The thesis is divided into three parts:

Part - I : Bis-Basic Amides.
Part - II : Bis-Thiazolines.
Part - III : Thiourethans.

PART - I.

Amides and esters are the two important types of compounds used as local anesthetics. Xylocaine\(^1\) is the best known example of the amide group of local anesthetics.

![Xylocaine](image)

Out of several types of basic amides prepared in this laboratory,

![Basic Amide](image)

\(\sigma{}'-\text{morpholino-N-(2-4-dimethyl benzyl)}\text{-acetamide}^2\) was more
active and less toxic as compared to xylocaine.

\[ \text{\(\alpha\)'-Morpholino-N-(-1-phenyl-2-phenylethyl)-acetamide}^3 \]

\[ \text{\(\alpha\)'-diethylamino-N-\(\bigwedge\)-1-(4-ethoxy phenyl)-2-phenylethyl\(\bigwedge\)-acetamide}^3 \]

were recent additions with higher activity as compared to xylocaine.

\[ \text{\(\alpha\)'-Secondary amino-N-(aryloxy alkyl)-acetamides}^4 \]

were found
to be two to four times as active as xylocaine and procaine.

Some, $\omega'$-secondary amino-N-(substituted benzyl)-acetanilides$^5$
were also found to be two to four times as active as xylocaine, and

$\omega'$-secondary amino-N-(aralkyl)-acetamides$^6$ were also found to be more active than xylocaine.

Some of these compounds exhibited analgesic, anticonvulsant, antiarrhythmic and hypnotic effects in addition to the significant local anesthetic activity. These encouraging results prompted us to exploit further variations in the fundamental structure.
Above mentioned diamines show interesting pharmacological properties. Therefore it was of considerable interest to synthesize some bis basic amides from these type of diamines and examine their various types of pharmacological activities.

The required substances were prepared by the following scheme.

(A)

(a) \[ R-C_6H_4-CHO \xrightarrow{\text{NaCN}} R-C_6H_4-C-C-C_6H_4-R \]

(b) The ketones were converted to amines by Leuckart reaction.

\[ R-C_6H_4 - C - C - C_6H_4-R \xrightarrow{\text{Leuckart reaction}} R-C_6H_4-CH - CH - C_6H_4-R \]
(c) \[ \text{R} = \text{H, 4-CH}_3, \text{4-OCH}_3, \text{and 4-Cl.} \]
\[ \text{NR}_1\text{R}_2 = \text{Diethylamino, Morpholino and Piperidino.} \]

(B)

(a) \[ \text{R-C}_6\text{H}_4-\text{CHO} + \text{R-C}_6\text{H}_4-\text{COCH}_3 \xrightarrow{\text{aq. Alkali}} \]
\[ \text{R-C}_6\text{H}_4-\text{CH} = \text{CH-C}_6\text{H}_4-\text{R} \]
\[ \text{Br}_2 \]
\[ \text{R-C}_6\text{H}_4-\text{CH} - \text{CH} - \text{C}_6\text{H}_4-\text{R} \xrightarrow{(1) \text{CH}_3\text{ONa}} (2) \text{HCl} \]
\[ \text{R-C}_6\text{H}_4-\text{C-CH}_2-\text{C}_6\text{H}_4-\text{R} \]
(b) The ketones were converted to amines by Leuckart reaction.

\[
\begin{align*}
R-C_6H_4-\text{O}-\text{CH}_2-C-C_6H_4-R & \xrightarrow{\text{Leuckart reaction}} \\
R-C_6H_4-\text{CH-CH}_2-\text{CH-C}_6H_4-R & \xrightarrow{\text{Cl-CH}_2\text{Cl}} \\
R-C_6H_4-\text{CH-CH}_2-\text{CH-C}_6H_4-R & \xrightarrow{\text{HNR}_1\text{R}_2} \\
R-C_6H_4-\text{NH-COCH}_2\text{Cl} & \\
R-C_6H_4-\text{NH-COCH}_2\text{Cl} & \\
R-C_6H_4-\text{NH-COCH}_2\text{NR}_1\text{R}_2 & \\
R-C_6H_4-\text{NH-COCH}_2\text{NR}_1\text{R}_2 & \\
\end{align*}
\]

where

\( R = \text{H, 4-CH}_3, 4-\text{COH}_3, \text{and 4-Cl}. \)

\( \text{NR}_1\text{R}_2 = \text{Diethylamino, Morpholino and Piperidino}. \)
(c) The ketones were converted to amines by Leuckart reaction.

(b) The ketones were converted to amines by Leuckart reaction.

(a) 
\[
\begin{align*}
\text{HOCO-CH} & \quad \xrightarrow{\text{SOCl}_2} \quad \text{Cl-CO-CH} \\
\text{CH-COCH} & \quad \text{ClCO-CH} \quad \text{Friedel-Crafts reaction} \quad \rightarrow \quad \text{R-C}_6\text{H}_4-\text{C}-\text{CH}=\text{CH-C}_6\text{H}_4-\text{R} \\
\text{CH-CO-C1} & \quad \text{CH2COCl} \\
\text{NaHSO}_3 & \quad \text{Alcohol} \\ 
\rightarrow & \quad \text{R-C}_6\text{H}_4-\text{C}-(\text{CH}_2)_2-\text{C-} \text{C}_6\text{H}_4-\text{R} \\
\end{align*}
\]

(b) 
\[
\begin{align*}
\text{R-C}_6\text{H}_4-\text{CH-(CH}_2)_2-\text{CH-C}_6\text{H}_4-\text{R} & \quad \xrightarrow{\text{Leuckart reaction}} \quad \text{NHCOCH}_2\text{Cl} \\
\text{NH}_2 & \quad \text{NH}_2 \\
\text{Cl-C-CH}_2\text{Cl} & \quad \text{HNR}_1\text{R}_2 \\
\text{NHCOCH}_2\text{Cl} & \quad \text{HNR}_1\text{R}_2 \\
\text{R-C}_6\text{H}_4-\text{CH-(CH}_2)_2-\text{CH-C}_6\text{H}_4-\text{R} & \quad \text{NH}_2 \\
\text{NHCOCH}_2\text{Cl} & \quad \text{HNR}_1\text{R}_2 \\
\text{R-C}_6\text{H}_4-\text{CH-(CH}_2)_2-\text{CH-C}_6\text{H}_4-\text{R} & \quad \text{NHCOCH}_2\text{Cl} \\
\text{NH}_2 & \quad \text{NH}_2 \\
\text{Cl-C-CH}_2\text{Cl} & \quad \text{HNR}_1\text{R}_2 \\
\end{align*}
\]
\[
\begin{align*}
&\text{NHCOCH}_2\text{NR}_1\text{R}_2 \\
&\begin{array}{c}
\text{R-}C_6H_4-\text{CH-}(\text{CH}_2)_2-\text{CH-}C_6H_4-\text{R} \\
\text{NHCOCH}_2\text{NR}_1\text{R}_2
\end{array}
\end{align*}
\]

where

\[
R = \text{H, 4-CH}_3, 4-\text{OCH}_3, 4-\text{Cl}, 2:4-(\text{CH}_3)_2, 2:5-(\text{CH}_3)_2, 3:4(\text{CH}_3)_2.
\]

\[
\text{NR}_1\text{R}_2 = \text{Diethylamino, Morpholino and Piperidino.}
\]

( D )

(a) \[
\begin{align*}
\text{HOOCC-(CH}_2)_3-\text{COOH} & \xrightarrow{\text{SOCl}_2} \text{ClCO-(CH}_2)_3-\text{COOH} \\
\text{Friedel-Crafts reaction} & \rightarrow \text{R-C}_6\text{H}_4-\text{C-(CH}_2)_3-\text{C}-C_6\text{H}_4-\text{R}
\end{align*}
\]

(b) The ketones were converted to amines by Leuckart reaction.

\[
\begin{align*}
\text{R-C}_6\text{H}_4-\text{C-(CH}_2)_3-\text{C}-
\end{align*}
\]

\[
\begin{align*}
\text{Leuckart reaction} & \rightarrow \text{R-C}_6\text{H}_4-\text{CH-(CH}_2)_3-\text{CH-C}_6\text{H}_4-\text{NH}_2
\end{align*}
\]

\[
\begin{align*}
\text{R-C}_6\text{H}_4-\text{CH-(CH}_2)_3-\text{CH-C}_6\text{H}_4-\text{NH}_2
\end{align*}
\]
Thiazolines show various pharmacological activities such as antitubercular, bactericidal, spasmolytic, antidiuretic, fungicidal, insecticidal and acaricidal.

Eisman et al found that thiazolines were more active than the corresponding sym. diaryl thioureas from which they were prepared.
Several sym. diarylthioureas have been shown to exhibit tuberculostatic, antileprotic, antifungal and antiviral activities. It was thought of interest to cyclize diarylthioureas to the corresponding thiazolines.

The required substances were prepared by the following scheme.

(a)

\[
\begin{align*}
R_1 & \quad \text{CO-(CH}_2\text{)_3-CO-} \quad R_1 \\
\downarrow & \quad \text{Br}_2 \quad \text{CCl}_4 \\
{\text{Br}} & \quad \text{Br} \\
R_1 & \quad \text{CO-CH-CH}_2\text{-CH-CO-} \quad R_1
\end{align*}
\]

(b)

\[
\begin{align*}
R_1 & \quad \text{CO-CH-CH}_2\text{-CH-CO-} \quad R_1 \\
\downarrow & \quad \text{Br} \quad \text{Br} \\
R_1 & \quad \text{CO-(CH}_2\text{)_3-CO-} \quad R_1
\end{align*}
\]

\[
\begin{align*}
\text{R}_2\text{NH-C=S} & \quad \text{HNR}_2 \\
\text{Alcohol} & \quad \text{Reflux} \\
\text{R}_2\text{NH-C=S} & \quad \text{HNR}_2 \\
\text{R}_2\text{N-C=S} & \quad \text{HNR}_2 \quad 2\text{HBr}
\end{align*}
\]
PART - III.

Thioureas show various pharmacological activities such as local anesthetics, fungistatic, insecticidal, anthelmintic and they show different types of biological activities.

It was, therefore, of considerable interest to prepare thiourethans from different alcohols.

The required substances were prepared by the following scheme.

\[ \text{R.OH} \xrightarrow{\text{Na}} \text{R-ONa} \xrightarrow{\text{R'NCS}} \text{R.OCSNHR'} \]

where

\( \text{R.OH} = \text{Ethylene glycol, propylene glycol, benzyl alcohol, 2-Morpholinomethyl cyclohexanol, 2-Diethylaminomethyl cyclohexanol, 1-phenyl-3-morpholino propanol, 1-phenyl-3-diethylamino propanol.} \)

\( \text{R'} = -\text{C}_6\text{H}_5, 4-\text{CH}_3-\text{C}_6\text{H}_4, 4-\text{OCH}_3-\text{C}_6\text{H}_4, 4-\text{Cl}-\text{C}_6\text{H}_4, \text{C}_6\text{H}_5-\text{CH}_2, n-\text{C}_4\text{H}_9. \)