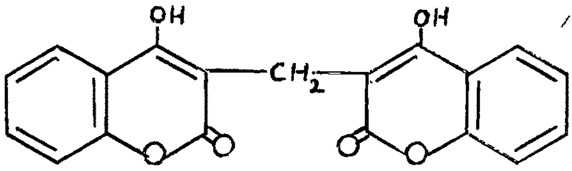
CHAPTER V

SYNTHESES OF BI(COUMARINOXY) METHANES

Syntheses of Bi(coumarinoxy) methanes

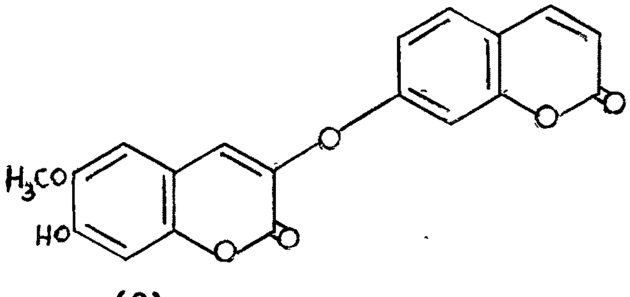
Methylenation may be regarded as a common natural process. In the group of plant phenolics, methylenation of a catechol unit is often encountered particularly in lignans, alkaloids and some flavonoids[1-9]. The presence of coumarin-type compounds in plants has been well established. Coumarin dimers were first shown to occur naturally when Link[10] reported the structure of 3,3'-methylenebis(4-hydroxycoumarin) [dicoumarol (1)] as two coumarin units connected by a methylene group.

bis-3-co [illegible]



(1)

A different type of coumarin dimer was reported by Tschesche and coworkers[11]. They identified daphnoretin(2)[12] as two coumarins linked by an ether bridge. Mihasi and coworkers[13,14] have recently isolated a third type of coumarin dimer (3) in which the two coumarins are linked through a carbon carbon bond. They named their compound



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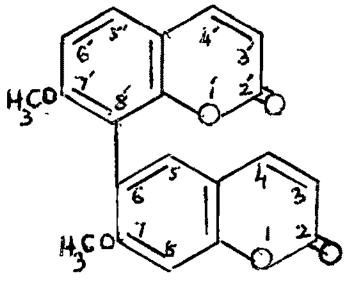
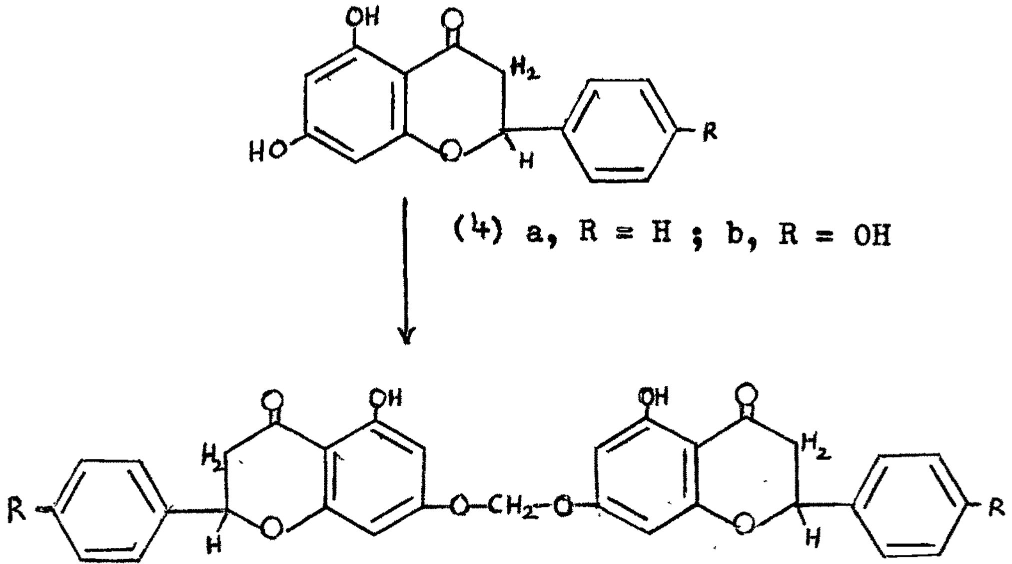


(3)

Matsukaze-lactone. Synthetic compounds of the latter structure are known and are called bicoumarinyls[15].

In the laboratory, methylenation appears simple when there are only two hydroxyl groups ortho to each other in a molecule, but when other hydroxyl groups are present, there is a possibility of competing reactions. Preferential methylenation of a catechol unit in 6,7-positions was successful in 5,6,7,4'-tetrahydroxyisoflavone[16] and vogoletin[17]. Generally in flavones and isoflavones, the resistant 5-hydroxyl group does not interfere. 7-Hydroxy compounds when heated with methylene iodide in the presence of potassium carbonate and acetone readily form bimolecular products linked by a methylenedioxy group.

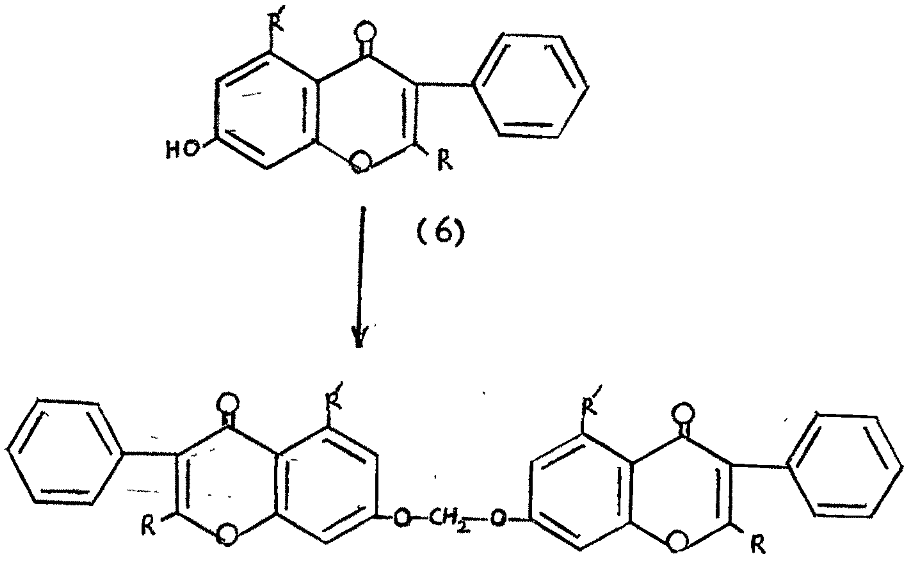
Grover, Jain and Seshadri[18] carried out the methylenation of 5,7-dihydroxyflavanone (4a) and naringenin (4b) and obtained (5a) and (5b) respectively.



(4) a, R = H ; b, R = OH

(5) a, R = H ; b, R = OH

The 7-hydroxyisoflavones (6 a,b and c) when subjected to methylenation using the potassium carbonate-acetone method readily yield the corresponding bi(7-isoflavonyloxy)methanes (7a,7b and 7c) respectively.

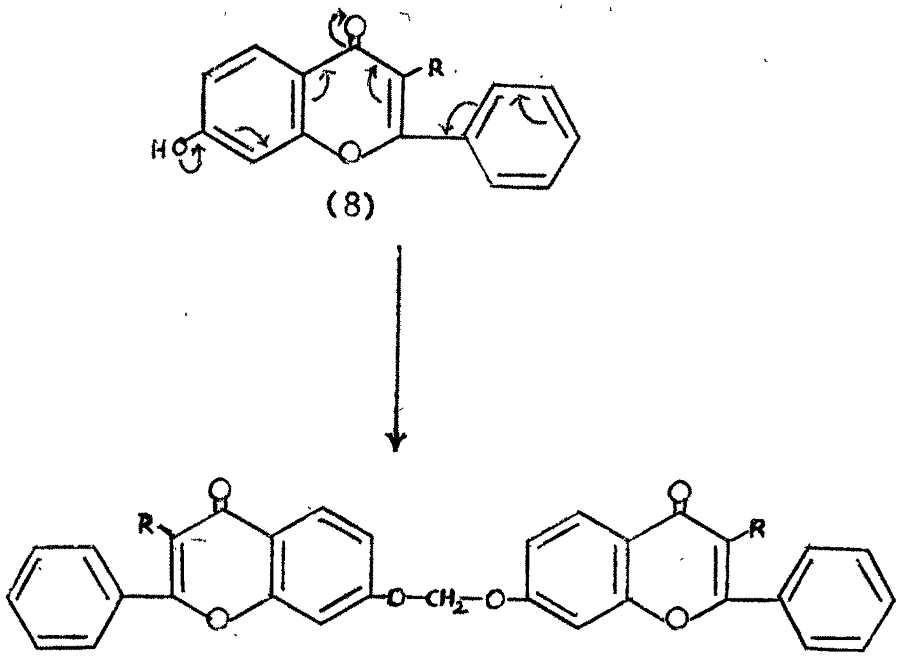


(6)

(7)

(a) R=R'=H ; (b) R=Me, R'=H ; (c) R=Me, R'=OH

In the case of flavones the reactivity of the 7-hydroxyl group is reduced due to the side phenyl which is also conjugated with the carbonyl group (8). Methylenation required a large period (60 hours) in order to convert(8a)as well as (8b) to (9a) and (9b) respectively.



(8)

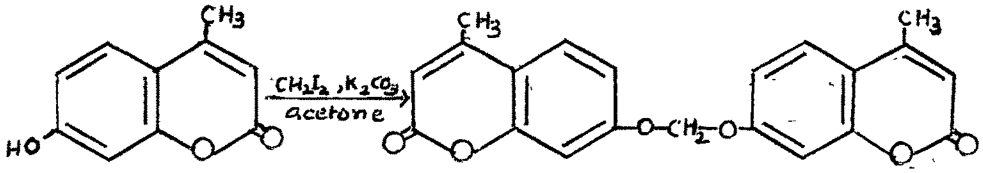
(9)

(a) R=H ; (b) R= OCH_3

The present work was carried out with a view to study the methylenation of different hydroxycoumarins. Methylenation was carried out by refluxing the mixture of hydroxycoumarin, anhydrous potassium carbonate, dry acetone and methylene iodide so that a where bimolecular compound linked by a methylenedioxy group was obtained.

Methylenation of 7-hydroxy-4-methylcoumarin : Bi(4-methyl-7-coumarinoxy)methane (10)

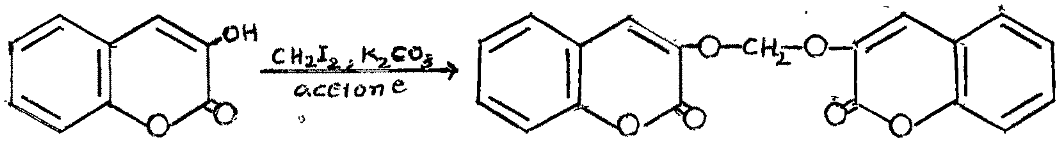
7-Hydroxy-4-methylcoumarin (11) when refluxed with methylene iodide in the presence of anhydrous potassium carbonate in boiling acetone gave a product which was insoluble in cold dilute alkali and did not give an alcoholic ferric chloride colouration. It also gave a positive gallic acid-sulphuric acid test, which indicated the presence of methylene dioxy group. On the basis of these properties and the analytical results it has been assigned the bi~~s~~(4-methyl-7-coumarinoxy)methane structure (10).



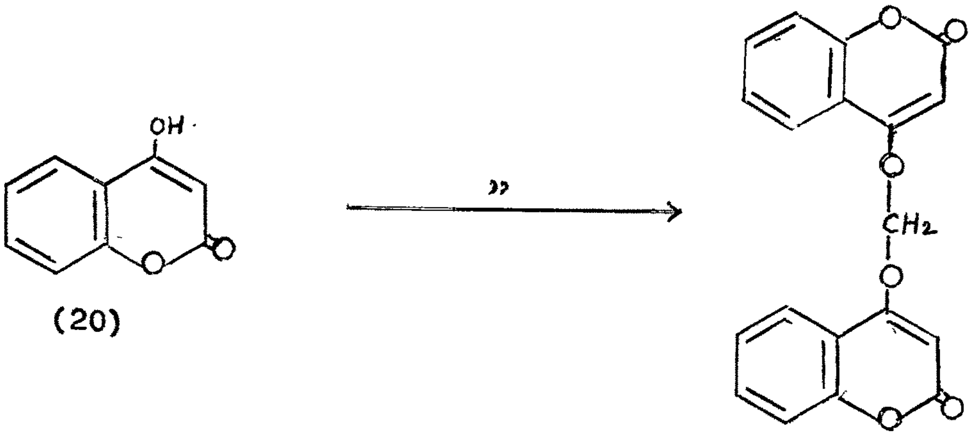
(11) (10)

Using the similar procedure bi(3-coumarinoxy)-(12), bi(4-coumarinoxy)-,(13), bi(4-methyl-5-coumarinoxy)-,(14), bi(4,7-dimethyl-5-coumarinoxy)-,(15), bi(4-methyl-6-coumarinoxy)-,(16), bi(7-coumarinoxy)-,(17) and bi(4-phenyl-7-coumarinoxy)-,(18) methane were synthesised from 3-hydroxy-(19), 4-hydroxy-(20), 5-hydroxy-4-methyl-(21), 5-hydroxy-4,7-dimethyl-(22), 6-hydroxy-4-methyl-(23), 7-hydroxy-(24) and 7-hydroxy-4-phenyl-(25) coumarin respecively.

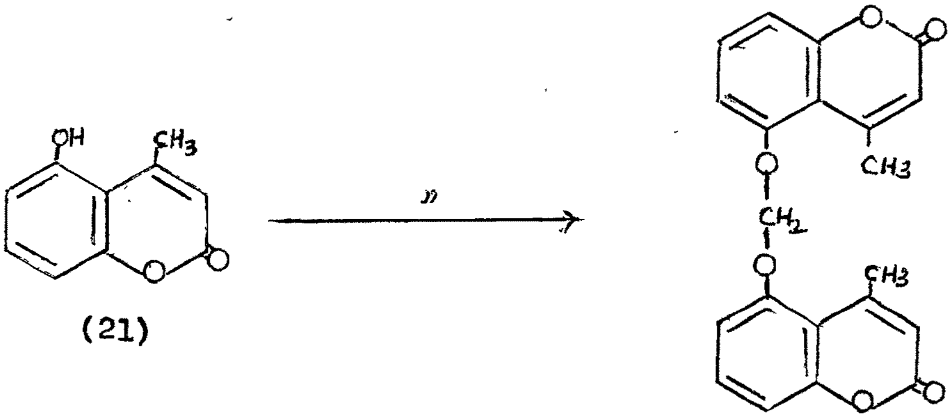
All these compounds were insoluble in dilute alkali, did not develope any ferric chloride colouration and gave positive gallic acid-sulphuric acid test. On the basis of these properties and the analytical data they were assigned the corresponding above structures.



(19) (12)



(20) (13)



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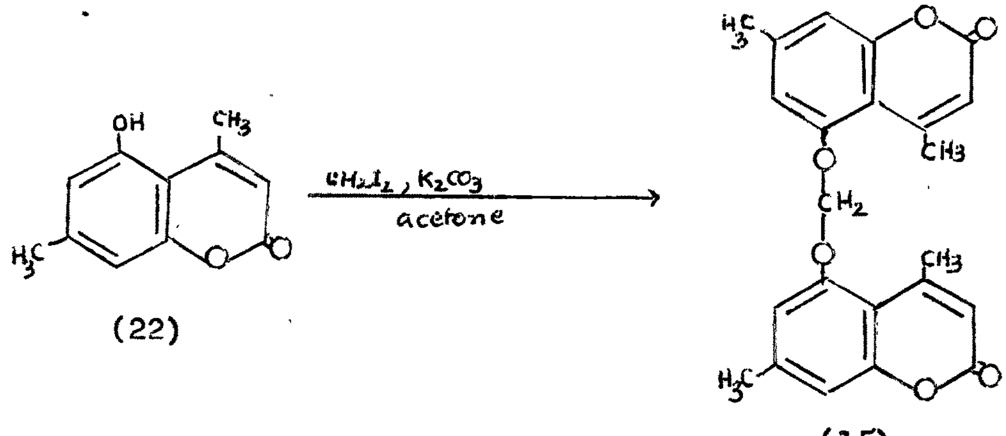

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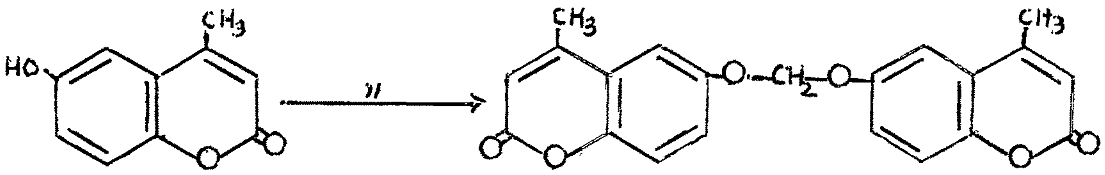
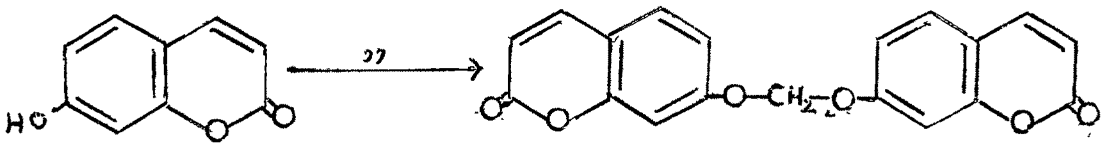
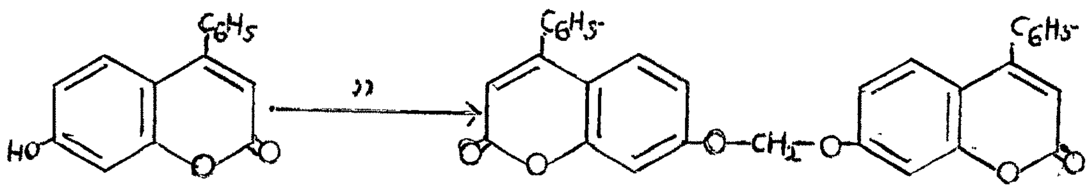


(23) (16)



(24) (17)



(25) (18)

EXPERIMENTAL

The methylenedioxy test was performed by heating the compound with gallic acid and concentrated sulphuric acid on a boiling water bath ; emerald green colour was taken as a positive reaction[19].

Methylenation of 7-Hydroxy-4-methylcoumarin : Bi(4-methyl-7-coumarinoxy)methane.

A mixture of 7-hydroxy-4-methylcoumarin (3.52 g.; 0.02 M), methylene iodide (2.68 g. ; 0.01 M) and anhydrous potassium carbonate (5 g.) was refluxed in dry acetone for 4 hours. The mixture was then filtered hot and after evaporation of the acetone the compound was washed with dilute sodium hydroxide solution and crystallised from acetic acid in colourless shining needles, m.p. 224°. Yield 0.5 g. The compound gave the green colouration in gallic acid, sulphuric acid solution by warming. It did not develope any ferric chloride colouration.

Analysis : Found : C,69.67 ; H,4.47 %.
$C_{21}H_{16}O_6$ requires : C,69.22 ; H,4.43 %.

Bi(3-coumarinoxy)methane :

A mixture of 3-hydroxycoumarin (3.24 g. ; 0.02 M),methylene iodide (2.68 g. ; 0.01 M), potassium carbonate (5 g.) and acetone was refluxed for 15 hours and worked up as above. The compound on crystallisation from acetic acid gave white crystals which melted at 259°.

Yield 0.1 g. gave green colouration with gallic-sulphuric acid mixture.

Analysis : Found : C,67.47 ; H,3.19 %.
$C_{19}H_{12}O_6$ requires : C,67.85 ; H,3.60 %.

Bi(4-coumarinoxy)methane :

A mixture of 4-hydroxycoumarin (3.24 g. ; 0.02 M), methylene iodide (2.68 g. ; 0.01 M), anhydrous potassium carbonate (5 g.) and dry acetone was refluxed for 35 hours. The product ~~was~~ crystallised from acetic acid in yellow shining needles, m.p. 255°. Yield 0.3 g. It gave a greenish colouration with gallic-sulphuric acid solution.

Analysis : Found : C,67.38 ; H,3.37 %.
$C_{19}H_{12}O_6$ requires : C,67.85 ; H,3.60 %.

Bi(4-methyl-5-coumarinoxy)methane :

5-Hydroxy-4-methylcoumarin (1.76 g. ; 0.01 M), methylene iodide (1.34 g. ; 0.005 M) and anhydrous potassium carbonate (2.5 g.) were refluxed in boiling acetone for 15 hours. The product was washed with dilute sodium hydroxide solution and crystallised from acetic acid in shining needles, m.p. 238°. Yield 0.5 g. It gave positive gallic-sulphuric acid test.

Analysis : Found : C,68.81 ; H,4.08 %.
$C_{21}H_{16}O_6$ requires : C,69.22 ; H,4.43 %.

Bi(4,7-dimethyl-5-coumarinoxy)methane :

A mixture of 5-hydroxy-4,7-dimethylcoumarin (3.8 g. ; 0.02 M), methylene iodide (2.68 g. ; 0.01 M) and anhydrous potassium carbonate was refluxed in acetone for 8 hours and was worked out as above. The compound was crystallised from acetic acid in colourless crystals, m.p. 277°. Yield 1 g.

Analysis : Found : C,70.36 ; H,5.39 %.
$C_{23}H_{20}O_6$ requires : C,70.40 ; H,5.14 %.

Bi(4-methyl-6-coumarinoxy)methane :

A mixture of 6-hydroxy-4-methylcoumarin (3.52 g. ; 0.02 M), methylene iodide (2.68 g. ; 0.01 M), anhydrous potassium carbonate (5 g.) and dry acetone was refluxed for 8 hours. On evaporation of acetone the separated product was washed with dilute alkali and crystallised from acetic acid in shining plates, m.p. 212°. Yield 0.7 g. It gave green colouration with gallic-sulphuric acid solution.

Analysis : Found : C,69.18 ; H,4.44 %.
$C_{21}H_{16}O_6$ requires : C,69.22 ; H,4.43 %.

Bi(7-coumarinoxy)methane :

7-Hydroxycoumarin (3.24 g. ; 0.02 M), methylene iodide (2.69 g. ; 0.01 M) and anhydrous potassium carbonate (5 g.) were refluxed in boiling acetone (60 ml.) for 8 hours. After giving the above treatment the compound was crystallised from acetic acid in colourless crystals m.p. 260°. Yield 0.7 g. It also gave positive gallic acid-sulphuric acid test.

Analysis : Found : C,67.69 ; H,3.78 %.
$C_{19}H_{12}O_6$ requires : C,67.85 ; H,3.60 %.

Bi(4-phenyl-7-coumarinoxy)methane :

A mixture of 7-hydroxy-4-phenylcoumarin (2.38 g. ; 0.01 M), methylene iodide (1.34 g. ; 0.005 M), anhydrous potassium carbonate (3 g.) and acetone was refluxed for 6 hours and the compound obtained was washed with alkali and crystallised from acetic acid in colourless crystals, m.p. 218°. Yield 0.3 g.

Analysis : Found : C,75.68 ; H,4.44 %.
$C_{31}H_{22}O_6$ requires : C,75.91 ; H,4.52 %.

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