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One pot synthesis of aryl substituted aurones

Céu M. Sousa [a,*], Jérôme Berthet [b], Stephanie Delbaere [b], Paulo J. Coelho [a]

[a] Centro de Química – Vila Real, Universidade de Trás-os-Montes e Alto Douro, Quinta dos Prados, 5001-801 Vila Real, Portugal
[b] Université Lille Nord de France, CNRS UMR 8516, UDSL, Faculté des Sciences Pharmaceutiques et Biologiques, F-59006 Lille, France

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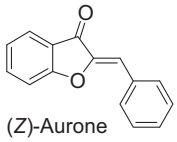
ABSTRACT

An efficient one-pot synthesis of new 4-hydroxy-2-(diarylmethylene)benzofuran-3(2*H*)-ones dyes (aryl substituted aurones) from 2′,6′-dihydroxyacetophenone, potassium *tert*-butoxide and aromatic ketones under thermal conditions is described.

1. Introduction

Aurones (2-benzylidenebenzofuran-3(2H)-ones) are natural occurring yellow dyes found especially in plants and in some marine organisms, usually in a hydroxylated form. Both *E* and Z isomers can be found in nature, although the latter is thermodynamically more stable and thus much more abundant. Besides their contribution to the pigmentation of flowers and fruits [1] aurones exhibit a wide variety of biological activities: they have been described as antifungal agents [2–4], antibacterial agents [5–9], insect antifeedant agents [10], antioxidants [11–14], as inhibitors of tyrosinase [15], iodothyronine-deiodinase [16], acetylcholinesterase [17], anticancer [18–20] and as possessing anti-inflammatory properties [10]. These compounds are usually prepared by three main methods: condensation between benzofuranones and benzaldehydes [10,15,17,18,21,22], oxidative cyclisation of 2′-hydroxychalcones [11] or by catalysed cyclisation of *ortho*-(1-hydroxyprop-2-ynyl)phenols or *ortho*-hydroxyaryl arylethynyl ketones [23–25]. In this paper we describe a fast and easy one-pot synthesis of new aryl substituted aurones starting from commercially available materials under thermal conditions.



(*Z*)-Aurone

2. Results and discussion

2′-Hydroxychalcones can be easily prepared, under mild conditions, by aldol condensation between 2′-hydroxyacetophenone and different benzaldehydes in the presence of base. This reaction is very general and these compounds are valuable intermediates in the synthesis of flavones [26–28] and aurones [11] (Scheme 1).

The reaction of 2′-hydroxyacetophenone with benzophenone in the presence of *t*-BuOK in toluene at reflux, gives the expected aryl substituted 2′-hydroxychalcone an useful compound that can be converted in acid medium to the 2,2-diphenylchroman-1-one, an important precursor for the synthesis photochromic chromenes [29,30]. In an attempt to prepare 2′,6′-dihydroxy-3-phenylchalcone we tried the reaction of 2′,6′-dihydroxyacetophenone with benzophenone in the presence of *t*-BuOK and using toluene as solvent, but no reaction was detected after 8 h at reflux. Changing the solvent to xylene led to the same result while when the reaction was performed in high boiling point solvents like DMSO, ethyleneglycol or nitrobenzene only degradation products were observed (Scheme 2).

* Corresponding author. Tel.: +351 259 350284; fax: +351 259 350480.
E-mail address: pcoelho@utad.pt (C.M. Sousa).

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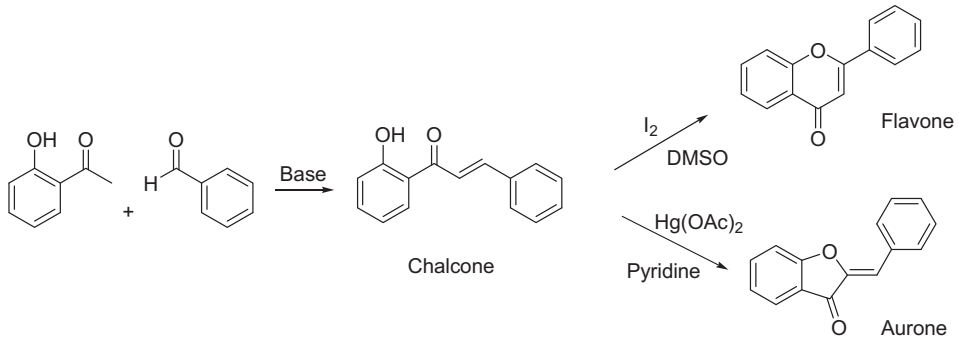
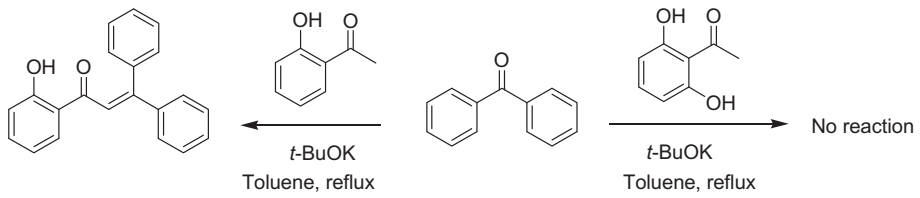


Scheme 1. Synthesis of flavones and aurones from 2′-hydroxychalcones.



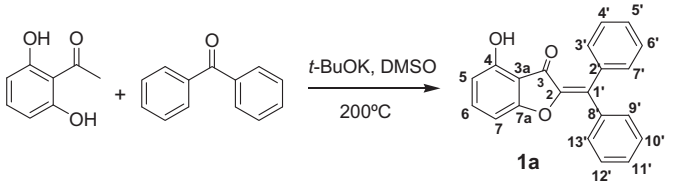
Scheme 2. Reaction of 2′-hydroxyacetophenone and 2′,6′-dihydroxyacetophenone with benzophenone.

However, heating a mixture of 2′,6′-dihydroxyacetophenone, potassium *tert*-butoxide and benzophenone in the presence of a very small amount of DMSO at 200 °C for 2 min affords a red mass that upon acid hydrolysis originated a deep yellow dye.

The ^{1}H NMR spectrum of this compound showed the expected aromatic signals but the absence of any signal that could be attributed to ethylenic protons, and the presence of only one phenolic proton pointed to a different structure. Mass spectrometry confirmed the molecular formula of the product as $C_{21}H_{14}O_3$ which indicates a difference of two hydrogen atoms from the predicted chalcone structure.

The structure of this new yellow dye was unambiguously established using 2D NMR experiments as being an aurone derivative (Scheme 3). ^{1}H–^{1}H scalar correlations were measured in COSY experiment (Fig. 1) from H-5 at 6.60 ppm up to H-7 at 6.76 ppm via H-6 at 7.51 ppm and for the two phenyl groups between H-3′/7′ at 7.60 ppm and H-4′/6′ at 7.44 ppm, and between H-9′/13′ at 7.37 ppm and H-10′/12′ at 7.50 ppm.

The HMBC spectrum (Fig. 2) evidences long-range C–H correlations between carbon C–4 at 156.9 ppm and aromatic protons H-5, H-6 and H-7, and the phenolic function at 8.06 ppm. The furanone quaternary carbons C-7a and C-3 were evidenced at 163.8 ppm and 184.8 ppm, respectively. Carbon C-7a is long-range correlated with H-5, H-6 and H-7, while carbon C-3 is correlated with H-5 and H-7. The carbon C-1′ at 133.0 ppm is long-range correlated with H-3′/7′ and H-9′/13′.



Scheme 3. Synthesis of 4-hydroxy-2-(diphenylmethylene)benzofuran-3(2H)-one dye **1a**.

The dye **1a** was obtained in 10% yield after column chromatography. Heating the reaction mixture for more than 2 min, or at higher temperature leads to more degradation while heating at lower temperature, leaves too much unreactive material. The reaction also works using *t*-butanol or DMF as solvent but with lower yields (7 and 8%, respectively) and the amount of solvent must be very low. If several mL are used only degradation products are detected. The best results were obtained using 60 mg of DMSO for 0.5 mmol of 2′,6′-dihydroxyacetophenone. Heating the reagents in an inert atmosphere (N_2) gave the same result.

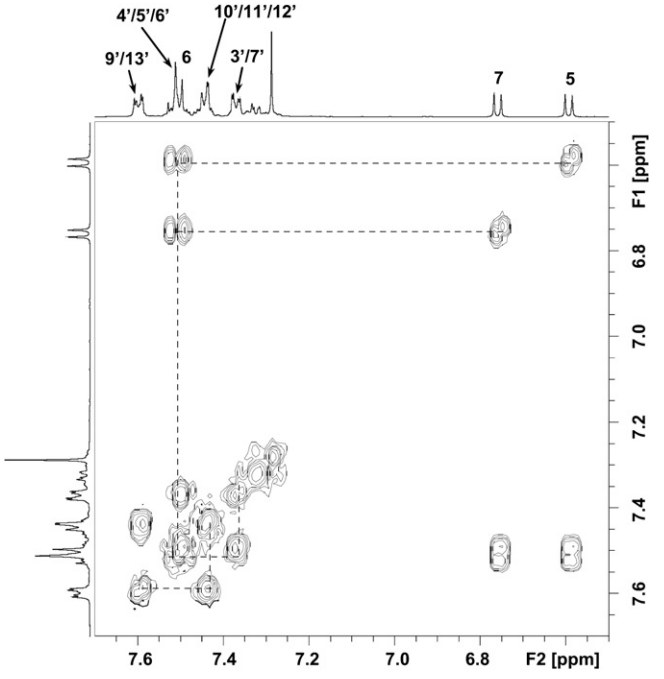


Fig. 1. ^{1}H–^{1}H COSY of **1a** in $CDCl_3$.