ABSTRACT

CHAPTER - I : Synthesis of 2'-chloroazobenzene-2-sulphenyl bromide.

1. Preparation of 2-benzylthio aniline:

(a). 1-chloro nitrobenzene (21) is treated with sodium sulphide and flower of sulphur in ethanol medium. The mixture on refluxing for two hours in water bath, 2, 2'-dinitro diphenyl disulphide (22) is formed.

\[
\begin{array}{c}
\text{NO}_2^- \text{Cl}^- + \text{Na}_2\text{S} \xrightarrow{\text{EtOH}, \Delta} \text{NO}_2^- \text{S-S-NO}_2^- \\
(21) & \quad (22)
\end{array}
\]

(b). 2, 2'-dinitro diphenyl disulphide (22) is treated with sodium hydroxide and sodium sulphide in ethanol and refluxed with water. The mixture on treatment with aqueous sodium hydroxide and benzyl chloride yields 1-benzylthio-2-nitrophenol (23).

\[
\begin{array}{c}
\text{NO}_2^- \text{S-S-NO}_2^- + \text{Na}_2\text{S} \xrightarrow{\text{NaOH, EtOH}} \text{NO}_2^- \text{SCH}_2\text{Ph} \\
(22) & \quad (23)
\end{array}
\]
(C) 1-thio benzyl-2-nitrophenol on reduction with iron powder and acetic acid in toluene yields 2-thiobenzyl aniline (13).

\[
\text{Fe/CH}_3\text{COOH} \rightarrow \text{Fe}_2\text{O}_3
\]

2. Preparation of 1-chloro-2-nitrosobenzene:

1-chloro-2 nitrosobenzene is prepared from 1-chloro-2-nitrobenzene by reduction with zinc and ethanol in presence of ammonium chloride. The hydroxyl amine derivative (24) resulted is then oxidized to 1-chloro-2-nitrosobenzene (17) with ice cold sodium dichromate and sulphuric acid.
3. Preparation of 2'-chloroazobenzene-2-benzyl sulphide:

2-benzyl thioaniline when condensed with 1-chloro-2-nitroso benzene in acetic acid medium at 60 °C yields 2'-chloroazobenzene-2-benzyl sulphide (18).

\[
\begin{align*}
\text{Cl}\text{-NO} + \text{H}_{2}\text{amine} \rightarrow \text{Cl}\text{-N=N-SCH}_{2}\text{Ph}
\end{align*}
\]

(17) (13) (18)

4. Preparation of 2'-chloroazobenzene-2-sulphenyl bromide:

2'-chloroazobenzene-2-benzyl sulphide (18) on brominolysis with bromine in acetic acid gave 2'-chloroazobenzene-2-sulphenyl bromide (19).

\[
\begin{align*}
\text{Cl-N=N-SCH}_{2}\text{Ph} \overset{\text{Br}_2, \text{CH}_3\text{COOH}}{\longrightarrow} \text{Cl-N=N-SBr}
\end{align*}
\]

(18) (19)
CHAPTER II: Physical characteristics of 2'-chloroazobenzene-2-sulphenyl bromide.

1. UV and visible spectra of 2'-chloroazobenzene-2-sulphenyl bromide:

UV and visible spectra of 2'-chloroazobenzene-2-sulphenyl bromide in chloroform and benzene show the K-band only. The disappearance of expected R-band due to the azo group, is perhaps due to the existence of the molecule in these solvent in the heterocyclic thia-diazonium structure (26).

\[
\text{Cl} \quad \text{Br}
\]

In ethanol medium both R-band and the K-band is observed. This is perhaps due to the ethanolysis of the thia-diazonium form (26) by the solvent molecule.

2. IR spectra of 2'-chloroazobenzene-2-sulphenyl bromide:

IR spectra of the compound (19) shows a weak band at 1585 cm\(^{-1}\) due to -N=N- stretching
3. **Study of the hydrolytic cleavage of S-Br bond of 2'-chloroazobenzene-2- sulphenyl bromide in aqueous solution**:

Hydrolytic cleavage of S-Br bond of the sulphenyl bromide (19) in aqueous solution is studied by monitoring the rate of change of pH with respect to time. The hydrolytic cleavage is found to be suppressed with addition of a common ion.

4. **Chromatographic characterization of 2'- chloroazobenzene-2- sulphenyl bromide**

Hptlc separation of a few azobenzene sulphenyl bromides along with 2'-chloroazobenzene-2- sulphenyl bromide is achieved with chloroform : cyclohexane (50:50) solvent system. Analog curve obtained from the hptlc chromatogram by scanning of the spots shows the separation profile of the sulphenyl bromides.

Studies on the separation of the sulphenyl bromide was also carried out by hplc using variety of solvent systems. The best separation of the compounds were achieved under reverse phase system with solvent mixture of acetonitrile : water (50:50).

5. **Mass spectra of the 2'- chloroazobenzene-2-sulphenyl bromide**

The mass fragmentation of the compound donot show the molecular ion. The other different fragmented ions are identified.
6 Thermal studies of 2'-chloroazobenzene-2-sulphenyl bromide.

Differential Scanning Calorimetry (DSC) of the compound (19) is done by variable heating method of Ozawa, in the temperature range of $100^\circ C$ to $350^\circ C$ at a heating rate of $10^\circ C$ per minute using air as a purge gas. The compound (19) gives an exothermal peak in the temperature range of $218^\circ C$ to $228^\circ C$. The absence of endothermal peak suggests that the compound does not have a clear melting point but it melts with decomposition.
CHAPTER III: Solvolysis and alkaline hydrolysis of 2'-chloroazobenzene-2- sulphenyl bromide.

1. The study of solvolytic properties of 2'-chloroazobenzene-2-sulphenyl bromide(19) shows that it is susceptible to solvolysis in water and in boiling ethanol. In both the cases the compound is converted to corresponding disulphide (38).

\[
\begin{array}{c}
\text{S}^- \\
\text{N} = \text{N} \\
\text{Cl}
\end{array}
\]

(38)

2. Alkaline hydrolysis of the compound(19) with equimolar quantities of sodium hydroxide gives a mixture of corresponding disulphide (38), monosulphide (43) and alkali sulphinate (40). The latter on acidification gives corresponding sulphinic acid (44).
3. Study of the solvolysis of 2'-chloroazobenzene-2-sulphenyl bromide with excess quantity of sodium hydroxide and sodium bicarbonate are carried out. The reactions are found to be analogous to that of the corresponding equimolar reaction of sodium hydroxide producing same set of products.
CHAPTER- IV : sulphenylation of active methylene compounds with 2'-chloroazobenzene-2- sulphenyl bromide.

1. The sulphenyl bromide (19) reacts with acetyl acetone to give the stable mono sulphenylated acetyl acetone (55).

Where,

\[
\text{Ar-S-HC} \quad \text{COCH}_3 \\
\text{COCH}_3
\]

(55)

2. Reaction of sulphenyl bromide (19) with acetoacetanilide in ethanolic medium gives β- keto sulphide (59).

\[
\text{Ar-S-HC} \quad \text{COCH}_3 \\
\text{CONHC}_6\text{H}_5
\]

(59)

3. 2'-Chloroazobenzene-2- sulphenyl bromide reacts with ethyl acetoacetate to give mono sulphenylated ethyl acetoacetate (60).
4. Reaction sulphenyl bromide (19) with diethyl malonate gives mono-sulphenylated diethyl malonate (61).

\[ \text{Ar-S-CH} \quad \text{COCH}_3 \quad \text{COC}_2\text{H}_5 \]

\[ \text{(60)} \]

\[ \text{Ar-S-CH} \quad \text{COOC}_2\text{H}_5 \]

\[ \text{COOC}_2\text{H}_5 \]

\[ \text{(61)} \]

In all the above reactions it is seen that all the active methylene groups have been mono sulphenylated by the sulphenyl bromide (19). The monosulphenylated active methylene compounds survived further sulphenylation in place of their second hydrogen atoms due to the insolubility of the monosulphenylated compounds in the reaction medium.

5. Attempts to prepare 1,3-thiazoles from the β-keto sulphide are failed and instead, sulphenyl bromide (19) is regenerated.
CHAPTER - V : Thioarylation of aromatic substrates with 2'-chloroazobenzene-2-sulphenyl bromide.

1. Reaction of sulphenyl bromide (19) with resorcinol in ethanol medium yields the thioether (70)

\[
\begin{align*}
&\text{OH} \\
&\text{SAr} \\
&\text{(70)}
\end{align*}
\]

2. Reaction of 2'-chloroazobenzene-2-sulphenyl bromide with m-aminophenol in ethanol medium gives thioether (71).

\[
\begin{align*}
&\text{OH} \\
&\text{NH}_2 \\
&\text{SAr} \\
&\text{(71)}
\end{align*}
\]

3. Reaction of sulphenyl bromide (19) with m-phenylene diamine in ethanol medium gives thioether (72).

\[
\begin{align*}
&\text{NH}_2 \\
&\text{NH}_2 \\
&\text{SAr} \\
&\text{(72)}
\end{align*}
\]
CHAPTER VI: Addition reaction of 2'-chloroazobenzene-2-sulphenyl bromide.

1. 2'-Chloroazobenzene-2-sulphenyl bromide reacts with styrene in dichloro methane medium in equimolar proportion to give the expected Markownikoff adduct, $\beta$-bromo thioether (77) as the major addition product along with a little amount of disulphide (38)

$$\begin{align*}
\text{Br} \\
\text{CH} \cdash \text{CH}_2 \cdash \text{SAr}
\end{align*}$$

(77)

2. The reaction of sulphenyl bromide (19) with styrene in 3:1 molar proportion in dichloro methane medium gives a mixture of expected $\beta$-bromo thioether (77), appreciable amount of disulphide (38) and 1, 2-dibromo-1-phenyl ethane (79).

$$\begin{align*}
\text{Br} \\
\text{CH} \cdash \text{CH}_2 \\
\text{Br}
\end{align*}$$

(79)
3. Equimolar reaction of sulphenyl bromide (19) with styrene in ethanol medium gives two products, one is expected Markownikoff's adduct $\beta$-bromo thioether (77) and the other one is solvent incorporated product $\beta$-ethoxy thioether (78)
CHAPTER VII: sulphenylation reactions of (A) Amino acids, (B) Dipeptides with 2'-chloroazobenzene-2- sulphenyl bromide.

(A): Sulphenylation of Aminoacids:

1. The aminoacids Glycine and Alanine, which donot have any other nucleophilic site except the amino group, can be N- sulphenylated with sulphenyl bromide (19). In ethanol medium and in equimolar proportion glycine and alanine give sulphenamides (87) and (88) respectively.

\[ \text{NHSAr} \quad \text{H}_2\text{C} \quad \text{COOH} \]
\[ \text{87} \]

\[ \text{NHSAr} \quad \text{CH}_3\text{HC} \quad \text{COOH} \]
\[ \text{88} \]

When reactions of glycine and alanine are carried out with the sulphenyl bromide (19) in 1:3 molar quantities in ethanol medium, respective sulphenamides (87), (88) are obtained as major product along with disulphide (89) and a little amount of respective sulphenimines (89) and (90).

\[ \text{C} = \text{N} - \text{SAr} \]
\[ \text{CH}_3\text{CH} = \text{SAr} \]
\[ \text{89} \]
\[ \text{90} \]
2. Regeneration of amino acids glycine and alanine from their mono-N-sulphenylated products (87) and (88).

The amino acids glycine and alanine are regenerated from their N-sulphenylated products (87) and (88) by the treatment with hydrogen bromide in dry ether.

3. Reactions with sulphur containing amino acids:

Sulphenyl bromide (19) reacts with cysteine in equimolar proportion in ethanol and acetic acid medium producing S-sulphenylated unsymmetrical disulphide (91).

\[
\text{Ar} - S - S - \text{CH}_2 - \text{HC} \quad \text{NH}_2 \quad \text{COOH}
\]

(91)

4. Regeneration of cysteine from unsymmetrical disulphide (91):

Cysteine is regenerated from unsymmetrical disulphide (91) by "thiol-disulphide" exchange reaction with 2-mercapto ethanol.

\[
\text{Ar} - S - S - \text{HC} \xrightarrow{\beta\text{-mercapto ethanol}} \text{HS} - \text{CH}_2 - \text{HC} \quad \text{NH}_2 \quad \text{COOH}
\]

(91)
5. Reaction with amino acid containing phenolic group:

Tyrosine reacts with sulphenyl bromide (19) in equimolar proportion in ethanol medium to give sulphenamide (92).

\[ \text{Ar.S—HN—CH—COOH} \] (92)

Tyrosine reacts with sulphenyl bromide (19) both in equimolar proportion and excess amount of the sulphenyl bromide in acetic acid medium. Phenolic thioether (93) results as the single product.

\[ \text{H2N—CH—COOH} \] (93)
6. Reaction with heterocyclic aminoacid:

Equimolar reaction of tryptophane with sulphenyl bromide (19) in ethanol medium gives sulphenamide (94) as the single product. But in acidic medium α- position of the indole ring is sulphenylated instead of the amino group to give the thioether (95).

(B). Sulphenylation of dipeptides:

Equimolar reactions of 2'-chloroazobenzene-2- sulphenyl bromide with dipeptides such as, tryptophyl-glycine, glycyyl-tryptophane and glycyyl-tyrosine in acetic acid medium, give respective thioethers (97), (99) and (101).
But the same dipeptides react with the sulphenyl bromide (19) in equimolar proportion in ethanol medium to give two products each. The major ones are respective mono N- sulphenylated products (96), (98) and (100), and the minor ones are being the respective thioethers (97), (99) and (101).
Regeneration of dipeptides:

Mono N-sulphenylated product (98) on treatment with hydrogen bromide in dry ether regenerates the dipeptide glycyl tryptophane.