Physical Organic Chemistry of Transition Metal Carbene Complexes. 2.[1] Kinetics and Mechanism of Reactions of [Methoxy(phenyl)carbene]pentacarbonylchromium(0) with Primary Aliphatic Amines in Aqueous Acetonitrile

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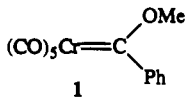
Abstract: A kinetic study of the aminolysis of [methoxy(phenyl)carbene]pentacarbonylchromium(0) with five primary aliphatic amines in 20% acetonitrile–80% water (v/v) at 25 °C is reported. Second-order rate constants (k_A) increase with amine and OH^- concentration, which indicates general base catalysis. Plots of k_A vs amine or OH^- concentration are curved and level off at high concentration; this implies a change in rate-limiting step and demonstrates that the reaction is stepwise. The mechanism is similar to that for ester aminolysis, i.e., the first step is nucleophilic addition of the amine to the substrate to yield a zwitterionic tetrahedral intermediate ($T_A^{\pm}$), followed by deprotonation of $T_A^{\pm}$ to form T_A^- which, in a third step, is converted to products by general acid catalyzed methoxide expulsion. In contrast to ester aminolysis, where general base catalysis is a consequence of rate-limiting deprotonation of $T_A^{\pm}$, rate-limiting conversion of T_A^- to products is responsible for the general base catalysis with the carbene complex. Possible reasons for this contrast include a stronger stabilization of T_A^- and $T_A^{\pm}$ and higher intrinsic barriers for the first and third steps of the reaction mechanism in the carbene-complex reaction. Structure–reactivity coefficients suggest that the transition state for the first step is $T_A^{\pm}$-like while the transition state for the third step is T_A^--like.

[Methoxy(phenyl)carbene]pentacarbonylchromium(0), **1**, is a prototype Fischer transition metal carbene complex.[2] It undergoes



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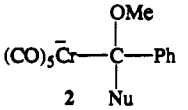

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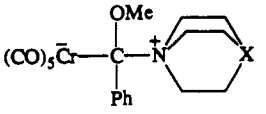
facile substitution of the methoxy group by nucleophiles. These nucleophilic substitution reactions are generally believed to proceed through a stepwise mechanism that involves an intermediate of the general structure **2**.[2] With rigid tertiary amines, e.g., Dabco or quinuclidine, as the nucleophile, a zwitterionic adduct, **3**, formed



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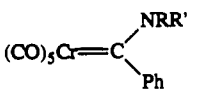

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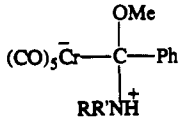
X = N or CH

in ethyl ether, has been isolated.[3] With NH_3 and primary and unhindered secondary amines the reaction leads to the corresponding amino carbene complexes, **4**;[4] no intermediate has been detected in these aminolysis reactions, but it is plausible that they pass through intermediates such as **5**.[5]



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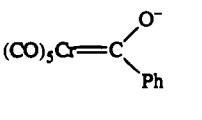

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Not much is known about the kinetics and mechanistic details of the aminolysis of **1** or of similar Fischer carbene complexes. A recent report indicates that the reaction of alkoxy carbene complexes with dimethylamine in THF is catalyzed by methoxide ion.[6] The only kinetic studies we are aware of are those of Werner et al.,[5] who investigated the reaction of **1** with several primary amines in *n*-decane, dioxane, methanol, and dioxane–methanol (1:1) mixtures. In these solvents, particularly in *n*-decane and dioxane, complications arise due to the low polarity of the medium, which makes mechanistic interpretations more difficult. For example, in *n*-decane the reaction follows fourth-order kinetics (third-order with respect to the amine), which was attributed to hydrogen bonding of one amine molecule to the methoxy oxygen of **1** and hydrogen bonding of another amine molecule to the amine that acts as the nucleophile.

The objective of the work presented here was to study the kinetics of the aminolysis in a much more polar solvent (20% acetonitrile–80% water). This should avoid the above complications and allow more clear-cut mechanistic conclusions. We are in fact able to provide the first substantial evidence for the stepwise nature of the mechanism by showing that the reaction is general base catalyzed at low but not at high base concentrations. Our results also allow us to establish the nature of this catalysis.

Results

General Features. The kinetics of the reaction of **1** with five primary amines (*n*-butylamine, 2-methoxyethylamine, 2-chloroethylamine, glycinamide, and glycine ethyl ester) were measured in 20% acetonitrile–80% water (v/v) at 25 °C. The conversion of **1** into the amine carbene complex **4** produces a blue shift in the UV spectrum. This is illustrated in Figure 1 with the example of the glycine ethyl ester reaction. The identity of the product was confirmed by comparison of the infinity spectrum of the reaction solution with the spectrum of the corresponding, independently synthesized amine carbene complex. Under most reaction conditions conversion of **1** to **4** was virtually quantitative; i.e., the hydrolysis of **1** to form **6** was negligible, as shown by comparing the rates of aminolysis with the known rates of hydrolysis.[7]

(1) Part 1: Gandler, J. R.; Bernasconi, C. F. *Organometallics* **1989**, *8*, 2282.

(2) For recent reviews, see: (a) Dötz, K. H.; Fisher, H.; Hofmann, P.; Kreissl, F. R.; Schubert, U.; Weiss, K. *Transition Metal Carbene Complexes*; Verlag Chemie: Deerfield Beach, FL, 1983. (b) Schubert, U., Ed. *Advances in Metal Carbene Chemistry*; Kluwer: Dordrecht, Holland, 1989.

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(5) Werner, H.; Fischer, E. O.; Heckl, B.; Kreiter, C. G. *J. Organomet. Chem.* **1971**, *28*, 367.

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(7) Bernasconi, C. F.; Stronach, M. W. Unpublished results.

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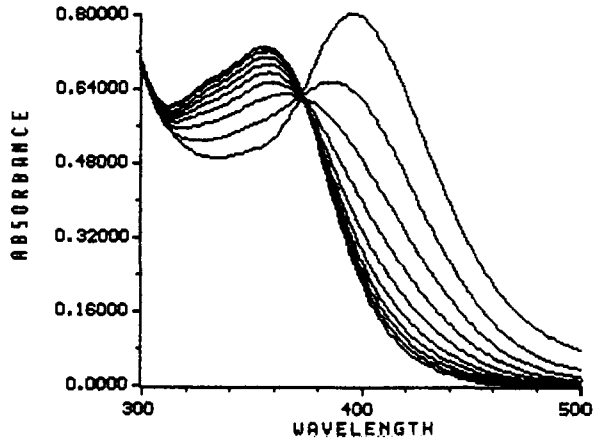


Figure 1. Conversion of **1** into **4** with 0.005 M glycine ethyl ester, pH 7.70. The first spectrum was taken after 3 s, and the time intervals are 12 s.

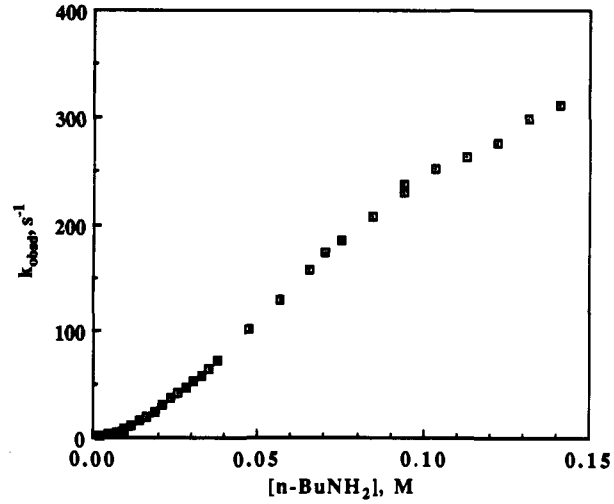


Figure 2. Reaction of **1** with *n*-butylamine. Pseudo-first-order rate constant as a function of amine concentration.

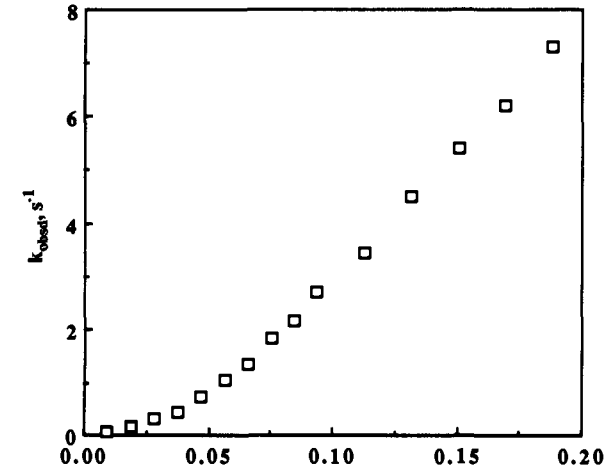


Figure 3. Reaction of **1** with glycine ethyl ester. Pseudo-first-order rate constant as a function of amine concentration.

The rates were generally quite fast and were measured in a stopped-flow spectrophotometer. All experiments were conducted under pseudo-first-order conditions with the amine as the excess component and the concentration of **1** between 4×10^{-5} and 10^{-4} M. The raw data are summarized in Tables S1–S10 of the supplementary material.[8] In all cases the observed pseudo-first-order rate constants, k_{obsd}, showed a nonlinear dependence on amine concentration. This is illustrated in Figures 2 and 3 for two representative examples (*n*-butylamine and glycine ethyl ester). These plots are indicative of a change from a second-order (or mixed first- and second-order) to a first-order dependence on amine concentration.

In the following analysis of the results all the data will be converted into second-order rate constants (k_A) by dividing k_{obsd} by the amine concentration.

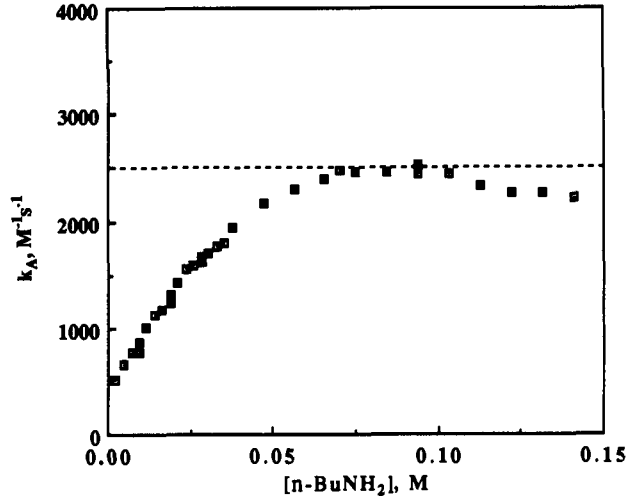


Figure 4. Reaction of **1** with *n*-butylamine. Second-order rate constant as a function of amine concentration.

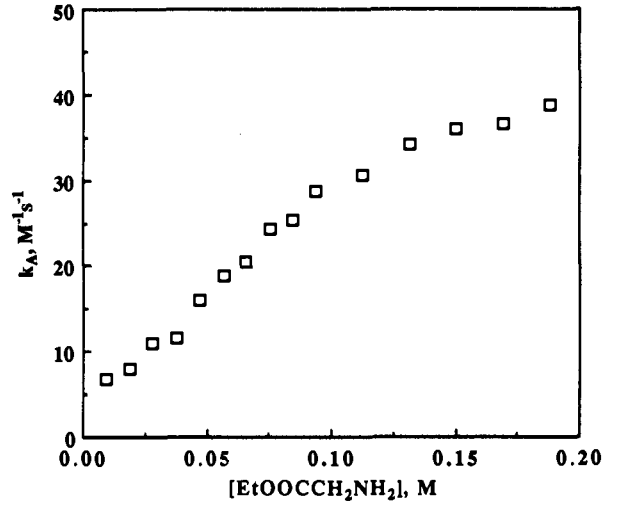


Figure 5. Reaction of **1** with glycine ethyl ester. Second-order rate constant as a function of amine concentration.

Table I. Reaction of [Methoxy(phenyl)carbene]pentacarbonylchromium(0) with Amines in 20% Acetonitrile–80% Water (v/v) at 25 °C[a]

RNH_2	pK_a^{AH}	k_1, $M^{-1}s^{-1}$	k_3^A/k_{-1}, M^{-1}	k_3^{OH}/k_{-1}, M^{-1}	k_3^{OH}/k_3^A
$CH_3(CH_2)_3NH_2$	10.67	2900	33.7	8.1×10^3	2.40×10^2
$CH_3OCH_2CH_2NH_2$	9.52	400	21.1	8.4×10^4	3.98×10^3
$ClCH_2CH_2NH_2$	8.61	91	19.5	2.8×10^5	1.44×10^4
$H_2NCOCH_2NH_2$	8.03	100	17.3	1.25×10^6	7.22×10^4
$EtOCOCH_2NH_2$	7.70	36	9.7	1.49×10^6	1.54×10^5

[a] μ = 0.5 M (KCl). Summary of kinetic parameters according to the mechanism of eq 1. Estimated errors are ±5% for k_1, ±10% for k_3^A/k_{-1} and k_3^{OH}/k_{-1}, and ±20% for k_3^{OH}/k_3^A.

(8) See the paragraph concerning supplementary material at the end of this paper.

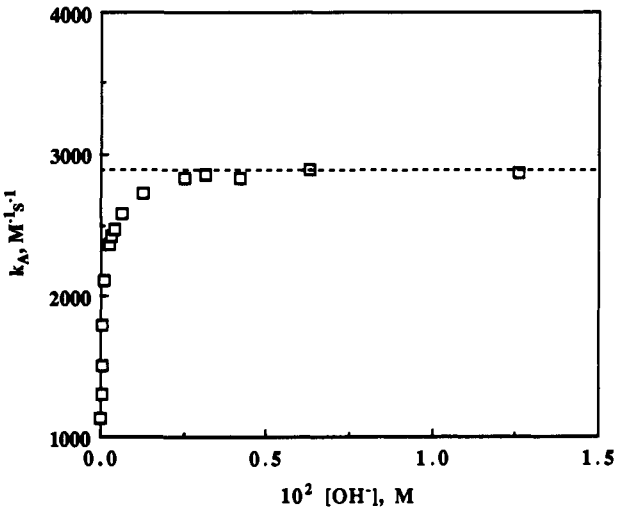


Figure 6. Reaction of **1** with *n*-butylamine. Second-order rate constant as a function of hydroxide ion concentration; [*n*-$BuNH_2$] = 0.047 M.

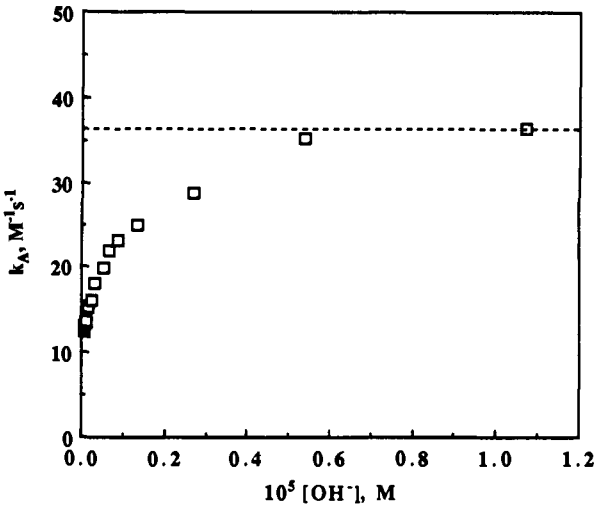


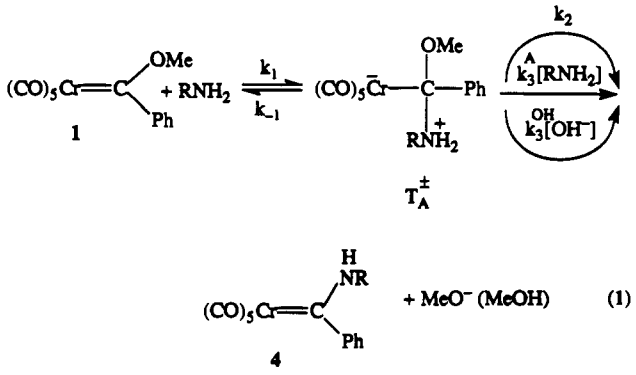
Figure 7. Reaction of **1** with glycine ethyl ester. Second-order rate constant as a function of hydroxide ion concentration; [$EtOOCCH_2NH_2$] = 0.094 M.

Dependence on Amine Concentration. The raw data are reported in Tables S1–S5.[8] Figures 4 and 5 show representative plots of $k_A = k_{obsd}/[RNH_2]$ for the reaction of **1** with *n*-butylamine and glycine ethyl ester. The plots are characterized by an initial rapid rise followed by a leveling off. With *n*-butylamine the leveling off is complete, i.e., k_A reaches a plateau, while for the more weakly basic amines (for amine pK_a values see Table I) the leveling off is not quite complete. The slight decrease in k_A in the *n*-butylamine reaction at the very highest amine concentrations is probably a medium effect whose origin has not been scrutinized further.

Dependence on Hydroxide Ion Concentration. The increase in k_A with amine concentration is most plausibly attributed to base catalysis, as elaborated upon in the Discussion. This interpretation implies that the reaction should also be accelerated by OH^-. Figures 6 and 7, constructed with the raw data reported in Tables S6–S10,[8] show that k_A indeed increases with increasing OH^- concentration. Similar plots were obtained for the other amines. Just as with the dependence on amine concentration, there is a leveling off at high OH^- concentration, and the plateau values are, within experimental error, the same as those reached when k_A is plotted vs amine concentration.

Discussion

Mechanism and Dissection of Kinetic Parameters. The kinetic results are consistent with the mechanism of eq 1; the k_3^A and



(1)

k_3^{OH} steps represent general base catalysis, the details of which will be discussed later. Applying the steady-state condition to $T_A^{\pm}$ leads to the rate law of eq 2.

$$-\frac{d[1]}{dt} = \frac{d[4]}{dt} = \frac{k_1(k_2 + k_3^A[RNH_2] + k_3^{OH}[OH^-])}{k_{-1} + k_2 + k_3^A[RNH_2] + k_3^{OH}[OH^-]}[1][RNH_2] \quad (2)$$

The second-order rate constant, $k_A = k_{obsd}/[RNH_2]$, is thus given by

$$k_A = \frac{k_1(k_2 + k_3^A[RNH_2] + k_3^{OH}[OH^-])}{k_{-1} + k_2 + k_3^A[RNH_2] + k_3^{OH}[OH^-]} \quad (3)$$

Under all experimental conditions used in this study the k_2 step for the noncatalyzed conversion of $T_A^{\pm}$ to products can be assumed to be negligible so that eq 3 reduces to eq 4.

$$k_A = \frac{k_1(k_3^A[RNH_2] + k_3^{OH}[OH^-])}{k_{-1} + k_3^A[RNH_2] + k_3^{OH}[OH^-]} = \frac{k_1\left(\frac{k_3^A}{k_{-1}}[RNH_2] + \frac{k_3^{OH}}{k_{-1}}[OH^-]\right)}{1 + \frac{k_3^A}{k_{-1}}[RNH_2] + \frac{k_3^{OH}}{k_{-1}}[OH^-]} \quad (4)$$

All features of Figures 4–7 can be understood as special cases of eq 4 as follows.

Case I. $(k_3^A/k_{-1})[RNH_2] + (k_3^{OH}/k_{-1})[OH^-] \ll 1$. Here eq 4 simplifies to eq 5; i.e., general base catalyzed conversion of $T_A^{\pm}$ to products is rate limiting. Equation 5 is consistent with the

$$k_A = k_1\frac{k_3^A}{k_{-1}}[RNH_2] + k_1\frac{k_3^{OH}}{k_{-1}}[OH^-] \quad (5)$$

linear increase in k_A with amine concentration at low $[RNH_2]$ (Figures 4 and 5) and the linear increase with OH^- at low $[OH^-]$ (Figures 6 and 7).

Case II. $(k_3^A/k_{-1})[RNH_2] \gg 1$. In this case eq 4 reduces to eq 6; i.e., nucleophilic attack is rate limiting. The k_1 value corresponds to the plateau values in Figures 4 and 5.

$$k_A = k_1 \quad (6)$$

Case III. $(k_3^{OH}/k_{-1})[OH^-] \gg 1$. Just as in case II, eq 4 simplifies to eq 6. The plateau values in Figures 6 and 7 should be the same as those in Figures 4 and 5, respectively. For the *n*-butylamine reaction the plateau in Figure 4 (2500 M^{-1} s^{-1}) is slightly lower than that in Figure 6 (2900 M^{-1} s^{-1}). This is attributed to the same medium effect that leads to a slight decrease in k_A at the highest *n*-butylamine concentration. In evaluating k_1 the plateau value from Figure 6 has been used. Similar medium effects were observed with 2-methoxyethylamine and glycinamide.

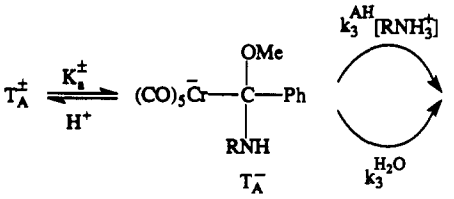
Our data also allowed us to evaluate the k_3^A/k_{-1} and k_3^{OH}/k_{-1} ratios. In principle, the best method for doing so would be to carry out a nonlinear least squares computer fit to all data for a given amine. However, because of some distortion of the data caused by medium effects at high amine concentrations, the following

"manual" analysis was preferred. From the initial slopes of the plots of k_A vs $[RNH_2]$ and assuming the validity of eq 5, a first approximation of $k_1k_3^A/k_{-1}$ and thus of k_3^A/k_{-1} was obtained. In a similar way a first approximation of k_3^{OH}/k_{-1} was derived from the initial slopes of the plots of k_A vs $[OH^-]$.

The k_3^A/k_{-1} ratios thus obtained indicated that at the amine concentrations used to determine the dependence of k_A and $[OH^-]$ (e.g., Figures 6 and 7) the term $(k_3^A/k_{-1})[RNH_2]$ exceeded 0.1 and thus was not completely negligible in the denominator of eq 4. Corrected k_3^{OH}/k_{-1} values were therefore obtained by equating the initial slopes of these plots with $(k_1k_3^{OH}/k_{-1})/\{1 + (k_3^A/k_{-1})[RNH_2]\}$ instead of $k_1k_3^{OH}/k_{-1}$. In a similar manner the first approximations of the k_3^{OH}/k_{-1} ratios showed that at the OH^- concentrations used to determine the dependence of k_A on amine concentration (e.g., Figures 4 and 5) $(k_3^{OH}/k_{-1})[OH^-]$ exceeded 0.1. Thus a better approximation of k_3^{OH}/k_{-1} was obtained from the k_A vs $[RNH_2]$ plots by equating the initial slopes with $(k_1k_3^A/k_{-1})/\{1 + (k_3^{OH}/k_{-1})[OH^-]\}$ instead of $k_1k_3^A/k_{-1}$.

The results of our analysis are summarized in Table I.

Nature of the Base Catalysis. The fact that the reaction is catalyzed not only by OH^- but also by the amine demonstrates general base catalysis. The most likely mechanism that can account for general base catalysis in our system is shown in eq 7: a rapid acid–base equilibrium between $T_A^\pm$ and T_A^- ($K_a^\pm$ is



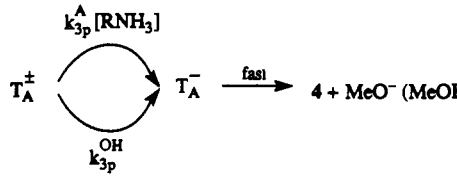
4 + MeO^- (MeOH) (7)

the acidity constant of $T_A^\pm$) followed by rate-limiting, general acid catalyzed leaving group departure. In terms of this mechanism, k_3^A and k_3^{OH} in eqs 1–4 are given by eqs 8 and 9, respectively, with K_a^{AH} being the acidity constant of RNH_3^+ and K_w the ionic product of water.

$$k_3^A = k_3^{AH}K_a^\pm/K_a^{AH} \quad (8)$$

$$k_3^{OH} = k_3^{H_2O}K_a^\pm/K_w \quad (9)$$

General base catalysis is, in principle, also consistent with rate-limiting deprotonation of $T_A^\pm$, eq 10. In this case the meaning of k_3^A and k_3^{OH} would be as in eqs 11 and 12, respectively. The

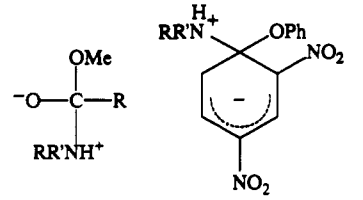


(10)

$$k_3^A = k_{3p}^A \quad (11)$$

$$k_3^{OH} = k_{3p}^{OH} \quad (12)$$

aminolysis of acyl esters, to which the reaction of Fischer carbene complexes with amines is frequently compared,[2,5] typically proceeds by an analogous mechanism with rate-limiting deprotonation of the corresponding zwitterion (e.g., **7**),[9] and so do many S_NAr reactions where the deprotonation of the zwitterionic Meisenheimer complex (e.g., **8**) is rate limiting.[10] On the other hand, in the aminolysis of strongly activated vinylic compounds, e.g., β-



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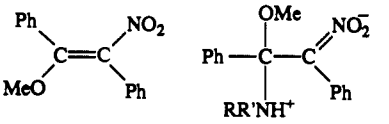

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methoxy-α-nitrostilbene (**9**), deprotonation of the corresponding zwitterionic intermediate (**10**) is fast and methoxide ion departure is rate limiting.[11]

In the present case, rate-limiting deprotonation of $T_A^\pm$ (eq 10) can be excluded on the basis of the k_3^{OH}/k_3^A ratios. These ratios increase from 240 for the *n*-butylamine reaction to 1.54×10^5 for the glycine ethyl ester reaction. If proton transfer were rate limiting, these ratios should, according to eqs 11 and 12, be given by

$$\frac{k_3^{OH}}{k_3^A} = \frac{k_{3p}^{OH}}{k_{3p}^A} \quad (13)$$

The rate constant k_{3p}^{OH} refers to an essentially diffusion controlled proton transfer;[12] it should be independent of the amine and have a value around 10^{10} M^{-1} s^{-1}.[12] The rate constant k_{3p}^A should also be independent of the amine since an increase in the acidity of RNH_3^+ should have a similar effect on the pK_a of $T_A^\pm$; hence the pK_a *difference* between $T_A^\pm$ and the respective RNH_3^+ is expected to be constant. Furthermore, the $pK_a^\pm$ of $T_A^\pm$ is likely to be somewhat lower than the pK_a of the respective RNH_3^+,[13] which would make the proton transfer from $T_A^\pm$ to RNH_2 thermodynamically favorable, with a rate constant close to diffusion control,[12] probably on the order of 4×10^8 to 2×10^9 M^{-1} s^{-1}.[14] Hence the k_3^{OH}/k_3^A ratios should be independent of the amine and have values on the order of 5–25. This contrasts with the experimental observation of a 640-fold change between *n*-butylamine and glycine ethyl ester; a plot of log k_3^{OH}/k_3^A vs pK_a^{AH} (not shown) yields a Brønsted β of −0.92 ± 0.04.

The strong increase in the k_3^{OH}/k_3^A ratios with decreasing basicity of the amine is easily accounted for in terms of the mechanism of eq 7. According to eqs 8 and 9 the k_3^{OH}/k_3^A ratio is given by eq 14. The K_a^{AH}/K_w ratio is proportional to K_a^{AH}

$$\frac{k_3^{OH}}{k_3^A} = \frac{k_3^{H_2O}}{k_3^{AH}}\frac{K_a^{AH}}{K_w} \quad (14)$$

and corresponds to $\beta = -1.00$. Combined with $\beta = -0.92 \pm 0.04$ for the k_3^{OH}/k_3^A ratio this implies a small increase in the $k_3^{H_2O}/k_3^{AH}$ ratio with increasing pK_a^{AH} that corresponds to a $\beta = 0.08 \pm 0.04$. This small increase appears to be mainly a consequence of the decreased catalytic activity of RNH_3^+ as it be-

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(13) The zwitterionic $T_A^\pm$ adducts in ester aminolysis (e.g., **7**) are typically slightly *less* acidic than the corresponding RNH_3^+,[9a,c,d] but this is probably a consequence of the close proximity of the highly concentrated negative charge. For example, $CH_3C(O^-)OEt(NH_2^+NH_2)$ was estimated to be ~1.3 pK_a units less acidic than $NH_2NH_3^+$, which explains why the k_{3p}^{OH}/k_{3p}^A ratio in the reaction of ethyl acetate with NH_2NH_2 is as high as 81.[9a] In $T_A^\pm$ derived from the carbene complex (**5**) the negative charge is likely to be significantly delocalized into the $(CO)_5Cr$ moiety (more on this below), which should reduce the $pK_a^\pm$-enhancing effect of the negative charge, as is known to be the case for **8**[10] and **10**.[11]

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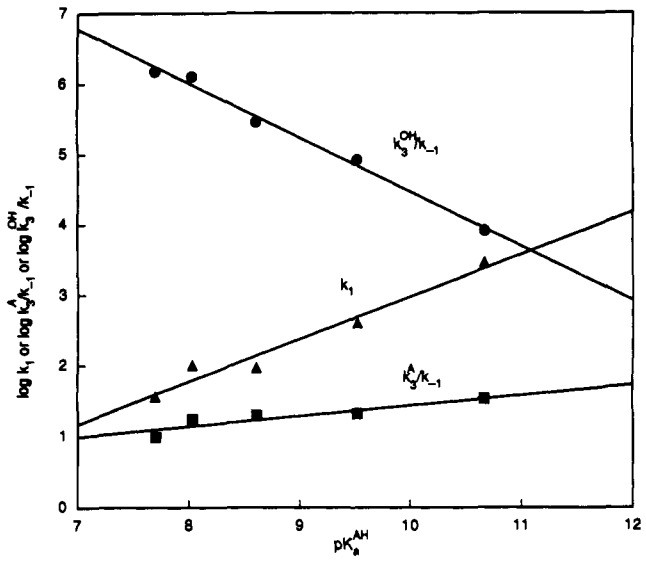
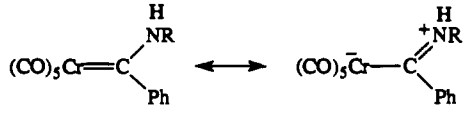


Figure 8. Brønsted-type plots of log k_1, log (k_3^A/k_{-1}), and log (k_3^{OH}/k_{-1}) vs pK_a^{AH}.

comes less acidic and lowers k_3^{AH}. Another potential factor that may affect the $k_3^{H_2O}/k_3^{AH}$ ratios is the "push" exerted by the nitrogen lone pair that leads to the resonance form **11b**.[2a] Such



11a **11b**

a push should enhance both $k_3^{H_2O}$ and k_3^{AH} as pK_a^{AH} increases; if these effects on the two rate constants were unequal, the rate constant ratio would be affected. In the next section it will be shown that this push, if it is present at all, must be very small.

Structure–Reactivity Relationships and Transition-State Structure. Figure 8 shows Brønsted-type plots for k_1, k_3^A/k_{-1}, and k_3^{OH}/k_{-1}. There is considerable scatter in the plot of log k_1 vs pK_a^{AH}. This is in large measure due to the positive deviation of the point for glycinamide, a deviation which has been observed in numerous other nucleophilic addition reactions.[15] An additional factor may be the strong sensitivity of the reaction to steric effects, as indicated by a preliminary study of the piperidine reaction which suggests a k_1 on the order of 25–30 M^{-1} s^{-1}.[7] This implies a $k_1(pip)/k_1(n\text{-}BuNH_2)$ ratio of ≈0.01, which contrasts with "normal" $k_1(pip)/k_1(n\text{-}BuNH_2)$ ratios of 3–16 in sterically unhindered systems.[11,15-17] Thus, even though all amines in the present study are primary, small differences in their steric effect could affect k_1 in a significant way.

A β_{nuc} (or $\beta(k_1)$) value of 0.60 ± 0.07 is obtained for the nucleophilic attachment step, suggesting that C–N bond formation is quite advanced at the transition state.[18] This contrasts with $\beta(k_1)$ values on the order of ~0.2[9a,b,17] in ester aminolysis.

The Brønsted β value for the k_3^{OH}/k_{-1} ratio is −0.77 ± 0.04. From eq 9 we deduce eq 15. $\beta(K_a^{\pm})$ can be set at ≈−1.0, while

$$\beta(k_3^{OH}/k_{-1}) = \beta(k_3^{H_2O}) + \beta(K_a^{\pm}) - \beta(k_{-1}) = -0.77 \pm 0.04 \quad (15)$$

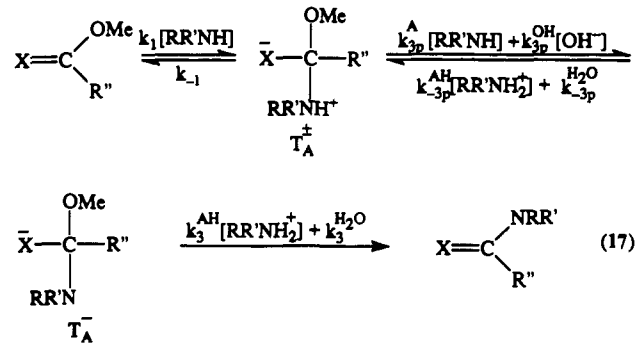
$\beta(k_{-1})$ may be estimated from $\beta(k_{-1}) = \beta(k_1) - \beta(K_1)$. On the basis of numerous reactions of amines with electrophilic olefins of the general structure PhCH=CXY, for which $\beta(K_1)$ values in the range of 0.7–0.9 were determined,[15,21] we shall assume a $\beta(K_1) \approx 0.80$. This yields an estimated $\beta(k_{-1}) \approx -0.20 \pm 0.07$. Solving eq 15 for $\beta(k_3^{H_2O}) = \beta_{push}$ affords ≈0.03 ± 0.07, i.e., the push is negligible, suggesting a transition state in which leaving group departure has made very little progress.

In a similar way the β value (0.15 ± 0.04) for the k_3^A/k_{-1} ratio can be used to estimate $\beta(k_3^{AH})$. According to eq 8 we can write

$$\beta(k_3^A/k_{-1}) = \beta(k_3^{AH}) + \beta(K_a^{\pm}) - \beta(K_a^{AH}) - \beta(k_{-1}) = 0.15 \pm 0.04 \quad (16)$$

With $\beta(K_a^{\pm}) \approx -1.0$, $\beta(K_a^{AH}) = -1.0$, and $\beta(k_{-1}) \approx -0.20 \pm 0.07$, eq 16 yields $\beta(k_3^{AH}) \approx -0.05 \pm 0.07$. This is again a very small β value, but it is significant that it is even lower than $\beta(k_3^{H_2O})$, reflecting not only the small push but also the opposing influence of the amine basicity due to the acid catalysis by RNH_3^+. (Note that $\beta(k_3^{H_2O}) - \beta(k_3^{AH}) = 0.08$ is the same as the value obtained directly from the $k_3^{H_2O}/k_3^{AH}$ ratios.) The fact that $\beta(k_3^{AH})$ is not much more negative indicates little sensitivty to the pK_a of the acid catalyst and suggests that proton transfer from RNH_3^+ to the departing group has made very little progress at the transition state, presumably because C–O bond cleavage has made very little progress. Thus both the small push and the weak sensitivity to the acidity of the catalyst give a consistent picture of a transition state that is very much intermediate-like (T_A^-). As indicated above, the relatively high $\beta(k_1)$ and low $\beta(k_{-1})$ suggest that the transition state of the first step is also close to the respective intermediate ($T_A^{\pm}$ in this case).

Comparisons with Acyl Ester Aminolysis. As mentioned earlier, there appears to be a strong similarity between the reactions of nucleophiles with Fischer carbene complexes and acyl esters. Specifically, the mechanism of aminolysis of these compounds is the same (eq 17, X = O, or X = $(CO)_5Cr$), except that with esters



(17)

base catalysis is due to rate-limiting proton transfer,[9] whereas with the Fischer carbene complexes it is due to rate-limiting leaving group departure. Why is there this contrast?

Proton transfer is rate limiting when $k_{-1} \gg k_{3p}^A[RR'NH] + k_{3p}^{OH}[OH^-]$ and $k_3^{AH}[RR'NH_2^+] + k_3^{H_2O} \gg k_{-3p}^{AH}[RR'NH_2^+] + k_{-3p}^{H_2O}$, while leaving group departure is rate limiting when $k_3^{AH}[RR'NH_2^+] + k_3^{H_2O} \ll k_{-3p}^{AH}[RR'NH_2^+] + k_{-3p}^{H_2O}$. Since the proton-transfer rate constants should be quite similar in both reactions,[12] the main reason for the contrast must be slower k_{-1}, k_3^{AH}, and $k_3^{H_2O}$ steps with the carbene complexes.

One source for these slower rates is the greater stability of $T_A^{\pm}$ and T_A^- derived from the carbene complexes; i.e., the $(CO)_5Cr$ moiety stabilizes the negative charge much more effectively than does oxygen. This higher stability manifests itself, e.g., in much higher k_1 values for the carbene complexes. For example, for the reaction of 2-methoxyethylamine with the carbene complex, k_1 = 400 M^{-1} s^{-1}, and for the reaction with phenyl acetate, k_1 = 4.2 × 10^{-3} M^{-1} s^{-1} (25 °C, water).[17] Another measure for the dif-

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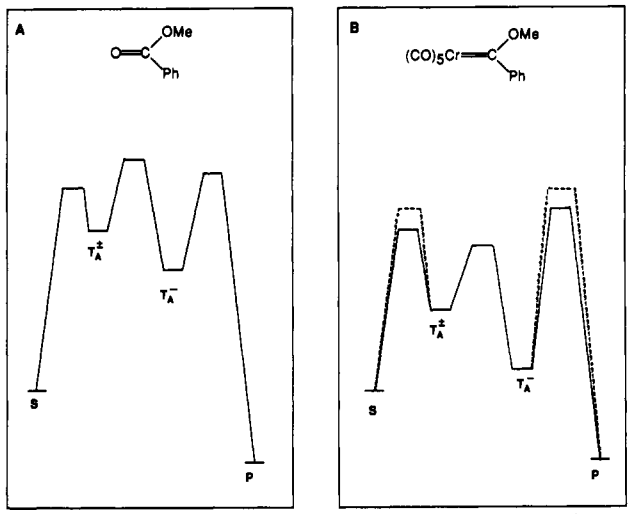
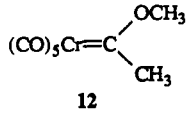


Figure 9. Schematic free energy vs reaction coordinate profiles for the reaction of an amine with an acyl ester and with [methoxy(phenyl)-carbene]pentacarbonylchromium(0). The dashed lines in part B indicate increased intrinsic barriers due to charge delocalization into the $Cr(CO)_5$ moiety; see text.

ferences in the stabilizing power is the much higher acidity of **12** (pK_a = 12.3)[1] compared to ethyl acetate (pK_a = 24.5).[22] Figure



12

9 shows a schematic representation of the free energy vs reaction coordinate profiles for the two reactions, reflecting the higher stability of $T_A^{\pm}$ and T_A^- derived from the carbene complexes and its effect on the rate-limiting step.

A second potential reason for the slower k_{-1}, k_3^{AH}, and $k_3^{H_2O}$ steps with the carbene complex is that the intrinsic barrier (in the Marcus[23] sense) of these steps is higher than that for the ester reactions. The effect of increased intrinsic barriers on the reaction profile is indicated by the dashed lines in Figure 9B. Such enhanced intrinsic barriers could come about if the negative charge in $T_A^{\pm}$ and T_A^- were significantly delocalized into the CO ligands, as is commonly observed in reactions that lead to delocalized or resonance-stabilized ions.[24] There is evidence of such delocalization in hydrido transition metal complexes.[25] If this is the case, vinylic substrates such as **9** (X = $C(NO_2)Ph$ in eq 17) would constitute a better analogy for the carbene complexes than acyl esters since the negative charge in $T_A^{\pm}$ or T_A^- is strongly delocalized (**10**), the intermediates are more stable, and the k_{-1}, k_3^{AH}, and $k_3^{H_2O}$ steps are relatively slow.[11,26]

Experimental Section

Materials. [Methoxy(phenyl)carbene]pentacarbonylchromium(0), **1**, was synthesized by the method of Fischer et al.[27] [(*n*-Butylamino)-(phenyl)carbene]pentacarbonylchromium(0), **4** (R = H, R′ = *n*-Bu), for spectral identification of the aminolysis product of **1** was prepared as described by Fischer and Leupold.[4c] Reagent grade *n*-butylamine and 2-methoxyethylamine were purified by distillation from KOH pellets. The other amines were available as hydrochloride salts and were converted to their free base without further purification.

Kinetic Runs and Spectra. Compound **1** decomposes in 20% acetonitrile–80% water within a few minutes due to hydrolysis,[7] which made it impractical to prepare reaction solutions in this solvent. However, in pure acetonitrile **1** is stable for several hours. Hence reaction solutions were freshly prepared in this solvent just before an experiment. A Durrum-Gibson D-110 stopped-flow apparatus was fitted with a small-bore syringe for the substrate solution (100% acetonitrile) and a normal-bore syringe for the amine buffer solution (mainly aqueous).[28] The buffer solutions were prepared in such a manner that the final solution after mixing was 20% acetonitrile–80% water (v/v) with an ionic strength of 0.5 M maintained by adding KCl. Rate constants were measured at 400 nm, which is close to the long-wavelength λ_{max} = 395 nm of **1**. Excellent first-order kinetics were observed over at least 3 half-lives in all experiments.

The absorption spectra shown in Figure 1 were measured on a Hewlett-Packard 8452A diode array spectrophotometer. The first spectrum was obtained ca. 3 s after injection of **1** into the cuvette containing the amine buffer, the subsequent spectra being obtained at 12-s intervals.

pH and pK_a Measurements. Solution pH was measured by calibrating the pH meter with standard aqueous buffers and then adding an empirical correction factor, Q_s, which accounts for changes in hydrogen ion activity and liquid junction potential due to changes in salt and solvent effects in order to obtain the true pH.[29]

$$pH = pH_{measd} + Q_s \qquad (18)$$

Experimentally, Q_s is the value required to adjust the measured pH of a 0.01 M HCl solution to a value of 2.00. For 20% acetonitrile–water (v/v) at 25.0 °C with μ = 0.5 M with KCl as compensating electrolyte, Q_s = −0.01. Measurement of the pH of a series of hydroxide solutions varying from 0.001 to 0.10 M in the same solvent gave a linear plot of log $[OH^-]$ vs pH with a slope of 1, indicating that the activity of hydroxide ion (γ) is not changing in this region. Using eq 19 gives pK_w = 14.27.

$$pK_w = pH_{measd}(0.010\ M\ KOH) + Q_s + 2.00 \qquad (19)$$

The pK_a values of the various amines in 20% acetonitrile–water (v/v) under standard conditions were determined by measuring the pH of various mixtures of amine buffers where $[BH^+]/[B]$ = 1/1.

Acknowledgment. This research was supported by Grant No. CHE-8921739 from the National Science Foundation.

Supplementary Material Available: Tables S1–S10 listing kinetic measurements (6 pages). This supplementary material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the American Chemical Society. Ordering information is given on any current masthead page.

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