Pergamon

Tetrahedron Letters, Vol. 35, No. 50, pp. 9459-9460, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $7.00+0.00

0040-4039(94)02047-7

Synthesis of 6,8-(Dibromo or Diiodo)-5-Hydroxy-2-(Phenyl or Styryl)chromones

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Abstract: A facile synthetic method has been developed for the preparation of 6,8-(dibromo or diiodo)--5-hydroxy-2-(phenyl or styryl)chromones. These compounds were obtained by either one-pot synthesis from 2'-benzyloxy-6'-hydroxychalcones or 2'-benzyloxy-6'-hydroxycinnamylideneacetophenones or from the corresponding 2-phenyl- or 2-styrylchromones.

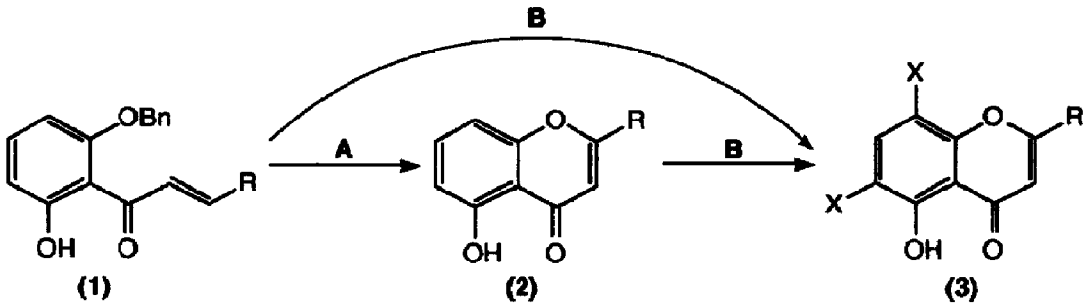
2-Phenyl- and 3-phenyl-substituted chromones, currently designated as flavones and isoflavones, are found in all plants where they participate in several biological functions.[1] However 2-styrylchromones are scarce in Nature. Two compounds of this type have been isolated from the blue-green algae *Chrysophaeum taylori*;[2] activity against certain leukemia cells has also been demonstrated by them.[2]

Natural halo-compounds are not very common in plants,[4] but some, such as halo-flavonoids, can be found in certain algae and fungi.[4,5] Many natural and synthethic halo-compounds show strong biological activity; and many pharmaceutical drugs,[6] fungicides, herbicides and insecticides are halide substituted compounds.[7]

Considering the important biological activity shown by chromones and certain halo-compounds it can be anticipated that halo-chromones might be useful in the pharmaceutical and / or agrochemical industries. To this end the synthesis of 6,8-dibromo- and 6,8-diiodo- derivatives of 5-hydroxy-2-(phenyl or styryl)chromones has been undertaken. This will allow these compounds to be available for biological evaluation in parallel with those without halide substituents.[8]

We have recently reported that catalytic amounts of iodine in DMSO performs the transformation of 2'-benzyloxy-6'-hydroxychalcones (**1a**) or 2'-benzyloxy-6'-hydroxycinnamylideneacetophenones (**1b**) into the respective 5-hydroxy-2-phenylchromones (**2a**) or 5-hydroxy-2-styrylchromones (**2b**)[8]. In this work, the diiodo derivatives (**3a.1**) and (**3b.1**) have been obtained by using 1.0 molar equivalents of iodine. Under these conditions, the reactions are consistent with electrophylic substitution processes at the most activated aromatic positions. However, when using compounds (**1a**) and (**1b**), the transformation of each one will involve a cyclization and cleavage of the benzylic protecting group, catalysed by the iodine:DMSO mixture, and also an electrophylic substitution process (Scheme 1). The corresponding brominated products (**3a.2**) and (**3b.2**) were obtained by simply replacing iodine with bromine.

This paper is dedicated to Prof. C. W. Jefford, Geneva University, on the occasion of his 65th birthday.



(1) (2) (3)

Bn = $CH_2C_6H_5$

a) R = Phenyl
b) R = Styryl

3a.1) R = Phenyl, X = I
3a.2) R = Phenyl, X = Br
3b.1) R = Styryl, X = I
3b.2) R = Styryl, X = Br

A - DMSO / I_2 or Br_2 (catalytical amount), reflux 30 min.
B - DMSO / I_2 or Br_2 (one equivalent), reflux 30 min.

Scheme 1

The structures of the products were determined using ^1H and ^{13}C NMR, mass spectrometry and elemental analysis. In particular for each compound (3) the ^1H and ^{13}C NMR resonances of H-7 and C-7 atoms appear, respectively, between δ 7.94-8.37 and 140.4-1551.3 ppm. In comparison with NMR results obtained for the non-halo-chromones (2), shifts to higher frequencies for the H-7 and C-7 resonances of (3) were observed, which are due to the deshielding effect of the *ortho* halide substituents.

Acknowledgements: Thanks are due to JNICT for a grant (1M/90) to purchase the Bruker AMX 300 NMR spectrometer and to University of Aveiro and "Centro de Química" for funding. One of us (D.C.G.A.P.) is also grateful to JNICT for the award of a student's grant.

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(*Received in UK* 20 *September* 1994; *accepted* 14 *October* 1994)