HETEROCYCLES, Vol. 3, No. 10, 1975

SYNTHESIS OF HEXA-O-METHYL-8,8"-BINARINGENIN

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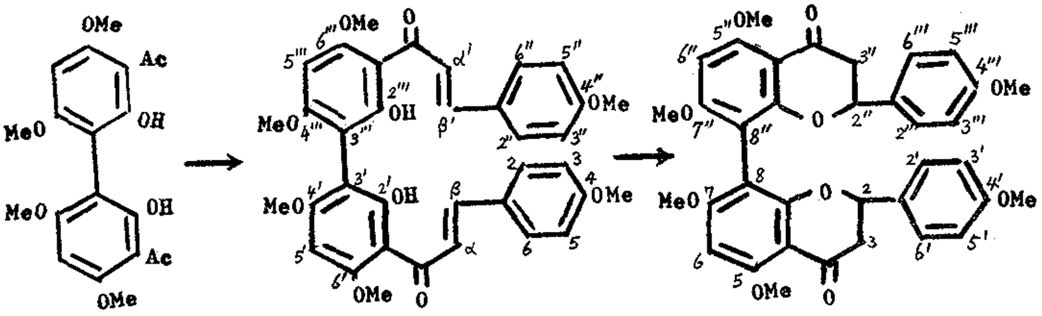
The hitherto unknown title compound was synthesized and its structure was confirmed by spectral evidence and by conversion by means of NBS to cupressuflavone derivative.

However synthetic hexa-O-methyl-8,8"-biapigenin, i.e. cupressuflavone hexamethyl ether, was reported by many workers,[1-4] the corresponding biflavanone (III) has not been recorded so far. As an extension on synthesis of biflavanoids[5] we now wish to report the two-step synthesis of the hitherto unknown biflavanone (III) from 3,3'-diacetyl-2,2'-dihydroxy-4,4',6,6'-tetramethoxybiphenyl (I).[4]



(I) (II) (III)

Friedel-Crafts reaction of 2,2',4,4',6,6'-hexamethoxybiphenyl with acetic anhydride and anhydrous aluminum chloride in nitrobenzene afforded I, m.p. 260-262°, yield 35% (lit., m.p. 262°, 25%;[3] m.p. 253-257°, 20%[4]).

Reaction of I with two moles of p-anisaldehyde in presence of alkali gave yellow bichalcone (II), m.p. 288-289°, yield 46% (lit.,[3] m.p. 282-285°); M$^+$ m/e 626; i.r.(KBr):~2500 (OH), 1600 (chelated CO), 1603, 1560, 1510 (arom.) cm^{-1}. The n.m.r. spectrum of II in DMSO-d_6-CDCl$_3$ showed six methoxyl groups at δ 3.71 (s, 12H, OMe-4,4',4",4"') and 3.88 (s, 6H, OMe-6',6"'); two aromatic protons at δ 6.19 (s, 2H, H-5',5"'); a set of A_2B_2 type doublets at δ 6.90 (d, J 9 Hz, 4H) and 7.64 (d, J 9 Hz, 4H), attributed to the eight aromatic protons at 3,3",5,5" and 2,2", 6,6" of the two 1,4-disubstituted rings B and E respectively; four protons at δ 7.83 (s) indicating the H-$\alpha,\alpha',\beta,\beta'$ of the two chalcone units.

Acidic cyclization of II by refluxing with alcoholic H_3PO_4 for two weeks afforded a mixture, which was treated by preparative t.l.c. to give a pale yellow crystal (III), yield 35%, m.p. 284-286°, $C_{36}H_{34}O_{10}$, M^+ m/e 626; R_f 0.24 (SiO_2, C_6H_6: EtOAc= 1:1); i.r. (KBr): 1680 (flavanone CO)cm^{-1}, no OH absorption. The n.m.r. spectrum of III in $CDCl_3$ showed six methoxyl groups at δ 3.66~3.90. The signal at δ 7.83 due to H-$\alpha,\alpha',\beta,\beta'$ of the chalcone II had disappeared and instead upfield signals appeared at δ 5.10 (dd, J 13 Hz, 3 Hz, 2H) and 2.60~2.87 (m, 4H), indicating the six protons at 2, 2", 3, and 3" positions of the two heterocyclic rings C and F of of the two flavanone units. The above results support strongly that during prolonged reflux with H_3PO_4 the ring closure of II had occurred, transforming the chalcone structure to the corresponding flavanone III. The structure of III was further supported by mass spectrum and by the dehydrogenation with NBS[6] yielding a biflavone derivative, m.p. 302-305° which was identical with authentic cupressuflavone hexamethyl ether (mixed m.p., t.l.c., i.r., and n.m.r.).

ACKNOWLEDGEMENTS We are grateful to Professor T. R. Seshadri for an authentic sample, to Professor W. C. Lin, Professor C. H. Yang and the Faculty members, Professor M. L. King and Mr. C. B. Wang of the National Defense Medical Center for n.m.r., u.v., i.r., and mass measurements. This work was supported by the National Science Council as the research project of the Chemistry Research Center, National Taiwan University.

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Received, 15th August, 1975