Hydrolysis of Fischer Carbene Complexes. Steric Effects of the π-Donor Group

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k_1^{OH} for R^1 = n-propyl >neo-pentyl >iso-propyl >menthyl
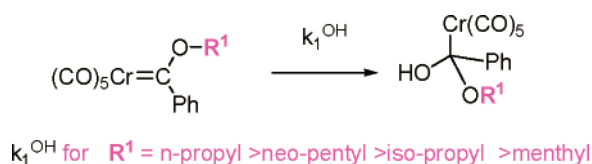
Rate constants for the hydrolysis of Fischer carbenes $(CO)_5Cr=C(OR)Ph$ (R = *n*-propyl, neopentyl, isopropyl, and menthyl) in 50% MeCN−50% water (v/v) at 25 °C are reported. The rate constants for the addition of −OH to the carbene carbon are 5.3, 3.7, 0.84, and 0.01 M^{-1} s^{-1}, respectively. These rate constants give linear correlations with the corresponding rate constants for the hydrolysis of esters such as acetate, benzoate, and formiate. The slopes of the plots of the observed rate constants for the carbenes vs the rate constants for the esters are 1.4 and 1.2 for acetate and benzoate, respectively, indicating that the factors that decrease the reactivity of the two types of compounds are similar, but the carbenes show higher sensitivity. The rate constants are well correlated with several steric parameters giving a value of −3.84 for the Charton's ψ parameter. The results show that the steric bulkiness of the R group is the main factor determining the reactivity differences for these carbene complexes.

Introduction

Fischer carbene complexes[1] constitute a subclass of transition-metal carbene complexes. Many Fischer carbene complexes are of the general structure **1**; an important feature is the presence of a π-donor heteroatom which stabilizes the electron-deficient carbene carbon.

M = Cr(0), Mo(0), W(0)
X = N, O, S
R^1 = alkyl
R^2 = alkyl, alkenyl, alkynyl, aryl
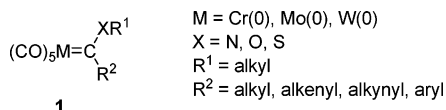
In regard to their reactivity, these metallic complexes are considered similar to esters,[2] where the carbon bound to the metal is the electrophilic center and the metal pentacarbonyl moiety takes the place of the carbonylic oxygen. The electron-withdrawing nature of the pentacarbonyl moiety is reflected in the strong acidity of the hydrogens in the α position with respect to the carbenic carbon; for instance, a pK_a of 12.3 for the carbene **2** has been reported,[3] which is about 14 orders of magnitude

lower than the pK_a for ethyl acetate.[4] In the last two decades, the development of the chemistry of these complexes has been vertiginous, especially in organic synthesis.[5−9]

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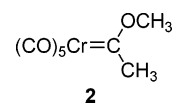
There have been relatively few kinetic studies in the early literature. These investigations focused mainly on reactions with amines[10−12] and phosphines[13,14] in weakly polar solvents. More recently, a number of studies regarding the mechanism and

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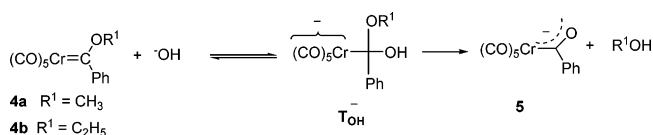
reactivity of a variety of nucleophiles such as alcohol and alkoxide ions,[15,16] water and OH⁻,[17−21] thiol and thiolate ions,[22−24] amines,[21,25−28] and $(CN)_2CH^-$ [29] were reported. Most of these studies involve prototypical carbenes such as **3**.
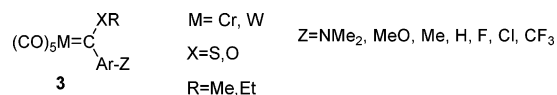
These studies led to important findings regarding the factors that determine the reactivity of Fischer carbene complexes. One important conclusion was that for the reaction with nucleophiles, the intrinsic barrier[30] for the reactions of the sulfur derivatives is higher than that for the alkoxy carbene derivatives mainly due to a steric effect that develops ahead of bond formation at the transition state.[31] On the other hand, the difference in reactivity of carbene complexes with $R^1 = CH_3$ and C_2H_5 was attributed to different π-donor ability of this two compounds. The available data do not allow the discussion regarding the contribution of steric effects in the alkoxy group.

It has been determined that the hydrolysis of carbene complexes can take one of two different pathways depending on the presence of acidic hydrogens at the α position of the carbenic carbon. The hydrolysis of the carbene complexes **2** occurs through the conjugate base of the carbene,[17,32] whereas for carbene complexes such as **4a** and **4b** the hydrolysis involves the nucleophilic attack of hydroxide or water to the carbene carbon with formation of the tetrahedral intermediate T_{OH^-}, Scheme 1.[18] The intermediate does not accumulate to detectable levels, and it was concluded that the addition of the nucleophile is the rate-limiting step in the whole pH range. The fast step is the decomposition of T_{OH^-} to give the acylate **5**, which slowly decomposes to benzaldehyde. For these complexes, it has been

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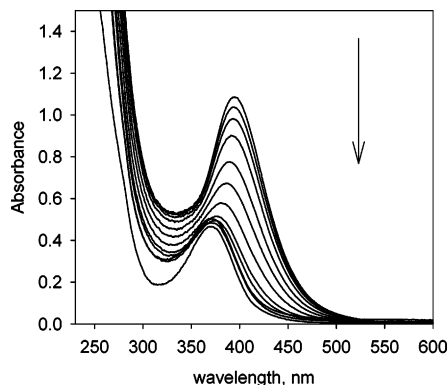(32) Bernasconi, C. F.; Sun, W. *Organometallics* **1995**, *14*, 5615.

SCHEME 1

shown that the metal has little influence on their reactivity. On the other hand, the reactivity decreases significantly when the R^1 substituent is changed from methyl (**4a**) to ethyl (**4b**).

We undertook a study to establish the importance of the steric effect on the nucleophilic attack to the carbenic carbon and we report here a kinetic study of the hydrolysis of carbenes **4c−f** where we have systematically changed the size of the alkoxy group. The data reported here together with data from the literature for compounds **4a,b** allows the separation of the contribution of the π-donor and steric effects of the groups, and lead to the conclusion that the steric effect is the main factor determining the reactivity differences in this family of compounds.

4c: R^1 = n-propyl
4d: R^1 = neo-pentyl
4e: R^1 = iso-propyl
4f: R^1 = menthyl
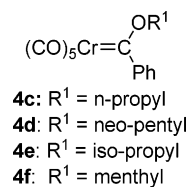
Results

General Aspects. The experiments were performed in 50% acetonitrile−50% water (v/v) as solvent at 25 °C. The reactions were monitored spectrophotometrically at or near the λ_{max} of the carbene complexes (395 nm). Figure 1 is illustrative of the evolution of the absorption spectra of **4e** with time. Similar behavior is observed with the other substrates (Figure S1, Supporting Information, for **4f**).[33] For **4e**, the rate constants were determined in buffer solutions of HCl, KOH, acetate, *N*-methylmorpholine (NMM), and carbonate, thus covering a pH range from 1 to 14 (Tables S3−S7, Supporting Information). Compounds **4c**, **4d**, and **4f** gave similar pH profiles (Tables S1, S2, and S8−S11, Supporting Information).[33] In all cases, the reaction rates were determined under pseudo-first-order conditions, with KOH, HCl, or the buffer in large excess with respect to the carbene complex. Under these experimental conditions, two kinetic processes were observed. The faster corresponds to the changes shown in Figure 1, and it may be attributed to the formation of the acylate **5**, while the second is associated to its decomposition.

The rate constants determined at 335, 395, and 425 nm gave the same values within experimental errors. These results indicate that there is no accumulation of the tetrahedral intermediate T_{OH^-} similarly as reported for **4a** and **4b**.[18]

Figure 2 shows a rate−pH profile for substrate **4e**. The values for k_{obsd} corresponding to pH between 5 and 10.5 were obtained as extrapolations to zero buffer concentration. Solutions of HCl and KOH were prepared in a concentration range of 0.001 to 0.1 M. The results for **4e** below pH 9 are only considered in comparative terms in this paper to verify that the behavior at low pH values is similar to that of the carbene complexes with R^1 = Me and Et. This is because under certain conditions there are some differences that will be addressed in a future report.

(33) See the Supporting Information.

FIGURE 1. Time-dependent absorption spectra of **4e** at pH 10.5 (carbonate buffer), temperature 25 °C. Total time elapsed between the first and the last spectrum is 7.4 h. The arrow indicates direction of change with time.
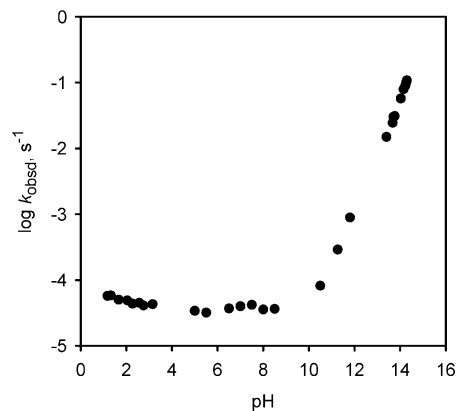

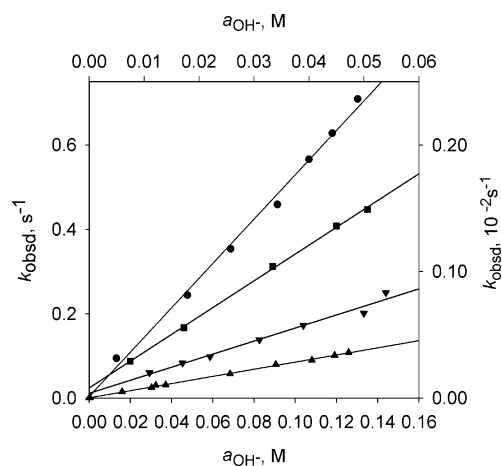**FIGURE 2.** pH−rate profile for the hydrolysis of **4e**.

FIGURE 3. k_{obsd} vs a_{OH} for complexes: **4c** (●), **4d** (▼) (top x axis, left y axis), **4e** (▲), **4f** (■) (bottom x axis, right y axis).

In Tables S1−S11 (Supporting Information) are listed the values for k_{obsd} at each pH value for the substrates studied.[33]

For the discussion that follows, we consider it relevant to demonstrate that the rate constants obtained from the spectral changes observed such as those shown in Figure 1 correspond in all cases to the formation of the acylate **5** and that the second kinetic process which corresponds to the decomposition of this compound does not interfere significantly with our measurements despite the important decrease in the magnitude of the rate constants in the series of substrates **4c−f**. The rate of decomposition of the acylate **5** should not depend on the nature of R_1 because the alcoxy substituent has been expelled from the tetrahedral intermediate T_{OH}^-. In the literature, it has been reported that at 0.1 M of KOH **4a** produces 1.2% of benzaldehyde after 1 h of reaction.[18] If a linear behavior is considered up to 10% conversion, it would take 8.3 h to reach this conversion percentage. In this period of time, under the least favorable conditions (substrate **4e** at pH 10.5), the conversion to the acylate **5** has reached nearly 90% of its total development. According to this, we can confirm that the measured rate constants correspond in all cases to the formation of the acylate **5**. The plot of the observed rate constants vs a_{OH} is linear for all of the substrates (Figure 3).

The information obtained from the slope and intercept of these plots will be discussed in the following section.

Discussion

Mechanism. The process described in the preceding section is attributed to the exchange of the OR^1 group by OH^- for all of the substrates studied.

In Scheme 2, we show the mechanism proposed in the literature for the formation of the acylate in the hydrolysis of carbene complexes **4a** and **4b**.[18] For the sake of simplicity in Scheme 2, only the reaction paths where the nucleophile is OH^- are explicit. Specifically, $k_1^{OH}a_{OH}$ represents the nucleophilic attack of OH^-, and $k_{-1}^{H_2O}$ indicates the spontaneous loss of OH^- from the intermediate T_{OH}^-. Regarding the formation of products from the tetrahedral intermediate in basic media, three pathways have been proposed:[18] $k_2^{H_2O}$ corresponds to the spontaneous expulsion of the alkoxide from T_{OH}^-, k_2^i corresponds to the intramolecular catalyzed expulsion of the alkoxide, and $k_3^{H_2O}$ represents the reaction via the dianionic form of the intermediate T_{OH}^{2-}.

As mentioned above, it is accepted that in the basic hydrolysis of the carbene complexes **4a** and **4b**, even when the equilibrium between **4** and T_{OH}^- and T_{OH}^{2-} is favorable to the tetrahedral intermediates, there is no accumulation of any intermediate because in basic solution the situation $k_1^{OH}a_{OH} \ll k_2^{H_2O} + k_2^i + k_3^{H_2O}K_a^T/a_H$ holds. This fact also leads to the conclusion that the k_1^{OH} step is rate limiting. When R^1 is changed to a bulkier alkoxy group it could be questioned if these structural variations might alter the reaction mechanism. If such accumulation were to occur, this should be reflected in a rate of product formation that is slower than the rate of decay of the substrate and would manifest itself in a wavelengh dependence of k_{obsd}. The wavelenth dependence was tested at 335 nm, λ_{max}, and 425 nm for **4c** and **4e** in the whole range of KOH concentrations. The observed variation in k_{obsd} was random and amounted to less than 10%, which is inconsistent with the accumulation of either T_{OH}^- or T_{OH}^{2-}; i.e., these species can be regarded as steady-state intermediates. This behavior can be explained in two different ways: On one side, the relative rate constants for the formation and decomposition of the tetrahedral intermediate are similar to those of **4a**, **4b**, i.e., $k_1^{OH}a_{OH^-} > k_{-1}^{H_2O}$ and $k_1^{OH}a_{OH} \ll k_2^{H_2O} + k_2^i + k_3^{H_2O}K_a^T/a_H$, or there could be a fast preequilibrium favorable to reactants and with the expulsion of the alkoxide as the rate-limiting step. For this last situation to occur, the conditions $k_{-1}^{H_2O} \gg k_2^{H_2O} + k_2^i + k_3^{H_2O}K_a^T/a_H$ and $k_1^{OH}a_{OH^-} < k_{-1}^{H_2O}$ must be met. Besides, it should also be assumed that the spectral changes due to the establishment of

SCHEME 2
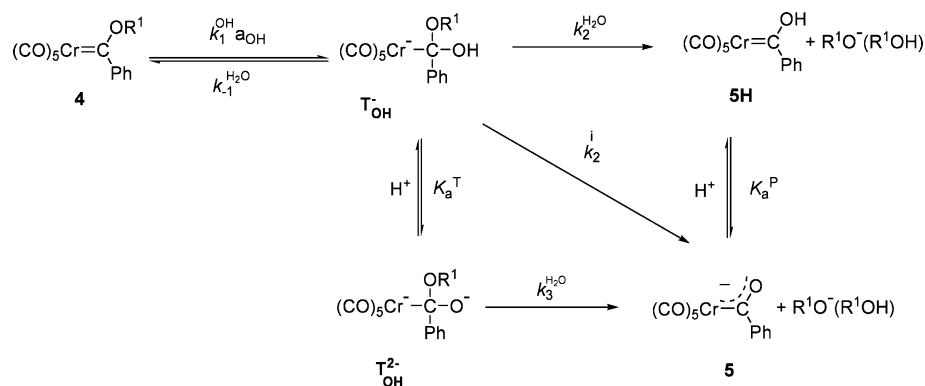
this equilibrium are below the detection level of our equipment, and thus, only one relaxation time is observed in the measured time scale. In this hypothetical situation, k_{obsd} is given by eq 1, where $k_2' = k_2^{H_2O} + k_2^i + k_3^{H_2O}k_a^T/a_H$ and $K_1 = k_1^{OH}/k_{-1}^{H_2O}$ represents the hypothetical equilibrium constant.

$$k_{obsd} = \frac{K_1 k_2'[OH^-]}{1 + K_1[OH^-]} \quad (1)$$

In this situation, we expect K_1 to be small enough so that the condition $K_1[OH^-] \ll 1$ holds; therefore, eq 1 simplifies to eq 2 and a linear relationship between k_{obsd} and a_{OH} should be observed, in agreement with the experimental results.

$$k_{obsd} = K_1 k_2'[OH^-] \quad (2)$$

According to eq 2, the slope of the plots k_{obsd} vs a_{OH} (Figure 3) should correspond to $k_1 k_2'$. If we assume a value for $K_1 \leq 0.5$ so that $K_1[OH^-] \ll 1$ is met in the whole a_{OH} range, then $k_2' = k_2^{H_2O} + k_2^i + k_3^{H_2O}K_a^T/a_H$ would take a value $\geq 10.6 \text{ s}^{-1}$ for **4c**.[34] The values of k_{-1} reported for a variety of nucleophiles of such a different nature as $-SR$ and $-P(R)_3$ all fall in the range $0.5-21 \text{ s}^{-1}$,[44] so there is no reason to believe that $k_{-1}^{H_2O}$ will be out of this range; therefore, the condition $k_{-1}^{H_2O} \gg k_2^{H_2O} + k_2^i + k_3^{H_2O}K_a^T/a_H$ cannot hold.

From the preceding analysis, it seems clear that for this series of carbene complexes there is no accumulation of the tetrahedral intermediate and that the formation of T_{OH}^- is the rate-determining step. It follows, then, that the slopes of the plots of log k_{obsd} vs a_{OH} (Figure 3) correspond to k_1^{OH} (Scheme 2), whereas the intercepts are associated with the nucleophilic attack by water.

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(34) To reach to this conclusion, we consider that the value of the slope of observed rate constant vs a_{OH} is $K_1 k_2' = 5.3 \text{ M}^{-1} \text{ s}^{-1}$ for compound **4c**, and using $K_1 \leq 0.5 \text{ M}^{-1}$ leads to $k_2' \geq 10.6$.

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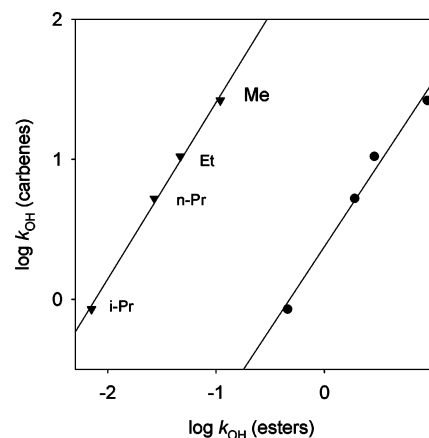
FIGURE 4. Correlation between the observed rate constant for the basic hydrolysis of esters and Fischer carbene complexes: (▼) $AcOOR^1$, (●) $BzOR^1$.

The relative efficiency of the different paths for the conversion of T_{OH}^- into products should not be very different from what was proposed for the carbene complexes **4a** and **4b**, i.e., $k_2^{H_2O} \ll k_2^i + k_3^{H_2O}K_a^T/a_H$. At most, this difference should become more marked due to the fact that the higher pK_a of the leaving groups must favor k_2^i and disfavor $k_2^{H_2O}$.[35]

Steric and Polar Effects of R^1. The main goal of this work was to evaluate the effects of the group R^1 on the reactivity of nonionizable alkoxy Fischer carbenes. According to our results, the most evident effect observed is the lower reactivity when the number of carbon atoms in R^1 is increased. It is also evident that the substitution degree on the carbon directly bound to the oxygen atom affects the reactivity noticeably. This statement is based on the comparison of the relative reactivities ($k_{Me}^{OH}/k_{R_1}^{OH}$) of **4b−e** with respect to **4a** ($R^1 =$ methyl). When $R^1 =$ ethyl (**4b**) this ratio is 2.5, whereas it is 5.0 for $R^1 = n$-propyl (**4c**) and 31.6 for $R^1 =$ isopropyl (**4e**). These comparisons show that the increase in two carbon atoms in R^1, maintaining the substitution degree, produces a 5-fold decrease in the reactivity. With the same increase in carbon atoms, but if the carbon directly bound to the oxygen atom is secondary, the reactivity decreases about 30 times. Taking into account that Fischer carbenes are usually compared with esters in regard to their reactivity,[36] it is interesting to verify if the effect of the group R^1 observed for these carbene complexes has any correlation with that produced on esters with the same alkyl substituent. Figure 4 shows the correlations found between the rate constants of alkaline hydrolysis for carbene complexes **4a**, **4b**, **4c**, and **4e** and the respective benzoates and acetates under similar

TABLE 1. Substituent Parameters for Alkoxy Groups and Second-Order Rate Constants for the Basic Hydrolysis of Fischer Carbenes, Alkyl Acetates, and Benzoates

| | substituent parameters | | | | | Fischer carbenes | | AcOOR[1] [a] | BzOR[1] [a] |
	R^{+} [b] $r^2 = 0.88$	E_s [c] $r^2 = 0.90$	E_s [d] $r^2 = 0.97$	E_{sCH2R} [e] $r^2 = 0.97$	ν_{OR} [a] $r^2 = 0.99$	K_1, M^{-1} [f]	k_1^{OH}, M^{-1} s^{-1} (log k)	log k	log k
Me	−1.07	0.00	0.00	−0.38	0.36	53.2[g]	26.6 (1.42)[g]	−0.96	0.95
Et	−1.07	−0.07	−0.38	−0.67	0.48	21.0−10.5	10.5 (1.02)[g]	−1.33	0.46
n-propyl	−1.09	−0.36	−0.67	−0.70	0.56	10.6−0.25	5.3 (0.72)[h]	−1.57	0.28
isopropyl	−1.19	−0.47	−1.08	−1.24	0.75	7.4−0.18	0.84 (−0.07)[h]	−2.15	−0.34
neopentyl						1.7−0.04	3.7[h]		
menthyl						0.02−5 10^{−4}	0.01[h]		

[a] Reference 41. [b] Reference 37. [c] Reference 38. [d] Reference 39. [e] Reference 40. [f] Calculated on the basis of the range of k_{-1} (0.5−21 s^{-1}) values reported in the literature (see text) unless otherwise noted. [g] Reference 18. [h] This work.
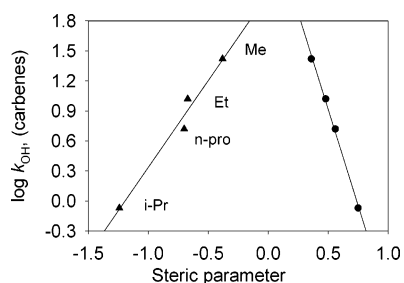
FIGURE 5. Dependence of k_1^{OH} for compounds **4** with steric parameters: (●) ν_{OR}, (▲) E_{CH2R}.

conditions. It is noteworthy that these correlations comprise primary R^1 groups (Me, Et, and *n*-propyl) as well as secondary ones (isopropyl). These linear correlations indicate that the effects produced by the increase in bulkiness of R^1 in the alkaline hydrolysis of Fischer carbenes are similar to those for the alkaline hydrolysis of benzoates and acetates. From the slopes of these plots (1.4 vs acetates and 1.2 vs benzoates, Figure 4), it can be concluded that the effects on the reactivity are more marked for the carbene complexes.

There is plenty of evidence that the π donor effect of the heteroatom is a major factor in determining the reactivity of Fischer carbene complexes because the ground state of a Fischer carbene can be represented as a combination of the resonance structures given in eq 3. However, the results reported here do not show a good correlation between k_1^{OH} and the corresponding parameter R^+ [37] ($r^2 = 0.88$; see Table 1).

In contrast, good to excellent correlations are observed between the values determined for k_1^{OH} and the steric parameters such as Taft's E_S[38] and its corrections: E_{SC},[39] E_{CH2R},[40] and Charton's ν_{OR}[41] (all correlations with $r^2 > 0.9$, the best being the one corresponding to the set ν_{OR} with $r^2 = 0.997$ (see Table 1 and Figure 5).

$$(CO)_5Cr=C{\overset{OR_1}{\underset{Ph}{}}} \longleftrightarrow (CO)_5Cr-C{\overset{+OR_1}{\underset{Ph}{}}} \qquad (3)$$
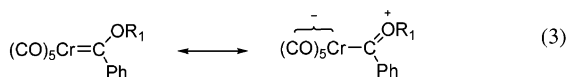
The correlations observed between log k_1^{OH} and ν_{OR} can be represented by eq 4, where Ψ represents the sensitivity of the reaction studied toward the steric parameter ν_{OR}.

$$\log k_1^{OH} = \Psi\nu_{OR_1} + h \qquad (4)$$

This equation allows the calculation of the steric parameter for $R^1 =$ menthyl as $\nu_{OR} = 1.26$, which has not been reported before, and it seems a reasonable value since the corresponding value for cyclohexyl is 0.81.[41] In Table 2 are summarized the

TABLE 2. Values ψ for the Basic Hydrolysis of Alkyl Benzoates, Acetates, Formiates, and Fischer Carbenes

	ψ
$(CO)_5Cr=C(Ph)OR_1$ [a]	−3.84
$O=C(Ph)OR_1$ [b]	−3.27
$O=C(CH_3)OR_1$ [c]	−2.92
$O=C(H)OR_1$ [d]	−1.40

[a] This work. [b] Set 1, ref 41. [c] Set 10, ref 41. [d] Set 20, ref 41.

values of Ψ for four sets of reactions that involve a tetrahedral intermediate. It is clear that as the reaction center becomes more crowded, the sensitivity with respect to the steric effects increases. Fischer carbenes are the most sensitive set due to the presence of the bulky $Cr(CO)_5$ moiety.

The π donor effect of the menthyl group is expected to be higher than that of the methyl group considering that the value of R^+ for OMe is −1.07 and that for the *O*-isopropyl group is −1.19.[37] However, the big size of the menthyl group may disrupt the structure of the carbene complex in the ground state, making it difficult for the group to exert its full π donor effect; therefore, the stability of the ground states of the corresponding carbene complexes are expected to be similar.

On the other hand, the size of the alkyl group increases the energy of the transition state for the formation of the tetrahedral intermediate, and consequently, the rate of the reaction decreases. We conclude that despite the fact that the ground state of the carbene complex may be somewhat stabilized for the increase in the number of the carbon atom in R^1, the diminution in reactivity appears to be the result of the a less stable transition state leading to a more crowed intermediate T_{OH}^-.

It is well-known that the steric effect is very important in the reactions of Fischer carbenes, and it is evident in the relative reactivity of primary and secondary amines of comparable basicity. While piperidine is more reactive than butylamine with activated aromatic compounds,[42] it is less reactive with thio-carbenes complexes, and this behavior was attributed to the operation of strong steric effect in the latter reactions.[27] Besides, it was reported that in the reactions of compound **4f** with PhLi the nucleophile adds to the aryl ring and not to the carbenic carbon due to the strong steric effect exerted by the menthyl group.[43]

Effects of R^1 on the Intrinsic Constants. Regarding the large change in reactivity produced by R^1 on Fischer carbenes, and taking into account that it has been demonstrated that there is an imbalanced transition state for these types of reactions,[44] an interesting question is this: are these changes in reactivity somehow a reflection of changes in intrinsic constants (k_0)?[45] To calculate the k_0 value we need to know the value of the equilibrium constant K_1 in Scheme 2 and consequently k_{-1}. To
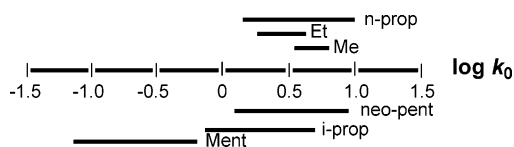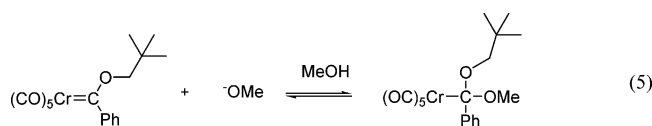
FIGURE 6. Schematic representation of the range of values of the intrinsic rate constants calculated for compounds **4**.

estimate this value, we have measured k_{-1} for equilibrium 5 [33] in methanol, and the obtained value is 1.3 s^{-1}, which is quite similar to the corresponding value reported for $R_1 = Me$, namely 1.1 s^{-1}.[46]

$$\text{(5)}$$

The similarity between these two values indicates that k_{-1} is not very sensitive to the size of R^1. Besides, as was mentioned above, the range of k_{-1} found in the literature is 0.5−21 s^{-1}; therefore, we can calculate the expected range for K_1 (Table 1) and from this the expected range for k_0,[47] which are schematically shown in Figure 6. In terms of the Principle of Nonperfect Synchronization,[48] two opposite effects should be considered. On one side, as the R^1 group becomes bulkier, the equilibrium is less favorable to the product (the tetrahedral intermediate) and the transition state should be more advanced (Hammond effect).[49,50] This effect should increase k_0 because the charge delocalization in the transition state is closer to that in the intermediate. On the other hand, the early development of the steric effect which destabilizes the product would tend to decrease k_0. As we can see in Figure 6, these two effects compensate each other for compounds **4a−d**, but for the compounds having the bulkier groups as isopropyl and menthyl the steric effect predominates and a strong decrease in the intrinsic rate constant is expected.

Experimental Section

General Methods. ^{1}H and ^{13}C NMR spectra were recorded on a 200-MHz instrument. IR spectra were recorded on a FT-IR spectrophotometer. Kinetic experiments were carried out on a stopped-flow spectrophotometer. UV−vis spectra were obtained on a conventional or a diode-array spectrophotometer.

General Procedure for the Synthesis of the Carbene Complexes 4. Carbene complexes **4c−f** were synthesized according to a modification of the procedure reported by Semmelhack et al.[51] The following is representative for all complexes: All procedures were carried out under an atmosphere of nitrogen using anhydrous solvents. An ether solution of phenyllithium (0.9−1.0 equiv) was added to a suspension of hexacarbonylchromium (1 equiv) in ether

at 0 °C. The solution turned yellow and then became orange. The reaction time was 1 h at ambient temperature. The solvent was removed under reduced pressure. The yellow solid was dissolved in a minimum amount of cold and degassed water, and tetramethylammonium bromide (3−4 equiv) was added. A red solid precipitated, the water was removed via cannula, and the solid dried under reduced pressure. The red solid was dissolved in anhydrous methylene chloride. Pivaloyl chloride (1.1 equiv) was added slowly at −45 °C. Then 7 mL of anhydrous dimethylformamide was added. The solution turned deep red and was allowed to react for 1.5 h at −45 °C. The alcohol (1.2−1.7 equiv) was added, and the reaction was allowed to reach ambient temperature slowly. The solvent was removed under reduced pressure, and the residue was purified by a chromatographic column with silica gel and using hexane as eluent. The carbene complexes were obtained as red solids or oils.

[Propoxy(phenyl)carbene]pentacarbonylchromium(0) (4c). Following the general procedure, 1.63 g (4.8 mmol, 26%) was obtained as a red oil from an ether solution of phenyllithium (18.4 mmol, 40 mL, 0.46 M), hexacarbonylchromium (4.08 g, 18.5 mmol), tetramethylammonium bromide (8.4 g, 54.5 mmol), pivaloyl chloride (2.4 mL, 19.5 mmol), dimethylformamide, and propyl alcohol (2.3 mL, 31 mmol). ^{1}H NMR (CDCl$_3$, 200 MHz): δ 1.12 (t, 3H), 2.03 (m, 2H), 4.79 (t, 2H), 7.3 (m, 5H). ^{13}C NMR (CDCl$_3$, 50 MHz): δ 10.4, 23.0, 82.6, 122.5, 128.1, 130.0, 153.7, 216.2, 224.3, 349.4. HRMS (nitrobenzyl alcohol): calcd for C$_{15}$H$_{12}$CrO$_6$ 340.0039, obtained 340.0035.

[Neopentoxy(phenyl)carbene]pentacarbonylchromium(0) (4d). Following the general procedure, 1.26 g (3.4 mmol, 18%) was obtained as a red oil from an ether solution of phenyllithium (16.4 mmol, 20 mL, 0.82 M), hexacarbonylchromium (4.09 g, 18.6 mmol), tetramethylammonium bromide (11.6 g, 75.6 mmol), pivaloyl chloride (2.5 mL, 20.3 mmol), dimethylformamide, and neopentylic alcohol (2.9 g, 33 mmol). ^{1}H NMR (CDCl$_3$, 200 MHz): δ 1.1 (s, 9H), 4.3 (s, 2H), 7.4 (m, 5H). ^{13}C NMR (CDCl$_3$, 50 MHz): δ 26.4, 32.7, 90.2, 122.1, 128.3, 129.7, 153.4, 216.3, 224.4, 349.8. HRMS (nitrobenzyl alcohol): calcd for C$_{17}$H$_{16}$CrO$_6$ 368.0352, obtained 368.0350.

[Isopropoxy(phenyl)carbene]pentacarbonylchromium(0) (4e). Following the general procedure, 1.52 g (24.5%) was obtained as a red solid (mp 78−79 °C) from an ether solution of phenyllithium (16.8 mmol, 30 mL, 0.56 M), hexacarbonylchromium (4.01 g, 18.2 mmol), tetramethylammonium bromide (8.5 g, 55.2 mmol), pivaloyl chloride (2.5 mL, 20.3 mmol), dimethylformamide, and isopropylic alcohol (1.7 mL, 22 mmol). ^{1}H NMR (CDCl$_3$, 200 MHz): δ 1.56 (d, 6H), 5.6 (m, 1H), 7.4 (m, 5H). ^{13}C NMR (CDCl$_3$, 50 MHz): δ 22.6, 85.7, 122.3, 128.1, 129.7, 153.8, 216.2, 224.4, 345.8. HRMS (nitrobenzyl alcohol): calcd for C$_{15}$H$_{12}$CrO$_6$ 340.0039, obtained 340.0043.

[Menthyloxy(phenyl)carbene]pentacarbonylchromium(0) (3f). Following the general procedure,[52] 1.83 g (24.5%) was obtained as a red oil from an ether solution of phenyllithium (16.8 mmol, 30 mL, 0.56 M), hexacarbonylchromium (4.01 g, 18.2 mmol), tetramethylammonium bromide (8.5 g, 55.2 mmol), pivaloyl chloride (2.5 mL, 20.3 mmol), dimethylformamide, and (+)-menthol (3.4 g, 22 mmol). ^{1}H NMR (CDCl$_3$, 200 MHz): δ 0.68 (d, 3H), 0.95 (m, 6H), 1.55 (m, 8H), 6.9−7.6 (m, 5H). ^{13}C NMR (CDCl$_3$, 50 MHz): δ 16.3, 21.1, 21.9, 22.9, 26.1, 31.2, 33.7, 41.9, 47.8, 92.1, 120.0, 127.1, 128.1, 128.4, 128.7, 153.1, 216.2, 224.8, 349.9.

Materials. Acetonitrile was reagent grade and was used without further purification. Water was taken from a Milli-Q water purification system. N-Methylmorpholine was refluxed over Na and

(45) The intrinsic rate constant k_0 is defined as the rate constant for the reaction without thermodynamic driving force, i.e., the rate constant when $K_1 = 1$; therefore, $k_0 = k_1 = k_{-1}$.

(46) Taking into account the statistical factor, the rate constant for the expulsion of MeO$^-$ from the intermediate is 0.55 s^{-1}.

(47) The intrinsic rate constant is calculated using the approximation $\log k_0 = \log k_1^{OH} - 0.5 \log K_1$.

(48) A product-stabilizing factor that develops late along the reaction coordinate or a reactant-stabilizing factor that is lost early always lowers k_0. Conversely, a product-destabilizing factor that develops late or a reactant destabilizing factor that is lost early increases k_0.

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freshly distilled before use. Reagente grade sodium acetate, sodium bicarbonate, and potassium chloride were used as received. A stock solution of KOH and HCl was prepared from solid KOH and fuming HCl 37% concd, reagents for analysis, respectively, with CO_2-free water. These solutions were titrated and used to prepare KOH and HCl solutions for the kinetic runs.

Kinetic Runs. For substrates **3c** and **3e** in KOH solutions, the rates were measured in a stopped-flow apparatus; all other rate determinations were performed in a conventional spectrophotometer. All reactions were run under pseudo-first-order conditions, with the substrate as the minor component and monitored by following the decreased in absorbance at the λ_{max} of the substrate (396 nm for **3c**, 397 nm for **3d**, 395 nm for **3e** and 394 nm for **3f**). Reaction solutions were always freshly prepared just prior to the experiment by injecting a small amount of stock solution of the carbene complex in pure acetonitrile into the 50% MeCN−50% water mixture

pH and pK_a Measurements. The pH in 50% acetonitrile−50% water was determined according to eq 6[53] with pH_{meas} referring to the reading of the pH meter calibrated with aqueous standard buffers.

$$pH = pH_{mess} + 0.18 \qquad (6)$$

The pK_a^{BH} value of sodium bicarbonate was determined by measuring the pH of various buffer ratios and plotting log([B]/[BH]) vs pH according to the Henderson−Hasselbach equation where the intercept is the pK_a and the slope is unity. The pH of the reaction solutions for stopped-flow experiments was measured in mock-mixing experiments that mimicked the stopped-flow runs. The pH of the runs residue for each solution was also measured and was the same as the mock-mixing experiments.

Supporting Information Available: Tables S1−S11 containing the k_{obs} values for all the substrates studies. IR and ^{1}H and ^{13}C NMR spectra of **4c−f** complexes; Figure S1 and detailed experimental data for determination of k_{-1} in MeO$^-$ addition to **4d**. This material is available free of charge via the Internet at http://pubs.acs.org.

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