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Research Note

Ultrasonic-assisted Synthesis of New Generation of Coumarins

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ABSTRACT

A convenient and efficient procedure for synthesis of Bis(4-HydroxyCoumarin) derivatives has been developed by a simple one-pot, one step ultrasonic-assisted reaction to produce Bis(4-HydroxyCoumarins) in room temperature. The present methodology offers several advantages, such as a simple procedure with an easy work-up, short reaction times, high yields, and the absence of any volatile and hazardous organic solvents.

Keywords: 4-HydroxyCoumarin; Ultrasonic-assisted; Salicylaldehyde; One-pot.

1. Introduction

Coumarins and their derivatives form an elite class of compounds, occupying an important place in the realm of natural products and synthetic organic chemistry. Their applications range from additives in food, perfumes, cosmetics, pharmaceuticals and in the preparation of insecticides [1], optical brighteners [2], dispersed fluorescent and tunable laser dyes [3], and alignment layers of liquid crystal [4]. Also, coumarins have varied bioactivities, for example, inhibition of platelet aggregation [5], anticancer and inhibition of steroid [6] reductase [7]. These properties have made coumarins into interesting targets for organic chemists. The last decade witnessed a series of publications on the development of synthetic protocols for this important heterocyclic scaffold. Thus, it is clearly evident that the need for the development

of new and flexible protocols is required, especially when they accommodate important functionalities and are broad in scope.

Many coumarin derivatives are used as photo chemotherapeutic drugs for PUVA (psoralen plus ultraviolet-A-radiation) therapy [8]. Coumarin compounds show a variety of applications i.e., coumarin-1-dye/biphenyl-periodic mesoporous organ silica is used as one of the key ingredient in light harvesting materials [9].

2. Experimental

The reagents were purchased from Aldrich and Merck companies. IR spectrum was recorded on a FT-IR spectrophotometer uses KBr pellets. NMR spectra were recorded on a Brucker 400 and 500 in CDCl3 and DMSO-d6 with TMS as internal reference with chemical shifts given in ppm and coupling constants in Hertz. A mixture of salcilaldehyde **1**, (1mmol) and 4-HydroxyCoumarin **2** (2mmol) was carried out in ultrasonic device; Bis(4-HydroxyCoumarins) **3** was obtained. As indicated by TLC (1:2 n-Hexane:AcOEt) solids were obtained (Figure 1).

3,3′-(2-Chloro,6-fluorobenzylidene)-bis(4-hydroxycoumarin), 92%, mp 286–288°C; IR (KBr, cm^{-1}): 3105, 2710, 1655, 1600, 1554, 1510, 1354, 1105, 778; 1H-NMR (500 MHz, CDCl3): δ: 10.7 (s, 1H), 8.09 (dd, J = 1.45, 8.04 Hz, 1H), 8.07 (dd, J = 1.45, 7.89 Hz, 1H), 7.47 (t, J = 7.77 Hz, 1H), 7.48 (t, J = 7.77 Hz, 1H), 7.42 (t, J = 7.30 Hz, 1H), 7.35 (t, J = 8.23 Hz, 1H), 7.15–7.35 (m, 5H), 5.56 (s, 1H).

3,3′-(4-Bromophenylmethylene)bis(4-hydroxy-2H-chromen-2-one), 89%, mp 241–243°C,1H NMR (500 MHz, CDCl3): δ: 7.87 (d ,2H, J = 8.34 Hz), 7.54 (t ,2H, J = 7.63 Hz), 7.21–7.43 (m ,6H), 7.09 (d ,2H, J = 8.25 Hz), 6.32 (s ,1H).

A mixture of salcilaldehyde **1**, (1mmol) and dimethylmalonate **2** (0.1ml, 1mmol) was carried out in ultrasonic device; 3-carboxilic coumarin **3** was obtained. Then diazonium salt **4**

was dropped into it until the reaction was completed and target compound was produced. As indicated by TLC (3:2 n-Hexane:AcOEt) colorful solids were obtained (Figure 1).

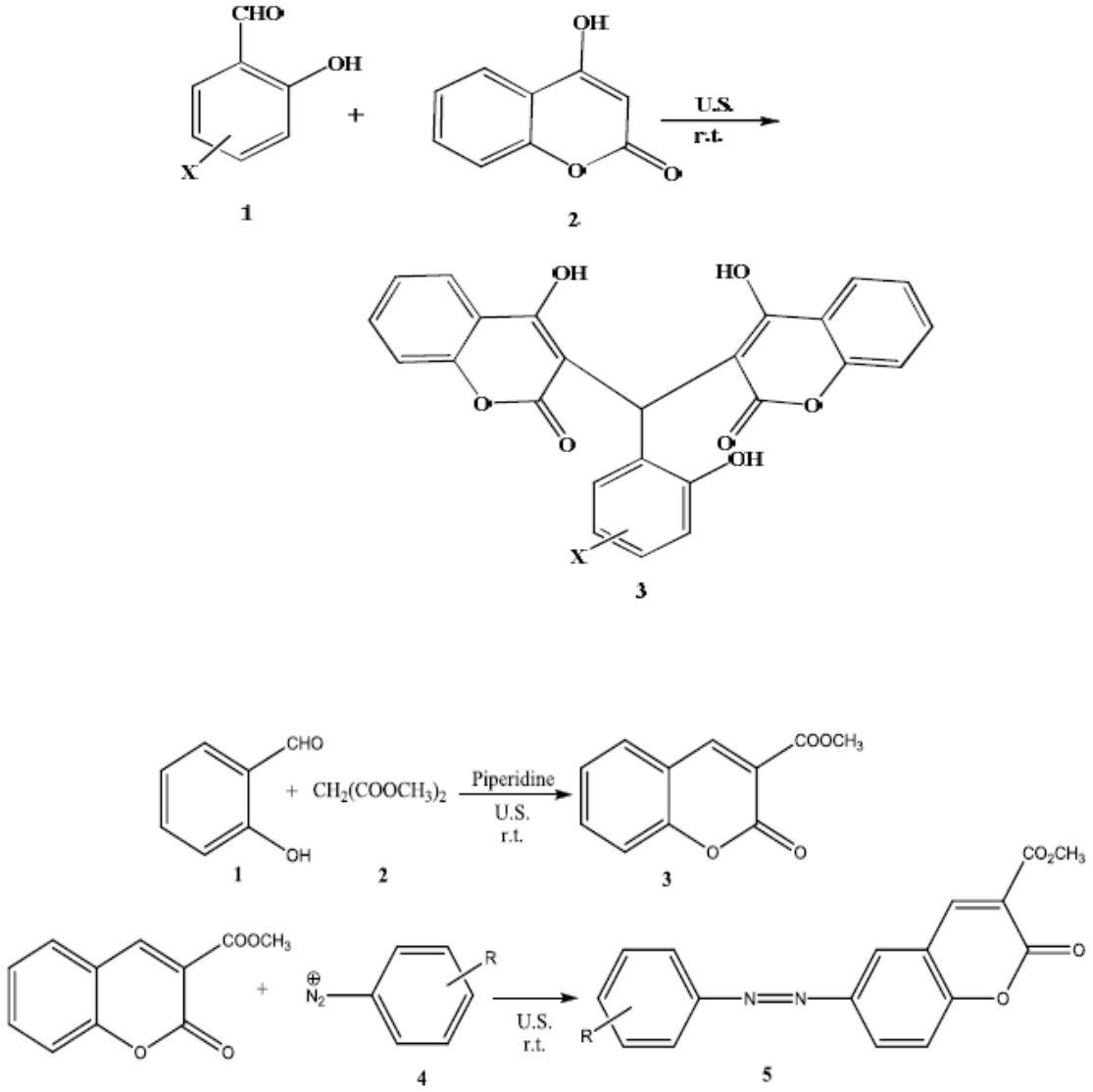

Fig.1. Synthesis of Bis(4-HydroxyCoumarin) and coumarins-3-carboxilate derivatives

3. Result and discussion

In continuation of our ongoing studies to synthesize of heterocyclic and pharmaceutical compounds at mild and practical protocols [10-12], herein we wish to report our experimental results on the aqueous and ultrasound assisted synthesis of new Bis(4-HydroxyCoumarin) derivatives using different substituted aldehydes and 4- Hydroxy Coumarin.

In an initial endeavor, the reaction of 4-bromo benzaldehyde with 4-HydroxyCoumarin under (i) reflux condition and (ii) ultrasonic irradiation in aqueous media afforded 3,3′-(4-Bromophenylmethylene)bis(4-hydroxy-2Hchromen-2-one). The product was characterized on the basis of spectroscopic data. In the 1HNMR spectrum the CH saturated group was observed at δ 6/32ppm as single signal. They were synthesized via knoevenagel reaction in the first step and electrophonic substitute reaction in the second one. We obtained the product in a good yield. The method offers several advantages such as: inexpensive solvent, short time reaction and the reaction is environmentally friendly.

4. Conclusion

In summary, we have developed a convenient method for the synthesis of Bis(4-HydroxyCoumarin) and coumarins-3-carboxilate derivatives. The reaction is clean and environment friendly. Most of these new compounds exhibit good biological activities as mentioned in introduction.

Acknowledgements

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