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Oxidation of paracetamol by *N*-chloro-*p*-toluene sulfonamide (Chloramine-T) in aqueous acid perchlorate medium: A kinetic and mechanistic pathway

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Kinetics and mechanism of oxidation of paracetamol by *N*-chloro-*p*-toluene sulfonamide (chloramine-T) have been studied in acid medium. Accounting for all such observations, a plausible reaction mechanism has been suggested. The activation parameters such as energy and entropy of activation have been calculated to be (58.63 ± 0.91) kJ mol^{-1} and (−88.75 ± 4.54) J K^{-1} mol^{-1} respectively employing Eyring equation. The stoichiometry of the reaction has been observed to be two moles of the oxidant for a mole of the substrate. The rate of the reaction is retarded by toluene-*p*-sulfonamide as well as hydrogen ion concentration. The oxidation product of paracetamol has been spectrally confirmed to be quinine oxime. To further support our proposed mechanism, density functional theory (DFT) computations at M06-2X/6-31G(d,p) level of theory have been performed, showing that activation energy barriers predict the same reactivity trend as shown by the kinetic experiments.

Keywords: Chloramine-T, Mechanism, Oxidation, Paracetamol, Reaction kinetics

The redox chemistry of *N*-Chloro-*p*-toluene sulfonamide[1] known as chloramine-T has been extensively studied both in aqueous acid[2-10] and alkaline[11-16] media. However, much is still desired about the speciation of chloramine-T species in aqueous acid and alkaline media. The species of chloramine-T are *p*H dependent and in acid medium it is more difficult to delineate its species because of interplay of such species governed by various types of equilibria.

Paracetamol is a well known drug also known as 4-hydroxyacetanilide or 4-acetaminophen or 4-acetamidophenol which has wider applications in pharmaceutical industry. It is also considered to be an antipyretic and analgesic compound with extremely useful therapeutic values in medicinal chemistry[17-20]. This drug has not, yet been exploited kinetically so far as its oxidation chemistry is concerned. As the oxidation studies are scanty[6,21-28], it is this reason that we were prompted to undertake the kinetics of oxidation of the paracetamol (heretofore written as PCM) with chloramine-T to know more about its pattern of reactivity and to perceive the logical conditions in such a manner that paracetamol can be determined quantitatively in solutions by this oxidant from the following viewpoints.

First, Chloramine-T is considered to be a potential oxidant in acid medium and has been frequently employed as an oxidimetric reagent in analytical chemistry. Our interest lies in the title study to find out such analytical conditions in such a manner that paracetamol can be estimated quantitatively in solutions by chloramine-T either titrimetrically or spectrophotometrically. Second, the title reaction appears to be an important probe mechanistically as this reagent is considered to be an important antisceptic and disinfectant reagent. Third, logical information regarding the speciation of chloramine-T species in acid medium can be ascertained.

Due to the clinical effects of paracetamol as an inhibitor are still indefinite, new findings are needed in the mode of action of paracetamol which is an advancement in physiological and pharmacological points of view. Oxidation reactions are useful in synthesis process of pharmaceutical drugs and organic compounds. Redox reactions are contributing in the modification of existing groups in compound. Paracetamol is a precursor of many pharmaceutical drugs and dyes. This study can be

useful to determine the paracetamol in drugs and its degradation. Therefore, understanding the role of mechanism of decomposition of this drug in aqueous medium is required to clear the probable pathway of its oxidation.

Experimental Section

Materials and method

N-Chloro-*p*-toluene sulfonamide was taken as its sodium salt (E. Merck, 98%) and its solution was prepared in doubly distilled water. Aqueous solution is quite stable if it is contained in glass vessels painted black from the out side, the stability is enhanced as the decomposition due to diffused photo-light is eliminated. Solution of chloramine-T was standardized iodometrically[29,30] by titrating an aliquot of this solution in the presence of potassium iodide in acidic medium. The librated iodine was titrated against sodium thiosulphate solution using starch as an indicator with sharp end point. Paracetamol (Acros, 98%) was employed as received without any further treatment. Aqueous solution of paracetamol was also kept in brown coloured glass bottles at refrigerator temperature (~5°C). However, fresh solution of paracetamol was always employed. Other reagents were of either AnalaR or guaranteed reagent grade and were employed as received. Doubly distilled water was employed throughout this study; second distillation was from alkaline potassium permanganate solution in an all glass still.

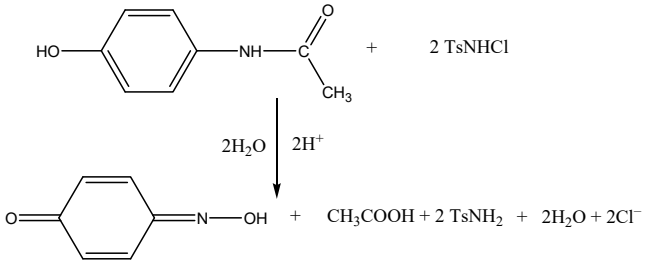
Procedure for kinetic analysis

The reaction mixtures containing all other ingredients except chloramine-T were taken in a glass stoppered and painted black from the outside Erlenmeyer flasks. These flasks were suspended in a water-bath thermostated at 30±0.1°C unless specified otherwise. The temperature pre-equilibrated solution of chloramine-T was added into reaction mixture to initiate the reaction, the time of initiation was recorded when half of the solution contents from the pipette were released into the reaction mixture. The reaction mixture was vigorously shaken and an aliquot (5 or 10 cm^3) of the reaction mixture was taken out at different time intervals to assay remaining chloramine-T iodometrically. None of the reaction ingredients interferes with this estimation. Initial rates were computed by employing plane-mirror method[31]. The rates in triplicate were reproducible to within ± 5%.

Stoichiometry and product analysis

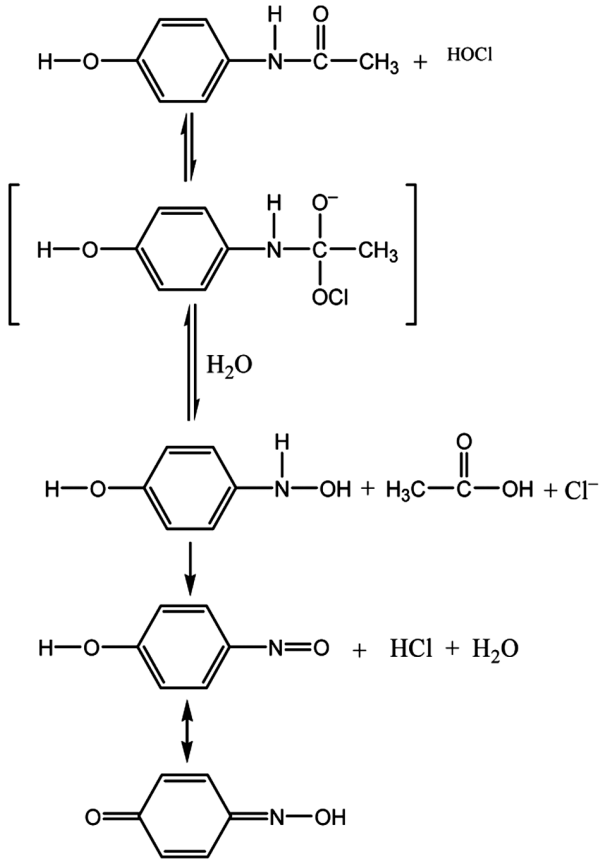
Stoichiometry of the reaction was determined by taking excess of chloramine-T concentration over that of paracetamol containing all other reaction ingredients. Such reactions were allowed to occur for more than 24 h in a thermostated water-bath at 30±0.1°C and the excess chloramine-T was estimated iodometrically.

The results indicate that one mole of PCM requires two moles of chloramine-T as represented by eqn (1).



… (1)

In so far the mode of electron transfer from paracetamol to oxidant is concerned, following tentative reaction Scheme 1 can be envisaged.



Scheme 1 — Mode of electron transfer from paracetamol to oxidant

Quinone oxime is the oxidation product of paracetamol under experimental conditions.

There are different reports regarding the end product of oxidation of paracetamol. The reaction mixture in this case turns to dark brown colour which might be quinone or quinoneoxime. However our attempts to identify and to establish the end product were trusted as the isolation of the product by diethyl ether were not successful. However results with $4e^-$ change correspond to the product to be quinoneoxime.

Oxidation product of paracetamol by Chloramine-T in acidic medium was identified as quinoneoxime with the help of chromatography, IR and NMR spectroscopy. This product oxime has also earlier been established[6]. Reduction product of CAT, $ArNH_2$ (where, Ar = *p*-$CH_3C_6H_4SO_2$) was isolated from the reaction mixture and recrystallized from dichloromethane-petroleum ether mixture (7:3, v/v) and identified by TLC (R_f = 0.84) with the solvent mixture petroleum ether: dichloromethane: 1-butanol (2:2:1, v/v/v) and with iodine as developing reagent.

Quinone oxime was purified from other reaction impurities by column chromatography. Thin layer chromatogram was conducted on Merck-Silica gel G plates in dichloromethane: methanol (9:1, v/v) and in column, chromatographic fractionation silica gel (60-120 mesh) was used and iodine was used as developing reagent.

Melting point

Melting point of 131.5°C was recorded in soft glass capillaries in an electrothermal melting point apparatus which is in very close agreement to that reported in literature (132°C).

Spectral analysis

IR (KBr): 1652 (>C=O, stretching), 1615 (C=N, stretching), 3332 (O-H, stretching) cm^{-1}.

^{1}H NMR (300.40 MHz, DMSO): δ 6.69 (d, 2H), δ 6.49 (d, 2H),δ 1.999 (s, 1H) ppm.

Results

Effect of Chloramine-T

The concentration of chloramine-T was varied from 1.0×10^{-3} to 5.0×10^{-3} mol dm^{-3} at two different but fixed concentrations of paracetamol *viz.* 4.0×10^{-2} and 5.0×10^{-2} mol dm^{-3} respectively and 0.01 mol dm^{-3} perchloric acid at 30°C. Since the reaction rate is affected by one of the reaction products such as *p*-toluene sulfonamide, initial rates (k_i, mol $dm^{-3}s^{-1}$) were calculated to avoid its interference (Table 1). The rates were plotted against the initial concentrations of chloramine-T. A straight line passing through the origin was obtained confirming first order dependence with respect to the oxidant. Second order plots were also made for comparable concentrations of the reactants (Fig. 1) and second order rate constants were calculated, and the results are given in Table 1.

Paracetamol dependence

The concentration of paracetamol was varied from 2.0×10^{-2} to 5.0×10^{-2} mol dm^{-3} at two different but fixed concentrations of chloramine-T *viz.* 2.0×10^{-3} and 3.0×10^{-3} mol dm^{-3} respectively at 30°C. The plot of initial rates (k_i, mol $dm^{-3}s^{-1}$) against the concentrations of paracetamol shows a straight line passing through the origin conforming first order with respect to the substrate. Second order plots were also made for comparable concentrations of the reactants (Fig. 2).

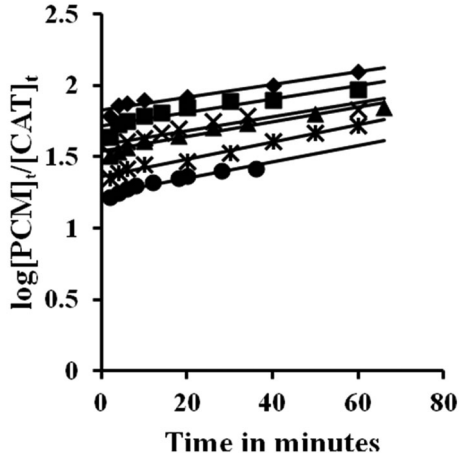
If first order is taken with respect to oxidant and substrate respectively, an empirical rate equation can be given as in eqn. 2.

Table 1 — Initial Rates (mol dm^{-3} s^{-1}) and Second Order Rate Constants (dm^3 mol^{-1} s^{-1}) in the Reaction of Paracetamol and Chloramine-T in Aqueous Acid Medium

$[HClO_4]$ = 0.01 mol dm^{-3} and 30°C

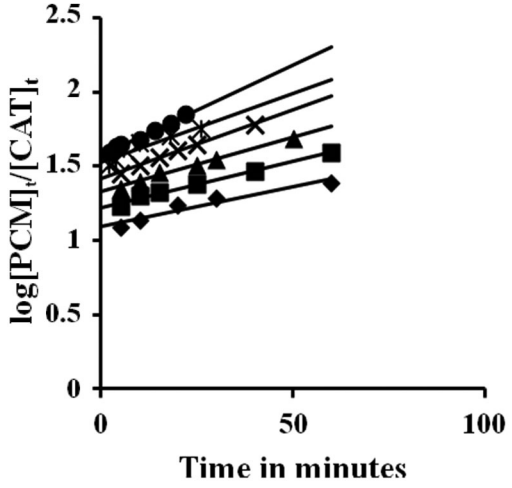
10^2 [PCM] mol dm^{-3}	10^3 [CAT] mol dm^{-3}	10^7 (k_i) mol dm^{-3} s^{-1}	10^2 (k′′) dm^3 mol^{-1} s^{-1}
4.0	1.0	4.50	1.12 (1.12)
4.0	1.5	6.66	1.11 (1.11)
4.0	2.0	8.33	1.12 (1.04)
4.0	2.5	10.80	1.13 (1.08)
4.0	3.0	13.30	1.11 (1.10)
4.0	3.5	16.60	1.12 (1.13)
4.0	4.0	20.0	1.11 (1.18)
5.0	1.0	5.50	1.13 (1.10)
5.0	3.5	19.58	1.10 (1.11)
5.0	4.0	23.30	1.13 (1.16)
5.0	4.5	26.60	1.13 (1.16)
5.0	5.0	28.30	1.12 (1.13)
2.0	2.0	4.33	1.13 (1.08)
2.5	2.0	5.50	1.12 (1.1)
3.0	2.0	6.66	1.10 (1.10)
3.5	2.0	7.50	1.12 (1.08)
4.0	2.0	8.33	1.14 (1.10)
4.5	2.0	10.0	1.13 (1.10)
5.0	2.0	11.6	1.12 (1.16)
2.0	3.0	6.25	1.12 (1.04)
2.5	3.0	8.33	1.13 (1.10)
3.0	3.0	10.0	1.13 (1.11)
3.5	3.0	11.6	1.14 (1.10)
4.0	3.0	13.3	1.12 (1.10)
4.5	3.0	15.0	1.12 (1.11)
5.0	3.0	17.0	1.13 (1.13)

Figures in parenthesis are calculated second order rate constants.



[CAT] = (1) ● 4.0×10^{-2}; (2) ✳ 3.0×10^{-3}; (3) ▲ 2.5×10^{-3}; (4) × 2.0×10^{-3}; (5) ■ 1.5×10^{-3}; (6) ♦ 1.0×10^{-3} mol dm^{-3}; [PCM] = 4.0×10^{-2} mol dm^{-3}; [$HClO_4$] = 0.01 mol dm^{-3} and 30°C

Fig. 1 — Second order plots of Chloramine-T



[CAT] = 2.0×10^{-3} mol dm^{-3}; [PCM] = (1) ♦ 2.0×10^{-2}; (2) ■ 2.5×10^{-2}; (3) ▲ 3.0×10^{-2}; (4) × 3.5×10^{-2}; (5) ✳ 4.0×10^{-2}; (6) ● 5×10^{-2} mol dm^{-3}; [$HClO_4$] = 0.01 mol dm^{-3} and 30°C

Fig. 2 — Second order plots of Paracetamol

$$-\frac{1}{2}\frac{d[CAT]}{dt} = A[CAT][PCM] \quad \ldots (2)$$

where 'A' is an empirical rate constant, [CAT] and [PCM] are the gross initial concentrations of chloramine-T and paracetamol respectively.

Effect of Hydrogen ion

The concentration of hydrogen ion was varied by employing perchloric acid at constant ionic strength I = 0.1 mol dm^{-3} (ionic strength = I was adjusted constant by employing lithium perchlorate) at 30, 35 and 40°C respectively. Sodium perchlorate was avoided because of chloride ion impurities and medium effect. The rate decreases with increasing hydrogen ion concentration (Fig. 3).

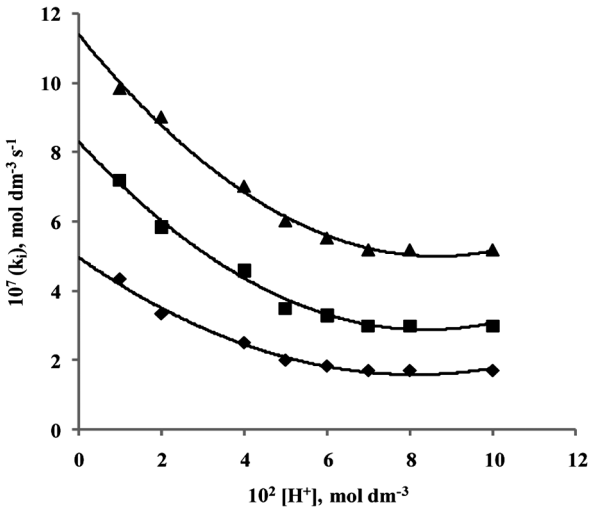


Fig. 3 — Variation of hydrogen ion

Thus to the empirical rate eqn. (2) accounting for hydrogen ion dependence, changes to eqn. (3)

$$-\frac{1}{2}\frac{d[CAT]}{dt} = \frac{A[CAT][PCM]}{C + D[H^+]} \quad \ldots (3)$$

where, C and D are other empirical constants.

Effect of ionic strength

The effect of ionic strength on the rate of reaction was studied by employing lithium perchlorate keeping constant concentrations of other reaction ingredients *viz.* [CAT] = 2.0×10^{-3} mol dm^{-3}, [PCM] = 2.0×10^{-2} mol dm^{-3} and [$HClO_4$] = 0.01 mol dm^{-3} at 30°C. The rate remains unaffected by ionic strength and thus rules out any interaction between charged species.

Effect of Toluene-*p*-Sulfonamide (PTS)

Toluene-*p*-sulfonamide (PTS) is one of the reduction products of chloramine-T. It is not much soluble in cold water and thus the solution was always prepared in hot water and that too was not of much higher concentration. However, hot solution of toluene-*p*-sulfonamide was added to the reaction mixtures in its variations. The rate was found to decrease with increasing concentration of toluene-*p*-sulfonamide. The rate inhibition by toluene-*p*-sulfonamide ascribes to the fact that an equilibrium

involving chloramine-T exists. It is because of this reason that, initial rates were evaluated throughout the kinetic study so that its affect is minimized to a large extent. Nevertheless, the effect of toluene-*p*-sulfonamide on the rate subsequently has been accounted for in the analysis of kinetic data.

Effect of Ruthenium (III) Chloride

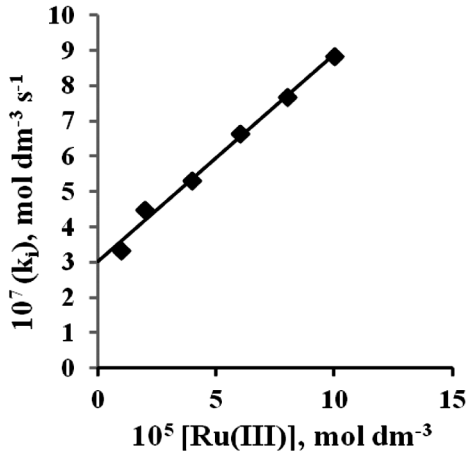
It has been reported[4] that ruthenium (III) chloride catalyzes the reaction. A brief study of effect of [Ru (III)] (for simplicity ruthenium chloride ($RuCl_3$) henceforth written as Ru (III)) by varying its concentration from 1.0×10^{-5} to 1.0×10^{-4} mol dm^{-3} at constant concentration of other reaction ingredients is performed. The rate increases with increasing concentration of Ru (III) and a plot of rate *versus* Ru (III) yields a straight line with non-zero intercept (Fig. 4) ascribing to the fact that uncatalysed reaction also simultaneously takes place in contrary to earlier observations[7]. In view of such an effect of Ru (III), the rate equation reported earlier must be revised as in eqn. 4.

$$-\frac{1}{2}\frac{d[CAT]}{dt} = \left[A^1 + B^1[Ru(III)]\right][CAT][PCM] \quad \ldots (4)$$

where A^1 and B^1 are other empirical rate parameters for steps in uncatalyzed and catalyzed reactions.

Effect of Temperature

The effect of temperature is studied at 30, 35 and 40°C keeping constant concentration of other reaction ingredients *viz.* [CAT] = 2.0×10^{-3} mol dm^{-3}, [PCM] = 2.0×10^{-2} mol dm^{-3}; I = 0.1 mol dm^{-3}. The energy and entropy of activation parameters were calculated by employing Eyring plot[32] and the values are (58.63±0.91) kJ mol^{-1} and (-88.75±4.54) Jmol^{-1} K^{-1}, respectively.



[CAT] = 2.0×10^{-3} mol dm^{-3}; [PCM] 2.0×10^{-2} mol dm^{-3}; [$HClO_4$] = 0.01 mol dm^{-3} and 30°C

Fig. 4 — Variation of Ruthenium (III)

Test for free radical

The reaction was also allowed to occur in a thermostated water-bath containing acrylonitrile/acrylic acid. There was no white sediment in the reaction mixture even after a long standing of 24 hours. This shows that no free radical participates in the reaction or if it acts. The radical reacts in the solvent cage under such circumstances. There is a possibility of fast interaction between chloramine-T and free radical in solvent cage and if it had not been a situation, a white precipitate would have been obtained in the reaction mixture on addition of acrylonitrile/acrylic acid.

Discussion

Much is reported about the chemistry of *N*-halo-*p*-toluene sulfonamide both in acid and alkaline medium and still there is further need to probe the speciation of chloramine-T species more particularly in acid medium than alkaline medium[5]. However, reactions in alkaline medium are slower, therefore, a catalyst is required in such reactions. The speciation of oxidant species in acid medium is more difficult owing to interplay of *p*H dependent species.

Chloramine-T species in acid medium are governed by equilibria (5)-(9)

$$RNClNa \rightleftharpoons RNCl^- + Na^+ \quad \ldots (5)$$

$$RNCl^- + H^+ \rightleftharpoons RNHCl \quad \ldots (6)$$

$$2RNHCl \rightleftharpoons RNH_2 + RNCl_2 \quad \ldots (7)$$

$$RNHCl + H_2O \rightleftharpoons RNH_2 + HOCl \quad \ldots (8)$$

$$HOCl \rightleftharpoons H^+ + OCl^- \quad \ldots (9)$$

Thus, the chloramine-T species in acid medium are RNHCl, $RNCl_2$, HOCl and OCl^-. Cl_2 is reactive only in the presence of chloride ion

$$RNHCl + Cl^- \rightleftharpoons Cl_2 + RNH^- \quad \ldots (10)$$

$$RNH^- \rightleftharpoons RNH_2 \quad \ldots (11)$$

Since rate is retarded by *p*-toluene sulfonamide, there is possibility of participation of either $RNCl_2$ or HOCl, however, RNHCl is negated in view of this effect. If $RNCl_2$ is the reactive species[33,34], the order with respect to chloramine-T should be two. If the experimental order with respect to chloramine-T has been observed to be one, the species $RNCl_2$ can be

negated. Thus to account for the order to be one, HOCl appears to be the reactive form of chloramine-T. Also, such a species accounts for the retarding effect of *p*-toluene sulfonamide.

Thus considering HOCl to be the reactive form of chloramine-T and molecular form of paracetamol to be the reactive form of the substrate, the following mechanism can be suggested.

$$RNHCl + H_2O \underset{}{\overset{K_1}{\rightleftharpoons}} RNH_2 + HOCl \quad \ldots (12)$$

$$HOCl + PCM \underset{}{\overset{K_2}{\rightleftharpoons}} C + [H^+] \quad \ldots (13)$$

$$C \underset{}{\overset{k'}{\rightleftharpoons}} C' + \text{Products} \quad \ldots (14)$$

$$C' + HOCl \xrightarrow{\text{fast}} \text{End products} \quad \ldots (15)$$

The loss of chloramine-T leads to the rate law (16)

$$-\frac{d[RNHCl]}{dt} = \frac{2k'K_1K_2[RNHCl]_T[PCM]}{[RNH_2][H^+] + K_1[H^+] + K_1K_2[PCM]} \quad \ldots (16)$$

Since order with respect to paracetamol is one, the eqn. (16) is reduced to eqn. (17)

$$-\frac{d[RNHCl]}{dt} = \frac{2k'K_1K_2[RNHCl]_T[PCM]}{[RNH_2][H^+] + K_1[H^+]} \quad \ldots (17)$$

$$= \frac{k'K_1K_2[RNHCl]_T[PCM]}{[H^+]([RNH_2] + K_1)} \quad \ldots (18)$$

where $[RNHCl]_T$ and [PCM] are the gross analytical concentrations of chloramine-T and paracetamol respectively. This eqn (18) is further reduced to eqn. (19)

$$-\frac{d[RNHCl]}{dt} \Big/ [RNHCl]_T[PCM] = k = \frac{2k'K_1K_2}{[H^+]([RNH_2] + K_1)} \quad \ldots (19)$$

where 'k' is an observed second order rate constant.

The double reciprocal of eqn.(19) yields eqn. (20)

$$1/k = \frac{[H^+][RNH_2]}{2k'K_1K_2} + \frac{[H^+]K_1}{2k'K_1K_2} = \frac{[H^+][RNH_2]}{2k'K_1K_2} + \frac{[H^+]}{2k'K_2} \quad \ldots (20)$$

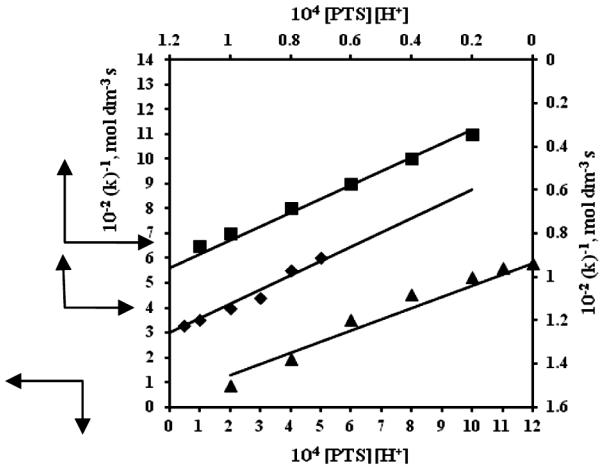
Another plot from eqn. (20) was made between 1/k and $[H^+][RNH_2]$ that yielded a straight line with non-zero intercept (Fig. 5).

The slope (S) and intercept (I) were calculated as represented by eqns. (21) and (22), respectively.

$$S = \frac{1}{2k'K_1K_2} \quad \ldots (21)$$

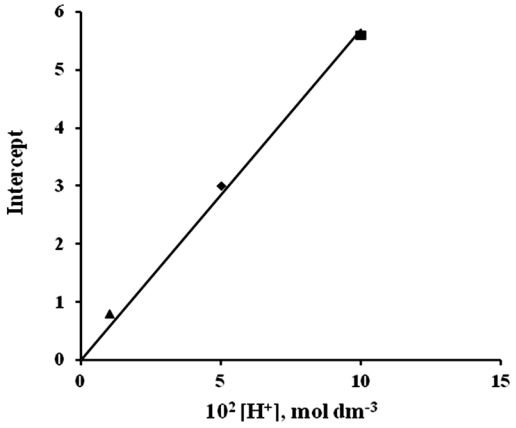
and

$$I = \frac{[H^+]}{2k'K_2} \quad \ldots (22)$$



[CAT] = 2.0 × 10^{-3} mol dm^{-3}; [PCM] = 2.0×10^{-2} mol dm^{-3}; [$HClO_4$] = ▲ 0.01, ♦ 0.05, ■ 0.1 mol $dm^{-3;}$ I = 0.1 mol dm^{-3}

Fig. 5 — A plot of ([PTS][H^+]) *vs* $(k)^{-1}$



[CAT] = 2.0 × 10^{-3} mol dm^{-3}; [PCM] = 2.0×10^{-2} mol dm^{-3}; [$HClO_4$] = ▲ 0.01, ♦ 0.05, ■ 0.1 mol dm^{-3}; I = 0.1 mol dm^{-3}; 30°C

Fig. 6 — A plot of intercept *versus* [H^+]

Further plot of intercept (I) *versus* [H^+] was made at 30°C and I = 0.1 mol dm^{-3} that yielded a straight line passing through the origin (Fig. 6).

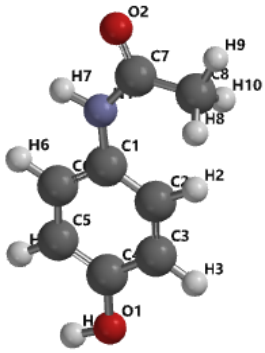
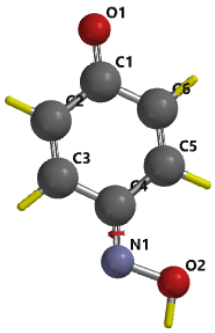
$k'K_2$ was calculated from the slope of the line. The ratio of this slope as obtained in eqn. (21) yielded 'K_1' to be 0.95 × 10^{-2} at 30°C respectively and I (Ionic strength) = 0.1 mol dm^{-3}. This value of K_1 is in the range as reported earlier. These values of $k'K_1K_2$ from the slope of eqn. 21, $[RNH_2]$ and [H^+] were further employed in the rate eqn. (19), and the values of $k_{(obs)}$ and $k_{(cal)}$ as mentioned in Table 2 are in fair agreement. However, such an agreement lacks in case of lower hydrogen ion concentrations.

Properties and mechanism of paracetamol drug is distinguished from the molecular properties of its analogs. Structure and binding of this drug are known to play an important role in its pharmacological actions. Among its analog, paracetamol is an important one and applied as antipyretic and analgesic drug. The nature of substituents on the ring at *para* position and lone pair present on nitrogen in $–NHCOCH_3$ group which is capable of non-covalent interaction with ruthenium have significant aspects in variations in different properties in transition state as pharmacological activity, reduction potential of their stability, *etc*. The theoretical calculations have been performed regarding PCM and Quinone-Oxime using Spartan software[35] with Density Functional Theory M06-2X functional with 6-31G(d,p) basis set, which is the best fit to thermal calculations[36]. To support our proposed mechanism, density functional theory (DFT) computations at M06-2X/6-31G(d,p) showed that activation energy barriers predict the same reactivity trend as shown by the kinetics experiments. The structural parameters and optimized structures are given in Table 3.

Table 2 — k_{obs} and k_{cal} values in the reaction of paracetamol and chloramine-T in acid perchlorate medium

10^3 [PTS] moldm^{-3}	[H^+] mol dm^{-3}	10^2 ($k_{obs.}$) dm^3 mol^{-1} s^{-1}	10^2 (k_{cal}) dm^3 mol^{-1} s^{-1}
1.0	0.05	0.3025	0.31
2.0	0.05	0.285	0.289
4.0	0.05	0.246	0.25
6.0	0.05	0.225	0.215
8.0	0.05	0.20	0.190
10.0	0.05	0.18	0.171
1.0	0.1	0.153	0.158
2.0	0.1	0.143	0.144
4.0	0.1	0.125	0.123
6.0	0.1	0.11	0.11
8.0	0.1	0.1	0.095
10.0	0.1	0.09	0.085

Table 3 — Structural parameters and optimized structures of paracetamol and quinoneoxime calculated using DFT M06-2X/6-31G(d,p) method.

Parameters	Paracetamol	Quinone-Oxime	
Molecular Structure			
Energy	423.69 kJ/mol	271.67 kJ/mol	
C_4-O_1	1.362 A°	C_1-O_1	1.474 A°
C_1-C_2	1.394 A°	C_1-C_2	1.336 A°
C_2-C_3	1.401 A°	C_2-C_3	1.485 A°
C_3-C_4	1.387 A°	C_3-C_4	1.488 A°
C_4-C_5	1.386 A°	C_4-C_5	1.337 A°
C_5-C_6	1.399 A°	C_5-C_6	1.474 A°
C_1-C_6	1.406 A°	C_1-C_6	1.224 A°
C_1-N_1	1.406 A°	C_4-N_1	1.299 A°
C7-N1	1.361 A°	N_1-O_1	1.400 A°
C_7-C_8	1.498 A°	-	-
C_7-O_2	1.235 A°	-	-
θ (C_3-C_4-O_1)	117.92°	θ (O_1-C_1-C_6)	121.36°
θ (C_3-C_4-C_5)	120.41°	θ (C_1-C_6-C_5)	121.54°
θ (C_2-C_1-C_6)	118.21°	θ (C_1-C_2-C_3)	121.31°
θ (C_2-C_1-N_1)	125.97°	θ (C_3-C_4-C_5)	115.97°
θ (C_1-N_1-C_7)	134.80°	θ (C_5-C_4-N_1)	126.22°
θ (N_1-C_7-O_2)	117.7°	θ (C_3-C_4-N_1)	117.81°
θ (O_2-C_7-C_8)	120.08°	θ (C_4-N_1-O_2)	112.11°
δ(Dihedral angle)	Almost same (180°)		

Conclusion

The oxidation product of paracetamol by chloramine-T in acid perchlorate medium is quinoneoxime, requiring two moles of oxidant for each mole of substrate. The reaction proceeds *via* an intermediate complex between oxidant and substrate. Eyring equation has been employed for calculation of energy and entropy of activation.

Conflict of Interest

There are no competing interests.

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