Concerted displacement mechanisms at trigonal carbon: the aminolysis of 4-aryloxy-2,6-dimethoxy-1,3,5-triazines

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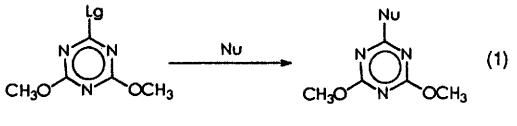
4-Aryloxy-1,3,5-triazines undergo bimolecular nucleophilic displacement reactions with amines and pyridines to yield the 4-substituted triazine and aryloxide ion. Rate constants in aqueous solution for the bimolecular reaction of morpholine and 4-dimethylaminopyridine with the title ethers obey the Hammett σ equations with Hammett ρ_{lg} values 1.65 and 0.82, respectively. Comparison of the ρ_{lg} values with the Hammett ρ_{eq} for the equilibrium constants indicates that build-up of effective charge on the departing ether oxygen in the transition structure is less than half of that for complete bond fission. Rate constants for the reaction of substituted pyridines with the 4-nitro- and 3,4-dinitro-phenyl ethers obey Brønsted equations with exponents β_{nuc} of 0.68 and 1.06, respectively. The build-up of effective charge in bond formation is greater than half of that expected for complete bond formation. Variation in β_{nuc} and ρ_{lg} as a function of leaving group and nucleophile structure, respectively, is consistent with substantial coupling between bond forming and bond breaking. The ratio of the Leffler exponents in the pyridinolysis reactions, α_{nuc}/α_{lg}, is greater than unity, consistent with an imbalance between bond fission and bond formation and indicating an accumulation of negative charge in the heteroaromatic nucleus in the transition structure 29% of that expected for adduct formation.

Introduction

The distinction between concerted and stepwise mechanisms of displacement reactions is one of the most fundamental problems in organic chemistry. Concerted mechanisms have been the subject of continued research since they were first suggested by Lewis for aliphatic substitution,[1] and are becoming increasingly important as the mechanisms of the action of enzymes are being unravelled. In recent years concerted mechanisms of nucleophilic displacements at various electrophilic centres have been studied using reactions for which it is possible to exclude putative $A_N + D_N$ mechanisms.[2]

Triazinyl group transfer between nucleophiles [eqn. (1)] has been shown to possess an A_ND_N mechanism involving a transition structure **1** when the ligands are phenolate ions,[3] whereas transfer between pyridines is $A_N + D_N$ involving a Meisenheimer-like adduct **2**.[4] The 1,3,5-triazinyl system has proved to be a useful vehicle [3,4] in studying the fundamental electronic processes involved at trigonal carbon during nucleophilic aromatic displacement reactions [eqn. (1)].[5,6] The endocyclic nitrogens have the advantage in kinetic studies over the analogous nitro-substituents in the aromatic nuclei because they confer reactivity,[6,7] without the spectral and chemical problems of nitro-substituents which can also act as leaving groups.[8] A disadvantage of the use of endocyclic nitrogen in studies of nucleophilic substitution at heteroaromatic centres is the possible interference by the 'ANRORC' process.[9]

The recent discovery of an A_ND_N mechanism[3] prompts studies to probe the relative timing of nucleophilic displacement reactions in heteroaromatic substitution [eqn. (1)] where the



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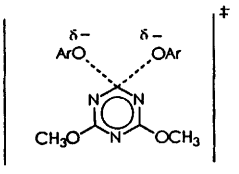
nucleophile and the leaving group have different structural types. This investigation is of the kinetics of aminolysis and pyridinolysis of the aryloxytriazine ethers [eqn. (1), Lg = OAr, Nu = morpholine or substituted pyridine]; it probes the change in effective charge [2] in the bonds undergoing fission and



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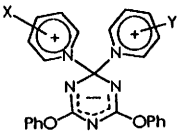

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formation which would be expected to be coupled in a concerted mechanism.

Previous studies have provided values of β_{eq} for transfer of the triazinyl species between substituted phenolate ions and a standard nucleophile (1.48)[3] and between substituted pyridines and a standard nucleophile (1.25).[4] These values may be employed to interpret the substituent effects on aminolysis or pyridinolysis of aryloxy triazines and to locate the transition structures in a More O'Ferrall–Jencks [10] diagram.

Experimental

Materials

Water used throughout the study was double distilled from glass and degassed before use. KCl, acetonitrile and buffers were of AR grade, and pyridines and morpholine were obtained commercially and purified by recrystallisation, redistillation or by sublimation. Dioxane was purified by passage of the AR grade material through active alumina and the filtrate tested for peroxides by use of KI solution. 2-(Substituted phenoxy)-4,6-dimethoxy-1,3,5-triazines were from a previous study.[3] 4-Morpholino-2,6-dimethoxy-1,3,5-triazine was prepared by stirring a mixture of morpholine (0.87 g), 4-chloro-2,6-dimethoxy-1,3,5-triazine (1.82 g), triethylamine (1.40 ml) and chloroform (50 ml) for 2 h, filtering, washing the filtrate with water and evaporating the dried solution. The yield was not optimised and the material, recrystallised from methanol in prisms, had mp 127–128 °C (Found: C, 47.50; H, 6.26; N, 24.64%. $C_9H_{14}N_4O_3$ requires C, 47.78; H, 6.24; N, 24.76%). 4-Hydroxy-2,6-dimethoxy-1,3,5-triazine was from a previous study and the identities and purity of the substrates were confirmed by NMR spectroscopy and TLC.

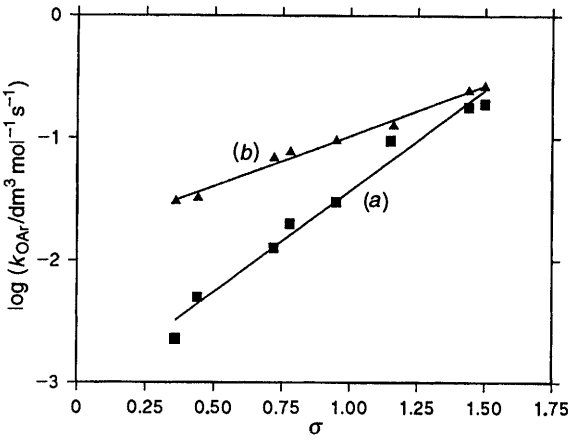


Fig. 1 Hammett σ-dependence for reaction of morpholine (*a*) and 4-dimethylaminopyridine (*b*) with 4-(substituted phenoxy)-2,6-dimethoxy-1,3,5-triazines. Data and conditions are from Tables 1 and 2 and the lines are drawn (*a*) from eqn. (3) and (*b*) from eqn. (4).

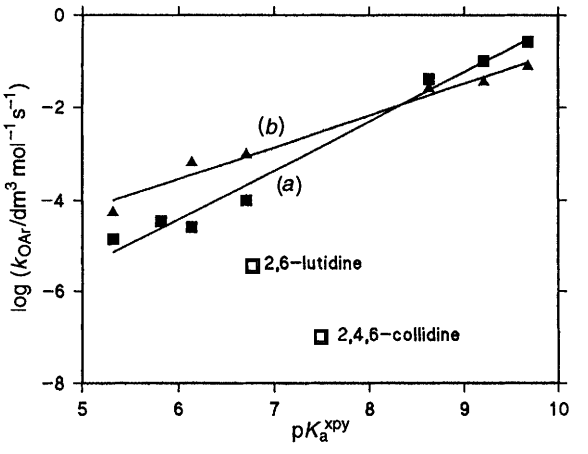


Fig. 2 Brønsted type dependence for reactions of substituted pyridines with 4-(3′,4′-dinitrophenoxy)-2,6-dimethoxy-1,3,5-triazine (*a*) and 4-(4′-nitrophenoxy)-1,2-dimethoxy-1,3,5-triazine (*b*). Data and conditions from Tables 3 and 4 and the lines are drawn (*a*) from eqn. (5) and (*b*) from eqn. (6); □ refer to reaction (*a*).

Kinetic methods

Rates of morpholinolysis and pyridinolysis were measured at 25 °C in a solvent mixture of composition 10% dioxane–water (v/v) with the ionic strength maintained at 0.25 mol dm^{-3} with KCl. A series of solutions were prepared with the same pH, ionic strength and solvent composition but with varying concentrations of the substituted pyridine or morpholine by diluting stock buffer solution with solution at the same pH which was lacking the pyridine or morpholine. Stock solutions of buffers were prepared by adding the solution of substituted pyridine or morpholine, dioxane, tris(hydroxymethylamino)-methane (TRIS) buffer at 0.025 mol dm^{-3}, HCl (1 mol dm^{-3}), and water to produce solutions of the required pH. Stock solutions of the substrates (the triazinyl species) were prepared in dimethyl sulfoxide at a concentration between 10 and 15 mg ml^{-1}.

The kinetics of the reactions were monitored at suitable wavelengths determined in preliminary experiments by repetitive scanning of the UV spectrum. The reactions were initiated by adding an aliquot (0.02 ml) of the stock triazine substrate solution to a silica cell containing the sample solution (2.5 ml) in the thermostatted cell compartment of a Unicam SP800 or Perkin-Elmer Lambda 5 spectrophotometer.

Data were fitted directly to theoretical equations for first-order kinetics by use of grid-search programs written in BASIC and using a BBC Master computer or an Opus VII desk top PC.

The method of initial rates[11] was employed for the reaction of the least basic pyridines with the 4-nitrophenoxy derivative and hindered pyridines with the 3,4-dinitrophenoxytriazine because these were too slow to be conveniently followed to completion. The first-order rate constants were obtained from the rate of change of absorbance at the wavelength in question divided by the total absorbance change computed for the complete release of the phenol under the conditions of the kinetic experiment. The data from initial rate studies were checked to be accurate for reactions which were also fast enough to follow to completion by use of the regular method for determining rate constants.

Product analysis

The amount of substituted phenol released in an aminolysis reaction was determined from the total change in absorbance at the kinetic wavelengths calculated using the concentration of substrate and the extinction coefficients of the phenol. The extinction coefficients were determined under the conditions of the kinetic experiments. Morpholinolysis reactions were also carried out under the conditions of the kinetic experiments but with larger quantities of triazine reactant. The product solutions were evaporated to dryness *in vacuo* and extracted with acetone; the acetone extracts were then subjected to TLC on fluorescent Kieselgel 60 F_{254} DC-Alufolien sheets with benzene eluent. The spots were developed by UV and their positions compared with those for standard 4-morpholino-2,6-dimethoxy-1,3,5-triazine and the hydrolysis product, 4-hydroxy-2,6-dimethoxy-1,3,5-triazine.

Results

Liberation of phenolate ion from the substrates in the presence of buffers containing pyridine or amine nucleophiles obeyed excellent pseudo first-order kinetics up to 90–95% of the total reaction. In the case of kinetics determined *via* initial rates it was assumed that the reactions were first-order. Rate constants are linearly dependent [eqn. (2)] on the concentration of the added

$$k_{obs} = k_{int} + k_2' [\text{nucleophile}]_{total} \quad (2)$$

amine or pyridine. Second-order rate constants were obtained by dividing the slope k_2' by FB, the fraction of reagent (substituted pyridine or morpholine) present in its nucleophilic form. The intercepts were negligible at the pHs studied and the effect of the TRIS buffer was negligible under the conditions of this study.

The amount of phenol produced in the kinetics of the reactions followed to completion agreed with the quantity expected on the basis of the known amount of triazine substrate and the extinction coefficient of the phenol at the wavelength and pH under investigation. Product analysis by TLC of the morpholinolysis reactions indicated that 4-morpholino-2,6-dimethoxy-1,3,5-triazine was the only product with no evidence of the intervention of the hydrolysis reaction.

The second-order rate constants are collected in Tables 1, 2, 3 and 4 together with the experimental conditions of concentration range of nucleophile and range of observed rate constants. The second-order rate constants fit eqns. (3), (4), (5) and (6) and the fit of the data to these equations is illustrated in

$$\log k_{morpholine} = 1.65 \pm 0.10\sigma - 3.08 \pm 0.10 \quad (r = 0.9890) \quad (3)$$

$$\log k_{dimethylaminopyridine} = 0.818 \pm 0.037\sigma - 1.80 \pm 0.04 \quad (r = 0.9941) \quad (4)$$

$$\log k_{3,4\text{-dinitro}} = 1.06 \pm 0.06 pK_a^{xpy} - 10.77 \pm 0.47 \quad (r = 0.9913) \quad (5)$$

Table 1 Reaction of 4-(substituted phenoxy)-2,6-dimethoxy-1,3,5-triazines in morpholine buffers[a]

Substituent	pK_a^{ArOH}	pH	FB[c]	Molarity range/mol dm^{-3}	Rate constant range/10^{-4} s^{-1}	$k_{morpholine}$/10^{-2} dm^3 mol^{-1} s^{-1}	λ/nm	σ
4-NO_2	7.14	8.88	0.768	0.04–0.2	6.8–27	1.99 ± 0.2	400	0.78
3,4-$(NO_2)_2$	5.28	9.02	0.820	0.04–0.2	34–240	19 ± 1.5	400	1.5
2-Cl-4-NO_2	5.45	9.03	0.824	0.04–0.2	18–94	7.1 ± 0.3	400	n/a[b]
3-NO_2	8.19	9.06	0.834	0.04–0.2	1.6–10	1.26 ± 0.08	400	0.72
3,5-$(NO_2)_2$	6.68	8.94	0.792	0.04–0.2	23–110	17.8 ± 0.3	400	1.44
3-Cl-4-NO_2	6.8	8.91	0.780	0.04–0.2	21–99	9.55 ± 0.6	400	1.15
4-Cl-3-NO_2	7.75	8.95	0.796	0.04–0.2	5.5–35	3.0 ± 0.25	400	0.95
4-Cl-2-NO_2	6.05	8.84	0.751	0.04–0.2	8.5–35	3.2 ± 0.3	400	n/a[b]
4-CHO	7.66	8.95	0.796	0.1–0.5	4.6–25	0.5 ± 0.047	365	0.44
3-CHO	8.99	9.45	0.928	0.25–0.4	5.4–7.5	0.23 ± 0.02	360	0.36

[a] 25 °C ionic strength maintained at 0.25 mol dm^{-3} with KCl, 10% v/v dioxane–water (< 1% dimethyl sulfoxide due to substrate stock); the number of data points was not less than 5 for each second order rate parameter. [b] Data for the 2-NO_2 and 2-Cl substituted phenoxy groups were not employed in the Hammett correlations. [c] FB = $1/(1 + 10^{pK_a - pH})$; morpholine has a pK_a of 8.36 under the conditions of this work.

Table 2 Reaction of 4-(substituted phenoxy)-2,6-dimethoxy-1,3,5-triazines in 4-dimethylaminopyridine buffers[a]

Substituent	pK_a^{ArOH}	pH	FB[b]	Molarity range/mol dm^{-3}	Rate constant range/10^{-3} s^{-1}	$k_{dimethylaminopyridine}$/$10^{-2}$ dm^3 mol^{-1} s^{-1}	λ/nm	σ
4-NO_2	7.14	10.25	0.788	0.02–0.15	1.64–9.9	7.74 ± 0.60	400	0.78
3,4-$(NO_2)_2$	5.28	10.68	0.909	0.03–0.15	3–23	26.3 ± 1	400	1.5
3-NO_2	8.19	10.66	0.905	0.03–0.15	3–10	6.90 ± 0.5	400	0.72
3-Cl-4-NO_2	6.8	10.86	0.938	0.03–0.15	3.8–11.4	12.6 ± 1.3	400	1.16
3,5-$(NO_2)_2$	6.68	10.72	0.916	0.03–0.15	7.4–35	0.24 ± 0.041	400	1.44
4-CHO	7.66	10.72	0.916	0.03–0.15	0.7–31	3.24 ± 0.27	365	0.44
4-Cl-3-NO_2	7.75	10.72	0.916	0.03–0.15	3.6–11	9.55 ± 1.1	400	0.95
3-CHO	8.99	10.78	0.926	0.03–0.15	1–3.9	3.02 ± 0.06	360	0.36

[a] Conditions as in footnote *a* of Table 1. [b] Fraction of base calculated as in footnote *c* of Table 1 employing the pK_a of 9.68 for 4-dimethylaminopyridine.

Table 3 Reaction of substituted pyridines with 4-(3′,4′-dinitrophenoxy)-2,6-dimethoxy-1,3,5-triazines in aqueous solution[a]

Substituent	pK_a^{xpy}	pH	FB[c]	Molarity range/mol dm^{-3}	Rate constant range/10^{-3} s^{-1}	$k_{3,4\text{-dinitro}}$/10^{-2} dm^3 mol^{-1} s^{-1}
4-$(CH_3)_2N$	9.68	9.0	0.173	0.1–0.5	5–12	26.3 ± 2.1
4-NH_2	9.21	8.5	0.163	0.01–0.05	0.15–0.79	10 ± 0.9
4-Morpholino	8.63	8.7	0.540	0.008–0.04	0.14–0.84	4 ± 0.2
4-CH_3O	6.71	8.5	0.984	0.1–0.45	0.16–0.52	(1.0 ± 0.020)10^{-2}
3,5-$(CH_3)_2$	6.14	8.5	0.996	0.1–0.5	0.05–0.16	(2.6 ± 0.05)10^{-3}
3-CH_3	5.82	8.3	0.997	0.1–0.5	0.025–0.22	(3.5 ± 0.07)10^{-3}
Parent	5.32	8.3	0.999	0.15–0.76	0.015–0.14	(1.4 ± 0.12)10^{-3}
2,6-Lutidine[b]	6.77	8.5	0.982	0.05–0.2	(1.8–7.1)10^{-4}	(3.64 ± 0.22)10^{-4}
2,4,6-Collidine[b]	7.48	8.5	0.913	0.1–0.3	(0.9–2.7)10^{-5}	< 10^{-5}

[a] Conditions as in footnote *a* of Table 1; wavelength for kinetic determinations was 400 nm. [b] Obtained by the method of initial rates as described in the text; 2,6-lutidine = 2,6-dimethylpyridine, 2,4,6-collidine = 2,4,6-trimethylpyridine. [c] Fraction of base calculated as in footnote *c* of Table 1 employing the pK_a^{xpy} of the nucleophilic pyridine.

Table 4 Reaction of substituted pyridines with 4-(4′-nitrophenoxy)-2,6-dimethoxy-1,3,5-triazines in aqueous solution[a,b]

Substituent	pK_a^{xpy}	pH	FB[c]	Molarity range/ mol dm^{-3}	Rate constant range/10^{-3} s^{-1}	$k_{4\text{-nitro}}$/10^{-2} dm^3 mol^{-1} s^{-1}
4-$(CH_3)_2N$	9.68	8.5	0.062	0.01–0.05	0.023–0.2	7.74 ± 0.1
4-NH_2	9.21	8.5	0.163	0.01–0.05	0.009–0.32	3.5 ± 0.5
4-CH_3	8.63	8.5	0.426	0.02–0.1	0.011–0.12	2.5 ± 0.6
4-CH_3O	6.71	8.38	0.979	0.01–0.05	(8.5–50)10^{-4}	0.10 ± 0.013
3,5-$(CH_3)_2$	6.14	8.4	0.995	0.01–0.05	(1.1–4.2)10^{-3}	(6.7 ± 1.1)10^{-2}
Parent	5.32	8.5	0.999	0.2–1.0	(3.6–8)10^{-3}	(5.4 ± 0.45)10^{-3}

[a] Conditions as in footnote *a* of Table 1; wavelength for kinetic determinations was 400 nm. [b] The results were obtained by the method of initial rates described in the text. The results were checked, in the 4-dimethylaminopyridine case, by comparison with the rate constants obtained by the standard method. [c] Fraction of base was calculated as in footnote *c* of Table 1 from the pK_a^{xpy} of the nucleophilic pyridine.

$$\log k_{4\text{-nitro}} = 0.680 \pm 0.053 pK_a^{xpy} - 7.61 \pm 0.42 \quad (r = 0.9879) \quad (6)$$

Figs. 1 and 2. The rate constant data for the hindered pyridines in Table 3 and the *ortho* substituents of Table 1 were not employed in the fits of eqns. (5) or (3), respectively.

Discussion

Aminolysis

The second order rate constants of Tables 1 to 4 refer to nucleophilic displacement of the phenoxide ion by the nitrogen nucleophile. Nucleophilic displacement at the triazine nucleus is

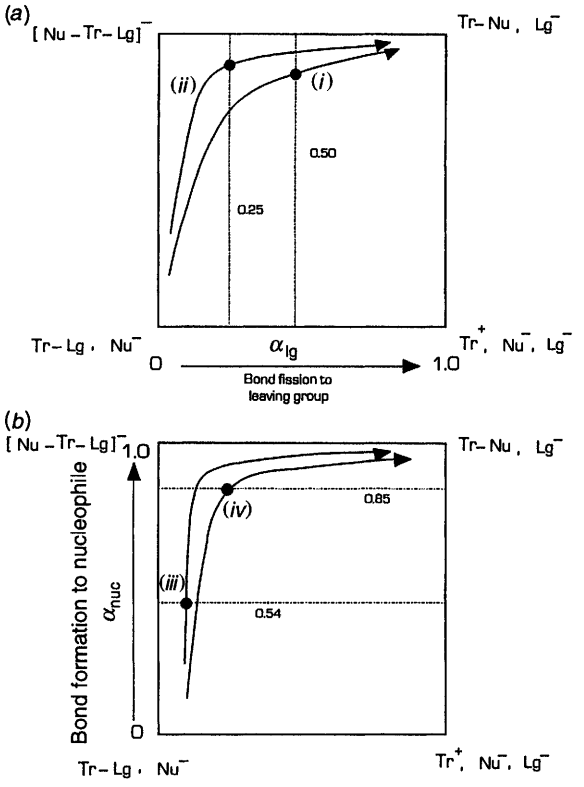


Fig. 3 More O'Ferrall–Jencks diagrams (*a*) for reaction of morpholine (*i*) and 4-dimethylaminopyridine (*ii*) with 4-(substituted phenoxy)-2,6-dimethoxy-1,3,5-triazines and (*b*) for reaction of substituted pyridines with 4-(4′-nitrophenoxy)-2,6-dimethoxy-1,3,5-triazine (*iii*) and 4-(3′,4′-dinitrophenoxy)-2,6-dimethoxy-1,3,5-triazine (*iv*). See text for discussion.

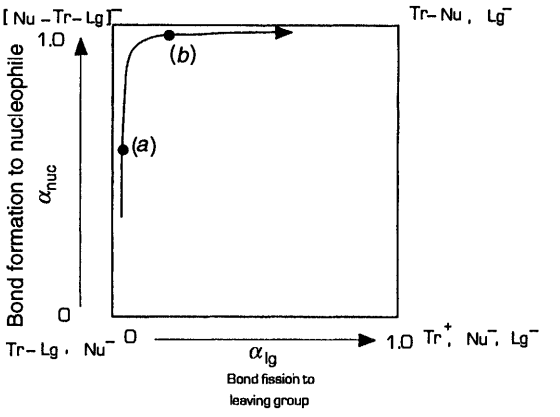


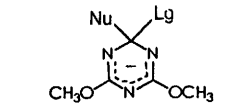
Fig. 4 More O'Ferrall–Jencks diagram for a stepwise displacement of leaving group by nucleophile at a triazine nucleus; (*a*) and (*b*) represent transition structures for rate limiting formation and decomposition respectively of the putative Meisenheimer adduct

confirmed by product analysis in the case of the morpholinolysis reactions, by the absence of the 4-hydroxy-2,6-dimethoxy-1,3,5-triazine hydrolysis product and because the rate constants for reaction of the hindered pyridines (2,4,6-collidine and 2,6-lutidine, Table 3) with the 3,4-dinitrophenoxytriazine fall substantially below those expected from unhindered pyridines of similar pK_a (Fig. 2). The second order rate constants for fission of the 4-nitrophenoxytriazine by morpholine (1.99×10^{-2} dm^3 mol^{-1} s^{-1}) and by 4-morpholinopyridine (2.5×10^{-2} dm^3 mol^{-1} s^{-1}) are much larger than that for the nucleophilic attack of 2-chlorophenoxide ion (8.68×10^{-4} dm^3 mol^{-1} s^{-1})[3] which has a similar pK_a; this result is also consistent with nucleophilic displacement by morpholinolysis and pyridinolysis. The aminolysis reaction is not subject to general base catalysis because the observed rate constants are linearly dependent on the amine concentration. Substitution of the amine or pyridine at the phenoxy nucleus is excluded by the results of the product analysis studies.

The absence of general base catalysis indicates that the proton transfer step in morpholinolysis is subsequent to the rate limiting step. Proton transfer is often rate limiting in aminolysis of aromatic and heteroaromatic systems[12] and has been observed in aminolysis of some 1,3,5-triazin-2-yl chlorides.[13] The protonated species which would be formed in the rate limiting step of morpholinolysis is consistent with the results of the pyridinolysis reactions where there is no proton which can be removed.

Bond fission

The Hammett σ relationships [eqns. (2) and (3)] indicate that bond fission is not sufficiently advanced in the transition structure for resonance interaction between the substituents on the phenoxy group and the charge on the leaving oxygen atom. Such resonance interactions would be assumed to manifest themselves by deviations from the Hammett plot in the case of π-acceptor substituents. This result is consistent with a stepwise process with rate limiting addition or a concerted one where substantial bond fission has not occurred in the transition structure. The greater selectivity for morpholinolysis ($\rho = 1.65$) compared with that for the stronger base and more reactive nucleophile 4-dimethylaminopyridine, (0.82), is in accord with the reactivity–selectivity regime.



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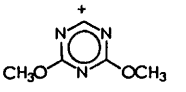

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The reaction can be described by a More O'Ferrall–Jencks diagram [Fig. 3(*a*)] where the top left and bottom right corners represent structures **3** and **4**, respectively. The values of ρ_{lg} may be calibrated by the value of ρ_{eq} determined previously (3.30)[14] to give the Leffler exponents[15] $\alpha_{lg} = 0.25$ and 0.5, which characterise the transition structures for attack of 4-dimethylaminopyridine and morpholine, respectively. Movement of the transition structure in the diagram from $\alpha_{lg} = 0.5$ to 0.25, resulting from increased basicity of the nucleophile, is toward that of the reactants consistent with the combination of a Hammond effect[16] (towards the lower left corner) and an anti-Hammond effect (towards the top left corner) in Fig. 3(*a*).

Bond formation

The β_{nuc} for the bond formation may be calibrated by the known value of β_{eq} (1.25) for transfer of the 1,3,5-triazin-2-yl group between pyridine nucleophiles[4] to give Leffler α_{nuc} values describing the transition structures of the rate limiting step for bond formation. The relative values of α_{nuc} of 0.54 and 0.85, respectively for 4-nitrophenoxy and 3,4-dinitrophenoxy leaving groups, are not consistent with the simple application of the reactivity–selectivity regime; the More O'Ferrall–Jencks diagram [Fig. 3(*b*)] illustrates the movement of the transition structure consequent on change of leaving group.

Concerted or stepwise process

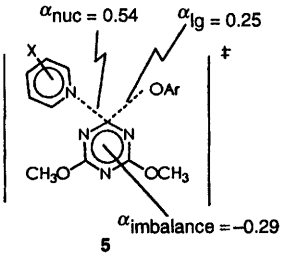
The reaction path traversing the edges of a More O'Ferrall–Jencks diagram (Fig. 4) represents a stepwise process involving a Meisenheimer-like adduct ([Nu–Tr–Lg]$^-$, **3**). The observation of a Hammett σ rather than a Hammett σ^- correlation would be consistent with rate limiting addition if the mechanism were stepwise. However, rate limiting addition is not consistent with the substantial change in the Leffler α_{lg} (0.5 to 0.25) as the basicity of the nucleophile is increased. Movement of the transition structure on the left hand limb of the diagram [Fig.

4(*a*)] is essentially constrained in a vertical direction for a stepwise process and variation in leaving group structure should therefore not be felt significantly in the bond formation step.

If the rate limiting step were bond fission the transition structure would be required to resemble the adduct, [Nu–Tr–Lg]$^-$ **3**, and to be close to the top left corner of the diagram [Fig. 4(*b*)] to account for a Hammett σ dependence. The change in base strength of the nucleophile would affect the vertical coordinate of Fig. 4 and should therefore have little affect on the horizontal position of the transition structure; the ρ value should therefore not change substantially with the basicity of the nucleophile. The change in acidity of the leaving phenol group should not change α_{nuc} substantially because movement of the position of the transition structure for a stepwise process [Fig. 4(*b*)] would be constrained in a horizontal direction. Moreover, the values of α_{nuc} for the stepwise process should be close to unity because the transition structure (judged against the vertical axis) would be close to that of the adduct. The observed variation and values of α_{nuc} and α_{lg} do not fit a stepwise ($A_N + D_N$) process but are fully consistent with an A_ND_N mechanism for aminolysis of aryloxytriazines.

Imbalance

Since the reactions studied here involve displacement of ligands by nucleophiles of different fundamental structure, it is not possible to compare effective charges for bond formation and bond fission because effective charge is defined by different ionisation equilibria in each case.[15c] A way round this problem is the use of Leffler 'methodology'[15b,c] which has been used before to discuss unsymmetrical reactions such as the phenolysis of sulfurylpyridines.[17] If the extent of bond formation (α_{nuc}) and bond fission (α_{lg}) are not the same in the transition structure, the Leffler parameters α_{nuc} and α_{lg} will not be the same and an imbalance[18] in effective charge will result. In a nucleophilic displacement reaction the sign of the equation $[1 - (\alpha_{nuc}/\alpha_{ig})]$ indicates the sign of the effective charge which accumulates in the electrophilic residue. The difference, $\alpha_{lg} - \alpha_{nuc}$, gives the apparent Leffler parameter $\alpha_{imbalance}$ which is a measure of the sign and amount of charge accumulating in the transition structure relative to the total amount possible if the transition structure resembled either the dissociative intermediate (analogous to **4** when $\alpha_{imbalance}$ would be $+1$) or the associative intermediate (analogous to **3** when $\alpha_{imbalance}$ would be -1). The ratio α_{nuc}/α_{lg} for the aminolyses of aryloxytriazines is greater than unity (2.16) for the standard leaving group (4-nitrophenolate ion, $\alpha_{nuc} = 0.54$) and standard nucleophile (4-dimethylaminopyridine, $\alpha_{lg} = 0.25$). This indicates that there is an imbalance[18] in the two bond changes, with bond formation being advanced over bond fission. The resultant build-up of negative charge on the triazine nucleus corresponds to a hypothetical Leffler value '$\alpha_{imbalance}$' of 0.29 and this is illustrated in structure **5**.



5

The imbalance corresponds to a build-up of negative charge, 29% of that which would be accumulated in the Meisenheimer-like adduct **3**. This imbalance compares with that observed in the case of the concerted transfer of the triazinyl group between phenoxide ions, where $\alpha_{imbalance}$ values of 0.29 and 0.45 are observed for the 4-nitrophenoxide ion and phenoxide ion attack, respectively.[3] The triazine nucleus in the transition structure in the stepwise process for pyridinolysis of pyridyl triazines[4] takes up about 50% of the negative charge prior to formation of the adduct **2**.

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