EXPERIMENTAL PART I
CHAPTER IV.

EXPERIMENTAL PART I.

This part deals with the preparation of phenyl 2-amino-4-thiazolyl ketones and phenyl 2-acetamido-5-bromo-4-thiazolyl ketones which involve the following steps during their synthesis.

1. Preparation of propiophenones.
2. Conversion of various propiophenones into corresponding α-isonitrosopropiophenones.
3. Hydrolysis of α-isonitrosopropiophenones to corresponding phenyl methyl α-diketones.
4. Bromination of the above α-diketones and condensation of α-bromo-α-diketones with thiourea to give phenyl 2-amino-4-thiazolyl ketones.
5. Chloromercuration of phenyl 2-acetamido-4-thiazolyl ketones to corresponding phenyl 2-acetamido-5-chloromercuri-4-thiazolyl ketones.
6. Replacement of chloromercuri group by bromine to obtain phenyl 2-acetamido-5-bromo-4-thiazolyl ketones.
1. **Propiophenones:**

(a) **Propiophenone:**

It was prepared according to the method described in *Practical Organic Chemistry* by A.I. Vogel, p.732 (1956).

(b) **4'-Methylpropiophenone:**

A solution of 0.5 mol. of sodium dried toluene in 200 ml. carbon disulphide was placed in a litre three-necked flask provided with a mercury sealed mechanical stirrer, a dropping funnel and a double surface reflux condenser having a drying tube. 1.1 mol. of anhyd. aluminium chloride was added in lots and the mixture stirred rapidly. Then 0.5 mol. of propionic anhydride was added dropwise from the dropping funnel so that the mixture refluxed gently. After complete addition, the mixture was gently heated under reflux for one and half hours, cooled, carbon disulphide distilled out and the residue decomposed with ice-hydrochloric acid mixture. The oil, separated, was taken up in ether and ether extract washed with water, 10 per cent sodium hydroxide and finally with water. The ether solution was dried over anhyd. calcium chloride, ether removed and the residue distilled under reduced pressure, b.p.105-7° at 8 mm. Yield 39.5 g. (86 per cent.).
(c) 4'-Ethoxypropiophenone:

Noller and Adams, (loc.cit.)

To a well stirred ice cold mixture of 200 ml. of carbon disulphide and 1.1 mol. of anhyd. aluminium chloride taken in a litre three-necked flask equipped with a mercury sealed stirrer, a dropping funnel and a double surface reflux condenser with a drying tube was added 0.5 mol. of anisole dropwise. The reaction mixture was kept at room temperature for about 5 hours and was further worked out as described in the previous method. Yield 38 per cent, b.p. 125-8° at 4-5 mm.

(d) 4'-Chloropropiophenone:

Zenitz and Hartung, J. Org. Chem., 11, 444 (1946)

To a solution of 0.5 mol. of freshly distilled chlorobenzene in 200 ml. carbon disulphide taken in a dry three-necked flask fitted with a mercury sealed mechanical stirrer, a dropping funnel and a double surface reflux condenser with a drying tube, were added 75 g. of anhyd. aluminium chloride in small lots, with stirring. Then, 47 g. of propionyl chloride was added dropwise from the dropping funnel so that the mixture refluxed gently. After complete addition, the mixture was further refluxed for three hours, the solvent distilled and the residue decomposed with ice and hydrochloric acid mixture. The
whole bulk was extracted with ether and the ethereal layer was washed with water, 10 per cent sodium hydroxide and finally with water. The ethereal solution was dried over anhyd. calcium chloride, ether removed and the residue distilled under vacuum. Yield 77 per cent, b.p.132-5° at 15 mm.

(a) 4'-Aminopropiophenone :

[Derick and Bornmann, J. Am. Chem. Soc., 35, 1286 (1913)]

50 g. of acetanilide, 100 g. of anhydrous aluminium chloride and 200 ml. carbon disulphide were mixed together in a litre three-necked flask equipped with a mercury sealed mechanical stirrer, a dropping funnel and a double wall reflux condenser with a drying tube. To the well stirred mixture, 75 g. of propionyl chloride was added through the dropping funnel and the mixture heated on water bath for 2 hours and finally on steam bath for about an hour. The solvent was distilled out and the residue was decomposed with sufficient crushed ice. The brown precipitate of crude 4'-acetamidopropiophenone was filtered, washed with water and dried under vacuum over anhyd. calcium chloride. Yield 38 per cent, pinkish plates from dil. alc., m.p.173°.

A mixture of 10 g. of 4'-acetamidopropiophenone and 50 ml. of 1:1 hydrochloric acid taken in a 250 ml.
round bottom flask was heated on the water bath for about two hours till homogenous solution was formed. The solution was cooled and poured into dil. sodium hydroxide containing ice lumps. The brown ppt. separated out was filtered, dried and purified by crystallisation from hot water in pale yellow plates, m.p.140°. Yield 4 g. (35 per cent.).

(f) 4'-Nitropropiophenone:

N. Sugimoto et al., Japan 1482, March 20, (1954); Chem. Abs., 49, 11707 (1955)

A solution of 10 g. of 4'-aminopropiophenone in 20.6 g. of 77 per cent nitric acid and 100 ml. of water was diazotised at 5° with 14.2 g. of 90 per cent sodium nitrite in 30 ml. water. The mixture was allowed to stand for an hour. Meanwhile, cuprous nitrite solution was prepared by adding 18 g. of powdered sodium sulphide in lots, with shaking, to a solution of 18 g. of hydrated copper sulphate in 60 ml. water, followed by addition of 29 g. of sodium nitrite in small lots. The Cu(NO) solution was cooled under ice. The above cold diazonium salt solution was added in small portions to the ice cold cuprous nitrite solution with shaking. The mixture was kept overnight and next day filtered. The residue was washed with water and dried in air. The filtrate was steam distilled
to get some more ketone. The crude compound was crystallised with dil. alc. in pale yellow shining needles, m.p. 90°. Yield 5.5 g.

(g) 2',4'-Dichloropropiophenone:


40 g. of m-dichlorobenzene and 50 g. of propionyl chloride were added to 300 ml. of carbon disulphide taken in a litre three-necked flask equipped with a mercury sealed mechanical stirrer and a double surface reflux condenser having a drying tube. To the stirred solution, 160 g. of powdered anhyd. aluminium chloride were added in small portions over a period of 15 minutes. The mixture was heated under reflux on a water bath for about 4 hours with continuous stirring. The solvent was distilled and the residue was further refluxed for another four hours on the steam bath. The reaction mixture was cooled and decomposed by pouring into 300 ml. of 6 N hydrochloric acid containing crushed ice. The heavy oil was separated and aqueous layer was extracted with ether. The ether solution was added to the above oil and ether layer was washed with water, 10 per cent sodium hydroxide and finally with water. The ethereal solution was dried over anhyd. calcium chloride, solvent removed and residue distilled under vacuum, b.p. 126° at 8 mm. Yield 89 per cent.
(h) 3',4'-Dichloropropiophenone and 2',5'-dichloropropiophenone:


(o- and p-Dichlorobenzenes were B.D.H. samples)

A mixture of 36 g. of dichlorobenzene and 51 g. of propionyl chloride was taken in a dry 500 ml. round bottom flask fitted with a reflux condenser having a calcium chloride guard tube at the mouth. 126 g. of finely powdered anhyd. aluminium chloride were added in small lots to the above mixture with shaking. The reaction mixture was refluxed on a steam bath for 5-6 hours and allowed to stand overnight. Next day, the mixture was decomposed with ice and hydrochloric acid and subjected to steam distillation. The distillate was extracted with ether, ethereal solution dried over anhyd. calcium chloride, solvent removed and residue fractionally distilled to separate the unreacted dichlorobenzenes and the required ketones.

3',4'-Dichloropropiophenone: Yield 48 g. (95 per cent.), b.p. 267-70°.

2',5'-Dichloropropiophenone: Yield 26 g. (49 per cent.), b.p. 253-60°.
2. oC-Isonitrosopropiophenones:

General method of preparation:

In a litre three-necked round bottom flask provided with a double surface reflux condenser having a drying tube, a mercury sealed mechanical stirrer and an air tight rubber cork carrying two gas delivery tubes, was placed a solution of 0.3 mol. of propiophenone in 300 ml. ether. The stirring was started and dry hydrogen chloride gas was passed through the stirred solution at the rate of 6-8 bubbles per second. After 30 minutes, methyl nitrite gas was passed into the solution through the second delivery tube. The gas was produced by adding 50 ml. of (1:1) sulphuric acid, dropwise, from a dropping funnel to a mixture of 30 g. of sodium nitrite, 18 ml. of distilled methanol and 18 ml. of water taken in a conical flask with a cork bearing a gas delivery tube and a dropping funnel. Within a short time the reaction mixture turned reddish brown and methyl nitrite gas was passed for an hour more. Hydrogen chloride gas was passed for extra 30 minutes. The reaction mixture was kept overnight. Next day, the mixture was poured into a 10 per cent sodium hydroxide solution containing ice lumps. The yellow aq. layer was separated and ether layer was washed with dil.
alkali till aqueous layer was colourless. The combined aq. solution was poured slowly into concentrated hydrochloric acid containing ice lumps. The ppt. thus obtained was filtered, washed with water and dried in air. It was purified by crystallising with suitable solvent.

(a) $\alpha$-Isonitrosopropiophenone:


Quantities taken:

<table>
<thead>
<tr>
<th>Propiophenone</th>
<th>40.2 g.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium nitrite</td>
<td>18.0 g.</td>
</tr>
<tr>
<td>Methanol</td>
<td>18 ml.</td>
</tr>
<tr>
<td>Water</td>
<td>18 ml.</td>
</tr>
<tr>
<td>Yield</td>
<td>34.2 g. (70 per cent.)</td>
</tr>
</tbody>
</table>

Snow coloured needles from toluene, m.p. 110°.

(b) $\alpha$-Isonitroso-$4'$-methylpropiophenone:

Hartung and Munch, J. Am. Chem. Soc., 51, 2264 (1929)

Quantities taken:

<table>
<thead>
<tr>
<th>$4'$-Methylpropiophenone</th>
<th>44.4 g.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium nitrite</td>
<td>18.0 g.</td>
</tr>
<tr>
<td>Methanol</td>
<td>18 ml.</td>
</tr>
<tr>
<td>Water</td>
<td>18 ml.</td>
</tr>
<tr>
<td>Yield</td>
<td>39.8 g. (75 per cent.)</td>
</tr>
</tbody>
</table>
White flakes from toluene, m.p.125°.

(c) ∞-Isonitroso-4'-methoxypropiophenone:


Quantities taken:
- 4'-Methoxypropiophenone 25.2 g.
- Sodium nitrite 9.0 g.
- Methanol 9 ml.
- Water 10 ml.
- Yield 25 g. (72 per cent.).

Colourless shining needles from hot water, m.p.131°.

(d) ∞-Isonitroso-4'-chloropropiophenone:

[Zenitz and Hartung, J. Org. Chem., 11, 446 (1946)]

Quantities taken:
- 4'-Chloropropiophenone 25.2 g.
- Sodium nitrite 9.0 g.
- Methanol 9 ml.
- Water 10 ml.
- Yield 25 g. (85 per cent.).

Snow coloured needles from toluene, m.p.120°.

(e) ∞-Isonitroso-4'-nitropropiophenone:

[Hartung and Foster, J. Am. Pharm. Assoc., 35, 15 (1946); Chem. Abs., 40, 2130 (1946)]

Quantities taken:
- 4'-Nitropropiophenone 18 g.
Sodium nitrite 8 g.
Methanol 3 ml.
Water 10 ml.
Yield 14.5 g. (70 per cent.).

Colourless needles from dilute alcohol, m.p. 133°.

(f) α-Isonitroso-2',4'-dichloropropiophenone:
Quantities taken:
2',4'-Dichloropropiophenone 30.5 g.
Sodium nitrite 9 g.
Methanol 10 ml.
Water 10 ml.
Yield 29.5 g. (85 per cent.)

Colourless plates from dil. alc., m.p. 115-6°.

Solubility: Soluble in alkali, alcohol, benzene, ether and acetone. Insoluble in water.

 Found: N, 6.00; Cl, 30.75. C₈H₆Cl₂NO₂ requires

 N, 6.03; Cl, 30.61 per cent.

(g) α-Isonitroso-3',4'-dichloropropiophenone:
Quantities taken:
3',4'-Dichloropropiophenone 30.5 g.
Methanol 10 ml.
Sodium nitrite 9 g.
Water 10 ml.
Yield 28.5 g. (83 per cent.).

Colourless shining needles from dil. alc., m.p.159°.

Solubility: Soluble in alkali, alcohol, benzene, ether, acetone and chloroform. Insoluble in water.

Found: N, 6.18; Cl, 30.59. C₉H₆Cl₂NO₂ requires
N, 6.03; Cl, 30.61 per cent.

(h) ∞-Isonitroso-2',5'-dichloropropiophenone:

Quantities taken:

- 2',5'-Dichloropropiophenone 30.5 g.
- Sodium nitrite 9 g.
- Methanol 10 ml.
- Water 10 ml.
- Yield 30.5 g. (87 per cent.)

Straw coloured needles from dil. alc., m.p.148°.

Solubility: Soluble in alkali, alcohol, benzene, toluene, ether, acetone and ethyl acetate.

Insoluble in water.

Found: N, 6.15; Cl, 30.77. C₉H₆Cl₂NO₂ requires
N, 6.03; Cl, 30.61 per cent.

3. Phenyl methyl α-diketones of 1-phenyl-1,2-propanediones:

General method of preparation:

In a litre round bottom flask arranged for steam distillation, 30 g. of ∞-isonitrosopropiophenone and 300 g.
of 10-15 per cent sulphuric acid were taken and the mixture was steam distilled until 2-3 litres of the distillate were collected. Sometimes, the distillation was continued till last portion of distillate was practically colourless and did not contain any oily droplets. The heavy oil or solid from the total distillate was separated and the aq. portion extracted with ether. The oil or solid was added to ethereal solution and it was washed with 2 per cent sodium bicarbonate solution. The washings were added to previous aq. layer and the whole bulk was saturated with pure sodium chloride. The mixture was extracted with ether in two or three portions and the combined ethereal solution dried over anhyd. sodium sulphate. The solvent was removed and residue distilled under vacuum in case of liquids. In case of solid, it was purified by crystallising with benzene.

(a) 1-Phenyl-1,2-propanedione :

\[ \text{Hartmann and Roll, Org. Syntheses, Coll. Vol. III, 20 (1955)} \]

Yield 25 g. (55 per cent.) from 50 g. of \( \ominus \)-iso-nitrosopropiophenone. Yellow oil, b.p. 98-100° at 7-8 mm. Hartmann and Roll (loc. cit.) report yield 60 per cent and b.p. 114-16° at 20 mm.
(b) 1-(4'-Methylphenyl)-1,2-propanedione:

Yield 11 g. (60 per cent.) starting with 20 g. of α-isonitroso-4'-methylpropiophenone. Orange coloured oil, b.p. 117-20° at 5-6 mm.

Found: C, 74.13; H, 6.20. \( \text{C}_{10}\text{H}_{10}O_2 \) requires C, 74.08; H, 6.17 per cent.

Semicarbazone:

Colourless tiny needles from dil. alc., m.p. 208° (decomp.).

(c) 1-(4'-Methoxyphenyl)-1,2-propanedione:

Yield 11 g. (60 per cent) starting with 20 g. of α-isonitroso-4'-methoxypropiophenone. Yellow silky needles from ligroin, m.p. 46-7°.

Fusco and Caggianelli, \( \text{Farm. Sci. e. tec. (Favia)}, 2, 125 \) (1948); Chem. Abs., 42, 1741 (1949) report m.p. 47°.

(d) 1-(4'-Chlorophenyl)-1,2-propanedione:

Yield 9.5 g. (50 per cent.) from 20 g. of α-isonitroso-4'-chloropropiophenone. Deep yellow oil, b.p. 140-4° at 20 mm.

Found: Cl, 19.52. \( \text{C}_{9}\text{H}_7\text{ClO}_2 \) requires Cl, 19.45 per cent.

Semicarbazone:

Colourless needles from dil. alc., m.p. 208-9°.
(e) 1-(4'-Nitrophenyl)-1,2-propanedione :

Yield 11 g. (69 per cent) from 20 g. of \( \alpha \)-iso-nitroso-4'-nitropropiophenone. Lemon yellow shining needles from ligroin, m.p.91°.


\( / \text{Found: } \text{N,7.35. Calc. for } \text{C}_{9}\text{H}_{7}\text{NO}_{4} \text{ N,7.25 per cent.} / \)

(f) 1-(2',4'-Dichlorophenyl)-1,2-propanedione :

Yield 7.5 g. (40 per cent.) from 20 g. of \( \alpha \)-iso-nitroso-2',4'-dichloropropiophenone. Orange coloured oil, b.p.142-7° at 10 mm.

\( / \text{Found: Cl,33.03. C}_{9}\text{H}_{6}\text{Cl}_{2}0 \text{ requires Cl,32.72 per cent.} / \)

Semicarbazone :

Colourless tiny needles from methanol, m.p.222-3°.

(g) 1-(3',4'-Dichlorophenyl)-1,2-propanedione :

Yield 7.5 g. (40 per cent) from 20 g. of \( \alpha \)-iso-nitroso-3',4'-dichloropropiophenone. Lemon yellow coloured shining needles from chloroform, m.p.48°.

\( / \text{Found: Cl,32.84. C}_{9}\text{H}_{6}\text{Cl}_{2}0_{2} \text{ requires Cl,32.72 per cent.} / \)

Semicarbazone :

Greyish granules from methanol, m.p.190°.
(h) 1-(2',5'-Dichlorophenyl)-1,2-propanedione :

Yield 7.2 g. (38 per cent) from 20 g. of α-iso-nitroso-2',5'-dichloropropiophenone. Orange coloured oily liquid, b.p. 154-7° at 12 mm. 

Found: Cl 32.68. C₉H₆Cl₂O₂ requires Cl 32.72 per cent.

Semicarbazone :

Colourless shining needles from dil. alc., m.p. 231-2° (decomp.).

4. Phenyl 2-amino-4-thiisoyl ketones or 2-amino-4-benzoylethiooles.

General method of preparation :

5 g. of a phenyl methyl α-diketone was brominated in presence of sun light by adding dropwise the solution of required quantity of bromine in carbon disulphide to the boiling solution of the compound in 50 ml. of carbon disulphide. The mixture was further heated under reflux for about 30 minutes. The solvent was distilled out, residue taken up in ether and excess of bromine was removed by washing the ethereal solution with 2 per cent sodium thiosulphate solution. The ethereal solution was dried over anhyd. sodium sulphate and molecular quantity of powdered thiourea was added to the clear ether solution of the above ω-bromo-α-diketone. Soon, the exothermic
reaction started and the mixture was gently refluxed for about 30 minutes. The residue was filtered, washed with ether and suspended in water to which dil. ammonium hydroxide was added to liberate the free base. The solid was filtered and purified by crystallising with suitable solvent.

They were characterised by preparing the following derivatives described below.

(i) Acetyl derivative:

About 1 g. of a dry compound was taken in a 100 ml. round bottom flask having a condenser with a guard tube. About 10 g. of acetic anhydride were added and the mixture was heated gently under reflux for 30 minutes. The hot reaction mixture was poured into 200 ml. of water. The solid, separated, was filtered out, washed with water and purified by crystallising with suitable solvent.

(ii) Benzoyl derivative:

About 0.5 g. of a compound was dissolved in minimum quantity of acetone taken in a conical flask. About 2 ml. of benzoyl chloride was added and the mixture was well shaken. Then about 10-15 ml. of 10 per cent sodium hydroxide was added and the mixture shaken vigorously. Immediately, about 50 ml. of sodium hydroxide were added to the above mixture and continued the shaking till there was no smell of benzoyl chloride. The solid separated.
was filtered, washed with water and dried. It was purified by crystallising with a suitable solvent.

(iii) Hydrochloride:

About 0.1 g. of a compound was dissolved in large excess of ether and the solution was saturated with dry hydrogen chloride gas. On keeping for some time the crystals separated out. But in case where some compounds could not form hydrochloride by the above method, the compound was taken in boiling water and a few drops of concentrated hydrochloric acid were added to dissolve the substance. On cooling, the crystals separated and were filtered from the solution and air dried.

(iv) Picrate:

The saturated solution of picric acid in alcohol was added to a solution of 0.05 g. of the compound in minimum quantity of ethyl alcohol when the picrate soon separated out. It was filtered, washed with alcohol and dried.

(v) Semicarbazone:

About 0.160 g. of a compound was dissolved in enough methanol. To this warm solution, a slight excess (1 : 1.5 molar proportion) of solution of semicarbazide hydrochloride in minimum quantity of water was added. Then
Some drops of pyridine were added. In some cases sodium acetate was used. In case the solution got turbid, some excess of methanol was added to produce clear solution. The mixture was refluxed for 30 minutes, concentrated, and diluted with water. The solid, separated, was filtered, washed and dried. It was purified by crystallising with a suitable solvent.

(a) Phenyl 2-amino-4-thiazolyl ketone:

Quantities taken:

1-Phenyl-1,2-propanedione 7.4 g.
Bromine 8.1 g.
Thiourea 3.8 g.
Yield 6.7 g. (66 per cent.).

Orange red shining plates from dil. alc., m.p. 161°.

Solubility: Soluble in chloroform, alcohol, warm benzene, and acetone. Sparingly soluble in ether and insoluble in water.

_\text{Found: N, 13.59. C}_{10}H_{10}N_{2}OS requires N, 13.73 per cent.}_

Derivatives:

(i) Acetyl derivative:

Straw coloured shining needles from dil. alc., m.p. 196°.
(ii) Benzoil derivative:

Colourless shining plates from dil. alc., m.p. 180-1°.

\[
\text{Found: } N, 9.12. \text{ requires } N, 9.09 \text{ per cent.}
\]

(iii) Hydrochloride:

Yellowish shining needles from ethyl alcohol, m.p. 99°.

\[
\text{Found: Eq. Wt., 238.6. } C_{10}H_{20}Cl \text{ requires Eq. Wt., 240.5.}
\]

(iv) Picrate:

Yellow shining silky needles from ethyl alcohol, m.p. 217° (decomp.).

(v) Semicarbazone:

Straw coloured shining needles from dil. alcohol, m.p. 220° (decomp.).

\[
\text{Found: } N, 27.00. \text{ requires } N, 26.82 \text{ per cent.}
\]

(b) 4-Methylphenyl 2-amino-4-thiazolyl ketone:

Quantities taken:

\[
\begin{align*}
1-(4'-\text{Methylphenyl})-1,2-\text{propanedione} & : 8 \text{ g.} \\
\text{Bromine} & : 8 \text{ g.} \\
\text{Thiourea} & : 3.8 \text{ g.} \\
\text{Yield} & : 7.5 \text{ g.} \quad (70 \text{ per cent.})
\end{align*}
\]

Light orange coloured shining needles from dil. alc., m.p. 153-4°.
Solubility: Soluble in alcohol, benzene, chloroform and acetone. Sparingly soluble in ether but insoluble in water.

\[
\text{Found: } N, 12.78. \quad C_{11}H_{10}N_2OS \text{ requires } N, 12.84 \text{ per cent.} \]

**Derivatives:**

(i) Acetyl derivative:

Pale yellow shining needles from dil. alc., m.p. 200-1°.

\[
\text{Found: } N, 11.02. \quad C_{13}H_{12}N_2O_3 \text{ requires } N, 10.76 \text{ per cent.} \]

(ii) Benzoyl derivative:

Straw coloured shining needles from methanol, m.p. 161-2°.

\[
\text{Found: } N, 8.59. \quad C_{18}H_{14}N_2O_2S \text{ requires } N, 8.69 \text{ per cent.} \]

(iii) Hydrochloride:

Colourless shining needles from ethyl alcohol, m.p. 215-6° (decomp.).

\[
\text{Found: Eq. Wt., 250.1. } C_{11}H_{11}ClN_2OS \text{ requires Eq. Wt., 254.5.} \]

(iv) Picrate:

Yellow shining tiny needles from ethyl alcohol, m.p. 206-7° (decomp.).

(v) Semicarbazone:

Straw coloured shining needles from dil. alc., m.p. 208° (decomp.).

\[
\text{Found: } N, 24.98. \quad C_{12}H_{13}N_5OS \text{ requires } N, 25.46 \text{ per cent.} \]

(c) 4-Methoxyphenyl 2- amino-4-thiazolyl ketone:

Quantities taken:

1- (4'- Methoxyphenyl)-1,2-propanedione  4.5 g.
Bromine  4.2 g.
Thiourea  2.0 g.
Yield  4.0 g.
(67 per cent.)

Orange coloured shining plates from dil. alcohol, m.p. 155-6°.

Solubility: Soluble in ethyl alcohol, benzene, acetone, chloroform and ethyl acetate. Insoluble in ether and water.

\[
\text{Found: N, 12.03. } \text{C}_{11}\text{H}_{10}\text{N}_{2}\text{O}_{2}\text{S requires N, 11.97 per cent.}
\]

Derivatives:

(i) Acetyl derivative:

Straw coloured shining needles from dil. alc., m.p. 197-8°.

\[
\text{Found: } \text{N, 10.05. } \text{C}_{13}\text{H}_{12}\text{N}_{2}\text{O}_{3}\text{S requires N, 10.15 per cent.}
\]

(ii) Benzoyl derivative:

Colourless shining needles from rectified spirit, m.p. 204-5°.

\[
\text{Found: N, 8.20. } \text{C}_{18}\text{H}_{14}\text{N}_{2}\text{O}_{3}\text{S requires N, 8.28 per cent.}
\]
(iii) Hydrochloride:

Colourless shining needles from ethyl alcohol, 
m.p.222° (decomp.).
\[\text{Found: Eq.Wt., 275.2. } \text{C}_{11}\text{H}_{11}\text{ClN}_2\text{O}_2\text{S requires Eq.Wt., 270.5}.\]

(iv) Picrate:

Yellow tiny needles from ethyl alc., m.p. 206-7°.

(v) Semicarbazone:

Straw coloured shining needles from dil. alcohol, 
m.p.231° (decomp.)
\[\text{Found: N, 23.95. } \text{C}_{12}\text{H}_{13}\text{N}_5\text{O}_2\text{S requires N, 24.05 per cent.}.\]

(d) 4-Chlorophenyl 2-amino-4-thiazolyl ketone:

Quantities taken:
- 1-({4′-Chlorophenyl})-1,2-propanedione 4.5 g.
- Bromine 4.2 g.
- Thiourea 2.0 g.
- Yield 4.0 g.
\[\text{(67 per cent).}\]

Pinkish shining needles from dil. alc., m.p. 158°.

Solubility: Soluble in ethyl alcohol, benzene, ethyl acetate, chloroform and acetone. Sparingly soluble in ether but insoluble in water.
\[\text{Found: N, 11.75; Cl, 14.79. } \text{C}_{10}\text{H}_{7}\text{ClN}_2\text{OS requires } \text{N, 11.74; Cl, 14.88 per cent.}.\]
**Derivatives:**

(i) Acetyl derivative:

Colourless shining needles from dil.alc., m.p. 217°.

\[ \text{Found: N, 9.90; C, 12.54; C}_{12H_{9}}C_{1N_{2}}O_{2}S \text{ requires} \]

\[ \text{N, 9.97; C, 12.66 per cent.} \]

(ii) Benzoyl derivative:

Colourless soft needles from dil.alc., m.p. 203-5°.

\[ \text{Found: N, 8.13; C, 10.47; C}_{17H_{11}}C_{1N_{2}}O_{2}S \text{ requires} \]

\[ \text{N, 8.18; C, 10.36 per cent.} \]

(iii) Hydrochloride:

Straw coloured needles from ethyl alcohol, m.p. 235°.

\[ \text{Found: Eq.Wt., 278.4. C}_{10H_{8}}Cl_{2}N_{2}O_{3} \text{ requires Eq.Wt., 275.} \]

(iv) Picrate:

Yellow shining needles from ethyl alcohol,

m.p. 209° (decomp.).

(v) Semicarbazone:

Colourless tiny needles from dil. alcohol,

m.p. 206-7° (decomp.).

\[ \text{Found: N, 23.89; C, 12.55; C}_{11H_{10}}C_{1N_{5}}O_{3} \text{ requires} \]

\[ \text{N, 23.69; C, 12.01 per cent.} \]

(e) 4-Nitrophenyl 2-amino-4-thiazolyl ketone:
Quantities taken:

1-(4'-Nitrophenyl)-1,2-propanedione 4.8 g.
Bromine 4.2 g.
Thiourea 2.0 g.
Yield 4.5 g. (72% per cent.)

Orange yellow powder from acetone, m.p. 172°.

Solubility: Soluble in pyridine and nitrobenzene on warming, but very sparingly soluble in hot ethyl alcohol, acetone and chloroform.

Insoluble in water.

Found: N, 16.93. \( \text{C}_{10}\text{H}_{7}\text{N}_{3}\text{O}_{3} \) requires N, 16.87 per cent.

**Derivatives:**

(i) Acetyl derivative:

Colourless shining needles from rectified spirit, m.p. 209°.

Found: H, 14.48. \( \text{C}_{12}\text{H}_{9}\text{N}_{3}\text{O}_{3} \) requires H, 14.43 per cent.

(ii) 2,4-Dichlorophenyl 2-amino-4-thiazolyl ketone:

Quantities taken:

1-(2',4'-Dichlorophenyl)-1,2-propanedione 5.0 g.
Bromine 4.0 g.
Thiourea 2.0 g.
Yield 3.0 g. (47% per cent.).

Straw coloured shining plates from rectified spirit, m.p. 204°.
Solubility: Soluble in chloroform, acetone, alcohol and benzene, but sparingly soluble in ether. Insoluble in water.

\[ \text{Found: } N, 10.36; Cl, 26.22. \text{ } \text{C}_{10} \text{H}_{4} \text{Cl}_{2} \text{N}_{2} \text{OS requires } N, 10.26; \text{ Cl}, 26.01 \text{ per cent. } \]

**Derivatives:**

(i) Acetyl derivative:

Colourless hexagonal plates from dil. alc., m.p. 179°.

\[ \text{Found: } N, 8.85; \text{ Cl}, 22.81. \text{ } \text{C}_{12} \text{H}_{8} \text{Cl}_{2} \text{N}_{2} \text{O}_{2} \text{S requires } N, 8.89; \text{ Cl}, 22.54 \text{ per cent. } \]

(ii) Benzoyl derivative:

Colourless shining needles from dil. alc., m.p. 151°.

\[ \text{Found: } N, 7.50; \text{ Cl}, 18.58. \text{ } \text{C}_{17} \text{H}_{10} \text{Cl}_{2} \text{N}_{2} \text{O}_{2} \text{S requires } N, 7.43; \text{ Cl}, 18.54 \text{ per cent. } \]

(iii) Hydrochloride:


\[ \text{Found: Eq. Wt., 310.3. } \text{C}_{10} \text{H}_{7} \text{Cl}_{3} \text{N}_{2} \text{OS requires Eq. Wt., 309.5.} \]

(iv) Picrate:

Yellow shining needles from ethyl alc., m.p. 218°.

(v) Semicarbazone:

Colourless shining needles from methanol, m.p. 198° (decomp.).

\[ \text{Found: } N, 20.54; \text{ Cl}, 22.04. \text{ } \text{C}_{11} \text{H}_{9} \text{Cl}_{2} \text{N}_{2} \text{OS requires } N, 21.22; \text{ Cl}, 21.52 \text{ per cent. } \]
(g) 3,4-Dichlorophenyl 2-amino-4-thiazolyl ketone:

Quantities taken:

1-(3',4'-Dichlorophenyl)-1,2-propanedione 5.0 g.
Bromine 4.0 g.
Thiourea 2.0 g.
Yield 3.2 g. (50 per cent.).

Colourless shining needles from benzene, m.p. 198-9°.

Solubility: Soluble in ethyl alcohol, benzene, pyridine, chloroform, ethyl acetate, and acetone.
Sparingly soluble in ether but insoluble in water.

Found: N, 10.18; Cl, 25.89; C₁₀H₆Cl₂N₂O₅S requires
N, 10.26; Cl, 26.01 per cent. J

Derivatives:

(i) Acetyl derivative:

Straw coloured shining needles from dil. alcohol, m.p. 218°.

Found: N, 9.06; Cl, 22.50. C₁₂H₁₀Cl₂N₂O₅S requires
N, 8.89; Cl, 22.54 per cent. J

(ii) Benzoyl derivative:

Colourless tiny needles from rectified spirit, m.p. 214-6°.

Found: N, 7.28; Cl, 19.03. C₁₇H₁₀Cl₂N₂O₂S requires
N, 7.43; Cl, 18.84 per cent. J
(iii) Hydrochloride:

Colourless needles from ethyl alcohol, m.p. 216°.

\[ \text{Found: Eq. Wt., 305.5. } C_{10}H_7Cl_3N_2O_3 \text{ required Eq. Wt., 309.5.} \]

(iv) Picrate:

Yellow tiny shining needles from ethyl alc., m.p. 191°.

(v) Semicarbazone:

Colourless shining needles from rectified spirit, m.p. 175°.

\[ \text{Found: N, 21.15; Cl, 22.10. } C_{11}H_9Cl_2N_5O_5 \text{ requires} \]

N, 21.22; Cl, 21.52 per cent.

(h) 2,5-Dichlorophenyl 2-amino-4-thiazolyl ketone:

Quantities taken:
- 1-(2',5'-Dichlorophenyl)-1,2-propanedione 5.0 g.
- Bromine 4.0 g.
- Thiourea 2.0 g.
- Yield 3.0 g. (47 per cent.).

Straw coloured shining needles from dil. alc., m.p. 168-9°.

Solubility: Soluble in ethyl alcohol, methanol, benzene, chloroform, acetone and ethyl acetate.
Sparingly soluble in ether but insoluble in water.

\[ \text{Found: N, 10.35; Cl, 26.10. } C_{10}H_6Cl_2N_2O_3 \text{ requires} \]

N, 10.26; Cl, 26.01 per cent.
Derivatives:

(i) Acetyl derivative:

Colourless shining needles from dil. alc., m.p. 190-1°.

Found: N, 6.59; Cl, 22.88. \( \text{C}_{12}\text{H}_8\text{Cl}_2\text{N}_2\text{O}_2\text{S} \) requires

N, 6.89; Cl, 22.54. per cent.

(ii) Benzoyl derivative:

Straw coloured shining plates from rectified spirit, m.p. 192-3°.

Found: N, 7.51; Cl, 18.90. \( \text{C}_{17}\text{H}_{10}\text{Cl}_2\text{N}_2\text{O}_2\text{S} \) requires

N, 7.43; Cl, 18.84 per cent.

(iii) Hydrochloride:

Colourless shining tiny needles from ethyl alcohol, m.p. 203°.

Found: Eq.Wt., 313.9. \( \text{C}_{10}\text{H}_7\text{Cl}_3\text{N}_2\text{OS} \) requires Eq.Wt., 309.5.

(iv) Picrate:

Yellow tiny needles from ethyl alc., m.p. 202-3°.

(v) Semicarbazone:

Straw coloured shining needles from dil. alcohol, m.p. 204° (decomp.).

Found: N, 21.06; Cl, 21.48. \( \text{C}_{11}\text{H}_9\text{Cl}_2\text{N}_5\text{OS} \) requires

N, 21.22; Cl, 21.52 per cent.
5. Phenyl 2-acetamido-5-chloromercuri-4-thiazolyl ketones:

**General method of preparation:**

To a hot solution of 0.5 g. of phenyl 2-acetamido-4-thiazolyl ketone in 20 ml. of ethyl alcohol was added an aq. solution containing 0.7 g. of mercuric chloride and 1.2 g. of sodium acetate, with shaking. The mixture was refluxed on water bath for an hour, cooled and filtered. The residue was washed with boiling water, then with 20 ml. of hot alcohol and finally with 20 ml. of ether. The residue was dried in air and was purified by dissolving in gl. acetic acid and reprecipitating on dilution of the clear solution with water. Most of the chloromercuri compounds were insoluble in common organic solvents but soluble in gl. acetic acid and mineral acids.

The various compounds are described in the following table.
Phenyl 2-acetamido-5-chloromercury-4-thiazolyl ketones.

\[
\text{Hg}_2\text{Cl}_2\text{N}=\text{NH-CO-CH}_3
\]

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<tbody>
<tr>
<td>1.</td>
<td>Nil, ( \text{C}_{12}\text{H}_9\text{ClHgN}_2\text{O}_2\text{S} )</td>
<td>White amorphous powder, m.p. 274°. Yield 82 per cent.</td>
<td>5.70</td>
<td>5.83</td>
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<td>2.</td>
<td>4-Methyl, ( \text{C}<em>{13}\text{H}</em>{11}\text{ClHgN}_2\text{O}_2\text{S} )</td>
<td>Greyish white amorphous powder, m.p. 286°. Yield 85 per cent.</td>
<td>5.72</td>
<td>5.66</td>
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<tr>
<td>3.</td>
<td>4-Methoxy, ( \text{C}<em>{13}\text{H}</em>{11}\text{ClHgN}_2\text{O}_3\text{S} )</td>
<td>Ash coloured white powdery mass, m.p. 284° (blackens). Yield 85 per cent.</td>
<td>5.40</td>
<td>5.43</td>
</tr>
<tr>
<td>4.</td>
<td>4-Chloro, ( \text{C}_{12}\text{H}_8\text{Cl}_2\text{HgN}_2\text{O}_2\text{S} )</td>
<td>Yellowish amorphous powder, m.p. 289°. Yield 80 per cent.</td>
<td>5.34</td>
<td>5.44</td>
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<td>1</td>
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<tr>
<td>5. 2,4-Dichloro.</td>
<td></td>
<td>Greyish white powdery mass, m.p. 255 ° (blackens). Yield 78 per cent.</td>
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<td>4.98</td>
</tr>
<tr>
<td></td>
<td>C_{12}H_7Cl_2HgN_2O_2S.</td>
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<tr>
<td>6. 3,4-Dichloro.</td>
<td></td>
<td>White amorphous powder, blackens at 272 ° but melts at 282 °. Yield 87 per cent.</td>
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<td>5.11</td>
</tr>
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<td></td>
<td>C_{12}H_7Cl_3HgN_2O_2S.</td>
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<tr>
<td>7. 2,5-Dichloro.</td>
<td></td>
<td>White amorphous powder, m.p. 255 ° (decomp.). Yield 80 per cent.</td>
<td></td>
<td>5.16</td>
</tr>
<tr>
<td></td>
<td>C_{12}H_7Cl_3HgN_2O_2S.</td>
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</table>

6. Phenyl 2-acetamido-5-bromo-4-thiazolyl ketones:

General method of preparation:

To 0.5 g. of phenyl 2-acetamido-5-chloromercuri 4-thiazolyl ketone was added 15 ml. of methanol saturated with sodium bromide. Then a few drops of bromine were added and heated on a water bath with shaking till the mixture turned into clear solution. After 15 minutes, some sodium
sulphite was added to remove excess of bromine. The mixture was further heated under reflux for another 30 minutes and filtered when hot. The clear filtrate was concentrated till it was turbid. The solid separated was filtered and crystallised with suitable solvent.

(a) Phenyl 2-acetamido-5-bromo-4-thiazolyl ketone:

Straw coloured shining needles from methanol, m.p. 199°. Yield 45 per cent.

Solubility: Soluble in alcohol, benzene, acetone, dioxan and chloroform. Insoluble in water.

\[ \text{Found: } N, 8.50; C_{12}H_9BrN_2O_2S \text{ requires } N, 8.62 \text{ per cent.} \]

(b) 4-Methylphenyl 2-acetamido-5-bromo-4-thiazolyl ketone:

Pale brown shining plates from methanol, m.p. 169°. Yield 40 per cent.

Solubility: Soluble in alcohol, benzene, acetone, dioxan and chloroform. Insoluble in water.

\[ \text{Found: } N, 8.10; C_{13}H_{11}BrN_2O_2S \text{ requires } N, 8.26 \text{ per cent.} \]

(c) 4-Methoxyphenyl 2-acetamido-5-bromo-4-thiazolyl ketone:

Greyish granules from alcohol-ligroin mixture, m.p. 177-8°. Yield 42 per cent.

Solubility: Soluble in alcohol, acetone, benzene, ether, chloroform and dioxan. Insoluble in water.
(d) 4-Chlorophenyl 2-acetamido-5-bromo-4-thiazolyl ketone:
Pale yellow shining plates from benzene-alcohol mixture, m.p.178°. Yield 40 per cent.
Solubility: Soluble in alcohol, acetone, chloroform, dioxan and benzene. Insoluble in water.

(f) 2,4-Dichlorophenyl 2-acetamido-5-bromo-4-thiazolyl ketone:
Light orange coloured shining plates from benzene-ligroin mixture, m.p.207°. Yield 38 per cent.
Solubility: Soluble in benzene, alcohol, acetone, dioxan, and chloroform. Insoluble in water.

(g) 3,4-Dichlorophenyl 2-acetamido-5-bromo-4-thiazolyl ketone:
Yellow shining plates from benzene-alcohol mixture, m.p.209°. Yield 35 per cent.
Solubility: Soluble in alcohol, acetone, dioxan, benzene and chloroform. Insoluble in water.
(h) 2,5-Dichlorophenyl 2-acetamido-5-bromo-4-thiasolyl ketone:

Pale yellow shining needles from dil. alcohol,
m.p. 200°. Yield 40 per cent.

Solubility: Soluble in alcohol, acetone, chloroform,
dioxan, benzene and ethyl acetate. Insoluble in water.

Found: N, 6.95. C_{12}H_{7}BrCl_{2}N_{2}O_{3} requires N, 7.10 per cent.