SYNOPSIS

Title: SYNTHESIS OF SULFONYL THIOUREAS/UREAS AND 1,3,4-THIADIAZOLES

The Thesis is divided into two parts.

PART - I 1-ARYL-3-ARYLSULFONYL THIOUREAS AND UREAS

In some patients, diabetes is owing to rapid destruction of insulin by enzymes. The sulphonamides are general enzymes inhibitors. 2-sulphanilamido-5-isopropyl-1,3,4-thiadiazole was the first compound which showed hypoglycemic activity probably by preventing enzymatic destruction of insulin (Janbon et al, Montpellier 1942, 21-22, 489).

\[
\begin{align*}
\text{H}_2\text{N} & \quad \text{SO}_2\text{NH} \\
& \quad \text{CH(CH}_3)\text{2}
\end{align*}
\]


\[\text{R} - \quad \text{SO}_2\cdot\text{NH} \cdot \text{CO} \cdot \text{NH} \cdot \text{R}^1\]
Thiourea derivatives have also been shown to reduce glucose content of blood (Budesinsky et al, Ceskoslov. farm 1959, 2, 129-35; Polazzo et al, Farmaco (pavia) Ed. Sci. 1959, 14, 358-62; Friedrich, Ger. (East) 16,086 Dec. 20, 1958 - Chem. Abstr. 1961. 52, 455).

As very few 1-Aryl/benzyl-3-Arylsulphonyl thioureas and ureas seem to have been studied, it was thought worth while to prepare 1-Aryl/benzyl-3-Arylsulphonyl thioureas and ureas.

(i) Thioureas have been prepared by the interaction of aryl sulphonyl amides with Aryl/benzyl isothiocyanates.

\[ R.SO_2NH_2 + R'NCS \]

\[ R SO_2NH.CS.NH R' \]

\[ R = p-CH_3.C_6H_4; \quad p-CH_3O.C_6H_4; \quad p-Cl.C_6H_4; \quad p-Br.C_6H_4 \]

\[ p-C_6H_5; \quad p-CH_3.CO.NH.C_6H_4; \quad p-NH_2.C_6H_4; \quad b-C_6H_5; \]

\[ R' = o, m, p-CH_2.C_6H_4; \quad o, p-CH_3O.C_6H_4; \quad o, p-Cl.C_6H_4 \]

\[ p-Br.C_6H_4; \quad 3:5-(CH_3)C_6H_3; o, p-CH_3.C_6H_4.CH_2; \]

\[ 2:4/2:5/3:4-(CH_3)C_6H_3.CH_2; o,p-Cl.C_6H_4.CH_2.p-Br.C_6H_4. \]

\[ -CH_2 \]
(ii) Ureas have been prepared by desulphurisation of above thioureas by alkaline hydrogen peroxide.

\[ R \text{SO}_2\text{NHCSNHR}' + H_2O \rightarrow R \text{SO}_2\text{NHCONHR}' \]

\( R \) and \( R' \) as above

(iii) By using benzyl sulphonamide in place of aryl sulphonamide 1-aryl/benzyl-3-benzylsulphonyl thioureas and ureas have been prepared as described above.

\[ RHCSNH' \quad R = C_6H_5.CH_2 \]
\[ R\text{NHCONHR}' \quad R' = O.CH_3.C_6H_4; p-CH_3O.C_6H_4 \]
\[ 3:5-(CH_3)_2.C_6H_4.CH_2; 2:4-(CH_3)_2.C_6H_3.CH_2 \]

PART II: 1, 3, 4 - THIADIAZOLES

it was of considerable interest to prepare 1,3,4-thiadiazoles from these compounds.

(i) 2 and 5 substituted 1,3,4-thiadiazoles have been prepared by the following three methods.

(a) \[ \text{R.NH-CS.NH.NH} \rightarrow \text{CH}_2 \cdot \text{R} \]

\[
\begin{array}{c}
\text{Oxidative cyclisation by FeCl}_3 \\
\end{array}
\]

\[
\begin{array}{c}
\text{N} \\
\text{N} \\
\text{R - NH-C} \\
\text{S} \\
\text{C - R'}
\end{array}
\]

\[ R = \text{m,p-Cl.C}_6\text{H}_4; \text{p-Br.C}_6\text{H}_4; \text{p-CH}_2\text{O.C}_6\text{H}_4; \text{o-CH}_3\text{C}_6\text{H}_4 \]
\[ \text{m,p-CH}_3\text{C}_6\text{H}_4; \text{p-Cl.C}_6\text{H}_4\cdot\text{CH}_2 \]

\[ R' = \text{o,p-Cl.C}_6\text{H}_4; \text{2:4-Cl}_2\text{C}_6\text{H}_3; \text{o,m,p-OH.C}_6\text{H}_4; \]
\[ \text{p-CH}_3\text{O.C}_6\text{H}_4; \text{p-N(CH}_3)_2\text{C}_6\text{H}_4 \]

(b) \[ \text{R.NH-CS.NH.NH}_2 + \text{R'.CO.Cl} \]

\[ \begin{array}{c}
\text{R.NH-CS.NH.NH.CO.R'} \\
\end{array} \]

\[
\begin{array}{c}
\text{HCl} \\
\end{array}
\]

\[
\begin{array}{c}
\text{N} \\
\text{N} \\
\text{R-NH-C} \\
\text{S} \\
\text{C - R'}
\end{array}
\]
(i) A few 5-mercapto-1,3,4-thiadiazoles have been prepared as follows:

\[
R \cdot \text{NH} \cdot \text{CS} \cdot \text{NH} \cdot \text{NH}_2 + \text{CS}_2 + \text{Na}_2\text{SO}_3 \text{ (Anhyd.)}
\]

(ii) Some of the thiadiazoles have been screened for antihistaminic activity.