CHAPTER 2

Experimental Methods

2.1 Materials

2.1.1 Preparation of N-Bromoacetamide

Twenty grams of acetamide (0.34 mole) was dissolved in 54 g of bromine (0.34 mole) contained in a 500 ml Erlenmeyer flask, and the solution was cooled to 0–5 °C in an ice bath. An ice-cold aqueous 50% potassium hydroxide solution was added in small portions with swirling and cooling until the color becomes a light yellow. Approximately 33–34 ml of the caustic solution was required. The nearly solid reaction mixture was allowed to stand at 0–5 °C for 2–3 hours.

The mixture was treated with 40 g of salt and 200 ml of chloroform and warmed on the steam bath with vigorous swirling. After 2–3 minutes the clear red chloroform layer was decanted from the semisolid lower layer, and the extraction was repeated twice more with 200 and 100 ml portions of chloroform respectively. The combined extracts were dried over sodium sulfate, the solution was filtered by gravity through a fluted filter into a 2 L Erlenmeyer flask, and 500 ml of hexane was added with swirling. White needles of N-bromoacetamide begin to form at once. After chilling for 1–2 hours, the crystals were collected with suction, washed with hexane, and air-dried. The yield was 19–24 g. (41–51%), m.p. 102–105°, purity 98–100%.
All the chemicals used were of AR grade. N-Chlorobenzamide were obtained from Sigma-Aldrich Chemical Co. Acetic acid (BDH) was first refluxed over chromic acid for 6 h and then distilled. Solutions of sodium perchlorate, perchloric acid and mercuric acetate were prepared in double distilled water. Double distilled water was employed in all kinetic runs.

### 2.1.2 Preparation of 4-oxoacids

The 4-oxo-4-(4'-methoxyphenyl)butanoic acid (S2), 4-oxo-4-(4'-methyl-phenyl)-butanoic acid (S3) and 4-oxo-4-(4'-chlorophenyl)-butanoic acid (S5) were obtained from Sigma-Aldrich Chemical Co. The remaining 4-oxoacids (S1, S4, S6, S7, S8 and S9) were prepared by Friedel-Crafts acylation of the substituted benzene with succinic anhydride\textsuperscript{282}

All the 4-oxo acids used in this study were crystallized twice from water and their purity was checked by their melting points.

#### 2.1.2.1 4-Oxo-4-phenylbutanoic acid (S1)

Succinic anhydride, 9 g was mixed with sodium dried benzene, 45 ml in a round bottomed flask fitted with a reflux condenser protected by a drying tube containing calcium chloride. The mixture was added with anhydrous aluminium chloride, 25 g all at once. The mixture was refluxed on a water bath with continued stirring for an hour. After
cooling, it was added with 50 ml of water and 20 ml of ice cold conc. HCl. The contents were then steam distilled to separate the unreacted benzene and cooled in freezing mixture. The colorless crystals of 4-oxo-4-phenylbutanoic acid separated from the solution were filtered and washed with a cold dilute solution of HCl and then with cold water. The crude product was dissolved in sodium carbonate solution, boiled for 10 minutes and filtered. The hot filtrate was treated with decolorizing carbon, 1 g, stirred and filtered. The filtrate was cooled, acidified with conc. HCl, 30 ml and further cooled in a freezing mixture. The oxoacid obtained was filtered, washed thoroughly with cold water and dried. Finally, the oxoacid was recrystallised in boiling water and dried for 12 h at 45-50°C.

2.1.2.2 4-Oxo-4-biphenylbutanoic acid (S4)

Biphenyl, 40 g was mixed with succinic anhydride, 18 g and nitrobenzene, 50 ml in a round bottomed flask. Anhydrous aluminium chloride, 50 g, was added in several portions and the mixture was refluxed in a water bath for two hours. The contents after cooling were added with ice cold HCl, 50 ml. then the reaction mixture was steam distilled and cooled. The crude product obtained was purified and recrystallised from alcohol.

2.1.2.3 4-Oxo-4-(4’-bromophenyl)butanoic acid (S6)

Bromobenzene was condensed with succinic anhydride. About 10 ml
of nitrobenzene was also added to the reaction mixture and refluxed for a long time. The oxoacid was recrystallised from hot water.

2.1.2.4 4-Oxo-4-(3’-nitrophenyl)butanoic acid (S7)

4-Oxo-4-phenylbutanoic acid, 5 g was added in small quantities to a ice cooled (< 5°C) mixture of fuming nitric acid, 10 ml and Con. H₂SO₄, 2 ml with constant stirring for about 30 minutes. The temperature of the reaction mixture was allowed to rise to 15°C, during the addition of the oxoacid. A clear solution was obtained and it was added slowly to crushed ice, with constant stirring. The product was formed as a precipitate. It was filtered and washed thoroughly with cold water. The oxoacid was purified and recrystallised in water.

2.1.2.5 4-Oxo-4-(1-naphthyl)butanoic acid (S8)

A mixture of naphthalene, 16 g and succinic anhydride, 8 g was added with stirring to a cold solution of nitrobenzene, 60 ml. Then it was added with anhydrous aluminium chloride, 22 g. The reaction mixture was kept overnight and treated with cold water and hydrochloric acid. A precipitate was formed and it was filtered. The precipitate contains 4-oxo-4-(2-naphthyl) butanoic acid and the filtrate contains 4-oxo-4-(1-naphthyl) butanoic acid. The filtrate containing 4-(1-naphthyl)-4-oxobutanoic acid was separately steam distilled and cooled to obtain the compound. The purification was carried out as usual and the oxoacid was recrystallised from methanol.
2.1.2.6 4-Oxo-4-(3’,4’-dimethylphenyl)butanoic acid (S9)

o-Xylene (25 ml), succinic anhydride (20g), finely powdered anhydrous aluminium chloride (60g) and tetrachloroethane (75 ml) were mixed in a round bottomed flask and the mixture was refluxed on a water bath for 2-3 hours. Then the contents were treated with ice cold HCl and steam distilled. The product obtained on cooling was purified and recrystallised from water.

2.1.3 Melting points of 4-oxoacids

The melting points of all the 4-oxoacids synthesized correspond to the values reported in the literature. These values along with their percentage yield are presented in following Table

<table>
<thead>
<tr>
<th>S.No</th>
<th>4-oxoacids</th>
<th>Lit. [Ref]</th>
<th>Melting Point (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S1</td>
<td>4-Oxo-4-phenylbutanoic acid</td>
<td>282</td>
<td>Observed 116</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Reported 116</td>
</tr>
<tr>
<td>S2</td>
<td>4-Oxo-4-(4’-methoxyphenyl)butanoic acid</td>
<td>283</td>
<td>Observed 146</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Reported 147</td>
</tr>
<tr>
<td>S3</td>
<td>4-Oxo-4-(4’-methylphenyl)butanoic acid</td>
<td>224</td>
<td>Observed 128</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Reported 129</td>
</tr>
<tr>
<td>S4</td>
<td>4-Oxo-4-biphenylbutanoic acid</td>
<td>284</td>
<td>Observed 184</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Reported 185</td>
</tr>
<tr>
<td>S5</td>
<td>4-Oxo-4-(4’-chlorophenyl)butanoic acid</td>
<td>231</td>
<td>Observed 132</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Reported 133</td>
</tr>
<tr>
<td>S6</td>
<td>4-Oxo-4-(4’-bromophenyl)butanoic acid</td>
<td>231</td>
<td>Observed 148</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Reported 149</td>
</tr>
<tr>
<td>S7</td>
<td>4-Oxo-4-(3’-nitrophenyl)butanoic acid</td>
<td>232</td>
<td>Observed 163</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Reported 164</td>
</tr>
<tr>
<td>S8</td>
<td>4-Oxo-4-(1-naphthyl)butanoic acid</td>
<td>226</td>
<td>Observed 129</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Reported 130</td>
</tr>
<tr>
<td>S9</td>
<td>4-Oxo-4-(3’4’-dimethylphenyl) butanoic acid</td>
<td>224</td>
<td>Observed 128</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Reported 129</td>
</tr>
</tbody>
</table>
2.1.4 Purification of solvents

Analar acetic acid (BDH) was refluxed for three hours with chromic acid. The acid was then distilled in a glass distillation apparatus and the fraction distilling at 117-118 °C was collected. The fraction collected has a boiling point of 118 °C.

Water purified, by a permutit ion exchanger, was distilled with a few crystals of potassium permanganate in a glass distillation apparatus. The distillate collected was used for preparing all the reagents and solutions.

2.2 Instrumentation

The reaction was followed potentiometrically by setting up a cell made up of the reaction mixture into which a platinum electrode and a standard calomel electrode were dipped. The emf of the cell was measured periodically using an Equip -Tronics potentiometer, while the reaction mixture was continuously stirred. An electrically operated thermostat was used to maintain the desired temperature with an accuracy of ±0.1 °C. A double walled 100 ml beaker with inlet-outlet water circulation facility, specially designed for this experiment, was used as reaction vessel.

2.3 Methods

2.3.1 Oxidation of 4-oxoacids by NCB

$N$-Chlorobenzamide was employed as oxidant for the oxidation of unsubstituted and substituted 4-oxoacids. The kinetics of oxidation of 4-oxoacids by NCB was studied by potentiometric method.
2.3.1.1 Kinetic measurements

The reactions were carried out in binary mixtures of acetic acid and water. Requisite amounts (appropriate volume of known concentration) of separately thermostated oxoacid, NCB, acetic acid, sodium perchlorate, perchloric acid solutions and water were pipetted out into the reaction vessel. The total volume of the reaction mixture being 50 ml, after the addition of all the solutions. The vessel was kept at the desired temperature (30 °C). The emf values of the reaction mixture were determined at definite intervals of time. The pseudo-first order rate constants were computed from the plots of ln (E_t - E_∞) versus time.

2.3.1.2 Product analysis

A typical product analysis was carried out as follows: 4-Oxo-4-phenylbutanoic acid (0.1 M), perchloric acid (1.0 M) and N-chlorobenzamide (0.5 M) were mixed together in 50 percent aqueous acetic acid so that the total volume of the mixture was 100 ml. The reaction mixture was allowed to stand for about 24 h to ensure the completion of the reaction. The gas evolved during the reaction was found out to be carbon dioxide. The solution was then shaken well with ether and aqueous layer was discarded. The ether layer was washed with distilled water several times, dried over anhydrous sodium sulphate and evaporated. The products were extracted with ether, dried and analyzed. Benzoic acid was identified by its m.pt. (121 °C) and estimated
quantitatively with a standard curve at $\lambda_{\text{max}} = 235$ nm and also tested with its characteristic spot test. Identification of the products, namely, benzoic acid, were also made by comparing the $R_f$ values of the authentic samples.

### 2.3.1.3 Stoichiometry

Different sets of reaction mixtures containing different quantities of NCB and 4-oxoacids at constant concentration of perchloric acid and sodium perchlorate were allowed to react for 24 h at 30° C and then analyzed. The remaining NCB was estimated. The results show that one mole of oxoacid consumes one mole of NCB.

\[
\text{C}_6\text{H}_5\text{COCH}_2\text{CH}_2\text{COOH} + \text{C}_6\text{H}_5\text{CONHCl} + 5\text{H}_2\text{O} \xrightarrow{\text{H}^+} \\
\text{C}_6\text{H}_5\text{COOH} + \text{C}_6\text{H}_5\text{CONH}_2 + 3\text{CO}_2 + 6\text{H}_2 + \text{HCl}
\]

### 2.3.2 Oxidation of 4-oxoacids by NBA

$N$-Bromoacetamide (AR grade) was employed as oxidant for the oxidation of unsubstituted and substituted 4-oxoacids. The kinetics of oxidation of 4-oxoacids by NBA was studied by potentiometric method.

#### 2.3.2.1 Kinetics measurements

The reactions were carried out in binary mixtures of acetic acid and water. Requisite amounts (appropriate volume of known concentration) of separately thermostated oxoacid, NBA, acetic acid, sodium perchlorate,
perchloric acid, mercury(II) acetate solutions and water were pipetted out into the reaction vessel. The total volume of the reaction mixture being 50 ml, after the addition of all the solutions. The vessel was kept at the desired temperature (30°C). The emf values of the reaction mixture were determined at definite intervals of time. The pseudo-first order rate constants were computed from the plots of ln (E_t - E_0) versus time.

2.3.2.2 Product analysis

A typical product analysis was carried out as follows: 4-Oxo-4-phenylbutanoic acid (0.1 M), perchloric acid (1.0 M) mercury(II) acetate (0.1 M) and NBA (0.5 M) were mixed together in 50 percent aqueous acetic acid so that the total volume of the mixture was 100 ml. The reaction mixture was allowed to stand for about 24 h to ensure the completion of the reaction. The gas evolved during the reaction was found out to be carbon dioxide. The solution was then shaken well with ether and aqueous layer was discarded. The ether layer was washed with distilled water several times, dried over anhydrous sodium sulphate and evaporated. The products were extracted with ether, dried and analyzed. Benzoic acid was identified by its m.pt. (121°C) and estimated quantitatively with a standard curve at $\lambda_{max} = 235$ nm and also tested with its characteristic spot test. Identification of the products, namely, benzoic acid, was also made by comparing the R_f values of the authentic samples.
2.3.2.3 Stoichiometry of oxidation

Different sets of reaction mixtures containing different quantities of NBA and 4-oxoacids at constant concentrations of perchloric acid, sodium perchlorate and mercury(II) acetate were allowed to react for 24 h at 30 °C and then analyzed. The remaining NBA was assayed iodometrically. The results are in good agreement with 1:1 stoichiometry

\[
\begin{align*}
C_6H_5COCH_2CH_2COOH & + CH_3CONHBr + 5H_2O \rightarrow H^+ \\
C_6H_5COOH & + CH_3CONH_2 + 3CO_2 + 6H_2 + HBr
\end{align*}
\]