Tetrahedron Letters No. 48, pp 4633 - 4636, 1971. Pergamon Press. Printed in Great Britain.

A NEW APPROACH TO THE SYNTHESIS OF SYMMETRICAL BIFLAVONES

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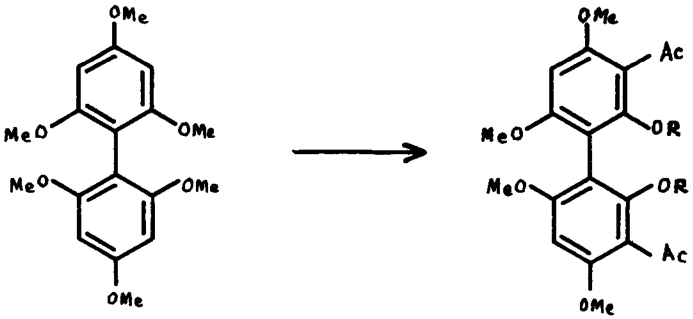
(Received in UK 20 October 1971; accepted for publication 27 October 1971)

Synthesis of cupressuflavone hexamethylether (IV R = Me) and cupressuflavone tetramethylether (IV R = H) have been reported $^{1-3}$ via 8-iodo, 5,7,4'-trimethoxyflavone. We now report the synthesis of these compounds by a new route.

Our key intermediate in this synthesis is 2,2'-dihydroxy 4,4', 6,6' tetramethoxy -3,3' diacetyl-biphenyl (II R = H). It was synthesised as follows:-

2,4,6-trimethoxy iodobenzene under Ullman conditions gave the symmetrical biphenyl (I) m.p. 158-59°, the NMR of which showed the presence of six OMe groups (τ 6.13,6.05) and four aromatic protons (τ 3.63).

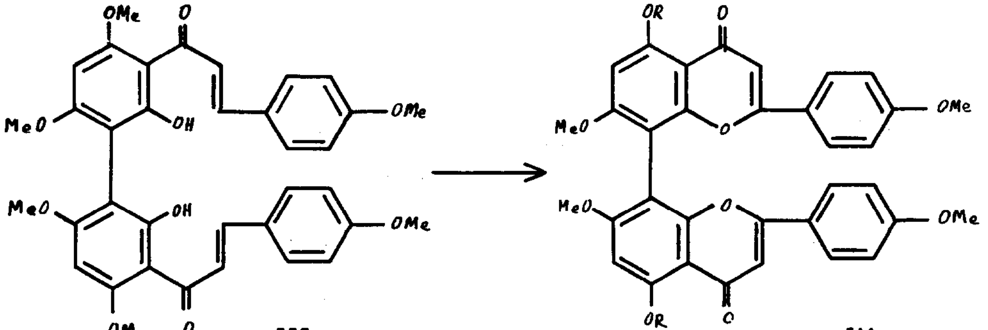


I

II

Friedal -Craft reaction on (I) with acetyl chloride and AlCl$_3$ in nitrobenzene under carefully controlled conditions gave (II R = Me), m.p. 161-63°. This structure is supported by its NMR and IR spectra. IR showed main peaks at 1695 cm^{-1} (arylketones) and 1600 cm^{-1} (aromatic). The signals associated with OMe protons occured at τ 6.15 (6H)$_s$, OMe at 4,4' , τ 6.28 (6H)$_s$, OMe at 6,6' and τ 6.6 (6H)$_s$, OMe at 2,2' . The up-field shift of OMe at 2,2' is characteristic of such biphenyls.^{4,5} Similar shielding phenomenon have been described for methyl, methoxyl and carbomethoxyl groups in "hindered" positions of various biphenyls.[6-8] It is used as a diagnostic tool for the positioning of methoxyl groups in various natural products.[9] The acetyl and aromatic protons of this compound resonated at τ 7.50 $(6H)_s$ and τ 3.73 $(2H)_s$ respectively. This structure is further supported by comparison of the compound obtained by Ullman coupling of 5-iodo, 2,4,6- trimethoxy acetophenone. Both compounds were identical in all respects (TLC, IR, NMR).

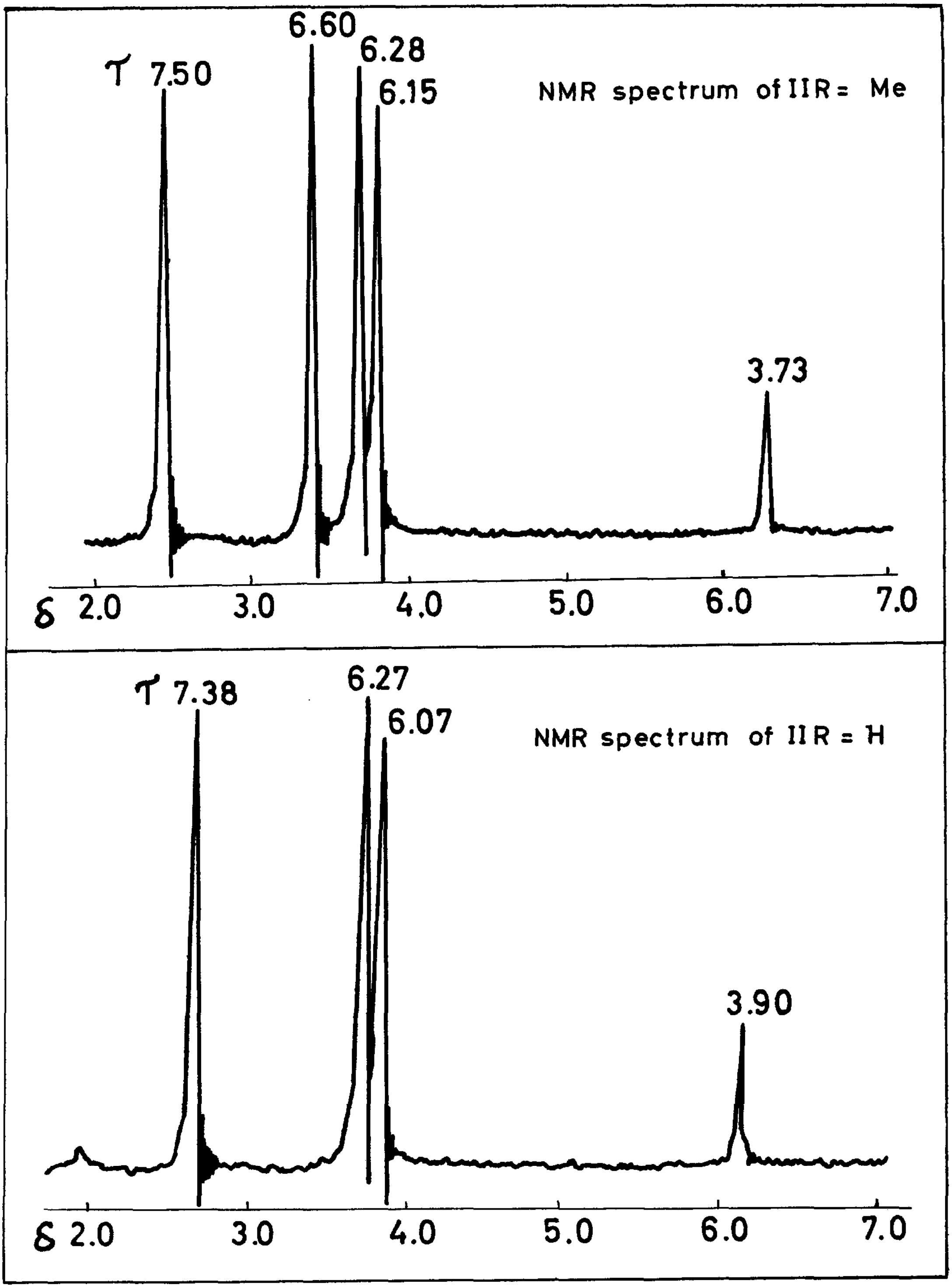
Treatment of (II R = Me) with BCl_3 at 0° gave a colourless crystalline product which showed three spots on TLC (silica). Repeated chromatography of the mixture on silica followed by fractional crystallization gave (II R = H), m.p. 262 in 25% yield. It gave +ve ferric test in alcohol. NMR spectrum of this compound showed signals at τ 6.07 $(6H)_s$ and τ 6.20 $(6H)_s$ which clearly indicated the presence of OMe groups at 4,4' and 6,6'. Two phenolic protons were detected by the peak at τ -4.0 $(2H)_s$, which readily exchanged with D_2O. This confirmed that demethylation had occured at 2,2'.



III

IV

Reaction of (II R = H) with 2 Moles of anisaldehyde in presence of alkali gave yellow needles of the bichalcone (III) m.p. 282-85°. Its NMR in DMSO indicated 4 vinylic protons at τ 2.35. AB doublet for the four -p-methoxyphenyl protons were centered at τ 2.72 (J = 8 cps). Oxidative cyclization of the bichalcone (III) with SeO_2 followed by column chromatography on silica gave (IV R = Me) m.p. 294-5°, identical (TLC, IR, NMR) with 5,5",7,7",4',4"'-hexa-O-methylcupressuflavone prepared by Ullman coupling of 8-iodo, 5,7,4'-trimethoxyflavone.[1]


τ 7.50
6.60
6.28
6.15
NMR spectrum of II R = Me
3.73
δ 2.0
3.0
4.0
5.0
6.0
7.0
τ 7.38
6.27
6.07
NMR spectrum of II R = H
3.90
δ 2.0
3.0
4.0
5.0
6.0
7.0

Demethylation of (IV R = Me) with BCl_3 at 0 gave (IV R = H) indistinguishable (TLC, IR, NMR) from 7,7",4',4"'-tetra-O-methylcupressuflavone synthesised by the known method[1].

All compounds gave satisfactory analyses.

Acknowledgement:

The authors wish to thank Dr. J.W. Hooper of Bristol Laboratories of Canada for helpful suggestions and doing the NMR spectra.

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