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Rate and Equilibrium Constants for the Formation and Decomposition of the Tetrahedral Intermediates of the Methanolysis of Methyl Benzoates

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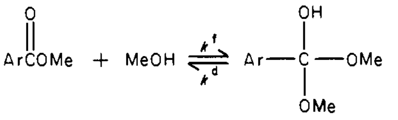
Abstract: Rate constants and equilibrium constants have been obtained for the equilibration of the tetrahedral intermediate $ArC(OMe)_2OH$ with methanol and methyl benzoate in 50% dioxane:water. Rate constants in the decomposition direction have been measured by generating the tetrahedral intermediate from an anilide acetal. Rate constants in the formation direction have been measured from the rate of exchange of CH_3OH with $PhCOOCD_3$. The equilibrium constant is evaluated as the ratio of the two rate constants. For $PhC(OMe)_2OH$ the formation equilibrium constant so obtained is 2.2×10^{-12} M^{-1}; this shows good agreement with a value obtained with use of a thermodynamic approach by Guthrie and Cullimore (*Can. J. Chem.* **1980**, *58*, 1281-94) for the intermediate $PhC(OH)_2OMe$. The formation (and decomposition) of $ArC(OMe)_2OH$ is subject to catalysis by both general acids and general bases, and the mechanisms of these reactions are discussed. The species $H_2PO_4^-$ shows enhanced reactivity, suggested to be due to a bifunctional mode of catalysis.

Acyl transfer reactions have been recognized for sometime now to proceed via discrete tetrahedral addition intermediates.[1,2] Although these intermediates are not normally observed in the acyl transfer reaction,[3] several experiments have recently been reported of their observation when generated from other more reactive precursors.[4]

In the preceding paper[5] we reported the detection of the species $ArC(OMe)_2OH$ as a transient intermediate in the hydrolysis of $ArC(OMe)_2NMeAr'$. This intermediate is the tetrahedral intermediate of the degenerate methanolysis of a methyl benzoate, and obviously bears a close relation to the tetrahedral intermediate of the hydrolysis of the same ester. Its observation from the anilide acetal precursor provides an opportunity to *directly* study its kinetics of decomposition and in this paper we report the results of such a study.



$$ArC(=O)OMe + MeOH \underset{k^d}{\overset{k^f}{\rightleftharpoons}} Ar-C(OH)(OMe)-OMe \quad (1)$$

Rates of formation k^f have also been measured with use of an appropriate isotopic tracer, and coupled with the decomposition rate constants to provide the equilibrium constant. This quantity is clearly not accessible by direct measurement since the equilibrium concentration of the adduct is so low. A method has been devised by Guthrie for estimating free energies of formation of tetrahedral intermediates, based on the measurement of free energies of stable analogues.[6,7] It is obviously of importance to see how our kinetically based numbers compare.

Table I. Rate Constants (50% Dioxane:Water, 25 °C) for $4\text{-}XC_6H_4C(OMe)_2OH$ Decomposition

constant[a]	4-MeO	4-Me	H	4-Br
k_{H^+}	4.5×10^4	3.0×10^4	1.9×10^4	6.6×10^3
k_0	0.7	0.7	0.6	0.5
k_{OH^-}	*b*	*b*	4×10^8	*b*
$k_{H_3PO_4}$	5.3×10^2	4.0×10^2	2.7×10^2	1.6×10^2
$k_{H_2PO_4^-}$	2.1×10^2	2.0×10^2	1.9×10^2	2.0×10^2
k_{CNCH_2COOH}	*b*	*b*	5.5×10^2	*b*
k_{ClCH_2COOH}	100	66	36	18
$k_{ClCH_2COO^-}$	*c*	*c*	4	8
k_{HCOOH}	38	29	13	9
k_{HCOO^-}	21	22	30	32

[a] Units of M^{-1} s^{-1}, except for k_0 (s^{-1}). [b] Not determined. [c] Not significant.

Table II. Exchange of Trideuteriomethyl 4-Methoxybenzoate in 50% Dioxane Containing 1 M HCl and 2.47 M MeOH

time, days	$ArCOOCH_3/ArCOOCD_3$[a]	k_{Ex},[b] s^{-1}
0	0.0000[c]	
12	0.0417	3.9×10^{-8}
14	0.0471	3.8×10^{-8}
26	0.0799	3.5×10^{-8}
36	0.1173	3.6×10^{-8}

[a] Ratio of peaks in mass spectra at 166:169. Error ± 0.0005. [b] $1/t \ln(1\text{-}ArCOOCH_3/ArCOOCD_3)$. [c] No peak at 166.

Experimental Section

The preparation of the anilide acetals and the kinetic methods used to study the hemiorthoester decomposition are described in the preceding paper.[5]

Trideuteriomethyl benzoates were prepared from the appropriate benzoyl chloride and perdeuteriomethanol (Aldrich). The labeled ester (0.5 g) was dissolved in 500 mL of a solution made up by placing in a volumetric flask 50% by volume dioxane, a known amount of CH_3OH, sufficient HCl to make the final HCl concentration 1 M, and water. The solution was placed in a water bath thermostated at 25 °C, and at appropriate times, a 100-mL portion was removed and extracted with ether, the ether portion washed with saturated sodium bicarbonate and dried

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[1] Bender, M. L. *Chem. Rev.* **1960**, *60*, 53-113.

[2] Jencks, W. P. "Catalysis in Chemistry and Enzymology"; McGraw-Hill: New York, 1968.

[3] A number of stable molecules with a tetrahedral intermediate structure are known, but these all have some special feature which results in the stabilization of the adduct form and/or destabilization of the carbonyl form. A summary of these examples can be found in reference 4b.

[4] (a) Capon, B.; Gall, J. H.; Grieve, D. M. A. *J. Chem. Soc., Chem. Commun.* **1976** 1034-1035. (b) Capon, B.; Grieve, D. M. A. *J. Chem. Soc., Perkin Trans. 2* **1980**, 300-302. (c) Capon, B.; Ghosh, A. K., *J. Am. Chem. Soc.* **1981**, *103*, 1765-1768. (d) Ahmad, M.: Bergstrom, R. G.; Cashen, M. J.; Kresge, A. J.; McClelland, R. A.; Powell, M. F. *J. Am. Chem. Soc.* **1977**, *99*, 4827-4829. (e) Ahmad, M.; Bergstrom, R. G.; Cashen, M. J.; Chiang, Y.; Kresge, A. J.; McClelland, R. A.; Powell, M. F. *ibid.* **1979**, *101*, 2669-2677. (f) McClelland, R. A.; Ahmad, M. *J. Org. Chem.* **1979**, *44*, 1855-1860. (g) McClelland, R. A.; Ahmad, M.; Bohonek, J.; Gedge, S. *Can. J. Chem.* **1979**, *57*, 1531-1540. (h) McClelland, R. A.; Alibhai, M. *Ibid.* **1981**, 59, 1169-1176.

[5] McClelland, R. A.; Patel, G. *J. Am. Chem. Soc.*, preceding paper.

[6] (a) Guthrie, J. P. *J. Am. Chem. Soc.*, **1973**, *95*, 6999-7003. (b) Guthrie, J. P. *Ibid.* **1974**, *96*, 3608-3615. (c) Guthrie, J. P. *Can. J. Chem.* **1975**, *53*, 898-906. (d) Guthrie, J. P. *Ibid.* **1976**, *54*, 3562-3573. (e) Guthrie, J. P.; Cullimore, P. A. *Can. J. Chem.* **1980**, *58*, 1281-1294.

[7] See also: Fastrez, J. *J. Am. Chem. Soc.* **1977**, *99*, 7004-7013.

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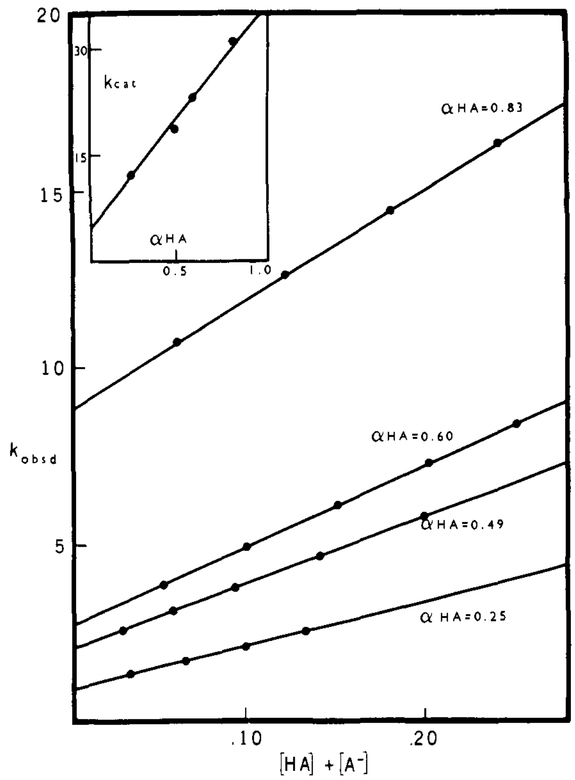


Figure 1. Observed rate constants for $PhC(OMe)_2OH$ decomposition in chloroacetic acid buffers. The insert plots the slope of the lines of the main figure vs. the fraction of the buffer in the acid form.

($MgSO_4$), and the ether removed. The remaining liquid was analyzed directly on an AEI MS9 mass spectrometer. The quantity measured, using a procedure previously described,[8] was the intensity ratio of peaks corresponding to $ArCOOCH_3$ and $ArCOOCD_3$.

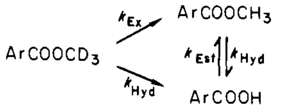
Results

Kinetics of Tetrahedral Intermediate Decomposition. As discussed in the previous paper,[5] the kinetic behavior associated with product formation from $ArC(OMe)_2NMeAr'$ in acid solution (pH <6) directly represents the kinetic behavior of the decomposition of $ArC(OMe)_2OH$. This decomposition is first order in a given solution, and the observed rate constants follow the pattern expected of the breakdown of a tetrahedral adduct of the carbonyl group.[9,10] Rate–pH profiles can be found in the preceding paper.

$$k_{obsd} = k_{H^+}{}^{d}[H^+] + k_0{}^{d} + k_{OH^-}{}^{d}[OH^-] + k_{HA}{}^{d}[HA] + k_B{}^{d}[B] \quad (2)$$

Figure 1 illustrates the effect of buffers; catalysis by both general acids and general bases is found. The various catalytic coefficients are summarized in Table I.

Kinetics of Formation of Tetrahedral Intermediate. Trideuteriomethyl benzoates were dissolved in solutions containing an acid catalyst, unlabeled methanol, and water (and 50% dioxane), and the exchange of CD_3O for CH_3O in the ester was followed by measuring in a mass spectrometer the ratio [$ArCOOCH_3$]/[$ArCOOCD_3$]. The result of a typical run is shown in Table II. With both methanol and water present, a hydrolysis reaction can also occur, and the following equation can be derived on rigorously solving the differential equations for the system.



(3)

Table III. Rate Constants for Methanol Exchange of Methyl Benzoates in 50% Dioxane Containing 1 M HCl

ester	[MeOH]	k_{Ex}, s⁻¹	$k_{H^+}{}^{f}$,^{a} M⁻¹ s⁻¹
$C_6H_5COOCD_3$	1.23	2.7×10^{-8}	3.8×10^{-8}
$C_6H_5COOCD_3$	2.47	5.2×10^{-8}	4.2×10^{-8}
$C_6H_5COOCD_3$	4.95	1.2×10^{-7}	5.0×10^{-8}
$4\text{-}MeOC_6H_4COOCD_3$	2.47	3.7×10^{-8}	3.0×10^{-8}
$4\text{-}BrC_6H_4COOCD_3$	2.47	5.7×10^{-8}	4.6×10^{-8}

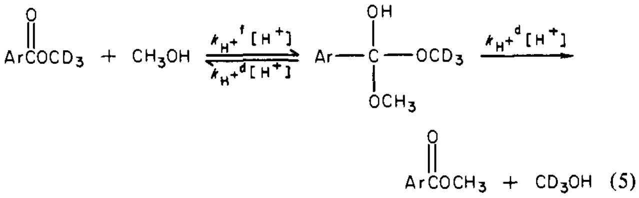
^{a} $2k_{Ex}/[MeOH][H^+]$.

$$k_{Ex} = 1/t \ln\left(1 - \frac{[ArCOOCH_3]}{[ArCOOCD_3]}\right) - 1/t \ln\left\{\left(\frac{k_{Est}}{k_{Hyd} + k_{Est}}\right)e^{k_{Hyd}t} + \left(\frac{k_{Hyd}}{k_{Hyd} + k_{Est}}\right)e^{-k_{Est}t}\right\} \quad (4)$$

The derivation makes the assumptions that steps reforming $ArCOOCD_3$ can be ignored, there is no isotopic effect on k_{Hyd}, and at zero time there is no $ArCOOCH_3$ present.

Obviously, accurate evaluation of k_{Ex}, the desired quantity, requires k_{Est} and k_{Hyd} to be known. A reasonable estimate of k_{Ex} can however be made in the absence of these. The substitution of various combinations of k_{Ex}, k_{Est}, and k_{Hyd} into eq 4 reveals that the contribution of the term containing k_{Est} and k_{Hyd} is small providing that k_{Ex} is not several orders of magnitude smaller than k_{Hyd} or k_{Est}[12] and providing that the exchange is allowed to occur only for a short period of time. In fact, in the limit as $t \to 0$ the extra term containing k_{Hyd} and k_{Est} goes to zero. Exchange kinetic runs were therefore carried out to only small degrees of conversion and exchange rate constants calculated at various times by ignoring the additional term (see Table II). Evidence that the values of k_{Ex} so calculated must be fairly reliable can be seen in the constancy of the numbers obtained. It can be shown with use of eq 4 that if the contribution from the extra term were important, the apparent k_{Ex} would increase with time.

First-order rate constants for exchange, evaluated as the average of several measurements as in Table II, are listed in Table III. To convert these to a formation rate constant for the tetrahedral intermediate, the assumption is made that this intermediate has an equal probability of breakdown in either direction, so that the formation rate is simply twice the exchange rate. Conversion



$$ArC(=O)OCD_3 + CH_3OH \underset{k_{H^+}{}^{d}[H^+]}{\overset{k_{H^+}{}^{f}[H^+]}{\rightleftharpoons}} Ar\text{—}C(OH)(OCH_3)\text{—}OCD_3 \xrightarrow{k_{H^+}{}^{d}[H^+]} ArC(=O)OCH_3 + CD_3OH \quad (5)$$

to a third-order rate constant, $k_{H^+}{}^{f}$, first order in ester, methanol, and hydronium ion is then carried out by dividing by the concentrations of methanol and hydronium ion (Table III).

The equilibrium constant for formation of the tetrahedral intermediate from methanol and methyl benzoate can now be evaluated as the ratio $k_{H^+}{}^{f}/k_{H^+}{}^{d}$. These values are listed in Table IV. Strictly speaking the two rate constants used in this calculation should refer to the same solvent conditions. There are in fact slight differences. The values of $k_{H^+}{}^{d}$ are measured in 50% dioxane:water, while values of $k_{H^+}{}^{f}$ are measured in a dioxane: water solution which contains methanol as well. This is of course

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[8] McClelland, R. A.; Ahmad, M. *J. Am. Chem. Soc.* **1977**, *99*, 5356–5360.

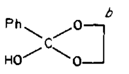
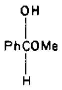
[9] Bell, R. P. *Adv. Phys. Org. Chem.* **1966**, *4*, 1–29.

[10] Funderburk, L. H.; Aldwin, L.; Jencks, W. P. *J. Am. Chem. Soc.* **1978**, *100*, 5444–5459.

[11] (a) There can be problems associated with the study of buffer catalysis in a mixed aqueous solvent such as dioxane:water because of salt effects.[11b] We feel, however, that the buffer contribution to the overall rate constant in the present case is sufficiently large (Figure 1) that there can be little doubt as to its reality. (b) Salomaa, P.; Kankaanpera; Lahti, M. *J. Am. Chem. Soc.* **1971**, *93*, 2084–2085.

[12] (a) This appears unlikely since water and methanol are normally regarded as having similar nucleophilicities.[12b] Moreover, literature values of k_{Est} for the acid hydrolysis of methyl benzoate are of the same order of magnitude as the values of k_{Ex} measured here.[12c] (b) Wenthe, A. M.; Cordes, E. H. *J. Am. Chem. Soc.* **1965**, *87*, 3173–3180. (c) Kirby, A. J. In "Comprehensive Chemical Kinetics", Bamford, C. H.; Tipper, C. F. H., Eds.; Elsevier: Amsterdam, 1972; Vol. 10, pp 57–208.

Table IV. Rate and Equilibrium Constants for the Formation of Hemiorthoesters and Hemiacetals

parameter	$ArC(OMe)_2OH^a$ for Ar = 4-$MeOC_6H_4$	C_6H_5	4-BrC_6H_4	 [b]	 $PhCH(OH)OMe$ [c]
K^f, M^{-1}	6.7×10^{-13}	2.2×10^{-12}	7.0×10^{-12}	$2.5 \times 10^{-9\,d}$	4×10^{-3}
$k_{H^+}{}^f$, $M^{-2}\,s^{-1}$	3.0×10^{-8}	4.2×10^{-8}	4.6×10^{-8}	$8 \times 10^{-7\,e}$	1×10^0
$k_0{}^f$, $M^{-1}\,s^{-1}$	4.7×10^{-13}	1.3×10^{-12}	3.5×10^{-12}	$4 \times 10^{-9\,f}$	2×10^{-5}
$k_{OH^-}{}^f$, $M^{-2}\,s^{-1}$		8.8×10^{-4}		$2 \times 10^{2\,e}$	2.8×10^3
$k_{H^+}{}^d$, $M^{-1}\,s^{-1}$	4.5×10^4	1.9×10^4	6.6×10^3	3×10^2	2.6×10^2
$k_0{}^d$, s^{-1}	0.7	0.6	0.5	1.5	5.2×10^{-3}
$k_{OH^-}{}^d$, $M^{-1}\,s^{-1}$		4×10^8		6×10^{10}	6.9×10^5

[a] 50% dioxane:water, 25 °C, $\mu = 0.1$. [b] Reference 4g, water, 25 °C, $\mu = 0.1$. [c] Reference 13, water. [d] Unitless. [e] $M^{-1}\,s^{-1}$. [f] s^{-1}.

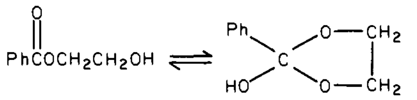
necessary since the exchange obviously cannot be observed in the absence of methanol. The $k_{H^+}{}^f$ data for $PhCOOCD_3$ obtained at different methanol concentrations however show little variation, the small trend that is present being within experimental uncertainty. In consequence it appears likely that the values of $k_{H^+}{}^f$ measured in the methanol:water mixtures are not much different from values which would be obtained in an infintely dilute methanol solution. A second solvent difference involves the ionic strength; $k_{H^+}{}^f$ refers to an ionic strength of 1.0 while $k_{H^+}{}^d$ refers to one of 0.1. Generally speaking rate constants for the A2 hydrolysis of esters are proportional to H^+ concentration even in nondilute acids (the Zucker–Hammett hypothesis[12c]), so that a second-order rate constant ($k_{obsd}/[H^+]$) measured in 0.1 M HCl is not that different from one obtained in 1.0 M HCl. The methanolysis reaction involved here is analogous to an A2 hydrolysis, and we feel therefore that the same conclusion can be made; the value of $k_{H^+}{}^f$ for 0.1 M HCl should not be too different from that measured in 1.0 M HCl.

Considering the complications in the determination of k_{Ex} due to the competing hydrolysis reaction, as well as the problems associated with the slightly different solvent conditions, the error in $k_{H^+}{}^f$ could be as great as ±20%. The values of $k_{H^+}{}^d$ have an error of no more than ±5%, since these are directly measured under the stated solvent conditions. Thus the error in the calculated value of K^f is ±25%.

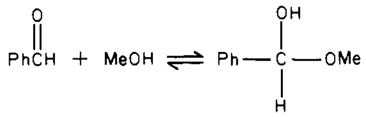
Discussion

Table IV lists rate and equilibrium constants for the formation and decomposition of the tetrahedral intermediate $ArC(OMe)_2OH$. The following comments on these results can be made.

(a) The numbers for $PhC(OMe)_2OH$ are fairly similar to those obtained with an analogous cyclic intermediate[4g] (eq 6), although

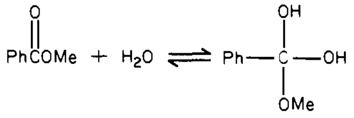

(6)

there is a slightly larger equilibrium constant in the intramolecular reaction. A comparison is also available with constants for a closely analogous hemiacetal[13] (eq 7). The latter is substantially


$$PhCHO + MeOH \rightleftharpoons PhCH(OH)OMe \quad (7)$$

more stable relative to its breakdown products, there being a factor of 10^9 difference in the values of K^f obtained with the ester and aldehyde. This difference shows up in the rate constants for both formation and decomposition; values of the former are 10^6–10^7 greater in the benzaldehyde system, while values of the latter are 10^2–10^3 smaller.

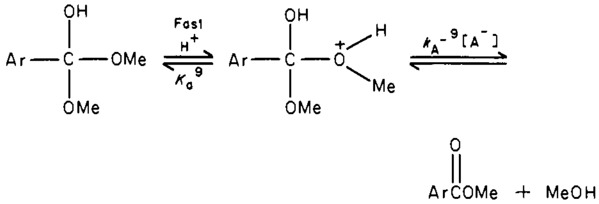
(b) Although Guthrie has not obtained a value of K^f for $PhC(OMe)_2OH$, a number is available for the closely related species $PhC(OH)_2OMe$, the tetrahedral intermediate of the hydrolysis of methyl benzoate. Converting the value listed by


$$PhCOOMe + H_2O \rightleftharpoons PhC(OH)_2OMe \quad (8)$$

Guthrie and Cullimore[6e] to unit molarity in water by dividing by 55, one obtains 1.5×10^{-12} M^{-1}. This compares remarkably well with the value of 2.2×10^{-12} M^{-1} which we obtain for $PhC(OMe)_2OH$. The very close agreement is undoubtedly somewhat fortuitous but it does indicate that the Guthrie approach does provide a good measure of the equilibrium constant. There are several cases where the Guthrie method has been applied for which a direct kinetic measurement is not likely ever to be possible (for example, amide tetrahedral intermediates[6b]).

(c) Although only $k_{H^+}{}^f$ was measured, values of $k_0{}^f$ and $k_{OH^-}{}^f$ are also available, as K^fk^d. The values of $k_0{}^f$ are particularly interesting because such values, either for a noncatalyzed alcoholysis or hydrolysis, are experimentally inaccessible for unactivated esters because of the slowness of the reaction. Our data provide a half-life for noncatalyzed addition of methanol to methyl benzoate in 1 M MeOH of 17 000 years at 25 °C. If the assumption is made that the rates of addition of methanol and water are the same, the half-life for the noncatalyzed hydrolysis of methyl benzoate will be about 50 times smaller, or 300 years. Guthrie and Cullimore have estimated a number of 30 years for this reaction.[6e]

Mechanisms. Two simple kinetically equivalent mechanisms can be suggested for acid-catalyzed adduct decomposition.[9]



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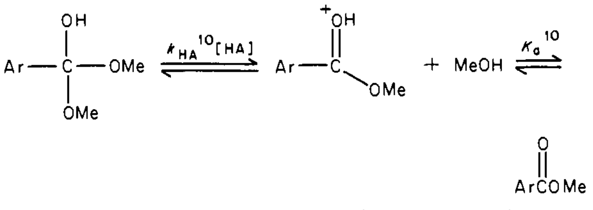

(10)

Although these have proven difficult to distinguish, arguments favoring the eq 9 mechanism have recently been presented for formaldehyde hydrate and hemiacetals.[10] For $ArC(OMe)_2OH$, however, this mechanism appears invalid. The dissociation constant $pK_a{}^9$ of the protonated tetrahedral intermediate can be estimated[14] to be of the order −6 (or more negative). In order

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[13] Harron, J.; McClelland, R. A.; Thankachan, C.; Tidwell, T. T. *J. Org. Chem.* **1981**, *46*, 903–910.

[14] (a) Based on pK_a values estimated for protonated ortho esters,[14b] and for protonated hemiacetals,[10] taking into account the acid-strengthening effect of the aryl group and the extra oxygen. (b) Kankaanpera, A.; Lahti, M. *Suom. Kemistil. B* **1969**, *42*, 427–429.

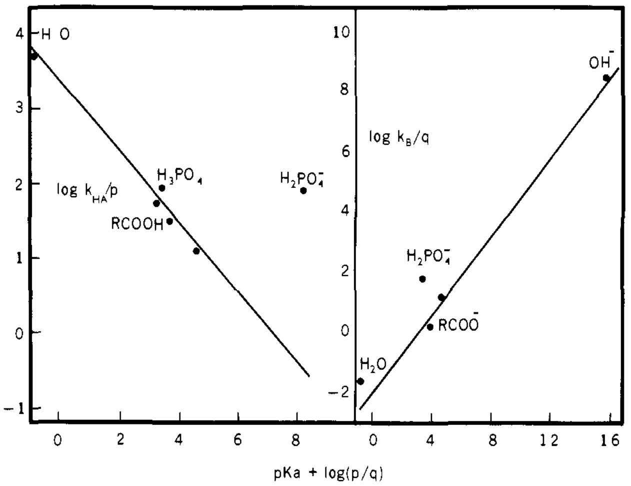


Figure 2. Brønsted plots for decomposition of PhC(OMe)$_2$OH.

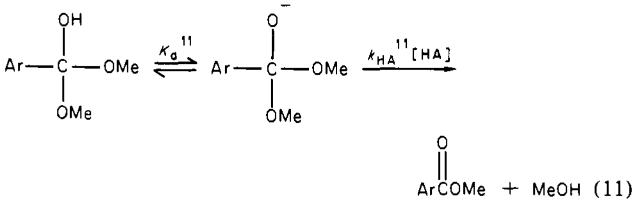
to account for the observed catalytic coefficient for PhC(OMe)$_2$OH decomposition catalyzed by formic acid, this pK_a requires a value of $k_{A}{}^{-9}$ of 10^{12} M^{-1} s^{-1}, a number which is clearly beyond the diffusion limit.

There are however equally as well problems with the eq 10 mechanism. In the decomposition direction, this has a rate-determining step directly analogous to the normal rate-determining step in the acid hydrolysis of a corresponding ortho ester. Although substituent effects are similar,[15] there are two aspects where a correlation is suspect. First PhC(OMe)$_2$OH decomposition exhibits significant general acid catalysis, with a Brønsted α value of 0.46 (Figure 2). ArC(OMe)$_3$ hydrolysis, on the other hand, is not subject to general acid catalysis[15b] (in water alone, although in 70% methanol:water such catalysis is apparently observed[15c,16]). Second, the k_{H^+} value for PhC(OMe)$_2$OH decomposition is three orders of magnitude greater than the k_{H^+} value for PhC(OMe)$_3$ hydrolysis.[5] A similar difference is seen between the rates of formaldehyde hemiacetal decomposition and formaldehyde acetal hydrolysis,[10] and was used as evidence against the eq 10 mechanism with the hemiacetal.[10,17]

These arguments suggest that the acid mechanism may be more involved than those depicted in eq 9 and 10 and we are currently carrying out further experiments relating to this question. One possibility is a "1-encounter" mechanism, in which the acid that donates the proton to the departing alkoxy group also acts as a general base to remove the OH proton before diffusional separation can occur.[18] A fully concerted mechanism in which the proton is simultaneously donated to OMe and removed from OH appears to be ruled out by the Ar substituent dependency, which implies a substantial development of positive charge at the pro-acyl carbon in the transition state.

One point which can be made is that, by the principle of microscopic reversibility, the acid-catalyzed addition of methanol, and presumably water, to a methyl benzoate is in fact general acid catalyzed and not specific acid catalyzed. General acid catalysis of lactonization reactions has been observed,[19] but as far as we are aware this is the first direct suggestion of general acid catalysis for alcoholysis (or hydrolysis) of a simple ester.[20]

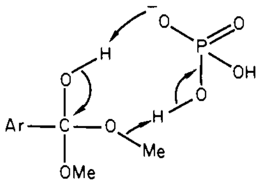
The mechanism of eq 11 has been suggested recently for general base decomposition of formaldehyde hemiacetals.[10] In this case,


$$\mathrm{Ar{-}C(OH)(OMe){-}OMe} \overset{K_a{}^{11}}{\rightleftharpoons} \mathrm{Ar{-}C(O^-)(OMe){-}OMe} \xrightarrow{k_{HA}{}^{11}[HA]} \mathrm{ArC(=O)OMe} + \mathrm{MeOH} \quad (11)$$

evaluation of the rate constant $k_{HA}{}^{11}$ required to produce the observed catalytic coefficients for ArC(OMe)$_2$OH decomposition, assuming a p$K_a{}^{11}$ of 11,[6d] produces values which are less than the diffusion limit for the carboxylate ions. The limited data available provide a large Brønsted β value (0.7–0.9) (Figure 2), suggestive of a considerable degree of proton transfer in the transition state, or in terms of the reaction of eq 11, a small degree of proton transfer to the tetrahedral intermediate anion. This is consistent with the highly reactive nature of this anion, which should be able to expel alcohol with little assistance from the acid HA. A large β value has previously been observed for the general-base-catalyzed lactonization of ethyl 2-(hydroxymethyl)benzoate,[21] where a similar cyclic tetrahedral intermediate is involved.

The pH-independent rate constants $k_0{}^{d}$ lie above the Brønsted lines for both the acids and bases (Figure 2), even after conversion to second order. This probably means that a different mechanism is involved. This suggestion is reinforced for the mechanism of eq 11 by the requirement that $k_{HA}{}^{11}$ be greater than 10^{11} M^{-1} s^{-1} if water were to be acting solely as a general base. The substituent effect of $k_0{}^{d}$ ($\rho \approx 0$) makes it unlikely that water is acting as a general acid. This ρ value may indicate a transition state in which the solvent simultaneously donates a proton to and removes a proton from the tetrahedral intermediate, perhaps in a cyclic fashion through a solvent bridge.[22]

One catalyst which deserves special comment is H$_2$PO$_4^-$, the points for which lie at least two orders of magnitude above the Brønsted lines for the other general acids and general bases (Figure 2). Unusual reactivity associatted with H$_2$PO$_4^-$ (or similar catalysts) has been observed now in a number of cases,[23] and can be explained either in terms of an electrostatic effect due to a different charge nature,[24] or in terms of bifunctional catalysis.[23,25] In the present case the electrostatic effect would seem to be ruled out. The substituent dependency on $k_{H_2PO_4^-}{}^{d}$ ($\rho \approx 0$) suggests that the catalyst is not acting as an acid. As a base catalyst the comparison actually involves species of the same charge type, H$_2$PO$_4^-$ vs. RCOO$^-$. A cyclic bifunctional mechanism would seem therefore to be involved. This is supported by the observed



substituent effect in Ar, which implies a transition state with little charge buildup on the central carbon.

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(15) (a) The ρ value for H$^+$-catalyzed hydrolysis of ArC(OMe)$_3$ is −1.16 in water[15b] and −2.02 in 70% methanol:water.[15c] For ArC(OMe)$_2$OH in 50% dioxane:water, ρ values are −1.6, −1.5, and −1.3 for, respectively, H$^+$, ClCH$_2$COOH, and HCOOH. (b) Bull, H. G.; Koehler, K.; Pletcher, T. C.; Ortiz, J. J.; Cordes, E. H. *J. Am. Chem. Soc.* **1971**, *93*, 3002–3011. (c) Kwart, H.; Price, M. B. *Ibid.* **1960**, *82*, 5123–5129.

(16) (a) See, however, ref 11b. Note also that the addition of water to oxocarbocations derived from acetophenone ketals is general base catalyzed.[16b] (b) Young, P. R.; Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 8238–8248.

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(20) The problem is not that the catalysis would not be observed, but working in the addition direction the rates are prohibitively slow in the pH region where buffer experiments must be carried out.

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