

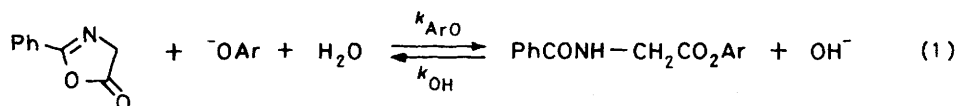
Rate and Equilibrium Studies of the Reaction of Oxyanions with 2-Phenyloxazol-5(4H)-one

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Equilibrium constants for the reaction of phenoxide ions with 2-phenyloxazol-5(4H)-one at 25 °C and 1M ionic strength obey a Brønsted relationship ($\log k_{\text{OH}}/k_{\text{ArO}} = \log K' = -1.73\text{p}K_{\text{ArOH}} - 15.81$) and are not subject to steric effects from *ortho*-substituents. Both forward and reverse rate parameters exhibit steric effects, and the Brønsted equations for *meta*- and *para*-substituted species are $\log k_{\text{OH}} = -0.81\text{p}K_{\text{ArOH}} + 9.75$, and $\log k_{\text{ArO}} = 0.95\text{p}K_{\text{ArOH}} - 6.40$. There is no break in the Brønsted line in the region of $\text{p}K_{\text{ArOH}}$ 5–11, consistent with a single transition-state. An upward deviation exists for oxyanions with low basicity ($\text{p}K_{\text{XOH}} < 5$); one of these oxyanions, betaine, has a solvent deuterium oxide isotope effect for its reaction with the oxazolone greater than 2, consistent with a general base mechanism for attack for these species. The results for nucleophilic attack of phenolate anions are in agreement with a *concerted* displacement at the carbonyl group.

Previous work from this laboratory¹ has examined the changes in effective charge on atoms in the forming and breaking bonds for the reaction of aryloxanions with 2-aryloxazol-5(4H)-ones [e.g. equation (1)]. We presented *prima facie* evidence¹ for a

mmol) was dissolved in dimethylformamide (5 ml) and added to the halogenophenol (5 mmol) in ethyl acetate (20 ml). The mixture was stirred for 4 h and the product urea then filtered off. The filtrate was evaporated *in vacuo* and the resultant crystalline



mechanism where fission of endocyclic C–O bonds and formation of ester C–O bonds have advanced to a similar extent in the transition state of the rate-controlling step.[†] The data for the effective charge on the exocyclic oxygen is derived from the Brønsted selectivities for k_{OH} and k_{ArO} for variation of the substituent on the phenolate nucleophile. Including the points for the attack of acetate and hydroxide ion in the Brønsted plot (Figure 6 in ref. 1) for the attack of phenolate ions on 2-phenyloxazol-5(4H)-one raises doubts as to the linearity of the plot; effective charges derived from the Brønsted slope could be ambiguous. Curvature could be construed as evidence for a change in rate-limiting step.

In order to counter this criticism we have investigated the linearity of the Brønsted relationship for attack of oxyanion nucleophiles [on 2-phenyloxazol-5(4H)-one] with $\text{p}K$ values ranging from 1.8 to 11. It proved impossible to measure the rate constants for attack of very weakly basic phenolate ions directly. We therefore resorted to the strategy of determining the dependence on $\text{p}K$ of the equilibrium constant for formation of the ester ($K' = k_{\text{OH}}/k_{\text{ArO}}$). A linear free energy relationship was observed, which we have used to calculate the equilibrium constant for the reaction of weakly basic oxyanions. A value of k_{ArO} may then be calculated from the *measured* value for k_{OH} .

The results of this work confirm our previous conclusion that large changes in bond order occur in both forming and breaking bonds in the transition state of the rate-limiting step.

Experimental

Materials.—Halogenophenyl esters of *N*-benzoylglycine were prepared in the following general way. *N*-Benzoylglycine (5

residue recrystallised. The methylphenyl esters of *N*-benzoylglycine were prepared by warming a mixture of *N*-benzoylglycine (2.5 g) and the phenol (1.8 g) with POCl_3 on a water-bath until homogeneous. The product was cooled and swirled with water (ca. 20 ml), and the oily liquid was decanted and treated with 2M-NaOH to extract residual phenol and acid. The material solidified and the product was dried and recrystallised. 2-Phenyloxazol-5(4H)-one, prepared as previously described,¹ had m.p. 88–89 °C (lit.,² m.p. 86 °C). 4-Nitrophenyl *N*-benzoylglycinate was prepared as described earlier.³ Structures of the esters and the oxazolone were confirmed by n.m.r. and i.r. spectroscopy. The carboxylic acids and phenols were recrystallised, redistilled, or sublimed from laboratory reagent grade materials.

Deuterium oxide (99.8% D), DCl in D_2O (99.0% D), and NaOD in D_2O (99.0%) were from Aldrich. Ordinary water was doubly distilled from glass; buffers and reagents used in the kinetic studies were either of analytical reagent grade or were redistilled or recrystallised prior to use. Microanalyses were carried out on the *N*-benzoylglycinate esters and these gave satisfactory results.[‡] Melting points are recorded in Table 1.

Methods.—N.m.r. spectra were recorded by Dr. D. O. Smith with a JEOL 100-MHz instrument; i.r. spectra were measured with a Perkin-Elmer 297 machine. U.v.–visible spectra were scanned repetitively with a Unicam SP 800 instrument fitted with an SP 825 automatic scanning device. Kinetics were measured by following the change in absorbance at a fixed wavelength with a Perkin-Elmer 124, a Unicam SP 800, or a Pye-Unicam SP6-550 instrument fitted with thermostatic water-bath and external potentiometric recorder. Measurements of

[†] We correct an error in ref. 1: β_{1g} for decomposition of aryl *N*-benzoylglycinates in alkali should be -0.8 and the value β_{1g}/β_{eq} for fission of the ester bond should be 0.49 in structure II.

[‡] Available as Supplementary Publication No. SUP 56383 (2 pp.). For details of Supplementary Publications see Instructions for Authors, in this issue.

Table 1. Alkaline hydrolysis of substituted phenyl *N*-benzoylglycinates^a

Subst.	M.p. (°C)	p <i>K</i> ^{ArOH}	<i>N</i> ^c	<i>k</i> _{OH} /mol ⁻¹ s ^{-1e}	Δ(pH) ^d	λ/nm ^f
3-Me	97–98	10.08	5	26.9	10.5–12	285
2-Me	112–113	10.28	5	12.9	10–12	285
3,5-Me ₂	120–121	10.19	5	28.8	10–12	296
2,4-Me ₂	125–126	10.60	5	10.5	10–12	290
2,3-Me ₂	99–101	10.54	5	8.32	10–11	295
2,5-Me ₂	105–106	10.41	4	10.0	10–12	295
2,6-Me ₂	135–136	10.63	5	0.370	11–12	292
2,4,6-Me ₃	147–148	10.9	5	0.190	11.5–12.5	300
2,3,6-Me ₃	121–122	10.64	5	0.490	11–12	295
F ₅	138–139	5.49	4	156 000	7–8	255
2,3,4,6-F ₄	137–138	5.56	5	109 000	7–8	255
2,3,4,5-Cl ₄ ^b	191–192	5.92	4	24 300	7–8	250
2,3,5-Cl ₃ ^b	131–132	6.43	4	11 400	7–8	255
2-Cl	115–116	8.48	5	336	8–9	235
4-NO ₂	170–171	7.14	6	7 150	6–11	400

^a At 25 °C; ionic strength kept at 1M with KCl. ^b 10% Ethanol used to complete dissolution of the ester. ^c Number of data points not including duplicates. ^d Buffers were: phosphate (6–7), tris(hydroxymethylamino)methane (7–9), hydrogen carbonate (9–10.5), and phosphate (10.5–12.5). Total added buffer concentrations were kept at 0.005M. ^e Errors in the derived rate parameters are less than 10%. ^f Wavelength for kinetic study.

pH were carried out with a Radiometer PHM 62 digital pH meter standardised with E.I.L. buffers to ± 0.02 pH units.

Kinetics were measured by adding a small volume (usually 25 μ l of the substrate dissolved in acetonitrile or ethanol) to the buffer solution (2.5 ml) containing the appropriate reagents. The buffer was held in a silica cell in the thermostatted cell compartment of the spectrophotometer. The spectrum was scanned repetitively to determine the optimal wavelength for the kinetic study. Experiments were then carried out as described above at the single wavelength, recording absorbance as a function of time. Pseudo-first-order rate constants were estimated by plotting $A_t - A_\infty$ versus time (A_t = absorbance at time t) on two-cycle semilogarithmic graph paper. The buffer solutions for reaction of oxyanions with 2-phenyloxazol-5(4*H*)-one were prepared by adjusting the pH of a solution of the oxygen acid (XOH), with buffer component at 0.005M and KCl 1M, to a convenient value. A reference buffer was prepared to the same specification but without added oxygen acid. Mixing of the two buffers enabled us to prepare solutions with oxygen acid at specified concentrations with the same pH and ionic strength. Buffers containing deuterium oxide as solvent were made up by adjusting the pD values of mixtures of the appropriate species in D₂O (pD = pH meter reading + 0.4).⁴

Statistical analyses of the data were performed using an Acorn BBC computer with programmes devised by Dr. A. D. Hall of this laboratory.

Results

Hydrolyses of the aryl *N*-benzoylglycinates obey good pseudo-first-order kinetics over at least 90% of the reaction; the rate constants are linear in hydroxide ion concentration [equation (2)]. Hydroxide ion concentrations (equivalent to activities at

$$\text{rate} = k_{\text{OH}}[\text{OH}][\text{ester}] \quad (2)$$

the pH values in question) were calculated from the pH and the ionic product of water at the temperature and ionic strength employed. The values of k_{OH} were determined from the slopes of the linear plots of pseudo-first-order rate constants versus hydroxide ion concentration (see Figure 1 for an example) and are recorded in Table 1. The values of k_{OH} , including the data from previous work⁵ and omitting 2,6-disubstituted phenyl esters and the 2-methyl- and 2-chloro-phenyl esters, obey an

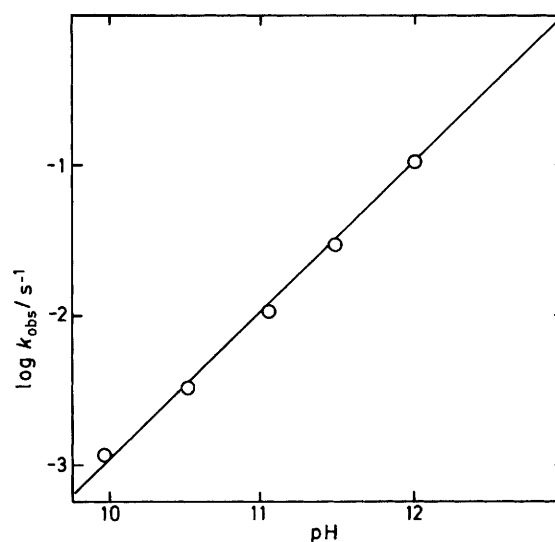


Figure 1. Dependence on pH of the hydrolysis of 2,5-dimethylphenyl *N*-benzoylglycinate at 25 °C and ionic strength made up to 1M with KCl; line calculated from data in Table 1

excellent linear Brønsted relationship with the p*K* of the leaving phenolate group [equation (3) and Figure 2]. There is no

$$\log k_{\text{OH}} = (-0.81 \pm 0.03)\text{p}K^{\text{ArOH}} + (9.75 \pm 0.24) \quad (r = 0.993) \quad (3)$$

deviation from the regression line if the 2- and 6-positions of the leaving phenol are occupied by fluorine atoms. The slope of the correlation line agrees well with the previous value for a smaller number of leaving groups (-0.8).⁵

The attack of oxyanions on the oxazolone gives good pseudo-first-order kinetics, and it is assumed that the rate law is equation (4). Values of k_{XO} were computed from the linear plot of k_{obs}

$$k_{\text{obs}} = k_{\text{intercept}} + k_{\text{XO}}[\text{XO}^-] \quad (4)$$

versus concentration of the oxyanion. The oxyanion concentration was determined from the added total hydroxy

species, the pH of the reaction mixture, and the pK value of the hydroxy group in question. The intercepts ($k_{\text{intercept}}$) for the linear plots (see Figure 3 for an example) agree with the values calculated from previous data¹ for the hydrolysis of the oxazolone at the measured pH value. The Brønsted correlation of k_{XO} with the pK of the attacking oxyanion group is illustrated in Figure 4. There is a good linear relationship for phenolate ion attack [equation (5)], provided phenolate ions without any

ortho-methyl groups are employed. The carboxylate ions show a positive deviation from this plot in the lower pK region.

Equilibrium constants for formation of the oxazolone from the aryl ester and hydroxide ion may be calculated from the values of k_{ArO} and k_{OH} from this paper and from previous studies.¹ The values $K' = k_{\text{OH}}/k_{\text{ArO}}$ are given in Table 2, and Figure 5 illustrates an excellent linear Brønstead correlation

$$\log k_{\text{ArO}} = (0.87 \pm 0.08)\text{pK}^{\text{ArOH}} - (5.67 \pm 0.75) \quad (r = 0.973) \quad (5)$$

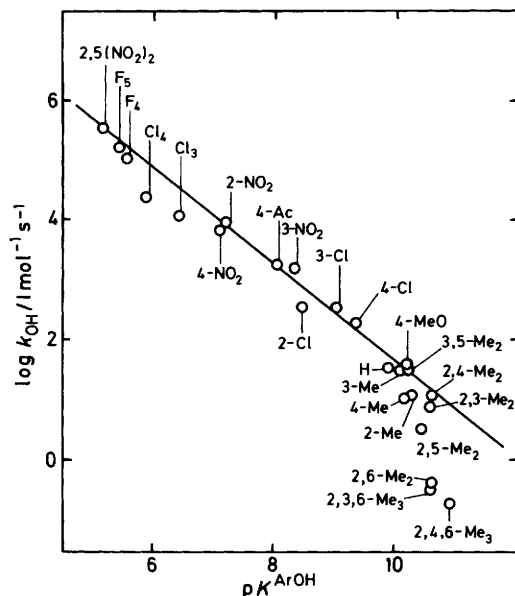


Figure 2. Brønsted plot for the alkaline hydrolysis of aryl *N*-benzoylglycinates at 25 °C and ionic strength made up to 1M with KCl; line is calculated from equation (3)

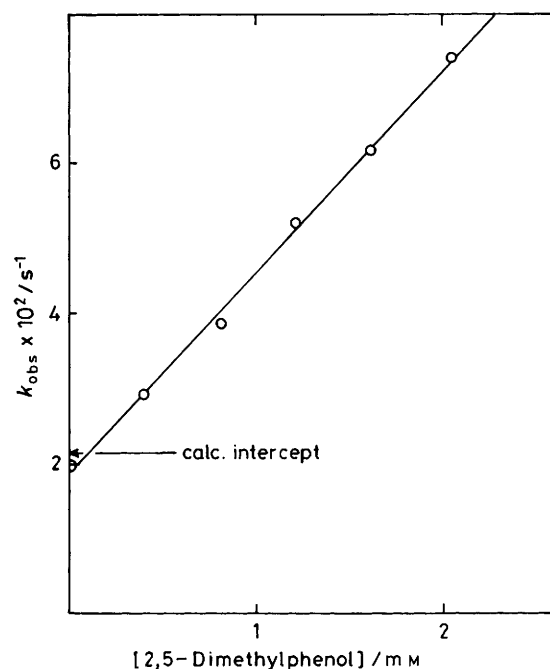


Figure 3. Reaction of 2,5-dimethylphenol buffers with 2-phenyloxazol-5-(4*H*)-one at 25 °C; ionic strength maintained at 1M with KCl and pH 8.97. The arrow shows the intercept ($2.12 \times 10^{-2} \text{ s}^{-1}$) calculated at pH 8.97 from parameters for the oxazolone hydrolysis described previously.¹ The line is calculated from the parameters in Table 2

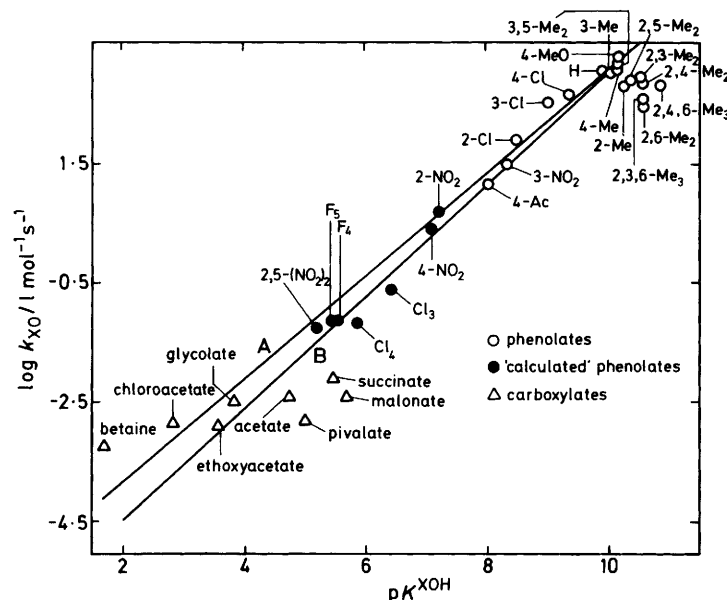


Figure 4. Dependence of k_{XO} on the acidity of the conjugate acid (XOH) for the reaction of the oxyanion with 2-phenyloxazol-5(4*H*)-one. Data and conditions are from Table 2. Line A is from equation (5) for observed values only; line B is from equation (7) and includes calculated values of k_{ArO} (see text)

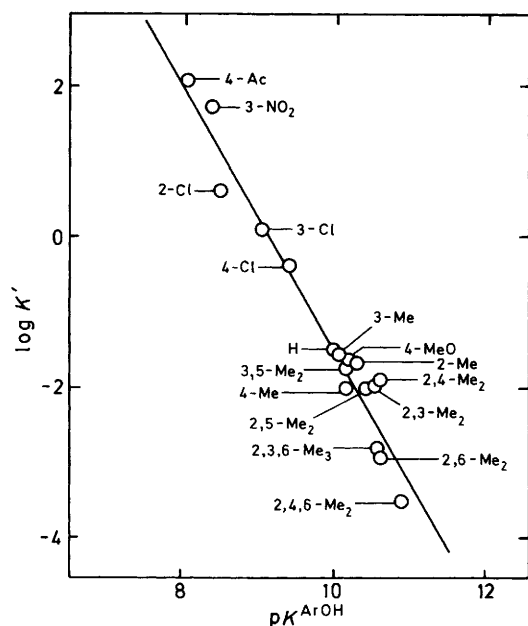


Figure 5. Brønsted dependence of the equilibrium constants K' on the pK value of the substituted phenol. Conditions are as in Table 3 and the line is from equation (6)

[equation (6)] which is independent of *ortho*-substitution in the phenol group.

$$\log K' = -(1.73 \pm 0.1)pK^{\text{ArOH}} + (15.81 \pm 0.97) \quad (r = 0.977) \quad (6)$$

It was difficult to measure, directly, the rate constants for attack of weakly basic phenolate ions, such as pentafluorophenolate, on the oxazolone. The reason is the very small equilibrium concentration of ester produced from the oxazolone for these nucleophiles. We can calculate K' from the correlation of equation (6) if we assume that the latter holds for all the phenols; this assumption is examined later. Since k_{OH} can be measured experimentally, we are then in a position to calculate k_{ArO} with a good degree of accuracy. Including the calculated values of k_{ArO} in the Brønsted correlation with the experimentally determined ones gives equation (7). The inclusion of the extra points increases the correlation coefficient and gives a slightly increased sensitivity [compare equation (5)] of k_{ArO} to the pK of the leaving phenol.

$$\log k_{\text{ArO}} = (0.95 \pm 0.03)pK^{\text{ArOH}} - (6.40 \pm 0.25) \quad (r = 0.993) \quad (7)$$

Discussion

The equilibrium constants for the reaction between phenolate anions and 2-phenyloxazol-5(4*H*)-one [equation (1)] exhibit an excellent linear Brønsted correlation (Figure 5). Sterically hindered 2,6-dimethyl-substituted species exhibit wide deviations from the linear Brønsted correlations for the individual rate constants (Figures 2 and 4). The absence of any steric effect on the equilibrium indicates that the steric interactions of the acyl group with the *ortho*-positions of the phenyl residue are the same as those between the hydroxy group and the *ortho*-positions in the phenol. This result is not surprising because the acyl group is free to rotate away from the

ortho-positions in the *N*-benzoylglycinate ester. The slope of the Brønsted correlation ($\beta_{\text{eq}} = -1.73$) indicates that the ground state of the *N*-benzoylglycinate ester has an effective charge of + 0.73 on the ether oxygen atom relative to the standard effective charge change of unity in the ionisation of phenol. The ground-state effective charge is to be compared with that of + 0.7 for acetate esters;⁶ this indicates that the *N*-benzoylglycyl group has an electropositivity similar to that of the acetyl group. The charge on the ether oxygen atom appears not very indicative of reactivity at the ester: ethyl *N*-benzoylglycinate has a rate constant of $1.1 \text{ l mol}^{-1} \text{ s}^{-1}$ at 25 °C (ref. 5), and ethyl acetate has a rate constant of $0.0061 \text{ l mol}^{-1} \text{ s}^{-1}$ at 25 °C (ref. 7) towards attack by hydroxide ion.

The rate constants for attack of oxyanions on the oxazolone may be determined experimentally for phenols with $pK > 8$. The reactivities of these nucleophiles and the equilibrium constants for ester formation are relatively high, so that the phenol needs only be present at low concentrations to have an effect. The u.v. absorption of the oxazolone species at 260 nm is therefore not 'blanked out', and absorbance changes can be readily monitored. Rate constants for reactions of carboxylate ions with the oxazolone can be measured because these species are usually transparent in the required u.v. wavelength range and can be obtained in high concentrations. The attack of weakly basic phenolate ions on the oxazolone cannot be monitored owing to equilibrium and reactivity problems which would require large concentrations of phenol to obtain a measurable kinetic change. Provided we can estimate the equilibrium constant for ester formation for these phenols [equation (6)], we should be able to calculate k_{ArO} , as the k_{OH} value is easily obtained experimentally. Equation (6) should hold over quite a large range of pK values and structural types provided the nucleophile is an oxyanion. Equilibrium constants for acyl-group transfer from oxygen, whether the acyl function is carbonyl, sulphonyl, or phosphyl, are only dependent on the pK of the donor hydroxy group.⁸⁻¹¹ We are therefore justified in using equation (6) to calculate the semi-empirical k_{ArO} value. The values of k_{ArO} for unhindered phenols fit a good linear Brønsted plot (Figure 4) with no hint of a break from pK 5 to 10. The values of k_{XO} for some of the carboxylate anions exhibit a positive deviation from the correlation for k_{ArO} . These anions possess a lower β value than that for the phenolate anions, and the substantial deuterium oxide solvent isotope effect (2.18; Table 2) for betaine is consistent with a general base catalysis mechanism. As the basicity of the carboxylate increases so will the contribution to k_{XO} from the nucleophilic mechanism; the acetate ion acts by a totally nucleophilic pathway as judged from its zero deuterium oxide solvent isotope effect.¹ It is impossible, under the present conditions, to measure the nucleophilic reactivity for oxyanions with pK values below that of acetic acid. The present observations indicate no change in rate-limiting step for attack of aryloxide ions, and this is confirmed by the linear Brønsted relationship for k_{OH} over an extensive range of pK of leaving phenol.

If the return step, in the oxazolone reaction [equation (8)] involving a putative tetrahedral intermediate, were slower than expected from the pK value of the attacking group, the change in rate-determining step would occur at the pK value of the phenoxide ion *lower* than that of the isoamide group (the leaving group, pK 11,¹ in ring fission). There is no reason to dispute that the leaving abilities of the oxyanions are *not* strictly pK -dependent. The return step might be slow for the hydrolysis of γ -butyrolactone in alkali because exchange of labelled oxygen between the carbonyl function and the solvent does not occur.¹² There is little doubt that a relatively long-lived tetrahedral intermediate participates in the lactone hydrolysis [equation (9)].

The absence of exchange at the carbonyl oxygen in equation

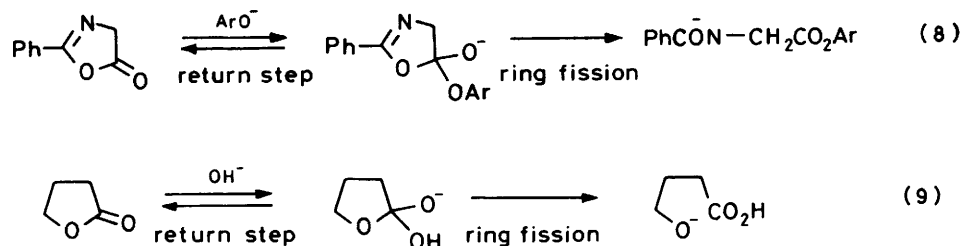
Table 2. Reaction of oxyanions with 2-phenyloxazol-5(4*H*)-one^a

Oxyanion	p <i>K</i>	<i>k</i> _{XO} /l mol ⁻¹ s ⁻¹ ^e	<i>N</i> ^f	pH	Conc. range of XOH(M)
Phenolates					
4-COMe	8.05	14.8	7	8.56	0.5–2 × 10 ⁻³
2-Me	10.28	634	6	9.13	0.4–2 × 10 ⁻³
3,5-Me ₂	10.19	1 320	6	9.01	0.4–2.5 × 10 ⁻³
2,5-Me ₂	10.41	1 050	6	8.97	0.5–2 × 10 ⁻³
2,3-Me ₂	10.54	820	6	8.95	0.4–2 × 10 ⁻³
2,4-Me ₂	10.60	7.54	6	8.94	0.4–2 × 10 ⁻³
2,6-Me ₂	10.63	297	6	8.97	0.4–2 × 10 ⁻³
2,4,6-Me ₃	10.90	626	6	8.96	0.4–2 × 10 ⁻³
2,3,6-Me ₃	10.64	359	6	8.96	0.4–2.5 × 10 ⁻³
Unsubstituted	9.95	1 050 (940) ¹	6	8.56	0.4–2 × 10 ⁻³
3-Me	10.08	995	9	8.56	0.3–2.5 × 10 ⁻³
Carboxylates					
Betaine	1.68	4.89 × 10 ⁻⁴ (2.24 × 10 ⁻⁴) ^c	4 (4)	5.00 (5.4) ^c	0.3–1
Chloroacetate	2.86	1.28 × 10 ⁻³	7	4.88	0.15–1
Ethoxyacetate	3.60	1.05 × 10 ⁻³	7	5.83	0.1–0.5
Glycolate	3.83	3.07 × 10 ⁻³	7	5.44	0.15–1
Acetate	4.76	3.60 × 10 ^{-3h}	6	7.84	0.2–1
Pivalate	5.01	1.55 × 10 ⁻³	7	7.02	0.05–0.3
Succinate ^b	5.48	7.74 × 10 ⁻³	6	7.89	0.1–0.3
Malonate ^b	5.69	3.60 × 10 ⁻³	7	7.38	0.05–0.3

Calc. values for phenolates (from experimental data for hydrolysis)^k

F ₅	<i>k</i> _{ArO(calc.)} ^g	<i>K'</i> _{calc.} ^h
2,3,5,6-F ₄	7.65 × 10 ⁻²	2.04 × 10 ⁶
2,3,4,5-Cl ₄	7.03 × 10 ⁻²	1.55 × 10 ⁶
2,3,5-Cl ₃	6.53 × 10 ⁻²	3.72 × 10 ⁵
4-NO ₂	0.233	4.90 × 10 ⁴
2-NO ₂	2.50	2.88 × 10 ^{3d}
2,5-(NO ₂) ₂	5.05	2.00 × 10 ^{3d}
	5.64 × 10 ⁻²	6.03 × 10 ^{6d}

^a Ionic strength maintained at 1M with KCl, 25 °C, wavelength for kinetic studies 260 nm. Background buffers were: pH 4.8–7, phosphate; 7–9.2, tris(hydroxymethylamino)methane; buffer concentration kept at 0.005M. ^b Dianion. ^c Values in parentheses refer to reaction carried out in D₂O solvent. ^d The *k*_{OH} value used to calculate this parameter is from previous work⁵ at 0.1M ionic strength; see footnote *d* of Table 3 for the effect of ionic strength. ^e Errors in the parameters are not greater than 10%; XOH is a general hydroxy species. ^f Number of data points, not including duplicates. ^g Units l mol⁻¹ s⁻¹; calculated from the equation *k*_{ArO(calc.)} = *k*_{OH}/*K'*_{calc.} ^h Calculated from the experimental linear free energy relationship [equation (7)]. ^k See Table 1 and text.



(9) indicates that either the return step or the proton-exchange reaction at the exocyclic oxygen atom is slow compared with ring fission. The higher energy of the *E*-configuration^{13a,b} of the ester in the ring compared with that of the *Z*-configuration of the acid product has been invoked^{13c} as an explanation of the zero oxygen exchange in the hydrolysis of the lactone. The return step, a dissociation reaction, has an entropy advantage over the ring-fission step of between 30 and 40 cal K⁻¹ mol⁻¹.^{13d} The entropy difference amounts to a free energy difference of about 9–13 kcal mol⁻¹ at 25 °C, and this would counterbalance an effect due to the energy difference between *E*- and *Z*-isomers (about 3 kcal mol⁻¹).^{13c} These arguments assume that the

thermodynamic energy differences for the complete reaction are reflected in the free energies of activation for the rates.

Proton transfer may be rate-limiting in the exchange reaction in the alkaline hydrolysis of the γ -butyrolactone; there is precedent for rate-limiting proton transfer in the alkaline hydrolysis–carbonyl exchange of methyl benzoates.¹⁴ The proton-transfer step is not important in the attack of phenolate ions on the oxazolone.

The energy difference caused by the *E*-configuration of the oxazolone would be expected, reasonably, to be exceeded by (a) the phenolate leaving groups of the return reaction being superior to the hydroxy group of the isoamide in ring fission and

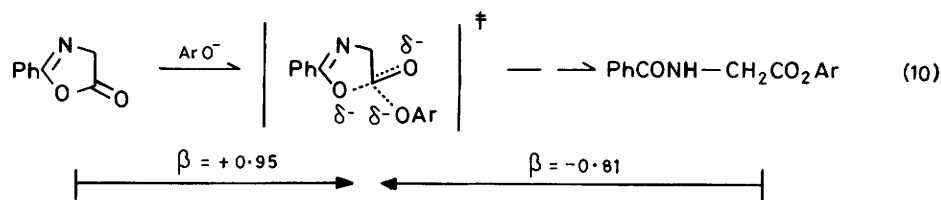


Table 3. Equilibrium constants for reaction between phenolate ions and 2-phenyloxazol-5(4*H*)-one^a

Phenolate	p <i>K</i> _{ArOH}	<i>k</i> _{OH} /l mol ⁻¹ s ⁻¹ ^b	<i>k</i> _{ArO} /l mol ⁻¹ s ⁻¹ ^b	<i>K'</i> ^c
3-Me	10.08	26.9	995	2.70 × 10 ⁻²
2-Me	10.28	12.9	634	2.03 × 10 ⁻²
3,5-Me ₂	10.19	28.8	1 320	2.18 × 10 ⁻²
2,4-Me ₂	10.60	10.5	754	1.39 × 10 ⁻²
2,3-Me ₂	10.54	8.32	820	1.01 × 10 ⁻²
2,5-Me ₂	10.41	10.0	1 050	9.52 × 10 ⁻³
2,6-Me ₂	10.63	0.370	297	1.25 × 10 ⁻³
2,4,6-Me ₃	10.90	0.190	626	3.04 × 10 ⁻⁴
2,3,6-Me ₃	10.64	0.490	359	1.36 × 10 ⁻³
2-Cl	8.48	336	89 ¹	3.78
4-COMe	8.05	1 780 ^d	14.8	120
3-NO ₂	8.35	1 590 ^d	31 ^e	51.3
3-Cl	9.02	392 ^d	340 ^e	1.15
4-Cl	9.38	194 ^d	470 ^e	0.413
Unsubstituted	9.95	33.8 ^d	1 050	3.22 × 10 ⁻²
4-OMe	10.20	39.2 ^d	1 800 ^e	2.18 × 10 ⁻²
4-Me	10.19	10.7 ^d	940 ^e	1.14 × 10 ⁻²

^a Ionic strength kept at 1M with KCl; 25 °C. ^b Data from Tables 1 and 2 except where stated. ^c *K'* = *k*_{OH}/*k*_{ArO}. ^d Data from ref. 5; ionic strength for these parameters is 0.1M. The ionic strength has little effect on *k*_{OH} as judged from a comparison of parameters for 4-nitrophenyl *N*-benzoylglycinate hydrolysis (*k*_{OH} = 7 150 at 1M and 7 200 l mol⁻¹ s⁻¹ at 0.1M from Table 1 and ref. 5, respectively). ^e Data from ref. 1.

(b) a favourable entropy of the return reaction. We conclude that ring fission in a stepwise mechanism [equation (8)] is likely to be the rate-limiting step at least for phenoxide ion nucleophiles with p*K* < 11 (the p*K* of the isoamide hydroxy group).¹ We should therefore expect a Hammett σ relationship to hold for the *k*_{OH} parameter for the reverse of equation (8) involving the putative tetrahedral intermediate. Considerable negative charge must form on the aryl oxygen atom in the transition state of the rate-limiting step because the values of *k*_{OH} for aryl esters⁵ follow a Hammett σ^- dependence. The data are consistent with a concerted pathway which, nonetheless, would involve a tetrahedral configuration of atoms in the transition state.

The oxygen in the leaving aryl group in the ester hydrolysis gains some 0.81 units of effective negative charge; if we assume effective charge changes are due to changes in bond order,⁶ the forming and breaking bonds in the transition state are roughly 0.5 of their total bond order in ground and product states [equation (10)]. A change in order of the C–OAr bond would be expected in the stepwise path from ground state to intermediate [reverse of equation (8)] due to the change in hybridisation of the carbonyl carbon atom and to the destruction of resonance possibilities of the ester. However, these factors would not place a negative charge on the aryl oxygen as is indicated by the Hammett σ^- relationship.

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