

Synthesis of some 3', 3'', 4', 4''-and 6, 6''-biflavonyls

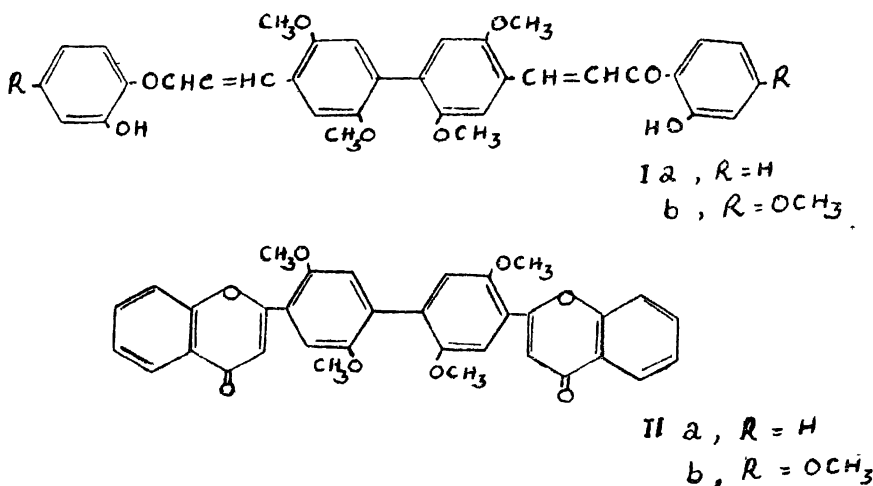
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The previous work¹ on the synthesis of biflavonyls has now been extended and several new biflavonyls have been synthesised.

2,2',6,6'-Tetramethoxy-3,3'-diformylbiphenyl² on condensation with 2-hydroxy-4-methoxy acetophenone gave 2',2''-dihydroxy-2,2',4,4',4''-hexamethoxy-3,3''-bichalconyl. It formed a diacetoxy derivative and gave the colour reactions of a chalcone. It was converted into 2',2'',4',4'',7,7''-hexamethoxy-3',3''-biflavonyl by refluxing with selenium dioxide in iso-amyl alcohol.

2',2''-Dihydroxy-4,4',4'',6,6''-hexamethoxy-3,3''-bichalconyl obtained from 2,2',4,4'-tetramethoxy-5,5'-diformylbiphenyl² and 2-hydroxy-4-methoxyacetophenone however did not give the expected biflavonyl on refluxing a suspension of the bichalconyl in iso-amyl alcohol in the presence of selenium dioxide. The original bichalconyl was obtained back.

2,2',5,5'-Tetramethoxy-4,4'-diformylbiphenyl² on condensation with 2-hydroxy acetophenone afforded the 2',2''-dihydroxy-2',2'',5,5''-tetramethoxy-4,4''-bichalconyl (Ia) which on cyclisation with selenium dioxide gave 2',2'',5',5''-tetramethoxy-4',4''-biflavonyl (IIa).



1. K. P. Mathai, Kanakalakshmi and S. Sethna, *This Journal* 1967, **44**, 148.

2. B. Kanakalakshmi, K. P. Mathai and S. Sethna, *This Journal*, 1966, **43**, 469.

Similarly 2',2''-dihydroxy-2,2'',4',4'',5,5''-hexamethoxy-4, 4''-bichalconyl (Ib) was obtained when 2,2',5,5'-tetramethoxy-4,4'-diformylbiphenyl³ was condensed with 2-hydroxy-4-methoxy acetophenone. The bichalconyl on cyclisation with selenium dioxide afforded the 2',2'',5,5'',7,7''-hexamethoxy-4',4''-biflavonyl (IIb).

4,4'-Dibenzoyloxy-3,3'-diacetylbiophenyl when subjected to Baker-Venkataraman rearrangement as modified by Looker *et al.*³ gave 4,4'-dihydroxy-3,3'-di(ω -benzoylacetyl) biphenyl which on cyclisation with con. H₂SO₄ furnished the 6,6''-biflavonyl as seen by direct comparison with the product obtained by Mathai and Sethna⁴ by other methods.

EXPERIMENTAL*

2',2''-Dihydroxy-2,2'',4',4'',5,5''-hexamethoxy-3,3''-bichalconyl : A mixture of 2,2',6,6'-tetramethoxy-3,3'-diformylbiphenyl (3.3 g.; 0.01 M) in alcohol, 2-hydroxy-4-methoxyacetophenone (6 g.; 0.04 M) and KOH (10 g. in 10 ml. water) was refluxed on a steam bath till the mixture became clear. It was kept overnight. The product obtained on acidification crystallised from benzene in orange needles, yield 75%, m.p. 215° (Found : C, 69.2; H, 5.6. C₃₆H₃₄O₁₀ Calc. for C, 69.0; H, 5.3%)

The diacetyl derivative : Prepared by refluxing the above bichalconyl derivative (1 g.) with acetic anhydride (10 ml.) and fused sodium acetate (3 g.). It crystallised from benzene in yellow plates, m.p. 165–66° (Found : C, 67.1; H, 5.3. C₄₀H₃₈O₁₂ Calc. for C, 67.4; H, 5.6%).

2',2'',4',4'',7,7''-Hexamethoxy-3',3''-biflavonyl : The bichalconyl (1 g.) was mixed with selenium dioxide (4 g.) and iso-amyl alcohol (40 ml.) and refluxed in an oil bath at 140–50° for 17 hr. It was filtered hot and the product precipitated out crystallised from xylene in pale yellow cubes, m.p. 255°. (Found : C, 69.5; H, 4.6. C₃₆H₃₀O₁₀ Calc. for C, 69.5; H, 4.8%).

2',2''-Dihydroxy-4,4',4'',6,6''-hexamethoxy-3,3''-bichalconyl : 2,2',4,4'-Tetramethoxy-5,5'-diformylbiphenyl (3.3 g.; 0.01 M) in alcohol was mixed with 2-hydroxy-4-methoxyacetophenone (6 g.; 0.04 M) and KOH (10 g. in 10 ml. water) and refluxed on a steam bath till the mixture became clear. It was kept overnight and the product obtained on acidification crystallised from nitrobenzene m.p. 320°, yield 71%. (Found : C, 68.7; H, 5.4, C₃₆H₃₄O₁₀ Calc. for C, 69.0; H, 5.4%).

The diacetyl derivative : Prepared as before and crystallised from benzene-petroleum ether in pale yellow needles, gave m.p. 191°. (Found : C, 67.1; H, 5.3. C₄₀H₃₈O₁₂ Calc. for C, 67.4; H, 5.6%).

2',2''-Dihydroxy-2,2',5,5''-tetramethoxy-4,4''-bichalconyl : 2,2',5,5'-Tetramethoxy-4,4'-diformylbiphenyl (3.3 g.; 0.01 M) in alcohol was mixed with *o*-hydroxyacetophenone (5.5 g.;

3. J. H. Looker, J. R. Edman and J. I. Dappen, *J. Heterocyclic Chem.*, 1964, 1, 141.

4. K. P. Mathai and S. Sethna, *This Journal*, 1964, 41, 347.

* All melting points are uncorrected.

0.04 *M*) and KOH (10 g. in 10 ml. water) and kept overnight. The product obtained on working up as usual crystallised from nitrobenzene in orange needles, m.p. 267°. Yield 65%. (Found : C, 72.0; H, 5.2. $C_{34}H_{30}O_8$ Calc. for C, 72.1; H, 5.3%).

The diacetyl derivative : Prepared as usual and crystallised from benzene-petroleum ether in yellow needles, m.p. 143°. (Found : C, 69.9; H, 5.4. $C_{38}H_{34}O_{10}$ Calc. for C, 70.1; H, 5.4%).

2',2''',5',5'''-Tetramethoxy-4',4'''-biflavonyl : The bichalconyl (1 g.) mixed with selenium dioxide (4 g.) was refluxed in iso-amyl alcohol in an oil bath at 140–50° for 16 hr. The product obtained on working up as usual crystallised from diphenyl ether, m.p. 288°. (Found : C, 73.0; H, 4.4. $C_{34}H_{26}O_8$ Calc. for C, 72.6; H, 4.6%).

2',2''',5',5'''-Hexamethoxy-4',4'''-bichalconyl : A solution of 2,2',5,5'-tetramethoxy-4,4'-diformyl biphenyl (3.3 g.; 0.01 *M*) and 2-hydroxy-4-methoxyacetophenone (6 g.; 0.04 *M*) in alcohol and KOH (10 g.; in 10 ml. water) was heated on a steam bath till the solution became clear. The reaction mixture was kept overnight and the product obtained on acidification crystallised from xylene in orange needles, m.p. 235°, yield 60%. (Found : C, 69.0; H, 5.5. $C_{36}H_{34}O_{10}$ Calc. for C, 69.0; H, 5.4%).

The diacetyl derivative : Prepared by refluxing the above bichalconyl derivative with acetic anhydride and sodium acetate for 1 hr. and crystallised from benzene-petroleum ether in pale yellow plates gave m.p. 150°. (Found : C, 67.5; H, 5.8. $C_{40}H_{38}O_{12}$ Calc. for C, 67.4; H, 5.6%).

2',2''',5',5''',7,7''-Hexamethoxy-4',4'''-biflavonyl : A mixture of the above bichalconyl derivative (1 g.), selenium dioxide (4 g.) and iso-amyl alcohol (40 ml.) was refluxed in an oil bath at 140–50° for 18 hr. It was filtered hot and the biflavonyl derivative which separated on cooling crystallised from xylene, m.p. 291°. (Found : C, 69.7; H, 5.1. $C_{36}H_{30}O_{10}$ Calc. for C, 69.5; H, 4.8%).

4,4'-Dibenzoyloxy-3,3'-diacetyl biphenyl : 4,4'-Dihydroxy-3,3'-diacetyl biphenyl (1 g.) was dissolved in acetone and benzoyl chloride (3 ml.) and anhydrous potassium carbonate (8 g.) was added. The reaction mixture was refluxed on a steam bath for 8 hr. and the product obtained on pouring into water crystallised from acetic acid, m.p. 175°. (Found : C, 75.6; H, 4.6. $C_{30}H_{22}O_6$ Calc. for C, 75.3; H, 4.6%).

4,4'-Dihydroxy-3,3'-di(ω-benzoylacetyl) biphenyl : The above dibenzoyloxy derivative (0.5 g.) was dissolved in minimum quantity of pyridine and powdered KOH (3 g.) was added with stirring. The reaction mixture, after keeping for 4 hr. at room temperature was poured in ice cold HCl. The product obtained crystallised from xylene, m.p. 253°. It was soluble in alkali and gave colouration with ferric chloride. (Found : C, 75.7; H, 4.4. $C_{30}H_{22}O_6$ Calc. for C, 75.3; H, 4.6%).

6,6''-Biflavonyl : The above β-diketone (0.5 g.) was mixed with con. H_2SO_4 (5 ml.) and kept at room temperature for 4 hr. The product obtained on pouring the reaction mixture in ice cold water crystallised from glacial acetic acid, m.p. 312°.

Mathai and Sethna⁴ prepared the same compound by other methods. Mixed m.p. with their sample was not depressed.

The cyclisation was also carried out by refluxing the β -diketone (0.5 g.) with glacial acetic acid (10 ml.) for 8 hr. The product obtained on cooling crystallised from acetic acid.

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