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Physical Organic Chemistry of Transition Metal Carbene Complexes.[1] Thermodynamic and Kinetic Acidities of $(CO)_5Cr{=}C(OCH_3)CH_3$ and $(CO)_5Cr{=}C(OCH_3)CH_2Ph$ in Aqueous Acetonitrile

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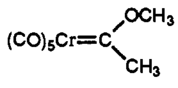
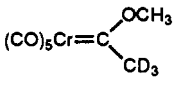
Abstract: Rate constants for proton transfer from (methoxymethylcarbene)pentacarbonylchromium(0), $(CO)_5Cr{=}C(OCH_3)CH_3$, to OH^- and amine bases and from (benzylmethoxycarbene)pentacarbonylchromium(0), $(CO)_5Cr{=}C(OCH_3)CH_2Ph$, to OH^-, amines, carboxylate ions, and H_2O were determined in 50% acetonitrile–50% water (v/v) at 25 °C. Intrinsic rate constants (k_o) were deduced from extrapolations of Brønsted plots. For $(CO)_5Cr{=}C(OCH_3)CH_3$ they are $\log k_o = 3.70$ (secondary amines) and 3.04 (primary amines) and for $(CO_5)Cr{=}C(OCH_3)CH_2Ph$ $\log k_o = 1.86$ (secondary amines), 1.51 (primary amines), and ~ 0.8 ($RCOO^-$). These $\log k_o$ values are consistent with significant resonance stabilization of the respective anions. Kinetic isotope effects on the order of 2.5–3.0 for the deprotonation of either metal carbene complex by OH^- and of 5.6 for the deprotonation of $(CO)_5Cr{=}C(OCH_3)CH_2Ph$ by piperidine were measured. These relatively low values may indicate substantial coupling of proton transfer to heavy atom motion, including bond changes in the CO ligands. The effect of changing solvent from water to 50% acetonitrile–50% water is to induce 2-fold and 4.8-fold increases in the rate of deprotonation of $(CO)_5Cr{=}C(OCH_3)CH_3$ by OH^- and piperidine, respectively. Possible reasons for these solvent effects, including electrostatic stabilization of the transition state of the piperidine reaction, are discussed.

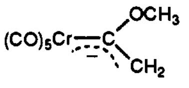
It has been known for over 25 years that (methoxymethylcarbene)pentacarbonylchromium(0), **1-CH₃**, a prototype Fischer carbene complex,[2] is a rather strong carbon acid. The first relevant report was Kreiter's observation of a rapid conversion of **1-CH₃** to **1-CD₃** in a dilute $NaOCH_3/CH_3OD$ solution.[3] Casey and Anderson[4] subsequently showed that in THF the acidity of **1-CH₃** is approximately the same as that of *p*-cyanophenol, an acid whose pK_a in water is 7.97.[5] In quoting this work, numerous authors have, rather misleadingly, referred to **1-CH₃** as a carbon acid with a pK_a of 8 which of course cannot be correct since *p*-cyanophenoxide ion and **1-CH₂⁻** should respond quite differently to a solvent change from THF to water.[6] The pK_a of **1-CH₃** in water was reported in 1989 to be 12.3.[8]


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

1-CH₃


$(CO)_5Cr{=}C(OCH_3)CD_3$

1-CD₃

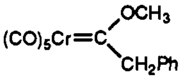

$(CO)_5Cr{\overset{-}{\cdots}}C(OCH_3){\cdots}CH_2$

1-CH₂⁻

A possible reason why the pK_a in water has not been determined much earlier is the instability of basic aqueous solutions of **1-CH₃**[9] which precludes equilibrium measurements by classical spectrophotometric procedures. The reported pK_a in water was based on a stopped-flow kinetic determination of the rate of deprotonation of **1-CH₃** by OH^-.[8]

Because of the instability of **1-CH₃** in basic solution—at 0.1 M KOH the decomposition half-life is less than 1 s—rates of proton transfer could only be determined with highly basic proton acceptors (OH^-, piperidine) that allow measurements in the direction **1-CH₃** → **1-CH₂⁻**. Measurements in the direction of **1-CH₂⁻** → **1-CH₃** would be highly desirable in order to expand the range of proton acceptors amenable to study. Such measurements require a capability of reacting **1-CH₂⁻** with acid within a second after it has been formed by deprotonation of **1-CH₃** with OH^-, i.e., before decomposition sets in. Such a capability has recently been acquired in our laboratory.

This paper presents the results of such a study and also of the proton transfer kinetics of (benzylmethoxycarbene)pentacarbonylchromium(0), **1-CH₂Ph**. Due to the low solubility of **1-CH₂Ph** in water, our investigation was carried out in 50% acetonitrile–50% water (v/v).


$(CO)_5Cr{=}C(OCH_3)CH_2Ph$

1-CH₂Ph

Results

General Features. When **1-CH₃** is placed into a KOH solution two reactions are observed. The faster of the two is in the millisecond time range. Figure 1 shows the spectral changes associated with this process as measured in a stopped-flow spectrophotometer. Addition of HCl to the reaction solution 150 ms after the reaction is initiated regenerates **1-CH₃** as determined by its UV/vis spectrum and confirmed by an HPLC analysis. Similar observations were made with **1-CH₂Ph** (Figure 2). The spectral changes are attributed to reversible deprotonation of the carbene complexes, a conclusion for which more evidence will be derived from the kinetics results. With both carbene

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[⊗] Abstract published in *Advance ACS Abstracts*, December 1, 1993.

(1) This is part 3 in this series. Part 2: Bernasconi, C. F.; Stronach, M. W. *J. Am. Chem. Soc.* **1993**, *115*, 1341.

(2) Dötz, K. H.; Fisher, H.; Hofmann, P.; Kreissl, F. R.; Schubert, U.; Weiss, K. *Transition Metal Carbene Complexes*; Verlag Chemie: Deerfield Beach, FL, 1983.

(3) Kreiter, C. G. *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 390.

(4) Casey, C. P.; Anderson, R. L. *J. Am. Chem. Soc.* **1974**, *96*, 1230.

(5) Fickling, M. M.; Fischer, A.; Mann, B. R.; Packer, J.; Vaughan, J. *J. Am. Chem. Soc.* **1959**, *81*, 4226.

(6) A pK_a = 8 for **1-CH₃** has even been quoted in a highly acclaimed text.[7]

(7) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987; p 806.

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

(9) This contrasts with the satisfactory stability of the **1-CH₃**/**1-CH₂⁻** system in THF.[4]

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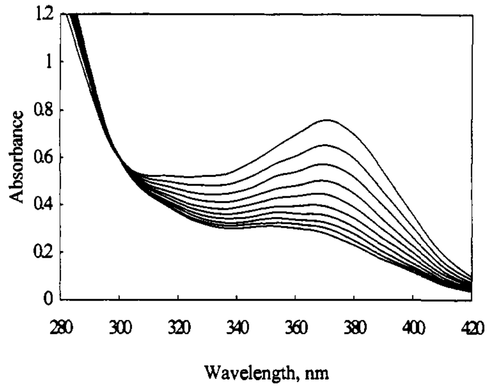

Figure 1. Time-resolved spectra of the proton transfer reaction of **1-CH$_3$** (1.20×10^{-4} M) with 0.1 M KOH in 50% acetonitrile–50% water (v/v) at 25 °C. The first spectrum was obtained within 1 ms after mixing and subsequent spectra at 10-ms intervals.

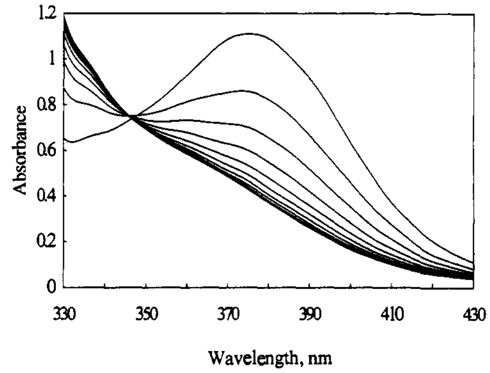

Figure 2. Time-resolved spectra of the proton transfer reaction of **1-CH$_2$-Ph** (1.20×10^{-4} M) with 0.04 M KOH in 50% acetonitrile–50% water (v/v) at 25 °C. The first spectrum was taken within 2.5 ms after mixing and subsequent spectra at 100-ms intervals.

complexes the deprotonation is followed by a slower process with a half-life of several seconds. A detailed kinetic investigation of this slower process, which leads to the formation of acetaldehyde in the case of **1-CH$_3$** and to β-methoxystyrene in the case of **1-CH$_2$Ph**, will be the subject of a future report.

Kinetics. Most experiments were performed in 50% acetonitrile–50% water (v/v) at 25 °C and an ionic strength of 0.1 M maintained with KCl. Rates were measured in KOH solutions and various amine buffers; with **1-CH$_2$Ph** kinetic determinations were also done in carboxylate buffers. Pseudo-first-order conditions, with the carbene complex as the minor component, were used throughout. Under these conditions the reaction may be represented by eq 1 with the observed pseudo-first-order rate

$$\mathbf{1\text{-}CH_2R} \underset{k_{-1}^{H}a_{H^+} + k_{-1}^{H_2O} + k_{-1}^{BH}[BH]}{\overset{k_1^{H_2O} + k_1^{OH}[OH^-] + k_1^{B}[B]}{\rightleftharpoons}} \mathbf{1\text{-}C^-HR} \qquad (1)$$

(R = **H** or Ph)

constant for equilibrium approach being given by eq 2.

$$k_{obsd} = k_1^{H_2O} + k_1^{OH}[OH^-] + k_{-1}^{H_2O} + k_{-1}^{H}a_{H^+} + k_1^{B}[B] + k_{-1}^{BH}[BH] \qquad (2)$$

1-CH$_3$. Runs with KOH were conducted in the **1-CH$_3$** → **1-CH$_2^-$** direction. The raw data are summarized in Table S1 of the supplementary material.[10] Figure 3 shows a plot of k_{obsd} vs [OH$^-$] which yields k_1^{OH} = slope = 456 ± 12 M^{-1} s^{-1}, $k_{-1}^{H_2O}$ = intercept = 0.91 ± 0.09 s^{-1}, and $K_1^{OH} = k_1^{OH}/k_{-1}^{H_2O}$ = 501 ± 71 M^{-1}. An independent check of K_1^{OH} is provided by measuring the absorbance change (ΔOD) induced by the reaction as a function of [OH$^-$]. These ΔOD measurements are included in Table S1.[10] ΔOD is related to K_1^{OH} by eq 3 with ΔOD_o being the absorbance

$$\frac{\Delta OD_o}{\Delta OD} = 1 + \frac{1}{K_1^{OH}[OH^-]} \qquad (3)$$

change at high [OH$^-$] where the equilibrium strongly favors **1-CH$_2^-$**. Figure 4 shows a plot according to eq 3 from which K_1^{OH} = 289 ± 20 M^{-1} was determined. In view of the fact that stock solutions of **1-CH$_3$** are not entirely stable (see Experimental Section) and the absorbances at the end of the reaction are based on an extrapolation because of the decomposition process referred to earlier, the agreement between the two K_1^{OH} values is remarkably good. In our subsequent discussion the kinetically determined value will be used.

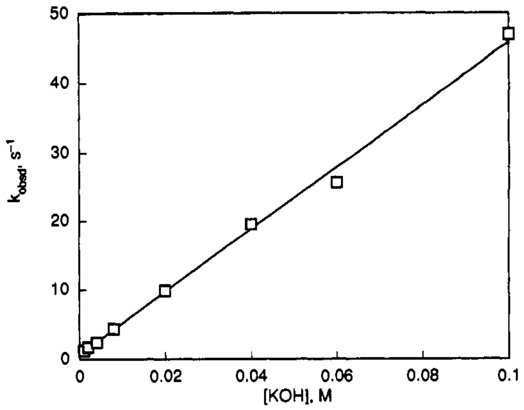

Figure 3. Plot of k_{obsd} vs [KOH] for the proton transfer reaction of **1-CH$_3$** with KOH in 50% acetonitrile–50% water (v/v) at 25 °C.

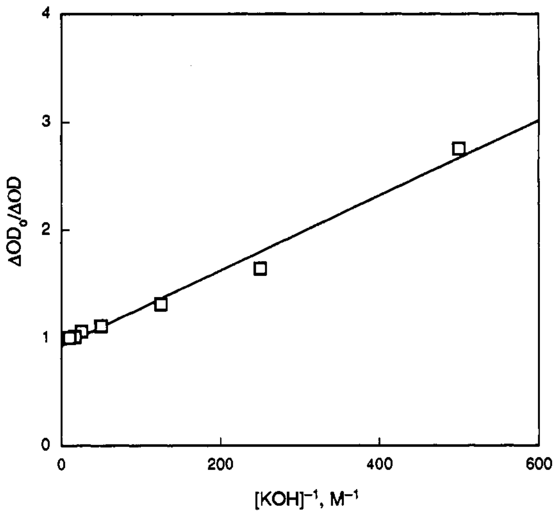

Figure 4. Plot of $\Delta OD_0/\Delta OD$ vs 1/[KOH] according to eq 3 for the proton transfer reaction of **1-CH$_3$** with KOH in 50% acetonitrile–50% water (v/v) at 25 °C.

The reaction with piperidine was measured by two methods. In the first, **1-CH$_3$** was mixed with piperidine solutions that contained 0.1 M KOH, i.e., the reaction was conducted in the **1-CH$_3$** → **1-CH$_2^-$** direction. In the second, the reaction was conducted in the **1-CH$_2^-$** → **1-CH$_3$** direction; i.e., **1-CH$_2^-$** was generated in a 0.02 M KOH solution and ca. 1 s later was mixed with 1:1 piperidine buffers at pH 11.01 ("pH-jump experiments"). In contrast to the experiments with OH$^-$ as the base, the absorbance changes were independent of amine concentration, an observation which is consistent with proton transfer as elaborated upon in the Discussion. Plots of k_{obsd} vs piperidine

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[10] See paragraph concerning supplementary material at the end of this paper.

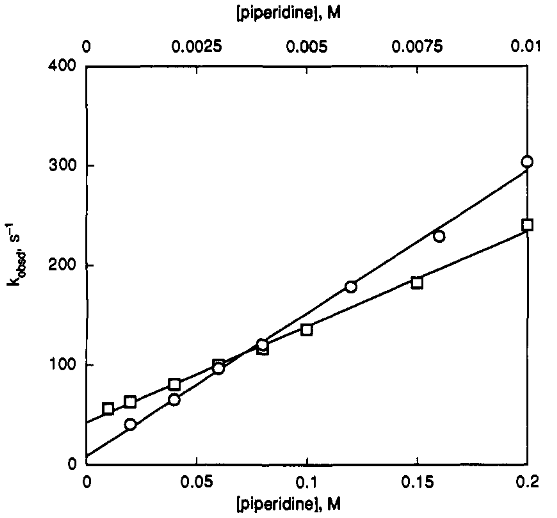

Figure 5. Plots of k_{obsd} vs [piperidine] for the proton transfer reaction of **1-CH$_3$** with piperidine: (□) in 0.1 M KOH, bottom *x* axis; (○) at pH 11.01, top *x* axis.

Table I. Summary of Rate Constants for Proton Transfer Reactions of **1-CH$_3$** in 50% Acetonitrile–50% Water at 25 °C[a,b]

Base	pK_a^{BH}	k_1^B, M^{-1} s^{-1}	k_1^{BH}, M^{-1} s^{-1}
n-BuNH$_2$	10.40	122	(1.52 ± 0.03) × 10^4
MeOCH$_2$CH$_2$NH$_2$	9.39	22.6	(2.88 ± 0.08) × 10^4
H$_2$NCOCH$_2$NH$_2$	8.14	5.01	(1.14 ± 0.04) × 10^5
piperidine	11.01	906 ± 21	(2.77 ± 0.07) × 10^4
piperazine	9.97	246	(8.23 ± 0.57) × 10^4
HEPA[c]	9.33	85.5	(1.25 ± 0.04) × 10^5
OH$^-$	16.64[d]	456 ± 12[e]	0.91 ± 0.09[e,f]

[a] μ = 0.1 M (KCl), pK_a^{CH} = 12.50. [b] Error limits are standard deviations in the slopes of k_{obsd} vs [BH] for amines and k_{obsd} vs [OH$^-$] in OH$^-$ reaction. [c] HEPA = *N*-(2-hydroxyethyl)piperazine. [d] pK_w = 15.19, see text. [e] $k_1^B = k_1^{OH}$; $k_{-1}^{BH} = k_{-1}^{H_2O}$. [f] In units of s^{-1}; error limits are standard deviation of the intercept of the plot of k_{obsd} vs [OH$^-$].

concentration for the two kinds of experiments are shown in Figure 5; the raw data are given in Table S2.[10] The slope of the first plot (906 M^{-1} s^{-1}) is approximated by k_1^B (k_{-1}^{BH}[BH] ≪ k_1^B[B] in eq 2), the slope of the second plot (2.86 × 10^4 M^{-1} s^{-1}) by k_{-1}^{BH} (k_1^B[B] ≪ k_{-1}^{BH}[BH]).

From k_1^B/k_{-1}^{BH} = 3.17 × 10^{-2} we obtain the ratio K_a^{CH}/K_a^{BH}, with K_a^{CH} and K_a^{BH} being the acid dissociation constants of **1-CH$_3$** and piperidinium ion, respectively. With pK_a^{BH} = 11.01 this yields pK_a^{CH} = 12.50. In conjunction with K_1^{OH} = 501 M^{-1} determined above one obtains pK_w = 15.19 from $K_w = K_a^{CH}/K_1^{OH}$. This pK_w value lies between that reported by Allen and Tidwell[11] (15.0) and by Barbosa et al. (15.39);[12] inasmuch as our ionic strength of 0.1 M lies between those reported in refs 11 (0.25 M) and 12 (0.0 M), our pK_w value seems very reasonable.

The runs with the other amines were all conducted in the **1-CH$_2^-$** → **1-CH$_3$** direction. The raw data are summarized in Tables S3 and S4.[10] The slopes of the plots of k_{obsd} vs [BH$^+$] (not shown) can all be approximated by k_{-1}^{BH} from which k_1^B was calculated as $k_1^B = k_{-1}^{BH}K_a^{CH}/K_a^{BH}$. The various constants determined in this manner are summarized in Table I.

Because our preliminary study of the reaction of **1-CH$_3$** with OH$^-$ and piperidine was done in water at 20 °C,[8] a few experiments aimed at assessing the impact of changing the solvent to 50% acetonitrile and the temperature to 25 °C are reported in Table II (raw data in Tables S5 and S6[10]). Furthermore, the kinetic isotope effect for the deprotonation of **1-CH$_3$** vs **1-CD$_3$** by OH$^-$ in various acetonitrile–water mixtures was determined (Tables III, S7, and S8[10]).

Table II. Effect of Changing the Solvent from Water to 50% Acetonitrile–50% Water and the Temperature from 20 to 25 °C on the Reaction of **1-CH$_3$** with OH$^-$ and Piperidine[a]

base	solvent	*T*, °C	pK_a^{BH}	pK_a^{CH}	k_1^B, M^{-1} s^{-1}
OH$^-$	H$_2$O	20	15.46[b]	12.3	135[b]
OH$^-$	H$_2$O	25	15.55	12.8	229
OH$^-$	50% MeCN	25	16.64	12.5	456
Pip	H$_2$O	20	11.51[b]	12.3	69[b]
Pip	H$_2$O	25	11.12	12.8	188
Pip	50% MeCN	25	11.01	12.5	906

[a] μ = 0.1 M (KCl). [b] μ = 0.5 M (KCl); data from ref 8.

1-CH$_2$Ph. The methodology was quite similar to that used with **1-CH$_3$**. However, because the pK_a^{CH} for **1-CH$_2$Ph** of 10.40 (see below) is about two units lower than that of **1-CH$_3$**, kinetic determinations in the direction **1-CH$_2$Ph** → **1-C$^-$HPh** were feasible not only with OH$^-$ and piperidine but with *n*-butylamine as well (Tables S9 and S10).[10] The pK_a^{CH} was determined from kinetic experiments in *n*-butylamine buffers at different pH values. According to eq 2 the slope of a plot of k_{obsd} vs [B] = [RNH$_2$] is given by eq 4. The slopes are summarized in Table S11.[10] A

$$\text{slope} = k_1^B + k_{-1}^{BH}\frac{a_{H^+}}{K_a^{BH}} = k_1^B\left(1 + \frac{a_{H^+}}{K_a^{CH}}\right) \quad (4)$$

plot of slope vs a_{H^+} is shown in Figure 6; it yields k_1^B = 75.5 ± 1.6 and pK_a^{CH} = 10.40 ± 0.05. The pK_a^{CH} value was confirmed by measurements of absorbance changes as a function of pH. The relevant relationship is given by eq 5. Average ΔOD values

$$\frac{\Delta OD_0}{\Delta OD} = 1 + \frac{a_{H^+}}{K_a^{CH}} \quad (5)$$

for a given pH are reported in Table S12.[10] A plot according to eq 5 (not shown) yields pK_a^{CH} = 10.49 ± 0.03. Even though the standard deviation is smaller than for the pK_a^{CH} value obtained via eq 4, ΔOD measurements are inherently less accurate, as discussed for the reaction of **1-CH$_3$** with OH$^-$, and hence the former value will be adopted.

The higher acidity of **1-CH$_2$Ph** also allowed pH-jump experiments with buffer acids of lower pK_a^{BH}, including carboxylic acids (Tables S13–S15),[10] because the protonation of **1-C$^-$HPh** is substantially slower than that of **1-CH$_2^-$**. From the pH dependence of buffer plot intercepts (Table S16)[10] k_{-1}^H for protonation of **1-C$^-$HPh** by H$_3$O$^+$ could also be obtained.

Table IV provides a summary of the various rate constants, while Table V (raw data in Tables S17 and S18)[10] reports kinetic isotope effects for the reaction of **1-CH$_2$Ph** with OH$^-$ and piperidine. The rate of deprotonation of **1-CD$_2$Ph** by piperidine was measured at pH 11.71 and 11.01. At pH 11.71, a_{H^+}/pK_a^{CH} in eq 4 is negligible and hence the slope of a plot of k_{obsd} vs [B] corresponds to k_1^B(**1-CD$_2$Ph**). At pH 11.01 at which [B] = [BH$^+$] eq 4 becomes slope = k_1^B(**1-CD$_2$Ph**) + k_{-1}^{BH}(**1-C$^-$DPh**). Since k_{-1}^{BH}(**1-C$^-$DPh**) should be approximately equal to k_{-1}^{BH}(**1-C$^-$HPh**), k_1^B(**1-CD$_2$Ph**) is calculated as slope − k_{-1}^{BH}(**1-C$^-$HPh**). The k_1^B(**1-CD$_2$Ph**) values obtained at the two pH's were the same within experimental error.

Discussion

Mechanism. There are several observations which demonstrate that the reactions described in this study represent a proton transfer according to eq 1 rather than nucleophilic attack on the carbene carbon. This point is not trivial since **1-CH$_3$** and similar carbene complexes are known to undergo aminolysis with primary and

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[11] Allen, A. D.; Tidwell, T. T. *J. Am. Chem. Soc.* **1987**, *109*, 2774.
[12] Barbosa, J.; Sanz-Nebot, V. *Anal. Chim. Acta* **1991**, *244*, 183.

Table III. Kinetic Isotope Effect on the Deprotonation of **1-CH$_3$** by OH$^-$ in Various MeCN–Water Mixtures at 25 °C

	5% MeCN	25% MeCN	50% MeCN	70% MeCN
k_1^{OH}(**1-CH$_3$**), M^{-1} s^{-1}	200 ± 5	369 ± 13	456 ± 12	553 ± 28
$k_1^{H_2O}$(**1-CH$_3$**), s^{-1}	8.81 ± 0.28	6.04 ± 0.71	0.91 ± 0.09	0.284 ± 0.069
K_1^{OH}(**1-CH$_3$**), M^{-1}	22.7 ± 1.3	61.1 ± 10.6	501 ± 71	(1.95 ± 0.75) × 10^3
pK_a^{CH}(**1-CH$_3$**)[a]	12.77 ± 0.03	12.81 ± 0.07	12.50 ± 0.06	13.16 ± 0.14
k_1^{OH}(**1-CD$_3$**), M^{-1} s^{-1}		124 ± 12	165 ± 14	213 ± 13
k_H/k_D[c]		2.98 ± 0.43	2.76 ± 0.33	2.60 ± 0.30
p$K_a^{H_2O}$[b] – pK_a^{CH}	~3.08[d]	~3.40[d]	4.51 ± 0.16	~4.14[d]

[a] From $K_1^{OH}K_w$, with pK_w = 14.13 in 5% MeCN, 14.59 in 25% MeCN, 15.19 in 50% MeCN, and 16.45 in 70% MeCN; pK_w in 5%, 25%, and 70% MeCN from ref 12; pK_w in 50% MeCN is our own. [b] p$K_a^{H_2O}$ = pK_w + log [H$_2$O]. [c] $k_H/k_D = k_1^{OH}$(**1-CH$_3$**)/k_1^{OH}(**1-CD$_3$**). [d] Uncertainty is unknown because of possible error in pK_w due to the difference in μ between literature (ref 12) data and ours.

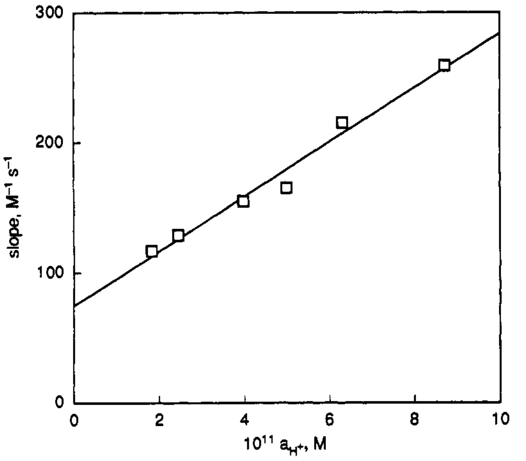


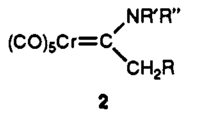
Figure 6. Plot of slope vs a_{H^+} according to eq 4 for the determination of pK_a^{CH} of **1-CH$_2$Ph**.

Table IV. Summary of Rate Constants for Proton Transfer Reactions of **1-CH$_2$Ph** in 50% Acetonitrile–50% Water at 25 °C[a,b]

base	pK_a^{BH}	k_1^B,[e] M^{-1} s^{-1}	k_1^{BH},[e] M^{-1} s^{-1}
n-BuNH$_2$	10.40	75.5 ± 1.6	75.5 ± 1.6
MeOCH$_2$CH$_2$NH$_2$	9.39	16.1	165 ± 2
H$_2$NCOCH$_2$NH$_2$	8.14	2.30	413 ± 44
NCCH$_2$NH$_2$	5.29	0.126	(1.61 ± 0.03) × 10^4
piperidine	11.01	225 ± 9	55 ± 2
piperazine	9.97	74.8	200 ± 8
HEPA[c]	9.33	25.2	295 ± 7
morpholine	8.70	19.5	978 ± 25
CH$_3$COO$^-$	5.93	0.299	(8.80 ± 0.40) × 10^3
ClCH$_2$CH$_2$COO$^-$	5.44	0.261	(2.37 ± 0.02) × 10^4
MeOCH$_2$COO$^-$	4.73	0.124	(5.80 ± 0.35) × 10^4
OH$^-$	16.64[d]	115 ± 2	0.0019
H$_2$O	–1.45	4.1 × 10^{-4}[f]	(1.02 ± 0.04) × 10^7

[a] μ = 0.1 M (KCl), pK_a^{CH} = 10.40. [b] Error limits are standard deviations in the slopes of k_{obsd} vs [BH] for amines and carboxylate ions and k_{obsd} vs [OH$^-$] in the OH$^-$ reaction. [c] HEPA = N-(2-hydroxyethyl)piperazine. [d] pK_w = 15.19, see text. [e] $k_1^B = k_1^{OH}$; $k_{-1}^{BH} = k_{-1}^{H_2O}$. [f] In units of s^{-1}.

secondary amines.[2,13]



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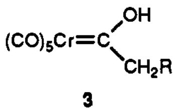

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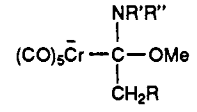
(1) The reactions are fully reversible, as demonstrated by regenerating **1-CH$_2$R** upon acidification of the reaction product shortly after its formation. This is inconsistent with the formation of any aminolysis product (**2**) or hydrolysis product (**3**) although it does not exclude reversible formation of the precursor intermediates of **2** and **3**, i.e., **4** and **5**, respectively.

Table V. Kinetic Isotope Effect on the Deprotonation of **1-CH$_2$Ph** by OH$^-$ and Piperidine in 50% Acetonitrile–50% Water at 25 °C

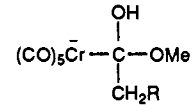
base	pK_a^{BH} – p$K_a^{H_2O}$	k_1^B(**1-CH$_2$Ph**), M^{-1} s^{-1}	k_1^B(**1-CD$_2$Ph**), M^{-1} s^{-1}	k_H/k_D[a]
OH$^-$	6.24	115 ± 2	45.5 ± 1.0	2.53 ± 0.10
piperidine	0.61	225 ± 9	40.8 ± 0.9	5.51 ± 0.35

[a] $k_H/k_D = k_1^B$(**1-CH$_2$Ph**)/k_1^B(**1-CD$_2$Ph**).



$(CO)_5\overset{-}{Cr}-\overset{NR'R''}{\underset{CH_2R}{C}}-OMe$

4



$(CO)_5\overset{-}{Cr}-\overset{OH}{\underset{CH_2R}{C}}-OMe$

5

(2) In the reaction of **1-CH$_3$** with piperidine and of **1-CH$_2$Ph** with piperidine and n-butylamine at high pH the absorbance changes (ΔOD) are independent of amine concentration for a given pH. This is inconsistent with an addition reaction (e.g., to form **4**) which should have a small ΔOD at low amine concentration because of an unfavorable equilibrium. On the other hand, a ΔOD value that does not change with amine concentration is consistent with proton transfer since the equilibrium position and hence ΔOD only depends on pH and not on amine concentration.

(3) There is a substantial primary kinetic hydrogen isotope effect on the reaction of **1-CH$_3$** with OH$^-$ and the reactions of **1-CH$_2$Ph** with OH$^-$ and piperidine, as expected for a proton transfer but difficult to rationalize for a nucleophilic reaction.

Brønsted Plots. The rate constants defined in eq 1 are summarized in Table I for **1-CH$_3$** and Table IV for **1-CH$_2$Ph**. Brønsted plots[14] are shown in Figures 7 and 8. For **1-CH$_3$** the range of buffers amenable to study was rather limited because rates of protonation of **1-CH$_2$$^-$** by carboxylic acids and the most acidic ammonium ions were too fast for the stopped-flow technique. Hence the Brønsted α and β values (Table VI) for **1-CH$_3$** should be regarded as somewhat crude, the relatively low standard deviations notwithstanding. An even worse problem exists with the Brønsted coefficients for the reaction of **1-CH$_2$Ph** with carboxylate ions because of the small pK_a^{BH} range of the carboxylic acids that were amenable to study.

The Brønsted coefficients are well within the range typically observed for proton transfers from carbon acids in water and mixtures of water with dipolar aprotic solvents.[16-18] Within the context of the traditional interpretation of Broønsted coefficients[20] our findings would imply that the degree of proton transfer at the transition state is comparable to that of the majority of C–H

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(13) (a) Klabunde, U.; Fischer, E. O. *J. Am. Chem. Soc.* **1967**, *89*, 7141. (b) Connor, J. A.; Fischer, E. O. *J. Chem. Soc. A* **1969**, 578. (c) Moser, E.; Fischer, E. O. *J. Organomet. Chem.* **1969**, *16*, 275. (d) Fischer, E. O.; Kollmeier, H. J. *Chem. Ber.* **1971**, *104*, 1339. (e) Fischer, E. O.; Leupold, M. *Chem. Ber.* **1972**, *105*, 599. (f) Fischer, E. O.; Heckl, B.; Werner, H. *J. Organomet. Chem.* **1971**, *28*, 359.

(14) Strictly speaking, they are Eigen[15] plots.

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

(16) (a) Bell, R. P. *The Proton in Chemistry*, 2nd ed.; Cornell University Press: Ithaca, New York, 1973; Chapter 10. (b) Kresge, A. J. In *Proton Transfer Reactions*; Caldin, E. F., Gold, V., Eds.; Wiley: New York, 1975; p 179.

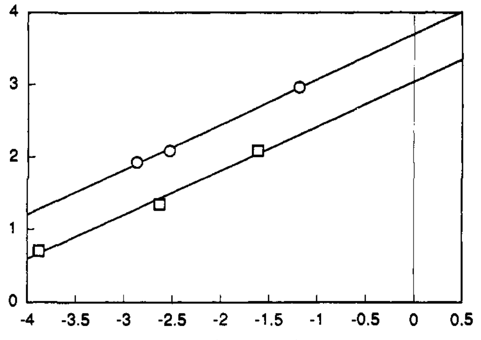


Figure 7. Brønsted plots for the proton transfer reaction of **1-CH$_3$** with primary (□) and secondary (○) amines. For the definitions of *p* and *q* see ref 22.

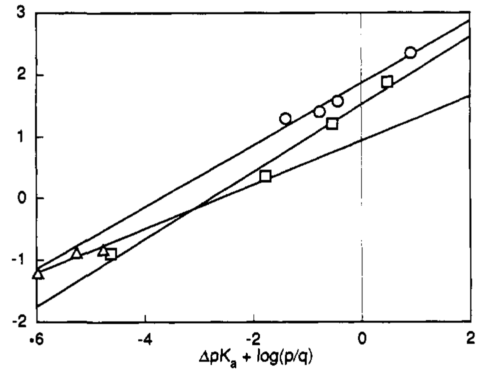


Figure 8. Brønsted plots for the proton transfer reaction of **1-CH$_2$Ph** with primary (□) and secondary amines (○) and carboxylate ions (△). For the definitions of *p* and *q* see ref 22.

Table VI. Brønsted Coefficients and Intrinsic Rate Constants

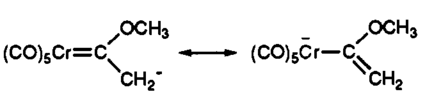
base type	β	α	$\log k_0$
		1-CH$_3$	
RNH$_2$	0.61 ± 0.06	0.39 ± 0.06	3.04 ± 0.17
R$_2$NH	0.62 ± 0.03	0.38 ± 0.03	3.70 ± 0.07
		1-CH$_2$Ph	
RNH$_2$	0.54 ± 0.04	0.46 ± 0.04	1.51 ± 0.10
R$_2$NH	0.48 ± 0.07	0.52 ± 0.07	1.86 ± 0.07
RCOO$^-$	0.33 ± 0.09	0.67 ± 0.09	0.79 ± 0.48

proton transfer reactions and may correspond roughly to a 50% to 60% transfer in the deprotonation of **1-CH$_2$R** by amines. However, this traditional interpretation has recently been challenged[21] and hence conclusions regarding the transition state based on Brønsted coefficients need to be viewed with caution.

Intrinsic Rate Constants. Intrinsic rate constants, defined as $k_o = k_1^B/q = k_1^{BH}/p$ when $pK_a^{BH} - pK_a^{CH} + \log(p/q) = 0$, are reported in Table VI as $\log k_o$.[22] It is well-known that there exists an approximate inverse relationship between $\log k_o$ for proton transfer from C–H acids and the degree of resonance stabilization of the resulting carbanion.[19,23] In a recent review the $\log k_o$ values for the deprotonation of a large number of carbon acids by various bases including primary and secondary amines as well as carboxylate ions were summarized and fit into four main categories.[19] The first category, with $\log k_o \geq 8.5$, comprises carbon acids whose conjugate bases are devoid of any resonance effects and hence behave essentially like "normal acids".[15] A second group with $\log k_o$ values between 6 and 7 consists mainly of nitriles and malononitriles. The third category which is the largest includes mainly C–H acids whose conjugate bases are stabilized by moderately strong resonance effects as provided by carbonyl, ester, fluorenyl, cyclopentadienyl, and *p*-nitrophenyl groups and some others, including arylnitroalkanes in Me$_2$SO or Me$_2$SO-rich solvents and acetonitrile. Their $\log k_o$ values fall between ca. 2.5 and 5.0. Finally, the fourth group is mainly composed of nitroalkanes in hydroxylic solvents with $\log k_o$ between −2 and ca. 2; these low intrinsic rate constants reflect the strong resonance stabilization of the nitronate ions, particularly in water where hydrogen bonding solvation enhances this effect by several orders of magnitude.

1-CH$_3$ falls about into the middle of the third category; for example, $\log k_o$ for the reaction with the secondary amines (3.70) is close to $\log k_o$ for the deprotonation of 2,4-dinitrophenylacetonitrile (3.70),[17a] 2,3,4,5-tetrachlorocyclopentadiene (3.59),[24] and Meldrum's acid (3.90)[19] by the same amines in 50% Me$_2$SO–50% water. This suggests that the amount of resonance stabilization of **1-CH$_2^-$** is comparable to that in the anions derived from 2,4-dinitrophenylacetonitrile, 2,3,4,5-tetrachlorocyclopentadiene, and Meldrum's acid.

The resonance stabilization of **1-CH$_2^-$** probably arises from contributions of the two resonance structures **6a** and **6b** as well



6a **6b**

as from additional charge delocalization into the carbonyl ligands. Direct support for delocalization into the CO ligands comes from IR data in THF (where **1-CH$_2^-$** is stable) which show that the CO stretching frequency is reduced from 1941 cm^{-1} in **1-CH$_3$** to 1898 cm^{-1} in **1-CH$_2^-$**.[4] Similar shifts were observed upon deprotonation of (2-oxacyclopentylidene)pentacarbonylchromium(0).[25]

IR frequency shifts due to charge delocalization into the carbonyl ligands also occur upon deprotonation of metal hydrido complexes such as (η^5-C$_5$H$_5$)M(CO)$_3$H with M = Cr, Mo, and W[26] and other similar complexes.[27] With anilines as proton acceptors, such deprotonations are characterized by $\log k_o$ values between 4.6 and 5.8 in acetonitrile,[28] significantly higher than for the deprotonation of **1-CH$_3$**. Apparently the degree of resonance stabilization of the corresponding anions is not as strong as in **1-CH$_2^-$**.

The intrinsic rate constants for the deprotonation of **1-CH$_2$Ph** are about 1.5 log units (RNH$_2$) to 1.8 log units (R$_2$NH) lower than for **1-CH$_3$**. This is reminiscent of the comparison between nitromethane and phenylnitromethane where k_o (R$_2$NH in 50% Me$_2$SO–50% water) for the latter is about 1.0 log unit lower than for the former.[17e] There are at least three factors that contribute to the lowering of $\log k_o$ for **1-CH$_2$Ph**. One is the additional

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(17) (a) Bernasconi, C. F.; Hibdon, S. A. *J. Am. Chem. Soc.* **1983**, *105*, 4343. (b) Bernasconi, C. F.; Bunnell, R. D. *Isr. J. Chem.* **1985**, *26*, 420. (c) Bernasconi, C. F.; Paschalis, P. *J. Am. Chem. Soc.* **1986**, *108*, 2969. (d) Bernasconi, C. F.; Terrier, F. *J. Am. Chem. Soc.* **1987**, *109*, 7115. (e) Bernasconi, C. F.; Kliner, D. A. V.; Mullin, A. S.; Ni, J. X. *J. Org. Chem.* **1988**, *53*, 3342.

(18) See also numerous references cited in ref 19.

(19) Bernasconi, C. F. *Adv. Phys. Org. Chem.* **1992**, *27*, 119.

(20) (a) Leffler, J. E.; Grunwald, E. *Rates and Equilibria of Organic Reactions*; Wiley: New York, 1963. (b) Kresge, A. J. *Acc. Chem. Res.* **1975**, *8*, 354. (c) Jencks, W. P. *Chem. Rev.* **1985**, *85*, 511. (d) Jencks, W. P. *Bull. Soc. Chim. Fr.* **1988**, 218.

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

(22) *p*, the number of equivalent protons on BH, and *q*, the number of equivalent basic sites on B, are commonly used statistical correction factors.[16]

(23) Bernasconi, C. F. *Acc. Chem. Res.* **1987**, *20*, 301. (b) Bernasconi, C. F. *Acc. Chem. Res.* **1992**, *25*, 9.

(24) Bernasconi, C. F.; Stronach, M. W. *J. Am. Chem. Soc.* **1990**, *112*, 8448.

(25) Casey, C. P.; Brunsvold, W. R. *J. Organomet. Chem.* **1976**, *118*, 309.

(26) Jordan, R. F.; Norton, J. P. *J. Am. Chem. Soc.* **1982**, *104*, 1255.

(27) Moore, E. J.; Sullivan, J. M.; Norton, J. R. *J. Am. Chem. Soc.* **1986**, *108*, 2257.

(28) Eididin, R. T.; Sullivan, J. M.; Norton, J. R. *J. Am. Chem. Soc.* **1987**, *109*, 3945.

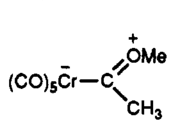
resonance stabilization of **1-C⁻HPh** brought about by charge delocalization into the phenyl group which is reflected in the lower pK_a^{CH} of **1-CH₂Ph** (10.4 vs 12.5). The second is a statistical factor of $^2/_3$ since **1-CH₂Ph** has only two equivalent protons compared to the three in **1-CH₃**. Finally there may be a steric effect that reduces k_o for **1-CH₂Ph**, especially for the reactions with secondary amines. Evidence for such a steric effect comes from the fact that the difference in log k_o for the reaction of **1-CH₂Ph** with primary and secondary amines, $\Delta \log k_o = \log k_o(R_2NH) - \log k_o(RNH_2) = 0.35$, is significantly smaller than $\Delta \log k_o = 0.74$ for **1-CH₃**. A difference in the order of 0.7 to 1.0 is considered "normal" for sterically unhindered proton transfers,[17a-d,24] while a smaller difference implies significant steric hindrance.[19,29] The higher intrinsic reactivity of secondary amines is a well-known phenomenon caused by the differences in the solvation energies of the respective protonated amines.[16a,30]

Kinetic Isotope Effects. The kinetic isotope effects are summarized in Tables III and V. The isotope effect of 5.51 for the reaction of **1-CH₂Ph** with piperidine is within the typical range observed for the deprotonation of C–H acids[31,32] although, considering that $pK_a^{BH} - pK_a^{CH}$ is close to zero,[31,33] our k_H/k_D value is at the low end of this range. The isotope effects for the deprotonation of both carbene complexes by OH^- also seem rather low even if the fact that $pK_a^{H_2O} - pK_a^{CH}$ is significantly different from zero is taken into account. Whether the slight variations in k_H/k_D with $pK_a^{H_2O} - pK_a^{CH}$ (Table III) reflect the expected trend of decreasing isotope effects with increasing pK_a difference[31,33] is uncertain because the standard deviations of k_H/k_D are of the same order of magnitude as the variations in k_H/k_D.

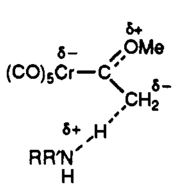
A possible explanation for the low isotope effects is that proton transfer is accompanied by a considerable amount of heavy atom reorganization,[34,35] more so than in the deprotonation of other C–H acids. This is because apart from compressing the C–C bond and stretching the M–C (carbene) bond, the M–C(CO) and C–O bonds are also affected.

Solvent Effects. The rate constants for deprotonation of **1-CH₃** by OH^- and piperidine in 50% acetonitrile–50% water at 25 °C are considerably higher than those in water at 20 °C reported in a preliminary communication.[8] The data summarized in Table II show that the change in solvent accounts for more than half of the increase (factor of 1.99 for OH^-, factor of 4.82 for piperidine). These solvent effects are probably the result of a complex interplay of various factors. For k_1^{OH} the increase in $pK_a^{H_2O} - pK_a^{CH}$ is likely an important factor; the fact that k_1^{OH} does not increase by more than 2-fold is perhaps surprising and may be related to the effect of acetonitrile on the water structure which is known to decrease the reactivity of small anionic nucleophiles in acetonitrile–water mixtures near 33 mol % acetonitrile.[36]

The relatively large solvent effect on the rate of the piperidine reaction cannot be accounted for by a larger $pK_a^{BH} - pK_a^{CH}$ difference. Apart from the likely absence of the above rate retarding effect of the water structure,[36] a possible rate enhancing factor is electrostatic stabilization of the transition state. There is much evidence which suggests that **7** represents an important and probably dominant resonance structure of **1-CH₃**.[2,37] This



7



8

implies that the negative charge that ends up on the $(CO)_5Cr$ moiety of the *anion* (**6b**) is already substantially developed in **1-CH₃** and must therefore be quite extensive in the transition state, as symbolized by a large δ– on **8**. Electrostatic accelerations of proton transfers are well documented[38,39] even in cases where the proton acceptor can only interact with *one* site of opposite charge, such as δ– on the carbon of **8**. Since there is an additional negative site on the $Cr(CO)_5$ moiety the electrostatic stabilization of **8** is likely to be unusually strong. This notion is supported by the fact that even in water the k_1^{pip}/k_1^{OH} ratio of 0.82 is significantly larger than that for the deprotonation of many typical carbon acids;[40] the strong increase of k_1^{pip} in 50% acetonitrile–50% water, which results in a k_1^{pip}/k_1^{OH} ratio of 1.99, is consistent with an enhanced electrostatic effect in the less polar solvent.[39]

Experimental Section

Materials. (Methoxymethylcarbene)pentacarbonylchromium(0), **1-CH₃**, was prepared as described by Fischer and Aumann:[44] yield 67%; mp 34.5–35.5 °C (lit.[44] mp 34 °C); ^{1}H NMR (250 MHz, $CDCl_3$) δ 2.97 (s, 3H, CH_3) and 4.72 (s, 3H, OCH_3).[45] (Benzylmethoxycarbene)pentacarbonylchromium(0), **1-CH₂Ph**, was synthesized according to Fischer et al.:[47] yield 49%; mp 39–39.5 °C (lit.[47] mp 39 °C); ^{1}H NMR (250 MHz, acetone-d_6) δ 4.70 (s, 2H, CH_2), 4.85 (s, 3H, CH_3), 7.27 (m, 5, Ph). All manipulations in the synthesis of **1-CH₃** and **1-CH₂Ph** were carried out using argon as the protective gas.

1-CD₃: **1-CH₃** (30 mg, 0.12 mmol) was dissolved in 1 ml of CD_3CN. D_2O (0.2 mL) and 30 μL of a 4.13 M NaOD solution (equivalent to 0.13 mmol of NaOD) were added. After being shaken for ca. 5 s the mixture was neutralized with 42 μL of a 3.22 M DCl solution (equivalent to 0.13 mmol of DCl). The upper layer of the biphasic mixture was separated and, after adding 0.2 mL of CD_3CN, the above H/D exchange procedure was repeated several times until the ^{1}H NMR spectrum no longer showed hydrogen in the methyl group. **1-CD₂Ph**: **1-CH₂Ph** (30 mg, 0.092 mmol) were dissolved in 1 mL of CD_3CN. D_2O (0.3 mL) and 50 μL of a 0.96 M NaOD solution were added. After the mixture was shaken for ca. 5 and neutralized with 30 μL of 1.74 M DCl the upper layer was separated and subjected to several H/D exchange cycles until the ^{1}H NMR spectrum showed less than 5% hydrogen in the methylene group.

All amines were refluxed over NaOH and freshly distilled under argon prior to use. The carboxylic acids were used as received. KOH and HCl solutions were prepared using "dilute it" from Baker Analytical. Acetonitrile was refluxed over CaH_2 and distilled under argon. Water was taken from a Milli-Q water purification system.

Kinetic Runs and Spectra. In 50% acetonitrile–50% water and 25 °C **1-CH₃** and **1-CH₂Ph** hydrolyze with an approximate half-life of 2 h.[41] Hence reaction solutions were always freshly prepared just prior to experiment by injecting a small amount of stock solution of the carbene

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[29] (a) Bernasconi, C. F.; Bunnell, R. D.; Terrier, F. *J. Am. Chem. Soc.* **1988**, *110*, 6514. (b) Farrell, P. G.; Terrier, F.; Xie, H.-Q.; Boubaker, T. *J. Org. Chem.* **1990**, *55*, 2546. (c) Bernasconi, C. F.; Fairchild, D. E. *J. Phys. Org. Chem.* **1992**, *5*, 409.

[30] Jencks, W. P. *Catalysis in Chemistry and Enzymology*; McGraw-Hill: New York, 1968; p 178.

[31] More O'Ferrall, R. A. In *Proton Transfer Reactions*; Caldin, E., Gold, V., Eds.; Wiley & Sons: New York, 1975; p 201.

[32] For a recent compilation of kinetic isotope effect data see: Casamassima, T. E.; Huskey, W. P. *J. Am. Chem. Soc.* **1993**, *115*, 14.

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[35] Melander, L.; Saunders, W. H., Jr. *Reaction Rates of Isotopic Molecules*; Wiley-Interscience: New York, 1980; p 152.

[36] Um, I.-H.; Lee, G.-J.; Yoon, H.-W.; Kwon, D.-S. *Tetrahedron Lett.* **1992**, *33*, 2023.

[37] Schubert, U. *Coord. Chem. Rev.* **1984**, *55*, 261.

[38] (a) Kresge, A. J. *Chem. Soc. Rev.* **1973**, *2*, 475. (b) Chwang, W. K.; Eliason, R.; Kresge, A. J. *J. Am. Chem. Soc.* **1977**, *99*, 805. (c) Dahlberg, D. B.; Kuzemko, M. A.; Chiang, Y.; Kresge, A. J.; Powell, M. F. *J. Am. Chem. Soc.* **1983**, *105*, 5387.

[39] Thibblin, A. *J. Am. Chem. Soc.* **1984**, *106*, 183.

[40] For example, k_1^{pip}/k_1^{OH} in water is 0.143 for nitromethane,[17c] 0.147 for phenylnitromethane,[17c] 0.269 for acetylacetone,[17b] 0.192 for 2,4-dinitrophenylacetonitrile,[41] and 0.332 for 9-cyanofluorene.[43,44]

[41] Bernasconi, C. F.; Sun, W., unpublished results.

[42] in 10% Me_2SO–90% water.

[43] Bernasconi, C. F.; Terrier, F. *J. Am. Chem. Soc.* **1987**, *109*, 7115.

[44] Fischer, E. O.; Aumann, R. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 879.

[45] Values from ref 43: δ 3.03 and 4.68 ppm, respectively.

[46] Fischer, E. O.; Massböl, A. *Chem. Ber.* **1967**, *100*, 2445.

[47] Fischer, E. O.; Kreiter, C. G.; Kollmeier, H. J.; Müller, J.; Fischer, R. D. *J. Organomet. Chem.* **1971**, *28*, 237.

complex in acetonitrile into the 50% acetonitrile–50% water reaction medium. All kinetic experiments were performed in an Applied Photophysics DX.17MV stopped-flow apparatus. For the pH-jump experiments, the substrate anion was first generated with KOH and 1 s later for **1-CH$_3$** and 2 s later for **1-CH$_2$Ph** the solution was mixed with the appropriate buffer, using the sequential mixing mode of the stopped-flow apparatus. The buffer solutions were prepared in such a manner that they would neutralize all the KOH used to generate the anion and the final solution had the appropriate pH and an ionic strength of 0.1 M maintained by adding KCl. Rate constants were measured either by monitoring substrate disappearance at 370–380 nm or, in the case of **1-CH$_2$Ph**, anion formation at 320 nm.

The spectra shown in Figures 1 and 2 were obtained from the absorbance values of kinetic traces generated at 5-nm intervals in the stopped-flow apparatus. Connecting the points and smoothing the curves is done by the computer software of the stopped-flow apparatus.

HPLC Analysis. The identity of **1-CH$_3$** and **1-CH$_2$Ph** regenerated by quenching the respective anions with HCl in the stopped-flow apparatus was confirmed by HPLC analysis. The effluent from the stopped-flow apparatus was run through an HP ODS Hypersil, 5 μm, 200 × 4.6 mm column and analyzed on a Hewlett-Packard 1090 HPLC apparatus with diode array detector. The eluent used was 80% acetonitrile–20% water.

pH and pK_a Measurements. The pH in 50% acetonitrile–50% water was determined from eq 6[11] with pH$_{\text{measured}}$ being the pH measured by the

$$\mathrm{pH} = \mathrm{pH}_{\text{measured}} + 0.18 \qquad (6)$$

pH meter calibrated with standard aqueous buffers. The pK_a of the various amines and carboxylic acids in 50% acetonitrile–50% water was determined as the pH of 1:1 buffers.

Acknowledgment. The research was supported by Grant No. CHE-9307659 from the National Science Foundation.

Supplementary Material Available: Tables S1–S18 containing kinetic data (15 pages). This 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 ACS; see any current masthead page for ordering information.