Synthesis of 2,5-Dihydroxy-7-methoxyflavanone, Cyclic Structure of the Benzoyl-(2,6-dihydroxy-4-methoxybenzoyl)-methane from *Populus nigra* Buds

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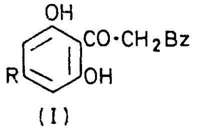
Summary Benzoyl-(2,6-dihydroxy-4-methoxybenzoyl)-methane, the natural product isolated from *Populus nigra*, has been synthesized and shown to have a cyclic structure.

It was recently suggested[1] that a compound, $C_{16}H_{15}O_5$, m.p. 170—172°, isolated from *Populus nigra* buds,[2] which was easily cyclodehydrated by acid into the flavone (III), had the structure (Ia). We now report the synthesis of this compound and show that its structure is, in fact (IIa). The stability of the natural compound in alkali led us to investigate the conversion of the flavone (III) into (Ia) by Na_2O_2 in pyridine,[3] but this failed. However, heating of (III) with anhydrous KOH in pyridine during 4 h at 115° gave a 60% yield of a product, identical with the natural one (m.p. and mixed m.p.; u.v. and i.r. spectra).

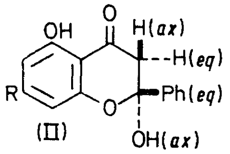
The classical Baker–Venkataraman process was then used for the total synthesis. 2,6-Dihydroxy-4-methoxyacetophenone[4] was benzoylated in aqueous NaOH; heating of the crude monobenzoate in pyridine with anhydrous KOH at 50° led to the desired product (30%).

The proposed structure (I), however, was not consistent with the physical data obtained for the synthetic and natural compounds. Thus the i.r. spectrum (KBr) showed only one carbonyl band (ν 1640 cm^{-1}) instead of the two (1640 and 1680 cm^{-1}) observed[5] for the colourless diketo-forms of *o*-hydroxydibenzoylmethanes. The mass spectrum showed an important peak at $M - 17$ (30%) corresponding to (IV), as expected for the structure (IIa) by comparison with the fragmentation pattern of flavanones.[6] The n.m.r.



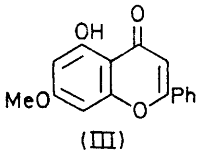
(I)

a ; R = MeO
b ; R = H

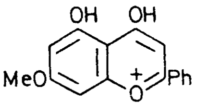


(II)

a ; R = MeO
b ; R = H



(III)



(IV)

spectrum [100 MHz; $(CD_3)_2CO$] at −60° clearly demonstrated the cyclic structure (II): δ 2·79 [d, J_{gem} 17 Hz, 3-H(*eq*)], 3·30 [q, J_{gem} 17 Hz, J (3-H–2-OH) 2 Hz, 3-H(*ax*)], 3·80 (s, OMe) 6·09 (s, 6- and 8-H) (*cf.* naringenin 7,4′-dimethyl ether[9]), 7·26 [d, J 2 Hz, 2-OH(*ax*)] 7·5 (3′-, 4′,- and 5′-H) and 7·8 (2′- and 6′-H), and 12·40 (s, 5-OH) p.p.m. The equatorial arrangement of the 2-phenyl group is indicated by the long-range coupling (2 Hz) between 2-OH and 3-H (*cf.* refs. 7 and 8). The observed positions of the 3-H signals are similar to those for flavanones,[10] and different from those expected for structure (I) (δ 4·5—4·7 p.p.m.[5]).

Wagner *et al.*[5] concluded from the u.v., i.r., and n.m.r. spectra of mono-*o*-hydroxydibenzoylmethanes that these compounds existed only in the enolic or keto-forms, no trace of 2-hydroxyflavanone tautomers being observable. This can be ascribed to strong interaction between the aromatic hydroxy-group and the adjacent carbonyl group. In our compound (I) however, another hydroxy-group is available for hemiacetalization of the non-bonded carbonyl group, thus favouring the 2-hydroxyflavanone structure.

All benzoyl-(2,6-dihydroxybenzoyl)methanes might then be expected to exist in the 2,5-dihydroxyflavanone form.

I.r. and n.m.r. spectra of synthetic benzoyl-(2,6-dihydroxybenzoyl)methane[11] showed that it existed in the cyclic form (IIb).

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