SUMMARY

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The present work was undertaken with a view to study some aspects of the chemistry of coumarins and it forms a part of the systematic study of coumarins going on in this laboratory since the past few years. The study includes the application of Mannich reaction to some coumarin derivatives and synthesis of Schiff bases, hydrazides, oxadiazoles, amides, anilides and sulfonamides of some coumarin derivatives. Biological screening of all the compounds of each class has also been carried out in search of potent antibacterial agents.

The structures of all types of compounds prepared during the course of work have been established by analytical data, IR, NMR and Mass spectra.

CHAPTER - I

INTRODUCTION

It deals with historical account of various biological activities, spectroscopic methods for elucidation of structure, methods of synthesis, reactions and applications of coumarins.

CHAPTER - II

PART - I : Synthesis of 7,8-dimethoxy-4-aminomethyl coumarins.

In order to introduce aminomethyl group in the coumarin ring system, two different methods were employed. In first approach, a known 7,8-dimethoxy-3- bromo-4-methylcoumarin was condensed with some secondary amines to get 7,8-dimethoxy-4-aminomethyl coumarins. Here, when piperidine was condensed two products were separated, one was 7,8-dimethoxy-3-piperidinyl-4-methylcoumarin and other was 7,8-dimethoxy-4-piperidinomethylcoumarin. Other secondary amines gave just single product i.e. the 4-aminomethylcoumarin derivatives. In second approach, 7,8-dimethoxy-4-bromomethyl coumarin was synthesised. When it was condensed with secondary

amines, it gave 4-aminomethyl coumarin derivatives, identical with those obtained by first approach. It was also condensed with different primary aromatic amines. All the compounds were tested for antibacterial activity at 100 and 500 ppm concentrations against E. coli and S. aureus by cup-plate method in DMF (in vitro). They were inactive against S. aureus while they were found to have moderate to good antibacterial activity against E. coli.

PART II : Mannich reaction on some hydroxy coumarins.

The mannich bases of the coumarins have been found to have antibacterial activity and act as the central nervous system stimulant. Some of the coumarin derivatives have been subjected to the Mannich reaction, incorporating aminoacids rather than usual amines as a base component. 7-hydroxy-, 7-hydroxy-4-methyl and 7-hydroxy-4-phenylcoumarin when subjected to Mannich reaction with optically active L-amino acids and formalin in 80% ethylalcohol gave corresponding Mannich bases. All the synthesised compounds were tested for antibacterial activity against E. coli and S. bacillus. They were found to possess feeble to moderate antibacterial activity.

CHAPTER - III

PART - I Synthesis of Schiff bases of coumarin derivatives.

The -HC=N-moiety required was incorporated in the coumarin derivatives by Schiff base formation. Several hitherto unknown Schiff bases have been prepared from acetyl, formyl and amino derivatives of coumarins. Here condensation of 7,8-dimethoxy-3-(3'-acetylphenyl aminomethyl)4-methylcoumarin, 7,8-dimethoxy-3-(4'acetyl coumarin, 7,8-dimethoxy-3-(4'-acetyl phenyl aminomethyl)4-methyl coumarin with various benzoic acid hydrazide in alcohol; condensation of 7,8-dihydroxy-6-formyl-4-methylcoumarin, 6'-hydroxy-5'-formyl-4-methyl, 7,8-benzocoumarin with various primary aromatic amines and condensation of 7-n-butoxy-3-aminocoumarin with various aromatic aldehyde furnished Schiff bases.

All of them were tested for their antibacterial activity against E. coli and S. aureus. Some of them have shown moderate activity against E. coli and S. aureus at 500 ppm concentration They were found inactive at 100 ppm concentration. Some of them were found to have moderate to good activity at 500 ppm concentration against E. coli but they were inactive againsi S. aureus at 500 ppm concentration. All the compounds were found inactive at 100 ppm concentration.

PART II : Synthesis of oxadiazolylcoumarin and hydrazides of coumarin derivatives.

8-Methoxy-5-bromocoumarin-3-carboxylic acid was condensed with various substituted benzoic acid hydradizes in $POCl_3$ to give substituted 1,3, 4-oxadiazoles

When 8-methoxy-5-bromocoumarin-3-carbonyl chloride was treated with various substituted benzoic acid hydrazides, it gave 8-methoxy-5-bromo-3-coumarinoyl substituted benzoic acid hydrazides. When these hydrazides were refluxed in $POCl_3$, it gave same, substituted 1,3,4-oxadiazoles. Screening of all the hydrazides and oxadiazoles was carried out against E. coli at 500 ppm concentration, were found to have feeble to moderate antibacterial activity but they were inactive at 100 ppm concentrations. Also, they did not show any activity against S. aureus at both the concentration.

CHAPTER IV : Synthesis of anilides and amides of coumarin derivatives.

A large number of carboxamides were prepared by condensing 8-methoxy- and 8-methoxy-5-bromocoumarin-3-carbonyl chloride with various L-aminoacids, DL-aminoacids. β-alanine and secondary amines. Carboxanilides were synthesised by treating 8-methoxy-, 8-methoxy-5-bromocoumarin-3-carbonyl chloride with different aromatic amines.

All of them were tested for their antibacterial activity and have some of them have shown moderate to good antibacterial activity at 500 ppm concentration against E. coli and S aureus but they were inactive against both the strains at 100 and 500 ppm

concentrations. Some of them were found moderately active against E. coli and S. aureus at 500 ppm concentrations but inactive at 100 ppm.

PART II : Synthesis of sulfonamides of coumarin derivatives

In search of better antibacterial agents, different sulfonamides prepared from with secondary amines were condensed with 8-methoxy-, 8-methoxy-5-bromocoumarin -3-carbonyl chloride to obtain corresponding sulfonamide derivatives. All of them were biologically tested against E. coli at 500 ppm concentration and found moderately active but found inactive at 100 ppm concentration. Also, they were inactive against S. aureus at 100 and 500 ppm concentrations.

CHAPTER V : Testing of antibacterial activity of compounds synthesised in Chapter II - IV

In this chapter, different methods of biological testing have been described. It also includes screening reports of all the compounds of each class, synthesised during the present work.