

The effect of solvent on the kinetics of the oxidation of 3-methyl-2,6-diphenyl-piperidin-4-one by quinolinium fluorochromate in aqueous organic media

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The kinetics of the oxidation of 3-methyl-2,6-diphenyl-piperidin-4-one by quinolinium fluorochromate (QFC) have been investigated in aqueous solutions of dimethyl sulphoxide, 1,4-dioxane, *tert*-butanol and acetone. The influence of the added co-solvent on the reactivity were analysed in the light of various simple and multiple regression equations, *viz* the Laidler-Eyring, Grunwald-Winstein, Swain and Kamlet-Taft equations. The obtained results showed that the solvation phenomenon plays a dominant role on the reactivity.

Keywords: kinetics, oxidation, solvent effect.

INTRODUCTION

Kinetic investigations of redox reactions in aqueous organic solvents and the subsequent correlation of the reaction rates with various solvent parameters provide important information regarding the mechanism of such reactions. Solvent variations may affect the kinetics and the energy of the electron transfer processes, particularly in mixed solvent media, in a complex manner as the physicochemical properties of mixed solvent media are often quite different from those of the pure solvents or of their ideal mixtures.¹ A number of solvent polarity scales, like relative permittivity, solvent ionizing power, *etc.*, have been established to quantify the influence of solvent on reactivity. In spite of the observation that single empirical parameters can be used as good approximations of solvent polarity, multiple solvent effects on kinetic processes are revealed only by using linear combinations of solvent parameters. Although the separation of solvent effects into various solvent-solvent-solute interactions mechanisms is purely formal, the multi-parameter approach to solvent effects has been shown to work well.² The objective of the present work, therefore, was to study the title reaction (as the kinetics and mechanism of this reaction are well understood in aqueous acetic acid medium^{3–7}) in four different water-organic solvent mixtures of various compositions, to check the utility of such solvent variation studies in the interpretation of mechanism.

EXPERIMENTAL

3-Methyl-2,6-diphenyl-piperidin-4-one⁸ and QFC⁹ were prepared and purified by literature methods. The other reagents and solvents used were of AnalaR grade. Doubly distilled water was used throughout the study. The reactions were performed under pseudofirst-order conditions by keeping an excess of the substrate over QFC. The progress of the reaction was followed by estimating the unreacted oxidant iodometrically at 25 °C. The rate constants were determined by the least squares method from the linear plots of log over QFC vs. time. Duplicate runs showed that the rate constants were reproducible to within 3%. Correlation analyses were carried out using Microcal Origin Computer Software. The goodness of the fit was discussed using the correlation coefficient (r), coefficient of multiple determination (R^2), standard deviation (sd) and Exner's statistical parameter (χ).¹⁰

RESULTS AND DISCUSSION

The oxidation of 3-methyl-2,6-diphenyl-piperidin-4-one by QFC was studied in aqueous mixtures of DMSO, 1,4-dioxane, *tert*-BuOH and acetone at 25 °C. The observed pseudofirst-order rate constants (k_{obs}), for different mole fractions of the added organic co-solvent, are collected in Table I. Since the results of the kinetics, stoichiometric and product analysis are similar to those of the oxidation of the title compound by pyridinium fluorochromate,¹¹ in this article I presents the effect of the added co-solvent on the kinetics alone. A probable mechanism consistent with the kinetic data is given in Scheme 1.

TABLE I. Pseudofirst-order rate constants ($10^4 k_{\text{obs}}$, s^{-1}) for the oxidation of 3-methyl-2,6-diphenyl-piperidin-4-one by QFC in various water-organic solvent mixtures at 25 °C

Solvent mixtures	Mole fraction of organic solvent						
	0.3	0.4	0.5	0.6	0.7	0.8	0.9
Water-DMSO	9.24	8.07	7.00	6.23	5.04	4.67	3.62
Water-dioxane	3.17	2.94	2.14	1.72	1.48	1.31	0.85
Water- <i>tert</i> -BuOH	2.01	1.75	1.31	0.99	0.92	0.73	0.61
Water-acetone	0.99	0.87	0.83	0.76	0.63	0.57	0.54

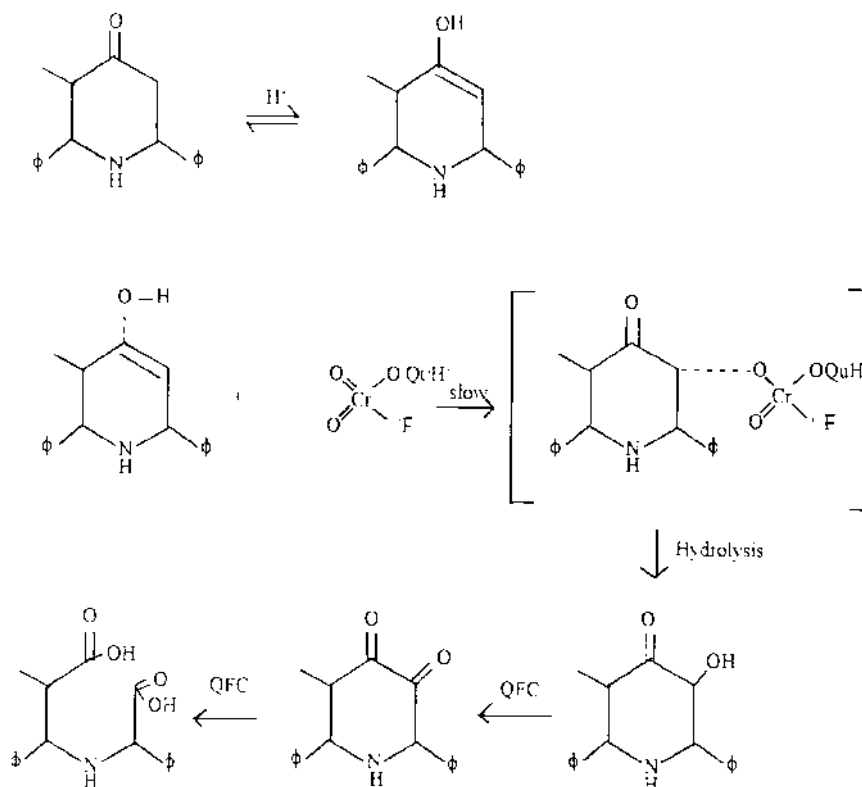
Substrate = 10×10^{-2} M; QFC = 10×10^{-3} M; $\text{ClCH}_2\text{COOH} = 5 \times 10^{-1}$ M

The proposed mechanism involves the formation of the enol in the first equilibrium step. QFC, being a two electron oxidant, prefers to attack the enol form in a slow second step leading to a transition state.¹² This undergoes fast hydrolysis and further oxidation to yield the main product. The above mechanism satisfactorily explains the different kinetic aspects and non-kinetic factors of the present investigation.

The influence of the relative permittivity of the solvent on the rate of the reaction was studied in four different water-organic solvent mixtures at seven different mole fractions (0.3-0.9) of organic co-solvent. It was observed that, in all the studied solvent mixtures, the k_{obs} values decrease with decreasing relative permittivity of the medium (*i.e.*, with increasing mole fraction of the added organic co-solvent). The influence of the relative permittivity on the rate can be described by the equation of Laidler and Eyring.¹³

$$d \ln k/d(1/\epsilon) = e^2 Z^2 (1/r - 1/r^*)/2kT$$

where k is the rate constant, Z the net charge, r the effective radius and r^* the radius of the activated species. A plot of $\log k_{\text{obs}}$ versus $1/\epsilon$ is linear ($r > 0.982$, $\epsilon < 0.23$)



Scheme 1. Mechanism of the oxidation of 3-methyl-2,6-diphenyl-piperidin-4-one by QFC.

with a negative slope in all the solvent mixtures studied. This is probably due to the fact that as the mole fraction of organic co-solvent in the medium increases, the concentration of the enol form, and hence the rate of the reaction, decreases.

The solvent effect was analysed using the Grunwald-Winstein equation.¹⁴

$$\log k = \log k_0 + mY$$

where Y is an empirical parameter (solvent ionizing power) characteristic of the given solvent and m is a substrate parameter measuring the substrate sensitivity to changes in the ionizing power of the medium. Plots of $\log k_{\text{obs}}$ vs. Y in water-1,4-dioxane and water-acetone mixtures (for the other two mixtures Y values are not available) are linear ($r > 0.991$, < 0.16) with positive slopes. The positive value of m (0.127 in water-1,4-dioxane and 0.075 in water-acetone mixtures) suggests that the transition state is more polar than the reactants.¹⁵ Such a transition state would be destabilized with increasing content of organic solvent in the medium and hence the rate of the oxidation would be decreased.

From idealized theories, the solvent relative permittivity is often predicted to serve as a quantitative measure of the solvent polarity. However, this approach is often

inadequate since these theories regard a solvent as a non-structured continuum, not composed of individual solvent molecules with their own solvent–solvent interactions and it does not take into account specific solute–solvent interactions, such as hydrogen bonding and electron pair donor–electron pair acceptor interactions, which often play a dominant role in solute–solvent interactions. No single macroscopic physical parameter could possibly account for the multitude of solute–solvent interactions on the molecular microscopic level.¹⁶ Thus, bulk solvent properties, like the relative permittivity and ionizing power can only poorly describe the microenvironment around the reacting species, which governs the stability of the transition state and thus the rate of the reaction. Hence, there have been a variety of attempts to quantify different aspects of solvent polarity and then use the resultant parameters to interpret solvent effects on reactivity through multiple regression. Various treatments for the above mentioned solvent–solvent–solute interactions based on linear solvation energy relationships (LSER) have been developed.¹⁰

The specific solvation is determined principally by the acidity and basicity of the solvent. Swain *et al.*¹⁷ believed that, in relation to specific solvation, the important characteristics of a solvent affecting chemical reactivity are its anion solvating tendency (*A*) and cation solvating tendency (*B*). Thus the observed kinetic data were analysed in terms of the Swain LSER.

$$\log k = aA + bB + c$$

The rates of oxidation in all the aqueous organic mixtures investigated show excellent correlation in the above LSER. The obtained correlation results are given below:

In water–DMSO mixture,

$$\log k_{\text{obs}} = 0.582 A - 3.410 B + 4.853 \quad 10^{17}$$

$$(N = 7, R^2 = 0.999, sd = 0.016, \quad = 0.04).$$

In water–1,4-dioxane mixture,

$$\log k_{\text{obs}} = 4.596 A - 8.492 B + 0.698$$

$$(N = 7, R^2 = 0.972, sd = 0.042, \quad = 0.20).$$

In water–*tert*-BuOH mixture,

$$\log k_{\text{obs}} = -159.002 A + 176.664 B - 21.095$$

$$(N = 7, R^2 = 0.986, sd = 0.028, \quad = 0.15).$$

In water–acetone mixture,

$$\log k_{\text{obs}} = 2.126 A - 5.992 B - 6.047 \quad 10^{-17}$$

$$(N = 7, R^2 = 0.999, sd = 0.014, \quad = 0.04).$$

From the magnitude of the coefficients *a* and *b*, the percentage contributions of *A* and *B* to the reactivity were calculated¹⁸ and the results are given in Table II. The excellent correlation indicates the existence of specific local electrostatic solute–solvent interactions. In all the solvent mixture, the cation solvating tendency plays the major role.

The negative sign of the coefficient of the term B , except in *tert*-BuOH–water mixtures, shows that the magnitude of the specific interaction between the reactants and the solvent is greater than that of the transition state–solvent interactions.¹⁹ This may be due to the fact that with increasing mole fraction of organic solvent in the mixture, the carbocation becomes increasingly solvated which hinders the approach of the large oxidant molecule to the carbon atom necessary for the formation of the transition state and hence the rate of oxidation is decreased. Further, as the organic solvent concentration increases in the mixture, more and more organic solvent molecules are introduced into the solvation shell, thereby increasing the hydrophobic environment of the enol form. Increasing hydrophobicity destabilizes the enol form and consequently the rate of the reaction is decreased. In *tert*-BuOH–water mixtures the positive sign of the coefficient of the B term shows that the magnitude of the specific interaction between the transition state and the solvent is greater than that between the reactants and the solvent. Since, *tert*-BuOH is a hydrogen bond donor solvent, increasing its mole fraction in the medium may result in increased solvation of the oxygen atom of the oxidant through hydrogen bonding and make its transfer to the substrate carbon difficult.

TABLE II. The percentage contributions of various solvent parameters to the reactivity in different aqueous organic solvent mixtures.

Solvent mixtures	Solvent parameters				
	Swain equation		Kamlet-Taft equation		
	A	B			*
Water–DMSO	15	85	33	16	51
Water–dioxane	35	65	08	25	67
Water– <i>tert</i> -BuOH	47	53	51	06	43
Water–acetone	26	74	15	44	41

In order to obtain a deeper insight into the specific co-solvent interactions which influence the reactivity, an attempt was made to adopt the solvatochromic comparison method developed by Kamlet and Taft.²⁰ This method may be used to unreveal, quantify, correlate and rationalize multiple interacting solvent effects on reactivity. The kinetic data were correlated with the solvatochromic parameters s , a and $*$ characteristic of the different mixtures using the following form of LSER.

$$\log k = A_0 + s * + a + b$$

where $*$ is an index of solvent dipolarity/polarizability which measures the ability of the solvent to stabilize a charge, or a dipole by virtue of its dielectric effect, s is the solvent HBD (hydrogen bond donor) acidity, a is the solvent HBA (hydrogen bond acceptor) basicity and A_0 is a regression value of the solute property in reference to cyclohexane. The regression coefficients s , a and b measure the relative susceptibilities of the solvent dependent solute property $\log k$ to the indicated solvent parameter. The rates of oxidation in all the water–organic solvent mixtures studied show excellent correlation with the solvent *via* the above LSER. The correlation results obtained are given below.

In water–DMSO mixture,

$$\log k_{\text{obs}} = -2.236 - 1.786 \epsilon^* + 1.182 \epsilon + 0.581$$

($N = 7$, $R^2 = 0.992$, $sd = 0.018$, $\epsilon = 0.11$).

In water–1,4-dioxane mixture,

$$\log k_{\text{obs}} = -5.775 + 2.177 \epsilon^* - 0.251 \epsilon + 0.841$$

($N = 7$, $R^2 = 0.980$, $sd = 0.041$, $\epsilon = 0.22$).

In water–*tert*-BuOH mixture,

$$\log k_{\text{obs}} = -2.047 + 4.128 \epsilon^* - 4.958 \epsilon - 0.561$$

($N = 7$, $R^2 = 0.993$, $sd = 0.023$, $\epsilon = 0.12$).

In water–acetone mixture,

$$\log k_{\text{obs}} = -4.443 + 0.871 \epsilon^* + 0.320 \epsilon - 0.935$$

($N = 7$, $R^2 = 0.973$, $sd = 0.023$, $\epsilon = 0.26$).

From the values of the regression coefficients, the contribution of each parameter on a percentage basis were calculated and are listed in Table II. The observation of this systematic multiple regression analysis leads to the following preliminary conclusions. i) In water–DMSO mixtures, the contribution of the solvent dipolarity/polarizability ϵ^* to the total solvent effect is predominant. The negative sign of the coefficient of this term indicates that the solvation of the reactants by the solvent mixture is extensive. Since DMSO is a HBA solvent, increasing its mole fraction in the mixture may shift the keto-enol equilibrium to the left and decrease the enol population in the medium and consequently decrease the rate of the reaction. ii) In water–acetone mixture, the contribution of the solvent HBA basicity ϵ to the total solvent effect is predominant. The negative sign of the coefficient of this term suggests that the solvent mixture solvates the reactants more than the transition state. Since acetone is a HBA solvent, increasing its mole fraction in the mixture may abstract the proton from the enol form and thereby shifts the equilibrium towards the keto form and consequently decrease the rate of the oxidation. Furthermore, the solvent dipolarity/polarizability ϵ^* also plays an appreciable role. The positive sign of this term indicates that solvation of the transition state is extensive. As a result of these two opposite effects the lowest rate was observed in this mixture. iii) The contribution of the solvent dipolarity/polarizability ϵ^* is greater in the case of the water–1,4-dioxane mixture. The transition state is more effectively solvated than the reactants as indicated by the positive sign of the coefficient of the term. Since 1,4-dioxane is a less polar solvent (having very low relative permittivity *ca.* 2.209), increasing its mole fraction in the mixture may destabilize the transition state, which is more polar than the reactants (as indicated by Grunwald-Winstein mY plot), and consequently decrease the rate of the reaction. iv) In water–*tert*-BuOH mixture, the solvation of the reactants by the solvent through its HBD property is found to be predominant. Since *tert*-BuOH is a HBD solvent increasing its mole fraction may discourage the removal of proton from carbonyl oxygen of the enol moiety to form the transition state and hence decrease the rate.

It can be concluded that the rate data indicate substantial solvent effects on the title reaction, showing strong dependencies on the nature and amount of the organic solvent added to the reaction medium.

ИЗВОД

УТИЦАЈ РАСТВАРАЧА НА КИНЕТИКУ ОКСИДАЦИЈЕ
3-МЕТИЛ-2,6-ДИФЕНИЛ-ПИПЕРИДИН-4-ОНА ХИНОЛИНИУМ ФЛУОРОХРОМАТОМ У
ВОДЕНОЈ СРЕДИНИ

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Испитивана је кинетика оксидације 3-метил-2,6-дифенил-пиперидин-4-она хинолиниум флуорохроматом (QFC) у воденим растворима диметилсулфоксида, 1,4-диоксана, *tert*-бутанола и ацетона. Утицаји додатих корастварача на реактивност анализирани су уз помоћ разних простих и регресионих једначина, као нпр. Laidler-Eyring, Grunwald-Winstein, Swain и Kamlet-Taft једначине. Добијени резултати показују да феномени солватације доминантно утичу на реактивност.

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REFERENCES

1. Y. Marcus, *Ion Solvation*, Wiley, New York, 1985
2. I. Tejera, A. Rodriguez, F. Sanchez, M. L. Moya, J. Burgess, *J. Chem. Soc.* **87** (1991) 2573
3. KR. Meenal, S. Lalitha, *J. Indian Chem. Soc.* **69** (1992) 741
4. KR. Meenal, R. Selvameena, *J. Indian Chem. Soc.* **69** (1992) 822
5. KR. Meenal, S. Lalitha, *J. Indian Chem. Soc.* **72** (1995) 693
6. KR. Meenal, D. Vimaladevi, *J. Indian Chem. Soc.* **73** (1996) 355
7. KR. Meenal, G. Ramanivimala, *J. Indian Chem. Soc.* **74** (1997) 43
8. V. Baliah, C. R. Noller, *J. Am. Chem. Soc.* **70** (1948) 3853
9. V. Murugesan, A. Pandurangan, *Indian J. Chem.* **31(B)** (1992) 377
10. J. Shorter, *Correlation Analysis of Organic Reactivity*, Research Studies Press, Letchworth, 1982
11. KR. Meenal, R. Selvameena, *J. Indian Chem. Soc.* **69** (1992) 303
12. J. S. Littler, *J. Chem. Soc.* (1962) 827
13. E. S. Amis, J. F. Hinton, *Solvent Effect of Chemical Phenomena*, Vol. 1, Academic Press, New York, 1973
14. A. H. Fainberg, S. Winstein, *J. Am. Chem. Soc.* **78** (1956) 2770
15. K. Karunakaran, K. P. Elango, *J. Phys. Org. Chem.* **8** (1995) 429
16. C. Reichardt, *Solvents and Solvent Effects in Organic Chemistry*, VCH, Weinheim, 1988, p. 339
17. C. G. Swain, M. S. Swain, A. L. Powell, S. Alunni, *J. Am. Chem. Soc.* **105** (1983) 502
18. Ref. 10, p. 220
19. P. Manikyamba, *Indian J. Chem.* **35A** (1996) 334
20. M. J. Kamlet, J. M. Abboud, M. H. Abraham, R. W. Taft, *J. Org. Chem.* **48** (1983) 2877.