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VANADIUM(III) CHLORIDE AS AN EFFECTIVE CATALYST FOR THE PECHMANN REACTION

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Good yields of substituted coumarins were obtained by a synthetic method involving the Pechmann reaction using vanadium(III)chloride (VCl_3) reagent to effect this condensation under solvent-free conditions.

Keywords: coumarins, vanadium(III) chloride, Pechmann reaction.

Coumarins and chromones are naturally occurring important plant constituents and occupy a unique place in natural and synthetic organic chemistry. Plants belonging to the natural orders of orchidaceae, leguminoceae, rutaceae, umberlliferae, and labiatae are rich sources of naturally occurring coumarins. Members of this group have a broad range of applications as fragrances, pharmaceuticals, and additives to food and cosmetics [1, 2]. Methyl coumarins occur in the heartwood of various plants and some of them possess antibiotic [3] and antiviral [4] properties, while others are used as fluorescent brighteners, photographic sensitizers, and dyes [5]. Coumarin derivatives have also found applications as CNS depressants [6], antitumour agents [7], HIV inhibitors [8], and as intermediates for the synthesis of the cardiac drug carbochromene [9]. The potent antibiotics chartrecisin [10] and coumarmycine [11] are also coumarin derivatives. Coumarins act as intermediates for the synthesis of polysubstituted heterocycles, which are most interesting compounds as potential biodegradable agrochemicals.

There are some well-known synthetic methods used for the synthesis of coumarins. All these methods center around the possibility of building up the pyrone ring on suitable benzene derivative. However, some of the classified methods, which have attained significant importance for the synthesis of coumarin derivatives, are Perkin [12], Pechmann [13], Pechmann–Duisburg, Knoevenagel [l4], Reformatsky [15], and Wittig reactions [16, 17]. The rapid development in the chemistry of coumarins is mainly due to the synthetic method universally known as the Pechmann reaction, which consists in the reaction of phenol with β-keto ester in the presence of sulfuric acid as a cyclizing agent. Since the Pechmann reaction proceeds from very simple starting materials and gives good yields of coumarin derivatives, it is the most widely used method for the preparation of various substituted coumarins. Various cyclizing reagents like H_2SO_4, P_2O_5, $FeCl_3$, $ZnCl_2$, $POCl_3$, $AlCl_3$, HCl, phosphoric acid, and trifluoroacetic acid [18-22] are known to affect the Pechmann condensation. A mixture of phenol, β-keto ester, and the acidic catalyst was allowed to stand for long time or was heated above 150°C in all the methods. Recently an attempt was made to use a solid acid catalyst for this reaction [23]. Application of ionic liquids [24] and sulfamic acid was also reported [25]. However, all these reactions require high

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TABLE 1. Synthesis of Substituted Coumarins from Phenols and β-Keto Esters* Catalyzed by VCl_3

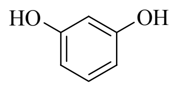
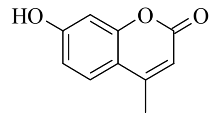
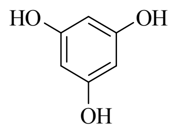
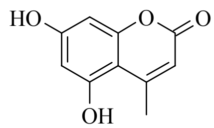
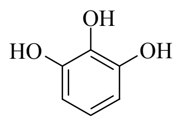
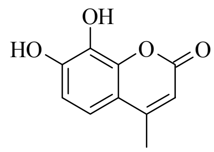
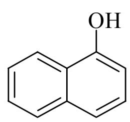
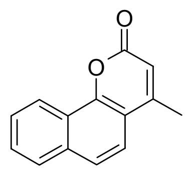
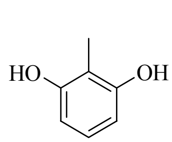
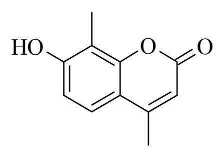
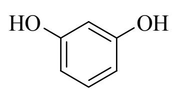
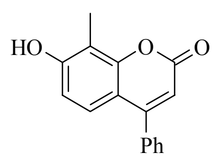
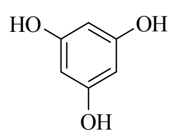
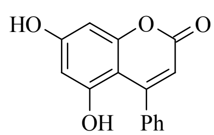
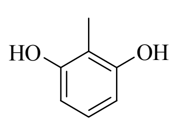
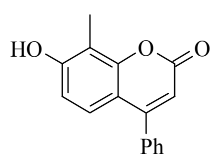
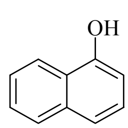
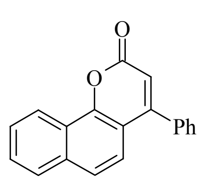
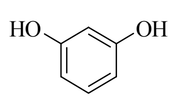
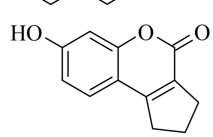
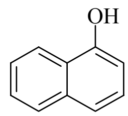
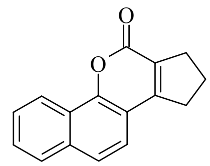
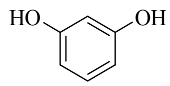
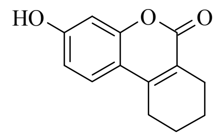
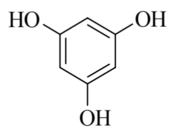
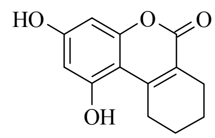
Entry	Phenol **1**	Product **3**	mp, °C*[2]	Yield, %
1	2	3	4	5
1			181-183	92
2			283-284	90
3			254-255	90
4			154-155	86
5			248-250	91
6			241-242	92
7			243-244	84
8			244-246	88
9			240-241	87
10			245-246	90

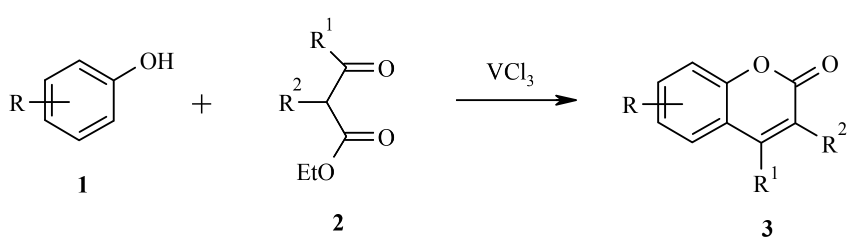
TABLE 1 (continued)

1	2	3	4	5
11			217-218	88
12			245-246	94
13			251-253	92

* β-Keto ester **2**: ethyl acetoacetate (1-5), ethyl benzoylacetate (6-9), 2-carbethoxycyclopentanone (10, 11), and 2-carbethoxycyclohexanone (12, 13).
*[2] mp according to the data of [25].

temperatures (150°C or above) or long reaction times; an excess amount of the catalyst is also a requirement for such reactions, and sometimes the yields are low. Several reports are also available on the use of microwaves for the accelerated synthesis of different coumarins [26-29].

We report in this communication a facile one-step synthesis of coumarin derivatives by the Pechmann reaction using vanadium(III) chloride as a new condensing agent. Simple workup, less reaction time, and solvent-free conditions are the advantages of using vanadium(III) chloride as a catalyst in the synthesis of coumarin derivatives by the application of the Pechmann reaction. This method is very effective and superior to earlier reported methods as it affords good yields without causing any side reaction.



The reaction was studied by using different concentrations of reactants and catalyst at different temperatures under neat conditions. The best results were achieved when the reactions were carried out at 50-55°C for 2 h using 10% of the catalyst with respect to the quantity of reactants in the absence of the solvent. The generality and scope of the reaction are summarized in Table 1.

EXPERIMENTAL

General Procedure for the Preparation of Coumarin Derivatives Using VCl_3. A mixture of the appropriate phenol (1 mmol) and β-keto ester (1 mmol) was stirred at 50-55°C for 2 h with VCl_3 (0.1 mmol). The progress of the reaction was monitored by TLC. After completion of the reaction the reaction mass was cooled to room temperature, water (25 ml) was added, and the whole stirred for 30 min. The solid obtained was filtered off, washed with water, and recrystallized from ethanol.

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