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Oxidation of chalcones by N - chloronicotinamide in aqueous acetic acid medium: A kinetic and mechanistic study

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ABSTRACT

The kinetics and oxidation of chalcones by N - chloronicotinamide has been studied in 80% acetic acid – 20% water (v/v) containing HCl and $NaClO_4$ in the temperature range between 307 and 319K. The reaction rate follows first order and zero order dependence with respect to [NCN] and [chalcone] respectively. The reaction is catalyzed by hydrogen ions. The rate increases with increase in the percentage of acetic acid and the plot of log k_{obs} versus 1/D is linear with a positive slope indicating the positive ion – dipole nature of the reaction. Variation of ionic strength and addition of the reaction product, nicotinamide has no effect on the rate. The product of oxidation is benzoic acid. A suitable mechanism consistent with the observed kinetics has been proposed.

Keywords: Kinetics, Oxidation, Chalcones, N – chloronicotinamide.

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INTRODUCTION

N - chloronicotinamide (NCN) has been extensively used in both chlorination and oxidation of many organic substrates. NCN [1] is one of the stable, mild, efficient and inexpensive N-halo compound [2] and is used as a source of electrophilic chlorine. Nicotinamide is a derivative of niacin (Vitamin B_3) with similar vitamin activity and plays an important role in certain biochemical mechanisms in human cells. The study becomes more important from the biological point of view. An extensive literature survey reveals that kinetics and mechanism of oxidation of amino acids [3], alcohols [4, 5], aldehydes [6], s-phenylmercapto acetic acid [7], and benzyl ethers [8] have been carried out using NCN. Literature survey reveals that there are no kinetic and mechanistic studies involving this useful compound with chalcones.

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Chalcones are of interest because they have a unique structural feature of having a >C=O functional group in conjugation with >C=C< and the whole molecule is in conjugation. Chalcones are oxidized by different oxidizing agents and in all these reactions either the >C=C< or >C=O group of the chalcone is attacked by the oxidant [9-18]. Chalcones are natural substance found in a number of plants or synthetically prepared. They display many biological activities [19] viz., antiviral, anti-inflammatory, antimicrobial, antimitotic, antitumor, cytotoxicity, analgesic and antipyretic properties. They also act as potential anti-ulcer, antifungal, anti-cancer [20] and antimalerial growth [21].

MATERIALS AND METHODS

Acetic acid was purified by standard method [22] and used. Chalcones were prepared in the laboratory [14]. Standard solution of NCN was prepared in water and its purity was checked iodometrically. Hydrochloric acid (AnalaR) was used as a source of $[H^+]$. Conductivity water was used throughout the studies. Other chemicals used were of analytical grade.

Kinetic measurements
The kinetic runs were carried out under pseudo-first order conditions ([chalcones] >> [NCN]. Rate studies were carried out at the desired temperature with an accuracy of ±0.5°C. The reaction was initiated by the rapid addition of known amounts of oxidant to reaction mixtures containing the required amount of chalcone, HCl, $NaClO_4$, acetic acid and water in glass stoppered pyrex boiling tubes; thermo-stated at 40°C. The progress of reaction was monitored by iodometric determination of unconsumed [NCN] in known aliquots of the reaction mixtures at different time intervals.

Stoichiometric analysis
The reaction mixture containing excess of NCN over chalcone (3:1) in the presence of HCl and $NaClO_4$ were kept at the room temperature for 36h. Estimation of unreacted NCN showed that one mole of chalcone reacted with one mole of NCN. Thus the overall stoichiometry of the oxidation reaction was found to be 1:1.

$$PhCOCH=CHPh + C_5H_4NCONHCl + 2H_2O \xrightarrow{H^+} PhCOOH + PhCH_2CHO + C_5H_4NCONH_2 + HCl$$
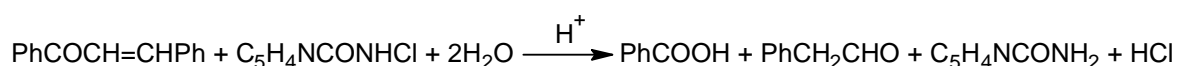
Product analysis
Product study was made keeping concentration of chalcone in excess over chalcone. The reaction was allowed to proceed to completion by keeping it in a thermostat at 40°C for 4h. The solution was shaken well with ether. The ethereal layer was washed with water several times and kept on a water bath for ether evaporation and cooled to get the product. Benzoic acid and phenyl acetaldehyde were identified as products and were detected by TLC and compared with those of the authentic samples. The presence of phenyl acetaldehyde among the reaction product was also detected by preparing their 2, 4 - dinitrophenyl hydrazine derivatives.

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RESULTS AND DISCUSSION

Effect of [N - chloronicotinamide]
The kinetics of oxidation of chalcones has been studied at various initial concentrations of the oxidant [NCN] and at fixed concentrations of other reactants. The reaction is first order in [NCN] as evidenced by the linearity plots of log [NCN] versus time.

Effect of [Chalcone]
In order to study the effect of [Chalcone] on the rate of the reaction, the reactions were studied over a tenfold variation in [Chalcone] at constant concentrations of all reactants at fixed temperature. The rates of reaction calculated at different [Chalcone] were found to be nearly the same for all concentrations of chalcone; exhibiting zero order kinetics with respect to [Chalcone].

Effect of [HCl]
The kinetic investigation has been made at various concentrations of HCl and at fixed concentrations of other reactants. Observed rate constants increases with increase in [HCl] **(Table – 1)**. Plots of log k_{obs} versus log [HCl] are linear (r = 0.998) with a slope value of unity (0.8 – 1.0) for all the substrates indicating first order in HCl.

Effect of percentage composition of acetic acid
The effect of dielectric constant on the rate of reaction has been studied by varying the percentage of acetic acid in the reaction mixture from 65% to 85% for the reaction carried out in acidic medium. An increase in the percentage of acetic acid increases the rate of reaction and the results are recorded in **(Table - 2)**. The plot of log k_{obs} versus 1/D (where D is the dielectric constant of the medium) is linear with a positive slope indicating the ion – dipole type of interaction.

Effect of [NaCl]
Addition of [Cl⁻] ion in the form of NaCl had no significant effect on the rate, indicating that no free chlorine was formed.

Effect of [NaClO$_4$] and [Nicotinamide]
Added neutral salts like KCl and NaClO$_4$ has no effect on the rate of oxidation. Added nicotinamide has negligible effect on the rate on the oxidation.

Table – 1 Effect of [HCl] on rate of the reaction at 313 K
[Chalcones] = 0.01M,   [NCN] = 0.003M,   [NaClO$_4$] = 0.1M,
Solvent (v/v) = 80% CH$_3$COOH – 20% H$_2$O

M	$k_1 \times 10^4 s^{-1}$						
	-H	4-Cl	4-Me	4-OMe	4-NO$_2$	3-Cl	3-NO$_2$
0.06	2.38	3.03	3.68	2.73	2.11	2.30	2.00
0.08	3.61	4.49	4.15	3.65	3.15	4.57	3.22
0.10	5.26	7.06	4.91	5.87	3.92	4.99	4.15
0.12	6.60	7.37	6.94	7.14	4.64	6.21	4.45
0.14	11.52	10.13	7.33	7.48	7.60	8.03	7.33

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Table – 2 Effect of solvent polarity on reaction at 313 K
[Chalcones] = 0.01M,   [NCN] = 0.003M,   [NaClO$_4$] = 0.1M,   [HCl] = 0.1M

CH$_3$COOH – H$_2$O %(v/v)	D	k_1 x 10^4s^{-1}						
		-H	4-Cl	4-Me	4-OMe	4-NO$_2$	3-Cl	3-NO$_2$
65 – 35	30.50	0.57	0.65	0.65	0.65	0.42	0.65	0.46
70 – 30	27.00	1.23	1.15	1.11	1.34	0.88	1.80	0.96
75 – 25	23.50	1.73	2.22	2.03	2.61	1.80	2.23	1.65
80 – 20	20.00	4.11	5.18	5.03	6.26	4.64	5.10	3.99
85 - 15	16.40	11.36	13.63	13.43	12.39	12.47	11.52	9.25

Table – 3 Effect of Temperature on the reaction rate
[Chalcones] = 0.01M,   [NCN] = 0.003M,   [HCl] = 0.1M,   [NaClO$_4$] = 0.1M,
Solvent (v/v) = 80% CH$_3$COOH – 20% H$_2$O

T (K)	k_{obs} x 10^4s^{-1}						
	-H	4-Cl	4-Me	4-OMe	4-NO$_2$	3-Cl	3-NO$_2$
307	2.46	3.65	3.38	2.65	2.53	3.11	2.46
310	3.65	4.91	5.72	3.65	3.03	4.15	2.73
313	5.34	6.76	6.53	4.41	4.11	4.72	5.07
316	6.45	9.67	8.83	6.62	5.83	6.83	5.26
319	9.83	14.27	13.05	8.06	8.37	9.86	7.41

Table - 4 Activation parameters for the oxidation of chalcones at 313 K

Substituents	Ea (kJ mol^{-1})	ln A	ΔH$^{\#}$ (kJ mol^{-1})	ΔG$^{\#}$ (kJ mol^{-1})	ΔS$^{\#}$ (JK^{-1} mol^{-1})
4 - Cl	85.41	25.26	82.81	88.74	-18.95
- H	84.02	24.75	81.42	87.92	-24.75
4 - NO$_2$	76.46	21.58	73.86	83.94	-32.21
3 - NO$_2$	72.76	20.37	70.16	81.61	-36.58
4 - Me	71.11	19.73	68.50	80.68	-38.91
3 - Cl	69.97	19.23	67.36	80.11	-40.72
4 – OMe	69.08	18.97	66.47	79.52	-41.67

An increase in [H$^+$] increases the rate indicating that the reaction is catalyzed by hydrolyzed ions. The stoichiometry of the reaction for all the substrates was found to be 1:1. The oxidation of all the chalcones has been studied at different temperatures (307 – 319 K). The results are shown in **(Table – 3)**. From the linear Arrhenius plots of log k_{obs} vs 1/T, the activation energy E$_a$ was calculated. Values of the other thermodynamic parameters are also evaluated (**Table - 4**). Addition of reaction mixture to aqueous acrylamide solution did not initiate polymerization showing the absence of free radical species.

Mechanism
The most possible mechanism for the oxidation of chalcones by NCN involves the protonation of NCN in the rate-determining step followed by the interaction with chalcone to give the products. Under the experimental conditions, the possible oxidizing species are Cl$_2$, HOCl, H$_2$OCl$^+$ and NCNH$^+$ in aqueous solution. The first order dependence of rate on [NCN] and the addition of nicotinamide having no effect on the rate indicate that HOCl may not be the reactive species [23]. Since there is no effect due to Cl$^-$ the possibility of involvement of Cl$_2$ is ruled out. If H$_2$OCl$^+$ is the active oxidizing species, a retardation of rate by added nicotinamide is expected.

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However no such effect is notice; hence the possibility of H_2OCl^+ as the oxidizing species is ruled out. Since the rate of the reaction increases with increase in [HCl], it is assumed that $NCNH^+$ is an effective oxidizing species in the present study and keeping the above data in consideration the following mechanism is proposed for the oxidation of chalcones by NCN.

$$NCN + H^+ \xrightleftharpoons{K'} NCNH^+$$

$$NCNH^+ + S \xrightleftharpoons{K} Complex \text{ (rapid)}$$

$$Complex \xrightarrow{k} Product \text{ (slow)}$$
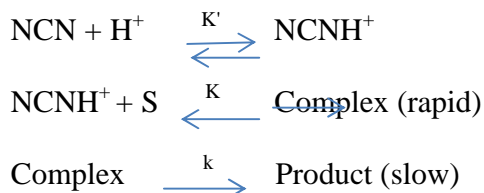
The mechanism shown in the above scheme leads to, under the condition that the formation constant K of the oxidant – substrate complex is large, the following rate law [24, 25].

$$-d\,[NCN]\,/\,dt = k\,K'\,[NCN]\,[H^+]$$

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