



STUDIES ON STRUCTURE–REACTIVITY CORRELATION IN SOME ORGANOREDOX REACTIONS

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ABSTRACT

Ortho and para substituted derivatives of piperidin-4-one have been prepared using the path suggested by Mannich reaction, in which different electron withdrawing and releasing groups were introduced. These compounds were oxidized by N-bromosuccinimide and the kinetics and mechanism of reactions have been calculated, compared and analysed. The study of comparative rates of oxidation of these compounds reflects the conclusions about the position and nature of the groups in the structure of compounds, which influence the nature of the groups in the structure of compounds and reactivity of oxidation.

Key words: Kinetics, Oxidation, NBS, Piperidin-4-one, Hammett equation, Mannich reaction, Arrhenius equation.

INTRODUCTION

N-bromosuccinimide, which is used for allylic bromination is selective oxidizing agent to oxidize a series of substituted aromatic ketones. As a result of oxidation of different ortho and para derivatives of piperidine-4-one by NBS, a correlation between rate constant or equilibrium constant and structural features of substituted aromatic ketones has been investigated by using Hammett- ρ , σ equation.

The results and conclusions of the investigation are reported here.

EXPERIMENTAL

The experimental procedure has been carried out in two main parts. In first part, the

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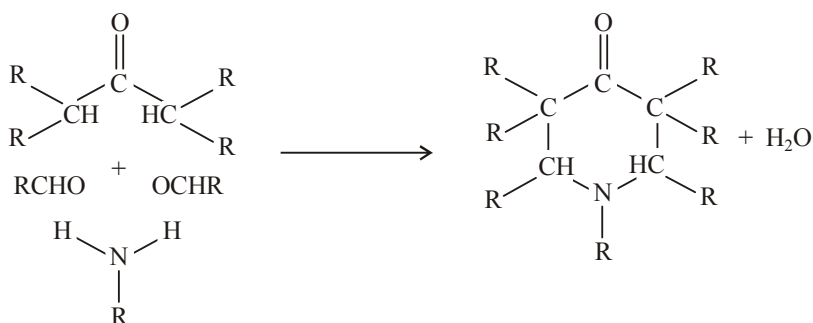
preparation of o- and p- substituted electron withdrawing and electron donating derivatives of piperidine-4-one and in the second part they were oxidised by NBS. The micro analysis and structure elucidation of piperidin-4-one derivatives were done by both microanalytical and spectral technique including I.R., U.V. and electronic spectra. Their molecular weights were determined by mass spectrometer at Instrumentation unit of North Eastern Hill University, NEHU, Shilong. Preparation of derivatives and their oxidation by NBS have been carried out in the Laboratory of Chemistry Deptt. of R. D. S. College, B. R. A. Bihar University, Muzaffarpur.

Preparation of derivatives

Seven derivatives of piperidin-4-one compounds were prepared by the path suggested by Mannich reaction with different substituents at 1,2,3,5 and 6 positions which are listed below:

1. 3, 5-Diethyl-2, 6-diphenyl piperidin-4-one
2. 3, 5-Diethyl-2, 6-diorthotolyl piperidin-4-one
3. 3, 5-Diethyl-2, 6-di-p-tolyl piperidin-4-one
4. 3, 5-Diethyl-2, 6-diortho chloro phenyl piperidin-4-one
5. 3, 5-Diethyl-2, 6-di-p-chloro phenyl piperidin-4-one
6. 3, 5-Diethyl-2, 6-di-para-anisyl piperidin-4-one
7. 3, 5-Diethyl-2, 6-diorthonitro phenyl piperidin-4-one

The usual procedure for the reaction is to reflux an aqueous or alcoholic solution of the ketone, aldehyde and amine or amine hydrochloride.



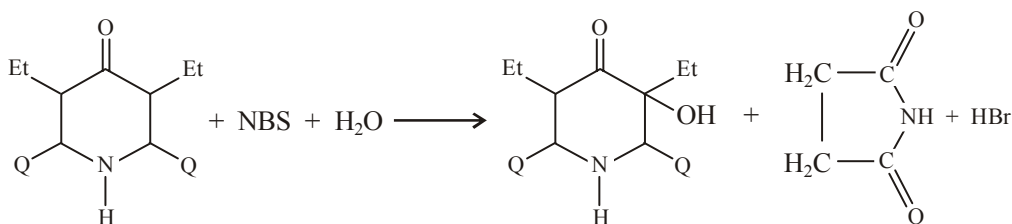
But when glacial acetic acid was used as solvent in place of water or alcohol then the reactions took place rapidly and the isolation of pure products was easy and the yields were very satisfactory. It was assumed that Mannich reaction might be more successful using acetic acid solvent rather than water or alcohol because the amino acetate might catalyze the reaction. It would dissociate more rapidly into the amine than would the amine hydrochloride and the temperature of the reaction could be raised without the loss of the gaseous amines, which was not the case when an aqueous or alcoholic solution of the amine were used.

Methods of derivatives preparation

Derivatives were prepared by using following procedure: 0.2 mole of amine or ammonium acetate was dissolved in 20 cc of glacial acetic acid. 0.4 mole of aldehyde and 0.2 mole of ketone were added to this solution. The mixture was heated upto the boiling point of solution and then allowed to cool to room temperature. The products were separated out as a crystalline solid which were filtered, washed and recrystallized.

Oxidation of derivatives

A variety of reaction conditions have been used to affect the oxidation of substituted piperidin-4-one with NBS. The ease of reaction is often dependent on the solvent employed. Mild oxidations with NBS are frequently carried out in aqueous acetone or aqueous dioxane solvent. The intensity of the reaction increases and selectively decreases when aq. tert-butyl alcohol or tert-butyl alcohol-pyridine are used as solvents. The role of pyridine is as a proton acceptor to remove the HBr formed, which otherwise would react with NBS to form Br₂.



The value of specific reaction rate was calculated from the slope of the plot of log (a-x) versus time. The result of kinetic study indicates that one mole of NBS reacted with one mole of piperidinone to afford α-ketol. The product was characterized by chromatography, I.R., U.V. and N. M. R. spectral studies. Under the experimental conditions [NBS] <<

piperidinone the plots of $\log(a-x)$ versus time were found to be linear indicating the order in [NBS] to be unity.

$$-d[\text{NBS}]/dt = K_{\text{eq}} K [\text{NBS}] [\text{piperidinone}]$$

The rate increased with increase in the concⁿ of piperidinone, the plot of $\log K$ versus $\log [\text{piperidinone}]$ was linear with unit slope indicating first order dependence in [piperidinone]. The reactions were carried out at four different temperatures in the range of 298 K-323 K. The rate and activation parameters were computed using Arrhenius equation.

Table 1: Rate and activation parameters

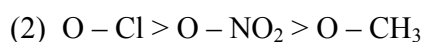
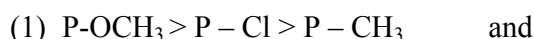
Compounds	E_a KJ mol ⁻¹	ΔH^\ddagger KJ mol ⁻¹	ΔG^\ddagger KJ mol ⁻¹	ΔS^\ddagger J K ⁻¹ mol ⁻¹	K^\ddagger dm ³ mol ⁻¹ s ⁻¹
3,5-Diethyl-2,6-diphenyl piperidin-4-one	80	78.2	85.1	- 22.2	2.28
3,5-Diethyl-2, 6-diorthotolyl piperidin-4-one	85.6	83.4	85.4	- 7.6	2.03
3,5-Diethyl-2,6-di-p-tolyl piperidin-4-one	90.0	87.6	85.5	5.4	1.97
3,5-Diethyl-2,6-diortho chloro phenyl piperidin-4-one	77.8	75.6	82.8	- 24.4	5.66
3,5-Diethyl-2,6-di-p-chloro phenyl piperidin-4-one	84.6	82.4	84.2	- 5.8	3.53
3,5-Diethyl-2,6-di-para-anisyl piperidin-4-one	60.8	58.2	82.6	- 80.4	5.80
3,5-Diethyl-2,6-diorthonitro phenyl piperidin-4-one	73.8	71.2	83.4	- 4.0	4.42

RESULTS AND DISCUSSION

The study of rate of oxidation of 3,5-dimethyl-2,6-diphenyl piperidin-4-one with different substituents at ortho, meta and para positions of the phenyl ring by NBS is considered to be of special interest because it exemplifies the inductive effect of the substituents on the reactivities of oxidation. It has been observed that there is considerable

difference in the reactivities of 2,6-diphenyl piperidin-4-one, 3-methyl-2,6-diphenyl piperidine-4-one and 3,5-dimethyl-2,6-dimethyl piperidin-4-one towards oxidation. In 3,5-dimethyl piperidin-4-one the decreased non bonded gauche interactions between enolic –OH and –CH₃ groups, which is possible only in highly distorted chair or twist conformation makes it least reactive.

Introducing the electron releasing and withdrawing groups in ortho and para positions of the ring in the least reactive 3,5-diethyl-2, 6-diphenyl piperidin-4-one existing in a nonchair conformation opens the way to a deeper understanding of structure-reactivity correlation in oxidation kinetics. The sequence of reactivity observed is -



Inductive effect offers a very simple explanation accounting for the above sequence. The electron releasing groups decrease the rate of oxidation while electron attracting groups enhance the rate of oxidation. This is in accordance with the fact that electron withdrawing groups facilitate the formation of cyclic transition state in the rate determining step where as electron releasing groups inhibit the formation of cyclic transition state in the rate determining step. Thus it has been concluded that the rate and mechanism of the reaction depends not only on the ortho, meta and para positions of substituents but also on the electron releasing and electron withdrawing nature of the substituents.

A slight deviation of reactivity is observed in O-NO₂ compounds. The unexpected fast rate for p-methoxy derivative may be due to the activation of the aromatic nucleus and hence ring bromination as a side reaction. But it is difficult to furnish positive evidence for the existence of ring brominated products in very fast reaction by isolation or otherwise.

There is further scope for study of the kinetic measurement of oxidation of meta substituted piperidine-4-one derivatives with NBS or other oxidizing agents. The comparison chart of the kinetics may explore new directions in the field of structure-reactivity correlation in organoredox reactions.

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