}, \text{M}^{-1}$ | $(1.72 \pm 0.15) \times 10^8$ | $(1.28 \pm 0.25) \times 10^7$ | $(6.96 \pm 0.27) \times 10^6$ | $(6.71 \pm 0.25) \times 10^5$ | |
| $k_2^{\text{H}}, \text{M}^{-1} \text{s}^{-1}$ | $(5.12 \pm 0.13) \times 10^8$ | $(2.65 \pm 0.09) \times 10^8$ | $(1.84 \pm 0.09) \times 10^8$ | | |
| k_{-1}, s^{-1} | 2.98 ± 0.33 | 20.7 ± 4.8 | 26.4 ± 2.3 | | |
| K_1, M^{-1} | $(7.82 \pm 1.25) \times 10^3$ | $(1.95 \pm 0.52) \times 10^3$ | $(1.61 \pm 0.18) \times 10^3$ | | |
| $k_2^{\text{BH}}, \text{M}^{-1} \text{s}^{-1 b}$ | | $(9.23 \pm 2.74) \times 10^1$ | $(6.47 \pm 0.91) \times 10^1$ | | |

^a Intercept in plot according to eq 8 is too small for determination of k_1 . ^b BH = *N*-methylmorpholinium ion; k_2^{BH} obtained from the k_2^{H}/k_{-1} ratios (Table 2) and k_{-1} .

acid catalysis on the conversion of the intermediate to products. Applying the steady-state approximation to eq 4 yields eq 6

$$\text{slope} = \frac{k_1(k_2 + k_2^{\text{H}}a_{\text{H}^+} + k_2^{\text{BH}}[\text{BH}])}{k_{-1} + k_2 + k_2^{\text{H}}a_{\text{H}^+} + k_2^{\text{BH}}[\text{BH}]} \quad (6)$$

for the slopes. Equation 6 may be simplified to eq 7

$$\text{slope} \approx \frac{k_1 k_2^{\text{H}} a_{\text{H}^+}}{k_{-1} + k_2^{\text{H}} a_{\text{H}^+}} \quad (7)$$

because independent runs showed that buffer catalysis ($k_2^{\text{BH}}[\text{BH}]$) is negligible compared to H^+ catalysis ($k_2^{\text{H}}a_{\text{H}^+}$) under most conditions of our experiments while the lack of product formation at high pH indicates k_2 for spontaneous leaving group departure to be very small. Inversion plots according to eq 8 are shown in Figure 4 for the reactions of

$$\frac{1}{k_{\text{obsd}}} = \frac{1}{k_1} + \frac{k_{-1}}{k_1 k_2^{\text{H}} a_{\text{H}^+}} \quad (8)$$

1a–d with $\text{HOCH}_2\text{CH}_2\text{S}^-$. Similar inversion plots were obtained with the other thiolate ions. They yield the k_1 and k_2^{H}/k_{-1} values summarized in Table 1. Even though the k_1 values have a relatively large standard error, they are in good agreement

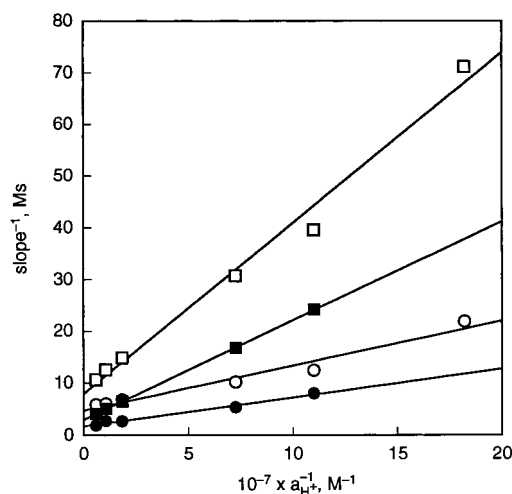


Figure 4. Reactions of **1a–d** with $\text{HOCH}_2\text{CH}_2\text{S}^-$. Plot of $1/k_{\text{obsd}}$ vs $1/a_{\text{H}^+}$ according to eq 8: (□) **1c**; (■) **1d**; (○) **1a**; and (●) **1b**.

with those obtained from the experiments at high pH (eq 5). The latter will be adopted in our subsequent discussion; they are also the values used to calculate k_2^{H}/k_{-1} from the slopes according to eq 8.

A few experiments were conducted where buffer catalysis is not negligible, to provide some representative k_2^{BH}/k_{-1} ratios. The best conditions were for the reactions of **1a–d** with

Table 2. Slopes of Plots of $k_{\text{obsd}}/[\text{RS}^-]$ vs *N*-Methylmorpholinium Concentration at pH 7.56 and k_2^{BH}/k_{-1} Ratios

| | HOCH ₂ CH ₂ S ⁻ | | MeO ₂ CCH ₂ CH ₂ S ⁻ | |
|---|---|---|--|---|
| | slope, ^a M ⁻² s ⁻¹ | k_2^{BH}/k_{-1} , ^b M ⁻¹ | slope, ^a M ⁻² s ⁻¹ | k_2^{BH}/k_{-1} , ^b M ⁻¹ |
| (CO) ₅ Cr=C(OMe)Ph (1a) | $(6.25 \pm 0.03) \times 10^5$ | 27.8 ± 1.5 | $(2.41 \pm 0.03) \times 10^5$ | 10.5 ± 0.3 |
| (CO) ₅ W=C(OMe)Ph (1b) | $(1.01 \pm 0.02) \times 10^6$ | 15.5 ± 0.8 | $(6.48 \pm 0.03) \times 10^5$ | 8.93 ± 0.10 |
| (CO) ₅ Cr=C(OEt)Ph (1c) | $(1.11 \pm 0.02) \times 10^5$ | 9.25 ± 0.66 | $(5.26 \pm 0.02) \times 10^4$ | 4.38 ± 0.13 |
| (CO) ₅ W=C(OEt)Ph (1d) | $(1.80 \pm 0.05) \times 10^5$ | 4.46 ± 0.30 | $(1.04 \pm 0.03) \times 10^5$ | 2.45 ± 0.13 |

^a Slope $\approx k_1 k_2^{\text{BH}}/k_{-1}$ (eq 9). ^b Calculated using k_1 determined via eq 5.

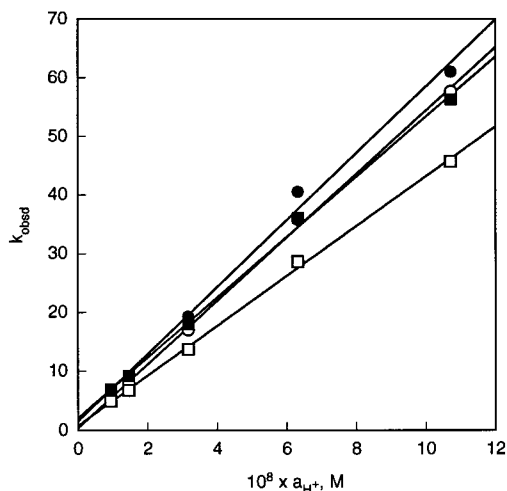


Figure 5. Reactions of **2a–d** ($R = n\text{-Pr}$) with H^+ in *N*-methylmorpholine buffers at constant *N*-methylmorpholinium ion concentration (5×10^{-3} M). Plots according eq 10: (●) **2b**; (○) **2a**, (■) **2d**; and (□) **2c**.

HOCH₂CH₂S⁻ and MeO₂CCH₂CH₂S⁻ in *N*-methylmorpholine buffers at pH 7.56. At this pH the $k_2^{\text{H}}a_{\text{H}^+}$ term is relatively small compared to $k_2^{\text{BH}}[\text{BH}]$ and $k_2^{\text{H}}a_{\text{H}^+} + k_2^{\text{BH}}[\text{BH}] \ll k_{-1}$, ensuring that conversion of the intermediate to products is rate limiting. Plots of $k_{\text{obsd}}/[\text{RS}^-]$ vs $[\text{BH}]$ (not shown) were linear with slopes given by eq 9. These slopes are reported in Table 2 along with the k_2^{BH}/k_{-1} ratios. Control experiments in the absence of thiolate ion showed that the observed catalysis by

$$\text{slope} \approx \frac{k_1 k_2^{\text{BH}}}{k_{-1}} \quad (9)$$

N-methylmorpholine is not due to nucleophilic addition to **1a–b** or base catalysis of hydrolysis of **1a–b** by *N*-methylmorpholine.

C. Reaction of the Intermediate with Acid. The respective intermediates of the reactions of **1a–d** with $n\text{-PrS}^-$, HOCH₂CH₂S⁻, and MeO₂CCH₂CH₂S⁻ were generated in the presence of 10^{-3} M RS^- at $\text{pH} = \text{p}K_{\text{a}}^{\text{RSH}}$; as mentioned earlier, in the reactions with MeO₂CCH₂S⁻ no intermediate could be observed due to rapid decomposition. The solutions containing the intermediate were then mixed with various *N*-methylmorpholine buffers ranging in pH from 6.97 to 8.05 in a stopped-flow spectrophotometer. The conversion of the intermediate to products was monitored at λ_{max} of the products. Plots of k_{obsd} vs a_{H^+} were linear according to eq 10, as shown in Figure 5 for a representative series. The intercepts (k_{-1}) were in general too small to yield a precise k_{-1} value. However, k_{-1} was obtained

$$k_{\text{obsd}} = k_2^{\text{H}}a_{\text{H}^+} + k_{-1} \quad (10)$$

based on k_2^{H} and the k_2^{H}/k_{-1} ratios determined under steady-state conditions (Table 1).

Discussion

The present work reports the first detailed kinetic study of a nucleophilic substitution of Fischer carbene complexes that allowed the direct observation of the tetrahedral intermediate and a complete dissection of the rate constants of various steps of the mechanism. Specifically, rate constants for nucleophilic addition of thiolate ions (k_1) and its reverse (k_{-1}), for hydronium ion catalyzed alkoxide ion expulsion from the intermediate (k_2^{H}), and for general acid-catalyzed alkoxide ion departure by *N*-methylmorpholinium ion (k_2^{BH}) for some selected reactions were obtained. Rate constants for spontaneous conversion of the intermediate to products (k_2) could not be determined, though, because this process is slower than the decomposition of the intermediate into unidentified byproducts. Rate constants for general acid-catalyzed leaving group expulsion by Et_3NH^+ and acetic acid could not be obtained either because the catalytic effect was too small against the background of the $k_2^{\text{H}}a_{\text{H}^+}$ process to yield accurate k_2^{BH} values.

A complete set of k_1 , k_{-1} , and k_2^{H} values was obtained for the reactions of **1a–d** with $n\text{-PrS}^-$, HOCH₂CH₂S⁻, and MeO₂CCH₂CH₂S⁻ (Table 1). For the reactions of **1a–d** with MeO₂CCH₂S⁻ only k_1 and the k_2^{H}/k_{-1} ratio could be determined because the intermediate decomposes too rapidly. The nature of the decomposition reaction is unknown.

The error limits associated with the various parameters reported in Table 1 are standard deviations. For k_1 they are relatively small, typically 3–6%. For k_2^{H} they are also quite small in most cases, typically 2–5%, except for the reactions of **1a** and **1b** with HOCH₂CH₂S⁻ where they are around 26%. These latter standard deviations reflect poor reproducibility of the kinetic results for these two reactions. The standard deviations for the k_2^{H}/k_{-1} ratios are mostly between 12 and 20%. This leads to even larger errors in k_{-1} obtained as $k_2^{\text{H}}/(k_2^{\text{H}}/k_{-1})$ and K_1 obtained as k_1/k_{-1} . However, these experimental uncertainties do not affect the major conclusions to be derived from the various parameters and their dependence on structure.

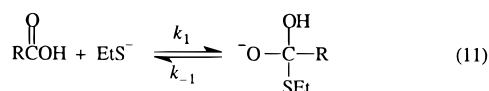
Rate and Equilibrium Constants for Nucleophilic Addition. A. The (CO)₅M Moiety as π -Acceptor. As pointed out by numerous authors,² there is a close formal analogy between the reaction of nucleophiles with Fischer carbene complexes and with carboxylic esters. However, quantitatively there is a large difference in that the equilibrium constants for nucleophilic addition to the carbene complexes are several orders of magnitude larger than for addition to esters. For example, K_1 for MeO^- addition to **1a** or **1b** in methanol was estimated to be 2×10^8 to 10^9 fold larger than for MeO^- addition to methyl benzoate.¹¹ Similarly, thiolate ion addition to **1a** or **1b** is strongly favored over thiolate ion addition to acyl carbon. Based on our K_1 values for $n\text{-PrS}^-$ addition to **1a** and **1b** and on Guthrie's¹⁶ estimate of $K_1 \approx 7.9 \times 10^{-14}$ M⁻¹ for EtS^- addition to acetic acid in water at 25 °C one obtains $K_1(\mathbf{1a})/K_1(\text{CH}_3\text{CO}_2\text{H}) \approx$

1.3×10^{17} and $K_1(\mathbf{1b})/K_1(\text{CH}_3\text{CO}_2\text{H}) \approx 1.7 \times 10^{17}$. These comparisons show even more dramatically that the $(\text{CO})_5\text{M}$ moiety is much more electron withdrawing than the carbonyl oxygen of an ester or a carboxylic acid.¹⁷ This is, in large measure, due to the π -acceptor ability of the $(\text{CO})_5\text{M}$ moiety which, in the adducts, leads to delocalization of the negative charge into the CO ligands.

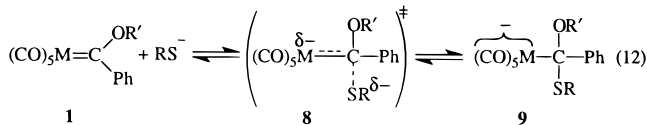
Evidence for this charge delocalization comes from the IR data which show that the CO stretching frequencies decrease substantially upon conversion of **1b** to **2b** or **1c** to **2c**. These frequency shifts are similar to those obtained in the formation of **5a** and **5b**¹¹ and of **7** or similar amine adducts;¹⁸ they indicate a decrease in the C=O double bond character of the CO ligands.

Additional evidence can be based on the well-documented inverse relationship between intrinsic rate constants¹⁹ of carbanion forming reactions and the degree of resonance stabilization of the carbanion. The underlying reason for this inverse relationship is that the development of the resonance effect lags behind bond formation or charge transfer at the transition state²¹ (transition state "imbalance"). According to this notion the intrinsic rate constant for nucleophilic addition to carbene complexes such as **1a–d** should be lower than that for nucleophilic addition to carboxylic acids or esters. This is because in the tetrahedral ester adduct the entire negative charge is localized on one oxygen atom, i.e., there is no resonance stabilization. Comparison of MeO^- addition to **1a** and **1b** in methanol with the same reaction of methyl benzoate and methyltrifluoroacetate indeed showed that the intrinsic rate constant for the carbene complex reactions is about 2 orders of magnitude lower than that for the ester reactions.¹¹ This indicates that the $(\text{CO})_5\text{M}$ moiety is a moderately strong π -acceptor.

A similar conclusion is reached when comparing the reactions of **1a** or **1b** with $n\text{-PrS}^-$ to the reactions of eq 11. By applying



the simplest version of the Marcus equation²² to Guthrie's estimate for K_1 and k_1 ²³ one obtains $\log k_0 \approx 3.5$ for $\text{R} = \text{CH}_3$ and $\log k_0 \approx 5.9$ for $\text{R} = \text{CF}_3$. Applying the same equation to the reaction of **1a** with $n\text{-PrS}^-$ yields $\log k_0 \approx 2.1$. Even though crude, these estimates clearly show that the intrinsic rate constant for the carbene complex reaction is substantially lower than that for the ester reactions,²⁴ just as is the case for MeO^- addition. As to the nature of the imbalance, the situation may be described by eq 12, which shows the charge at the transition state mostly



localized on the metal while in the adduct the charge is mostly

(17) The reasons why these equilibrium constant ratios are so much larger than the corresponding ratios for MeO^- addition will be discussed in section B.

(18) Kreissl, F. R.; Fischer, E. O. *Chem. Ber.* **1974**, *107*, 183.

(19) The intrinsic rate constant of a reaction with forward rate constant k_1 and reverse rate constant k_{-1} is defined as $k_0 = k_1 = k_{-1}$ when $K_1 = k_1/k_{-1} = 1$. The intrinsic rate constant is a purely kinetic measure of the reaction barrier that is not influenced by any thermodynamic driving force.²⁰

(20) Marcus, R. A. *J. Chem. Phys.* **1965**, *43*, 679.

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

(22) $\log k_0 = \log k_1 - 0.5 \log K_1$ ²⁰

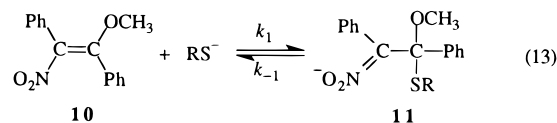
Table 3. Rate and Equilibrium Constants for the Reactions of $\text{MeO}_2\text{CCH}_2\text{CH}_2\text{S}^-$ with **1a** and **10**

| | (CO) ₅ Cr=C(OMe)Ph (1a) | Ph(NO ₂)C=C(OMe)Ph (10) | 1a/10 |
|------------------------------------|--|---|--------------|
| | 50% MeCN–50% H ₂ O ^a | 50% DMSO–50% H ₂ O ^{b,c} | |
| $k_1, \text{M}^{-1} \text{s}^{-1}$ | 2.30×10^4 | 3.60×10^2 | 63.9 |
| k_{-1}, s^{-1} | 6.55 | 8.99×10^{-2} | 72.9 |
| K_1, M^{-1} | 3.51×10^3 | 4.00×10^3 | 0.88 |

^a 25 °C. ^b 20 °C. ^c Reference 12b.

delocalized into the CO ligands, a point emphasized by the bracket symbol in **9**.

Another comparison of interest is that between the thiolate ion addition to **1a–d** with the analogous reaction of β -methoxy- α -nitrostilbene, eq 13.^{12a,b} This comparison is particularly appropriate because the two reactions have similar equilibrium



constants. For example, K_1 for the reaction of **10** with $\text{MeO}_2\text{CCH}_2\text{CH}_2\text{S}^-$ in 50% DMSO–50% water at 20 °C is almost identical to K_1 for the reaction of **1a** with the same nucleophile in 50% MeCN–50% water at 25 °C (Table 3). On the other hand, the *rate* constants in both directions are almost 2 orders of magnitude higher for **1a** than for **10**, indicating that the intrinsic rate¹⁹ constant is higher by the same amount. We conclude that even though the $(\text{CO})_5\text{M}$ moieties are moderately strong π -acceptors, they are not as strong as the nitro group, i.e., the resonance component that contributes to the stabilization of **2a–d** is not as strong as that for **11**. The same conclusion is reached when comparing the intrinsic rate constants for the deprotonation of **4a** or **4b** with those for PhCH_2NO_2 .³

B. Dependence on the Nucleophile. (1) In comparison with MeO^- addition to **1a** and **1b**, the K_1 and k_1 values for thiolate addition are substantially higher despite the much lower proton basicities of the thiolate ions. For example, for **1a** $K_1(n\text{-PrS}^-)/K_1(\text{MeO}^-) = 151$ and $k_1(n\text{-PrS}^-)/k_1(\text{MeO}^-) = 174$, for **1b** $K_1(n\text{-PrS}^-)/K_1(\text{MeO}^-) = 122$ and $k_1(n\text{-PrS}^-)/k_1(\text{MeO}^-) = 226$. This contrasts with $\text{p}K_a = 11.94$ for $n\text{-PrSH}$ vs $\text{p}K_a = 18.31$ for methanol in methanol.²⁵ These comparisons demonstrate the well-known high carbon basicity and high nucleophilicity of sulfur bases which have been mainly attributed to their strong polarizability²⁶ or "softness".²⁷ **1a** and **1b** may be considered to be particularly soft, hence optimizing the favorable soft–soft interactions with thiolate ions and accentuating the unfavorable soft–hard interactions with the hard methoxide ion. An additional factor, particularly important in hydroxylic solvents, is the weaker solvation of thiolate ions compared to MeO^- .

(2) Another observation that may be understood in terms of soft–soft/soft–hard/hard–hard interactions is the much larger $K_1(\mathbf{1a})/K_1(\text{CH}_3\text{CO}_2\text{H})$ ratio ($\approx 1.3 \times 10^{17}$) for the addition of $n\text{-PrS}^-$ to **1a** vs addition of EtS^- to $\text{CH}_3\text{CO}_2\text{H}$, compared to

(23) For $\text{R} = \text{CH}_3$, $\log K_1 \approx -13.1$ and $\log k_1 \approx -3.1$; for $\text{R} = \text{CF}_3$, $\log K_1 \approx -5.3$ and $\log k_1 \approx 3.3$.¹⁶

(24) The actual difference between $\log k_0$ for the reaction of **1a** + $n\text{-PrS}^-$ and the reactions of eq 11 is probably even greater because $\log k_0$ for the reactions of eq 11 in 50% MeCN–50% water is expected to be higher than that in pure water.^{21a, c}

(25) Rochester, C. H.; Rossall, B. *Trans. Faraday Soc.* **1969**, *65*, 1004.

(26) (a) Sander, E. G.; Jencks, W. P. *J. Am. Chem. Soc.* **1968**, *90*, 6154. (b) Hine, J. *Structural Effects on Equilibria in Organic Chemistry*; Wiley: New York, 1975; p 225.

(27) (a) Pearson, R. G.; Songstad, J. *J. Am. Chem. Soc.* **1967**, *89*, 1827.

(b) Pearson, R. G. *Surv. Prog. Chem.* **1969**, *5*, 1.

Table 4. Brønsted Coefficients for the Dependence of k_1 , k_{-1} , K_1 , and k_2^H on pK_a^{RSH} ^a

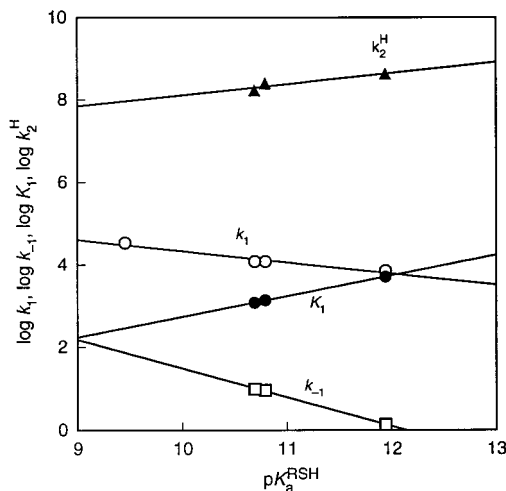
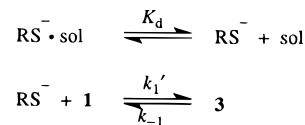
| | 1a | 1b | 1c | 1d |
|---|------------------|------------------|------------------|------------------------|
| $\beta_{nuc} = d \log k_1/d pK_a^{RSH}$ ^{a,b} | -0.28 ± 0.05 | -0.25 ± 0.04 | -0.28 ± 0.05 | -0.26 ± 0.04 |
| $\beta_{lg} = d \log k_{-1}/d pK_a^{RSH}$ ^{c,d} | -0.55 ± 0.08 | -0.57 ± 0.06 | -0.70 ± 0.06 | -0.75 ± 0.06 |
| $\beta_{eq} = d \log K_1/d pK_a^{RSH}$ ^{c,d} | 0.36 ± 0.09 | 0.39 ± 0.06 | 0.50 ± 0.06 | 0.54 ± 0.06 |
| $\beta_{push} = d \log k_2^H/d pK_a^{RSH}$ ^{b,c} | 0.27 ± 0.16 | 0.27 ± 0.17 | 0.26 ± 0.13 | 0.31 ± 0.09 (0.36) |

^a Based on 4 points (n-PrS⁻, HOCH₂CH₂S⁻, MeO₂CCH₂CH₂S⁻, MeO₂CCH₂S⁻). ^b Error limits are standard deviations plus ± 0.02 . ^c Based on 3 points (n-PrS⁻, HOCH₂CH₂S⁻, MeO₂CCH₂CH₂S⁻). ^d Error limits are standard deviations plus ± 0.04 .

$K_1(\mathbf{1a})/K_1(\text{PhCO}_2\text{Me}) \approx 2 \times 10^8$ to 10^9 for the addition of MeO⁻ to **1a** vs addition of MeO⁻ to methylbenzoate (see previous section). The reaction of **1a** with a thiolate is particularly favorable because it leads to a soft–soft interaction while the reaction of acetic acid with a thiolate ion is disfavored because it leads to a hard–soft interaction. This tends to make the $K_1(\mathbf{1a})/K_1(\text{CH}_3\text{CO}_2\text{H})$ ratio particularly large. On the other hand, the reaction of **1a** with MeO⁻ is disfavored because it represents a soft–hard combination while the reaction of methyl benzoate with MeO⁻ is favored because of the hard–hard combination. Hence both factors reduce the $K_1(\mathbf{1a})/K_1(\text{PhCO}_2\text{Me})$ ratio.²⁹

(3) A third point of interest in comparing thiolate ion with methoxide ion addition to the Fischer carbene complexes is that the $k_1(\text{n-PrS}^-)/k_1(\text{MeO}^-)$ ratios are similar to the $K_1(\text{n-PrS}^-)/K_1(\text{MeO}^-)$ ratios or even slightly larger. This implies that the *intrinsic* rate constants are larger for thiolate ion addition than for MeO⁻ addition. Again applying the simplest version of the Marcus equation,²² $\log k_0 \approx 2.11$ for **1a** + n-PrS⁻ vs $\log k_0 \approx 0.96$ for **1a** + MeO⁻,¹¹ and $\log k_0 \approx 2.56$ for **1b** + n-PrS⁻ vs $\log k_0 \approx 1.25$ for **1b** + MeO⁻.¹¹ Similar findings have recently been reported when comparing thiolate and alkoxide ion addition to olefinic and vinylic substrates.^{12c,d} The differences in the intrinsic rate constants are the result of transition states that are imbalanced with respect to the factors that are responsible for the differences in the equilibrium constants, i.e., the stronger solvation of alkoxide ions and the soft–soft interactions in the thiolate ion reactions. Specifically, following generally observed behavior,³⁰ the partial desolvation of the nucleophile that occurs as it enters the transition state should be more advanced than bond formation. This has the effect of reducing the intrinsic rate constants, and more so for the reactions with the more strongly solvated alkoxide ions.^{12c} Regarding the soft–soft interactions, it is not unreasonable to assume that they are more advanced than bond formation at the transition state,³¹ which has the effect of enhancing the intrinsic rate constants for the thiolate ion reactions. Hence both factors reinforce each other in increasing the difference in the intrinsic rate constants of these reactions.

(4) The dependence of K_1 , k_1 , and k_{-1} on pK_a^{RSH} for the reactions of **1b** is shown in Figure 6; the corresponding Brønsted plots for **1a**, **1c**, and **1d** (not shown) are very similar. The slopes, β_{nuc} , β_{lg} , and β_{eq} are summarized in Table 4. The β_{nuc} values are, within experimental error, the same for all carbene

**Figure 6.** Brønsted plots for the reaction of **1b** with thiolate ions.**Scheme 1**

complexes. The β_{lg} and β_{eq} values show no significant dependence on the metal but some dependence on the alkoxy group; in view of the relatively large uncertainties³² and the fact that the β_{lg} and β_{eq} were obtained based on three points only, with two points referring to very similar pK_a^{RSH} values, it is not clear whether the apparent dependence on the alkoxy group is significant and no interpretation will be attempted.

The most interesting features are the fact that β_{nuc} is negative and that β_{eq} is much smaller than unity. Negative β_{nuc} are unusual but not without precedent.³³ According to Jencks,³⁴ they may result from the requirement of partial desolvation of the nucleophile prior to reaction. Whether this desolvation is part of the nucleophilic attack, a point of view favored by us^{12a,c} and implied by the discussion in the previous section, or as a separate step,^{30b} is unclear. However, the following analysis is simpler if desolvation is assumed to be a separate preequilibrium step and hence the two-step model will be adopted here. It is illustrated by Scheme 1.

In terms of Scheme 1, the experimental k_1 value corresponds to $K_d k_1'$, with K_d being the equilibrium constant for partial

(28) (a) Parker, A. J. *Chem. Rev.* **1969**, *69*, 1. (b) Bordwell, F. G.; Hughes, D. L. *J. Org. Chem.* **1982**, *47*, 3224. (c) Taft, R. W. *Prog. Phys. Org. Chem.* **1983**, *14*, 247.

(29) The fact that $K_1(\mathbf{1a})$ for the reaction with n-PrS⁻ refers to 50% MeCN–50% water while $K_1(\text{CH}_3\text{CO}_2\text{H})$ was estimated in water cannot account for more than a minor part of the large $K_1(\mathbf{1a})/K_1(\text{CH}_3\text{CO}_2\text{H})$ ratio for the thiolate ion reactions.

(30) (a) Hupe, D. J.; Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 451. (b) Jencks, W. P.; Brant, S. R.; Gandler, J. R.; Fendrich, G.; Nakamura, C. J. *Am. Chem. Soc.* **1982**, *104*, 7054.

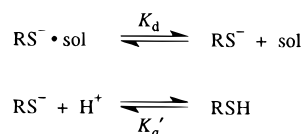
(31) Bernasconi, C. F.; Killion, R. B., Jr. *J. Am. Chem. Soc.* **1988**, *110*, 7506.

(32) The error limits given for β_{lg} and β_{eq} are larger than the standard deviations (see footnote *d* in Table 4) because of the relatively large errors in the k_2^H/k_{-1} ratios (Table 1) from which k_{-1} and K_1 are calculated, and additional uncertainties arising from experimental errors in the pK_a^{RSH} values. This latter factor was also considered in assigning error limits to β_{nuc} (footnote *b* in Table 4).

(33) Negative β_{nuc} values have been reported for some phosphoryl transfer reactions to amines³⁴ and for reactions of highly reactive carbocations with amines;^{35,36} β_{nuc} values close to zero have also been found in the reaction of diphenylketene with amines.³⁷

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

Scheme 2



desolvation of the nucleophile. In the simplest approach, β_{nuc} may be approximated by eq 14.

$$\beta_{\text{nuc}} = \frac{d \log k_1}{d \text{p}K_a^{\text{RSH}}} = \frac{d \log K_d k'_1}{d \text{p}K_a^{\text{RSH}}} = \frac{d \log K_d}{d \text{p}K_a^{\text{RSH}}} + \frac{d \log k'_1}{d \text{p}K_a^{\text{RSH}}} = \beta_d + \beta'_{\text{nuc}} \quad (14)$$

Since desolvation becomes more difficult as the basicity of RS^- increases, $\beta_d < 0$. If β'_{nuc} is small, β_{nuc} may be dominated by β_d and become negative. For $|\beta_d| > \beta'_{\text{nuc}}$, eq 14 underestimates the effect of the desolvation step on β_{nuc} , while for $|\beta_d| < \beta'_{\text{nuc}}$, it overestimates it. This is because it neglects the effect of the desolvation step on $\text{p}K_a^{\text{RSH}}$. If this is taken into account (Scheme 2), $\text{p}K_a^{\text{RSH}}$ corresponds to $\log K_d + \text{p}K'_a$ and β_{nuc} is given by

$$\beta_{\text{nuc}} = \frac{d(\log K_d + \log k'_1)}{d(\log K_d + \text{p}K'_a)} \quad (15)$$

Defining $\beta'_{\text{nuc}} = d \log k'_1/d \text{p}K'_a$ and $\beta_d = d \log K_d/d \text{p}K'_a$ converts eq 15 to eq 16.³⁸

$$\beta_{\text{nuc}} = \frac{\beta_d + \beta'_{\text{nuc}}}{\beta_d + 1} \quad (16)$$

Even though usually not negative, β_{nuc} values are typically quite low for thiolate ion addition to a variety of electrophiles.^{12b,30a,31,39–41} This implies a transition state with little bond formation.⁴²

The fact that β_{eq} is smaller than unity indicates that the carbon basicities of the thiolate ions toward the carbene complexes are not quite proportional to their proton basicities. This is a common pattern in reactions of thiolate ions with electrophiles.^{12b,c,31,41} It may be related to the high polarizability of the thiolate ions in the sense that, just as the *absolute* carbon basicities are dominated by the soft–soft interactions and rather insensitive to the factors that determine proton basicities, the effect of the R group of RS^- on the carbon basicity is also attenuated relative to its effect on the proton basicity. The partial desolvation of the nucleophile (Scheme 2) contributes to the reduction in β_{eq} in a similar way as to the reduction in β_{nuc} .

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

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

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

(38) For example, if $\beta_d = -0.30$ and $\beta'_{\text{nuc}} = 0.10$, $\beta_{\text{nuc}} = -0.29$ (eq 16) and -0.20 (eq 14).

(39) (a) Gilbert, H. F.; Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 7931.

(40) Ritchie, C. D.; Gandler, J. R. *J. Am. Chem. Soc.* **1979**, *101*, 7318.

(41) (a) Bernasconi, C. F.; Schuck, D. F. *J. Org. Chem.* **1992**, *57*, 2365.

(b) Bernasconi, C. F.; Ketner, R. J. *J. Org. Chem.* **1998**, *63*, 6266.

(42) This is the traditional view,⁴³ although this view has been challenged⁴⁴ as well as defended.⁴⁵

(43) (a) Hammond, G. S. *J. Am. Chem. Soc.* **1955**, *77*, 554. (b) Leffler, J. E.; Grunwald, E. *Rates and Equilibria of Organic Reactions*; Wiley: New York, 1963; p 156. (c) Kresge, A. J. *Acc. Chem. Res.* **1975**, *8*, 354.

(44) (a) Pross, A. *J. Org. Chem.* **1984**, *49*, 1811. (b) Bordwell, F. G.; Hughes, D. L. *J. Am. Chem. Soc.* **1985**, *107*, 4737. (c) Pross, A.; Shaik, S. *New J. Chem.* **1989**, *13*, 427.

Using the same reasoning as in the derivation of eq 16, one may derive eq 17 with β'_{eq} defined as $d(\log k'_1/k_{-1})/d \text{p}K'_a = d$

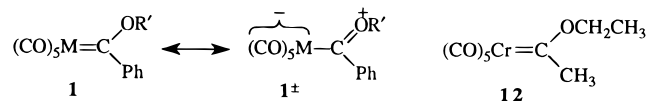
$$\beta_{\text{eq}} = \frac{\beta_d + \beta'_{\text{eq}}}{\beta_d + 1} \quad (17)$$

$\log K'_1/d \text{p}K'_a$ and β_d defined as before. From eq 17 it is apparent that $\beta_{\text{eq}} = \beta'_{\text{eq}}$ if $\beta'_{\text{eq}} = 1$, irrespective of the value of β_d , but for $\beta_{\text{eq}} < 1$ and $\beta_d < 0$ one obtains $\beta_{\text{eq}} < \beta'_{\text{eq}}$; the difference between β_{eq} and β'_{eq} becomes larger the smaller β'_{eq} .

C. Dependence on the Metal and on the Alkoxy Group.

The reactions of the tungsten complexes are somewhat favored over those of the chromium complexes. The effect on the K_1 values is rather minimal but somewhat larger on the rate constants: the $K_1(\mathbf{1b})/K_1(\mathbf{1a})$ and $K_1(\mathbf{1d})/K_1(\mathbf{1c})$ ratios vary between 1.27 and 1.53, the $k_1(\mathbf{1b})/k_1(\mathbf{1a})$ and $k_1(\mathbf{1d})/k_1(\mathbf{1c})$ ratios between 2.56 and 3.54 (Table 5). Similar results were found for MeO^- addition to **1a** and **1b** in methanol: $K_1(\mathbf{1b})/K_1(\mathbf{1a}) = 111/70.1 = 1.58$ and $k_1(\mathbf{1b})/k_1(\mathbf{1a}) = 186/77.1 = 2.41$. These findings are also consistent with a report that the acidity of **4b** ($\text{p}K_a = 12.36$)⁴⁶ is slightly higher than that of **4a** ($\text{p}K_a = 12.50$).^{9b}

The rather minimal dependence of the equilibrium constants on the metal may be the result of the extensive dispersion of the negative charge into the CO ligands of the adducts.⁴⁷ Since this leaves little charge on the metal, the identity of the metal has little effect on the stability of the adduct. An additional factor is related to the strong contribution of $\mathbf{1}^\pm$ to the structure of $\mathbf{1}$.² Because $\mathbf{1}^\pm$ leads to substantial negative charge on the $(\text{CO})_5\text{M}$



moiety of the carbene complex, the greater stabilization of the negative charge by the $(\text{CO})_5\text{W}$ moiety in the adduct is partially offset by a similar effect on the carbene complex. Support for this notion has been discussed elsewhere.¹

The fact that the k_1 values show a somewhat greater dependence on the metal than K_1 and that not only k_1 but also k_{-1} is larger for the tungsten complexes is noteworthy; it means that the *intrinsic* rate constant¹⁹ is somewhat higher for the tungsten complexes than for the chromium complexes. This can be understood with reference to eq 12. If the fractional charge on the *metal* is greater at the transition state (**8**) than in the adduct (**9**) and tungsten is better able to support negative charge than chromium, the greater stabilization resulting from the change from chromium to tungsten will affect the transition state more than the adduct and increase k_1 more than K_1 .

Regarding the dependence on the alkoxy group, the K_1 values are somewhat lower for the ethoxy carbene complexes than for the methoxy carbene complexes: the $K_1(\mathbf{1a})/K_1(\mathbf{1c})$ and $K_1(\mathbf{1b})/K_1(\mathbf{1d})$ ratios vary between 1.73 and 2.90 (Table 5). The same is true for the k_1 values with the $k_1(\mathbf{1a})/k_1(\mathbf{1c})$ and $k_1(\mathbf{1b})/k_1(\mathbf{1d})$ ratios varying between 1.61 and 1.97 (Table 5). The lower K_1 and k_1 values for the ethoxy carbene complexes may be attributed to the stronger π -donation ($\mathbf{1}^\pm$) by the ethoxy group compared to the methoxy group. The same effect is seen in the higher $\text{p}K_a$ values of **12** (12.98)⁴⁶ compared to **4a** (12.50).^{9b}

Leaving Group Departure. The mechanism of acid-catalyzed leaving group departure is probably concerted, with

(45) Jencks, W. P. *Chem. Rev.* **1985**, *85*, 511.

(46) Bernasconi, C. F.; Sun, W. *Organometallics* **1997**, *16*, 1926.

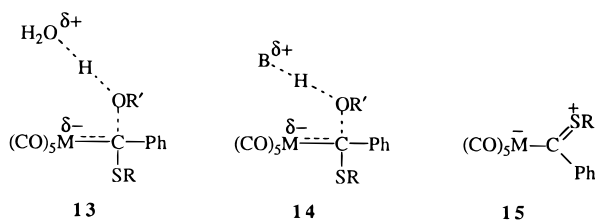
(47) See structure **9**.

Table 5. Equilibrium and Rate Constant Ratios

| ratio | n-PrS ⁻ | HOCH ₂ CH ₂ S ⁻ | MeO ₂ CCH ₂ CH ₂ S ⁻ | MeO ₂ CCH ₂ S ⁻ |
|---|--------------------|--|--|--|
| alkoxy group dependence of first step | | | | |
| $K_1(\mathbf{1a})/K_1(\mathbf{1c})$ | 2.07 ± 0.79 | <i>a</i> | 2.90 ± 0.98 | |
| $k_1(\mathbf{1a})/k_1(\mathbf{1c})$ | 1.90 ± 0.20 | 1.87 ± 0.17 | 1.92 ± 0.06 | 1.97 ± 0.13 |
| $K_1(\mathbf{1b})/K_1(\mathbf{1d})$ | 1.73 ± 0.71 | <i>a</i> | 2.76 ± 1.18 | |
| $k_1(\mathbf{1b})/k_1(\mathbf{1d})$ | 1.81 ± 0.19 | 1.61 ± 0.11 | 1.71 ± 0.16 | 1.65 ± 0.23 |
| metal dependence of first step | | | | |
| $K_1(\mathbf{1b})/K_1(\mathbf{1a})$ | 1.27 ± 0.59 | <i>a</i> | 1.27 ± 0.53 | |
| $k_1(\mathbf{1b})/k_1(\mathbf{1a})$ | 3.14 ± 0.34 | 2.90 ± 0.22 | 3.16 ± 0.07 | 2.56 ± 0.28 |
| $K_1(\mathbf{1d})/K_1(\mathbf{1c})$ | 1.53 ± 0.49 | <i>a</i> | 1.33 ± 0.46 | |
| $k_1(\mathbf{1d})/k_1(\mathbf{1c})$ | 3.30 ± 0.33 | 3.37 ± 0.29 | 3.54 ± 0.14 | 3.06 ± 0.36 |
| alkoxy group dependence of second step | | | | |
| $k_2^H(\mathbf{1a})/k_2^H(\mathbf{1c})$ | 1.27 ± 0.05 | 1.31 ± 0.39 | 1.18 ± 0.03 | |
| $k_2^H(\mathbf{1b})/k_2^H(\mathbf{1d})$ | 1.11 ± 0.07 | 1.42 ± 0.41 | 1.11 ± 0.07 | |
| $k_2^{BH}(\mathbf{1a})/k_2^{BH}(\mathbf{1c})$ | | <i>b</i> | 1.59 ± 0.58 | |
| $k_2^{BH}(\mathbf{1b})/k_2^{BH}(\mathbf{1d})$ | | <i>b</i> | 2.26 ± 1.05 | |
| metal dependence of second step | | | | |
| $k_2^H(\mathbf{1b})/k_2^H(\mathbf{1a})$ | 1.06 ± 0.07 | <i>b</i> | 1.03 ± 0.03 | |
| $k_2^H(\mathbf{1d})/k_2^H(\mathbf{1c})$ | 1.21 ± 0.06 | 0.99 ± 0.08 | 1.10 ± 0.07 | |
| $k_2^{BH}(\mathbf{1b})/k_2^{BH}(\mathbf{1a})$ | | <i>b</i> | 2.12 ± 0.94 | |
| $k_2^{BH}(\mathbf{1d})/k_2^{BH}(\mathbf{1c})$ | | <i>b</i> | 1.49 ± 0.58 | |

^a Experimental errors in the K_1 values are too large to give meaningful ratios. ^b Experimental errors in the k_2^H and k_2^{BH} values are too large to give meaningful ratios.

transition states **13** for the k_2^H and **14** for the k_2^{BH} steps, respectively. The k_2^H values are all above $10^8 \text{ M}^{-1} \text{ s}^{-1}$, the highest being $5.69 \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$ (**1b**/n-PrS⁻); this is only about 1 order of magnitude below the limit for diffusion-controlled reactions.⁴⁸



There is an increase in k_2^H with increasing basicity of the thiolate ion. This indicates the operation of an electronic push by the RS group, presumably because of developing resonance (**15**) in the transition state. From the slopes of plots of $\log k_2^H$ vs pK_a^{RSH} (Figure 6) the β_{push} values summarized in Table 4 are obtained.

The k_2^H and k_2^{BH} values are slightly larger for the methoxy derivatives: the $k_2^H(\mathbf{1a})/k_2^H(\mathbf{1c})$ and $k_2^H(\mathbf{1b})/k_2^H(\mathbf{1d})$ ratios vary between 1.11 and 1.42, and the $k_2^{BH}(\mathbf{1a})/k_2^{BH}(\mathbf{1c})$ and $k_2^{BH}(\mathbf{1b})/k_2^{BH}(\mathbf{1d})$ ratios vary between 1.59 and 2.26 (Table 5). In acid-catalyzed alkoxide ion departure the relative progress of C–O bond cleavage vs oxygen protonation determines which leaving group leaves faster. If C–O bond cleavage is ahead of proton transfer, the energetics of the reaction should be more reflective of C–O bond cleavage than of the proton transfer and hence the less basic leaving group (MeO⁻) should leave faster. On the other hand, if proton transfer is ahead of C–O bond cleavage the opposite holds and the ethoxy derivative should react faster. Our results suggest that the former situation applies.

Regarding the dependence of k_2^H and k_2^{BH} on the metal, the effect on k_2^H is too small and the uncertainties in the k_2^{BH} values are too large to discern a significant difference in reactivity.

Conclusions

(1) The stabilization of the tetrahedral intermediate by the (CO)₅M moiety in the reactions of **1a–d** with nucleophiles is much stronger than the stabilization of the intermediate by the carbonyl oxygen in the reaction of esters with nucleophiles. This is, in large measure, due to the π -acceptor ability of the (CO)₅M moiety. Evidence for charge delocalization in the intermediate comes from IR data and the comparatively low intrinsic rate constants for nucleophilic addition.

(2) The extent to which K_1 for nucleophilic addition to carbene complexes exceeds K_1 for addition to acyl carbon depends strongly on soft–soft, soft–hard, and hard–hard interactions between nucleophile and electrophile. Soft–soft combinations such as thiolate ions/carbene complexes are particularly favorable, and so are hard–hard combinations such as alkoxide ions/acyl compounds. Less favorable are soft–hard or hard–soft combinations such as thiolate ions/acyl compounds and alkoxide ions/carbene complexes, respectively.

(3) The intrinsic rate constants are higher for thiolate ion addition to carbene complexes than for MeO⁻ addition. This appears to be the result of partial desolvation of the nucleophile being ahead of bond formation and the fact that solvation of thiolate ions is weaker than that of MeO⁻. A contributing factor may be early development of soft–soft interactions in the transition state.

(4) β_{nuc} for the k_1 step is negative, indicating that bond formation has made little progress at the transition state and partial desolvation of the nucleophile prior to reaction plays a dominant role. The desolvation step is also partly responsible for the small β_{eq} values.

(5) The dependence of K_1 on the metal is almost negligible, but there appears to be a significant dependence of the intrinsic rate constant on the metal (W > Cr). This suggests a transition state imbalance that places a greater fractional negative charge on the metal at the transition state than in the adduct; in the adduct the charge is mainly dispersed into the CO ligands.

(6) K_1 and k_1 are somewhat lower for the ethoxy carbene complexes compared to the methoxy derivatives. This reflects

(48) Eigen, M. *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 1.

the stronger π -donation by the ethoxy group in the neutral carbene complex.

(7) Acid-catalyzed leaving group departure is probably concerted. The k_2^H values increase with increasing basicity of the thiolate ion, reflecting the increased "push" by the RS group due to developing resonance in the product (**15**).

Experimental Section

Instrumentation. ^1H and ^{13}C NMR spectra were recorded in CDCl_3 on a 500 MHz Varian Unity instrument. UV-vis spectra were obtained on a Hewlett-Packard 8452A diode array spectrophotometer. IR spectra were taken with a Perkin-Elmer 1600 FT IR spectrophotometer. Kinetic experiments were performed on an Applied Photophysics DX.17MV stopped-flow apparatus (fast reactions) or Hewlett-Packard spectrophotometer (slow reactions).

Materials. 1a–d were available from a previous study.¹⁵ The alkane thiols were distilled under argon prior to use. Triethylamine and *N*-methylmorpholine were refluxed over CaH_2 and freshly distilled prior to use. Acetic acid was used as received. KOH and HCl solutions were prepared using "dilut-it" from Baker Analytical. Acetonitrile was used as received. Water was taken from a Milli-Q ion exchange water purification system. 50% MeCN–50% water mixtures were degassed by three cycles of the freeze–pump–thaw method.

Identification of Products. All products (**3a** and **3b**) showed the characteristic absorption spectrum of thioalkoxy carbene complexes (Figure 1, spectrum B for **3b** and Figure 1 in ref 13 for **3a**). For **3a** and **3b** (R = n-Pr) the absorption spectra obtained from kinetic runs of the reactions of n-PrS[−] with **1c** and **1b**, respectively, were indistinguishable from samples of **3a** and **3b** that were synthesized independently. The synthesis was performed under conditions that were as similar as possible to those in the kinetic experiments, as follows. An 8 mmol sample of **1b** or **1c** was added to a mixture of 40 mL of MeCN and 4 mL of water under Ar and stirred. n-PrS[−]K⁺ (32 mmol) was added while stirring. After 5 min HCl was added dropwise until the pH was ~ 4 . Stirring was continued for 1 h. The following procedures were carried out in the open air. The solution was reduced to a small volume by rotovap. Water (40 mL) was added followed by 100 mL of *n*-hexane. The aqueous layer was removed and the hexane layer was extracted with 50 mL of water, collected, and dried over Na_2SO_4 . The solution was filtered and reduced by rotovap to leave a dark red oily residue. This residue was filtered through a silica plug and an HPLC filter plug (0.1 μm). After removal of most of the solvent by rotovap the sample was dried under high vacuum at $-78\text{ }^\circ\text{C}$ for 24 h. ^1H NMR (**3a**): δ 0.89 (t, 3H, $\text{SCH}_2\text{CH}_2\text{CH}_3$), 1.54 (m, 2H, SCH_2CH_2 -

CH_3), 2.70 (t, 2H, $\text{SCH}_2\text{CH}_2\text{CH}_3$), 6.6 (d, 2H, Ph), 7.4 (m, 3H, Ph). ^1H NMR (**3b**): δ 0.91 (t, 3H, $\text{CH}_2\text{CH}_2\text{CH}_3$), 1.48 (m, 2H, $\text{SCH}_2\text{CH}_2\text{CH}_3$), 2.49 (t, 2H, $\text{SCH}_2\text{CH}_2\text{CH}_3$), 6.7 (d, 2H, Ph), 7.5 (m, 3H, Ph). ^{13}C NMR (**3a**): δ 13.0 ($\text{SCH}_2\text{CH}_2\text{CH}_3$), 21.3 ($\text{SCH}_2\text{CH}_2\text{CH}_3$), 46.5 ($\text{SCH}_2\text{CH}_2\text{CH}_3$), 126.8–128.7, 157.5 (Ph), 215.5 (cis CO), 228.6 (trans CO), 362.6 ($=\text{C}$). ^{13}C NMR (**3b**): δ 13.3 ($\text{SCH}_2\text{CH}_2\text{CH}_3$), 21.2 ($\text{SCH}_2\text{CH}_2\text{CH}_3$), 46.9 ($\text{SCH}_2\text{CH}_2\text{CH}_3$), 127.4–128.9, 157.9 (Ph), 197.4 (cis CO), 209.0 (trans CO), 329.4 ($=\text{C}$).

NMR of Intermediate. The intermediate derived from the reaction of **1b** with n-PrS[−] was stable enough to be characterized by NMR. ^1H NMR: δ 1.35 (t, 3H, $\text{SCH}_2\text{CH}_2\text{CH}_3$), 1.96 (m, 2H, $\text{SCH}_2\text{CH}_2\text{CH}_3$), 2.44 (t, 2H, $\text{SCH}_2\text{CH}_2\text{CH}_3$), 4.04 (s, 3H, OCH₃), 7.66 (m, 5H, Ph). ^{13}C NMR: δ 13.7 ($\text{SCH}_2\text{CH}_2\text{CH}_3$), 22.5 ($\text{SCH}_2\text{CH}_2\text{CH}_3$), 38.8 ($\text{SCH}_2\text{CH}_2\text{CH}_3$), 49.0 (OCH₃), 52.4 ($>\text{C}<$), 127.4–128.6 (Ph), 202.5 (cis CO), 207.6 (trans CO).

Kinetics. All reactions were conducted under pseudo-first-order conditions with a large excess of thiol/thiolate or, for the experiments **2**[−] \rightarrow **3**, of buffer over the substrate. Runs in which **1a–d** were reacted with RSH buffers were monitored at $\lambda = 396\text{ nm}$, which is at or near λ_{max} of **1a–d**. Runs where the intermediate was reacted with an acidic buffer were monitored at 454 (W) or 464 (Cr) nm, i.e., at or near the λ_{max} of **3a–d**. These latter runs were conducted in the sequential mixing mode of the stopped-flow apparatus as follows. A 10^{-3} M solution of the carbene complex was first mixed with a 10^{-3} M solution of the thiolate ion. After being aged for 0.5 to 5 s to allow generation of the intermediate, the solution was mixed with the appropriate acidic buffer.

pH and pK_a Measurements. The pH in 50% MeCN–50% water was determined according to eq 18⁴⁹ with pH_{meas} referring to the reading of the pH meter calibrated with standard buffers. All pH measurements

$$\text{pH} = \text{pH}_{\text{meas}} + 0.18 \quad (18)$$

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. The pK_a^{RSH} values of the thiols were determined potentiometrically.

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