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Novel, Efficient, and Green Procedure for the Knoevenagel Condensation Catalyzed by Diammonium Hydrogen Phosphate in Water

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Abstract: Knoevenagel condensation of various aromatic and heteroaromatic aldehydes with active methylene compounds such as methyl and ethyl cyanoacetate, malononitrile, and cyanoacetamide proceeds smoothly with stirring in water in the presence of 4 mol% of diammonium hydrogen phosphate. The reactions were carried out at room temperature in short periods with a very simple workup procedure and good to high yields.

Keywords: Alkene, diamamonium hydrogen phosphate, Knoevenagel condensation, water

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INTRODUCTION

The Knoevenagel condensation of aldehydes with active methylene compounds is an important and widely employed method for carboncarbon bond formation in organic synthesis.^[1] The versatile Knoevenagel reaction has numerous applications in the elegant synthesis of fine chemicals,^[2] in the hetero Diels-Alder reaction,^[3] and in synthesis of carbocyclic and heterocyclic compounds of biological significance.^[4] The reaction is usually catalyzed by bases such as amines or their ammonium salts, ammonia, and sodium ethoxide in organic solvents.^[5] Lewis acids,^[6] zeolites.^[7] and heterogenous catalysts^[8] have also been employed to catalyze the reaction. Recently, the solvent-free Knoevenagel condensation on solid support promoted by infrared,^[9] ultrasound,^[10] or microwave irradiation^[11] and also in support-free stoichiometric molten condition^[12] has been a matter of interest. However, most of the reported procedures were carried out in organic solvents with a notable amount of waste. It should be emphasized that most solvent-free methods still require organic solvents during workup, and this is so for the catalyst-free Knoevenagel reaction in water.^[13] Kaupp et al.^[14] reported a green method for the Knoevenagel condensation by the molten catalyst and in the absence of solvent. Yet high reaction temperatures (150-170°C) and long reaction times were required for a complete reaction. There are also some new catalysts such as TPP (triphenylphosphane),^[15] urea,^[16] ionic liquids,^[17] and TBAH (tetrabutylammonium hydroxide)^[18] that were used for the Knoevenagel condensation.

Nowadays, in the development of a new synthesis, ecological points of view must also be taken into account. In this process the solvents are especially important, because they are generally used in large quantities. Many organic solvents are ecologically harmful, and their use should therefore be minimized as far as possible or even avoided altogether. One ideal alternative under investigation as solvent for organic reactions is water^[19]; many biochemical processes occur in the presence of water, and the diversity of the in vivo reactions has prompted chemists to rediscover the potential of water as a solvent. Some efforts have been made to perform the Knoevenagel condensation in aqueous medium as well as in the absence of organic solvents. (Scheme 1)^[20]

RESULTS AND DISCUSSION

I continue our interest in the Knoevenagel condensation and its applications in the synthesis of bioactive molecules,^[21] we hereby report a very simple, green, and highly efficient method for the condensation of various aromatic and heteroaromatic aldehydes (1) with several active methylene compounds (2) such as malononitrile, methyl- and ethyl cyanoacetate, and cyanoacetamide. The reactions were carried out in water at room temperature in the presence of

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4 mol% of diammonium hydrogen phosphate. It was exciting to observe that, except in a few cases, all reactions run rapidly and were completed in just a few minutes, giving excellent yields of the Knoevenagel product **3**.

It was also shown that natural phosphate,^[22] AlPO₄-Al₂O₃,^[23] natural phosphate doped with potassium fluoride,^[24] and phosphate complexes^[25] are efficient catalysts for the Knoevenagel condensation, but all the reported methods need extraction with organic solvents or advance preparation of the catalyst. Diammonium hydrogen phosphate is a very cheap, nontoxic, and commercially available compound that can be used in practice without any special precaution. To the best of our knowledge, there is only one report on the application of diammonium hydrogen phosphate in the synthesis of some classes of heterocyclic compounds.^[26]

At first, the reaction of 4-chlorobenzaldeyde with malononitrlie was selected as a model to examine the effects of catalyst ranging from 0-10% at room temperature. The best yield was obtained when the reaction was carried out in the presence of 4 mol% of diammonium hydrogen phosphate in aqueous media. No other by-product was formed during the course of the reaction. Electron-deficient aldehydes gave relatively higher yields than electron-rich counterparts.

In conclusion, we have demonstrated that the Knoevenagel condensation between aromatic and heteroaromatic aldehydes with active methylene compounds can be effectively performed at room temperature in the presence of a catalytic amount (4 mol%) of diammonium hydrogen phosphate in aqueous media, which provides a simple route to the synthesis of trisubstituted alkenes. The present method has many obvious advantages compared to those reported in literature, including simplicity of the methodology, ease of product isolation (only simple filtration), good yields, short reaction times, use of a very cheap catalyst, and being environmentally benign (Table 1).

EXPERIMENTAL

Melting points were recorded on an Electrothermal 9100 melting-point apparatus and are not corrected. IR spectra were recorded on a FT-IR Perkin-Elmer GX spectrophotometer using KBr disks. ¹H NMR spectra

	Ar	R	Yield ^a (%)	Mp (°C)	
Product				Found	Reported
3a	4-Cl-C ₆ H ₄	CN	70	161	162[27]
3b	$4-Me_2N-C_6H_4$	CN	80	179	179-180 ^[23]
3c	$4-NO_2-C_6H_4$	CN	85	160	160 ^[18,27]
3d	C ₆ H ₅	CO_2Me	90	89	89 ^[5a,21a]
3e	4-Cl-C ₆ H ₄	CO_2Me	75	122	
3f	2,4-Cl ₂ -C ₆ H ₃	CO_2Me	90	78	79-80
3g	3-OH-C ₆ H ₄	CO_2Me	87	145	
3h	$4 - Me_2N - C_6H_4$	CO_2Me	92	146	146 ^[18]
3i	$3-NO_2-C_6H_4$	CO_2Me	92	135	135 ^[18]
3j	$4-NO_2-C_6H_4$	CO_2Me	90	178	$178^{[18]}$
3k	PhCH=CH-	CO ₂ Me	90	144	145 ^[21a]
31	2-Furyl	CO_2Me	85	94	95 ^[15,21a]
3m	2-Thienyl	CO_2Me	80	113-114	
3n	$4-Cl-C_6H_4$	CO ₂ Et	82	91-92	91 ^[23]
30	4-Me ₂ N-C ₆ H ₄	CO ₂ Et	83	125	125 ^[18]
3р	$3-NO_2-C_6H_4$	CO ₂ Et	95	139	139 ^[18]
3q	2-Furyl	CO ₂ Et	90	91-93	91–93 ^[16]
3r	2-Thienyl	CO ₂ Et	80	106	$105 - 108^{[18]}$
3s	$3-NO_2-C_6H_4$	CONH_2	90	156-159	
3t	$4-NO_2-C_6H_4$	$CONH_2$	70	235-236	237-238 ^[16]

Table 1. Synthesis of alkenes catalyzed by diammonium hydrogen phosphate in aqueous media

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^{*a*}In all cases, the yields are related to pure isolated compounds.

were recorded on Bruker DRX 500 (500 MHz) Avance spectrometer in CDCl₃ using TMS as the internal standard.

General Procedure for the Preparation of Alkenes at Room Temperature

To a stirred solution of malononitrile (2.2 mmol, 145 mg) in water (10 ml), diammonium hydrogen phosphate (7 mg, 0.04 mmol) and benzaldehyde (212 mg, 2 mmol) were added. Progress of the reaction was monitored by thin-layer chromatography (TLC) (eluent: petroleum ether–EtOAc, 3:1). After 10 min, the solid material was isolated by simple filtration. Further purification for some samples was made by recrystallization from EtOH.

Selected Data for Compounds 3a-t

3a: 2-(4-Chlorophenylmethylene)malononitrile: mp: 161° C [lit.: 162° C]^[27]; IR (KBr, cm⁻¹): 3038, 2227, 1583, 1486; ¹H NMR (δ , CDCl₃) 7.56

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(d, 2H, J = 8.4 Hz, H-Ar), 7.77 (s, 1H, H-C=C), 7.89 (d, 2H, J = 8.4 Hz, H-Ar).

3b: 2-(4-N,N-dimethylphenylmethylene)malononitrile: mp: 179°C [lit.: 179–180]^[18,23]; IR (KBr, cm⁻¹): 3010, 2208, 15609.

3c: 2-(4-Nitrophenylmethylene)malononitrile: mp: 160° C [lit.: 160]^[18,27]; IR (KBr, cm⁻¹): 3038, 2227, 1582, 1519; ¹H NMR (δ , CDCl₃) 7.88 (s, 1H, H-C=C), 8.10 (d, 2H, J = 7.20 Hz, H-Ar), 8.39 (d, 2H, J = 7.2 Hz, H-Ar).

3d: Methyl-(E)-2-cyano-3-phenyl-2-propenoate: mp: 89°C [lit.: 89]^[5a,21a]; IR (KBr, cm⁻¹): 3038, 2227, 1725, 1608, 1428; ¹H NMR (δ, CDCl₃) 3.90 (s, 3H, OMe), 7.70–8.15 (m, 5H, Ar), 8.25 (s, 1H, H-C=C).

3e: Methyl-(E)-2-cyano-3-(4-chlorophenyl)-2-propenoate: mp: 122°C; IR (KBr, cm⁻¹): 3060, 2227, 1725, 1583; ¹H NMR (δ , CDCl₃) 3.99 (s, 3H, OMe), 7.53 (d, 2H, J = 8.60 Hz, H-Ar), 7.98 (d, 2H, J = 8.60 Hz, H-Ar), 8.25 (s, 1H, H-C-C).

3f: Methyl-(E)-2-cyano-3-(2,4-dichlorophenyl)-2-propenoate: mp: 78°C; IR (KBr, cm⁻¹): 3050, 2250, 1731, 1577; ¹H NMR (δ , CDCl₃) 4.00 (s, 3H, OMe), 7.45 (dd, 1H, J = 8.50, 1.70 Hz, H-Ar), 7.59 (d, 1H, J = 1.70 Hz, H-Ar), 8.25 (d, 1H, J = 8.50, H-Ar), 8.65 (s, 1H, H-C=C).

3g: Methyl-(E)-2-cyano-3-(3-hydroxyphenyl)-2-propenoate: mp: 145°C; IR (KBr, cm⁻¹): 3412, 3032, 2227, 1725, 1596; ¹H NMR (δ , CDCl₃) 3.98 (s, 3H, Me), 5.90 (brs, 1H, OH), 7.12 (m, 1H, Ar), 7.41 (t, 1H, J = 7.80 Hz, H-Ar), 7.47 (d, 1H, J = 7.80 Hz, H-Ar), 8.25 (s, 1H, H-C=C).

3h: Methyl-(E)-2-cyano-3-(4-N,N-dimethylphenyl)-2-propenoate: mp: 146°C [lit.: 146]^[18]; IR (KBr), [cm⁻¹] 2907, 2215, 1715, 1610, 1575; ¹H NMR (δ , CDCl₃) 3.10 (s, 6H,-NMe), 3.90 (s, 3H, OMe), 6.70 (d, 2H, J = 9 Hz, H-Ar), 7.90 (d, 2H, J = 9 Hz, H-Ar), 8.20 (s, 1H, =CH).

3i: Methyl-(E)-2-cyano-3-(3-nitrophenyl)-2-propenoate: mp: 135°C [lit.: 135°C]^[18]; IR (KBr, cm⁻¹) 3080, 2226, 1720, 1609, 1536, 1359.

3j: Methyl-(E)-2-cyano-3-(4-nitrophenyl)-2-propenoate: $178^{\circ}C$ [lit.: $178^{\circ}C$]^[18]; IR (KBr, cm⁻¹) 3119, 2847, 2225, 1731, 1613; ¹H NMR (δ , CDCl₃) 4.0 (s, 3H, OMe), 8.15 (d, 2H, J = 9 Hz, Ar), 8.34 (s, 1H, H–C=C), 8.38 (d, 2H, J = 9 Hz, Ar).

3k: Methyl-(E)-2-cyano-5-phenyl-2,4-pentadieneoate: 145°C [lit.: 145°C]^[21a]; IR (KBr, cm⁻¹) 3031, 2220, 1611,1583; ¹H NMR (δ, CDCl₃) 3.94 (s, 3H, OMe), 7.33 (m, 2H, HC=C), 7.42–7.48 (m, 3H, H-Ar), 7.63 (m, 2H, H-Ar), 8.06 (dd, 1H, *J* = 11, 2.9 Hz, HC=C).

31: Methyl-(E)-2-cyano-3-(furyl)-2-propenoate: 94° C [lit.: 95° C]^[15,21a]; IR (KBr, cm⁻¹) 3135, 2961, 2221, 1725, 1538; ¹H NMR (δ , CDCl₃) 3.95 (s, 3H, OMe), 6.70 (dd, 1H, J = 4.0, 1.9 Hz, H-Furyl), 7.45 (d, 1H, J = 4.0 Hz, H-Furyl), 7.78 (d, 1H, J = 1.9 Hz, H-Furyl), 8.05 (s,1H, H-C=C).

3m: Methyl-(E)-2-cyano-3-(thienyl)-2-propenoate: 113° C IR (KBr, cm⁻¹) 3090, 2961, 2220, 1719, 1596; ¹H NMR (δ , CDCl₃) 3.96 (s, 3H, OMe), 7.27 (d, 1H, J = 4.50 Hz, H-thienyl), 7.83 (d, 1H, J = 4.50 Hz, H-thienyl), 7.89 (d, 1H, J = 3, 50 Hz, H-thienyl), 8.39 (s, 1H, H-C=C).

3n: Ethyl-(E)-2-cyano-3-(4-chlorophenyl)-2-propenoate: $91-92^{\circ}$ C [lit.: 91° C]^[23]; IR (KBr, cm⁻¹) 3050, 2950, 2220, 1725, 1608; ¹H NMR (δ , CDCl₃) 1.45 (t, 3H, *J* = 7.12 Hz), 4.43 (q, 2H, *J* = 7.12 Hz, OCH₂), 7.52 (d, 2H, *J* = 8.56 Hz, H-Ar), 7.97 (d, 2H, *J* = 8.56 Hz, H-Ar), 8.23 (s, 1H, H-C=C).

30: Ethyl-(E)-2-cyano-3-(4-N,N-dimethylphenyl)-2-propenoate: 125° C [lit.: 125° C]^[18]; IR (KBr, cm⁻¹) 2944, 2212, 1713, 1611, 1575; ¹H NMR: (δ , CDCl₃) 1.40 (t, 3H, J = 8 Hz, CH₃), 3.10 (s, 6H, 2NMe), 4.30 (q, 2H, J = 8 Hz, OCH₂), 6.70 (d, 2H, J = 9 Hz, H-Ar), 7.90 (d, 2H, J = 9 Hz, H-Ar), 8.10 (s, 1H, HC=C).

3p: Ethyl-(E)-2-cyano-3-(3-nitrophenyl)-2-propenoate: $139^{\circ}C$ [lit.: $139^{\circ}C$]^[18]; IR (KBr, cm⁻¹) 3036, 2226, 1727, 1609, 1537; ¹H NMR: (δ , CDCl₃): $\delta = 1.50$ (t, 3H, J = 7.2 Hz, CH₃), 4.40 (q, 2H, J = 7.2 Hz, OCH₂), 7.6– 8.80 (m, 4H, Ar), 8.32 (s, 1H, =CH).

3q: Ethyl-(E)-2-cyano-3-(furyl)-2-propenoate: $91-93^{\circ}$ C [lit.: $91-93^{\circ}$ C]^[16]; IR (KBr, cm⁻¹) 3130, 3040, 2223, 1716, 1621; ¹H NMR (δ , CDCl₃) 1.42 (t, 3H, J = 7.2 Hz, Me), 4.40 (q, 2H, J = 7.2 Hz, OCH₂) 6.69 (dd, 1H, J = 3.6, 1.5 Hz, H-Furyl), 7.44 (d, 1H, J = 3.6 Hz, H-Furyl), 7.75 (d, 1H, J = 1.5 Hz, H-Furyl), 8.05 (s,1H, H-C=C).

3r: Ethyl-(E)-2-cyano-3-(thienyl)-2-propenoate: $106^{\circ}C$ [lit.: $105-108^{\circ}C$]^[15,18]; IR (KBr, cm⁻¹) 3086, 2219, 1717, 1599; ¹H NMR: (δ , CDCl₃) 1.39 (t, 3H, J = 7.1 Hz, CH₃), 4.36 (q, 2H, J = 7.1 Hz, CH₂), 7.26 (t, J = 4.79 Hz, 1H, H-Thienyl), 7.81 (d, J = 4.90 Hz, 1H, H-Thienyl) 7.88 (d, J = 3.70 Hz, 1H, H-Thienyl), 8.37 (s, 1H, H-C=C).

3s: 2-Cyano-3-(3-nitrophenyl)-2-propenamide: 156–159°C; IR (KBr, cm⁻¹) 33418, 3129, 2227, 1706, 1608; ¹H NMR (δ, CDCl₃) 5.80 (brs, 1H, NH),

6.30 (brs, 1H, NH), 7.77 (t, 1H, J = 8 Hz, H-Ar), 8.32 (d, 1H, J = 7.7 Hz, H-Ar), 8.43 (d, 1H, J = 7.7 Hz, H-Ar), 8.45 (s, 1H, H-C=C), 8.77 (d, 1H, J = 1.67 Hz, H-Ar).

3t: 2-Cyano-3-(4-nitrophenyl)-2-propenamide: $235-238^{\circ}C$ [lit.: $237-238^{\circ}C$]^[16]; IR (KBr, cm⁻¹) 3438, 3347, 2227, 1688, 1596; ¹H NMR (δ , CDCl₃) 7.35 (brs, 1H, NH), 7.45 (brs, 1H, NH), 8.12 (d, 2H, J = 8.7 Hz, H-Ar), 8.39 (d, 2H, J = 8.7 Hz, H-Ar), 8.44 (s, 1H, H-C=C).

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REFERENCES

- (a) Jones, G. The Knoevenagel condensation reaction. In *Organic Reactions*; John Wiley: New York, 1967; Vol. 15, p. 204; (b) Tietze, L.; Beifuos, V. The Knoevenagel condensation, In *Comprehensive Organic Synthesis*; B. M. Trost and I. Fleming, Eds.; Pergamon Press: Oxford, 1991; Vol. 2, pp. 341–392 Chapter 1.11.
- 2. Freeman, F. Properties and reactions of ylidene malononitriles. *Chem Rev.* **1981**, *81*, 329.
- (a) Borah, H. N.; Deb, M. L.; Boruah, R. C.; Bhuyan, P. J. Stereoselective intramolecular hetero Diels-Alder reaction of 1-oxa-1,3-butadienes: Synthesis of novel annelated pyrrolo[1,2-a]indoles. *Tetrahedron Lett.* 2005, 46, 3391.
- 4. Tietze, L. F. Domino reactions in organic synthesis. Chem. Rev. 1996, 96, 115.
- (a) Ayoubi, S. A.; Texier-Boullet, F.; Hamelin, J. Minute synthesis of electrophilic alkenes under microwave irradiations. *Synthesis* 1994, 258, and references therein;
 (b) Ayoubi, S. A.; Texier-Boullet, F. Clay-mediated synthesis of gem-bis(alkoxy-carbonyl)alkenes under microwave irradiation. *J. Chem. Res. Synop.* 1995, 208;
 (c) Choudary, B. M.; Kantam, M. L.; Neeraja, V.; Rao, K. K.; Figueras, F.; Delmotte, L. Layered double hydroxide fluoride: A novel solid base catalyst for C-C bond formation. *Green Chem.* 2001, *3*, 257;
 (d) Narasaiha, A. V.; Basak, A. K.; Visali, B.; Nagaiah, K. An eco-friendly synthesis of electrophilic alkenes catalyzed by dimethyl aminopyridine under solvent-free conditions. *Synth. Commun.* 2004, *34*, 2893.
- 6. (a) Prajapati, D.; Lekhok, K. C.; Sandhu, J. S.; Ghosh, A. C. Lithium bromide as a new catalyst for carbon–carbon bond formation in solid state. *J. Chem. Soc. Perkin Trans. 1* 1996, 959; (b) Rao, P. S.; Ratnam, R. V. Zinc chloride as a new catalyst for Knoevenagel condensation. *Tetrahedron Lett.* 1991, *32*, 5821; (c) Narsaiah, A. V.; Nagaiah, K. An efficient Knoevenagel condensation catalyzed by LaCl₃ · 7H₂O in hetergenous medium. *Synth. Commun.* 2003, *33*, 3825.

- (a) Wang, Q. L.; Ma, Y.; Zuo, B. Knoevenagel condensation catalyzed by USY zeolite. *Synth. Commun.* **1997**, *27*, 4107; (b) Reddy, T. I.; Varma, R. S. Rareearth (RE) exchanged NaY zeolite promoted Knoevenagel condensation. *Tetrahedron Lett.* **1997**, *38*, 1721.
- Lu, Y.; Ren, Z.; Cao, W.; Tong, W.; Gao, M. Solent-free synthesis of ethyl α-cyanocinnamate in the presence of CaO. Synth. Commun. 2004, 34, 2047.
- Obrador, E.; Castro, M.; Tamariz, J.; Zepeda, G.; Miranda, R.; Delgado, F. Knoevenagel condensation in heterogeneous phase catalyzed by IR radiation and tonsil actisil FF. *Synth. Commun.* **1998**, *28*, 4649.
- Li, J. T.; Chen, G. F.; Wang, S. X.; He, L.; Li, T. S. Synthesis of arylmethylenemalononitrile catalyzed by KF-Al₂O₃ under ultrasound. *Aus. J. Chem.* 2005, 58, 231.
- (a) Loupy, A.; Petit, A.; Hamelin, J.; Texier-Boullet, F.; Jacqualt, P.; Mathe, F. New solvent-free organic synthesis using focused microwave. *Synthesis* 1998, 1213; (b) Hayes, B. L. Recent advances in microwave assisted synthesis. *Aldrichimica Acta* 2004, 73, 66.
- Ren, Z.; Cao, W.; Tong, W. The Knoevenagel condensation reaction of aromatic aldehydes with malononitrile by grinding in the absence of solvents and catalyst. *Synth. Commun.* 2002, *32*, 3475.
- Bigi, F.; Carloni, S.; Ferrari, L.; Maggi, R.; Mazzacani, A.; Sartori, G. Clean synthesis in water, part 2: Uncatalyzed condensation reaction of Meldrum's acid and aldehydes. *Tetrahedron Lett.* 2001, 42, 5203.
- Kaupp, G.; Naimi-Jamal, M. R.; Schmeyers, J. Solvent-free Knoevenagel condensation and Michael additions in the solid state and in the melt with quantitative yield. *Tetrahedron* 2003, 59, 3753.
- Yadav, J. S.; Reddy, B. S.; Basak, A. K.; Visali, B.; Narsaiah, A. V.; Nagaiah, K. Phosphane-catalyzed Knoevenagel condensation: A facile synthesis of α-cyanoacrylates and α-cyanoacrylonitriles. *Eur. J. Org. Chem.* 2004, 546.
- Sun, Q.; Shi, L. X.; Ge, Z. M.; Cheng, T. M.; Li, R. T. An efficient and green procedure for the Knoevenagel condensation catalyzed by urea. *Chin. J. Chem.* 2005, 23, 745.
- (a) Harjani, J. R.; Nara, S. J.; Salunkhe, M. M. Lewis acidic ionic liquids for the synthesis of electrophilic alkenes via the Knoevenagel condensation. *Tetrahedron Lett.* 2002, 43, 1127; (b) Chen, Z. C.; Zheng, Q. G. Organic reactions in ionic liquids: Knoevenagel condensation catalyzed by ethylenediammonium diacetate. *Synthesis* 2003, 555.
- Balalaie, S.; Barajanian, M. Tetra-butylammonium hydroxide (TBAH) catalyzed Knoevenagel condensation: A facile synthesis of α-cyanoacrylates, α-cyanoacrylonitriles, and α-cyanoacrylamides. *Synth. Commun.* 2006, 36, 533–539.
- (a) Grieco, P. A. In Organic Synthesis in Water; Thomson Science: London, 1998; pp. 1–304; (b) Li, C. J.; Chan, T. H. Organic Reactions in Aqueous Media; John Wiely and Sons: New York, 1997; pp. 1–189; (c) Lindstrom, U. M. Stereoselective organic reaction in water. Chem. Rev. 2002, 102, 2751.
- (a) Hangarge, R. V.; Sonwane, S. A.; Jarikote, D. V.; Shingare, M. S. Water mediated uncatalyzed facile synthesis of ylidenenitriles of 4-oxo-4H-1-benzopyran-3-carbaldehyde. *Green Chem.* 2001, *3*, 310; (b) Wang, S.; Ren, Z.; Cao, W.; Tong, W. The Knoevenagel condensation of aromatic aldehydes with malonitrile or ethylcyanoacetate in the presence of CTMAB in water. *Synth. Commun.* 2001, *31*, 673; (c) Deb, M. L.; Bhuyan, P. J. Uncatalyzed Knoevenagel condensation in aqueous medium at room temperature. *Tetrahedron Lett.* 2005, *46*, 6453.

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- 21. (a) Balalaie, S.; Nemati, N. Ammonium acetate-basic alumina catalyzed Knoevenagel condensation under microwave irradiation and solvent-free condition. *Synth. Commun.* **2000**, *30*, 869; (b) Balalaie, S.; Nemati, N. One-pot preparation of coumarins by Knoevenagel conditions under solvent-free condition and microwave irradiation. *Heterocycl. Commun.* **2001**, *7*, 67.
- (a) Sebti, S.; Saber, A.; Rhihil, A. Phosphate naturel et phosphate trisodique; nouveaux catalyseurs solides de la condensation de Knoevenagel en milieu heterogene. *Tetrahedron Lett.* **1994**, *35*, 9399; (b) Sebti, S.; Nazih, R.; Tahir, R.; Saber, A. Fluorapatite/sodium nitrate as a solid support for the Knoevenagel reaction. *Synth. Commun.* **2001**, *31*, 993.
- Cabello, J. A.; Campelo, J. M.; Garcia, A.; Luna, D.; Marians, J. M. Knoevenagel condensation in the heterogenous phase using AlPO₄-Al₂O₃ as a new catalyst. *J. Org. Chem.* **1984**, *49*, 5195.
- Sebti, S.; Smahli, A.; Solhy. A. Natural phosphate doped with potassium flouride and modified with sodium nitrate: Efficient catalysts for the Knoevenagel condensation. *Tetrahedron Lett.* 2002, 43, 1813.
- Bennazha, J.; Zahouilly, M.; Boukhari, A.; Hole, E. A. Investigation of catalytic activity of solid state phosphate complexes in the Knoevenagel condensation. *J. Mol. Catal. A.* 2003, 202, 247.
- Salehi, P.; Dabiri, M.; Khosropour, A. R.; Roozbehniya, P. Diammonium hydrogen phosphate: A versatile and cheap reagent for one-pot synthesis of dihydropyrimidinones, quinazolinones, and azalactones under solvent-free conditions. *J. Iran. Chem. Soc.* 2006, *3*, 98–104.
- Moison, H.; Texier-Boullet, F.; Foucaud, A. Knoevenagel, Wittig and Wittig– Horner reactions in the presence of magnesium oxide or zinc oxide. *Tetrahedron* 1987, 43, 537.