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Synthesis of new derivatives of chalcones from euparine extracted of *Petasites hybridus*

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Abstract: One-pot reaction of 1-(6-hydroxy-2-isopropenyl-1-benzofuran-yl)-1-ethanone and benzaldehyde derivatives in the presence of sodium hydroxide in mixture of ethanol and water as the solvent was described as efficient synthetic procedure for preparation of chalcone derivatives in excellent yield. In these reactions, 1-(6-hydroxy-2-isopropenyl-1-benzofuran-yl)-1-ethanone was extracted from rhizomes of *Petasites hybridus* from northern Iran. The structure of this compound was determined by ^{1}H, ^{13}C NMR spectroscopy.

Keywords: Euparine, Chalcone, Benzaldehyde derivatives, *Petasites hybridus*.

Introduction

The chemistry of chalcones has generated intensive scientific studies throughout the world. Especially interest has been focused on the synthesis and biodynamic activities of chalcones. The name "Chalcones" was given by Kostanecki and Tambor [1]. These compounds are also known as benzalacetophenone or benzylidene acetophenone. In chalcones, two aromatic rings are linked by an aliphatic three carbon chain. Chalcone bears a very good synthon so that variety of novel heterocycles with good pharmaceutical profile can be designed. Different methods are available for the preparation of chalcones [2-4]. The most convenient method is the Claisen-Schimdt condensation of equimolar quantities of arylmethylketone with aryl aldehyde in the presence of alcoholic alkali [5]. Chalcones are used to synthesize several derivatives like cyanopyridines, pyrazolines isoxazoles and pyrimidines having different heterocyclic ring systems [6-9]. Also, benzofuran derivatives exist in some natural products, euparine or 1-(6-hydroxy-2-isopropenyl-1-benzofuran-yl)-1-ethanone **1** was extracted from rhizomes of *Petasites hybridus* [10]. This compound is soluble in water. It is noteworthy to mention that these classes of compounds have potent biological and medicinal properties and are used in the treatment of severe migraine and MS diseases. Phytochemical analyses of *Petasites hybridus* extracts reveal different patterns of medicinal products and a few reports were observed about the tilted plant [11-14]. Herein, we describe an efficient synthesis of chalcones via the reaction of 1-(6-hydroxy-2-isopropenyl-1-benzofuran-yl)-1-ethanone 1 and benzaldehyde derivatives 2 in the presence of sodium hydroxide in mixture of ethanol and water as the solvent (Scheme **1**).

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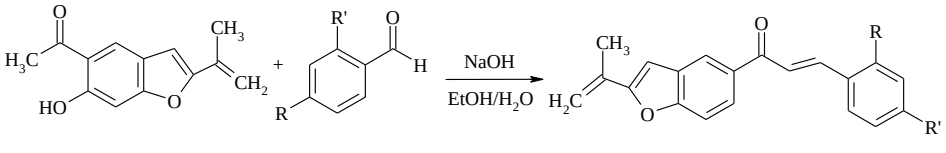
Results and discussion

As indicated in Scheme **1**, 1-(6-hydroxy-2-isopropenyl-1-benzofuran-yl)-1-ethanone **1**, with benzaldehyde derivatives **2** in the presence of sodium hydroxide in mixture of ethanol and water as the solvent to produce chalcone derivatives **3** in good yields (Scheme **1**). Structures of compounds **3a–3d**

were deduced from their IR, ^{1}H NMR and ^{13}C NMR spectra. The ^{1}H NMR spectrum of **3a** exhibited one singlet for the hydroxyl group at (δ 13.24 ppm). Also two singlets display at (3.88 and 2.17 ppm) for methoxy and methyl groups at (3.75 and 3.82 ppm) respectively. The proton decoupled ^{13}C NMR spectrum of **3a** showed distinct resonances in agreement with the proposed structure. Three single resonances at δ = 193.3; 162.8 and 161.9 ppm are observed in the ^{13}C NMR spectrum of **3a**, which are attributed to the carbonyl groups.

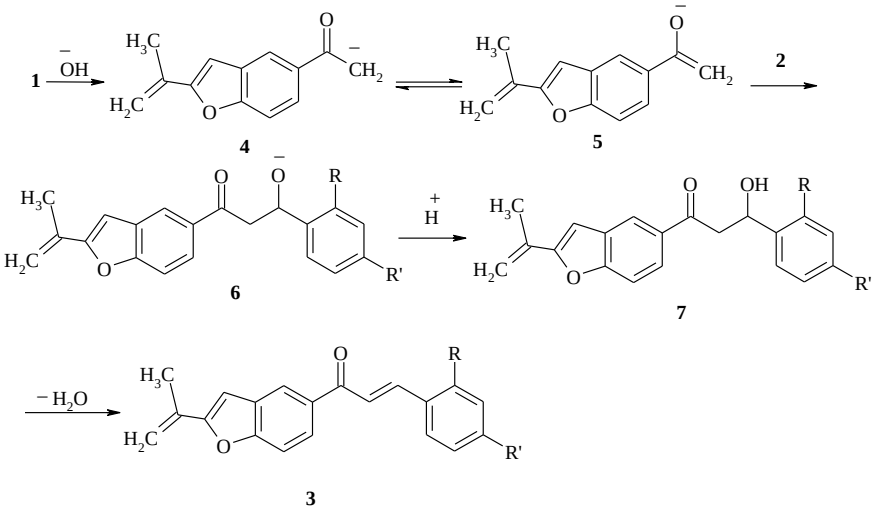


1 **2** **3**

2, 3	R	R'	yield % of **3**
a	CH_3O	H	95
b	H	CH_3O	93
c	CH_3	H	94

Scheme 1: Schematic synthesis of chalcones.

Although we have not established the mechanism of these reactions, a possible explanation is proposed in Scheme **2**. It is reasonable to assume that the enolate **5** results from an initial addition of the 1-(6-hydroxy-2-isopropenyl-1-benzofuran-yl)-1-ethanone **1** and sodium hydroxide in water. Enolate **5** attack to benzaldehyde derivatives **2** as the nucleophile to produce intermediate **6**. Finally by elimination of H_2O chalcone derivatives **3** was produced.with in mixture of resulting in the formation of **3.**



Scheme 2: Possible mechanism for the formation of chalcones 3.

Conclusion

A facile method describes for the synthesis of chalcone derivatives from extracted benzofurane derivatives with benzaldehyde derivatives in the presence of sodium hydroxid in mixture of ethanol and water as the solvent. The present method carries the advantage that, not only is the reaction performed under neutral conditions, but also the substrates can be reacted without any prior activation or modification. The simplicity of the present procedure makes it an interesting alternative to complex multistep approaches.

Experimental

Compound **1** was extracted from rhizomes of *Petasites hybridus* in northern Iran [10]. Other chemicals were obtained from were obtained from

Fluka and were used without further purification. ^{1}H NMR and ^{13}C NMR spectra were obtained with a Bruker FT-400 spectrometer in chloroform-d[1], and tetramethylsilane (TMS) was used as an internal standard.

General procedure:

To a stirred mixture of 1-(6-hydroxy-2-isopropenyl-1-benzofuran-yl)-1-ethanone (2 mmol) and sodium hydroxide (2.1 gr) in water/ethanol (20/12 cc) as the solvent, benzaldehyde derivatives (2 mmol) was added slowly. The reaction mixture was stirred for 7 h at room temperature. The resulting precipitate was separated by filtration and recrystallized from diethyl ether (Et_2O) to afford the pure title compounds.

E-1-(6-hydroxy-3-(prop-1-en-2-yl)benzofuran-5-yl)-3-(4-methoxy phenyl) prop-2-en-1-one (**3a**):

^{1}HNMR(400 MHz, $CDCl_3$): 2.17 (*s*, 3H, Me) , 3.88 (*s*, 3H, MeO), 5.22 (*s*, 1H, CH), 5.79 (*s*, 1H, CH), 6.60 (*s*, 1H, CH), 7.00 (*d*, 2H, ^{3}J = 8.4Hz, 2CH), 7.05 (*s*, 1H, CH), 7.61 (*d*, 1H, ^{3}J =15.2Hz, CH), 7.68 (*d*, 2H, ^{3}J = 8.8Hz, 2 CH), 7.94 (*d*,1H, ^{3}J = 15.2Hz, CH), 8.13 (*s*, 1H, CH), 13.24 (*s*, 1H, OH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 38.2, 55.5, 59.5, 99.7, 102.5, 113.6, 114.5, 117.3, 118.0, 121.8, 123.3, 127.5, 130.5, 132.2, 145.0, 157.8, 161.9, 162.8, 193.3 ppm.

E-1-(6-hydroxy-3-(prop-1-en-2-yl)benzofuran-5-yl)-3-(2-methoxyphenyl)prop-2-en-1-one (**3b**):

^{1}HNMR(400 MHz, $CDCl_3$): 2.13(s, 3H, CH_3), 3.97(s, 3H, OCH_3), 5.20 (s, 1H, CH), 5.70 (s, 1H, CH), 6.62 (s, 1H, CH), 6.02 (d, 1H, CH), 7.02(t,^{3}J = 9Hz, 1H, CH), 7.04(s, 1H, CH), 7.43 (t, 1H, ^{3}J = 9Hz, CH), 7.69 (d, 1H, ^{3}J = 6Hz, CH), 7.83(d, 1H, ^{3}J = 15Hz, CH), 8.11(s, 1H, CH); 8.26 (d, 1H, ^{3}J = 18Hz, CH), 13.24(s, 1H, OH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.2, 19.2, 55.6, 99.6, 102.5, 111.3, 113.5, 117.3, 120.8, 121.1, 121.8, 122.5, 123.7, 129.5, 132.1, 132.2, 140.8, 158.9, 162.7, 193.9 ppm.

E-1-(6-hydroxy-3-(prop-1-en-2-yl) benzofuran-5-yl)-3-P-tolylprop-2-en-1-one (**3c**):

^{1}H NMR(400 MHz, $CDCl_3$): 2.15 (*s*, 3H, Me), 2.65 (*s*, 3H, Me), 5.22 (*s*, 1H, CH), 5.80 (*s*, 1H, CH), 6.61 (*s*, 1H, CH), 7.07 (*s*, 1H, CH), 7.15(*d*, 2H, ^{3}J = 8.4 Hz, 2 CH), 7.46 (*d*, 2H, ^{3}J = 8.4Hz, 2CH), 7.67 (*d*, 1H, ^{3}J =17.2 Hz, CH), 7.94 (*d*, 1H, ^{3}J = 16Hz, CH), 8.12 (*s*, 1H, CH), 13.05 (*s*, 1H, OH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): 38.2, 59.5, 99.7, 102.5, 113.7, 117.2, 119.4, 121.9, 122.4, 128.8, 129.8, 131.2, 132.2, 141.5, 145.3, 157.8, 159.7, 162.8, 193.4 ppm.

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