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Clay Catalysis: Solventless Condensation of Benzofuran-3(2*H*)-One with α,β-Dicarbonyl Compounds under Microwave Irradiation: Synthesis of New Acyl-Aurones †

Karima Boussafi [1,2], Didier Villemin [1,*] and Nathalie Bar [1]

[1] Laboratoire de Chimie Moléculaire et Thioorganique, UMR CNRS 6507, INC3M, FR 3038, ENSICAEN et Université de Caen Normandie, 14050 Caen, France; boussafi.karima@yahoo.fr (K.B.); nathalie.bar@ensicaen.fr (N.B.)

[2] Algeria, Département de Chimie, Faculté des Sciences Exactes et Informatique, Université Mohamed Seddik Ben Yahia Jijel, Jijel 18000, Algeria

* Correspondence: didier.villemin@ensicaen.fr

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Abstract: Aurones are natural bioactive dyes found in plants, and many of them are biologically active. We reported herein that α,β-dicarbonyl compounds condense with 3-coumarones without a solvent under microwave irradiation with clay as a catalyst. Novel acylaurones were obtained in good yields; the more stable *E*-isomer was formed stereoselectively.

Keywords: aurone; clay catalysis; coumaranone; microwave

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1. Introduction

Aurones are natural products [1], and some aurone derivatives have been used recently in medicinal chemistry [2,3]. The aurones were generally synthesized by condensation of coumaran-3-ones with aldehydes under acido-basic conditions [4–6]. While ketones generally do not condense easily in these conditions with 3-coumaranones, we report herein that the more electrophilic α,β-dicarbonyl compounds [7] lead to these condensations providing new tetrasubstituted aurones. To our knowledge, the tetrasubstituted aurones already described in the literature were obtained only via ring formation [8].

In order to avoid the benzylic rearrangement [9] of the α,β-dicarbonyl compounds in a basic medium, we have preferred to use acidic catalysis rather than a basic one. Since 1989 [10], we have described the clays as good catalysts in a solvent-free Knoevenagel reaction under microwave irradiation (Scheme 1).

Scheme 1. Acidic catalyzed condensation of 3-coumaranone with α,β-dicarbonyl compounds.

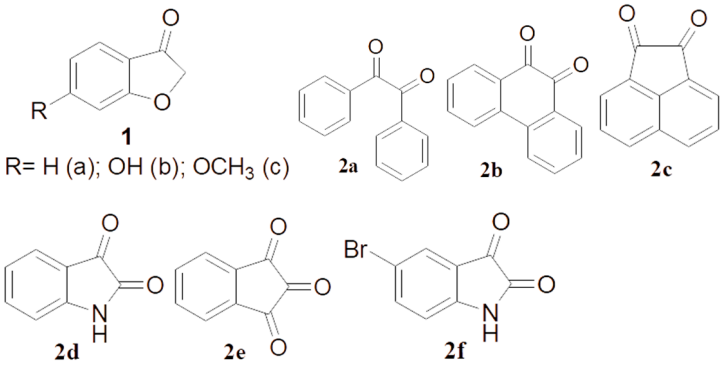
2. Results and Discussion

According to this methodology, an equimolar mixture of benzofuran-3(2*H*)-one and a dicarbonyl compound adsorbed on clay in a closed tube was irradiated using a microwave at 2450 MHz in a resonance cavity Anton Paar Monowave 300. The reactions of coumaranone **1a** and benzil **2a** are used as a model reaction to test the clays K10, KSF, or Algerian clay of Maghnia (Maghia) treated with sulphuric acid [11] as a catalyst. All these clays conduct similar yields (around 80%) after microwave irradiation.

Under these conditions, novel acylaurones not previously described were prepared according to Scheme 1. The irradiation conditions and the yields are reported in Table 1. The new products were characterized using mass spectroscopy, ^{1}H, and ^{13}C NMR spectroscopy.

Table 1. Synthesis of new acylaurones under microwave activation.

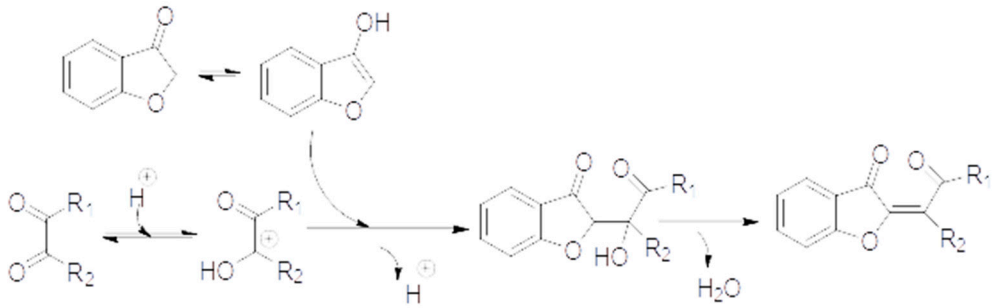
Starting reactants



Coumaranone 1a–b	α,β-dicarbonyl 2	Conditions	Product, Yield %
1a	**2a**	200 °C, 15 min	**3a**, 80
1a	**2b**	200 °C, 10 min	**3a**, 75
1a	**2c**	200 °C, 10 min	**3a**, 72
1a	**2d**	200 °C, 10 min	**3d**, 70
1a	**2e**	200 °C, 15 min	**3e**, 70
1b	**2a**	180 °C, 10 min	**3f**, 67
1b	**2b**	180 °C, 10 min	**3g**, 65
1b	**2c**	180 °C, 10 min	**3h**, 63
1b	**2d**	180 °C, 10 min	**3i**, 60
1b	**2f**	180 °C, 10 min	**3j**, 70
1c	**2a**	180 °C, 10 min	**3k**, 65
1c	**2b**	180 °C, 10 min	**3l**, 80

3. Mechanisms

A probable mechanism for this acidic condensation involves the addition of an α-hydroxy-acylium cation on the enol form of the 3-coumaranone according to Scheme 2:



Scheme 2. Probable mechanism of acidic catalyzed condensation of 3-coumaranone with α,β-dicarbonyl compounds.

4. Stereochemistry

Two stereoisomers can be formed in the acidic catalyzed condensation of 3-coumaranone with carbonyl compounds. In the case of aldehydes, only the more stable Z-isomer was produced. In the case of α,β-dicarbonyl compounds, only one stereoisomer was formed (TLC, NMR). We focused on the case of the two stereoisomers of **3a**, and we have predicted the ^{13}C NMR spectra of Z and E **3a** with Spartan software [12]: the more stable E-isomer displays a ^{13}C NMR spectrum corresponding to the compound found.

5. Experimental

5.1. General Information

The ^{1}H NMR and ^{13}C NMR spectra were recorded on a Brüker AC 400 spectrometer at 400 MHz. Samples were recorded in $CDCl_3$ solutions using TMS as an internal standard. The chemical shifts are expressed in δ units (ppm) and quoted downfield from TMS. The multiplicities are reported as s, singlet; d, doublet; t, triplet; q, quartet; and m, multiplet.

Mass spectra were recorded on Xevo G2-XS QTof Waters.

Microwave irradiations were performed at 2450 MHz with an Anton–Paar Monowave 300.

Computation was performed with Spartan 14 software (DFT, with B3LYP 3-21G basis) on a Dell workstation.

5.2. Starting Reactants

The 6-hydroxybenzofuran-3(*2H*)-one (**1b**) and 6-methoxybenzofuran-3(*2H*)-one (**1c**) were prepared according to the literature. Benzofuran-3(*2H*)-one (**1a**), isatin (**2d**), bromo-5-isatin (**2f**), benzil (**2a**), phenanthraquinone (**2b**), acenaphthoquinone (**2c**), and ninhydrine (**2e**) are commercial (Alfa).

Clays used: the Algerian clay of Maghnia was treated with sulfuric acid according to the conditions described by us in the literature [11]. K10 and KSF clays (Süd Chemie) are commercially available from Aldrich.

5.3. Typical Experiment

The mixture of dicarbonyl compound **2** (1 mmol) and 3-coumaranone **1a** (1 mmol) was dissolved in methanol (10 mL), the clay K10 (2 g) was added, and the solvent was evaporated under vacuum with a rotary evaporator. The powder placed in a G10 tube was irradiated using a microwave (see conditions Table 1) with a Monowave 300 of Anton Paar. The powder was extracted with methanol (3 × 20 mL), and the solvent was evaporated. The resulting solid was chromatographed using preparative TLC (AcOEt/cyclohexane = 1/3). The colored acylaurones (orange to red) were characterized by ^{1}H, ^{13}C NMR, and mass spectroscopy.

For example:

(E)-2-(2-oxo-1,2-diphenylethylidene)benzofuran-3(*2H*)-one (**3a**)

Obtained fom benzil **2a** and 3-coumaranone **1a** as an orange solid, $C_{22}H_{14}0_3$, Mp = 175 °C; Rf = 0.64 (AcOEt).

^{1}H NMR: (400 MHz, CD_3Cl) δ 8.07 (m, 1Har); 7.88 (m, 1Har); 7.72 (m, 1Har); 7.63 (m, 1Har); 7.55 (m, 1Har); 7.54 (m, 1Har); and 7.46 (m, 1Har).

^{13}C NMR: (400 MHz, CD_3Cl) δ 197.5 (CO); 182.6 (CO), 163.4, 156.2, 137.9, 135.2; 134.5; 132.6; 129.2; 128.9; 128.6; 128.5; 123.4; and 119.1

HRMS (M+1): 327.1021 calculated for $C_{22}H_{14}0_3$; found: 327.1020.

IR (cm^{-1}): 1681 (νCO); 1668 (νCO; 1600-1450(νC=C); and 1220 (-O-C).

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