

Reactivity of Some Heterocyclic Ketone Thiosemicarbazones towards Chloramine-T: A Kinetic and Mechanistic Study

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Kinetics of oxidation of piperidinone thiosemicarbazones (PTSC) by Chloramine-T (CAT) in aqueous acetic acid medium have been investigated in the presence of perchloric acid. Oxidation of all the substrates showed first order kinetics in [CAT] and fractional order in [PTSC]. The reactions show inverse fractional order dependence on $[H_3O^+]$. Variation in ionic strength of the medium and addition of the reduced product of the oxidant, viz., *p*-toluenesulphonamide have only negligible effect on the rate of oxidation. The rate of reaction increases with decrease in the dielectric constant of the medium. Added acrylamide fails to polymerize eliminating the possibility of free radical pathway for the reaction. The stoichiometry of the reaction and the product analysis have also been carried out. From the kinetic data obtained at different temperatures the various activation parameters have been computed and a plausible mechanism proposed.

Key Words: Kinetic, Oxidation, Chloramine-T, Thiosemicarbazones.

INTRODUCTION

Chloramine-T (CAT) has been used as a versatile oxidising agent for a variety of organic compounds in aqueous and partially aqueous media in the presence of acids and alkalis¹⁻⁵. The present investigation is aimed to explore the potentiality of CAT as an oxidant for thiosemicarbazones of few heterocyclic ketones, to explain the mechanism of the reaction and correlating reactivity with structure.

EXPERIMENTAL

The thiosemicarbazones PTSC-1 to PTSC-7 used in the present investigation were prepared by following the literature procedures⁶⁻⁸. CAT, E. Merck (GR) was purified and used. All other chemicals used were of excellent grade.

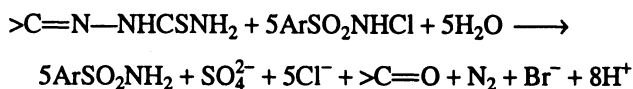
Kinetic measurements

Pseudo first order conditions with $[substrate] \gg [CAT]$ were maintained for the kinetic measurements. Ionic strength was maintained using $NaClO_4$. The reactions were carried out in darkened flasks to avoid photocatalysis, if any. The

progress of the reaction was monitored for two half lives. The pseudo first order rate constants k_{obs} are reproducible within $\pm 3\%$.

Stoichiometry and product analysis

The reaction mixture containing excess of oxidant over substrate in aqueous acetic acid was kept at room temperature in the presence of perchloric acid for a day. The products of oxidation were identified by standard tests⁹. The stoichiometric investigations showed that 1 mol of the substrate consumed 5 mol of oxidant. Thus the reaction may be represented as:



RESULTS AND DISCUSSION

The computed first order rate constant k_{obs} remains constant with increase in [CAT] (Table-1) indicating first order dependence of rate on [CAT]. The rate increases with increase in [substrate] (Table-1) and the order in [substrate] is

TABLE-1
PSEUDO FIRST ORDER RATE CONSTANTS (k_{obs}) FOR THE
OXIDATION OF *r*-2-*cis*-6-DIPHENYL-*trans*-3-METHYL-
PIPERIDIN-4-ONE THIOSEMICARBAZONE (PTSC-2)
BY CHLORAMINE-T (CAT)

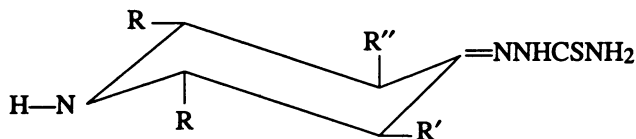
[HClO ₄] = 0.2 M, Temp. = 283 K				
[CAT] ₀ × 10 ⁻³ M	[SUB] ₀ × 10 ² M	Solvent % AcOH	[Cl ⁻] × 10 ⁴ M	k_{obs} × 10 ⁴ s ⁻¹
1.278	1.183	15	—	1.514
1.598	1.183	15	—	1.515
1.759	1.183	15	—	1.519
1.917	1.183	15	—	1.504
1.598	1.183	15	—	1.515
1.598	1.775	15	—	2.020
1.598	2.366	15	—	2.559
1.598	2.958	15	—	2.792
1.598	1.183	15	—	1.515
1.598	1.183	20	—	1.556
1.598	1.183	30	—	1.719
1.598	1.183	40	—	1.883
1.598	1.183	50	—	1.967
1.598	1.183	15	4.1	1.520
1.598	1.183	15	6.2	1.515
1.598	1.183	15	8.2	1.530
1.598	1.183	15	10.1	1.530

fractional. The data in Table-2 show that the rate has inverse dependence on $[H_3O^+]$ and the order with respect to $[H_3O^+]$ is fractional. Change in the ionic strength of the medium (Table-2) has only negligible effect on the reaction rate. However, a decrease in dielectric constant of the medium (by increasing the percentage of acetic acid) enhances the rate (Table-1). Further, a plot of $\log k_{obs}$ vs. $1/D$ (where D is dielectric constant of the medium) is a curve with positive slope⁶ indicating the interaction of neutral molecule or an ion and a dipole in the slow step. Added *p*-toluenesulphonamide, the reduction product, has no effect on rates. Under identical conditions the values of $10^5 k_{obs}$ (s^{-1}) for the compound PTSC-2 in the presence of 2.92, 4.38, 5.84, 8.76×10^{-3} mol dm^{-3} *p*-toluenesulphonamide are 15.15, 15.25, 15.19, 15.35 respectively. Added acrylamide fails to polymerize thus excluding free radical pathway. Increase in temperature from 283 to 303 K accelerates the rate and the various thermodynamic parameters have also been evaluated (Table-3).

TABLE-2
EFFECT OF VARYING PERCHLORIC ACID
CONCENTRATION AND IONIC STRENGTH OF
THE MEDIUM ON THE RATE OF OXIDATION
OF PTSC-2 BY CAT

[SUB] = 1.183×10^2 M, Solvent = 15% AcOH
[CAT] = 1.598×10^{-3} M, Temp. = 283 K

[HClO ₄] (M)	[NaClO ₄] (M)	k_1 ($\times 10^4 s^{-1}$)
0.20	0.30	1.515
0.30	0.20	1.204
0.35	0.15	1.126
0.40	0.10	1.026
0.20	0.10	1.504
0.20	0.20	1.525
0.20	0.30	1.515
0.20	0.40	1.518



Compound	R	R'	R''	Compound	R	R'	R''
PTSC-1	Ph	H	H	PTSC-5	Ph	Me	Me
PTSC-2	Ph	Me	H	PTSC-6	<i>p</i> -tolyl	Me	H
PTSC-3	Ph	Et	H	PTSC-7	<i>p</i> -anisyl	Me	H
PTSC-4	Ph	<i>iso</i> -pr	H	—	—	—	—

TABLE-3
PSEUDO FIRST ORDER RATE CONSTANTS FOR THE OXIDATION
OF VARIOUS THIOSEMICARBAZONS (PTSC-1 TO PTSC-7) BY CAT

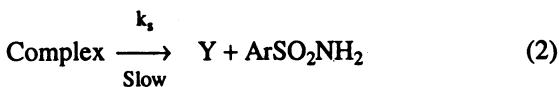
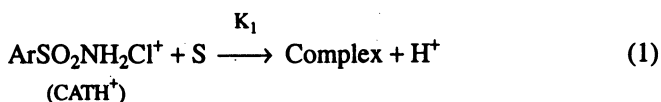
[CAT] = 1.598×10^{-3} M, Solvent = 15% AcOH
[HClO₄] = 0.2 M, Temp. = 283 K

Compound	k_1 ($\times 10^4$ s ⁻¹)	ΔH^\ddagger (kJ mol ⁻¹)	ΔS^\ddagger (J mol ⁻¹ K ⁻¹)	ΔG^\ddagger (kJ mol ⁻¹)
PTSC-1	1.457	40.69	-174.43	90.05
PTSC-2	1.515	42.04	-169.25	89.94
PTSC-3	1.712	42.38	-167.06	89.66
PTSC-4	1.952	46.01	-153.22	89.37
PTSC-5	1.724	41.20	-171.11	89.62
PTSC-6	1.628	40.25	-175.00	89.77
PTSC-7	1.468	40.76	-174.04	90.01

Mechanism and rate law

Chloramine-T (CAT) is a fairly strong electrolyte. In aqueous acidic media, depending upon pH, $\text{ArSO}_2\text{NCl}^-$, ArSO_2NHCl , HOCl , $\text{ArSO}_2\text{NH}_2\text{Cl}^+$ and H_2OCl^+ have been reported as oxidising species¹⁰⁻¹². Under the experimental conditions at $[\text{HClO}_4] = 0.2$ M, the possible oxidising species may be $\text{ArSO}_2\text{NH}_2\text{Cl}^+$ or H_2OCl^+ . If H_2OCl^+ is the active species, retardation of rate by added *p*-toluenesulphonamide could be expected. But no such effect is observed. Molecular chlorine as oxidising species is excluded since the added sodium chloride has no significant effect on rate.

Based on these observations, the following mechanism is proposed:



where S is substrate.

This scheme leads to the rate law

$$\text{Rate} = -\frac{d[\text{CAT}]}{dt} = \frac{k_s K_1 [\text{CATH}^+]_T [\text{S}]}{K_1 [\text{S}] + [\text{H}^+]} \quad (4)$$

$$k_{\text{obs}} = \frac{k_s K_1 [\text{S}]}{K_1 [\text{S}] + [\text{H}^+]} \quad (5)$$

As expected a plot of $1/k_{\text{obs}}$ vs. $1/[\text{S}]$ at constant $[\text{H}^+]$ and of $1/k_{\text{obs}}$ vs. $[\text{H}^+]$ at constant $[\text{S}]$ were linear. Further the double reciprocal plot of $1/k_{\text{obs}}$ vs. $1/[\text{S}]$ has

an intercept on the rate axis confirming the intermediate formation of a complex. A good agreement between the rate constant values, experimental and recalculated (from the linear plots of k_{obs} vs. $1/[\text{H}^+]$ and k_{obs} vs. $[\text{S}]$) further lend support to the mechanism proposed (Table-4).

TABLE-4
COMPARISON OF RECALCULATED AND EXPERIMENTAL
VALUES OF RATE CONSTANTS FOR THE OXIDATION
OF PTSC-2 IN AQUEOUS ACETIC ACID BY CAT

[CAT] = 1.598×10^{-3} M, Temp. = 283 K

[SUB] $\times 10^2$ M	[H ⁺] (M)	k_{obs} ($\times 10^4$ s ⁻¹) (experimental)	k_{obs} ($\times 10^4$ s ⁻¹) (recalculated)
1.183	0.20	1.515	1.560
1.775	0.20	2.020	1.994
2.366	0.20	2.559	2.428
2.958	0.20	2.792	2.863
1.183	0.20	1.515	1.560
1.183	0.30	1.204	1.200
1.183	0.35	1.126	1.110
1.183	0.40	1.026	1.042

Structure and reactivity

An analysis of the rate constants of various substituted PTSC's (Table-3) reveal that the reaction rate is susceptible to the inductive influence of the substituents. All the piperidinones used to prepare the substrates PTSC-1 to PTSC-7 have been shown from ¹H and ¹³C NMR studies to exist in the chair form with the aryl and alkyl substituents in the most stable equatorial positions^{6, 13, 14}. The mechanism proposed envisages the simultaneous attack of positive chlorine of CATH⁺ on the imino nitrogen of thiosemicarbazone and the positive N of CATH⁺ on C₄ of the substrate. This would be facilitated by the presence of electron releasing substituents at the reaction site. In the substrates used, the electron releasing substituents are present at C₃ or at C₅. Hence their effect is somewhat less pronounced. The 3-alkyl substituted substrates react slightly faster than 3-unsubstituted ones, the relative reactivity being 3-isopropyl > 3-ethyl > 3-methyl. This is to be expected since the electron releasing ability of these groups follows the same order. The 3,5-dimethyl substituted substrate reacts faster than 3-alkyl substituted and 3-unsubstituted substrates. This may be due to the additional inductive effect of second methyl substituent present on C₅. The inductive influence of the substituents on the rate of the reaction may be further confirmed by the observation that the 2,6-*p*-tolyl substrates react slightly faster than the 2,6-phenyl substituted substrates as methyl group is electron releasing and 2,6-*p*-anisyl substrate reacts slightly slower, as methoxy group is electron withdrawing.

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