Reversibility of the Ring-opening Step in the Acid Hydrolysis of Cyclic Acetophenone Acetals

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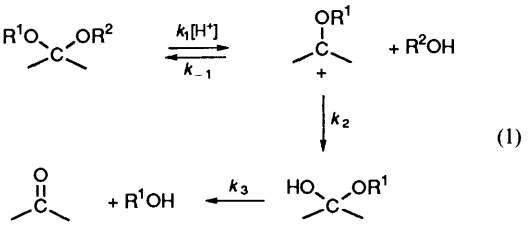
The acid-catalysed hydrolysis of the vinyl ethers α-(2-hydroxyethoxy)styrene **1a** or α-(3-hydroxypropoxy)styrene **1b** yields a mixture of acetophenone and a cyclic acetophenone acetal, 2-methyl-2-phenyl-1,3-dioxolane **3a** or 2-methyl-2-phenyl-1,3-dioxane **3b**. Ratios [acetophenone] : [**3**] have been determined by HPLC and by UV spectroscopy as 15 (from **1a**) and 10 (from **1b**). The acetals undergo further hydrolysis, but this is considerably slower than that of the vinyl ethers, and the above numbers represent products of kinetic control. These product ratios are equal to the rate constant ratios $k_2:k_{-1}$ for the partitioning of the oxocarbocations 1-(2-hydroxyethoxy)-1-phenylethyl **2a** or 1-(3-hydroxypropoxy)-1-phenylethyl **2b** between reaction with solvent water molecules and with the internal hydroxy group. These cations are also formed as intermediates in the hydrolysis of the cyclic acetals **3**. That k_2 is an order of magnitude greater than k_{-1} signifies that the rate-limiting step in this hydrolysis is the ring-opening forming the oxocarbocation, and that there is little reversibility in aqueous solutions. The hydrolysis reactions of these cyclic acetals are considerably slower than that of an acyclic analogue, the dimethyl acetal of acetophenone, by factors of 1.0×10^3 for **3a** and 1.8×10^2 for **3b**. This study demonstrates that these rate retardations cannot be accounted for by reversibility of the ring-opening step. The presence of the ring results in an inherent decrease in the rate constant for the H^+-catalysed formation of the oxocarbocation.

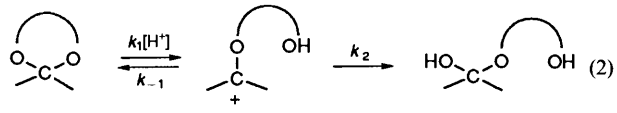
A three-stage reaction mechanism is now generally accepted for the acid-catalysed hydrolysis of acetals of aldehydes and ketones.[1,2] Two intermediates are involved, an oxocarbocation and a hemiacetal, and there is the possibility of three rate-limiting steps.



(1)

With acyclic acetals, the first stage, the acid-catalysed formation of the oxocarbocation, is generally rate-limiting. This reaction can occur with general-acid or specific-acid catalysis, depending on the stability of the cation and the nature of the leaving group.[2,3] The second stage, the hydration of the oxocarbonium ion is usually very fast.[4-7] The third stage occurs by hydronium ion, hydroxide ion and water-catalysed pathways.[8-10] While this is rapid at higher pH where the base-catalysed breakdown occurs, there are now examples where the H^+-rates of the first stage and third stage are comparable, so that the hemiacetal accumulates and the third stage is partially or wholly rate-limiting in the overall hyrolysis. This situation has been most clearly demonstrated for unsymmetrical acetals where the first stage is faster than the third because of a good leaving group[12,13] or because of the differential effects of ring strain.[14-17] However, a small amount of hemiacetal has been demonstrated to accumulate during the hydrolysis of the symmetrical dimethyl and diethyl acetals of benzaldehyde[18,19] and acetophenone.[20]

With acyclic acetals the first stage forming the oxocarbonium ion is essentially irreversible, since under normal hydrolytic conditions the concentration of water is in vast excess, so that $k_2 \gg k_{-1}[R^2OH]$.† With cyclic acetals however, this condition need not apply, since here the initial C–O bond breaking does not result in departure of the alcohol from the remainder of the molecule.



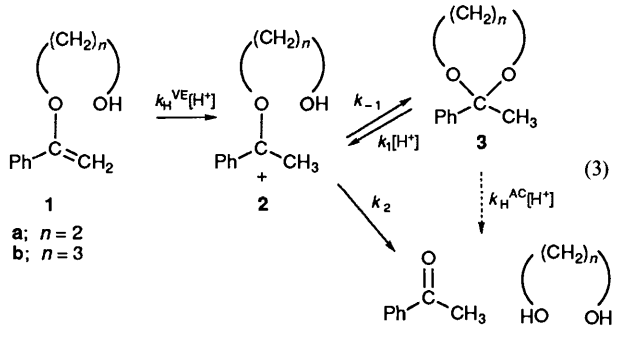
(2)

The reverse of the first step is thus intramolecular, and could conceivably compete with water addition. In a case where $k_{-1} > k_2$, the H^+-catalytic coefficient k_H for the disappearance of acetal becomes $k_1k_2:k_{-1}$. Such a mechanism has been classified $A2^+$,[21] because of the involvement of a water molecule in the rate-limiting step. Such a situation would mean that the observed k_H would be smaller than k_1, the rate constant for the H^+-catalysed ring-opening. This would explain the general observation that cyclic acetals undergo hydrolysis considerably more slowly than acyclic analogues ('by factors of 1.5 to 4.4 powers of ten').[21] In addition, entropies of activation for the hydrolysis of cyclic acetals, especially 1,3-dioxolanes, are usually more negative than those of acyclic derivatives.[21-25] This has been interpreted in terms of a bimolecular mechanism, although the values are not as negative as those of A2 processes such as ester hydrolysis,[26] leading to other explanations such as restricted rotation in the ring-opening.[22] Unequivocal evidence for reversibility has been obtained in several cases—for the ethylene glycol and trimethylenediol acetals of tropone, where the reactions of the intermediate oxocarbonium ion can be directly studied,[27] for ethylene glycol and cyclohexane-1,2-diol acetals of 4-dimethylaminobenzaldehyde, where curved rate–pH or buffer–pH plots point to changes in rate-limiting steps,[28,29] and for benzaldehyde acetals of norbornane-*exo*-2-*exo*-3-diol, where epimerization at the acetal carbon competes

† The convention is employed of expressing k_2 as a first-order rate constant. Thus, $k_2 = k_2'[H_2O]$ where k_2' = second-order rate constant for water addition to the cation and $[H_2O] = 55$ mol dm^{-3} For dilute solutions of acyclic acetals undergoing hydrolysis in water, $k_2'[H_2O]$ will always be greater than $k_{-1}[R^2OH]$.

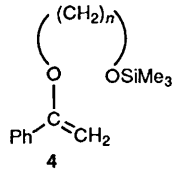
with hydrolysis.[30] In contrast, the 1,2-acetonide of glycerol does not racemize during hydrolysis, suggesting little reversibility (or if reversible, the C–O bond always forms with the oxygen that was originally attached).[24]

In this paper we address the question of the reversibility of the ring-opening in the hydrolysis of the ethylene glycol and trimethylene diol acetals of acetophenone **3a** and **3b**. The approach has involved the generation of the cation intermediate derived from the acetal *via* an independent route, the protonation of the vinyl ether **1**. The ratio of acetal to acetophenone produced in this hydrolysis is equal to the partitioning ratio $k_{-1}:k_2$, the ratio that determines whether or not the acetal hydrolysis is reversible. This particular system was chosen since oxocarbocations of type **2** are known to form as free cations in water,[4-7] and thus should have sufficient lifetime to select between the internal and external nucleophile (see later). In addition, the H^+-catalysed hydrolysis of vinyl ethers of type **1** was known to be considerably faster than the hydrolysis of the cyclic acetals **3** ($k_H^{VE} > k_H^{AC}$), so that the determination of the products of kinetic control in the hydrolysis of **1** was anticipated. Moreover the breakdown of hemiacetals derived from acetophenone is very fast, even under acidic conditions,[20] so that vinyl ether and acetal hydrolyses can be studied without the added complication of considering this step.



Results

The vinyl ethers **1a** and **1b** were prepared from the acetals **3a** and **3b**, by opening the ring with trimethylsilyl trifluoromethanesulfonate in the presence of an equivalent amount of Hunig's base,[31] followed by removal of the trimethylsilyl group of the so-formed vinyl ethers **4a** and **4b**. The latter process was



carried out *in situ*, since attempts to isolate the deprotected compounds resulted in significant decomposition. The trimethylsilyl group proved to be removable in acetonitrile–water mixtures containing a small amount of sodium carbonate. HPLC analyses of these solutions showed the clean conversion of the precursor **4** into a single new compound, with no contamination from acetophenone or the acetal **3**.

Product analyses were carried out with HPLC, employing acetate and formate buffers with pH in the range 3.5–4.5. Quantitation was based upon standard curves of peak area *versus* concentration, using authentic samples of acetophenone and the acetals **3**, and the base solutions of **1**. Results of a typical experiment are shown in Fig. 1. With both vinyl ethers,

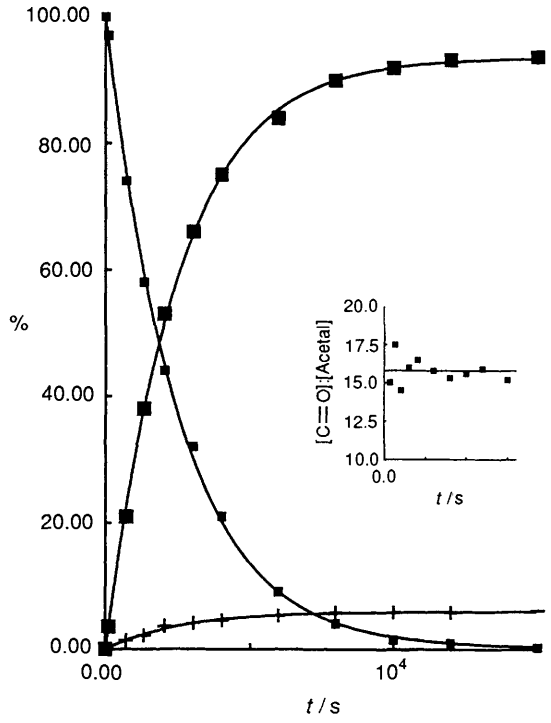


Fig. 1 Disappearance of α-(2-hydroxyethoxy)styrene **1a** (■), and appearance of acetophenone (■) and 2-methyl-2-phenyl-1,3-dioxolane **3a** (+) in a formate buffer ([HCOOH] = 0.01, [HCOONa] = 0.01 mol dm^{-3}, pH = 3.66 at ionic strength 0.1 mol dm^{-3} and 25.0 °C). The insert plots the [acetophenone]:[**3a**] ratio as a function of time.

acetophenone is the major product, but the appropriate acetal can be detected, the two products forming with the same exponential rate as that observed for the decay of the vinyl ether. The acetals of course are also undergoing hydrolysis, and at very long times, only acetophenone is observed. The acetal hydrolysis, however, is considerably slower than that of the vinyl ethers. This is demonstrated in terms of the H^+-catalytic coefficients in the next section. For the experiments in the carboxylate buffers, the rate difference is even larger, since the vinyl ether hydrolysis is catalysed by the carboxylic acid as well, while the acetal hydrolysis is not. As shown in the insert in Fig. 1, even at relatively substantial conversions of **1**, the acetophenone:acetal ratio is, to within experimental error, constant. This ratio is also independent of pH and buffer concentration. The values for the two compounds are given in Table 1, under the heading $k_2:k_{-1}$.

Spectroscopic kinetic studies were carried out in HCl solutions of various concentrations. A typical result is illustrated in Fig. 2. The absorption spectra of α-alkoxystyrenes overlap that of acetophenone, although there are differences in intensity; at the λ_{max} of the ketone, 250 nm, the vinyl ether is about 70% as strongly absorbing. Acetophenone acetals also absorb in the same region, but very much more weakly, the extinction coefficient being 3% of that of acetophenone at 250 nm. Two-component increases in absorbance at 250 nm are in fact observed with **1**. In simple terms, the first increase represents the conversion of the vinyl ether into acetophenone plus a small amount of acetal, and the second, the formation of additional ketone associated with the slower further hydrolysis of the acetal. These changes can be fit with the use of non-linear least squares to the equation for a double exponential, eqn. (4),

$$A = A_\infty + X_1 \exp(-k_{fast}t) + X_2 \exp(-k_{slow}t) \quad (4)$$

where A_∞ is the absorbance at overall completion, k_{fast} and k_{slow} are the exponential coefficients for the two kinetic phases, and X_1 and X_2 are pre-exponential factors. As shown in the

Table 1 Rate constants in the hydrolysis of acetophenone acetals and α-alkoxystyrenes (25.0 °C, ionic strength 0.1 mol dm^{-3})

Substrate	Parameter	Value
2-Methyl-2-phenyl-1,3-dioxolane	$k_2:k_{-1}$	15.5 ± 1.0[a]
	$k_2:k_{-1}$	13.7 ± 0.8[b]
	k_H^{Ac}/dm^{-3} mol s^{-1}	0.510 ± 0.030[c]
	k_H^{Ac}/dm^{-3} mol s^{-1}	0.521 ± 0.023[d]
	k_1/dm^{-3} mol s^{-1}	0.55[e]
2-Methyl-2-phenyl-1,3-dioxane	$k_2:k_{-1}$	9.9 ± 0.7[a]
	$k_2:k_{-1}$	10.6 ± 0.6[b]
	k_H^{Ac}/dm^{-3} mol s^{-1}	3.09 ± 0.04[c]
	k_H^{Ac}/dm^{-3} mol s^{-1}	3.11 ± 0.12[d]
	k_1/dm^{-3} mol s^{-1}	3.40[e]
Acetophenone dimethyl acetal	$k_1 = k_H^{Ac}$/dm^{-3} mol s^{-1}	525 ± 15[f]
		750[g]
α-(2-Hydroxyethoxy)styrene	k_H^{VE}/dm^{-3} mol s^{-1}	42.5 ± 1.3[h]
α-(3-Hydroxypropoxy)styrene	k_H^{VE}/dm^{-3} mol s^{-1}	87.9 ± 1.9[h]
α-Methoxystyrene	k_H^{VE}/ dm^{-3} mol s^{-1}	53.3[i]
α-Ethoxystyrene	k_H^{VE}/dm^{-3} mol s^{-1}	118[i]

[a] Based upon analysis of products of hydrolysis of **1**. [b] Based upon analysis of absorbance changes in the hydrolysis of **1**. [c] $k_{slow}/[H^+]$ in experiments starting with **1**. [d] Starting with acetal. [e] $k_H^{Ac} \times (1 + k_{-1}/k_{-2})$. [f] This work. [g] Reference 20, ionic strength 0.5 mol dm^{-3}. [h] $k_{fast}/[H^+]$. [i] A. J. Kresge, D. S. Sagatys and H. L. Chen, *J. Am. Chem. Soc.*, 1977, **99**, 7228.

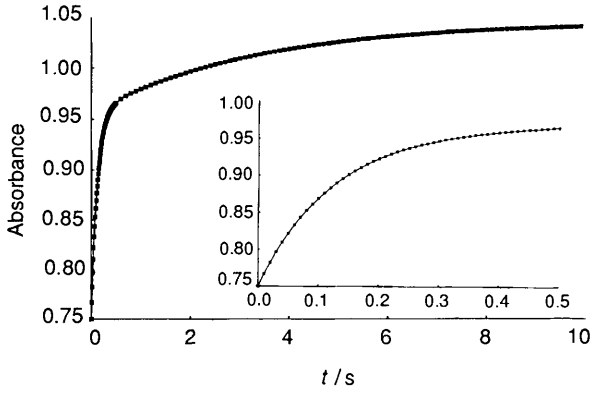


Fig. 2 Absorbance change at 250 nm (λ_{max} of acetophenone) on mixing α-(3-hydroxypropoxy)styrene **1b** (1.5×10^{-4} mol dm^{-3}) in 0.002 mol dm^{-3} NaOH with an equal volume of 0.200 mol dm^{-3} HCl. Data were computer fit to eqn. (4) using non-linear least-squares to provide the parameters $A_\infty = 1.045$, $k_{fast} = 8.40\ s^{-1}$, $k_{slow} = 0.303\ s^{-1}$, $X_1 = -0.206$, and $X_2 = -0.089$.

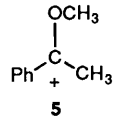
Appendix, k_{fast} is equal to the observed rate constant for disappearance of the vinyl ether ($k_H^{VE}[H^+]$), while k_{slow} is the observed rate constant for the hydrolysis of the acetal ($k_H^{Ac}[H^+]$). Both k_{fast} and k_{slow} exhibit the expected linear dependence in H^+-concentration, and, as shown in Table 1, the values of k_H^{Ac} are in excellent agreement with those obtained starting with the acetal. While the expression for X_1 is complex, the pre-exponential X_2 provides the initial acetal:acetophenone partitioning, eqn. (5), where $\varepsilon_3:\varepsilon_{C=O}$ is the ratio of

$$\frac{k_{-1}}{k_{-1} + k_2} = \left(\frac{-X_2}{A_\infty(1 - \varepsilon_3/\varepsilon_{C=O})}\right)\left(1 - \frac{k_{slow}}{k_{fast}}\right) \quad (5)$$

extinction coefficients of the acetal and acetophenone. As can be seen in Table 1, values of $k_2:k_{-1}$ calculated with this method are in good agreement with those obtained from the product analyses. It can be noted that $k_{-1}:(k_{-1} + k_2)$ is in fact approximately equal to $-X_2:A_\infty$, since both $\varepsilon_3:\varepsilon_{C=O}$ and $k_{slow}:k_{fast}$ are significantly less than one.

Discussion

There is now substantial evidence that vinyl ethers undergo hydrolysis with rate-limiting protonation of the C=C bond, affording oxocarbocation intermediates analogous to those obtained during the hydrolysis of acetals.[32,33] Thus, hydroxy-substituted vinyl ethers such as **1** give an independent entry into the oxocarbocations formed with cyclic acetals, providing a way of measuring the partitioning of this intermediate between internal and external nucleophiles. There are two further requirements for this to work. The first, which is easily demonstrated in the present case, is that the vinyl ether protonation be sufficiently faster than the hydrolysis of the cyclic acetal that the products of kinetic control from the former can be readily determined. The second is that the cations produced from the acetal and vinyl ether precursors indeed be identical. These two cations are formed in different ways, and are likely initially in different conformations, so that what is required is that they have sufficient lifetime to achieve conformational equilibrium. This can also be demonstrated to be the likely situation for the cations involved in this work. The lifetime of the methoxy analogue **5** in water has been estimated,



5

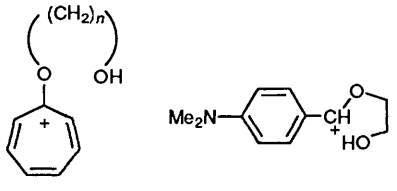
as 10 ns[4] and 20 ns[7] from competition experiments with sulfite and azide and the assumption of diffusion control in the added nucleophile, and as 18 ns by extrapolation from direct measurements in concentrated aqueous H_2SO_4.[5] These are clearly in good agreement, and in fact the first number is now considered to be a slight over-estimate.[7] The cations **2a** and **2b** of course have different alkoxy substituents, but it can be argued that these will have little effect. For example, considering the rate constants k_H^{VE} for the vinyl ether protonation as an indicator of cation stability, the 2-hydroxyethyl group of **2a** has an effect similar to methyl, while 3-hydroxypropyl of **2b** is slightly more stabilizing. These effects are, however, small, so

that 10–20 ns is not an unreasonable estimate for the lifetimes of the two hydroxy-substituted cations as well. This should be sufficient time for these cations to have achieved conformational equilibrium before reacting with water (or with the internal hydroxy group). It will also mean that there should be equilibration of the solvent shell about the cation.

With this background, the conclusion of this study is that with both systems the ring-closing reaction is an order of magnitude slower than the reaction with solvent water molecules. Thus, the rate-limiting step in the hydrolysis of the cyclic acetophenone acetals **3a** and **3b** is essentially the H^+-catalysed ring-opening. The second-order rate constant for this hydrolysis (k_H^{Ac}) is given by $k_1/(1 + k_{-1}/k_2)$, and, since $k_{-1}/k_2 \sim 0.1$, this is only slightly reduced from k_1. This leads to the second important conclusion, namely that the significant differences in rates between the cyclic acetals and the acyclic analogue (Table 1) cannot be accounted for by reversibility of the ring-opening step. The presence of the ring results in an inherent decrease in the rate constant k_1 for the H^+-catalysed formation of the oxocarbocation.

A further interesting result is the close similarity between the two cyclic systems. In particular, the rate constant k_{-1} for forming the five-membered ring from **2a** is very similar to the value for forming the six-membered ring from **2b**. This is surprising since the latter is a 6-*endo-trig* process, allowed by Baldwin's rules, while the former constitutes a formally disallowed 5-*endo-trig* reaction.[34] Both processes are in fact slightly faster than the addition of water, considering the latter in bimolecular terms. The differences, however, are not large,* and the conclusion must be that the cyclizations are neither especially fast nor especially slow. The explanation for this is not immediately obvious. Deslongchamps and co-workers have recently analysed a similar ring closing in terms of the energetics of the conformers that are capable of reacting, and such factors may be important here as well.[37]

Partitioning ratios for the hydrolysis of cyclic acetals have been determined in two other related systems, the tropone derivatives **6a** and **6b**,[27] and the *p*-dimethylaminobenzaldehyde-derived **7**.[28] In these cases ring closure is favoured to a small



6a; $n = 2$, $k_{-1}:k_2 = 4.3$
6b; $n = 3$, $k_{-1}:k_2 = 1.6$

7; $k_{-1}:k_2 = 1–2$

extent over the solvent reaction, so that there is significant reversibility in the hydrolysis of the cyclic acetal. These systems differ from the actophenone acetals, in that the cations are considerably more stable, with significant charge delocalization in the tropylium ring in **6** and to the amino group in **7**. In this sense therefore the cyclizations have a component of an *exo-trig* reaction. This may mean that the angle of approach of the intramolecular OH group in the ring-closing reaction is slightly different, resulting in the reaction becoming somewhat more favourable than the reaction with water.

Experimental

2-Methyl-2-phenyl-1,3-dioxolane (**3a**), 2-methyl-2-phenyl-1,3-dioxane (**3b**) and acetophenone dimethyl acetal are known compounds and were prepared by standard routes.[38–41]

The vinyl ethers **4** were prepared following the procedure of Gassman and Burns,[31] typically by reacting 0.030 mol of the acetal **3** with 0.036 mol of trimethylsilyl trifluoromethanesulfonate and 0.040 mol of ethyldiisopropylamine in 50 cm^3 of chloroform for 4 h. Products were isolated as previously described,[31] and were purified by vacuum distillation through a short column.

α-(2-*Trimethylsilyloxyethoxy*)*styrene* (**4a**): b.p. 69–71 °C (0.4 mmHg); $\delta(CDCl_3)$ 0.16 (s, 9 H), 3.96 (s, 4 H), 4.21 (d, 1 H, J = 2.8 Hz), 4.66 (d, 1 H, J = 2.8 Hz), 7.3–7.4 (m, 3 H), 7.6–7.7 (d, 2 H) (Found: C, 65.9; H, 8.6. Calc. for $C_{13}H_{20}O_2Si$: C, 66.05; H, 8.53%).

α-(3-*Trimethylsilyloxypropoxy*)*styrene* (**4b**): b.p. 76–78 °C (0.4 mmHg); $\delta(CDCl_3)$ 0.15 (s, 9 H), 2.05 (q, 2 H, J = 6.2 Hz), 3.83 (t, 2 H, J = 6.2 Hz), 3.97 (t, 2 H, J = 6.2 Hz), 4.23 (d, 1 H, J = 1.7 Hz), 4.67 (d, 1 H, J = 1.7 Hz), 7.3–7.4 (m, 3 H), 7.6–7.7 (d, 2 H) (Found: C, 67.4; H, 8.9. Calc. for $C_{13}H_{20}O_2Si$: C, 67.15; H, 8.86%).

HPLC separations and quantitative analyses of products were carried out with a Waters 600E multisolvent delivery system, equipped with a Waters 486 tunable absorbance detector. A Waters Radial-Pak™ C18 column was employed, with isocratic elution with 70:30 methanol–water at 1 cm^3 per min. The detector wavelength was set to 250 nm for the first two peaks, corresponding to the acetophenone (4.5 min) and the vinyl ether **1** (6 min for **1a**, 6.5 min for **1b**) after which it was changed to 220 nm for analysis of the acetal **3** (7.5 min for **3a**, 8.0 min for **3b**).

Stock solutions of **1** of concentration 0.01–0.1 mol dm^{-3} were prepared by adding the protected vinyl ethers **4** to 50:50 acetonitrile–water containing a small amount (*ca.* 2 mmol dm^{-3}) of Na_2CO_3. Quantitative removal of the trimethylsilyl group was rapid, as verified with the above HPLC system. Thus, solutions of **4** prepared without the base gave a single HPLC peak with a long retention time (~ 30 min), while the solutions with base gave a single peak with the retention time above. No peaks for acetophenone or the appropriate acetal **3** were present. Repeated injections showed that the base solutions of **1** were stable over several days.

Reactions were initiated by adding 0.1 cm^3 of the stock solution to 10 cm^3 of an appropriate aqueous acid. The ionic strength of the aqueous solution was maintained with sodium chloride at 0.1 mol dm^{-3}, and the solution was thermostatted before and after addition at 25.0 °C. This solution was analysed at appropriate time intervals with the above HPLC system. Quantitative measurements were based upon standard curves constructed with the authentic samples of acetophenone and its acetals.

Spectroscopic measurements were carried out with a Cary 2200 UV–VIS spectrophotometer or a Hi-Tech Scientific SF-51 stopped-flow spectrometer. Reactions in the former were carried out by adding the stock solution of **1** to a thermostatted aqueous solution in the UV cuvette. For the stopped-flow reactions, the stock solution was diluted 100-fold into 0.002 mol dm^{-3} NaOH, and this solution mixed in a 1:1 ratio with the appropriate acid. Increases in absorbance at 250 nm were monitored, and the absorbance–time traces analysed by non-linear least-squares fitting to the double exponential equation [eqn. (4)].

Acknowledgements

Acknowledgement is made to the Natural Sciences and Engineering Research Council of Canada for support of this research in the form of a research grant (R. A. M.) and an undergrate research scholarship (B. W.).

* Part of the difference could arise from the inherently better nucleophilicity of alcohols towards carbocations.[35,36]

Appendix

Derivation of Absorbance–Time Dependence.—For the kinetic system (**Ac** = acetophenone)

$$\mathbf{1} \xrightarrow{k_a} \mathbf{3}$$

$$\mathbf{1} \xrightarrow{k_b} \mathbf{Ac}$$

$$\mathbf{3} \xrightarrow{k_c} \mathbf{Ac}$$

the solution to the rate equations, with at zero time, $[\mathbf{1}] = [\mathbf{1}_0]$, $[\mathbf{3}] = 0 = [\mathbf{Ac}]$, is

$$[\mathbf{1}] = [\mathbf{1}_0] \exp[-(k_a + k_b)t]$$

$$[\mathbf{3}] = [\mathbf{1}_0]\left(\frac{k_a}{k_c - (k_a + k_b)} \{\exp[-(k_a + k_b)t] - \exp(-k_c t)\}\right)$$

$$[\mathbf{Ac}] = [\mathbf{1}_0]\left\{1 - \frac{k_c - k_b}{k_c - (k_a + k_b)} \exp[-(k_a + k_b)t] + \frac{k_a}{k_c - (k_a + k_b)} \exp(-k_c t)\right\}$$

For spectroscopic measurements, the observed absorbance is the sum of those due to the three compounds, so that for a path-length of unity,

$$A = \varepsilon_1[\mathbf{1}] + \varepsilon_3[\mathbf{3}] + \varepsilon_{Ac}[\mathbf{Ac}]$$

where the ε values represent individual extinction coefficients. The absorbance after complete conversion into acetophenone is A_∞ and this equals $\varepsilon_{Ac}[\mathbf{1}_0]$. Thus, after substitution of the integrated rate equations,

$$A = A_\infty + A_\infty\left[\frac{\varepsilon_1}{\varepsilon_{Ac}} + \frac{\varepsilon_3}{\varepsilon_{Ac}}\left(\frac{k_a}{k_c - (k_a + k_b)}\right) - \left(\frac{k_c - k_b}{k_c - (k_a + k_b)}\right)\right] \exp[-(k_a + k_b)t] + A_\infty\left(\frac{k_a(1 - \varepsilon_3/\varepsilon_{Ac})}{k_c - (k_a + k_b)}\right) \exp(-k_c t)$$

The experimental absorbance–time curves (Fig. 2) are fit to a double exponential equation with five variables: A_∞, two exponential constants $k_{fast} > k_{slow}$, and two pre-exponential factors X_1 and X_2, each of which is negative at the λ_{max} of acetophenone (250 nm) since absorbance increases throughout.

$$A = A_\infty + X_1 \exp(-k_{fast} t) + X_2 \exp(-k_{slow} t)$$

The following relations then apply,

$k_{fast} = k_a + k_b$ = rate constant for disappearance (protonation) of vinyl ether **1**.

$k_{slow} = k_c$ = rate constant for hydrolysis of acetal **3** to acetophenone.

X_1 = complex

$$X_2 = A_\infty\left(\frac{k_a(1 - \varepsilon_3/\varepsilon_{Ac})}{k_c - (k_a + k_b)}\right)$$

On rearrangement, and appropriate substitution of k_{fast} and k_{slow},

$$\frac{k_a}{k_a + k_b} = \left(\frac{-X_2}{A_\infty(1 - \varepsilon_3/\varepsilon_{Ac})}\right)\left(1 - \frac{k_{slow}}{k_{fast}}\right)$$

The quantity $k_a/(k_a + k_b)$ is the fraction of the vinyl ether **1** that is converted into acetal **3** under conditions of kinetic control, and this ratio is directly equally to $k_{-1}/(k_{-1} + k_2)$.

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