SUMMARY OF THE PRESENT WORK
SUMMARY

CHAPTER I

In this Chapter previous work carried out in this laboratory which led to the present investigation is discussed. The acid-catalysed cyclodehydration of alkyl/aryl \( \gamma \)-aminoethylketones and disproportionation of the intermediate 1,2-dihydroquinolines and quinolines has been studied by Tilak et al.\(^1\). The mechanism of the formation of quinolines and tetrahydroquinolines from 1,2-dihydroquinoline and its precursors such as alkyl/aryl \( \gamma \)-aminoethylketones is analogous to the acid-catalysed disproportionation of \( \Delta^3 \)-thiachromens\(^3,4\) and \( \Delta^3 \)-chromenes\(^5\). This disproportionation involves an intermolecular hydride transfer between one molecule of dihydroquinoline acting as hydride donor and another molecule of the same as in its protonated form as a hydride acceptor. Tilak et al.\(^6\) were interested in the synthesis of quinoline derivatives which would not involve disproportionation observed in the above synthesis. When cis-2-(3'-methoxyphenylaminomethylene)cyclohexanone was treated with PPA 7-methoxy-1,2,3,4-tetrahydrophenanthridine was obtained whereas treatment with aniline hydrochloride/anhydrous ZnCl\(_2\) in boiling ethanol gave 6-methoxy-1,2,3,4-tetrahydroacridine. Cis-(3'-methoxyphenylaminomethylene)-cycloalkanones were also cyclodehydrated by formic acid, lactic acid and other acidic reagents. Acid-catalysed
Chart 1

1. \[
\text{H}_3\text{C}-\text{N}\text{H}_2\text{C}_6\text{H}_4\text{O}\text{CH}_3 \xrightarrow{\text{NaBH}_4} \text{H}_3\text{C}-\text{N}\text{H}_2\text{C}_6\text{H}_4\text{OH} \xrightarrow{} \text{H}_3\text{C}-\text{N}\text{H}_2\text{C}_6\text{H}_4\text{H}
\]

2. \[
\text{H}_3\text{C}-\text{N}\text{H}_2\text{C}_6\text{H}_4\text{O}\text{H} \xrightarrow{\text{NaBH}_4} \text{H}_3\text{C}-\text{N}\text{H}_2\text{C}_6\text{H}_4\text{OH} \xrightarrow{} \text{H}_3\text{C}-\text{N}\text{H}_2\text{C}_6\text{H}_4\text{H}
\]

3. \[
\text{H}_3\text{C}-\text{N}\text{H}_2\text{C}_6\text{H}_4\text{O} \xrightarrow{\text{NaBH}_4} \text{H}_3\text{C}-\text{N}\text{H}_2\text{C}_6\text{H}_4\text{OH} \xrightarrow{} \text{H}_3\text{C}-\text{N}\text{H}_2\text{C}_6\text{H}_4\text{H}
\]

4. \[
\text{H}_3\text{C}-\text{N}\text{H}_2\text{C}_6\text{H}_4\text{O} \xrightarrow{\text{NaBH}_4} \text{H}_3\text{C}-\text{N}\text{H}_2\text{C}_6\text{H}_4\text{OH} \xrightarrow{} \text{H}_3\text{C}-\text{N}\text{H}_2\text{C}_6\text{H}_4\text{H}
\]

5. \[
\text{H}_3\text{C}-\text{N}\text{H}_2\text{C}_6\text{H}_4\text{H} \xrightarrow{} \text{H}_3\text{C}-\text{N}\text{H}_2\text{C}_6\text{H}_4\text{H}
\]

6. \[
\text{H}_3\text{C}-\text{N}\text{H}_2\text{C}_6\text{H}_4\text{H} \xrightarrow{} \text{H}_3\text{C}-\text{N}\text{H}_2\text{C}_6\text{H}_4\text{H}
\]

7. \[
\text{H}_3\text{C}-\text{N}\text{H}_2\text{C}_6\text{H}_4\text{H} \xrightarrow{} \text{H}_3\text{C}-\text{N}\text{H}_2\text{C}_6\text{H}_4\text{H}
\]

8. \[
\text{H}_3\text{C}-\text{N}\text{H}_2\text{C}_6\text{H}_4\text{H} \xrightarrow{} \text{H}_3\text{C}-\text{N}\text{H}_2\text{C}_6\text{H}_4\text{H}
\]
cyclodehydration of 3-arylamino-1-alkanols gave a mixture of 2,3-disubstituted-1,2,3,4-tetrahydroquinoline and 3,4-disubstituted-1,2,3,4-tetrahydroquinoline. In one case 1-(3'-methoxyphenyl)-2-phenylazetidine was obtained which rearranged slowly to 7-methoxy-2-phenyl-1,2,3,4-tetrahydroquinoline. The mechanism of formation of the rearranged tetrahydroquinolines, through the intermediate azetidine has been suggested.

CHAPTER II-A

The cyclodehydration of 3-arylamino-butane-1-ol derivatives which led to 2,4-disubstituted-1,2,3,4-tetrahydroquinoline is presented in this Chapter. Whereas in the cyclodehydration of 1, 7 and 8 were expected, the rearranged product 5 was formed. Cyclodehydration of 3 gave 6 and the rearranged tetrahydroquinolines 7 and 8. In the cyclodehydration of 2, 7 and 8 were expected, but the rearranged product 5 was formed. Cyclodehydration of 4 gave 6. A great deal of stereospecificity in the formation of tetrahydroquinolines was observed (Chart 1).

CHAPTER II-B

Synthesis of 4-methyl-2-phenylquinoline and 7-methoxy-2-methyl-4-phenylquinoline is described. Reduction of the quinoline by sodium and alcohol gave the corresponding tetrahydroquinolines. The tetrahydroquinolines were useful in identifying the compounds described in Chapter II-A, III, IV and V.
CHAPTER III

In the rearrangement reactions mentioned in Chapter II-A, N-arylazetidines were likely intermediates. However, except in case of 3-(3'-methoxyphenylamino)-1-phenylpropane-1-ol where 1-(3'-methoxyphenyl)-2-phenylazetidine was isolated, in none of the p-arylamino carbinols the azetidines could be isolated in the cyclodehydration reaction (using 70% H₂SO₄). In order to elucidate the above rearrangement reactions a good synthesis of N-arylazetidines was necessary. In the synthesis described in this Chapter, the OH group of the β-arylamino alkanol is probably converted into oxophosphonium bromide group by interaction with triphenylphosphine dibromide. The oxophosphonium bromide group then probably acts as a good leaving group when the reaction product is treated with triethylamine. Some of the N-arylazetidines synthesised by this method are given in Chart 2. However, this method could not be applied for the cyclodehydration of 3-(3'-methoxyphenylamino)-1,3-diphenylpropane-1-ol and 3-(3'-methoxyphenylamino)-1,2-diphenylpropane-1-ol. Probable explanation for this failure may be that the NH and OH groups are bonded intramolecularly and no free OH is available for conversion into the leaving group. This suggestion finds support from a study of the IR spectra of the carbinols.

CHAPTER IV

To study the stereoselectivity in the rearrangement
\[ R_1 = \varnothing, \ R_2 = R_3 = H \]
\[ R_1 = \varnothing, \ R_2 = CH_3; R_3 = H \]
\[ R_1 = CH_3; R_2 = H; \ R_3 = CH_3 \]
\[ R_1 = \varnothing; \ R_2 = H; \ R_3 = CH_3 \]
of *N*-arylazetidines resulting into 1,2,3,4-tetrahydroquinoline, a stereoselective synthesis of 2,4-disubstituted-*N*-arylazetidine was necessary. 1-(3'-Methoxyphenylamino)-1-phenylbutane-3-ol 13, prepared by the sodium borohydride reduction of α-(3'-methoxyphenylamino)-styryl methyl ketone, on cyclodehydration under above conditions, yielded cis-1-(3'-methoxyphenyl)-2-methyl-4-phenylazetidine 17 as the major product. On the other hand, when β-(3'-methoxyphenylamino)-β-phenethyl methyl ketone was reduced by sodium borohydride an isomeric carbinol (14) was obtained which gave on cyclodehydration trans-1-(3'-methoxyphenyl)-2-methyl-4-phenylazetidine 18 as the major product. In an analogous manner, cyclodehydration of 3-(3'-methoxyphenylamino)-1-phenylbutane-1-ol 15, prepared by the sodium borohydride reduction of β-(3'-methoxyphenylamino)-crotonophenone, gave 17. Finally the carbinol 16, obtained by NaBH₄ reduction of β-(3'-methoxyphenylamino)-propyl phenyl ketone, on cyclodehydration gave 18 as the major product. The sequence of the reaction is presented in Chart 3.

CHAPTER V

Rearrangement (ring expansion) of cis- and trans-1-(3'-methoxyphenyl)-2-methyl-4-phenylazetidines 17 and 18 to give tetrahydroquinolines by (1) pyrolysis at 290°, under nitrogen atmosphere, (2) by exposure to ultraviolet light from a medium pressure mercury vapour lamp and (3) by
\[ \text{CHART-3} \]
treatment with 70% sulphuric acid is discussed in this Chapter. Mechanism of the formation of the also tetrahydroquinolines is discussed in this Chapter.
REFERENCES