Kinetic Study of Oxidation of N-Methyl-2,6-Diphynyl–Piperidin-4-One Oxime [NMPO] - Effect of Varying the Substrate [NMPO]

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Abstract
PCC and N-methyl-2,6-diphynyl-piperidin-4-One Oxime were prepared, PCC by the method of Corey and Suggs. Then acetic acid was purified. Other reagents such as Analar samples of Sodium Perchlorate and Trichloroacetic acid was used as such. Doubly distilled water was used throughout. The purity of PCC was checked by estimating Cr(IV) iodometrically. The reaction was done at constant temperature (±0.10 C) and was followed iodometrically. The liberalized iodine was titrated against standardized sodium thiosulphate. The titration was repeated for the subsequent intervals of time. The first order rate constant was found from the slope of the log litre plots by least square method. First kinetic study of oxidation of N-methyl-2,6-diphynyl-piperidin-4-one oxime [NMPO] - by varying the concentration of the Substrate [NMPO].

1. Introduction
Pyridinium Chlorochromate (PCC), an efficient reagent for the oxidation of primary and secondary alcohols to the carbonyl compounds was discovered by Corey and Suggs1. The structure of the complex could be either (XII) or (XIII)1.

PCC exists as stable orange red crystalline solid (Molecular weight 215.45). It is freely soluble in cold water, benzene, acetic acid, glycerol, alcohols, chlorobenzene and nitrobenzene2. The aqueous solution of PCC is more stable for a fairly long period. It liberates iodine quantitatively from acidified potassium iodide as shown below:

$$2PyHOCOCl + 6KI + 3H_2SO_4 \rightarrow C_7O_7 + 3K_2SO_4 + 3H_2 + PyHCl + 3H_2O \quad [1]$$

Here two moles of PCC liberated six equivalents of iodine and hence the equivalent weight of PCC is equal to molecular weight/3.

Brown, Gundu Rao and Kukerni2 with a view to study the oxidation of Primary alcohols with PCC and in particular, to determine the stereochemistry of the reaction, added varying amounts of PCC to 1-octanol in methylene chloride. The progress of the reaction was followed by gas chromatography technique3. They predicted a two electron transfer, unlike in the case of chromic acid oxidation involving commonly a three electron transfer.

$$RCH_2OH + C_8H_7NHCrO_4Cl \rightarrow RCHO + C_8H_7NHCl + CrO_2 + H_2O \quad [2]$$

Even in the oxidation of 2-propanol with Thus, chromic acid, chromium (VI) species once formed is completely inert as an oxidant3.
The kinetics and mechanism of the oxidation of substituted mandelic acid by PCC was reported by Banerji4. The reaction was followed under pseudo-first order conditions, uncatalysed as well as acid catalysed in 1:1 (v/v) methylene chloride - nitrobenzene mixture.

The order was found to be one each in (oxidant) (substrate), and (H+). Increase in the percentage of nitrobenzene decreased the rate in accordance with the suggestion that the rate – determining step, in the presence of an acid involved a protonated Cr(VI) species. No free radical was trapped5. The substituted mandelic acids gave an excellent fit into the Hammett equation, with a negative ρ - value. A suitable mechanism was also suggested.

Based on the experimental results, two types of rate – determining hydride – ion transfer mechanisms are proposed:

Direct rate determining hydride – ion transfer from alcohol to protonated PCC and Prior formation of a chromate-ester between alcohol and PCC before the rate – determining hydride-ion transfer.

Chromate-ester formation is not likely to be susceptible to any considerable structural influence6. The large negative reaction constant can arise thus only from the differential effects of the substituents on the rate-determining step.

The kinetics of oxidation of ten primary alcohols by PCC in dichloromethane- nitrobenzene mixture at 30°C was studied under acid catalysed and uncatalysed conditions. In each primary alcohol the main product of the oxidation was the corresponding aldehyde. The reaction was first order each with respect to (alcohol) and the (oxidant)7. The order with respect to (H+) was one, showing the involvement of the protonated PCC. The reaction did not induce polymerization of acrylonitrile. The values of the reaction constants, for the uncatalysed and acid catalysed oxidation were –1.93 and –1.75 respectively. Both the hydride-ion transfer and the chromate-ester formation mechanisms have been suggested8.

Michaelis–Menten type of oxidation of dimethyl, dipropyl and diphenyl sulphides, in chlorobenzene - nitrobenzene mixture, studied by Panigrahi and Mahapatro7, was not very fact as compared to CrO3 oxidation. The reaction in chlorobenzene-nitrobenzene mixture in the presence of dichloroacetic acid showed a first order dependent each on (aniline), (PCC) and (dichloroacetic acid). The product of the reaction in each case was found to be azobenzene and p–benzoquinone. In one scheme the prior formation of an ester in a reversible step preceded by a hydride-ion shift was reported. In the other scheme, an equilibrium complex formation involving dichloroacetic acid, as a hydrogen bonded component of PCC was represented (XIV).

A novel oxidation of tetra substituted furan with PCC by Akbar et al.9 has led to a covalent synthesis of 4-acetoxy-3-acetyl or methoxy-carbonyl-4-substituted phenylbut-3-en-2-one.

The kinetics of oxidation of methylphenyl sulphide and several Para-substituted phenylmethyl sulphides by PCC was followed in binary solvent mixtures of 60% (v/v)
aqueous acetic acid and 50% (v/v) chlorobenzene–nitrobenzene by Rajasekaran et al\textsuperscript{10}.

Banerji, during the oxidation of benzhydrols\textsuperscript{11} and diols\textsuperscript{12} by PCC in dimethyl sulphoxide proposed the following cyclic hydride-ion transfer mechanism (XV).

\begin{center}
\includegraphics[width=0.2\textwidth]{mechanism.png}
\end{center}

2. Experimental Part

2.1 General Procedure for the N-methylation of Piperidin-4-ones

The piperidone (10g) was dissolved in 100ml of acetone and anhydrous potassium carbonate (10g) and methyl iodide (5ml) were added to the solution. The mixture was heated on a water bath for three hours. Acetone was removed and the residue was poured into water (150ml). The solid N-methypiperidone separated was filtered and recrystallised from ethanol\textsuperscript{13}.

2.2 General Procedure for the N-methylation of Piperidin-4-one oximes

The piperidone (0.1mol) was dissolved in ethanol (50ml). Saturated solutions of hydroxylamine hydrochloride and sodium acetate in water were added. The mixture was refluxed on a water bath for one hour. Then it was cooled, poured into water and the solid oxime obtained was filtered. All the oximes were recrystallised from ethanol.

3. Kinetic Procedure

The purity of PCC was checked by estimating Cr(IV) iodometrically. The present reaction was arranged to be under pseudo-first order conditions by keeping a large excess of oxime over PCC. The reaction was done at constant temperature (± 0.1\textdegree C) and was followed iodometrically. The N-Methyl-2,6-diphenylpiperidin-4-one Oxime (NMPO) in acetic acid, Pyridinium Chlorochromate in acetic acid and acetic acid were thermally equilibrated\textsuperscript{18}. In a sample run the oxime solution, acetic acid were pipette out in to a flask kept in the thermostat. The oxidant was added lastly. Aliquots (2ml) were drawn and quenched into solution of 2 M sulphuric acid (10ml). To this were added potassium iodide (20ml, 20%) and starch s indicator. The liberalized iodine was titrated against standardized sodium thiosulphate. The titration was repeated for the subsequent intervals of time. The duplicate rate measurements were reproducible up to 3%. The first order rate constant was found from the slope of the log liter plots by least square method\textsuperscript{14}.

3.1 Substrate Effect

Piperidone oxime I: 1. Methyl-2,6-diphenyl-piperidin-4-oxime (NMPC)

| Run – 6 | Effect of Substrate |
|---------|---------------------|
| [NMPO] = 0.501 \times 10^{-2} M | [AcOH] = 100 % |
| [PCC] = 9.02 \times 10^{-4} M | Temperature = 35 \textdegree C |

| Time  | Titre | log titre |
|-------|-------|-----------|
| 63    | 10.6  | 1.0253    |
| 274   | 10.1  | 1.0043    |
| 650   | 9.1   | 0.9590    |
| 930   | 8.5   | 0.9294    |
| 1225  | 8.0   | 0.9031    |
| 1555  | 7.3   | 0.8633    |
| 1855  | 6.7   | 0.8261    |
| 2122  | 6.3   | 0.7993    |
| 2440  | 5.9   | 0.7708    |

r = 0.999
k = \text{2.50 \times 10}^{-4} \text{.sec}^{-1}
\dot{r} = 3.13 \times 10^{-3}

Run – 7
Effect of Substrate

| Time  | Titre | log titre |
|-------|-------|-----------|
| 65    | 10.7  | 1.0294    |
| 313   | 9.8   | 0.9912    |
| 730   | 8.4   | 0.9242    |
| 990   | 7.6   | 0.8808    |
| 1293  | 6.8   | 0.8325    |
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| Run – 8 |
|---------|
| Effect of Substrate |
| [NMPO] = 1.253 X 10^{-2} M    | [AcOH] = 100 % |
| [PCC] = 9.02 X 10^{-4} M    | Temperature = 35 °C |
| Time | Titre | log titre |
| Secs. | ml | |
| 60 | 10.3 | 1.0130 |
| 309 | 9.4 | 0.9730 |
| 610 | 8.3 | 0.9191 |
| 928 | 7.2 | 0.8573 |
| 1216 | 6.5 | 0.8129 |
| 1436 | 5.8 | 0.7709 |
| 1695 | 5.4 | 0.7324 |
| 1970 | 4.8 | 0.6812 |

r = 0.999
k = 3.71 X 10^{-4} . sec^{-1}
Sd. = 2.92 X 10^{-3}

| Time | Titre | log titre |
| Secs. | ml | |
| 75 | 9.8 | 0.9912 |
| 282 | 8.8 | 0.9445 |
| 598 | 7.4 | 0.8692 |
| 780 | 6.7 | 0.8261 |
| 954 | 6.0 | 0.7781 |
| 1170 | 5.5 | 0.7403 |
| 1358 | 4.9 | 0.6902 |
| 1548 | 4.5 | 0.6532 |

r = 0.999
k = 4.38 X 10^{-4} . sec^{-1}
Sd. = 2.60 X 10^{-3}

| Run – 9 |
|---------|
| Effect of Substrate |
| [NMPO] = 1.00 X 10^{-2} M    | [AcOH] = 100% |
| [PCC] = 9.02 X 10^{-4} M    | Temperature = 35 °C |
| Time | Titre | log titre |
| Secs. | ml | |
| 63 | 10.4 | 1.0170 |
| 350 | 9.1 | 0.9590 |
| 647 | 8.1 | 0.9085 |
| 918 | 7.2 | 0.8573 |
| 1207 | 6.3 | 0.7993 |
| 1520 | 5.5 | 0.7403 |
| 1759 | 4.9 | 0.6902 |
| 1978 | 4.5 | 0.6532 |

r = 0.999
k = 4.03 X 10^{-4} . sec^{-1}
Sd. = 3.30 X 10^{-3}

| Run – 10 |
|---------|
| Effect of Substrate |
| [NMPO] = 2.005 X 10^{-2} M    | [AcOH] = 100 % |
| [PCC] = 9.02 X 10^{-4} M    | Temperature = 35 °C |
| Time | Titre | log titre |
| Secs. | ml | |
| 75 | 9.8 | 0.9912 |
| 282 | 8.8 | 0.9445 |
| 598 | 7.4 | 0.8692 |
| 780 | 6.7 | 0.8261 |
| 954 | 6.0 | 0.7781 |
| 1170 | 5.5 | 0.7403 |
| 1358 | 4.9 | 0.6902 |
| 1548 | 4.5 | 0.6532 |

r = 0.999
k = 5.33 X 10^{-4} . sec^{-1}
Sd. = 4.11 X 10^{-3}
4. Discussion

4.1 Effect of Varying NMPO Concentration on the Reaction Rate

The reaction was investigated by varying the substitute concentration at constant PCC concentration. With the increase in the concentration of the substrate the rate of the reaction was found to increase. The order with respect to NMPO was found to be fractional as evidenced by the linear plot of logk1 versus log (NMPO) with slope equal to 0.53.

\[
[PCC] \times 10^{-3} \quad k \times 10^4 \quad \text{sec}^{-1} \\
0.45 \quad 3.74 \quad 4.14 \\
0.90 \quad 3.71 \quad 4.26 \\
1.13 \quad 3.58 \quad 4.11 \\
1.35 \quad 3.44 \quad 4.05 \\
1.58 \quad 3.13 \quad 4.23
\]

Table 2a

\[
3 + \log [\text{NMPO}] \\
0.70 \quad 0.40 \\
1.00 \quad 0.57 \\
1.10 \quad 0.61 \\
1.18 \quad 0.64 \\
1.30 \quad 0.73
\]

\[
r = 0.997 \\
\text{Slope} = 0.53 \\
\text{Sd.} = 1.03 \times 10^{-2}
\]

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