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SYNTHESIS OF HEXAMETHYL ETHERS OF AGATHISFLAVONE AND CUPRESSUFLAVONE

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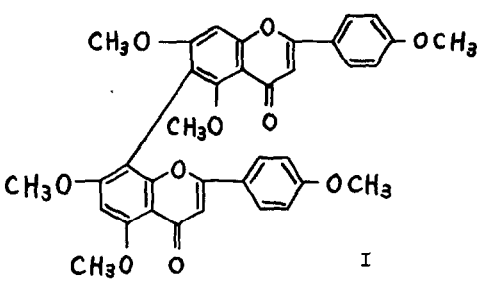
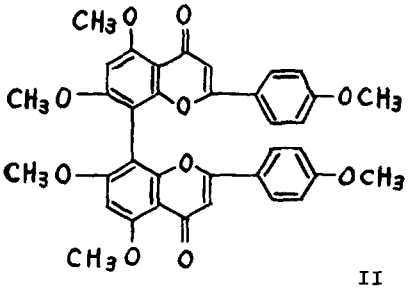
Agathisflavone hexamethyl ether (I) has been synthetically obtained only by Wessely-Moser rearrangement of cupressuflavone hexamethyl ether (II) with hydrogen iodide followed by methylation.[1] We now report a complete synthesis of this compound (I) starting from an asymmetrically substituted biphenyl derivative (V). A new synthesis of cupressuflavone hexamethyl ether (II)[2,3,4] is also reported[5] in this paper using a symmetrical compound (IV).



I



II

Friedel-Crafts reaction of 2,2',4,4',6,6'-hexamethoxybiphenyl (III) with acetic anhydride and $AlCl_3$ in nitrobenzene gave 2,2'-dihydroxy-3,3'-diacetyl-4,4' 6,6'-tetramethoxybiphenyl (IV) in 20 % yield. However, a similar reaction of III with acetyl chloride and $AlCl_3$ in diethyl ether solution gave three compounds, IV, V, and VI in 15, 23, and 16 % yield respectively after separation of the reaction products by silica gel column chromatography. The structures of these compounds were supported by NMR (Table 1) and mass spectral data.

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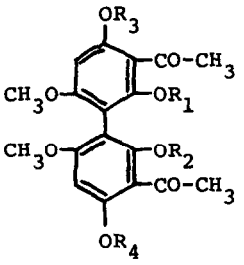
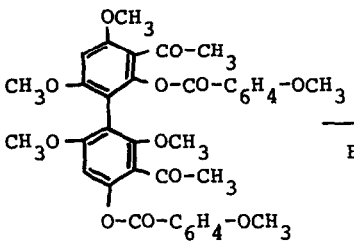


IV $R_1=R_2=H$, $R_3=R_4=CH_3$ mp 254-257°

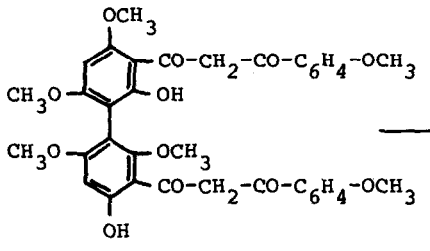
V $R_1=R_4=H$, $R_2=R_3=CH_3$ mp 185-186°

VI $R_1=H$, $R_2=R_3=R_4=CH_3$ mp 213-215°



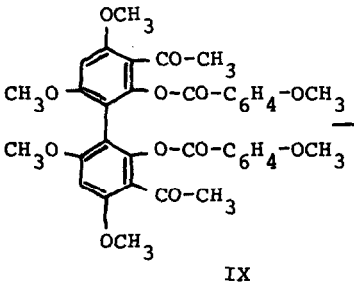
VII

B.V.R.



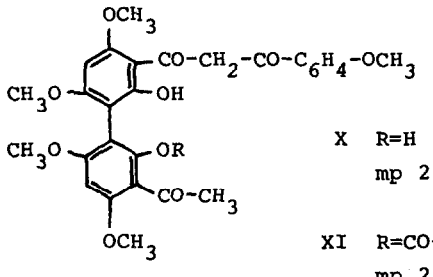
VIII

I



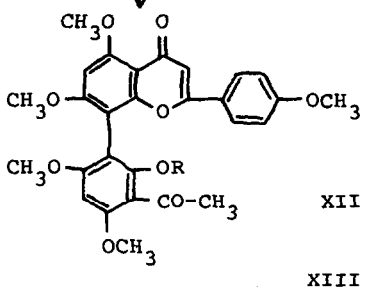
IX

B.V.R.



X R=H mp 260-264°

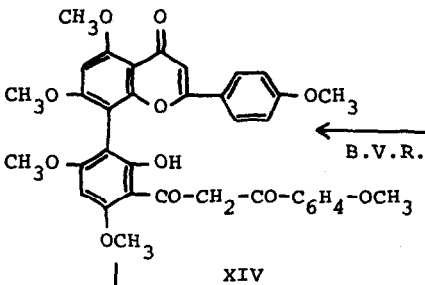
XI $R=CO-C_6H_4-OCH_3$ mp 212-215°



XII R=H mp 230-232°

XIII $R=CO-C_6H_4-OCH_3$ mp 160-165°

B.V.R.



XIV

II

Table 1. NMR Data (ppm) of Biphenyl Derivatives.

Compounds	IV	V	VI
OAc	2.62 (6H)	2.67 (6H)	2.52, 2.65
OMe	3.80 (6H) 3.93 (6H)	3.48, 3.73, 3.83, 3.96	3.48, 3.76, 3.81, 3.86, 3.96
Aromatic H	6.06 (2H)	6.10, 6.28	6.07, 6.36
OH	13.94 (2H)	13.55, 13.95	13.98

All signals are singlet and taken in $CDCl_3$ solution.

The compound V, on treatment with p-anisoyl chloride in pyridine gave an anisoyl compound (VII), mp 174-177°, which yielded a β-diketone (VIII), mp 108-112° by Baker-Venkataraman rearrangement.[6] Agathisflavone hexamethyl ether (I), mp 262-265° was obtained by ring closure of VIII and the UV, IR and NMR spectra were all identical with those of an authentic sample (I) obtained by methylation of natural products.

Similarly, the following method provided a new synthetic route of II. The Baker-Venkataraman rearrangement of an anisoyl compound (IX), mp 263-265° derived from IV afforded two compounds, X and XI in 25 and 5 % yield respectively along with 42 % recovery of starting material (IX). The structures of X and XI were confirmed by NMR and mass spectral data. This finding is much different from the former rearrangement of VII to VIII. It seems that the hydroxy group of XI will prevent the further rearrangement in the same molecule. XIII was obtained by ring closure of XI or by acylation of XII derived from X. The Baker-Venkataraman rearrangement of XIII was performed to give a compound XIV, mp 255-257°, which gave II, mp 293-294° on formation of the second flavone ring and it was identified with an authentic sample (II) by mixed mp determination and by comparisons of spectral data.

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