

SYNTHESIS OF SOME FLAVONE COMPONENTS OF THE
EUPHORBIACEAE.

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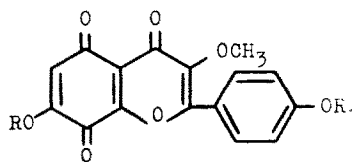
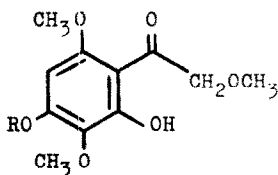
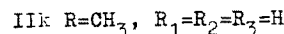
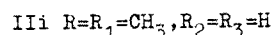
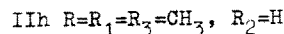
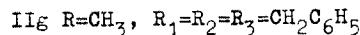
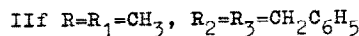
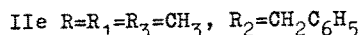
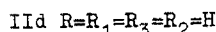
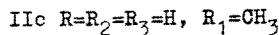
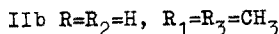
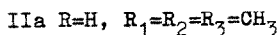
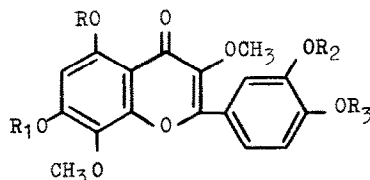
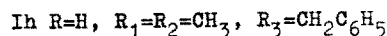
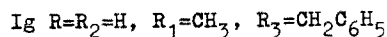
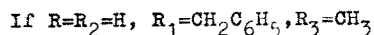
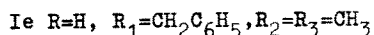
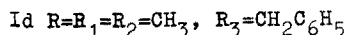
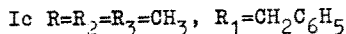
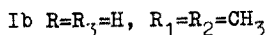
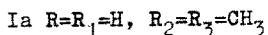
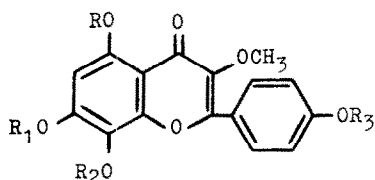
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Occurrence of six closely related flavones in the Euphorbiaceae family has been reported recently in a series of papers by Henrick, Jefferies et. al. 5,7-Dihydroxy-3,4',8-trimethoxyflavone (Ia) was isolated from Beyeria spp.¹, 4',5-dihydroxy-3,7,8-trimethoxyflavone (Ib), 5-hydroxy-3,3',4',7,8-pentamethoxyflavone (IIa) and 3',5-dihydroxy-3,4',7,8-tetramethoxyflavone (IIb) from Ricinocarpus stylosus², finally 3',4',5-trihydroxy-3,7,8-trimethoxyflavone (IIc) and 3',4',5,7-tetrahydroxy-3,8-dimethoxyflavone (IId) from Ricinocarpus muricatus³. This communication deals with the synthesis of these flavones. No synthesis of Ib, IIb, IIc and IId has been reported; the synthesis of Ia⁴ and IIa⁵ preceded their isolation from natural sources.

The common type of key-intermediate for the syntheses were the fully alkylated flavones (Ic, Id, IIe, III, II_G), readily accessible by fusion of 2-hydroxy-4-benzyl-oxy-3,6, ω -trimethoxyacetophenone (IIIa)⁶ or 2-hydroxy-3,4,6, ω -tetramethoxy-acetophenone (IIIb)⁷ with the appropriate acid anhydride and the sodium salt of the same acid (Allan-Robinson method). Elimination of the 5-methyl group was accomplished by oxidation or treatment with AlCl₃.

According to this scheme Ic (m.p. 178-130^o, prepared from III a and anisic anhydride) was treated with one molar equivalent of AlCl₃ in boiling acetonitrile to yield 5-hydroxy-

7-benzyloxy-3',4'-8-trimethoxyflavone (Ie, m.p. 172-173°, lit.⁴ 170-171°). Catalytic debenzylation gave 5,7-dihydroxy-3,4',8-trimethoxyflavone (Ia, m.p. 174-175.5°, lit.¹ 173-175°). An alternative approach to Ia was the oxydation of Ic with nitric acid to the quinoflavone IVa (m.p. 201-204°) and subsequent reduction with Na₂S₂O₄ to the corresponding hydroquinone If (m.p. 187-188.5°, lit.⁴ 186-187°), that was partially methylated to Ie.



IIIa $R=CH_2C_6H_5$ IVa $R=CH_2C_6H_5$, $R_1=CH_3$ IIIb $R=CH_3$ IVb $R=CH_3$, $R_1=CH_2C_6H_5$

Similarly oxidation of Id (m.p. 146-148^o, prepared from IIIb and 4-benzoyloxybenzoic anhydride) to the quinoflavone IVb (m.p. 220-222^o), reduction to the hydroquinone Ig (m.p. 209-210^o) partial methylation to Ih (m.p. 178-179^o) and finally debenylation gave rise to 4',5-dihydroxy-3,7,8-trimethoxyflavone (Ib, m.p. 266-267^o, lit.² 266-268^o. Diacetate: m.p. 183-184^o, lit.² 183-185^o).

Though nitric acid oxidation could be extended also on the 3',4'-disubstituted flavones IIe, II f and II g, low yields made this route impractical. Consequently these were debenzylated to the corresponding hydroxyflavones IIh, IIIi and IIk, and the synthesis completed by partial demethylation with $AlCl_3$ in boiling acetonitrile. It was observed, that demethylation of the 5-methoxy group was always accompanied with that in the 3-position. In accordance with previous findings⁴, no simultaneous demethylation of both functions has been experienced.

Accordingly IIe (m.p. 166-168^o, prepared from IIIb and benzylisovanillic anhydride) was debenzylated to IIh (m.p. 221-223^o), II f (m.p. 132-133^o, prepared from IIIb and dibenzyl-protocatechuic anhydride) to IIIi (m.p. 245-247^o) and II g (m.p. 150-151^o, prepared from IIIa and dibenzyl-protocatechuic anhydride) to IIk (m.p. 268-270^o).

Partial demethylation of IIh with two molar equivalents of $AlCl_3$ in boiling acetonitrile for 2 hr. afforded 3',5-dihydroxy-3,4',7,8-tetramethoxyflavone (IIb) of m.p. 185-186^o and 193^o/lit.² 184-185^o and 192-193^o. Diacetate: m.p. 180-182, lit.² 179-180^o).

A similar treatment of IIIi gave 3'4'5-trihydroxy-3,7,8-trimethoxyflavone (IIc) of m.p. 248-250^o) lit.³ 249-240^o. Triacetate: m.p. 183-184^o, lit.³ 184-185^o).

Demethylation of IIk with three molar equivalents of

AlCl_3 in boiling acetonitrile for 4 hr. yielded 3',4',5,7-tetrahydroxy-3,8-dimethoxyflavone (II_d) of m.p. $300-301^\circ$ dec.), (lit.³ $301-303^\circ$.)

Tetraacetate: m.p. $158-160^\circ$ (prisms from aqueous AcOH) and $150-151^\circ$ needles from MeOH), (lit.³ $149-150^\circ$ (MeOH)).

II_a can be prepared by partial methylation of any of the flavones II_b, II_c or II_d. Actually II_b was treated with one molar equivalent of $(\text{CH}_3)_2\text{SO}_4$ (K_2CO_3 , acetone) to yield 5-hydroxy-3,3',4'-7,8-pentamethoxyflavone of m.p. $161-162^\circ$ of m.p. $161-162^\circ$ (lit.² $161-162^\circ$).

References

1. R.M. Dawson C.A. Henrick, P.R. Jefferies and E.J. Middleton, Aust. J. Chem. 18, 1871 (1965).
2. C.A. Henrick and P.R. Jefferies, Aust. J. Chem. 17
934/1964
3. C.A. Henrick and P.R. Jefferies, Tetrahedron, 21,
3219/1965
4. S.C. Bhrara, A.C. Jain and T.R. Seshadri, Indian J. Chem.
3, 68 (1965).
5. R.M. Horowitz and B. Gentili, J. Org. Chem. 26, 2899 (1961)
6. V.D.N. Sastri and T.R. Seshadri, Proc. Indian Acad. Sci.
24A 238 (1946).
7. V.V.S. Murti, L.R. Row and T.R. Seshadri, Proc. Indian Acad. Sci. 24A, 233 (1946).