CHAPTER 5

Intramolecular Cyclisations of

2-Nitrophenyl Aryl thioethers upon Protonation

In Mass Spectrometry
5.1. Scope

Cyclisation reactions have been fascinating to researchers in organic chemistry in designing the synthesis of heterocyclic molecules. Lewis acids are also known to catalyze such cyclisation reactions [1-3]. Analogous to these reactions, aromatic nitro compounds can also undergo intramolecular cyclisations in presence of strong acids. This is possible only if the nitro group can be protonated and can participate as an electrophile in cyclisation reactions. The acid catalyzed cyclisation reactions of 4’-chloro-2-nitro-N-phenyl aniline [4] and β-Nitro substituted Meso- Tetraphenylporphyrins [5-7], have been reported.

We have detailed in chapter three of this thesis, a novel cyclisation of 2-nitrophenyl phenyl ether initiated by the protonation of nitro group followed by fragmentations to afford heterocyclic ions. We have also established in the previous chapter of this thesis that a similar electrophilic cyclisation of 2-nitro-N-phenyl aniline takes place in a mass spectrometer upon protonation. The cyclic intermediate formed eliminates H₂O and OH radical to afford heterocyclic fragment ions. Although mass spectrometric rearrangements usually involve odd-electron ions, these studies illustrate that similar rearrangements are possible for even-electron ions as well. This also demonstrate that these type of gas-phase cyclisations take place even in low energy ionisation processes like ESI and that upon protonation, nitro group can become an electrophile to bring about cyclisation reactions in the gas-phase.

Moreover, the [M-SO₂]⁺ fragment ion in the EI mass spectrum of 2-nitrophenyl 4-tolyl sulphide was proposed to be formed [8] as a result of double oxygen transfer from the nitro group to the sulphur atom. The expulsion of a hydrogen radical from the [M-SO₂]⁺ ion affords a cyclic structure, which forms the base peak in the mass spectrum.
An EI mass spectrometric investigation of 2-NO$_2$-C$_6$H$_4$-Z-C$_6$H$_4$Me (Z = SO, Se) gave examples of oxygen transfers to SO and Se functions [9]. The EI induced oxygen transfers from the nitro group in 2-nitrophenyl-2-pyridyl sulphide [10], S- Nitrophenyl substituted 2,5-dimercapto-1, 3,4- thiazoles [11] and 5,5’-dimercapto-2, 2’-bis(1,3,4-thiadiazolyl) S [12] have been studied. Rearrangements triggered by single or double oxygen transfer from the nitro group to the sulfur atom, followed by the loss of SO or SO$_2$ were also observed.

The literature survey revealed that there are no reports on cyclisation of 2-nitrophenyl phenyl thioether (2-nitrophenyl phenyl sulphide) or their substituted derivatives on protonation under fast atom bombardment, chemical or electrospray ionisations. So the study of the mass spectral behavior of protonated 2-nitrophenyl-phenyl thioether (a compound in which ether oxygen is replaced by sulphur) and their substituted derivatives in mass spectrometry was considered important from the point of view of mechanism and synthetic strategy. Moreover, we have identified this system as one that may be useful in extending our knowledge regarding the role of nitro group as electrophile upon protonation, in cyclisation reactions in the gas-phase.
5.2. Results and Discussion

Nitrophenyl aryl thioethers 1 to 4 (Scheme 5.2.1) were synthesized and their mass spectra were examined to investigate the possible rearrangements upon protonation, leading to cyclisation reactions of the even-electron molecular ions generated by FAB, Electrospray and Chemical ionizations.

![Scheme 5.2.1](image)

The FAB mass spectrum of the [M+H]$^+$ ion of 2-nitrophenyl phenyl sulphide, the thioether 1 (1-nitro-2- phenylthio benzene) Fig. 5.2.1, shows the fragment ions of m/z 232, 231, 215, 214, 198, 184, 168 and 167. The ion of m/z 232 corresponds to the protonated molecule, [M+H]$^+$, while the ion of m/z 231 is due to the radical cation of thioether 1. The ion of m/z 184 may be due to the loss of the elements of H$_2$NO$_2$ while the ion of m/z 167 is assigned to the loss of SO$_2$H radical. The ion of m/z 167 can also be due to the loss of SO$_2$ from the ion of m/z 231. The MI mass spectrum of the protonated molecule of m/z 232, Fig. 5.2.2, shows abundant fragment ions of m/z 215, 214, 202, 184 and 168 indicating that these ions are produced by the fragmentation process of the molecular ion of m/z 232. The ion of
$m/z$ 215 corresponds to the loss of an OH radical. The ion of $m/z$ 214 due to H$_2$O loss and the ion of $m/z$ 198 formed by the loss of two OH radicals, both from the $[M+H]^+$ ion are analogous to the established mass spectral fragmentations of 2-nitrophenyl phenyl ether and 2-nitro-N-phenyl aniline under identical conditions. The ion of $m/z$ 202 is assigned to the loss of NO from the $[M+H]^+$ ion.

![Fig. 5.2.1. The FAB MS of $[M+H]^+$ ion of 2-nitrophenyl phenyl Sulphide (thioether 1)](image)

![Fig. 5.2.2. The FAB-MI-MS of the $[M+H]^+$ ion of 2-nitrophenyl phenyl sulphide](image)
Since the ion of \( m/z \) 231, \( M^+ \), is more abundant than the ion of \( m/z \) 232, \( [M+H]^+ \), in the FAB mass spectrum, Fig. 5.2.1, of thioether 1, there may be some \(^{13}\text{C}\)-isotomer contribution from \( M^+ \) in the MS/MS spectra, Fig. 5.2.2 and 5.2.3, of the \( [M+H]^+ \) ion.

The FAB-CAD mass spectrum of the thioether 1, Fig. 5.2.3 also shows peaks for fragment ions of \( m/z \) 215 and 214 due to the eliminations of an OH radical and \( \text{H}_2\text{O} \). The ion of \( m/z \) 198 formed by the loss of a second OH radical from the ion of \( m/z \) 215 appears to be less abundant indicating that its formation is a high-energy process. Moreover, Fig. 5.2.3 shows other unusual fragment ions of \( m/z \) 184, 168 and 167 due to the eliminations of \( \text{SO} \), \( \text{SO}_2 \) and \( \text{SO}_2\text{H} \) radical. The fragment ion of \( m/z \) 184 can as well be formed by the loss of the elements of \( \text{H}_2\text{NO}_2 \). The abundance of ions of \( m/z \) 167 and 184 increases significantly in the FAB-CAD mass spectrum indicating that these ions are probably, generated by step-wise processes from the molecular ion whereas the ions of \( m/z \) 215 and 214 are formed from the molecular ion directly. To get more insight to the proposed cyclisation upon protonation, the CI mass spectrum of thioether 1, Fig. 5.2.4, was studied.
The CI mass spectrum of the [M+H]+ ion of the thioether 1 shows the fragment ions of m/z 232 (much higher abundance compared to m/z 231), 215, 214, 202, 184, 168 and 167 very similar to the mass spectral fragmentations under FAB ionisation.

The CI-MI mass spectrum of the [M+H]+ ion of 2-nitrophenyl phenyl sulphide.

The CI-MI mass spectrum of the protonated molecule, [M+H]+ ion of m/z 232, Fig. 5.2.5, also shows fragment ions of m/z 215, 214, 202, 198, 184, 168 and 167 indicating that these ions are produced by the fragmentation process of the molecular ion of m/z 232. The CI mass spectral fragmentations of thioether 1 are analogous to its FAB mass spectral
dissociations indicating that the gas-phase reactions of the thioether upon protonation under FAB and CI follow the same course. The different pathways for the fragmentation process of the protonated molecule, [M+H]$^+$ ion of $m/z$ 232 under FAB and CI are illustrated in Scheme 5.2.2.

Scheme 5.2.2. Schematic representation of the fragmentation pathways for the [M+H]$^+$ ion from thioether 1.

5.2.1. Mechanism of eliminations of H$_2$O and two OH radicals from protonated thioether 1.

The proposed step-wise eliminations of two OH radicals or a molecule of H$_2$O from the protonated thioether 1 are unusual and but are analogous to the mass spectral fragmentations of protonated 2-nitrophenyl phenyl ether and 2-nitro-N-phenyl aniline discussed in the previous chapters. The step-wise elimination of two OH radicals and a molecule of H$_2$O from the protonated thioether 1 afford the fragment ions of $m/z$ 198 and 214 respectively. Attempts to establish the structures of the fragment ions $m/z$ 214 and 198 by a comparative mass spectral study with an appropriate reference were not successful. So, for establishing a suitable mechanism of cyclisation and consequent fragmentations, ab initio molecular orbital calculations were performed by using Density Functional Theory.
Scheme 5.2.3. Proposed mechanism for the eliminations of H₂O and two OH radicals.
The heats of formations of the intermediates, transition states and products proposed in the mechanism, Scheme 5.2.3, for the step-wise elimination of two OH radicals and H₂O from protonated thioether 1, were estimated. In the calculations the heats of formations are stated relative to that for the [M+H]⁺ ion. It is envisaged that the protonated molecule [M+H]⁺ rearranges to the cyclic intermediate M2a, by an electrophilic substitution initiated by the protonated nitro group. Then, M2a transforms into various cyclic structures from M2b to M2f through OH migration followed by reversible hydrogen shifts. The highest transition state energy barrier, TS2, for the eliminations of H₂O and OH is 38.3 Kcal/mol. [M+H- H₂O]⁺ ion of m/z 214, possesses the structure Mc, if the elimination of H₂O takes place from M2d. In the rearranged structure M2g for the molecular ion there are two OH groups on the nitrogen atom. The intermediate M2g is formed from M2a through a reversible 1,3-hydrogen shift. The ion [M+H-H₂O]⁺ can have another structure Ma, if the elimination of H₂O occurs from M2g. But, the preferred structure for [M+H- H₂O]⁺ is Mc as the heat of formation of Ma is -46.7 kcal/mol while that for Mc is -81.6 kcal/mol. The elimination of the first OH radical takes place from structure M1f to form [M+H-OH]⁺ while the loss of a second OH⁻ affords Mb [phenothiazine-H]⁺. Both structures M2c and M2f contain two OH groups, Schemes 5.2.3, and the presence of these OH groups may account for H/D exchange if the thioether 1 is ionized by attaching D⁺. In fact the [M+D]⁺ ion of m/z 233 generated by chemical ionization of thioether 1 using methane-D₄ dissociates via loses of OH, H₂O/ OD and HDO to afford fragment ions of m/z 216, 215 and 214 as indicated in its MI, Fig.5.2.6 (a) and CAD, Fig.5.2.6 (b) mass spectra. In addition, the fragment ions of m/z 198 and 199 are also formed from [M+D]⁺ ion indicating that there is H/D scrambling during the loss of the second OH radical.
To ascertain the structure of the ion of $m/z$ 214 ($[M+H-H_2O]^+$) from thioether 1, its FAB-CAD mass spectrum, Fig. 5.2.7a was recorded. The mass spectrum revealed that this ion could fragment via extrusion of a molecule of CO to produce the ion of $m/z$ 186. This suggests that the preferred structure Mc, (appears to be a protonated cyclic ketone) for the ion of $m/z$ 214 given in Scheme 5.2.3 is justifiable. A possible mechanism for the extrusion
of CO from Mc has been proposed in Scheme 5.2.4 based on ab initio calculations performed by using DFT.

\[
\begin{align*}
&Mc: \text{[M+H-H}_2\text{O]}^+ \quad m/z \ 214 \\
&\Delta H_f = -81.6 \text{ Kcal/mol}
\end{align*}
\]

\[
\begin{align*}
&m/z \ 186 \\
&\Delta H_f = -60.3 \text{ Kcal/mol}
\end{align*}
\]

Scheme 5.2.4. Proposed mechanism for the extrusion of CO from the ion of \(m/z\) 214

Further, the CAD mass spectrum of the collisionally produced ion of \(m/z\) 214 was studied by performing MS\(^3\) experiment on the ESI generated \([M+H]^+\) ion of thioether 1. The CAD mass spectrum, Fig. 5.2.7b showed an intense peak corresponding to the ion of \(m/z\) 186 confirming that \([M+H-H_2O]^+\) ion can dissociate via the expulsion of CO but no peak

Fig. 5.2.7b, CAD–MS of the collisionally produced ion of \(m/z\) 214 by MS\(^3\) Experiment on ESI generated \([M+H]^+\) ion of thioether 1.
corresponding to the ion of \( m/z \) 184. This clearly establishes that \text{Me}, a protonated cyclic ketone, is the structure of the ion of \( m/z \) 214. This is in good agreement with the results of the molecular orbital calculations and the ESI-CAD-MS of the \([M+H]^+\) ion of thioether 1.

Moreover, the CI-CAD mass spectrum of the ion of \( m/z \) 215 (\([M+H-OH]^+\)), Fig. 5.2.8, show peaks corresponding to the ions of \( m/z \) 198, 184 and 182 formed by the eliminations of OH, NOH and SH radicals respectively. This is in accordance with the structure given in Scheme 5.2.3 for \([M+H-OH]^+\) ion, in which there is an OH group on the nitrogen atom. Therefore one of the pathways for the formation of the ion of \( m/z \) 184 is by the step-wise eliminations of OH and NOH radicals from protonated thioether 1. The high relative abundances of the ions of \( m/z \) 184 and 182 compared to that of the ion of \( m/z \) 198 in Fig. 5.2.8 show that the enhanced eliminations of NOH and SH radicals reduces the possibility of the elimination of a second OH radical from the \([M+H-OH]^+\) ion. This accounts well for the low abundance of the ion of \( m/z \) 198 formed by the successive elimination of two OH radicals from protonated thioether 1, Fig. 5.2.8.

The different pathways for the fragmentation processes of the ion of \( m/z \) 215 from
compound 1 ([M+H-OH]+) in collision dissociation on chemical ionisation are illustrated in Scheme 5.2.5.

![Scheme 5.2.5. Proposed fragmentation processes of the ion of m/z 215 from thioether 1](image_url)

**Scheme 5.2.5.** Proposed fragmentation processes of the ion of m/z 215 from thioether 1

### 5.2.2. Mechanism of eliminations of SO, SO\(_2\) and SO\(_2\)H radical from protonated thioether 1.

In addition to the eliminations of H\(_2\)O and two OH radicals, the FAB-MI and CI-MI and CAD mass spectrum of the thioether 1, shows other unusual fragment ions of m/z 184, 168 and 167 due to the loss of SO, SO\(_2\) and SO\(_2\)H radical. These mass spectral fragmentations can be explained if the sulphur atom of the thioether 1 is acting as an intramolecular reducing agent accepting oxygen atoms from the nitro group. To gain some insight to the mechanism, the CI-MI spectrum of the ion of m/z 234 ([M+H+2]+ ion) having \(^{34}\)S in the protonated thioether 1, **Fig. 5.2.9** was studied. The presence of the ion of m/z 186 in addition to the ion of m/z 184 indicates that there are competitive fragmentation pathways for the formation of the ion of m/z 184 from the [M+H]+ ion. The ion of m/z 186 is formed by the step-wise loss of OH and NOH radicals so that \(^{34}\)S is retained. The ion of m/z 184 in the mass spectrum is due to [M+H-SO]+ where \(^{34}\)S is eliminated.
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The high relative abundance of the ion of m/z 186 indicate that the step-wise loss of OH and NOH is the major pathway for the formation of the ion of m/z 184 from the [M+H]+ ion. The relative abundance of the ions of m/z 168 and 167 are unaffected indicating that these ions are formed by the expulsions of 34SO2 and 34SO2H radical.

To aid the elucidation of a suitable mechanism for the cyclisation and consequent eliminations of SO, SO2 and SO2H radical, ‘ab initio’ molecular orbital calculations were performed using Density Functional Theory. In the calculations the heats of formations are stated relative to that for the [M + H]+ ion.

Fig. 5.2.9, The CI-MI mass spectrum of the [M+H]+ ion of 2-nitrophenyl phenyl Sulphide of m/z 234 with 34S isotope.
Scheme 5.2.6. Proposed mechanism for the elimination of SO, SO₂ and SO₂ H radical.
The proposed mechanism, Scheme 5.2.6 involves the transfer of an OH from the nitro group to the sulphur forming the intermediate, $M_{3b}$, followed by the back transfer of the H from the O to the N to form, $M_{3d}$, effecting the first step in the reduction. $M_{3d}$ transforms into $M_{3e}$ by the migration of the phenyl group. This intermediate $M_{3e}$ can extrude SO to afford the ion of $m/z$ 184. The second oxygen is transferred from the nitro group to the sulfur via a cyclic five-membered intermediate, $M_{3g}$ before the final cyclisation to form $M_{3i}$ and stabilizes to the intermediate $M_{3j}$ by aromatisation of the ring. The extrusion of SO$_2$ from $M_{3j}$ can take place directly or indirectly via intermediates $M_{3k}$ and the ion-dipole complex (IDC) to form the ion of $m/z$ 168. The IDC can also expel SO$_2$H radical to form the ion of $m/z$ 167.

For the confirmation of the structure of the ion of $m/z$ 184, its FAB-CAD mass spectrum, Fig. 5.2.10 (a) was compared with the EI-CAD mass spectrum of the radical cation of dibenzothiophene, Fig. 5.2.10 (b). The relative abundances of the characteristic fragment ions of $m/z$ 139 and 152 in the CAD mass spectrum of the radical cation of dibenzothiophene observed in the ratio 2:1 are seen in the same ratio in the FAB-CAD mass spectrum of ion of $m/z$ 184 generated from thioether 1. This supports that the ion of $m/z$ 184 generated from protonated thioether 1 is a mixture two isobaric ions, as proposed in Schemes 5.2.5 and 5.2.6, in which one possess a dibenzothiophene radical cation structure.

Moreover, the FAB-CAD mass spectrum of the ion of $m/z$ 184 generated from thioether 1 show peaks corresponding to the fragment ions of $m/z$ 167 and 166 due to the expulsions of OH radical and H$_2$O. These fragmentations suggest that the other isobaric ion $[C_{12}H_{10}NO]^{+}$ of $m/z$ 184 i.e. $[M+H- SO]^{+}$, Scheme 5.2.7, can isomerise to another structure having an OH group.
A tentative structure, P1, for the ion of m/z 184 and a rationalization for its fragmentation pathways are proposed, Scheme 5.2.7.

Scheme 5.2.7, The fragmentation pathways for the ion of m/z 184.
To confirm the proposed mechanisms, the accurate mass measurements are done using ESI-CAD mass spectrum of the \([\text{M+H}]^+\), ion of the thioether 1. High-resolution mass spectral data, Table 5.2.1 are in good agreement with the elemental compositions for the ions of \(m/z\) 215, 214, 202, 186, 184, 168 and 167 proposed in mechanisms, Schemes 5.2.3, 5.2.4, 5.2.5 and 5.2.6.

### 5.2.3, ESI mass spectral study of thioether 1 upon protonation

The ESI experiment was conducted by using a quadrupole time-of-flight instrument (Q-Tof). Electrospray ionization provides better protonation efficiency under low energy conditions and hence the ESI mass spectrum of thioether 1, Fig.5.2.11 was recorded. The ESI mass spectrum shows the \([\text{M+H}]^+\) ion of \(m/z\) 232. The ESI-CAD mass spectrum, Fig.5.2.12, shows fragment ions of \(m/z\) 215, 214, 202, 186, 184 168 and 167 similar to the mass spectral behaviour under CI and FAB ionization. The ion of \(m/z\) 215 corresponds to the loss of an OH radical and the ion of \(m/z\) 214 is due to \(\text{H}_2\text{O}\) loss. It is interesting to note that the ion of \(m/z\) 198 due to the loss of a second OH radical from the ion of \(m/z\) 215 disappears in the ESI-CAD mass spectrum supporting the fact that the expulsion of a second OH radical is a high-energy process.

![Fig. 5.2.11](image-url)
The ions of \( m/z \) 202, 168 and 167 are due to the eliminations of NO, \( \text{SO}_2 \) and \( \text{SO}_2\text{H} \) radicals respectively from the \([\text{M+H}]^+\) ion. The ion of \( m/z \) 184 can be generated either by the expulsion of SO from the \([\text{M+H}]^+\) ion or by the elimination of NOH from the fragment ion of \( m/z \) 215. The ion of \( m/z \) 186 is assigned to the loss CO from the fragment ion of \( m/z \) 214. The ESI-CAD mass spectrum was recorded at a resolution of 15000 and hence the exact mass of the fragment ions could be determined using the ion of \( m/z \) 232 as the internal standard. The high-resolution mass spectral data thus obtained are in good agreement with the calculated masses for the elemental compositions of the fragment ions, Table 5.2.1. The fragment ion of \( m/z \) 184 is composed of isobaric ions of two different elemental compositions as shown in Table 5.2.1 one of them corresponding to the elimination of SO from the \([\text{M+H}]^+\) and the other corresponding to the expulsion of NOH from the ion \( m/z \) 215. The peak due to the ion of \( m/z \) 184 at a resolution of 15000 is shown in Fig. 5.2.13. It may be noted that the fragment ion formed by the elimination of SO is the major component of the ion of \( m/z \) 184 present in the ESI-CAD mass spectrum unlike in the FAB-CAD mass spectrum. This supports the step-wise mechanism requiring high energy for the formation of the ions.

![Graph showing ESI-CAD-MS of the [M+H]^+ ion of thioether 1](image_url)
the ion of \( m/z \) 184 containing sulfur, \( \text{C}_{12}\text{H}_{8}\text{S}^+ \), Scheme 5.2.5, compared to the elimination of SO in one step to yield the ion of \( m/z \) 184 without sulfur, \( \text{C}_{12}\text{H}_{10}\text{NO}^+ \).

<table>
<thead>
<tr>
<th>Fragment ion</th>
<th>Nominal Mass</th>
<th>Molecular Formula</th>
<th>Observed Mass</th>
<th>Calculated Mass</th>
</tr>
</thead>
<tbody>
<tr>
<td>([\text{M}+\text{H-} \text{OH}]^+)</td>
<td>215</td>
<td>( \text{C}<em>{12}\text{H}</em>{9}\text{NOS} )</td>
<td>215.0406</td>
<td>215.0405</td>
</tr>
<tr>
<td>([\text{M}+\text{H-} \text{H}_2\text{O}]^+)</td>
<td>214</td>
<td>( \text{C}<em>{12}\text{H}</em>{8}\text{NOS} )</td>
<td>214.0322</td>
<td>214.0326</td>
</tr>
<tr>
<td>([\text{M}+\text{H-} \text{NO}]^+)</td>
<td>202</td>
<td>( \text{C}<em>{12}\text{H}</em>{10}\text{OS} )</td>
<td>202.0463</td>
<td>202.0453</td>
</tr>
<tr>
<td>([\text{M}+\text{H-} \text{H}_2\text{O-CO}]^+)</td>
<td>186</td>
<td>( \text{C}_{11}\text{H}_8\text{NS} )</td>
<td>186.0378</td>
<td>186.0377</td>
</tr>
<tr>
<td>([\text{M}+\text{H-} \text{SO}]^+)</td>
<td>184</td>
<td>( \text{C}<em>{12}\text{H}</em>{10}\text{NO} )</td>
<td>184.0769</td>
<td>184.0762</td>
</tr>
<tr>
<td>([\text{M}+\text{H-} \text{OH-NOH}]^+)</td>
<td>184</td>
<td>( \text{C}<em>{12}\text{H}</em>{8}\text{S} )</td>
<td>184.0343</td>
<td>184.0347</td>
</tr>
<tr>
<td>([\text{M}+\text{H-} \text{SO}_2]^+)</td>
<td>168</td>
<td>( \text{C}<em>{12}\text{H}</em>{10}\text{N} )</td>
<td>168.0815</td>
<td>168.0813</td>
</tr>
<tr>
<td>([\text{M}+\text{H-} \text{SO}_2\text{H}]^+)</td>
<td>167</td>
<td>( \text{C}_{12}\text{H}_9\text{N} )</td>
<td>167.0732</td>
<td>167.0735</td>
</tr>
</tbody>
</table>

**Table 5.2.1.** Measured accurate masses of the fragment ions from the ESI-CAD mass spectrum of the \([\text{M}+\text{H}]^+\), ion of 2-nitrophenyl phenyl sulphide (Thioether 1).

**Fig. 5.2.13.** Measured accurate masses of the isobaric ions of \( m/z \) 184 from the ESI-CAD MS of the \([\text{M}+\text{H}]^+\), ion of thioether 1.
Another interesting mass spectral reaction of the thioether 1 upon electrospray ionization is the oxidation of the molecule at the emitter electrode in an electrospray ion source. This is manifested in the ESI mass spectrum (solvent mixture of acetonitrile and water in the ratio 1:1) Fig. 5.2.14, which contains an unusual peak corresponding to an ion of m/z 248, sixteen amu higher than the molecular mass of the thioether 1.

The spectrum was repeated by injecting a solution of the thioether 1 in a 1:1 mixture of acetonitrile and water containing 1% formic acid to the ESI source of the mass spectrometer. It shows an increase in the relative abundance of the ion of m/z 248 compared to the [M+H]+ ion (m/z 232) of the thioether 1. So it may be assumed that the ion of m/z 248 may be due to the sulfoxide, [M+H+O]+ ion, [protonated 1-nitro-2- (phenyl sulfinyl) benzene] generated by oxidation of the thioether 1, at the emitter electrode in an electrospray ion source. The ions of m/z 254 is the [M + Na]+ ion of the thioether 1 and the ion of m/z 270 is the [M + Na]+ ion of the oxidation product, 1-nitro-2- (phenylsulfinyl) benzene.
Accurate mass measured for the ion of \( m/z \) 248 is 248.0381 (measured by using sodium trifluoroacetate as internal standard) is within 1.6 ppm of the exact mass 248.0377 calculated for the elemental composition of the \([M+H+O]^+\) ion, \(C_{12}H_{10}NO_3S\). To confirm the structure of the ion of \( m/z \) 248, its ESI-CAD mass spectrum, Fig. 5.2.15 was compared with that of 1-nitro-2- (phenylsulfinyl) benzene [the sulphoxide of thioether 1] an appropriate reference, Fig. 5.2.16 produced by the oxidation of thioether 1 by using sodium periodate. The two spectra are closely similar indicating that the electrochemical oxidation of the thioether 1 in the ion source produces the sulphoxide.

Further, the fragment ions of \( m/z \) 217 ([M+H- NOH]^+), 184 ([M+H- SO_2]^+), and 167 ([M+H- (SO_2+OH)]^+) present in both the CAD mass spectra, Fig. 5.2.15 and Fig. 5.2.16 of the molecular ion of \( m/z \) 248 indicate that analogues to the thioether 1, the corresponding sulphoxide also undergo gas-phase cyclisation upon protonation. The fragment ion of \( m/z \) 170 corresponds to the elimination of a molecule of benzene from the ion of \( m/z \) 248 and it can be considered as a characteristic fragmentation of sulfoxides. An outline of the mechanism, Scheme 5.2.8 is proposed for explaining the mass spectral fragmentations of the ion of \( m/z \) 248. The high-resolution mass spectral data, Table 5.2.2, obtained are in good agreement with the calculated masses for the elemental compositions of the fragment ions proposed in the mechanism. So the mechanism proposed for the formation of the fragment
ions in the ESI-CAD mass spectrum of the ion of \( m/z \ 248 \) is substantiated and hence their structures are justified.

\[
\text{Scheme 5.2.8, Mass spectral fragmentations pathways for the ion of } m/z 248 \text{ on ESI-CAD analysis.}
\]

<table>
<thead>
<tr>
<th>Fragment ion</th>
<th>Nominal mass</th>
<th>Molecular Formula</th>
<th>Observed mass</th>
<th>Calculated mass</th>
</tr>
</thead>
<tbody>
<tr>
<td>([\text{M}+\text{H}-\text{NOH}]^+)</td>
<td>217</td>
<td>( \text{C}_{12}\text{H}_9\text{O}_2\text{S} )</td>
<td>217.0325</td>
<td>217.0319</td>
</tr>
<tr>
<td>([\text{M}+\text{H}-\text{SO}_2]^+)</td>
<td>184</td>
<td>( \text{C}<em>{12}\text{H}</em>{10}\text{NO} )</td>
<td>184.0767</td>
<td>184.0762</td>
</tr>
<tr>
<td>([\text{M}+\text{H}-\text{C}_6\text{H}_6]^+)</td>
<td>170</td>
<td>( \text{C}_6\text{H}_4\text{NO}_3\text{S} )</td>
<td>169.9906</td>
<td>169.9909</td>
</tr>
<tr>
<td>([\text{M}+\text{H}- (\text{SO}_2+\text{OH})]^+)</td>
<td>167</td>
<td>( \text{C}_{12}\text{H}_9\text{N} )</td>
<td>167.0725</td>
<td>167.0734</td>
</tr>
</tbody>
</table>

\text{Table 5.2.2, Measured accurate masses of the fragment ions from the ESI-CAD mass spectrum of the [M+H]^+, ion of } m/z 248 \text{ from thioether 1.}
5.2.3, FAB and ESI mass spectral study of Thioethers 2-4 upon protonation.

For a comparative study, the FAB mass spectral fragmentations of the thioether 4, the para nitro isomer of thioether 1, (4-nitrophenyl phenyl sulphide) was investigated.

The FAB mass spectrum of the thioether 4, Fig. 5.2.17, indicates that the para nitro isomer also dissociates via loss of OH radical to produce an ion of \( m/z \) 215. The loss of the first OH radical, however, does not necessarily require the presence of the nitro group at the ortho position. But the ion of \( m/z \) 198 due to the elimination of another OH radical is absent here indicating that this require a nitro group at the ortho position. The fragment ions of \( m/z \) 214, 198, 168 and 167 are absent in the MI, Fig.5.2.18, of the molecular ion of thioether 4, the para nitro isomer indicating that the formation of these fragment ions require that the nitro group be present at the ortho position. The peaks corresponding to the ions of \( m/z \) 215, 202,186 and 184 are seen in the FAB-MI mass spectrum of the thioether 4 revealing that these ions can be generated even without a nitro group at the ortho position and hence probably follows a different mechanism and these ions can be isobaric with the corresponding ions produced for the ortho nitro isomer 1, Scheme 5.2.9.
To explore the elemental compositions of fragment ions and electrochemical oxidation, the ESI mass spectrum of the thioether 4, Fig. 5.2.19 was studied. The spectrum shows the [M+H]⁺ ion of m/z 232 and the unusual peak corresponding to an ion of m/z 248, sixteen amu higher than the molecular mass of the thioether 4 due to the oxidation of the molecule at the emitter electrode in an electrospray ion source.

The ESI-HR-CAD mass spectrum of the thioether 4, Fig. 5.2.20, showed peaks due to ions of m/z 215, 202, 186 and 184 as in its FAB-MI mass spectrum. The high-resolution mass spectral data obtained are in good agreement with the calculated masses for the
elemental compositions of the fragment ions, **Table.5.2.3** The ions of *m/z* 215, 202, 186 and 184 are assigned to the loss of OH radical, NO, NO₂ and (NO+H₂O) respectively from the [M+H]⁺ ion. The fragment ion of *m/z* 186 of the ortho isomer, thioether 1, corresponds to the loss of H₂O and CO from the molecular ion whereas that of the para isomer is due to the loss of NO₂. The fragment ion of *m/z* 184 in the CAD mass spectrum of the ortho isomer is mainly due to the loss SO from the [M+H]⁺ ion but that of the para isomer (comparatively low abundance) is due the loss of [NO+H₂O] from the [M+H]⁺ ion.

<table>
<thead>
<tr>
<th>Fragment ion</th>
<th>Nominal mass</th>
<th>Molecular Formula</th>
<th>Observed mass</th>
<th>Calculated Mass</th>
</tr>
</thead>
<tbody>
<tr>
<td>[M+H-NO]⁺</td>
<td>202</td>
<td>C₁₂H₁₀Oₛ</td>
<td>202.0447</td>
<td>202.0453</td>
</tr>
<tr>
<td>[M+H-NO₂]⁺</td>
<td>186</td>
<td>C₁₂H₁₀S</td>
<td>186.0478</td>
<td>186.0504</td>
</tr>
<tr>
<td>[M+H-NO-H₂O]⁺</td>
<td>184</td>
<td>C₁₂H₈S</td>
<td>184.0349</td>
<td>184.0348</td>
</tr>
</tbody>
</table>

**Table.5.2.3**, Measured accurate masses of the fragment ions from the ESI-CAD mass Spectrum of the [M+H]⁺ ion of thioether 4.
The accurate mass measurements have shown that the ion of $m/z$ 248 has the elemental composition $\text{C}_{12}\text{H}_{10}\text{NO}_3\text{S}$ (measured mass - 248.0387; calculated mass - 248.0381, internal standard; sodium trifluoroacetate), which corresponds to the sulfoxide, confirming the oxidation of the thioether molecule at the emitter electrode. To ascertain the structure of the ion of $m/z$ 248 in the ESI mass spectrum of thioether 4, its ESI-CAD mass spectrum, Fig. 5.2.21, was recorded.

![Fig. 5.2.21, ESI-CAD mass spectrum, of the ion of m/z 248 formed by the electrochemical oxidation of the thioether 4.](image)

The ion of $m/z$ 231 is due to OH loss from the ion of $m/z$ 248 (Measured mass - 231.0362, calculated mass - 231.0350) while the ion of $m/z$ 202 is due to NO$_2$ loss (measured mass - 202.0454, calculated mass - 202.0453). The ion of $m/z$ 169.9912 (calculated mass 169.9909) is due to the characteristic elimination of benzene, $[\text{M+H-C}_6\text{H}_6]^+$, analogous to the fragmentation of the sulfoxide of the ortho isomer. Scheme 5.2.10.
To gain more insight into the proposed cyclisation and the oxidation of the molecule at the emitter electrode in the electrospray ion source, the ESI mass spectra of thioether 2 (4-chloro-2-nitro-1-(phenylthio) benzene), para chloro derivative of thioether 1, was recorded Fig. 5.2.22. The ESI mass spectrum was recorded by injecting a solution of the thioether 2 in a 1:1 mixture of acetonitrile and water containing 1% formic acid to the ESI source of the mass spectrometer. The spectrum showed the [M+H]^+ ion of m/z 266 and [M+H+O]^+ ion of m/z 282 similar to thioether 1.

The ESI-CAD mass spectrum of [M+H]^+ ion of m/z 266, Fig.5.2.23, shows fragment ions of m/z 249, 248, 236, 220, 218, 202 and 201 similar to the mass spectral behaviour of thioether 1 upon electrospray ionization.
The ion of \( m/z \) 249 corresponds to the loss of an OH radical and the ion of \( m/z \) 248 is due to \( \text{H}_2\text{O} \) loss. The ions of \( m/z \) 236, 202 and 201 are due to the eliminations of NO, \( \text{SO}_2 \) and \( \text{SO}_2\text{H} \) radicals respectively from the \([\text{M}+\text{H}]^{+}\) ion of thioether 2. The ion of \( m/z \) 218 can be generated either by the expulsion of SO from the \([\text{M}+\text{H}]^{+}\) ion or by the elimination of NOH from the fragment ion of \( m/z \) 249. The ion of \( m/z \) 220 is assigned to the loss CO from the fragment ion of \( m/z \) 248. These fragmentation pathways observed for thioether 2, Scheme 5.2.11, are in line with the mechanisms proposed in Scheme 5.2.3, 5.2.4 and 5.2.6 for explaining the mass spectral fragmentations of thioether 1. Further, The fragment ion of \( m/z \) 183 is due to the loss of Cl from the ion of \( m/z \) 218 while the ion of \( m/z \) 167 which forms the base peak is assigned to \([\text{M}+\text{H}- (\text{SO}_2+\text{Cl})]^{+}\).
Moreover, the oxidation of the thioether 2 takes place at the emitter electrode in electrospray ion source analogues to thioether 1. This is manifested in the ESI mass spectrum, Fig. 5.2.22, which contains an unusual peak corresponding to an ion of $m/z$ 282, sixteen amu higher than the molecular mass of thioether 2. Accurate mass measured for the ion of $m/z$ 282 is 281.9991 (calculated mass 281.9992) with the elemental composition of $C_{12}H_9NO_3SCl$ for the $[M+H+O]^+$ ion which corresponds to the formation of the sulfoxide.

To ascertain the structure of the ion of $m/z$ 282 from the thioether 2, its high-resolution ESI-CAD mass spectrum, Fig. 5.2.24, was recorded. The high-resolution mass spectral data thus obtained are in good agreement with the calculated masses for the elemental compositions of the fragment ions, Table.5.2.4. This data revealed that the fragment ions from the ion of $m/z$ 282 are chlorine analogues of the mass spectral fragment ions generated from the ion of $m/z$ 248 except for the ions of $m/z$ 183,167 and 166. These ions are due to the presence of the chlorine atom and their composition is given in Table.5.2.4.
**Chapter 5**

**Cyclisation of nitro thioethers**

![JMG-103 2-NITRO CHLOROTHIOETHER CAD 282](image)

**Fig. 5.2.24, ESI- CAD mass spectrum, of the ion of m/z 282**

<table>
<thead>
<tr>
<th>Fragment ion</th>
<th>Nominal Mass</th>
<th>Molecular Formula</th>
<th>Observed Mass</th>
<th>Calculated Mass</th>
</tr>
</thead>
<tbody>
<tr>
<td>[M+H- NOH]^+</td>
<td>251</td>
<td>C_{12}H_{8}O_{2}SCl</td>
<td>250.9930</td>
<td>250.9938</td>
</tr>
<tr>
<td>[M+H- SO_{2}]^+</td>
<td>218</td>
<td>C_{12}H_{9}NOCl</td>
<td>218.0357</td>
<td>218.0373</td>
</tr>
<tr>
<td>[M+H-C_{6}H_{6}]^+</td>
<td>204</td>
<td>C_{6}H_{3}NO_{3}SCl</td>
<td>203.9512</td>
<td>203.9523</td>
</tr>
<tr>
<td>[M+H- (SO_{2}+OH)]^+</td>
<td>201</td>
<td>C_{12}H_{9}NCl</td>
<td>201.0340</td>
<td>201.0346</td>
</tr>
<tr>
<td>[(M+H- SO_{2})-Cl]^+</td>
<td>183</td>
<td>C_{12}H_{9}NO</td>
<td>183.0680</td>
<td>183.0684</td>
</tr>
<tr>
<td>[M+H- (SO_{2}+Cl+O)]^+</td>
<td>167</td>
<td>C_{12}H_{9}N</td>
<td>167.0731</td>
<td>167.0734</td>
</tr>
<tr>
<td>[M+H- (SO_{2}+OH)-Cl]^+</td>
<td>166</td>
<td>C_{12}H_{8}N</td>
<td>166.0650</td>
<td>166.0657</td>
</tr>
</tbody>
</table>

**Table.5.2.4, Measured accurate masses of the fragment ions from the ESI-CAD mass Spectrum of the ion of m/z 282 generated from thioether 2.**

So it is evident that the oxidation of thioether 2 in an electrospray ion source yields the sulphoxide which undergoes gas-phase cyclisation upon protonation, analogous to the thioether 1, leading to eliminations of SO_{2} and NOH. The fragmentation pathways of the
[M+H]+ ion of the sulfoxide \(m/z\) 282 is shown in Scheme 5.2.12. The characteristic elimination of benzene from the sulfoxide is also observed analogous to the sulfoxides of thioethers 1, 2 and 4.

Scheme 5.2.12, ESI-CAD-MS fragmentations pathways for the ion of \(m/z\) 282.

To gain more support for the proposed cyclisation and the oxidation of the thioethers in an electrospray ion source, the ESI mass spectrum of thioether 3, 4-chloro-1-[(4-methyl phenyl) sulfinyl]-2 nitrobenzene, para methyl analogue of thioether 2, was recorded, Fig. 5.2.25. The spectrum showed the \([M+H]^+\) ion of \(m/z\) 280 and \([M+H+O]^+\) ion of \(m/z\) 296.
The ESI-CAD mass spectrum, Fig. 5.2.26, shows fragment ions of \( m/z \) 263, 262, 250, 234, 232, 216 and 215 analogous to the mass spectral fragmentations of thioethers 1 and 2.

The ion of \( m/z \) 263 corresponds to the loss of an OH radical and the ion of \( m/z \) 262 is due to \( \text{H}_2\text{O} \) loss. The ions of \( m/z \) 250, 216 and 215 are due to the eliminations of NO, SO\(_2\) and SO\(_2\)H radicals respectively from the \([M+H]^+\) ion of thioether 3. The ion of \( m/z \) 232 can be generated either by the expulsion of SO from the \([M+H]^+\) ion or by the elimination of NOH from the fragment ion of \( m/z \) 263. The ion of \( m/z \) 234 is assigned to the loss CO from the fragment ion of \( m/z \) 262. The fragmentation pathways observed for thioether 3, Scheme 5.2.13, are in line with the mechanisms proposed in Scheme 5.2.3, 5.2.4 and 5.2.6 for explaining the mass spectral fragmentations of thioether 1. The fragment ion of \( m/z \) 197 is due to the loss of Cl from the ion of \( m/z \) 232 while the ion of \( m/z \) 181 is assigned \([M+H-(SO_2+Cl)]^+\). The fragment ions of \( m/z \) 197 and 181 are methyl analogues of the fragment ions of \( m/z \) 183 and 167 observed in the ESI-CAD mass spectrum of the \([M+H]^+\) ion of thioether 2.
Scheme 5.2.13

The accurate mass measured for the ion of $m/z$ 296 in the ESI mass spectrum, Fig. 5.2.25, the sulfoxide formed by the oxidation of the thioether 3 is 296.0143 (calculated mass 296.0148) which corresponds to the elemental composition of $C_{13}H_{11}NO_3SCl$ for the $[M+H+O]^+$ ion. To elucidate the structure of the ion of $m/z$ 296, its ESI-CAD mass spectrum, Fig. 5.2.27, was recorded.

![ESI-CAD mass spectrum of the ion of m/z 282](image)

**Fig. 5.2.27**, ESI-CAD mass spectrum of the ion of $m/z$ 282
The high-resolution mass spectral data thus obtained are in good agreement with the calculated masses for the elemental compositions of the fragment ions, Table 5.2.5. This data revealed that the fragment ions for the ion of m/z 296 are methyl analogues of the mass spectral fragment ions generated from the ion of m/z 282 except for the ions of m/z 204. It is interesting to observe that the ion of m/z 204 is formed from the ion of m/z 296 by the expulsion of a molecule toluene similar to the expulsion of benzene from the ion of m/z 282. This support the proposed the mechanism, schemes 5.2.8 and 5.2.12 for the fragmentations pathways for the sulphoxides.

<table>
<thead>
<tr>
<th>Fragment ion</th>
<th>Nominal Mass</th>
<th>Molecular Formula</th>
<th>Observed Mass</th>
<th>Calculated Mass</th>
</tr>
</thead>
<tbody>
<tr>
<td>[M+H- NOH]+</td>
<td>265</td>
<td>C_{13}H_{10}O_{2}SCl</td>
<td>265.0098</td>
<td>265.0085</td>
</tr>
<tr>
<td>[M+H- SO_{2}]^+</td>
<td>232</td>
<td>C_{13}H_{11}NOCl</td>
<td>232.0494</td>
<td>232.0524</td>
</tr>
<tr>
<td>[M+H-C_{7}H_{8}]^+</td>
<td>204</td>
<td>C_{6}H_{3}NO_{3}SCl</td>
<td>203.9520</td>
<td>203.9523</td>
</tr>
<tr>
<td>[M+H- (SO_{2}+OH)]^+</td>
<td>215</td>
<td>C_{13}H_{10}NCI</td>
<td>215.0499</td>
<td>215.0497</td>
</tr>
<tr>
<td>[(M+H- SO_{2})-Cl]^+</td>
<td>197</td>
<td>C_{13}H_{11}NO</td>
<td>197.0836</td>
<td>197.0835</td>
</tr>
<tr>
<td>[M+H- (SO_{2}+Cl+O)]^+</td>
<td>181</td>
<td>C_{13}H_{11}N</td>
<td>181.0889</td>
<td>181.0886</td>
</tr>
<tr>
<td>[M+H- (SO_{2}+OH)-Cl]^+</td>
<td>180</td>
<td>C_{13}H_{10}N</td>
<td>180.0805</td>
<td>180.0808</td>
</tr>
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Table 5.2.5, Measured accurate masses of the fragment ions from the ESI-CAD mass Spectrum of the ion of m/z 296 generated from thioether 3.

A mechanism, Scheme 5.2.14 is proposed for explaining the ESI-CAD mass spectral fragmentations of the ion of m/z 296. This establishes that the oxidation of the thioether 3 in an electrospray ion source generates the corresponding sulphoxide and it undergoes gas-phase cyclisation upon protonation analogues to the thioethers 1 and 2.
Scheme 5.2.14, ESI-CAD-MS fragmentations pathways for the ion of m/z 296
5.3. Conclusion

The FAB, CI and ESI mass spectra of 2-nitrophenyl phenyl sulfide [1-nitro-2-(phenylthio) benzene] were investigated. The mass spectra of the para nitro isomer were examined for comparison. The protonated thioether rearranges to a cyclic intermediate which fragments either by the step-wise eliminations of two OH radicals or by the elimination of a molecule of H₂O, analogous to the protonated 2-nitrophenyl phenyl ether and 2-nitro-N-phenyl aniline in the gas-phase as discussed in the previous chapters. Here the protonated nitro group participates as an electrophile in the cyclisation reaction to afford the heterocyclic intermediate. The step-wise eliminations of two OH radicals from the heterocyclic intermediate affords [phenothiazine-H]+ while the elimination of H₂O generates a protonated heterocyclic ketone. In addition a novel ortho effect of nitro group involving cyclisations due to oxygen transfers from the nitro group to the sulphur atom occurs in the molecular ions of 2-nitropheylphenyl sulfide which resulted in the expulsions of SO followed by OH and SO₂ loss followed by H radical.

Moreover, the sulfide undergoes oxidation at the emitter electrode in the ESI source during ionization, depending on the pH of the solution. Tandem mass spectrometric experiments, accurate mass measurements and DFT molecular modeling supported the proposed mechanisms and structures of the fragment ions and the intermediates. Similar proton induced gas-phase cyclisations are observed in the mass spectra of the choro- and chloro-methyl analogues of 2-nitrophenyl-phenyl sulfide but not in the case of the para nitro isomer. These unusual gas-phase reactions leading to the cyclisation of [M+H]⁺ ions of 2-nitrothioethers generated by FAB, CI and ESI, where the protonated nitro group participates in electrophilic cyclisations are reported for the first time.
5.4. Experimental Details

1. Preparation of 1-nitro-2-(phenylthio) benzene (thioether 1) [13].

   Thiophenol - 4.4 g  
   1-chloro-2-nitrobenzene - 6.4 g  
   Dry Ethanol - 50cc  
   Metallic Sodium - 1.4 g

   50 ml dry alcohol is taken in 250 ml R.B. flask fitted with a CaCl₂ guard tube. 1.4 g of small pieces of metallic Na (0.06 mol) is slowly added. After the reaction is complete, thiophenol (4.4g, 0.04 mol) is added drop wise to the reaction mixture and is stirred well. 6.4 g (0.04 mol) of 1-chloro-2-nitrobenzene dissolved in alcohol is added. The mixture is stirred well and refluxed over a water bath for 1 hour. On cooling yellow coloured crystals of thioether 1 separated. The product is filtered, washed with water and dried. It is purified by recrystallisation from hot alcohol. Yield was 79%.

   Melting point  
   Observed  
   Reported [13]  
   82°C  
   82°C

   IR (KBr) cm⁻¹: 3050 (aromatic CH stretch), 1588, (aromatic C=C stretch), 1512, 1333 (Asymmetric and symmetric N=O stretch of Ar-NO₂), 1249 (C-O stretch), 684 (C-S stretch)

   ¹H NMR (in CDCl₃): δ 7.8 -8.0 (d, 1 H), 7.0 –7.6 (m, 7 H), 6.8 (d, 1H).

2. Preparation of 4-chloro-2-nitro-1-(phenylthio) benzene (thioether 2) [13]

   Thiophenol - 4.4 g  
   1.4-dichloro-2-nitrobenzene - 7.8 g  
   Dry Ethanol - 50 cc  
   Metallic Sodium - 1.4 g
50 ml dry alcohol is taken in 250 ml R.B. flask fitted with a CaCl₂ guard tube. 1.4 g of metallic Na (1.4 g 0.06 mol) is added in small quantities and is allowed to react completely. Then thiophenol (0.04 mol) is added drop wise to the reaction mixture and stirred well. 7.8 g (0.04 mol) of 1.4-dichloro-2-nitrobenzene dissolved in alcohol is then added. The mixture refluxed over a water bath for 1 hour. On cooling yellow coloured crystals of thioether 2 is separated. The product is filtered, washed, dried and recrystallised from hot alcohol. Yield was 82%.

<table>
<thead>
<tr>
<th>Melting point</th>
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</tr>
</thead>
<tbody>
<tr>
<td>85°C</td>
<td></td>
<td>86°C</td>
</tr>
</tbody>
</table>

\[\text{IR (KBr) cm}^{-1}: 3100 (\text{aromatic CH stretch}), 1602, 1567, (\text{aromatic C=C stretch}), 1522, 1327 (\text{Asymmetric and symmetric N=O stretch of Ar-NO₂}), 801 (\text{Ar-Cl stretch}), 714 (\text{C-S stretch}), \]

\[\text{\textsuperscript{1}H NMR (in CDCl₃)}: \delta 8.2 (s, 1 H), 7.0 –7.5 (m, 7 H). \]

3. **Preparation of 4-chloro-1-[{(4-methyl phenyl) sulfinyl}-2-nitrobenzene** [13].

   (Thioether 3)

   4-methyl benzene thiol \((p\)-thiocresol\) - 5.0 g
   1.4-dichloro-2-nitrobenzene - 7.8 g
   Dry Ethanol - 50cc
   Metallic Sodium - 1.4 g

50 ml dry alcohol is taken in 250 ml R.B. flask fitted with a CaCl₂ guard tube. Small pieces of metallic Na (0.06 mol) are added slowly. After the reaction is complete, \(p\)-thiocresol (5.0 g, 0.04 mol) is added drop wise to the reaction mixture and is stirred well. 7.8 g (0.04 mol) of 1.4-dichloro-2-nitrobenzene dissolved in alcohol is added. The mixture is stirred well and refluxed over a water bath for 1 hour. On cooling orange coloured crystals
of thioether 3 separated. The product is filtered through a quantitative filter paper, washed with water and dried. It is purified by recrystallisation from hot alcohol. Yield was 80%.

<table>
<thead>
<tr>
<th>Melting point</th>
<th>Observed</th>
<th>Reported [15]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>121°C</td>
<td>121°C</td>
</tr>
</tbody>
</table>

**IR (KBr) cm⁻¹:** 3080 (aromatic CH stretch), 1597, 1557, (aromatic C=C stretch), 1517, 1331 (Asymmetric and symmetric N=O stretch of Ar-NO₂), 815 (Ar-Cl stretch), 715 (C-S stretch),

**¹H NMR (in CDCl₃):** δ 8.2 (s, 1 H), 7.0 –7.5 (m, 5 H), 6.8 (d, 1H) 2.4(s, 3H).

4. **Preparation of 4-nitro-2-(phenylthio) benzene (thioether 4)** [13].

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiophenol</td>
<td>-</td>
<td>4.4 g</td>
</tr>
<tr>
<td>1-chloro-4-nitrobenzene</td>
<td>-</td>
<td>6.4 g</td>
</tr>
<tr>
<td>Dry Ethanol</td>
<td>-</td>
<td>50cc</td>
</tr>
<tr>
<td>Metallic Sodium</td>
<td>-</td>
<td>1.4 g</td>
</tr>
</tbody>
</table>

50 ml dry alcohol is taken in 250 ml R.B. flask fitted with a CaCl₂ guard tube. Small pellets of metallic Na (0.06 mol) is added one after another and is allowed to react exothermically. After the reaction is complete, thiophenol (4.4g, 0.04 mol) is added drop wise to the reaction mixture and is stirred well. 6.4 g (0.04 mol) of 1-chloro-4-nitrobenzene dissolved in alcohol is added. The mixture is stirred well and refluxed over a water bath for 1 hour. On cooling yellow coloured crystals of thioether 4 separated. The product is filtered, washed, dried and purified by recrystallisation from hot alcohol. Yield was 80%.

**Melting point** 58°C (Observed), 57°C (Reported [16])

**IR (KBr) cm⁻¹:** 3050 (aromatic CH stretch), 1578, (aromatic C=C stretch), 1510, 1335 (Asymmetric and symmetric N=O stretch of Ar-NO₂), 684 (C-S stretch)

**¹H NMR (in CDCl₃):** δ 8.2 (d, 2 H), 7.0 –7.5 (m, 7 H),
5.5 References

7. M.A. Faustino, M.G.P.M.S. Neves, M.G.H.Vincente, A.M.S. Silvia and J.A.S Cavaleiro
13. a. Chemical Abstracts: 1937, 31, 14136,