This article was downloaded by: [Monash University Library] On: 12 March 2013, At: 01:13 Publisher: Taylor & Francis Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



## Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information: <u>http://www.tandfonline.com/loi/lsyc20</u>

# An Efficient Knoevenagel Condensation Catalyzed by $LaCI_3$ .7H<sub>2</sub>O in Heterogeneous Medium<sup>#</sup>

A. Venkat Narsaiah <sup>a</sup> & Dr. K. Nagaiah <sup>a</sup>

<sup>a</sup> Organic Chemistry Division, Fine Chemicals Laboratory, Indian Institute of Chemical Technology, Hyderabad, India Version of record first published: 16 Aug 2006.

To cite this article: A. Venkat Narsaiah & Dr. K. Nagaiah (2003): An Efficient Knoevenagel Condensation Catalyzed by LaCl<sub>3</sub>.7H<sub>2</sub>O in Heterogeneous Medium<sup>#</sup>, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 33:21, 3825-3832

To link to this article: <u>http://dx.doi.org/10.1081/SCC-120025194</u>

### PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: http://www.tandfonline.com/page/terms-and-conditions

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae, and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand, or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.



©2003 Marcel Dekker, Inc. All rights reserved. This material may not be used or reproduced in any form without the express written permission of Marcel Dekker, Inc.

SYNTHETIC COMMUNICATIONS<sup>®</sup> Vol. 33, No. 21, pp. 3825–3832, 2003

## An Efficient Knoevenagel Condensation Catalyzed by LaCl<sub>3</sub>.7H<sub>2</sub>O in Heterogeneous Medium<sup>#</sup>

A. Venkat Narsaiah and K. Nagaiah\*

Organic Chemistry Division, Fine Chemicals Laboratory, Indian Institute of Chemical Technology, Hyderabad, India

#### ABSTRACT

Knoevenagel condensation was carried out in absence of solvent with a mild Lewis acid Lanthanum(III) chloride, to prepare substituted alkenes. A systematic study of the reaction to establish the generality of the method has been undertaken with various aldehydes and active methylene compounds.

*Key Words:* Lanthanum chloride; Knoevenagel condensation; Active methylene compounds; Substituted alkenes; Trimethoprim.

3825

DOI: 10.1081/SCC-120025194 Copyright © 2003 by Marcel Dekker, Inc. 0039-7911 (Print); 1532-2432 (Online) www.dekker.com

<sup>\*</sup>Correspondence: Dr. K. Nagaiah, Organic Chemistry Division, Fine Chemicals Laboratory, Indian Institute of Chemical Technology, Tarnaka, Hyderabad-500 007, India; Fax: +91-40-27160512; E-mail: nagaiah@iict.ap.nic.in.

SM4

©2003 Marcel Dekker, Inc. All rights reserved. This material may not be used or reproduced in any form without the express written permission of Marcel Dekker, Inc.

3826

#### Narsaiah and Nagaiah

#### INTRODUCTION

The reaction of active methylene carbon with carbonyl compounds is a classical synthetic route to make carbon–carbon bond. Knoevenagel<sup>[1]</sup> condensation is one of the most important preparating method for substituted alkenes and it has numerous applications in the elegant synthesis of fine chemicals which are valuable precursors to a wide variety of target molecules in pharmaceutical industry. It may be carried out either in homogeneous or heterogeneous phase. Ammonium<sup>[2]</sup> salts (primary, secondary, and tertiary) generally catalyzed these reactions. There are few reports with Lewis<sup>[3]</sup> acids (ZnCl<sub>2</sub>, TiCl<sub>4</sub>-Base). In recent years, the use of inorganic solid<sup>[4]</sup> supports as catalyst (Al<sub>2</sub>O<sub>3</sub> LiBr SiO<sub>2</sub>, AlPO<sub>4</sub>-Al<sub>2</sub>O<sub>3</sub>, Clay-KSF, K<sub>10</sub>-ZnCl<sub>2</sub>, and xonolite, Silicagel functionalized with amine group), is well known. Most of the organic reactions have been studying in solvent medium. But there is a considerable interest in developing solvent-free green processes. It may be conventional or nonconventional where as in conventional, the reactants, reagents, and catalyst were mixed and heated to a required temperature without any solvent.

In continuation of our ongoing research efforts to develop newer, environmentally benign methods for chemical transformations, we decided to investigate the effect of a milder Lewis acid i.e., Lanthanum(III) chloride as a catalyst for Knoevenagel condensation. The earlier known work in this area is permitted only to the reactions of acetalization,<sup>[5]</sup> selective reductions in association with sodium borohydride<sup>[6]</sup> (NaBH<sub>4</sub>) and lithium aluminum hydride (LAH).<sup>[7]</sup>

Herein, we wish to report the use of a new catalyst, Lanthanum(III) chloride heptahydrate, for the preparation of substituted alkenes in heterogeneous phase in the absence of solvent at 80–85°C (Sch. 1). It can perform, the reaction to produce the products in high purity and excellent yields. The efficient Knoevenagel condensation between diethyl malonate, dicyano malonate, ethyl cyano malonate, and different aldehydes, consequently a systematic and comparative study of this reaction



Scheme 1.

©2003 Marcel Dekker, Inc. All rights reserved. This material may not be used or reproduced in any form without the express written permission of Marcel Dekker, Inc.

Knoevenagel Condensation Catalyzed by LaCl<sub>3</sub>.7H<sub>2</sub>O





Scheme 2.

to establish the generality of the method has been undertaken with various aromatic aldehydes, bearing a variety of functional groups such as electron donating groups (hydroxy, methoxy, chloro, methyl) and electron withdrawing group (nitro) and aliphatic aldehydes were also studied. Aliphatic aldehydes did not give good results but aromatic aldehydes reacts faster and in excellent yields. The reaction conditions and the corresponding yields of these active methylene species suggest their reactivity order is  $CN > CO_2Et$ . The results obtained with various aldehydes and different malonates were shown in Table 1.

In the reaction of 3,4,5-trimethoxybenzaldehyde and active methylene compound of ethyl cyano acetate, the product obtained compound **6** was treated with Pd/c to saturate the double bond. This saturated product **7** on condensation with guanidine<sup>[8]</sup> by literature procedure gives a product which is a well known antibacterial agent called "Trimethoprim." This is an easy and convenient method for the preparation of Trimethoprim (Sch. 2).<sup>[9]</sup>

In conclusion, we have demonstrated the general utility of Lanthanum(III) chloride heptahydrate in the Knoevenagel condensation. The reaction of carbonyl substrates and active methylene compounds, using  $LaCl_3.7H_2O$  in catalytic (0.01 equiv.) amount to produce the corresponding olefinic products in excellent yields, without using any solvent and easy work-up procedures.

#### **EXPERIMENTAL**

#### General Procedure for the Synthesis of Substituted Alkenes

To a mixtures of the carbonyl compound (10 mmol) and active methylene compound (10 mmol) was added Lanthanum(III) chloride

©2003 Marcel Dekker, Inc. All rights reserved. This material may not be used or reproduced in any form without the express written permission of Marcel Dekker, Inc.

#### 3828

#### Narsaiah and Nagaiah

	ε			5 5		
Entry	R	$R^1$	$R^2$	Product <sup>a</sup>	Time (h)	Yield <sup>b</sup>
1	Н	CN	CO <sub>2</sub> Et	CN CO <sub>2</sub> Et	1.5	89
2	4-CH <sub>3</sub>	CN	CO <sub>2</sub> Et	H <sub>3</sub> C	2.0	85
3	2-Cl 4-Cl	CN	CN	CI CI CN	1.0	90
4	4-OCH <sub>3</sub>	CO <sub>2</sub> Et	CO <sub>2</sub> Et	Me O CO <sub>2</sub> Et	2.5	86
5	Н	CO <sub>2</sub> Et	CO <sub>2</sub> Et	CO <sub>2</sub> Et	2.5	84
6	4-OCH <sub>3</sub>	CN	CN	MeO	1.5	90
7	4-OH	CN	CO <sub>2</sub> Et	HO CO <sub>2</sub> Et	2.5	85
8	4-NO <sub>2</sub>	CO <sub>2</sub> Et	CO <sub>2</sub> Et	O2N CO2Et	2.5	87
9	2-Cl 4-Cl	CN	CO <sub>2</sub> Et	CI CO <sub>2</sub> Et	1.5	88
10	Н	CN	CN	CN CN	1.0	95
11	4-OH	CO <sub>2</sub> Et	CO <sub>2</sub> Et	HO CO <sub>2</sub> Et	3.0	80
12	4-0CH <sub>3</sub>	CN	CO <sub>2</sub> Et	MeO CO <sub>2</sub> Et	2.0	88

Table 1. Knoevenagel condensation catalyzed by Lanthanum(III) ch	loride.
--	---------

<sup>b</sup>Isolated yields.

(1 mmol) heptahydrate at room temperature. After being stirred for few minutes, the resulting mixture was heated at  $80-85^{\circ}$ C in an oil bath for required time (see in Table 1). Then it was cooled to room temperature, the solidified material was dissolved in ethyl acetate and washed with water. The organic layer was dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated to

<sup>&</sup>lt;sup>a</sup>All the products were characterized by comparison of their M.p, IR and <sup>1</sup>HNMR spectra with those of authentic samples.<sup>[10]</sup>

©2003 Marcel Dekker, Inc. All rights reserved. This material may not be used or reproduced in any form without the express written permission of Marcel Dekker, Inc.

#### Knoevenagel Condensation Catalyzed by LaCl<sub>3</sub>.7H<sub>2</sub>O

3829

yield crude product, which was purified by column chromatography. (Silicagel 60–120 mesh).

#### Preparation of Ethyl 3,4,5-Trimethoxy Benzylidene Malononitrile (6)

To a mixture of 3,4,5-trimethoxy benzoldehyde (1.96 gm, 10 mmol) and ethyl cyano acetic acid (1.13 gm, 10 mmol) was added Lanthanum(III) chloride hyptahydrate (0.245 g, 1 mmol). The contents were heated to  $80-85^{\circ}$ C for 1 h. Then cooled to room temperature and the solidified mass was dissolved in ethyl acetate (25 mL) washed with water the organic layer was dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated to yield crude product, which was purified by column chromatography to yield a white solid (2.62 g, 90%). <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  8.08 (s, 1H), 7.27 (s, 2H), 4.3 (q, 2H, O<u>CH</u>-CH<sub>3</sub>, J=6.5 Hz), 3.9 (two singlets, 9H), 1.35–1.45 (t, 3H, J=6 Hz). IR (CDCl<sub>3</sub>): 3100–2800, 2210, 1705, 1600 cm<sup>-1</sup>.

#### Preparation of Ethyl Ester 2-(3,4,5-Trimethoxy Benzyl) Cyano Acetic Acid (7)

A mixture of alkene compound<sup>[6]</sup> (2.0 g), Ethyl acetate (20 mL) and 10% pd/c (150 mg) were stirred under hydrogen atmosphere (Balloon) for 5 h at room temperature. The reaction mixture was filtered and purified by column chromatography to yield pure product, light brown solid. The yield was quantitative (96%). <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  6.5 (s, 2H), 4.2–4.35 (q, 2H, J = 8 Hz), 3.8–3.9 (two singlets, 9H), 3.6–3.7 (q, 1H, J = 6 Hz), 3.1–3.2 (q, 2H), 1.25–1.35 (t, 3H, J = 6 Hz).

In the similar manner, the Knoevenagel condensations of aldehydes (Showed in Table 1) were performed to obtain the corresponding malano esters. The spectral data of entry 1–12 are as follows:

**Entry-1.** IR (Neat). 3100–2800, 2210, 1710,  $1600 \text{ cm}^{-1}$ . <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  8.25 (s, 1H), 8.0 (d, d, 2H), 7.5 (m, 3H), 4.35–4.4.45 (q, 2H, O<u>CH</u><sub>2</sub>-CH<sub>3</sub>, J = 7 Hz), 1.38–1.48 (t, 3H, OCH<sub>2</sub>-<u>CH</u><sub>3</sub>, J = 7 Hz).

**Entry-2.** IR (Neat): 3100–2860, 2215, 1715, 1610 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  8.2 (s, 1H), 7.8 (d, 2H, J=8.0 Hz), 7.3 (d, 2H, J=7.5 Hz), 4.4 (q, 2H, OCH<sub>2</sub>-CH<sub>3</sub> J=6.5 Hz), 2.4 (s, 3H, Ar-CH<sub>3</sub>), 1.4 (t, 3H, OCH<sub>2</sub>-CH<sub>3</sub>, J=6.5 Hz).

**Entry-3.** IR (Neat): 3050–2800, 2220, 1710,  $1600 \text{ cm}^{-1}$ . <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  8.23 (s, 1H), 8.18 (s, 2H), 7.6 (d, 1H), 7.5 (d, d, 1H, J=8 Hz).

©2003 Marcel Dekker, Inc. All rights reserved. This material may not be used or reproduced in any form without the express written permission of Marcel Dekker, Inc.

#### Narsaiah and Nagaiah

**Entry-4.** IR (Neat): 3100–2800, 1730, 1605 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  7.6 (s, 1H), 7.35 (d, 2H, J=8.0 Hz), 6.8 (d, 2H, J=8.0 Hz), 4.4 (q, 2H, J=7.0 Hz), 4.3 (q, 2H, J=7.0 Hz), 3.8 (s, 3H, OCH<sub>3</sub>), 1.4 (t, 3H, J=7.0 Hz), 1.3 (t, 3H, J=7.0 Hz, OCH<sub>2</sub>-<u>CH<sub>3</sub></u>).

**Entry-5.** IR (Neat): 3100–2800, 1730, 1630 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  7.8 (s, 1H), 7.5–7.3 (m, 5H, Ar-H), 4.4 (q, 2H, J=7.0 Hz, O<u>CH</u><sub>2</sub>-CH<sub>3</sub>), 4.3 (q, 2H, J=7.0 Hz, O<u>CH</u><sub>2</sub>-CH<sub>3</sub>), 1.32 (t, 3H, J=7.0 Hz, OCH2-<u>CH</u><sub>3</sub>), 1.26 (t, 3H, J=7.0 Hz, OCH2-<u>CH</u><sub>3</sub>).

**Entry-6.** IR (Neat): 3100–2800, 2230, 1700,  $1620 \text{ cm}^{-1}$ . <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  7.95 (d, 2H, J = 8.5 Hz), 7.65 (s, 1H), 7.0 (d, 2H, J = 8.5 Hz), 3.95 (s, 3H, OCH<sub>3</sub>).

Entry-7. IR (Neat): 3460–3180, 3080–2900, 2220, 1710, 1600 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  8.2 (s, 1H), 7.9 (d, 2H, J=8.0 Hz), 7.0 (d, 2H, J=8.0 Hz), 4.4 (q, 2H, O<u>CH</u><sub>2</sub>-CH<sub>3</sub> J=7.0 Hz), 1.4 (t, 3H, OCH<sub>2</sub>-<u>CH</u><sub>3</sub>, J=7.0 Hz).

**Entry-8.** IR (Neat): 3100–2850, 1725, 1638 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  8.2–8.0 (d, 2H, J = 10 Hz), 7.8 (s, 1H), 7.7–7.6 (d, 2H, J = 10 Hz), 4.45–4.3 (m, 4H), 1.35–1.25 (t, 6H).

**Entry-9.** IR (Neat): 3100–2850, 2210, 1710,  $1600 \text{ cm}^{-1}$ . <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  8.6 (s, 1H), 8.3 (d, 1H, J=8.5 Hz), 7.6 (d, 1H), 7.45 (d, d, 1H, J=8.0 Hz), 4.4 (q, 2H, O<u>CH</u><sub>2</sub>-CH<sub>3</sub>), 1.45 (t, 3H, OCH<sub>2</sub>-<u>CH</u><sub>3</sub>).

**Entry-10.** IR (Neat): 3100–2800, 2230, 1700, 1620 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  7.9 (d, 2H, J = 8.5 Hz), 7.8 (s, 1H), 7.5–7.7 (m, 3H).

**Entry-11.** IR (Neat): 3340, 3100–2900, 1730, 1630 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  7.7 (s, 1H), 7.4 (d, 2H, J = 8.0 Hz), 6.9 (d, 2H, J = 8.0 Hz), 6.75 (br, s, 1H, <u>OH</u>), 4.4 (q, 2H, <u>OCH</u><sub>2</sub>-CH<sub>3</sub> J = 7.0 Hz), 4.3 (q, 2H, J = 7.0, OCH<sub>2</sub>-CH<sub>3</sub>), 1.3 (t, 6H, J = 7.0 Hz, OCH<sub>2</sub>-CH<sub>3</sub>).

**Entry-12.** IR (Neat): 3100–2800, 2210, 1705,  $\overline{1600} \text{ cm}^{-1}$ . <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  8.15 (s, 1H), 8.0 (d, 2H, J = 7.0 Hz), 7.0 (d, 2H, J = 7 Hz), 4.3–4.43 (q, 2H, <u>OCH</u><sub>2</sub>-CH<sub>3</sub>, J = 7 Hz), 3.9 (s, 3H, OCH<sub>3</sub>), 1.35–1.4 (t, 3H, OCH<sub>2</sub>-<u>CH<sub>3</sub></u>, J = 7 Hz).

#### REFERENCES

- 1. Knoevenagel, E. Condensationen zwischen malonester und aldehyden unter dem einfluss von ammoniak und organischen amminen. Chem. Ber. **1898**, *31*, 2596.
- (a) Jones, G. Organic Reactions; The Knoevenagel condensation reaction, Wiley: New York, 1967; Vol. XV, 204 p; (b) Popp, F.D.; McEwen, W.E. Chem. Rev. 1958, 58, 321.

#### 3830

3831

©2003 Marcel Dekker, Inc. All rights reserved. This material may not be used or reproduced in any form without the express written permission of Marcel Dekker, Inc.

#### Knoevenagel Condensation Catalyzed by LaCl<sub>3</sub>.7H<sub>2</sub>O

- (a) Rao, P.S.; Venkataratnam, R.V. Zinc chloride as a new catalyst for Knoevenagel condensation. Tetrahedron Lett. **1991**, *32*, 5821;
  (b) Lehnert, W. Verbesserte variante der Knoevenagel-kondensation mit TiCl<sub>4</sub>/THF/pyridine (I). Tetrahedron Lett. **1970**, *54*, 4723.
- 4. (a) Texier-Boullet, F.; Foucaud, A. Knoevenagel condensation catalysed by aluminium oxide. Tetrahedron Lett. 1982, 23, 4927; (b) Chalais, S.; Laszlo, P.; Mathy, A. Catalysis of the Knooevenagel condensation. Tetrahedron Lett. 1985, 26, 4453; (c) Cabello, J.A.; Campelo, J.M.; Garcia, A.; Luna, D.; Marinas, J.M. J. Org. Chem. 1984, 49, 5195; (d) Bram, G.; Loupy, A.; Villemin, D. In Solid Supports and Catalyst in Organic Synthesis; Smith, K., 1992, Ellis Horwood, Prentice Hall: Chichester, 1992; Ch. 12; (e) Villemin, D.; Martin, B. J. Chem. Res. (S) 1994, 146; (f) Angeletti, E.; Canepa, C.; Martinetti, G.; Venturello, P. Amino groups immobilized on Silica gel; An efficient and reusable heterogeneous catalyst for the Knoevenagel condensation. J. Chem. Soc. Perkin Trans. 1. 1989, 105; (g) Abdallah-E, Ayobbis, S.; Texier-Boullet, F. J. Chem. Res. (S) 1995, 208; (h) Cruz, P.D.L.; Barra, D.E.; Loupy A.; Lang, F. Silica gel catalysed Knoevenagel condensation in dry media under microwave irradiation. Tetrahedron Lett. 1996, 37, 1113; (i) Prajapati, D.; Lekhok, K.C.; Sandhu, J.S.; Ghosh, A.C. Lithium bromide as a new catalyst for carbon-carbon bond formation in the solid state. J. Chem. Soc., Perkin Trans. 1. 1996, 959; (j) Reddy, T.I.; Varma, R.S. Rare-earth (RE) exchanged NaY zeolite promoted Knoevenagel condensation. Tetrahedron Lett. 1997, 38, 1721; (k) Franca, B.; Luca, C.; Raimondo, M.; Giovanni, S. Montmorillonite KSF as an inorganic, water stable and reusable catalyst for the Knoevenagel synthesis of Coumarin-3-carboxylic Acids. J. Org. Chem. 1999, 64, 1033-1035.
- Luche, J.L.; Gemal, A.L. Efficient synthesis of acetals catalysed by rare earth Chlorides. J. Chem. Soc., Chem. Commun. 1978, 976.
- Gomal, A.L.; Luche, J.L. Lanthanoids in organic synthesis. 6. The reducation of α-enones by sodium borohydride in the presence of lanthanoid chlorides: Synthetic and Mechanistic Aspects. J. Amer. Chem. Soc. 1981, 103, 5454.
- Fukuzawa, S.; Fujinami, J.; Yamauchi, S.; Sakai, S. 1,2-Reioselective reduction of α,β-unsaturated carbonyl compounds with lithium aluminium hydride in the presence of lanthanoid salts. J. Chem. Soc. Perkin Trans 1. **1986**, 1929.
- 8. Mary Smal, H.T.; Cheung, A.; Davis, P.E. Selectively <sup>13</sup>C-enriched 2,4-Diamines-5-(3,4,5-trimethoxy benzyl) pyrimidine (trimethoprim)

©2003 Marcel Dekker, Inc. All rights reserved. This material may not be used or reproduced in any form without the express written permission of Marcel Dekker, Inc.

#### 3832

#### Narsaiah and Nagaiah

and 2,4-diaminopyrimidine. J. Chem. Soc. Perkin Trans 1. 1986, 747.

- (a) Roth, B.; Falco, E.A.; Hitchings, G.H.; Bushby, S.R.M. J. Med. Pharm. Chem. **1962**, *5*, 1103; (b) Sebti, S.; Nazih, R.; Rahir, R.; Salhi, L.; Saber, H. Fluorapatite: new solid catalyst of the Knoevenagel reaction in heterogenous media with solvent. Applied Catalysis A **2000**, *197*, L187–L190.
- (a) Curini, M.; Francesco, E.; Maria, C.M.; Orneli, R.; Andre,T.; Potassium exchanged layered zirconium phosphate as base catalyzed in Knoevenagel condensation. Synthetic Communi. 2002, 33 (3), 355–362; (b) Sang-Yun, Y.K.; Pan-Suk, K.; Tae-Woo, Kwon. Microwave enhanced Knoevenagel condensation of ethyl cyano acetate with aldehydes. Synthetic Communi. 1997, 27 (4), 533–541.

Received in the UK May 17, 2003