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# Kinetics and Mechanism of Oxidation of Piperidin-4-one Semicarbazones by Pyridinium Fluorochromate

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The kinetics of oxidation of 2,6-diphenyl-piperidin-4-one semicarbazone (PPS) and some 3-alkyl substituted 2,6-diphenyl-piperidin-4-one semicarbazones (X = -H, -Me, -Et, -*i*Pr, -3,3-diMe) by pyridinium fluorochromate have been studied in aqueous acetic acid medium. The reactions are catalyzed by acid. The acid catalyzed reactions being very fast, precluded determination of their order in acid medium. The effect of added sodium sulphate and the influence of dielectric strength together indicate the reaction to be an ion-diploe type. The stoichiometry is 1:1 and the product of oxidation is the corresponding ketone. Activation energies and related thermodynamic parameters have been calculated. A suitable mechanism and hence a corresponding rate equation has been derived. An attempt has also been made to rationalize the structure reactivity correlation.

**Key Words: Alkyl substituted semicarbazones, Pyridinium fluorochromate, Kinetics, Mechanism.**

## INTRODUCTION

Oxidizing agents with chromium(VI) as the central atom have always enjoyed a special privilege of a very commonly used oxidant owing to their being versatile, operationally simple and easily accessible[1,2]. Two such reagents *viz.*, pyridinium chlorochromate (PCC)[3] and pyridinium fluorochromate (PFC)[4] are important addition to the list of oxidants.

Kinetic investigations of 4-piperidones[5] and cyclic ketones[6] with PFC have been carried out by previous workers. Oxidation kinetics of oximes and semicarabzones are limited. Simple and easy methods of their preparation attract the researchers. Many valuable natural products containing carbonyl groups are crystallized out only in the form of their biological sources[7]. Kinetic studies of oximes and semicarabzones by PMS[8] and acetophenone semicarbazone by PFC[9] have been carried out in our laboratory.

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Literature search has unveiled the fact that the use of PFC for the oxidation of 2,6-diphenyl piperidin-4-one semicarbazones is lacking. Hence the present investigation is initated in an effort to probe into the kinetic and mechanistic aspects of PFC oxidation of semicarbazones.

## EXPERIMENTAL

Pyridinium fluoro-chromate (PFC) (a complex of chromium trioxide, pyridine and hydrofluoric acid) was prepared[4] and it's purity checked by iodometric method. 2,6-Diphenyl piperidin-4-one semicarbazone and 3-alkyl substituted 2,6-diphenyl piperidin-4-one semicarbazones were prepared from the respective ketones[10] and their melting point checked. Acetic acid used as the solvent was purified by the standard procedure[11]. All other chemicals used were of AR grade.

Kinetic runs were carried out under pseudo-first order conditions of [semicarbazones] >> [PFC] in aqueous acetic acid medium 90 % (v/v) at constant ionic strength (0.021 mol $dm^{-3}$) maintained by the addition of $Na_2SO_4$. As the reactions were immeasurably fast in the presence of a mineral acid, the kinetic runs were followed in the absence of acid. The rates of reactions were measured at four different temperatures in the range 278 to 308 K. The dependence of the reaction rates of [PFC] was observed by varying the concentration of PFC in the range 8.0-1.20 × $10^{-4}$ mol $dm^{-3}$. The concentration of semicarbazone was varied in the range 0.8-1.2 × $10^{-2}$ mol $dm^{-3}$. The influence of ionic strength of the medium on the reaction rate was investigated by changing the concentration of the added sodium sulphate in the range 0.018-0.027 mol $dm^{-3}$. Effect of solvent polarity on the reaction rates was studied by varying the proportions of AcOH in the solvent mixture 80-95 % (v/v).

**Test for free radical intermediates:** There was no polymerization of the added acrylonitrile monomer in the reaction mixture. This points out that there are no free radical intermediates in this reaction.

**Stoichiometry and product analysis:** The stoichiometry of the reaction was estimated by allowing a known excess of PFC to react with a known concentration of semicarbazone in 90 % (v/v) acetic acid medium. The stoichiometry of the reaction was found to be 1:1. These reaction mixtures were extracted with ether and the ethereal layers were concentrated and used for the product analysis. One drop of the test solution was warmed with seven drops of 0.2 % aqueous azobenzene phenylhydrazone in sulphuric acid and four drops of concentrated sulphuric acid and cooled. Then a few drops of alcohol and enough chloroform were added to form a lower layer, followed by three drops of concentrated hydrochloric acid. The chloroform layer became coloured on shaking, indicating the presence of the parent ketone[12]. The product was further confirmed by TLC experiments.

## RESULTS AND DISCUSSION

The oxidation of 2,6-diphenyl piperidin-4-one semicarabazone and 3-alkyl substituted 2,6-diphenyl piperdin-4-one semicarbazone by PFC in aqueous acetic acid medium yields the corresponding ketones.

**Order with respect to oxidant:** The reaction was carried at different concentrations of pyridinium fluorochromate. The fact that the plots of log [PFC] *vs.* time were straight lines even beyond 80 % completion of the reaction, indicates that the reaction is first order in PFC. However, the pseudo-first order rate constants decrease with increase in concentration of gross PFC (Table-1). Similar observations have been made earlier in different oxidation studies[13-15] including the oxidation by PFC[6,7]. The plots of log [PFC] *vs.* time (min) at different initial concentrations of substrate were linear and the values of $k_{obs}$ ($s^{-1}$) evaluated from the slopes were found to be dependent on the initial concentrations of the substrate.

TABLE-1
RATE DATA FOR THE OXIDATION OF 3-ETHYL SUBSTITUTED 2,6-DIPHENYL PIPERIDIN-4-ONE SEMICARBAZONE BY PFC AT 293 K

| [PFC] × $10^4$ (mol $dm^{-3}$) | [Et-PPS] × $10^2$ (mol $dm^{-3}$) | [$Na_2SO_4$] × $10^3$ (mol $dm^{-3}$) | AcOH:$H_2O$ % (v/v) | $k_1 \times 10^4$ ($s^{-1}$) |
|---|---|---|---|---|
| 9.0 | 1.00 | 0.021 | 90:10 | 28.17 |
| 10.0 | 1.00 | 0.021 | 90:10 | 25.83 |
| 11.0 | 1.00 | 0.021 | 90:10 | 23.18 |
| 12.0 | 1.00 | 0.021 | 90:10 | 21.88 |
| 10.0 | 0.80 | 0.021 | 90:10 | 19.96 |
| 10.0 | 0.90 | 0.021 | 90:10 | 22.65 |
| 10.0 | 1.10 | 0.021 | 90:10 | 28.79 |
| 10.0 | 1.00 | 0.018 | 90:10 | 25.77 |
| 10.0 | 1.00 | 0.024 | 90:10 | 25.87 |
| 10.0 | 1.00 | 0.027 | 90:10 | 25.88 |
| 10.0 | 1.00 | 0.021 | 80:20 | 43.18 |
| 10.0 | 1.00 | 0.021 | 85:15 | 31.67 |
| 10.0 | 1.00 | 0.021 | 95:05 | 21.11 |

*at 283K, 12.39; *at 288K, 18.69; *at 298K, 32.63.

**Order with respect to substrate:** The plot of log [k] *vs.* log [substarte] was linear with unit slope showing the first order dependence on the substrate (Fig. 1). The second order rate constant $k_2$ is invariant supporting the first order dependence on [substrate].

**Effect of [$H^+$]:** Attempted acid catalyzed[16] reactions being very fast, precluded determination of their order in acid medium and hence the reaction is carried out in the absence of mineral acid.

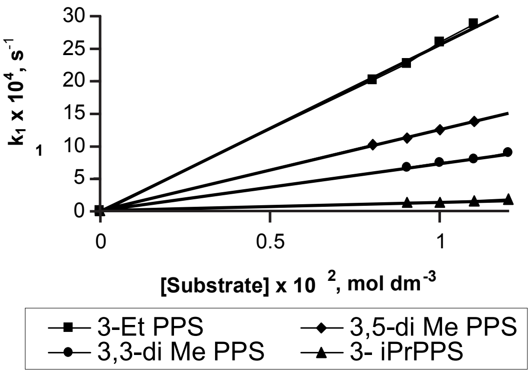


Fig. 1. Evaluation of $K_2$ at 293 K

**Influence of ionic strength:** The added sodium sulphate has negligible effect showing the participation of an ion and dipole in the rate determining step.

**Dependence on solvent polarity:** The rate decreases with decrease in dielectric constant of the medium indicating that there is a charge development in the transition state involving a more polar activated complex than the reactants, a neutral molecule semicarbazone and the protonated PFC.

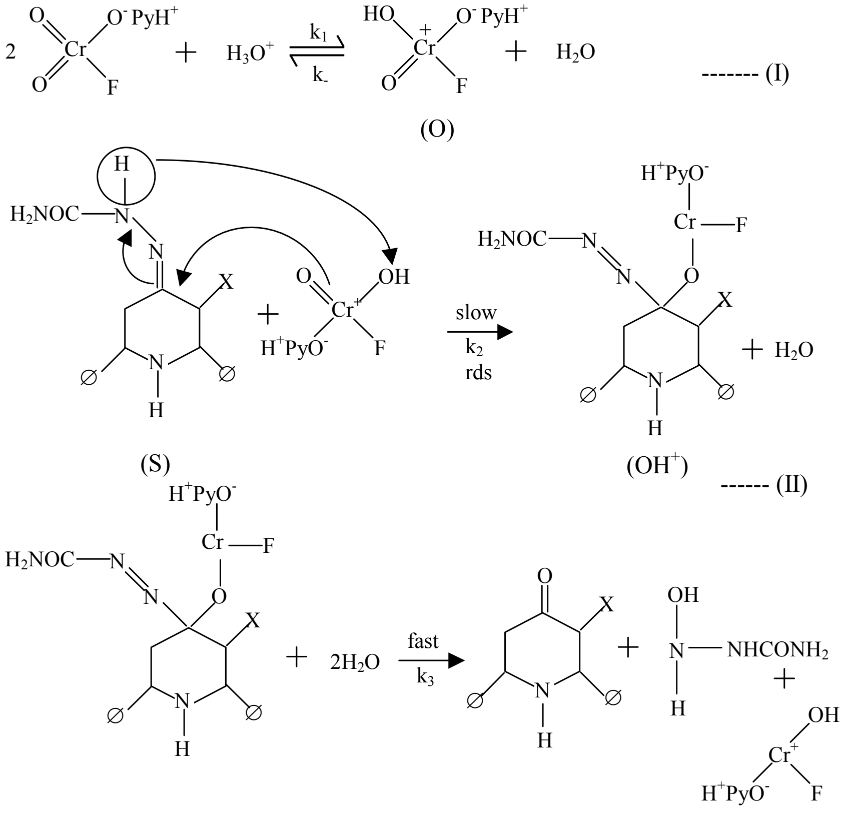
**Rate and activation parameters:** From the observed kinetic data, the second order rate constants for the oximes were found to increase with increase in temperature. The plots of log $k_2$ *vs.* 1/T were linear indicating that the Arrhenius law is being obeyed. The thermodynamics parameters $E_a$ (KJ $mol^{-1}$), $\Delta G^{\#}$ (KJ $mol^{-1}$), $\Delta H^{\#}$ (KJ $mol^{-1}$) and $\Delta S^{\#}$ ($JK^{-1}$ $mol^{-1}$) have been computed and tabulated (Table-2).

TABLE-2
RATE AND ACTIVATION PARAMETERS FOR SEMICARBAZONES OF 3-ALKYL SUBSTITUTED 2,6-DIPHENYL PIPERIDIN-4-ONE

| Substrate | $K_2 \times 10^2$ ($dm^3$ $mol^{-1}$) | | | | | | | $E_a$ (KJ $mol^{-1}$) | $\Delta H^{\#}$ (KJ $mol^{-1}$) | $\Delta S^{\#}$ ($JK^{-1}$ $mol^{-1}$) | $\Delta G^{\#}$ (KJ $mol^{-1}$) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | 278 K | 283 K | 288 K | 293 K | 298 K | 303 K | 308 K | | | | |
| PPS | 76.70 | 85.50 | 94.00 | 99.00 | - | - | - | 12.75 | 10.32 | -247.89 | 85.40 |
| 3-Me PPS | 50.00 | 65.10 | 78.50 | 93.00 | - | - | - | 27.19 | 24.75 | -199.13 | 83.10 |
| 3-Et PPS | - | 12.40 | 18.70 | 25.80 | 32.60 | - | - | 51.70 | 49.26 | -126.19 | 86.23 |
| 3,5-diMe PPS | - | 7.90 | 10.10 | 12.40 | 14.78 | - | - | 30.18 | 27.74 | -205.71 | 88.01 |
| 3,3-diMe PPS | - | - | 5.22 | 7.30 | 9.52 | 11.50 | - | 40.84 | 38.40 | -173.73 | 89.31 |
| 3-ipr PPS | - | - | - | 1.34 | 2.18 | 3.22 | 4.18 | 65.64 | 63.20 | -103.23 | 93.45 |

**Mechanism:** The oxidation reactions are catalyzed by acid. The acid-catalyzed reactions being very fast precluded determination of their order in acid medium. A large increase in the oxidation rate with acidity suggests the involvement of a protonated $Cr^{6+}$ species in the rate determining step. The participation of such species is well known in PFC oxidation.

In the present study, the slow formation of a positively charged PFC ester between the semicarbazone and the protonated PFC by the removal of water molecule is proposed as reported in the chromic acid oxidation of alcohols[17] and PCC oxidation of oximes of azabicyclic ketones[18]. The PFC ester then undergoes hydrolysis quickly to give the corresponding ketone. In the light of the experimental results a suitable mechanism has been proposed which is presented in **Scheme-I**.



X = -H, -Me, -Et, -iPr, -3,3-diMe, ---3,5-diMe
rds = Rate determining steps. ϕ = Phenyl group

Cr(IV)

**Scheme-I**

**Structure and reactivity:** From the magnitude of the rate constants, the reactivity trends observed for semicarbazones of different 3-alkyl substituted 2,6-diphenyl-piperidin-4-one.

3-H > 3-Me > 3-Et > 3,5-diMe > 3,3-diMe > 3-*i*Pr

It is observed that the reactivity decreases as the size of the alkyl substituent increases. For example, 3-methyl-2,6-diphenyl-piperidin-4-one semicarbazone reacts slower than 2,6-diphenyl-piperidin-4-one semicarbazone.

This indicates that there should be more steric crowding in the transition state than in the ground state. This trend can be attributed to the change of the central carbon atom from a trigonal to a tetragonal state. It is evident that the increase in the steric crowding is proportional to the bulkiness of the substituent in the third position.

That is why the reactivity decreases in the order is:

3-H > 3-Me > 3-Et > 3,5-diMe > 3,3-diMe > 3-*i*Pr

Thus all the experimental data observed in this investigation collectively prove the proposed mechanism to be the only possible one.

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