SUMMARY

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Furo-benzo-α-pyrones or furocoumarins, furo-benzo--γ-pyrones or furochromones and coumestans are found in nature. In 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 substances of extra ordinary variety and interest.

The present work deals with the synthesis of furocoumarins, furochromones, furoxanthones and furocoumestan derivatives.

Chapter I.

Studies in the synthesis of furocoumarins :

Linear and angular furo-benzo-α-pyrones are synthesised having alkyl, aryl and alicyclic substituentss in different positions.

Synthesis of psoralene derivatives :

Pechmann condensation of 2-bromo resorcinol with ethyl benzoyl acetate in the presence of conc. sulphuric acid gave 8-bromo-7-hydroxy-4-phenylcoumarin, which on allylation with allyl bromide in dry acetone and anhydrous potassium carbonate afforded 8-bromo-7-allyloxy-4-phenyl-coumarin. This, on Claisen rearrangement by refluxing it with dimethyl aniline in an atmosphere of nitrogen gave

7-hydroxy-6-allyl-4-phenylcoumarin, bromine being eliminated during the reaction. The structure of 7-hydroxy-6-allyl-4-phenylcoumarin was confirmed on the basis of I.R. and N.M.R. spectra. 7-Hydroxy-6-allyl-4-phenylcoumarin triturated with conc. sulphuric acid to give 2-methyl-5-phenyl-7H-2,3-dihydrofuro [3,2g] [1] benzopyran-7-one, which on dehydrogenation with palladised charcoal in diphenyl ether gave 2-methyl-5-phenyl-7H-furo [3,2-g] [1] benzopyran-7-one.

2-Bromo resorcinol, on similar condensation with ethyl cyclohexanone-2-carboxylate gave 4-bromo-3-hydroxy-7,8,9,10-tetrahydro-6H-dibenzo [b,d] pyran-6-one. This on allylation and Claisen migration gave 2-allyl-3-hydroxy-7,8,9,10-tetrahydro-6H-dibenzo [b,d] pyran-6-one, the structure of which was confirmed by I.R. and N.M.R. spectra. This compound on ring closure with conc. sulphuric acid followed by dehydrogenation gave 9-methyl-5H-benzo furo [6,5-c][1] benzopyran-5-one.

9-Methyl-1,2,3,4-tetrahydro-5H-benzofuro [6,5-c] [1] benzopyran-5-one was also synthesised by a different route developed by Kaufmann et al. (J. Org. Chem. 27, 2567, 1962). 2-Allyl-3-hydroxy-7,8,9,10-tetrahydro-6H-dibenzo[b,d] pyran-6-one on acetylation with acetic anhydride and sodium acetate gave 2-allyl-3-acetoxy-7,8,9,10-tetrahydro-6H-dibenzo [b,d] pyran-6-one, which on bromination with bromine in acetic acid afforded 3-acetoxy-2-(2',3'-dibromopropyl)-

7,8,9,10-tetrahydro-6H-dibenzo [b,d] pyran-6-one. Cyclisation of the dibromopropyl acetate to 9-methyl-1,2,3,4-tetrahydro--5H-benzofuro [6,5-c][1] benzopyran-5-one was accomplished by treatment with potassium hydroxide in absolute alcohol.

Pechmann condensation of 2-bromo resorcinol with ethyl cyclopentanone-2-carboxylate gave 6-bromo-7-hydroxy-1,2,3,4-tetrahydro cyclopenta [c] benzopyran-4-one, which on allylation and Claisen migration, afforded 8-allyl-7-hydroxy-1,2,3,4-tetrahydro cyclopenta [c] [1] benzopyran--4-one. The structure of this compound was confirmed by N.M.R. and I.R. spectra. This underwent ring closure with conc. sulphuric acid but failed to give final compound on dehydrogenation with palladised charcoal. So the final compound 8-methyl-1,2,3,4-tetrahydro cyclopenta [c] furo [3,2-g] [1] benzopyran-4-one was prepared by Kaufmann's method as described above, which consisted of acetylation of ortho-hydroxy-allyl compound, bromination and reaction with alcoholic potassium hydroxide.

Synthesis of angular furocoumarin derivatives :

Synthesis of 7H-furo- [3,2-f] [1] benzopyran-7-one and its 2-methyl derivative have been achieved.

6-Hydroxycoumarin was converted to its allyl ether by refluxing it with allyl bromide in dry acetone and anhydrous potassium carbonate, which underwent Claisen migration to give 5-allyl-6-hydroxycoumarin. The structure of this compound was confirmed by N.M.R. and I.R. spectra.

This compound on treatment with osmium tetroxide and potassium periodate in ethyl acetate-eater, afforded 5-acetaldehydo-6-hydroxycoumarin, which on heating with polyphosphoric acid gave 7H-furo- [3,2-f] [1] benzopyran--7-one. The structure of this compound was confirmed by U.V. and I.R. spectra.

5-Allyl-6-hydroxycoumarin on trituration with conc. sulphuric acid followed by dehydrogenation with palladised charcoal in boiling diphenyl ether furnished 2-methyl-7H-furo-[3,2-f] [1] benzopyran-7-one. The structure of which was confirmed by U.V. and I.R. spectra.

Synthesis of difuro-coumarin derivatives :

4-Hydroxy-7-allyloxycoumarin was allylated with allyl bromide in dry acetone and anhydrous potassium carbonate afforded 4,7-diallyloxycoumarin. This when subjected to Claisen rearrangement by refluxing it with dimethyl aniline gave two products. These were characterised as 2-methyl-7-hydroxy-6-allyl-4-oxo-4H-dihydro furo (3,2-c) benzopyran and 5-methyl-7-allyloxy-4-oxo-4H-2,3-dihydro furo(3,2-c) benzopyran. 2-Methyl-7-allyloxy-4-oxo-4H-2,3-dihydro furo(3,2-c)benzopyran on Claisen migration gave 2-methyl-7-hydroxy-6-allyl--4-oxo-4H-dihydro furo (3,2-c) benzopyran. 2-Methyl-7-hydroxy-6-allyl-4-oxo-4H-dihydro furo(3,2-c) benzopyran on cyclisation with conc. sulphuric acid followed by dehydrogenation with palladised charcoal in diphenyl ether furnished

2,7-dimethyl-4-oxo-4H-difuro(3,2-c ; 2',3'-H) benzopyran. Similar series of reactions on 4,7-diallyloxy-8-methyl-coumarin and 4,6-diallyloxycoumarin gave 2,6,7-trimethyl-4-oxo-4H-difuro (3,2-c ; 3',2'-g) benzopyran and 2,9-dimethyl-4-oxo-4H-difuro (3,2-c ; 3',2'-f) benzopyran, respectively. U. V., I.R. and N.M.R. spectra of di furo coumarins were recorded for confirmation of the structures.

Chapter II.

Studies in the synthesis of furo-benzo-γ-pyrones :

Linear and angular furochromones and xanthones are synthesised by building up a furan ring on o-hydroxy allyl chromone derivatives or o-hydroxy acyl derivatives, depending upon the position of the substituent required.

Synthesis of furochromone derivatives :

Thermal condensation of 2-methyl resorcinol with cyclopentanone-2-carboxylic acid ethyl ester in refluxing diphenyl ether gave 7-hydroxy-8-methyl-1,2,3,4-tetrahydro-cyclopenta (b) benzopyran-4-one, which on allylation afforded 7-allyloxy-8-methyl-1,2,3,4-tetrahydro cyclopenta (b) benzo-pyran-4-one. This allyloxy chromone when subjected to Claisen rearrangement by refluxing it with dimethyl aniline afforded 7-hydroxy-6-allyl-8-methyl-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one, which on treatment with osmium tetroxide and potassium periodate in ethyl acetate - water afforded

7-hydroxy-6-acetaldehydo-8-methyl-1,2,3,4-tetrahydrocyclopenta-(b) benzopyran-4-one. This on treatment with polyphosphoric acid gave 9-methyl-1,2,3,4-tetrahydrocyclopenta (b) furo (3,2-g) benzopyran-4-one.

6-Allyl-7-hydroxy-8-methyl-1,2,3,4-tetrahydro-cyclopenta (b) benzopyran-4-one on trituration with conc. sulphuric acid gave 7,9-dimethyl-1,2,3,4,6,7-hexahydro cyclopenta (b) benzopyran-4-one. The dihydro furo chromone was dehydrogenated to 7,9-dimethyl-1,2,3,4-tetrahydro cyclo-penta (b) furo (3,2-g) benzopyran-4-one, when refluxed with diphenyl ether in the presence of palladised charcoal.

Thermal condensation of resorcinol with cyclopen-tanone-2-carboxylic acid ethyl ester in refluxing diphenyl ether gave 7-hydroxy-1,2,3,4,-tetrahydro cyclopenta (b) benzo-pyran-4-one, which when refluxed with allyl bromide in dry acetone and anhydrous potassium carbonate afforded 7-allyloxy-1,2,3,4-tetrahydro cyclopenta (b) benzopyran-4-one. This allyloxy chromone when subjected to Claisen rearrangement by refluxing it with dimethyl aniline gave 7-hydroxy-8-allyl-1,2,3,4-tetrahydro cyclopenta (b) benzopyran-4-one. Cyclisa-tion with conc. sulphuric acid gave 8-methyl-1,2,3,4,8,9-hexahydro-cyclopenta (b) furo (2,3-h) benzopyran-4-one. Dehydrogenation of this compound with palladised charcoal in diphenyl ether as well as with DDQ in benzene failed to give 8-methyl-1,2,3,4,-tetrahydro cyclopenta (b) furo (3,2-g) benzopyran-4-one.

In the following synthesis furochromone having methyl group in the 3-position of the furan ring along with the substituents in the γ-pyronyl ring was prepared,

7-Hydroxy-1,2,3,4-tetrahydro-cyclopenta (b) benzopyran-4-one on acetylation with acetic anhydride and fused sodium acetate gave 7-acetoxy-1,2,3,4-tetrahydro-cyclopenta (b) benzopyran-4-one, which on Fries migration in the presence of anhydrous aluminium chloride, gave 7-hydroxy-8-acetyl-1,2,3,4-tetrahydro-cyclopenta (b) benzopyran-4-one. This was condensed with ethyl bromo acetate in dry acetone and anhydrous potassium carbonate to give ethyl-8-acetyl--4-oxo-1,2,3,4-tetrahydro-cyclopenta (b) benzopyronyloxy-7-acetate, which was hydrolysed with a mixture of acetic acid and hydrochloric acid (1 : 1) to 8-acetyl-4-oxo-1,2,3,4-tetrahydrocyclopenta (b) benzopyronyloxy-7-acetic acid. The acid was cyclised with acetic anhydride and freshly fused sodium acetate to 9-methyl-1,2,3,4-tetrahydro cyclopenta (b) furo (2,3-h) benzopyran-4-one. The structures of the compounds were confirmed by U.V., I.R. and N.M.R. spectra.

Synthesis of furoxanthone derivatives :

Thermal condensation of 2-methyl resorcinol with cyclohexanone-2-carboxylic acid ethyl ester refluxing diphenyl ether gave 6-hydroxy-5-methyll,2,3,4-tetrahydroxanthone, which on allylation followed by Claisen rearrangement gave 6-hydroxy-7-allyl-5-methyl-1,2,3,4-tetrahydroxanthone. This

compound on treatment with osmium tetroxide and potassium periodate in ethyl acetate-water afforded 6-hydroxy-7-acetaldehydo-5-methyl-1,2,3,4-tetrahydroxanthone, which on treatment with polyphosphoric acid gave 5-methyl-1,2,3,4-tetrahydro furo (2',3'-6,7) xanthone.

5',5-Dimethyl-1,2,3,4-tetrahydro furo (2',3'-6,7) xanthone was synthesised by Kaufmann's method. 7-Allyl-6-hydroxy-5-methyl-1,2,3,4-tetrahydroxanthone on acetylation with acetic anhydride and sodium acetate gave 7-allyl-6-acetoxy-5-methyl-1,2,3,4-tetrahydroxanthone, which on bromination with bromine in acetic acid afforded 6-acetoxy-7-(2',3 -dibromo propyl)-5-methyl-1,2,3,4-tetrahydroxanthone. Cyclisation of the dibromopropyl compound to 5',5-dimethyl-1,2,3,4-tetrahydro-furo (2 ,3 -6,7) xanthone was accomplished by treatment with potassium hydroxide in absolute alcohol.

7-Allyl-6-hydroxy-5-methyl-1,2,3,4-tetrahydro-xanthone on trituration with conc. sulphuric acid gave 5',5-dimethyl-1,2,3,4,4',5'-hexahydro furo (2',3'-6,7)xanthone. The dihydrofuro xanthone on reaction with palladised charcoal in diphenyl ether gave 5',5-dimethyl-furo (3',2'-2,3)xanthone. U.V., I.R. and N.M.R. spectra of some of the compounds were recorded to confirm the structure of the compounds.

Thermal condensation of resorcinol with cyclohexanone-2-carboxylic acid ethyl ester in refluxing diphenyl ether gave 6-hydroxy-1,2,3,4-tetrahydroxanthone which when refluxed with allyl bromide in dry acetone and anhydrous potassium

carbonate afforded 6-allyloxy-1,2,3,4-tetrahydroxanthone. This allyloxyxanthone when subjected to Claisen rearrangement by refluxing it with dimethyl aniline gave 6-hydroxy-5-allyl--1,2,3,4-tetrahydroxanthone. The structure of this compound was confirmed by N.M.R. and I.R. spectra. 6-Hydroxy-5-allyl--1,2,3,4-tetrahydroxanthone on treatment with osmium tetroxide and potassium periodate in ethyl acetate-water, followed by heating with polyphosphoric acid afforded 1,2,3,4-tetrahydrofuro (3',2'-5,6) xanthone.

6-Hydroxy-5-allyl-1,2,3,4-tetrahydroxanthone on trituration with conc. sulphuric acid gave 5'-methyl-1,2,3,4, 4',5'-hexahydro (3',2'-5,6)xanthone. The dihydro furo xanthone was dehydrogenated to 5'-methyl-furo (3',2'-4,3)xanthone, when refluxed with diphenyl ether in the presence of palladised charcoal.

6-Hydroxy-1,2,3,4-tetrahydroxanthone on acetylation with acetic anhydride and fused sodium acetate gave 6-acetoxy-1,2,3,4-tetrahydroxanthone, which on Fries migration in the presence of anhydrous aluminium chloride gave 6-hydroxy-5-acetyl-1,2,3,4-tetrahydro xanthone. This was condensed with ethyl bromo acetate in dry acetone and anhydrous potassium carbonate to give ethyl-5-acetyl-1,2,3,4-tetrahydro-6-xanthonyloxy-acetate, which was hydrolysed with a mixture of acetic acid and hydrochloric acid (1 : 1) to 5-acetyl-1,2,3,4-tetrahydro-6-xanthonyloxy acetic acid. The acid was cyclised

with acetic anhydride and fused sodium acetate to 4'-methyl 1,2,3,4-tetrahydro furo (3',2'-5,6) xanthone. 4'-Methyl-furo (3',2'-4,3) xanthone was prepared by dehydrogenation of 4'-methyl-1,2,3,4-tetrahydro furo (3',2'-5,6) xanthone with with palladised charcoal in diphenyl ether. The structures of the compounds are supported by U.V., I.R. and N.M.R. spectra.

Chapter III.

Studies in the synthesis of furo-coumestan derivatives :

Furocoumestans of this type are synthesised for the first time in the present work by building up a furan ring on coumestan derivatives. Coumestan derivatives were synthesised from different 4-hydroxycoumarins by using Wanzlick's method. Furan ring was then built up on o-hydroxy-allyl coumastan derivatives.

4-Hydroxy-7-allyloxycoumarin was prepared by reaction of 4-allyloxy-2-hydroxy-acetophenone with sodium and diethyl carbonate, which on dehydrogenative coupling with catachol in the presence of potassium iodate gave 3-allyloxy-8,9-dihydroxycoumestan. 3-Allyloxy-8,9-dihydroxy-coumestan was methylated with dimethyl sulphate in the presence of anhydrous potassium carbonate in dry acetone to give 3-allyloxy-8,9-dimethoxy coumestan, which underwent Claisen rearrangement, when refluxed with dimethyl aniline

under nitrogen atmosphere to give 3-hydroxy-4-allyl-8,9-dimethoxy coumestan. The ring closure of 3-hydroxy-4-allyl-8,9-dimethoxy coumestan to 5'-methyl-8,9-dimethoxy-4',5'-dihydro furo (2,3-h) coumestan, was accomplished by trituration with conc. sulphuric acid. This was dehydrogenated by refluxing it with diphenyl ether in the presence of palladised charcoal (10 %) to 5'-methyl-8,9-dimethoxy furo (2,3-h) coumestan. The structure of this compound was confirmed by U.V. and I.R. spectra.

Synthesis of 4,5'-dimethyl-8,9-dimethoxy-furo (3,2-g) coumestan and 5'-methyl-8,9-dimethoxy-furo (2,3-f) coumestan was similarly achieved starting from 7-allyloxy-5-methyl-4-hydroxycoumarin and 6-allyloxy-4-hydroxycoumarin respectively The U.V., I.R. and N.M.R. spectra of the above compounds are also recorded to confirm the structures.