CHAPTER II

SYNTHESIS OF SOME BIFLAVONYLS STARTING WITH BIPHENYL DERIVATIVES.

CHAPTER II

Synthesis of some Biflavonyls starting with biphenyl derivatives.

Theoretical

The presence of flavones in plants has been known since many years. The structures of many of them have been established and a large number of them have been synthesised. It is only in recent years that the presence of a new class of flavanoids where two flavone nuclei are joined together and which are therefore designated as biflavonyls has been discovered.

The story of biflavonyls begins with the isolation by Furukawa[1] of a yellow phenolic product in 1932 from the autumn leaves of the Gingko biloba or maidenhair tree. To this yellow phenolic compound he gave the 5,8-dihydroxy-4'-methoxyflavone structure but the synthesis of this compound showed that the structure was incorrect. Examination of Furukawa's evidence led Baker[2] and his co-workers to suggest that the yellow product of Furukawa which they named " ginkgetin ", probably had a

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[1] Furukawa, Sci.Papers.Inst.Phys.Chem.Res., Tokyo, 19, 27 (1932) ; 21, 278 (1933) ; C.A. 27, 5745.

[2] Baker and Simmonds., J.Chem.Soc., 1940, 1370 ;
Baker and Flemons. Ibid., 1948, 2138;
Baker, Flemons and Winter. Ibid., 1949, 1560.

higher molecular weight than that corresponding to a normal flavanoid structure. So they synthesised various flavanoids including furanoflavones ; but they were all different from ginkgetin. Later, Nakazawa[3] showed that ginkgetin has a formula $C_{32}H_{22}O_{10}$ but the formula suggested by him on the basis of degradation products was later found to be incorrect. The discovery of other natural products like kayaflavone and sotetsuflavone and their study led to the conclusion that all three had similar skeletal structures and that these were biflavonyl derivatives.

Ollis[4] has summarised the work done on biflavonyls upto 1961.

Naturally occurring biflavonyls : Several natural biflavonyls have been isolated during the past few years and their structures have been established by degradation methods and by physical methods such as ultra violet and infra red spectra. Ginkgetin, isoginkgetin, sciadopitysin, kayaflavone, sotetsuflavone are some of the important biflavonyl derivatives isolated from gingko biloba, sciadopitys verticillata (umbrella pine), gymnosperm

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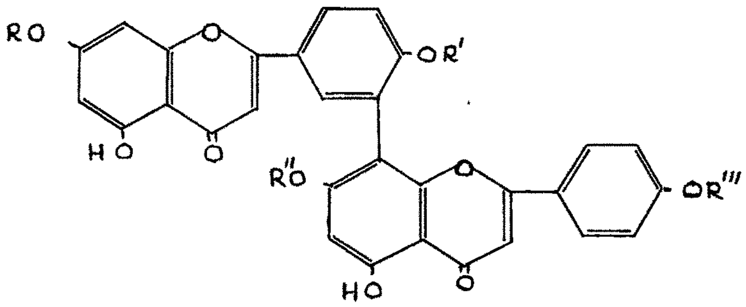
3. Nakazawa. J.Pharm.Soc., Japan., 61, 174, 228 (1941).

4. W.D.Ollis. " Chemistry of Natural Phenolic Products," Pergamon Press. 1961. See chapter on Biflavonyls.

torreyanucifera sièb et. zucc and cycad cycas revoluta Thunb, respectively. The structures of the above biflavonyls have been established. The structures with the references to publications of the principal investigators are given below:



	R	R'	R''	R'''
Ginkgetin[1,3]	Me	Me	H	H
Isoginkgetin[2]	H	Me	H	Me
Sciadopitysin[5]	Me	Me	H	Me
Kayaflavone[6]	H	Me	Me	Me
Sotetsuflavone[7]	H	H	H	H

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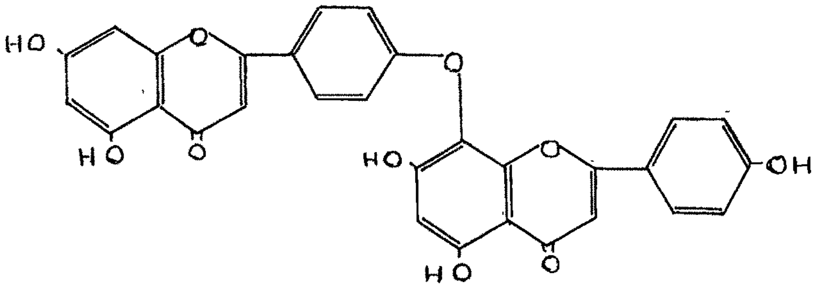
5. Kariyone and Kawano., J.Pharm.Soc., Japan., 76, 448 etc. (1956) ; C.A., 54, 3405 (1960).
6. Kariyone and Sawada., J.Pharm.Soc., Japan., 78, 1010, 1013, 1016 (1958).
7. Baker, Ollis and Robinson., Proc.Chem.Soc., 1961, 269.

Hinokiflavone[8] isolated from the leaves of " Cryptomeria japonica " has been shown to be a biflavonyl ether.



Hinokiflavone

The biflavonyls are probably produced in the plant by oxidative coupling of a flavanoid precursor such as epigenin or a closely related compound. This could be followed by methylation of the di-epigeninyl in various positions and this is in aggrement with the simultaneous occurrence of various biflavonyls in the same plant. It is also supported by the biflavonyl ether structure of hinokiflavone since it is recognised that oxidative coupling of phenols can lead either to diaryls or diaryl ethers. It would be of interest if it could be proved that a labelled epigenin is converted into labelled biflavonyls by feeding it to a suitable plant.

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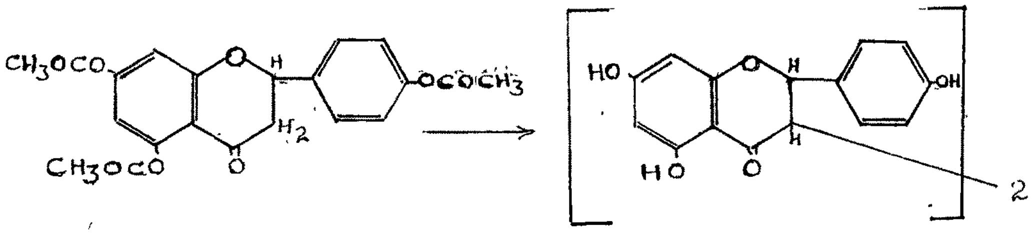
[8] Fukui and Kawano. J.Amer.Chem.Soc., 81, 6331 (1959).

<u>Synthetic biflavonyls</u> : Mahesh and Seshadri[9] in their attempt to oxidise narigenin triacetate with Fenton's reagent[10] obtained 4,4''',5,7,5'',7''-hexahydroxy-3,3''-biflavanonyl as a byproduct. They did not give a definite proof for this compound ; but gave the bimolecular structure to this compound because of the availability of a number of organic bimolecular compounds when the simple ones are oxidised with Fenton's[10] reagent.



Chen and Liu[11] synthesised 3,3'-biflavonyl by the Ullmann reaction on 3-bromoflavone. They further reported that the Ullmann reaction on 6-bromo, 7-bromo, 4'-iodo and 6-bromo-4'-methoxy flavanol derivatives did not succeed.

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[9] Mahesh and Seshadri., J.Chem.Soc., 1955, 2503.

[10] Merz and Waters., J.Chem.Soc., 1949, 2427.

[11] Chen and Liu., J.Taiwan Pharm.Soc., <u>5</u>, 53 (1953) ; C.A., <u>49</u>, 5464 (1955).

Other symmetrical biflavonyls have been synthesised through the Ullmann reaction on their appropriate halogenoflavones. Thus 3-bromo, 6-iodo, 6-iodo-4'-methoxy, 7-iodo, 7-iodo-4'-methoxy, 8-iodo, 8-bromo, 8-chloro, 3'-iodo and 4'-iodo flavone derivatives were converted into their respective biflavonyls by Chen et al[12]. Jurd[13] synthesised 7,7'-dimethoxy-8,8'-biflavonyl and 7,7',4,4'-tetramethoxy-8,8'-biflavonyl from the corresponding 8-iodoflavone derivatives by the Ullmann reaction. Demethylation of the above methoxy biflavonyls with aluminium chloride in boiling benzene gave the corresponding hydroxy biflavonyls. In this laboratory Shah[14] has synthesised symmetrical biflavonyls by the Ullmann reaction on 7-methoxy-8-iodoflavone, and 7-methoxy-6-iodo-3-benzoyl flavone. Recently, ginkgetin was synthesised by Nakazawa and Ito[15] by the cross Ullmann reaction ~~on~~ between 3'-iodo-5-benzoyloxy-4',7-dimethoxy flavone and 5-benzoyloxy-8-iodo-4',7-dimethoxy flavone in the presence of activated copper powder and subsequent hydrolysis with 10 % sulphuric acid in acetic acid.

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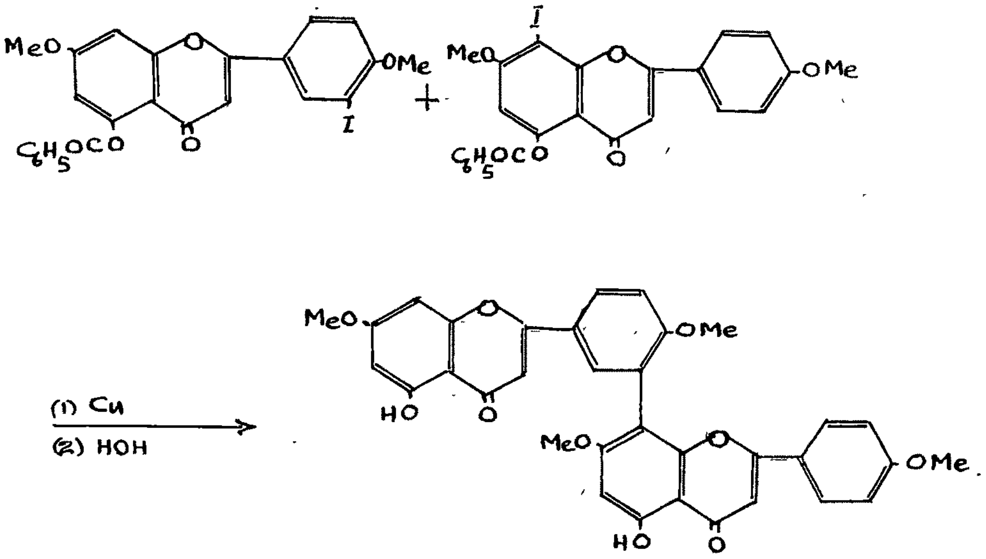
12. Chen et al., Proc.Chem.Soc., 1959, 232.

13. Jurd., Chem.Ind., 1961, 322.

14. Shah M.V., Current Science., 31, 57 (1962).

15. Nakazawa and Ito., Chem.Pharm.Bull (Tokyo) 11, (3) 282 (1963) ; C.A., 59, 1574 (1963).



Ginkgetin

Other possible routes to symmetrical biflavonyls :

Other approaches to the synthesis of symmetrical biflavonyls are possible and it was thought of interest to investigate some of them. One approach is to start with a suitable biphenyl derivative and to build up the heterocyclic ring on each one of the phenyl rings. This can be done by various methods and some of these are given below.

(a) Kostanecki-Robinson acylation[16] A ketone of the type (I) can be subjected to Kostanecki-Robinson acylation by

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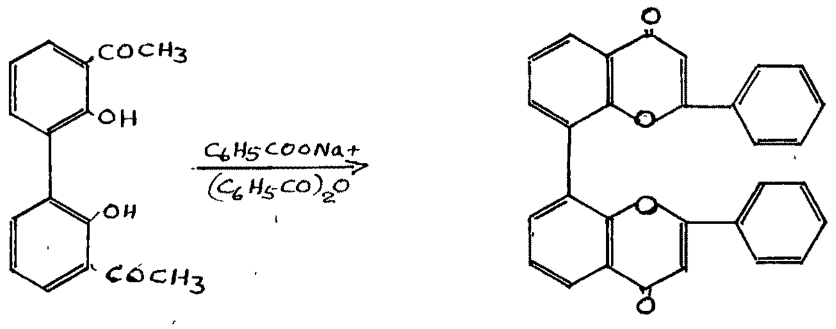
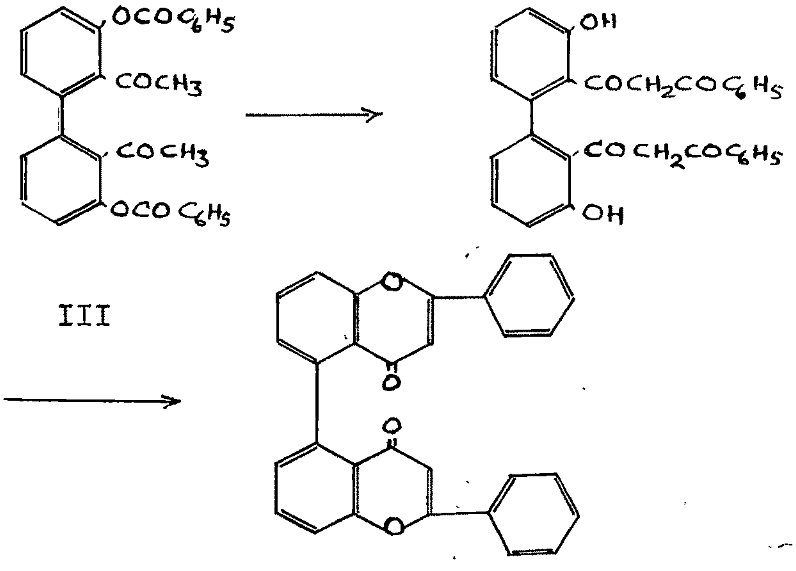
[16] Kostanecki and Rozycki., Ber., 34, 102 (1901) ; Allan and Robinson., J.Chem.Soc., 125, 2192 (1924).

heating with the sodium salt of an aromatic acid and its anhydride and the biflavonyls (II) can be synthesised.



I II

(b) A biphenyl derivative such as (III) can be subjected to Baker-Venkataraman[17] transformation and a biflavonyl such as (IV) can be synthesised.



III

IV

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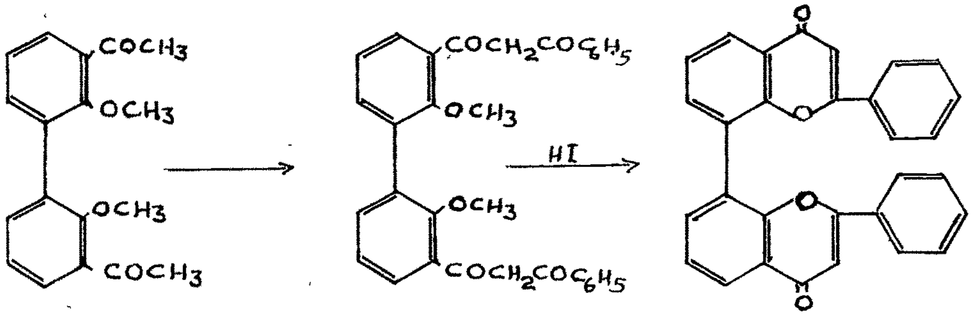
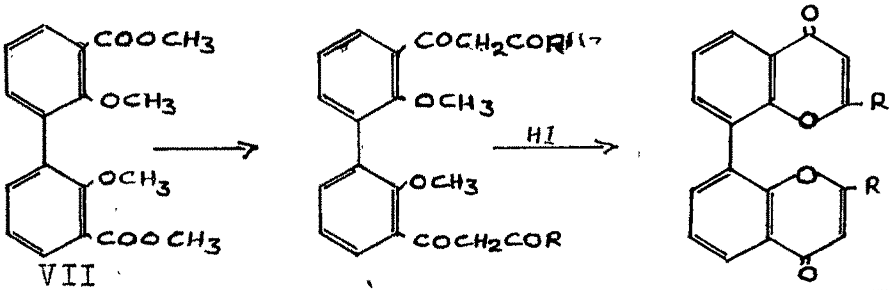
[17] Baker., J.Chem.Soc., 1386 (1933).
Mahal and Venkataraman., Current Science., 4, 214 (1933) ; J.Chem.Soc., 1934, 1767.

(c) Cyclization of B-diketones[18,19] - A biphenyl derivative such as (V) can be condensed with the ester of an aromatic acid and the B-diketone obtained subjected to cyclisation in the presence of hydriodic acid.



V VI

Alternately, an ester such as (VII) can be condensed with an aromatic ketone and the β-diketone formed cyclized with hydriodic acid to the corresponding biflavonyl. (VIII).



VII VIII

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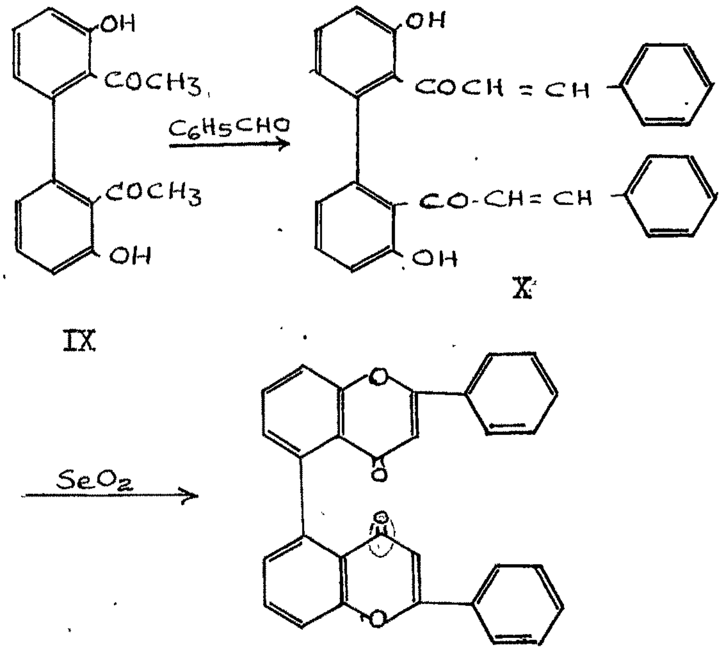
[18] Kostanecki., Ber., 33, 330, 471 (1900).

[19] Idem., Ibid., 33, 1998 (1900).

In all the above cases it will be clear that by starting with appropriate biphenols one could synthesise biflavonyls with the linkage between the two flavone nuclei in different positions i.e. at 5,5''; 6,6''; 7,7'' and 8,8''-positions.

(d) Kostanecki's chalcone method[20] - A ketone from a biphenyl such as (IX) can be condensed with an aromatic aldehyde and the bichalconyl derivative (X) formed can be cyclised and dehydrogenated with selenium dioxide[21] to get the biflavonyl derivative (XI).



IX

X

XI

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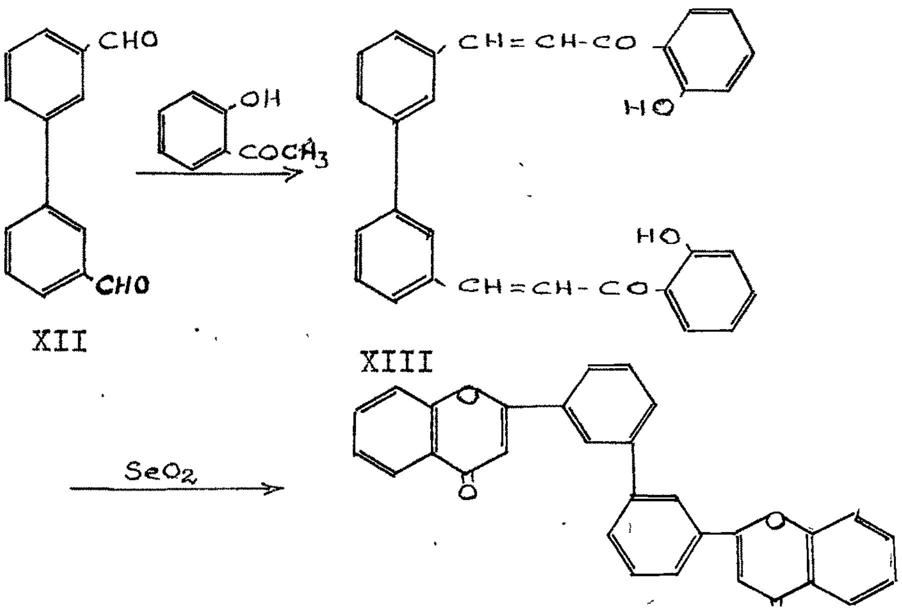
[20] Kostanecki and Rossbach., Ber., 29, 1488 (1896).

[21] Nadkarni and Wheeler., J.Chem.Soc., 1320 (1938).
Chakravarti and Dutta., J.Ind.Chem.Soc., 16, 639 (1939).

Alternately, one could start with a diformyl derivative of a biphenyl such as XII and condense it with an o-hydroxy acetophenone, to get a bichalconyl (XIII) which can then be cyclised and dehydrogenated to a biflavonyl derivative (XIV).



XII

XIII

XIV

It will be seen from the above that by starting with a biketone derivative of a biphenyl one can obtain biflavonyls with linkage between the two flavone nuclei in the benzenoid part of the molecule and by starting with a diformyl derivative of a biphenyl one can synthesise a biflavonyl where the two flavonyl nuclei are linked through the side phenyl nuclei.

The present work deals with the synthesis of various symmetrical biflavonyls starting with biphenyl derivatives and using some of the above mentioned approaches.

Synthesis of 6',6'''-dimethoxy-3',3'''-biflavonyl :-

4,4'-Dimethoxy-3,3'-diformylbiphenyl (I), prepared by the chloromethylation of 4,4'-dimethoxy biphenyl[22] and the subsequent Sommelet reaction on the resulting 3,3'-dichloromethyl derivative, was condensed with 2-hydroxy acetophenone(II) in the presence of alcoholic potassium hydroxide. The orange red product obtained gave tests for a chalcone such as (1) red colouration with concentrated sulphuric acid, (2) yellow colouration with dry acetone solution of citric acid-boric acid mixture (Wilson test[23]) and (3) a faint colouration with alcoholic ferric chloride.[24] Moreover it gave a diacetyl derivative when refluxed with acetic anhydride and fused sodium acetate. 2',2'''-Dihydroxy-6,6''-dimethoxy-3,3''-bichalconyl (III) structure has therefore been assigned to this product. The above bichalconyl derivative (III) on refluxing with selenium dioxide in amyl alcohol gave a light yellow compound which gave a yellow colouration with sulphuric acid. The Wilson test was negative. 6',6'''-Dimethoxy-3',3'''-biflavonyl (IV) structure

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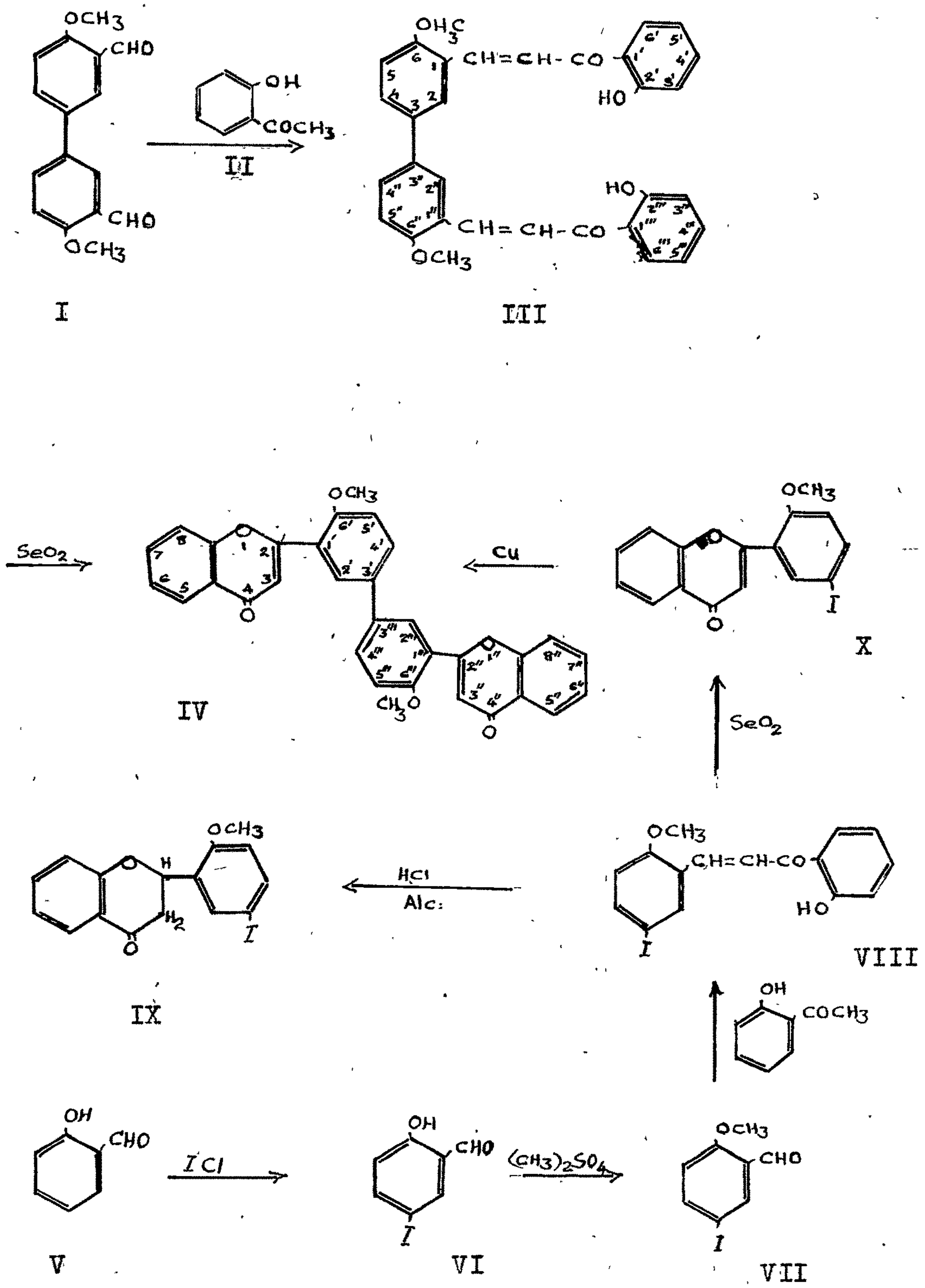
[22] Mathai and Sethna., J.Ind.Chem.Soc., **40**, 347 (1963).

[23] Wilson., J.Am.Chem.Soc., **61**, 2303 (1939).

[24] Faint colouration may be due to the sparing solubility of the bichalconyl derivative in alcohol.


OCH3
CHO
CHO
OCH3
I
OH
COCH3
II
OHC
CH=CH-CO
HO
HO
CH=CH-CO
OCH3
III
SeO2
OCH3
CH3O
IV
Cu
OCH3
I
X
SeO2
OCH3
H
H2
I
IX
HCl
Alc.
OCH3
CH=CH-CO
HO
I
VIII
OH
COCH3
OH
CHO
V
ICl
OH
CHO
I
VI
(CH3)2SO4
OCH3
CHO
I
VII

was assigned to this compound.

The same biflavonyl derivative was synthesised for comparison by an alternate method as follows : Salicylaldehyde (V) was treated with iodine monochloride at low temperature to get the 5-iodo salicylaldehyde[25] (VI) which on methylation with dimethyl sulphate gave 2-methoxy-5-iodo benzaldehyde (VII) which on condensation with 2-hydroxy acetophenone (II) in the presence of alcoholic potassium hydroxide gave 2'-hydroxy-2-methoxy-5-iodochalcone (VIII). The chalcone structure was established by the formation of the monoacetyl derivative and the pos~~s~~itive ferric chloride and Wilson tests and deep red colouration with sulphuric acid. On refluxing with alcoholic hydrochloric acid a colourless compound isomeric with the chalcone was obtained to which 2'-methoxy-5'-iodoflavanone (IX) structure has been assigned. The above iodochalcone on heating with selenium dioxide in amyl alcohol gave 2'-methoxy-5'-iodoflavone (X) which when refluxed in diphenyl ether with copper bronze gave a product identical with the biflavonyl (IV) described above.

6',6''',7,7''-Tetramethoxy-3',3'''-biflavonyl :-4,4'-Dimethoxy-3,3'-diformyl biphenyl (I) on condensation with 2-hydroxy-4-methoxy acetophenone(XI) in the presence of alcoholic potassium hydroxide gave an orange red product which

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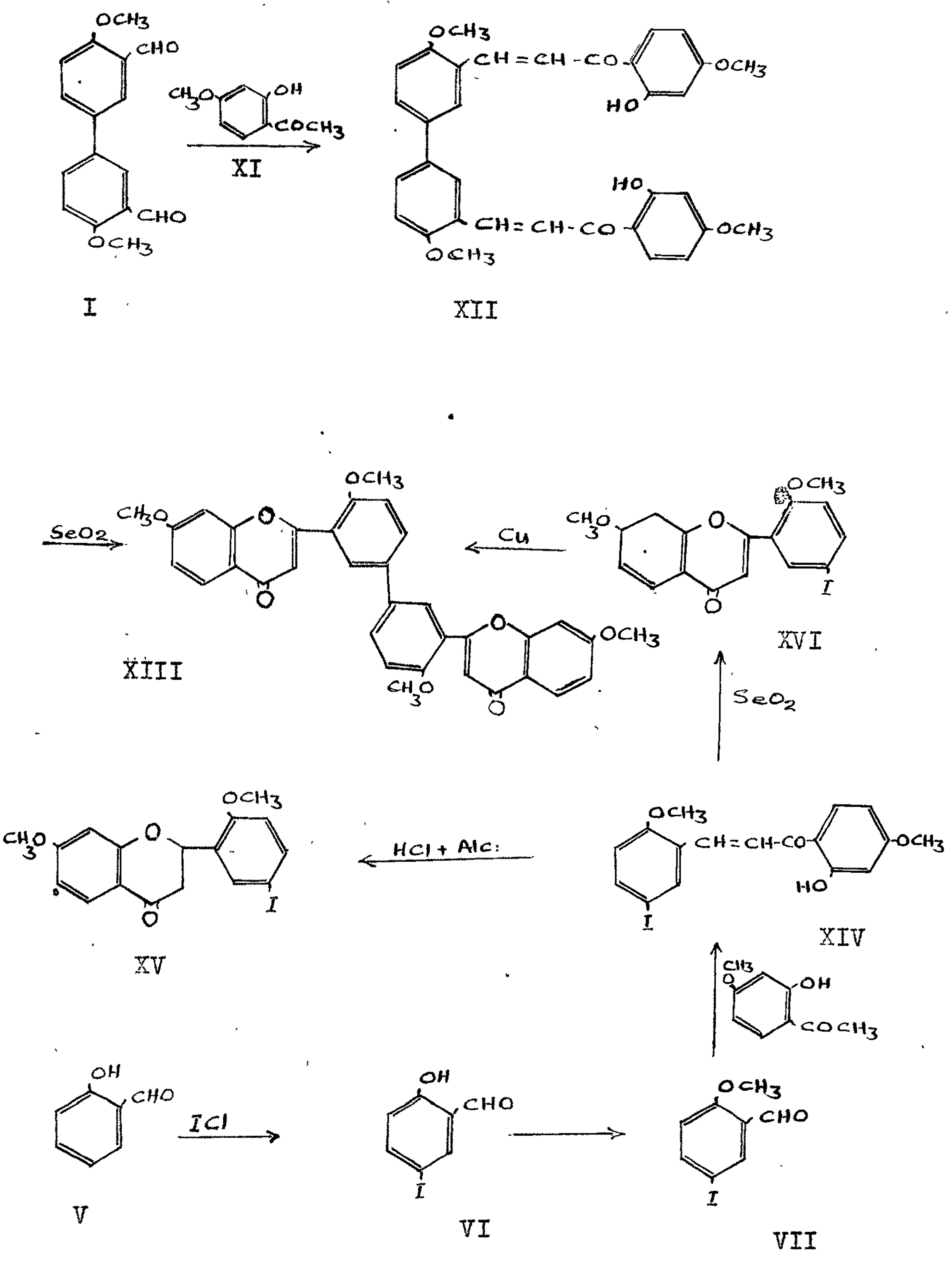
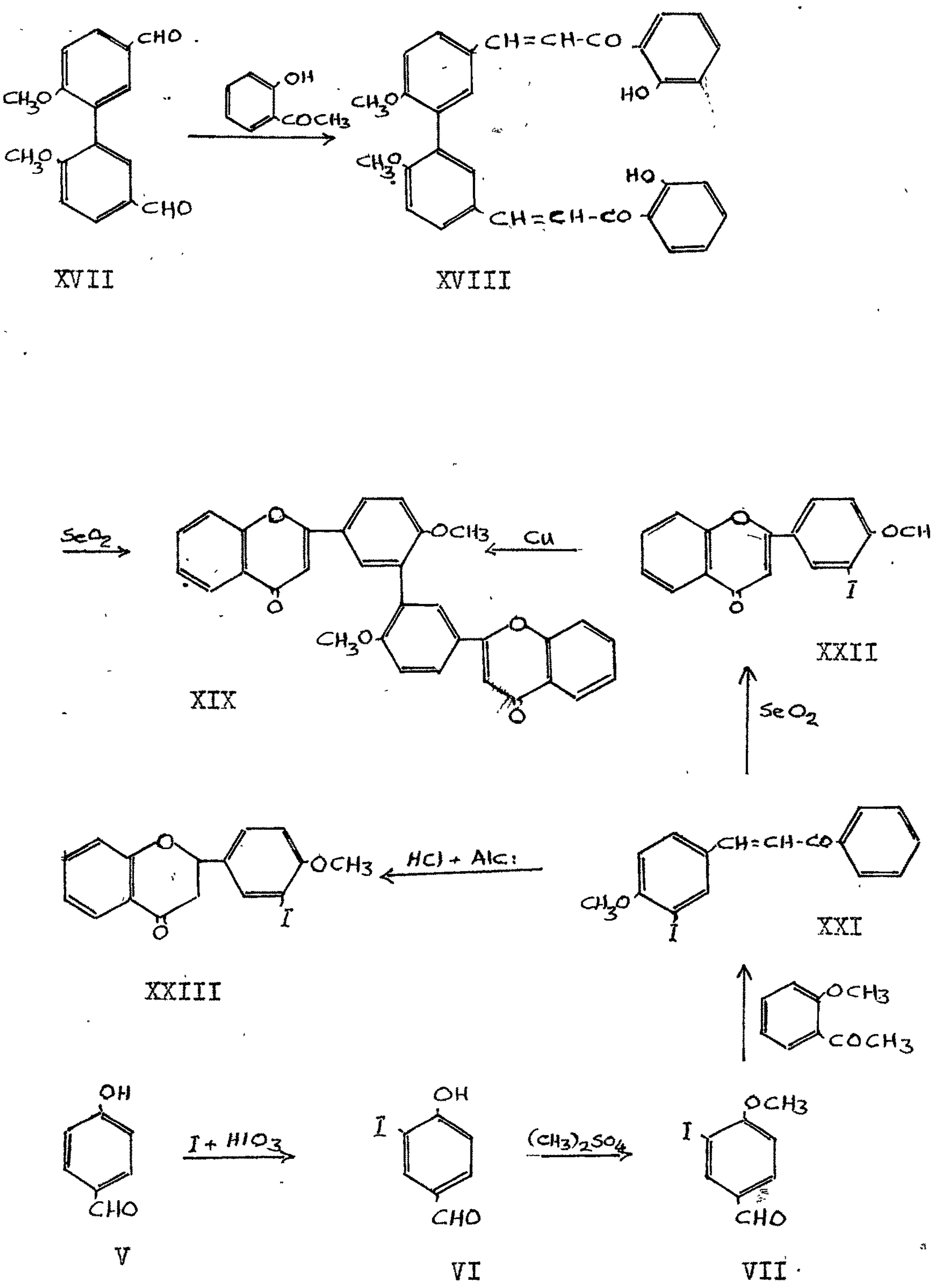
[25] Visser., Archiv der Pharmazie., 235, 558


I
XI
XII
SeO2
XIII
Cu
XVI
SeO2
XV
HCl + Alc:
XIV
V
ICl
VI
VII

gave tests for a chalcone, and a colourless diacetyl derivative. 2',2'''-Dihydroxy-4',4''',6,6''-tetramethoxy-3,3''-bichalconyl (XII) structure has been assigned to the product. On refluxing with selenium dioxide in amyl alcohol it gave a pale yellow product to which 6',6'''-7,7''-tetramethoxy-3',3'''-biflavonyl (XIII) structure has been assigned. The same biflavonyl derivative was prepared by an alternate synthesis given below.

2-Hydroxy-4-methoxy acetophenone (XI) was condensed with 2-methoxy-5-iodo benzaldehyde (VII) in alcoholic potassium hydroxide. The resulting compound has been assigned the 2,4'-dimethoxy-2'-hydroxy-5-iodo chalcone (XIV) structure on the basis of the formation of a mono-acetyl derivative and the ferric chloride and sulphuric acid colour reactions and a positive Wilson test. The iodo-chalcone was isomerised to the corresponding flavanone (XV) by refluxing with hydrochloric acid in alcoholic solution. The chalcone (XIV) was converted into 2',7-dimethoxy-5'-iodoflavone (XVI) by heating with selenium dioxide in amyl alcohol solution. The iodo flavone (XVI) when subjected to Ullmann reaction gave a biflavonyl derivative identical with 6',6'''-7,7''-tetramethoxy-3',3'''-biflavonyl (XIII) described above.

<u>4',4'''-Dimethoxy-3',3'''-biflavonyl</u> :- 2,2'-Dimethoxy-5,5'-diformyl biphenyl (XVII) prepared by the chloromethylation of 2,2'-dimethoxy biphenyl and subsequent Sommelet reaction on the resulting 5,5'-dichloromethyl derivative, on


CHO
CH3O
CH3O
CHO
OH
COCH3
CH=CH-CO
HO
CH3O
CH3O
HO
CH=CH-CO
XVII
XVIII
SeO2
OCH3
Cu
CH3O
XIX
OCH3
I
XXII
SeO2
OCH3
HCl + Alc.
I
XXIII
CH=CH-CO
CH3O
I
XXI
OCH3
COCH3
OH
CHO
I + HIO3
I
OH
CHO
(CH3)2SO4
I
OCH3
CHO
V
VI
VII

condensation with 2-hydroxy acetophenone (II) in the presence of alcoholic potassium hydroxide gave a yellow product which gave tests for a chalcone and also gave a colourless diacetyl derivative. 2',2'''-Dihydroxy-4,4''-dimethoxy-3,3''-bichalconyl (XVIII) structure has therefore been assigned to the product. The above bichalconyl derivative on refluxing with selenium dioxide in amyl alcohol gave 4',4'''-dimethoxy-3',3'''-biflavonyl (XIX). The same biflavonyl was also prepared by an alternate method given below.

2'-Hydroxy-4-methoxy-3-iodo chalcone (XXI) was prepared by the condensation of 2-hydroxy acetophenone (II) with 4-methoxy-3-iodo benzaldehyde[26] (XX) in the presence of alcoholic potassium hydroxide. On treatment with selenium dioxide in amyl alcohol it gave 4'-methoxy-3'-iodo flavone (XXII) which on Ullmann reaction gave a product identical with 4',4'''-dimethoxy-3',3'''-biflavonyl (XIX) described above. 2'-Hydroxy-4-methoxy-3-iodo chalcone (XXI) was converted into the isomeric 4'-methoxy-3'-iodo-flavanone (XXIII) by refluxing with alcoholic hydrochloric acid. It also gave a mono acetyl derivative.

4',4''',7,7''-Tetramethoxy-3',3'''-biflavonyl :-2,2'-Dimethoxy-5,5'-fiformyl biphenyl (XVII) on condensation with 2-hydroxy-4-methoxy acetophenone (XI) in the presence of alcoholic potassium hydroxide gave 2',2'''-dihydroxy-4,4',4'',4'''-tetramethoxy-3,3''-bichalconyl (XXIV). It gave a

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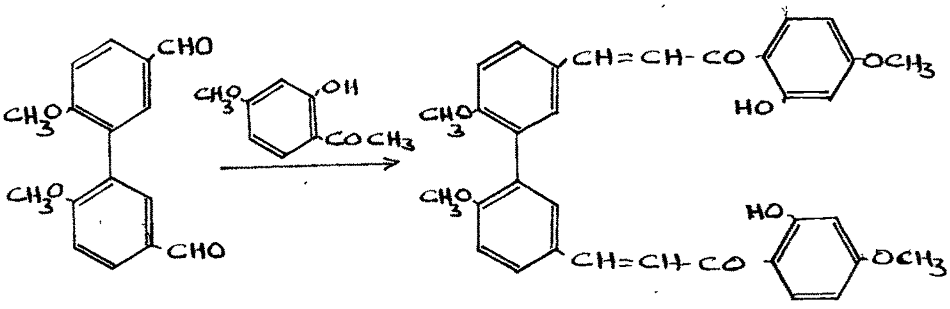
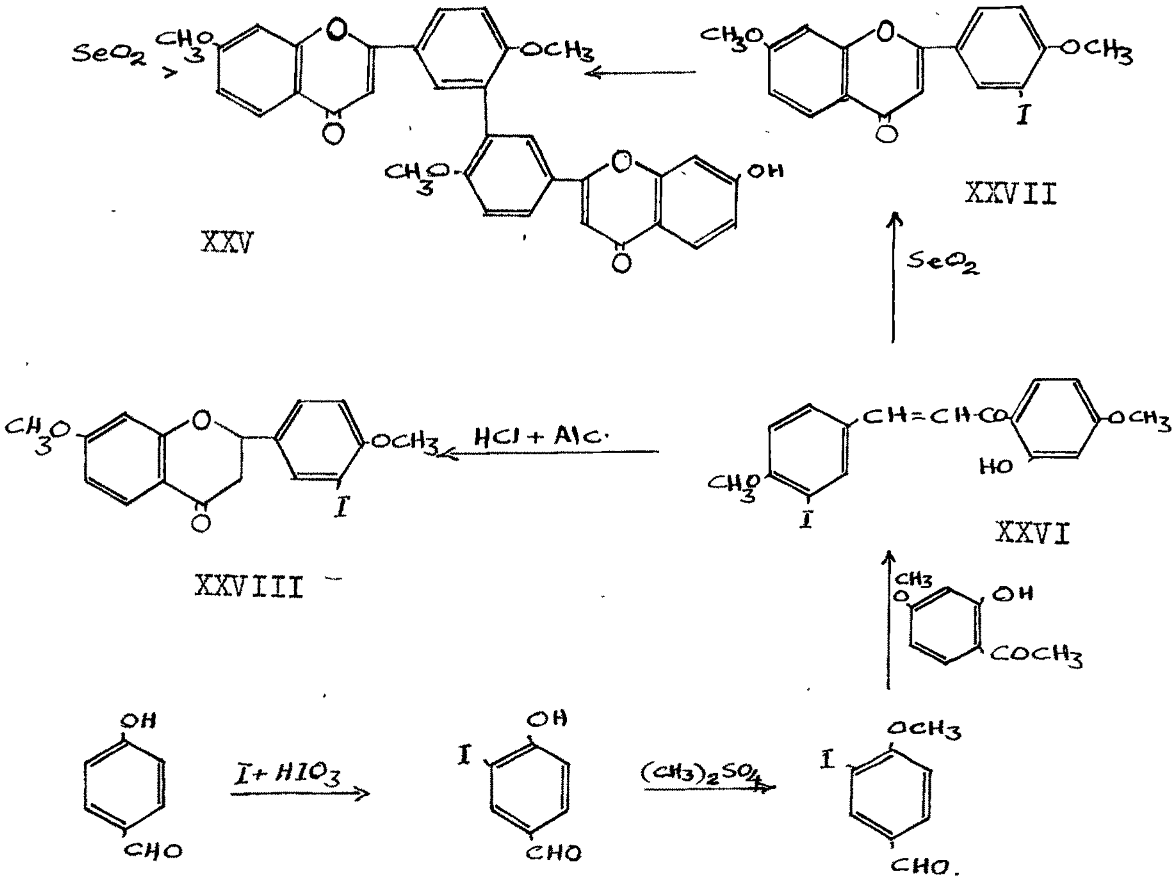
[26] Seidel., J.Prakt.Chem., (2), 52, 41.



XVII

XXIV



XXV

XXVII

XXVIII

XXVI

XX

a diacetyl derivative and tests for a chalcone. When refluxed with selenium dioxide in amyl alcohol it gave the expected 4',4''',7,7''-tetramethoxy-3',3'''-biflavonyl (XXV) whose structure was confirmed by preparing the same by an alternate method given below.

2'-Hydroxy-4,4'-dimethoxy-3-iodo chalcone (XXVI) was prepared by condensing 2-hydroxy-4-methoxy acetophenone (XI) with 4-methoxy-3-iodo benzaldehyde[26] (XX) in the presence of alcoholic alkali. The above iodo chalcone (XXVI) was converted into 4',7-dimethoxy-3'-iodoflavone (XXVII) by treating it with selenium dioxide in amyl alcohol. The iodo flavone (XXVII) on Ullmann reaction gave a biflavonyl which was identical with 4,4''',7,7''-tetramethoxy-3',3'''-biflavonyl (XXV) described above. 2'-Hydroxy-4,4'-dimethoxy-3-iodo chalcone (XXVI) on refluxing with alcoholic hydrochloric acid gave the isomeric 4',7-dimethoxy-3-iodo flavanone (XXVIII). It also gave a diacetyl derivative.

<u>6,6''-Biflavonyl</u> :- 4,4'-Dihydroxy-3,3'-diacetyl biphenyl[27] (XXIX) on condensation with benzaldehyde (XXX) in the presence of alcoholic potassium hydroxide gave a red product which gave a diacetyl derivative and it gave positive tests for a chalcone. 6',6'''-Dihydroxy-3',3'''-bichalconyl (XXXI) structure has therefore been assigned to the product. On refluxing with alcoholic hydrochloric

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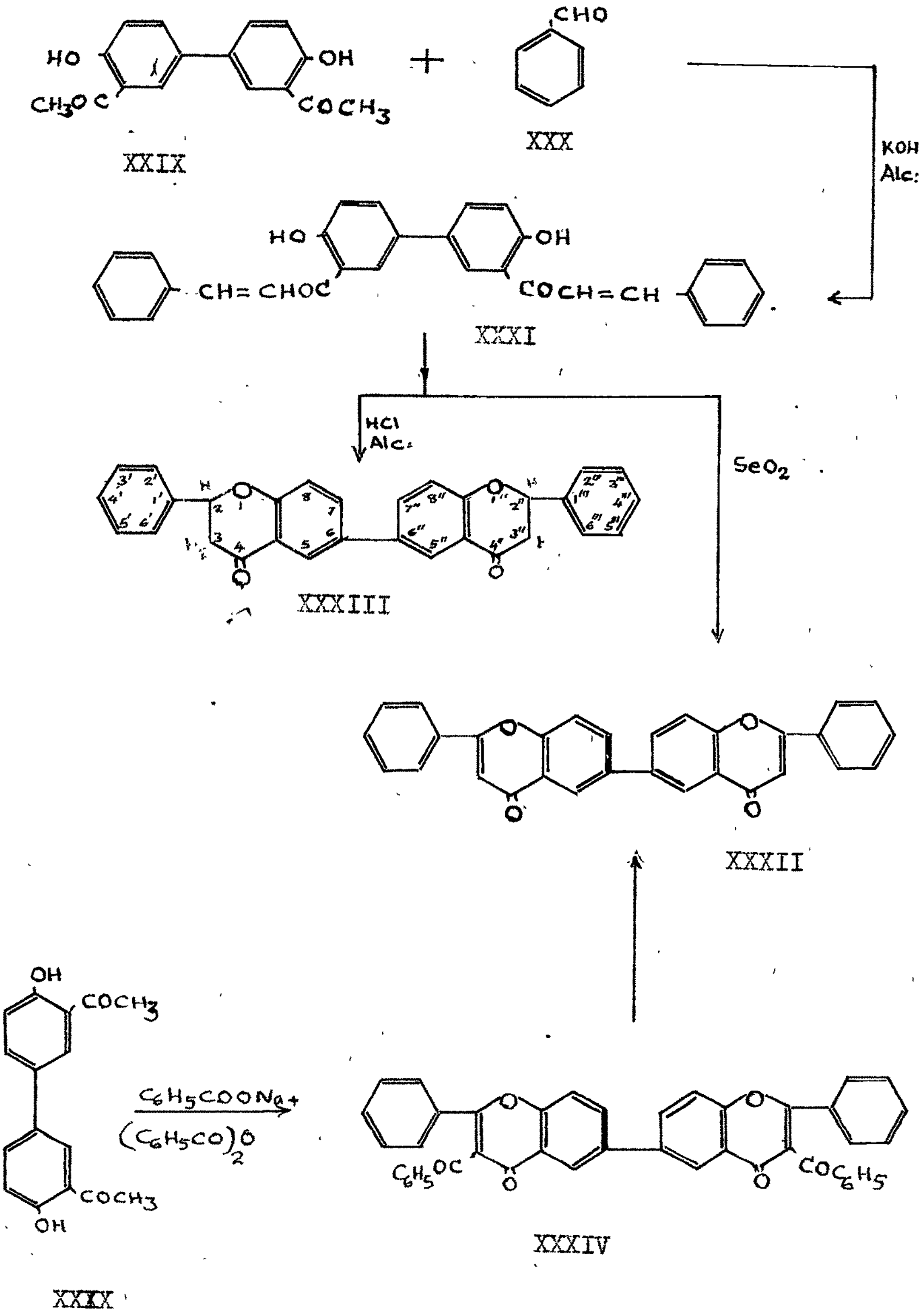
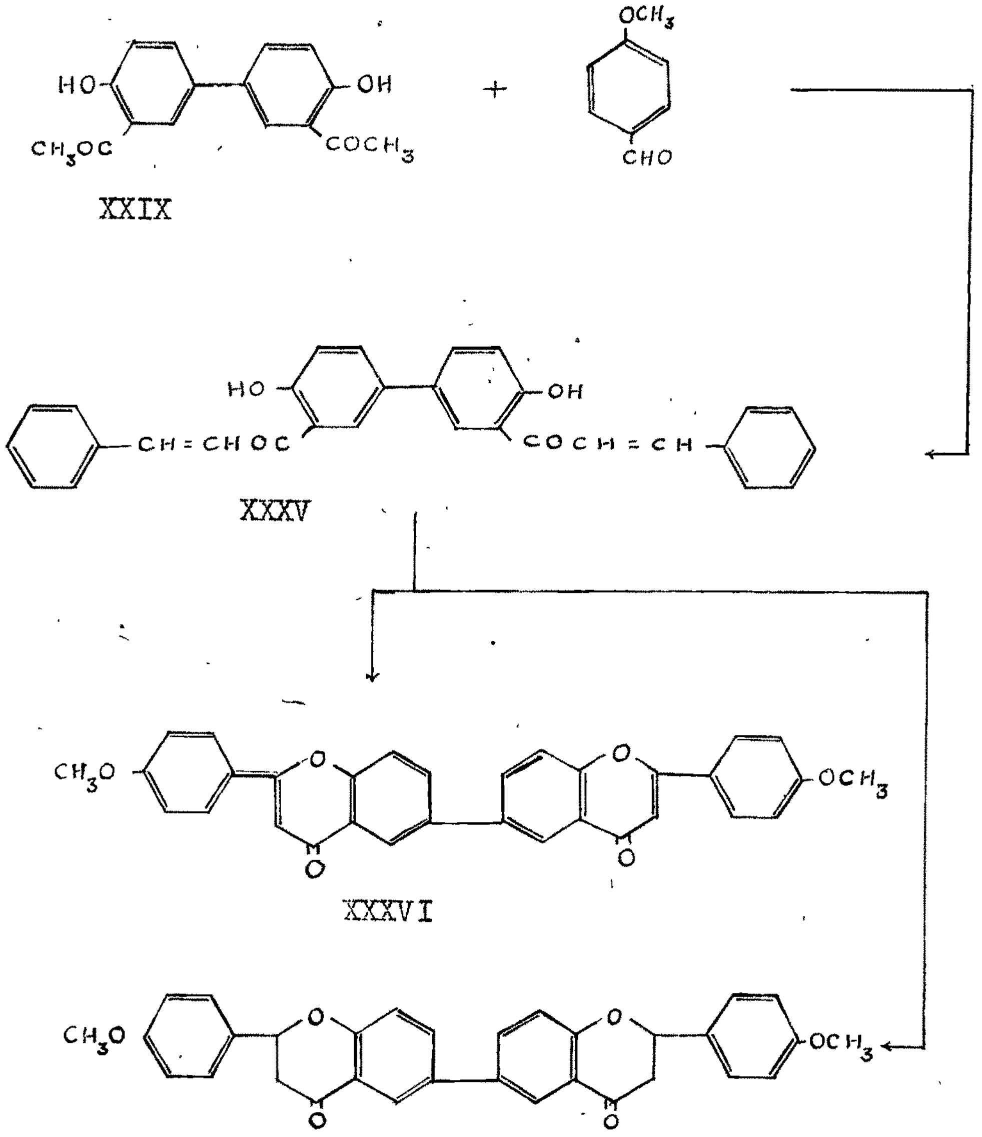
[27] Boon-Long., J.Pharm.Assoc., Siam 1, No. 4,5 (1948) ; C.A., 43, 5017 (1949).


HO
OH
CH₃OC
COCH₃
XXIX
+
CHO
XXX
KOH
Alc:
HO
OH
CH=CHOC
COCH=CH
XXXI
HCl
Alc:
SeO₂
XXXIII
XXXII
OH
COCH₃
COCH₃
OH
C₆H₅COONa+
(C₆H₅CO)₂O
C₆H₅OC
COC₆H₅
XXXIV
XXXX

acid it gave the colourless isomeric 6,6''-biflavanone (XXXIII). 6',6'''-Dihydroxy-3',3'''-bichalconyl (XXXI) when refluxed with selenium dioxide in amyl alcohol gave the expected 6,6''-biflavonyl (XXXII), m.p. 306°. Chen et al.[12] who prepared the same biflavonyl derivative by the Ullmann reaction on 6-iodoflavone have reported m.p. 305-7°. The same biflavonyl (XXXII) was also obtained when 4,4'-dihydroxy-3,3'-diacetyl biphenyl (XXIX) was subjected to Kostanecki-Robinson benzoylation at 210-15° and the benzoyl derivative (XXXIV) obtained was hydrolysed with 2 % alcoholic sodium hydroxide. Kostanecki-Robinson reaction at lower temperature gave only the O-benzoyl derivative.

4',4'''-Dimethoxy-6,6''-biflavonyl :- Similarly 4,4'-dihydroxy-3,3'-diacetylbiphenyl[27] (XXIX) on condensation with anisaldehyde (XXXIV) in the presence of alcoholic potassium hydroxide gave an orange coloured product to which 6',6'''-dihydroxy-4,4''-dimethoxy-3',3'''-bichalconyl (XXXV) structure has been assigned on the basis of the formation of a diacetyl derivative and colour reactions. It was converted into the 4',4'''-dimethoxy-6,6''-biflavonyl(m.p.318°) (XXXVI) by refluxing it with selenium dioxide in amyl alcohol. The same biflavonyl has been prepared by Chen et al[12] who have reported m.p. 315-20°. 4',4'''-Dimethoxy-6,6''-biflavanonyl (XXXVII) was also prepared by refluxing the bichalconyl derivative (XXXV) with alcoholic hydrochloric acid.



XXIX

XXXV

XXXVI

XXXVII

EXPERIMENTAL

2,2'''-Dihydroxy-6,6''-dimethoxy-3,3''-bichalconyl :- A mixture of 4,4'-dimethoxy-3,3'-diformyl biphenyl (2.7 g. ; 0.01 mole), 2-hydroxy acetophenone (5.5 g. ; 0.04 mole), alcohol (50 c.c.) and potassium hydroxide (15 g. in 15 c.c. of water) was refluxed over a steam bath till the solution became clear (30 minutes). The solution turned deep red. It was cooled and kept for 3 days. The red sodium salt of the bichalconyl derivative crystallised out which was collected, washed with a little alcohol and again dissolved in alcohol by boiling. This was then acidified with hydrochloric acid, the precipitated orange product crystallised from nitrobenzene in orange needles, m.p. 263-4°. The filtrate after the removal of the sodium salt on acidification gave a further quantity of the bichalconyl derivative. Total yield was 3 g. It gave a positive Wilson test and a deep red colouration with con.sulphuric acid. With alcoholic ferric chloride it gave only a faint brown colour.

Analysis : 4.040 mg. of the substance gave 11.236 mg. of carbon dioxide and 1.790 mg. of water.

Found : C = 75.9 % ; H = 5.0 %.

$C_{32}H_{26}O_6$ requires : C = 75.9 % ; H = 5.1 %.

2,2''',6,6'''-Tetramethoxy-3,3''-bichalconyl :- The above bichalconyl derivative (1 g.) was mixed with dry acetone (50 c.c.), dimethyl sulphate (3 c.c.) and anhydrous potassium carbonate and refluxed over a steam bath for

4 hrs. The solvent was removed and the mixture was diluted with water. The precipitated tetramethoxy derivative crystallised from benzene in light yellow crystals, m.p. 217°.

Analysis : 4.362 mg. of the substance gave 12.152 mg. of carbon dioxide and 2.146 mg. of water.

Found : C = 76.0 % ; H = 5.5 %.

$C_{34}H_{30}O_6$ requires : C = 76.4 % ; H = 5.6 %.

5-Iodo salicylaldehyde :- Iodine monochloride (6.6 g.; 0.04 mole) was added drop wise to a well cooled salicylaldehyde (5 g. ; 0.04 mole) while stirring. The mixture was kept at room temperature for 2 hrs. It was diluted with water and the precipitate washed with sodium bisulphite and sodium bicarbonate. It crystallised from petroleum ether in white needles, m.p. 102°. Visser, (Archiv. der. Pharmazie., 235, 558,) ~~who~~ prepared the same compound by a different method, has reported the same m.p.

Analysis : 12.378 mg. of the substance gave 11.722 mg. of silver iodide.

Found : I = 51.2 %.

$C_7H_5IO_2$ requires : I = 51.2 %.

2-Methoxy-5-iodobenzaldehyde :- A mixture of 5-iodo salicylaldehyde (4 g.), excess of dimethyl sulphate (4 c.c.), anhydrous potassium carbonate (20 g.) and dry acetone was refluxed over a steam bath till the yellow colour just disappeared (15 minutes). The reaction mixture was poured into water and the precipitated methoxy derivative was washed with sodium hydroxide and crystallised from alcohol in colourless needles, m.p. 145-46°.

Analysis : 13.134 mg. of the substance gave 11.572mg. of silver chloride.

Found : I = 48.3 %.

$C_8H_7IO_2$ requires : I = 48.5 %.

2'-Hydroxy-2-methoxy-5-iodochalcone :- To a mixture of 2-methoxy-5-iodobenzaldehyde (2.6 g. ; 0.01 mole) and 2-hydroxy acetophenone (2.7 g. ; 0.02 mole) in alcohol (25 c.c.), potassium hydroxide (5 g. ; in 5 c.c. water) was added and the mixture kept over night in a well stoppered flask. The mixture after dilution with water and acidification gave orange red coloured precipitate which was crystallised from alcohol acetone mixture in orange coloured needles, m.p. 134-35°. Yield 3.5 g. It gave the following tests:(1) Orange colour with conc.sulphuric acid. (2) Brown colour with ferric chloride. (3) Positive Wilson test.

Analysis : 4.044 mg. of the substance gave 7.476 mg. of carbon dioxide and 1.056 mg. of water. 14.932 mg. of the same substance gave 9.272 mg. of silver iodide.

Found : C = 50.5 % ; H = 2.9 % ; I = 33.6 %.

$C_{16}H_{13}O_3I$ requires : C = 50.5 % ; H = 3.4 % ; I = 33.4 %.

The acetyl derivative Prepared from the above chalcone (1 g.) by heating with acetic anhydride (5 g.)

and fused sodium acetate (2 g.) on a steam bath for 2 hr. It crystallised from dilute acetic acid, m.p. 94°.

Analysis : 4.928 mg. of the substance gave 9.224 mg. of carbon dioxide and 1.418 mg. of water. 14.572 mg. of the same substance gave 8.232 mg. of silver iodide.

Found : C = 51.1 % ; H = 3.2 % ; I = 30.5 %.
$C_{18}H_{15}IO_4$ requires : C = 51.2 % ; H = 3.6 % ; I = 30.1 %.

2'-Methoxy-5'-iodoflavanone :- 2'-Hydroxy-2-methoxy-5-iodochalcone (0.5 g.) was refluxed with alcohol (50 c.c.) containing hydrochloric acid (5 c.c.) for 24 hrs. over a steam bath. It was filtered hot and on cooling the colourless crystals of iodoflavanone separated which was recrystallised from benzene, m.p. 138°. Mixed m.p. with the isomeric iodochalcone was depressed by over 10°.

Analysis : 4.826 mg. of the substance gave 8.920 mg. of carbon dioxide and 1.578 mg. of water. 13.450 mg. of the same substance gave 8.372 mg. of silver iodide.

Found : C = 50.4 % ; H = 3.6 % ; I = 33.6 %.
$C_{16}H_{13}O_3I$ requires : C = 50.5 % ; H = 3.4 % ; I = 33.4 %.

2'-Methoxy-5'-iodoflavone :- 2'-Hydroxy-2-methoxy-5-iodochalcone (1 g.) was dissolved in dry iso amyl alcohol (25 c.c.) and the solution refluxed with selenium dioxide (3 g.) in an oil bath at 140-50° for 10 hrs. It was filtered hot and the filtrate on cooling gave crystals of the flavone. It crystallised from benzene in colourless needles, m.p. 136-37°. Mixed m.p. with the iodochalcone was depressed by more than 10°. The mother liquor on removal of the solvent by steam distillation gave a further crop of iodoflavone.

Analysis : 4.888 mg. of the substance gave 9.032 mg. of carbon dioxide and 1.110 mg. of water. 14.332 mg. of the same substance gave 8.874 mg. of silver iodide.

Found : C = 50.4 % ; H = 2.5 % ; I = 33.5 %.

$C_{16}H_{11}O_3I$ requires : C = 50.8 % ; H = 2.9 % ; I = 33.6 %.

6',6'''-Dimethoxy-3',3'''-biflavonyl :- A mixture of 2',2'''-dihydroxy-6,6''-dimethoxy-3,3''-bichalconyl (1 g.), selenium dioxide (6 g.) and dry isoamyl alcohol (30 c.c.) was refluxed in an oil bath at 135-45° for 18 hrs. It was filtered hot and on cooling the biflavonyl derivative separated. It crystallised from nitrobenzene-toluene mixture, in light yellow needles, m.p. 271°. On removal of isoamyl alcohol by steam distillation it gave further quantity of biflavonyl.

Analysis : 4.466 mg. of the substance gave 12.328 mg. of carbon dioxide and 1.694 mg. of water. (It left a residue of 0.052 mg.)

Found : C = 76.2 % ; H = 4.3 %.

$C_{32}H_{22}O_6$ requires : C = 76.5 % ; H = 4.4 %.

The same biflavonyl was prepared by the Ullmann reaction on 2'-methoxy-5'-iodoflavone as follows : A mixture of 2'-methoxy-5'-iodoflavone (2 g.) and copper bronze (3 g.)

was refluxed in diphenyl ether (4^0 c.c.) over a wire gauze for 5 hrs. It was filtered hot and the filtrate was steam distilled to remove the diphenyl ether. The product obtained on repeated crystallisation from nitrobenzene gave light yellow needles of biflavonyl. M.P. and mixed m.p. with the biflavonyl described above was 271°.

2',2'''-Dihydroxy-6,6'',4',4'''-tetramethoxy-3,3''-bichalconyl :- A mixture of 4,4'-dimethoxy-3,3'-diformylbiphenyl (2.7 g. ; 0.01 mole) and 2-hydroxy-4-methoxy acetophenone (6 g. ; 0.04 mole), alcohol (60 c.c.) and potassium hydroxide (15 g. in 15 c.c. water) was refluxed on a steam bath till the mixture became clear (30 minutes). It was kept for 3 days. On working up as before the deep orange coloured chalcone was obtained which crystallised from nitrobenzene in long orange red crystals, m.p. 223°. Yield 3 g.

Analysis : 4.634 mg. of the substance gave 12.298 mg. of carbon dioxide and 2.192 mg. of water.

Found : C = 72.4 % ; H = 5.3 %.

$C_{34}H_{30}O_8$ requires : C = 72.1 % ; H = 5.3 %.

The diacetyl derivative :- of the above bichalconyl was prepared as usual by refluxing the bichalconyl derivative (1 g.) with acetic anhydride (10 c.c.) and fused sodium acetate (3 g.). It crystallised from acetic acid in colourless needles, m.p. 182°.

Analysis : 5.016 mg. of the substance gave 12.854 mg. of carbon dioxide and 2.456 mg. of water.

Found : C = 69.9 % ; H = 5.5 %.

$C_{38}H_{34}O_{10}$ requires : C = 70.2 % ; H = 5.2 %.

2'-Hydroxy-2,4'-dimethoxy-5-iodochalcone :- A mixture of 2-methoxy-5-iodobenzaldehyde (2.7 g. ; 0.01 mole) and 2-hydroxy-4-methoxyacetophenone (3 g. ; 0.02 mole) in alcohol (50 c.c.) and potassium hydroxide (10 g. in 10 c.c. water) was kept over night in a well stoppered flask. On acidification with hydrochloric acid the iodochalcone was obtained which crystallised from alcohol-acetone mixture in bright orange coloured needles, m.p.134°. Yield 3.3 g. It gave an orange colour with conc.sulphuric acid, a deep brown colour with ferric chloride and a positive Wilson test.

Analysis : 4.962 mg. of the substance gave 9.058 mg. of carbon dioxide and 1.562 mg. of water. 13.566 mg. of the same substance gave 7.694 mg. of silver iodide.

Found : C = 49.8 % ; H = 3.5 % ; I = 30.7 %.

$C_{17}H_{15}O_4I$ requires : C = 49.8 % ; H = 3.7 % ; I = 31.0 %.

The acetyl derivative - of the above iodochalcone was prepared as usual gave light yellow crystals from acetic acid, m.p. 142°.

Analysis : 4.734 mg. of the substance gave 8.704 mg. of carbon dioxide and 1.490 mg. of water. 16.228 mg. of the same substance gave 8.538 mg. of silver iodide.

Found : C = 50.2 % ; H = 3.5 % ; I = 28.4 %.
$C_{19}H_{17}O_5I$ requires : C = 50.4 % ; H = 3.8 % ; I = 28.1 %.

2',7-Dimethoxy-5'-iodoflavanone :- A mixture of 2'-hydroxy-2,4'-dimethoxy-5-iodochalcone (1 g.) was refluxed with alcoholic hydrochloric acid over a steam bath for 24 hrs. Alcohol was removed by distillation and the mixture was diluted with water. The precipitated flavanone crystallised from benzene in colourless crystals, m.p. 150°. Mixed m.p. with the isomeric chalcone was depressed by over 10°.

Analysis : 4.912 mg. of the substance gave 8.922 mg. of carbon dioxide and 1.590 mg. of water. 10.732 mg. of the same substance gave 6.072 mg. of silver iodide.

Found : C = 49.6 % ; H = 3.6 % ; I = 30.6 %.
$C_{17}H_{15}O_4I$ requires : C = 49.8 % ; H = 3.7 % ; I = 31.0 %.

2',7-Dimethoxy-5'-iodoflavone :- A mixture of 2'-hydroxy-2,4'-dimethoxy-5-iodochalcone (1 g.), selenium dioxide (3 g.) and isoamyl alcohol (20 c.c.) was refluxed in an oil bath at 140-50° for 10 hrs. It was filtered hot and the filtrate on cooling gave colourless crystals of the flavone. On removing the alcohol from the filtrate by steam distillation a further crop of the flavone was obtained. It crystallised from benzene, m.p. 210°. Yield 0.5 g.

Analysis : 4.612 mg. of the substance gave 8.392 mg. of carbon dioxide and 1.270 mg. of water. 11.988 mg. of the same substance gave 6.930 mg. of silver iodide.

Found : C = 49.7 % ; H = 3.1 % ; I = 31.3 %.

$C_{17}H_{13}O_4I$ requires : C = 50.0 % ; H = 3.2 % ; I = 31.1 %.

6',6''',7,7''-Tetramethoxy-3',3'''-biflavonyl :-

(A) From 2',2'''-dihydroxy-6,6'',4',4'''-tetramethoxy-3,3''-bichalconyl .- The above bichalconyl (1 g.) was mixed with selenium dioxide (6 g.) and isoamyl alcohol (40 c.c.) and refluxed in an oil bath at 140-50° for 16 hrs. It was filtered hot. On cooling, light yellow biflavonyl derivative precipitated out which crystallised from nitrobenzene-xylene mixture, m.p. 317°. On Removal of isoamyl alcohol from the filtrate by steam distillation gave a further crop of the biflavonyl. Yield 0.5 g.

Analysis : 4.884 mg. of the substance gave 12.896 mg. of carbon dioxide and 2.000 mg. of water.

Found : C = 72.1 % ; H = 4.6 %.

$C_{34}H_{26}O_8$ requires : C = 72.6 % ; H = 4.6 %.

(B) By the Ullmann reaction on 2',7-dimethoxy-5'-iodoflavone :- A mixture of 2',7-dimethoxy-5'-iodoflavone (1 g.) and copper bronze (2 g.) was refluxed with diphenyl ether over a wire gauze for 5 hrs. It was filtered hot and the solvent was removed by steam distillation. The product obtained was crystallised from nitrobenzene. M.P. and mixed m.p. with the above biflavonyl was 317°.

2',2'''-Dihydroxy-4,4''-dimethoxy-3,3''-bichalconyl :- To a mixture of 2,2'-dimethoxy-5,5'-diformyl biphenyl (2.7 g.), prepared by the chloromethylation of 2,2'-dimethoxy biphenyl and subsequent Sommel~~k~~et reaction on the resulting 5,5'-dichloromethyl derivative[22] (p.54), 2-hydroxy acetophenone (5 g. ; 0.04 mole) in alcohol (50 c.c.) potassium hydroxide (10 g. ; 10 c.c. water) was added and the mixture heated on a steam bath till a clear solution was obtained. It was kept at room temperature for 10 hours and worked up as before. The bichalconyl derivative obtained crystallised from nitrobenzene in deep yellow needles, m.p. 260°. Yield 3.5 g. It was insoluble in common organic solvents such as ether,alcohol,benzene etc. But it was soluble in alcoholic sodium hydroxide. It gave orange colour with con.sulphuric acid, faint colouration with alcoholic ferric chloride and a positive Wilson test.

Analysis : 4.018 mg. of the substance gave 11.128 mg. of carbon dioxide and 1.942 mg. of water.

Found : C = 75.6 % ; H = 5.4 %.

$C_{32}H_{26}O_6$ requires : C = 75.9 % ; H = 5.1 %.

The diacetyl derivative of the above bichalconyl was prepared as before and crystallised from acetic acid in light yellow crystals, m.p. 95°.

Analysis : 4.358 mg. of the substance gave 11.676 mg. of carbon dioxide and 2.020 mg. of water.

Found : C = 73.1 % ; H = 5.2 %.

$C_{36}H_{30}O_8$ requires : C = 73.2 % ; H = 5.1 %.

<u>2'-Hydroxy-4-methoxy-3-iodochalcone</u> :- To a mixture of 4-methoxy-3-iodo benzaldehyde (2.6 g. ; 0.01 mole) and 2-hydroxy acetophenone (2.7 g. ; 0.02 mole) in alcohol (30 c.c.),potassium hydroxide (10 g. ; 10 c.c. water) was added and the mixture kept overnight. The iodochalcone obtained on working up as usual crystallised from alcohol-acetone mixture in orange red needles, m.p. 169°. Yield 3.5 g. It gave a red colouration with conc.sulphuric acid, a deep brown colour with alcoholic ferric chloride and a positive Wilson test.

<u>Analysis</u> : 4.922 mg. of the substance gave 9.094 mg. of carbon dioxide and 1.514 mg. of water. 15.086 mg. of the same substance gave 9.290 mg. of silver iodide.

Found : C = 50.4 % ; H = 3.4 % ; I = 33.3 %.

$C_{16}H_{13}O_3I$ requires : C = 50.5 % ; H = 3.4 % ; I = 33.4 %.

<u>The acetyl derivative of</u> the above iodochalcone was prepared as usual and crystallised from acetic acid in colourless needles, m.p. 129°.

<u>Analysis</u> : 5.006 mg. of the substance gave 9.428 mg. of carbon dioxide and 1.638 mg. of water. 15.654 mg. of the same substance gave 8.738 mg. of silver iodide.

Found : C = 51.4 % ; H = 3.7 % ; I = 30.2 %.

$C_{18}H_{15}O_4I$ requires : C = 51.2 % ; H = 3.6 % ; I = 30.1 %.

4'-Methoxy-3'-iodoflavanone :- 2'-Hydroxy-4-methoxy-3-iodochalcone (0.5 g.) was refluxed with alcohol(50 c.c.) containing hydrochloric acid (5 c.c.) for 24 hrs. The alcohol was removed by distillation and the precipitated iodoflavanone was crystallised from benzene in colourless needles, m.p. 160°. Mixed m.p. with the isomeric iodochalcone was lowered by over 15°.

Analysis : 4.832 mg. of the substance gave 8.932 mg. of carbon dioxide and 1.392 mg. of water. 12.870 mg. of the same substance gave 7.914 mg.of silver iodide.

Found : C = 50.5 % ; H = 3.4 % ; I = 33.4 %.
$C_{16}H_{13}O_3I$ requires : C = 50.5 % ; H = 3.2 % ; I = 33.2 %.

4'-Methoxy-3'-iodoflavone :- 2'-Hydroxy-4-methoxy-3-iodochalcone (1 g.) was mixed with selenium dioxide (3 g.) and isoamyl alcohol (20 c.c.) and refluxed in an oil bath for 10 hrs. The reaction mixture was filtered hot and the product obtained on cooling crystallised from toluene in light yellow needles, m.p. 192°. Jurd who also prepared the same iodoflavone by the Baker-Venketaraman transformation method has reported the m.p. 193°.

Analysis : 4.652 mg. of the substance gave 8.646 mg. of carbon dioxide and 1.198 mg. of water. 12.092 mg. of the same substance gave 7.506 mg. of silver iodide.

Found : C = 50.7 % ; H = 2.9 % ; I = 33.6 %.
$C_{16}H_{11}O_3I$ requires : C = 50.8 % ; H = 2.9 % ; I = 33.6 %.

4',4'''-Dimethoxy-3',3'''-biflavonyl :

(A) From 2',2'''-dihydroxy-4,4''-dimethoxy-3,3''-bichalconyl: The above bichalconyl (1 g.) was refluxed in isoamyl alcohol (30 c.c.) with selenium dioxide (6 g.) in an oil bath at 140-50° for 16 hrs. It was filtered hot and on cooling light yellow crystals of the biflavonyl derivative separated which were recrystallised from nitrobenzene. On removing the isoamyl alcohol by steam distillation a further crop of the biflavonyl was obtained, m.p. 327°. It was insoluble in common organic solvents such as ether, alcohol, benzene and acetone but soluble in acetic acid.

Analysis : 4.734 mg. of the substance gave 13.214 mg. of carbon dioxide and 2.030 mg. of water.

Found : C = 76.2 % ; H = 4.8 %.

$C_{32}H_{22}O_6$ requires : C = 76.5 % ; H = 4.4 %.

(B) By the Ullmann reaction on 4'-methoxy-3'-iodoflavone :- A mixture of 4'-methoxy-3'-iodoflavone (1 g.) copper bronze(2 g.) and diphenyl ether (25 c.c.) was refluxed on a wire gauze for 4 hrs. The product obtained on working up as before was crystallised from nitrobenzene in light yellow crystals. M.P. and mixed m.p. with the above biflavonyl was 327°.

2',2'''-Dihydroxy-4,4',4'',4'''-tetramethoxy-3,3''-bichalconyl:-

A mixture of 2-hydroxy-4-methoxy acetophenone (6 g. ; 0.04 mole) and 2,2'-dimethoxy-5,5'-diformyl biphenyl(2.6 g.; 0.01 mole) in alcohol (50 c.c.) and potassium hydroxide (10 g. ; 10 c.c. water) was kept overnight in a well stoppered flask and then diluted and acidified. The precipitated bichalconyl derivative crystallised from nitrobenzene in yellow needles, m.p. 257°. Yield 3 g. It was insoluble in common organic solvents such as ether, alsohol,benzene and acetone. It gave a red solution with alcoholic sodium hydroxide but it was insoluble in free alkali. It gave an orange coloured solution with conc. sulphuric acid, a faint colouration with alcoholic ferric chloride and a positive Wilson test.

<u>Analysis</u> : 4.030 mg. of the substance gave 10.604 mg. of carbon dioxide and 2.008 mg. of water.

Found : C = 71.8 % ; H = 5.6 %.

$C_{34}H_{30}O_8$ requires : C = 72.1 % ; H = 5.3 %.

<u>The diacetyl derivative</u> of the above bichalconyl was prepared as usual and crystallised from acetic acid in light yellow needles, m.p. 160°.

<u>Analysis</u> : 4.506 mg. of the substance gave 11.500 mg. of carbon dioxide and 2.202 mg. of water.

Found : C = 69.7 % ; H = 5.5 %.

$C_{38}H_{34}O_{10}$ requires : C = 70.2 % ; H = 5.2 %.

<u>2'-Hydroxy-4,4'-dimethoxy-3-iodochalcone</u> :- This was prepared by keeping overnight a mixture of 2-hydroxy-4-methoxy acetophenone (6 g. ; 0.04 mole), 4-methoxy-3-iodo benzaldehyde (2.6 g. ; 0.01 mole) in alcohol (50 c.c.) and potassium hydroxide (10 g. in 100 c.c. water). The mixture on dilution and acidification gave the iodochalcone which was crystallised from alcohol-acetone mixture in bright

orange coloured needles, m.p. 163°. Yield 3.2 g. It gave red colouration with conc. sulphuric acid, a deep brown colouration with alcoholic ferric chloride and a positive Wilson test.

<u>Analysis</u> : 4.002 mg. of the substance gave 7.282 mg. of carbon dioxide and 1.418 mg. of water. 13.034 mg. of the same substance gave 7.458 mg. of silver iodide.

	Found	: C = 49.7 % ; H = 4.0 % ; I = 30.9 %.
$C_{17}H_{15}O_4I$	requires	: C = 49.7 % ; H = 3.7 % ; I = 31.0 %.

<u>The acetyl derivative</u> of the above iodochalcone was prepared as usual and crystallised from acetic acid in light yellow needles, m.p. 130°.

<u>Analysis</u> : 4.554 mg. of the substance gave 8.454 mg. of carbon dioxide and 1.444 mg. of water. 13.040 mg. of the same substance gave 6.754 mg. of silver iodide.

	Found	: C = 50.7 % ; H = 3.6 % ; I = 28.0 %.
$C_{19}H_{17}O_5I$	requires	: C = 50.4 % ; H = 3.8 % ; I = 28.0 %.

<u>4',7-Dimethoxy-3'-iodoflavanone</u> :- 2'-Hydroxy-4,4'-dimethoxy-3-iodochalcone (1 g.) was refluxed with alcoholic hydrochloric acid (30:5) on a steam bath for 24 hrs. The alcohol was distilled off and the separated flavanone was crystallised from alcohol in pale yellow needles, m.p.143°. Mixed m.p. with the isomeric chalcone was depressed by about 8°.

Analysis : 4.938 mg. of the substance gave 8.986 mg. of carbon dioxide and 1.582 mg. of water. 12.562 mg. of the same substance gave 7.152 mg. of silver iodide.

Found : C = 49.7 % ; H = 3.6 % ; I = 30.8 %.
$C_{17}H_{15}O_4I$ requires : C = 49.8 % ; H = 3.7 % ; I = 31.0 %.

4',7-Dimethoxy-3'-iodoflavone :- 2'-Hydroxy-4,4'-dimethoxy-3'-iodochalcone (1 g.) was refluxed with selenium dioxide (3 g.) in isoamyl alcohol (20 c.c.) in an oil bath at 140-50° for 10 hrs. The reaction mixture was worked up as before and the iodoflavone was crystallised from toluene in light yellow needles, m.p. 217°. Jurd who prepared the same iodoflavone by the Baker-Venketaraman method has reported the m.p. 219°.

Analysis : 4.116 mg. of the substance gave 7.608 mg. of carbon dioxide and 1.346 mg. of water. 14.406 mg. of the same substance gave 8.228 mg. of silver iodide.

Found : C = 50.4 % ; H = 3.7 % ; I = 30.9 %.
$C_{17}H_{13}O_4I$ requires : C = 50.0 % ; H = 3.2 % ; I = 31.1 %.

4',4''',7,7''-Tetramethoxy-3',3'''-biflavonyl :- 2',2'''-Dihydroxy-4,4'',4',4'''-tetramethoxy-3,3''-bichalconyl(1 g.) mixed with selenium dioxide (6 g.) was refluxed in isoamyl alcohol (50 c.c.) in an oil bath at 140-50° for 16 hrs. The product obtained on working up as before was crystallised from nitrobenzene in light yellow crystals, m.p. 305°. It was insoluble in alcohol,ether and acetone but soluble in hot acetic acid and nitrobenzene.

Analysis : 4.642 mg. of the substance gave 12.328 mg. of carbon dioxide and 2.060 mg. of water.

Found : C = 72.5 % ; H = 5.0 %.

$C_{34}H_{26}O_8$ requires : C = 72.6 % ; H = 4.6 %.

By the Ullmann reaction on 4',7-dimethoxy-3'-iodoflavone:- A mixture of 4',7-dimethoxy-3'-iodoflavone (1 g.) and copper bronze (2 g.) was taken in diphenyl ether (25 c.c.) and refluxed on a wire gauze for 4 hrs. The product obtained on working up as before crystallised from nitrobenzene, m.p. and mixed m.p. with the above biflavonyl was 305°.

6',6'''-Dihydroxy-3',3'''-bichalconyl :- To 4,4'-Dihydroxy-3,3'-diacetyl biphenyl (2.7 g. ; 0.01 mole) and potassium hydroxide, benzaldehyde (6.3 g. ; 0.06 mole) and alcohol (60 c.c.) were added followed by more potassium hydroxide (10 g. ; 10 c.c. water). The mixture was kept overnight at room temperature. The dark red solution was diluted with water and extracted with ether. The ether layer was rejected. The aqueous layer was acidified and the precipitated material was crystallised from toluene in red needles, m.p. 203°.

Analysis : 4.884 mg. of the substance gave 14.496 mg. of carbon dioxide and 2.118 mg. of water.

Found : C = 81.0 % ; H = 4.9 %.

$C_{30}H_{22}O_4$ requires : C = 80.7 % ; H = 4.9 %.

The diacetyl derivative of the above bichalconyl was prepared as before and crystallised from acetic acid in colourless needles, m.p. 112°.

Analysis : 4.218 mg. of the substance gave 11.830 mg. of carbon dioxide and 1.794 mg. of water.

Found : C = 76.5 % ; H = 4.8 %.

$C_{34}H_{26}O_6$ requires : C = 77.0 % ; H = 4.9 %.

6,6''-Biflavanonyl :- 6,6'''-Dihydroxy-3,3'''-bichalconyl (1 g.) was refluxed with alcohol (60 c.c.) containing hydrochloric acid (10 c.c.) and refluxed on a steam bath for 30 hrs. The alcohol was distilled off and the separated biflavanonyl derivative was crystallised from benzene in white needles, m.p. 252°.

Analysis : 4.272 mg. of the substance gave 12.700 mg. of carbon dioxide and 1.846 mg. of water.

Found : C = 81.1 % ; H = 4.8 %.

$C_{30}H_{22}O_4$ requires : C = 80.7 % ; H = 4.9 %.

Kostanecki-Robinson benzoylation of 4,4'-dihydroxy-3,3'-diacetylbiphenyl : **3,3''-Dibenzoyl-6,6''-biflavonyl** - A mixture of 4,4'-dihydroxy-3,3'-diacetyl biphenyl (1 g.), sodium benzoate (4 g.) and benzoic anhydride (12 g.) was heated at 210-15° in an oil bath for 10 hrs. It was cooled, washed with sodium bicarbonate and crystallised from nitrobenzene in white needles(1 g.), m.p. 335°. (Found C = 80.4 % ; H = 3.7 % ; $C_{44}H_{26}O_6$ requires C = 80.9 %; H = 4.0 %). When the temperature was kept at 180-90° only the O-benzoyl derivative was formed instead of the flavone.

(A) 6,6''-Biflavonyl - (A) from 6,6'''-dihydroxy-3,3'''-bichalconyl :- 6,6'''-Dihydroxy-3,3'''-bichalconyl (1 g.) was mixed with selenium dioxide (5 g.) and isoamyl alcohol (25 c.c.) and refluxed in an oil bath at 140-50° for 16 hrs. It was filtered hot and on cooling crystals of biflavonyl separated out. It was crystallised from nitrobenzene in light yellow needles, m.p. 305°.

Chen et al.[12] who prepared the same biflavonyl by a different method reported the same m.p.

Analysis : 5.004 mg. of the substance gave 14.866 mg. of carbon dioxide and 1.934 mg. of water.

Found : C = 81.1 % ; H = 4.3 %.

$C_{30}H_{18}O_4$ requires : C = 81.5 % ; H = 4.1 %.

(B) From 3,3''-dibenzoyl-6,6''-biflavonyl :- 3,3''-Dibenzoyl-6,6''-biflavonyl was refluxed with 2 % alcoholic sodium hydroxide over a steam bath for 2 hrs. The residue after filtration, on repeated crystallisation from nitrobenzene gave 6,6''-biflavonyl identical with the one described above.

6,6'''-Dihydroxy-4,4''-dimethoxy-3,3'''-bichalconyl :- 4,4'-Dihydroxy-3,3'-diacetyl biphenyl (2.7 g. ; 0.01 mole) was dissolved in sodium hydroxide and anisaldehyde (8 g.; 0.06 mole) was added. Alcohol was added to the above mixture till the anisaldehyde completely dissolved. Potassium hydroxide (10 g. ; 10 c.c. water) was then added and the mixture kept overnight. The red reaction mixture was diluted with water and extracted with ether. The ether layer was discarded. The aqueous layer was acidified and the precipitated bichalconyl derivative was crystallised from nitrobenzene in red needles, m.p. 226°. It gave the red colouration with conc.sulphuric acid, brown colouration with alcoholic ferric chloride and yellow colouration with Wilson reagent.

<u>Analysis</u> : 4.450 mg. of the substance gave 12.446 mg. of carbon dioxide and 1.964 mg. of water.

Found : C = 76.3 % ; H = 4.9 %.

$C_{32}H_{26}O_6$ requires : C = 75.9 % ; H = 5.1 %.

<u>The diacetyl derivative</u> of the above biflavonyl was prepared as before and crystallised from benzene in colourless needles, m.p. 170°.

<u>Analysis</u> : 4.664 mg. of the substance gave 12.454 mg. of carbon dioxide and 2.039 mg. of water.

Found : C = 72.9 % ; H = 4.9 %.

$C_{36}H_{30}O_8$ requires : C = 73.2 % ; H = 5.1 %.

<u>4',4'''-Dimethoxy-6,6''-biflavanonyl</u> :- 6',6'''-Dihydroxy-4,4''-dimethoxy-3',3'''-bichalconyl (1 g.) was refluxed with alcoholic hydrochloric acid on a steam bath for 30 hrs. The product obtained was recrystallised from benzene in colourless needles, m.p. 250°.

<u>Analysis</u> : 4.536 mg. of the substance gave 12.664 mg. of carbon dioxide and 2.096 mg. of water.

Found : C = 76.2 % ; H = 5.2 %.

$C_{32}H_{26}O_6$ requires : C = 75.9 % ; H = 5.1 %.

4',4'''-Dimethoxy-6,6''-biflavonyl :- A mixture of 6',6'''-dihydroxy-4,4''-dimethoxy-3',3'''-bichalconyl (1 g.) selenium dioxide (5 g.) and isoamyl alcohol (30 c.c.) was refluxed on an oil bath at 140-50° for 16 hrs. The product obtained crystallised from nitrobenzene in light yellow needles, m.p. 318°. Chen et al.[12] who prepared it by a different method have given the m.p. 315-20°.

Analysis : 4.692 mg. of the substance gave 12.954 mg. of carbon dioxide and 2.064 mg. of water.

Found : C = 75.4 % ; H = 4.9 %.

$C_{32}H_{22}O_6$ requires : C = 76.5 % ; H = 4.4 % .