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, oxadiazoles, hydrazides, anilides, amides and sulfonamides of some coumarin derivatives. Biological screening of representative compounds of each class has also been carried out in search of potent antibacterial agents.

The structures of all 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 and chemical reactions of coumarins.

CHAPTER - II

PART-I : Mannich reaction on some hydroxycoumarins

The Mannich bases of the coumarins have been found

to have antibacterial activity and as the central nervous system stimulant. Some of the coumarin derivatives have been subjected to the Mannich reaction, incorporating amino-acids rather than usual amines as a base component. 7-Hydroxy-7-hydroxy-4-phenyl-, 7-hydroxy-5-methyl- and 7-hydroxy-8-acetyl-4-methylcoumarin when subjected to Mannich reaction with glycine and other DL-aminoacids and formalin in 80% ethanol gave corresponding Mannich bases. Some of the compounds were tested for their antibacterial activity against strain E.coli, S.aureus, S. typhosa and S.albus at 100 and 500 ppm concentration using cup-plate method. Mannich bases obtained from 7-hydroxy-4-phenylcoumarin were found to possess feeble to moderate antibacterial activity.

PART-II : Synthesis of some 8-methoxy-5-substituted amino-methylcoumarins

In order to introducce aminomehyl group in the coumarin ring system, a known 8-methoxy-5-chloromethylcoumarin was condensed with various simple and substituted aliphatic, aromatic and heterocyclic primary and secondary amines to furnish the new series of 8-methoxy-5-substituted aminomethyl coumarin[5]. Some of the aminomethyl derivatives synthesised were found to have moderate antibacterial activity. They were found active against E.coli, S.aureus, S.typhosa and B.subtilis at 100 and 500 ppm concentration.

CHAPTER-III

PART-I : Synthesis of some Schiff bases of coumarin derivatives

The -CH=N- moiety required was incorporated in the coumarin derivatives by Schiff base formation. Several hitherto unknown Schiff bases have been prepared from formyl and amino derivatives of coumarins. The formyl derivatives were prepared from 8-methoxy-5-chloromethylcoumarin and 8-hydroxy coumarin by treating them with hexamine. These were then condensed with various amines and substituted acid hydrazides to get Schiff bases.

Similarly, number of Schiff bases were synthesised from 8-methoxy-5-(o-amino)-phenylaminomethylcoumarin. This amine component was prepared by reaction of 8-methoxy-5-chloromethylcoumarin with o-phenylenediamine. Condensation of various substituted benzaldehydes with amine component furnished Schiff bases.

Another series of Schiff bases were obtained by condensing 7-hydroxy-4-methyl-8-acetylcoumarin with various substituted acid hydrazides.

Several Schiff bases have shown moderate to good activity against E.coli, S.aureus, S. albus and B.subtilis, at 100 and 500 ppm concentration.

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

8-Methoxycoumarin-3-carboxylic acid was condensed with various substituted acid hydrazides in $POCl_3$ to give substituted 1,3,4-oxadiazoles.

When 8-methoxy-3-carbonylchloride was treated with various substituted benzoic acid hydrazides, it gave 8-methoxy-3-coumarinoyl substituted benzoic acid hydrazides. When these hydrazides were treated with $POCl_3$, it gave the same, substituted 1,3,4-oxadiazoles.

Some oxadiazoles also have been prepared by condensation of acid chloride of 8-methoxy coumarin-3-carboxylic acid and 2-aryl-5-amino-1,3,4-oxadiazoles. Some selected oxadiazole derivatives were tested for their antibacterial activity and some of them were found active against E.coli, S.aureus, S.albus and B.subtilis. They exhibited moderate to good activity.

A number of acid hydrazides were synthesised from 8-methoxy-3-carbonylchloride and 8-methoxy-5-chloromethylcoumarin by condensing them with various substituted acid hydrazides.

CHAPTER-IV

PART-I : Synthesis of anilides, amides and sulfonamides of coumarin derivatives

Number of anilides and amides of 8-methoxycoumarin-3-carboxylic acid were prepared via acid chloride employing various aliphatic, alicyclic, aromatic and heterocyclic primary and secondary amines.

Some of the selected anilides prepared during the course of work were screened and found to have appriciable antifungal activity. They were found to be active against the fungi Cryptococcus neoformans, Sportrichum Schenckii and Trichophyton mentagrophytes at 25 ppm concentration.

In search of better antibacterial agents, different sulfonylchlorides were condensed with 8-methoxycoumarin-3-(o-amino) carboxanilide and 8-methoxy-5-(o-amino) phenylaminomethylcoumarin to obtain corresponding sulfonamido derivatives. Some of the sulfonamido derivatives were found to possess moderate to good activity E.coli, S.aureus, S.albus and S.typhosa.

PART-II : Testing of antibacterial activity of compounds synthesised in Chapter-II to IV

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