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Physical Organic Chemistry of Transition Metal Carbene Complexes. Part 20:[1] Kinetics and Mechanism of Reactions of $(CO)_5M{=}C(OMe)C_6H_4X$ (M=Cr and W) with Primary Aliphatic Amines in Aqueous Acetonitrile. Substituent Effects

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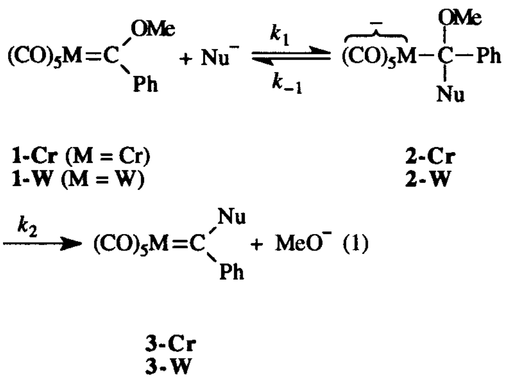
Abstract—A kinetic study of the reactions of $(CO)_5Cr{=}C(OMe)C_6H_4X$ (X=4-Cl, 4-F, H, 4-Me, 4-OMe and 4-NMe_2) and the respective tungsten carbene complexes with primary aliphatic amines (mainly *n*-butylamine) in 50% MeCN–50% water (v/v) at 25°C is reported. The rate law is complex and shows OH^- and amine catalysis at low amine and OH^- concentrations but not at high concentrations. The results are consistent with a three-step mechanism: the first step is nucleophilic addition of the amine to the carbene complex to form a zwitterionic steady state intermediate, $T_A^{\pm}$, which, in the second step, is followed by a rapid deprotonation of $T_A^{\pm}$ to form the anionic steady state intermediate T_A^-, while the third step involves water and RNH_3^+ catalyzed methoxide ion expulsion, respectively, to form the substitution product, $(CO)_5M{=}C(NHR)C_6H_4X$ (M=Cr or W). It is shown that the third step is rate limiting at low OH^- and amine concentrations while the first step is rate limiting at high OH^- and/or amine concentrations. The reasons why $T_A^{\pm}$ and T_A^- cannot be observed directly are discussed and a detailed analysis of the substituent effects on various kinetic parameters is presented. © 2000 Published by Elsevier Science Ltd.

Introduction

The chemistry of Fischer carbene complexes[2] has seen a spectacular development since the first synthesis of such complexes by Fischer and Maasböl in 1964[3]; it now represents an important branch of organometallic chemistry. The major thrust of this development has been the synthesis and characterization of innumerable carbene complexes and their use as synthons and catalysts.[2,4] This intensive synthetic activity is in sharp contrast with the modest efforts towards kinetic and thermodynamic studies of even the simplest reactions of prototypical Fischer carbene complexes. About ten years ago we initiated a program aimed at filling this gap with an emphasis on the study of proton transfers and nucleophilic addition/substitution processes.[5] These latter reactions are the focus of the present paper.

The nucleophilic substitution of a methoxy group in (methoxyphenylcarbene)pentacarbonyl complexes of chromium(0) or tungsten(0), **1-M** (**1-Cr** for M=Cr, **1-W** for M=W), has generally been assumed to proceed by a stepwise mechanism analogous to that of the reaction of carboxylic esters with nucleophiles.[6–10] This mechanism is shown in Eq. (1) for the reaction with an anionic nucleophile.



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The most compelling evidence for this mechanism has come from the direct detection of the intermediate (**2-M**) in the reactions of **1-Cr** and **1-W**[11] with thiolate ions in aqueous acetonitrile and the demonstration that the observed intermediate is indeed on the reaction coordinate of the substitution process.[12] Earlier indications of the plausibility of the two step mechanism included the isolation of adducts such as **4-Cr** (X=N or CH) from ether solutions of **1-Cr** and DABCO or quinuclidine,[13] and the spectroscopic detection of **5-Cr** and **5-W** in methanolic NaOMe solutions.[14]

With NH_3, primary amines and unhindered secondary amines as nucleophiles substitution of the alkoxy group

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Keywords: Fischer carbenes; nucleophilic substitution; general acid/base catalysis; Hammett plots.

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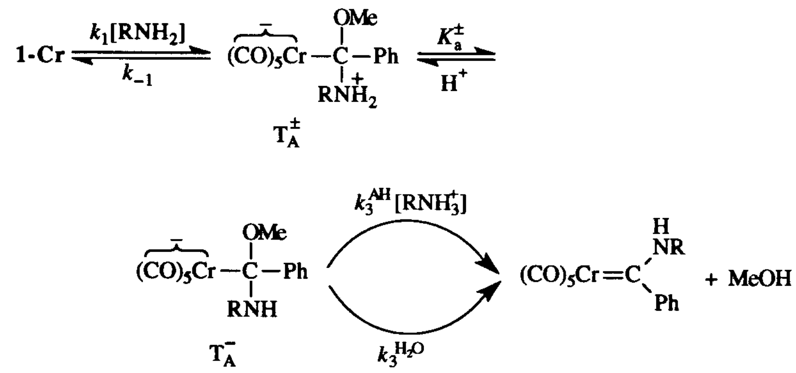
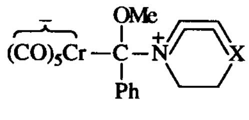
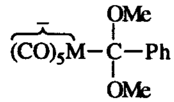


Scheme 1.

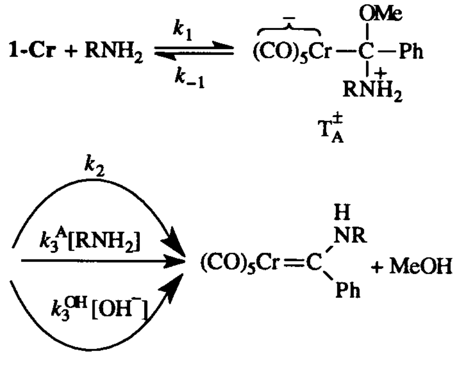
occurs but no intermediate is detectable in such reactions.[7] However, indirect evidence for a stepwise mechanism has been presented based on the kinetics of the reaction of **1-Cr** with a series of aliphatic amines in 20% MeCN–80% water.[7g] The reactions can be represented by Eq. (2); k_2 refers to spontaneous conversion of the intermediate to products while k_3^A [RNH$_2$] and k_3^{OH}[OH$^-$] refer to amine and OH$^-$ catalyzed pathways, respectively.



4-Cr



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



(2)

These reactions were shown to undergo a change in rate limiting step from amine and OH$^-$ catalyzed leaving group departure at low amine and OH$^-$ concentrations to nucleophilic attack at high amine and/or OH$^-$ concentrations; such change, of course, implies the operation of at least two steps and the presence of at least one intermediate. A detailed analysis of the kinetic data demonstrated that the k_3^A and k_3^{OH} pathways can, in turn, be broken down into two steps, a rapid reversible deprotonation of the zwitterion, $T_A^{\pm}$, followed by general acid catalyzed leaving group departure. This is shown in Scheme 1, with the k_3^{AH} step referring to a transition state such as **6**[15] and the $k_3^{H_2O}$ step to a transition state such as **7**[15]; the k_2 step has been omitted from the scheme because it is negligible under the reaction conditions. According to Scheme 1 k_3^A in Eq. (2) takes on the meaning of Eq. (3), k_3^{OH} in Eq. (2) that of Eq. (4), with $K_a^{\pm}$ and K_a^{AH} being the acid dissociation constants of $T_A^{\pm}$ and of RNH$_3^+$, respectively, and K_w being the ionic product of the solvent.

$$k_3^A = k_3^{AH} K_a^{\pm} / K_a^{AH} \tag{3}$$

$$k_3^{OH} = k_3^{H_2O} K_a^{\pm} / K_w \tag{4}$$

In this paper we focus on the effect of phenyl substituents on the kinetics of the reaction of *n*-butylamine with **1-Cr-X** and **1-W-X** in 50% MeCN–50% water (v/v) where X=Cl, F, H, Me, MeO and Me$_2$N. A few experiments referring to the reaction of ClCH$_2$CH$_2$NH$_2$ with **1-Cr-H** are also reported.

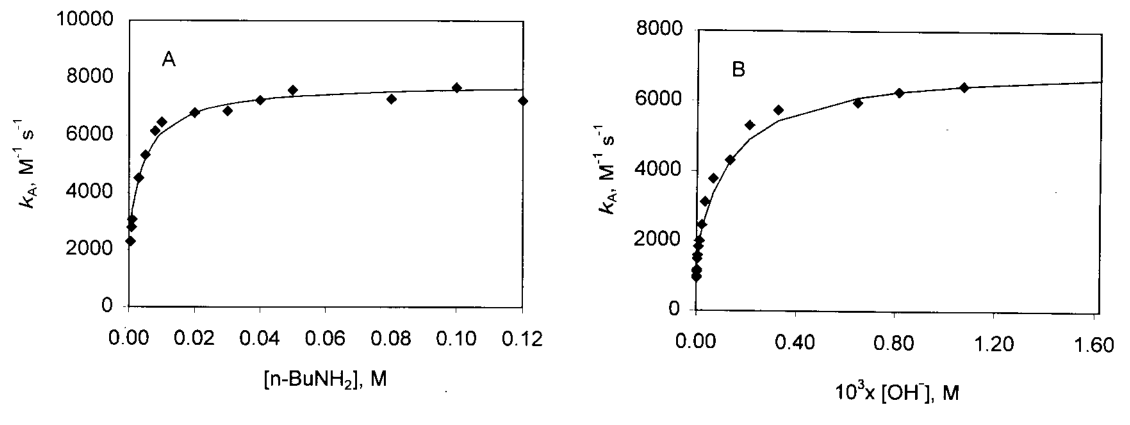
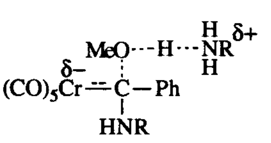


Fig. 1. Reaction of **1-W-Cl** with *n*-BuNH$_2$ in 50% MeCN–50% water: (A) k_A as a function of [*n*-BuNH$_2$] at pH 10.88; (B) k_A as a function of [OH$^-$] at [*n*-BuNH$_2$]=10^{-3} M.



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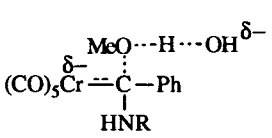

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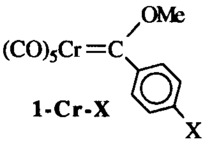
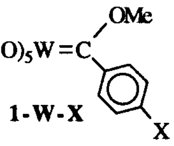


1-Cr-X



1-W-X

Results

General features

The general features of the kinetic experiments which were all conducted under pseudo-first-order conditions, with the carbene complex as the minor component, have been described earlier.[7g] Competing hydrolysis of the carbene complex was negligible and hence second order rate constants for aminolysis were calculated based on Eq. (5). For all carbene complexes the k_A values generally increased

$$k_A = \frac{k_{\text{obsd}}}{[\text{RNH}_2]} \tag{5}$$

non-linearly with increasing amine and OH^- concentration and, in most cases, reached a plateau. Fig. 1A shows a representative plot of k_A vs. amine concentration at constant pH while Fig. 1B shows a representative plot of k_A vs. OH^- concentration at constant amine concentration. In a number of experiments, rates were measured both at $\lambda_{\max}$ of the substrate (396 nm) and of the product (295 nm); the k_{obsd} values were the same within experimental error. This indicates that there is no accumulation of an intermediate to detectable levels even at the highest *n*-butylamine concentrations (0.2 M) and highest pH (14.1) used.[18]

Data analysis

The kinetic data were analyzed based on the scheme of Eq. (2), with $T_A^{\pm}$ treated as steady state intermediate and k_2 assumed to be negligible compared to $k_3^{A}[\text{RNH}_2] + k_3^{OH}[OH^-]$. Thus k_A is given by Eq. (6).

$$k_A = k_1 \frac{(k_3^A/k_{-1})[\text{RNH}_2] + (k_3^{OH}/k_{-1})[OH^-]}{1 + (k_3^A/k_{-1})[\text{RNH}_2] + (k_3^{OH}/k_{-1})[OH^-]} \tag{6}$$

The plateau values of the plots shown in Fig. 1A and B correspond to $k_A = k_1$ and are reached when either $((k_3^A/k_{-1})[\text{RNH}_2] \gg 1$ or $(k_3^{OH}/k_{-1})[OH^-] \gg 1$; the initial slopes correspond to $(k_1 k_3^A/k_{-1})/\{1 + (k_3^{OH}/k_{-1})[OH^-]\}$ in Fig. 1A and to $(k_1 k_3^{OH}/k_{-1})/\{1 + (k_3^A/k_{-1})[\text{RNH}_2]\}$ in Fig. 1B.

The determination of k_1, k_3^A/k_{-1} and k_3^{OH}/k_{-1} was achieved by non-linear regression analysis of the plots of k_A vs. amine and OH^- concentration. Due to problems discussed below the set of k_1, k_3^A/k_{-1} and k_3^{OH}/k_{-1} values which would give the best fit for the plot of k_A vs. $[\text{RNH}_2]$ would not always give the best fit for the plot of k_A vs. $[OH^-]$, and the parameters that gave the best fit for the $[OH^-]$ dependence would not give the best fit for the $[\text{RNH}_2]$ dependence. In these cases, the k_3^A/k_{-1} values obtained from the fit to the $[\text{RNH}_2]$ dependence, and the k_3^{OH}/k_{-1} values obtained from the $[OH^-]$ dependence are reported. This choice reflects the fact that the former fit is more sensitive to the value of k_3^A/k_{-1} than that of k_3^{OH}/k_{-1} while for the latter fit the opposite is true. For the k_1 values which would typically differ by less than 10%, the average from the two fits is reported.

There are probably several reasons why a single set of k_1, k_3^A/k_{-1} and k_3^{OH}/k_{-1} values did not always give an optimal fit for both the amine and OH^- concentration dependence. The most important one is attributed to difficulties in maintaining good pH control, mainly in the experiments where $[OH^-]$ was the variable. Since the rates had to be determined by the stopped-flow method, the pH of the reaction solution could not be measured directly but was determined by mock mixing experiments outside the stopped-flow apparatus. A conservative estimate of the accuracy of these pH values is ±0.02 units which corresponds to ±5% error in $[OH^-]$. Errors in $[OH^-]$ not only affect OH^--catalysis but also lead to errors in the concentration of free amine, especially at $\text{pH} < \text{p}K_a^{AH}$ where, for a given total amine concentration, the free amine concentration is proportional to $[OH^-]$. Furthermore, an error in the free amine concentration affects k_A in two ways, one via Eq. (5), the other because of amine catalysis. Hence, depending on pH and $[\text{RNH}_2]$, the compounded error in k_A may range from ±3% to ±15%.

Another potential source of slight discrepancies is the operation of salt effects at high amine concentrations where $[\text{RNH}_3^+]$ is also high and the potassium ion is replaced by RNH_3^+ as the cation in the supporting electrolyte. Such salt effects may, in part, be responsible for the small differences in the k_1 values obtained from the plots of k_A vs. $[OH^-]$ compared to the plots of k_A vs. $[\text{RNH}_2]$.

Discussion

Mechanism

As discussed in more detail elsewhere,[7g] the only reasonable interpretation of the kinetic data is in terms of the stepwise mechanism of Eq. (2). Particularly compelling is the fact that the plateau values of the curvilinear plots of k_A vs. amine concentration are the same as for the plots of k_A vs. OH^- concentration and represent k_1 for the limiting situation where $k_3^A[\text{RNH}_2]k_{-1} + k_3^{OH}[OH^-]/k_{-1} \gg 1$. With regard to the nature of the base catalysis (k_3^A and k_3^{OH} steps), two possibilities exist. One is that deprotonation of $T_A^{\pm}$ is rate limiting, followed by rapid MeO^- expulsion. Such rate limiting deprotonation of the corresponding zwitterionic tetrahedral intermediate is typically observed in the aminolysis of acyl esters[19] and in numerous S_NAr reactions.[20] The second possibility is the one shown in Scheme 1 where rapid equilibrium deprotonation is

Table 1. Summary of the kinetic parameters for the reactions of **1-W-X** and **1-Cr-X** with *n*-BuNH$_2$ and the reaction of **1-Cr-X** with ClCH$_2$CH$_2$NH$_2$

X	σ	k_1[a] ($M^{-1}\ s^{-1}$)	k_3^A/k_{-1}[b] (M^{-1})	k_3^{OH}/k_{-1}[b] (M^{-1})	k_3^{OH}/k_3^A[c]
1-W-X+*n*-BuNH$_2$ (50% MeCN–50% water)					
Cl	0.23	7800	250	2.3×10^4	92
F	0.06	5000	130	1.5×10^4	115
H	0	4500	100	1.0×10^4	100
Me	−0.17	2600	40	5.0×10^3	125
MeO	−0.27	1200	20	2.8×10^3	140
Me$_2$N	−0.83	40	6.0	7.9×10^2	132
1-Cr-X+*n*-BuNH$_2$ (50% MeCN–50% water)					
Cl	0.23	3200	250	2.2×10^4	88
F	0.06	2100	120	1.2×10^4	100
H	0	1600	100	1.2×10^4	120
Me	−0.17	1000	65	7.0×10^3	108
MeO	−0.27	340	50	8.0×10^3	160
Me$_2$N	−0.83	27	7.0	9.8×10^2	140
1-Cr-H+ClCH$_2$CH$_2$NH$_2$ (50% MeCN–50% water)					
H		130	35	1.1×10^5	3.5×10^3
1-Cr-H+*n*-BuNH$_2$ (20% MeCN–80% water)[d]					
H		2900	34	8.1×10^3	238
1-Cr-H+ClCH$_2$CH$_2$NH$_2$ (20% MeCN–80% water)[d]					
H		91	19	2.8×10^5	1.47×10^4

[a] Estimated uncertainty ±10% or better.
[b] Estimated uncertainty ±30% or better.
[c] Estimated uncertainty ±60% or better.
[d] Ref. 4g.

followed by rate limiting general acid catalyzed MeO$^-$ departure.

For the reaction of **1-Cr-H** in 20% MeCN–80% water it was shown that the results are consistent with Scheme 1 but inconsistent with rate limiting proton transfer.[7g] Specifically, the k_3^{OH}/k_3^A ratios which revealed a systematic increase with decreasing basicity of the amine ($k_3^{OH}/k_3^A = 238$ for *n*-BuNH$_2$, p$K_a^{AH} = 10.67$; 3.98×10^3 for MeOCH$_2$CH$_2$NH$_2$, p$K_a^{AH} = 9.52$; 1.47×10^4 for ClCH$_2$CH$_2$NH$_2$, p$K_a^{AH} = 8.61$; 7.22×10^4 for H$_2$NCOCH$_2$NH$_2$, p$K_a^{AH} = 8.03$; 1.54×10^5 for EtOCOCH$_2$NH$_2$, p$K_a^{AH} = 7.70$), were dramatically different from the ratios expected for rate limiting proton transfer. If proton transfer were rate limiting, k_3^{OH} would refer to a diffusion controlled reaction with $k_3^{OH} \approx 10^{10}\ M^{-1}\ s^{-1}$,[21] irrespective of the amine; k_3^A should have a value on the order of 4×10^8 to $2\times10^9\ M^{-1}\ s^{-1}$,[22] which is also independent of the amine because the pK_a difference between $T_A^{\pm}$ and RNH_3^+ is expected to be essentially independent of the amine. This leads to expected k_3^{OH}/k_3^A ratios on the order of 5 to 25, independent of the amine. On the other hand, the strong increase in the k_3^{OH}/k_3^A ratios with decreasing amine basicity is easily understood in terms of Scheme 1 for which k_3^{OH}/k_3^A is proportional to the acidity constant of RNH_3^+, K_a^{AH} Eq. (7); there is some

$$\frac{k_3^{OH}}{k_3^A} = \frac{k_3^{H_2O}}{k_3^{AH}}\frac{K_a^{AH}}{K_w} \tag{7}$$

attenuation of this proportionality because the stronger acid catalysis by the more acidic RNH_3^+ results in an increase in k_3^{AH} with decreasing basicity of the amine but this attenuation is small.

The current results were obtained in 50% MeCN–50% water (v/v), a solvent which has become standard in most of our recent studies.[5] The change from 20% MeCN–80% water used in the previous study[7g] to 50% MeCN–50% water is not expected to affect any of the kinetic parameters in a major way and hence it is safe to assume that the same mechanism (Scheme 1) prevails in both solvents. This expectation is confirmed by the fact that for the reactions of **1-Cr-H** with *n*-BuNH$_2$ and ClCH$_2$CH$_2$NH$_2$ the k_1 values and the k_3^{OH}/k_3^A ratios are quite similar to the corresponding parameters in 20% MeCN–80% water (Table 1).

Why is T_A^- not detectable?

In the reactions of **1-Cr-H** and **1-W-H** with thiolate ions, the corresponding intermediates (**2-Cr** and **2-W** with Nu$^-$=RS$^-$ in Eq. (1)) accumulate to detectable levels[12] because the equilibrium of the first step is quite favorable (i.e. $K_1[RS^-]>1$)[23] and the conversion of the intermediate to products is slower than its formation from the reactants (i.e. $k_1[RS^-]/k_2>1$).[24] For example, for the reaction of **1-Cr-H** with MeO$_2$CCH$_2$CH$_2$S$^-$ (p$K_a^{RSH} = 10.69$), $K_1 = 3.51\times10^3\ M^{-1}$, $k_1=2.30\times10^4\ M^{-1}\ s^{-1}$ and $k_2\leq4.0\times10^{-3}\ s^{-1}$;[25] thus the condition $K_1[RS^-]\geq1$ is met for $[RS^-]\geq2.85\times10^{-4}$ M while the condition $k_1[RS^-]/k_2\geq1$ is met at even lower [RS$^-$].

This situation contrasts with that for the reactions of **1-Cr-X** and **1-W-X** with amines. Here the fact that k_{obsd} determined at λ_{max} of the product is the same as k_{obsd} determined at λ_{max} of the reactant shows that there is no accumulation of an intermediate to detectable levels. In view of how amply the conditions for intermediate detection are met for the thiolate ion reactions, it may seem surprising that T_A^- in Scheme 1 is not detectable and remains a steady state intermediate even at the highest amine concentrations (0.2 M) and highest pH

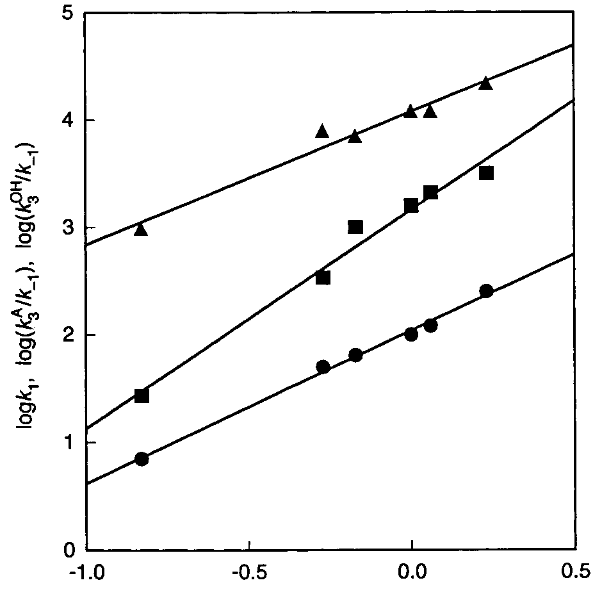


Fig. 2. Reaction of **1-Cr-X** with n-BuNH$_2$ in 50% MeCN–50% water. Hammett plots for k_1 (■), k_3^A/k_{-1} (●) and k_3^{OH}/k_{-1} (▲).

(14.1) used.[26] It is instructive to analyze the reasons why T_A^- does not accumulate to measurable levels.

The necessary conditions for T_A^- to become detectable are shown in Eqs. (8) and (9).[27] Based on

$$(K_1K_a^{\pm}/a_{H^+})[RNH_2] > 1 \tag{8}$$

$$k_1[RNH_2]/(k_3^{AH}[RNH_3^+] + k_3^{H_2O}) > 1 \tag{9}$$

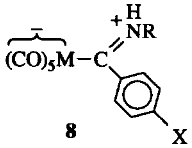
analogies with the reactions of β-methoxy-α-nitrostilbene with amines[28] and thiolate ions[29] we estimate that K_1 for n-BuNH$_2$ addition to **1-Cr-H** is 10^5 to 10^6 lower than K_1 for MeO$_2$CCH$_2$CH$_2$S$^-$,[30] i.e. 3×10^{-3} to 3×10^{-2} M^{-1}, and that the p$K_a^{\pm}$ of $T_A^{\pm}$ is at least 1.4 units lower than pK_a^{AH},[31] i.e. p$K_a \lesssim 9.0$ for the n-BuNH$_2$ adduct. Hence at the highest pH values used (14.1) we expect $K_1K_a^{\pm}/a_{H^+} \approx 4\times10^2$ to 4×10^3 M^{-1} and hence $K_1K_a^{\pm}[RNH_2]/a_{H^+} \approx 80$ to 800 at the highest amine concentrations used. In other words, the 'equilibrium condition' of Eq. (8) is met, implying it is the 'kinetic condition' of Eq. (9) which is not met. Apparently, the loss of MeO$^-$ from T_A^- is much faster than the loss of MeO$^-$ from the corresponding intermediates in the thiolate ion reactions. This must be mainly the result of the strong electronic push by the lone pair on the amine nitrogen due to the developing resonance that stabilizes the product (**8**). This conclusion is similar to that reached for the reasons why an intermediate is observed in the reactions of β-methoxy-α-nitrostyrene with thiolate ions but not in the reactions with strongly basic amines.[28]

Table 2. Hammett ρ values for the reactions of n-BuNH$_2$ with **1-Cr-X** and **1-W-X**

	1-Cr-X	1-W-X
k_1	2.03±0.15	2.23±0.21
k_3^A/k_{-1}	1.42±0.05	1.56±0.18
k_3^{OH}/k_{-1}	1.24±0.11	1.40±0.13

Substituent effects

An increase in the electron withdrawing strength of the phenyl substituent leads to an increase in k_1, k_3^A/k_{-1} and k_3^{OH}/k_{-1} (Table 1). Hammett plots for these parameters are shown in Fig. 2 for the reactions of **1-Cr-X**; similar plots (not shown) were obtained for the reactions of **1-W-X**. The ρ values are summarized in Table 2.



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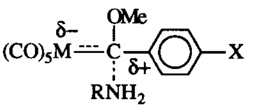

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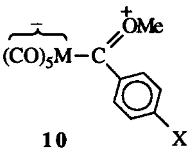

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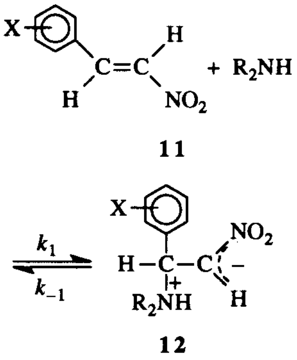
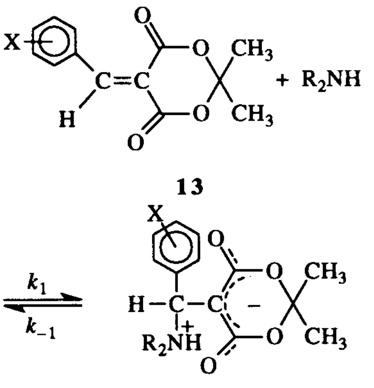
k_1. The positive ρ values for k_1 are of similar magnitude as for the nucleophilic addition of OH$^-$ in 50% MeCN–50% water (ρ=2.25 for **1-Cr-X** and ρ=1.79 for **1-W-X**)[1] or of MeO$^-$ in methanol (ρ=2.19 for **1-Cr-X** and ρ=2.60 for **1-W-X**).[1] They are the combined result of several factors. One is the stabilization of the incipient negative charge on the (CO)$_5$M moiety at the transition state (**9**) by electron withdrawing substituents. However, this factor may be largely or completely offset by a destabilization of the incipient positive charge on the amine nitrogen. A more important factor must therefore be the destabilization, by electron withdrawing substituents, of the highly electrophilic carbene carbon in the reactants. Another way to describe this effect is to consider the resonance structure **10** of the carbene complex. Inasmuch as the negative charge in **10** is quite remote from the phenyl substituent due to delocalization into the CO ligands, while the positive charge is concentrated on the oxygen atom and thus closer to X, the destabilizing substituent effect on the positive charge must be much greater than the stabilizing effect on the negative charge, resulting in a net increase in reactivity of the carbene complex.

This interpretation is supported by a comparison with the reactions of piperidine with phenyl substituted β-nitrostyrenes (**11**)[32] or benzylidene Meldrum's acids (**13**).[33] In these cases there is no π-donating methoxy group attached to the electrophilic carbon and hence there must be less destabilization of the reactant by electron withdrawing X-groups. Indeed, the $\rho(k_1)$ values are only 0.27 for **11**[11,32,34] and 0.35 for **13**,[13,33,34], respectively, reflecting the compensating substituent effects on the incipient positive and negative charges at the transition states.



(10)

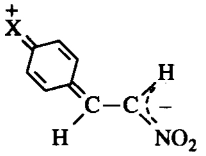


13

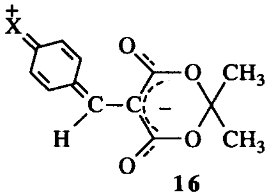
14

(11)

The presence of a methoxy group in the Fischer carbenes and its absence from **11** or **13** leads to another interesting contrast. The k_1 values for the piperidine reaction with the 4-OMe and especially the 4-Me$_2$N derivatives of β-nitrostyrene and benzylidene Meldrum's acids show substantial deviations from the Hammett plots.[32,33] These deviations were attributed to the π-donor effect of these substituents (**15**,**16**). No such deviations are found with the Fischer carbenes, presumably because the π-donor effect of the phenyl substituents is overshadowed by the stronger π-donor effect of the methoxy group directly attached to the carbene carbon.



15



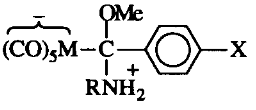
16

k_3^{A}/k_{-1} and k_3^{OH}/k_{-1}. The substituent effects on the k_3^{A}/k_{-1} and k_3^{OH}/k_{-1} ratios which are given by Eqs. (12) and (13), respectively, are best discussed by considering each term in Eqs. (12) and (13) separately. For k_{-1}, electron withdrawing substituents should slow down the reaction since it is the reverse of the k_1 step.

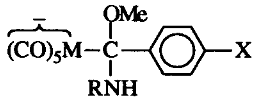
$$\frac{k_3^{\mathrm{A}}}{k_{-1}} = \frac{k_3^{\mathrm{AH}}}{k_{-1}}\frac{K_{\mathrm{a}}^{\pm}}{K_{\mathrm{a}}^{\mathrm{AH}}} \tag{12}$$

$$\frac{k_3^{\mathrm{OH}}}{k_{-1}} = \frac{k_3^{\mathrm{H_2O}}}{k_{-1}}\frac{K_{\mathrm{a}}^{\pm}}{K_{\mathrm{w}}} \tag{13}$$

Negative $\rho(k_{-1})$ values have indeed been observed for the reversible MeO$^-$ addition to **1-Cr-X** ($\rho=-1.91$) and **1-W-X** ($\rho=-1.60$) in methanol.[1] However, the absolute $\rho(k_{-1})$ values for the amine reactions are probably smaller than for the MeO$^-$ reactions because of the offsetting effect of the positive charge on the amine nitrogen both in the adduct (**17**) and the transition state (**9**).



17



18

For k_3^{AH} and $k_3^{\mathrm{H_2O}}$ which refer to the conversion of **18** to **6** and **7**, respectively, the partial loss of negative charge again suggests a negative ρ value. There is no offsetting effect from the partial loss of a positive charge, therefore the ρ values for k_3^{AH} and $k_3^{\mathrm{H_2O}}$ are potentially more negative than $\rho(k_{-1})$ although this will depend on the reactant- vs. product-like nature of the respective transition states.

$K_{\mathrm{a}}^{\pm}$ will definitely be enhanced by electron withdrawing substituents and this appears to be the major contribution to the positive ρ values observed for the k_3^{A}/k_{-1} and k_3^{OH}/k_{-1} ratios.

Effect of the metal

The k_1 values for the tungsten complexes are about 2.5 fold higher than for the chromium complexes. Similar k_1(W)/k_1(Cr) ratios have been reported for the reactions with methoxide ion in methanol[14] and with various thiolate ions in 50% MeCN–50% water.[12] They show a consistent pattern of somewhat enhanced electrophilic reactivity of the tungsten complexes. On the other hand, the k_3^{A}/k_{-1} and k_3^{OH}/k_{-1} ratios for the chromium and tungsten complexes are, within experimental error, indistinguishable.

With respect to the substituent dependence of k_1, k_3^{A}/k_{-1} and k_3^{OH}/k_{-1}, there is no significant difference between the chromium and tungsten complexes as reflected in the respective ρ values (Table 2).

Conclusions

1. The reaction of **1-M-X** with primary aliphatic amines leads to nucleophilic substitution of the methoxy group by the three-step mechanism of Scheme 1. At low amine and OH$^-$ concentration, RNH$_3^+$ and water catalyzed methoxide ion departure is rate limiting while at high amine and/or high OH$^-$ concentration nucleophilic attack is rate limiting.
2. The two intermediates, $\mathrm{T_A^{\pm}}$ and $\mathrm{T_A^{-}}$, remain undetectable even at high amine concentration and high pH, conditions which favor $\mathrm{T_A^{-}}$ over the substrate thermodynamically, i.e. $(K_1K_{\mathrm{a}}^{\pm}/a_{\mathrm{H^+}})[\mathrm{RNH_2}] > 1$. It is concluded that the reason why $\mathrm{T_A^{-}}$ cannot be observed is that its rate of conversion to products is faster than the rate of its formation, i.e. $k_1[\mathrm{RNH_2}]/(k_3^{\mathrm{H_2O}} + k_3^{\mathrm{AH}}[\mathrm{RNH_3^+}]) < (\ll)1$.
3. The positive ρ values for k_1 are in large measure the result of a destabilization of the carbene complexes by electron withdrawing substituents. The potential contribution to the ρ value by the substituent effect on the incipient negative charge in the transition state is likely

to be offset by the effect on the incipient positive charge.

4. The absence of strong deviations from the Hammett plots for the 4-OMe and 4-NMe_2 derivatives may be attributed to the dominance of the π-donor effect of the methoxy group directly attached to the carbene carbon.
5. The main contribution to the positive ρ values for the k_3^A/k_{-1} and k_3^{OH}/k_{-1} ratios comes from the enhancement in $K_a^{\pm}$ by electron withdrawing substituents.
6. The change from chromium to tungsten results in an approximately 2.5 fold increase in k_1, which is in line with similar increases in reactions of the same carbene complexes with other nucleophiles.

Experimental

Materials

All the carbene complexes were available from a previous study.[1] *n*-Butylamine was refluxed over sodium or $Ca(OH)_2$ and distilled and stored under argon. 2-Chloroethylamine was recrystallized from an ethanol–toluene mixture as its hydrochloride salt. Reagent grade acetonitrile was used throughout. The water used was taken from a Milli-q purification system. Stock solutions of KOH and HCl were prepared from Baker 'Dilut-it' prepackaged solutions.

Solutions and pH measurements

All solutions were prepared in 50% MeCN–50% water (v/v) at 25°C and an ionic strength of 0.1 M maintained with KCl. pH measurements were made in mock mixing experiments outside the stopped-flow apparatus. A Model 611 Orion research digital pH meter calibrated with standard aqueous buffers was used. Actual pH values were calculated by adding 0.18 to the measured pH, according to Allen and Tidwell.[35]

Kinetic experiments

All measurements were made with an Applied Photophysics DX.17MV stopped-flow apparatus. Pseudo-first-order conditions, with the carbene complex as the minor component, were used throughout. Due to rapid hydrolysis, substrate solutions in 50% MeCN–50% water were always freshly prepared from a stock solution in pure MeCN immediately prior to a kinetic experiment. Typical substrate concentrations were on the order of 10^{-4} M. The reactions were usually monitored at or near λ_{max} of the carbene complex (λ_{max}=396 nm) although some runs were also followed at or near λ_{max} of the product (λ_{max}=295 nm). For **1-M-NMe$_2$** the reactions were monitored at 450 nm.

Acknowledgements

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sition states the charge is mainly localized on the metal is based on a large body of evidence that in reactions where a delocalized ion is formed, the delocalization lags behind bond changes at the transition state ('transition state imbalance') while in reactions where a delocalized ion is converted to a non-delocalized product, localization of the charge occurs ahead of bond changes.[16,17].

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17. For evidence pertaining specifically to the addition of nucleophiles to Fischer carbene complexes, see Ref. 1.

18. A high pH would favor the accumulation of T_A^- as elaborated upon in the Discussion.

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23. $K_1=k_1/k_{-1}$.

24. Both of these conditions must be met for an intermediate to become observable.

25. This upper limit for k_2 was estimated as follows. The rate constant for H^+-catalyzed conversion of the intermediate to products, k_2^H, is $1.99\times10^8\ M^{-1}\ s^{-1}$.[1] At pH 10.69 where $k_2^H a_{H^+} = 4.06\times10^3$ there is no measurable conversion to products by the k_2 pathway, indicating that $k_2<4.06\times10^{-3}\ s^{-1}$.

26. Under typical reactions conditions, $K_a^{\pm}/a_{H^+} \gg 1$ which means that $[T_A^-] \gg [T_A^{\pm}]$ and hence only T_A^- is a realistic candidate for being a detectable intermediate.

27. If the conditions of Eqs. (8) and (9) were met, T_A^- would accumulate to a level that is equal to the initial carbene complex concentration or approaching it. However, if $(K_1K_a^{\pm}/a_{H^+})[RNH_2]$ and/or $k_1[RNH_2](k_3^{AH}[RNH_3^+] + k_3^{H_2O})$ were about unity or even somewhat less than unity, T_A^- would still be detectable although at a concentration that is lower than the initial carbene complex concentration.

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30. K_1 for $MeO_2CCH_2CH_2S^-$ addition to β-methoxy-α-nitrostyrene is $4.0\times10^3\ M^{-1}$[29] while K_1 for *n*-$BuNH_2$ addition to the same substrate may be estimated to be $\sim10^2\ M^{-1}$. This latter estimate is based on $K_1=3.7\times10^{-6}\ M^{-1}$ for methoxyamine ($pK_a^{AH} = 4.70$) addition, a $\beta_{eq}=0.92$ for amine additions and an α-effect correction factor of 60.[28b]

31. The $pK_a^{\pm}$ value of the $T_A^{\pm}$ type adduct between β-methoxy-α-nitrostyrene and methoxyamine is 2.5 units lower than the pK_a^{AH} of methoxyamine. Since the $\overbrace{(CO)_5Cr}$ moiety may be somewhat less electron withdrawing than the $\underline{C}(Ph)NO_2^-$ moiety, a somewhat smaller acidifying effect for $\overbrace{(CO)_5Cr}$ is assumed.

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