

SYNTHESIS OF (\pm)-HEPTA-O-METHYLFUKUGETIN AND HEPTA-O-METHYLSAHARANFLAVONE

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Previously¹⁻³⁾ we reported the structures of biflavanoid pigments, (\pm)-fukugetin (I), (+)-fukugetin (II), (\pm)-3'-O-methylfukugetin (III) and fukugiside (IV) isolated from the fresh bark of Garcinia spicata Hook. f. (Guttiferae). The study of these compounds including the assignment of the coupling positions of ring I-C and ring II-A⁴⁾ of the biflavanoids was made at that time by chemical and spectroscopic data. In the present study, the synthesis of (\pm)-hepta-O-methylfukugetin (V) and hepta-O-methylsaharanflavone (VI)⁵⁾ has been attempted to establish the structures of these compounds (I - IV).

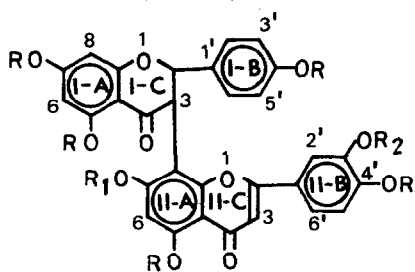
Chloromethylation of luteolin tetramethylether (VII)⁶⁾ with paraformaldehyde and hydrogen chloride⁷⁾ gave a 8-chloromethyl compound (VIII), m.p. 228^o, n.m.r. (60 Mc. in CDCl₃) τ 5.05 (2H, s., -CH₂-Cl), in a 70% yield. Catalytic reduction of VIII over palladium-carbon in acetic acid gave a C-methyl compound (IX), m.p. 237-238^o, n.m.r. τ 7.70 (3H, s., -CH₃), which was found to be identical with 8-methyl-5,7,3',4'-tetramethoxyflavone synthesized according to the procedure of Seshadri et al.⁸⁾ VIII was treated with KCN in benzene to give a cyanide (X), m.p. 238^o, m/e 381 (M⁺), n.m.r. τ 6.08 (2H, s., -CH₂-CN). Hydrolysis of X with sulfuric acid - acetic acid - water (2:2:1) gave an acid (XI), which was converted into the acid chloride (XII). Esterification of the acid chloride (XII) with phloroglucinol dimethyl ether gave XIII, m.p. 201-202^o, n.m.r. τ 5.86 (2H, s., -CH₂-CO), τ 5.98 - 6.34 (six methoxyl groups), which underwent the Fries rearrangement in the presence of titanium tetrachloride in nitrobenzene^{9,10)} at room temperature to give the required ketoflavone (XIV), m.p. 235-236^o, m/e 536 (M⁺), n.m.r. τ 5.98 - 6.40 (six methoxyl groups), τ 5.41 (2H, s., -CH₂-CO-), τ 2.56 - 4.05 (six aromatic and one olefinic protons),

τ -3.71 (1H, s., -OH), in a 50% yield. Anisoylation of XIV gave a compound (XV), m.p. 135-136°. Condensation of XI with phloroglucinol dimethyl ether in the presence of polyphosphoric acid also gave the same compound (XIV), in a low yield. The treatment of XIV with dimethyl sulfate gave a methyl ether (XVI), m.p. 218-219°, m/e 550 (M^+), which was identical with a ketone prepared by the condensation of XI with phloroglucinol trimethyl ether in the presence of polyphosphoric acid. The synthetic compound (XIV) was identical in all respects (m.p., mixed m.p., i.r., n.m.r., mass spectra and t.l.c.) with the ketoflavone obtained by the alkaline hydrolysis¹⁾ of (\pm)-hepta-O-methylfukugetin.

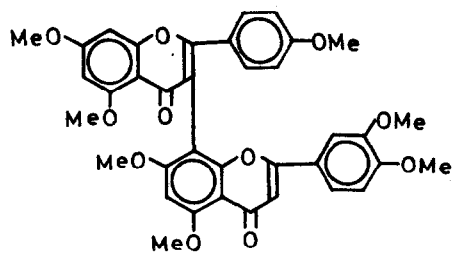
The ketoflavone (XIV) was condensed with anisaldehyde in the presence of 50% potassium hydroxide in pyridine to give a chalcone (XVII), m.p. 134-136°, in a 30% yield. Acetylation of XVII with acetic anhydride and pyridine gave a monoacetate (XVIII), m.p. 219-220°. The synthetic chalcone (XVII) and its acetate (XVIII) were identical in all respects (m.p., mixed m.p., i.r., n.m.r., t.l.c.) with the samples derived from (\pm)-hepta-O-methylfukugetin¹⁾. Finally, XVII was cyclized in a boiling 2.5% methanolic sulfuric acid to give a biflavonyl (V), m.p. 213-214°, m/e 654 (M^+). This compound (V) was proved to be completely identical with (\pm)-hepta-O-methylfukugetin in terms of their m.p., mixed m.p., i.r., n.m.r., mass spectra and t.l.c. comparisons. Thus, it has been definitely established that the coupling positions of ring I-C and ring II-A of the flavanone-flavone compounds isolated from Garcinia spicata are C-3 and C-8, respectively.

Cyclization of XIV with anisic anhydride and sodium anisate afforded the required biflavonyl (VI) (Allan-Robinson method),^{11,12)} m.p. 152°, in a 30% yield, which was also obtained by the oxidation of V with iodine-potassium acetate in acetic acid in a 80% yield. The synthetic biflavonyl (VI) was identified as hepta-O-methylsaharanflavone by comparative analyses (m.p., mixed m.p., i.r., n.m.r., t.l.c.) with a standard sample prepared from (\pm)-fukugetin according to the procedure of Pelter et al.⁵⁾.

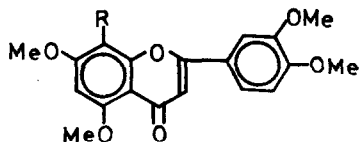
Studies on the total synthesis of (\pm)-fukugetin are in progress. Satisfactory analytical and spectroscopic data were obtained for all new compounds.



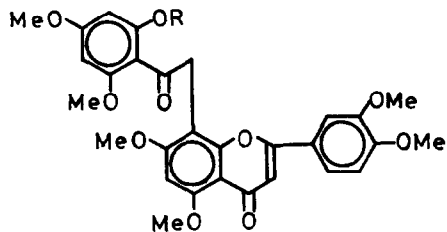
- I, II : R = R₁ = R₂ = H
 III : R = R₁ = H, R₂ = Me
 IV : R = H, R₁ = β-D-gluc, R₂ = H
 V : R = R₁ = R₂ = Me



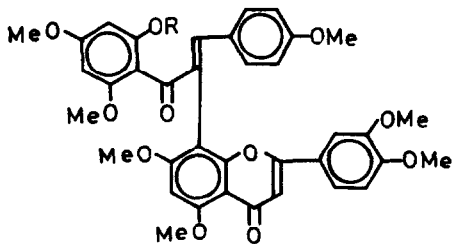
VI



- VII : R = H
 VIII : R = CH₂Cl
 IX : R = CH₃
 X : R = CH₂CN
 XI : R = CH₂COOH
 XII : R = CH₂COC1
 XIII : R = CH₂COO-C₆H₃(OMe)₂



- XIV : R = H
 XV : R = CO-C₆H₄(OMe)
 XVI : R = Me



- XVII : R = H
 XVIII : R = Ac

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