SUMMARY

Chapter-I: Introduction

Many heterocyclic 2H-1-benzopyran-2-ones and their derivatives have attracted considerable interest because of their various physiological and biochemical properties. Some of the naturally occurring 2H-1-benzopyran-2-ones are found to be active as antibiotics, anticoagulants, rodenticides, insecticides, fungicides etc. Some 2H-1-benzopyran-2-one derivatives also have blood cholesterol lowering properties. Recently, it has been noted that some of 2H-1-benzopyran-2-one derivatives could be used as modulator receptor for the treatment of estrogen related conditions including breast cancer.

In view of these interesting properties, it was thought worthwhile to investigate biological influence of some new substituted 2H-1-benzopyran-2-ones and other related derivatives.

Chapter-II: Synthesis of Aminopsoralens

In the present work 3-acetamido-6-methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one and some of its derivatives having substituted secondary aminomethyl groups at C-6 position have been prepared. For this, 2,4-dihydroxybenzaldehyde was condensed with acetyl glycine which gave 3-acetamido-7-acetoxy-2H-1-benzopyran-2-one, followed by refluxing in dry DMF and acetonylation with chloroacetone to furnish 3-acetamido-7-acetonyloxy-2H-1-benzopyran-2-one. Cyclization of 3-acetamido-7-acetonyloxy-2H-1-benzopyran-2-one with alcoholic KOH under reflux yielded, exclusively, 3-acetamido-6-methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one i.e. 3-acetamido-6-methylpsoralen.

3-Acetamido-6-methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one was, then, photobrominated using NBS in $CHCl_3$ under reflux to give 3-acetamido-6-bromomethyl-2H-furo[3,2-*g*]-1-benzopyran-2-one. This brominated compound was condensed with various acyclic and cyclic secondary amines to give corresponding 3-acetamido-6-substituted aminomethyl-2H-furo[3,2-*g*]-1-benzopyran-2-ones.

Chapter-III

Section-I : Synthesis of psora-Schiff bases

Some Schiff bases from 3-acetamido-6-methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one have been prepared. For this, 3-acetamido-6-methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one was subjected to hydrolysis using aq. HCl in methanol to give 3-amino-6-methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one, followed by condensation in benzene/ethanol with various substituted benzaldehydes, having electron withdrawing and electron releasing groups, which afforded corresponding Schiff bases.

Section-II : Synthesis of psora-azetidinones

A strategy was applied for the synthesis of azetidinones in which an active -C=N center of psora-Schiff bases is treated with chloroacetyl chloride as well as phenoxyacetyl chloride in triethyl amine. Various Schiff bases with electron withdrawing as well as electron releasing groups were subjected to form azetidin-2-ones.

Chapter-IV: It includes following four sections.

Section-1: Claisen rearrangement and Wittig reactions of Cinnamylated 2H-1-benzopyran-2-ones

2,4-Dihydroxybenzaldehyde was condensed with cinnamyl chloride in dry acetone giving monocinnamyloxy and dicinnamyloxy derivatives. Monocinnamyloxy derivative in refluxing N,N-dimethylaniline did not show any product and was recovered unchanged.

Dicinnamyloxy derivative was subjected to tandem-Wittig reaction and Claisen rearrangement in N,N-dimethylaniline with equimolar proportion of the ylide, carbethoxy methylene triphenyl phosphorane, which gave two products 8-methyl-9-phenyl-8,9-dihydro-2H-furo[2,3-*h*]-1-benzopyran-2-one and 8-methyl-9-phenyl-6-(1-phenylprop-2-enyl)-8,9-dihydro-2H-furo[2,3-*h*]-1-benzopyran-2-one.

2,4-Dihydroxybenzaldehyde was condensed with diethylmalonate in presence of pyridine and piperidine to give ethyl-7-hydroxy-2H-1-benzopyran-2-one-3-carboxylate. Cinnamylation of ethyl-7-hydroxy-2H-1-benzopyran-2-one-3-carboxylate in dry DMF afforded ethyl-7-cinnamyloxy-2H-1-benzopyran-2-one-3-carboxylate which in refluxing N,N-dimethylaniline did not show any rearrangement and starting material was recovered.

Section-2: Knovaenegel and Claisen reactions of Allylated and Cinnamylated 2H-1-benzopyran- 2-ones

2,4-Dihydroxy-3-methylbenzaldehyde on allylation gave corresponding monoallyloxy and diallyloxy derivatives. The diallyloxy compound on Knoevenegel condensation with ethylcyanoacetate in presence of pyridine and piperidine gave ethyl-2,4-diallyloxy-3-methyl-α-cyanocinnamate which in refluxing N,N-dimethylaniline underwent Claisen rearrangement giving 6-allyl-3-cyano-7-hydroxy-8-methyl-2H-1-benzopyran-2-one.

Similarly, dicinnamyloxy derivative of 2,4-dihydroxybenzaldehyde on Knoevenegel condensation with ethylcyanoacetate in presence of pyridine and piperidine gave ethyl-2,4-dicinnamyloxy-α-cyanocinnamate which in refluxing N,N-dimethylaniline underwent Claisen rearrangement giving 3-cyano-7-hydroxy-6-(1-phenylprop-2-enyl)-2H-1-benzopyran-2-one.

Section-3: Claisen rearrangement and Wittig reactions of Prenylated 2H-1-benzopyran-2-ones

2,4-Dihydroxybenzaldehyde was condensed with prenylbromide, followed by Wittig reaction with ethyl carboethoxy methylene triphenyl phosphorane in THF giving ethyl-2-hydroxy-4-prenyloxycinnamate and 2,4-diprenyloxy cinnamate. Diprenyloxy compound in refluxing N,N-dimethylaniline underwent Claisen rearrangement giving an alkali insoluble compound 6-(3-methylbutan-2-enyl)-8,8-dimethyl-9,10-dihydro-2H-pyrano[2,3-*h*]-1-benzopyran-2-one, which showed IR band at 1703 cm^{-1} indicating lactone ring formation and H-NMR in $CDCl_3$ exhibited signals in the range δ 5.0-6.25 for two protons and one proton respectively confirming prenyl chain.

Diallyloxy derivative of 2,4-dihydroxybenzaldehyde on Knovaenegel condensation with ethyl cyano acetate yielded 3-cyano-7-(1,1-dimethylprop-2-enyloxy)-2H-benzopyran-2-one.

Section-4: Synthesis of novel 2H-1-benzopyran-2-ones using ι -2-amino-1-butanol

Several novel substituted amido angelicins and amido cinnamyloxy derivative were prepared from dihydrofurofused benzopyran-2H-one and cinnamyloxy benzopyran-2H-one respectively.

Ethyl 8-methyl-8,9-dihydro-2H-furo[2,3-*h*]-1-benzopyran-2-one-3-carboxylate was treated with ι-2-amino-1-butanol in DMF, which gave an amido derivative 3-{N-(1-hydroxybutan-2-yl)methanamido}-8-methyl-8,9-dihydro-2H-furo[2,3-*h*]-1-benzopyran-2-one. This amido derivative in refluxing N,N-dimethylaniline did not show any change and was recovered. But in refluxing $POCl_3$, 3-{N-(1-hydroxybutan-2-yl)methanamido}-8-methyl-8,9-dihydro-2H-furo[2,3-*h*]-1-benzopyran-2-one afforded 3-Cyano-8-methyl-4-(1-methylpropanyl)-8,9-dihydro-2H-furo [2,3-*h*]-1-benzopyran-2-one.

Similarly, ethyl 7-cinnamyloxy-2H-1-benzopyran-2-one-3-carboxylate on treatment with ι -2-amino-1-butanol afforded an amido derivative 7-Cinnamyloxy-3-{N-(1-hydroxybutan-2-yl)methanamido}-2H-1-benzopyran-2-one which did not undergo Claisen rearrangement in refluxing N,N-dimethylaniline and was recovered unchanged.

Chapter-V

Biological activity of psora-Schiff's bases and psora-azetidinones

Psora-azetidinones, with new lactam ring, have been synthesized and with a view to understand effective antibiotic properties, their antibacterial activities have been studied. The activity was observed in stationary phase in which the compounds inhibited the growth of *E.Coli.* bacteria in the growing stage. Some psora-azetidinones have been found to show remarkable inhibition while some others showed mild inhibition. In the

case of few aminopsoralens and Schiff bases, no clear zones of inhibition were found. However, some aminopsoralens and psora-Schiff bases, showed little antibacterial effect. The concentration of the compound employed was 100-500 mM.

The antibacterial activity shown by newly synthesized 2H-1-benzopyran-2-ones may be useful in preparing more effective analogues and homologues.