SYNTHETIC EXPERIMENTS IN THE BENZOPYRONE SERIES

Part XLVII. A New Synthesis of 3-Hydroxy Primetin Derivatives

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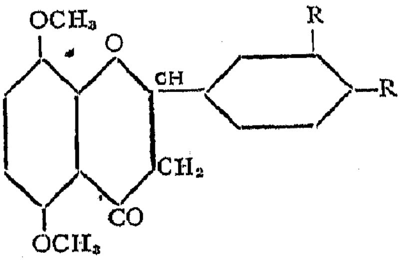
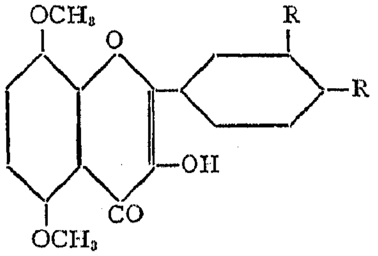
THREE-Hydroxy primetin was prepared earlier by Seshadri *et al.*[1] by nuclear oxidation using 3-methoxy-5-hydroxy flavone. In view of the recent simplification in the preparation of 2-hydroxy-3 : 6-dimethoxy acetophenone,[2] the alternative method using this ketone as the starting point has now been adopted. Condensation with benzaldehyde to yield the corresponding chalkone has already been reported by Ballio and Pocchiari.[3] The chalkone has now been converted into the corresponding flavanone (I *a*) and finally into the dimethoxy flavonol (II *a*) using a modification[4] of the method of Kostanecki. The trimethoxy flavone (III *a*) obtained on methylation agrees with the sample prepared earlier.[1] As a useful reference compound for analytical study in this series, alkali fission of the trimethoxy flavone (III *a*) has been carried out and the properties of 2-hydroxy-ω : 3 : 6-trimethoxy acetophenone (IV) recorded.

Using veratraldehyde in the above series of condensations 3 : 5 : 8 : 3′ : 4′ pentamethoxy flavone (III *b*) and the corresponding pentahydroxy flavone have also been prepared. The same pentamethyl ether is obtained by the

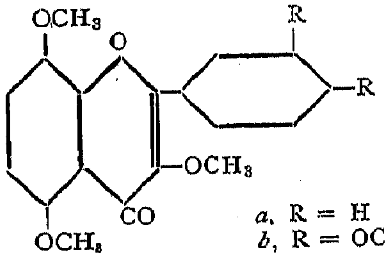


I

a, R = H
b, R = OCH₃

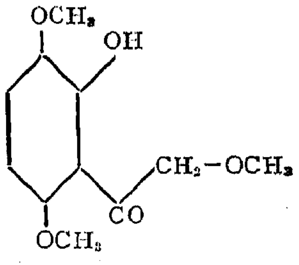


II



a, R = H
b, R = OCH₃

III



IV

condensation of the fission ketone (IV) with the anhydride and sodium salt of veratric acid (Allan-Robinson condensation). That there is no isomeric change during the demethylation of the flavonol methyl ether (II *b*) by means of hydriodic acid has also been proved by the remethylation of the pentahydroxy flavone whereby the same pentamethoxy flavone (III *b*) is again formed. A similar report was made earlier in the preparation of 3-hydroxy primetin.[1]

Recently Kurth and Hubbard[5] isolated a pentahydroxy flavone from Ponderosa Pine Bark and concluded that it should have the constitution of 3 : 5 : 8 : 3′ : 4′-pentahydroxy flavone. The properties recorded in this paper for the synthetic pentahydroxy flavone, its acetate and methyl ether do not agree with those of the natural product and its derivatives.

EXPERIMENTAL

5 : 8-*Dimethoxy flavanone* (*I* a)

2-Hydroxy-3 : 6-dimethoxy chalkone[3] (1·5 g.) was refluxed with alcohol (100 c.c.) and conc. sulphuric acid (2·5 c.c.) for 35 hours, diluted with water (100 c.c.) and the alcohol distilled off under reduced pressure. The solid product crystallised from ethyl acetate as colourless prismatic needles and rods, m.p. 163–64° C. Yield, 1·0 g. (Found: C, 71·7; H, 5·6; $C_{17}H_{16}O_4$ requires C, 71·8; H, 5·6%). It gave no colour with alcoholic ferric chloride solution.

3-*Hydroxy*-5 : 8-*dimethoxy flavone* (*II* a)

The dimethoxy flavanone (0·5 g.) was dissolved in alcohol (50 c.c.) and to the boiling solution iso-amyl nitrite (3 c.c.) and conc. hydrochloric acid (30 c.c.) were added alternately in small quantities at a time, with stirring. The solution turned bright yellow first and finally bright reddish orange. The hot solution was allowed to cool slowly and stand for 2 hours with occasional shaking. It was then diluted with water (200 c.c.) and within a few minutes crystals of the flavonol separated out. This was filtered off and crystallised from ethyl alcohol as yellow needles and long rectangular plates, m.p. 191–92° C. Yield, 70 mg. (Found: C, 66·8; H, 4·5; $C_{17}H_{14}O_5$, $\frac{1}{2}$ H_2O requires C, 66·5; H, 4·9%). A further quantity (30 mg.) was obtained from the mother liquor which was extracted with ether. The ether solution was extracted with sodium hydroxide (2%) and the alkaline solution acidified and re-extracted with ether. On distilling off the solvent an oil was obtained. It was heated with a mixture of glacial acetic acid and concentrated hydrochloric acid (1 : 1; 10 c.c.) on a water-bath for 30 minutes. On dilution with water a solid product was obtained which on crystallisation from ethyl