romatic nucleophilic substitution reactions
2-chloro-1-methylpyridinium iodide with phenols

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The kinetics and mechanism of nucleophilic substitution reactions of 2-chloro-1-methylpyridinium iodide (PI) with phenols have been studied spectrophotometrically. The reactions are first-order with respect to PI and phenols and the II reaction order is second. The Bronsted coefficient $\beta$ for series is $0.09 \pm 0.02$, which is in agreement for the nucleophilic substitution reactions. From the Hammett correlation, $\rho$ was found to be $-0.29 \pm 0.07$. Activation parameters for the reaction have been reported. The isokinetic temperature is calculated (321 K) and it is observed that the isokinetic reactions are enthalpy controlled. A two-step reaction mechanism is consistent with the observed results in which the reaction of an intermediate is rate determining.

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Study the kinetics of the reactions between 2-chloro-1-methylpyridinium iodide (PI) with phenols. Such reactions can give information on the substituent effects and on the application of linear free energy relationship.

Materials and Methods

2-chloro-1-methylpyridinium iodide (PI) and the phenols were of A. R. grade and obtained from Mark Co. (Germany). Distilled methanol was used throughout the experiments. The phenols were standardised according to standard procedure. UV spectra were recorded employing a computer-controlled Shimadzu UV-1601PC UV-visible spectrophotometer. The spectrophotometer was equipped with a thermoelectric temperature controller (Shimadzu TCC-240A) which maintained constant temperature of the reaction mixture to $\pm 0.1^\circ C$.

Kinetic Measurements

The substitution reactions were followed spectrophotometrically in methanol under pseudo-first order condition, where [phenoxide] >> [PI]. The reactions were also studied at different temperatures to evaluate the activation parameters. A stock solution of 2-chloro-1-methylpyridinium iodide was prepared (4.1 x 10$^{-3}$ mol dm$^{-3}$) in methanol. Solutions of different sodium phenoxides were prepared by dissolving a weight amount of the required phenol in a known volume of methanol and the required quantity (half molarity) of standardised sodium methoxide in methanol. A sufficient excess of phenol over base was taken to ensure virtually complete conversion of methoxide into phenoxide. The concentrations of the phenoxides were considered for the calculations of rate constant. Solutions of PI and sodium phenoxides were thermostated separately to the desired temperature. A suitable initial concentration (1.0 x 10$^{-4}$ mol dm$^{-3}$) of pyridinium iodide for kinetic measurements was obtained by directly injecting 0.05 mL of stock solution with a micro syringe into the measuring cell containing phenol solution (2 mL). The reactions were followed by monitoring the disappearance of an UV absorbance band of the phenoxide by the kinetic mode or time scan mode of the spectrophotometer in the region of 298-327 nm. For the reactions studied, the spectra at the en
of the reactions are similar to the spectra of the corresponding substitution products in the same solvent. The reactions were followed for several half-lives and the rate constants and the activation parameters were calculated using standard expression and the method of least squares. The first-order rate constants were calculated by the following Eqn (1).

$$\ln (A_t - A_\infty) = -k_{a0}t + \ln (A_0 - A_\infty) \quad \ldots (1)$$

Where $A_0$, $A_t$ and $A_\infty$ are the values of the absorbance at zero time, time $t$ and infinite time, respectively. The values of $A_\infty$ for each kinetic run were taken as the experimentally determined value.

**Results and Discussion**

Under the present experimental condition, where $[\text{phenoxide}] >> [\text{PI}]$, the plots of $\ln (A_t - A_\infty)$ versus time ($t$) were linear, indicating that the order of the reaction with respect to [PI] is unity. In order to observe the effect of [phenoxide] on $k_{a0}$, the phenoxide concentrations were varied within the range of $2.0 \times 10^{-3} - 4.0 \times 10^{-3}$ mol dm$^{-3}$, keeping the [PI] constant (the concentration of PI was $1.0 \times 10^{-2}$ mol dm$^{-3}$). The pseudo-first order rate constants were found to increase linearly with increasing phenol concentration. The second-order rate constants $k_2$ for different phenols were calculated from the slope of the plots of $k_{a0}$ versus [phenoxide], by using the equation $k_2 = k_{a0}/[\text{phenoxide}]$ which is linear and passed through the origin$^3$. So, the substitution reactions are first-order with respect to PI and the different phenols, indicating that the overall reaction is second-order.

In these reactions the chlorine on PI acts as an electron withdrawing as well as a good leaving group when the nearby positively charged quaternary nitrogen helps to produce partially positively charged carbon centre. The quaternary nitrogen atom activates to undergo nucleophilic aromatic substitution by an addition-elimination mechanism. The experimental observation and the kinetic data indicate that the reaction between PI and different phenols follow the second-order kinetics with the two-stage mechanism. An addition-elimination mechanism is suggested similar to the commonly accepted$^{10,12}$ aromatic bimolecular two-stage procedure in which the formation of the intermediate is the rate-determining step with rapid decomposition of this intermediate product ($k_3 >> k_1, k_2$). This assumption is made on the basis of clean second-order kinetics, first-order in both substrate and different phenols and dependence of the rates on the nature and position of substituent in the nucleophile. In PI, partially positively charged carbon centre acts as an electrophile (Scheme I).

![Scheme I](image)

The relative reactivity or nucleophilicity of the different phenols (Table I) can be explained in terms of the resonance or conjugative effect, inductive effect and steric effect$^3$. As expected for nucleophilic reactions, electron-donating substituents in the

<table>
<thead>
<tr>
<th>Phenols</th>
<th>$pK_a$</th>
<th>$\sigma$</th>
<th>$k_{a0}/10^3$ (s$^{-1}$)</th>
<th>$k_{a0}/10^3$ (mol$^{-1}$ dm$^3$ s$^{-1}$)</th>
</tr>
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<tr>
<td>Phenol</td>
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<td>9.18</td>
<td>0.23</td>
<td>4.14</td>
<td>4.53</td>
</tr>
</tbody>
</table>

Rate constants are reproducible to $\pm 5\%$. 

Table I — Rate constants for the reactions of 2-chloro-1-methylpyridinium iodide (PI) with different phenols

{Temp. = 40° ± 0.1°C, Solvent = methanol, [PI] = $1.0 \times 10^{-4}$ mol dm$^{-3}$}
phenols increase the rate, while electron-withdrawing ones decrease it.

The Bronsted free energy relationship holds good for our results as it does for the structurally closely related compounds. The value of Bronsted constant is positive ($\beta = 0.09 \pm 0.02$) and is in agreement with the nucleophilic substitution reaction. Since $\beta$ values are generally associated with the degree of bond formation in the transition-state, its value indicates the formation of an oxygen-carbon bond in the transition-state during the reaction of PI with phenoxides. It is customary to correlate the effect of $m$- and $p$-substituents in the benzene ring by the Hammett relationship. Multiparameter treatments of the data are not justified in our case, owing to the small number of substituents considered. Plot of log-$k_2$ values versus the Hammett $\sigma$ constants for the different substituents in phenol is linear for compound PI. The value of $\rho$ calculated is $-0.29 \pm 0.07$. This negative $\rho$ value implies that the substituents are on the nucleophile.

### Activation parameters

The negative values of entropy of activation (Table II) reflect that the transition states are more rigid than the initial stage, and this is expected for bimolecular substitution reaction. For the current reaction series the entropy of activation $\Delta S^s$ is substituent dependent. Though there are substituents in the $o$-position, the variation in $\Delta S^s$ values can be explained in terms of direct steric interaction and in changes in solvation between the reactants and transition state. Electron-donating substituents in phenoxide ion, though their resonance and/or inductive effect, localize the formal charge in the oxygen atom. This favours the formation of a more ordered transition state, reflecting a higher entropy value of activation (Table II). Whereas, phenoxide ions containing electron-withdrawing substituents differ in their nature so that the formal charge on oxygen delocalize over a great part of this ion leading to a lower negative entropy value of activation. The frequency factors of ionic reactions depend in a very simple and important way on the ionic charges in the transition-state. For reactions between ions of opposite signs, the frequency factors are generally higher. The value of the frequency factor should decrease as the entropy of the transition state decreases, i.e. as the negative value of $\Delta S^s$ increases. This correlation holds good for different phenols.

The nearly constant value of $\Delta G^r$ indicates that similar mechanisms are operative for the substitution reactions of phenols. According to Leffler isokinetic relationship, it is found that the activation enthalpies and entropies of the eight different phenols are linearly related ($r = 0.9987$). The linear correlation also implies that the series of the reactions studied follow the same mechanism. The isokinetic temperature computed from the slope of this linear plot is 321 K. As the isokinetic temperature is above the experimental temperature range (308 - 323 K) the reaction is assumed to be enthalpy controlled.

### References