Induction of 2,3-Aryl Migrations in 3-Bromoflavanones

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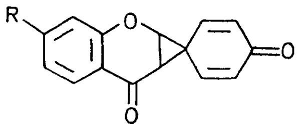
Summary 3-Bromoflavanones with electron releasing substituents in the 4′-position undergo a ready, silver-promoted, 2,3-aryl shift to yield isoflavones.

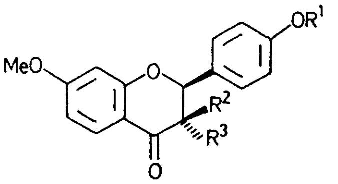
THE mechanism of the biosynthesis of isoflavones from flavonoid precursors has long been a matter of interest, involving as it does an unusual aryl shift.[1,2] A hypothesis that the rearrangement is due to oxidative attack on a chalcone[3] has received much experimental backing;[4] in particular this process would involve the protonation or alkylation of a spirodienone of type (**1**).

An earlier hypothesis involved the rearrangement of 3-hydroxyflavanones or their derivatives.[1] No successful *in vitro* rearrangements of such compounds have however been reported, in contrast to the successful rearrangement of 3-substituted flavans.[5] The difficulties expected with the flavanone derivatives[6] merely reflect the well discussed general problem of producing α-keto carbonium ions.[7,8] 3-Bromoflavanones have been reacted with nucleophilic reagents (including AgOAc, AgOBz, AgONO) to give mixtures of dihydroflavonol derivatives and flavones.[9]

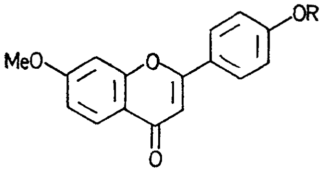
With the aim of finding new routes to isoflavonoid compounds and also ultimately of providing *in vitro* analogies to the proposed biosynthesis we have been investigating some new rearrangements of flavonoid compounds. We now report a new 1,2-aryl migration of 3-bromoflavanones induced by the silver ion. Our 3-bromoflavanones were prepared as a mixture of *cis*- and *trans*-isomers (in contrast to previous reports) by the action of cupric bromide upon the corresponding flavanones.[10] When the 3-bromoflavanones (**2**, R^1 = H or Me) were treated with aq. K_2CO_3, aq. NaOH, triethylamine, pyridine, butyl lithium or trityl sodium only the flavones (**3**, R = H or Me) were formed, the *cis*-3-bromoflavanones reacting most rapidly.



(1)



(2) *cis*, R^2=Br, R^3=H
trans; R^2=H, R^3=Br



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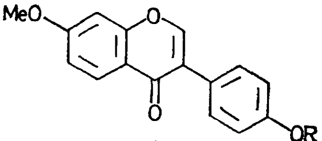

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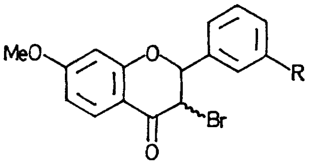
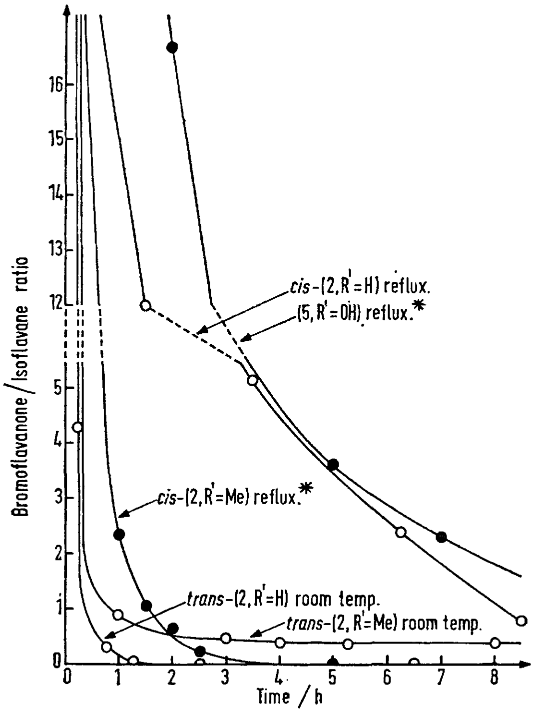


(5)

However when the same 3-bromoflavanones were treated with silver hexafluoroantimonate in methylene dichloride,[8] then a 2,3-aryl shift occurred and the isoflavones (**4**, R = H or Me) were obtained as products. The same reaction took place, although more slowly, when silver perchlorate was used. The yields from the *trans*-isomers were of the order of 50—60%.

The rates of the $AgSbF_6$ induced reactions were followed by h.p.l.c. (see Figure) though the great range of activity plus the fact that in some cases other products (*e.g.* flavones) were formed simultaneously did not allow quantitative comparison. However, the rates are particularly fast for the *trans*-3-bromoflavanones bearing an electron releasing group at the 4′-position. This suggests a concerted mechanism for the migration of these compounds. For the corresponding *cis*-3-bromoflavanones presumably a pre-equilibration step or the formation of a carbonium ion (or ion-pair) is required before reaction can proceed. The very slow migration observed with (**5**, R = OH)† and (**5**, R = H)‡ serves to substantiate the idea of a concerted migration for the *trans*-isomers.



*Substantial quantity of flavone also formed.

Figure Rates of $AgSbF_6$-catalysed reactions

In at least one case (**2**, R^1 = H) the spirodienone (**1**, R = OMe) could be an intermediate but so far all attempts to trap it by alkylation or protonation have been unsuccessful, as has spectroscopic detection.

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† A mixture of *cis*- and *trans*-isomers was used.

‡ The reaction was so slow that it was unplottable in the Figure.

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