SUMMARY

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The benzo[b] pyrones are of two types, benzo-α-pyrones and benzo-γ-pyrones. The more systematic name given to them are 2H-benzo[b]pyran-2-ones and 4H-benzo[b]-pyran-4-ones. Chromones, flavones, flavonols and isoflavones form a class of benzo-γ-pyrone derivatives, while xanthones are the analogues of benzo-γ-pyrones. In the recent years the interest in the study of these compounds has been enhanced as a result of the discovery of their interesting physiological properties. Moreover, they occupy a prominent position among the plant products and comprise a body of organic subtances of extraordinary variety and interest.

The present work deals with the study of a novel thermal dimerization reaction of 2-hydroxychromanones and a new one step synthesis of xanthones, and also with the synthesis of furochromones, furoxanthones and 2'-pyrono-xanthone derivatives.

Chapter I

A brief survey of recently reported chromones and xanthone derivatives is given.

Chapter II

Studies in the Synthesis of Chromone derivatives :

Chromone derivatives unsubstituted in 2- and 3-positions were rarely reported in the literature and such

few derivatives have been recently isolated from natural sources. Therefore, present work was under taken to synthesise different chromone derivatives carrying no substituent at C-2 and C-3.

Synthesis of furochromones :

Claisen condensation of 2-hydroxy-4-allyloxy-acetophenone with ethyl formate in presence of pulverized sodium gave 2-hydroxy-7-allyloxychromanone and not the acyclic 3-(2-hydroxy-4-allyloxyphenyl)-3-oxo-3H-propanal. The structure of this product was confirmed on the basis of UV, IR and NMR spectra. This on dehydration with dilute sulphuric acid gave 7-allyloxychromone, which on Claisen rearrangement in dimethylaniline afforded 7-hydroxy-8-allylchromone. This on treatment with osmium tetroxide-potassium periodate in ethyl acetate-water gave an intermediate 8-acetaldehydo product, which was cyclized to 7H-furo(2,3-h)benzopyran-7-one using polyphosphoric acid.

7-Hydroxy-8-allylchromone, on treatment with conc. sulphuric aiacid gave 2-methyl-2,3-dihydro-7H-furo(2,3-h)-benzopyran-7-one. This on dehydrogenation with palladized charcoal (10 %) in diphenyl ether gave 2-methyl-7H-furo-(2,3-h)benzopyran-7-one. The structures of final and intermediate products were confirmed on the basis of spectral data.

Similarly starting from 2-hydroxy-3-methyl-4-

allyloxy-, 2-hydroxy-5-allyloxy- and 2-hydroxy-4-methyl-5-allyloxy-acetophenone, the synthesis of 9-methyl-5H-furo-(3,2-g)benzopyran-5-one, 2,9-dimethyl-5H-furo(3,2-g)benzo-pyran-5-one, 4H-furo(3,2-f)benzopyran-4-one, 2-methyl-4H-furo(3,2-f)benzopyran-4-one, 9-methyl-4H-furo(3,2-f)benzo-pyran-4-one and 2,9-dimethyl-4H-furo(3,2-f)benzopyran-4-one were described with their spectral studies.

Synthesis of Cyclohexa- and Cyclopentafurochromones :

Resorcinol on thermal condensation with ethyl cyclohexanone-2-carboxylate in diphenyl ether gave 8-hydroxy-1,2,3,4-tetrahydro-5H-dibenzo [b,e] pyran-5-one. This on allylation with allyl bromide in presence of anhydrous potassium carbonate in dry acetone followed by Claisen rearrangement in dimethylaniline afforded 9-allyl-8-hydroxy derivative which was acetylated with acetic anhydride-pyridine and gave acetate derivative. This was brominated with bromine in glacial acetic acid to give dibromo derivative, which on treatment with ethanolic potassium hydroxide solution yielded 9-methyl-1,2,3,4-tetrahydro-5H-benzofuro[4,5-b][2]benzopyran-5-one. Its structure was confirmed on the basis of its NMR spectrum.

Similarly resorcinol on thermal condensation with ethyl cyclopentanone-2-carboxylate gave 7-hydroxy-1,2,3,-trihydro-4H-cyclopenta[b]benzopyran-4-one. This on similar series of reactions gave an acidic derivative and not 8-methyl-

1,2,3-trihydro-4H-cyclopenta[b]furo[2,3-h]benzopyran-4-one. The acidic product was characterized as 6-[2'-methyl-4'-hydroxybenzofuran-5'-yl]-6-oxo-6H-hexanoic acid on the basis of IR and NMR spectra. The mechanism of its formation is also shown.

The compound 8-allyl-7-hydroxy-1,2,3-trihydro-4H-cyclopenta[b]benzopyran-4-one obtained in above described route, was triturated with conc. sulphuric acid to give a cyclized product, 8-methyl-1,2,3,8,9-pentahydro-4H-cyclopenta[b]furo-[2,3-h]benzopyran-4-one. However this could not be dehydrogenated to 8-methyl-1,2,3-trihydro-4H-cyclopenta[b]furo[2,3-h]-benzopyran-4-one by palladized charcoal (10 %) in diphenyl ether or by DDQ in dry benzene.

A Novel thermal dimerization reaction of 2-hydroxychromanone derivatives :

During the study of furochromones, we observed that the 2-hydroxychromanone derivatives were quite unstable at their melting temperature and heated 20-30° above their melting temperatures, they dimerized to give yellow coloured products. The formation of 1-(7-allyloxy-8-methyl-3-chromonyl)-2-(2-hydroxy-3-methyl-4-allyloxybenzoyl)-ethylene, 1-[2,3-dihydro-2,9-dimethyl-5-oxo-5H-furo(3,2-g)benzopyran-6-yl]-2-[2,3-dihydro-2,7-dimethyl-6-hydroxy-5-benzofuranoyl]-ethylene and 1-(7-allyloxy-3-chromonyl)-2-(2-hydroxy-4-allyloxybenzoyl)-ethylene from corresponding 2-hydroxychromanones was described.

The structures of these product were confirmed by spectral data and also by their synthesis from corresponding chromone derivatives using sodium ethoxide.

Chapter III

Studies in the synthesis of xanthone derivatives :

Section I

A new one step synthesis of xanthones :

Many xanthones have been isolated from plants and other sources, having divers pharmacological properties. Xanthones and their derivatives have been prepared by the condensation of o-hydroxy-benzoic acid derivatives with monohydric, dihydric and trihydric phenols in the presence of a condensing agent using known methods. But the present method is very convenient and gives quantitative yields. Smooth condensation of the ethyl or a methyl ester of an o-hydroxy-aromatic acid and a phenol is achieved by heating the mixture under reflux in biphenyl ether, without addition of a condensing agent.

Phenols, such as phloroglucinol, orcinol, pyrogallol, 1-naphthol or 2-naphthol, when condensed with ethyl salicylate, give directly the corresponding xanthone derivatives, whereas phenols like resorcinol, 2-methylresorcinol and catechol, give the corresponding hydroxyxanthones as well as the intermediate phenyl salicylate derivatives, less reactive phenols such as hydroquinone, 3,4-o-xylenol and m-cresol give only the

corresponding phenyl salicylate derivatives.

In case of resorcinol, a mixture of 1-hydroxy- and a 3-hydroxyxanthone were obtained in which 3-hydroxyxanthone was preponderant. With orcinol, 1-hydroxy-3-methyl- and 3-hydroxy-1-methylxanthone were obtained, the former as the major product. These results indicate that γ-substitution in resorcinol nucleus took place in both cases, which is rather difficult without a condensing agent.

The structures of all the condensation products were confirmed by preparing acetate or methyl ether derivatives and also by spectral data.

Synthesis of 2'-Pyronoxanthones :

The present synthesis, could not be applied only to phenols but also to heterocyclic compounds containing one or more hydroxy groups. Ethyl salicylate on condensation with coumarins, such as 4-methyl-7-hydroxy-, 4,8-dimethyl-7-hydroxy-, 4,7-dimethyl-5-hydroxy- and 5-methyl-7-hydroxy-coumarin gave the corresponding 2'-pyronoxanthones viz., 4'-methyl-2'-pyrono(6',5'- 1,2)xanthone, 4,4'-dimethyl-2'-pyrono(5',6'-2,3)xanthone, 1,4'-dimethyl-2'-pyrono(6',5'-3,4)-xanthone and 3-methyl-2'-pyrono(6',5'-1,2)xanthone.

The 2'-pyronoxanthones cannot be synthesised by the condensation of ethyl acetoacetate with a hydroxyxanthone through any known method. The structures of above pyronoxanthones were confirmed on the basis of IR and NMR spectra.

Section II

Synthesis of furoxanthones :

3-Hydroxy-, 3-hydroxy-1-methyl-, 3-hydroxy-4-methyl- and 3,6-dihydroxy-4-methylxanthone on allylation with allyl bromide in presence of anhydrous potassium carbonate in dry acetone followed by Claisen rearrangement in dimethylaniline gave corresponding o-hydroxyallylxanthones.

3-Hydroxy-4-allyl- and 3-hydroxy-2-allyl-4-methylxanthone on oxidation with osmium tetroxide-potassium periodate in ethyl acetate-water followed by cyclization with PPA afforded furo(2',3'-3,4)xanthone and 4-methylfuro(3',2'-2,3)xanthone respectively. They were also synthesised starting from the condensation of resorcinol and 2-methylresorcinol with ethyl cyclohexanone-2-carboxylate.

3-Hydroxy-4-allyl-, 3-hydroxy-4-allyl-1-methyl-, 3-hydroxy-2-allyl-4-methyl- and 3,6-dihydroxy-2,5-diallyl-4-methylxanthone on cyclization with conc. sulphuric acid followed by dehydrogenation with palladized charcoal (10 %) in diphenyl ether afforded 5'-methylfuro(2',3'-3,4)xanthone, 1,5'-dimethylfuro(2',3'-3,4)xanthone, 4,5'-dimethylfuro(3',2'-2,3)xanthone and 4,5',5"-trimethyldifuro(3',2'-2,3) and (3",2"-5,6)xanthone respectively.

3-Hydroxy-4-methylxanthone on acetylation followed by Fries migration with anhydrous aluminium chloride gave 2-acetyl-3-hydroxy-4-methylxanthone. This on condensation with ethyl bromoacetate in dry acetone followed by hydrolysis with alkali and cyclization with acetic anhydride — sodium acetate gave 4,4'-dimethylfuro(3',2'-2,3)xanthone.