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Selectfluor Promoted Environmental-Friendly Synthesis of 2H-Chromen-2-ones Derivatives under Various Reaction Conditions

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A simple, clean and benign route to the synthesis of 2H-chromen-2-ones derivatives through one-pot condensation of β-ketoesters and substituted phenols in the presence of 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bistetrafluoroborateis (Selectfluor^{TM} F-TEDA-BF_4) as catalyst under solvent free reaction conditions was experimented. The application of ultrasonic irradiation improved the yields and reduced the reaction times. The use of selectfluor catalyst is feasible because of its stability, commercial value, easy handling, easy recovery and good activity. To extend our research, the ability of selectfluor for the synthesis of 2-aminochromene derivatives was also examined.

Keywords: Selectfluor, Solvent free, Phenol, β-Ketoesters, Chromen, Ultrasound

INTRODUCTION

1-Chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bistetrafluoroborateis (Selectfluor^{TM} F-TEDA-BF_4, Fig. 1) is the most valuable reagent for electrophilic fluorination reaction [1-4]. Recently, it has been used as a versatile mediator or catalyst for various other functionalisations of organic compounds. Its application for selective and effective oxidation of alcohols [5], bromination [6], iodination [7], nitration and thiocyanation of some organic compounds [8] is reported.

Coumarins have attracted considerable interest because they possess various biological activities such as antiviral [9], antibacterial [10], antimicrobial [11], antiinflammatory [12], anticancer [13] activity as well as inhibition of platelet aggregation [14] and inhibition of steroid 5a-reductase [15]. Some coumarins have been used as photosensitizers [16], fluorescent and laser dyes [17]. These compounds are also utilized in drug and pesticidal preparations [18]. Moreover, these compounds can be used as fragrances, pharmaceuticals, agrochemicals [19] and as antioxidants in lipid peroxidation [20]. Application of coumarin derivatives for the synthesis of some fused ring heterocyclic compounds is also reported [21,22]. Several publications have described the preparation of coumarin derivatives from the reaction of phenols with β-keto esters in the presence of different catalysts such as $ZrCl_4$, $ZnCl_2$, $AlCl_3$, $ZnCl_2/Al_2O_3$, H_2SO_4, TBACl, P_2O_5, montmorillonite clay and $Cu(ClO_4)_2$ [23-29]. However, some of these methods suffer from one or more disadvantages such

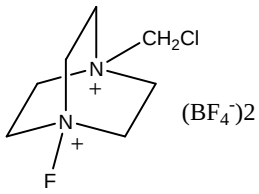

Fig. 1

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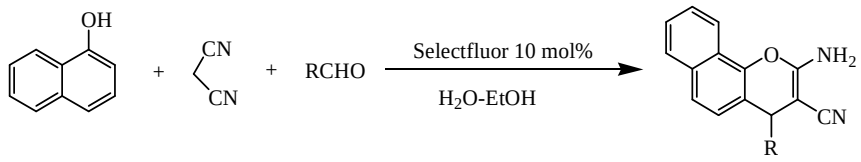


R = 2,4-dichlorobenzaldehyde 93% Yield

R = 4-(dimethylamino)benzaldehyde 94% Yield

Scheme 1

as long reaction times, harsh reaction conditions, tedious work-up procedure, use of highly flammable and expensive reagents, formation of by-products, and low yields of the desired products. Therefore, introduction of new methods and catalysts for the preparation of coumarin is axiomatic.

Here, we would like to report the catalytic activity of selectfluor reagent in the one-pot synthesis of 2H-chromen-2-ones derivatives under stirring at room temperature or ultrasonic irradiation conditions (Scheme 1). Also, the ability of selectfluor for the synthesis of 2-aminochromene derivatives is reported.

EXPERIMENTAL

Chemicals and Apparatus

All chemicals used in this research were purchased from Merck and Aldrich Company. NMR spectra were recorded on a Bruker DRX300 spectrometer operating at 300 MHz for ^{1}H nuclei and 75 MHz for ^{13}C nuclei with tetramethylsilane as the internal standard. Mass spectra were recorded using a VG70-SE spectrometer operating at nominal accelerating voltage of 70 eV. Thin layer chromatography (TLC) was run on silica percolated aluminium plates (Merck Kieselgel F254). Melting points were determined on a Kofler hot-stage apparatus. A multiwave ultrasonic generator (Bandlin Sonopuls Gerate-Typ: UW 3200, Germany) equipped with a converter/ transducer and titanium oscillator (horn), 12.5 mm in diameter, operating at 30 kHz with a maximum power output of 780W, was used for the ultrasonic irradiation.

General Procedure for the Preparation of 2H-Chromen-2-ones Derivatives

Method A. Selectfluor (10 mol%) was added to a mixture of substituted phenol (10 mmol) and metyl acetoacetate (15 mmol) and the reaction mixture was stirred at room temperature for 80-90 min. After the completion of the reaction (monitored by TLC), CH_2Cl_2 was added after which the reaction mixture was filtered. The solvent was evaporated to obtain crude solid and recrystallized from ethanol to afford pure product.

Method B. Selectfluor (10 mol%) was added to a mixture of substituted phenol (10 mmol) and metyl acetoacetate (15 mmol) and the reaction mixture was irradiated with ultrasound for 15-40 min. After the completion of the reaction (monitored by TLC), CH_2Cl_2 was added following which the reaction mixture was filtered. The solvent was evaporated to obtain crude solid and recrystallized from ethanol to afford pure product.

General Procedure for the Preparation of 2-Aminochromene Derivatives

Selectfluor (10 mol%) was added to a mixture of substituted aldehyde (1 mmol), malononitrile (1 mmol), α- or β-naphthol (1 mmol) in H_2O-EtOH (10 ml, 1:1) solvent and the reaction mixture was stirred at room temperature for 90 min. After the completion of the reaction (monitored by TLC), CH_2Cl_2 was added and then the reaction mixture was filtered. The solvent was evaporated to obtain crude solid and recrystallized from ethanol to afford pure product.

RESULTS AND DISCUSSION

The reaction between phenol and ethyl acetoacetate was selected as the model reaction for optimization of various parameters. The reaction was started with different amounts of catalyst ranging from 5 to 30 mol% of selectfluor separately

(Table 1).

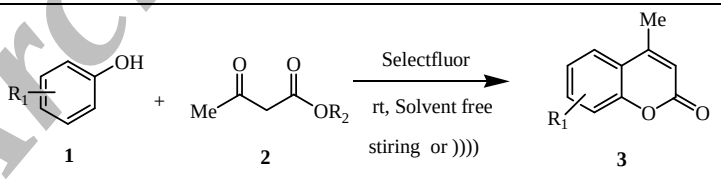
The best results were obtained using 10 mol% of the catalyst. It was found that above and below 10 mol% of selectfluor, the yield of the product decreased. In the absence of the catalyst yield was found to be very low (Table 1). To make it clean and green, the reaction was triggered under solvent free reaction conditions.

The effect of ultrasound irradiation on this procedure was investigated. The synthesis of 4-methyl-2H-chromen-2-one took place in the presence of 0, 5, 10, 15, 20 and 30 mol% of selectfluor with and without ultrasound irradiation (Table 1). In all the reactions, it was found that the use of ultrasound radiations resulted in faster reaction and higher yields. A wide range of substituted phenols was used to give maximum yields (Table 2). All products have been described previously and are fully characterized by NMR, IR and melting point by

Table 2. Effect of the Catalytic Amounts of Selectfluor with or Without Sonication for Synthesis of 4-Methyl-2H-chromen-2-one at Room Tempratur

Entry	SF (mol%)	Method A		Method B	
		Time (min)	Yield (%)	Time (min)	Yield (%)
1	0	60	0	60	0
2	5	60	45	35	55
3	10	60	65	30	82
4	15	60	70	30	73
5	20	70	90	40	75
6	30	70	87	40	75

Table 2. Synthesis of Substituted 2H-Chromen-2-ones 3



1 **2** **3**

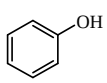
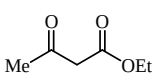
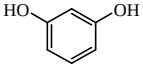
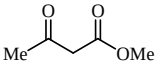
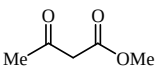
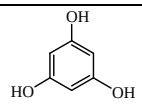
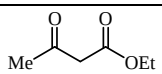
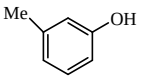
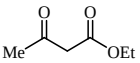
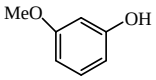
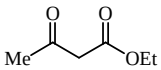
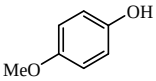
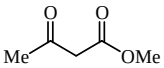
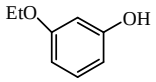
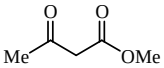
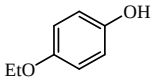
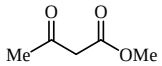
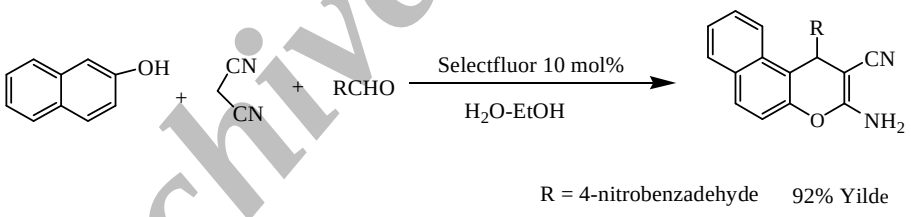
Entry	Phenol (1)	β-diketone (2)	Method A		Method B	
3a			Time (min)	Yield (%)	Time (min)	Yield (%)
3b			90	70	40	82
3c			85	75	20	92
3d			80	80	15	95

Table 2. Continued

3e			85	79	15	94
3f			90	73	30	90
3g			80	80	25	91
3h			85	83	20	92
3i			90	80	30	90
3j			90	82	35	90



Scheme 2

comparison with the reported literature data.

As part of our ongoing interest in the selectfluor catalyzed reactions for various organic transformations, we examined three-component one-pot synthesis of 2-aminochromene derivatives by condensing malononitrile, α- or β-naphthol and aromatic aldehydes in aqueous ethanol in the presence of selectfluor as a heterogeneous and reusable catalyst. Treatment of 4-(dimethylamino)benzaldehyde or 2,4-dichloro-benz-aldehyde, malononitrile, and α-naphthol in the presence of selectfluor in aqueous ethanol under refluxing conditions resulted in the formation of 2-amino-2-chromene (Scheme 1). Under similar reaction conditions, β-naphthol gave 2-amino-2-chromenes in excellent yield (Scheme 2)

CONCLUSIONS

Selectfluor is not only one of the most valuable reagents for electrophilic fluorination but also can be used as a versatile catalyst for environmental-friendly synthesis of 2H-chromen-2-ones derivatives. Unlike some reported methods, this method offers several noteworthy advantages including good yields of products, easy work-up, in combination with stability, non-toxicity, easy preparation and cheapness of the catalyst. On the other hand, ultrasonic irradiation increased the

catalytic activity and higher product yields were obtained.

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