PdCl₂ Catalyzed and Uncatalyzed N-Oxidation of Naratriptan with Alkaline Chloramine-T: Delineation of Reaction Mechanisms and Kinetic Modelings

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Received: 24 April 2015 / Accepted: 31 August 2015 / Published online: 18 September 2015
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Abstract Naratriptan (NTT), chemically known as N-methyl-2-[3-(1-methyl piperidin-4-yl)-1-H-indol-5-yl] ethane sulfonamide, is an indole derivative widely used in the treatment of migraine headaches. The literature survey indicates that there is no report on the oxidation of NTT from the view point of its kinetic and mechanistic aspects. Also none has examined the task of platinum group metal ions as catalysts in the oxidation of this drug. Therefore, in the present research, oxidation of NTT with chloramine-T (CAT) in alkaline medium has been investigated at 298 K through systematic kinetic study in order to explore the mechanistic picture of this redox system in presence and absence of palladium (II) chloride (Pd(II)) catalyst. The reaction shows a first-order dependence of rate each on

[CAT]₀ and [NTT]₀, and an inverse-fractional-order dependence on [NaOH] for both the Pd(II) catalyzed and uncatalyzed reactions. The order with respect to Pd(II) catalyst is fractional. Addition of *P*-toluenesulfonamide decreases the rate. The dielectric effect is negative. 2-[3-(1-methyl-1-oxidopiperidin-4-yl)-1H-indol-5-yl]ethanesulfonic acid and methylamine were identified as oxidation products of NTT. Activation parameters were deduced. The Pd(II) catalyzed reactions are about five-fold faster than the uncatalyzed reactions. The observed results have been explained by plausible mechanisms and the related rate laws have been worked out.

Graphical Abstract The Stoichiometry of the reaction is

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Keywords Naratriptan · Oxidation-kinetics · PdCl₂ catalysis · Chloramine-T · Mechanism

1 Introduction

Naratriptan (NTT), also known as N-methyl-2-[3-(1-methyl piperidin-4-yl)-1-H-indol-5-yl] ethane sulfonamide, is an indole derivative commonly used as a second generation triptan drug [1]. NTT is a selective 5-HT receptor agonist with high affinity at the 5-HT_{1B}/5HT_{1D} receptor sub type. It is also useful to suppress moderate to acute migraine headaches [1]. NTT is available in the form of hydrochloride salt. Due to its pharmaceutical relevance, several analytical techniques have been reported for the determination of this drug [2–4]. Surprisingly, no information is available on the oxidation-kinetics of NTT with any reagent in order to understand its mechanistic chemistry. Accordingly, the mechanism and kinetic modeling of this drug is unknown. Oxidation-kinetics of NTT is of much significance as it throw some light on the fate of this drug in biological systems. Besides, this kind of study would be helpful to researchers who are working on the mechanistic chemistry of this drug in biological systems. Additionally, the role of platinum group metal ions in the catalytic transformation of this drug has not yet been investigated.

The most important class of organic *N*-haloamines are the *N*-chloro derivatives of aromatic sulfonamides, which contain positive halogen. Organic *N*-haloamines show diverse chemical behavior. Their versatile nature is due to their ability to act as source of halonium cations, hypohalite species and *N*-anions which act both as bases and nucleophiles [5]. As a result, these reagents react with a wide range of functional groups affecting an array of molecular transformations [6–9]. Sodium *N*-chloro *P*-toluenesulfonamide or chloramine-T (CAT) is the prominent member of this class of compounds and behaves as a mild oxidizing agent in both acidic and alkaline media. Its oxidation mechanism has been kinetically well proven [10–15]. It is commercially available, inexpensive, water-tolerant, non-toxic and hence easy to operation [10]. It was therefore CAT was chosen as an oxidant in the present research.

Platinum group metal ions have been employed as homogeneous catalysts for the study of kinetics and mechanism of various redox reactions [11]. The mechanisms of catalysis to some extent is complicated by the formation of different intermediate complexes, free radicals and different oxidation states [16, 17]. Palladium (II) chloride (Pd(II)) has been used as a catalyst in the oxidation of several substrates in alkaline medium and some of them have been proved to be suitable for kinetic analysis [11, 18–22]. This background instigated us to carry out the detailed study on the kinetics and mechanism of NTT-CAT redox system in alkaline medium with and without Pd(II)

catalyst. The target of this research are: (i) to accumulate all the possible kinetic data, (ii) to elucidate plausible mechanisms, (iii) to characterize the oxidation products, (iv) to put forward appropriate rate laws, (v) to ascertain the various reactive species and (vi) to reveal the catalytic activity of Pd(II) in alkaline medium.

2 Experimental and Methods

2.1 Materials

Chloramine-T was purchased from Merck and purified by the method of Morris et al. [23]. Aqueous solution of CAT was prepared afresh, standardized by iodometric method and preserved in a brown bottle to prevent any of its photochemical deterioration. Analytical grade of NTT was procured from Sigma and was used as received. Aqueous solution of NTT was freshly prepared whenever required. A solution of Pd(II) (s.d. fine-chem. Ltd.) was prepared in 20 m mol dm^{−3} HCl and used as a catalyst in alkaline medium. Allowance was made for the amount of HCl present in catalyst solution. Reagent grade chemicals and double distilled water were used throughout the work.

2.2 Kinetic Procedure

All kinetic runs were carried out under pseudo-first-order conditions by keeping a large excess of [NTT]₀ over [CAT]₀ at constant temperature of 298 K. Raagaa Ultra Cold Chamber with digital temperature control (Chennai, India) was used to regulate the temperature with an accuracy of ±0.1 °C. The kinetic procedure followed is similar to that reported earlier [12]. Reactions were carried out in glass stoppered boiling tubes whose outer surface was coated black to eliminate photochemical effects. For each kinetic run, appropriate amounts of NTT, NaOH, Pd(II) (in case of catalyzed reaction) solutions and water (to keep the total volume constant for all kinetic runs) were taken in the boiling tube and thermostated at 298 K for thermal equilibrium. A measured amount of CAT solution, also thermostated at the same temperature, was rapidly added to the mixture with stirring in the boiling tube. The progress of the reaction was monitored by withdrawing 5 ml aliquots of the reaction mixture at different time intervals and determining the unreacted CAT iodometrically. The course of the reaction was followed for more than two half-lives. The pseudo-first-order rate constants (k' s^{−1}), calculated from linear plots of log [CAT] versus time were reproducible within ±5 %. The regression coefficients (R^2) of the linear plots were calculated using an fx-100z scientific calculator.

2.3 Instruments Used

The product was characterized by the following instruments. GC–MS data (Agilent technologies mass spectrometer), IR data (Agilent technologies cary 630 FTIR spectrometer), NMR analysis (Bruker 400 MHz NMR spectrometer), Elemental Analysis (Vario micro Elementar CHNS analyser), melting point (Guna melting point apparatus). The complex study was done by using UV Vis spectrophotometer (Elico SL 159).

3 Results

3.1 Reaction Stoichiometry

Different ratios of CAT to NTT in the presence of 3.0×10^{-3} mol dm $^{-3}$ NaOH and 2.0×10^{-5} mol dm $^{-3}$ Pd(II) (in case of catalyzed reaction) were equilibrated at 298 K for 24 h. The unreacted CAT in the reaction mixture was determined by iodometry and the analysis showed that one mole of NTT consumed one mole of CAT in both cases. Accordingly, the following stoichiometric equation can be formulated:

3.2 Product Characterization

A mixture of 0.18 g of NTT and 0.5 g of CAT was taken in a dry round bottom flask and dissolved in water. To this mixture, NaOH and PdCl $_2$ solutions were added and stirred at 298 K for 12 h. After completion of the reaction (monitored by TLC), the reaction products were neutralized with acid and extracted with ether. The organic

products were subjected to spot tests and chromatographic analysis (TLC technique), which revealed the formation of 2-[3-(1-methyl-1-oxidopiperidin-4-yl)-1H-indol-5-yl] ethanesulfonic acid and methylamine as the oxidation products of NTT and *P*-toluenesulfonamide as the reduction product of CAT for both the catalyzed and uncatalyzed reactions. These products were separated by column chromatography and 2-[3-(1-methyl-1-oxidopiperidin-4-yl)-1H-indol-5-yl] ethanesulfonic acid was confirmed by GC–MS analysis. The mass spectrum showed a molecular ion peak at 338 amu, confirming 2-[3-(1-methyl-1-oxidopiperidin-4-yl)-1H-indol-5-yl] ethanesulfonic acid (Fig. 1). 2-[3-(1-methyl-1-oxidopiperidin-4-yl)-1H-indol-5-yl] ethanesulfonic acid was also further characterized by IR, NMR, Elemental Analysis. An absorption peak at 3282 cm $^{-1}$ for OH (str) and 1574 cm $^{-1}$ for NO (str) was observed (Fig. 2) NMR (400 MHz DMSO (d $_6$)) (Fig. 3): δ 11.0 (s, 1H), 9.9 (s, 1H), 7.5 (s, 1H), 7.1 (s, 1H), 6.9–7.0 (m, 2H), 3.3–3.4 (m, 2H), 3.2–3.3 (m, 4H), 3.0 (m, 3H), 2.7 (s, 3H), 2.0–2.1 (m, 4H). Elemental analysis: calc.(%). C = 58.78, H = 6.55, N = 8.28, S = 9.48 Found: C = 58.80, H = 6.52, N = 8.25, S = 9.45 Yield and melting point of the product was found to be 82 % and 218 °C respectively.

Fig. 1 GC-Mass spectrum of 2-[3-(1-methyl-1-oxidopiperidin-4-yl)-1H-indol-5-yl] ethanesulfonic acid with its molecular ion peak at 338 amu

Fig. 2 IR spectrum of 2-[3-(1-methyl-1-oxidopiperidin-4-yl)-1H-indol-5-yl] ethanesulfonic acid

Table 2 Effect of varying concentrations of oxidant, substrate and medium on the reaction rate at 298 K

10^4 [CAT] ₀ (mol dm ⁻³)	10^3 [NTT] ₀ (mol dm ⁻³)	10^3 [NaOH] (mol dm ⁻³)	10^4 k' (s ⁻¹)
0.3	1.2	3.0	2.60
0.6	1.2	3.0	2.55
1.0	1.2	3.0	2.60
2.0	1.2	3.0	2.58
4.0	1.2	3.0	2.62
1.0	0.6	3.0	1.10 (0.18)
1.0	0.9	3.0	1.77 (0.19)
1.0	1.2	3.0	2.60 (0.21)
1.0	1.8	3.0	3.40 (0.19)
1.0	2.4	3.0	5.52 (0.22)
1.0	1.2	1.5	4.22
1.0	1.2	2.0	3.68
1.0	1.2	3.0	2.60
1.0	1.2	6.0	1.42
1.0	1.2	10.0	0.92

Values in parenthesis refer to second-order rate constants

Table 3 Effect of varying dielectric constant of the medium on the reaction rate at 298 K

% MeOH (v/v)	D	10^4 k' (s ⁻¹)	
		Uncatalyzed	Pd(II) catalyzed
0	76.73	2.60	12.0
5	74.50	2.14	10.5
10	72.37	1.71	9.00
20	67.48	0.96	6.10

Experimental conditions: [CAT]₀ = 1.0×10^{-4} mol dm⁻³, [NTT]₀ = 1.2×10^{-3} mol dm⁻³, [NaOH] = 3.0×10^{-3} mol dm⁻³, and [Pd(II)] = 2.0×10^{-5} mol dm⁻³ (in case of catalyzed reaction)

Fig. 4 Plots of log k' versus 1/D

increase in MeOH concentration decreases the rate of the reaction (Table 3) for both the catalyzed and uncatalyzed reactions. Further, plots of log k' versus 1/D gave straight lines (Fig. 4 $R^2 > 0.9974$) with negative slopes. The dielectric constant values of MeOH-H₂O mixtures reported in the literature [26, 27] were employed. Blank experiments showed that MeOH did not undergo any oxidation with CAT under the present experimental conditions.

Addition of *P*-toluenesulfonamide (PTS, 0.3 to 4.0×10^{-4} mol dm⁻³), to the reaction mixture retards the rate (Table 4) in both catalyzed and uncatalyzed reactions, indicating that it is involved in the pre-equilibrium steps. Further, plots of log k' versus log [PTS] were linear (Fig. 5 $R^2 > 0.9822$) with negative slopes, confirming a negative-fractional-order dependence of rate on (PTS). The effect of Cl⁻ was studied by adding 4.0×10^{-3} mol dm⁻³ NaCl solution to the reaction mixture. The effect of NaCl on the

Table 4 Effect of varying concentration of *P*-toluenesulfonamide on the reaction rate at 298 K

10^4 [PTS] (mol dm ⁻³)	10^4 k' (s ⁻¹)	
	Uncatalyzed	Pd(II) catalyzed
0.3	5.95	15.3
0.5	3.03	12.5
1.0	2.60	12.0
2.0	1.53	10.7
4.0	0.95	8.50

Experimental conditions: [CAT]₀ = 1.0×10^{-4} mol dm⁻³, [NTT]₀ = 1.2×10^{-3} mol dm⁻³, [NaOH] = 3.0×10^{-3} mol dm⁻³, and [Pd(II)] = 2.0×10^{-5} mol dm⁻³ (in case of catalyzed reaction)

Fig. 5 Plots of $\log k'$ versus $\log [\text{PTS}]$

rate of the reaction was trivial in both the cases, suggesting that no chlorine was formed in the reaction. Our preliminary experiments showed that the change in ionic strength of the medium by adding 0.4 mol dm^{-3} NaClO_4 solution to the reaction mixture had no effect on the rate of the reaction in both the cases. Hence, all the kinetic runs were carried out in the absence of any added salt. The effect of temperature on the reaction rate was studied by performing the kinetic experiments at various temperatures (288–308 K) keeping other experimental conditions constant. From the linear Arrhenius plots of $\log k'$ versus $1/T$ ($R^2 > 0.9927$), activation parameters (E_a , $\Delta H^\ddagger$, $\Delta G^\ddagger$, $\Delta S^\ddagger$ and $\log A$) for the overall reaction were computed for

Table 5 Effect of varying temperature on the reaction rate and activation parameters for the oxidation of NTT with CAT in alkaline medium with and without Pd(II) Catalyst

Temperature (K)	$10^4 k' (\text{s}^{-1})$		K_C
	Uncatalyzed	Pd(II) catalyzed	
288	1.32	6.58	4.20
293	1.80	9.34	6.03
298	2.60	12.0	7.52
303	3.20	16.1	10.2
308	5.18	21.3	12.9
E_a (kJ mol $^{-1}$)	50.4	40.9	40.2
$\Delta H^\ddagger$ (kJ mol $^{-1}$)	47.9 ± 0.01	38.5 ± 0.04	37.7 ± 0.01
$\Delta G^\ddagger$ (kJ mol $^{-1}$)	93.7 ± 0.3	89.6 ± 0.26	67.9 ± 0.06
$\Delta S^\ddagger$ (JK $^{-1}$ mol $^{-1}$)	-153 ± 0.2	-171 ± 0.13	-101 ± 0.16
$\log A$	8.83	7.18	8.62

Experimental conditions: $[\text{CAT}]_0 = 1.0 \times 10^{-4} \text{ mol dm}^{-3}$, $[\text{NTT}]_0 = 1.2 \times 10^{-3} \text{ mol dm}^{-3}$, $[\text{NaOH}] = 3.0 \times 10^{-3} \text{ mol dm}^{-3}$, and $[\text{Pd(II)}] = 2.0 \times 10^{-5} \text{ mol dm}^{-3}$ (in case of catalyzed reaction)

both the catalyzed and uncatalyzed reactions. All these results are tabulated in Table 5. The reaction mixture failed to initiate polymerization reaction in presence of aqueous acrylamide solution indicating the absence of free radicals.

4 Discussion

Chloramine-T acts as an oxidizing agent in both acid and alkaline solutions, with a two electron change per mole, giving PTS and NaCl. The redox potential of CAT-PTS system [28] is pH dependent and decreases with increase in pH of the medium (E_{redox} 1.139, 0.778, 0.614 and 0.5 V at pH 0.65, 7.0, 9.7 and 12, respectively). Consequently, the nature of the active oxidizing species of CAT depends on the pH of the medium as well as observed kinetic results. Chloramine-T behaves as a strong electrolyte in aqueous solutions [28]. Depending on the pH of the medium, CAT furnishes following types of reactive species in solutions [23, 28, 29].

(here Ts = $\text{CH}_3\text{C}_6\text{H}_4\text{SO}_2^-$).

Therefore the possible oxidizing species in acidified CAT solutions are TsNHCl, TsNCl₂, HOCl and possibly $\text{H}_2\text{O}^+\text{Cl}$. In alkaline solutions of CAT, TsNCl₂ does not exist and the possible oxidizing species are TsNHCl, TsNCl[−], HOCl and OCl[−]. From these four possibilities, the reactive species of CAT can be selected based on the observed kinetic data.

An inverse fractional order dependence of the rate on $[\text{NaOH}]$ clearly indicates the hydrolysis of CAT (TsNCINa) which results in the generation of the conjugate acid TsNHCl which has been observed [30–34] in many reactions of CAT. This is attributed to the following reaction where TsNHCl is assumed to be reactive species.

Further, Hardy and Jhonston [29] have made detailed calculations on the relative concentrations of the reactive species in alkaline bromamine-B solutions and reported that HOBr is also the predominant species in alkaline medium. Since *N*-haloamines have similar properties and hence one can expect similar equilibrium for alkaline CAT solutions also as shown below,

It is also noted that, if HOCl is an active species a retardation of rate by the added PTS is expected, which is true in the present case. Hence HOCl is considered to be the most probable reactive species in both the cases.

4.1 Reaction Scheme and Rate Law without Pd(II) Catalyst

Based on the preceding discussion and observed kinetic results, the following reaction mechanism (Scheme 1) can be formulated for the oxidation of NTT with CAT in alkaline medium.

Detailed mechanism involving the electrons transfer during the oxidation of NTT with CAT in alkaline medium and the structure of complex-I is shown in Scheme 2. In Scheme 2, in the initial alkali retarding fast step [step(i)], CAT undergoes hydrolysis to give the conjugate acid TsNHCl. In the successive equilibrium fast step (ii), TsNHCl further undergoes hydrolysis to give HOCl which is the active oxidizing species, with the elimination of TsNH₂. In the next slow/rate determining step [step(iii)], the lone pair of electrons present on the nitrogen of NTT attacks the chloronium ion of HOCl to form an intermediate complex-I. This intermediate complex with several fast steps involving the interaction with OH[−] ions and undergoes hydrolysis yields the ultimate products.

From the slow/rds of Scheme 1, the reaction rate is

$$\text{Rate} = k_3[\text{HOCl}][\text{NTT}] \quad (11)$$

According to the reaction Scheme 1, total concentration of [CAT]_t, which is given by the Eq. (12)

$$[\text{CAT}]_t = [\text{TsNCINa}] + [\text{TsNHCl}] + [\text{HOCl}] \quad (12)$$

From steps (i) and (ii) of Scheme 1,

$$[\text{TsNCINa}] = \frac{[\text{HOCl}][\text{NaOH}][\text{TsNH}_2]}{K_1 K_2 [\text{H}_2\text{O}]^2} \quad (13)$$

and

$$[\text{TsNHCl}] = \frac{[\text{HOCl}][\text{TsNH}_2]}{K_2 [\text{H}_2\text{O}]} \quad (14)$$

By substituting for [TsNCINa] and [TsNHCl] from Eqs. (13) and (14) respectively, in Eq. (12) and solving for [HOCl], we get

$$[\text{HOCl}] = \frac{K_1 K_2 [\text{CAT}]_t [\text{H}_2\text{O}]^2}{[\text{TsNH}_2] \{ [\text{NaOH}] + K_1 [\text{H}_2\text{O}] + K_1 K_2 [\text{H}_2\text{O}]^2 \}} \quad (15)$$

By substituting for [HOCl] from Eq. (15) in Eq. (11), the following rate law is obtained,

$$\text{Rate} = \frac{K_1 K_2 k_3 [\text{CAT}]_t [\text{NTT}] [\text{H}_2\text{O}]^2}{[\text{TsNH}_2] \{ [\text{NaOH}] + K_1 [\text{H}_2\text{O}] \} + K_1 K_2 [\text{H}_2\text{O}]^2} \quad (16)$$

Rate law (16) is in accordance with the kinetic findings, wherein a first-order dependence of rate each on [CAT]₀ and [NTT]₀, and a negative fractional-order dependence on both [NaOH] and [TsNH₂] was noticed.

4.2 Reactive Species of PdCl₂

Palladium(II) chloride is known to form different complexes in acid and alkaline media. In acidic solution, it exists in the [PdCl₄]^{2−} complex anionic form. However, in alkaline solution, the possible Pd(II) complex species are [Pd(OH)Cl₃]^{2−}, [Pd(OH)₂Cl₂]^{2−}, [Pd(OH)₃Cl]^{2−} and [Pd(OH)₄]^{2−}. The species [Pd(OH)₃Cl]^{2−} and [Pd(OH)₄]^{2−} are not commonly found as they are insoluble. Further, the rate decreased with increase in [OH[−]] and lack of effect of [Cl[−]] on the rate of reaction clearly rules out [Pd(OH)Cl₃]^{2−} as the reactive species. The existence of [Pd(OH)₂Cl₂]^{2−} is confirmed at higher base concentration. Hence, [Pd(OH)₂Cl₂]^{2−} complex ion has been assumed to be the reactive species in the present study.

Further, formation of the intermediate complex-II between oxidant and catalyst was evidenced by recording UV–Visible spectra of CAT, Pd(II) and CAT + Pd(II) mixture in aqueous alkaline medium. Absorption maxima

Scheme 1 A general reaction scheme for the oxidation of NTT by CAT in alkaline medium

Fig. 6 UV-Vis spectra of (a) CAT, (b) Pd(II) and (c) CAT + Pd(II) mixture in alkaline medium

appear at 222, 358 and 351 nm for CAT, Pd(II) and CAT + Pd(II) mixture, respectively. A hypsochromic shift of 7 nm from 358 to 351 of Pd(II) implies that the complexation occurs between the oxidant CAT and the catalyst Pd(II) (Fig. 6).

4.3 Reaction Scheme and Rate Law with Pd(II) Catalyst

In the light of the above considerations, a mechanism (Scheme 3) is proposed for the Pd(II) catalyzed oxidation

generated in the same way as shown in Scheme 2 [steps (i) and (ii)]. In the next fast step (step (iii)), the lone pair of electrons on oxygen of HOCl coordinates to metal center of active catalyst species forming an intermediate complex-II. In the next slow/rds [step (iv)], the substrate NTT reacts with complex-II forming an another intermediate complex (III) with the regeneration of catalyst species. In the next several fast steps, this complex interacts with hydroxyl ions and H₂O leading to the formation of final products.

From the slow/rds of Scheme 3,

$$\text{Rate} = k_8[\text{Complex-II}][\text{NTT}] \quad (17)$$

From Scheme 3, the total effective concentration of CAT is,

$$[\text{CAT}]_t = [\text{TsNCINa}] + [\text{TsNHCl}] + [\text{HOCl}] + [\text{Complex - II}] \quad (18)$$

From steps (i) (ii) and (iii) of Scheme 3, we obtain

$$[\text{TsNCINa}] = \frac{[\text{Complex-II}][\text{NaOH}][\text{TsNH}_2]}{K_5K_6K_7[\text{Pd(II)}][\text{H}_2\text{O}]^2} \quad (19)$$

$$[\text{TsNHCl}] = \frac{[\text{Complex-II}][\text{TsNH}_2]}{K_6K_7[\text{Pd(II)}][\text{H}_2\text{O}]} \quad (20)$$

$$[\text{HOCl}] = \frac{[\text{Complex-II}]}{K_7[\text{Pd(II)}]} \quad (21)$$

By substituting for [TsNCINa], [TsNHCl] and [HOCl] from Eqs. (19), (20) and (21), respectively into Eq. (18), and solving for [Complex-II] one obtains,

$$[\text{Complex-II}] = \frac{K_5K_6K_7[\text{CAT}]_t[\text{Pd(II)}][\text{H}_2\text{O}]^2}{[\text{TsNH}_2]\{[\text{NaOH}] + K_5[\text{H}_2\text{O}]\} + K_5K_6[\text{H}_2\text{O}]^2 + K_5K_6K_7[\text{Pd(II)}][\text{H}_2\text{O}]^2} \quad (22)$$

of NTT with CAT in alkaline medium to substantiate the experimental observations.

By substituting for [Complex-II] from Eq. (22) into Eq. (17), the following rate law is obtained,

$$\text{Rate} = \frac{K_5K_6K_7k_8[\text{CAT}]_t[\text{NTT}][\text{Pd(II)}][\text{H}_2\text{O}]^2}{[\text{TsNH}_2]\{[\text{NaOH}] + K_5[\text{H}_2\text{O}]\} + K_5K_6[\text{H}_2\text{O}]^2 + K_5K_6K_7[\text{Pd(II)}][\text{H}_2\text{O}]^2} \quad (23)$$

The structures of the Complex-II and Complex-III are shown in Scheme 4, wherein a detailed mechanistic interpretation of NTT-CAT reaction in presence of NaOH and Pd(II) catalyst is illustrated. In Scheme 4, the reactive oxidizing species is also HOCl, which is

This rate law satisfactorily fits well to the experimental results wherein a first-order dependence of rate on both [CAT]₀ and [NTT]₀ a negative fractional-order on each [NaOH] and [TsNH₂], and a fractional-order on [Pd(II)] on the rate of reaction was noticed.

Scheme 2 A descriptive mechanistic interpretation for the oxidation of NTT by CAT in alkaline medium**Scheme 3** A general reaction scheme for Pd(II)-catalyzed oxidation of NTT by CAT in alkaline medium

Scheme 4 A descriptive mechanistic interpretation for the Pd(II) catalyzed oxidation of NTT by CAT in alkaline medium

The general equation relating for uncatalyzed and catalyzed reactions has been derived by Moelwyn–Hughes [35] and correlated as,

$$k_1 = k_0 + K_C[\text{catalyst}]^x \quad (24)$$

Here k_1 is the observed pseudo-first-order rate constant in the presence of Pd(II) catalyst, k_0 is that for the

uncatalyzed reaction, K_C is the catalytic constant and x is the order of the reaction with respect to Pd(II). In the present investigations x value was found to be 0.83. The value of K_C was calculated using the equation,

$$K_C = (k_1 - k_0)/[\text{Pd(II)}]^{0.83} \quad (25)$$

The values of K_C have been evaluated at different temperatures (288–308 K) and K_C was found to vary with temperature. A plot of $\log K_C$ versus $1/T$ was linear ($R^2 = 0.9965$). The values of energy of activation and other thermodynamic parameters for the Pd(II) catalyst were computed and summarized in Table 5.

Further, for the standard run at 298 K, a plot of k' versus Pd(II) (Table 1) was found to be linear ($R^2 = 0.9944$) with an intercept equal to k_0 , which was found to be $2.70 \times 10^{-4} \text{ s}^{-1}$. This value fits well with the rate constant ($k' = 2.60 \times 10^{-4} \text{ s}^{-1}$) determined experimentally for the uncatalyzed reaction at 298 K (Table 1). This clearly implies that both Pd(II) catalyzed and uncatalyzed reactions proceed concurrently.

Under identical set of experimental conditions, it was observed that Pd(II) was an efficient catalyst for this redox system by making the reaction to go five-fold faster than the uncatalyzed reactions (Tables 1 and 2). Hence, the observed rate of oxidation obtained in presence of Pd(II) catalyst justifies the need of a catalyst for the facile oxidation of NTT with CAT in alkaline medium. The activation parameters determined for the Pd(II) catalyzed and uncatalyzed reactions explain the catalytic effect on the reaction. The catalyst Pd(II) forms a complex with the oxidizing species (HOCl), which increases the oxidizing property of the oxidant than in absence of Pd(II) catalyst. Further, the catalyst suitably modifies the reaction path by lowering the energy of activation (Table 5).

It is essential to be aware of the effect of solvents on the rates of the reactions, since most of the organic reactions are carried out in solution. Solvent effect provides information on the nature of the reactive species in the rate determining step as well as the structure of the activated complex. The effect of solvent on the reaction kinetics has been described in detail in the well-known publications [36–40]. A negative methanol effect observed in the present investigations supports for the proposed mechanisms. For the limiting case of zero angle of approach between two dipoles or an ion dipole system, Amis [39] has showed that a plot of $\log k_{\text{obs}}$ versus $1/D$ gives a straight line, with a negative slope for a reaction between a negative ion and a dipole or between two dipoles, while a positive slope results for a positive ion–dipole interaction. The negative dielectric effect observed in the present studies clearly supports the dipole-negative ion and dipole–dipole nature of rate determining steps for Pd(II) catalyzed and uncatalyzed reactions, respectively (Schemes 2 and 4). Hence, the Amis concept agrees with the present observations. The rate constants of ionic reactions depend upon the charges carried by the ions and also upon the ionic strength of the medium. The primary salt effect observed supports the Schemes 2 and 4. Increase in the ionic strength of the

medium does not affect the rate for both Pd (II) catalyzed and uncatalyzed reactions. It clearly signifies the involvement of a neutral molecule (s) in the rate determining steps of Schemes 2 and 4. It is in accordance with Bronsted and Bjerrum theory of salt effects [41].

The proposed mechanisms are also validated with the moderate values of energy of activation and other thermodynamic parameters (Table 5). Values of $\Delta H^\ddagger$ indicate that the reactions are enthalpy controlled. The transition state is expected to be strongly solvated, which is indicated by the positive $\Delta G^\ddagger$ values. The large negative values of $\Delta S^\ddagger$ indicate that the transition state is more rigid than initial state with less degrees of freedom. Frequency factor (A) values specify the frequency of collisions and the orientation of reactive molecules. Proposed Schemes and derived rate laws are further supported by the observed stoichiometry of the reaction.

5 Conclusion

The kinetics of the oxidation of NTT by CAT in alkaline medium in the presence and absence of Pd(II) catalyst obeys the experimental rate laws: $-d[\text{CAT}]/dt = k [\text{CAT}]^1 [\text{NTT}]^1 [\text{NaOH}]^{-0.83} [\text{PTS}]^{-0.73}$ and $-d[\text{CAT}]/dt = k [\text{CAT}]^1 [\text{NTT}]^1 [\text{NaOH}]^{-0.88} [\text{Pd(II)}]^{0.83} [\text{PTS}]^{-0.23}$, respectively. 2-[3-(1-methyl-1-oxidopiperidin-4-yl)-1H-indol-5-yl] ethanesulfonic acid and methylamine were identified as the oxidation products of NTT. Activation parameters have been evaluated. The Pd(II) catalyzed reaction is about fivefold faster than the uncatalyzed reaction. Based on the kinetic data suitable mechanisms and relevant rate laws have been worked out.

Acknowledgments One of the authors (SD) is gratefully acknowledge the UGC, New Delhi for awarding UGC-BSR meritorious scholarship. The Authors are also thankful to Prof. M.A. Pasha of this department for his valuable suggestions on the proposed reaction schemes.

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