

# A MECHANISTIC INVESTIGATION OF THE OXIDATION OF CHALCONES BY N-CHLOROSUCCINIMIDE IN AQUEOUS ACETIC ACID MEDIUM

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## ABSTRACT

The oxidation kinetics of chalcones [ $C_6H_5COCH=CHC_6H_4X$ ]; {X = H, 4-Me, 4-OMe, 4-Cl, 4-NO<sub>2</sub>, 3-Cl and 3-NO<sub>2</sub>} by N-chlorosuccinimide (NCS) in 80% aqueous acetic acid has been investigated. The reaction follows first - order kinetics with respect to [NCS] and zero order in [chalcone]. A decrease in the dielectric constant of the medium increases the rate. The rate increased with increase in acidity. Chloride ions positively influence the rate of the reaction. Addition of succinimide (>NH) has no significant effect on the rate of oxidation. Activation parameters of the reactions were determined by studying the reaction at different temperatures (34–46 °C). Based on the kinetic results and product analysis, a probable mechanism has been proposed for the oxidation of chalcones by NCS.

**Keywords:** Kinetics, oxidation, chalcone, N-chlorosuccinimide, mechanism.

## 1. INTRODUCTION

Recently, attention has been paid to the wide range of properties of N-halo compounds due to their ability to act as a source of halonium ions, hypohalite species and nitrogen anions, which act as bases and nucleophiles<sup>1-2</sup>. N-halo compounds have extensively been used as oxidizing agents for the catalysed and uncatalysed reaction<sup>3-11</sup>. Additionally, N-halo compounds have also been widely used as halogenating reagents of organic compounds<sup>12, 13</sup>.

Chalcones either natural or synthetic are known to exhibit various biological activities. They have been reported to possess antioxidant<sup>14-17</sup>, antimalarial<sup>18</sup>, antileishmanial<sup>19</sup> and anti-inflammatory<sup>20</sup>. The presence of a reactive  $\alpha$ ,  $\beta$ -unsaturated keto function in chalcones is found to be responsible for their antimicrobial activity, which may be altered depending on the type and position of substituent on the aromatic rings. Kinetics and mechanism of oxidation of benzylamines<sup>21</sup>, primary alcohols<sup>22</sup>, aromatic

aldehydes<sup>23</sup>, aromatic sulphides and arylmercaptoacetic acids<sup>24</sup>, benzyl phenyl ethers<sup>25</sup>, diphenyl selenide<sup>26</sup> and secondary amines<sup>27</sup> have been reported. For lack of information on similar studies using N-chlorosuccinimide (NCS) as an oxidant, the kinetic study has been taken up with a view to finding out the reactive species and mechanism of reaction.

## 2. EXPERIMENTAL

### 2.1. MATERIALS AND REAGENTS

N-chlorosuccinimide (AnalaR) was purchased from Qualigens Chemicals and its solution was always prepared fresh and its strength was checked by iodometric method. Acetic acid (AnalaR, BDH) was purified by standard method and 80% of acetic acid – 20% water mixture was used. Chalcones were prepared by the condensation of substituted aldehydes with acetophenone in alcoholic NaOH medium. The purity of the chalcones was checked by their melting point, IR and TLC

method. Triply distilled water was used throughout the course of investigation.

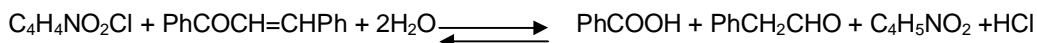
## 2.2. KINETIC MEASUREMENTS

For the kinetic runs, a measured amount of NCS pre – equilibrated at 40 °C was rapidly added to a thermally equilibrated mixture containing the appropriate amounts of the chalcone,  $\text{HClO}_4$ ,  $\text{NaCl}$ ,  $\text{CH}_3\text{COOH}$  and water. The progress of the reaction was monitored for two half lives by the iodometric determination of unreacted NCS in a measured aliquot

withdrawn at regular intervals of time. The pseudo first - order rate constant for each kinetic run was evaluated from the slope of the linear plot of  $\log(a-x)$  versus time, using the method of least squares.

## 2.3 STOICHIOMETRY AND PRODUCT ANALYSIS

Stoichiometric runs, performed with an excess of NCS revealed that one mole of the oxidant was consumed by one mole of chalcone.



For identification of the product, the reaction mixture was left to stand for 24h under kinetic conditions. It was then extracted with ether. The ether layer was separated, dried and identified as benzoic acid and phenyl acetaldehyde by TLC, IR and NMR.

## 3. RESULTS AND DISCUSSION

### 3.1. ORDER OF REACTION

The rate and other experimental data were obtained for all the chalcones. Since the results are similar, only the data for the oxidation of benzylidene acetophenone ( $\text{Ph-CH=CH-CO-Ph}$ , BAP) are reproduced here. The kinetics of oxidation of chalcones by NCS was investigated at several initial concentrations of the reactants in acid medium. With the substrate in excess, at constant  $[\text{HClO}_4]$ ,  $[\text{NaCl}]$ ,  $\text{CH}_3\text{COOH}$  and temperature, plots of  $\log [\text{NCS}]_0$  versus time were linear indicating a first order dependence on  $[\text{NCS}]_0$ . The pseudo – first order rate constants calculated from these plots are given in (Table I). Further the values of  $k$  calculated from these plots are unaltered with the variation of  $[\text{NCS}]_0$  confirming the first order dependence on  $[\text{oxidant}]_0$ . Values of  $k$  did not change with increase in  $[\text{chalcone}]_0$  indicating zero – order dependence on  $[\text{chalcone}]$ .

### 3.2. EFFECT OF ACIDITY

The rate increased with increase in  $[\text{HClO}_4]$  and the linear plot of  $\log k$  vs  $\log [\text{HClO}_4]$  ( $r=0.9943$ ) with a slope of 1.0 indicating unit order dependence of the reaction rate on  $[\text{HClO}_4]$  (Table I).

### 3.3. EFFECT OF HALIDE ION

Effect of  $[\text{Cl}^-]$  on the rate of reaction has also been studied by increasing the  $[\text{NaCl}]$  at constant  $[\text{HClO}_4]$  (Table I). Increase in  $[\text{Cl}^-]$  has a positive effect on the rate. The plot of  $\log k$  versus  $\log [\text{NaCl}]$  is linear ( $r=0.9971$ ) with unit

slope indicating first – order dependence of rate on  $[\text{Cl}^-]$ .

### 3.4. EFFECT OF IONIC STRENGTH

The effect of ionic strength on the rate of the reaction is studied by increasing  $[\text{NaClO}_4]$ . It has been observed that the reaction remains constant with increase in  $[\text{NaClO}_4]$ . Hence  $\text{NaClO}_4$  act as inert salt, maintaining constant ionic strength.

### 3.5. EFFECT OF VARYING SOLVENT COMPOSITION

The increase in percentage of acetic acid in the reaction mixture increases the rate (Table I). Plot

of  $\log k$  versus  $1/D$  ( $D$  is the dielectric constant of the medium) is found to be linear ( $r = 0.9912$ ) with positive slopes, indicating that an interaction between a positive ion and a dipolar molecule.

### 3.6. EFFECT OF SUCCINIMIDE

Effect of added succinimide ( $>\text{NH}$ ) on the rate of the reaction was studied at different initial concentration of succinimide. Addition of succinimide has no effect on the rate of oxidation.

### 3.7. INDUCED POLYMERIZATION

The reaction mixture fails to initiate polymerization of aqueous acrylamide solution, indicating the absence of free radicals. This indicates that a one electron oxidation giving rise to free radicals is unlikely in the present reaction.

### 3.8. EFFECT OF TEMPERATURE

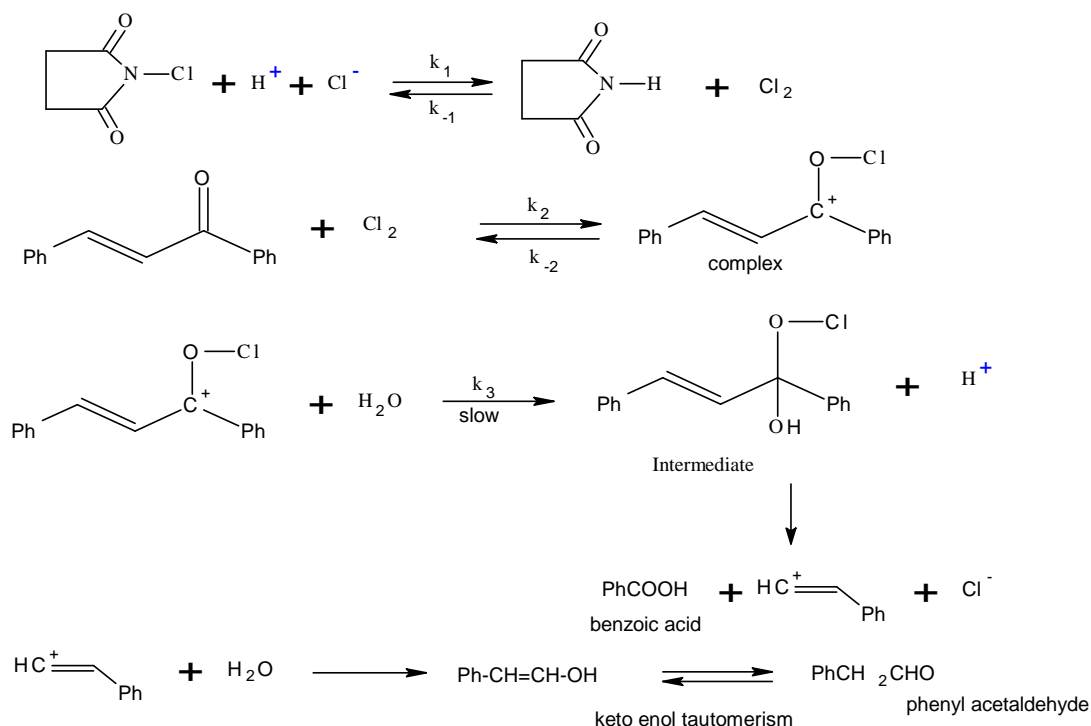
In order to investigate the effect of temperature on the reaction rate, the reaction was performed at 34, 37, 40, 43 and 46 °C. Arrhenius and the activation parameters were evaluated (Table I). Arrhenius plot of  $\log k$  versus  $1/T$  was linear. From the plot, the

activation and thermodynamic parameters are evaluated.

### 3.9. MECHANISM AND RATE LAW

Under the experimental conditions, the possible oxidizing species<sup>28</sup> are  $\text{Cl}_2$ ,  $\text{HOCl}$ ,  $\text{H}_2\text{OCl}^+$  and  $\text{NCSH}^+$  in aqueous solution. The oxidations of alcohols and aliphatic ketones by N-chlorosuccinimide<sup>29</sup> and N-bromosuccinimide<sup>30</sup> have been reported to take place through the intermediate forms of

protonated species of the oxidant like  $\text{NCSH}^+$  and  $\text{NBSH}^+$ . If  $\text{NCSH}^+$  is the active oxidant, the reaction must show hydrogen ion catalysis only. Since both hydrogen and chloride ions are found to catalyze the reaction in the present case, molecular chlorine has been assumed to act as the effective oxidant. It has been reported that in aqueous acidic solutions in presence of chloride ion, NCS produces a steady, but small, concentration of molecular chlorine<sup>31-33</sup>.



$$\text{Rate} = k_3 [\text{complex}]$$

Applying steady-state approximation to the molecular chlorine and the complex, the following rate law is deduced.

$$\text{Rate} = \frac{k_1 k_2 k_3 [\text{chalcone}] [\text{NCS}] [\text{H}^+] [\text{Cl}^-]}{k_{-2} + k_3 \{k_{-1} [\text{SH}] + k_2 [\text{chalcone}]\}}$$

where  $[\text{SH}] = [\text{succinimide}]$

Assuming  $k_{-1} [\text{SH}] \ll k_2 [\text{chalcone}]$

$$\text{Rate} = \frac{k_1 k_3 [\text{NCS}] [\text{H}^+] [\text{Cl}^-]}{k_{-2} + k_3}$$

The above rate law accounts for the first order dependence of rate on  $[\text{NCS}]$ ,  $[\text{H}^+]$ ,  $[\text{Cl}^-]$  and zero order dependence on  $[\text{chalcone}]$ .

### CONCLUSION

Kinetic studies demonstrate that the intermediate unstable complex decomposes in the slow rate determining step to give the corresponding benzoic acid and phenyl acetaldehyde as the products. High dielectric constant of the medium facilitates the

reactivity. The mechanism is further supported by the value of energy of activation and other thermodynamic parameters. The fairly high positive values of free energy of activation and enthalpy of activation indicates that the transition state is highly solvated, while the negative entropy of activation suggests the

formation of the compact activated complex with fewer degrees of freedom. First order with respect to each NCS,  $H^+$ ,  $Cl^-$  and zero order

with respect to chalcones are supported by derived rate law.

**Table 1: Effect of variation of [NCS], [BAP], [HClO<sub>4</sub>], [NaCl], [HOAc] on the reaction rate at 313 K**

[NCS] 10 <sup>3</sup> (M)	[BAP] 10 <sup>2</sup> (M)	[HClO <sub>4</sub> ] (M)	[NaCl] (M)	HOAc % (v/v)	k 10 <sup>4</sup> (s <sup>-1</sup> )
2.0	1.0	0.10	0.10	80 – 20	1.77
3.0	1.0	0.10	0.10	80 – 20	1.60
4.0	1.0	0.10	0.10	80 – 20	1.46
5.0	1.0	0.10	0.10	80 – 20	1.80
6.0	1.0	0.10	0.10	80 – 20	1.77
3.0	0.5	0.10	0.10	80 – 20	1.46
3.0	1.0	0.10	0.10	80 – 20	1.60
3.0	1.5	0.10	0.10	80 – 20	1.84
3.0	2.0	0.10	0.10	80 – 20	1.69
3.0	2.5	0.10	0.10	80 – 20	1.50
3.0	1.0	0.06	0.10	80 – 20	0.96
3.0	1.0	0.80	0.10	80 – 20	1.31
3.0	1.0	0.10	0.10	80 – 20	1.60
3.0	1.0	0.12	0.10	80 – 20	1.92
3.0	1.0	0.14	0.10	80 – 20	2.07
3.0	1.0	0.10	0.05	80 – 20	0.85
3.0	1.0	0.10	0.10	80 – 20	1.60
3.0	1.0	0.10	0.15	80 – 20	2.52
3.0	1.0	0.10	0.20	80 – 20	3.32
3.0	1.0	0.10	0.25	80 – 20	4.20
3.0	1.0	0.10	0.10	65 – 35	0.15
3.0	1.0	0.10	0.10	70 – 30	0.54
3.0	1.0	0.10	0.10	75 – 25	0.73
3.0	1.0	0.10	0.10	80 – 20	1.60
3.0	1.0	0.10	0.10	85 – 15	3.95

**Table 2: Effect of Temperature on the reaction rate**  
[NCS] =  $3 \times 10^3$  M; [Chalcone] =  $1 \times 10^2$  M; [HClO<sub>4</sub>] = 0.10 M;  
[NaCl] = 0.10 M; Solvent (v/v) = 80 % HOAc – 20% H<sub>2</sub>O

T (K)	k x 10 <sup>4</sup> (s <sup>-1</sup> )						
	4-H	4-Cl	4-Me	4-OMe	4-NO <sub>2</sub>	3-Cl	3-NO <sub>2</sub>
307	0.99	1.00	0.93	1.01	0.92	0.95	0.97
310	1.34	1.23	1.24	1.34	1.23	1.38	1.34
313	1.60	1.71	1.66	1.88	1.58	1.77	1.69
316	2.46	2.36	2.38	2.40	2.22	2.49	2.35
319	3.13	3.05	2.92	3.15	2.92	3.01	3.06

**Table 3: Activation parameters for the oxidation of chalcones at 313 K**

Substituents	E <sub>a</sub> (kJ mol <sup>-1</sup> )	ln A	ΔH <sup>‡</sup> (kJ mol <sup>-1</sup> )	ΔG <sup>‡</sup> (kJ mol <sup>-1</sup> )	ΔS <sup>‡</sup> (JK <sup>-1</sup> mol <sup>-1</sup> )
4-H	78.94	20.66	76.26	87.78	-35.68
4-Me	79.82	21.02	77.14	88.24	-34.36
4-NO <sub>2</sub>	78.69	20.55	76.01	87.66	-36.06
4-OMe	77.58	20.31	74.90	86.82	-36.92
3-NO <sub>2</sub>	77.62	20.22	74.94	86.97	-37.25
4-Cl	78.20	20.45	75.51	87.28	-36.44
3-Cl	78.69	20.67	76.01	87.52	-35.65

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