THEORETICAL PART I
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The purpose of synthesising various substituted thiophenols having substituents like dichloro, bromochloro methylbromo, methoxybromo, chloro, dichloroalkoxy and n-alkyl is indicated in the body of the introductory part. These thiophenols have been prepared during the present investigation either from Leuckart reaction on anilines or from reduction of benzenesulphonyl chlorides.

A. Leuckart reaction :-

This is the only convenient method for the preparation of substituted thiophenols starting from anilines which are easily accessible.

The method involves -

(i) Preparation of diazonium salts,

(ii) Coupling of the diazonium salt with potassium ethylxanthate followed by hydrolysis of the complex obtained and,

(iii) Isolation of the thiophenol.

(i) Diazonium salts.

For the diazotisation of arylamines a solution of sodium nitrite is added to a cold solution of arylamine...
dissolved in aqueous mineral acids usually hydrochloric acid. However, James R. Cox et al., \textit{J. Org. Chem.}, 25, 1083 (1960) recommends dil. sulphuric acid for sterically hindered anilines like 2,6-dimethylaniline.

(ii) Coupling.

Leuckart \textit{J. prakt. Chem.}, 41, 186 (1890) studied the reaction between aryldiazonium chloride and potassium ethylxanthate. According to him the course of the reaction is as follows.

\[
\begin{align*}
\text{II} & \quad \text{I} \\
\begin{array}{c}
\text{N} \equiv \text{N} - \text{Cl} \\
\text{S} \quad \text{S} \quad \text{S} \\
\text{K} \quad \text{S} \quad \text{C} - \text{O}_2\text{H}_5
\end{array} & \quad - \text{N}_2 \\
\begin{array}{c}
\text{S} \quad \text{C} - \text{O}_2\text{H}_5
\end{array}
\end{align*}
\]

In order to avoid the accumulation of the complex (I) which decomposes between 50-60° with evolution of nitrogen, the addition of diazonium salt to potassium ethylxanthate was effected between 60-70°. It was assumed that aryl ethylxanthate was the only product obtained on coupling. Recently Cox et al., (loc. cit.) analysed the complex fully and showed that the complex contains considerable
amount of diaryl dithiolcarbonate besides aryl ethylxanthate.

\[
\text{ArN}_2\text{Cl} + \text{K}_2\text{SCS.C}_2\text{H}_5 \rightarrow \text{II} + \text{Ar-S-C-S-Ar}
\]

Exhaustive study in this regard has been made by him with anilines having sterically hindering groups like 2,6-di-methylaniline, electron attracting groups like NO\(_2\) and electron donating groups like \(\text{OCH}_3\). The yields of aryl ethylxanthate (II) and diaryl dithiolcarbonate (III) obtained in the case of various anilines studied by him are summarised in the following table.

<table>
<thead>
<tr>
<th></th>
<th>(ArS)(_2)CO</th>
<th>ArS.J3.C(_2)H(_5)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yield per cent</td>
<td>Yield per cent</td>
</tr>
<tr>
<td>(a) Aniline</td>
<td>30</td>
<td>50</td>
</tr>
<tr>
<td>(b) 2-Methylaniline</td>
<td>50</td>
<td>42</td>
</tr>
<tr>
<td>(c) 2,6-Dimethylaniline</td>
<td>62</td>
<td>23</td>
</tr>
<tr>
<td>(d) 4-Nitroaniline</td>
<td>27</td>
<td>42</td>
</tr>
<tr>
<td>(e) 4-Methoxyaniline</td>
<td>20</td>
<td>36</td>
</tr>
</tbody>
</table>

From the above table it can be concluded that the formation of diaryl dithiolcarbonate predominates over aryl ethylxanthate in case of sterically hindered anilines. The yield of aryl ethylxanthate is highest in the case of unsubstituted aniline.
pH control:

It seems that exact control of pH during coupling is not a significant factor, as coupling can be carried in both alkaline and neutral mediums. Examples follow.

Bordwell and Andersen \( \textit{J. Am. Chem. Soc.}, 75, 6019-22 \) (1953) coupled m-bromobenzenediazonium chloride and m-nitrobenzenediazonium chloride using a mixture of potassium ethylxanthate and sodium carbonate. They pointed out that alkaline medium should be maintained throughout the coupling reaction.

However, Greenwood and Stevenson \( \textit{J. Chem. Soc.}, 1516 \) (1953), Müller and Read \( \textit{J. Am. Chem. Soc.}, 55, 1224 \) (1933) and Suter and Hansen \( \textit{J. Am. Chem. Soc.}, 54, 4102 \) (1932) neutralised the diazonium chloride solution by a buffer using sodium acetate prior to coupling with potassium ethylxanthate. These views were confirmed recently by Cox et al., (loc.cit.) who employed both alkaline and perfectly neutral mediums during coupling reactions.

Hydrolysis of the complex.

This can be very well accomplished by treating the complex with,

(a) Water and sodium hydroxide

P.F. Wiley \( \textit{J. Org. Chem.}, 16, 812 \) (1951) and
The thiophenols are susceptible to air oxidation especially in alkaline medium. Hence during hydrolysis care should be taken to prevent the formation of disulphide which can be achieved by

1) Carrying the hydrolysis in an atmosphere of nitrogen as recommended by Bordwell and Andersen (loc.cit.) or by

2) Addition of glucose in presence of alcohol which creates a reducing medium as suggested by Suter and Hansen (loc.cit.).

Cox et al., (loc.cit.) showed that diaryl dithiolcarbonate could be converted into diaryl disulphide by refluxing with alcoholic potassium hydroxide for four hours, followed by addition of bromine till the colour just persisted. Probably the action of bromine is to convert thiophenol formed by the hydrolysis of diaryl dithiolcarbonate to disulphide.

\[
\begin{align*}
0 && \text{Ar-S-C-S-Ar} \xrightarrow{\text{NaOH}} & \text{ArSK} \xrightarrow{\text{Br}} & (\text{ArS})_2 \\
\end{align*}
\]

In the light of these observations it is advisable to employ
alcoholic sodium or potassium hydroxide and glucose during hydrolysis. The hydrolysis period should be sufficiently long, especially in the case of sterically hindered thio-phenols, since it has been pointed out previously that yield of diaryl dithiolcarbonate is more in the case of sterically hindered anilines.

(iii) Isolation:

The free thiophenols can be obtained by acidification of the hydrolysed product using a mineral acid. However, it has been pointed out in many cases that the formation of disulphide is inevitable even in spite of the above precautions taken during hydrolysis. But the disulphide can be converted easily to thiophenol by the action of zinc dust and mineral acid like hydrochloric or sulphuric acid. Suter and Hansen (loc.cit.) obtained p-methoxy and p-ethoxythiophenols in 70-76 per cent yield by reduction of hydrolysed product, while Bordwell and Andersen (loc.cit.) have reported only 40 per cent yield, for m-bromothiophenol when it was isolated as such without reduction. The free thiophenols can be obtained by subjecting the reaction mixture to steam distillation or by extraction with solvents like ether, benzene and chloroform etc.
Bearing all the above facts in mind the following conditions have been observed so as to get the maximum yields of various thiophenols prepared in the present work.

(i) The free acid present in diazonium salt was neutralised using enough sodium acetate.

(ii) Coupling of the diazonium chloride with potassium ethylxanthate was carried out with stirring between 70-5°.

(iii) Hydrolysis was carried out in most cases for 10-20 hours employing glucose and alcoholic potassium hydroxide and

(iv) The reduction was effected by zinc and sulphuric acid prior to isolation of thiophenol with benzene.

Various thiophenols prepared by employing this method are described in Table No. I.

The yields of thiophenols for sterically hindered anilines are low by xanthate hydrolysis method because the formation of diaryl dithiolcarbonate is more in preference to aryl ethylxanthate. It was shown by Cox et al., (loc. cit.) that diaryl dithiolcarbonate could be reduced to thiophenols by employing lithium aluminium hydride. Hence, for sterically hindered thiophenols it is advisable to carry out the reduction with lithium aluminium hydride. 2,6-Dimethylthiophenol was prepared in 84 per cent yield

B. Thiophenols from arylsulphonyl chlorides.

The method involves

(a) Preparation of arylsulphonyl chlorides and

(b) Reduction of sulphonyl chlorides to thiophenols.

Arylsulphonyl chlorides.

These are generally prepared by the action of chlorosulphonic acid, though reagents like phosphorus pentachloride upon alkali sulphonate and chlorine in water solution on sulphinates can be used.

The action of chlorosulphonic acid, is either for introducing sulphonic acid \( (SO_3H) \) group or chlorosulphonyl group. Two standard procedures have been devised for chlorosulphonation. The first method consists in carrying chlorosulphonation in chloroform solution, while the second method uses no solvent. However, both methods employ a relatively large excess of chlorosulphonic acid in order to convert the intermediate sulphonic acid formed, to corresponding sulphonyl chloride, as completely as possible.

\[
\text{ArH} + \text{SO}_3\text{HCl} \rightarrow \text{ArSO}_3\text{H} + \text{HCl}
\]

\[
\text{ArSO}_3\text{H} + \text{SO}_3\text{HCl} \rightarrow \text{ArSO}_2\text{Cl} + \text{H}_2\text{SO}_4
\]
In absence of solvent, sulphone formation occurs to a varying extent as side reaction has been observed by Huntress and Garten (/J. Am. Chem. Soc., 62, 511 (1940)/ during chlorosulphonation of fluorobenzene, chlorobenzene, iodobenzene, o-dichlorobenzene, and o-dibromobenzene by the action of chlorosulphonic acid at 50° in absence of solvent. Hence sulphonyl chlorides are usually prepared by the action of chlorosulphonic acid in presence of chloroform.

During the present work 3-bromo-4-methoxybenzene sulphonyl chloride and 3-bromo-6-methoxybenzenesulphonyl chloride have been prepared by the action of chlorosulphonic acid on o- and p-bromoanisoles dissolved in chloroform at room temperature.

**Reduction of sulphonyl chlorides.**

\[
\text{RSO}_2\text{Cl} + \text{H} \rightarrow \text{RSH}
\]

The reduction of arylsulphonyl chlorides with metals in alkaline or neutral solutions e.g., calcium in aqueous alkali as suggested by P.T.Cleve (/Ber., 12, 2180 (1886)/) and zinc dust in water or alcohol employed by W.Palmaer (/Ber., 21, 3263 (1888)/) yields sulphinates. Sodium or potassium in toluene converts p-tolylsulphonyl chloride to disulphone (/C.M.Suter, Organic Chemistry of.../
Sulphur, p.498 (1944). Hence with mild reducing agents, the reduction of sulphonyl chloride stops at the sulphonate stage. However, sulphonyl chlorides can be reduced completely to thiophenols by using drastic reducing agents using metal and mineral acids like hydrochloric acid or sulphuric acid as can be seen from the following examples.

1. Zinc or iron in acetic acid when employed by Werner Heffter (Ber., 22, 2261 (1895)) to reduce benzenesulphonyl chloride converted to metal sulphinate, but the presence of hydrochloric acid or sulphuric acid zinc effected complete reduction to thiophenol (Werner, I nn., 321, 274 (1902)).

2. Tin forms tin complex with thiophenols as observed by Archer and Suter (J. Am. Chem. Soc., 74, 4307 (1952)) during reduction of 2,5-dichlorobenzenesulphonyl chloride with tin and hydrochloric acid. When they isolated the thiophenol from acid solution prior to steam distillation they obtained tin tetra-(2,5-dichlorothiophenolate) together with 2,5-dichlorothiophenol.

3. Hansch and Blondon (J. Am. Chem. Soc., 70, 1561 (1948)) prepared o-ethylthiophenol in 68 per cent yield and o-n-propylbenzenethiol in 76 per cent yield by reduction of corresponding sulphonyl chloride with zinc and sulphuric acid. Similarly Gilman and Broadbent (J. Am. Chem. Soc., 69,
prepared 4-isopropylthiophenol in 63.5 per cent yield by reduction of 4-isopropylbenzenesulphonyl chloride using zinc dust and sulphuric acid.

During the present work 3-bromo-4-methoxybenzenesulphonyl chloride and 3-bromo-6-methoxybenzenesulphonyl chloride have been reduced using zinc and dilute sulphuric acid to get the corresponding thiophenols in 70 and 68 per cent respectively.

The above two thiophenols are described in Table No.I.

The use of lithium aluminium hydride for reduction of aliphatic and aromatic sulphonyl chlorides was first realised by Marvel and Caesar (/J.Am.Chem.Soc., 72, 1033 (1950)). They prepared p-thiocresol by reducing p-methylbenzenesulphonyl chloride with this reagent.
\[
2RSO_2Cl + 3\text{LiAlH}_4 \rightarrow \text{LiAlCl}_2(SR)_2 + 6\text{H}_2 + 2\text{LiAlO}_2
\]

With this reagent, Strating and Backer \(^7\) \textit{Rec.trav.chim.}, 62, 638 (1950); \textit{Chem.Abs.}, \( ^4 \text{44}, 7222 \) (1950) \(^7\) have reported 76 per cent yield for p-tert.butylthiophenol.

C. \textbf{Miscellaneous methods:}

Though the above two methods have got general applicability for the preparation of thiophenols, they are not suitable in some instances when thiophenols having desired substituents at particular positions are to be synthesised. So the following are some of the examples for the preparation of such thiophenols.

(a) \textbf{By the action of thiourea or metalhydrosulphide on active halides.}

Thiourea reacts in presence of abs. alcohol with active heterocyclic or aromatic halides to form isothio-uronium salts which on alkaline hydrolysis followed by acidification yield mercaptans. e.g., Phillips and Shapiro \(^6\) \textit{J.Chem.Soc.}, 584 (1942) \(^7\) prepared 2-mercapto-5-nitropyridine by reacting 2-chloro-5-nitropyridine with thiourea and subsequent treatment with ammonia. Price and Stacy \( ^6 \text{68}, 499 \) (1946) \(^7\) prepared p-nitrothiophenol in 16-22 per cent yield by refluxing p-chloro-nitrobenzene in alcohol and thiourea. The thiol compound
was obtained by adding sodium hydroxide and acidifying the filtrate with dil. hydrochloric acid. John R. Thirtle \( {/\text{J. Am.Chem.Soc.}, 68, 342 (1946) } \) prepared 2-mercaptopyridine in 87 per cent yield by the action of potassium hydrosulphide in propylene glycol on 2-bromopyridine at 175°.  

(b) **By the action of sulphur on organometallic reagents.**

\[
\text{ArLi} \xrightarrow{S} \text{ArSLi} \xrightarrow{\text{H}_2\text{O}} \text{ArSH} \xrightarrow{\text{H}^+} \text{ArSH}
\]

Phenyllithium and p-dimethylaminophenyllithium react with sulphur to give a complex which on hydrolysis with dil. hydrochloric acid yield corresponding thiophenols. \( {/B.R.Baker \text{ et al., J.Org.Chem., 12, 171 (1947) } \) F.G. Bordwell et al., \( {/J.Am.Chem.Soc., 76, 1082 (1954) } \) prepared thiophenol by reacting propylene sulphide with phenyllithium to yield RS(CH\(_2\))\(_3\)Li and subsequent reduction with lithium aluminium hydride.

(c) **Action of phosphorous sulphides on phenols.**

Lydia Monti and Gian Gualberto gallo \( {/Gazz.chim. ital, 83, 319-26 (1953); Chem.Abs., 48, 12111 (1954) } \) prepared 2- and 4-mercaptoquinolines by the action of phosphorous pentasulphide on 2- and 4-hydroxyquinolines and Klingsberg and Domenick papa \( {/J.Am.Chem.Soc., 73, 4988 (1951) } \) prepared 2-mercapto-3,5-diiodopyridine by the action of phosphorous pentasulphide on 2-hydroxy-3,5-diiodopyridine.
(d) By Cleavage of 2,4-dinitrophenyl sulphide.

Kharasch and Swidler /J.Org.Chem., 19, 1704 (1954) devised a novel method for preparing thiophenols. 2,4-Dinitrosulphenyl chloride was reacted with an aromatic substance to yield corresponding aryl 2,4-dinitrophenyl sulphide, which was cleaved by alkali and acidified to yield desired thiophenols. By this method thiophenol (80 per cent), p-thiocresol (80 per cent), p-xenylthiol (70 per cent), p-bromothiophenol (79 per cent) and p-chlorothiophenol (76 per cent) were obtained.

(e) By alkylating thiophenols in presence of aluminium chloride.

Kenneth L.Kreuz. U.S. 2,753,378 (1956 July) prepared 2-methyl-4-tert-butylthiophenol by alkylating 2-methylthiophenol with tert-butyl alcohol in presence of petroleum ether and aluminium chloride. Similarly with thiophenol, 4-tert-butylthiophenol was obtained.

(f) By cleaving the Herz compound.

Farrington and Warburton /Australian J.Chem., 8, 545-9 (1955); Chem.Abs., 50, 10102 (1956) prepared 2-amino-5-chlorothiophenol, by reacting p-chloroaniline with $S_2Cl_2$ and treating the Herz compound so formed, with sodium hydroxide and sodium hydrosulphite.
<table>
<thead>
<tr>
<th>S.No.</th>
<th>Name of the compound</th>
<th>Yield per cent</th>
<th>Properties</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>2,3-Dichlorothiophenol</td>
<td>65</td>
<td>Colourless thick liquid, b.p. 108-10° at 7-8 mm., solidifies to colourless needles, m.p. 58-9°.</td>
</tr>
<tr>
<td></td>
<td>Lead salt</td>
<td></td>
<td>Yellow powder, does not melt up to 282°</td>
</tr>
<tr>
<td></td>
<td>Mercury salt</td>
<td></td>
<td>Colourless powder, m.p. 235°.</td>
</tr>
<tr>
<td>2.</td>
<td>2-Bromo-4-methylthiophenol</td>
<td>70</td>
<td>Colourless liquid, b.p. 103-4° at 5 mm., n\text{D}^{25} 1.6148.</td>
</tr>
<tr>
<td></td>
<td>Lead salt</td>
<td></td>
<td>Yellow powder, blackens at 235°.</td>
</tr>
<tr>
<td></td>
<td>Mercury salt</td>
<td></td>
<td>Colourless powder, m.p. 218-19°.</td>
</tr>
<tr>
<td>3.</td>
<td>2-Methyl-4-bromothiophenol</td>
<td>62</td>
<td>Colourless liquid, b.p. 114° at 4-5 mm., n\text{D}^{25} 1.6185.</td>
</tr>
<tr>
<td></td>
<td>Lead salt</td>
<td></td>
<td>Yellow powder, does not melt up to 260°.</td>
</tr>
<tr>
<td></td>
<td>Mercury salt</td>
<td></td>
<td>Colourless powder, decom. at 184°.</td>
</tr>
<tr>
<td></td>
<td>Chemical Formula</td>
<td>Properties</td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>----------------------</td>
<td>---------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>3-Chloro-4-bromo-thiophenol</td>
<td>Colourless liquid, b.p. 122-4°C at 3-4 mm., solidifies to colourless solid, m.p. 40-2°C. Yellow powder, blackens at 169°C. Colourless powder, does not melt up to 270°C.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lead salt</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mercury salt</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>2-Bromo-5-chloro-thiophenol</td>
<td>Colourless liquid, b.p. 104-5°C at 5 mm., solidifies on keeping. Yellow powder, does not melt up to 270°C (blackens at 243°C). Colourless powder, does not melt up to 270°C.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lead salt</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mercury salt</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>p-n-Butylthiophenol</td>
<td>Colourless liquid, b.p. 100-3°C at 3-4 mm., nD^25 1.5400. Colourless powdery mass, blackens at 250°C.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mercury salt</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>o-n-Butylthiophenol</td>
<td>Colourless liquid, b.p. 97-8°C at 3-4 mm., nD^27 1.5420. Colourless powder, decomposes at 145°C.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>8. 2-Chloro-4-methoxy thiophenol</td>
<td></td>
<td>48 Colourless liquid, b.p.121-24° at 4-5 mm., n_D^25 1.5948.</td>
</tr>
<tr>
<td></td>
<td>Lead salt</td>
<td></td>
<td>Yellow powder, m.p. 240° (shrinks at 210°).</td>
</tr>
<tr>
<td></td>
<td>Mercury salt</td>
<td></td>
<td>Colourless powder, does not melt up to 310° (blackens at 270°).</td>
</tr>
<tr>
<td></td>
<td>9. 2,5-Dichloro-4-methoxythiophenol</td>
<td></td>
<td>Colourless liquid, b.p. 136-8° at 7 mm. Solidifying to colourless tiny shining needles.</td>
</tr>
<tr>
<td></td>
<td>Lead salt</td>
<td></td>
<td>Yellow powder, blackens at 255°.</td>
</tr>
<tr>
<td></td>
<td>Mercury salt</td>
<td></td>
<td>Colourless powder, blackens at 242°.</td>
</tr>
<tr>
<td></td>
<td>10. 2,6-Dichloro-4-methoxythiophenol</td>
<td></td>
<td>Colourless liquid, b.p. 136-9° at 5 mm., n_D^25 1.6030. Solidifies after keeping.</td>
</tr>
<tr>
<td></td>
<td>Lead salt</td>
<td></td>
<td>Yellow powder, blackens at 240°.</td>
</tr>
<tr>
<td></td>
<td>11. 2-Chloro-4-ethoxy thiophenol</td>
<td></td>
<td>Colourless liquid, b.p. 123-24° at 5 mm., n_D^27 1.5790.</td>
</tr>
<tr>
<td></td>
<td>Lead salt</td>
<td></td>
<td>Yellow powder, does not melt up to 272°.</td>
</tr>
</tbody>
</table>
12. 3-Chloro-4-(n-butoxy)-thiophenol

Mercury salt

13. 3-Bromo-4-methoxy-thiophenol

Lead salt

Mercury salt

14. 3-Bromo-6-methoxy-thiophenol

Lead salt

---

Pale yellow liquid, b.p. 137-9° at 5 mm., n_D^25 1.5555.

Colourless powder, m.p. 134-5°.

Colourless liquid, b.p. 165-8° at 25 mm., n_D^24 1.6295.

Orange powder from alcohol, m.p. 170°.

Colourless powder from alcohol, m.p. 230°.

Colourless liquid, b.p. 156° at 20 mm.
Solidifying to colourless needles, m.p. 66°.

Colourless amorphous powder from alcohol, blackens at 190°.