

Rapid Iodination of 4-Chloroacetanilide in Aqueous Medium by Iodine Monochloride using Rpe: A Kinetic Approach

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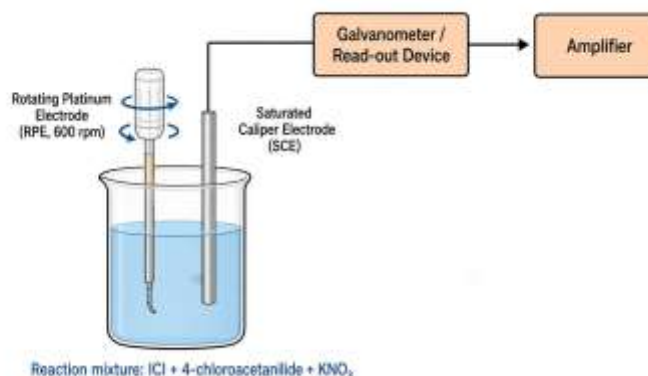
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Abstract

The kinetics of the rapid iodination of 4-chloroacetanilide with iodine monochloride were examined in aqueous solution across five temperatures. The process proved to be markedly fast and second-order overall, displaying a half-life of 480 s and a rate constant of $4.16 \text{ M}^{-1} \text{ s}^{-1}$ at 23°C . Because of the high speed of the reaction, hydrodynamic voltammetry was employed to monitor the progress of iodination. From the measurements, the specific rate constant, activation energy, entropy of activation and the pre-exponential factor were obtained. These kinetic and thermodynamic quantities permit a direct assessment of the reactivity of 4-chloroacetanilide under the conditions studied. [1]

Keywords: Hydrodynamic Voltammetry, Iodination, Iodine Monochloride, Kinetics, RPE

Hydrodynamic Voltammetry Setup for Rapid Iodination Kinetics



I.Introduction

Aromatic halogen compounds occupy a central place in synthetic organic chemistry.[1] They serve as key intermediates for organometallic reagents [2,3]and participate in important transition-metal-catalysed couplings such as the Negishi reaction.[4] The halogen substituent also confers useful properties that allow these molecules to function as pharmaceuticals, herbicides, pesticides and flame retardants.[5,7]

Iodination of aromatic rings, an electrophilic aromatic substitution,[8] is especially valuable for preparing natural-product intermediates and bioactive iodoarenes. [9-11] Because the reaction is sensitive to the electrophilicity of the reagent, the nucleophilicity of the substrate and steric factors, a quantitative understanding of substrate reactivity is essential. In aqueous solution the iodinations are extremely rapid, and conventional kinetic methods are inadequate; literature data for aqueous media are correspondingly scarce.

Iodine monochloride, being polar, attacks the aromatic ring more readily than molecular iodine and avoids the complications associated with tri-iodide formation or protonated hypohalous acids.[12] Half-lives of only a few seconds are typical, yet dilution converts the second-order processes into systems that can be followed by hydrodynamic voltammetry at a rotating platinum microelectrode. The consumption of ICl is monitored directly, furnishing complete rate constants and thermodynamic parameters for the iodination of the regioisomers of cresol, nitrophenol and chlorophenol relative to phenol itself. Product identities were confirmed by standard analytical methods. [13]These data permit a clear assessment of how substituent character and molecular planarity govern reactivity under aqueous conditions.[15]

II.Materials and Methods :

All reagents were obtained from commercial suppliers and used without further purification. Analytical-grade iodine monochloride, 4-chloroacetanilide and potassium nitrate were employed to prepare stock solutions in double-distilled water.

A. Kinetic measurements by hydrodynamic voltammetry

A rotating platinum electrode (RPE) was constructed from a 30 cm long, 5 mm diameter inverted T-shaped glass tube filled with mercury. A 1 cm length of 1 mm diameter platinum wire was sealed into the tip so that 0.5 cm projected into the solution. Electrical contact was made by a copper wire immersed in the mercury. The electrode was driven at a constant 600 rpm by a synchronous motor through a pulley arrangement. The inverted T geometry ensured efficient stirring of the reaction mixture during rotation. A saturated calomel electrode (SCE) served as the reference electrode and was connected as the positive pole of the circuit.

B. Calibration of the diffusion current

For the iodination of 4-chloroacetanilide the RPE and SCE were immersed in 50.0 cm³ of 0.01 M potassium nitrate supporting electrolyte. A potential of +0.1 V versus SCE was applied and the galvanometer spot was adjusted to zero. The supporting electrolyte was then replaced by 50.0 cm³ of 1×10^{-3} M iodine monochloride containing 0.01 M potassium nitrate. The galvanometer shunt was set so that the light-spot deflection remained on scale; a 1.0 cm deflection corresponded to a diffusion current of 1.0 nA. This shunt setting was kept constant for all temperatures examined.

Calibration solutions containing iodine monochloride in the range 1×10^{-4} M to 5×10^{-4} M were prepared after the solutions had reached the thermostat temperature used for the subsequent kinetic runs. Diffusion-current readings (expressed as galvanometer deflection) were recorded for each concentration. Linear plots of diffusion current versus iodine monochloride concentration were obtained at every temperature (Table 2.1 and Fig. 2.1). Both the iodine monochloride and the 4-chloroacetanilide solutions experienced a twofold dilution when mixed in the reaction vessel.

Table 1 Calibration of the Diffusion Current of ICl at Various Temperatures for the Uncatalyzed Iodination of 4-chloroacetanilide in Aqueous Medium. (± 0.2 nA Error)

[ICl]/ 10^{-4}M	Diffusion Current/nA				
	18°C	23°C	28°C	33°C	38°C
1	2.42	3.70	3.77	4.44	5.11
2	4.85	7.00	7.54	8.88	10.23
3	7.27	9.30	11.31	13.33	15.35
4	9.70	11.70	15.08	17.77	20.46
5	15.05	15.50	18.86	22.22	25.58

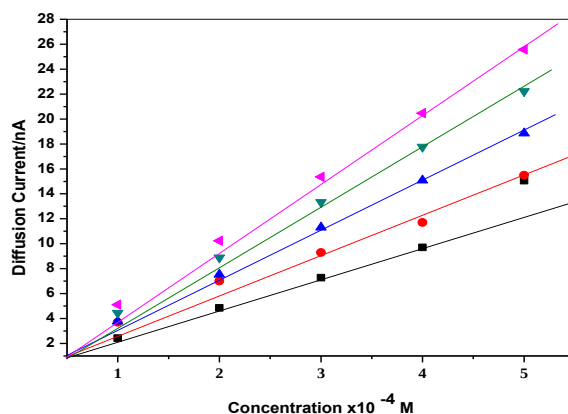


Fig. 1 Calibration of the diffusion current of ICl at various temperatures for the uncatalyzed iodination of 4 chloroacetanilide in aqueous medium

Table 2 Kinetics of Uncatalyzed Iodination of 4-chloroacetanilide at 23.0°C by ICl in Aqueous Medium (± 0.2 nA Error)

Time/sec	Diffusion Current/nA	[ICl]/ 10^{-4}M	[ICl] $^{-1}/10^{-3}\text{M}^{-1}$
0	15.60	5.05	1.980
30	14.60	4.70	2.127
60	13.80	4.45	2.247
90	13.00	4.20	2.380
120	12.50	4.05	2.469
150	11.80	3.80	2.631
180	11.30	3.65	2.739
210	10.80	3.50	2.857
240	10.40	3.35	2.985
270	10.00	3.25	3.076
300	9.60	3.20	3.125
330	9.20	3.00	3.333
360	8.90	2.90	3.448

Table 3 Constant Parameters in the Kinetics of Uncatalyzed Iodination of 4-chloroacetanilide in Aqueous Medium at All Temperatures

Sr.no.	Parameters	Values	Unit's
1.	Potential applied at the RPE Vs SCE	0.1	V
2.	Initial concentration of iodine-monochloride	5×10^{-4}	M
3.	Initial concentration of 4-chloroacetanilide	5×10^{-4}	M
4.	Concentration of potassium nitrate	1×10^{-2}	M
5.	Total volume of the reaction mixture	50.0	cm ³

After the two reactant solutions had been mixed to give a final volume of 50 cm³, the following procedure was adopted. Twenty-five cubic centimetres of 5×10^{-4} M iodine monochloride containing 1×10^{-2} M potassium nitrate were placed in one flask and equilibrated at the required temperature in a thermostat. An identical volume of 5×10^{-4} M 4-chloroacetanilide, also containing 1×10^{-2} M potassium nitrate, was held in a second flask in the same thermostat. Once both solutions had reached the set temperature they were poured simultaneously into the reaction vessel, which already contained the rotating platinum electrode and the saturated calomel electrode. The moment of mixing was recorded on a stop-watch that had been started in advance, and the progressive fall in diffusion current arising from residual iodine monochloride was noted every thirty seconds as the displacement of the galvanometer light spot. Measurements continued until approximately one half-life of the reaction had elapsed (Table 2.2). The initial concentrations present after dilution to 50 cm³ are listed in Table 2.3. Unreacted iodine monochloride concentrations at successive times were obtained from the appropriate temperature calibration plot. Because the reaction is second-order and the reactants were present in equimolar amounts, a plot of the reciprocal of the iodine monochloride concentration against time was linear; its slope furnished the second-order rate constant k_2 (Fig. 2.2). Kinetic runs for the remaining eight systems were performed in the same way, the initial reactant concentrations being adjusted so that the decay of the diffusion current could be recorded at convenient but rapid intervals.

III. Experimental Errors

Calibration and kinetic measurements were each repeated three times to confirm reproducibility. Galvanometer readings remained consistent within ± 0.2 nA. Given the instrument's sensitivity and response characteristics, the uncertainty in the measured nanocurrents arising from residual iodine monochloride did not exceed 1 %. Preparation of the stock solutions introduced a weighing error of no more than 0.25 %, set by the balance sensitivity. Taken together, these contributions limited the overall experimental uncertainty in the derived activation energy (E_a) and entropy of activation ($\Delta S^\ddagger$) to ≤ 2 %.

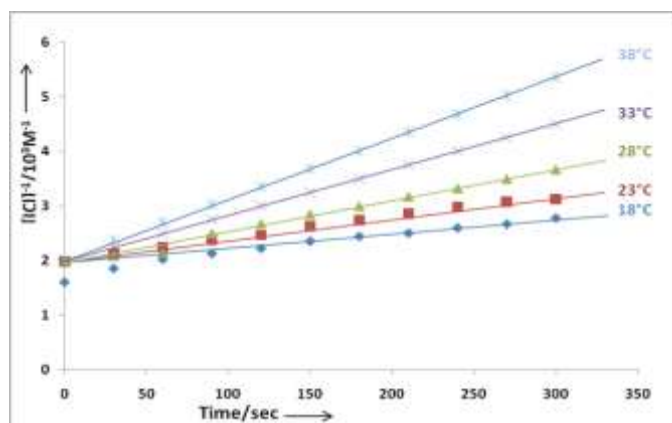
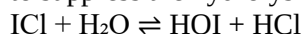


Fig. 2 Kinetics of the uncatalyzed iodination of 4-chloroacetanilide by ICl in aqueous medium at various temperatures

IV. Results and Discussion

A. Optimization of reaction conditions

To compare the relative reactivities of the substrates, the experimental conditions had first to be carefully optimized. Although iodination is normally the slowest of the halogenation reactions, it becomes markedly faster when the polar reagent iodine monochloride is used in place of molecular iodine. Iodine monochloride was therefore selected for its superior electrophilic character. Under the conditions employed, 4-chloroacetanilide proved to be among the more reactive aromatic substrates. Because the reactions are rapid, the progress of iodination was followed by measuring the diffusion-limited current of residual iodine monochloride at a rotating platinum electrode. The method requires a high concentration of supporting electrolyte; potassium nitrate was chosen both for this purpose and to suppress the hydrolysis of iodine monochloride through the common-ion effect: [16]



Ionic strength was held constant throughout, ensuring that the dipolar iodine monochloride molecule remained the sole iodinating species. The kinetic and thermodynamic parameters obtained under these conditions have been interpreted in terms of stereoelectronic and electrophilic-substitution principles.

B. Thermodynamic and kinetic analysis

The iodination of 4-chloroacetanilide by iodine monochloride was monitored at a platinum microelectrode rotated at 600 rpm. A potential of +0.1 V versus the saturated calomel electrode was applied, and the diffusion current arising from unreacted iodine monochloride was recorded every 30 s with a moving-coil mirror galvanometer (sensitivity 1 nA cm⁻¹). Separate calibrations of galvanometer deflection against iodine monochloride concentration were performed at each temperature used for the kinetic runs. Unreacted concentrations at successive times were then read from the appropriate calibration plot.

Measurements were made at five temperatures so that the activation energy could be determined (Table 3.1 and Fig. 3.1). Rate constants were reproducible to within $\pm 2\%$ after allowance for all experimental uncertainties. Initial reactant concentrations were chosen to permit convenient recording of the decaying current. From the temperature dependence of the rate constants the activation energy, frequency factor and entropy of activation were evaluated for each of the nine systems examined. The data for 4-chloroacetanilide were analysed in particular to establish a quantitative structure–reactivity relationship. A summary of the kinetic and thermodynamic parameters is given in Table 3.2.

Table 4 Variation of the Specific Reaction Rate of Iodination of 4-chloroacetanilide by ICl in Aqueous Medium with Temperature ($\leq 2\%$)

Temp/ ^o C	Temp/K	[T] ⁻¹ /10 ⁻³ K ⁻¹	k/M ⁻¹ s ⁻¹	Log k
18	291	3.4364	2.77	0.4421
23	296	3.3783	4.16	0.6190
28	301	3.3222	5.50	0.7403
33	306	3.2679	8.33	0.9206
38	311	3.2154	11.11	1.0457

Table 5 Kinetic parameters for the iodination of 4-chloroacetanilide in aqueous medium by using iodine-monochloride at 23°C

Sr. no.	Description	Experimental values
1.	Specific Reaction Rate / $\text{M}^{-1}\text{s}^{-1}$	4.16
2.	Energy Of Activation / kJmol^{-1}	45.953
3.	Frequency Factor / $10^8\text{M}^{-1}\text{s}^{-1}$	5.33
4.	Entropy Of Activation / $\text{JK}^{-1}\text{mol}^{-1}$	-88.459

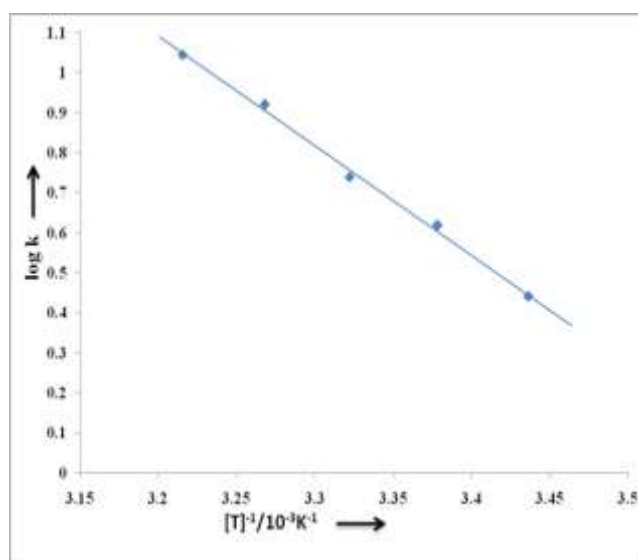
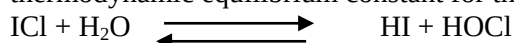


Fig. 3 Variation of the specific reaction rate of iodination of 4-chloroacetanilide by ICl in aqueous medium at different temperatures

V.Conclusions

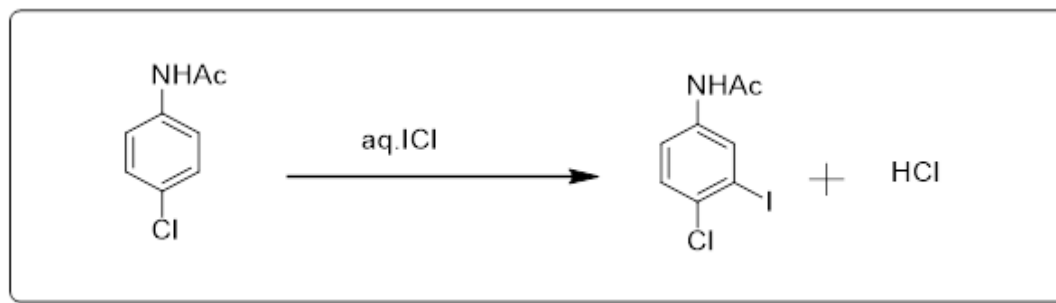
Iodine monochloride is the strong iodinating reagent in the present reaction in view of the thermodynamic equilibrium constant for the equilibrium,



A calibration curve relating the diffusion-limited current measured at the rotating platinum electrode versus the saturated calomel electrode to the concentration of iodine monochloride was constructed and found to be linear, as expected. Equimolar concentrations of iodine monochloride and 4-chloroacetanilide were employed throughout the kinetic runs. The plot of the reciprocal of the residual iodine monochloride concentration against time was linear, confirming that the reaction is strictly second-order. Although the process is intrinsically rapid, dilution of the reactant solutions lengthens the half-life sufficiently for the decay of the very low residual iodine monochloride concentration to be followed conveniently by hydrodynamic voltammetry.

Kinetic measurements were performed at five temperatures, allowing the activation energy (E_a), the entropy of activation ($\Delta S^\ddagger$) and the frequency factor (A) to be evaluated. Molecular iodine, being only sparingly soluble in water, does not react with 4-chloroacetanilide at a measurable rate under the same conditions. In contrast, the polar interhalogen iodine monochloride attacks the aromatic ring readily. The rate of this electrophilic aromatic substitution is governed by both the electrophilicity of the reagent and steric factors. The acetamido substituent is ortho/para-directing, while the chlorine atom, although deactivating through its inductive effect, also exerts a mesomeric influence. In accordance with the substitution pattern expected for a meta-disubstituted benzene bearing both donor and

acceptor groups, iodination occurs preferentially ortho to the chlorine. The quantitative kinetic data obtained in the present work are consistent with this regiochemical outcome.



The experimental design itself embodies several principles of green chemistry: the half-lives are short and the reactant concentrations are kept deliberately low, thereby minimising material consumption and waste.

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VII. References

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