Timing of Bonding Changes in Fundamental Reactions in Solutions: Pyridinolysis of a Triazinylpyridinium Salt

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Pyridinolysis of 1-(4,6-diphenoxy-1,3,5-triazin-2-yl)pyridinium chloride with substituted pyridines in aqueous solution exhibits a non-linear Brønsted correlation possessing a break-point at the pK_a of the pyridine nucleophile equal to that of the leaving group: the results are consistent with the intervention of a Meisenheimer-like intermediate and the full effective charge map for solution states along the reaction coordinate indicates substantial bonding change in the formation of the transition states.

Recent work has demonstrated that phenolysis of a 2-(4-nitrophenoxy)-1,3,5-triazine occurs *via* a concerted mechanism[1] in contrast to the generally expected stepwise process for nucleophilic aromatic substitution.[2]

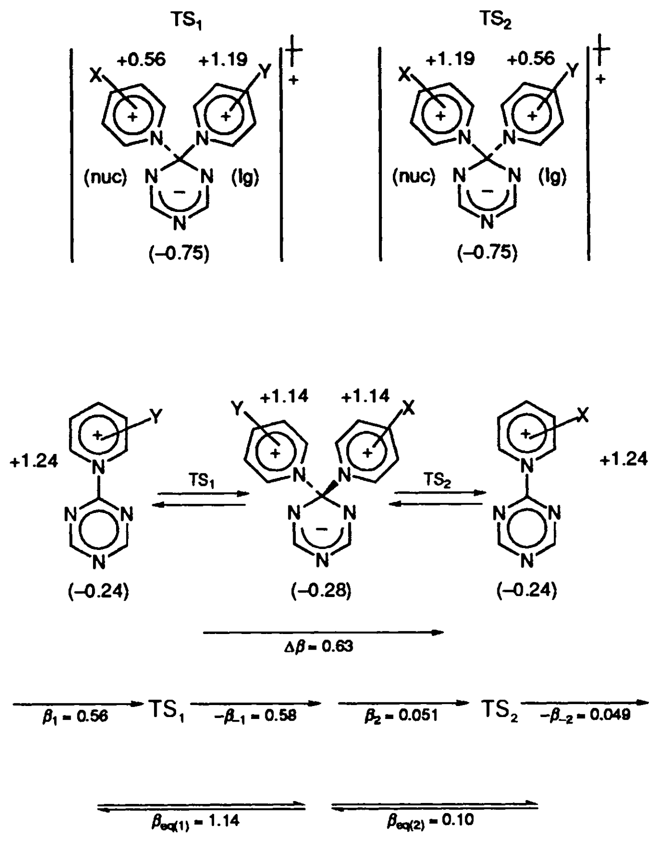
This paper reports a study of the kinetics of the displacement of pyridines from triazinylpyridinium salts† to determine the scope of the concerted mechanism. The results, determined from measurement of both forward and reverse reactions, indicate an intermediate and enable a map to be constructed of the effective charge on the substituted pyridine nucleophile through the whole reaction (Scheme 1).

The kinetics of a two-step process (Scheme 1) for the forward reaction of the triazinyl chloride (**1**) with substituted pyridines (Xpy) is predicted by the simple equation: $\text{rate}_{\text{forward}} = k_1k_2[\text{Xpy}][\mathbf{1}]/(k_{-1} + k_2) = k_{\text{Xpy}}[\text{Xpy}][\mathbf{1}]$. The reverse reaction of pyridine with triazinyl-substituted pyridinium ions (**2**) has a similar rate equation: $\text{rate}_{\text{reverse}} = k_{-\text{Xpy}}[\text{py}][\mathbf{2}]$ and $k_{-\text{Xpy}} = k_{-1}k_{-2}/(k_{-1} + k_2)$. Rates were followed by UV-spectroscopy and there is no evidence for a stoichiometric build-up of intermediates. Non-linear Brønsted-type correlations (illustrated in Fig. 1) are observed for k_{Xpy} and $k_{-\text{Xpy}}$ against the pK_a of the substituted pyridine and the data fit the equations (1a) and (1b)[5a] providing excellent evidence for a stepwise process with a non-accumulating intermediate (**3**).‡

$$k_{\text{Xpy}} = 2k_{\text{py}}10^{\beta_1}/(1 + 10^{\Delta pK\Delta\beta}) \qquad (1a)$$

$$k_{-\text{Xpy}} = 2k_{\text{py}}10^{-\beta_{-2}}/(1 + 10^{-\Delta pK\Delta\beta}) \qquad (1b)$$

The value of Leffler's α-parameter[6] is identical for formation of an intermediate from reactant and product in a symmetrical reaction and this enables it, and the individual β_{-1} and β_2 parameters, to be calculated from the observed values for $\Delta\beta$, β_1 and β_{-2}. The α value for formation of the Meisenheimer intermediate from both directions is 0.49 and indicates that charge is approximately half built up at the transition state of these reaction steps. The data also yield values for the parameters $\beta_{\text{eq}1}$ and $\beta_{\text{eq}2}$ (1.14 and 0.10 respectively) and these indicate that most of the change in charge (and hence probably most of the bonding change) occurs in step 1 of Scheme 1



Scheme 1 Reaction map for the effective charges on the parent pyridine during pyridinolysis of the triazinylpyridinium species. The effective charges on the triazine nucleus (−0.24→−0.75→−0.28→−0.75→−0.24) are the differences between the sums of the effective charges on the pyridines and the net charge on the system of +1.0. The effective charges on the attacking pyridine (Xpy) (0→+0.56→+1.14→+1.19→+1.24) are obtained from the successive summation of β_1, $-\beta_{-1}$, β_2 and $-\beta_{-2}$. Effective charges on the leaving pyridine (Ypy) are obtained by a similar method. The 4,6-substituents on the triazinyl nucleus are omitted for clarity.

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† The pyridinium species were prepared from 4,6-diphenoxy-1,3,5-triazin-2-yl chloride[3a] with the appropriate pyridine in tetrahydrofuran solvent.[3b] Pseudo-base formation and subsequent ring opening of the pyridinium ring proved a complicating feature in the kinetics (as observed previously with *N*-acylpyridinium salts)[4] but this only occurred at high pH and the values of k_{Xpy} and $k_{-\text{Xpy}}$ are corrected for this where necessary.

‡ These equations may be derived[5b] from the mechanism in Scheme 1 assuming that the microscopic rate constants (k_n) have linear Brønsted correlations with exponents β_n. $\Delta\beta = +\beta_{-1} + \beta_2$, $\Delta pK = pK_{\text{Xpy}} - pK_{\text{py}}$, k_{py} is the rate constant for the identity reaction of **1** with pyridine. The values of β are all measured relative to the forward direction (left to right in the Scheme) so that a normally negative β_{-1} for k_{-1} would be positive. This will affect the signs of exponents relative to those in ref. 5(*b*).

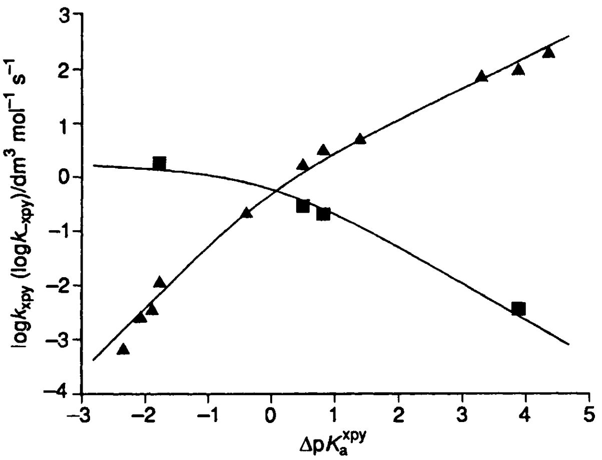

Fig. 1 Brønsted type dependence of the reaction of substituted pyridines with 1-(4,6-diphenoxy-1,3,5-triazin-2-yl)pyridinium chloride (k_{xpy}, ▲) and pyridine with 4,6-diphenoxy-1,3,5-triazin-2-yl-substituted pyridinium chlorides (k_{-xpy}, ■). Conditions: 25 °C, ionic strength maintained at 0.25 mol dm^{-3} with KCl; dioxan/water = 1 : 9 (v/v) and pH values maintained by the pyridine nucleophiles acting as their own buffers. Identities of the pyridines in increasing order of pK_a are: 3-Cl; 3-CH_3OCO; 3-CH_3CO; 4-$CONH_2$; 3-CH_3O; 3-CH_3; 3,5(CH_3)$_2$; 4-CH_3O; 4-morpholino; 4-NH_2; 4(CH_3)$_2$N. The lines are calculated from eqns. (1a) and (1b) using parameters given in the text and Scheme 1.

consistent with the charge change being less insulated from the substituents than in step 2 when substituents in the nucleophilic pyridine are varied.

Although the substituent variation is in the nucleophile for the forward reaction we are able to calculate effective charge change on the leaving group because the reaction is symmetrical. Scheme 1 illustrates the effective charge map derived from the experimental Brønsted β values for the identity reaction when X = Y = H. The unattributed numbers in Scheme 1 are values of effective charge based on the standard ionisation equilibrium of the conjugate acid of pyridines;[6,7] pyridines and their conjugate acids have effective charge defined as zero and +1 units respectively. The numbers in parentheses are effective charges at the triazine nucleus obtained by difference.

The value of β_{eq} for the complete transfer of the triazinyl group (1.24) between pyridine nucleophiles may be compared with those for other systems where a group is transferred between substituted pyridines.[8] The triazinyl group is about as electrophilic as the phosphoryl, sulfuryl or hydrogen groups (β_{eq} respectively 1.07, 1.25 and 1.00) in contrast to the carbonyl group which has a β_{eq} of 1.6 in transfer between pyridine.

The Meisenheimer type structure in the transfer of the triazinyl group between pyridines has sufficient stability, unlike that of the putative intermediate for transfer between aryl oxide ions (**4**), to enable it to be expressed as a discrete intermediate. The data of this report and that of the previous work on the phenoxy species[1] indicates that the triazinyl group transfer system occupies a borderline region of mechanism where changes in leaving group structure cause significant change in mechanism. It is possible to speculate on the effect of the 4,6-substituents on the stability of the putative intermediate but it is probable that an electrostatic interaction is the major factor in stabilising (**3**) over (**4**). The putative tetrahedral intermediates in transfer of the analogous acyl group between pyridines[4] or aryl oxide ion[9] are not stable enough to compete with the concerted mechanism. It is likely that the more localised negative charge in the structures for acyl group transfer causes them to be less stable with respect to reactant or product states compared with the energies in the triazinyl system where the putative intermediate has less localised charge.

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