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Natural phosphate as new, highly efficient and reusable heterogeneous catalyst for the selective preparation of beta-enaminoesters under solvent-free conditions

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Abstract

Natural phosphate (NP) has been found to be a new and highly efficient heterogeneous catalyst for the synthesis of β-enaminoesters, by simple condensation of various primary amines with β-dicarbonyl under solvent-free conditions.

Keywords: Natural phosphate (NP), b-enaminoesters, solvent-free conditions

1. Introduction

β-enaminoesters represent an importance rang of functionalized building blocks, such as synthetic intermediates for the preparation of various heterocyclic and biologically active compounds [1-2]. Consequently, various approaches toward the synthesis of β-dicarbonyl compounds have been explored during the past years. The direct enamination of b-dicarbonyl with amines is one of most straightforward methodology for the preparation of β-enaminoesters in the presence of various promoting agents [3-5]. However, these methods suffer from drawbacks, such as long reaction time, low yield, high temperature, costly catalyst, and poor regioselectivity [6-8].

Moroccan subsoil is rich in phosphate ore, it contains two-thirds of global reserves; The mineralogical constitution of phosphate is quite diverse, more than 200 species have been recorded. The phosphate ores are rich in apatite "fluorapatite" but they contain a lot of chemical impurities that affect the apatite structure. A several previous studies have been done in the order to approximate the actual structure of the natural phosphate [9]. Natural phosphate has been shown in a wide range of catalytic reactions involving different types of organic reactions [10-13].

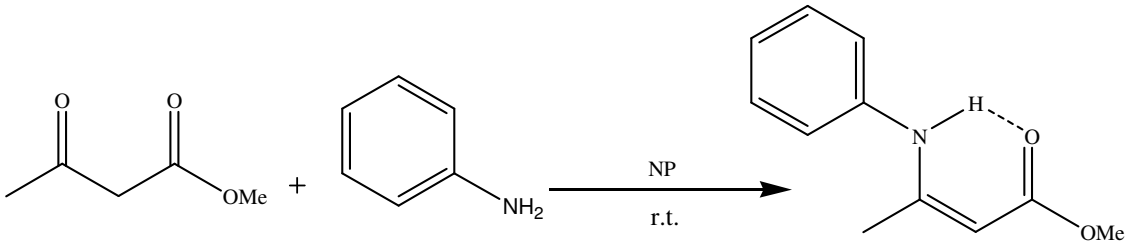
Recently, green catalyst has received considerable attention as a stable, inexpensive, non-toxic ans readily producible from available materials, for various organic reactions, under mild heterogeneous conditions to afford the corresponding products in excellent yields with high selectivity. As part of our ongoing project, to develop more efficient and environmentally benign methods for organic synthesis using economic and eco-friendly catalyst [14-19].

Herein, we report a new, clean and efficient solvent-free strategy for the preparation of β-enaminoesters from aromatic as well as aliphatic amines and β-dicarbonyl in the presence of NP.

2. Result and discussion

At first, the condensation of methyl acetoacetate (1 mmol) and aniline (1.1 mmol), was examined in presence of different solvents, and different amounts of NP.

In order to optimize the reaction conditions with respect to amount of catalyst and effect of solvent. The results are listed in table 1. As it can be seen from table 1, the reasonable results were obtained when the reaction was carried out using 0.3 g NP, at room temperature in the absence of solvent.



Scheme 1: Synthesis of β-Enaminoesters Catalyzed by NP.

Table 1. The Condensation of Aniline and Methyl-acetoacetate under Various Different Conditions.

Entry	Amount of NP (g)	Solvent	Time (h)	Yield (%)[b]
1	0.1	EtOH	2	60
2	0.1	MeOH	2	62
3	0.1	CH_3CN	2	70
4	0.1	CH_2Cl_2	2	68
5	0.1	H_2O	2	50
6	0.1	none	2,5	70
7	0.2	none	2	82
8	0.3	none	1	90

[a] All reactions were run with methyl acetoacetate(1 mmol) and aniline (1,1 mmol), 5 ml of solvent.
[b] isolated yields

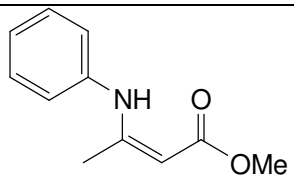
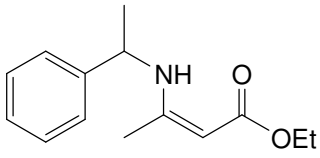
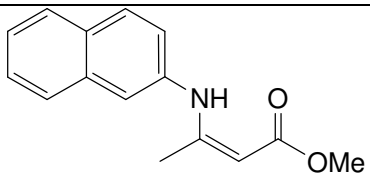
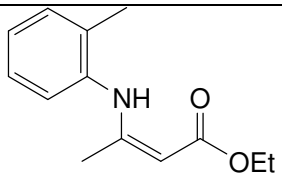
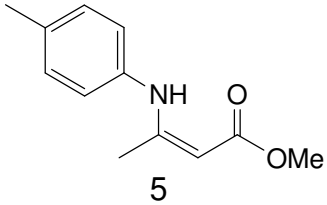
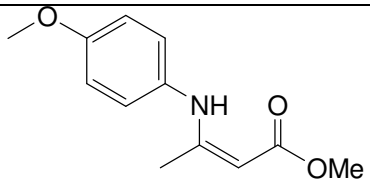
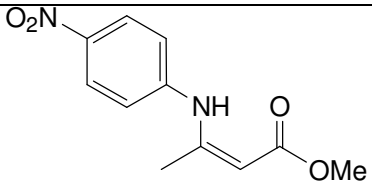
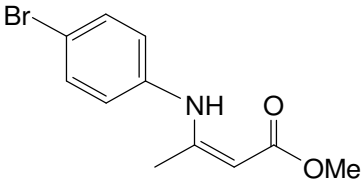
Using these optimized conditions, the reaction of β-dicarbonyl with a range of primary amines was examined to explore the scope of reaction.

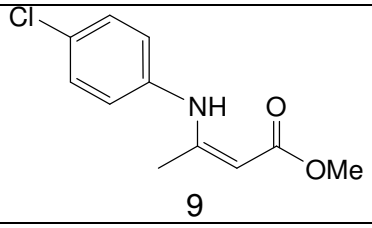
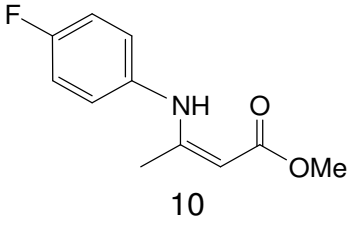
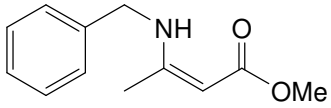
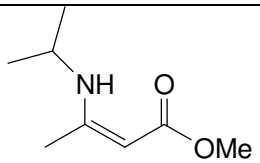
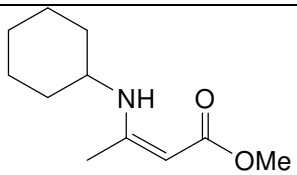
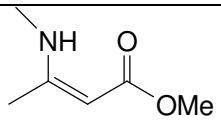
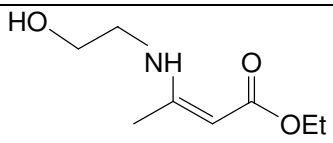
As shown in table 2, a series of aromatic amines bearing either electron-donating or electron-withdrawing groups on aromatic ring were investigated. This method efficiently condensed anilines having electron-donating groups in positions 4 with β-dicarbonyl, to give the corresponding β-enaminoesters in good yield (table 2, entries 5-6).

Whereas, anilines with strong electron with-drawing groups such as 4-nitro-aniline did not give any product under the present conditions (table 2, entry 7).Aliphatic amines also reacted efficiently to give the corresponding β-enaminoesters in excellent yield (table 2, entries 12-15), and the reaction time was shorter than that of aromatic amines (table 2, entries 12-15).

The present protocol proved to be efficient in term of chemoselectivity [14-19]. The amine reacted selectively with the ketone of β-dicarbonyl. The (Z) configuration was confirmed by intramolecular hydrogen bonding, the proton of the –NH- group appearing at a lower field (δ> 8.2). Therefore, this condensation was stereospecific.

Table 2. Synthesis of Different β-Enaminoesters Using NP as Catalyst under Solvent-free Conditions.

Entry	Product [a]	Time (h)	Yield (%)[b]
1	 1	1	90
2	 2	1,2	82
3	 3	5	88
4	 4	1,5	77
5	 5	1,5	97
6	 6	2	88
7	 7	5	none
8	 8	2	70

9	 9	1,5	92
10	 10	1,5	96
11	 11	30min	98
12	 12	20min	96
13	 13	25min	94
14	 14	20min	98
15	 15	20min	92

[a] All products were identified by comparison of their physical and spectral data with those of authentic samples [14-19].

Finally, the reusability of NP was further investigated in subsequent reactions, taking the additions of aniline to ethyl acetoacetate as an example. The catalyst was easily recovered by simple filtration after diluting of the reaction mixture with ethyl acetate and was reused after being dried under vacuum. NP was reused for four runs without evident loss of activity.

3. Conclusion

In summary, we have reported PN as a highly efficient heterogeneous reusable catalyst for chemoselective enamination of β-dicarbonyl compounds with aliphatic and aromatic amines under solvent-free conditions. In addition, the important features of this procedure are mild reaction conditions, high yield, and operational simplicity which make it a useful and attractive strategy for the preparation of N-substituted β-enamino carbonylic compounds.

Experimental Section

Instruments

Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on a Bruker Avance 300 spectrometer at 300 MHz. Carbon-13 nuclear magnetic resonance (^{13}C NMR) was recorded on Bruker Avance 300 spectrometer at 75 MHz. Chemical shifts are reported as d values in parts per million (ppm) relative to tetramethylsilane (TMS) for all recorded. Low resolution mass spectra were recorded on Termofinnigan Polaris-Q mass spectrometer. Starting materials and reagents used in the reactions were obtained commercially from Acros, Aldrich, Fluka and were used without purification, unless otherwise indicated.

Catalytic studies

To a magnetically stirred mixture of the β-dicarbonyl compounds (1 mmol) and amines (1.1 mmol), NP (0.3 g) was added and the reaction mixture was stirred at room temperature for the appropriate time. The reaction was monitored by TLC. After completion of the reaction, the reaction mixture was diluted with ethyl acetate. The catalyst was separated by filtration, then the solution was washed with ethyl acetate (5 mL) and dried over anhydrous sodium sulfate, filtered and the solvent was evaporated under vacuum. The residue was purified by flash column chromatography to afford the desired product. All isolated pure products were compared with the known compounds [14-19].

(Z)-Methyl 3-(phenylamino) but-2-enoate (1)

^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.9 (s, 3H), 3.75 (s, 3H), 4.6 (s, 1H), 7.09-7.22 (m, 7H), 10.5 (br s, 1H, NH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 20.28, 50.11, 85.92, 124.40, 124.88, 129.02, 139.37, 158.54, 170.45. EIMS (*m/z*) 192.1 (M+1).

(Z)-Ethyl 3-(2-methyl, benzylamino) but-2-enoate (2)

^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.29 (t, J=6.77, 3H), 1.53 (m, 3H), 1.99 (s, 3H), 4.96 (q, J=6.8, 2H), 4.33 (s, 1H), 4.46 (m, 1H), 6.93-7.13 (m, 3H, Ar), 8.93 (br s, 1H, NH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 12.94, 17.68, 23.14, 51.03, 56.49, 81.79, 123.19, 125.13, 127.11, 130.31, 143.42, 159.47, 168.81. EIMS (*m/z*) 219.1 (M+1).

(Z)-Methyl 3-(naphtylamino) but-2-enoate (3)

^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.77 (s, 3H), 3.62 (s, 3H), 4.67 (s, 1H), 7.13-7.96 (m, 7H), 10.48 (br s, 1H, NH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 20.03, 50.14, 85.17, 122.81, 123.46, 124.29, 124.71, 125.16, 125.8, 126.37, 128.19, 126.72, 126.52, 159.9, 170.7. EIMS m/z 241.1 (M+1, 100).

(Z)-Ethyl 3-(o-tolylamino) but-2-enoate (4)

^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.21 (t, J=6.9 Hz, 3H), 2.07 (s, 3H), 2.24 (s, 3H), 4.03 (q, J=6.9 Hz, 2H), 4.70 (s, 1H), 6.98-7.17 (m, 4H), 10.28 (br s, 1H, NH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 12.31, 15.64, 17.65, 56.25, 83.12, 123.56, 133.74, 133.49, 133.73, 135.39, 157.26, 168.21. EIMS (*m/z*) 206.1 (M+1).

(Z)-Methyl 3-(p-tolylamino) but-2-enoate (5)

^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.96 (s, 3H), 2.33 (s, 3H), 3.5 (s, 3H), 4.6 (s, 1H), 6.98-7 (m, 4H), 10.28 (br s, 1H, NH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 20.01, 30.10, 49.80, 84.71, 123.56, 133.74, 133.49, 133.73, 135.39, 159.26, 170.73. EIMS (*m/z*) 206.1 (M+1).

(Z)-Methyl 3-(p-methoxyanilinlamino) but-2-enoate (6)

^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.76 (s, 3H), 3.51 (s, 3H), 4.55 (s, 1H), 6.83-6.93(m, 4H), 10.12 (br s, 1H, NH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 19.94, 50.14, 85, 115, 116, 126.25, 126.62, 135, 158, 161, 170. EIMS m/z 222.1 (M+1, 100).

(Z)-Methyl 3-(p-bromoanilinlamino) but-2-enoate (8)

^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.88 (s, 3H), 3.57 (s, 3H), 4.62 (s, 1H), 6.83-7.33(m, 4H), 10.24 (br s, 1H, NH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 19.94, 50.14, 86, 116, 117, 126.25, 126.62, 135, 158, 161, 170. EIMS (*m/z*) 271.1 (M+1).

(Z)-Methyl 3-(p-fluoroanilinlamino) but-2-enoate (10)

^{1}H NMR ($CDCl_3$, 300 MHz) δ : 1.77 (s, 3H), 3.52 (s, 3H), 4.55 (s, 1H), 6.83-6.93 (m, 4H), 10.12 (br s, 1H, NH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 19.94, 50.14, 85.46, 115.66, 115.96, 120.25, 125.7, 135.2, 158.76, 162.01, 170.70. EIMS m/z 209.1 (M+1, 100).

(Z)-Methyl 3-(benzylamino) but-2-enoate (11)

^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.75 (s, 3H), 3.47 (s, 3H), 4.27 (s, 2H), 4.36 (s, 1H), 7.09-22 (m, 7H), 8.86 (br s, 1H, NH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 19.25, 46.64, 49.76, 83.55, 126.5, 127.28, 128.78, 139.02, 160.99, 170.45. EIMS (*m/z*) 206.1 (M+1).

(Z)-Methyl 3-(isopropylamino) but-2-enoate (12)

^{1}H NMR ($CDCl_3$, 300 MHz) δ: 0.88 (d, J = 7.0 Hz, 6H); 1.52 (t, J = 7.0 Hz, 3H), 1.92 (s, 3H), 3.66 (m, 1H), 4.02 (q, J = 7.0 Hz, 2H), 6.87 (s, 1H), 8.20 (brs, 1H), ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 18.33, 23.59, 43.80, 48.93, 81.82, 159.92, 170.03 , EIMS (m/z) 157.1 (M+1).

(Z)-Methyl 3-(cyclohexylamino) but-2-enoate (13)

^{1}H NMR ($CDCl_3$, 300 MHz) δ: 0.8 (m, 2H), 1.1 (s, 4H), 1.2 (m, 1H), 3.4 (s, 3H), 4.2 (s, 1H), 8.6 (br s, 1H, NH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ : 20.20, 22.41, 24.62, 35.82, 49.20, 51.63, 81.30, 160.11, 170.42. EIMS (*m/z*) 198.1 (M+1).

(Z)-Methyl 3-(methylamino) but-2-enoate (14)

^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.66 (s, 3H), 2.69 (d, 3H), 3.32 (s, 3H), 4.15(s, 1H), 8.20 (br s, 1H, NH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ:19.02, 29.86, 49.7, 82.02, 162, 170.7. EIMS m/z 130.1 (M+1, 100).

(Z)-Ethyl 3-(ethanol-amino) but-2-enoate (15)

^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.3(t, *J* =7.34, 3H), 1.82 (s,3H), 3.40(q, 2H), 3.38(t,2H), 3.75(t ,2H), 4.01(q, 2H), 4.45(s,1H), 8.61(Bsr, 1H, NH). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.48; 19.48; 45.17; 58.38; 61.50; 82.37; 162.24;170.74. EIMS (*m/z*) 160.08 (M+1).

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