An Open Transition State in Carbonyl Acyl Group Transfer in Aqueous Solution

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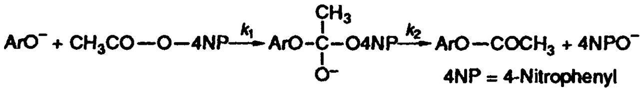
The second-order rate constants have been measured for the reaction of substituted phenolate ions with 2,4-dinitrophenyl acetate, 2,4-dinitrophenyl 4-methoxy-2,6-dimethylbenzoate and acetic anhydride in aqueous solution at 25 °C. The data are over a wide range of phenolate ion basicity and obey good Brønsted equations which have β_{nuc} values of, respectively, 0.57 ± 0.03, 0.15 ± 0.07 and 0.59 ± 0.05.

The principal conclusion of this work is that the identity reaction of 2,4-dinitrophenolate ion with 2,4-dinitrophenyl 4-methoxy-2,6-dimethylbenzoate has an open transition state, namely one with very weak bonds to entering and departing ligands. The transition state possesses a Kreevoy tightness parameter (τ) of 0.18. The open transition state arises from the stabilising effect of the acyl group substituents on the benzoylium ion and their destabilising effect on the putative tetrahedral intermediate as well as the weak basicities of the nucleophile and nucleofuge. This is the first example of an open transition state in an acyl group transfer which does not require the assistance of a negatively charged internal nucleophile.

The data for 2,4-dinitrophenyl acetate may be employed to calculate an identity rate constant (k_{ii}) for the reaction of 2,4-dinitrophenolate ion with the ester. This data may be fitted to a theoretical Lewis–Kreevoy plot (log k_{ii} *vs.* pK_i) possessing both positive and negative values of β_{ii} (slope of the line). Microscopic medium effects place a limit to the accuracy of predictions of rate constants, including k_{ii}, from linear free energy relationships.

Recent work has provided evidence that the transfer of the carbonyl acyl group (RCO–) between weakly basic oxyanions is concerted in aqueous solution.[1,2] Other weakly basic nucleophiles have been shown to react with carbonyl groups *via* a concerted † pathway, namely a single-step reaction.[3,4]

Evidence for the single-step pathway in phenolate ion attack involves the observation of a linear Brønsted type plot for variation in phenolate ion over a wide range of basicity greater and less than that for the leaving phenolate ion. The observation of a substantial value of the p_{xy} parameter (variation of either β_{nuc} or β_{lg} with pK_{lg} or pK_{nuc}, respectively) indicates variation of transition-state structure with nucleophile basicity.[1,2] If eqn. (1) were the mechanism of the acyl group transfer the observed Brønsted data require that a larger change in effective charge occurs in step 2 than in step 1; the expectation, for this putative stepwise mechanism, is that step 1, which has a full bonding change in ArO–C, should have a larger change in charge on the oxygen than in step 2 which only involves a hybridisation change on carbon.

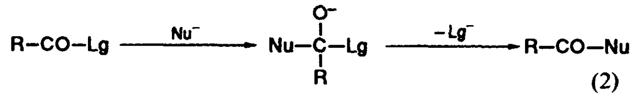


$$ArO^- + CH_3CO{-}O{-}4NP \xrightarrow{k_1} ArO{-}\overset{CH_3}{\underset{O^-}{C}}{-}O4NP \xrightarrow{k_2} ArO{-}COCH_3 + 4NPO^-$$

4NP = 4-Nitrophenyl

(1)

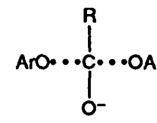
Classical work supports the stepwise associative [eqn. (2)][5] and dissociative [eqn. (3)][6] paths for displacement reactions by nucleophiles at carbonyl centres. Eqn. (2) is based on evidence for reactions involving strongly basic entering and leaving nucleophiles.[5a,b,7a,b] The mechanism of eqn. (3), the S_N1 mechanism,‡[7b] is favoured when the leaving group is weakly basic and when the function (R) possesses a group which can effectively stabilise the acylium ion.[6,8,9]



$$R{-}CO{-}Lg \xrightarrow{Nu^-} Nu{-}\overset{O^-}{\underset{R}{C}}{-}Lg \xrightarrow{-Lg^-} R{-}CO{-}Nu \qquad (2)$$

$$R{-}CO{-}Lg \xrightarrow{-Lg^-} R{-}CO^+ \xrightarrow{+Nu^-} R{-}CO{-}Nu \qquad (3)$$

It is of interest to study the p_{xy} parameter which indicates structure variation[2] to predict and demonstrate a system where the transition state structure of a carbonyl acyl transfer reaction is open (**1**). Such a prediction is most easily carried out for identity reactions.



$$ArO\cdots\overset{R}{\underset{O^-}{C}}\cdots OAr'$$

1

This paper presents data for the reaction of substituted phenolate ions with carbonyl centres possessing weakly basic leaving groups. Previous work[2] on the transfer of the acetyl group between phenolate ion nucleophiles indicated that the slope of a Lewis–Kreevoy plot (β_{ii}) varies with pK_a giving rise to a curved plot.§ A positive value of β_{ii} indicates an associative mechanism with a tight transition state whereas a negative β_{ii}

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† A reaction with a single step has a concerted mechanism except for the case where only one major bond change is occurring; thus the ionisation of methyl iodide is not defined to be concerted although the re-hybridisation involving bond angle and bond length changes are probably in concert with C–I bond fission. A synchronous mechanism is defined as a concerted mechanism where all the bonding changes have occurred to the same extent in the transition state.

‡ In the new nomenclature the S_N1 mechanism of eqn. (3) is a $D_N + A_N$.[7c,d] The ElcB mechanism under the old nomenclature[7d] becomes: $D_HA_H + D_N + A_N + D_NA_N$. Acid chlorides are proposed to undergo uncatalysed hydrolysis *via* the S_N1 mechanism.[7e–j]

§ We propose that this type of free energy plot be named a 'Lewis–Kreevoy' plot to distinguish it from other types of plots and to honour the individuals responsible for progressing the application of identity reaction mechanistic studies.

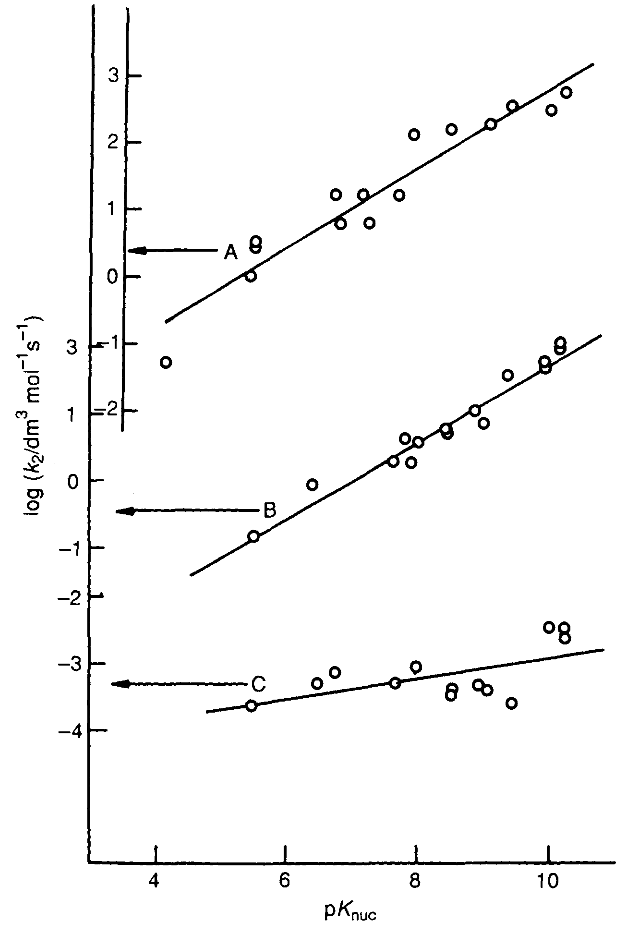


Fig. 1 Brønsted dependences for attack of phenolate ions on various acetate derivatives: A, acetic anhydride; B, 2,4-dinitrophenyl acetate; C, 2,4-dinitrophenyl 4-methoxy-2,6-dimethylbenzoate. Lines are calculated from coefficients in Table 2 and the data from Table 1, which also records the conditions.

value is for an open dissociative process. As seen later the provision of the very weakly basic 2,4-dinitrophenolate ion as acceptor and donor nucleophile for the acetyl group induces a negative β_{ii} value which is not sufficient to give rise to a significantly open transition state. This paper shows that provision of substituents on the R group of the acyl function suffices to force the transition state to become open in character.[10]

The evidence from polar effects applied in this work refers to structures of solution states; we are not in a position to discuss the electronic structures as if they were single entities *in vacuo* although our graphical representations would appear to indicate this.

Experimental

Materials were as described earlier.[1,2] The ester 2,4-dinitrophenyl 4-methoxy-2,6-dimethylbenzoate was prepared according to the method described by Thea *et al.*;[11a] the material was recrystallised from toluene and had m.p. 138–139 °C (lit., m.p. 138–139 °C).[11a] The 2,4-dinitrophenyl acetate was prepared by dissolving the phenol (2 g) in acetic anhydride (30 cm^3) with H_2SO_4 (0.25 cm^3). The solution was kept overnight and the solvent removed to yield a solid which was recrystallised from methanol–ether; it had m.p. 72–73 °C (lit., m.p. 72 °C).[11b] Other esters were prepared by either of the following methods: A, Chattaway's procedure[11c] employing NaOH and acetic anhydride or B, refluxing a solution of the phenol with a slight excess of pyridine and acetyl chloride in diethyl ether or dichloromethane followed by extraction with dilute HCl, drying ($MgSO_4$) and evaporation. The phenyl esters were either distilled or recrystallised from suitable solvents. The m.p. and b.p. characteristics are given in Table 1. Phenols were obtained commercially, except 4-chloro-3-nitrophenol which was obtained from 4-amino-3-nitrophenol by the Sandmeyer process.[11d] Substrates were checked for purity by NMR spectroscopy, TLC and elemental analysis.

Kinetic and other methods, including the equipment employed here are described in a previous paper.[1,3a] Data were fitted to theoretical equations by use of programs operating on an Opus IV or V PC or by use of 'grid-search' programs written in BASIC and employing a BBC Master 128 computer.

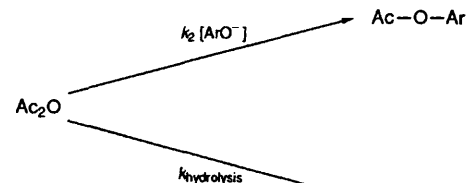
Results

Reactions of aryl esters in buffers containing phenolate ion were followed by UV–VIS spectroscopy at the optimal wavelength; they obeyed good first-order kinetics up to at least 90% of the total reaction. First-order plots were obtained from linear plots of log ($A_\infty - A_t$) *vs.* t where A_t is the absorbance at the given wavelength at time t. The first-order rate constants were dependent on total phenol concentration in the buffer and second-order rate constants for attack of phenolate ion on the esters were obtained from eqn. (4) where FB is the fraction of

$$k_2 = \frac{\mathrm{d}k_{\mathrm{obs}}/\mathrm{d}[\mathrm{phenol}]_{\mathrm{totl}}}{\mathrm{FB}} \qquad (4)$$

total phenol present as its conjugate base; previous studies[1,2] confirm this equation. The data for the reactions for attack of phenolate ions on 2,4-dinitrophenyl acetate and 4-methoxy-2,6-dimethylbenzoate are recorded in Table 1.

Reactions of acetic anhydride in buffers containing phenolate ions were followed spectrophotometrically employing wavelengths corresponding to the absorption of the phenols. Acetic anhydride undergoes an hydrolysis reaction as well as a reaction with nucleophiles under these conditions. In a typical reaction the rate of change of absorbance decreases as time progresses obeying a first-order rate law. The rate constant corresponding to the change was invariably very close to that for hydrolysis and sufficient concentration of the acetic anhydride was necessary in order to obtain sufficient nucleophilic attack to form a measurable amount of aryl ester [eqn. (5)]. An equation may be written [eqn. (6)] where the overall rate constant is



(5)

$$\text{Rate} = k_{\text{hydrolysis}} + k_2[\mathrm{Ac_2O}][\mathrm{ArO^-}] \qquad (6)$$

equal to that of the sum of hydrolysis and other nucleophilic reactions. The nucleophilic pathway takes less reaction flux than that for hydrolysis. The value of k_2 may be obtained from the initial rate at which time both acetic anhydride and phenol have not been depleted. The initial rate is converted from a change in absorbance to a change in molarity by division by the extinction coefficient of the phenol under the conditions. The initial rate was determined in either of two ways: the first-order rate constant for the overall change in absorbance was measured and the rate at $t = 0$ calculated from this; the absorbance data was fitted to a polynomial with Opus or BBC microcomputers and the rate at $t = 0$ taken from the coefficients. The initial rates were linear in phenolate ion and acetic anhydride concentrations and the second-order rate constants were obtained by division by acetic anhydride and phenolate ion concentrations; the derived parameters are recorded in Table 1. Although it was not employed in this work the rate constant for nucleophilic attack of the phenolate ion could have been obtained from the overall first-order rate constant and the product analysis is obtained by comparing the final absorbance change with that expected for complete reaction of phenolate ion with anhydride.

The parameters for attack of phenolate ion on acetic anhydride are in reasonable agreement with those determined by Leppanen *et al.*;[12a] Leppanen employed a pH-stat method under conditions which differ from those for our study.

The reactions of substituted phenolate ions with acetic anhydride and the two 2,4-dinitrophenyl esters obey good Brønsted equations (Table 2) which are illustrated in Fig. 1. The data for reaction of phenolate ions with 2,4-dinitrophenyl acetate is in reasonable agreement with that of Jencks and Gilchrist[12b] for three substituents determined under different conditions.

The Brønsted lines from this work are employed to calculate the identity rate constants (k_{ii}) for the attack of 2,4-dinitrophenolate ion on the 2,4-dinitrophenolate ester of acetic acid and 4-methoxy-2,6-dimethylbenzoic acid and these are recorded in Table 2.

Table 1 Kinetic data for the reaction of phenolate ion nucleophiles with acetyl derivatives[a]

Phenol	pK_a	[Ac_2O]/ 10^4 dm^3 mol^{-1} [b]	pH[c]	N[d]	k_2/dm^3 mol^{-1} s^{-1} [e]	[ArOH]/ mol dm^{-3} [f]	Rate[g]	λ[h]
Reaction of substituted phenolate ions with acetic anhydride								
						× 10^6	10^6 dm^3 mol^{-1} s^{-1}	
2,4-(NO_2)$_2$	4.11	386	5.00	5	0.054	33–163	0.9–2.6	400
F_5	5.49	3.62	6.00	5	3.6	180–910	4.5–19	266
2,3,5,6-F_4	5.5	4.00	6.00	5	3.0	180–890	8–32	275
2-Cl-4-NO_2	5.45	12.6	5.70	5	1.1	3–162	0.2–0.8	400
2,3,5-Cl_3	6.43	8.46	7.52	4	8.9	144–700	21–55	303
2,4,5-Cl_3	6.72	5.25	7.50	5	18	140–800	40–105	300
4-NO_2	7.14	6.8	7.00	10	18	15–80	2.5–10.7	400
2-NO_2	7.23	8.46	7.45	8	6.4	120–460	56–160	400
4-CHO	7.66	15	8.00	5	18	20–98	3.8–17	330
4-CN	7.90	12.2	9.60	5	14	19–950	190–760	275
2-Cl	8.98	6.32	8.00	5	160	19–920	28–110	300
3-Cl	9.02	7.23	8.00	5	200	170–860	25–110	275
4-Cl	9.38	11.8	8.00	5	370	91–460	46–78	280
2,6-Cl_2	6.78	7.58	7.50	5	6.3	84–420	3.8–17	300
Parent	9.99	12.3	9.00	5	320	150–750	60–270	276
4-MeO	10.20	31.1	8.00	5	610	85–420	18–55	288
Reaction of substituted phenolate ions with 2,4-dinitrophenyl 4-methoxy-2,6-dimethylbenzoate								
					× 10^3	× 10^3	10^{-5} s^{-1}	
4-Me	10.20		8.93	4	3.1	14–34	6–6.3	
F_5	5.49		8.96	4	0.24	8.8–22	3.2–3.6	
4-CHO	7.66		8.98	3	0.48	11–28	4.1–5.0	
3-Cl	9.02		9.03	4	0.35	13–32	3.3–3.7	
2-Cl	8.48		8.95	3	0.30	10–22	2.6–2.9	
4-MeO	10.2		9.03	4	2.20	9.9–25	4.9–6.2	
Parent	9.99		9.02	5	3.10	1.0–28	4.7–5.9	
4-Cl	9.38		9.05	4	0.23	13–33	4.7–4.9	
3-EtO_2C	8.90		9.09	4	0.46	8.9–28	3.4–3.8	
4-EtO_2C	8.50		9.20	5	0.39	1.0–23	3.4–4.4	
4-CN	7.95		8.88	4	0.93	1.0–25	6.4–8.5	
2,3,5-Cl_3	6.43		8.94	4	0.48	2–28	4.3–5.7	
2,4,5-Cl_3	6.72		8.99	3	0.71	6.9–14	4.5–5.0	
Reaction of substituted phenolate ions with 2,4-dinitrophenyl acetate								
						× 10^3	s^{-1}	
3-Cl	9.02		9.05	4	6.5	4.9–20	0.039–0.08	
4-CHO	7.66		8.84	4	1.8	4–21	0.0086–0.04	
4-CN	7.96		8.99	4	1.9	4–16	0.009–0.03	
4-Cl	9.38		9.10	5	35	4.8–24	0.035–0.25	
Parent	9.99		9.45	4	42	6.3–25	0.05–0.27	
4-Me	10.2		9.51	5	90	4.4–22	0.11–0.51	
4-MeO	10.2		9.53	4	107	1.1–11	0.037–0.23	
2-Cl	8.48		8.99	5	5.8	4.7–24	0.014–0.11	
4-F	9.95		9.34	6	53	1.3–32	0.016–0.36	
4-CH_3CO	8.05		8.86	5	3.6	5–25	0.012–0.075	
2,3,5-Cl_3	6.43		8.72	5	0.87	3.7–18.7	0.0065–0.02	
2,4-Cl_2	7.85		8.9	4	4.3	5.4–27	0.015–0.1	
4-EtO_2C	8.5		8.95	4	5.0	4.3–22	0.05–0.11	
2-EtO_2C	8.9		9.22	5	10.4	4.3–21	0.034–0.17	
2,3,5,6-F_4	5.53		8.59	5	0.15	5.4–27	0.008–0.11	

Table 1 (*continued*)

Phenol	pK_a	[Ac_2O]/ 10^4 dm^3 mol^{-1} [b]	pH [c]	*N* [d]	k_2/dm^3 mol^{-1} s^{-1} [e]	[ArOH]/ mol dm^{-3} [f]	Rate [g]	λ [h]
Reaction of phenolate ion with substituted phenyl acetates [j,k]								
						$\times 10^3$	10^3 s^{-1}	
3-CHO	8.00		8.98	5	0.12	10–50	0.15–0.36	350
3-Cl	9.02		8.94	4	0.21	1–5	0.15–0.25	280
3-CN	8.57		8.97	5	0.47	5–26	0.45–1.4	300
4-CN	7.95		8.99	5	0.60	5–25	0.25–1.6	300
2,5-Cl_2	7.50		9.01	5	0.39	10.6–53	0.49–2.2	306
2,3-Cl_2	7.70		8.99	6	0.30	10.6–53	0.36–1.8	304
4-Cl-3-NO_2	7.75		8.98	6	1.18	11.5–57	1.64–6.73	380
2-Cl-4-NO_2	5.45		9.01	6	1.97 [j]	5–26	1.75–5.96	410
2-Cl	8.48		8.98	6	0.085	12–62	0.17–0.59	310

[a] General conditions: 25.0 °C, 0.1 mol dm^{-3} Tris buffer, 0.1 mol dm^{-3} ionic strength maintained with solvent: dioxane–water, 40% v/v and 2,4-dinitrophenyl 4-methoxy-2,6-dimethylbenzoate at 3.10^{-4} mol dm^{-3}. Acetic anhydride reactions were studied at 0.5 mol dm^{-3} ionic strength. The 2,4-dinitrophenyl acetate concentration was 0.2×10^{-4} mol dm^{-3}. [b] Concentration of acetic anhydride in the reaction cell. [c] Average pH for all the runs. [d] Number of data points, not including duplicates. [e] Error range not more than 10% of the quoted figure. [f] Concentration range of total nucleophilic species. [g] Range of observed rates or rate constants. [h] Wavelength, λ, for kinetic runs; the 2,4-dinitrophenyl esters were studied at 400 nm. [i] This data (see previous work)[2] was repeated under the present conditions because of the slight effect on the rates. [j] Phenyl acetates prepared for this work were: 4-cyano, m.p. 58–59 °C (lit., 57 °C; B. Lack, *Ber. Dtsch. Chem. Ges.*, 1884, **17**, 1571); 3-cyano, m.p. 62.5–63.5 °C (lit., 60 °C; A. Clemm, *Ber. Dtsch. Chem. Ges.*, 1891, **24**, 826); 3-Chloro, b.p. 98–100 °C,/2 Torr (lit., 116.5 °C/21 Torr; W. J. Wohlleben, *Ber. Dtsch. Chem. Ges.*, 1909, **42**, 4369); 4-chloro-3-nitro, m.p. 83–84 °C (lit., 83–85 °C; R. Meldola, G. H. Woolrott and E. Wray, *J. Chem. Soc.*, 1896, **69**, 1321); 3-formyl, b.p. 115 °C/0.8 Torr (lit., 263 °C/760 Torr; F. Tiemann and R. Ludwig, *Ber. Dtsch. Chem. Ges.*, 1892, **25**, 2043); 2-chloro, b.p. 85–87 °C/1.4 Torr (lit., b.p. 103 °C/15 Torr; W. J. Wohlleben, *Ber. Dtsch. Chem. Ges.*, 1909, **42**, 4369); 2,3-dichloro, b.p. 104–106 °C/1 Torr (Found: C, 46.8; H, 2.7. $C_8H_6Cl_2O_2$ requires C, 46.9; H, 2.9%); 2,5-dichloro, m.p. 42.5–43.5 °C (Found: C, 46.6; H, 2.9. $C_8H_6Cl_2O_2$ requires C, 46.9; H, 2.9%). [k] Kinetics measured using 5% MeOH–water as solvent except for those of the 2,5-dichloro-, 2,3-dichloro-, 2-chloro-4-nitro-, 4-chloro-3-nitro- and 2-chloro-esters which were measured using water as the solvent; kinetic parameters measured under both solvent conditions to 2-chloro-4-nitro- and 2,3-dichloro-esters gave identical data with the error limits.

Table 2 Brønsted parameters, identity rate constants and τ values for reaction of phenolate ions with various electrophiles[a]

	pK_a [b]	β	Int [c]	log k_{ii} [d]	τ [e,f]
Electrophile [g]		β_{nuc}			
Acetic anhydride		0.58 ± 0.047	−3.04 ± 0.36		
2,4-Dinitrophenyl 4-methoxydimethyl benzoate	4.11	0.15 ± 0.067	−4.45 ± 0.57	−3.84 ± 0.85	0.18 ± 0.08
2,4-Dinitrophenyl acetate	4.11	0.57 ± 0.033	−4.00 ± 0.29	−1.65 ± 0.41	0.67 ± 0.04
4-Chloro-2-nitrophenyl acetate	6.46	0.64 ± 0.05 [h]		−1.98 ± 0.69	0.75 ± 0.06
4-Nitrophenyl acetate	7.14	0.75 ± 0.04 [h]		−1.93 ± 0.57	0.88 ± 0.05
4-Formylphenyl acetate	7.66	0.79 ± 0.04 [h]		−1.96 ± 0.63	0.92 ± 0.05
3-Nitrophenyl acetate	8.35	1.04 ± 0.09 [h]		−1.69 ± 0.58	1.22 ± 0.11
Nucleophile [i]		β_{lg}			
PhO^-	9.99	−0.33 ± 0.06 [h]		−0.82 ± 0.99	1.61 ± 0.07
3-$ClC_6H_4O^-$	9.02	−0.37 ± 0.04 [h]		−1.22 ± 0.64	1.56 ± 0.05
4-$CNC_6H_4O^-$	7.96	−0.51 ± 0.09 [h]		−2.08 ± 1.3	1.40 ± 0.05
4-$CHOC_6H_4O^-$	7.66	−0.46 ± 0.06 [h]		−2.01 ± 0.83	1.46 ± 0.07
2,3,5-$Cl_3C_6H_2O^-$	6.43	−0.82 ± 0.10 [h]		−1.91 ± 1.39	1.04 ± 0.12
2,4,5-$Cl_3C_6H_2O^-$	6.72	−0.79 ± 0.11 [h]		−1.88 ± 1.59	1.07 ± 0.13

[a] Conditions for the first three electrophiles (Ac_2O, 24DNPMDMB and 24DNPA) are taken from Table 1. The Brønsted law is log $k = \beta pK$ + intercept. [b] The pK_a of the conjugate acid of the leaving group or attacking group is taken from the compilation of Jencks and Regenstein (W. P. Jencks and J. Regenstein, *Handbook of Biochemistry and Molecular Biology*, 3rd edn., ed. G. Fasman, Chemical Rubber Co., Cleveland, Ohio, 1976, p. V21. [c] The intercept (see footnote *a*). [d] This value is obtained from the Brønsted equation of the p*K* of the nucleophile or leaving group. [e] The value of τ is obtained from β values from equations given in the Appendix. [f] The value of β_{eq} employed to calculated α and τ values is taken to be 1.7[13c] The average value of β_{eq} calculated from the observed kinetic β value and that calculated from eqns. (7) or (8) for the reverse kinetic β is 1.45 ± 0.52; this low value has a rather large error limit which encompasses the literature value. [g] The variant nucleophile is the substituted phenolate ion series. [h] Data taken from ref. 2. [i] The variant electrophile is the substituted phenyl acetate series.

The values of β_{nuc} (Table 2) for acyl transfer between phenolate anions obey eqn. (7) which differs from the one

$$\beta_{nuc} = (0.095 \pm 0.032)pK_{lg} + (0.118 \pm 0.23) \quad (n = 5, r = 0.858) \quad (7)$$

previously quoted[2] due to refinement by use of extra experimental data from this study; eqn. (8) is from previous work.[2]

$$\beta_{lg} = (0.15 \pm 0.03)pK_{nuc} - (1.73 \pm 0.23) \quad (n = 6, r = 0.932) \quad (8)^2$$

The large difference between β_{nuc} for 2,4-dinitrophenyl acetate found here (Table 2) and that found by the Kwon, Lee and Um[13b] (0.038 ± 0.19) is accommodated by the large deviation arising from the fewer points used in their Brønsted plots.

The difference, $\beta_{eq} = \beta_{nuc} - \beta_{lg}$, should theoretically be independent of pK_a, but the experimental error on the slopes of

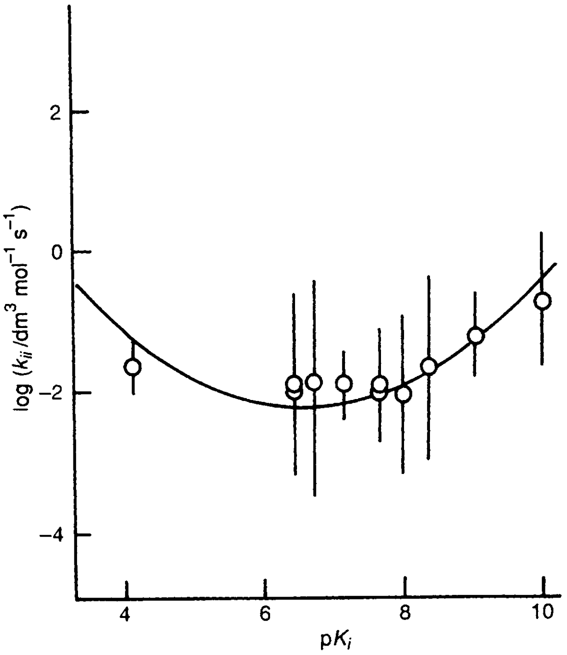


Fig. 2 The Lewis–Kreevoy plot for identity reactions involving attack of phenolate ions on phenyl acetates. The data are from Table 2 and the line is calculated from eqn. (9) employing values of p_{xy}, $(N + L)$ and C given in the results section.

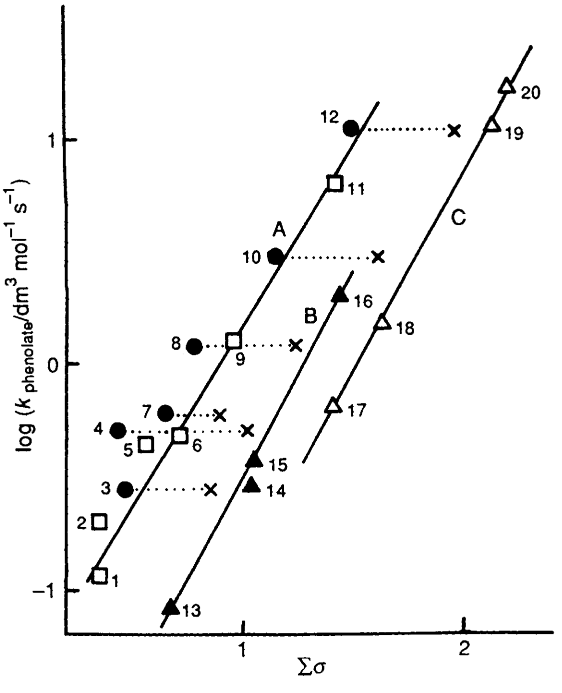


Fig. 3 Hammett dependence for attack of phenolate ion on substituted phenyl acetates. Data are from Table 1 and ref. 2.*

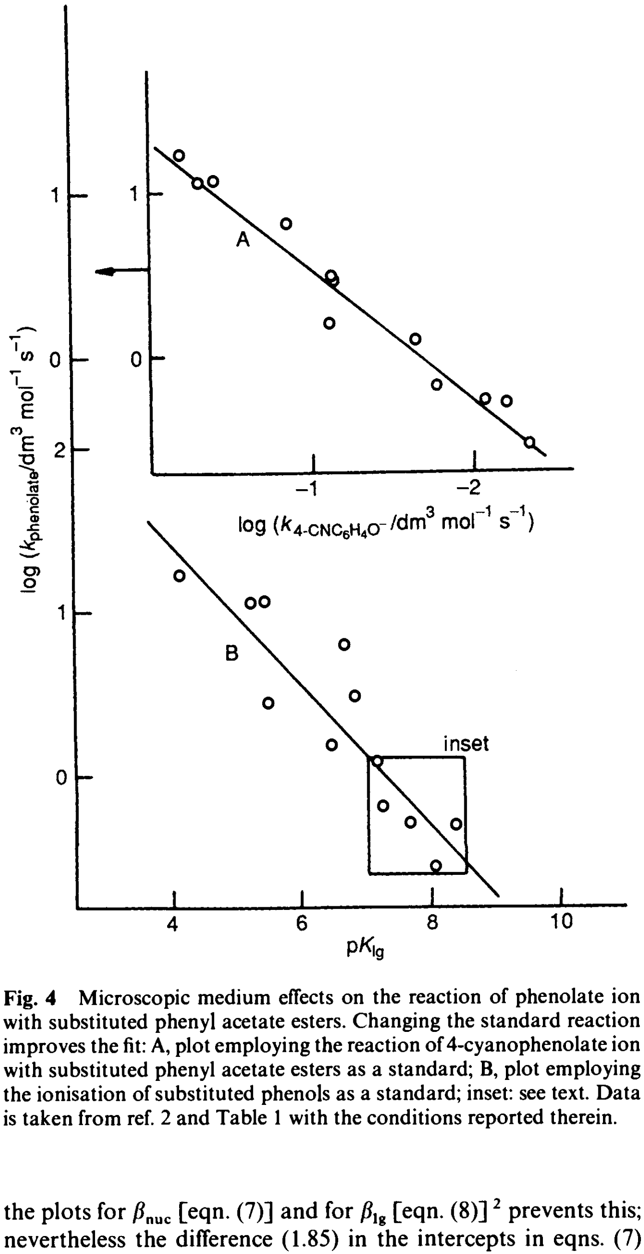


Fig. 4 Microscopic medium effects on the reaction of phenolate ion with substituted phenyl acetate esters. Changing the standard reaction improves the fit: A, plot employing the reaction of 4-cyanophenolate ion with substituted phenyl acetate esters as a standard; B, plot employing the ionisation of substituted phenols as a standard; inset: see text. Data is taken from ref. 2 and Table 1 with the conditions reported therein.

the plots for β_{nuc} [eqn. (7)] and for β_{lg} [eqn. (8)][2] prevents this; nevertheless the difference (1.85) in the intercepts in eqns. (7) and (8) is within the error limits of the expected value (1.7)[13c] for β_{eq}. The data for β_{lg} and β_{nuc} may be forced to fit the condition ($\beta_{\text{eq}} = \beta_{\text{nuc}} - \beta_{\text{lg}} = 1.7$) assuming p_{xy} is the same for each equation (see Appendix). When this is done the values of p_{xy}, N and L (see Appendix) are, respectively, 0.16, −0.21 and −1.91.

The values of log k_{ii} (Table 2) should fit the theoretical eqn. (9) [see eqn. 7(*a*) in the Appendix]. The parameter pK_i is the pK_a of the conjugate acid of the phenolate ion nucleophile involved in the identity reaction; p_{xy} is defined by Jencks and Jencks.[13a] The value of the disposable parameter, C, is obtained by fit of the experimental data for log k_{ii} to eqn. (9) by a grid search program

$$\log k_{ii} = p_{xy}\text{p}K_i^2 + (N + L)\text{p}K_i + C \qquad (9)$$

employing the parameters $p_{xy} = 0.16$, $(N + L) = -2.12$. The fit of the calculated eqn. (10) with $C = 4.8$ is illustrated in Fig. 2.

The dependence of the second-order rate constant for attack of phenolate ion on substituted phenyl acetates is illustrated in Figs. 3 and 4. The data for Fig. 3, the Hammett dependence, is taken from Table 2 in an earlier work[2] and Table 1. The data for the substituents with resonating potential fit the line defined by the non-resonating substituents consistent with the operation of a Hammett σ dependence rather than σ⁻ correlation. The

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* The σ values (including the notional ones for *ortho* substituents) are taken from Perrin's complication (D. D. Perrin, Boyd Dempsey and E. P. Serjeant, 'pK_a *Predictions for Organic Acids and Bases*,' Chapman and Hall, London and New York, 1981). Line A is for esters with no *ortho* substituents and the crosses indicate 'σ⁻' points for this set; the line is derived from values for those substituents with no expected classical resonance interaction (□); substituents with capacity for resonance interaction (●) fit this line. Lines B and C correlate data for sets with 2-chloro (▲) and 2-nitro (△) substituents, respectively; no significance is attached to the value of the '*ortho*' σ constants employed in these correlations. Identification is: 1, 3-CHO; 2, 3-Cl; 3, 4-Ac; 4, 4-CHO; 5, 3-CN; 6, 3-NO_2; 7, 4-CN; 8, 4-NO_2; 9, 4-Cl, 3-NO_2; 10, 3-Cl, 4-NO_2; 11, 3,5-$(NO_2)_2$; 12, 3,4-$(NO_2)_2$; 13, 2-Cl; 14, 2,3-Cl_2; 15, 2,5-Cl_2; 16, 2-Cl, 4-NO_2; 17, 2-NO_2; 18, 4-Cl, 2-NO_2; 19, 2,5$(NO_2)_2$; 20, 2,4-$(NO_2)_2$.

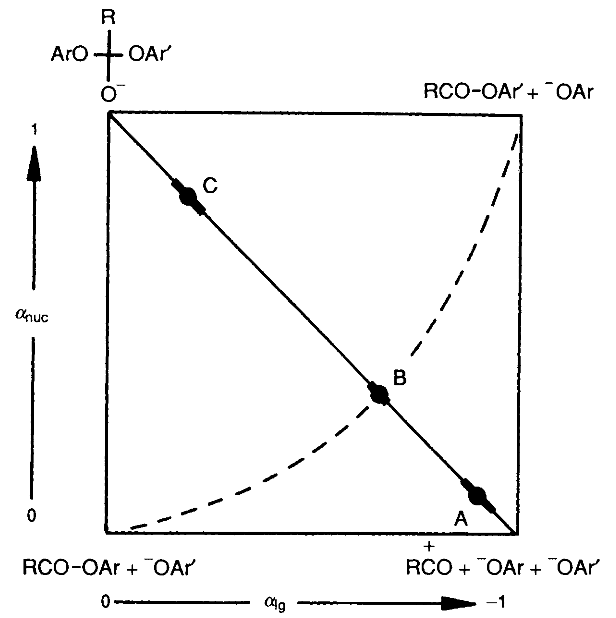


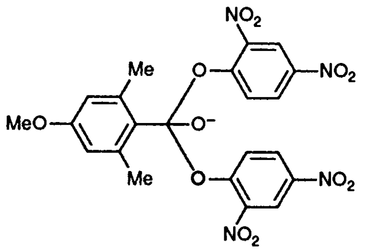
Fig. 5 Reaction map for the attack of substituted phenolate ions on substituted phenyl esters. Positions on the tightness diagonal (Kreevoy)[22] represent transition state structures (given by τ values)[22] for identity reactions of A, 2,4-dinitrophenyl 4-methoxy-2,6-dimethylbenzoate; B, 2,4-dinitrophenyl acetate; C, phenyl acetate (data from Table 2). Confidence limits on the τ values are given by the thick lines. The dashed line is the notional path through the reaction map for the identity reaction of 2,4-dinitrophenolate ion with 2,4-dinitrophenyl acetate.

diagram indicates that separate lines exist for phenyl esters with no *ortho* substituents and for phenyl esters with 2-chloro and with 2-nitro substituents. The *ortho* σ values are employed for the latter correlations where contributions from the *ortho* substituent will be relatively constant. Fig. 4 illustrates the Brønsted dependence of the rate constants and the dependence on the analogous reaction between 4-cyanophenolate ion and aryl acetates.

Discussion

Open or 'Exploded' Transition State.—The main conclusion from this work is that suitable adjustment of the substituents of the acyl group enables the transition state to assume an almost completely open structure where forming and breaking bonds are very weak. The value of α_{nuc} for attack of phenolate ions on 2,4-dinitrophenyl 4-methoxy-2,6-dimethylbenzoate is 0.089 if the reasonable assumption is made that β_{eq} (Appendix) for transfer of the benzoyl group from phenyl esters is 1.7. The derived value of τ (0.18) indicates that the identity reaction of 2,4-dinitrophenolate ion with the ester is even more imbalanced than that for the acetyl group transfer between the same nucleophiles. The imbalance in the benzoyl group transfer is similar to that seen in transfer for the sulfuryl ($-SO_3^-$) and phosphoryl ($-PO_3^{2-}$) groups between pyridine nucleophiles ($\tau = 0.18$ and 0.14, respectively)[14a,b] where internal negatively charged nucleophiles are available to stabilise the acylium component of the transition state.

The transfer of a general acyl group between phenolate ion nucleophiles may be represented by a reaction map as shown in Fig. 5. It is not possible in this study to place numbers for the energies of the states at the corners of the reaction map for the benzoate esters although Guthrie[3e] has done this for the acetyl group transfer case. However, it is reasonable that the top left state of the diagram should be more energetic for the 4-methoxy-2,6-dimethylbenzoate case than for the acetate because of steric crowding of the putative tetrahedral addition compound **2**. The energy of the right bottom state should be lower for the benzoate because of resonance interactions between the 4-methoxy group and the acylium centre **3**. The net result is a surface which is more skewed for the methoxydimethylbenzoyl group transfer than for the acetyl case and which therefore forces the transition state of the identity reaction between dinitrophenolate anions towards the benzoylium ion corner in the diagram.



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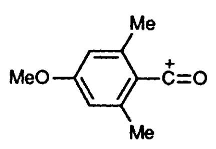

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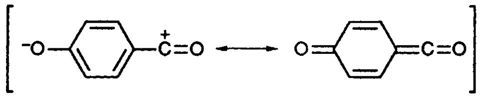

4

Provision in the acylium ion of an interacting negative atom can force the mechanism to involve a discrete acylium ion intermediate. Such an intermediate occurs when the acyl function is the conjugate base of 4-hydroxy-2,6-dimethylbenzoate where the acylium ion **4** is stabilised by the neutralisation of the cationic character.[11a,14c,d] Other examples include the transfer of the carbamoyl and acetoacetyl type groups between nucleophiles where isocyanate and ketene intermediates have been demonstrated.[14e,f]

Lewis–Kreevoy Plots.—The Brønsted equation for attack of phenolate ions on 2,4-dinitrophenyl acetate (Table 2) indicates a Leffler α_{nuc} value of 0.336; this gives rise to a τ value of 0.67 (Fig. 5) for the identity reaction for 2,4-dinitrophenolate ion attack. This parameter indicates a transition state with significant imbalance of charge in a dissociative process. Previous work[2] has indicated that the Lewis–Kreevoy plot of log k_{ii} *versus* the pK_a of the ligand should possess curvature if β_{nuc} and β_{lg} are linearly related, respectively, to pK_{lg} and pK_{nuc}. Such plots should be paraboloid and curvature has been demonstrated for the transfer of the acetyl and diphenylphosphoryl groups between phenolate anions. The data for β_{nuc} and β_{lg} for acetyl transfer including the new point have been re-worked to yield a new set of p_{xy}, $(N + L)$ and C parameters and the line predicted from eqn. (9) (with only one disposable parameter, C) is compared with the experimental data in Fig. 2. It is doubtful if the present approach can yield any better certainty in log k_{ii} unless very large numbers of points are to be used in the individual Brønsted plots; even if these were available the problem of deviations due to microscopic medium effects would still pertain. The explicit determination of identity rate constants by use of isotope incorporation is not always possible; such an approach would be very difficult in the present case. The skeptic could draw a straight line through the error bars in Fig. 2, but the data is more accurate than to just give a range of values for log k_{ii}, and the curvature in the line is predicted from eqns. (7) and (8) and is not due to a fit to the points in Fig. 2.

The physical meaning of Fig. 2 is that reactions with a positive β_{ii} value (where the pK_a of the conjugate acid of the nucleophile or nucleofuge places the point on the upward going plot) possess a build up of negative charge on the central acyl group in the transition state. Points on the downward plot (negative β_{ii}) involve a depletion of negative charge on the central acyl function. In the central portion of the curve, where $\beta_{ii} = 0$, there is no charge change on the central acyl group and a synchronous mechanism operates. The pK_i where $\beta_{ii} = 0$ is predicted (see the Appendix for the equation) to be 6.63.

Hammett σ and σ⁻ Dependences.—The observation of a Hammett σ^- dependence in rate or equilibria is regarded as evidence that the resonance interaction between charge at the reaction centre and electron-withdrawing substituents such as 4-cyano, 4-nitro or 4-acetyl- undergoes a change between the two states being measured.[15b] So far as we are aware the diagnosis (for σ^-) has mostly referred to a change between 'full' resonance and 'no' resonance. Intermediate positions of bond formation or fission have been reported for the alkaline hydrolysis of phenyl esters;[15c,d] the better fit of the data to a Yukawa–Tsuno type equation in this case could be merely due to the use of an extra parameter which brings scatter due to microscopic medium effects (see later) into line. Attack of substituted phenolate ions on 4-nitrophenyl acetate,[1] 2,4-dinitrophenyl acetate (this work), 4-nitrophenyl diphenylphosphinate,[15e] epoxides[16] and chloro-2,4-dinitrobenzene[17] all exhibit σ^- Hammett plots. These results can be interpreted to mean that the oxyanion loses its ability to resonate with the 'σ^-' substituents in the respective transition states relative to the phenolate ion ground state. The values of ρ_{nuc} for these reactions are less than those of ρ_{eq} (where these are known) for the overall addition of the phenolate ion to form the ArO–X bond. On the basis of this comparison the observation of a σ^- dependence for attack of substituted phenolate ions on a standard aryl acetate ester is not consistent with complete bond formation; the data indicate that the resonance component of the ground state is lost essentially in advance of full bond formation to the oxygen. The converse presumably holds namely that in the reverse reaction where the phenolate ions are lost from substituted phenyl acetates the resonance component is the last to be restored; this implies that the Hammett dependence in the above reactions (for attack of a standard phenolate ion on aryl acetates) should have a σ dependence. This is indeed observed for this work (Fig. 3; attack of phenolate ion on aryl acetates) and also that of Hoz and Buncel.[18a] Since the value of α_{lg} is small for attack of phenolate ion or 4-chlorophenolate ion, indicating little bond fission, it is not surprising that a σ rather than a σ^- Hammett dependence is observed even in a concerted reaction.

There are acyl group transfer reactions where a Hammett σ^- dependence is observed in both forward and reverse reactions namely the decomposition of carbamate monoanions[18b] and the reaction of phenolate ions with cyclic sultones.[18c]

The Hammett σ dependence in attack of phenolate or hydroxide ion on aryl acetates is consistent with either putative stepwise or putative single step processes. Addition of strongly basic nucleophiles to aryl esters is expected to be the rate-limiting step in a two-step process; these nucleophiles would also place the transition state of the single step process in the top left quadrant of Fig. 3 where bond fission lags behind bond formation.

Departure of weakly basic nucleofuges in acetyl group transfer (as in attack of substituted phenolate ions on 2,4-dinitrophenyl acetate) would involve bond formation in advance of bond fission giving rise to a σ^- Hammett dependence; the single step process would possess a transition state structure in a region of Fig. 5 also giving a σ^- dependence. It is not possible to study, at this stage, the nucleophilic attack of a very weakly basic oxyanion on aryl acetates because of difficulties in driving the equilibria. It is noted that carboxylate ion attack in reactions driven by an intramolecular process, namely the cyclisation of aryl glutarate and succinate monoanions[19a] and aryl hippurates[19b,c] (to form respectively, glutaric and succinic anhydrides and phenyloxazolinone), possess Hammet σ^- dependences; these results can be explained by both stepwise and single step processes.

Diagnosis of Concerted Mechanisms.—Diagnosis of a concerted mechanism (a mechanism with only one transition state between reactant and product) for a reaction requires a method which 'counts' the number of transition states along the pathway. Methods which diagnose structure, such as those measuring balance or the nature of the Hammett dependence, do not diagnose whether a reaction is concerted or not. The extent of bond formation and fission in the transition state can bear any relationship with each other and the ratio of $\alpha_{\text{lg}}/\alpha_{\text{nuc}}$ is defined as numerical measure of balance. In a synchronous concerted mechanism the balance is unity as it is for transition states which lie on the tightness diagonal. The effect of metal ions (Suh and Heo)[20a] and the experiments of Haberfield and Trattner[20b] refer to structure indicators and as such do not 'count' transition states as required in the diagnosis of concertedness. The observation of extensive bond fission in a nucleophilic displacement could indicate either a concerted mechanism or a stepwise one where bond fission is rate limiting.

Kwon, Lee and Um[13b] have shown that $\beta_{\text{nuc}} - \beta_{\text{lg}}$ for 3-nitrophenyl acetate reacting with phenolate ion nucleophiles is less than 1.7 (β_{eq})[13c] consistent with the existence of an extra transition state. However, the data on which they base their value of β_{lg} (for attack of 3-nitrophenolate anion on aryl acetates) requires extrapolation of β_{lg} values from a plot of β_{lg} *vs.* pK_{nuc} where the deviations are large; Kwon, Lee and Um chose to employ the β_{lg} (their value $= -0.51$) for the attack of 4-cyanophenolate ion (to approximate to that for the 3-nitrophenolate ion) to combine with β_{nuc} for phenolate ion attack on 3-nitrophenyl acetate (their value of $\beta_{\text{nuc}} = 0.91 \pm 0.05$).[13b] Re-calculation from the data of their paper[13b] indicates a value of $\beta_{\text{lg}} = -0.65 \pm 0.35$; the large standard error on this value is similar to that on the β_{lg} obtained from extrapolation from the β_{lg} plot. The difference between ($\beta_{\text{nuc}} - \beta_{\text{lg}}$) and the literature value of β_{eq}[13c] is less than the standard error on $\beta_{\text{nuc}} - \beta_{\text{lg}}$ ($0.4 = 0.35 + 0.05$). A similar problem with accumulation of errors arises if the data of this paper are employed in the above arguments.

Microscopic Medium Effects.—Recent work of Buncel, Um and Hoz[18a] has pointed out the existence of microscopic deviations from a linear Brønsted plot;[15e,21] they show that over a small range of pK_a with five substituents there is no obvious correlation for attack of 4-chlorophenolate ion with substituted phenyl acetates.[18a] The lack of correlation will be accentuated if the ordinate is to a smaller scale than is the abscissa, as is often the case in Hammett representations. The deviations are not due to experimental error and when a larger range and number of points are taken a linear Brønsted correlation becomes apparent (albeit, one including non-experimental scatter); Fig. 4 illustrates the fit for attack of phenolate ion on aryl acetates including an inset demonstrating the ranges taken by Hoz, Um and Buncel for 4-chlorophenolate ion nucleophile. The deviations are caused by the slight differences in microscopic medium in comparison of the effect of substituent on the energy differences between ground and transition states in the reaction with ground and product states in the standard ionisation.

A much improved fit is obtained in free energy correlations when a more closely related standard reaction is employed which is closely related to the reaction in hand and microscopic media differences can then be expected to be almost identical; comparison of the rate constants for phenolate ion attack with those for 4-cyanophenolate ion reaction (Fig. 4) indicates that the sum of the residuals is 0.759 compared with 2.63 and 2.76

for the respective Brønsted correlations for both of these nucleophiles.

Acetate Ion as a Leaving Group.—The α_{nuc} value (0.34) for the reaction of phenolate ions with acetic anhydride is close to that for the 2,4-dinitrophenyl acetate reaction. The bond formation in phenolate ion attack on acetic anhydride is similar to that in the 2,4-dinitrophenyl acetate reaction although the rate constants for the acetic anhydride reactions are some ten times larger than those of the 2,4-dinitrophenyl ester. The return reaction, namely nucleophilic attack of acetate ion on aryl acetates is some two powers of ten less reactive than that of the phenolate ion of pK_a identical with that of acetic acid. Such a reduced nucleophilic reactivity enables significant general base catalysis of hydrolysis in the acetate reaction.[15a]

Appendix

Definitions.—The value of the tightness parameter τ is given by eqn. (1a);[22] it ranges from 0–2 and refers to the structure of

$$\tau = 2\alpha_{nuc} = 2 + 2\alpha_{lg} \tag{1a}$$

the transition state of an identity reaction which lies along the diagonal as illustrated in Fig. 5. Thus, a τ value of 0 refers to an acylium ion-like transition state at the bottom right corner of the map of Fig. 5. A τ value of 2 is at the top left and a τ value of 1 refers to a synchronous mechanism with a transition state structure at the centre of the map. The Leffler parameters α_{nuc} and α_{lg} have opposite signs and refer to the ratios β_{nuc}/β_{eq} and β_{lg}/β_{eq} respectively. In the case of identity reactions the value of α_{nuc} is given by the simple relationship $\alpha_{nuc} = 1 + \alpha_{lg}$. The following equations hold for identity reactions [eqns. (2*a*) and (3*a*)].

$$\delta = \beta_{ii}/\beta_{eq} = \alpha_{nuc} + \alpha_{lg} = \tau + 1 \tag{2a}$$

$$\beta_{ii} = \mathrm{d}\log k_{ii}/\mathrm{dp}K_i = \beta_{nuc} + \beta_{lg} \tag{3a}$$

Given that the values of β are linearly related to pK_a we can define eqns. (4*a*) and (5*a*) and these values can then be related to $\log k_{ii}$ and β_{ii} through eqns. (6*a*) and (7*a*).

$$\beta_{nuc} = p_{xy}\mathrm{p}K_{lg} + N \tag{4a}$$

$$\beta_{lg} = p_{xy}\mathrm{p}K_{nuc} + L \tag{5a}$$

$$\beta_{ii} = 2p_{xy}\mathrm{p}K_i + N + L \tag{6a}$$

$$\log k_{ii} = p_{xy}\mathrm{p}K_i^2 + (N + L)\mathrm{p}K_i + C \text{ [eqn. (9) in text]} \tag{7a}$$

Substitution into eqn. (6*a*) for $\beta_{ii} = 0$ indicates that a synchronous mechanism will exist at a pK_i when eqn. (8*a*) holds.

$$\mathrm{p}K_{i(\mathrm{synchronous})} = (N + L)/2p_{xy} \tag{8a}$$

The Leffler parameters are qualified by subscript 'lg' or subscript 'nuc' to indicate their assignment to the extent of fission or formation respectively of the two bonding changes in the transition state.

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