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A Convenient Procedure for Friedlander Synthesis of Quinoline Derivatives Catalyzed by Zirconium Dodecylphosphonate as an Efficient and Reusable Catalyst

Soheila Ghassamipour [a,*], Mohammad Mehdi Ghanbari [b], Elham Barmshouri [a], Mohammad Sadegh Moaddeli [a]

[a] *Department of Chemistry, Marvdasht Branch, Islamic Azad University, Marvdasht, Iran*

[b] *Young Researchers Club, Marvdasht Branch, Islamic Azad University, Marvdasht, Iran*

Abstract

2-Amino-substituted ketones react with α-methylene ketones under solvent-free conditions at 90 °C in the presence of a catalytic amount of zirconium dodecylphosphonate to create the corresponding quinolines in excellent yields. This procedure recommends numerous advantages such as easy work-up, use of mild, reusable and safe catalyst, short reaction timeand high yields. The new compounds have been characterized by ^{1}H-NMR, ^{13}C-NMR, mass and elemental analysis data.

Keywords: Zirconium dodecylphosphonate, Quinolines, Solvent-free, Reusable catalyst

Introduction

Nitrogen-containing heterocyclic compounds are an important class of heterocyclic compounds since many of these chemical compounds, exhibit biological activities such as anti-platelet [1] anti-malaria [2] anti-inflammatory [3] and anti-asthmatic agents [4] Quinolines are important category of these compounds that are synthesized by various methods. These methods Include Skraup [5] Doebner-Von Miller [6] and Friedlander ones [7]. Also, synthesis of quinolines by *N*-aryl nitrilium compounds [8], alkenylation/ cyclization of ortho-amino ketones [9], utilizing ortho-amino aromatic vinyls [10] and lately use of Aza-Dielz-Alder reaction [11] are the other procedures. However, among these methods, the Friedlander synthesis is the most convenient one for this purpose. This method can occur under base [12], Bronsted [13] and Lewis acids [14] catalyzed conditions. But, higher yields were achieved from the acid catalyzed reactions. Alternatively, most of these methods suffered from many disadvantages such as; deactivation of α-amino ketones by protonation of amino group in strong Bronsted acid media, difficulties in work-up, loss of catalyst, harsh reaction conditions and the use of stoichiometric and/ or relatively expensive reagents. As part of our current studies on the development of new heterocyclic systems [15], the problems listed above and in connection with our ongoing research on the catalytic properties of dodecylphosphonic acid and its salts [16], we now report zirconium dodecylphosphate ($Zr(DP)_2$) as a reusable and efficient catalyst for preparation of quinoline derivatives by Friedlander synthesis.

*Corresponding author
Tel.: +98 728 3311145, +98 9173070745
Fax: +987283311172
E-mail address:soheilaghassamipour@gmail.com

Experimental

2-Amino-substituted ketone (1) and α-methylene ketone (2) were obtained from Merck and were used without further purification. Zirconium dodecylphosphonate were prepared by known methods [16a]. Melting points (uncorrected) were measured on an Electrothermal 9100 apparatus. Elemental analyses for C, H and N were performed using a Heraeus CHN-O-Rapid analyzer. The experimental data were in good agreement with the calculated values. ^{1}H and ^{13}C NMR spectra were measured with a Bruker DRX-400 Avance spectrometer. Mass spectra were recorded on a Hewleet-Packard 5993C spectrometer.

General Procedure for the Preparation of quinoline derivatives using Zr(DP)$_2$ as catalyst

A mixture of 2-amino-substituted ketone (1 mmol), α-methylene ketone (1.2-1.5 mmol) and Zr(DP)$_2$ (0.1 mmol) was heated at 90 °C with stirring for the appropriate time (Table 2). The extent of reaction was monitored by TLC and mixture of iodine/ silica gel. After completion of the reaction, 3 mL petroleum ether (b.p. 60˚C) was added to the reaction mixture. The pure product was filtrated and dried. Then 2 mL dichloromethane was added to residue solution. The catalyst was precipitated and dried for the next reaction.

(2,4-Dimethylquinolin-3-yl) (phenyl) methanone (**Table 3, Entry 13**): Pale yellow solid, m.p: 141 ˚C, Anal. Calcd for $C_{18}H_{15}NO$ (261.32): C, 82.73; H, 5.79; N, 5.36. Found: C, 82.65; H, 5.75; N, 5.30. MS: *m/z* (%): 261 (M+,100)246 (48), 209 (40), 184 (6), 105 (38), 77 (66), 51 (13).^{1}H NMR (400 MHz, DMSO): δ= 2.43 (3H, s, CH_3), 2.47 (3H, s, CH_3), 7.57-7.77 (7H, m, CH), 8.08 (1H, d, $^3J_{HH}$ =8.0 Hz, CH), 8.20 (1H, d, $^3J_{HH}$ = 8.0 Hz, CH). ^{13}C NMR (100 MHz, DMSO): δ=18.2 (CH_3), 22.7 (CH_3), 124.5, 125.6, 126.2, 126.9, 127.7, 128.5, 129.2, 129.4, 130.7, 132.5, 134.7, 136.1, 153.3, 197.2 (C=O).

Benzyl 2, 4-dimethylquinoline-3-carboxylate (**Table 3, Entry 14**): Yellow oil, Anal. Calcd for $C_{19}H_{17}NO_2$ (291.34): C, 78.33; H, 5.88; N, 4.81. Found: C, 78.15; H, 5.75; N, 4.72.MS: *m/z* (%): 291(M^+,100), 246 (18), 218 (15), 149 (20), 107 (42), 91 (66), 77 (5), 57 (10). ^{1}H NMR (400 MHz, $CDCl_3$): δ=2.61 (3H, s, CH_3), 2.67 (3H, s, CH_3), 5.46 (s, 2H, CH_2), 7.39-7.72 (7H, m, CH), 7.96-7.98 (1H, d, $^3J_{HH}$ = 8.4 Hz, CH), 8.03 (1H, d, $^3J_{HH}$ =8.4 Hz, CH). ^{13}C NMR (100 MHz, $CDCl_3$): δ=19.7 (CH_3), 23.7 (CH_3), 67.5 (CH_2), 123.9, 125.7, 126.3, 127.6, 128.7, 128.8, 128.9, 129.1, 130.2, 135.1, 141.8, 146.9, 154.3, 168.9 (C=O).

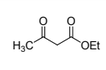
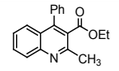
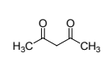
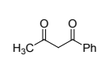
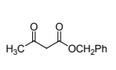
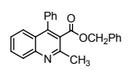
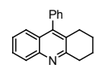
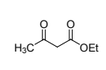
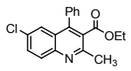
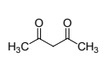
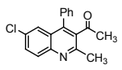
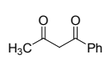
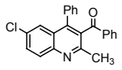
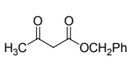
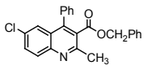
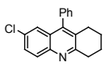
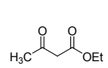
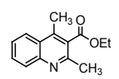
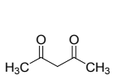
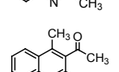
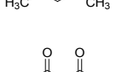
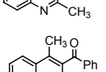
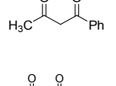
Results and discussion

In the beginning of our studies, the reaction of 2-amino-5-chlorobenzophenon and ethyl acetoacetate was utilized as a model for finding the optimization conditions (Scheme 1, Table 1). First we started to investigate the behavior of zirconium dodecylphosphonate as

Table 1. Optimization of Reaction Conditions in the Presence of Zr(DP)$_2$

Entry	Solvent	Catalyst (mol %)	Temp. (˚C)	Time	Isolated Yield (%)
1	Solvent-free	10	25	1 h	-
2	Solvent-free	10	50	1h	15
3	Solvent-free	10	90	15 min	98
4	Solvent-free	5	90	1 h	87
5	Solvent-free	20	90	30min	96
6	Solvent-free	-	90	1 h	25

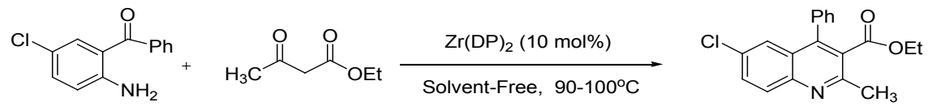
Table 2. Zr(DP)$_2$-catalyzed Friedlander reaction between *o*-aminoaryl ketones and various β-diketones/ ketoesters

Entry	o-aminoketone	Ketone	Product[a]	Mp (˚C) Found (Lit.)	Isolated Yields (%)	Time (min)
1				94 (97) [15d]	92	35
2				113 (114) [15d]	85	30
3				133 (134) [15d]	90	40
4				91-93 (90-93) [15d]	78	60
5				141 (141) [15d]	94	30
6				107 (108) [15d]	98	15
7				153 (151) [15d]	93	40
8				211 (211) [15d]	90	75
9				121 (123) [15d]	87	43
10				78 (78) [15d]	95	35
11				270 (270-272)[18]	86	10
12				Oil [19]	90	40
13				141	95 [a]	3 (h)
14				Oil	88	30

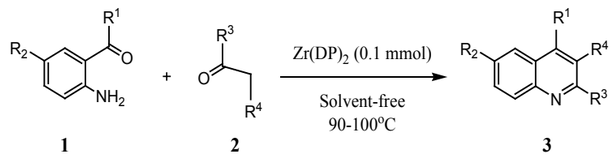
[a]All the products were characterized on the basis of their ^{1}H NMR and ^{13}C NMR spectral analysis and compared with the literature data (Ghassamipour & Sardarian, 2008; Poor Heravi, 2009; Barbero, 2010)

Table 3. Comparison of catalytic activity of Zr(DP)$_2$, DPA and $ZrOCl_2.8H_2O$

Entry	Catalyst	Conditions	Temp. (˚C)	Time (min)	Isolated Yields (%)
1	Zr(DP)$_2$	Solvent-free	90	15	98
2	DPA	Solvent-free/H_2O	90	20/96	98/82
3	$ZrOCl_2.8H_2O$	Solvent-free	90	30	70



Scheme 1



1 **2** **3**

Scheme 2

catalyst at different temperatures in solvent-free conditions with or without catalyst (Entry 1-6, Table 1). Lower amount of catalyst, 5 mol %, led to longer time for completion of the reaction and higher amount, 20 mol %, did not show significant improvement in the yield and the reaction time. With the aim of studying the generality of the method, a series of ortho-aminoaryl ketones were reacted with various β-diketones/ ketoesters under the optimized conditions (Scheme 2). The results are summarized in Table 2.

As shown in Table 2, a variety of β-diketones or ketoesters and simple ketones such as cyclohexanone reacted with ortho-aminoaryl ketones to efficiently generate, the corresponding quinolines. In most cases, adding petroleum ether to the reaction mixture caused precipitation of product. Then, the catalyst was separated by adding dichloromethane to filtrate and reuse directly without any activation. For example, the reaction of 2-aminobenzophenone and ethyl acetoacatate gave the corresponding quinoline in 92, 92, 90 and 89 % yields over four runs. In continuation, we have compared the catalytic activity of zirconium dodecylphosphonate with dodecylphosphonic acid and $ZrOCl_2.8H_2O$ (starting materials for synthesis of $Zr(DP)_2$) in the preparation of ethyl 6- chloro-2-methyl-4-phenylquinoline-3-carboxylate (Table 3, Entry 6), as a model product (Table 3).

Conclusions

Conclusively, Zirconium dodecylphosphonate have been introduced as a new catalyst that easy recovered and produced correspounding quinolines in great yields under solvent-free conditions. This procedure in Compared with our recent work (Ghassamipour, 2009) has two advantages: recovery of catalyst and high yields. In previous methods we were not able to recover the corresponding catalyst in solvent-free conditions in addition the yields in aqueous media were lower than under solvent-free conditions. So zirconium dodecylphosphonate can be used as a reusable and efficient catalyst for preparation of several quinoline derivatives by Freidlander synthesis. Thus, the first application of $Zr(DP)_2$ in organic chemistry has been introduced by our research team.

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References

[1] T. Ch. Ko, M. J. Hour, J. Ch. Lein, Ch. M. Teng, K. H. Lee, Sh. Ch. Kuo, I. J. Huang, Bioorganic and Medicinal Chemistry Letters. 11 (2001) 279.
[2] J. Tracey, L. Webster, Drugs Used in Chemothetapy of Protozoal Infections, Pergamon Press, New York. 1996.

[3] G. Roma, M. D. Braccio, G. Grossi, F. Mattioli, M. Ghia, Eur. J. Med. Chem. 35 (2000) 1021.
[4] D. Dube, M. Blouin, C. Brideau, C. C. Chan, S. Desmarais, D. Ethier, J. P. Falgueyret, R. W. Friesen, M. Girard, Y. Girard, J. Guay, D. Riendeau, P. Tagari, R. N. Young, Bioorganic and Medicinal Chemistry Letters. 8 (1998) 1255.
[5] H. Skraup, Monatsh. Chem. 1 (1880) 316.
[6] (a). O. Doebner, W. V. Miller, Ber. 14 (1881) 2812. (b). O. Doebner, W. V. Miller, Ber. 16 (1883) 1664. (c). O. Doebner, W. V. Miller, Ber. 17 (1884) 1712.
[7] P. Friedlander, Chem. Ber. 15 (1882) 2572.
[8] M. Al-Talib, J. C. Jochims, Q. Wang, A. Hamed, A. H. Ismail, Synthesis. (1992) 875.
[9] B. Jiang, Y. G. Si, J. Org. Chem. 67 (2002) 9449.
[10] B. S. Lee, J. H. Lee, D. Y. Chi, J. Org. Chem. 67 (2002) 7884.
[11] K. Turhan, E. Pelit, Z. Turgut, Synthetic Communications. 39 (2009) 1729.
[12] (a) E. A. Fehnel, J. Med. Chem. 37 (1994) 2129. (c) B. Kalluraya, S. Sreenivasa, Farmaco, 53 (1998) 399. (d) T. M. Das, S. Nagarajan. Carbohydrate Research. 344 (2009) 1028.
[13] (a). L. Sterkowski, A. Czamy, Journal of Fluorine Chemistry, 104 (2000) 281. (b) G. W. Wang, C. S. Jia, Y. W. Dong, Tetrahedron Letters. 47 (2006) 1059. (c) M. Dabiri, M. Baghbanzadeh, M. S. Nikcheh, Monatsh. Chem. 138 (2007) 1249. (d) S. Ghassamipour, A. R. Sardarian, Tetrahedron Letters. 50 (2009) 514. (e). X. L. Zhang, Q. Y. Wang, S. R. Sheng, Q. Wang, X. L. Liu, Synthetic Communications. 39 (2009) 3293. (f). D. Garella, A. Barge, D. Upadhyaya, Z. Rodriguez, G. Palmesano, G. Cravotto, Synthetic Communications. 40 (2009) 120. (g) J. Akbari, A. Heydari, H. R. Calor, S. A. Kohan, J. Comb. Chem. 12 (2009) 137.
[14] (a) J. S. Yadav, V. S. Reddy, P. Sreedhar, R. K. Srinivasa, K. Nagaiah, Synthesis. (2004) 2381. (b) B. Das, K. Damodar, N. Chowdhury, R. A. Kumar, J. Mol. Catal. A: Chemical. 274 (2007) 148. (c) M. Dabiri, S. Bashiribod, Molecules. 14 (2009) 1126. (d) S. Bose, M. Idrees, N. M. Jakka, J. V. Rao, J. Comb. Chem. 12 (2009) 100. (d). M. Barbero, S. Bazzi, S. Cadamuro, S. Dughera, Tetrahedron Letters. 51 (2010) 2342. (e) E. Soleimani, M. M. Khodaei, N. Batooie, S. Samadi, S. Chem. Pharm. Bull. 58 (2010) 212. (f) R. Ghorbani-Vaghei, S. Akbari-Dadamahaleh, Phosphorus, Sulfur, and Silicon. 185 (2010) 319.
[15] (a) S. Ghassamipour, A. R. Sardarian, J. Iran. Chem. Soc.7 (2010) 237. (b) M. M. Ghanbari, Chem Month. 142 (2011) 794. (c) I. Yavari, M. M. Ghanbari, J. Azizian, F. Sheikholeslami, J. Chem. Res. (2011) 87. (d) I. Yavari, M. M. Ghanbari, A. S. Shahvelayati, M. Ghazvini, Phosphorus, Sulfur, Silicon, Relat. Elem. 185 (2010) 2551.
[16] K. Segawa, N. Kihara, H. Yamamoto, J. Mole. Catal. 1992, 74, 213.