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Kinetics of Iodination of Substituted Hydroxy Aromatic Ketones by Iodine and Iodic Acid

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Abstract

The kinetics of iodination of the substituted hydroxy aromatic ketones using iodine and iodic acid in ethanol has been studied under varying conditions. The rates show first order kinetics each in iodine and hydroxy aromatic ketones and zero order with respect to iodic acid. The rates of reactions are measured at different temperature and activation parameters for all hydroxy aromatic ketones computed. The correlation between the enthalpies and free energies of activations is reasonably linear with an isokinetic temperature 379.44K. Similarly log A values of all the hydroxy aromatic ketones are optimized corresponding to E_a of hydroxy aromatic ketones through the equation, log A = log k_{obs} + E_a / 2.303 RT.

Keywords: *Kinetics, iodination, hydroxy aromatic ketones, iodine, iodic acid.*

Introduction

The iodination of aromatic carbonyl compounds has been the subject of numerous studies due to the potential of the product to serve as intermediate in organic synthesis. Iodination of aromatic rings is an electrophilic substitution reaction with wide applications in organic synthesis particularly in the synthesis of pharmaceuticals [1-6]. Aromatic iodides have been used in the synthesis of many interesting natural products [7] and also as bioactive materials [8]. They also have importance in medicinal and pharmaceutical research[9].

To study the kinetics of organic compounds number of reagents such as molecular iodine [10-11], iodine monochloride[12], N-iodosuccinimide[13] have been used. But most of reagents used are toxic, expensive and generates hazardous waste [14].The iodine and iodic acid an efficient solid iodinating agent which has no hazardous effect and ecofriendly.

Further one of the important tool in deciding the mechanism of reaction is the study of substituent effect and thermodynamic parameters. The linear free energy relationship (LFER), have been found useful for correlating reaction and equilibrium constants. The isokinetic relationship is also an important tool for deciding the nature of a mechanism.

This article focuses on the study of kinetics and mechanism of iodination of hydroxy aromatic ketones by iodine and iodic acid in ethanol.

Materials and Methods

Experimental section

All the chemicals and solvent used were of analytical grade. 5-Chloro, 4, 6-Dimethyl, 5-Methyl, 4-Methyl, 3-Chloro hydroxy aromatic ketones were synthesized by known method. [15]

Kinetic measurements:

The reactions were carried out under pseudo first order conditions by keeping an excess of substrate over, iodine and iodic acid. The progress of reaction was followed by estimating the concentration of unreacted iodine spectrophotometrically at wavelength 545 nm. The rate constants were determined by least square method, from the linear plots of log OD versus time. Replicate runs showed that the rate constants were reproducible to within $\pm$ 3%.

Stoichiometric and product analysis:

Stoichiometric of iodine and iodic acid and hydroxyl aromatic ketone reaction was determined by allowing the reaction mixture containing hydroxy ketone, iodine and iodic acid in 5:2:1 molar ratio in ethanol to go to completion at room temperature. Then the reaction mixture was poured in water to get solid product. The iodinated product was analyzed using preparative TLC on silica gel, and comparing the melting point of product with the known sample.

Results and Discussion

The results of iodination of substituted hydroxy aromatic ketones by iodine and iodic acid are presented in table 1-4.

Effect of variation of [substrate]:

At constant [Iodine] and [Iodic acid], the increase in [substrate] enhances the reaction rate. The plot of log k_{obs} versus log [substrate] for different initial concentration of substrate is linear with unit slope indicating the first order dependence on substrate (table-1).

Table 1: Effect of Variation of [substrate] on Reaction Rate

[Substarate]	$k_1 \times 10^4$ sec^{-1}					
	4,6-di CH_3	4-CH_3	5-CH_3	3-CH_3	5-Cl	3-Cl
0.05 M	5.56	5.1	4.98	4.81	4.73	4.57
0.045M	5.03	4.59	4.43	4.32	4.23	4.02
0.040M	4.44	4.08	3.98	3.74	3.76	3.62
0.035M	3.89	3.57	3.48	3.24	3.29	3.19
0.03M	3.33	3.06	2.96	2.82	2.82	2.75

[Iodine]= 0.005 M, [Iodic acid] = 0.005 M, Temperature = 301 K Solvent = Ethanol

Effect of variation of [Iodine]:
At constant [Substrate] and [Iodic acid], the increase in [iodine] enhances the reaction rate. The first order plots of log OD versus time were linear. The plot of log k_{obs} versus log [Iodine] for different initial concentration of iodine is linear with unit slope indicating the first order dependence on iodine (table-2).

Table 2: Effect of Variation of [Iodine] on Reaction Rate

[Iodine]	k_1 **x** 10^4 **sec**$^{-1}$					
	4,6-di CH_3	4-CH_3	5-CH_3	3-CH_3	5-Cl	3-Cl
0.005 M	5.56	5.1	4.98	4.81	4.73	4.57
0.0045M	5.03	4.63	4.48	4.27	4.2	4.09
0.004M	4.5	4.12	3.88	3.78	3.65	3.65
0.0035M	3.71	3.62	3.28	3.68	3.17	3.15
0.003M	3.47	3.19	2.78	2.6	2.62	2.55

[Iodine]= 0.005 M, [Iodic acid] = 0.005 M, Temperature = 301 K Solvent = Ethanol

Effect of variation of [Iodic acid]:
At constant [substrate] and [Iodine], the increase in [Iodic acid] did not affect the rate of reaction. . The pseudo first order rate constants computed from the plots remained unaffected by the change in [Iodic acid], establishing the zero order dependence of the rate on iodic acid in all cases (table-3).

Table 3: Effect of Variation of [Iodic acid] on Reaction Rate

[Iodic acid]	k_1 **x** 10^4 **sec**$^{-1}$					
	4,6-di CH_3	4-CH_3	5-CH_3	3-CH_3	5-Cl	3-Cl
0.005 M	5.69	5.08	4.98	4.81	4.73	4.57
0.0045M	5.67	5.01	4.93	4.89	4.70	4.59
0.004M	5.70	5.15	4.88	4.82	4.69	4.51
0.0035M	4.69	5.10	4.81	4.80	4.71	4.54
0.003M	4.59	5.20	4.91	4.79	4.65	4.59

[Iodine]= 0.005 M, [Iodic acid] = 0.005 M, Temperature = 301 K Solvent = Ethanol

Effect of temperature:
The study of iodination of different hydroxyl aromatic ketones has been subjected to different temperature range 296 K to 316 K by keeping the concentration of substrate and reagent constant. The rate constants are given in table 4. The plots of log *k* versus 1/T are linear. Activation parameters are presented in table 5.

Energy-entropy relationship:
The entropy of activation and heat of reaction are correlated by the equation 1.

$$\Delta H^{\#} = \Delta H^{0} + \beta \Delta S^{\#} \text{ ---------- (1)}$$

Where β is the isokinetic temperature .The isokinetic plot for the reaction between hydroxy aromatic ketones and iodine and iodic acid in ethanol.

Table – 4 Rate Constant of Iodination of 2'-Hydroxy Propiophenone by Iodine and Iodic Acid at Different Temperature

Sr.No.	Temperature →	296K	301K	306K	311K	316K
	Name of Substrate	$k \times 10^4$ sec^{-1}				
1	2'-Hydroxy-4'-6'-Di-methyl Propiophenone	4.89	5.56	6.23	7.14	8.04
2	2'-Hydroxy-4'-Methyl Propiophenone	4.48	5.10	5.90	6.63	7.49
3	2'-Hydroxy-5'-Methyl Propiophenone	4.40	4.98	5.65	6.47	7.25
4	2'-Hydroxy-3'-Methyl Propiophenone	4.36	4.81	5.50	6.22	7.07
5	5'-Chloro-2'-Hydroxy Propiophenone	4.30	4.70	5.38	6.12	6.79
6	3'-Chloro-2'-Hydroxy Propiophenone	4.05	4.50	5.18	5.64	6.43

[Substrate]: 5.0 x 10^{-2} M, [Iodic Acid]: 5.0 x 10^{-3} M, [Iodine]: 5.0 x 10^{-3} M, Solvent: Ethanol

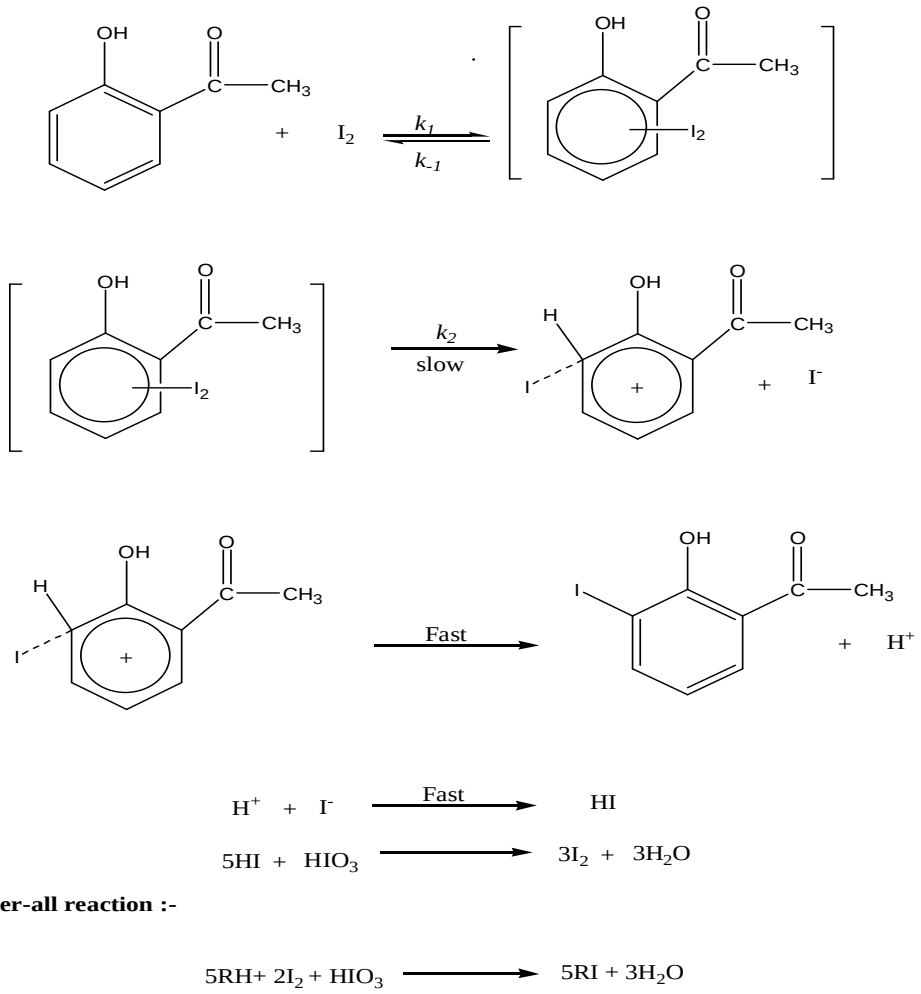
Table – 5 Activation Parameters

Sr. No.	Name of substrate	kx10^4sec^{-1}	Freq.Factor log(A) L/mole/sec	Ea$^{\#}$ KJ/mole	$\Delta H^{\#}$ KJ/mole	$-\Delta S^{\#}$ J/mole	$\Delta G^{\#}$ KJ/mole
1	2'-Hydroxy-4'-6'-Di methyl-propiophenone	5.56	4.26	18.799	16.296	249.82	91.492
2	2'-Hydroxy-4'-methyl-propiophenone	5.10	4.52	19.530	17.027	247.99	91.673
3	2'-Hydroxy-5'-methyl-propiophenone	4.98	4.56	19.669	17.166	247.84	91.767
4	2'-Hydroxy-3'-methyl-propiophenone	4.81	5.03	20.870	18.367	244.13	91.852
5	5'-Chloro-2'-hydroxy propiophenone	4.70	5.19	21.444	18.941	242.43	91.912
6	3'-Chloro-2'-hydroxy propiophenone	4.50	5.37	21.827	19.324	241.40	91.986

[Ketone] = 5.0 x 10^{-2} M, [Iodic Acid] = 5.0 x 10^{-3} M, [Iodine] = 5.0 x 10^{-3} M, Temperature= 301K

The isokinetic tempeature (379.44 K) greater than experimental temperature. The values of entropy of activation also suggest that the reaction is entropy as well as enthalpy controlled. The values of free energies of activation of reaction were found to be move or less similar. This trend also supports the identical reaction mechanism being followed in these reactions. The linear relationship in Exner plot [16, 17] at 3 + log k_{296K} and 3 + log k_{301K} observed in present study also supports the conclusion drawn from isokinetic temperature.

Probable Mechanism of Iodination of Hydroxy Aromatic Ketone by Iodine and Iodic Acid



Over-all reaction :-

$$5RH + 2I_2 + HIO_3 \longrightarrow 5RI + 3H_2O$$

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