

Physical Organic Chemistry of Transition Metal Carbene Complexes. 25. Kinetic and Thermodynamic Acidities of Substituted (Methylthiophenylcarbene)pentacarbonyl Tungsten(0) and (Benzoxymethylcarbene)pentacarbonyl Tungsten(0) in Aqueous Acetonitrile. Evidence for Transition State Imbalances[†]

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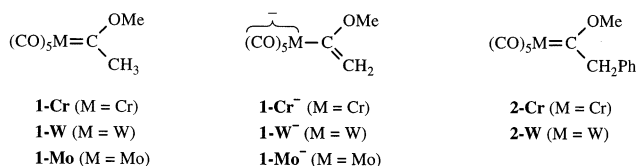
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Abstract: A kinetic study of the reversible deprotonation of substituted (methylthiophenylcarbene)pentacarbonyltungsten(0) ((CO)₅W=C(SC₆H₄Z)CH₃) and of substituted (benzoxymethylcarbene)pentacarbonyltungsten(0) ((CO)₅W=C(OCH₂C₆H₄Z)CH₃) by primary aliphatic and secondary alicyclic amines in 50% MeCN–50% water (v/v) at 25 °C is reported. From the dependence of the deprotonation rate constants on amine basicity and on carbene complex acidity (variation of Z), Brønsted β_B and α_{CH} values, respectively, were obtained. The α_{CH} values were found to be smaller than the β_B values. These results indicate a transition state imbalance in which the loss of the carbene complex stabilizing π-donor effect of the OCH₂Ar and SAR groups lags behind the proton transfer. These findings confirm a previously formulated hypothesis as to how π-donor groups attached to the carbene carbon of carbene complexes can affect transition state imbalances and mask the experimental manifestation of such imbalances. It is also shown that the transition state structure of the reactions examined in this work is subject to changes with changing amine basicity and carbene complex acidity; these changes can be expressed by ρ_{xy} cross correlation coefficients, which are positive.

Introduction

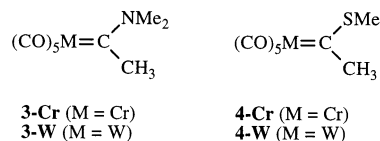
The methyl group of pentacarbonyl chromium or tungsten carbene complexes of the Fischer type is remarkably acidic.¹ For example, the pK_a of **1-Cr** in 50% MeCN–50% water (v/v) is 12.50,² while that of **1-W** is 12.36.³ This high acidity can be



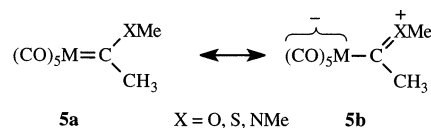
attributed to the strong stabilization of the respective conjugate anions, **1-M⁻**, by delocalization of the negative charge into the (CO)₅M moieties.^{1,4}

The acidities are strongly affected by the π-donor group attached to the carbene carbon. This is seen in the fact that **3-Cr**

or **3-W** cannot be deprotonated in an aqueous solvent,⁵ and in the pK_a values of **4-Cr** (9.05)⁶ or **4-W** (8.37)⁶ which are 3.45 and 3.99 units lower than those of the respective methoxy analogues in the same solvent. This dependence on the π-donor



group is indicative of the strong stabilization of the neutral carbene complexes by π-donation (**5a** ↔ **5b**);^{1,7} the decreasing acidity in the order **4-M** > **1-M** > **3-M** reflects the increasing strength of the π-donor effect in the order MeS < MeO < Me₂N.⁸



The rates of deprotonation/protonation of the α-carbon of Fischer carbene complexes are relatively slow, indicating rather

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[†] Part 24: Bernasconi, C. F.; Sun, W. *J. Am. Chem. Soc.* **2002**, *124*, 2299.

(1) For a recent review, see: Bernasconi, C. F. *Chem. Soc. Rev.* **1997**, *26*, 299.

(2) Bernasconi, C. F.; Sun, W. *J. Am. Chem. Soc.* **1993**, *115*, 12526.

(3) Bernasconi, C. F.; Sun, W. *Organometallics* **1997**, *16*, 1926.

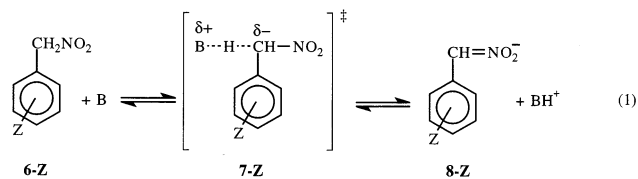
(4) Casey, C. P.; Anderson, R. L. *J. Am. Chem. Soc.* **1974**, *96*, 1230.

(5) Bernasconi, C. F.; Leyes, A. E.; Ragains, M. L.; Shi, Y.; Wang, H.; Wulff, W. D. *J. Am. Chem. Soc.* **1998**, *120*, 8632.

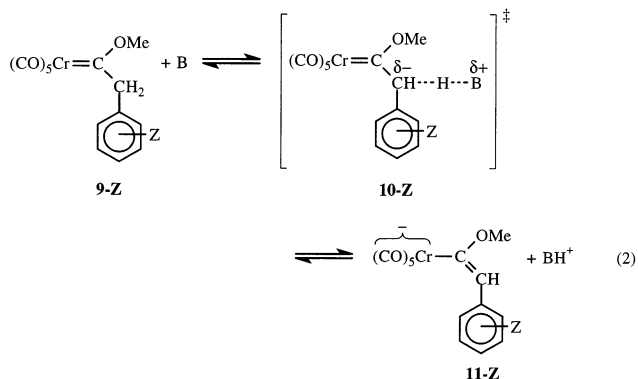
(6) Bernasconi, C. F.; Ali, M. *J. Am. Chem. Soc.* **1999**, *121*, 3039.

high Marcus intrinsic barriers (ΔG_o^\ddagger) or low intrinsic rate constants (k_o),¹⁰ as is typical for carbon acids that are converted to delocalized carbanions.¹² The main reason for the high intrinsic barriers is that the transition state is imbalanced in the sense that charge delocalization lags behind proton transfer.¹³

Independent evidence for the presence of transition state imbalances comes from Brønsted coefficients, specifically from a comparison of Brønsted α_{CH} values obtained by varying a remote substituent in the carbon acid, with the Brønsted β_{B} value obtained by varying the buffer base such as a series of amines or carboxylate ions.¹² The best-known example is the reaction shown in eq 1 ($\text{B} = \text{R}_2\text{NH}$), where $\alpha_{\text{CH}} = 1.29$ and $\beta_{\text{B}} = 0.56$.^{14,15}

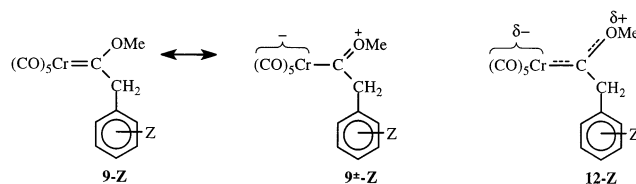


Because Fischer carbene complexes such as **1-M**, **2-M**, and **4-M** show characteristics similar to those of purely organic carbon acids such as **6-Z**, that is, their conjugate anions are highly delocalized, and the intrinsic barriers to proton transfer are quite high,¹ one would expect that here, too, transition state imbalance is the reason for the high intrinsic barriers. This prediction has recently been tested for the reaction shown in eq 2¹⁶ ($\text{B} =$ primary aliphatic and secondary alicyclic amines). If the transition state is imbalanced as shown in **10-Z**, one should have observed $\alpha_{\text{CH}} > \beta_{\text{B}}$ as in the case of eq 1. However, α_{CH}



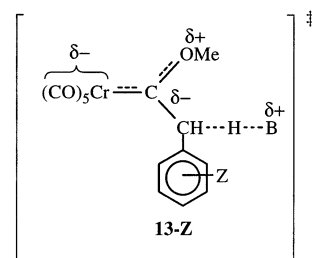
and β_{B} are, within the experimental uncertainties, indistinguishable (RNH_2 : $\alpha_{\text{CH}} = 0.56 \pm 0.03$ and $\beta_{\text{B}} = 0.54 \pm 0.04$; R_2NH : $\alpha_{\text{CH}} = 0.53 \pm 0.02$ and $\beta_{\text{B}} = 0.48 \pm 0.07$).¹⁶ This

unexpected result was attributed to the π -donor effect of the MeO (**9-Z** \leftrightarrow **9[±]-Z**: **12-Z**) group which masks the imbalance by reducing α_{CH} to become approximately equal to β_{B} .



The key to an explanation put forward in ref 16 is that, inasmuch as the contribution of **9[±]-Z** leads to resonance stabilization of the carbene complexes, this resonance is expected to add to the intrinsic barrier of proton transfer. This is because its loss at the transition state should be ahead of the proton transfer.¹² As Z becomes more electron withdrawing, the greater electron deficiency of the carbene carbon induces a stronger π -donor effect by the methoxy group. There are two consequences. One is that the increased contribution of the resonance structure **9[±]-Z** partially compensates for the destabilization of the electron-deficient carbene carbon by the electron-withdrawing inductive effect of Z . The second is that the increased resonance stabilization of the carbene complex increases the intrinsic barrier, and hence the rate (k_1^{B}) enhancement caused by the polar effect of Z will be attenuated. This attenuation is proportional to the electron-withdrawing strength of Z , and hence the slope of the Brønsted plot (α_{CH}) is reduced.¹⁷

An alternative view, perhaps simpler but by no means contradicting the above explanation, is to assume that the partial positive charge on the MeO group of **12-Z** is largely maintained at the transition state, implying that **13-Z** is a more accurate representation of the transition state than **10-Z**. This means that the stabilizing effect of an electron-withdrawing Z substituent on the negatively charged carbon is partially offset by its destabilizing effect on the positively charged oxygen.¹⁸ Hence α_{CH} is reduced.

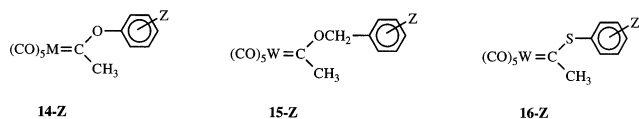


The objective of the present paper is to test this explanation by examining whether **13-Z** is a reasonable representation of the transition state. Our approach is to use substituents on the π -donor group to examine whether the partial positive charge on the π -donor atom of the carbene complex is substantially conserved at the transition state. An ideal system for such a study would be carbene complexes of the type **14-Z**. However,

- (7) Dötz, K. H.; Fischer, H.; Hofmann, P.; Kreissl, F. R.; Schubert, U.; Weiss, K. *Transition Metal Carbene Complexes*; Verlag Chemie: Deerfield Beach, FL, 1983.
- (8) $\sigma_{\text{R}} = -0.15$ (MeS), -0.43 (MeO), and -0.56 (Me₂N).⁹
- (9) Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165.
- (10) The intrinsic barrier, ΔG_o^\ddagger (intrinsic rate constant, k_o), of a reaction is the barrier (rate constant) in the absence of a thermodynamic driving force.¹¹ For a reaction with a forward rate constant k_1 and a reverse rate constant k_{-1} , $k_o = k_1 = k_{-1}$ when K_1 (equilibrium constant) = 1, and $\Delta G_o^\ddagger = \Delta G_1^\ddagger = \Delta G_{-1}^\ddagger$ when $\Delta G^\circ = 0$.
- (11) Marcus, R. A. *J. Phys. Chem.* **1968**, *72*, 891.
- (12) (a) Bernasconi, C. F. *Acc. Chem. Res.* **1987**, *20*, 301. (b) Bernasconi, C. F. *Adv. Phys. Org. Chem.* **1992**, *27*, 119. Bernasconi, C. F. *Acc. Chem. Res.* **1992**, *25*, 9.
- (13) This situation refers to the deprotonation of the carbon acid by a buffer base. In the reverse direction where a buffer acid protonates the carbanion, the imbalance manifests itself in a loss of resonance that is ahead of proton transfer.

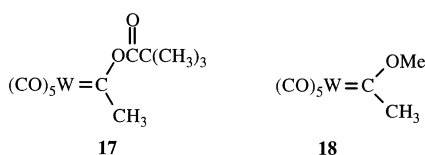
- (14) In water.
- (15) Bordwell, F. G.; Boyle, W. J., Jr. *J. Am. Chem. Soc.* **1972**, *94*, 3907.
- (16) Bernasconi, C. F.; Sun, W. *J. Am. Chem. Soc.* **2002**, *124*, 2299.
- (17) See Figure 5 in ref 16.
- (18) The effect of Z on the negatively charged $(\text{CO})_5\text{Cr}$ moiety is expected to be smaller than that on the positively charged oxygen because the negative charge is more dispersed than the positive one.

we were unsuccessful in preparing these carbene complexes in sufficient yield and purity suitable for kinetic investigation.¹⁹ We therefore chose complexes such as **15-Z** and **16-Z** for our investigation. Even though their preparation also becomes more difficult as Z is made more electron withdrawing, a number of such compounds were successfully synthesized and amenable to kinetic determinations.



Results

General Features. The following carbene complexes were synthesized: **15-Z** with Z = 4-OMe, 4-Me, H, and 4-Cl; **16-Z** with Z = 4-OMe, 4-Me, H, 4-Br, and 3-Br. The synthesis of **15-Z** involved the reaction of the pivaloyl ester, **17**, with the corresponding benzyl alcohol, while the synthesis of **16-Z** was based on the reaction of the methoxy carbene complex, **18**, with the corresponding thiophenols.

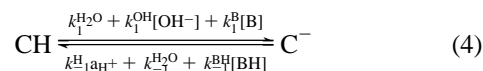


Deprotonation of all carbene complexes occurs readily in a variety of basic buffers; it typically takes place in the millisecond time range and is measurable in a stopped-flow spectrophotometer. Recovery of the carbene complex upon acidification of its conjugate anion immediately after its formation established the reversibility of the proton transfer. With the thiophenyl complexes (**16-Z**), this recovery was on the order of $\geq 95\%$, with the benzyloxy carbene complexes $\sim 85\text{--}90\%$. The lower recovery yields for the latter complexes reflect the faster hydrolysis of the carbanion, a reaction that occurs with all deprotonated carbene complexes.²¹ Because of the short lifetime of the carbanions derived from the benzyloxy carbene complexes, the kinetics of their reprotonation had to be conducted in a double-mixing stopped-flow apparatus that allows the mixing of the carbanion with an acidic buffer less than 1 s after the carbanion has been generated.

Kinetic Experiments. Rates were determined in KOH solutions and in various primary aliphatic and secondary alicyclic amine buffers; some measurements were also performed in acetate buffers. All experiments were conducted in 50% MeCN–50% water (v/v) at 25 °C. Pseudo-first-order conditions, with the carbene complex or its anion as the minor component, were used throughout. The observed pseudo-first-order rate constants for approach to equilibrium are given in eq 3, with the various rate constants defined in eq 4 (B = buffer base, BH = buffer acid, CH = carbene complex, C⁻ =

carbanion). Depending on the pH, the reactions were run either in the forward direction (CH → C⁻ at pH > pK_a^{CH}) or in the reverse direction (C⁻ → CH at pH < pK_a^{CH}).

$$k_{\text{obsd}} = k_1^{\text{H}_2\text{O}} + k_{-1}^{\text{H}} a_{\text{H}^+} + k_1^{\text{OH}} [\text{OH}^-] + k_{-1}^{\text{H}_2\text{O}} + k_1^{\text{B}} [\text{B}] + k_{-1}^{\text{BH}} [\text{BH}] \quad (3)$$



All rate constants and pK_a^{CH} values determined in this study as described below are summarized in Tables 1 (**15-Z**) and 2 (**16-Z**).

Kinetic pK_a^{CH} Determination. For **15-Z**, the pK_a^{CH} was determined from experiments in piperidine buffers at various pH values as follows. At a given pH, plots of k_{obsd} versus [B] were linear with slopes given by eq 5. A representative set of such plots is shown in Figure 1. From a plot of the slopes versus

$$\text{slope} = k_1^{\text{B}} \left(1 + \frac{a_{\text{H}^+}}{K_a^{\text{CH}}} \right) \quad (5)$$

a_{H^+} , a value for k_1^{B} and K_a^{CH} could then be obtained (Figure 2), and k_{-1}^{BH} was calculated as $k_{-1}^{\text{BH}} = k_1^{\text{B}} K_a^{\text{BH}} / K_a^{\text{CH}}$, with K_a^{BH} being the acidity constant of piperidinium ion.

In an analogous way, the pK_a^{CH} values of **16-Z** were determined in *N*-methylmorpholine and/or acetate buffers.

Kinetics in Various Amine Buffers and KOH Solutions. The kinetic experiments with amines were conducted at a constant pH that was close to the pK_a^{BH} of the amine buffer ([B]:[BH⁺] ≈ 1:1). The k_1^{B} values were obtained by solving eq 5 for k_1^{B} which is the only unknown, and k_{-1}^{BH} was again calculated as $k_{-1}^{\text{BH}} = k_1^{\text{B}} K_a^{\text{BH}} / K_a^{\text{CH}}$. The deprotonation of OH⁻ was performed in KOH solution at concentrations ranging from 0.01 to 0.1 M. Plots of k_{obsd} versus [KOH] provided k_1^{OH} as the slope; the intercept was too small to yield a reliable value for $k_{-1}^{\text{H}_2\text{O}}$, but $k_{-1}^{\text{H}_2\text{O}}$ could be calculated as $k_{-1}^{\text{H}_2\text{O}} = k_1^{\text{OH}} K_w / K_a^{\text{CH}}$ with K_w being the ionic product of the solvent.²²

Spectrophotometric pK_a^{CH} Determination. For **16-Z**, the respective anions were stable enough to allow for the determination of the pK_a^{CH} by applying eq 6, where A_{max} is the absorbance at pH << pK_a^{CH}, A_{min} is the absorbance at pH >>

$$\text{pH} = \text{pK}_a^{\text{CH}} + \log \frac{A_{\text{max}} - A}{A - A_{\text{min}}} \quad (6)$$

pK_a^{CH}, and A is the absorbance at pH ≈ pK_a^{CH}. The pK_a^{CH} was obtained as the intercept of a plot of pH versus $\log\{(A_{\text{max}} - A)/(A - A_{\text{min}})\}$. These spectrophotometric pK_a^{CH} values are included in Table 2; they are in excellent agreement with the ones determined kinetically. However, the kinetic pK_a^{CH} values are deemed more accurate because they are not affected by the slight decomposition of the anion during the spectrophotometric measurements, and they will be the ones adopted in the Discussion.

(19) We followed the synthetic procedures described by Jiang, Fuentes, and Wulff.²⁰ For unknown reasons, this synthesis could not be reproduced by one of the authors nor by one of us (V.R.) while working in Professor Wulff's laboratory.

(20) Jiang, W.; Fuentes, M. J.; Wulff, W. D. *Tetrahedron* **2000**, *56*, 2183.
 (21) (a) Bernasconi, C. F.; Flores, F. X.; Sun, W. *J. Am. Chem. Soc.* **1995**, *117*, 4875. (b) Bernasconi, C. F.; Sun, W. *Organometallics* **1995**, *14*, 5615. (c) Bernasconi, C. F.; Leyes, A. E. *J. Chem. Soc., Perkin Trans. 2* **1997**, 1641. (d) Bernasconi, C. F.; Leyes, A. E.; García-Río, L. *Organometallics* **1998**, *17*, 4940.

(22) pK_w = 15.19 in 50% MeCN–50% water (v/v) at 25 °C, $\mu = 0.1$ M (KCl).²

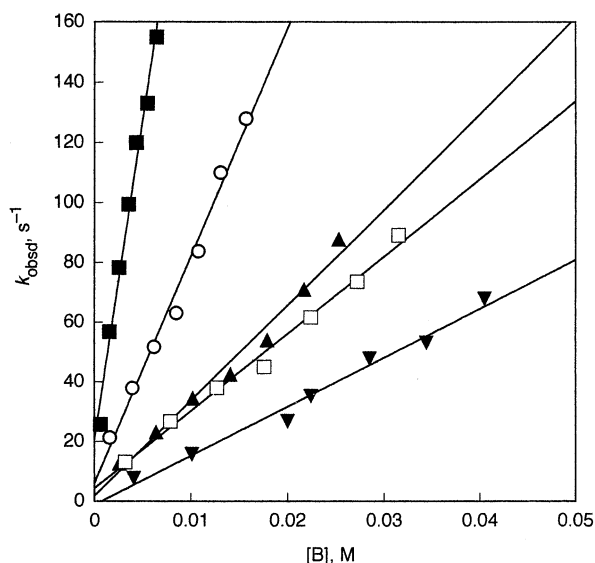


Figure 1. Selected plots of k_{obsd} versus piperidine concentration for the reaction of **15-Cl** with piperidine. ■, pH 10.17; ○, pH 10.66; ▲, pH 11.03; □, pH 11.25; ▼, pH 11.66.

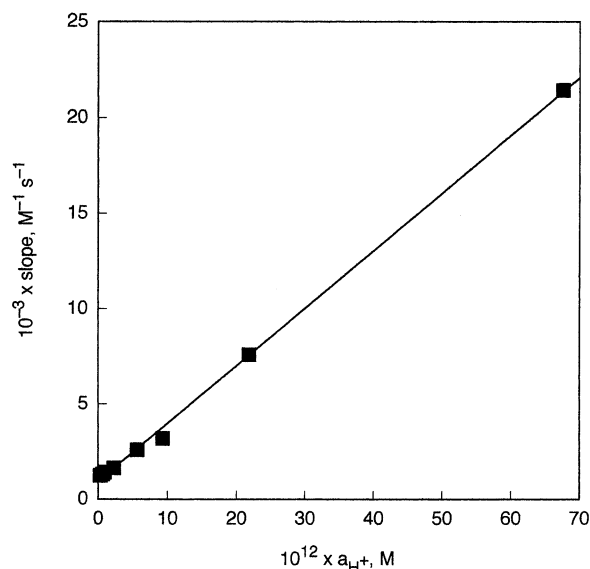
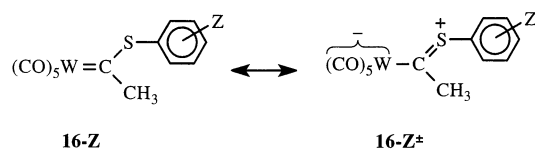


Figure 2. Plot of slope versus a_{H^+} according to eq 5 for the reaction of **15-Cl** with piperidine.

1-M (12.50 for $M = \text{Cr}$, 12.36 for $M = \text{W}$) were interpreted the same way.⁶ Note that the π -donor effects completely



overshadow the inductive effects because the stronger inductive effect of the oxygen²³ in **15-Z** should have a greater acidifying effect than the sulfur in **16-Z**.

The second factor is the stronger electron-withdrawing inductive effect of the phenyl as compared to that of the benzyl group.²⁴ This is the likely reason that the $pK_{\text{a}}^{\text{CH}}$ difference between **15-Z** and **16-Z** is even larger than that between **1-M** and **4-M**.

(23) $\sigma_1 = 0.30$ (MeO) and 0.20 (MeS).⁹

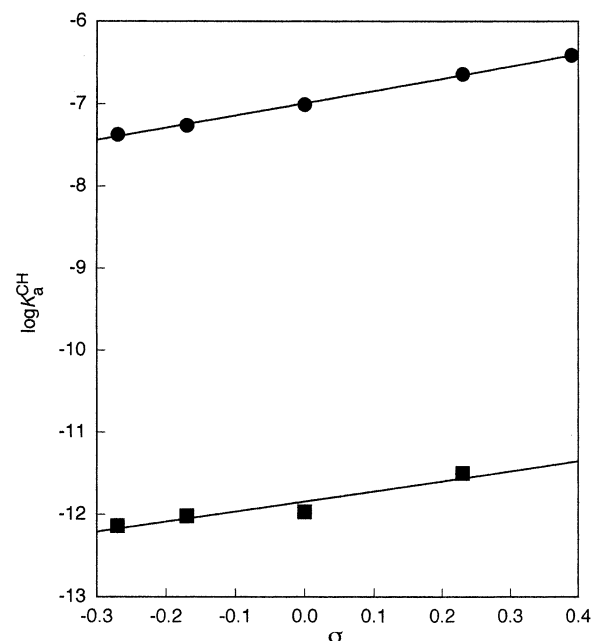


Figure 3. Hammett plots of $\log K_{\text{a}}^{\text{CH}}$ for **15-Z** (■) and **16-Z** (●).

Substituent Effects on the Acidity Constants. Figure 3 shows plots of $\log K_{\text{a}}^{\text{CH}}$ versus Hammett σ values. They yield $\rho = 1.22 \pm 0.27$ for **15-Z** and $\rho = 1.48 \pm 0.04$ for **16-Z**, respectively. These ρ -values probably reflect a combination of carbanion stabilization and carbene complex destabilization by electron-withdrawing substituents. The destabilization of the carbene complexes may be attributed to the build-up of positive charge on the oxygen atom of **15-Z** (**15-Z $^{\pm}$**) and on the sulfur atom of **16-Z** (**16-Z $^{\pm}$**), which results from the π -donor effect of these atoms.

The finding that ρ for **15-Z** is only slightly lower than that for **16-Z**, despite the greater distance of the phenyl group from the heteroatom as well as from the site of the negative charge in the anion, is noteworthy. It must be the result of the greater positive charge on the oxygen of the oxa carbene complexes as compared to that on the sulfur of the thia complexes. This enhances the destabilizing effect of the electron-withdrawing substituents on the oxa carbene complexes and compensates for the greater distance of the phenyl group from the heteroatom.

Brønsted Coefficients. A. Cross Correlations. Figure 4 shows representative Brønsted plots of $\log(k_1/q)$ versus $pK_{\text{a}}^{\text{BH}} - pK_{\text{a}}^{\text{CH}} + \log(p/q)$ ²⁵ for the determination of β_{B} , while Figure 5 shows representative plots of $\log k_1^{\text{B}}$ versus $\log K_{\text{a}}^{\text{CH}}$ for the determination of α_{CH} . The α_{CH} values are summarized in Table 3, while the β_{B} values are reported in Table 4.

Some of the Brønsted coefficients are associated with significant standard deviations, especially some of the α_{CH} values. For the latter, the relatively small $pK_{\text{a}}^{\text{CH}}$ range is a likely contributing factor to these deviations. Nevertheless, looking at the totality of all Brønsted coefficients, there is a definite trend toward increasing α_{CH} values with decreasing $pK_{\text{a}}^{\text{BH}}$ and toward a decrease in β_{B} with decreasing $pK_{\text{a}}^{\text{CH}}$. These trends are more evident for the reactions of **15-Z** than for the reactions of **16-Z**.

(24) $F = 0.12$ (C_6H_5) and -0.04 ($\text{C}_6\text{H}_5\text{CH}_2$).⁹

(25) q and p are statistical factors: q is the number of equivalent basic sites on B, while p is the number of equivalent protons on BH^+ .

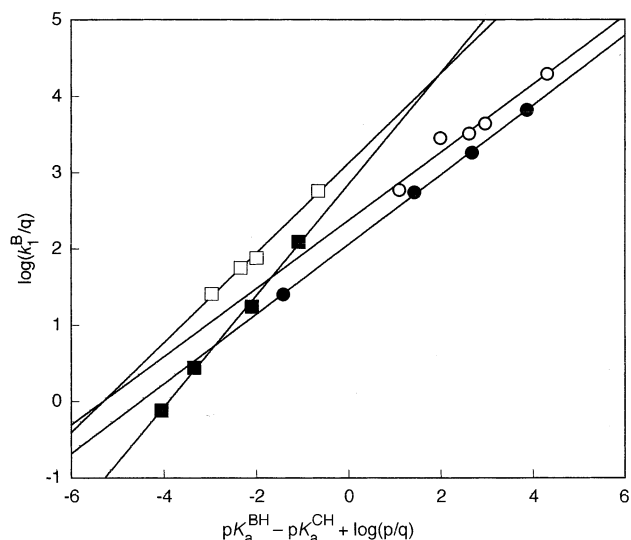


Figure 4. Representative Brønsted plots for dependence on base: □, **15-H/R₂NH**; ■, **15-H/RNH₂**; ○, **16-H/R₂NH**; ●, **16-H/RNH₂**.

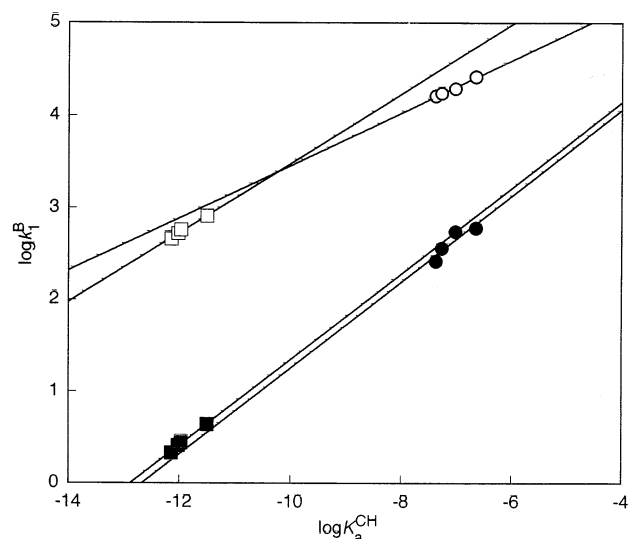


Figure 5. Representative Brønsted plots for the dependence on the carbene complex: □, **15-Z/piperidine**; ■, **15-Z/H₂NCOCH₂NH₂**; ○, **16-Z/piperidine**; ●, **16-Z/H₂NCOCH₂NH₂**.

The changes in α_{CH} and β_{B} can be expressed by the p_{xy} cross correlation coefficient which is defined by eq 7 and is obtained as the slope of plots of α_{CH} versus $pK_{\text{a}}^{\text{BH}}$ or of β_{B} versus $pK_{\text{a}}^{\text{CH}}$, respectively.²⁶ The respective p_{xy} values are included in Tables 3 and 4. Note that the p_{xy} values calculated as $\alpha_{\text{CH}}/\partial pK_{\text{a}}^{\text{BH}}$ are considered more reliable than those calculated as $\beta_{\text{B}}/\partial pK_{\text{a}}^{\text{CH}}$ because the $pK_{\text{a}}^{\text{BH}}$ range is larger than the $pK_{\text{a}}^{\text{CH}}$ range.

$$p_{xy} = \frac{\partial \alpha_{\text{CH}}}{-\partial pK_{\text{a}}^{\text{BH}}} = \frac{\partial \beta_{\text{B}}}{\partial pK_{\text{a}}^{\text{CH}}} \quad (7)$$

Similar changes leading to positive p_{xy} cross correlation coefficients have been observed for the deprotonation of other carbon acids such as **19-Z**,²⁷ **20-Z**,²⁸ and **21-Z**.²⁹ They indicate

- (26) (a) Jencks, D. A.; Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 7948. (b) Jencks, W. P. *Chem. Rev.* **1985**, *85*, 511.
 (27) Bernasconi, C. F.; Wenzel, P. J. *J. Am. Chem. Soc.* **1996**, *118*, 11446.
 (28) Murray, C. J.; Jencks, W. P. *J. Am. Chem. Soc.* **1990**, *112*, 1880.
 (29) Bernasconi, C. F.; Fairchild, D. E. *J. Phys. Org. Chem.* **1992**, *5*, 409.

Table 3. Brønsted α_{CH} Values and p_{xy} Cross Correlation Coefficients for the Reactions of **15-Z** and **16-Z** with Various Bases

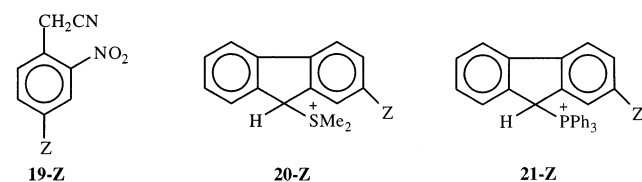
B	$pK_{\text{a}}^{\text{BH}}$	α_{CH}	$p_{xy} = \partial \alpha_{\text{CH}} / -\partial pK_{\text{a}}^{\text{BH}}$
(CO)₅W=C(OCH₂C₆H₄Z)CH₃ (15-Z)			
OH ⁻	16.64	0.41 ± 0.04	0.049 ± 0.007
piperidine	11.01	0.35 ± 0.03	
piperazine	9.97	0.38 ± 0.02	
HEPA ^a	9.33	0.43 ± 0.03	
morpholine	8.70	0.46 ± 0.05	
<i>n</i> -BuNH ₂	10.40	0.24 ± 0.03	0.062 ± 0.023
MeOCH ₂ CH ₂ NH ₂	9.39	0.39 ± 0.05	
H ₂ NCOCH ₂ NH ₂	8.14	0.44 ± 0.02	
EtOCOCH ₂ NH ₂	7.43	0.43 ± 0.05	
(CO)₅W=C(SC₆H₄Z)CH₃ (16-Z)			
OH ⁻	16.64	0.21 ± 0.09	0.017 ± 0.004
piperidine	11.01	0.29 ± 0.01	
piperazine	9.97	0.33 ± 0.03	
HEPA ^a	9.33	0.32 ± 0.03	
morpholine	8.70	0.34 ± 0.02	
PIPALD ^b	7.81	0.35 ± 0.07	0.030 ± 0.013
<i>n</i> -BuNH ₂	10.40	0.28 ± 0.07	
MeOCH ₂ CH ₂ NH ₂	9.39	0.26 ± 0.05	
H ₂ NCOCH ₂ NH ₂	8.14	0.30 ± 0.01	
NCCH ₂ NH ₂	5.29	0.41 ± 0.03	

^a HEPA: 1-(2-hydroxyethyl)piperazine. ^b PIPALD: 1-piperazine carboxaldehyde.

Table 4. Brønsted β_{B} Values, p_{xy} Cross Correlation Coefficients, and $\log k_0$ Values for the Reactions of **15-Z** and **16-Z** with Secondary Alicyclic (R₂NH) and Primary Aliphatic (RNH₂) Amines

carbene complex	$pK_{\text{a}}^{\text{CH}}$	β_{B}	$p_{xy} = \partial \beta_{\text{B}} / \partial pK_{\text{a}}^{\text{CH}}$	$\log k_0$
Secondary Alicyclic Amines (R₂NH) + 15-Z				
15-OMe	12.14	0.56 ± 0.05	0.135 ± 0.049	3.11 ± 0.11
15-Me	12.02	0.58 ± 0.05		3.12 ± 0.06
15-H	11.97	0.58 ± 0.02		3.14 ± 0.03
15-Cl	11.50	0.49 ± 0.05		2.92 ± 0.13
Primary Aliphatic Amines (RNH₂) + 15-Z				
15-OMe	12.14	0.75 ± 0.04	0.089 ± 0.010	2.95 ± 0.13
15-Me	12.02	0.73 ± 0.03		2.88 ± 0.09
15-H	11.97	0.73 ± 0.03		2.86 ± 0.09
15-Cl	11.50	0.69 ± 0.02		2.60 ± 0.06
Secondary Alicyclic Amines (R₂NH) + 16-Z				
16-OMe	7.37	0.46 ± 0.05	0.031 ± 0.007	2.40 ± 0.13
16-Me	7.26	0.46 ± 0.06		2.36 ± 0.16
16-H	7.01	0.44 ± 0.06		2.39 ± 0.17
16-Br (p)	6.64	0.44 ± 0.05		2.56 ± 0.16
16-Br (m)	6.41	0.43 ± 0.06		2.34 ± 0.20
Primary Aliphatic Amines (RNH₂) + 16-Z				
16-OMe	7.37	0.49 ± 0.04	0.025 ± 0.009	1.97 ± 0.09
16-Me	7.26	0.47 ± 0.02		2.00 ± 0.06
16-H	7.01	0.47 ± 0.01		1.97 ± 0.03
16-Br (p)	6.64	0.46 ± 0.01		1.93 ± 0.08
16-Br (m)	6.41	0.46 ± 0.02		1.92 ± 0.07

changes in transition state structure that can be understood on the basis of a reaction coordinate diagram with separate axes



for α_{CH} and β_{B} , as described by Murray and Jencks.²⁸ Such a diagram is shown in Figure 6, for the example of the reaction

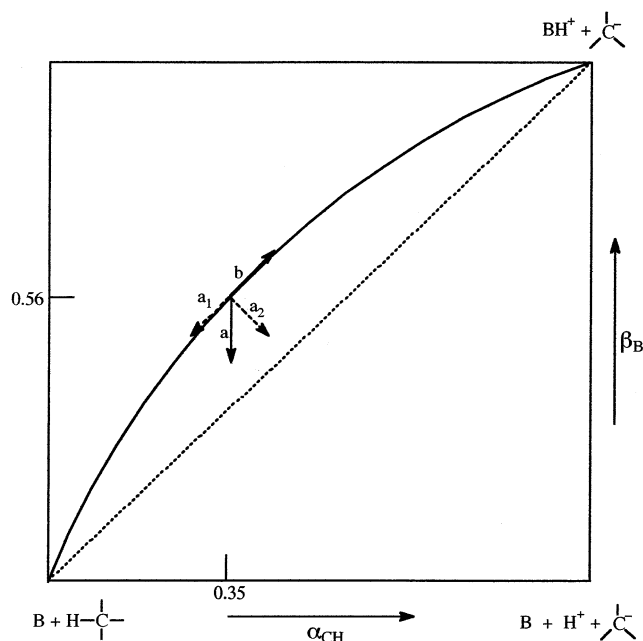


Figure 6. Reaction coordinate diagram for the reaction of **15-OMe** with piperidine ($\alpha_{\text{CH}} = 0.35$ and $\beta_{\text{B}} = 0.56$), see text.

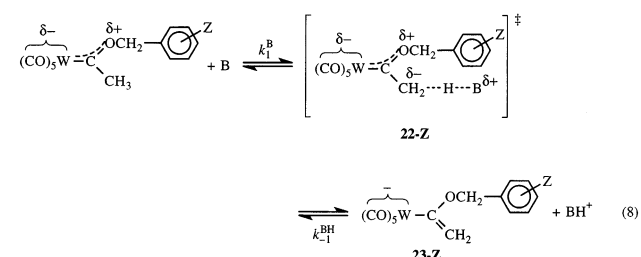
of **15-OMe** with piperidine ($\alpha_{\text{CH}} = 0.35$, $\beta_{\text{B}} = 0.56$). This diagram presumes that β_{B} can be regarded as an approximate measure of proton transfer to the base and that α_{CH} is related to the progress of proton dissociation from the carbon acid. It is important to realize, though, that this does not imply a linear relationship between proton transfer and the Brønsted parameters, only that an increase in β_{B} means more protonation of the base and an increase in α_{CH} means a greater loss of the proton from the carbon acid (the meaning of α_{CH} and β_{B} is considered further in the next section).

With reference to Figure 6, a change to a more acidic carbon acid lowers the right-hand edge of the diagram because the carbanion becomes more stable. This induces the transition state to shift along the reaction coordinate toward the lower left corner (arrow a_1) and perpendicular to the reaction coordinate toward the lower right-hand corner (arrow a_2). The resulting vector (arrow a) suggests that the transition state moves in the direction of less protonation of the base, implying a lower β_{B} as observed (Table 4).

A change to a less basic amine raises the energy of the upper right-hand corner because BH^+ becomes less stable. This induces the transition state to move toward this corner as indicated by arrow b . It implies a more productlike transition state in terms of both a greater degree of protonation of the base and more progress in the dissociation of the proton from the acid; that is, both α_{CH} and β_{B} should increase. The increase in α_{CH} is clearly seen in Table 3; the increase in β_{B} should manifest itself in a downward curvature of the plots of $\log(k_1^{\text{B}}/q)$ versus $\text{p}K_{\text{a}}^{\text{BH}} - \text{p}K_{\text{a}}^{\text{CH}} + \log(p/q)$. However, the relatively small $\text{p}K_{\text{a}}^{\text{BH}}$ range and small number of amines, coupled with experimental scatter, make detection of this curvature impossible. Even in more optimum situations, such curvature is often difficult to detect. For example, in the reaction of **20-Br** with eight primary amines spanning a $\text{p}K_{\text{a}}^{\text{BH}}$ range of 7.3 units, the data at best suggest but definitely do not clearly establish the presence of such curvature.²⁸

B. Transition State Imbalance. As stated in the Introduction, a possible explanation of why for the reaction of **9-Z** with amines the expected transition state imbalance (**10-Z** in eq 2) does not manifest itself in an α_{CH} value that exceeds β_{B} is that the π -donor effect of the MeO group lowers α_{CH} . Specifically, the lowering of α_{CH} can be understood if one assumes that the π -donor effect is substantially maintained at the transition state (**13-Z**).

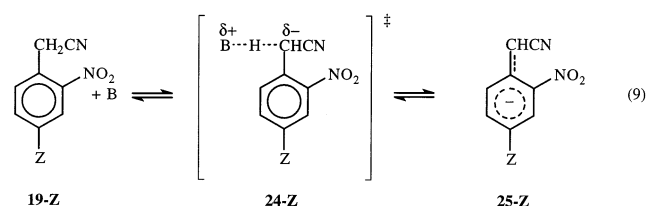
The results of the present study allow a test of this assumption. The analogue of **13-Z** in the reactions of **15-Z** or **16-Z** with amines is shown as **22-Z** for the example of the oxo carbene complexes. Maintaining most of the partial positive charge on



the oxygen at the transition state should lead to a disproportionately small substituent effect on k_1^{B} relative to that on K_{a}^{CH} . This would translate into a disproportionately small α_{CH} relative to the progress of proton transfer, that is, relative to β_{B} .

Our results show this to be the case. A factor that renders the quantitative evaluation of the difference between α_{CH} and β_{B} somewhat less than straightforward is the fact that the α_{CH} and β_{B} values are not constant, as discussed in the previous section. We shall therefore use average α_{CH} and β_{B} values for our assessment of the difference between α_{CH} and β_{B} . These average Brønsted coefficients are summarized in Table 5. They clearly show that $\alpha_{\text{CH}} < \beta_{\text{B}}$ for the reactions of both **15-Z** and **16-Z** with both types of amines.³⁰

Our observation that $\alpha_{\text{CH}} < \beta_{\text{B}}$ is reminiscent of the situation in the deprotonation of **19-Z**, **20-Z**, and **21-Z**. In both situations, there is creation of a partial negative charge on the carbon that loses a proton, and, in both cases, the Z-substituent is located relatively far away from that carbon at the transition state (e.g., **24-Z**). In the deprotonation of **19-Z**, **20-Z**, and **21-Z**, this negative charge moves closer to Z and becomes a full negative charge in the product ion (e.g., **25-Z**). In the deprotonation of



15-Z and **16-Z**, the negative charge also moves closer to Z, but here the effect is a neutralization of positive charge on the

(30) A referee has questioned the use of average α_{CH} and β_{B} values. Irrespective of which combination of α_{CH} and β_{B} is used to compare the two, the result is always qualitatively the same; that is, $\alpha_{\text{CH}} < \beta_{\text{B}}$, even when the highest α_{CH} value is being compared with the lowest β_{B} value for a given system. Because the main point is to show that $\alpha_{\text{CH}} < \beta_{\text{B}}$ rather than to obtain a quantitatively precise value of the difference between α_{CH} and β_{B} , using averages seems to be the most satisfactory approach.

Table 5. Average Values for α_{CH} , β_{B} , and $\log k_0$

parameter	R ₂ NH	RNH ₂
(CO) ₅ W=C(OCH ₂ C ₆ H ₄ Z)CH ₃ (15-Z)		
α_{CH}	0.41 ± 0.05	0.37 ± 0.09
β_{B}	0.55 ± 0.04	0.73 ± 0.03
$\beta_{\text{B}} - \alpha_{\text{CH}}$	0.15	0.36
$\log k_0$	3.07 ± 0.10	2.82 ± 0.15
(CO) ₅ W=C(SC ₆ H ₄ Z)CH ₃ (16-Z)		
α_{CH}	0.33 ± 0.02	0.33 ± 0.07
β_{B}	0.45 ± 0.01	0.47 ± 0.01
$\beta_{\text{B}} - \alpha_{\text{CH}}$	0.12	0.14
$\log k_0$	2.41 ± 0.09	1.96 ± 0.03

oxygen or sulfur atom (e.g., **23-Z**). In terms of substituent effects, that is, α_{CH} versus β_{B} , the result is the same in both situations.

C. Intrinsic Rate Constants. The intrinsic rate constants are reported as $\log k_0$ in Table 4; they are defined as $\log k_0 = (\log k_1^{\text{B}}/q)$ when $\text{p}K_{\text{a}}^{\text{BH}} - \text{p}K_{\text{a}}^{\text{CH}} + \log(p/q) = 0$ and were obtained by interpolation or extrapolation of the Brønsted plots of $(\log k_1^{\text{B}}/q)$ versus $\text{p}K_{\text{a}}^{\text{BH}} - \text{p}K_{\text{a}}^{\text{CH}} + \log(p/q)$. The following points are noteworthy.

(1) For any given type of carbene complex/amine combination, the $\log k_0$ values are virtually independent of the Z substituent, although a slight trend toward lower values with more electron-withdrawing substituents can be detected, which for the reactions of **15-Z** with the primary amines appears to be outside the experimental error. A slight dependence on Z is expected due to the dependence of β_{B} on Z, but in view of the experimental uncertainties in the $\log k_0$ values which vary between ±0.03 and ±0.20, this dependence is too small to warrant further scrutiny. We shall therefore use average $\log k_0$ values, listed in Table 5, for our discussion.

(2) The $\log k_0$ values for the reactions of the oxa carbene complexes (**15-Z**) are virtually the same as for the reactions of the corresponding methoxy carbene complex (**1-W**), that is, $\log k_0(\mathbf{15-Z}) = 3.07$ versus $\log k_0(\mathbf{1-W}) = 3.18$ for the reactions with secondary alicyclic amines,³ and $\log k_0(\mathbf{15-Z}) = 2.82$ versus $\log k_0(\mathbf{1-W}) = 2.73$ for the reactions with the primary aliphatic amines.³ This is a reasonable result because the electronic effects of a methoxy and a benzyloxy group are expected to be quite similar, and the greater steric bulk of the benzyloxy as compared to the methoxy group is unlikely to significantly affect the rates due to the remoteness from the reaction site. The situation for the thia carbene complexes is similar, that is, $\log k_0(\mathbf{16-Z}) = 2.41$ versus $\log k_0(\mathbf{4-W}) = 2.50$ ⁶ for the reactions with the secondary alicyclic amines, and $\log k_0(\mathbf{16-Z}) = 1.96$ versus $\log k_0(\mathbf{4-W}) = 2.17$ ⁶ for the reactions with the primary aliphatic amines.⁶

(3) As was found to be the case for the reactions of **1-W** and **4-W**, the $\log k_0$ values for the reactions of the oxa carbene complexes (**15-Z**) are significantly higher than those for the reactions of the thia carbene complexes (**16-Z**): $\Delta \log k_0 = \log k_0(\mathbf{15-Z}) - \log k_0(\mathbf{16-Z}) = 3.07 - 2.41 = 0.66$ for R₂NH, and $\Delta \log k_0 = 2.82 - 1.96 = 0.86$ for RNH₂. This compares with $\Delta \log k_0 = \log k_0(\mathbf{1-W}) - \log k_0(\mathbf{4-W}) = 3.18 - 2.50 = 0.68$ for R₂NH and $\Delta \log k_0 = 2.73 - 2.17 = 0.56$ for RNH₂. The reasons for these differences in k_0 have been analyzed in great detail in ref 6 and are not repeated here. Briefly, the differences in $\log k_0$ result from a combination of a stronger decrease in k_0 for the thia than for the oxa derivatives caused

by a steric effect and a stronger increase in k_0 for the oxa than for the thio carbene complexes resulting from the electron-withdrawing inductive effect of the heteroatom. There may also be a small opposing effect due to the stronger π -donation of the alkoxy group, but the first two factors are dominant.

Conclusions

The main motivation for the work presented in this paper was to test the notion that it is the π -donor effect of the MeO group which is responsible for lowering α_{CH} in the deprotonation of **9-Z** by amines so that $\alpha_{\text{CH}} \approx \beta_{\text{B}}$ instead of $\alpha_{\text{CH}} > \beta_{\text{B}}$. The specific hypothesis, in its simplest form, was that the π -donor effect and with it the partial positive charge on the MeO group of **12-Z** is largely maintained at the transition state (**13-Z**). As a result, the stabilizing effect of electron-withdrawing substituents on the negatively charged carbon is partially offset by its destabilizing effect on the positively charged oxygen, and hence α_{CH} is reduced.

The results of the present study have confirmed this hypothesis by showing that, in the deprotonation of **15-Z** and **16-Z** by amines, $\alpha_{\text{CH}} < \beta_{\text{B}}$, a result that implies that the neutralization of the partial positive charge on the oxygen or sulfur atoms, respectively, has indeed only made little progress at the transition state.

Other conclusions that emerge from this work can be summarized as follows.

(1) The much higher acidity of the thia as compared to the oxa carbene complexes is mainly the result of the weaker π -donor effect of the phenylthio group versus that of the benzyloxy group. The fact that the phenyl group of **16-Z** is inductively electron withdrawing while the benzyl group of **15-Z** is not electron withdrawing contributes to making **16-Z** more acidic than **15-Z**.

(2) The increased acidity of **15-Z** and **16-Z** with increasingly more electron-withdrawing Z substituents reflects a combination of carbanion stabilization and carbene complex destabilization. The latter is mainly the result of the partial positive charge on the oxygen (**15-Z[±]**) or sulfur atoms (**16-Z[±]**), respectively.

(3) The transition state structure varies somewhat as a function of Z and of amine basicity, as evidenced by the increase in α_{CH} with decreasing $\text{p}K_{\text{a}}^{\text{BH}}$ and the decrease in β_{B} with decreasing $\text{p}K_{\text{a}}^{\text{CH}}$. These changes imply a greater degree of proton transfer with decreasing amine basicity and with decreasing carbene complex acidity.

Table 6. ¹H NMR Chemical Shifts^a

carbene complex	CH ₃	aryl	Z	CH ₂
(CO) ₅ W=C(OCH ₂ C ₆ H ₄ Z)CH ₃ (15-Z)				
15-OMe	2.91 (s)	6.98 and 7.40	3.86 (s)	5.75 (s)
15-Me	2.93 (s)	7.26 and 7.36	2.41 (s)	5.76 (s)
15-H	2.94 (s)	7.46		5.76 (s)
15-Cl	2.95 (s)	7.35 and 7.43		5.76 (s)
(CO) ₅ W=C(SC ₆ H ₄ Z)CH ₃ (16-Z)				
16-OMe	3.07 (s)	6.99 and 7.27	3.87 (s)	
16-Me	3.06 (s)	7.26 and 7.36	2.41 (s)	
16-H	3.06 (s)	7.41		
16-Br (p)	3.02 (s)	7.21 and 7.42		
16-Br (m)	3.05 (s)	7.4 and 7.7		

^a In CDCl₃, 250 MHz.

Table 7. ^{13}C NMR Chemical Shifts^a

carbene complex	CO	aryl	CH ₂	=C	CH ₃	Z
$(\text{CO})_5\text{W}=\text{C}(\text{OCH}_2\text{C}_6\text{H}_4\text{Z})\text{CH}_3$ (15-Z)						
15-OMe	203.5 (cis) 197.5 (trans)	160.7, 130.8 126.1, 114.6	86.9	330.5	52.7	55.6
15-Me	203.6 (cis) 197.5 (trans)	149.6, 131.0 129.9, 128.9	87.6	330.8	52.7	21.5
15-H	203.6 (cis) 197.5 (trans)	134.1, 128.6 128.5, 128.2	86.6	330.5	52.6	
15-Cl	203.4 (cis) 197.5 (trans)	136.0, 130.5 129.6, 128.7	85.1	331.9	52.7	
$(\text{CO})_5\text{W}=\text{C}(\text{SC}_6\text{H}_4\text{Z})\text{CH}_3$ (16-Z)						
16-OMe	208.1 (cis) 197.7 (trans)	161.5, 133.1 129.2, 115.4		334.0	49.4	55.6
16-Me	208.1 (cis) 197.8 (trans)	141.3, 134.6 133.7, 129.8		333.2	49.4	21.6
16-H	203.6 (cis) 197.9 (trans)	138.2, 131.7 130.9, 129.3		333.5	49.7	
16-Br (p)	204.3 (cis) 197.4 (trans)	134.1, 133.4 133.2, 130.2		331.9	52.4	
16-Br (m)	208.1 (cis) 197.9 (trans)	136.0, 134.3, 134.0 131.5, 130.2		331.4	50.0	

^a In CDCl_3 , 250 MHz.

Experimental Section

Synthesis of Carbene Complexes. All solvents were dried and degassed by standard procedures. All glassware was flame dried prior to use. Standard syringe and septum methods were employed, and all reactions were performed under argon.

$(\text{CO})_5\text{W}=\text{C}(\text{OCH}_2\text{C}_6\text{H}_4\text{Z})\text{CH}_3$ (**15-Z**). The synthesis of **15-Z** was based on a modification of procedures described by Wulff et al.²⁰ for the synthesis of (aryloxymethylcarbene)pentacarbonylchromium(0) complexes but using pivaloyl chloride³¹ as the acylating

reagents of $(\text{CO})_5\text{W}=\text{C}(\text{CH}_3)\text{O}^- \text{NMe}_4^+$. First 2.86 g (6.6 mmol) of $(\text{CO})_5\text{W}=\text{C}(\text{CH}_3)\text{O}^- \text{NMe}_4^+$ was mixed with pivaloyl chloride in a 1.1:1 ratio in 40 mL of CH_2Cl_2 at -40°C . The solution was stirred at -30°C for 45 min. At this point, an equimolar amount of substituted benzyl alcohol was added, and the ensuing mixture was stirred for another 45 min at -30°C . After the solvent was removed under vacuum, the resulting orange substance was dissolved in hexane and filtered through a Büchner funnel with one layer of Celite and one layer of silica gel treated with Et_3N to remove solid impurities. The solvent was partially removed, whereupon the carbene complex crystallized. The ^1H NMR and ^{13}C NMR data are summarized in Tables 6 and 7.

$(\text{CO})_5\text{W}=\text{C}(\text{SC}_6\text{H}_4\text{Z})\text{CH}_3$ (**16-Z**). These carbene complexes were synthesized as described by Lam et al.³⁴ The ^1H NMR and ^{13}C NMR data are reported in Tables 6 and 7.

Kinetics, Spectra, and pH Measurements. The procedures described earlier^{2,6} were used.

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