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Zirconyl (IV) Chloride Catalyzed Solvent-Free Von Pechmann Synthesis Of Coumarins

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ABSTRACT

Zirconyl (IV) chloride is used as an efficient catalyst in the Von Pechmann condensation reaction of phenols with β-keto esters leading to the formation of coumarin derivatives in excellent yields under solvent-free conditions.

KEYWORDS

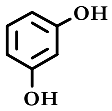
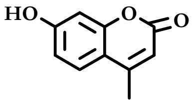
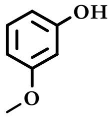
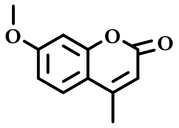
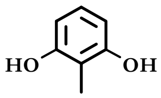
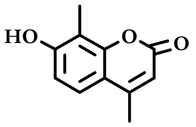
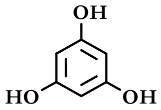
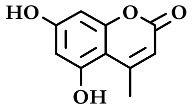
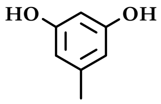
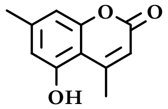
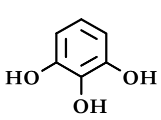
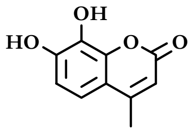
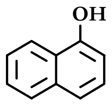
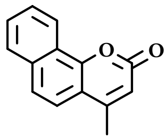
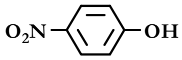
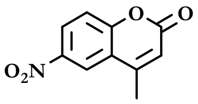
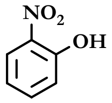
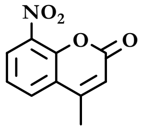
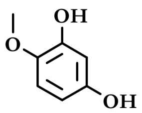
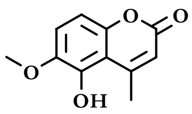
Zirconyl (IV) chloride;
Von Pechmann reaction;
Coumarin;
Solvent-free.

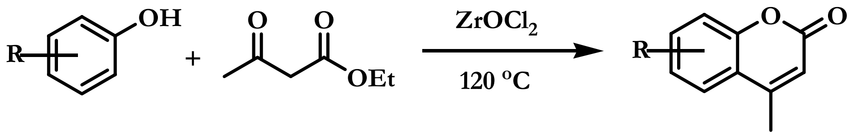
INTRODUCTION

The Pechmann reaction is the most widely applied method for synthesizing coumarins and it involves the condensation of phenol with β-ketonic esters in the presence of a variety of acidic condensing agents and gives good yields of 4-substituted coumarins[1,2]. Coumarins occupy an important place in the realm of natural and synthetic organic chemistry. Coumarin compounds are used for the synthesis of fluorocoumarins, chromones, coumarones, 2-acyl resorcinol[3], additive in food and cosmetics[4] and possess the biological activity like anthelminthic, hypnotic, insecticidal and anticoagulants[5]. Coumarin have synthesised by several methods including Von Pechman reaction[6], Perkin reaction[7] Knovenenagel condensation[8,9] Reformatsky reaction[10] and Wittig reaction[11,12].

Several acid catalyst have been used in the Von Pechman reaction[6], including sulfuric acid[6], phosphorus pentoxide[13,14], aluminum chloride[15], trifluoacetic acid[16] and many more. However these catalyst have to be used in excess, for example sulfuric acid,[10-12] equivalents, trifluoroacetic acid, 3-4 equivalents. Phosphorus pentoxide is required in 5-fold excess. Further such reactions require longer reaction time and in some cases the yields are poor. Recently Von Pechman reaction has been carried out

TABLE 1: Zirconyl (IV) chloride promoted synthesis of coumarins

Entry	Phenol	Product	M.P.(^{o}C)	Yield (%)
1.			184 185 [20]	95
2.			162 160-162 [21]	88
3.			138-141 137-139 [16]	88
4.			279-282 280-285 [20]	85
5.			258 258-259 [17]	82
6.			236 236-238 [22]	78
7.			152 150-151 [17]	82
8.			152 150-151 [17]	79
9.			183-185 184-186 [17]	75
10.			165-166 164-165 [20]	75



SCHEME 1

(1-10)

successfully using microwave irradiation[17,18] and in ionic liquids[19] as alternative to conventional methods.

Due to their easy availability and low toxicity Zr(IV) salt have recently attracted much attention. This has been reflected in their application, specially, zirconium(IV) chloride ($ZrCl_4$) as an Lewis acid for various transformations. Zirconyl (IV) chloride ($ZrOCl_2{\cdot}8H_2O$) is moisture stable, readily available and inexpensive oxysalt of zirconium and its handling is easier in comparison to that of the moisture sensitive zirconium (IV) chloride.

In continuation of our work to develop new synthetic methodologies[20] herein, we report a general and practical route for the Pechman condensation using $ZrOCl_2{\cdot}8H_2O$ as the catalyst as shown in SCHEME 1. In the presence of $ZrOCl_2{\cdot}8H_2O$, the reaction of ethyl acetoacetate and resorcinol was carried out in one-pot condition at 120 ^{0}C and resulted in the formation of 7-hydroxy-4-methyl coumarin in 95 % yield. To extend the scope of this reaction and to generalize the procedure, we investigated the reaction of a series of monhydric and polyhydric Phenol with a β-ketoesters to obtain the corresponding coumarins. (TABLE 1). Many pharmacologically relevant substitution patterns on the aromatic ring could be introduced with high efficiency and most importantly, phenols carrying either electron-donating or electron withdrawing substituents all reacted very well, giving moderate to excellent yields with high purities. In general we observed that the reaction proceeded faster than conventional ones and the yields were comparable.

In conclusion, we have demonstrated an efficient and simple alternative for the preparation of substituted coumarins via solvent-free Pechman condensation using zirconyl (IV) chloride as catalyst. Prominent among the advantages of this new method are operational simplicity, good yields, shorter reaction times, very inexpensive, easily available catalyst and easy workup procedure employed.

EXPERIMENTAL

A mixture of resorcinol (1.1 g·10 mmole), ethyl acetoacetate (1.3 g·10 mmole) and $ZrOCl_2{\cdot}8H_2O$ (2mmole) was refluxed at 120°C for 90 minutes (monitored by TLC). The reaction mixture, after being cooled to room temperature, was poured into crushed ice (40 g.) and stirred for 5-10 min. The crystalline products were collected by filtration , washed with ice cold water and then recrystallized from ethanol to afford pure 7-hydroxy-4-methylcoumarin as yellowish prism.

m.p.184°C

^{1}HNMR ($CDCl_3$) δ ppm: 2.2 (s,3H,-CH_3), 6.1(s,1H), 6.83(d,1H), 6.97(s,1H), 7.5(d,1H);

Mass (ES/MS) : m/z 175 (M - H)

IR (KBr) 2985, 1740, 1625 cm.

This procedure was followed for the preparation of all the substituted coumarins listed in the TABLE 1. All the compounds were identified by modern analytical techniques like IR, ^{1}HNMR and mass spectra and melting point were compared with those reported.

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