Physical organic chemistry of transition metal carbene complexes. Part 11.[1] Kinetics and mechanism of the hydrolysis of (2-oxacyclopentylidene)pentacarbonylchromium(0) in aqueous acetonitrile

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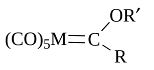
A kinetic study of the hydrolysis of the title compound, 6, in 50% acetonitrile–50% water (v/v) at 25 °C is reported. The organic products are 2-hydroxytetrahydrofuran in equilibrium with small amounts of 4-hydroxybutanal. There are two possible mechanisms that can account for the hydrolysis. (*i*) Rate limiting reaction of the conjugate anion of 6 (6^-) with water, buffer acids and H_3O^+, followed by $(CO)_5Cr$ catalyzed hydrolysis of the resulting 2,3-dihydrofuran. (*ii*) Ring opening of 6 through nucleophilic substitution on the carbene carbon by OH^-, water or by buffer base catalyzed water attack, followed by breakdown of the intermediate substitution product into final hydrolysis products. Kinetic solvent isotope effects can be interpreted by either mechanism. Based on more conclusive isotope effect experiments in the hydrolysis of $(CO)_5Cr{=}C(OR')CH_3$ ($R' = CH_3$ or CH_3CH_3) and $(CO)_5Cr{=}C(OMe)CH_2Ph$ reported earlier, the first mechanism is preferred by reason of analogy, at least in basic solution. In acidic solution the mechanistic ambiguity could not be resolved, not even for $(CO)_5Cr{=}C(OMe)CH_3$ which was reinvestigated in HCl and DCl solutions.

Introduction

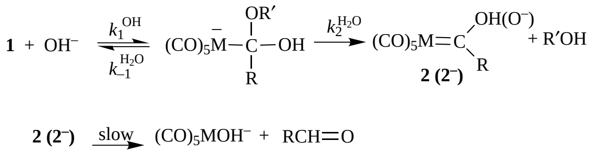
Fischer-type carbene complexes of the general structure **1**



$$(CO)_5M{=}C\begin{matrix}OR'\\R\end{matrix}$$

1 (M = Cr or W)

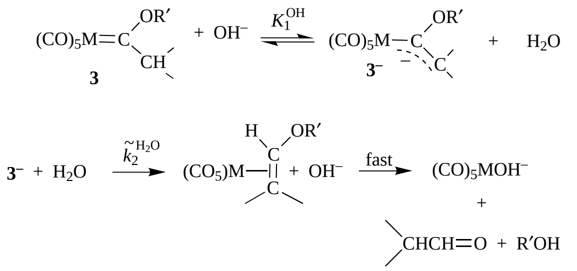
undergo hydrolysis to form an aldehyde RCH=O and alcohol R′OH as the organic products in most cases.[2–4] However, the mechanism which leads to these products is not the same for all carbene complexes but depends on the nature of the R group. If R does not contain a hydrogen on the carbon α to the carbene carbon, *e.g.* R = phenyl, the only plausible mechanism available is that shown in Scheme 1.[2,4] Scheme 1 represents the reaction



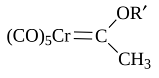
Scheme 1

in basic solution where **2** is predominantly present as its anion; formation of **2** ($\mathbf{2^-}$) is quite fast and occurs *via* a tetrahedral intermediate whose formation is rate limiting. The transformation of **2** ($\mathbf{2^-}$) into final products is a known,[5] but mechanistically poorly understood reaction, which occurs on a much slower timescale than the formation of **2** ($\mathbf{2^-}$).[4]

If R contains a hydrogen on the carbon adjacent to the carbene carbon, *e.g.* R = CH_3, there is a competing mechanism which is more efficient than that of Scheme 1. It involves rapid deprotonation of the carbene complex followed by rate limiting reaction of the anion with a proton donor to generate the corresponding vinyl ether.[3] This vinyl ether appears to be complexed with $(CO)_5M$ which activates it toward rapid hydrolysis to the corresponding aldehyde. Such activation is necessary because vinyl ethers are stable under basic conditions; the effectiveness of this activation has been demonstrated independently in the basic hydrolysis of $CH_2{=}CHOEt$.[3] The mechanism is shown in Scheme 2 for the reaction in basic solution. A major piece of evidence for this mechanism is the large kinetic solvent isotope effect found in the hydrolysis of **4a**,[3] **4b**,[3] **5a**[6] and **5b**[6] in 50% acetonitrile–50% water which is inconsistent with the mechanism of Scheme 1. In the case of **5a** and **5b** the nucleophilic substitution mechanism could also be excluded based on the isolation of $PhCH{=}CHOCH_3$ instead of $PhCH_2$-$CH{=}O$ as the hydrolysis product. The reason why, in this case, the vinyl ether was not hydrolyzed is attributed to a lower stability and/or shorter lifetime of the complex between $(CO)_5Cr$ and $PhCH{=}CHOMe$ due to steric crowding.[6] Based on recent estimates[4] the pathway *via* Scheme 2 for the hydrolysis of **4a** in basic solution appears to be approximately five-fold faster than the pathway *via* Scheme 1.

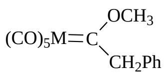


Scheme 2



$$(CO)_5Cr{=}C\begin{matrix}OR'\\CH_3\end{matrix}$$

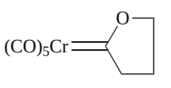
4a (R′ = CH_3)
4b (R′ = CH_3CH_2)



$$(CO)_5M{=}C\begin{matrix}OCH_3\\CH_2Ph\end{matrix}$$

5a (M = Cr)
5b (M = W)

In this paper we wish to examine whether the hydrolysis of (2-oxacyclopentylidene)pentacarbonylchromium(0), **6**, follows



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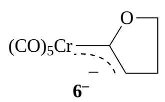


6$^-$

the mechanism of Scheme 1 or Scheme 2. Complex **6**, just as **4a**, **4b**, **5a** and **5b** contains an acidic proton α to the carbene carbon and hence one might expect its hydrolysis to follow Scheme 2. It will be shown, however, that the results for **6** are less clear cut and are consistent with either mechanism. A reinvestigation of **4a** in HCl solution, coupled with a kinetic solvent isotope effect study, also reveals mechanistic ambiguities in acidic solution with this compound.

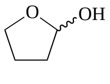
Results

General features and product study

Unless stated otherwise, all experiments were carried out in 50% MeCN–50% water (v/v) at 25 °C. When **6** is added to a KOH solution at [KOH] $\geqslant$ 0.01 M, two reactions are observed by monitoring the UV–VIS spectrum. The faster of the two is in the subsecond range and can be attributed to the reversible deprotonation of **6** that leads to the anion **6**$^-$. A detailed study of this process has been reported recently.[1]

The slower process is irreversible and in strongly basic solution occurs on a timescale of several seconds but becomes progressively slower as the pH is decreased. At pH $\leqslant$13.2 ([OH$^-$] < 0.01 M) it is the only visible reaction because the acid–base equilibrium between **6** and **6**$^-$ strongly disfavors **6**$^-$, making the proton transfer undetectable. Fig. 1 shows time resolved absorption spectra of the reaction of **6** in a 0.005 M KOH solution.

The organic products of the slow process are the hemiacetal 2-hydroxytetrahydrofuran (**7**) in equilibrium with small amounts of its acyclic form, 4-hydroxybutanal (**8**). Identification of **7** and **8** was achieved by ^{1}H and ^{13}C NMR spectroscopy. A solution of 0.024 M **6** and 0.01 M NaOD in 75% CD_3CN–25% D_2O (a higher proportion of organic solvent than in the kinetic experiments was necessary to make **6** more soluble) was left to react and its NMR spectrum compared to that of an authentic sample of **7** in equilibrium with **8**. This latter sample was generated by acid hydrolysis of 2,3-dihydrofuran with 0.01 M DCl in 75% CD_3CN–25% D_2O and then made basic with NaOD, to mimic the conditions of the reaction of **6**. Both the ^{1}H and ^{13}C NMR spectra of hydrolyzed **6** were the same as those of the hydrolyzed 2,3-dihydrofuran, except that in the ^{1}H NMR spectrum of the hydrolyzed **6** the signal for the anomeric hydrogen in **7** was missing. The replacement of the anomeric hydrogen by a deuterium atom is consistent with hydrolysis conducted in the presence of D_2O.



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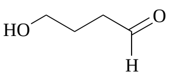

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Kinetics

Rates of hydrolysis of **6** were measured in the pH range 1.0–14.2. All kinetic determinations were made under pseudo-first-order conditions with **6** as the minor component. The ionic strength was maintained at 0.1 M with KCl. The observed pseudo-first-order rate constants, k_{obsd}, are reported elsewhere.[7] Experiments were performed in HCl solutions (pH 1.01–1.71), methoxyacetic acid (pH 4.73), acetic acid (pH 5.93), *N*-methylmorpholine (*N*-MeMor) (pH 7.43–8.43) and triethylamine buffers (pH 9.31–12.0), and in KOH solutions (pH 12.18–14.18). In all buffers, general base catalysis was observed. Intercepts of the linear plots of k_{obsd} *vs.* buffer concentration were combined with the HCl and KOH data to construct the pH–rate profile shown in Fig. 2. The slight downward curvature at the high pH end is consistent with the onset of a shift of the acid–base equilibrium towards the anion (**6**$^-$), as expected on the basis of $pK_a^{CH} = 14.47$ for **6**.[1] The relatively large scatter in the plateau region of the pH–rate profile is mainly attributed to the slowness of the reaction, which necessitated the use of the inherently less precise initial rates method to evaluate k_{obsd} (see Experimental section). Between pH 4.3 and 8.4 an additional source of error comes from the extrapolation of relatively steep plots of k_{obsd} *vs.* buffer concentration.

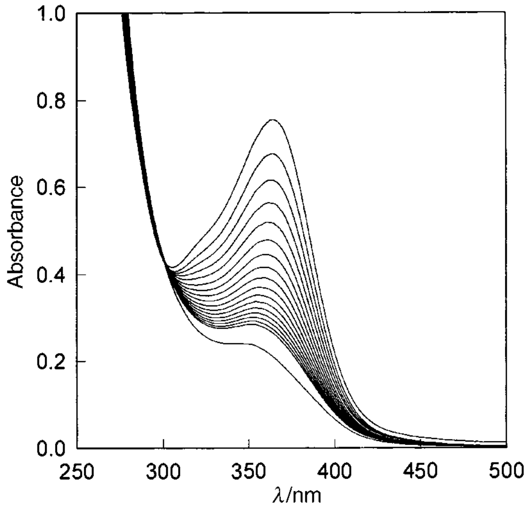


Fig. 1 Time resolved absorption spectra for the hydrolysis of **6** in a 0.005 M KOH solution (pH 12.9). Spectra taken every 15 s in a Hewlett-Packard 8452A diode array spectrophotometer. Spectrum of the final product was taken after 8 min.

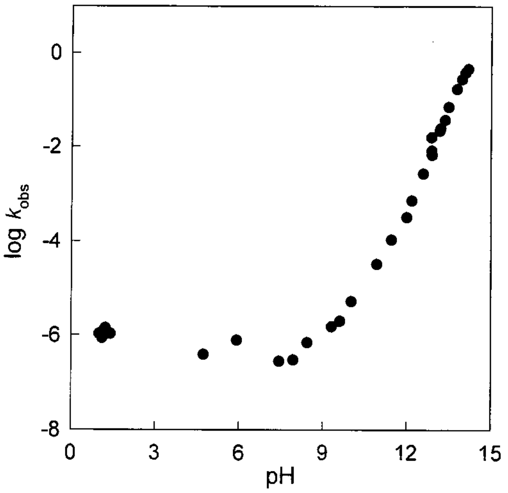
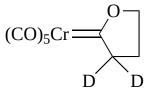


Fig. 2 pH–rate profile of the hydrolysis of **6** in 50% CH_3CN–50% H_2O

Kinetic isotope effects

The deuterated carbene complex, [$^2H_2$]**6**, was reacted with 0.005–0.1 M KOD in 50% MeCN–50% D_2O. Just as for the reaction of **6** with KOH in 50% MeCN–50% water, the deuteron transfer and hydrolysis could be observed as separate processes. A plot of k_{obsd} *vs.* [KOD] for the hydrolysis reaction is



[$^2H_2$] **6**

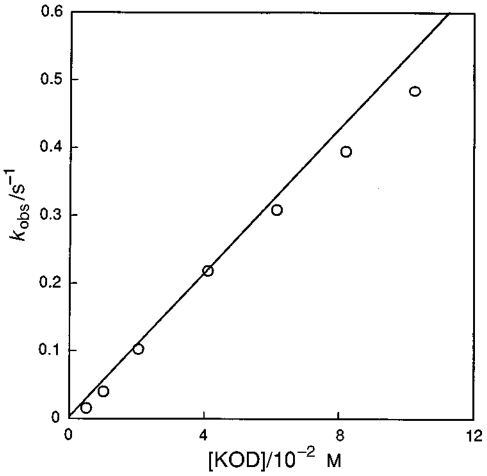


Fig. 3 Plot of k_{obsd} *vs.* [KOD] for the reaction of $[^2H_2]$**6** in 50% CH_3CN–50% D_2O

shown in Fig. 3. Just as in the pH–rate profile of the reaction of **6** with KOH in 50% MeCN–50% water there is a slight downward curvature at the highest KOD concentrations which is consistent with a shift of the acid–base equilibrium towards the anion. The initial slope of the plot is 5.30 ± 0.18 $\text{M}^{-1}\ \text{s}^{-1}$; the corresponding quantity for the reaction of **6** with KOH obtained from the pH–rate profile in 50% MeCN–50% water is 5.20 ± 0.09 $\text{M}^{-1}\ \text{s}^{-1}$.

Experiments where $[^2H_2]$**6** was reacted with KOH in MeCN–H_2O or where **6** was reacted with KOD in MeCN–D_2O did not yield easily interpretable results as discussed elsewhere.[1]

Attempts at measuring hydrolysis rates in DCl–MeCN–D_2O solutions were unsuccessful. As can be seen from the pH–rate profile in Fig. 2, hydrolysis of **6** at low pH is very slow, with k_{obsd} values in the order of 10^{-6} s^{-1}. As mentioned earlier, this necessitated the use of the initial rates method which is subject to larger experimental errors than standard first order kinetics. The k_{obsd} values obtained in HCl solutions were nevertheless of acceptable quality. However, experiments in DCl–MeCN–D_2O gave erratic results, probably because the rates are considerably lower than in HCl–MeCN–H_2O and possible formation of byproducts may be a more serious problem. Hence, we used **4a** whose hydrolysis in HCl solution is about 50-fold faster than hydrolysis of **6**,[3] as a model to determine the kinetic solvent isotope effect (KSIE) in acidic solution.

Two types of experiments were performed. (*i*) Reactions of **4a** with DCl in 50% MeCN–50% D_2O. The kinetic traces deviated slightly from ideal first-order behavior at short reaction times, probably because H/D exchange occurs in competition with hydrolysis; if $[^2H]$**4a**, $[^2H_2]$**4a** and $[^2H_3]$**4a**† have slightly different reactivities this could account for the deviations. Nevertheless, approximate k_{obsd} values could be determined. They are summarized in Table 1, along with the corresponding k_{obsd} in HCl–MeCN–H_2O. (*ii*) Reactions of $[^2H_3]$**4a** with DCl in 50% MeCN–50% D_2O. In these experiments the kinetic traces showed strict first-order behavior which is consistent with the above interpretation of the slight deviations from first-order kinetics with **4a**. The k_{obsd} values are also reported in Table 1. The KSIE calculated for the two types of experiments are 2.98 and 3.19, respectively.

Discussion

Mechanism

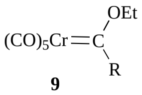
In anhydrous solvents, base catalyzed decomposition of Fischer carbene complexes that have acidic hydrogens adjacent to the carbene carbon typically lead to vinyl ethers. This has been shown for **4a** and other similar complexes in the presence of neat pyridine and *N*-methylmorpholine, or of quinuclidine in hexane,[8] and also for **6** in pyridine which leads to 2,3-dihydrofuran.[9] In the presence of water, on the other hand, only **5a** leads to the corresponding vinyl ether ($PhCH{=}CHOCH_3$)[6] while **4a** and **4b** lead to the hydrolysis products of the respective vinyl ethers.[3] We now find that the decomposition of **6** in 50% MeCN–50% water also leads to the hydrolysis product of 2,3-dihydrofuran, **8** (which rapidly cyclizes to **7**), rather than to 2,3-dihydrofuran.

Table 1 Rate constants for the hydrolysis of **4a** in MeCN–H_2O–HCl and MeCN–D_2O–DCl, and of $[^2H_3]$**4a** in MeCN–D_2O–DCl at 25 °C

[LCl]/10^{-2} M	k_{obsd}/10^{-5} s^{-1}
4a + HCl in 50% MeCN–50% H_2O	
0.58	4.62
2.26	4.88
4.52	4.91
6.80	4.91
11.3	5.26
	average 4.92
4a + DCl in 50% MeCN–50% D_2O	
0.52	1.63
4.0	1.57
8.0	1.45
10.0	1.88
	average 1.65[a]
$[^2H_3]$**4a** + DCl in 50% MeCN–50% D_2O	
0.52	1.25
2.0	1.47
4.0	1.65
6.0	1.62
10.0	1.67
	average 1.54[b]

[a] $k_{obsd}(H_2O)/k_{obsd}(D_2O) = 2.98$. [b] $k_{obsd}(H_2O)/k_{obsd}(D_2O) = 3.19$.

Formation of vinyl ethers is easily accounted for by reaction of $\mathbf{3}^-$ with a proton donor which leads to protonation of the carbene carbon and cleavage of the bond between the metal and carbene carbon. On the other hand, formation of the hydrolysis products of the expected vinyl ether poses a more complex mechanistic problem and may be explained in two different ways. (*i*) The reaction does not involve $\mathbf{3}^-$ (or $\mathbf{6}^-$ in the case at hand) as the intermediate but proceeds by a nucleophilic substitution mechanism, as is the case for **1** with R = Ph in aqueous acetonitrile[4] and for **9** (R = Ph, CH=CHR and others)



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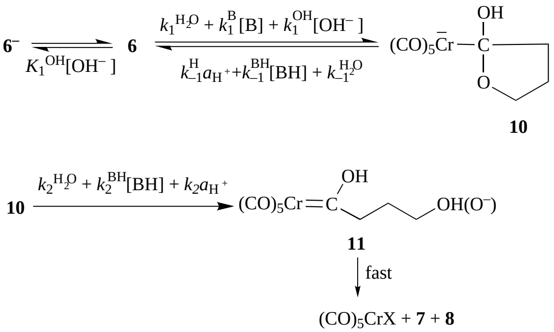
in THF in the presence of small amounts of water.[2] This mechanism, applied to the hydrolysis of **6**, is shown in Scheme 3 where $(CO)_5CrX$ is likely to be a mixture with X being either OH^-, MeCN or a buffer base. Scheme 3 is essentially the mech-



Scheme 3

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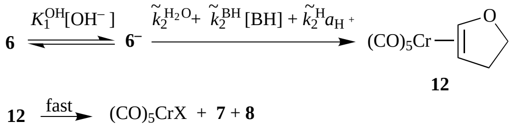
† $[^2H]$**4a**: $(CO)_5Cr{=}C(OCH)_3CH_2D$; $[^2H_2]$**4a**: $(CO)_5Cr{=}C(OCH_3)CHD_2$; $[^2H_3]$**4a**: $(CO)_5Cr{=}C(OCH_3)CD_3$.

anism of Scheme 1, but it accounts for the deprotonation equilibrium of **6** and includes terms not only for reversible OH^- attack ($k_1^{OH}[OH^-]$, $k_{-1}^{H_2O}$) and spontaneous breakdown of the tetrahedral intermediate ($k_2^{H_2O}$) but also for reversible nucleophilic attack by water ($k_1^{H_2O}$, $k_{-1}^{H}a_{H^+}$), reversible buffer catalyzed water attack ($k_1^{B}[B]$, $k_{-1}^{BH}[BH]$), and for the H^+ and BH catalyzed breakdown of the intermediate ($k_2^{H}a_{H^+}$, $k_2^{BH}[BH]$). (*ii*) Alternatively, the reaction does involve $\mathbf{3}^-$ ($\mathbf{6}^-$ in the present case) as the intermediate and leads to the vinyl ether but the latter is rapidly hydrolyzed because of complexation with $(CO)_5Cr$. This mechanism is shown in Scheme 4 which is an elaboration of Scheme 2 to include $\tilde{k}_2^{H}a_{H^+}$ and a $\tilde{k}_2^{BH}[BH]$ term.‡



Scheme 4

The mechanisms of Schemes 3 and 4 are kinetically indistinguishable. If nucleophilic attack in Scheme 3 is assumed to be rate limiting,§ k_{obsd} is given by eqn. (1), while k_{obsd} for Scheme

$$k_{obsd} = \frac{k_1^{H_2O} + k_1^{B}[B^-] + k_1^{OH}[OH^-]}{1 + K_1^{OH}[OH^-]} \qquad (1)$$

4 is given by eqn. (2). At pH ≪ pK_a^{CH} ($K_1^{OH}[OH^-] \ll 1$), eqns. (1)

$$k_{obsd} = \frac{K_1^{OH}[OH^-]}{1 + K_1^{OH}[OH^-]}(\tilde{k}_2^{H}a_{H^+} + \tilde{k}_2^{BH}[BH] + \tilde{k}_2^{H_2O}) \qquad (2)$$

and (2) simplify to eqns. (3) and (4), respectively; at pH ≫ pK_a^{CH}

$$k_{obsd} = k_1^{H_2O} + k_1^{B}[B] + k_1^{OH}[OH^-] \qquad (3)$$

$$\begin{aligned} k_{obsd} &= K_1^{OH}K_w\tilde{k}_2^{H} + K_1^{OH}\tilde{k}_2^{BH}[OH^-][BH] + K_1^{OH}\tilde{k}_2^{H_2O}[OH^-] = \\ &\quad K_a^{CH}\tilde{k}_2^{H} + \frac{K_a^{CH}}{K_a^{BH}}\tilde{k}_2^{BH}[B] + \frac{K_a^{CH}}{a_{H^+}}\tilde{k}_2^{H_2O} \end{aligned} \qquad (4)$$

($K_1^{OH}[OH^-] \gg 1$; $k_1^{H_2O} \ll k_1^{OH}[OH^-]$; $\tilde{k}_2^{H}a_{H^+} \ll \tilde{k}_2^{H_2O}$), and in the absence of buffer, eqns. (1) and (2) simplify to eqns. (5) and (6), respectively.

$$k_{obsd} = k_1^{OH}/K_1^{OH} \qquad (5)$$

$$k_{obsd} = \tilde{k}_2^{H_2O} \qquad (6)$$

Due to the high pK_a^{CH} of **6** (14.47), most of our kinetic data can be treated by eqns. (3) or (4). The various rate constants (k_1^{OH}, k_1^{B} and $k_1^{H_2O}$ according to Scheme 3, or $\tilde{k}_2^{H_2O}$, $\tilde{k}_2^{BH}$ and $\tilde{k}_2^{H}$ according to Scheme 4) that give the best fit to the pH–rate profile are summarized in Table 2.

Table 2 Rate constants for rate limiting steps in the hydrolysis of Fischer carbene complexes at 25 °C. Interpretation in terms of Scheme 3 and Scheme 4.[a]

Reactive agent	**6** $pK_a^{CH} = 14.47$	**4a**[b] $pK_a^{CH} = 12.50$	**5a**[b] $pK_a^{CH} = 10.40$
Scheme 3 (k_1^{OH}, k_1^{B}, $k_1^{H_2O}$)			
OH^- (16.63)[c]	5.20	7.84×10^1	5.24×10^2
Et_3N (10.31)[c]	1.94×10^{-4}		4.88×10^{-2}
N-MeMor (7.43)[c]	2.10×10^{-5}	3.49×10^{-3}	1.71×10^{-3}
AcO^- (5.93)[c]	6.32×10^{-5}	8.61×10^{-3}	2.91×10^{-3}
$MeOCH_2COO^-$ (4.73)[c]	6.01×10^{-6}		
H_2O (−1.44)[c]	9.8×10^{-7}	6.01×10^{-5}	1.71×10^{-5}
Scheme 4 ($\tilde{k}_2^{H_2O}$, $\tilde{k}_2^{BH}$, $\tilde{k}_2^{H}$)			
H_2O (16.63)[d]	0.98	0.16	8.5×10^{-3}
Et_3NH^+ (10.31)[d]	2.80		6.0×10^{-2}
N-MeMorH$^+$ (7.43)[d]	2.2×10^2	4.1×10^2	1.6
AcOH (5.93)[d]	2.19×10^4	3.2×10^4	8.6×10^1
$MeOCH_2COOH$ (4.73)[d]	3.3×10^4		
H_3O^+ (−1.44)[d]	2.9×10^8	1.9×10^8	4.3×10^5

[a] k_1^{OH}, k_1^{B}, $\tilde{k}_2^{BH}$ and $\tilde{k}_2^{H}$ in units of $M^{-1}\ s^{-1}$; $k_1^{H_2O}$ and $\tilde{k}_2^{H_2O}$ in units of s^{-1}. [b] Ref. 19. [c] Numbers in parentheses are pK_a of conjugate acid. [d] pK_a.

Before discussing these rate constants, we ask whether one can distinguish between the two mechanisms. In basic solution, where the $k_1^{OH}[OH^-]$ [eqn. (1)] or the $\tilde{k}_2^{H_2O}$ [eqn. (2)] term is dominant, a distinction between the two mechanisms is, in principle, possible on the basis of the kinetic solvent isotope effects (KSIE). For Scheme 3, these isotope effects are given by eqns. (7) and (8), respectively; for Scheme 4, the isotope effects are given by eqns. (9) and (10), respectively.

$$\frac{k_{obsd}(H_2O)}{k_{obsd}(D_2O)} = \frac{K_1^{OD}k_1^{OH}}{K_1^{OH}k_1^{OD}} \quad (pH \gg pK_a^{CH}) \qquad (7)$$

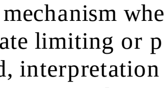
$$\frac{k_{obsd}(H_2O)}{k_{obsd}(D_2O)} = \frac{k_1^{OH}}{k_1^{OD}} \quad (pH \ll pK_a^{CH}) \qquad (8)$$

$$\frac{k_{obsd}(H_2O)}{k_{obsd}(D_2O)} = \frac{\tilde{k}_2^{H_2O}}{\tilde{k}_2^{D_2O}} \quad (pH \gg pK_a^{CH}) \qquad (9)$$

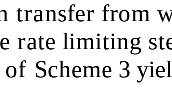
$$\frac{k_{obsd}(H_2O)}{k_{obsd}(D_2O)} = \frac{K_1^{OH}\tilde{k}_2^{H_2O}}{K_1^{OD}\tilde{k}_2^{D_2O}} \quad (pH \ll pK_a^{CH}) \qquad (10)$$

Analysis of the KSIE data according to eqns. (7)–(10) affords the results reported in Table 3. The primary KIE reported in the table under 'Scheme 4' were estimated by assuming a secondary KSIE of 1.41 in all cases.¶

Focusing first on **4a** and **4b**, interpretation of the results in terms of Scheme 4 implies sizable primary KIE values, consistent with a mechanism where proton transfer from water to $\mathbf{4a}^-$ or $\mathbf{4b}^-$ is rate limiting or part of the rate limiting step.‡ On the other hand, interpretation in terms of Scheme 3 yields k_1^{OH}/k_1^{OD} ratios that are unrealistically high, especially for $\mathbf{4b}^-$; typically OD^- shows nucleophilic reactivity equal to or somewhat higher than OH^-,[13,14] *e.g.*, in the hydrolysis of **13** which must proceed


$(CO)_5Cr{=}C(OMe)Ph$

13


$(CO)_5W{=}C(OEt)Ph$

14

by a nucleophilic mechanism, the k_1^{OH}/k_1^{OD} ratio is 1.0 ± 0.04,[4] while for **14** it is 0.91 ± 0.05.[4] Hence the nucleophilic mechanism is unattractive and can be excluded for **4a** and **4b**.[3]

The situation with **6** is less clear cut. For Scheme 4, the results yield a primary KIE of about 2.2 which is rather small, while for the nucleophilic mechanism we obtain $k_1^{OH}/k_1^{OD} = 0.98$ which is about the same as for the hydrolysis of **13**. This suggests that

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‡ In Scheme 4 formation of **12** is assumed to be a concerted reaction whereby protonation of the carbene carbon of the anion and metal–carbon bond cleavage are coupled, *i.e.* occur in a single step. As elaborated upon elsewhere,[3] the alternative possibility (in the case of **4a** and **4b**) of rate limiting protonation of the anion on the metal followed by fast reductive elimination is less attractive.

§ Alkoxide ions are typically better leaving groups than OH^- in ester hydrolysis[10] and other reactions;[11] hence the reaction of **10** to form **11** is expected to be faster than reaction of **10** to revert back to **6** which makes the nucleophilic attack step rate limiting.

¶ The secondary KSIE is estimated based on $(k_H/k_D)_{sec} = (\varphi_{L_2O}^2/\varphi_{OL^-})^a$ with φ_{L_2O} and φ_{OL^-} being the respective fractionation factors.[12] It is assumed that the fractionation factors in 50% MeCN–50% L_2O are the same as in pure L_2O, *i.e.* 1.0 for L_2O and 0.5 for OL^- (ref. 12); *a* is assumed to be 0.5.

Table 3 Kinetic solvent isotope effects on the hydrolysis of Fischer carbene complexes at 25 °C. Interpretation in terms of Scheme 3 and Scheme 4

	Scheme 3	Scheme 4	
	k_1^{OH}/k_1^{OD}	$(\tilde{k}_2^{H_2O}/\tilde{k}_2^{D_2O})_{exp}$	$(\tilde{k}_2^{H_2O}/\tilde{k}_2^{D_2O})_{prim}$
4a	*ca.* 1.32 [a]	4.15 [b]	*ca.* 2.93 [c]
4b	*ca.* 2.22 [a]	7.0 [b]	*ca.* 4.95 [c]
6	*ca.* 0.98 [d]	3.06 [e]	*ca.* 2.17 [c]
5a	*ca.* 0.88 [a]	2.78 [b]	*ca.* 1.97 [c]

[a] Obtained from eqn. (7) after correcting for $K_1^{OD}/K_1^{OH} = 3.15$. [b] Obtained directly from eqn. (9). [c] Estimated assuming a secondary KSIE of 1.41, see text. [d] Obtained directly from eqn. (8). [e] Obtained from eqn. (10) after correcting for $K_1^{OH}/K_1^{OD} = 0.317$.

in the case of **6** the mechanism of Scheme 3 might be operative, or the two mechanisms might be in competition with each other; no definite conclusion is possible at this point. Nevertheless, there are a number of features which seem to favor Scheme 4. The first is an analogy with the reactions of **4a** and **4b**. The second is that in the case of **5a**, where formation of PhCH=CHOMe as the hydrolysis product is difficult to reconcile with Scheme 3 and hence Scheme 4 is the only reasonable mechanism, the KSIE is about as small as for **6**. The third is that in the absence of water, base catalyzed decomposition of **6** leads to 2,3-dihydrofuran,[9] which implies a mechanism like Scheme 4 and not Scheme 3.

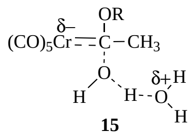
In acidic solution, where the $\tilde{k}_2^{H}a_{H^+}$ term [eqn. (2)] or $k_1^{H_2O}$ term [eqn. (1)] is dominant, no reliable data for the KSIE could be obtained for **6** but the KSIE for hydrolysis of **4a** was determined as $k_{obsd}(H_2O)/k_{obsd}(D_2O) = 3.1$ (average value). Interpretation in terms of Scheme 4 yields eqn. (11), while interpretation in terms of Scheme 3 yields eqn. (12). With respect to eqn.

$$\frac{k_{obsd}(H_2O)}{k_{obsd}(D_2O)} = \frac{K_a^{CH}(H_2O)\tilde{k}_2^{H}}{K_a^{CD}(D_2O)\tilde{k}_2^{D}} \quad (11)$$

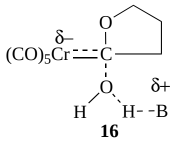
$$\frac{k_{obsd}(H_2O)}{k_{obsd}(D_2O)} = \frac{k_1^{H_2O}}{k_1^{D_2O}} \quad (12)$$

(11), the $\tilde{k}_2^{H}/\tilde{k}_2^{D}$ ratio may be estimated as follows. The K_1^{OH}/K_1^{OD} ratio was found to be 0.317 based on kinetic measurements.[1] Assuming that $pK_a^{D_2O} - pK_a^{H_2O} = 0.86$ as in pure water[15] yields $K_a^{CH}(H_2O)/K_a^{D_2O}(CD) = (K_1^{OH}/K_1^{OD})(K_a^{H_2O}/K_a^{D_2O}) = 2.3$. This, then, affords $\tilde{k}_2^{H}/\tilde{k}_2^{D} = 1.35$ *via* eqn. (11). The $\tilde{k}_2^{H}/\tilde{k}_2^{D}$ ratio is a composite of a primary KIE and a secondary KSIE. The latter can be estimated to be about 0.69,‖ leaving a primary KIE of about 2.24. This is quite a small value but possibly consistent with a very unsymmetrical transition state[16] and/or with a concerted process[16b] where proton transfer to the carbene carbon of **4a**⁻ is coupled to carbon–metal bond cleavage.

If Scheme 3 prevails, we have $k_1^{H_2O}/k_1^{D_2O} = 3.1$. This is the same as the $k_1^{H_2O}/k_1^{D_2O}$ ratio in the hydrolysis of **13**[4] and close to corresponding ratios for reactions of numerous electrophiles with water;[13] these isotope effects suggest a mechanism where two water molecules are involved,[13] *e.g.* one acting as nucleophile and the other as base catalyst, as in **15**. As shown by the



15



16

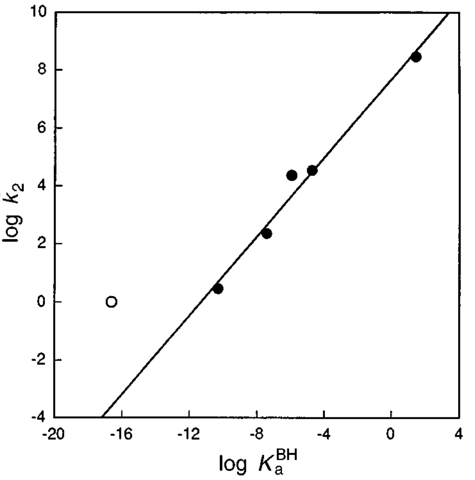


Fig. 4 Brønsted plot of the $\tilde{k}_2$ rate constants (●: $\tilde{k}_2^{BH}$ and $\tilde{k}_2^{H}$; ○: $\tilde{k}_2^{H_2O}$) according to Scheme 4. Slope = 0.68 ± 0.05 based on $\tilde{k}_2^{BH}$ for Et_3NH^+, *N*-MeMorH⁺ and $MeOCH_2COOH$.

preceding analysis no definite choice between Scheme 4 and 3 can be made with respect to the mechanism of the pH-independent pathway in acidic solution.

Rate constants

The individual rate constants calculated from the experimental data for Schemes 3 and 4 are summarized in Table 2 along with the corresponding rate constants for the hydrolysis of **4a** and **5a**. Fig. 4 shows a Brønsted plot of the rate constants for the $\tilde{k}_2$ steps according to Scheme 4. The points for the two tertiary ammonium ions and methoxyacetic acid define a straight line of slope $\alpha = 0.68 \pm 0.05$; there is a small positive deviation for acetic acid and a large positive deviation for water while the point for H_3O^+ is on the line. The positive deviation of the water point and the fact that the point for H_3O^+ is on the line contrast with the more common observation that these points typically deviate negatively from most Brønsted plots.[17] It suggests that, due to the bulkiness of the buffer acids, their $\tilde{k}_2^{BH}$-values are strongly depressed by steric crowding in the transition state. The slight positive deviation for acetic acid may, at least in part, also reflect a smaller steric effect for this less bulky acid. The data for **4a** and **5a** are more limited but the corresponding Brønsted plots (not shown) display the same features as Fig. 4.

An alternative Brønsted plot for base catalysis (not shown) may be constructed based on the rate constants (k_1) for Scheme 3. It yields a straight line of slope $\beta = 0.32 \pm 0.05$ defined by the two amines, methoxyacetate ion and water, and shows a small positive deviation for AcO⁻ and a large positive deviation for OH⁻. Again the positive deviations can be understood in terms of steric hindrance, this time of base catalysis by the bulky buffer bases.

The rather substantial steric effect which manifests itself in both Brønsted plots is probably more easily understood in terms of Scheme 4 than of Scheme 3. This is because proton transfer from the buffer acid to **6**⁻, **4a**⁻ or **5a**⁻ is likely to be direct, *i.e.* not to involve a bridging water molecule.[18] Such direct transfers require a closer approach of the buffer molecule to the carbene complex in the transition state than in a transition state like **16** for base catalyzed water attack. This reasoning is suggestive rather than compelling but it is in agreement with the evidence from kinetic solvent isotope effects, especially for **4a** and **4b**. On the other hand, no conclusion can be reached, based on the Brønsted plots, regarding the question of whether the hydrolysis pathway might proceed by a different mechanism in acidic solution (Scheme 3) than in basic solution.

The dependence of the rate constants on the specific carbene complex calls for comment. In a previous paper[1] the low acidity

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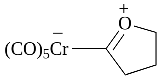
‖ The secondary KSIE is estimated based on $(k_H/k_D)_{sec} = (\varphi^2_{L_3O^+}/\varphi_{L_2O})^{\alpha}$ with $\varphi_{L_3O^+}$ and φ_{L_2O} being the respective fractionation factors.[12] They are assumed to be the same as in pure L_2O, *i.e.* 1.0 for L_2O and 0.69 for L_3O^+.[12] α = 0.68 is based on the Brønsted plot discussed below.

of **6** (pK_a = 14.47) compared to that of **4a** (pK_a = 12.50)[19] was shown to be mainly the result of stabilization of the acid form (**6**) rather than to a destabilization of the anion (**6**$^-$). The extra stabilization of **6** was primarily attributed to enhanced π-donation from the oxygen to the carbene carbon (**6**$^\pm$), a consequence of the ring structure which locks the oxygen into a position for better π-overlap than is the case for **4a**. Irrespective of whether Scheme 3 or 4 prevails, the substrate dependence of the various rate constants lends further support to this conclusion. Assuming Scheme 4 is the correct mechanism, we note that the rate constants for the reaction of **6**$^-$ and **4a**$^-$ with proton donors are quite similar but substantially larger than for the reactions of **5a**$^-$ with the same proton donors. This lower reactivity of **5a**$^-$ may be attributed to the stabilization of **5a**$^-$ by the phenyl group, the same stabilization that is responsible for the higher acidity of **5a** (p$K_a^{\mathbf{CH}}$ = 10.40)[19] compared to that of **4a** (p$K_a^{\mathbf{CH}}$ = 12.50). On the other hand, the comparable reactivities of **6**$^-$ and **4a**$^-$ indicate comparable stabilities of **6**$^-$ and **4a**$^-$, consistent with the notion that the pK_a difference between **6** and **4a** is not the result of different stabilities of **6**$^-$ and **4a**$^-$, but the result of different stabilities of **6** and **4a**. If Scheme 3 is operative, the same conclusion emerges: nucleophilic attack on **4a** and **5a** occurs with comparable rates and is considerably faster than attack on **6**, reflecting the fact that only **6** enjoys extra stabilization from enhanced π-donation by the oxygen atom (**6**$^\pm$).



6$^\pm$

Conclusions

The hydrolysis of **6** yields 2-hydroxybutanal (**8**) which rapidly cyclizes to the hemiacetal **7**. This finding is consonant with results for the hydrolysis of **4a** and **4b** which yields acetaldehyde and the respective alcohol under similar conditions. The most likely hydrolysis mechanism is that shown in Scheme 4; as with **4a** and **4b**, it is consistent with the kinetic solvent isotope effect although this isotope effect is less conclusive for the reaction of **6** than it was for the reactions of **4a** and **4b**. Tentative support for the mechanism of Scheme 4 also comes from a consideration of steric effects on the hydrolysis rate constants.

Irrespective of whether Scheme 3 or 4 prevails, the difference between the individual rate constants (k_1 for Scheme 3 or $\tilde{k}_2$ for Scheme 4) for **6** and **4a** supports an earlier conclusion that the lower acidity of **6** compared to that of **4a** is mainly the result of enhanced π-donation by the oxygen in **6** (**6**$^\pm$).

Experimental

Materials

(2-Oxacyclopentylidene)pentacarbonylchromium(0), **6**, was a gift from Professor Hegedus; it was recrystallized from dry pentane before use, mp 63.5–65.0 °C (lit. 63.5–65.0 °C[20]). [$^2H_2$]**6** was prepared by dissolving known amounts of **6** in 1.0 ml of 70% CD_3CN–30% D_2O in the presence of catalytic amounts of NaOD (<0.005 M). H/D exchange was monitored by ^1H NMR spectroscopy until no residual signal for the acidic protons of **6** at 3.6 ppm was observed. The resulting [$^2H_2$]**6** was not isolated, *i.e.* the NMR solutions were directly used for the kinetic experiments. (Methoxymethylcarbene)pentacarbonylchromium(0), **4a**, and [$^2H_3$]**4a** were available from a previous study.[3] Triethylamine, and *N*-methylmorpholine were refluxed over sodium for at least 5 h in an argon atmosphere and were then fractionally distilled. Acetic acid and methoxyacetic acid were used as received. HCl and KOH solutions were prepared by diluting prepackaged stock solutions (Baker Analytical). KOD was prepared by dissolving KOH in D_2O; the concentration of the resulting solution was determined by potentiometric titration. Acetonitrile was purchased from Fisher Scientific and used as received. Water was obtained from a Millipore water purification system. Water and acetonitrile used in the hydrolysis experiments at pH ⩽7.43 were degassed by the freeze–pump–thaw method to minimize substrate oxidation by dissolved oxygen over long reaction times. CD_3CN, D_2O and DCl were used as received.

Product analysis by NMR

All ^1H and ^{13}C NMR spectra for the product study were recorded in 75% CD_3CN–25% D_2O with a 250 MHz Bruker spectrometer.

Solutions and pH measurements

All kinetic experiments were conducted in 50% CH_3CN–50% H_2O (v/v) or 50% CH_3CN–50% D_2O (v/v) solutions at 25 °C, I = 0.1 M (KCl). All pH measurements were made with an Orion 611 pH-meter equipped with a glass electrode and a 'SureFlow' (Corning) reference electrode. Actual pH values were calculated by adding 0.18 to the measured pH, according to Allen and Tidwell[21] The pK_a values of triethylamine and *N*-methylmorpholine were determined by standard potentiometric techniques. The pK_a values of the other buffers were known from a previous study.[19]

Kinetics

Typical substrate concentrations were 5–10 × 10^{-5} M. Rates were measured in a Perkin-Elmer Lambda 2 or Hewlett-Packard 8452A diode array UV–VIS spectrophotometer. Kinetics were followed by monitoring the disappearance of the substrate at 364 nm. Rate constants (k_{obsd}) were obtained by computer fit programs (Applied Photophysics and Enzfitter[22]). Rates at pH ⩽10.31 were very low and hence k_{obsd} was determined by the initial rates method: reactions were monitored for 1–5 h, after which enough 2M KOH was added to neutralize the acidic component of the buffer and increase the pH of the solution to ≈12. Reactions were then further monitored until the infinity value (OD_∞) was reached. Pseudo-first-order rate constants were calculated according to eqn. (13), where S is the

$$k_{\mathrm{obsd}} = S/\Delta OD_0 \qquad (13)$$

slope of the plot of OD *vs.* time for the first 1–5 h, and $\Delta OD_0 = OD_\infty - OD_0$.

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