CHAPTER IV

DISCUSSION AND PROBABLE MECHANISM
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Syntheses of 2-mercapto-3-arylquinazol-4-ones:

In this study of the syntheses of 2-mercapto-3-arylquinazol-4-ones two methods were employed, (i) using arylthioureas and (ii) using arylisothiocyanates. In the first case the best yield was obtained by heating an anthranilic acid with an arylthiourea in 2:3 molar proportions at 190-200°C for 2-1/2 to 3 hours. Reaction was also studied using sodium bisulphate as a catalyst without any improvement in the yield. In the second case, the best condition was heating anthranilic acid with an arylisothiocyanate on a steam bath for 1-1/2 hours. The yield was better when ethanol was used as a solvent than without a solvent.

With anthranilic acid the yields ranged from 50 to 65 per cent depending upon arylthioureas and 60 to 75 per cent depending upon arylisothiocyanates. In case of 4- and 5-bromoanthranilic acids the yields were 35 to 50 per cent for arylthioureas and 50 to 65 per cent for arylisothiocyanates. The most poor yields were with 3:5-dibromoanthranilic acid where it ranged from 30 to 40
per cent for arylthioureas and 35 to 55 per cent for aryliothiocyanates.

In the syntheses of these 2-mercapto-3-arylquinazol-4-ones the best results were for 3-p-anisyl, which were 40 to 65 per cent by the thiourea method and 55 to 75 per cent by the isothiocyanate method. This is followed by 3-p-tolyl \((1)\) 35 to 65, \((ii)\) 50 to 70 per cent \(\bigwedge\), 3-phenyl \((1)\) 35 to 55, \((ii)\) 45 to 65 per cent \(\bigwedge\) and 3-p-chlorophenyl \((1)\) 30 to 55, \((ii)\) 40 to 65 per cent \(\bigwedge\) in that order. The poorest results are for 3-p-nitrophenyl \((1)\) 30 to 50 and \((ii)\) 35 to 60 per cent. Thus it is evident that electron withdrawing groups in anthranilic acid as well as the thiourea or isothiocyanate decrease the yield, while electron releasing group in the thiourea or isothiocyanate increase the yield.

\textbf{Physical Properties:}

The 2-mercapto-3-arylquinazol-4-ones are insoluble in water and aqueous sodium bicarbonate, but dissolve in aqueous sodium hydroxide to give a yellow solution. They are soluble in acetone and acetic acid but moderately in ethanol. They give colourless lead salts and yellow copper salts with the respective metal acetates.
Reactions:

The 2-mercapto-3-arylquinazol-4-ones were easily oxidised to the corresponding 3-arylquinazol-2:4-diones in acidified 5 per cent aqueous potassium permanganate at room temperature.

With 5 per cent aqueous iodine the corresponding disulphides were obtained which in most of the cases be reduced back to the original 2-mercapto compound by tin and hydrochloric acid and oxidised to the respective 2:4-dione by acidic permanganate. However in the case of the disulphides from 3-p-nitropherylquinazol-4-ones no definite product could be isolated on reaction with tin and hydrochloric acid.

Reaction with methyl iodide in presence of sodium methoxide gave the corresponding 2-methylthio ether which could easily be oxidised to the corresponding sulphones using acidic permanganate. The 2-mercapto-3-p-nitropherylquinazol-4-ones failed to react with methyl iodide.

Similarly the 2-mercapto-3-arylquinazol-4-ones reacted with 2:4-dinitrochlorobenzene in presence of pyridine. The yellow 2:4-dinitrophenyl thio ethers so obtained were oxidised with acidic permanganate to the
corresponding sulphones. The 2-mercapto-3-arylquinazol-4-ones also condensed with chloroacetic acid and \( \omega \)-bromoacetophenone to give the corresponding sulphides. Only two quinazol-4-ones did not react with the latter.

The 2-mercapto-3-arylquinazol-4-ones when heated with sulphuric acid isomerised to the corresponding 2-arylamo-6-keto-4:5-benzo-1:3-thiazines. The 2-mercapto-3-p-anisylquinazol-4-ones did not isomerise when heated with sulphuric acid.

**Probable Mechanism:**

(I) The condensation of phenylthiourea with anthranilic acid proceeds via three steps giving a diphenyl thiourea derivative (A). This is in parallel with the reaction of arylamines with aryl thioureas. First (i) a nucleophilic attack by the arylamino group on the carbon of \( \text{C} = \text{S} \), (ii) transfer of a proton from the arylamines -\( \text{NH}_2 \) to -\( \text{NH}_2 \) of arylthiourea, followed by (iii) elimination of \( \text{NH}_3 \) to form \( \text{N}_1 \)-aryl-\( \text{N}_3 \)-2-(carboxy-phenyl)-thiourea (A). This further gets cyclised by a nucleophilic attack to the carboxyl carbon via the usual three steps (i) the nucleophilic attack (ii) transfer of a proton from -\( \text{NH} \) to -\( \text{OH} \) and (iii) elimination of \( \text{H}_2\text{O} \) resulting in the final product (I).
thio-enamine
(I)

thio-ketamine
(I)
The investigation of reactions of the functional group $-\mathcal{S}H$ in 2-mercapto-3-arylquinazol-4-one (I) have been described earlier. On comparison with aryl mercapto group and in the light of experimental condition the following probable mechanism is proposed.

II:1 Reactions in alkaline medium:

This will first lead to the formation of a mercaptide anion (I). A nucleophilic attack by this anion on the substrate carbon of the reagent methyliodide (a), chloroacetate (b) and phenacylbromide (c).

(a) $R = H, X = I$  
(b) $R = \text{COOH}, X = \text{Cl}$  
(c) $R = \text{CoPh}, X = \text{Br}$  

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II:2 Reactions in poor basic medium like pyridine:

The lower basicity has an adverse effect on the formation of a mercaptide anion(I), however the non-bonding electrons of sulphur of the mercapto group are polarizable and there will be sufficient nucleophilicity. Hence the chlorine of the 2;4-dinitrochlorobenzene(d) is replaced by an initial nucleophilic attack followed by removal of the proton by a weak base-pyridine.
II:3. Oxidation in acidic medium:

In acidic conditions the oxidation of 2-mercapto-3-arylquinazolin-4-one (I) by aqueous potassium permanganate probably proceeds by the following mechanism.

Owing to the easily polarisable non-bonding electron of sulphur in thio-ketamine form there will be co-ordination with Mn$^{+7}$ of MnO$_4$$^{-1}$. This will render carbon substrate in position 2. It will be attacked by a weak nucleophile H$_2$O, followed by the removal of a proton and finally a keto group will be generated in position 2 giving (II).
2-Methylmercapto-3-arylquinazol-4-one (IV) and 2(2',4'-dinitrophenyl) mercapto-3-arylquinazol-4-one (VI) are oxidised by acidic potassium permanganate. In this case thiolactonic form is not possible, however non-bonding electron of sulphur can be donated to Mn⁷⁺ of MnO₄⁻¹. This will not be favourable to render carbon substrate in position 2. However sulphur becomes electron deficient and hence experiences nucleophilic attack of H₂O. This will raise the oxidation state of sulphur from -2 to +2 giving a sulphone derivatives (V) and (VII).

\[ \text{IV, } R = \text{CH}_3 \]
\[ \text{IV, } R = \ \begin{array}{c} \text{NO}_2 \\ \text{NO}_2 \end{array} \]
\[ \text{V, } R = \text{CH}_3 \]
\[ \text{VII, } R = \ \begin{array}{c} \text{NO}_2 \\ \text{NO}_2 \end{array} \]
III Rearrangement by sulphuric acid:

(X)