Physical Organic Chemistry of Transition Metal Carbene Complexes. 12.[1] Spectroscopic Detection and Kinetic Characterization of the Intermediate in the Nucleophilic Substitution Reaction of $(CO)_5Cr{=}C(OCH_3)Ph$ with Thiolate Ions in Aqueous Acetonitrile

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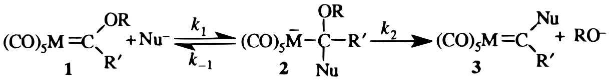
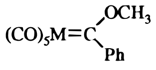
Fischer-type carbene complexes undergo facile nucleophilic substitution by the two-step mechanism illustrated in eq 1 for the reaction of a prototype carbene complex.[2] The evidence for



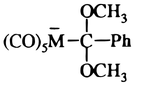
$$(CO)_5M{=}C(OR)R' \;(\mathbf{1}) + Nu^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} (CO)_5\bar{M}{-}C(OR)(Nu){-}R' \;(\mathbf{2}) \xrightarrow{k_2} (CO)_5M{=}C(Nu)R' \;(\mathbf{3}) + RO^- \qquad (1)$$

this mechanism has mostly been based on analogy with reactions of carboxylic esters. However, direct observation of **5-M** in the reaction of **4-M** with MeO$^-$ in methanol has recently been reported[3] and kinetic evidence for **6-Cr** in the reaction of **4-Cr** with primary aliphatic amines has been presented.[4] Furthermore, in the reaction of **7-Cr** with NaSPh in methanol/benzene, Lam *et al.*[5] observed conversion of **7-Cr** to an unidentified species which, upon treatment with HCl, yielded **8-Cr**. From this they inferred that the unidentified species is **9-Cr**.



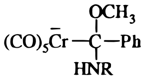
$(CO)_5M{=}C(OCH_3)Ph$

4-M (M = Cr or W)



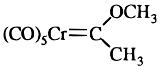
$(CO)_5\bar{M}{-}C(OCH_3)_2{-}Ph$

5-M (M = Cr or W)



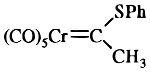
$(CO)_5\bar{Cr}{-}C(OCH_3)(HNR){-}Ph$

6-Cr



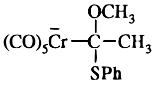
$(CO)_5Cr{=}C(OCH_3)CH_3$

7-Cr



$(CO)_5Cr{=}C(SPh)CH_3$

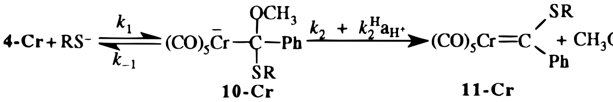
8-Cr



$(CO)_5\bar{Cr}{-}C(OCH_3)(SPh){-}CH_3$

9-Cr

In this communication, we report the first direct spectroscopic observation and kinetic characterization of the intermediate in a "real" substitution reaction, i.e., one where the products are different from reactants.[6] It is the reaction of **4-Cr** with $CH_2CH_2CH_2S^-$ and $HOCH_2CH_2S^-$ in 50% MeCN−50% water (v/v), eq 2. Figure 1 shows absorption spectra of **4-Cr** in the presence of *n*-propanethiol in an *N*-methylmorpholine buffer at pH 7.38. This pH is well below the $pK_a^{RSH} = 11.94$ of *n*-propanethiol and hence the concentration of the thiolate ion is small (4×10^{-7} M). There is a clean conversion of **4-Cr** (a) to **11-Cr** (b) whose spectrum is identical to that of authentic **11-Cr**. The isosbestic point indicates that there is no accumulation of an intermediate (**10-Cr**) under these conditions. Similar observations were made for the reaction of **4-Cr** with $HOCH_2CH_2S^-$.



$$\mathbf{4\text{-}Cr} + RS^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} (CO)_5\bar{Cr}{-}C(OCH_3)(SR){-}Ph \;(\mathbf{10\text{-}Cr}) \xrightarrow{k_2 + k_2^H a_{H^+}} (CO)_5Cr{=}C(SR)Ph \;(\mathbf{11\text{-}Cr}) + CH_3O^- \qquad (2)$$

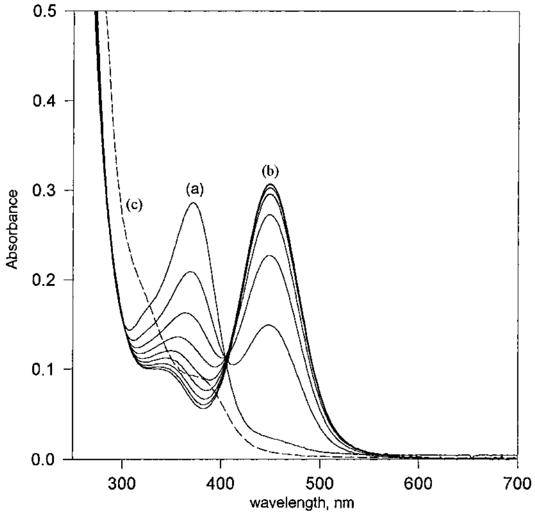


Figure 1. Conversion of **4-Cr** (a) to **11-Cr** (b) in the presence of 4×10^{-7} M $CH_3CH_2CH_2S^-$ in an *N*-methylmorpholine buffer at pH 7.38. Spectra taken every 5 s for 2 min. Spectrum c corresponds to **10-Cr** generated in the presence of 10^{-3} M $CH_3CH_2CH_2S^-$ at pH 11.0.

A different situation arises with higher thiolate ion concentrations at a pH close to pK_a^{RSH} (Figure 1c). Here **4-Cr** is rapidly converted to a new species whose spectrum resembles neither that of **4-Cr** nor that of **11-Cr**. This species is stable for several minutes but upon acidification yields the product (**11-Cr**). We conclude that the new species is **10-Cr**.

Rates of the formation of **10-Cr** were measured by stopped-flow spectrometry. In the presence of excess thiolate ion, the observed pseudo-first-order rate constant showed a linear dependence on [RS$^-$] according to eq 3 from which k_1 could be

$$k_{obsd} = k_1[RS^-] + k_{-1} \qquad (3)$$

obtained; on the other hand, the intercepts of the plots of k_{obsd} vs [RS$^-$] were too small to yield accurate k_{-1} values.

Rates were also measured in *N*-morpholine buffers ($HOCH_2CH_2S^-$) and triethylamine buffers ($CH_3CH_2CH_2S^-$) at different pH values. Under these conditions **10-Cr** is a steady-state intermediate. In each buffer a plot of k_{obsd} vs thiolate ion concentration is linear with pH-dependent slope and negligible intercept. A representative plot of 1/slope vs $1/a_{H^+}$ is shown in Figure 2. These results are consistent with eq 4 derived for steady-state conditions; tests for buffer catalysis showed that it

$$\text{slope} = \frac{k_1k_2 + k_1k_2^H a_{H^+}}{k_{-1} + k_2 + k_2^H a_{H^+}} \qquad (4)$$

is negligible at low buffer concentrations. The linearity of the plot indicates that k_2 for spontaneous loss of MeO$^-$ is negligible compared to $k_2^H a_{H^+}$ for acid catalysis so that eq 4, after inversion, simplifies to eq 5. Analysis according to eq 5 yields the k_1 and k_2^H/k_{-1} values reported in Table 1. The agreement between the k_1 values obtained via eqs 5 and 3 is excellent.

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[1] Part 11: Bernasconi, C. F.; Leyes, A. E. *J. Chem. Soc., Perkin Trans. 2* **1997**, 1641.

[2] Dötz, K. H.; Fischer, H.; Hofmann, P.; Kreissl, F. R.; Schubert, U.; Weiss, K. *Transitional Metal Complexes*; Verlag Chemie: Deerfield Beach, FL, 1983.

[3] Bernasconi, C. F.; Flores, F. X.; Gandler, J. P.; Leyes, A. E. *Organometallics* **1994**, *13*, 2186.

[4] Bernasconi, C. F.; Stronach, M. W. *J. Am. Chem. Soc.* **1993**, *115*, 1341.

[5] Lam, C. T.; Senoff, C. F.; Ward, J. E. H. *J. Organomet. Chem.* **1974**, *70*, 273.

[6] In contrast to the reaction of **4-M** with MeO$^-$ that leads to the symmetrical **5-M.**[3]

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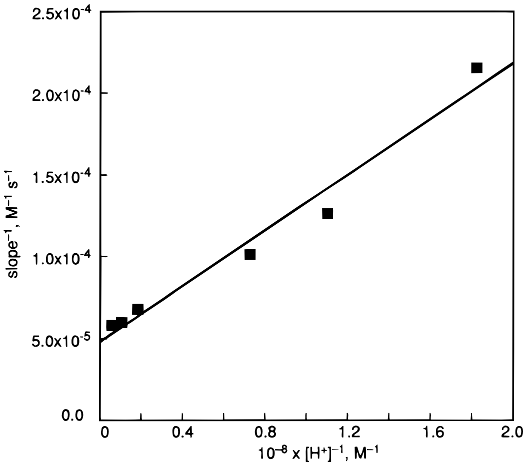


Figure 2. Plot of slope^{-1} vs $a_{H^+}^{-1}$ for the reaction **4-Cr** with $HOCH_2CH_2S^-$.

$$\frac{1}{\text{slope}} = \frac{1}{k_1} + \frac{k_{-1}}{k_1 k_2{}^H a_{H^+}} \tag{5}$$

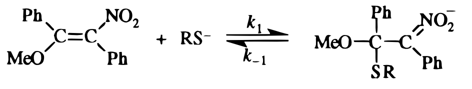
In a third type of experiment **10-Cr** was generated in a thiolate ion solution at pH > 11 and then rapidly mixed in the stopped-flow apparatus with a series of *N*-methylmorpholine buffers at pH between 6.98 and 8.04. The k_{obsd} values showed a linear dependence on a_{H^+} according to eq 6, with k_{-1} being too small to yield an accurate value. This is consistent with the fact that

$$k_{obsd} = k_2^H a_{H^+} + k_{-1} \tag{6}$$

the spectrum of the product is virtually identical with that of **11-Cr**, with no measurable contribution from **4-Cr**. These data yielded k_2^H; in conjunction with k_2^H/k_{-1} this then allowed calculation of k_{-1} which, in combination with k_1, yielded K_1 (Table 1).

With respect to the rate and equilibrium constants, the following points are noteworthy.

(1) The equilibrium constants ($K_1 = k_1/k_{-1}$) for RS$^-$ addition to **4-Cr** are high, much higher than for MeO$^-$ addition in methanol ($K_1 = 70.1$ M^{-1}),[3] despite the lower proton basicity of the thiolate ions. This reflects the well-known high carbon basicity of sulfur bases which has been attributed to their high polarizability[7] or "softness".[8] The K_1 values are comparable to K_1 for $HOCH_2CH_2S^-$ addition to **12** (eq 7) in 50% DMSO−50% water[9] (Table 1),



12 **13** (7)

suggesting that stabilization of the negative charge in **10-Cr** by the $(CO)_5Cr$ moiety is comparable to that in **13** by the $C(NO_2)Ph$ moiety.

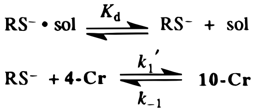
(2) The k_1 and k_{-1} values for the reaction of **4-Cr** with $HOCH_2CH_2S^-$ are about 2 orders of magnitude higher than for the reaction of **12** with the same nucleophile. With the K_1 values being about the same for both reactions, this result indicates that the *intrinsic* rate constant, k_o,[10] for the reaction of **4-Cr** is ~2 orders of magnitude higher than for the reaction of **12**. The reason for this state of affairs in undoubtedly the same as the reason k_o for deprotonation of **7-Cr** by OH$^-$ is about 2 orders of magnitude higher than k_o for deprotonation of $PhCH_2NO_2$,[11] i.e., the resonance component that contributes to the stabilization of the anion derived from the Fischer carbenes is not quite as strong as that for nitronate ions.[12]

Table 1. Rate and Equilibrium Constants for the Reactions of **4-Cr** with Thiolate Ions in 50% MeCN−50% Water (v/v) at 25 °C

	$CH_3CH_2CH_2S^-$ + **4-Cr**[a]	$HOCH_2CH_2S^-$ + **4-Cr**[a]	$HOCH_2CH_2S^-$ + **12**[b]
pK_a^{RSH}	11.94	10.79	10.56
k_1, M^{-1} s^{-1} [c]	$(1.34 \pm 0.07) \times 10^4$	$(2.25 \pm 0.09) \times 10^4$	3.90×10^2
k_1, M^{-1} s^{-1} [d]	$(1.40 \pm 0.15) \times 10^4$	$(2.08 \pm 0.25) \times 10^4$	
k_2^H/k_{-1}, M^{-1} [e]	$(4.29 \pm 0.93) \times 10^8$	$(6.98 \pm 1.24) \times 10^7$	
k_2^H, M^{-1} s^{-1}	$(5.39 \pm 0.11) \times 10^8$	$(4.42 \pm 0.11) \times 10^8$	
k_{-1}, s^{-1}	1.26 ± 0.28	6.33 ± 1.10	5.10×10^{-2}
$K_1 = k_1/k_{-1}$, M^{-1}	$(1.06 \pm 0.24) \times 10^4$	$(3.55 \pm 0.63) \times 10^3$	7.65×10^3

[a] In 50% MeCN−50% H_2O at 25 °C, this work. [b] In 50% DMSO−50% H_2O at 20 °C, ref 9. [c] From eq 3. [d] From eq 5. [e] From eq 5 using k_1 from eq 3.

Scheme 1



(3) The dependence of k_1 on the basicity of the thiolate ion is unusual in that k_1 for $HOCH_2CH_2S^-$ is slightly larger than that for $CH_3CH_2CH_2S^-$, even though $HOCH_2CH_2S^-$ is *less* basic than $CH_3CH_2CH_2S^-$. This suggests a negative β_{nuc} value of approximately −0.2. Negative β_{nuc} values are rare but not without precedent.[14] According to Jencks,[14] they may result from the requirement for partial desolvation of the nucleophile prior to reaction, as illustrated in Scheme 1. In terms of Scheme 1, the experimental k_1 value corresponds to $K_d k_1'$ and hence β_{nuc}(obsd) = $d(\log k_1)/d(pK_a^{RSH}) = d(\log(K_d k_1'))/d(pK_a^{RSH}) = d(\log K_d)/d(pK_a^{RSH}) + d(\log k_1')/d(pK_a^{RSH}) = \beta_d + \beta'_{nuc}$. Since desolvation is more difficult for a more basic nucleophile, $\beta_d < 0$. If β'_{nuc} is small (early transition state), β_{nuc}(obsd) may be dominated by β_d and become negative.

(4) The dependence of K_1 on pK_a^{RSH}, as measured by $\beta_{eq} = d(\log K_1)/d(pK_a{}^{RSH}) = 0.41 \pm 0.17$ is quite small. Even though the experimental uncertainty is large,[15] β_{eq} is clearly smaller than unity, which is common for thiolate ion addition to electrophiles.[9,16]

(5) With respect to conversion of **10-Cr** to products, no k_2 value for spontaneous expulsion of MeO$^-$ could be measured because this reaction is too slow to compete with decomposition of **10-Cr** into unidentified byproducts. However, at pH < 8 acid-catalyzed conversion of **10-Cr** to products (k_2^H) is a clean reaction. The k_2^H value for the reaction of $CH_3CH_2CH_2S^-$ is slightly higher than with $HOCH_2CH_2S^-$. This is consistent with increased "push" by the more basic $CH_3CH_2CH_2S$ group, due to the π donation by the sulfur atom.

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[7] (a) Sander, E. G.; Jencks, W. P. *J. Am. Chem. Soc.* **1968**, *90*, 6154. (b) Hine, J.; Weimar, R. D., Jr. *J. Am. Chem. Soc.* **1965**, *87*, 3387.

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

[9] Bernasconi, C. F.; Fassberg, J.; Killion, R. B.; Rappoport, Z. *J. Am. Chem. Soc.* **1990**, *112*, 3169.

[10] For a reaction with the forward rate constant k_1 and the reverse rate constant k_{-1}, the intrinsic rate constant is defined as $k_o = k_1 = k_{-1}$ when $K_1 = k_1/k_{-1} = 1$ ($\Delta G° = 0$).

[11] Bernasconi, C. F. *Chem. Soc. Rev.* **1997**, *26*, 299.

[12] For a discussion of the relationship between intrinsic rate constants and resonance see ref 13.

[13] (a) Bernasconi, C. F. *Acc. Chem. Res.* **1987**, *20*, 301. (b) Bernasconi, C. F. *Adv. Phys. Org. Chem.* **1992**, *27*, 119.

[14] Jencks, W. P.; Haber, M. T.; Herschlag, D.; Nazaretian, K. L. *J. Am. Chem. Soc.* **1986**, *108*, 479.

[15] β_{eq} is based on two points only and the K_1 values have a large uncertainty.

[16] (a) Bernasconi, C. F.; Killion, R. B., Jr. *J. Am. Chem. Soc.* **1988**, *110*, 7506. (b) Bernasconi, C. F.; Schuck, D. F. *J. Org. Chem.* **1992**, *57*, 2365.