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# Ceric Ammonium Nitrate (CAN): An Efficient Catalyst for the Coumarin Synthesis via Pechmann Condensation using Conventional Heating and Microwave Irradiation

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**Abstract:** An efficient and convenient method for the synthesis of substituted coumarins via Pechmann condensation of different phenols with ethylacetoacetate in the presence of ammonium cerium(IV) nitrate as the catalyst in a solvent-free media using both conventional heating and microwave irradiation.

**Keywords:** Ceric ammonium nitrate (CAN), Coumarins, β-ketoesters, Pechmann condensation

## INTRODUCTION

Coumarins and chromones are naturally occurring important plant constituents and occupy a unique place in natural and synthetic organic chemistry. Coumarin derivatives have a wide range of biological and therapeutic properties such as anthelmintic, anticoagulant, hypnotic, and insecticide properties.[1] Furthermore, they are used as additives in food, perfumes, cosmetics, and pharmaceuticals,[1] optical brighteners,[2] and dispersed fluorescent and laser dyes.[3] Some polycyclic coumarins such as calanolides,[4] isolated from *Calophyllum genus*, and others[5] have

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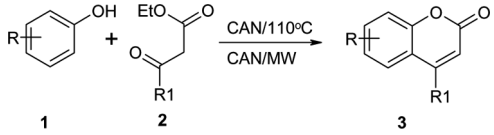



*Scheme 1.*

shown potent anti-HIV activity. Coumarins are prepared by different reactions such as the Pechmann reaction,[6] Knoevenagel reaction,[7] and Wittig reaction.[8] The Pechmann reaction is the most common, a two-component coupling reaction of phenol and β-keto ester in the presence of sulfuric acid as a cyclizing agent.

The reaction can also be catalyzed by different Brønsted and Lewis acids, such as PPA,[9] $InCl_3$,[10] $ZrCl_4$,[11] $Yb(OTf)_3$,[12] *p*-TsOH,[13] $BiCl_3$,[14] and $I_2$ or AgOTf.[15] Because of recent efforts toward green chemistry, attempts are being made to replace stoichiometric Brønsted and Lewis acids by nonstoichiometric solid acids, such as montmorillonite clay[16] and cation-exchanged resin.[17] Application of ionic liquids was also reported.[18]

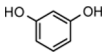
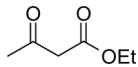
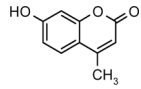
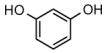
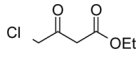
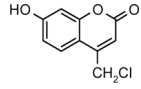
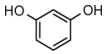
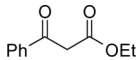
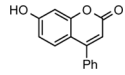
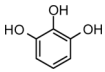
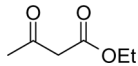
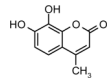
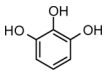
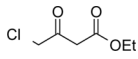
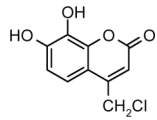
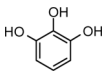
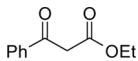
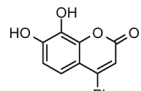
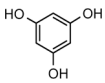
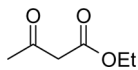
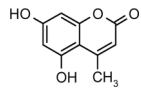
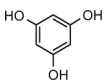
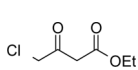
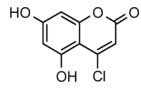
Even though various procedures are reported, disadvantages (including low yields, prolonged reaction times, use of an excess of reagents/catalysts, and use of toxic solvents) necessitate the development of an alternative for the synthesis of coumarin derivatives.

Recently, ceric ammounium nitrate (CAN) has emerged as a promising solid acid catalyst for various chemical transformations.[19] In continuation of our work[20] on the development of new synthetic methodologies using acid catalysts and microwave irradiation, we have observed that CAN is an efficient catalyst for the condensation of phenol with *β*-ketoester in solvent-free media under conventional heating and microwave irradiation (Scheme 1).

## RESULTS AND DISCUSSION

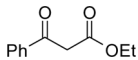
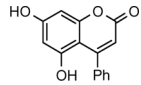
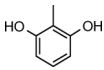
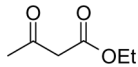
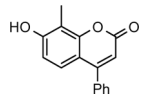
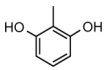
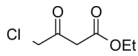
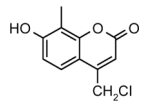
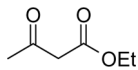
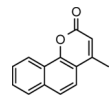
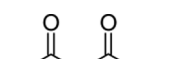
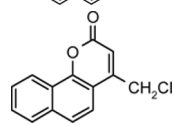
In the conventional procedure (method A), phenol was heated with β-ketoester at 110 °C under solvent-free conditions in the presence of CAN to afford the corresponding coumarin in 10–15 min. As part of our ongoing work with microwave irradiation,[20] phenol was irradiated with β-ketoester under solvent-free conditions in the presence of CAN in a microwave oven (method B) to yield the desired coumarin in 2–3 min (Table 1).

**Table 1.** Ceric ammonium nitrate (CAN)–catalyzed Pechmann synthesis of coumarins

| Phenol | β-ketoester | Coumarin | Method A | | Method B | | Mp (°C) |
|---|---|---|---|---|---|---|---|
| | | | Time (min) | Yield (%)[a] | Time (min) | Yield (%)[a] | |
|  |  |  | 10 | 94 | 2 | 96 | 185[12a] |
|  |  |  | 10 | 92 | 3 | 95 | 180[12c] |
|  |  |  | 15 | 93 | 3 | 95 | 257[12b] |
|  |  |  | 10 | 95 | 2 | 96 | 242[12a] |
|  |  |  | 10 | 96 | 2 | 96 | 134[12d] |
|  |  |  | 15 | 92 | 3 | 94 | 195[12b] |
|  |  |  | 10 | 95 | 3 | 96 | 280[12a] |
|  |  |  | 10 | 93 | 2 | 95 | 187[12d] |

(*Continued*)

**Table 1.** Continued

| Phenol | β-ketoester | Coumarin | Method A Time (min) | Method A Yield (%)[a] | Method B Time (min) | Method B Yield (%)[a] | Mp (°C) |
|---|---|---|---|---|---|---|---|
|  |  |  | 15 | 95 | 3 | 96 | 245[12b] |
|  |  |  | 10 | 96 | 3 | 97 | 264[12b] |
|  |  |  | 10 | 94 | 3 | 94 | 285[12b] |
|  |  |  | 15 | 94 | 3 | 95 | 153[12b] |
|  |  |  | 15 | 93 | 3 | 96 | 166[12b] |

[a]Yields refer to pure products, and all products were characterized by comparison of their physical data and $^1$H NMR, IR, and mass spectral data with those of authentic samples.

## EXPERIMENTAL

### General Procedure: Conventional Heating Method (Method A)

A mixture of the phenol **1** (1 mmol), β-ketoester **2** (1 mmol), and CAN (0.1 mmol) was stirred at 110 °C for the appropriate time according to (Table 1). Completion of the reaction was indicated by thin-layer chromatography (TLC). The reaction was cooled to room temperature, diluted with ethyl acetate, washed with water, and dried over $Na_2SO_4$.

The solvent was removed under vacuum, and the residue was purified by flash chromatography to yield the corresponding coumarin **3**.

### Microwave Irradiation Method (Method B)

A mixture of the phenol **1** (1 mmol), β-ketoester **2** (1 mmol), and CAN (0.1 mmol) was added, and the mixture was inserted in a microwave oven (BPL, 800T model) on a silica-gel solid support and irradiated at 300 W for the appropriate time (Table 1). Completion of the reaction was indicated by TLC. The reaction was cooled to room temperature, diluted with ethyl acetate, washed with water, and dried over $Na_2SO_4$. The solvent was removed under vacuum, and the residue was purified by flash chromatography to yield the corresponding coumarin **3**.

## CONCLUSION

We have demonstrated an efficient and very simple procedure for the synthesis of substituted coumarins by the Pechmann condensation of phenols with β-ketoesters in solvent-free media under conventional heating and microwave irradiation using CAN, which is an inexpensive, nontoxic, and readily available catalyst. Prominent among the advantages of this new procedure are easy workup, good yields, short reaction times, and operational simplicity.

## ACKNOWLEDGMENT

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