

Effect of Substituent on The Oxidation of Some Heterocyclic Semicarbazones by Quinolinium Fluorochromate

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Kinetics of oxidation of 2,6-diphenylpiperidin-4-one semicarbazone and some 3-alkyl substituted-2,6-diphenylpiperidin-4-one semicarbazones by quinolinium 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-dipole 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. The reaction is subjected to steric hindrance by the alkyl substituent.

Key Words: Kinetic, Oxidation, Semicarbazones.

INTRODUCTION

Oxidizing agents with chromium(VI) as the central atom have always enjoyed a special privilege of a commonly used oxidant owing to their being versatile, operationally simple and easily accessible^{1,2}. One such reagent is quinolinium fluorochromate due to its selective and mild oxidizing action³. Kinetic investigation of semicarbazones with Cr(VI) and other oxidizing agents have been carried in our laboratory^{4,5}. The formation of semicarbazone derivative is a common method of isolating purifying, identifying and characterizing carbonyl compounds⁶. This is especially true with natural products. A variety of hydrolytic, oxidative and reductive procedures have been described for the conversion of semicarbazones into aldehydes and ketones of which oxidative hydrolysis of semicarbazone is more suitable. Literature search has unveiled the fact that the use of quinolinium fluorochromate (QFC) for the oxidation of semicarbazone is lacking. Hence the present investigation is initiated with an effort to probe into the kinetic and mechanistic aspects of QFC oxidation of semicarbazones.

EXPERIMENTAL

Kinetic procedure: Quinolinium fluorochromate (QFC), a complex of chromium trioxide, quinoline and hydrofluoric acid was prepared and its purity checked by melting point, iodometric method and conductance study³. 2,6-Diphenylpiperidin-4-ones and their semicarbazones were prepared by the reported methods⁷⁻⁹. Their

purity was checked from their melting points. Acetic acid used as the solvent was purified by the standard procedure¹⁰. The kinetic runs were carried out in 90 % aqueous acetic acid medium in the temperature range of 278-313 K maintaining pseudo-first order conditions. The concentration of semicarbazone was kept in considerable excess over that of QFC. Kinetic measurements were initiated by mixing required volumes of pre-equilibrated reactant solutions. The experiment was followed spectrophotometrically at 355 nm by monitoring the disappearance of QFC. The rate constants were found to be reproducible within ± 3 %.

RESULTS AND DISCUSSION

Order with respect to oxidant: The concentration of QFC was varied in the range $0.8-1.2 \times 10^{-3}$ mol dm⁻³. The plots of log [QFC] vs. time were straight line indicating that the reaction is first order with respect to QFC. However the pseudo-first order rate constants decrease with increase in concentration of gross QFC (Table-1, Fig. 1) Similar observations have been made earlier in different oxidation studies¹¹⁻¹³ including the oxidation by QFC¹⁴.

TABLE-1
RATE DATA FOR OXIDATION OF SEMICARBAZONE OF 3-ISOPROPYL-2,6-DIPHENYLPYPERIDIN-4-ONE BY QUINOLINIUM FLUCROCHROMATE

| QFC $\times 10^3$ (mol dm ⁻³) | [3-iPrPPS] \times 10 ² (mol dm ⁻³) | μ (mol dm ⁻³) | AcOH:H ₂ O % (v/v) | $k_1 \times 10^3$ s ⁻¹ Temp. 293 K |
|--|--|-------------------------------|----------------------------------|--|
| 0.8 | 1.00 | - | 90:10 | 1.18 |
| 0.9 | 1.00 | - | 90:10 | 1.01 |
| 1.0 | 1.00 | - | 90:10 | 0.98 |
| 1.1 | 1.00 | - | 90:10 | 0.83 |
| 1.0 | 0.50 | - | 90:10 | 0.50 |
| 1.0 | 0.75 | - | 90:10 | 0.73 |
| 1.0 | 1.25 | - | 90:10 | 1.23 |
| 1.0 | 1.00 | - | 75.25 | 7.08 |
| 1.0 | 1.00 | - | 80.20 | 3.67 |
| 1.0 | 1.00 | - | 85.15 | 1.74 |
| 1.0 | 1.00 | 0.15 | 90:10 | 1.05 |
| 1.0 | 1.00 | 0.30 | 90:10 | 1.12 |
| 1.0 | 1.00 | 0.60 | 90:10 | 1.11 |

Order with respect to substrate: The concentration of semicarbazone was varied in the range of $0.5-1.5 \times 10^{-2}$ mol dm⁻³ maintaining the fixed concentration of QFC. The plots of log [QFC] vs. time (s) at different initial concentration of semicarbazone were linear and the values of k_{obs} (s⁻¹) evaluated from the slopes were found to be dependent on the initial concentration of substrate. The values of k_{obs} (s⁻¹) plotted against [substrate] gave a straight line passing through the origin, showing a first order dependence with respect to [substrate] as well as the absence of self decomposition of semicarbazone. From the slopes of the above plots, the second order rate constant k_2 dm³ mol⁻¹ s⁻¹ was evaluated.

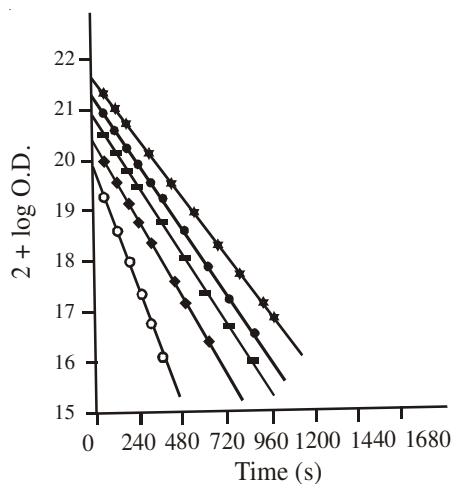


Fig. 1

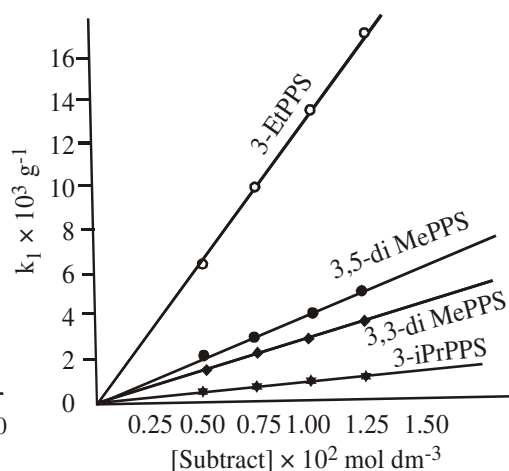


Fig. 2

TABLE-2
SECOND ORDER RATE CONSTANT AT DIFFERENT TEMPERATURES AND
ACTIVATION PARAMETERS FOR SEMICARBAZONE OF 3-SUBSTITUTED-
2,6-DIPHENYLPEPERIDIN-4-ONES AT 293 K

| Substitute | $k_2 \times 10^2 \text{ (mol}^{-1} \text{ dm}^3 \text{ s}^{-1}\text{)}$ | | | | | $E_a \text{ (KJ mol}^{-1}\text{)}$ | $H^\ddagger \text{ (KJ mol}^{-1}\text{)}$ | $S^\ddagger \text{ (JK}^{-1} \text{ mol}^{-1}\text{)}$ | $G^\ddagger \text{ (KJ mol}^{-1}\text{)}$ |
|------------|---|--------|--------|-------|-------|------------------------------------|---|--|---|
| | 283 K | 288 K | 293 K | 298 K | 303 K | | | | |
| 3-H | 76.80 | 109.00 | 132.00 | | | 41.51 | 39.08 | -72.41 | 60.30 |
| 3-Me | 43.40 | 69.10 | 99.80 | | | 50.10 | 47.66 | -46.92 | 61.51 |
| 3-Et | 6.76 | 8.67 | 14.00 | 15.60 | | 42.10 | 39.66 | -125.79 | 76.57 |
| 3,3-di Me | 1.41 | 2.95 | 4.08 | 5.67 | | 46.54 | 44.10 | -113.93 | 80.43 |
| 3,5-di Me | 2.00 | 2.95 | 4.08 | 5.67 | | 48.58 | 46.14 | -124.00 | 79.52 |
| 3-iPr | | | 0.98 | 1.24 | 1.77 | 43.39 | 40.96 | -143.50 | 83.00 |

Effect of $[H^+]$ and ionic strength: Attempted acid catalyzed¹⁵ 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. The added sodium sulphate has negligible effect showing the participation of an ion and dipole in the rate determining step.

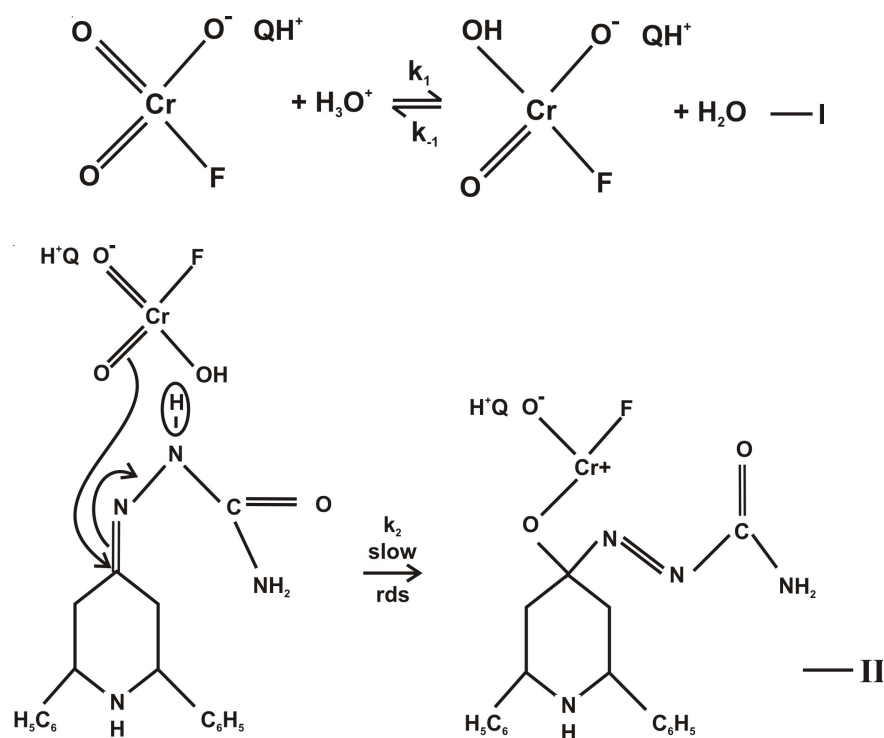
Effect of dielectric constant: The rate decreases with decrease in dielectric constant of the medium indicating that there is a charge development in the transition state involving a more polar activated complex than the reactants, a neutral semicarbazone molecule and the protonated QFC.

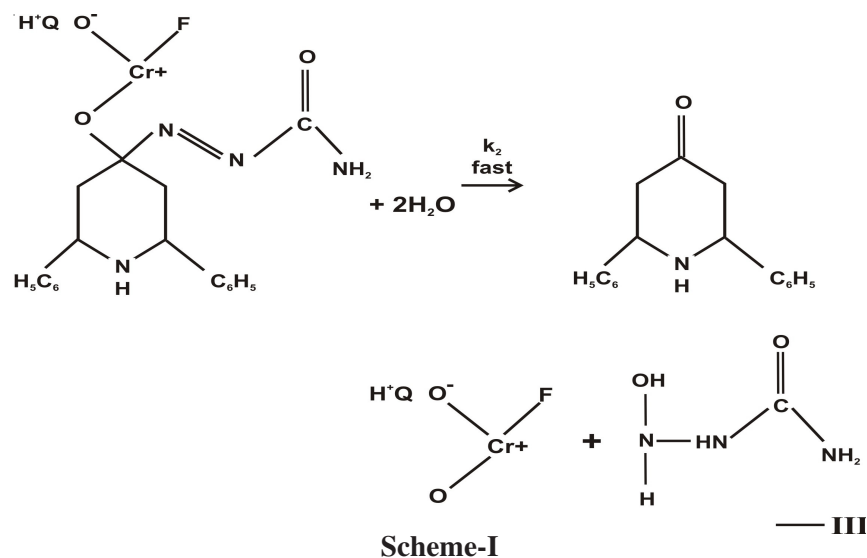
Test for free radical intermediate: There was no polymerization of the added acrylonitrile monomer in the reaction mixture. This point out that there is no free radical intermediate in this reaction.

Stoichiometry and product analysis: A known excess of QFC was allowed to react with known concentration of substrate in 90 % (v/v) aqueous acetic acid medium. The stoichiometry of the reaction was found to be 1:1. The reaction mixture was extracted with ether, the ether layer concentrated and was found that the product is the corresponding ketone which was confirmed by tlc experiments and qualitative methods.

Rate and activation parameters: From the observed kinetics the rate law for the disappearance of QFC is given as
$$-\frac{d[\text{QFC}]}{dt} = k_1[\text{QFC}][\text{substrate}]$$

Mechanism: 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 QFC oxidation. In the present study, the slow formation of positively charged QFC ester between the semicarbazone and the protonated QFC by the removal of water molecule is proposed as reported in the chromic acid oxidation of alcohols¹⁶, PCC oxidations of oximes of azabicyclic ketones¹⁷, PFC⁵ and acid dichromate¹⁸ oxidation of semicarbazones. The QFC 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**.





Influence of structure on reaction rates: From the rate constants the reactivity trend observed in the present study is PPS > 3-MePPS > 3-EtPPS > 3,3-diMePPS > 3,5-diMePPS > 3-iPrPPS. In the case of piperidin-4-one semicarbazone the steric effect of the 3-alkyl substituent is well pronounced. The rate data shows that the introduction of a methyl group near the reaction center, disfavours the reaction. The 3-alkyl substituent remarkably influences the properties of the functional group in the 4-position of 2,6-diphenylpiperidine ring system. The dissociation constant of the cyanohydrin of the ketone is much enhanced by the 3-alkyl substituent¹⁹. Similarly, the chromic acid oxidation of axial and equatorial 3-alkyl-2,6-diphenylpiperidin-4-ones²⁰ and the acid permanganate oxidation of the ketone are accelerated by the 3-alkyl substituent.

Based on the rate data values for the oxidation of 2,6-diphenylpiperidin-4-one semicarbazone and 3-MePPS, one would expect the rate of reaction of 3,5-dimePPS to be comparable with 3-MePPS. The much lower value may be due to the difference in conformation of this semicarbazone. Similar trend is observed in oxidation of 3-alkyl-2,6-diphenylpiperidin-4-one oximes by pyridinium fluorochromate¹⁷.

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