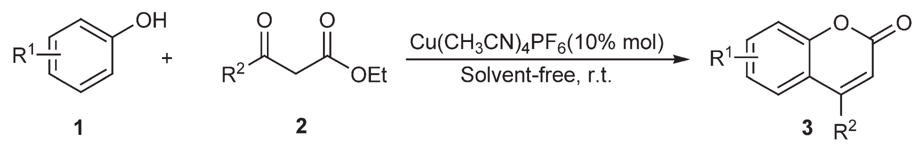
Tetrakis(acetonitrile)copper(I) Hexafluorophosphate Catalyzed Coumarin Synthesis via Pechmann Condensation under Solvent-Free Condition

Ebrahim Soleimani,* Mohammad Mehdi Khodaei,* Nasim Batooie, and Saadi Samadi

Department of Chemistry, Razi University, Kermanshah 67149, Iran
*E-mail: e_soleimanirazi@yahoo.com
Received October 2, 2010
DOI 10.1002/jhet.814
Published online 21 November 2011 in Wiley Online Library (wileyonlinelibrary.com).



Tetrakis(acetonitrile)copper(I) hexafluorophosphate ($Cu(CH_3CN)_4PF_6$) is used as an efficient catalyst in the Pechmann condensation reaction of phenols with ethyl acetoacetate leading to the formation of coumarin derivatives in excellent yields under solvent free conditions at ambient temperature. The method is simple, solvent-free and gives excellent yields in a short reaction time.

J. Heterocyclic Chem., **49**, 409 (2012).

INTRODUCTION

Coumarins occupy an important place in the realm of natural and synthetic organic chemistry. They are 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]. In addition, coumarins have been synthesised by several methods, including Pechmann [5], Perkin [6], Knoevenagel [7], Reformatsky [8], Wittig reactions [9], and Flash Vacuum Pyrolysis [10]. Among these, the Pechmann reaction is the most widely used method, as the reaction involves the use of simple starting materials, that is, phenols and β-ketoesters, in the presence of a variety of acidic condensing agents and gives good yields of 4-substituted coumarins. Several acid catalysts have been used in the Pechmann reaction including sulfuric acid [5], aluminum chloride [11], phosphorus pentoxide [12], trifluoroacetic acid [13], and others. However, these catalysts have to be used in excess; for instance, sulfuric acid in ten equivalents, trifluoroacetic acid in three to four equivalents, and phosphorus pentoxide is required in five equivalents. In all these methods, mixtures of the reagents were allowed to stand overnight or for a number of days, depending on their reactivity, or were heated above 150°C, and unwanted side products such as chromones were obtained. Recently, a number catalysts such as $BiCl_3$ [14], $Sm(NO_3)_3{\cdot}6H_2O$ [15], $InCl_3$ [16], $TiCl_4$ [17], $Yb(OTf)_3$ [18], *p*-Toluenesulfonic acid [19], AgOTf [20], ceric ammonium nitrate [21], montmorillonite clay [22], silica sulfuric acid [23], chloroaluminate ionic liquid [24], heteropolyacids [25], $Bi(NO_3)_3{\cdot}5H2O$ [26], sulphamic acid [27], sulfonic acid nanoreactor [28], and $FeCl_3$ [29] under ultrasound irradiation [30] have been used in the Pechmann condensation. However, each of these methods has its own advantages but also suffers from one or more disadvantages, such as prolonged reaction times, low yields, use of harmful organic solvents, and requirement of excess of catalyst and reagents, and harsh reaction conditions.

In continuation of our work to develop new synthetic methodologies [31], herein we are gratified to report an efficient and a convenient method for the synthesis of 4-substituted coumarins **3** using a novel $Cu(CH_3CN)_4PF_6$ catalyst in the Pechmann condensation reaction of phenols **1** with β-ketoesters **2** under solvent-free conditions at room temperature. The method has advantages in terms of yields, short reaction times, ease of operation, use of relatively nontoxic catalyst, room temperature conditions, and will make a useful and important addition to the present methodologies (Scheme 1).

RESULT AND DISCUSSION

To study the feasibility of the $Cu(CH_3CN)_4PF_6$ catalyzed Pechmann condensation, the reaction of resorcinol with ethyl acetoacetate was selected as a model. Our initial experiments focused on the optimization of the amount of $Cu(CH_3CN)_4PF_6$. We observed that only 10 mol % of $Cu(CH_3CN)_4PF_6$ could effectively catalyze the reaction at a comparatively mild reaction

Scheme 1

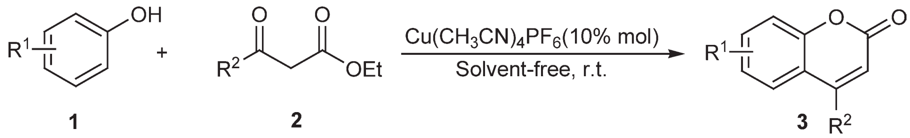


Table 1

Syntheses of coumarins via Pechmann condensations of phenols with ethyl acetoacetate in presence $Cu(CH_3CN)_4PF_6$ under solvent free condition at room temperature.

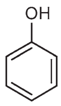
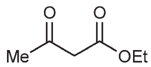
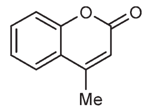
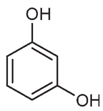
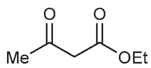
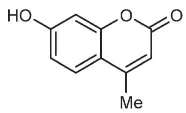
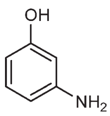
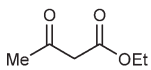
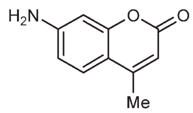
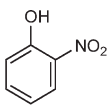
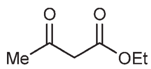
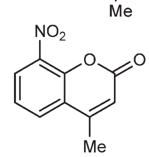
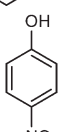
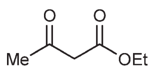
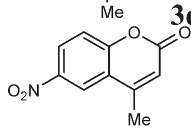
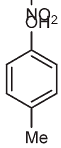
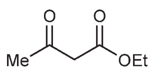
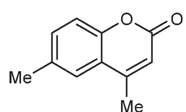
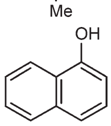
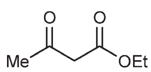
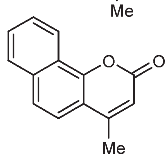
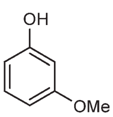
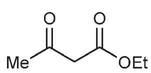
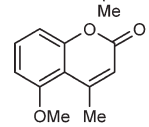
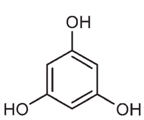
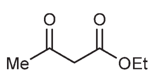
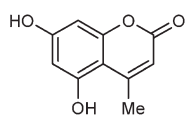
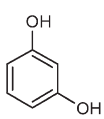
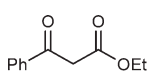
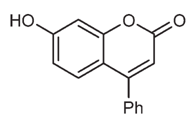
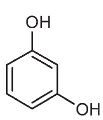
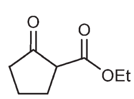
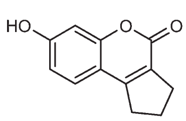
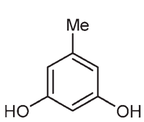
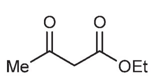
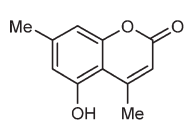
Entry	Phenol	B-Ketoester	Product	Time (min)	Isolated yield (%)	Mp (°C) Found	Mp (°C) Reported
1			 **3a**	30	98	79–81	78–80 [15]
2			 **3b**	10	95	182–184	185 [24]
3			 **3c**	10	98	220–224	222–224 [16]
4			 **3d**	17	82	182–185	184–186 [15]
5			 **3e**	10	90	150–152	151–154 [15]
6			 **3f**	10	99	149–151	150–151 [32]
7			 **3g**	35	99	152–154	155 [24]
8			 **3h**	12	98	159–161	160–162 [15]
9			 **3i**	9	95	279–283	280–285 [24]
10			 **3j**	20	82	242–244	240–242 [24]
11			 **3k**	30	81	242–245	244–246 [24]
12			 **3l**	15	83	245–247	244–246 [24]

Table 2

Comparison of the efficiencies of various catalysts used in the synthesis of coumarins via Pechmann condensation.

Catalyst	Conditions/T (°C)	Time (min)	Yield (%)	Reference
$Bi(NO_3)_3{\cdot}5H2O$	Solvent-free/80	15–300	47–94	26
Sulphamic acid	Solvent-free/130	20–80	62–96	27
$BiCl_3$	Solvent-free/75	60–120	66–93	14
$InCl_3$	Solvent-free/65	30–120	65–98	16
HClO4·SiO2	Solvent-free/130	30–90	65–97	33
$H_{14}[NaP_5W_{30}O_{110}]$	Solvent-free/130	40–300	70–95	25
$Sm(NO_3)_3{\cdot}6H_2O$	Solvent-free/80	15–90	45–98	15
$[MBsIm][CF_3SO_3]$	Solvent-free/80	30–360	61–95	34
SnO2	Solvent-free/70	45–120	72–93	35
$Cu(CH_3CN)_4PF_6$	Solvent-free/25	5–35	90–98	This work

temperature of room temperature. An increase in the catalyst to 15 mol % showed no substantial improvement in the yield, though a slight improvement in the reaction time was observed. This encouraged us to study the scope of the reaction under the optimized reaction parameters in the presence of 10 mol % of catalyst under solvent-free condition at room temperature. The results of using $Cu(CH_3CN)_4PF_6$ as a catalyst in the reaction of various phenols with ethyl acetoacetate are summarized in Table 1. Various functionalities present in phenols, such as hydroxy, amino, methyl, and nitro groups were tolerated. In all these cases, the corresponding 4-substituted coumarins were obtained in excellent yields.

To show the merit of $Cu(CH_3CN)_4PF_6$ in comparison with other reported catalysts, we summarized some of the results for the synthesis of coumarins via Pechmann condensation obtained by other workers. It is clear from Table 2 that the current method is simpler, more efficient, and less time consuming for the synthesis of coumarins derivatives.

$Cu(CH_3CN)_4PF_6$ is a free-flowing, white, microcrystalline powder that does not darken on long-term storage in an inert atmosphere. Exposure to air for longer than about 1 h results in minor surface oxidation due to the slightly hygroscopic nature of the complex. The complex is moderately soluble in polar solvents and is remarkably stable to air oxidation in CH_3CN solution. $Cu(CH_3CN)_4PF_6$ was synthesis based on literature [36].

CONCLUSIONS

In conclusion, we have developed a simple and an efficient synthesis of substituted coumarins via Pechmann condensations using $Cu(CH_3CN)_4PF_6$ catalyst under solvent-free conditions. This method offers some advantages in terms of simplicity of performance, low reaction times, room temperature condition, good to excellent yields, solvent-free condition, and it follows along the line of green chemistry. This protocol could serve as a valuable alternative to known reaction systems.

EXPERIMENTAL

A mixture of the phenol (1 mmol) and the ethyl acetoacetate (1 mmol) was well stirred with $Cu(CH_3CN)_4PF_6$ (0.037 g, 0.1 mmol) at room temperature for the appropriate time according to Table. After completion of the reaction, the reaction mixture was poured onto crushed ice, and the resulting crude product was filtered off and recrystallised from ethanol to give the pure product.

All the products are known compounds, which were characterized by IR and ^{1}H-NMR spectral data and their melting points compared with literature reports.

Acknowledgment. We gratefully acknowledge financial support from the Research Council of Razi University.

REFERENCES AND NOTES

[1] Singer, L. A.; Kong, N. P. J Am Chem Soc 1966, 88, 5213.

[2] ÓKennedy, R.; Thornes, R. D. Coumarins; Biology, Applications and Mode of Action; Wiley: Chichester, 1997.

[3] Zahradnik, M. The Production and Application of Fluorescent Brightening Agents, Wiley, 1992.

[4] Murray, R. D. H.; Mendez, J.; Brown, S. A. The Natural Coumarins; Occurrence, Chemistry and Biochemistry; Wiley: New York, 1982.

[5] Pechmann, H. V.; Duisberg, C. Chem Ber 1884, 17, 929.

[6] Jonson, J. R. Org React 1942, 1, 210.

[7] Brufola, G.; Fringuelli, F.; Piermatti, O.; Pizzo, F. Heterocycles 1996, 43, 1257.

[8] Shriner, R. L. Org React 1942, 1, 1.

[9] Yavari, I.; Hekmat-Shoar, R.; Zonouzi, A. Tetrahedron Lett 1998, 39, 2391.

[10] Cartwright, G. A.; McNab, H. J Chem Res (S) 1997, 296.

[11] Sentha, S. M.; Shah, N. M.; Shah, R. C. J Chem Soc 1938, 228.

[12] Robertson, A.; Sandrock, W. F.; Henry, C. B. J Chem Soc 1931, 2426.

[13] Woods, L. L.Sapp, J. J Org Chem. 1962, 27, 3703.

[14] De, K. S.; Gibbs, R. A. Synthesis 2005, 1231.

[15] Bahekara, S. S.; Shinde, D. B. Tetrahedron Lett 2004, 45, 7999.
[16] Bose, D. S.; Rudradas, A. P.; Babu, M. H. Tetrahedron Lett 2002, 43, 9195.
[17] Valizadeh, H.; Shockravi, A. Tetrahedron Lett 2005, 46, 3501.
[18] Wang, L.; Xia, J.; Tian, H.; Qian, C.; Ma, Y. Ind J Chem 2003, 42B, 2097.
[19] Sugino, T.; Tanaka, K. Chem Lett 2001, 4, 110.
[20] Jie, W.; Tianning, D.; Wei, S.; Yizhe, L. Synth Commun 2006, 39, 2949.
[21] Reddy, Y. T.; Sonar, V. N.; Crooks, P. A.; Dasari, P. K.; Reddy, P. N.; Rajitha, B. Synth Commun 2008, 38, 2082.
[22] Frere, S.; Thiery, V.; Besson, T. Tetrahedron Lett 2001, 42, 2791.
[23] Dabiri, M.; Salehi, P.; Zolfigol, M. A.; Baghbanzadeh, M. Heterocycles 2007, 71, 677.
[24] Khandekar, A. C.; Khadilkar, B. M. Synlett 2002, 152.
[25] Heravi, M. M.; Khorasani, M.; Derikvand, F.; Oskooie, H. A.; Bamoharram, F. F. Catal Commun 2007, 8, 1886.
[26] Alexander, V. M.; Bhat, R. P.; Samant, S. D. Tetrahedron Lett 2005, 46, 6957.
[27] Singh, P. R.; Singh, D. U.; Samant, S. D. Synlett 2004, 1909.
[28] Karimi, B.; Zareyee, D. Org Lett 2008, 10, 3989.
[29] Kumar, V.; Tomar, S.; Patel, R.; Yousaf, A.; Parmar, V. S.; Malhotra, S. V. Synth Commun 2008, 38, 2646.
[30] Gutiérrez-Sánchez, C.; Calvino-Casilda, V.; Pérez-Mayoral, E.; Martín-Aranda, R. M.; López-Peinado, A. J. Catal Lett 2009, 128, 318.
[31] Soleimani, E.; Khodaei, M. M.; Batooie, N.; Samadi, S.; Chem Pharm Bull 2010, 58, 212.
[32] Li, T. S.; Zhang, Z. H.; Yang, F.;J Chem Res (S) 1998, 38.
[33] Maheswara, M.; Siddaiah, V.; Damu, G. L. V.; Rao, Y. K.; Rao, C. V. J Mol Catal A Chem 2006, 255, 49.
[34] Gu, Y.; Zhang, J.; Duan, Z.; Denga, Y. Adv Synth Catal 2005, 347, 512.
[35] Sowmiya, M.; Sharma, A.; Parsodkar, S.; Mishra, B. G.; Dubey, A. Appl Catal A Gen 2007, 333, 272.
[36] Kubas, G. J. Inorg Syn 1979, 19, 90.