



Kinetics and Mechanism of Oxidation of Chalcones by 1,3-Dichloro-5,5-dimethyl Hydantoin

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Mechanistic study on oxidation of chalcone by 1,3-dichloro-5,5-dimethyl hydantoin (DCDMH or DCH) in aqueous acetic acid medium have been carried out. The reaction follows a fractional order (0.63) with respect to substrate and first order with respect to the oxidant. Increase in percentage of acetic acid increased the rate of the reaction. The added H^+ did not affect the reaction rate. The oxidation reaction fails to initiate polymerization with acrylonitrile and free radical mechanism is ruled out. The thermodynamic and activation parameters for the oxidation have been determined and discussed. Based on the observations a probable mechanism and rate law were proposed.

Keywords: Chalcone, 1,3-Dichloro-5,5-Dimethylhydantoin, Kinetics, Oxidation.

INTRODUCTION

Chalcones¹ (1,3-diaryl-2-propen-1-ones) are naturally occurring compounds, largely distributed in plants, fruits and vegetables. They belong to the flavanoid group of compounds. Literature studies²⁻⁵ reveals that these compounds are of chemical and pharmacological interest because they exhibit many biological activities such as antimicrobial, antioxidant, anti-malarial, antitumor, antidepressant, antiinflammatory, anti-HIV and anticancer. Chalcones are α,β -unsaturated ketones⁶ consisting of two aromatic rings (ring A and B) having diverse array of substituents. Rings are interconnected by a highly electrophilic three carbon α,β -unsaturated carbonyl system that assumes linear or nearly planar structure. They contain the ketoethylenic group ($-\text{CO}-\text{CH}=\text{CH}-$). Chalcones possess conjugated double bonds and a completely delocalized π -electron system on both benzene rings. They can be obtained by several methods and Claisen-Schmidt's condensation (aldol condensation) is the most used one.

Chalcones are oxidized by different oxidizing agents and in all these reactions either the $>\text{C}=\text{C}<$ or $>\text{C}=\text{O}$ group of the chalcone is attacked by the oxidant. The kinetics and oxidation of chalcones by various oxidants like pyridinium chloro-chromate⁷, trichloro isocyanuric acid⁸, chromic acid⁹, quinaldinium dichromate¹⁰, chloramine- T ¹¹, N-chlorosuccinimide¹², quinaldinium fluorochromate¹³ have been extensively carried out by many eminent workers. In recent years, the kinetic studies on the oxidation and halogenation of organic compounds by N-halo compounds are gaining importance due to their applications in organic synthesis and also due to kinetic

aspects¹⁴. N-Halo compounds have extensively been used as oxidizing agents for the catalyzed and uncatalyzed reactions¹⁵⁻²⁰. Since the N-halo compounds exhibit appreciable stability both in acid and alkaline medium, it is used as a redox titrant in analytical chemistry.

1,3-Dichloro-5,5-dimethyl hydantoin is a N-chloro compound and is usually represented as DCDMH or DCH. It has found limited application and only few reports¹⁵⁻²⁰ are available of its uses in organic synthesis.

Literature survey reveals that no report was available on the kinetics of oxidation of chalcones by 1,3-dichloro-5,5-dimethyl hydantoin.

EXPERIMENTAL

All the chemicals and solvents used were of analytical grade (Merck, India). Chalcone and 1,3-dichloro-5,5-dimethyl hydantoin (Sigma-Aldrich) were used as such. All the solutions used in the study were made by using double distilled water. All the reagents were freshly prepared just before the reactions were carried out. All the reactions were carried out in a thermostat and the temperature was maintained at $\pm 0.1^\circ\text{C}$.

Kinetic measurements: The kinetic studies were carried out in an aqueous acetic medium. The reactions were performed by maintaining a large excess of [chalcone] over [DCDMH]. The reaction mixture was homogeneous throughout the course of the reaction. The reaction rate was found by estimating the amount of the unconsumed DCDMH iodometrically up to 80 % of completion of the reaction. The rate constants (k_{obs}) were determined from the slopes of linear plots of $\log[\text{titre}]$ versus

time. Replicate runs showed that the rate constants for the oxidation reactions were reproducible within + 3 %.

Rate law:

$$k_{\text{obs}} = \frac{-d[\text{DCDMH}]}{dt} = \frac{K_1 k_3 [\text{chalcone}] + K_1 K_2 k_4 [\text{chalcone}][\text{H}^+]}{K_1 + K_1 K_2 [\text{H}^+]}$$

Stoichiometry: The stoichiometry of the reaction was found out by doing several sets of experiments by varying [DCDMH]. The unconsumed DCDMH remained after completion of the reaction showed 1:1 (chalcone : DCDMH) stoichiometry.

Product analysis: The concentration of DCDMH is kept in excess over chalcone. The reaction was allowed to complete by keeping in a thermostat at 40 °C for 4 h. 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 found to be the major products of oxidation and were detected by TLC and compared with those of the authentic samples.

Data analysis: Correlation studies were carried out using Microcal origin (version 6) computer software. The goodness of the fit was discussed using the correlation coefficient, *r*, in the case of simple linear and *R* in the case of multiple linear regression analysis.

RESULTS AND DISCUSSION

Factors influencing the rate of oxidation of chalcone by 1,3-dichloro-5,5-dimethyl hydantoin such as [chalcone], [DCDMH], [H⁺] and dielectric constant have been studied. Rate of the reaction and activation parameters were calculated.

Effect of [Chalcone]: At a constant [DCDMH], [H⁺] and fixed percentage of acetic acid, kinetic runs were carried out with various initial concentrations of chalcone, which yielded rate constants whose values depended on [chalcone]. The pseudo-first order rate constants (*k*_{obs}) thus obtained were found to increase with [chalcone] (Table-1). The plot (Fig. 1) of log *k*_{obs} versus log[chalcone] is linear with a slope of 0.63 showing that the reaction is fractional order in [chalcone]. The plot (Fig. 2) of 1/*k*_{obs} versus 1/[chalcone] is linear with definite intercept on the rate ordinate, which indicates the operation of Michaelis-Menten mechanism.

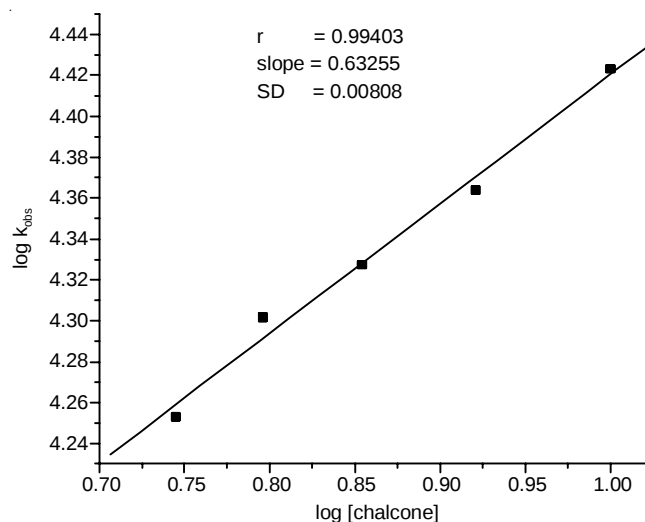


Fig. 1. Plot of log *k*_{obs} versus log [chalcone] for oxidation of chalcone by 1,3-dichloro-5,5-dimethyl hydantoin in acetic acid medium

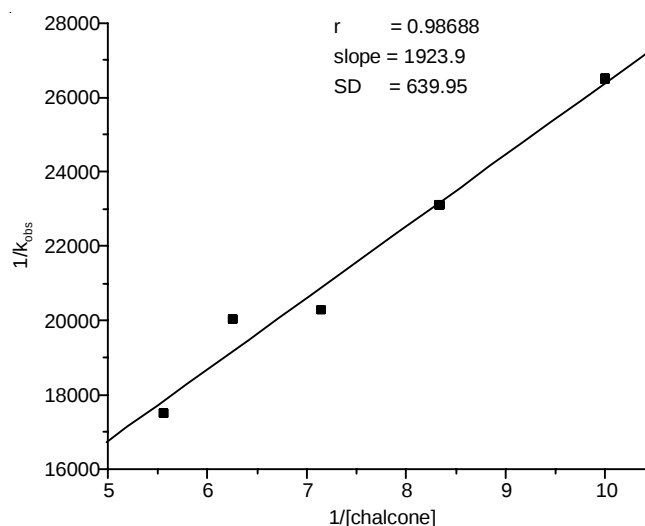


Fig. 2. Plot of 1/*k*_{obs} versus 1/[chalcone] for oxidation of chalcone by 1,3-dichloro-5,5-dimethyl hydantoin in acetic acid medium

Effect of [DCDMH]: The kinetics of oxidation of chalcone has been studied at various initial concentrations of the oxidant (DCDMH) (1.5×10^{-3} mol dm⁻³) and at fixed concentrations

TABLE-1
PSEUDO-FIRST ORDER RATE CONSTANTS FOR THE OXIDATION OF
CHALCONE BY 1,3-DICHLORO-5,5 DIMETHYL HYDANTOIN AT 303 K

[Chalcone] × 10 (mol dm ⁻³)	[DCDMH] × 10 ³ (mol dm ⁻³)	[H ⁺] × 10 (mol dm ⁻³)	CH ₃ COOH % (V/V)	<i>k</i> _{obs} × 10 ⁵ (s ⁻¹)
1.0	5.0	4.0	30	3.77
1.2	5.0	4.0	30	4.33
1.4	5.0	4.0	30	4.63
1.6	5.0	4.0	30	5.15
1.8	5.0	4.0	30	5.71
1.0	1.0	4.0	30	9.87
1.0	2.0	4.0	30	6.14
1.0	3.0	4.0	30	5.49
1.0	4.0	4.0	30	3.97
1.0	5.0	4.0	30	3.77
1.0	5.0	2.4	30	3.38
1.0	5.0	4.0	30	3.77
1.0	5.0	5.6	30	4.53
1.0	5.0	7.2	30	5.20
1.0	5.0	8.8	30	5.67

of other reactants. The plot of $\log [\text{DCDMH}]$ versus time was found to be linear indicating first order dependence on the reaction rate and from the slope of such plots pseudo-first order rate constants were evaluated.

Effect of $[\text{H}^+]$: The required concentrations of $[\text{H}^+]$ solutions were prepared from the stock solution of 4 M concentration. The reaction rate constants measured with various $[\text{H}^+]$ (2.4 – $8.8 \times 10^{-1} \text{ mol dm}^{-3}$) were found to increase with increase in $[\text{H}^+]$ ion concentration (Fig. 3). Order of the reaction with respect to $[\text{H}^+]$ is 0.39.

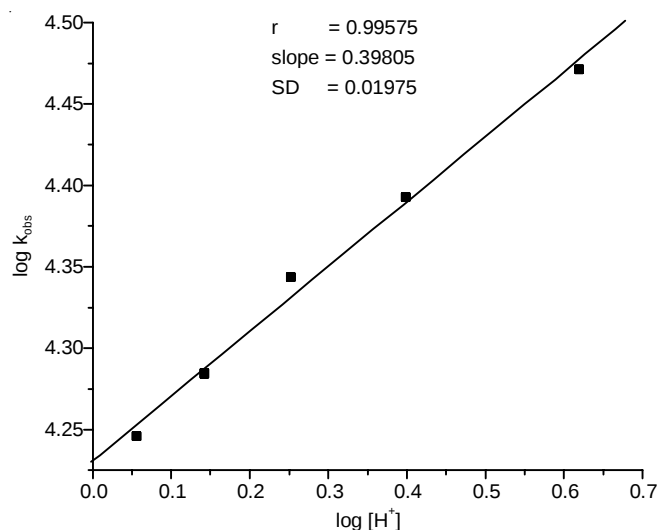


Fig. 3. Plot of $\log k_{\text{obs}}$ versus $\log [\text{H}^+]$ showing the effect of H^+ concentration on reaction rate

Effect of dielectric constant: In order to determine the effect of dielectric constant (polarity) of the medium on rate, the oxidation of chalcone by 1,3-dichloro-5,5-dimethyl hydantoin was studied in aqueous acetic acid mixtures of various compositions (Table-2). The data clearly revealed that the rate increases with increase in the percentage of acetic acid⁸.

TABLE-2 EFFECT OF DIELECTRIC CONSTANT ON THE REACTION RATE AT 303 K		
$\text{CH}_3\text{COOH}:\text{H}_2\text{O}$	D^a	$k_{\text{obs}} \times 10^5 (\text{s}^{-1})$
10:90	41.47	2.33
20:80	45.48	3.45
30:70	49.71	3.77
40:60	53.83	6.35
50:50	57.95	7.83
[DCDMH] = $5 \times 10^{-3} \text{ mol dm}^{-3}$, [chalcone] = 0.1 mol dm^{-3} , $[\text{H}^+] = 4 \text{ mol dm}^{-3}$, ^a values are calculated from the values of pure solvent		

Test for free radical intermediate: Addition of monomers like acrylonitrile to the reaction mixture under inert conditions did not induce any polymerization indicating the absence of free radicals in the reaction mixture⁸.

Rate and activation parameters: The effect of temperature was studied in the range of 283–323 K and the results were shown in Table-3. The Arrhenius plot of $\ln k_{\text{obs}}/T$ versus $1/T$ was found to be linear (Fig. 4). The value of energy of activation (E_a) was found to be $9.74081 \text{ kJ mol}^{-1} \text{ K}^{-1}$ and $\Delta H^\ddagger = 7.2204 \text{ kJ mol}^{-1}$, $\Delta S^\ddagger = -196.60 \text{ J K}^{-1} \text{ mol}^{-1}$, $\Delta G^\ddagger = 66.79 \text{ kJ}$

TABLE-3 EFFECT OF TEMPERATURE ON THE REACTION RATE					
Temp. (K)	283	293	303	313	323
$k_{\text{obs}} (\text{s}^{-1}) \times 10^5$	1.23	2.33	3.77	7.51	9.96
[DCDMH] = $5 \times 10^{-3} \text{ mol dm}^{-3}$, [chalcone] = 0.1 mol dm^{-3} , $[\text{H}^+] = 4 \text{ mol dm}^{-3}$, Acetic acid:water = 40:10					

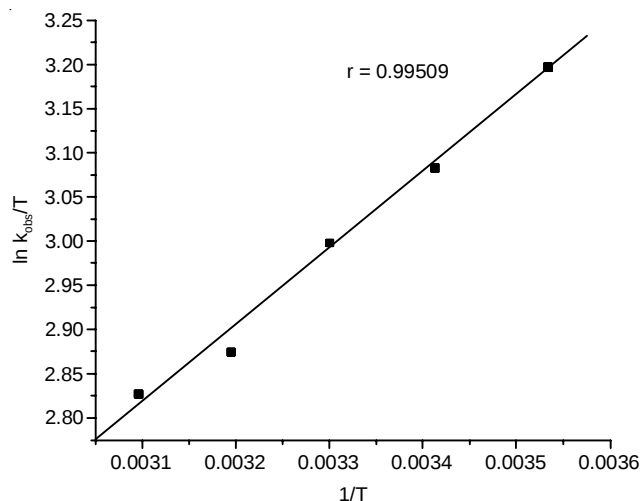


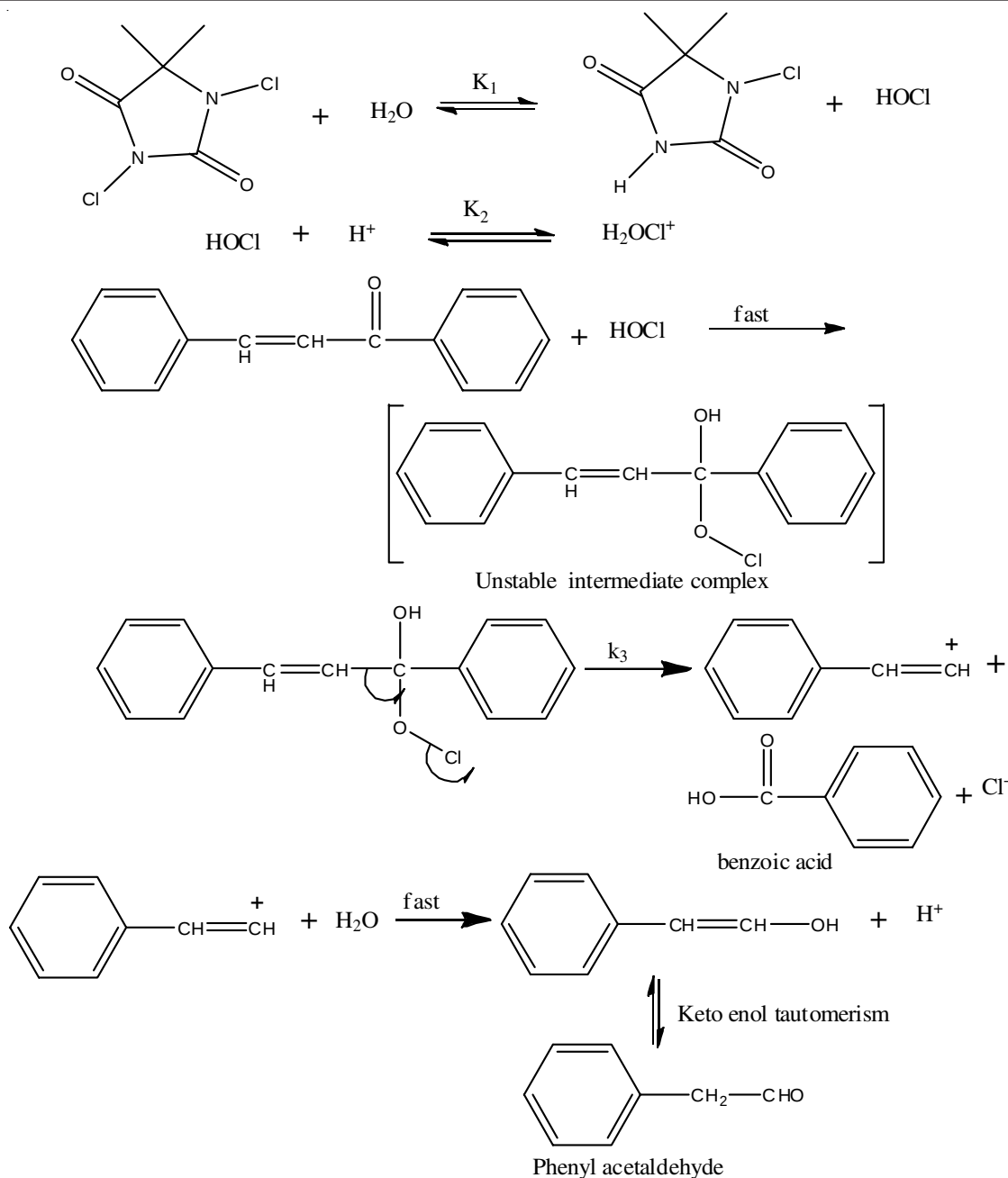
Fig. 4. Plot of $\ln k_{\text{obs}}/T$ versus $1/T$ showing the effect of temperature on reaction rate

mol^{-1} . It is clear from these values that both the parameters $\Delta H^\ddagger$ and $\Delta S^\ddagger$ are important in controlling the rates of reactions though the enthalpy factor appears to be more predominating. The value of $\Delta S^\ddagger$ is negative indicating the loss of entropy during the formation of activated complex.

Mechanism: Chalcone contains two functional groups, viz. $>\text{C}=\text{C}<$ and $>\text{C}=\text{O}<$ and the whole molecule is in conjugation. In strongly acidic media, DCDMH may get protonated producing electrophilic species and these species will get hydrolyzed in the presence of acid to give the reactive species such as HOCl and H_2OCl^+ . Since H_2OCl^+ is the reactive species it attacks either at $>\text{C}=\text{C}<$ or at $>\text{C}=\text{O}<$ or as an alternate path these can chlorinate phenyl rings. As no chlorination products were detected, the nuclear chlorination of phenyl rings was ruled out. The other possibility is the attack at $>\text{C}=\text{C}<$ or $>\text{C}=\text{O}<$. The functional group $>\text{C}=\text{C}<$ may not be attacked by HOCl as $>\text{C}=\text{C}<$ group is deactivated by two phenyl rings in conjugation. The other alternative is the attack at $>\text{C}=\text{O}<$. The keto functional group is highly polarized and HOCl forms an unstable intermediate complex with chalcone at this site. This unstable complex decomposes in a rate determining step to give the final products such as benzoic acid and phenyl acetaldehyde. In accordance with the above observations and stoichiometry of the reaction, the following reactions are involved to constitute the most probable mechanism of the reaction (Scheme-I).

Conclusion

In conclusion, 1,3-dichloro-5,5-dimethyl hydantoin (DCDMH) has been proven to be an excellent oxidant for the oxidation of chalcone. The kinetic and thermodynamic parameters for the oxidation of chalcone by DCDMH were determined and the reaction scheme was proposed. The thermodynamic data obtained, supported the proposed mechanism.



Scheme-I: Probable mechanism for the oxidation of chalcone by DCDMH

REFERENCES

- M.A. Rahman, *Chem. Sci. J.*, **29**, 1 (2011).
- S.S. Lim, H.S. Kim and D.U. Lee, *Bull. Korean Chem. Soc.*, **28**, 2495 (2007).
- R.J. Anto, K. Sukumaran, G. Kuttan, M.N.A. Rao, V. Subbaraju and R. Kuttan, *Cancer Lett.*, **97**, 33 (1995).
- J. Vaya, A.P. Belinky and M. Aviram, *Free Radic. Biol. Med.*, **23**, 302 (1997).
- H.L. Yadav, P. Gupta, P.S. Pawar, P.K. Singour and U.K. Patil, *Med. Chem. Res.*, **20**, 461 (2011).
- P.M. Sivakumar, P.K. Prabhakar and M. Doble, *Med. Chem. Res.*, **20**, 482 (2011).
- D.D. Sung and A. Nadar, *Bull. Korean Chem. Soc.*, **20**, 1487 (1999).
- J. Anilkumar and S. Sondu, *Indian J. Chem.*, **46A**, 1792 (2007).
- N.C. Khandual, K.K. Satpathy and P.L. Nayak, *J. Chem. Soc. Perkin II*, 328 (1974).
- B. Kuotsu, E. Tiewsoh, A. Debroy and M.K. Mahanti, *J. Org. Chem.*, **61**, 8875 (1996).
- S.P. Vajjayanthi and N. Mathiyalagan, *J. Chem. Biol. Phys. Sci.*, **2**, 1281 (2012).
- S.P. Vajjayanthi and N. Mathiyalagan, *Int. J. Res. Pharm. Chem.*, **2**, 722 (2012).
- K.G. Sekar and S.K. Periyasami, *J. Chem. Pharm. Res.*, **4**, 2153 (2012).
- E. Kolvari, A. Ghorbani-Choghamarani, P. Salehi, F. Shirini and M.A. Zolfigol, *J. Iran. Chem. Soc.*, **4**, 126 (2007).
- J. Mukherjee and K.K. Banerji, *J. Org. Chem.*, **46**, 2323 (1981).
- A.K. Singh, V. Singh, S. Rahmani, A.K. Singh and B. Singh, *J. Mol. Catal. A*, **197**, 91 (2003).
- R. Filler, *Chem. Rev.*, **63**, 21 (1963).
- P.V. Balasubramanian and N. Mathiyalagan, *J. Chem. Pharm. Res.*, **3**, 522 (2011).
- N.S. Srinivasan and N. Venkatasubramanian, *Tetrahedron Lett.*, **11**, 2039 (1970).
- K. Vivekanandan and K. Nambi, *J. Indian Chem. Soc.*, **76**, 198 (1999).