SUMMARY

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Benzo-α-pyrones or coumarins are found in nature in abundance as furanocoumarins, pyranocoumarins or coumestan derivatives. They have also gained the importance as they are having physiological activity and so in recent years the synthesis of such coumarin derivatives is of interest.

The present work deals with the synthesis of pyranocoumarins, furanocoumarins, some isoprenylated coumarins and pyranocoumestans.

Chapter I : Prenylation of 4-hydroxycoumarins

Prenylation of 4-hydroxycoumarin derivatives is carried out by different prenylating reagents giving pyrano- or furanocoumarin derivatives.

4-Hydroxycoumarin, when condensed with 2-methyl--but-3-en-2-ol in the presence of BF_3-etherate gave 3,4-dihydro-5-oxo-5H-2,2,-dimethylpyrano(3,2-c)benzopyran. This on dehydrogenation with DDQ in dry benzene afforded 5-oxo-5H-2,2,-dimethylpyrano(3,2-c)benzopyran in 30 % yield as a mixture with dihydro derivative. The structure of these were confirmed by IR, UV and NMR spectra.

4-Hydroxy-6-methylcoumarin was condensed with 2-methyl-but-3-en-2-ol in the presence of BF_3-etherate to give 3,4-dihydro-5-oxo-5H-2,2,9-trimethylpyrano(3,2-c)benzo-pyran which was ultimately dehydrogenated to 5-oxo-5H-2,2,9-

-trimethylpyrano(3,2-c)benzopyran by DDQ. The structure was confirmed by spectral data.

5-Oxo-5H-2,2,7-trimethylpyrano(3,2-c)benzopyran, 5-oxo-5H-7,8-benzo-2,2-dimethylpyrano(3,2-c)benzopyran, 5-oxo-5H-5,6-benzo-2,2,dimethylpyrano(3,2-c)benzopyran and 3,4-dihydro-5-oxo-5H-8-methoxy-2,2-dimethylpyrano(3,2-c)-benzopyran were synthesised by condensing 4-hydroxy-8-methyl-, 4-hydroxy-7,8-benzo-, 4-hydroxy-5,6-benzo- and 4-hydroxy-7-methoxycoumarin respectively, with 2-methyl-but-3-en-2-ol in the presence of BF_3-etherate and dehydrogenated partially by refluxing with DDQ in dry benzene.

Abnormal Claisen product, 2,3-dihydro-4-oxo-4H--2,2,3-trimethylfurano(3,2-c)benzopyran was obtained by condensing 4-hydroxycoumarin with 1-chloro-3-methyl-but-2-ene in the presence of anhydrous potassium carbonate and potassium iodide in acetone followed by Claisen migration of 4-prenyloxy-coumarin by refluxing it with dimethylaniline. The structure of the compound was confirmed by the spectral data.

Similarly, 2,3-dihydro-4-oxo-4H-2,2,3,8-tetramethyl-furano(3,2-c)benzopyran, 2,3-dihydro-4-oxo-4H-2,2,3,6-tetra-methylfurano(3,2-c)benzopyran, 2,3-dihydro-4-oxo-4H-7-methoxy-2,2,3-trimethylfurano(3,2-c)benzopyran and 2,3-dihydro-4-oxo--4H-7,8-benzo-2,2,3-trimethylfurano(3,2-c)benzopyran were synthesised as abnormal Claisen products by condensing 4-hydroxy-6-methyl-, 4-hydroxy-8-methyl-, 4-hydroxy-7-methoxy- and 4-hydroxy-7,8-benzocoumarin with 1-chloro-3-methyl-but-2-

-ene followed by Claisen migration.

4-Hydroxycoumarin on condensation with 3-chloro--3-methyl-but-1-yne in the presence of anhydrous potassium carbonate and potassium iodide in acetone gave 2,3-dihydro--4-oxo-4H-2-methylene-3,3-dimethylfurano(3,2-c)benzopyran. The structure of the compound was confirmed by its IR, UV and NMR spectra. To confirm the structure, it was further hydrogenated with hydrogen in the presence of palladised charcoal (10 %) to give 2,3-dihydro-4-oxo-4H-2,3,3-trimethylfurano(3,2-c)benzopyran and ozonolysis of 2,3-dihydro-4-oxo--4H-2-methylene-3,3-dimethylfurano(3,2-c)benzopyran gave 2,3-dihydro-2,4-dioxo-4H-3,3-dimethylfurano(3,2-c)benzopyran, the structure of both the compounds were confirmed by the spectral data.

4-Hydroxy-6-methylcoumarin on condensation with 3-chloro-3-methyl-but-1-yne gave 2,3-dihydro-4-oxo-4H-2-methylene-3,3,8-trimethylfurano(3,2-c)benzopyran which on hydrogenation gave 2,3-dihydro-4-oxo-4H-2,3,3,8-tetramethylfurano(3,2-c)benzopyran and on ozonolysis gave 2,3-dihydro--2,4-dioxo-4H-3,3,8-trimethylfurano(3,2-c)benzopyran. Similarly, 2,3-dihydro-4-oxo-4H-2-methylene-3,3,6-trimethyl--furano(3,2-c)benzopyran, 7,8-benzo-2,3-dihydro-4-oxo-4H-2-methylene-3,3-dimethylfurano(3,2-c)benzopyran and 5,6-benzo-2,3-dihydro-4-oxo-4H-2-methylene-3,3-dimethylfurano(3,2-c)-benzopyran were synthesised and subsequently hydrogenated from corresponding 4-hydroxycoumarin derivative.

Chapter II :

This Chapter is divided in three sections. Section I consists of the synthesis of pyranocoumastan derivatives, Section II includes the synthesis of furanocoumarin derivatives and the Section III describes the synthesis of pyrano-furano-coumarin and di-furanocoumarin derivatives.

Section I : Synthesis of pyranocoumestan derivatives :

Pyranocoumestans of this type are synthesised earlier and reported by different workers. Pyranocoumestans prepared from different 4-hydroxycoumarin derivatives by Wanzlick method are reported.

3,4-Dihydro-6-acetyl-5-hydroxy-2,2-dimethylchromene, when reacted with diethyl carbonate and pulverised sodium gave 2,2-dimethyl-3,4-dihydro-8-hydroxy-6-oxo-6H-pyrano-(2,3-h)benzopyran which on dehydrogenative coupling with catechol in the presence of potassium iodate and sodium acetate yielded 8,9-dihydroxy-2,2-dimethyl-3,4-dihydropyrano(2,3-h)-coumestan. This was methylated with dimethyl sulphate in the presence of anhydrous potassium carbonate in acetone to 8,9-dimethoxy-2,2-dimethyl-3,4-dihydropyrano(2,3-h)coumestan. The structure was confirmed by its IR and NMR spectra. It could not be dehydrogenated to 8,9-dimethoxy-2,2-dimethylpyrano-(2,3-h)coumestan.

8,9-Dimethoxy-2,2-dimethylpyrano(2,3-h)coumestan was prepared by condensing 2,2-dimethyl-6-acetyl-5-hydroxy-

-chromene with sodium and diethyl carbonate to give 2,2-dimethyl-8-hydroxy-6-oxo-6H-pyrano(2,3-h)benzopyran followed by condensation with catechol in the presence of potassium iodate and sodium acetate to 8,9-dihydroxy-2,2-dimethylpyrano-(2,3-h)coumestan and subsequent methylation.

Synthesis of 3,4-dihydro-8,9-dimethoxy-2,2-dimethylpyrano(3,2-g)coumestan, 8,9-dimethoxy-2,2-dimethylpyrano(3,2-g)coumestan, 3,4-dihydro-8,9-dimethoxy-2,2,13-tri--methylpyrano(3,2-g)coumestan and 8,9-dimethoxy-2,2,13-trimethylpyrano(3,2-g)coumestan was achieved starting from 3,4--dihydro-2,2-dimethyl-6-hydroxy-7-acetyl-, 2,2-dimethyl-6--hydroxy-7-acetyl-, 3,4-dihydro-2,2,8-trimethyl-6-hydroxy--7-acetyl- and 6-hydroxy-7-acetyl-2,2,8-trimethylchromene, respectively. The structures of above compounds were assigned on the basis of spectral data.

Section II : Synthesis of furanocoumarins :

An angular type of furanocoumarin, 7-hydroxy-2--methyl-6-phenyl-5-oxo-5H-furano(2,3-h)benzopyran was synthesised. 4-Allyloxy-2-hydroxyphenylbenzyl ketone on condensation with sodium and diethyl carbonate gave 7-allyloxy--4-hydroxy-3-phenylcoumarin. This on methylation gave 4-methoxy--coumarin derivative, which on subsequent Claisen migration gave 8-allyl-4,7-dihydroxy-3-phenylcoumarin and 8-allyl-7--hydroxy-4-methoxy-3-phenylcoumarin. These on cyclisation with concentrated sulphuric acid gave 2,3-dihydro-7-hydroxy--2-methyl-6-phenyl-5-oxo-5H-furano(2,3-h)benzopyran.

Dehydrogenation of this compound with palladised charcoal (10 %) gave 7-hydroxy-2-methyl-6-phenyl-5-oxo-5H-furano-(2,3-h)benzopyran. Similarly, 2,3-dihydro-7-hydroxy-2-methyl-6-(p-methoxyphenyl)-5-oxo-5H-furano(2,3-h)benzopyran was synthesised from 4-allyloxy-2-hydroxy(p-methoxyphenyl)-benzyl ketone.

A psoralene type of furanocoumarin, 2,9-dimethyl-5-hydroxy-6-phenyl-7-oxo-7H-furano(3,2-g)benzopyran, was synthesised by carrying out the similar series of reactions starting with 4-allyloxy-2-hydroxy-3-methylphenylbenzyl ketone.

Section III : Synthesis of pyranofuranocoumarins and di-furanocoumarin :

3,4-Dihydro-2,2-dimethyl-8-hydroxy-6-oxo-6H-pyrano-(2,3-h)benzopyran on allylation with allyl bromide gave 8-allyloxy-3,4-dihydro-2,2-dimethyl-6-oxo-6H-pyrano(2,3-h)-benzopyran which on subsequent Claisen migration gave 2,3,6,7-tetrahydro-2,8,8-trimethyl-4-oxo-4H-furano(3,2-c)pyrano-(2',3'-h)benzopyran. This failed to give its dehydrogenated product. On allylating 2,2-dimethyl-8-hydroxy-6-oxo-6H-pyrano(2,3-h)benzopyran gave 8-allyloxy-2,2-dimethyl-6-oxo-6H-pyrano(2,3-h)benzopyran which on Claisen migration gave 2,3-dihydro-2,8,8-trimethyl-4-oxo-4H-furano(3,2-c)pyrano-(2',3'-h)benzopyran.

Similarly, 2,3,9,10-tetrahydro-2,8,8-trimethyl-4-oxo-4H-furano(3,2-c)pyrano(3',2'-g)benzopyran starting

from 3,4-dihydro-2,2-dimethyl-6-hydroxy-8-oxo-8H-pyrano--(3,2-g)benzopyran and 2,6,8,8-tetramethyl-4-oxo-4H-furano--(3,2-c)pyrano(3',2'-g)benzopyran from 3,4-dihydro-2,2,10--trimethyl-6-hydroxy-8-oxo-8H-pyrano(3,2-g)benzopyran were synthesised.

7-Allyloxy-4-prenyloxy-8-methylcoumarin on Claisen migration gave 2,3-dihydro-7-allyloxy-4-oxo-4H-2,2,3,6-tetramethylfurano(3,2-c)benzopyran and 2,3-dihydro-8-allyl-7--hydroxy-4-oxo-4H-2,2,3,6-tetramethylfurano(3,2-c)benzopyran. The second product on cyclisation with sulphuric acid followed by dehydrogenation with DDQ gave 2,3-dihydro-4-oxo--4H-2,2,3,6,8-pentamethyldifurano(3,2-c : 3',2'-g)benzopyran. The structure was confirmed by the spectral data.

4-Hydroxy-8-methyl-7-prenyloxycoumarin was prepared from 2,4-dihydroxy-3-methylacetophenone by first prenylating it with 1-chloro-3-methyl-but-2-ene and then reacting it with diethyl carbonate and sodium. This was then allylated with allyl bromide and further on Claisen migration gave 2,3-dihydro-7-hydroxy-2,6-dimethyl-4-oxo-4H-8-prenyl-furano(3,2-c)benzopyran.

Chapter III : Prenylation of 3-hydroxycoumarins :

3-Hydroxycoumarin was condensed with 1-chloro--3-methyl-but-2-ene in the presence of anhydrous potassium carbonate and potassium iodide in acetone to give 3-prenyloxy-coumarin. This on Claisen migration gave 3-hydroxy-4-prenyl-coumarin, the structure of this was confirmed by the spectral

data. Further cyclisation of this failed to give cyclised product by all the usual methods. This was reacted with acetic anhydride in the presence of pyridine to give 3-acetoxy derivative.

3-Hydroxy-6-methylcoumarin was similarly condensed with 1-chloro-3-methyl-but-2-ene to give 6-methyl-3-prenyloxy-coumarin, which was converted to 3-hydroxy-6-methyl-4-prenyl--coumarin by Claisen migration and to 3-acetoxy-6-methyl-4-prenylcoumarin by acetylation. 3-Hydroxy-8-methyl-4-prenyl-coumarin, 3-hydroxy-5,6-benzo-4-prenylcoumarin and 3-hydroxy-8-methoxy-4-prenylcoumarin were synthesised by carrying out the above series of reactions starting with 3-hydroxy-8-methyl-, 3-hydroxy-5,6-benzo-, and 3-hydroxy-8-methoxy-coumarin respectively.

3-Hydroxycoumarin, when condensed with 3-chloro-3-methyl-but-1-yne in the presence of anhydrous potassium carbonate and potassium iodide in acetone gave 3-propargyloxy-coumarin which on Claisen migration gave 2-isopropylfurano-(2,3-c)coumarin or 9-oxo-9H-2-isopropylfurano(2,3-c)benzopyran. The structure was confirmed by the spectral data.

Similarly, 9-oxo-9H-2-isopropyl-5-methylfurano-(2,3-c)benzopyran, 9-oxo-9H-2-isopropyl-7-methylfurano-(2,3-c)benzopyran and 8-methoxy-3-propargyloxycoumarin were synthesised from 3-hydroxy-6-methyl-, 3-hydroxy-8-methyl- and 3-hydroxy-8-methoxycoumarin respectively.