Steric Effects on the Cyclisation of Chalcone Dibromides

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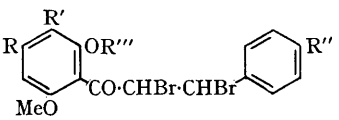
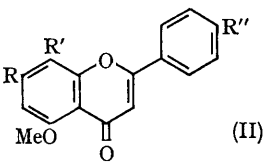
IN practice, the most convenient general method of synthesis of flavones (II) is that discovered by Emilewicz and Kostanecki.[1] It involves the bromination of 2′-hydroxy(or acetoxy)-chalcones and cyclisation of the resulting chalcone dibromides (I) with aqueous ethanolic alkali. Its use, however, has been greatly curtailed by the fact that the many naturally occurring flavones with 5,7-disubstitution patterns could not be obtained[2] by this method—the corresponding chalcone dibromides yielded aurones (III) and not flavones. Re-examination of the reaction, using phloracetophenone-derived chalcone dibromides, has now shown that the products are mixtures, with flavones as the major constituents. The isolation of the aurone component only in earlier work was, presumably, due to its being the less soluble of the two components in ethanol, the usual solvent for crystallisation.

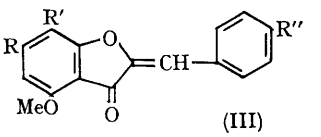
The Table below lists: (i) the chalcone dibromides examined, (ii) the yields of neutral products obtained from these dibromides, and (iii) the composition of these products (the crude reaction products were chromatographed on alumina columns; the aurones, which were eluted first, required further purification and, hence, only the proportions of



(I)



(II)



(III)

a; R = OMe; R′ = Br; R″ = R‴ = H.
b; R = R″ = OMe; R′ = Br; R‴ = H.
c; R = R′ = R″ = H; R‴ = Ac.
d; R = R″ = H; R′ = Br; R‴ = Ac.

flavones, as a percentage of the total neutral product, are given).

It is apparent from these results that the steric effects of the 6′-methoxyl group[8] are not the principal cause of aurone formation by these dibromides; (Ic), the simplest 2′-acetoxy-6′-methoxychalcone dibromide, gave relatively little aurone. The introduction of a 3′-bromo-substituent into (Ic), to give 2′-acetoxy-3′-bromo-6′-methoxychalcone dibromide (Id), had the unexpected effect of decreasing the percentage of flavone found from 89% to 46% and suggests that aurone formation by phloracetophenone-derived chalcone dibromides may be due[9] to the combined steric effects of the two substituents, the 3′-bromo and the 6′-methoxy, *ortho* to the developing heterocyclic ring.

TABLE

(i) Dibromide	(ii) Yield (%)	(iii) Products	
(Ia)[3]	93	(IIa)[3] 54%	(IIIa)[2,4] (m.p. 258—259°)
(Ib)[3]	95	(IIb)[3] 62%	(IIIb)[2] (m.p. 243—245°)
(Ic) (m.p. 142—143°)	91	(IIc)[5] 89%	(IIIc)[6]
(Id) (m.p. 172—173°)	44	(IId)[7] 46%	(IIId) (m.p. 202—203°)

The spectroscopic and analytical data for all new compounds are consistent with the assigned structures.

(*Received, May 10th*, 1966; *Com.* 312.)

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