SYNTHESIS OF 5:6-DIHYDROXYFLAVONOLS—PART I

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5:6-DIHYDROXYFLAVONOLS have not so far been synthesised. In connection with the constitution of patuletin it is now found necessary to prepare them and study their properties and reactions. 5:6-Dihydroxy-flavone (IV) was made by Baker in the course of his study of primetin; starting from 2:6-dihydroxy-acetophenone (I) the various stages of his synthesis are represented below:

Since the \(\omega\)-methoxy derivative of (III) is not available the method of Allan and Robinson cannot be used for the synthesis of the flavonols. Consequently the original procedure of Kostanecki has been adopted. This paper records the condensation of ketone (III) with vanillin and of 5:6-dimethoxy-2-hydroxy-acetophenone (V) with veratric aldehyde and anisaldehyde to obtain the corresponding chalkones (VI). The conditions for getting the best yields were worked out initially using resacetophenone and its 4-methyl ether. Addition of an excess of the aldehyde component, and the use of strong aqueous alcoholic potash were found to be advantageous. It was noted that in all the cases reported here, some quantity of the flavanones (VII) accompanied the corresponding chalkones.

The conversion of the chalkones (VI) to the flavanones (VII) was carried out by means of aqueous alcoholic sulphuric acid. Even here the products
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were mixtures, a portion of the original chalkones remaining unchanged. 5:6:3′:4′-Tetramethoxy-flavanone was first obtained by methylating 5:3′-dimethoxy-6:4′-dihydroxy-flavanone using methyl iodide and potassium carbonate in acetone medium. The identity of the compound was established by synthesis directly from (V) and veratric aldehyde. This is rather remarkable since in other cases of flavanones like naringin and hesperidin the methylation of the hydroxyl groups is accompanied by the opening of the flavanone ring and final methylation of the hydroxyl thus set free. The factors that contribute to this difference are not quite clear.

The chalkones described in this paper are bright red in colour whereas the flavanones are colourless. Only the former yield colour with ferric chloride whereas the latter alone give red colour when reduced with magnesium and hydrochloric acid, the colour being definitely weaker with the fully methylated flavanones. In general the chalkones are markedly less soluble.

The synthesis of the flavonols from the flavanones and their study will be reported later.

Experimental

2:5:4′-Trihydroxy-6:3′-dimethoxy chalkone. (VI. \( R_1 = H, R_2 = OH, R_3 = OCH_3 \)).—2: 5-Dihydroxy-6-methoxy acetophenone \(^{1} \) (4·0 g.) and vanillin (8·0 g.) were dissolved in alcohol (40 c.c.). To this solution aqueous potassium hydroxide (75 g. in 100 c.c. water) was added with stirring and the mixture refluxed on a water-bath for about 15 minutes. While still hot, the flask was corked tight and allowed to stand for about 24 hours. The reddish-brown liquid was then diluted to about 200 c.c. with water and acidified with hydrochloric acid with cooling under the tap, when an orange-red precipitate separated out. On crystallising it twice from alcohol deep-red