Physical Organic Chemistry of Transition Metal Carbene Complexes. 27.[†] Substituent Effects on the Nucleophilic Substitution of [Aryl(thiomethyl)carbene]pentacarbonylchromium(0) Complexes by Amines in Aqueous Acetonitrile

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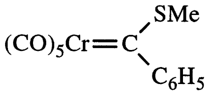
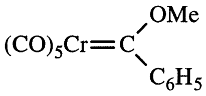
A kinetic study of the reactions of $(CO)_5Cr{=}C(SMe)C_6H_4Z$ (Z = 4-CF_3, 4-Cl, 4-F, 4-Me, 4-MeO, and 4-Me_2N) with *n*-butylamine, 2-chloroethylamine, piperidine, and 1-(2-hydroxyethyl)piperazine in 50% MeCN−50% water (v/v) at 25 °C is reported. In all cases the nucleophilic attachment of the amine to the carbene complex is rate limiting, which contrasts with the previously reported aminolysis of the methoxy analogues ($(CO)_5Cr{=}C(OMe)C_6H_4Z$), where leaving group departure is rate limiting in most cases. The substituent effect on the nucleophilic attachment step is much weaker (average $\rho = 0.55$) than for the methoxy analogue ($\rho = 2.03$). It is shown that the small ρ value for $(CO)_5Cr{=}C(SMe)C_6H_4Z$ is "normal" and reflects the near cancellation of the substituent effects on the partial positive and partial negative charges at the transition state. These findings provide evidence that the high ρ value for $(CO)_5Cr{=}C(OMe)C_6H_4Z$ is "abnormal" and the result of the strong π-donor effect of the methoxy group on the reactant carbene complex.

Introduction

In a previous paper we reported a kinetic study of the nucleophilic substitution of [phenyl(thiomethyl)carbene]pentacarbonylchromium(0), **1-SMe**, by a series of primary aliphatic and secondary alicyclic amines in 50% MeCN−50% water.[1] A major focus of that study was a comparison with earlier investigations of the reaction of the methoxy analogue, **1-OMe**, with amine nucleophiles.[2,3] The mechanism of the aminolysis reaction which is shown in Scheme 1 is undoubtedly the same for the two types of carbene complexes. However, differences in the rate constants of the individual steps for the two substrates affect the incidence or absence of base catalysis by OH^- and the amine. Base catalysis is observed when leaving group departure is rate limiting, i.e., when $(k_3^{H_2O}K_a^{\pm}/k_{-1}K_w)[OH^-] < 1$ and $(k_3^{AH}K_a^{\pm}/k_{-1}K_a^{AH})[RR'NH] < 1$; K_w is the ionic product of the solvent, and K_a^{AH} is the acidity constant of $RR'NH_2^+$. With **1-OMe**, catalysis was observed for a wide range of amines.[2,3] However, the change from **1-OMe** to **1-SMe** induces a large decrease in k_{-1}, a moderate increase in $k_3^{H_2O}$ and $K_a^{\pm}/K_w$, and a slight decrease in k_3^{AH} and $K_a^{\pm}/K_a^{AH}$. As a result, the $(k_3^{H_2O}K_a^{\pm}/k_{-1}K_w)$ and $(k_3^{AH}/K_a^{\pm}/k_{-1}K_a^{AH})$ ratios increase so that $(k_3^{H_2O}K_a^{\pm}/k_{-1}K_w)[OH^-] > 1$ and $(k_3^{AH}K_a^{\pm}/k_{-1}K_a^{AH})$-$[RR'NH] > 1$ under most conditions, which means k_1 is rate limiting and no base catalysis is observed.

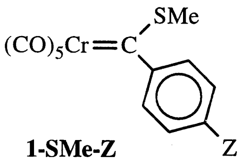


1-SMe

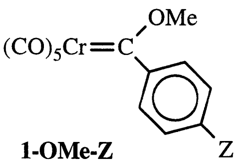


1-OMe

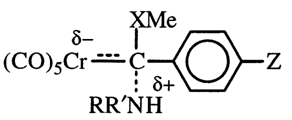
In the present paper we report a substituent effect study on k_1 of the reactions of **1-SMe-Z** with various amines in 50% MeCN−50% water (v/v). The focus is on how the change from X = O to X = S in **1-XMe** affects the sensitivity of k_1 to substituent effects. For the reaction of **1-OMe-Z** with n-$BuNH_2$, the Hammett ρ value was found to be 2.03.[3] For a reaction that has a zwitterionic transition state (**3**), this ρ value seems large because the effect of Z on the partial negative charge should be largely offset by its effect on the partial



1-SMe-Z



1-OMe-Z



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[†] Part 26: Bernasconi, C. F.; Bhattacharya, S. *Organometallics* **2003**, *22*, 426.

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Scheme 1

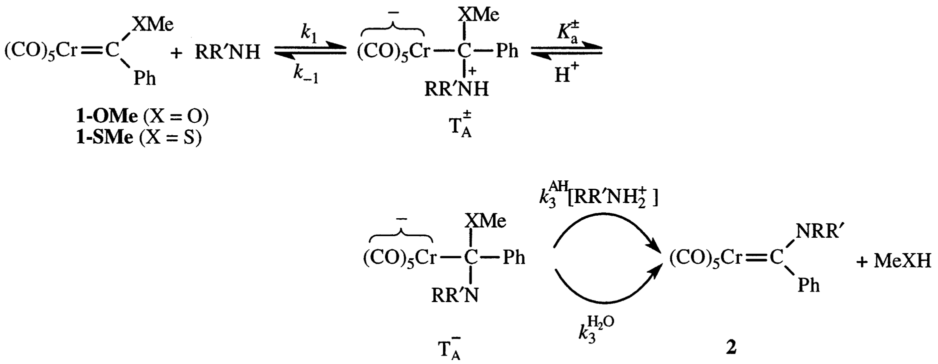

Table 1. Summary of k_1 Values for the Reactions of 1-SMe-Z with Amines in 50% MeCN−50% Water (v/v) at 25 °C[a,b]

Z (σ)	n-BuNH$_2$ pK_a^{AH} = 10.40	ClCH$_2$CH$_2$NH$_2$ pK_a^{AH} = 8.05	piperidine pK_a^{AH} = 11.01	HEPA[c] pK_a^{AH} = 9.33
CF$_3$ (0.54)	19.1 ± 0.6	3.04 ± 0.05	6.74 ± 0.25	0.803 ± 0.04
Cl (0.23)	15.4 ± 0.8	2.05 ± 0.04	4.82 ± 0.14	0.625 ± 0.03
F (0.06)	11.8 ± 0.6	1.69 ± 0.07	4.03 ± 0.09	0.592 ± 0.02
H (0.00)	9.56 ± 0.16[d]	1.20 ± 0.02[d]	2.84 ± 0.09[d]	0.453 ± 0.02[e]
Me (−0.17)	7.44 ± 0.18	1.19 ± 0.05	2.84 ± 0.10	0.395 ± 0.02
MeO (−0.27)	8.18 ± 0.26	0.984 ± 0.017	3.30 ± 0.06	0.358 ± 0.01
Me$_2$N (−0.83)	3.20 ± 0.19	0.457 ± 0.011	1.17 ± 0.05	0.174 ± 0.01

[a] μ = 0.1 M (KCl). [b] In units of M^{-1} s^{-1}. [c] 1-(2-Hydroxyethyl)piperazine. [d] From ref 1. [e] This work.

positive charge, resulting in a very small ρ value. It was suggested that the large ρ value is the consequence of the strong π-donor effect of the MeO group.[3] If this interpretation is correct, ρ for the reaction of **1-SMe-Z** with amines should be smaller because the π-donor effect of the MeS group is smaller.[4] The results of the present study confirm this hypothesis.

Results

The kinetics of the reactions of n-BuNH$_2$, ClCH$_2$CH$_2$NH$_2$, piperidine, and 1-(2-hydroxyethyl)piperazine with **1-SMe-Z** (Z = CF$_3$, Cl, F, Me, MeO, Me$_2$N) were investigated in 50% MeCN−50% water (v/v) at 25 °C. The reactions were run in 1:1 amine buffers corresponding to pH = pK_a^{AH} as described previously for **1-SMe**.[1] All reactions were strictly first order in both the carbene complex and the amine; that is, no amine or OH$^-$ catalysis was observed. This implies that k_1 in Scheme 1 is rate limiting. A number of representative plots of the observed pseudo-first-order rate constants versus amine concentration are shown in Figure 1. The k_1 values obtained from the slopes of such plots are summarized in Table 1.

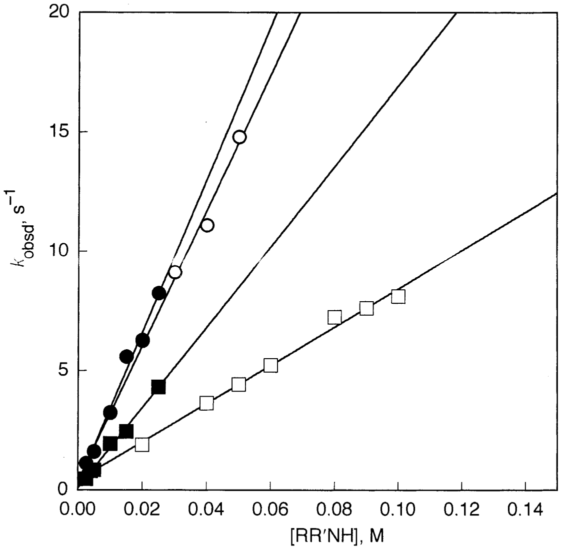

Figure 1. Representative plots of k_{obsd} versus amine concentration: ●, n-BuNH$_2$ with **1-SMe-NMe$_2$**; ○, piperidine with **1-SMe-Me**; ■, ClCH$_2$CH$_2$NH$_2$ with **1-SMe-F**; □, HEPA with **1-SMe-CF$_3$**.

Discussion

Absence of Base Catalysis. Since the focus of the present paper is on the nucleophilic attachment step (k_1), the four amines chosen for this study were among the ones that in their reactions with **1-SMe** did not lead to base catalysis. As it turned out, the reactions of these amines with the *substituted* carbene complexes did not show base catalysis either, implying that in all cases $(k_3^{AH}K_a^{\pm}/k_{-1}K_a^{AH})$[RR′NH] ≫ 1 and/or $(k_3^{H_2O}K_a^{\pm}/k_{-1}K_w)$[OH$^-$] ≫ 1 under our reaction conditions. This outcome was not necessarily predictable because the Z-substituents are expected to affect k_{-1}, k_3^{AH}, $k_3^{H_2O}$, and $K_a^{\pm}$ and hence the $k_3^{AH}K_a^{\pm}/k_{-1}K_a^{AH}$ and $k_3^{H_2O}K_a^{\pm}/k_{-1}K_w$ ratios. Specifically, electron-withdrawing substituents should decrease k_{-1}, $k_3^{H_2O}$, and k_3^{AH}, but increase $K_a^{\pm}$, while electron-donating substituents should have the opposite effect. Thus, if, for example, the influence of Z on k_{-1}, $k_3^{H_2O}$, and k_3^{AH} was about the same, the net effect of electron-donating substituents would be to decrease $k_3^{AH}K_a^{\pm}/k_{-1}K_a^{AH}$ and $k_3^{H_2O}K_a^{\pm}/k_{-1}K_w$ ratios due to the lower $K_a^{\pm}$. Such a decrease was indeed observed for the reaction of n-BuNH$_2$ with **1-OMe-Z**.[3] However, for the reactions of **1-SMe-Z** this effect is apparently not large enough, even for Z = Me$_2$N, to lead to $(k_3^{AH}K_a^{\pm}/$

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(4) σ_R(OMe) = −0.43,[5] σ_R(SMe) = −0.15.[5]

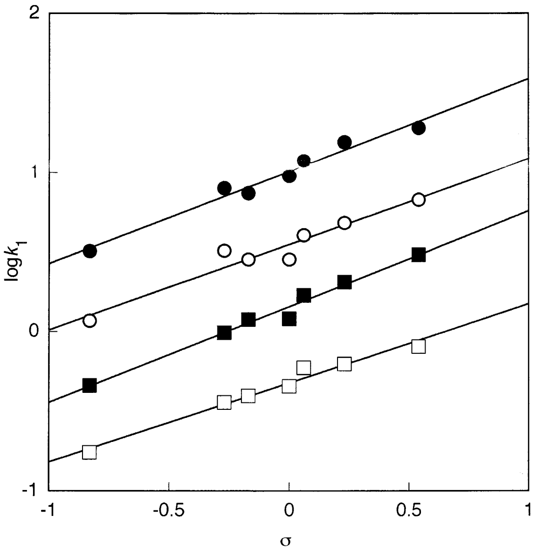


Figure 2. Hammett plots for the reactions of **1-SMe-Z** with amines: ●, n-BuNH$_2$; ○, piperidine; ■, ClCH$_2$CH$_2$NH$_2$; □, HEPA.

Table 2. Hammett ρ Values

	1-SMe-Z		1-OMe-Z	
amine	k_1 (M^{-1} s^{-1})[a]	ρ	k_1 (M^{-1} s^{-1})[a]	ρ
n-BuNH$_2$	9.56[b]	0.59 ± 0.04	1600[c]	2.03[d]
ClCH$_2$CH$_2$NH$_2$	1.20[b]	0.60 ± 0.04		
piperidine	2.84[e]	0.50 ± 0.17		
HEPA[f]	0.453[e]	0.50 ± 0.04		

[a] Z = H. [b] $\beta_{nuc} = 0.30$ based on n-BuNH$_2$, MeOCH$_2$CH$_2$NH$_2$, H$_2$NCOCH$_2$NH$_2$, and ClCH$_2$CH$_2$NH$_2$ (ref 1). [c] $\beta_{nuc} = 0.46$ based on n-BuNH$_2$ and ClCH$_2$CH$_2$NH$_2$ (ref 3). [d] Reference 3; $\rho = 2.23$ for (CO)$_5$W=C(OMe)C$_6$H$_4$Z (ref 3). [e] $\beta_{nuc} = 0.42$ based on piperidine, piperazine, HEPA, and morpholine (ref 3). [f] 1-(2-Hydroxyethyl)piperazine.

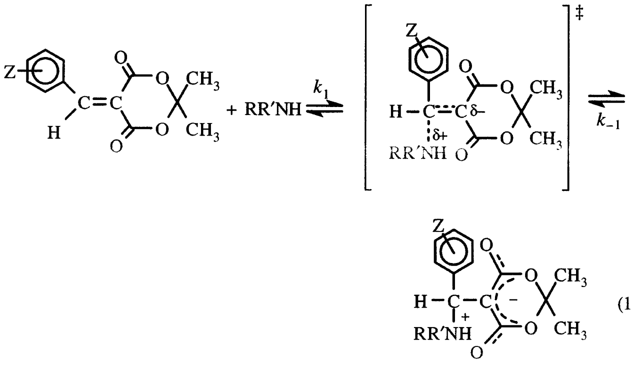
$k_{-1}K_a^{AH}$)[RR′NH] < 1 and/or $(k_3^{H_2O}K_a^{\pm}/k_{-1}K_w)[OH^-] < 1$, which are the necessary conditions for observing catalysis.

Substituent Effect on k_1. Figure 2 shows Hammett plots for the four reaction series of this study, while Table 2 summarizes the ρ values. The plots are of reasonably good quality except that the point for the methoxy derivative tends to show a fairly significant positive deviation, especially for the reaction with piperidine. The most likely explanation for this deviation seems to be an experimental problem in obtaining good first-order kinetic plots and in getting very accurate rate constants. This could be due to some unidentified side reaction, as suggested by observing a less than sharp isosbestic point in the time-resolved visible spectra.

The ρ values are all quite similar and in the range 0.5−0.6, although the ones for the reactions with the secondary alicyclic amines appear slightly lower than those for the reactions with the primary amines. However, in view of the relatively high standard deviations of the individual ρ values a detailed interpretation of the slight differences does not seem warranted and we will use the average value of 0.55 ± 0.05 in the subsequent discussion.

The main point of interest is that ρ for the reactions of **1-SMe-Z** is substantially lower than $\rho = 2.03$ for the reaction of **1-OMe-Z**.[3] Two factors contribute to our results. One is that the transition state of the reactions of **1-SMe-Z** is probably somewhat more reactant-like than that of the reactions of **1-OMe-Z**. The relevant β_{nuc} values which may be taken as an indication of C−N bond formation at the transition state[6] are given in the footnotes of Table 2. The β_{nuc} value of 0.30 for the reaction of **1-SMe** with primary aliphatic amines is lower than the corresponding $\beta_{nuc} = 0.46$ for **1-OMe**, suggesting less C−N bond formation for the MeS derivative. However, the difference in these β_{nuc} values is too small to explain an almost 4-fold decrease in ρ. Furthermore, the correlation between ρ and β_{nuc} seems weak, as seen by the fact that for the reaction of **1-SMe** with the secondary alicyclic amines ρ is not larger than ρ with the primary amines, despite a higher β_{nuc} value (0.42). We conclude that an earlier transition state cannot be the whole explanation for the low ρ value and probably is not even the main contributing factor.

The second principal factor is the reduced π-donor effect of the MeS group compared to that of the MeO group,[4] as suggested in the Introduction. In the absence of extraneous factors such as a π-donor group one would expect the substituent effect on a reaction that leads to a zwitterionic transition state to be small as long as the distances of the substituent from the sites of positive and negative charge are about the same. These conditions are met, for example, for the transition states of the reactions of amines with substituted benzylidene Meldrum's acids (eq 1)[13] and β-nitrostyrenes (eq 2),[14] respectively.



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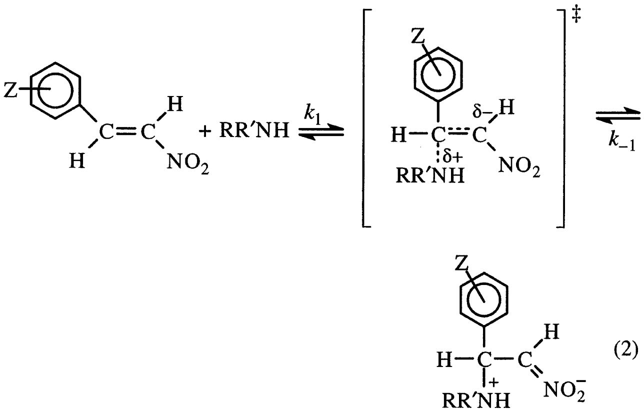

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(6) This is the traditional view,[7−10] although this view has been challenged.[11,12]

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The $\rho(k_1)$ values for these reactions conducted in 50% DMSO−50% water (v/v) are 0.35 (eq 1) and 0.27 (eq 2), respectively. These low ρ values clearly reflect the fact that the substituent effect on the negative charge is largely offset by an opposing effect on the positive charge. Interestingly, the $\rho(K_1) = 0.06$ value for the *equilibrium* constant of eq 2 is even lower than $\rho(k_1)$; this constitutes additional convincing proof of the opposing substituent effects and negates an alternative interpretation of the low $\rho(k_1)$ values based on assuming a highly reactant-like transition state.

How can we understand the role of the π-donor effect of the MeO group in enhancing the ρ value? The key to such understanding is to consider the substituent effect not only on the transition state but also on the reactant. The carbene complex is stabilized by the π-donor effect, which means that the carbene complex has considerable zwitterionic character due to a strong contribution of the resonance form **4**.[15−17] The effect of an electron-withdrawing Z-substituent on **4** should be overall destabilizing, which enhances the reactivity of the carbene complex. This is because the negative charge is largely delocalized into the CO ligands, while the positive charge is concentrated on the methoxy oxygen. As a consequence, the destabilizing substituent effect on the positive charge is stronger than the stabilizing effect on the remote negative charge. For **1-SMe-Z** the π-donor effect is much weaker,[4] which means the corresponding zwitterionic resonance structure is less important and hence the substituent effect on the reactant is diminished.

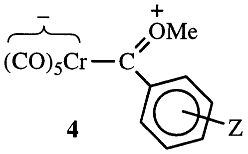

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Table 3. ^{1}H NMR Data for 1-SMe-Z^a

	chemical shift (ppm)		
	SMe	C_6H_4	Z
Z = F	2.34 (s)	6.63 (d), 7.22 (d)	
Z = Cl	2.33 (s)	6.62 (d), 7.33 (d)	
Z = CF_3	2.30 (s)	6.76 (d), 7.02 (d)	
Z = CH_3	2.31 (s)	6.57 (d), 7.10 (d)	2.39 (s)
Z = OCH_3	2.36 (s)	6.70 (d), 6.99 (d)	3.87 (s)
Z = $N(CH_3)_2$	2.44 (s)	6.62 (d), 6.86 (d)	3.07 (s)

^{a} 500 MHz in $CDCl_3$.

Experimental Section

Methods. Schlenk techniques were used in synthesizing and handling the carbene complexes, with argon as the protecting gas. The **1-SMe-Z** complexes were prepared by reaction of the corresponding methoxy complexes, **1-OMe-Z**,[18] with NaSMe, using the procedure of Lam et al.[19] described for the synthesis of $(CO)_5W{=}C(SPh)C_6H_4Z$ type complexes. The products were identified by ^{1}H NMR; the NMR data are summarized in Table 3.

All other materials and reagents were obtained or purified as described earlier.[1]

Procedures and Instrumentation. The preparation of solutions, pH measurements, kinetic methodology, and instrumentation were the same as described earlier.[1]

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