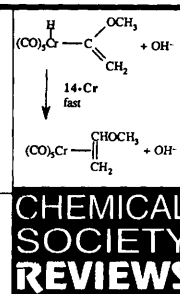


# Developing the physical organic chemistry of Fischer carbene complexes



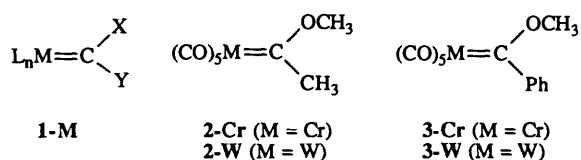
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Fischer carbene complexes have over the last 25 years become a major focus of many synthetic groups. On the other hand, until recently there have been only a few kinetic and/or thermodynamic studies of even the simplest reactions of these complexes. A number of such studies have now been carried out in my laboratory. This review summarizes the results obtained thus far and focuses on three areas: (1) thermodynamic and kinetic acidities of carbene complexes that contain an ionizable proton on the carbon adjacent to the carbene carbon; (2) mechanism and structure-reactivity relationships in the reactions of carbene complexes with nucleophiles; (3) mechanism of hydrolysis of carbene complexes with and without ionizable protons.

## 1 Introduction

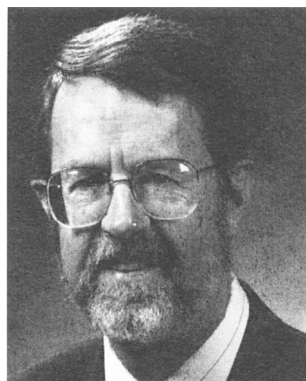
Fischer carbene complexes are compounds of the general structure **1-M**.<sup>1</sup> M is a transition metal, L are ligands while X



and Y represent a variety of groups including alkyl, aryl, vinyl, alkynyl, amino, alkoxy, alkylthio, halo and others; typically one of these groups is a  $\pi$ -donor such as alkoxy, amino or alkylthio which provides stabilization of the electron deficient carbene carbon.

Since the first targeted synthesis of (methoxymethylcarbene)pentacarbonylchromium(0), **2-W**, by Fischer and Maasböl,<sup>2</sup>

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California, Santa Cruz, in 1967, where he has been a Professor of Chemistry since 1977. His current research interests are in physical organic chemistry with particular attention to proton transfers, nucleophilic addition to electrophilic alkenes, nucleophilic vinylic substitution, and reactions of Fischer carbene complexes. He is the author of over 150 research publications and of the book 'Relaxation Kinetics.'

the chemistry of Fischer carbene complexes has developed in an explosive fashion and become an important branch of organometallic chemistry. The major thrust of this development has been the synthesis and characterization of hundreds of such complexes and their use as synthons and catalysts.<sup>3</sup> This intensive synthetic activity is in sharp contrast to the modest efforts toward kinetic and thermodynamic studies of even the simplest reactions of prototypical Fischer carbene complexes such as **2-Cr**, **2-W**, **3-Cr** and **3-W**. For example, the substitution of the methoxy group in complexes such as **2-Cr** or **3-Cr** by amines,<sup>1,4</sup> thiolate ions<sup>1,5</sup> carbanions<sup>1</sup> and other nucleophiles<sup>1</sup> is well documented, yet only very few kinetic investigations of such processes have been reported, e.g. the reaction of amines with **2-Cr**<sup>6</sup> and with (dithiomethylcarbene)pentacarbonylchromium(0).<sup>7</sup> Examples of other processes that have been the subject of kinetic studies include the thermolysis of 2-(oxacyclopentylidene)pentacarbonylchromium(0),<sup>8</sup> CO-exchange reactions,<sup>9</sup> substitution of CO ligands by alkynes,<sup>10</sup> the addition of amines to the triple bond of an  $\alpha,\beta$ -acetylenic pentacarbonylchromium carbene complex<sup>11</sup> and the reaction of several carbene complexes with tertiary phosphines and phosphites.<sup>12</sup>

A few years ago we started a research program aimed at studying the kinetics of reactions of **2-M**, **3-M** (throughout this review we use the symbols **2-M**, **3-M**, etc. when more than one derivative is meant, e.g. the Cr or W derivative) and related carbene complexes with nucleophiles and bases in polar solvents, mainly aqueous acetonitrile. Our objective is to firmly establish the mechanisms of these reactions and to develop a better understanding of their structure-reactivity behaviour. This review summarizes our results obtained thus far and focuses on three areas: (i) thermodynamic and kinetic acidities of complexes such as **2-M** that contain an acidic proton on the  $\alpha$ -carbon (carbon adjacent to the carbene carbon); (ii) mechanism and structure-reactivity relationships in the reactions of complexes such as **3-M** with nucleophiles; (iii) mechanism of hydrolysis of carbene complexes with and without an acidic proton on the  $\alpha$ -carbon.

## 2 Kinetic and thermodynamic acidities

### 2.1 General features and methods

The first indication that carbene complexes of the type **2-M** are relatively strong carbon acids was Kreiter's<sup>13</sup> observation of the rapid conversion of **2-Cr** to  $(\text{CO})_5\text{Cr}=\text{C}(\text{OCH}_3)\text{CD}_3$  in dilute  $\text{NaOCH}_3\text{-CH}_3\text{OD}$  solutions. Casey and Anderson<sup>14</sup> subsequently showed that in tetrahydrofuran (THF) the acidity of **2-Cr** is approximately the same as that of *p*-cyanophenol. In aqueous solution acidity measurements are more difficult because of rapid hydrolytic decomposition of the conjugate anion. This is probably the reason why an acidity constant in water was not reported until 1989 when a kinetic study of the deprotonation of **2-Cr** yielded a  $\text{p}K_a^{\text{CH}}$  of 12.3 (the superscript CH will be used to distinguish  $\text{p}K_a^{\text{CH}}$  from the  $\text{p}K_a$  of other acids).<sup>15</sup> This value was obtained from the relationship  $K_a^{\text{CH}} = (k_1^{\text{OH}}/k_{-1}^{\text{H}_2\text{O}})K_w$  where  $k_1^{\text{OH}}$  and  $k_{-1}^{\text{H}_2\text{O}}$  are the rate constants for the proton transfer reaction [eqn. (1)] and  $K_w$  is the ionic product of the solvent;  $k_1^{\text{OH}}$  and  $k_{-1}^{\text{H}_2\text{O}}$  were determined as

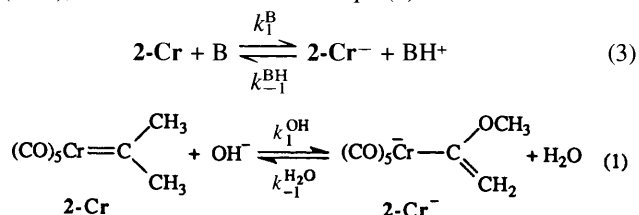
slope and intercept, respectively, of a plot of the observed pseudo-first-order rate constant for equilibrium approach vs.  $[\text{OH}^-]$  [eqn. (2)]. The  $k_{\text{obs}}$  values were obtained in a stopped-flow spectrophotometer. Applying the same methodology,

$$k_{\text{obs}} = k_1^{\text{OH}}[\text{OH}^-] + k_{-1}^{\text{H}_2\text{O}} \quad (2)$$

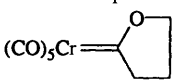
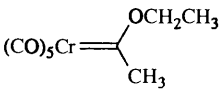
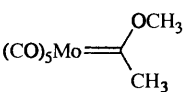
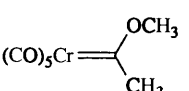
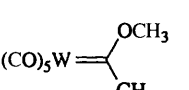
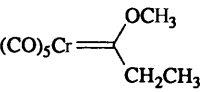
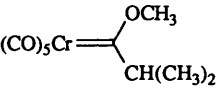
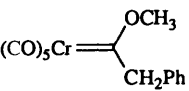
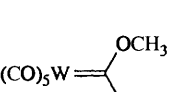
$k_1^{\text{OH}}$ ,  $k_{-1}^{\text{H}_2\text{O}}$  and  $\text{p}K_{\text{a}}^{\text{CH}}$  were determined for a number of carbene complexes, mainly in acetonitrile–water (50:50);<sup>16–18</sup> the results are summarized in Table 1. In cases where the  $\text{p}K_{\text{a}}^{\text{CH}}$  was substantially lower than 12, *i.e.* for **8-Cr** and **8-W** (for numbering of compounds, see Table 1), the intercepts of the plot of  $k_{\text{obs}}$  vs.  $[\text{OH}^-]$  were too small for a reliable determination of  $k_{-1}^{\text{H}_2\text{O}}$ . In these cases the  $\text{p}K_{\text{a}}^{\text{CH}}$  values were determined based on the rate of deprotonation of the carbene complex by butylamine and reprotonation of **2-Cr**<sup>-</sup> by  $\text{BuNH}_3^+$ .<sup>16,17</sup> A different problem prevented application of eqn. (2) for the determination of  $k_{-1}^{\text{H}_2\text{O}}$  for **6-Cr** and **7-Cr**. In these cases the rate constants for hydrolysis of the respective anions ( $k_2^{\text{H}_2\text{O}}$  in Scheme 3, see below) are of the same order of magnitude as  $k_{-1}^{\text{H}_2\text{O}}$ , which, at low  $[\text{OH}^-]$ , leads to strong coupling between proton transfer and hydrolysis.<sup>19</sup> As a result, eqn. (2) breaks down and  $k_{-1}^{\text{H}_2\text{O}}$  had to be determined by a method which is based on measuring hydrolysis rates under two extreme conditions. One was at high  $[\text{OH}^-]$  where  $k_1^{\text{OH}}[\text{OH}^-] \gg k_{-1}^{\text{H}_2\text{O}}$  and  $k_1^{\text{OH}}[\text{OH}^-] \gg k_2^{\text{H}_2\text{O}}$  so that  $k_2^{\text{H}_2\text{O}}$  could be obtained directly. The other was at low

enough  $[\text{OH}^-]$  so that the anions (*e.g.* **2-Cr**<sup>-</sup> in Scheme 3) are steady state intermediates and the observed rate constant for hydrolysis is given by  $k_1^{\text{OH}} k_2^{\text{H}_2\text{O}}[\text{OH}^-]/(k_{-1}^{\text{H}_2\text{O}} + k_2^{\text{H}_2\text{O}})$ ;  $k_{-1}^{\text{H}_2\text{O}}$  was then obtained as the only unknown in this steady state expression.

Rate constants for proton transfer to various amines were also measured. Because of the relatively high  $\text{p}K_{\text{a}}^{\text{CH}}$  values of the carbene complexes the deprotonation is thermodynamically unfavourable in most cases and hence the rates had to be determined by generating the anion in KOH solution and then reacting it with the protonated amine. In order to prevent hydrolysis, the anion was generated in a double-mixing stopped-flow spectrophotometer and reacted with the protonated amine buffer within 50–100 ms after its formation. Some representative results are summarized in Table 2;  $k_1^{\text{B}}$  refers to the deprotonation of the carbene complex by the amine (B) and  $k_{-1}^{\text{BH}^+}$  to the protonation of the anion by the respective ammonium ion ( $\text{BH}^+$ ), as illustrated for **2-Cr** in eqn. (3).



**Table 1** Summary of  $\text{p}K_{\text{a}}^{\text{CH}}$  values and rate constants for proton transfer to hydroxide ion in MeCN–water (50:50) at 25 °C

Carbene Complex	$\text{p}K_{\text{a}}^{\text{CH}}$	$\text{p}K_{\text{a}}^{\text{CH}}(\text{corr})$	$k_1^{\text{OH}}/$	$k_1^{\text{OH}}(\text{corr})/$	$k_2^{\text{H}_2\text{O}}/$	$\log k_0^{\text{OH}}(\text{corr})$
 <b>(4-Cr)<sup>a</sup></b>	14.47	14.77	74	37	14	1.36
 <b>(5-Cr)<sup>b</sup></b>	12.98	13.46	241	80.3	1.48	1.03
 <b>(2-Mo)<sup>b</sup></b>	12.81	13.29	181	60.3	0.75	0.82
 <b>(2-Cr)<sup>c</sup></b>	12.50 <sup>d</sup>	12.98	456	152	0.91	1.07
 <b>(2-W)<sup>b</sup></b>	12.36	12.84	284	94.7	0.42	0.80
 <b>(6-Cr)<sup>e</sup></b>	12.32	12.62	46.8	23.4	0.064	0.09
 <b>(7-Cr)<sup>e</sup></b>	12.27	12.27	2.97	2.97	$3.57 \times 10^{-3}$	-0.99
 <b>(8-Cr)<sup>c</sup></b>	10.40	10.70	115	57	$1.90 \times 10^{-3}$	-0.48
 <b>(8-W)<sup>b</sup></b>	10.18	10.48	140	70	$1.35 \times 10^{-3}$	-0.36

<sup>a</sup> Ref. 18. <sup>b</sup> Ref. 17. <sup>c</sup> Ref. 16. <sup>d</sup>  $\text{p}K_{\text{a}}^{\text{CH}}$  in water is 12.3, ref. 16. <sup>e</sup> Ref. 19. <sup>f</sup> In units of  $\text{dm}^3 \text{mol}^{-1} \text{s}^{-1}$ . <sup>g</sup> In units of  $\text{s}^{-1}$ . <sup>h</sup> The  $\log k_0^{\text{OH}}(\text{corr})$  values have an estimated uncertainty of  $\pm 0.25$  log units.

**Table 2** Summary of representative rate constants for proton transfer to amines in MeCN–water (50 : 50) at 25 °C<sup>a</sup>

B	$pK_a^{BH}$	$k_1^B$	$k_{-1}^{BH}$	$\log k_o^B(\text{corr})$
	<b>4-Cr<sup>b</sup></b> ( $pK_a^{CH} = 14.47$ )			
Piperidine	11.01	47	$1.36 \times 10^5$	ca. 3.40
	<b>2-Cr<sup>c</sup></b> ( $pK_a^{CH} = 12.50$ )			
Piperidine	11.01	906	$2.77 \times 10^4$	} 3.52
Piperazine	9.97	246	$8.23 \times 10^4$	
BuNH <sub>2</sub>	10.40	122	$1.52 \times 10^4$	} 2.85
MeOCH <sub>2</sub> CH <sub>2</sub> NH <sub>2</sub>	9.39	22.6	$2.88 \times 10^4$	
H <sub>2</sub> NCOCH <sub>2</sub> NH <sub>2</sub>	8.14	5.01	$1.14 \times 10^4$	
	<b>6-Cr<sup>d</sup></b> ( $pK_a^{CH} = 12.32$ )			
Piperidine	11.01	48.2	$9.82 \times 10^2$	ca. 2.19
	<b>7-Cr<sup>d</sup></b> ( $pK_a^{CH} = 12.27$ )			
Piperidine	11.01	0.194	3.55	ca. -0.11
	<b>8-Cr<sup>c</sup></b> ( $pK_a^{CH} = 10.40$ )			
Piperidine	11.01	225	55	} 1.70
Piperazine	9.97	74.8	200	
Morpholine	8.70	19.5	978	} 1.37
BuNH <sub>2</sub>	10.40	75.5	75.5	
MeOCH <sub>2</sub> CH <sub>2</sub> NH <sub>2</sub>	9.39	16.1	165	
H <sub>2</sub> NCOCH <sub>2</sub> NH <sub>2</sub>	8.14	2.30	413	
NCC <sub>2</sub> H <sub>2</sub> NH <sub>2</sub>	5.29	0.126	$1.61 \times 10^4$	

<sup>a</sup> In units of dm<sup>3</sup> mol<sup>-1</sup>. <sup>b</sup> Ref. 18. <sup>c</sup> Ref. 16. <sup>d</sup> Ref. 19.

In most cases the range of amines amenable to study was limited by the fact that protonation of the anion by BH<sup>+</sup> was too fast for the stopped-flow technique. This problem was generally more severe for carbene complexes with the highest  $pK_a^{CH}$  values, especially **4-Cr** ( $pK_a^{CH} = 14.47$ ) which only allowed measurements with piperidinium ion.<sup>18</sup> This contrasts with **8-Cr** ( $pK_a^{CH} = 10.40$ ) for which  $k_{-1}^{BH}$  with buffers as weakly basic as aminoacetonitrile could still be measured.<sup>16,17</sup> As discussed in Section 2.4, factors other than a low  $pK_a^{CH}$  contribute to the low  $k_{-1}^{BH}$  values for **8-Cr** and some other complexes, e.g. **6-Cr** and **7-Cr**.

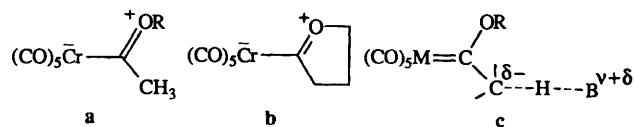
## 2.2 Effect of structure on $pK_a^{CH}$ values

The  $pK_a^{CH}$  values of the carbene complexes listed in Table 1 range from 10.18 for **8-W** to 14.47 for **4-Cr**. This compares with a  $pK_a^{CH}$  of 25.6 for ethyl acetate in aqueous solution,<sup>20</sup> indicating that the electron withdrawing effect of the (CO)<sub>5</sub>M-moieties is much stronger than that of the ester carbonyl oxygen. This may be attributed to charge dispersion into the CO ligands, a point to which we will return below. Regarding the variation of the  $pK_a^{CH}$  values with structure the following features are noteworthy.

(i) The  $pK_a^{CH}$  values are not very sensitive to the metal. This is seen from a comparison of **2-Mo**, **2-Cr** and **2-W**, and of **8-Cr** with **8-W**. This result implies that the stabilization of the anion by the (CO)<sub>5</sub>M moiety is similar for the three metals; it is in marked contrast to the strong metal dependence of the  $pK_a$  values of metal hydrido complexes of the type ( $\eta^5$ -C<sub>5</sub>H<sub>5</sub>)M(CO)<sub>3</sub>H. In acetonitrile these  $pK_a$  values are 13.3 for M = Cr, 13.9 for M = Mo and 16.1 for M = W; in methanol they are 6.4, 7.2 and 9.0, respectively.<sup>21</sup> This trend for the hydrido complexes would be difficult to reconcile with the results for the carbene complexes if it were assumed that the  $pK_a$  values of the hydrido complexes reflect a strong increase in the stabilization of the anions, ( $\eta^5$ -C<sub>5</sub>H<sub>5</sub>)M(CO)<sub>3</sub>, along the series W < Mo < Cr. However, Norton has shown that the differences in the acidities of the hydrido complexes are not due to differences in the stabilization of the anions, but can be traced to differences in the M–H bond dissociation enthalpies,<sup>21a</sup> i.e. there is no contradiction between Norton's and our results.

(ii) The effect of changing the alkoxy group can be seen by comparing **4-Cr**, **5-Cr** and **2-Cr**. The change from methoxy (**2-Cr**) to ethoxy (**5-Cr**) leads to an increase in  $pK_a^{CH}$  of 0.48

units. Inasmuch as the resonance structure **a** appears to play a dominant role in the stabilization of carbene complexes,<sup>1</sup> the higher  $pK_a^{CH}$  for **5-Cr** is most plausibly attributed to increased stabilization of **a** by stronger electron donation when R = ethyl instead of methyl.<sup>17</sup> In the case of **4-Cr**, the stabilization of the carbene complex by  $\pi$ -donation from the oxygen (**b**) is even more effective because, by virtue of the cyclic structure of **4-Cr**, the oxygen is locked into a position for better  $\pi$ -overlap with the carbene carbon.<sup>18</sup> <sup>53</sup>Cr NMR data are in agreement with this notion.<sup>22</sup> The result is a substantial further increase in  $pK_a^{CH}$ .



(iii) Substituting one of the  $\alpha$ -hydrogens by a phenyl group increases the acidity by more than two  $pK_a$ -units (**8-Cr** vs. **2-Cr** and **8-W** vs. **2-W**). This acidifying effect is mainly the result of additional resonance stabilization of the anion provided by the phenyl group.

(iv) Substituting one or two  $\alpha$ -hydrogens by methyl groups (**6-Cr** and **7-Cr** vs. **2-Cr**) has an acidifying influence which is particularly apparent when considering the statistically corrected  $pK_a^{CH}$ ,  $pK_a^{CH}(\text{corr})$ , which are included in Table 1. They are  $pK_a(\text{corr}) = 12.98, 12.62$  and  $12.27$  for the CH<sub>3</sub>, CH<sub>2</sub>CH<sub>3</sub> and CH(CH<sub>3</sub>)<sub>2</sub> derivatives, respectively. This acidity enhancement may be attributed to an increase in stability of the respective anions (**7-Cr** > **6-Cr** > **2-Cr**) caused by the methyl groups. Assuming that the dominant resonance structure of the anions has the negative charge mainly delocalized into the (CO)<sub>5</sub>Cr moiety [see, e.g. **2-Cr** in eqn. (1)], the increased stability in the order **7-Cr** > **6-Cr** > **2-Cr** simply reflects the well-known stabilization of alkenes by methyl groups.<sup>23</sup> This stabilization is commonly interpreted in terms of hyperconjugation<sup>23</sup> although other factors may contribute to it.<sup>19,23</sup> The increase in acidity of nitroalkanes in the order CH<sub>3</sub>NO<sub>2</sub> ( $pK_a^{CH} = 10.22$ ) < CH<sub>3</sub>CH<sub>2</sub>NO<sub>2</sub> ( $pK_a^{CH} = 8.60$ ) < (CH<sub>3</sub>)<sub>2</sub>CHNO<sub>2</sub> ( $pK_a^{CH} = 7.74$ ) has been explained in similar terms.<sup>24</sup>

## 2.3 Kinetic acidities: comparison with other carbon acids

Proton transfer rate constants for the reactions with OH<sup>-</sup> are summarized in Table 1, those for the reactions with amines in Table 2; the tables include statistically corrected (for the number of protons on the carbene complex) rate constants [ $(k_1^{OH}(\text{corr}), k_1^B(\text{corr}))$ ]. Intrinsic rate constants,  $k_o(\text{corr})$ , based on the statistically corrected  $k_1^{OH}$  and  $k_1^B$  values are also reported; they refer to deprotonation of the carbon acid by a hypothetical base such that the statistically corrected equilibrium constant is equal to 1. For the reactions with OH<sup>-</sup>,  $k_o^{OH}(\text{corr})$  was estimated based on the relationship  $\log k_o^{OH}(\text{corr}) = \log k_1^{OH}(\text{corr}) - 0.5 \log K_1^{OH}(\text{corr})$  [ $K_1^{OH}(\text{corr}) = K_a^{CH}(\text{corr})/K_w$  with  $K_w = 6.46 \times 10^{-16}$  mol<sup>2</sup> dm<sup>-6</sup> being the ionic product of the solvent<sup>16</sup>] which corresponds to the simplest version of the Marcus<sup>25</sup> equation. The  $\log k_o^{OH}(\text{corr})$  values are included in Table 1; because they are estimates, there is probably an uncertainty of about ca.  $\pm 0.25$  log units in these values. For the reactions with amines,  $\log k_o^B(\text{corr})$  was obtained by extrapolation or interpolation of Brønsted plots to  $pK_a^{BH} - pK_a^{CH}(\text{corr}) + \log(p/q) = 0$  where  $pK_a^{BH}$  is the  $pK_a$  of the protonated amine and  $p$  and  $q$  are the statistical factors for B and BH<sup>+</sup>, respectively. The  $\log k_o^B(\text{corr})$  values are reported in Table 2.

Because they are independent of the thermodynamic driving force of the proton transfer the intrinsic rate constants provide a useful measure of the purely kinetic barrier (intrinsic reactivity) of the reaction. This intrinsic reactivity can be related to salient structural differences between the transition state and carbon acid and/or its conjugate anion. Indeed, there exists an inverse relationship between  $\log k_o$  for proton transfer from carbon

acids activated by  $\pi$ -acceptors and the degree of resonance stabilization by charge delocalization in the carbanion.<sup>26</sup> Table 3 summarizes  $\log k_o$  values for a number of representative examples; for a more complete list see ref. 26(b).

The reason for this inverse relationship is that the transition state is imbalanced in the sense that resonance development in the incipient carbanion lags behind proton transfer.<sup>26</sup> This means that at the transition state the negative charge is closer to the  $\alpha$ -carbon than to the  $\pi$ -acceptor [e.g. the  $(CO)_5M$  moiety], as illustrated in exaggerated form by structure **c** ( $\nu = -1$  for  $B = OH^-$ ,  $\nu = 0$  for  $B = \text{amine}$ ). As a result, the stabilization of the transition state is disproportionately weak compared to that of the carbanion which depresses the intrinsic rate constant, the more so the greater the resonance stabilization of the anion. This effect is an example of a much more general phenomenon known as the principle of nonperfect synchronization or PNS;<sup>26</sup> this principle states that whenever in a reaction the development of a product-stabilizing factor (in our case resonance) lags behind the main bond changes (in our case proton transfer), there is a reduction in the intrinsic rate constant.

The  $\log k_o^{OH}(\text{corr})$  and  $k_o^B(\text{corr})$  values for the deprotonation of the carbene complexes fall into the range between  $-0.99$  and  $1.36$  for  $\log k_o^{OH}(\text{corr})$  (Table 1) and between  $-0.11$  and  $3.52$  for  $\log k_o^B(\text{corr})$  (Table 2). These ranges are below the  $\log k_o^{OH}$  and  $\log k_o^B$  values of the deprotonation of most carbon acids except the nitroalkanes (see Table 3). The implication is that the conjugate anions of the carbene complexes derive a substantial fraction of their stabilization from resonance, probably mainly by virtue of charge dispersion into the CO ligands of the  $(CO)_5M$  moieties. This interpretation is consistent with IR data of anions such as **2-Cr**<sup>-</sup> or **4-Cr**<sup>-</sup> in THF (where the anions are stable) which show a substantial reduction in the CO stretching frequency upon deprotonation of **2-Cr** or **4-Cr**, respectively.<sup>14,27</sup>

#### 2.4 Kinetic acidities: dependence on carbene complex structure

We first consider deprotonation of the carbene complexes by  $OH^-$ . Except for the trend towards higher rate constants with increasing thermodynamic acidities in the series **4-Cr** < **5-Cr** < **2-Cr**, the  $k_1^{OH}$  values do not correlate well with the  $pK_a^{CH}$  values. For example, the most acidic compounds (**8-Cr** and **8-W**) have  $k_1^{OH}(\text{corr})$  values that are less than twofold higher than for the least acidic carbene complex (**4-Cr**), despite a difference in  $pK_a^{CH}(\text{corr})$  of more than four units; or  $k_1^{OH}(\text{corr})$  for **2-Cr** is 2.7-fold higher than for **8-Cr** yet its  $pK_a^{CH}(\text{corr})$  is 2.3 units higher than for **8-Cr**; or  $k_1^{OH}(\text{corr})$  for **7-Cr** is 7.9-fold lower than for **6-Cr** yet the  $pK_a^{CH}(\text{corr})$  of **7-Cr** is 0.35 units lower, etc.

The poor correlation between  $k_1^{OH}(\text{corr})$  and  $pK_a^{CH}(\text{corr})$  is the result of significant variations in the *intrinsic* rate constants.

There is only one group of carbene complexes for which the  $\log k_o^{OH}(\text{corr})$  values are all approximately the same. They are **5-Cr** (1.03), **2-Mo** (0.82), **2-Cr** (1.06) and **2-W** (0.80); considering that the  $\log k_o^{OH}(\text{corr})$  values are estimates, the slight variation in these numbers is too small to warrant any attempt at interpretation. Even **4-Cr** (1.36) probably belongs to this group as will be shown below when comparing intrinsic rate constants for the reactions with piperidine. We conclude that changes in metal or alkoxy group have no or, at best, only a small effect on the  $\log k_o^{OH}(\text{corr})$  values. These are the cases where kinetic acidity correlates reasonably well with thermodynamic acidity.

In contrast, substituting one or two  $\alpha$ -protons by a phenyl or by methyl groups results in a substantial lowering of  $\log k_o^{OH}(\text{corr})$ . For **8-Cr** and **8-W** this reduction can be mainly attributed to the resonance effect of the phenyl group which stabilizes the anions **8-Cr**<sup>-</sup> and **8-W**<sup>-</sup>; this resonance effect is in addition to the resonance effect of the  $(CO)_5M$  moiety and further reduces the already relatively low  $k_o^{OH}$  values of typical carbene complexes such as **2-Cr** or **2-W**.

The  $k_o^{OH}$ -reducing effect of methyl groups is the result of a combination of several factors.<sup>19</sup> The first is that, due to the imbalanced nature of the transition state, the stabilizing effect of the methyl groups that manifests itself in the anions (**6-Cr**<sup>-</sup> and **7-Cr**<sup>-</sup>) and is responsible for the increased thermodynamic acidities of **6-Cr** and **7-Cr** is only minimally developed at the transition state. By virtue of the PNS,<sup>26</sup> this factor alone would lead to reduced  $k_o^{OH}$  values. However, there are additional factors that actually destabilize the transition state and further decrease  $k_o^{OH}$ . One is the repulsive interaction between the partial negative charge on the  $\alpha$ -carbon (see **c**) and the inductive/field effect of the alkyl group. Another is the repulsive field effect between the partial negative charge on the hydroxide ion ( $B^\nu = OH^-$  in **c**) and the alkyl groups. The third factor is steric crowding which is particularly significant in the reaction of **7-Cr**. The latter three factors lead to a decrease in  $k_1^{OH}(\text{corr})$  in the series **2-Cr** > **6-Cr** > **7-Cr**; since the thermodynamic acidities increase in the order **2-Cr** < **6-Cr** < **7-Cr** the result is a negative Brønsted  $\alpha$  value which is reminiscent of similarly negative  $\alpha$  values for the deprotonation of  $CH_3NO_2$ ,  $CH_3CH_2NO_2$  and  $(CH_3)_2CHNO_2$  (nitroalkane anomaly).<sup>24</sup>

Turning to the proton transfer reactions involving amines, we note that  $k_o^B(\text{corr})$  shows the same qualitative dependence on carbene complex structure as  $k_o^{OH}(\text{corr})$ . In particular,  $k_o^B(\text{corr})$  is essentially independent of the metal and the alkoxy group, while substituting  $\alpha$ -hydrogens by phenyl and methyl groups depresses  $k_o^B(\text{corr})$ . These reductions in  $k_o^B(\text{corr})$  are somewhat larger than the corresponding reductions in  $k_o^{OH}(\text{corr})$ . This is the result of greater steric crowding in the transition state because of the larger size of the amines compared to  $OH^-$ ; the effect is seen to be particularly important with **7-Cr**, the bulkiest carbene complex.<sup>19</sup>

Table 3  $pK_a^{CH}$  and  $\log k_o^B$  values for representative carbon acids<sup>a</sup>

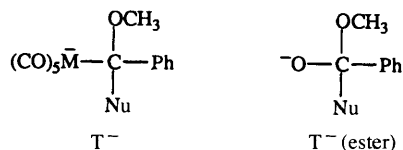
Carbon acid	Solvent	$pK_a^{CH}$	$pK_a^{CH}(\text{corr})$	$\log k_o^{OHb}$	$\log k_o^B(\text{corr})^c$	$\log k_o^B(\text{corr})^d$
HCN	H <sub>2</sub> O	9.0	9.0			ca. 8.60
CH <sub>2</sub> (CN) <sub>2</sub>	H <sub>2</sub> O	11.2	11.5		ca. 6.95	
9-Cyanofluorene	50% DMSO	9.53	9.53	ca. 2.69	4.58	3.76
Meldrum's acid	50% DMSO	4.70	5.00		3.75	
CH <sub>3</sub> COOEt	H <sub>2</sub> O	25.6	26.08	> 2.8 <sup>e</sup>		
4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> CN	50% DMSO	12.62	12.92	2.62	3.62	2.88
1,3-Indandione	50% DMSO	6.35	6.65	0.91	2.95	2.27
Acetylacetone	50% DMSO	9.12	9.42	1.25	2.58	1.90
2,4-(NO <sub>2</sub> ) <sub>2</sub> C <sub>6</sub> H <sub>3</sub> CH <sub>2</sub> CN	50% DMSO	8.06	8.36	1.49	2.60	1.70
CH <sub>3</sub> NO <sub>2</sub>	50% DMSO	11.32	11.80	0.04	0.53	
PhCH <sub>2</sub> NO <sub>2</sub>	50% DMSO	7.93	8.23	-0.91	-0.41	

<sup>a</sup> Taken from ref. 26; note that in ref. 26 the  $pK_a^{CH}$  and  $\log k_o^B$  values were not corrected for the number of acidic protons on the carbon acid. <sup>b</sup> The  $\log k_o^{OH}$  values have an estimated uncertainty of  $\pm 0.25$  log units. <sup>c</sup> B = Secondary alicyclic amines. <sup>d</sup> B = Primary aliphatic amines. <sup>e</sup> Estimated based on data in ref. 20.

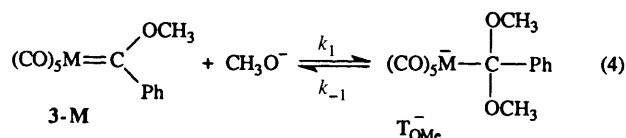
### 3 Reactions of nucleophiles at the carbene carbon

#### 3.1 Methoxide ion as nucleophile

Fischer carbene complexes show a strong qualitative similarity to carboxylic esters with respect to their reactions with nucleophiles, *i.e.* they undergo nucleophilic substitution by an addition–elimination mechanism involving a tetrahedral intermediate ( $T^-$ ). However, there is a major quantitative difference in that the tetrahedral intermediates derived from carbene complexes are much more stable than  $T^-(\text{ester})$ .



In favourable cases this allows a direct detection of the tetrahedral adduct, *e.g.* in the reaction of **3-Cr** and **3-W** with  $\text{MeO}^-$  in methanol, eqn. (4).<sup>28</sup> The rate constants  $k_1$  and  $k_{-1}$  for



eqn. (4) are summarized in Table 4 along with the equilibrium constants  $K_1 = k_1/k_{-1}$ . For the corresponding reaction of methyl benzoate a  $K_1$  value of  $1 \times 10^{-7}$  to  $5 \times 10^{-7} \text{ dm}^3 \text{ mol}^{-1}$  has been estimated.<sup>28</sup> This value implies that  $K_1$  for methoxide ion addition to the carbene complexes is  $2 \times 10^8$  to  $10^9$ -fold higher than for addition to the corresponding ester; it demonstrates that the  $(\text{CO})_5\text{M}$  moiety is a much stronger electron acceptor than the carbonyl oxygen in the ester, presumably, at least in part, because of a resonance effect brought about by delocalizing the negative charge into the CO ligands of  $T_{\text{OMe}}^-$ . This is the same effect that is largely responsible for the much higher acidity of **2-Cr** ( $\text{p}K_a = 12.5$ ) compared to ethyl benzoate (26.5) discussed earlier.

**Table 4** Rate and equilibrium constants for methoxide ion addition to **3-Cr** and **3-W** in methanol at 25 °C<sup>a</sup>

	<b>3-Cr</b>	<b>3-W</b>
$k_1/\text{dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$	77.1	186
$k_{-1}/\text{s}^{-1}$	1.10	1.68
$K_1/\text{dm}^3 \text{ mol}^{-1}$	70.1	111
$\log k_o$	0.96	1.25

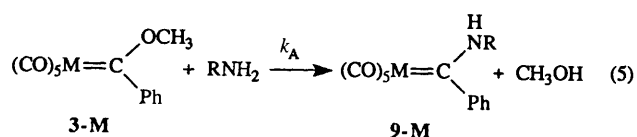
<sup>a</sup> Ref. 28.

Further evidence for the importance of resonance in the stabilization of  $T_{\text{OMe}}^-$  comes from the intrinsic rate constants,  $k_o$ , for nucleophilic addition. They have been estimated in a similar way as  $k_o^{\text{OH}}(\text{corr})$  for the deprotonation of acidic carbene complexes by  $\text{OH}^-$ , *i.e.*  $\log k_o \approx \log k_1 - 0.5 \log K_1$ ; for both **3-Cr** and **3-W**  $\log k_o \text{ ca. } 1$  (Table 4). This compares with  $\log k_o \text{ ca. } 3.1$  estimated for the reaction of methyl benzoate with methoxide ion.<sup>28</sup> The substantially lower  $\log k_o$  for the carbene complexes is most easily understood as the result of the resonance contribution to the stability of  $T_{\text{OMe}}^-$ . As in the case of resonance stabilized carbanions generated by deprotonation of carbon acids activated by  $\pi$ -acceptors, the delocalization of the charge in  $T_{\text{OMe}}^-$  presumably lags behind bond formation at the transition state and leads to a reduction of  $k_o$  (PNS effect).<sup>26</sup>

Regarding the dependence of reactivity on the metal, it is noteworthy that the rate and equilibrium constants are quite similar for both complexes (Table 4). This is consistent with the very small metal dependence of  $\text{p}K_a^{\text{CH}}$  and proton transfer rate constants when comparing **2-W** with **2-Cr** or **8-W** with **8-Cr** (Tables 1 and 2).

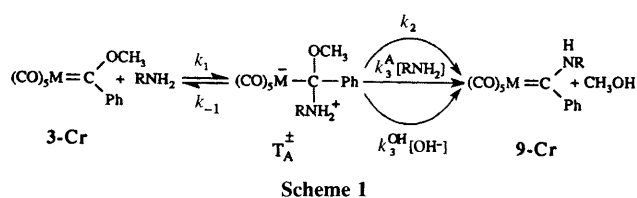
#### 3.2 Amines as nucleophiles

Aminolysis of Fischer carbene complexes with  $\text{NH}_3$ , primary amines and unhindered secondary amines is a facile reaction that leads to the corresponding amino carbene complex, *e.g.* eqn. (5).<sup>1,4,6</sup> A kinetic study of this reaction with **3-Cr** and

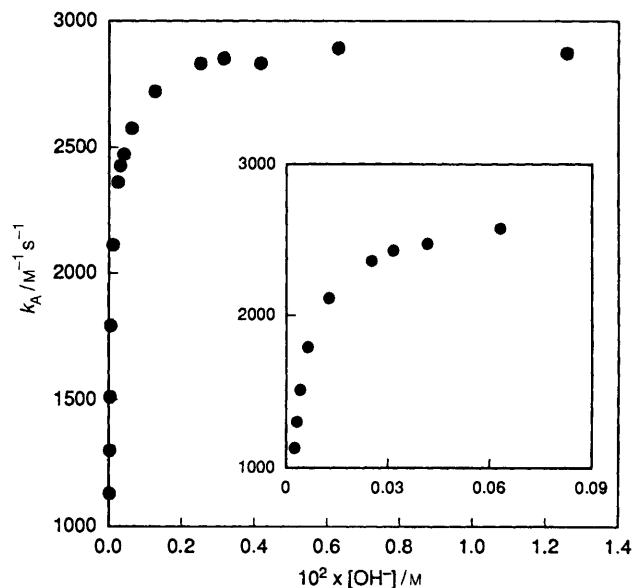


primary amines in decane, dioxane, methanol and dioxane–methanol mixtures was reported by Werner *et al.*<sup>6</sup> However, in these solvents complications arise due to the low polarity which makes mechanistic interpretations difficult. More definite results were obtained from a kinetic investigation of the same reaction in acetonitrile–water (20 : 80 v/v).<sup>29</sup>

Even though the presumed tetrahedral intermediate does not accumulate to detectable levels, the kinetic data provided compelling evidence that the reaction involves such an intermediate and proceeds through the mechanism shown in Scheme 1. The evidence for the involvement of  $T_{\text{A}}^\pm$  was based on



the observation of base catalysis by the amine and by  $\text{OH}^-$ , and specifically on how the second-order rate constant,  $k_A$  [see eqn. (5)], depends on the amine and hydroxide ion concentration. The dependence on  $\text{OH}^-$  is shown in Fig. 1 for the reaction with



**Fig. 1** Second-order rate constant of the reaction of **3-Cr** with butylamine in MeCN–water (20 : 80) at 25 °C as a function of hydroxide ion concentration

butylamine; it indicates a change from rate-limiting base catalysed conversion of the intermediate ( $T_{\text{A}}^\pm$ ) to products at low base concentrations to rate-limiting nucleophilic attack on **3-Cr** at high base concentrations. This is consistent with eqn. (6) for  $k_A$  based on the steady state approximation. Note that  $k_2$  for the spontaneous conversion of  $T_{\text{A}}^\pm$  to **9-Cr** has been omitted from eqn. (6) because this term was negligible under the experimental conditions. Analysis of the data according to eqn. (6)

provided the  $k_1$ ,  $k_3^A/k_{-1}$ ,  $k_3^{OH}/k_{-1}$  and  $k_3^{OH}/k_3^A$  values summarized in Table 5.

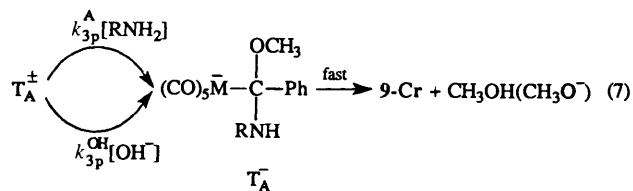
$$k_A = \frac{k_1(k_3^A[\text{RNH}_2] + k_3^{OH}[\text{OH}^-])}{k_{-1}(k_3^A[\text{RNH}_2] + k_3^{OH}[\text{OH}^-])} \quad (6)$$

**Table 5** Kinetic parameters of the reaction of **3-Cr** with primary amines in MeCN–water (20 : 80) at 25 °C<sup>a</sup>

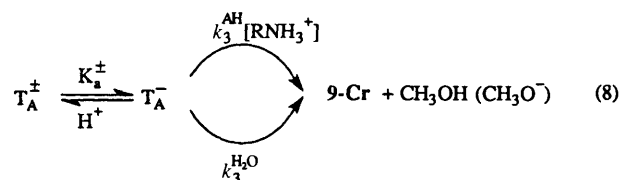
RNH <sub>2</sub>	pK <sub>a</sub> <sup>AH</sup>	k <sub>1</sub> <sup>b</sup>	k <sub>3</sub> <sup>A</sup> /k <sub>-1</sub> <sup>c</sup>	k <sub>3</sub> <sup>OH</sup> /k <sub>-1</sub> <sup>c</sup>	k <sub>3</sub> <sup>OH</sup> /k <sub>3</sub> <sup>A</sup>
BuNH <sub>2</sub>	10.67	2900	33.7	8.1 × 10 <sup>3</sup>	2.40 × 10 <sup>2</sup>
CH <sub>3</sub> OCH <sub>2</sub> CH <sub>2</sub> NH <sub>2</sub>	9.52	400	21.1	8.4 × 10 <sup>4</sup>	3.98 × 10 <sup>3</sup>
ClCH <sub>2</sub> CH <sub>2</sub> NH <sub>2</sub>	8.61	91	19.5	2.8 × 10 <sup>5</sup>	1.44 × 10 <sup>4</sup>
H <sub>2</sub> NCOCH <sub>2</sub> NH <sub>2</sub>	8.03	100	17.3	1.25 × 10 <sup>6</sup>	7.22 × 10 <sup>4</sup>
EtOCOCH <sub>2</sub> NH <sub>2</sub>	7.70	36	9.7	1.49 × 10 <sup>6</sup>	1.54 × 10 <sup>5</sup>

<sup>a</sup> Ref. 29. <sup>b</sup> In units of dm<sup>3</sup> mol<sup>-1</sup> s<sup>-1</sup>. <sup>c</sup> In units of dm<sup>3</sup> mol<sup>-1</sup>.

Regarding the mechanism of the base catalysed conversion of T<sub>A</sub><sup>±</sup> to products, there are two reasonable possibilities. The first involves rate-limiting deprotonation of T<sub>A</sub><sup>±</sup> followed by rapid methoxide ion expulsion, eqn. (7). For this mechanism, one can



equate  $k_3^A$  and  $k_3^{OH}$  with the respective rate constants for deprotonation of T<sub>A</sub><sup>±</sup> by the amine ( $k_{3p}^A$ ) and hydroxide ion ( $k_{3p}^{OH}$ ). In the second mechanism proton transfer occurs as a rapid pre-equilibrium step followed by general acid catalysed leaving group departure, eqn. (8); here  $k_3^A$  corresponds to  $k_3^{AH}K_a^{AH}/K_a^{AH}$  and  $k_3^{OH}$  to  $k_3^{H_2O}K_w/K_w$ , with  $K_a^{AH}$  being the acidity constant of RNH<sub>3</sub><sup>AH</sup> and  $K_w$  the ionic product of the solvent.

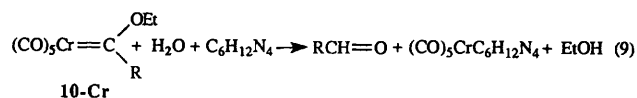


In the aminolysis of carboxylic esters, the deprotonation of the corresponding zwitterionic intermediate is usually rate limiting.<sup>30</sup> However, for the reaction of **3-Cr** with primary amines conversion of T<sub>A</sub><sup>±</sup> to products occurs by the mechanism of eqn. (8).<sup>29</sup> This conclusion was based on the following analysis of  $k_3^{OH}/k_3^A$  values (Table 5). If proton transfer were rate limiting, the  $k_3^{OH}/k_3^A$  ratios should be equal to  $k_{3p}^{OH}/k_{3p}^A$ . The rate constant  $k_{3p}^{OH}$  refers to a diffusion controlled proton transfer and should have a value of ca. 10<sup>10</sup> dm<sup>3</sup> mol<sup>-1</sup> s<sup>-1</sup>, independent of the amine.<sup>31</sup>  $k_{3p}^A$  should also be independent of the amine since the pK<sub>a</sub> difference between T<sub>A</sub><sup>±</sup> and RNH<sub>3</sub><sup>AH</sup> should be roughly constant; it was estimated to be in the order of 4 × 10<sup>8</sup> to 2 × 10<sup>9</sup> dm<sup>3</sup> mol<sup>-1</sup> s<sup>-1</sup>.<sup>32</sup> Hence the  $k_3^{OH}/k_3^A$  ratio should be independent of amine and have values of the order of 5–25. This contrasts with the experimental ratios that increase with decreasing pK<sub>a</sub><sup>AH</sup> from 240 to 1.54 × 10<sup>5</sup>. This increase which corresponds to a Brønsted coefficient,  $d(k_3^{OH}/k_3^A)/dpK_a^{AH}$ , of –0.92 is easily accounted for by the mechanism of eqn. (8) according to which the  $k_3^{OH}/k_3^A$  ratios correspond to  $k_3^{H_2O}K_w/K_a^{AH}/k_3^{AH}K_w$ . The Brønsted coefficient of –0.92 indicates that the  $k_3^{OH}/k_3^A$  ratios are not quite proportional to  $K_a^{AH}$  because of a small compensating effect by the  $k_3^{H_2O}/k_3^{AH}$  ratios which decrease slightly with decreasing amine basicity, reflecting the increasing catalytic effect of RNH<sub>3</sub><sup>AH</sup> on  $k_3^{AH}$  with decreasing pK<sub>a</sub><sup>AH</sup>.

Because the rates of interconversion between T<sub>A</sub><sup>±</sup> and T<sub>A</sub><sup>-</sup> by proton transfer should be about the same in the aminolysis with **3-Cr** and that of the corresponding methyl ester, the change from rate-limiting proton transfer for the ester to rate-limiting methoxide ion departure for **3-Cr** must be the result of lower  $k_3^{AH}$  and  $k_3^{H_2O}$  values with the carbene complex. These reduced  $k_3^{AH}$  and  $k_3^{H_2O}$  values reflect the combined effects of the increased stability of T<sub>A</sub><sup>-</sup> derived from **3-Cr** and the lower intrinsic rate constant for leaving group departure, both a consequence of the strong delocalization of the negative charge into the (CO)<sub>5</sub>Cr moiety of T<sub>A</sub><sup>-</sup>.

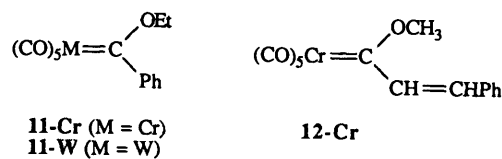
### 3.3 Hydroxide ion and water as nucleophiles

Until recently, the hydrolysis of carbene complexes has received very little attention. The first study was that reported in 1993 by Aumann *et al.*<sup>33</sup> who investigated the reaction of several substrates of the type **10-Cr** (R = Ph, CH=CHPh,



C<sub>4</sub>H<sub>3</sub>S, CH=CHC<sub>4</sub>H<sub>3</sub>S and C≡CPh) in THF containing small quantities of water. In the presence of urotropine (hexamethylenetetramine, C<sub>6</sub>H<sub>12</sub>N<sub>4</sub>) the aldehyde RCH=O is formed in ≥90% yield with all R groups except when R is C≡CPh; in this latter case the triple bond undergoes nucleophilic attack by the amine.

We recently published a kinetic study of the hydrolysis of **3-Cr**, **3-W**, **11-Cr**, **11-W** and **12-Cr** in acetonitrile–water

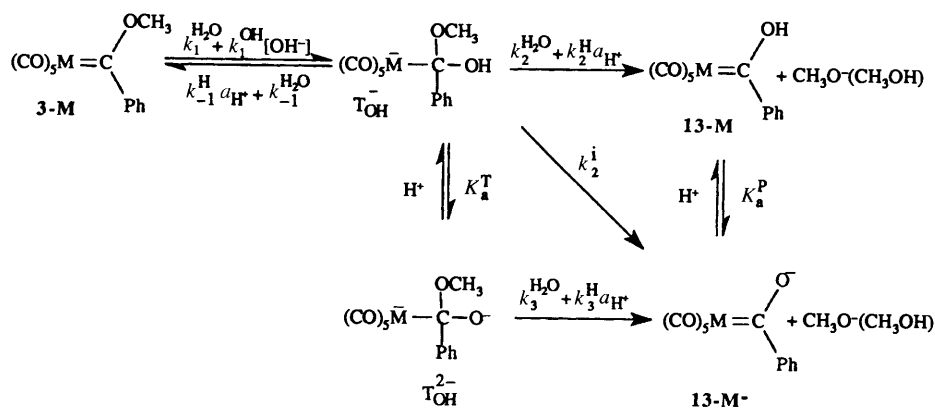


(50 : 50).<sup>34</sup> Two processes were observed. The first, faster one, corresponds to conversion of the carbene complexes to (hydroxyphenylcarbene)pentacarbonylchromium(0) or the tungsten analogue, while the second process leads to the formation of benzaldehyde (from **3-M** and **11-M**) or cinnamaldehyde (from **12-Cr**), consistent with the findings of Aumann *et al.*<sup>33</sup> The rate law for the first process examined over a wide pH range is given by eqn. (10) with  $k_B[B]$  representing buffer base catalysis.

$$k_{\text{obs}} = k_{\text{H}_2\text{O}} + k_{\text{OH}}[\text{OH}^-] + k_B[\text{B}] \quad (10)$$

The data were interpreted in terms of Scheme 2 (shown for the specific case of **3-M**) which is an elaboration of the mechanism proposed by Aumann *et al.*<sup>33</sup> and reminiscent of the mechanism of carboxylic ester hydrolysis. Scheme 2 takes into account all potential pathways under basic as well as acidic conditions. Specifically,  $k_1^{H_2O}$  and  $k_1^{OH}[\text{OH}^-]$  represent nucleophilic addition of water and OH<sup>-</sup>, respectively, while  $k_{-1}^H a_{H^+}$  and  $k_{-1}^{H_2O}$  refer to H<sup>+</sup>-catalysed and spontaneous loss of OH<sup>-</sup> from T<sub>OH</sub><sup>-</sup>, respectively. Regarding product formation, the scheme allows for the possibility of either direct conversion of T<sub>OH</sub><sup>-</sup> to products by unimolecular ( $k_2^{H_2O}$ ), H<sup>+</sup>-catalysed ( $k_2^H a_{H^+}$ ) or intramolecularly acid catalysed ( $k_2^I$ ) expulsion of CH<sub>3</sub>O<sup>-</sup>, or of reaction *via* the dianionic form of the intermediate (T<sub>OH</sub><sup>2-</sup>), again with either spontaneous ( $k_3^{H_2O}$ ) or H<sup>+</sup>-catalysed ( $k_3^H$ ) loss of CH<sub>3</sub>O<sup>-</sup>. Note, that for simplicity the buffer catalysed pathways have been omitted from the scheme.

The question whether T<sub>OH</sub><sup>-</sup> accumulates to detectable levels at high pH is an interesting one. It was estimated that the equilibrium constant for OH<sup>-</sup> addition to **3-M** in acetonitrile–water (50 : 50) is at least as large as that for MeO<sup>-</sup> addition to **3-M** in methanol ( $K_1$  ca. 100 dm<sup>3</sup> mol<sup>-1</sup>, Table 4), suggesting that T<sub>OH</sub><sup>-</sup> might be detectable. However, T<sub>OH</sub><sup>-</sup> was not observable



Scheme 2

even at the highest  $\text{OH}^-$  concentrations (0.1 M) used. This implies that conversion of  $\text{T}_{\text{OH}}^-$  to products is much faster than its formation, i.e.  $k_2^{\text{H}_2\text{O}} + k_2^{\text{H}^+} + K_a^{\text{T}}k_3^{\text{H}^+} \gg k_1^{\text{OH}}[\text{OH}^-]$ , turning  $\text{T}_{\text{OH}}^-$  into a steady state intermediate whose formation ( $k_1^{\text{OH}}$ ) is rate limiting. Further analysis indicated that it is  $k_2^{\text{H}_2\text{O}}$  and/or  $K_a^{\text{T}}k_3^{\text{H}^+}$  rather than  $k_2^{\text{H}_2\text{O}}$  that greatly exceed  $k_1^{\text{OH}}[\text{OH}^-]$ . In acidic solution water attack on the carbene complex ( $k_1^{\text{H}_2\text{O}}$ ) is rate limiting.

The  $k_1^{\text{OH}}$  and  $k_1^{\text{H}_2\text{O}}$  values are summarized in Table 6. The following points are noteworthy. (i) The rate constants depend little on the metal as seen by comparing **3-Cr** with **3-W** or **11-Cr** with **11-W**. This is consistent with observations made for the reaction of **3-Cr** and **3-W** with  $\text{MeO}^-$  in methanol.<sup>28</sup>

**Table 6** Summary of  $k_1^{\text{H}_2\text{O}}$  and  $k_1^{\text{OH}}$  values for nucleophilic attack on various carbene complexes in MeCN–water (50 : 50) at 25 °C<sup>a</sup>

Carbene complex	$k_1^{\text{H}_2\text{O}}/\text{s}^{-1}$	$k_1^{\text{OH}}/\text{dm}^3 \text{mol}^{-1} \text{s}^{-1}$
$(\text{CO})_5\text{Cr}=\text{C}(\text{OMe})\text{Ph}$ ( <b>3-Cr</b> )	$2.9 \times 10^{-3}$	26.6
$(\text{CO})_5\text{Cr}=\text{C}(\text{OEt})\text{Ph}$ ( <b>11-Cr</b> )	$4.5 \times 10^{-4}$	10.5
$(\text{CO})_5\text{Cr}=\text{C}(\text{OMe})\text{CH}=\text{CHPh}$ ( <b>12-Cr</b> )	$1.8 \times 10^{-4}$	14.6
$(\text{CO})_5\text{W}=\text{C}(\text{OMe})\text{Ph}$ ( <b>3-W</b> )	$2.8 \times 10^{-3}$	26.3
$(\text{CO})_5\text{W}=\text{C}(\text{OEt})\text{Ph}$ ( <b>11-W</b> )	$4.7 \times 10^{-4}$	17.6

<sup>a</sup> From Ref. 34.

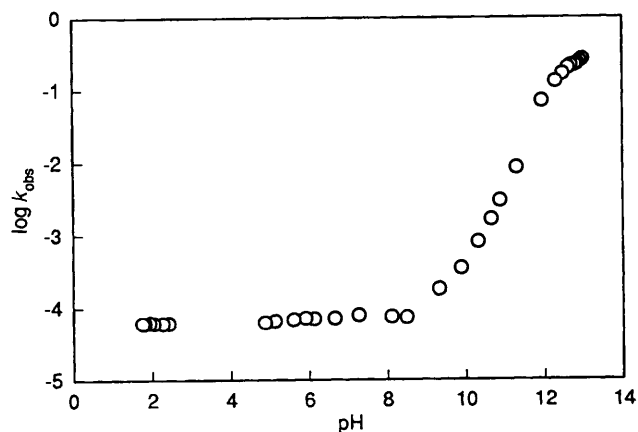
(ii) Substitution of a methoxy for an ethoxy group (**11-Cr** vs. **3-Cr** and **11-W** vs. **3-W**) lowers the reactivity. This is the result of more effective reactant state stabilization by  $\pi$ -donation by the ethoxy group, the same effect which decreases the acidity and rate of deprotonation of **5-Cr** compared to **2-Cr**. This effect manifests itself more strongly in the  $k_1^{\text{H}_2\text{O}}$  values than in the  $k_1^{\text{OH}}$  values and suggests that the transition state is relatively late for water addition and relatively early for  $\text{OH}^-$  addition, consistent with the Hammond postulate<sup>35</sup> or reactivity–selectivity principle.<sup>36</sup>

(iii) The reactivity of  $\text{OH}^-$  towards **12-Cr** is marginally lower than that towards **3-Cr** but attack by water on **12-Cr** is 16 fold slower than on **3-Cr**. The lower reactivity of **12-Cr** may be attributed to extra resonance stabilization of **12-Cr** by the styryl group.<sup>34</sup> The larger effect on  $k_1^{\text{H}_2\text{O}}$  than on  $k_1^{\text{OH}}$  may again be the result of a later transition state for the water reaction.

## 4 Hydrolysis of ionizable carbene complexes

### 4.1 Thermal reaction

The hydrolysis of **2-Cr**,<sup>37</sup> **4-Cr**,<sup>38</sup> **5-Cr**,<sup>37</sup> **8-Cr**<sup>39</sup> and **8-W**<sup>39</sup> (for structures see Table 1) has been thoroughly investigated in acetonitrile–water (50 : 50). The organic products of the hydrolysis were: acetaldehyde and methanol for **2-Cr**, acetaldehyde and ethanol for **5-Cr**,  $\beta$ -methoxystyrene for **8-Cr** and **8-W**, and 2-hydroxytetrahydrofuran in equilibrium with small amounts of 4-hydroxybutanal for **4-Cr**. Fig. 2 shows a typical pH–rate profile. The points below pH 8.5 represent a ‘water reaction’,

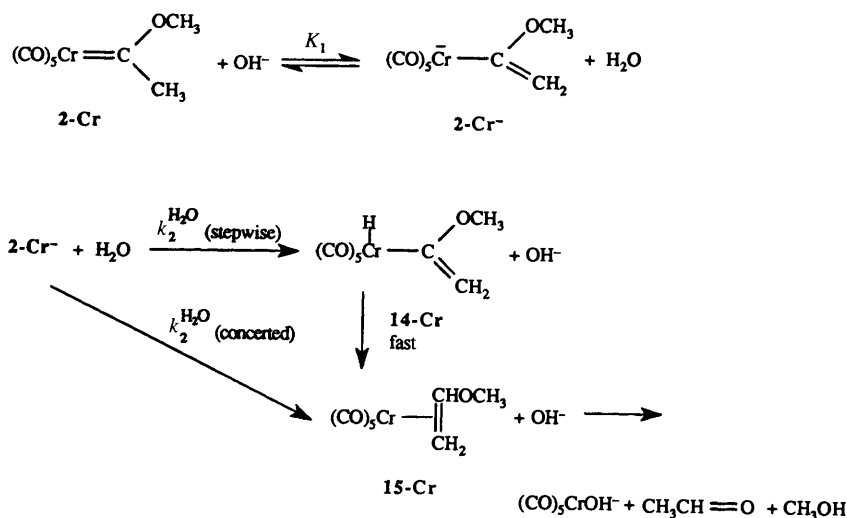


**Fig. 2** The pH–rate profile of the hydrolysis of **2-Cr** in MeCN–water (50 : 50) at 25 °C

those above pH 8.5 an  $\text{OH}^-$  catalysed reaction while the levelling off at  $\text{pH} > 12$  is due to the ionization of the carbene complex (see Section 2). The hydrolysis is subject to general base catalysis; the points on the pH–rate profile between pH 4.8 and 11.3 were obtained by extrapolation of buffer plots to zero buffer concentration.

The pH dependence of the hydrolysis of all compounds studied is, in principle, consistent with the mechanism of Scheme 2 for the hydrolysis of **3-M**, and so are the products of the reactions of **2-Cr**, **4-Cr** and **5-Cr**. However, the products obtained in the hydrolysis of **8-Cr** and **8-W** and the fact that in basic solution the hydrolysis of all the compounds is subject to a substantial kinetic solvent isotope effect are inconsistent with Scheme 2, at least at  $\text{pH} > 8.5$ . The mechanism that accounts best for all experimental observations at  $\text{pH} > 8.5$ , including the isotope effect, is shown in Scheme 3 for the example of **2-Cr**. It involves fast deprotonation of **2-Cr** followed by rate limiting reaction of **2-Cr**<sup>-</sup> with water to form **15-Cr**; complexation between  $(\text{CO})_5\text{Cr}$  and the vinyl ether activates the latter towards basic hydrolysis which rapidly leads to the vinyl alcohol and tautomerization to the aldehyde. Control experiments demonstrated that the kind of complexation indicated by **15-Cr** indeed promotes rapid hydrolysis of the vinyl ether.<sup>37</sup> In the reaction of **8-Cr** and **8-W** complexation of the vinyl ether ( $\beta$ -methoxystyrene) appears to be weak, presumably because of steric crowding, and hence the reaction essentially stops at the  $\beta$ -methoxystyrene stage although small amounts of  $\text{PhCH}_2\text{CH}=\text{O}$  could be detected with **8-W**.

Regarding the conversion of **2-Cr**<sup>-</sup> into **15-Cr**, there are two possible pathways, stepwise and concerted. The stepwise pathway consists of rate-limiting protonation on the metal



Scheme 3

followed by rapid reductive elimination while the concerted pathway involves protonation on the carbene carbon which is simultaneous with bond cleavage between the metal and the carbene carbon. No firm distinction between these two pathways is possible but the concerted alternative is preferred because the stepwise mechanism requires the  $pK_a$  of **14-Cr** to be unrealistically high.<sup>37</sup>

The fact that the base catalysed hydrolysis of ionizable carbene complexes proceeds by the mechanism of Scheme 3 instead of the nucleophilic mechanism of Scheme 2 implies that the former is energetically more favourable. For the nucleophilic mechanism to be competitive with Scheme 3 in the case of **2-Cr** the rate constant for  $\text{OH}^-$  attack on **2-Cr** would have to be approximately three times higher than for  $\text{OH}^-$  attack on **3-Cr**.<sup>34</sup> This contrasts with the expectation that it is **3-Cr** which should be the more electrophilic carbene complex, due to the electron withdrawing inductive effect of the phenyl group. The potential  $\pi$ -donor effect of the phenyl group is negligible because this group was found to have an orthogonal orientation both in the solid state<sup>40</sup> and a solution.<sup>41</sup>

Regarding the 'water reaction' ( $\text{pH} < 8.5$ ), whether it follows Scheme 3 with conversion of **2-Cr** to **15-M** involving  $\text{H}_3\text{O}^+$  instead of water, or Scheme 2 with the  $k_1^{\text{H}_2\text{O}}$ -step being rate limiting, remains an open question.<sup>38</sup>

#### 4.2 Light-induced reaction

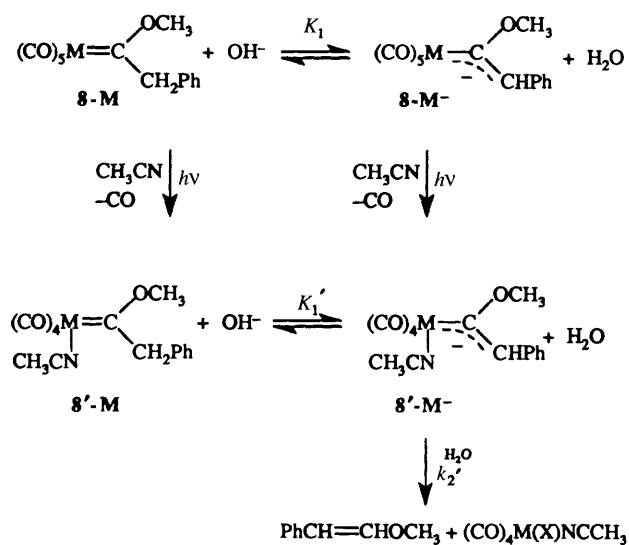
The hydrolysis of **8-Cr** and **8-W** is catalysed by light.<sup>39</sup> Accelerations in the presence of high light intensities of the order of five- to six-fold have been observed. A possible mechanism for this photochemical process is shown in Scheme 4.<sup>39</sup> This mechanism is consistent with the fact that  $\text{PhCH}=\text{CHOCH}_3$  is the main organic product of the reaction, just as for the thermal reaction, and with a kinetic solvent isotope effect that is similar to that for the thermal process and suggests that reaction of **8-M** with water is rate limiting. The results did not, however, allow a distinction between the two pathways that lead to **8'-M**. Note that the increased reactivity of **8'-M** compared to **8-M** is consistent with a higher electron density induced by replacing one of the strongly electron withdrawing CO ligands by acetonitrile.

The hydrolysis of **7-Cr**<sup>19</sup> is also catalysed by light although the effect is smaller than for **8-Cr** and **8-W** and the phenomenon was not studied in detail. On the other hand, no light-induced rate accelerations have been observed for the hydrolysis of **2-Cr**,<sup>37</sup> **4-Cr**,<sup>38</sup> **5-Cr**<sup>37</sup> or **6-Cr**.<sup>19</sup> It is unclear at this point what structural factors are responsible for inducing catalysis by light.

#### 5 Conclusion

Until recently there has been a dearth of kinetic and thermodynamic data on fundamental reactions involving Fischer carbene complexes. Over the last few years, we have begun to fill this void by studying the thermodynamic and kinetic acidities of ionizable carbene complexes, and the kinetics of nucleophilic addition and substitution at the carbene carbon of phenyl carbene complexes. In these processes Fischer carbene complexes show a behaviour that is qualitatively similar to that of carboxylic esters but differs dramatically in its quantitative manifestations because of the much stronger electron withdrawing effect of the  $(\text{CO})_5\text{M}$  moiety compared to that of a carbonyl oxygen. For example, the thermodynamic acidities of the ionizable carbene complexes are 11–15  $pK_a$  units higher than that of ethyl acetate, and the equilibrium constants for  $\text{MeO}^-$  addition to **3-M** are *ca.*  $10^9$ -fold higher than for  $\text{MeO}^-$  addition to methyl benzoate. On the other hand, the rate constants for proton transfer and nucleophilic addition do not show as dramatic an increase; this is because the strong electron-withdrawing effect of the  $(\text{CO})_5\text{M}$  moieties is mainly the result of  $\pi$ -delocalization which lowers the intrinsic rate constants of these processes, thereby attenuating the effect of the stronger thermodynamic driving force on the actual rates.

Regarding the hydrolysis of ionizable Fischer carbene complexes, our studies have shown that a reaction pathway



Scheme 4



through the ionized carbene complex is more favourable than the classic nucleophilic mechanism governing hydrolysis of the non-ionizable complexes. For this reaction there is no counter-part in the hydrolysis of esters. In some cases the pathway through the ionized carbene complex is further enhanced by light.

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