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Research Article

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Study of the Catalytic Constant of Phosphate Base in the Kinetics of Iodination of Pyrazole by Molecular Iodine in Aqueous Medium

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ABSTRACT

The rapid kinetics of base catalysed iodination of pyrazole by molecular iodine has been studied in aqueous medium using phosphate buffer. The reaction is electrophilic substitution reaction and rate sows second order kinetics. The specific reaction rates have been determined at constant pH of 7 and temperature 23°C at various base concentrations of the buffer component in the range of 0.02 M to 0.1 M. The catalytic constant of the reaction is calculated from the slope of the graph of specific reaction rate versus base concentration which is found to be 675.4 $M^{-2}s^{-1}$*. The reaction has been also studied kinetically at different pH and at constant base concentration of 0.1 M of the buffer component used. The rapidity of the reaction necessitates the use of special technique namely hydrodynamic voltammetry to study the progress of reaction. The decay of the unreacted iodine is followed by measuring the decrease in diffusion current at rotating platinum electrode. The linear proportionality of specific reaction rates with the concentration of base component provides the quantitative verification for the base catalysed reaction.*

Keywords: Rapid kinetics; Base catalysed; Hydrodynamic voltammetry; Quantitative assessment

INTRODUCTION

Pyrazole is known to be the 1, 2 azole which is five-membered aromatic heterocyclic compound containing two adjacent nitrogen in a ring [1]. It is a weak base. Pyrazole undergoes the different types of reactions which forms number of derivative of pyrazole. In the recent years the attention has been paid pyrazole derivatives which are synthesized based on the pyrazole as central core. The various pyrazole derivatives have great interest in agrochemical pharmaceuticals, and chemical industries [2,3]. Derivatives of pyrazole represent one of the most active classes of compounds and possess a wide spectrum of biological activities [4,5]. Some of these are found to be used in medicine such as analgesia, anti-inflammatory drugs, antifungal, anti-bacterial, antiviral etc. [6].

Halogenations of such azoles are also of great interest since some of the halogenated five membered aromatic heterocycles are found to be biologically active against various fungi and bacteria [7]. Therefore halogenation of such aromatic heterocyclic compounds and their kinetics study seems to be important in synthetic organic chemistry. The measurement of reaction rates and examination of factors which influence them are essential in such study of reaction mechanism and their chemical reactivity.

Halogenation of aromatic substrates is known to be electrophilic substitution reaction in aqueous medium. The iodination is observed to be the slowest and base-catalysed [8]. Earlier investigators have been studied the base catalysis of iodination of aromatic substrate [9] but the changes in base concentration of buffer used were ignored. An attempt of the base catalysed iodination reactions of aromatic substrate in which consequences of change of pH as well as change in the base concentration of buffer used were made by Dangat et al. [10] and Bonde et al. [11].

The kinetics of iodination of pyrazole by molecular iodine in aqueous medium has been studied by earlier investigators which lacks use of buffer component [12]. In the present study, attempt has been made to investigate the iodination of pyrazole in aqueous medium using molecular iodine in the presence of phosphate buffer. The iodine solution used in the study is totally devoid of I^-ions hence the formation of I^{3-} ions by molecular iodine is prevented. Since the reaction is electrophilic in nature, the role of I_3^- as an iodinating agent is expected to be negligible.

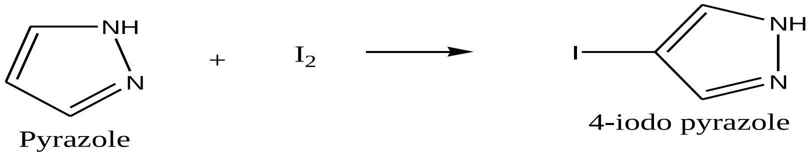
The present study have been under taken to kinetically verify the effect of change in pH and the change in concentration of the base component of the buffer used on the iodination of pyrazole. The pH and the base concentration of the buffer component are maintained as per the requirement using Henderson-Hasselbalch equation [13] as:

$$pH = pk_a + \frac{log\left[base\right]}{\left[acid\right]}$$

In first attempt the [base]/[acid] is varied at constant pH of 7, however second time the pH is varied at constant base concentration and changing acid concentration.

Iodination of aromatic substrates by molecular iodine in aqueous medium generally follows second order kinetics. The reactions are observed to be too rapid to study by conventional kinetic methods. Thus the simple yet efficient technique namely hydrodynamic voltammetry [14] have been employed in the present kinetic study. Convenient kinetic measurements of unreacted iodine are possible since the half-lives can be extended by diluting solutions. The progress of the reaction is measured in terms of the diffusion current using Rotating Platinum Electrode (RPE) and the Saturated Calomel Electrode (SCE), the reference electrode. In the reaction under study, iodine is the only species among the reactants and products which is electro-reproducible at the RPE, its decay during the course of reaction is thus followed in terms of decrease in the diffusion current at RPE.

The reaction under study is shown below:



Iodination of Pyrazole by Molecular Iodine

The product formed in the reaction is mono iodo derivative of pyrazole and the iodination takes place at position –4 in a pyrazole ring [12].

EXPERIMENTAL SECTION

Chemicals

A.R. Grade pyrazole, iodine crystals, potassium nitrate, disodium hydrogen phosphate, sodium dihydrogen phosphate, sodium thiosulphate and starch were used in the present study to prepare the stock solution of required concentration using double distilled water. Iodine solution was standardized prior to the study using standard solution of sodium thiosulphate and freshly prepared starch indicator.

Calibration of Diffusion Current

The RPE and SCE were dipped in 50 cm^3 of 1×10^{-2} M potassium nitrate which is the supporting electrolyte. A potential of +0.1 V *versus* the SCE was applied at RPE. The galvanometer light spot was adjusted to zero deflection on the scale. The potassium nitrate solution was then replaced by 2×10^{-4} M iodine solution containing 100 fold potassium nitrate and the required amount of buffer component to maintain 7 pH. The shunt was adjusted for the maximum deflection of the galvanometer light spot within the limit of scale which is found to be at 30.8 cm. By keeping this shunt value constant the calibration and kinetic measurement for diffusion current were recorded at pH 7. The diffusion current in nA were recorded at various concentrations of iodine in the range of 0.4×10^{-4} M to 2×10^{-4} M in terms of deflection of galvanometer light spot on the scale in cm.

The calibration readings were carried out only after the solutions have attained the thermostat temperature, at which kinetic readings are to be observed subsequently. In a similar manner the calibration of diffusion current of iodine was repeated at various pH and various base concentration of buffer component. The plot of diffusion current *versus* concentration of iodine was found to be linear.

Kinetic Measurements

The solutions of 10 cm^3 each of 1×10^{-3} M iodine, 0.1 M potassium nitrate, 0.5 M disodium hydrogen phosphate, and 0.811 M sodium dihydrogen phosphate were kept in one flask. Similarly 10 cm^3 of 1×10^{-3} M Pyrazole was kept in another flask. Both the flasks were kept in the thermostat to attain the desired temperature. After the solutions attained the temperature of the thermostat, they were mixed in the reaction vessel in which the SCE and the RPE were set up. At the moment of mixing a stopwatch was started. As the reaction proceeds, the decaying concentration of iodine was measured in terms of decrease in the diffusion current at every 10 seconds interval in terms of deflection of galvanometer light spot on a scale.

The above procedure of kinetic measurements was repeated twice for checking the reproducibility of the galvanometer measurements, and these were found to be within the limits of ± 0.3 cm. From the observed deflection during the kinetic study, the concentrations of the unreacted iodine $[I_2]$ at various instants were obtained using the calibration curve. A plot of $[I_2]^{-1}$ *versus* time is found to be linear with intercept equals to initial concentration of iodine which confirms the reaction follows second order kinetics. From the slope of this plot, specific reaction rate 'k' was determined at the desired temperature (Figure 1).

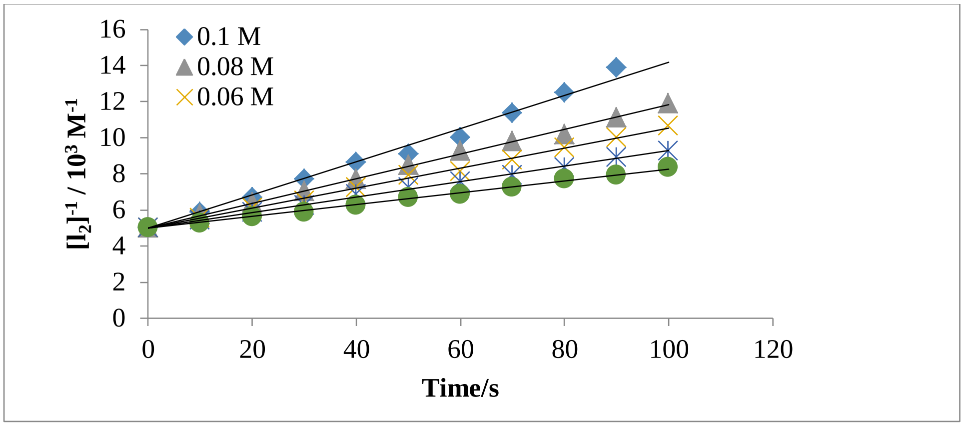


Figure 1. Kinetics of the base catalyzed iodination of pyrazole by molecular iodine at pH=7 and various base concentration

The kinetic measurements were repeated in a similar manner for the various pH and various base concentration of buffer components.

RESULTS AND DISCUSSION

The iodination of aromatic substrate is known to be a base catalysed reaction. The present study comprises the kinetic investigation of base catalysed iodination of pyrazole by molecular iodine using phosphate buffer in aqueous medium. The effect of change of base concentration of the buffer used at a constant pH on the specific reaction rates of iodination of pyrazole has been studied kinetically. The pH of reaction has been maintained constant by using the Henderson-Hasselbalch equation:

$$pH = pk_a + \frac{\log\left[base\right]}{\left[acid\right]}$$

The specific reaction rate at constant pH of 7 and temperature of 23°C has been determined for the various base concentration ranges from 2 × 10^{-2} M to 1 × 10^{-1} M. The results of which are shown in Table 1. The kinetic measurements have an error of not more than ± 2.0 % in view of the reproducibility of the diffusion current.

The study has also been compared to the uncatalyzed reaction which was studied by earlier investigator. The results shows that with increase in concentration of base component of buffer used, the specific reaction rate of the iodination of pyrazole increases, establishing that the increase in specific reaction rate is totally due to increase in concentration of base since no other salt is added during the reaction which may cause the increase in specific reaction rate. From the above study the catalytic constant for phosphate base has been determined (Figure 2).

Table 1. Determination of the base catalytic constant

Concentration of disodium hydrogen phosphate (Base)/M	Specific reaction rate/$M^{-1}s^{-1}$
0.02	32.43
0.04	43.29
0.06	54.17
0.08	67.58
0.1	90.42

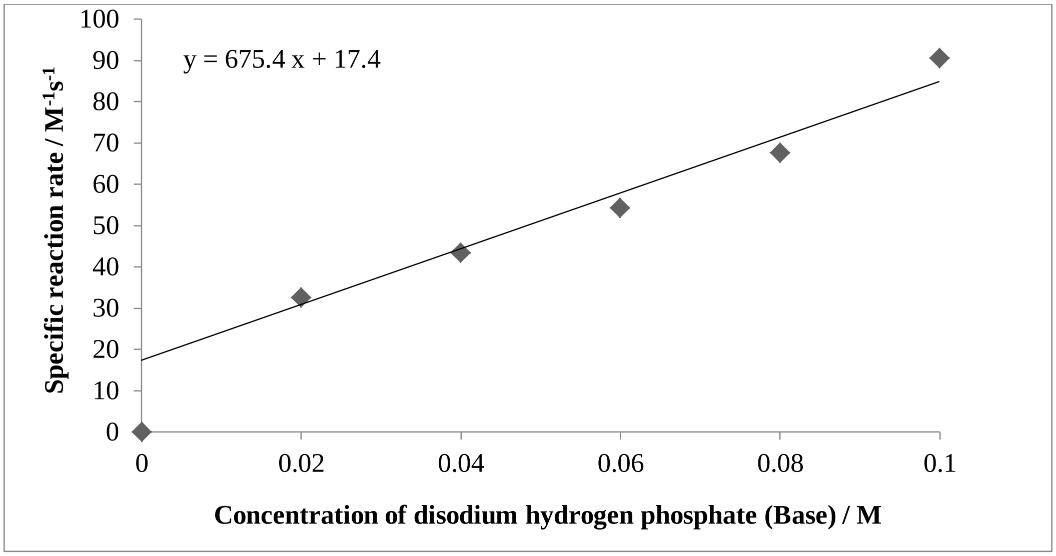


Figure 2: Concentration of disodium hydrogen phosphate base/M

Base Catalytic constant=Slope of the graph of specific reaction rate versus concentration of disodium hydrogen phosphate=675.4 $M^{-2}s^{-1}$.

Uncatalysed rate constant=Intercept of the above plot=17.4 $M^{-1}s^{-1}$.

Generally in halogenations of aromatic substrates the formation of an adduct is usually the rate determining step and deprotonation is a fast step. Iodination however, is an exception in which the deprotonation is slow therefore it is the rate determining step, which involves breaking of C-H bond in the ring. It is because of this, the reaction is highly susceptible to base catalysis where the removal of proton is fast, which increases the specific reaction rate.

The reaction has been also studied at three different pH *viz.* 6.5, 7.0 and 7.5, keeping the constant base concentration of 1×10^{-1} M. The results of which are shown in Table 2. It is found that the specific reaction rate increases with the increase in pH. This is because the percentage of pyrazole anion increases with increase in pH.

Table 2. Variation of the specific reaction rate of iodination of Pyrazole with pH at constant base concentration=0.1 M

pH	**Specific reaction rate/M^{-1} s^{-1}**
6.5	18.18
7.0	90.42
7.5	425.00

The molecular iodine solution used in the present study is totally devoid of I^- ions. The polarization of electrophile *viz.* iodine, due to inductive effect of the substrate ring is much more prominent in the absence of I^- ions. Hence positive end of the dipole in the iodine molecule ($I^{\delta+}$) acts as an effective electrophile. However in the presence of potassium iodide or I^- the formation of I_3^- takes place as:

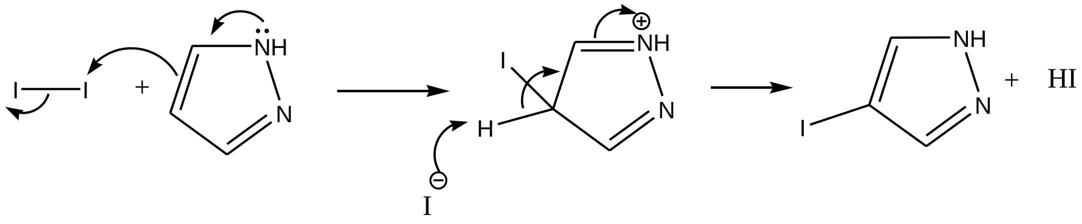
$$I_2 + I^- \rightleftharpoons I_3^-$$

But I_3^- is not being electrophilic in nature which does not bring about electrophilic substitution. Also, the hydrolysis constant for the equilibrium is very low [15] and further hypoiodous acid does not undergo iodination at any appreciable rate. Hence the iodination could be entirely attributed to the molecular iodine.

$$I_2 + H_2O \rightleftharpoons IOH + I^- + H^+$$

The mechanism of iodination of pyrazole by molecular iodine can be explained as follows. The polarization of iodine (I_2) molecule takes place in presence of polar solvent to create the bond dipole of I - I bond. This dipole allows the iodine to have a formal positive charge on one iodine atom ($I^{\delta+}$) and formal negative charge on the another iodine atom ($I^{\delta-}$). The pi electron cloud of the double bond of the substrate *viz.* pyrazole attacks the positive end of dipole i.e. $I^{\delta+}$ or electrophile’ creating a resonance stabilized carbocation. Substrate losses its aromaticity in this step and becomes unstable. The negative end of the dipole i.e. $I^{\delta-}$ abstract the proton and the molecule regains the aromaticity by deprotonation of the carbocation.

The plausible mechanism is shown in Scheme 1.



Scheme 1. Iodination of pyrazole using molecular iodine

CONCLUSION

The assessment of kinetics of iodination of pyrazole by molecular iodine in aqueous medium has been verified quantitatively. The iodination seems to be base catalyzed. The specific reaction rate increases with increase in base concentration of buffer component used at constant pH. The base catalytic constant has been determined using above study. Hydrodynamic voltammetry technique has been found to be efficient to study such rapid kinetics of halogenation since the current due to unreacted iodine can be determined at Rotating Platinum Electode.

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