Effective charge development in the transfer of the acetyl group between nucleophiles in acetonitrile solution: acetolysis and butylaminolysis of substituted phenyl esters

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Equilibrium and rate constants have been measured for the phenolyses of acetic anhydride in acetonitrile solution. Acetolysis of substituted phenyl acetates by acetate ion possesses a Brønsted β_{lg} value of -1.50 which, together with a β_{eq} value of 2.86, indicates substantial fission of the C–OAr bond in the transition structure. The value of β_{eq} is employed to identify the rate-limiting steps in aminolyses in acetonitrile.

Butylaminolysis of substituted phenyl acetates in acetonitrile solution yields amide and substituted phenolate anion and the kinetics obey the general rate law:

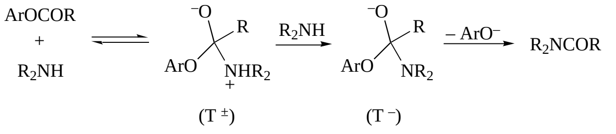
$$\text{Rate} = k_1[\text{ester}][\text{amine}] + k_2[\text{ester}][\text{amine}]^2 + k_3[\text{ester}][\text{amine}][\text{18-crown-6}]$$

Free energy plots of log k_1 and log k_2 exhibit breaks near pK_a^{ArOH} values of 9 and 8, respectively, and these can be interpreted by a mechanism which involves a common zwitterionic adduct $T^{\pm}$, which partitions to give the product by two routes: A involving direct expulsion of the phenolate ion leaving group (k_1 parameter) and B involving proton transfer prior to phenolate ion expulsion (k_2 parameter). The formation of $T^{\pm}$ is rate-limiting for the A path and C–OAr bond fission is rate-limiting for the B mechanism

Introduction

Reactions catalysed by enzymes involve complexation of the substrate into an active site on the globular protein.[1] The complexed substrate often fits snugly within the active site leaving little or no space for solvent, *e.g.* in acetylcholinesterase;[2a] the microscopic medium of the bound reactants in subsequent steps in the catalysis is thus not likely to resemble the water of the uncatalysed system.[2b,c] Constituents of the active site are required to provide solvation-like interactions to enable the catalysis to proceed.[3,4] The strong solvating power of water usually overrides any advantage to be gained from potential solvation by a model catalyst; studies of reactions in non-aqueous media are therefore of importance and moreover the microscopic medium of a non-aqueous solvent could enhance interactions which would otherwise be minor in water.

Aminolysis of phenyl esters in aqueous solution proceeds by initial nucleophilic attack at the carbonyl carbon to give a tetrahedral intermediate $T^{\pm}$ with subsequent proton transfer to yield T^- and C–OAr bond cleavage to yield the product amide (Scheme 1). The breakdown of the tetrahedral intermediate in butylaminolysis is rate limiting in chlorobenzene and involves a proton transfer to a base, usually a second molecule of the amine, followed by fast, non-rate-limiting expulsion of the phenoxide ion.[5] Crown ethers and glymes can also trap the $T^{\pm}$ intermediate presumably by providing solvation of the cationic centre which is not available in chlorobenzene solvent.[5,6]



Scheme 1

Knowledge of changes in effective charge is one of the most powerful tools to use as a standard against which to measure bonding in transition structures in aqueous and non-aqueous systems.[7] In order to interpret effective charge completely it is necessary to possess standard values for β_{eq}.[7] This work reports the measurement of the Brønsted β_{eq} value for transfer of the acetyl group to phenolate ion nucleophiles in acetonitrile solvent. Knowledge of β_{eq} is required to interpret the effective charge data for butylaminolysis of substituted phenyl acetates in acetonitrile and adds to the β_{eq} data already known for water and chlorobenzene.[8] This report demonstrates that the butylaminolyses in acetonitrile involve a mechanism with at least two steps.

Experimental

Materials

4-Chlorophenyl, 3-chlorophenyl, 4-fluorophenyl and 3-acetylphenyl and phenyl acetates were prepared by the method of Chattaway.[9a] Product purity was checked by ^{1}H NMR spectroscopy and elemental analysis; analytical and physical data are recorded in Table 1. Other substituted phenyl acetates were available from previous studies in this laboratory.[10] 18-Crown-6 was purchased from the Aldrich Chemical Co. and was purified by recrystallisation from acetonitrile prior to use. Acetonitrile was from BDH and was distilled from P_2O_5 and then from CaH_2 before use. Butylamine was distilled twice, once from KOH pellets, then from CaH_2 and stored in a dark bottle. Potassium salts of the various substituted phenols and KOAc were prepared and purified as described earlier.[8]

Methods

Kinetics of the reaction of butylamine with substituted phenyl acetates were measured by addition of an aliquot (0.02 ml) of a solution of the ester in acetonitrile to a solution (2.5 ml) of butylamine in acetonitrile of varying concentration of butylamine in a silica cell held at 25 °C in a Perkin-Elmer Lambda 5 UV–VIS spectrophotometer. The absorbance change at a previously determined wavelength was recorded as a function of time. Pseudo-first- and second-order rate constants were fitted to theoretical equations using grid-search programs operating on an Opus VII microcomputer. The dependence of the rate constant for aminolysis of phenyl acetate upon the concentration of 18-crown-6 was determined by varying the crown ether concentration against a fixed concentration of butylamine. The kinetics of the reaction of phenyl acetates with

Table 1 Rate constants for the butylaminolysis of substituted phenyl acetates[a] in acetonitrile solution[b]

Phenol	$\Delta k_{obs}/10^{-3}$ s^{-1}	Δ[BuNH$_2$]/mM	N[c]	pK_a^{ArOH}	$k_1/10^{-3}$ M^{-1} s^{-1}[d]	$k_2/10^{-3}$ M^{-1} s^{-1}[e]	λ/nm[f]	$\Delta\varepsilon/10^3$[a]
2,4,5-Cl$_3$	2.3–23	4–40	6	6.72	574 ± 2	<300	293	1.15
4-NO$_2$	0.82–30.4	2–100	10	7.14	299 ± 2	<100	400	11.5
2,5-Cl$_2$	1.4–14	10–100	6	7.51	132 ± 1	99 ± 11	282	1.03
4-CN	0.32–98	6–800	12	7.95	39 ± 2	104 ± 4	283	2.36
3-NO$_2$	2.06–71	80–1000	7	8.38	21 ± 0.7	50 ± 1	350	0.835
3-CN	1.2–35	100–1000	6	8.57	9.2 ± 0.2	25 ± 0.2	280	1.85
3-Cl	1.3–24	400–2000	9	9.02	<2.0	6.04 ± 0.06	279	1.23
3-Ac	0.39–6.9	400–2000	9	9.19	<0.21	1.75 ± 0.01	325	1.65
4-Cl	0.36–7.1	400–2000	9	9.26	<0.30	1.78 ± 0.01	285	1.37
4-F	0.17–1.3	600–2000	9	9.95	<0.20	0.34 ± 0.006	284	2.13
Parent[b]	0.13–0.57	800–2000	8	9.99	<0.075	0.15 ± 0.004	275	1.48

[a] Phenyl acetates prepared for this work were 3-chloro, bp 55–56 °C/0.3 mmHg (lit.[9b] 116.5 °C/21 Torr. Found C, 56.21; H, 4.01). $C_8H_7ClO_2$ requires C, 56.33; H, 4.14%); 3-acetyl, bp 122–128 °C/0.5 mmHg (Kügelrohr), mp 43.5–44 °C (lit.[9c] bp 147 °C/9 mmHg, mp 44–44.5 °C. Found C, 67.22; H, 5.45. $C_{10}H_{10}O_3$ requires C, 67.41; H, 5.66%); 4-chloro, bp 78.5–80 °C/0.6 mmHg (lit.[9b] 108 °C/12 mmHg. Found C, 56.13; H, 3.96. $C_8H_7ClO_2$ requires C, 56.33; H, 4.14%); 4-fluoro, bp 58.5–59.5 °C/1.0 mmHg (lit.[9d] 85–87 °C/16 mmHg. Found C, 62.33; H, 4.33. $C_8H_7FO_2$ requires C, 62.34; H, 4.58%); parent, bp 85–86 °C/15 mmHg (lit.[9e] 196.7 °C/760 mmHg. Found C, 70.79; H, 5.94. $C_6H_8O_2$ requires C, 70.58; H, 5.92%). [b] Rate constants were derived from pseudo-first-order rate constants measured at 25 °C. [c] Number of data points not including duplicates. [d] Second-order rate constants for butylaminolysis; ester concentrations ranged from 40–500 μM. [e] Third-order rate constant for butylaminolysis. [f] Wavelength for kinetic runs. [g] Extinction coefficient for the change in absorbance at the given wavelength. [h] The value of $k_3 = (3.1 \pm 0.1) \times 10^{-3}$ M^{-1} s^{-1}.

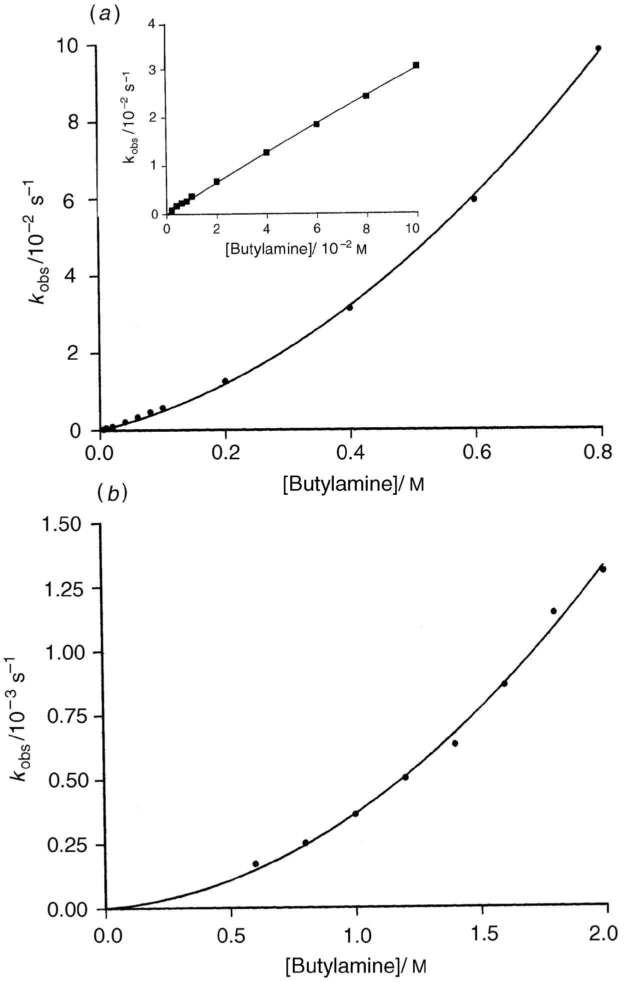


Fig. 1 (*a*) Butylaminolysis of 4-cyanophenyl acetate in acetronitrile solution (both k_1 and k_2 are measurable). Inset: butylaminolysis of 4-nitrophenyl acetate in acetonitrile solution (only k_1 is measurable). Lines are drawn from data in Table 1 using eqn. (1); conditions as in Table 1. (*b*) Butylaminolysis of 4-fluorophenyl acetate in acetonitrile solution. This illustrates a case where k_2 is measurable and k_1 can only be obained as an upper limit. Line is from eqn. 1 using data from Table 1; conditions as in Table 1.

KOAc and of acetic anhydride with KOAr in acetonitrile were measured using the techniques described for chlorobenzene solvent using 18-crown-6 as a solubilising agent.[8]

Product analysis was carried out on the aminolysis of 4-nitrophenyl acetate after the solvent was evaporated, diluted with water and acidified. The solution was extracted with dichloromethane and the extracts dried and evaporated; the thick oil was then subjected to NMR and IR analysis.

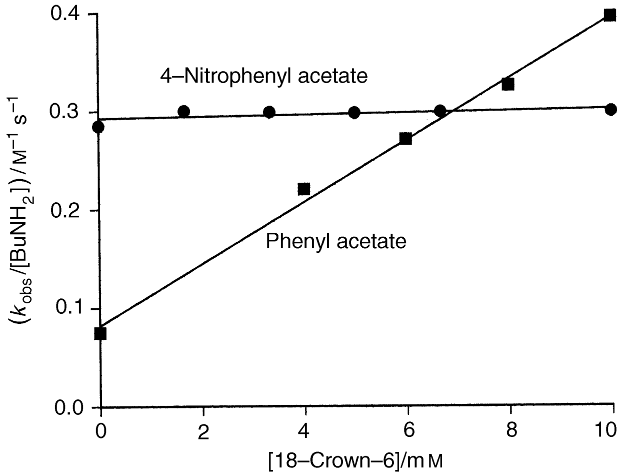


Fig. 2 Butylaminolysis of 4-nitrophenyl and phenyl acetates in the presence of increasing concentrations of 18-crown-6 in acetonitrile at 25 °C. The line for the 4-nitrophenyl ester is calculated from k_1 from Table 1. The line for the phenyl ester is calculated from a value of k_3, $k_1^{upper\ limit}$ and k_2 from Table 1; k_{obs}/[BuNH$_2$] values for phenyl acetate are multiplied by 10^3. Experiments were carried out with [butylamine] at 10 and 100 mM for 4-nitrophenyl and phenyl esters, respectively.

Results

The rates for disappearance of ester in aminolysis and acetolysis reactions fitted good first-order kinetics up to greater than 90% of the total reaction. Product analysis in the case of aminolysis indicated that the amide had been formed in quantitative yield and this was checked by the quantitative release of 4-nitrophenolate ion as determined from the total absorbance change and the extinction coefficient at the experimental wavelength. The pseudo-first-order rate constants (k_{obs}) for reactions of butylamine with substituted phenyl acetates in acetonitrile obey the general rate equation [eqn. (1)] and this is

$$k_{obs} = k_1[\mathrm{BuNH_2}] + k_2[\mathrm{BuNH_2}]^2 + k_3[\mathrm{BuNH_2}][\text{18-crown-6}] \quad (1)$$

illustrated in Fig. 1(*a*) and the derived parameters and conditions of the experiments are recorded in Table 1. The value of k_3 for phenyl acetate is recorded in Table 1 but the value for 4-nitrophenyl acetate is negligible (see Fig. 2).

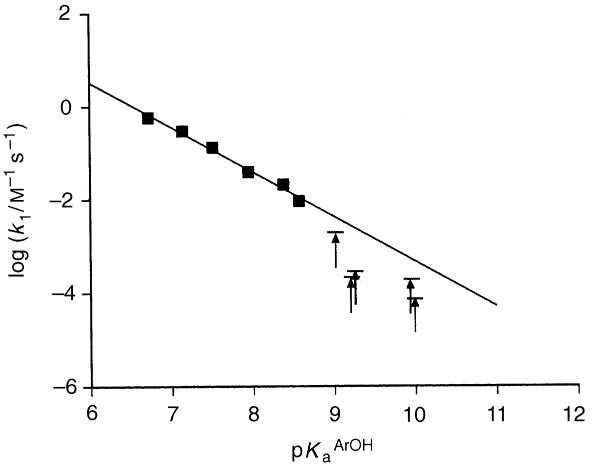


Fig. 3 Dependence of k_1 on pK_a^{ArOH} for butylaminolysis of substituted phenyl acetates in acetonitrile. The line is drawn from eqn. (2) and the conditions are as in Table 1.

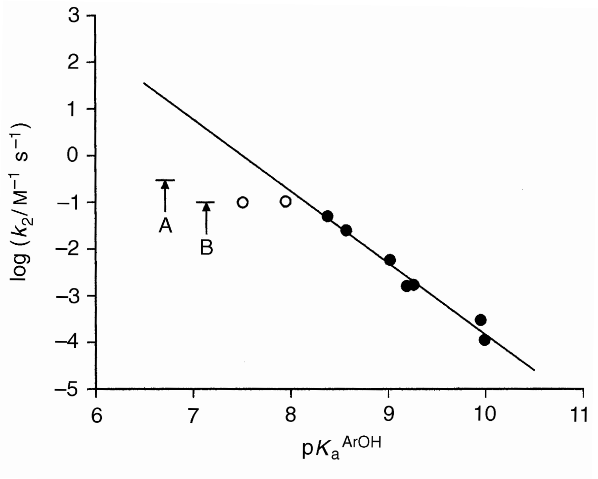


Fig. 4 Dependence of k_2 on pK_a^{ArOH} for butylaminolysis of substituted phenyl acetates in acetonitrile. The line is from eqn. (3) and conditions are from Table 1.

Only first-order dependencies on amine concentration were found for the butylaminolyses of 2,4,5-trichlorophenyl and 4-nitrophenyl acetates and the values of k_2 for these esters given in Table 1 are upper limits. The reaction flux for butylaminolysis of 4-fluorophenyl acetate 3-chloro, 3-acetyl, 4-chloro and phenyl acetates with butylamine was taken essentially by the k_2 parameter and only upper limits for the k_1 terms were measurable [see Fig. 1(*b*)]; the data are recorded in Table 1.

The parameter k_1 obeys a Brønsted relationship [eqn. (2)]

$$\log k_1 = (-0.96 \pm 0.052)\mathrm{p}K_a + (6.28 \pm 0.41)\ (r = 0.9941) \quad (2)$$

(the data for the upper limits are not included, see Discussion) illustrated in Fig. 3. When the data for the upper limits and for the 4-cyano and 2,5-dichloro substitutents are excluded (see Discussion) the k_2 parameter obeys eqn. (3) illustrated in Fig. 4.

$$\log k_2 = (-1.54 \pm 0.11)\mathrm{p}K_a + (11.56 \pm 0.98)\ (r = 0.9883) \quad (3)$$

Pseudo-first-order rate constants for acetolysis of substituted phenyl acetates by KOAc in acetonitrile obey the rate law [given in eqn. (4)]. The solutions contained amounts of 18-crown-6 in

$$k_{obs} = k_{AcO}[\mathrm{AcO^-K^+}] \quad (4)$$

excess of the acetate concentration. Separate experiments showed that the crown concentration did not affect k_{obs} for a single acetate concentration when present at greater concentrations than the acetate ion. The data are shown in Table 2 and the second-order rate constants obey a Brønsted-type equation [eqn. (5)], where pK_a^{ArOH} refers to water as solvent.

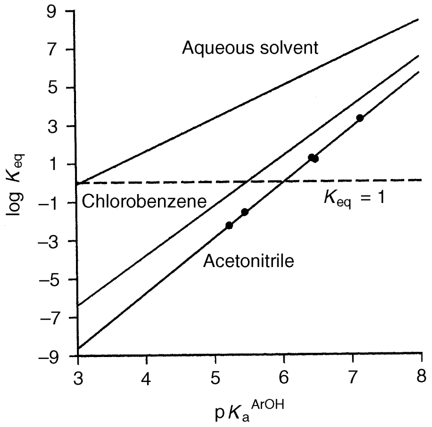


Fig. 5 Equilibrium constants for formation of ester from phenolate ion and acetic anhydride for water, chlorobenzene and acetronitrile solvents; lines for water and chlorobenzene are calculated from equations given in ref. 8. Data and conditions for acetonitrile from Table 3; line is calculated from eqn. (8).

$$\log k_{AcO} = (-1.5 \pm 0.25)\mathrm{p}K_a^{ArOH} + 9.63 \pm 1.52\ (r = 0.9638) \quad (5)$$

The phenolyses of acetic anhydride in acetonitrile were measured at low concentrations of the phenoxide ion with excess crown and the resultant kinetics were pseudo-first-order in concentration of the phenoxide ion which was depleted through the reaction. The rate constants for formation of ester are linearly dependent on acetic anhydride concentration [eqn. (6)] and the resultant data are collected in Table 3; the

$$k_{obs} = k_{ArO}[\mathrm{Ac_2O}] \quad (6)$$

parameter, k_{ArO}, fits a Brønsted-type law [eqn. (7)]. 18-Crown-6

$$\log k_{ArO} = (1.32 \pm 0.2)\mathrm{p}K_a^{ArOH} - 7.58 \pm 1.26\ (r = 0.9659) \quad (7)$$

was observed to have no effect on phenolysis rates when present in excess of the KOAr salt. The absorption changes for phenolysis and acetolysis are independent, respectively, of the acetic anhydride and KOAc concentrations and are those expected for complete conversion. Division of k_{ArO} by k_{AcO} gives the equilibrium constant for formation of ester from phenolate ion and acetic anhydride (K_{eq}) and the values recorded in Table 3 satisfy eqn. (8).

$$\log K_{eq} = (2.86 \pm 0.049)\mathrm{p}K_a^{ArOH} - 17.21 \pm 0.3\ (r = 0.9996) \quad (8)$$

The phenolysis of acetic anhydride in acetonitrile was checked for the incursion of very low concentrations of water by adding a subsequent aliquot of the phenolate ion to the cuvette some 15 min after the previous reaction had completed. The absence of a change in the rate constant for disappearance of the phenolate ion indicated that the acetic anhydride solution in the cuvette was stable during the period of the experiments and that any water present had no effect on the kinetics.

Discussion

Acetolysis

Transfer of the acetyl function to the acetate ion from ester or to the phenolate ion from acetic anhydride proceeds to completion under the conditions of the kinetic measurements. We are therefore justified in assuming that the experimental parameters k_{ArO} and k_{AcO} are respectively single forward and reverse rate

Table 2 Reaction of substituted phenyl acetates with acetate ion in acetonitrile solution[a]

Substituent	pK_a^{ArOH}	Δ[AcOK]/mM[b]	λ/nm[c]	Δ[Crown]/mM[d]	$\Delta k_{obs}/10^3\ s^{-1}$[e]	N[f]	$k_{AcO}/M^{-1}\ s^{-1}$[g]	$\Delta\varepsilon/10^3$[h]
2,5-$(NO_2)_2$	5.22	0–4	465	0–8	0–240	4	59.0	1.89
2-Cl, 4-NO_2	5.45	0–20	400	0–40	0–138	3	6.83	6.86
2,3,5-Cl_3	6.43	0–40	293	0–79	0–19	3	0.371	1.44
4-Cl, 2-NO_2	6.48[i]	0–40	400	0–79	0–55	4	1.33	1.76
4-NO_2	7.14	0–101	400	0–198	0–2.6	3	0.0260	16.2

[a] Rate constants were derived from pseudo-first-order rate constants measured at 25 °C; ester concentration ranged between 5 and 250 μM. [b] Range of potassium acetate concentration. [c] Wavelength for kinetic runs. [d] Range of crown ether concentrations. [e] Range of pseudo-first-order rate constants. [f] Number of data points not including duplicate runs. [g] Second-order rate constants for acetolysis derived from the slope of the rate constant *versus* acetate ion concentration; error is less than ±5%. [h] Extinction coefficient for the change in absorbance at the given wavelength. [i] An error is noted in a recent publication where the pK_a of 4-chloro-2-nitrophenol is incorrectly quoted as 6.05;[21] the error does not affect the conclusions of that paper.

Table 3 Reaction of acetic anhydride with substituted phenolate ions in acetonitrile[a]

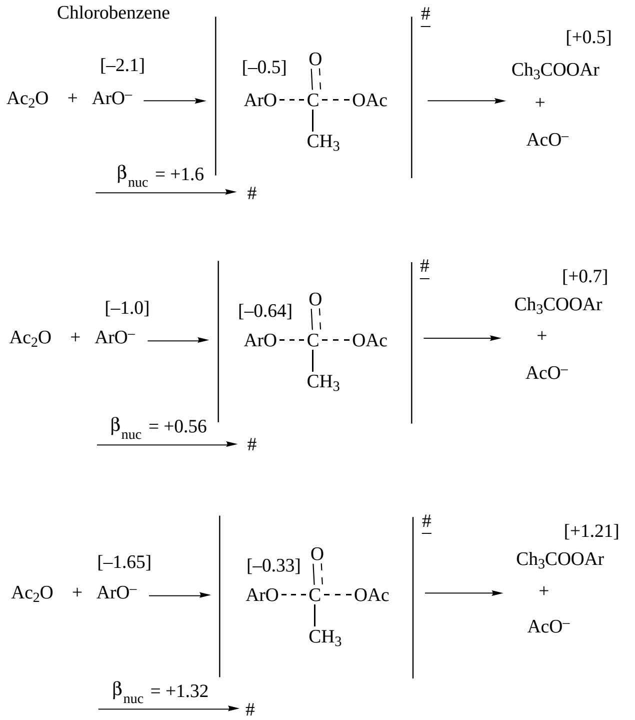
Substituent	K_{eq}[b]	λ/nm[c]	Δ[Ac_2O]/mM[d]	Δ[Crown]/mM[e]	$\Delta k_{obs}/10^{-3}\ s^{-1}$[f]	N[g]	$k_{ArO}/M^{-1}\ s^{-1}$[g]	$\Delta\varepsilon/10^3$[h]
2,5-$(NO_2)_2$	5.46×10^{-3}	480	0–6	0.1–0.490	0–1.5	3	0.322	3.20
2-Cl, 4-NO_2	2.7×10^{-2}	415	0–6	0.1–0.420	0–6.00	3	0.186	20.0
2,3,5-Cl_3	17.5	235	0–11	0.1–0.570	0–72.0	4	6.52	1.68
4-Cl, 2-NO_2	15.0	455	0–0.12	0.1–0.566	0–2.40	3	20.0	3.50
4-NO_2	1.92×10^3	430	0–2.0	0.1–1.98	01–100	4	50.0	21.6

[a] Rate constants were derived from pseudo-first-order rate constants (depletion of ArOK) measured at 25 °C; ArOK concentrations ranged between 70 and 100 μM. [b] $K_{eq} = k_{ArO}/k_{AcO}$. [c] Wavelength for kinetic runs. [d] Range of acetic anhydride concentration. [e] Range of crown ether concentrations. [f] Range of pseudo-first-order rate constants. [g] Number of data points not including duplicate runs. [h] Extinction coefficient for the change in absorbance at the given wavelength. [i] Second-order rate constant for phenolysis derived from the slope of the rate constant *versus* acetic anhydride concentration; error is less than ±5%.

constants. The technique described here has been employed previously to estimate equilibrium constants for acylation in chlorobenzene and acetonitrile.[11] The Brønsted dependence of K_{eq} [eqn. (8)] is illustrated in comparison with that for chlorobenzene and water in Fig. 5. The equilibrium constants for acetonitrile, chlorobenzene and water become unity at phenol pK_a values at 6.0, 5.5 and 3.1, respectively, (Fig. 5) and it follows that an acetylating agent more energetic than acetic anhydride is required to yield esters from phenols with smaller pK_a values than these in the respective solvents. Eqn. (8) and equations relating the effect of pK_a^{ArOH} to the equilibrium constant for formation of ester in chlorobenzene and water[8] predict that the equilibrium constants become almost identical for a phenol with pK_a^{ArOH} between 10 and 11 (see Fig. 5); this indicates that synthesis is more favoured in water than in acetonitrile or chlorobenzene for all accessible phenols.

The large value of β_{eq} of 2.86 for acetonitrile indicates more charge destruction in the equilibrium for acetylation of phenolate ions consistent with the poorer solvating power of acetonitrile compared with that of water ($\beta_{eq} = 1.7$). The pK_a values for the ionisation of phenols in acetonitrile, obtained from Magoński and Pawlak[12] and Kolthoff and Chantooni,[13] obey a Brønsted equation (p$K_a^{CH_3CN} = (1.65 \pm 0.08)pK_a^{H_2O} + 9.68 \pm 0.46$; $r = 0.9833$). Relative to acetonitrile as standard the β_{eq} for the transfer of the acetyl group between phenolate ions is therefore 2.86/1.65 = 1.73. The charge change in the acetyl group transfer relative to that of the ionisation in each solvent is thus about the same as that for water and slightly larger than that of chlorobenzene (1.4).†

There is considerable evidence that the reactions of phenolate ions with phenyl esters in aqueous solution have concerted mechanisms[14] (but see Buncel,[15] Kwon[16a] and Basaif[16b] and their co-workers). Since acetonitrile is less tolerant of ions than water it is proposed that the concerted mechanism for acyl transfer reactions of phenolate ions is more favoured in acetonitrile than in water. The various β values for the proposed concerted processes in all three solvents combine to give effective charge maps as shown in Scheme 2. The ratio of effective charge on the phenol oxygen from reactant to transition state relative to that from reactant to product (Leffler's α parameter; $\alpha = \beta_{nuc}/\beta_{eq}$)[7] differs significantly for the three solvents ($\alpha^{aq} = 0.33$, $\alpha^{CH_3CN} = 0.46$ and $\alpha^{Cl} = 0.62$).



Scheme 2 (Values in brackets are effective charges)

Butylaminolysis

The observation of aminolysis with kinetic terms first- and second-order in amine [k_1 and k_2, respectively, in eqn. (1)] is consistent with results from other studies.[2b,5,17] It is interesting to compare our results with those reported by Bruice and Mayahi[18] for the ammonolysis of substituted phenyl acetates in

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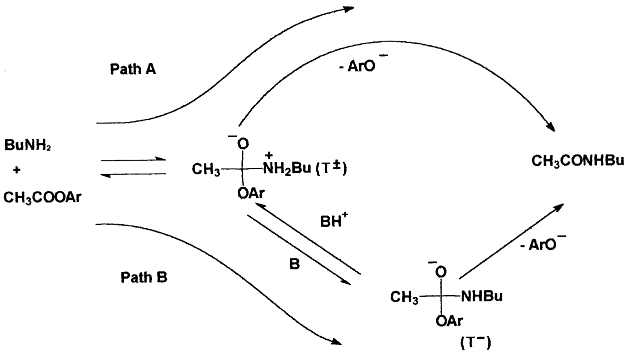
† The ionisation of phenols in water is used as the standard equilibrium for the free energy relationships because this enables the β values to be directly compared with those of other systems which utilise the water standard. Provided the same standard is used throughout it does not matter which is used and water is the most appropriate because of the large number of literature pK_a values. In the present case pK_a values of some of the phenols are not available for acetonitrile solution.

aqueous solution. Aminolysis reactions of 4-nitro- and 3-nitrophenyl acetates in water are not subject to base catalysis whilst 4-chlorophenyl, phenyl and *p*-cresyl acetates showed both uncatalysed and base-catalysed terms. The rate-determining step for aminolysis of phenyl acetates in aqueous solution is first-order in amine concentration for nucleofuges from relatively acidic phenols and leads to the formation of the tetrahedral intermediate (T$^{\pm}$). As the leaving ability decreases there is a change towards a rate-limiting step which is second-order in amine concentration[19] and the breakdown of T$^{\pm}$ is the rate-limiting step. For some of the most strongly basic nucleofuges the concentration of butylamine required to obtain rate data enters the range where the medium is significantly altered (up to 2 M in acetonitrile corresponds to a 20/80 v/v solvent system). The data fit eqn. (1) with negligible values for k_1 (Fig. 3) (k_3 is not appropriate in the absence of crown additive); the fit of the k_2 parameter to a Brønsted equation [eqn. (3), Fig. 4] indicates that the medium effect is likely to be small.

Data in Fig. 3 indicates that the upper limits on k_1 for the substituents with p$K_a^{ArOH} > 9$ are much lower than the line subtended from the 'measurable' data [eqn. (2)] and that the dependency is not linear over the whole of the range of pK_a; eqn. (2) represents one limb of a free energy relationship involving a break due to a change in the rate-limiting step. Substituents with p$K_a^{ArOH} < 9$ have a Brønsted β_{lg} value much less than that for the overall β_{eq} and the mechanism therefore has a rate-limiting step not involving C–OAr bond fission; path A in Scheme 3 illustrates the mechanism proposed to account for these results. The change in effective charge on the aryl oxygen in the transition structure gives rise to a Leffler α_{lg}[7] value of 0.34 consistent with formation of T$^{\pm}$ as the rate-limiting step.



Scheme 3

The upper limits on the parameter k_2 are well below the values predicted from the linear relationship illustrated in Fig. 4. Moreover, the values of k_2 for the 2,5-dichloro- and 4-cyano-substituents are also below the line consistent with a break in the free energy relationship around a pK_a^{ArOH} of 8. The slope of the free energy relationship for the substituents with p$K_a^{ArOH} > 8.4$ [eqn. (3)] has a Leffler α_{lg} value of 0.54 consistent with C–OAr bond fission in the rate-limiting step. At pK_a^{ArOH} values above that of the break-point the fission of the C–OAr bond in T$^-$ (path B in Scheme 3) is proposed as the rate-limiting step. The rate-limiting step for the k_2 term in the aminolysis of esters from phenols with p$K_a < 8$ is likely to be the proton transfer step in pathway B (Scheme 3).

The observation of the catalytic effect of added crown ether (k_3) for the butylaminolysis of phenyl acetate in acetronitrile is consistent with mechanism B whereby the interaction of the crown with T$^{\pm}$ provides an alternative pathway from direct proton transfer. A similar mechanism has been postulated for butylaminolysis in chlorobenzene[5] and in other aminolyses where non-basic species such as crowns or amides stabilise T$^{\pm}$.[17c] Since the rate-limiting step for the aminolysis of the 4-nitrophenyl acetate is formation of T$^{\pm}$ in mechanism A the steps subsequent to its formation (including those of path B) would be kinetically 'silent' and thus no effect of crown ether would be expected; this prediction is borne out experimentally (Fig. 2) confirming the overall mechanism.

The kinetics for the pyrrolidinolysis of substituted phenyl acetates in acetonitrile are described by both k_1 and k_2 terms[20] and substituent effects on both these parameters are large. Comparison with the data from this work confirms the original conclusion that C–OAr bond fission is rate limiting for both mechanisms. In the case of pyrrolidinolysis the conditions are such that no change in the rate-limiting step takes place within the range of substituents studied.

Acknowledgements

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