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Quantitative Aspects of ANRORC Substitution Reactions in *N*-Arylpyridinium Salts

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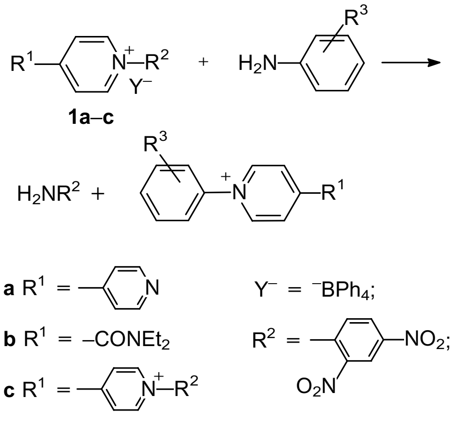
An isoparametric correlation with respect to reagent structure has been obtained for the reaction of 4-R^1-*N*-(2,4-dinitrophenyl)-pyridinium salts with arylamines in acetonitrile at 25 °C; the quantitative data describe the sequence of slow steps (S_N Ar type) in the multi-step mechanism of the ANRORC substitution.

Reactions of 4-R^1-*N*-arylpyridinium salts with arylamines involve different reaction centres, depending both on the structure of the *N*-arylpyridinium salt and on the nucleophile.[1–4] We found that the reactions of 4-R^1-*N*-(2,4-dinitrophenyl)pyridinium salts with primary aromatic amines in acetonitrile at 25 °C occur quantitatively and irreversibly through a nucleophilic substitution pathway (Scheme 1).



R^3 = 4-NH$_2$, 4-OMe, 4-Me, 3-Me, H, 3-OMe, 3-F

Scheme 1

The mechanism of the reactions studied has been previously classified as ANRORC substitution (addition of a nucleophile followed by ring opening, closure and elimination of the leaving group).[5–7] This mechanism can be characterized more precisely as $S_N(\text{ANRORC})^n$ (where ‘n’ means ‘normal’), since after cyclisation the nucleophile occupies the leaving group position.

Previously[5] we performed a kinetic analysis of the reaction of salt **1c** with arylamines in acetonitrile (spectrophotometric monitoring of the accumulation of 2,4-dinitroaniline, $\lambda = 370$ nm). The salt cation serves as the reactive species. When excess nucleophile is present, the reaction occurs through two parallel pathways: a non-catalytic one (k_0, dm^3 mol^{-1} s^{-1}) and that catalysed by the second arylamine molecule (k_b, dm^6 mol^{-2} s^{-1}). These pathways determine the rate of the overall multi-step substitution process. Similar kinetic regularities were also observed in the case of salts **1a** and **1b**.[†] The experimental values of k_0, k_b and the constants of the substituents in the reagents (σ^0) are shown in Table 1. When the electron-withdrawing properties of the substituents in the substrate and in the nucleophile increase, the bimolecular reaction rate constant (k_0) decreases. Good Hammett–Taft-type correlations between log k_0 and the constants of the substituents in the substrate and in the nucleophile with negative sensitivity parameters (ρ^0) are observed. The absolute values of the factors of sensitivity with respect to the structure of the nucleophile increases in the order: $-(3.3 \pm 0.2)$ **1a**, $-(4.6 \pm 0.2)$ **1b**, $-(6.1 \pm 0.6)$ **1c**, while the factor of sensitivity to substrate structure changes from $-(8.3 \pm 0.2)$ (R^3 = 4-NH$_2$) to $-(1.94 \pm 0.04)$ (R^3 = 3-F).

Thus, an isoparametric dependence with respect to the structure of the reagents is found in the reaction series studied. To quantitatively estimate the isoparametric phenomenon, we used equations (1)–(4), which provide the best fit of the experimental data.

$$\log k_{0(\mathrm{R})} = \log k_{0(\mathrm{H})} + \rho_i^0\sigma_i^0 + \rho_j^0\sigma_j^0 + q\sigma_i^0\sigma_j^0 \tag{1}$$

$$\log k_{0(\mathrm{R})} = -(1.04 \pm 0.08) - (4.6 \pm 0.3)\sigma_i^0 - (6.5 \pm 0.4)\sigma_j^0 + (8.01 \pm 1.0)\sigma_i^0\sigma_j^0 \tag{2}$$

$$R = 0.990;\ N = 21;\ S = 0.169$$

$$\log k_{b(\mathrm{R})} = \log k_{b(\mathrm{H})} + \rho_i^0\sigma_i^0 + \rho_j^0\sigma_j^0 + \rho_\mathrm{R}^+\sigma_\mathrm{R}^+ + q\sigma_i^0\sigma_j^0 \tag{3}$$

$$\log k_{b(\mathrm{R})} = (0.6 \pm 0.1) - (6.3 \pm 0.5)\sigma_i^0 - (10.0 \pm 0.9)\sigma_j^0 - (1.6 \pm 0.2)\sigma_\mathrm{R}^+ + (1.0 \pm 0.2)\sigma_i^0\sigma_j^0 \tag{4}$$

$$R = 0.989;\ N = 21;\ S = 0.348$$

In the case of catalytic constants, the constants of direct polar conjugation in arylamines (σ_R^+) should be taken into account. The negative value of ρ_i^0 with respect to substrate structure (−4.6) can be explained by the fact that the ρ^0 observed is an algebraic sum from separate reaction steps.

[†] Salts **1a,b** were obtained by an exchange reaction of the corresponding chloride salts with NaBPh$_4$ in methanol.[9]

Table 1 Non-catalytic (k_0, dm^3 mol^{-1} s^{-1}) and catalytic (k_b, dm^6 mol^{-2} s^{-1}) constants for the reaction of 4-R^1-*N*-(2,4-dinitrophenyl)pyridinium cations with arylamines in acetonitrile, 25 °C.

	1a, σ^0 0.40[a]		**1b**, σ^0 0.26[a]		**1c**, σ^0 0.09[a]		R^3
R^3	$k_0 \times 10^4$	$k_b \times 10^2$	$k_0 \times 10^3$	k_b	$k_0 \times 10^2$	k_b	σ^0 (ref. 8)
4-NH$_2$	280 ± 20	17200 ± 800	400 ± 80	2800 ± 100	1150 ± 300	4.5 ± 10^5	−0.38
4-OMe	29 ± 7	63 ± 2	43 ± 7	23.2 ± 0.8	16 ± 2	180 ± 20	−0.15
4-Me	36 ± 7	4.3 ± 0.2	25 ± 3	3.2 ± 0.1	24 ± 3	7.4 ± 0.7	−0.14
3-Me	17 ± 6	3.3 ± 0.3	8 ± 0.9	0.70 ± 0.06	7 ± 1	2.7 ± 0.4	−0.07
H	15 ± 5	0.62 ± 0.04	4.4 ± 0.8	0.14 ± 0.01	1.5 ± 0.3	1.59 ± 0.07	0
3-OMe	9.5 ± 0.9	1.21 ± 0.05	2.8 ± 0.2	$(8.5 \pm 0.2) \times 10^{-2}$	1.8 ± 0.2	0.68 ± 0.04	0.06
3-F	1.01 ± 0.06	$(1.24 \pm 0.07) \times 10^{-2}$	0.18 ± 0.02	$(2.8 \pm 0.2) \times 10^{-4}$	$(3.7 \pm 0.3) \times 10^{-2}$	$(6.3 \pm 0.7) \times 10^{-4}$	0.35

[a] The σ^0 values for the cations of salts **1a,c** were calculated from a partial correlation obtained for the salts with R^1 = H, CONEt$_2$, NHCOMe and 3-fluoroaniline. The *meta*-position of the substituent with respect to the reaction centre was taken into account.

The following critical values were obtained from equations (2) and (4):

$$\hat{\sigma}_i^0 = 0.8 \pm 0.2,\ \log \hat{k}_0 = -4.7 \pm 0.3;$$
$$\hat{\sigma}_j^0 = 0.6 \pm 0.1,\ \log \hat{k}_0 = -4.9 \pm 0.3$$

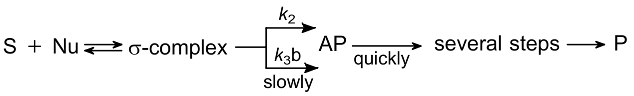
$$\hat{\sigma}_i^0 = 0.9 \pm 0.3,\ \log \hat{k}_b = -5.0 \pm 0.2,\ \hat{\sigma}_j^0 = 0.6 \pm 0.2$$

Thus, catalysis by the second amine molecule is absent at the isoparametric point, $\hat{k}_b = \hat{k}_0$.

It has been reported on an experimental basis[5] that expanding beyond the isoparametric region with respect to the structure of the arylamine ($\sigma_j^0 \geqslant 0.6$) results in a change in the rate-determining step.

The mechanism of the multi-step substitution process studied involves equilibrium formation of a σ-complex (formation of a C–N bond between the arylamine and the α-carbon atom in the pyridinium salt) followed by its slow monomolecular decomposition (k_2) and that catalysed by the second molecule of the amine (k_3b) to give an acyclic product (AP). The latter undergoes rapid cyclisation through several steps to give the reaction products (P), namely, a new pyridinium salt and 2,4-dinitroaniline. Scheme 2 is a generalised view of these processes.

The slow steps in Scheme 2, which determine the overall rate of the process, are of the same type as those found in base-catalysed reactions of the S$_N$Ar activated nucleophilic substitution.[10,11] In other words, the S$_N$Ar mechanism can be regarded as the rate-determining step in the ANRORC substitution mechanism.



Scheme 2

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