Available online at www.sciencedirect.com
SCIENCE DIRECT®
Tetrahedron Letters 45 (2004) 7999–8001
Tetrahedron Letters

Samarium(III) catalyzed one-pot construction of coumarins

Sushilkumar S. Bahekar[a] and Devanand B. Shinde[b,*]

[a]Department of Chemistry, National Cheang Kung University, Tainan, Taiwan
[b]Department of Chemical Technology, Dr. Babasaheb Ambedkar Marathwada University, Aurangabad 431004 (MS), India

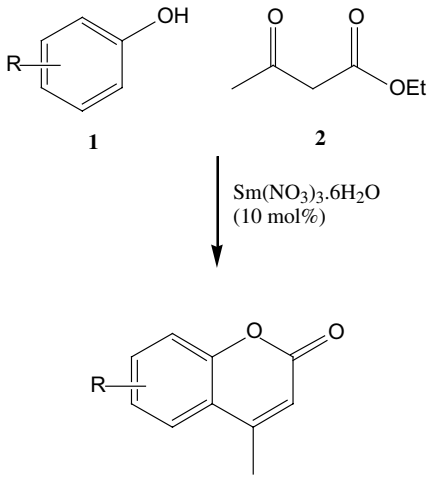
Received 30 June 2004; revised 21 August 2004; accepted 2 September 2004

Abstract—Samarium(III) nitrate hexahydrate as a catalyst is used as an alternative to conventional acid catalysts in the von Pechmann condensation of phenols with ethyl acetoacetate leading to the formation of coumarin derivatives.

Coumarins occupy an important place in the realm of natural products and synthetic organic chemistry. They have been used as anticoagulants,[1] additives in food and cosmetics,[2] and in the preparation of insecticides, optical brighteners,[3] and dispersed fluorescent and laser dyes.[4] Coumarins have synthesized by several methods including the von Pechmann,[5] Perkin,[6] Knoevenagel,[7,8] Reformastsky,[9] and Wittig[10,11] reactions.

The Pechmann reaction is the most widely applied method for synthesizing coumarins as it involves the condensation of phenols with β-ketonic esters in the presence of a variety of acidic condensing agents and gives good yields of 4-substituted coumarins.[12,13] Several acid catalyst have been used in the Pechmann reaction[5] including sulfuric acid,[5] phosphorus pentoxide,[14,15] aluminum chloride,[16] trifluoroacetic acid,[17] and many more.[12] However, these catalysts have to be used in excess, for example sulfuric acid, 10–12 equiv,[13] trifluoroacetic acid, 3–4 equiv.[17] Further the disposal of acidic waste leads to environmental pollution. The Pechmann reaction has been carried out successfully using microwave irradiation[18,19] and in ionic liquids[20] as alternatives to conventional methods.

In recent years, Sm(III) has been used as an efficient Lewis acid for various transformations such as carbon–carbon bond formation,[21] aldol condensations,[22] and β-diketone and α-selenoketone synthesis.[23,24] In this letter we report a general and practical route[25] for the Pechmann condensation using Sm(III) as the catalyst under solvent-free conditions as shown in Scheme 1. This is a novel, one-pot condensation that not only preserves the simplicity of the Pechmann condensation reaction but also consistently produces excellent yields of the coumarin derivatives[19] and greatly decreases environmental pollution. In the presence of $Sm(NO_3)_3 \cdot 6H_2O$ (10 mol%) the reaction of ethyl acetoacetate (**1**, 1 mmol), resorcinol (**2**a, 1 mmol) was carried out in one-pot reaction under solvent-free conditions for 20 min at 80 °C, and resulted in the formation of 7-hydroxy-4-methylcoumarin in 98% yield. A wide range of structurally varied phenols reacted smoothly and very quickly to give



Scheme 1.

Keywords: Coumarins; Pechmann condensation; Lewis acid catalysts.
* Corresponding author. Tel.: +91 0240 2401831; fax: +91 0240 2401833; e-mail: ssbahekar@rediffmail.com

0040-4039/$ - see front matter © 2004 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2004.09.013

Table 1. Synthesis of coumarins via von Pechmann condensation of phenols with β-ketoesters catalyzed by $Sm(NO_3)_3{\cdot}6H_2O$

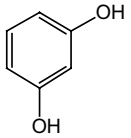
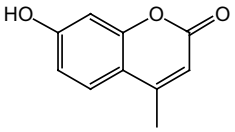
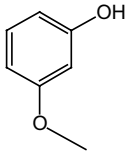
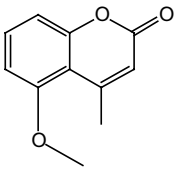
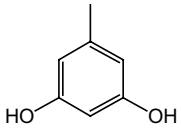
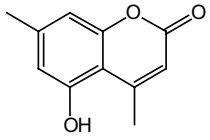
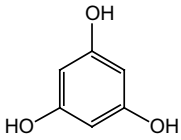
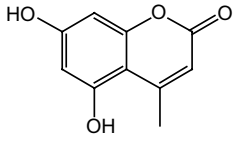
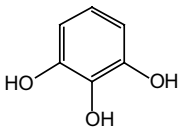
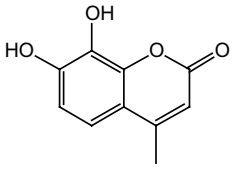
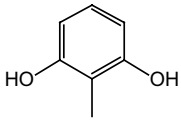
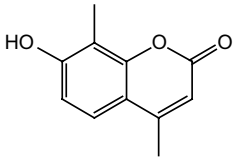
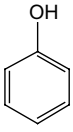
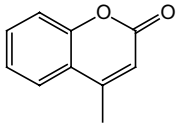
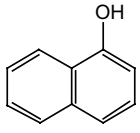
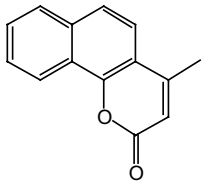
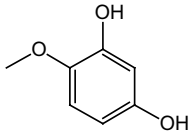
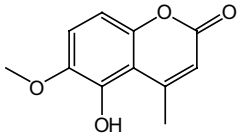
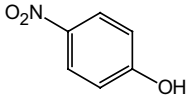
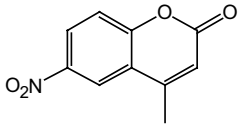
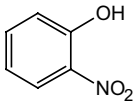
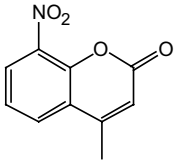
Entry	Phenol **2**	Time[c] (min)	Product **3**[a,d]	MP	Yields[b] (%)
1		20		185–187 185[27]	98
2		25		160–162 161–162[26]	94
3		15		257–258 258–259[18]	89
4		25		281–283 280–285[27]	95
5		20		236–239 236–238[28]	92
6		30		138–139 137–139[17]	90
7		90		78–80 82[26]	50
8		60		154–156 155[27]	85
9		40		163–164 164–165[27]	45
10		20		151–154 150–151[18]	75

Table 1 (*continued*)

Entry	Phenol **2**	Time[c] (min)	Product **3**[a,d]	MP	Yields[b] (%)
11		35		183–185 184–186[18]	70

[a] All products were characterized by comparison of their mp, IR, and ^{1}H NMR spectra with those of authentic samples.
[b] Isolated yields.
[c] All reactions refluxed at 80 °C.
[d] Elemental analyses (±0.4% of the calculated values) were obtained for all compounds.

the corresponding coumarins in high yield and purity as listed in 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.

To study the substituent effects on the reactivity of the phenol, the reaction was performed on a variety of phenols. The reaction worked well and the results are illustrated in Table 1. For most of the substrates, the reaction time was reduced drastically even at ambient conditions in contrast to reported procedures[12,13] and gave an excellent yield of the coumarins. Substrates having electron-donating groups *para* to the site of electrophilic substitution gave maximum yields in the minimum time.

In conclusion, we have developed[25] a novel and simple modification of the von Pechmann condensation reaction using $Sm(NO_3)_3{\cdot}6H_2O$ as the catalyst under solvent-free conditions.

References and notes

1. Singer, L. A.; Kong, N. P. *J. Am. Chem. Soc.* **1966**, *88*, 5213.
2. O'Kennedy, R.; Thornes, R. D. *Coumarins: Biology, Applications and Mode of Action*; Wiley & Sons: Chichester, 1997.
3. Zahradnik, M. *The Production and Application of Fluorescent Brightening Agents*; Wiley & Sons, 1992.
4. Murray, R. D. H.; Mendez, J.; Brown, S. A. *The Natural Coumarins: Occurrence, Chemistry and Biochemistry*; Wiley & Sons: New York, 1982.
5. von Pechmann, H.; Duisberg, C. *Chem. Ber.* **1884**, *17*, 929.
6. Jonson, J. R. *Org. React.* **1942**, *1*, 210.
7. Jones, G. *Org. React.* **1967**, *15*, 204.
8. Brufola, G.; Fringuelli, F.; Piermatti, O.; Pizzo, F. *Heterocycles* **1996**, *43*, 1257.
9. Shriner, R. L. *Org. React.* **1942**, *1*, 1.
10. Narasimahan, N. S.; Mali, R. S.; Barve, M. V. *Synthesis* **1979**, 906.
11. Yavari, I.; Hekmat-Shoar, R.; Zonouzi, A. *Tetrahedron Lett.* **1998**, *39*, 2391.
12. Sethna, S.; Phadke, R. *Org. React.* **1953**, *7*, 1.
13. Russell, A.; Frye, J. R. *Org. Synth.* **1941**, *21*, 22.
14. Simmonis, H.; Remmert, P. *Chem. Ber.* **1914**, *47*, 2229.
15. Robertson, A.; Sandrock, W. F.; Henry, C. B. *J. Chem. Soc.* **1931**, 2426.
16. Sethna, S. M.; Shah, N. M.; Shah, R. C. *J. Chem. Soc.* **1938**, 228.
17. Woods, L. L.; Sapp, J. *J. Org. Chem.* **1962**, *27*, 3703.
18. de la Hoz, A.; Moreno, A.; Va'zquez, E. *Synlett* **1999**, 608.
19. Fre're, S.; Thie'ry, V.; Besson, T. *Tetrahedron Lett.* **2001**, *42*, 2791.
20. Potdar, M. K.; Mohile, S. S.; Salunkhe, M. M. *Tetrahedron Lett.* **2001**, *42*, 9285.
21. Yu, Y.; Lin, R.; Zhang, Y. *Tetrahedron Lett.* **1993**, *34*, 4547.
22. Bao, W.; Zhang, Y.; Wang, J. *Synth. Commun.* **1996**, *26*, 3025.
23. Ying, T.; Bao, W.; Zhang, Y. *Synth. Commun.* **1996**, *26*, 2905.
24. Ying, T.; Bao, W.; Zhang, Y. *Synth. Commun.* **1996**, *26*, 1517.
25. Typical experimental procedure: A mixture of resorcinol (1.1 g, 10 mmol) and ethyl acetoacetate (1.3 g, 10 mmol) was heated under reflux in the presence of $Sm(NO_3)_3{\cdot}6H_2O$ (10 mol%) for 20 min on 80 °C (TLC) under nitrogen. The reaction mixture, after being cooled to room temperature, was poured onto crushed ice (40 g) and stirred for 5–10 min. The crystalline products were collected by filtration under suction (water aspirator), washed with ice-cold water, and then recrystallized from hot ethanol to afford pure 7-hydroxy-4-methylcoumarin **3a**[27] as colorless prisms (1.73 g, 98%), mp 185–187 °C. ^{1}H NMR ($CDCl_3$) 2.2 (s, 3H, $-CH_3$), 6.1 (s, 1H), 6.83 (d, 1H), 6.97 (s, 1H), 7.5 (d, 1H); IR (KBr) 2985, 1740, 1625 cm. This procedure was followed for the preparation of all the substituted coumarins listed in Table 1. All the compounds were identified by comparison of analytical data (IR, ^{1}H NMR, and mass spectra) and mp's with those reported.
26. Abram, N. B.; Jack, D.; William, L. W. *J. Med. Chem.* **1986**, *29*, 1094.
27. Khandekar, A. C.; Khadilkar, B. M. *Synlett* **2002**, 152.
28. Konstantina, C. F.; Gautam, D. R.; Hadjipavlou-Litina, D. J.; Kontogiorgis, C. A.; Litinas, K. E.; Nicolaides, D. N. *J. Chem. Soc., Perkin Trans. 1* **2001**, 3073.