INTRODUCTION PART - II
THIADIAZOLES

The widespread occurrence of heterocyclic compounds in nature as alkaloids, vitamins, pigments and a variety of plant and animal cell constituents, their vital role in biological processes: their availability from agricultural wastes and as products volatilized in coking of coal; and their economic value as solvents, dyes and pharmaceuticals are factors which have directed the attention of organic chemists to this field since the earliest days of the science. A generous third of the compounds listed in Beilstein have heterocyclic nuclei, over half of the types of compounds produced by nature have heterocyclic systems. As a result information has accumulated until to day heterocyclic Chemistry constitutes major branch of organic chemistry ranking in importance with the aliphatic and isocyclic branches.

Thiadiazoles are related to thiazoles as shown below:

\[
\begin{align*}
N & \quad CH \\
CH & \quad CH \quad \text{Thiazole ring} \\
HC & \quad N \\
HC & \quad N \\
HC & \quad N \\
N & \quad CH \\
N & \quad CH \\
N & \quad CH \\
N & \quad CH \\
S & \quad S \\
S & \quad S \\
S & \quad S
\end{align*}
\]

1:2:3- 1:2:5- 1:2:4- 1:3:4-thiadiazole.
The large number of patents appearing in technical literature regarding thiadiazole derivatives show its importance in different fields of chemical applications.


Several thiadiazole derivatives exhibit antithyroid activity. 5-Amino-1:3:4-thiadiazole-2-thiol exhibited marked

Substances having the formula 2-amino-5-substituted 1:3:4-thiadiazole (substituents are Ethyl, cyclopropyl, Benzyl, propenyl, butyl, butenyl, methyl, vinyl) have been claimed to be antibacterial agents (U.S. patent 2,497,825 Feb. 14, 1950 - Chem. Abstracts 1950 44, 59196), 2,5-Dimer-captothiadiazole, (Ernst Shraufstrutter Z. Naturforsch. 5b, 190-5 (1950) - Chem. Abstracts 1950, 44, 8999) and 4-phenyl-5-thioxo-4:5-dihydro-1:3:4-thiadiazole-2-sulfonamide (U.S. patent No. 2,883,390 Chem. Abstracts 1959, 52, 16156) show antibacterial activity. Whereas Mercury containing 2,5-dimer-capto-1:3:4-thiadiazole derivatives are useful as insecticides (German patent 951, 869 Nov. 8 (1956) - Chem. Abstracts 1959, 53, 4306). Antibacterial properties are also shown by 5-(Nitro-Amino)-2-(furyl/substitutedfuryl)-1:3:4-thiadiazoles (William

Thiadiazoles of the type

\[
\begin{align*}
\text{N} & \quad \text{N} \\
\text{R} - \text{C} & \quad \text{C} - \text{NH}.\text{SO}_2.\text{C}_6\text{H}_4.\text{NH}_2.\text{P} \\
\text{S} &
\end{align*}
\]

where is \( 4-(\text{H}_2\text{C})-3-(\text{OH}) \) \( \text{C}_6\text{H}_3 \) and \( R \) is 1:3:4-thiadiazole-2-yl, have also reported antitubercular activity (Antibiotics & Chemotherapy, 5, 129-31 (1955) - Chem. Abstracts 1955, 42, 12707 f ).


5-benzylamino-thiadiazole or derivatives are valuable as antihistamines U.S. patent 2,619,489 Nov. 25, 1952 - Chem. Abstracts 1953, 47, 10009 h). 2-phenyl-1:3:4-thiadiazole

2:5-Bis (4-nitrobenzylthio)-1:3:4-thiadiazoles are good acaricides (British patent 748, 422 - chem. abstracts 1957, 51, 12910).

Benzyl group is found to be physiologically active as can be seen from Marfanil (sulphamylon) (Domagk, Deut. Med. Wochschr, 1942, 21, 448) and Hibicon (Kushner et al., J. Org. Chem., 1951, 16, 1283 and Hibital (Benzyl-4-carbamyl-1-piperazine carboxylate (Goldman and Williams, J. Org. Chem. 1953, 18, 815).

\[ \begin{align*}
H_2N - CH_2 & \quad \text{SO}_2\text{NH}_2 \quad \text{(Marfanial)} \\
\text{Cl} \cdot CH_2 \cdot CH_2 & \cdot CO \cdot NH \cdot CH_2 & \quad \text{CO}_2H \\
\text{CH}_2 & \cdot OOCC - N & \quad \text{H}_2\text{C} \quad \text{CH}_2 & \quad \text{NH}_2 \quad \text{CO} - \text{NH}_2 \quad \text{(Hibital)}
\end{align*} \]

The above indicate the importance of benzyl, phenyl and mercapto groups in endowing a compound with physiological activity.

Thiosemicarbazides and thiosemicarbazones have been found to show antitubercular activity (Domagk et al., Naturwissenschaften, 1946, 315; Domagk, Nord. Med. 1947, 32, 1322; Domagk ibid.; 1950, 61, 8; Hoggarth et al., Brit. J. Pharm. 1949, 4, 248; Martin, Brit. J. Exp. Path., 1950, 31, 189).
It was therefore of considerable interest to examine heterocyclic compounds from such phenyl/benzyl-thiosemicarbazides and phenyl/benzyl-thiosemicarbazones. With this in view several 2-arylamino-5-(aryl/benzyl or alkyl)-1:3:4-thiadiazoles have been prepared.

These 1:3:4-thiadiazoles were prepared as shown below by four routes:

(1) \[
\text{R-NH} \cdot \text{C} \cdot \text{NH} \cdot \text{NH}_2 + \text{R}^\prime \cdot \text{CO} \cdot \text{Cl} \\
\rightarrow \text{R-NH} \cdot \text{C} \cdot \text{NH} \cdot \text{NH} \cdot \text{CO} \cdot \text{R}^\prime \\
\rightarrow \text{HCl} \\
\]

(2) \[
\text{R-NH} \cdot \text{C} \cdot \text{NH} \cdot \text{N} = \text{CH} \cdot \text{R}^\prime \xrightarrow{\text{FeCl}_3} \text{R}^\prime \cdot \text{C} \cdot \text{NH} \cdot \text{R} \\
\]

(3) \[
\text{R-NH} \cdot \text{C} \cdot \text{NH} \cdot \text{NH}_2 + \text{R}^\prime \cdot \text{COOH} \\
\rightarrow \text{H}_2\text{SO}_4 \\
\]

R & R' are aryl groups.

R, = Aryl groups
R = Alkyl groups
These substances were prepared as described in theoretical part II page 135.