



MICROWAVE ASSISTED SOLVENT FREE KNOEVENAGEL CONDENSATION OF AROMATIC ALDEHYDES WITH ETHYLCYANOACETATE CATALYZED BY NH₄OAc

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ABSTRACT

Ammonium acetate catalyses the efficient Knoevenagel condensation of aromatic aldehydes **1a-e** with active methylene compound **2** in solvent-free conditions under microwave irradiation to give arylidene derivatives **3a-e**. The reaction is clean, shorter reaction time and mild reaction condition compared to conventional methods. Functional groups such as nitro, hydroxy and chloro survived under the reaction condition. The yield is high and the purity is good. The method is convenient and useful.

Keywords: Arylidenes-acrylates, aldehydes, ethylcyanoacetate, Knoevenagel condensation, microwave irradiation, solvent free

INTRODUCTION

Organic reactions under solvent free (Tanaka and Tod 2000; Loupy 2000) have increasingly attracted chemists' particularly from the viewpoint of green chemistry (Anastas *et al.* 1998) Knoevenagel reaction is an important carbon-carbon bond forming reaction, which is generally catalyzed by base or Lewis acid in the liquid phase system. In recent years, chemists paid more and more attention to the clean synthesis of alkenes by Knoevenagel condensation. During the past two decades, considerable attention has been focused on the application of microwave in organic synthesis and a handful of papers in this field were reported. Microwave-assisted organic synthesis (MAOS) under solvent free condition has a significant impact on synthetic chemistry because of its intrinsic advantages, like it reduces the reaction time, energy and manpower, increases the reaction yields, and suppresses the reaction side product (Wolkenberg *et al.* 2004, Varma *et al.* 1999). Due to the easier work up, milder reaction conditions and higher selectivity the use of inorganic solids as catalysts is rapidly increasing. In general, the Knoevenagel condensations is catalyzed by organic bases such as aliphatic amines, ethylenediamine and piperidine. The Knoevenagel condensations between aldehydes and malonitrile in dry media catalyzed by

ZnCl₂ (Rao *et al.* 1991), silica gel (Cruz *et al.* 1996)) have been reported. Environmentally friendly solid bases such as AlPO₄-Al₂O₃ Cabello J. A. *et al.* 1984), ZnO or MgO (Moison *et al.* 1987) have been employed in Knoevenagel condensation. No attention has been paid to the use of readily available and cheaper NH₄OAc as catalyst. Bhuiyan *et al.* (2012) reported the synthesis of arylidenemalonitriles by the reaction of malonitriles and aldehydes. The reagent ethylcyanoacetate is an active methylene compound largely used in the Knoevenagel condensation. The acrylates thus obtained have applications in industry, agriculture, and medicine. So far literature study, it is observed that the Knoevenagel condensation between active methylene compound ethyl cyanoacetate with derivatives of aldehydes under solvent free condition has not been reported yet. Herein we report our study on the Knoevenagel condensation of various aldehydes with ethyl cyanoacetate under solvent free using NH₄OAc as catalyst.

MATERIALS AND METHODS

Melting point were recorded Gallenkamp melting point apparatus and are uncorrected. The thin layer chromatography was performed on Kieselgel GF254 and visualization was accomplished by iodine vapour

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or UV light. ^1H NMR spectra were recorded on a JEOL JNM ECS FT NMR at 400 MHz spectrometer using tetramethylsilane as an internal standard. Coupling constant J are given in Hz. Infrared spectra were observed on a Shimadzu FTIR- spectrometer (IR prestige 21). Analytical TLC was performed on pre-coated alumina sheet and the product were visualized by UV light. All reactions were carried out in a commercially available Samsung microwave oven (Samsung, MW76ND).

General procedure for the synthesis of acrylate:

To an equimolecular mixture of aromatic aldehyde **1** and ethyl cyanoacetate **2** was added catalytic amount of ammonium acetate (NH_4OAc) in a Pyrex glass 50 ml beaker and mixed thoroughly with the help of glass rod. The mixture was then subjected to microwave irradiation at 300 W for 50 to 120 sec. The progress of the reaction was followed by TLC (hexane:ethyl acetate). After complete conversion and cooling of the reaction, the solid mass was recrystallized using ethyl acetate and n-hexane solvent mixture.

Ethyl 2-cyano-3-(4-chlorophenyl)acrylate (1a): white crystals, Mp: 85-87 °C. IR(KBr) $\nu_{\text{max}}(\text{cm}^{-1})$: 3050 (aromatic =C-H), 2995 (alkene =C-H) 2225 ($\text{C}\equiv\text{N}$), 1725($\text{C}=\text{O}$), 1600($\text{C}=\text{C}$). ^1H NMR δ_{ppm} 8.20 (s, 1H), 7.93(d, 2H), 7.49(d, 2H), 4.40(q, 2H), 1.40(t, 3H).

Ethyl 2-cyano-3-(4-methoxyphenyl)acrylate (1b): light yellow crystals. Mp: 78-80 °C. IR(KBr) $\nu_{\text{max}}(\text{cm}^{-1})$: 3028 (aromatic =C-H), 2993 (alkene =C-H), 2845 (CH_3 C-H), 2216 ($\text{C}\equiv\text{N}$), 1712($\text{C}=\text{O}$), 1585($\text{C}=\text{C}$). ^1H NMR δ_{ppm} 8.17 (s, 1H), 8.01(d, 2H, $J = 7.2$ Hz), 7.0(d, 2H, $J = 7.2$ Hz), 4.37(q, 2H, $J = 8$ Hz), 1.39(t, 3H, $J = 7.2$ Hz), 3.89(s, 3H). ^{13}C NMR (CDCl_3) δ_{ppm} 163.75, 163.14, 154.41, 134, 124.33, 114.70, 116.21, 99.34, 62.33, 55.50, 14.17.

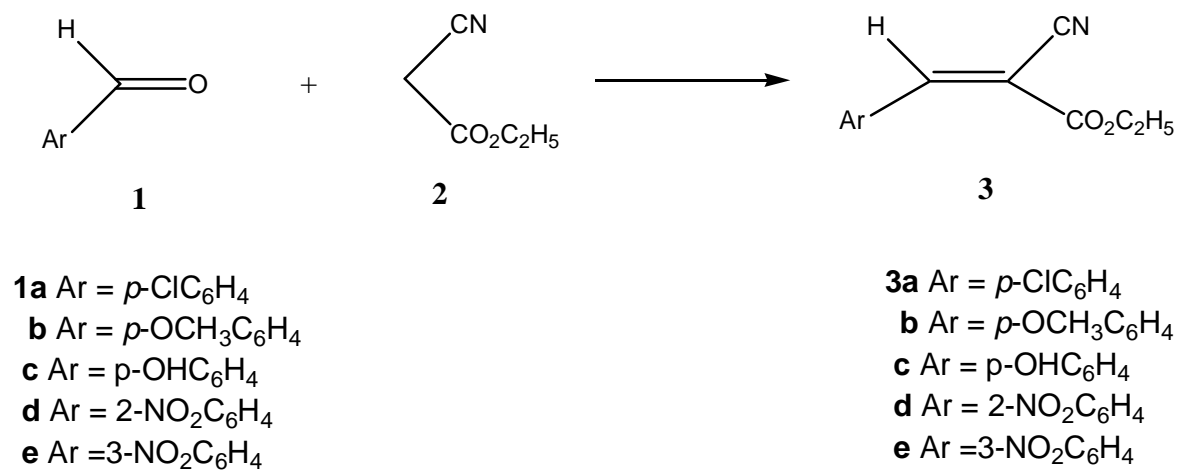
Ethyl 2-cyano-3-(4-hydroxyphenyl)acrylate (1c): light yellow crystals. Mp: 172-173 °C IR(KBr) $\nu_{\text{max}}(\text{cm}^{-1})$: 3288 (OH str.), 3040 (aromatic C-H), 2987 (alkene =C-H), 2233 ($\text{C}\equiv\text{N}$), 1732($\text{C}=\text{O}$), 1585($\text{C}=\text{C}$). ^1H NMR δ_{ppm} 8.23 (s, 1H), 8.0 (d, 2H, $J = 7.0$ Hz), 6.95(d, 2H, $J = 7.0$ Hz), 4.27(q, 2H, $J = 7.0$ Hz), 1.28(t, 3H, $J = 7.2$ Hz), 3.34(s, 1H). ^{13}C NMR (CDCl_3) δ_{ppm} 163.45, 163.12, 154.22, 134.55, 124.33, 122, 116.86, 97.42, 62.45, 14.55.

Ethyl 2-cyano-3-(2-nitrophenyl)acrylate (1d): light yellow crystal. Mp: 100-102 °C. IR(KBr) $\nu_{\text{max}}(\text{cm}^{-1})$: 3107(aromatic C-H), 2910(alkene =C-H), 2229 ($\text{C}\equiv\text{N}$), 1727($\text{C}=\text{O}$), 1622($\text{C}=\text{C}$). ^1H NMR δ_{ppm} 8.73(s, 1H), 8.28 (d, 1H, $J = 9.2$ Hz), 7.82(d, 1H, $J = 6.8$ Hz), 7.85(t, 1H, $J = 8$ Hz), 7.72(t, 1H, $J = 6.8$ Hz), 4.43(q, 2H, $J = 7.2$ Hz), 1.42(t, 3H, $J = 7.2$ Hz). ^{13}C NMR (CDCl_3) δ_{ppm} 161, 153.09, 147.37, 134.49, 132.17, 130.58, 128.11, 125.41, 113.89, 108.64, 63.17, 14.10.

Ethyl 2-cyano-3-(3-nitrophenyl)acrylate (1e): White powder. Mp: 125-127 °C. IR(KBr) $\nu_{\text{max}}(\text{cm}^{-1})$: 3070(aromatic C-H), 2994(alkene =C-H), 2960(- CH_3), 2225 ($\text{C}\equiv\text{N}$), 1718($\text{C}=\text{O}$), 1606($\text{C}=\text{C}$). ^1H NMR δ_{ppm} 8.70(s, 1H), 7.72-8.41 (m, 4H), 4.41(q, 2H), 1.41(t, 3H). ^{13}C NMR (CDCl_3) δ_{ppm} 161.45, 151.82, 148.56, 134.49, 135.13, 132.84, 130.52, 127.05, 125.90, 114.52, 106.60, 63.26, 14.09.

RESULTS AND DISCUSSION

Various methods for the synthesis of aryledene-malonitriles and α -cyanoacrylates already mentioned in the introduction. In this paper, we wish to present our findings on the NH_4OAc catalysed condensation of active methylene compound such as ethyl cyanoacetate with several aromatic aldehydes. Treatment of *p*-chlorbenzaldehyde with ethyl cyanoacetate in presence of catalytic amount of ammonium acetate under microwave irradiation resulted in the formation of ethyl-2-cyano-3-(4-chlorophenyl)acrylate (**1a**) in 86% yield under solvent free condition. Several acrylates compound **1b-e** have been synthesized in a similar manner under microwave irradiation by treatment of aromatic aldehydes **1** with active methylene compound ethyl cyanoacetate **2** in the presence of catalytic amount of NH_4OAc by modified Knoevenagel reaction (Scheme 1) and table 1. In general the reactions are clear and free from the Michael adduct. The compounds obtained were characterized by NMR and IR spectroscopy. The ^1H NMR spectra of **3a-e** showed the olefinic proton around δ 8 – 9 ppm (in CDCl_3) as singlet peaks. In the IR spectra of **3a-e** absorption was observed at 1712 – 1732 cm^{-1} for carbonyl, and 2216 - 2229 for CN groups. The similar products obtained by thermal procedure by other workers are shown in table 2 (Jhillu *et al.* 2004). The spectroscopic data of all the products were identical with those reported in the literature (Su *et al.* 2003, Delga *et al.* 1995, Jhillu *et al.* 2004).

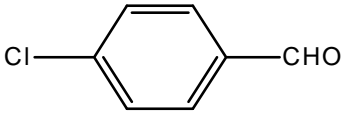
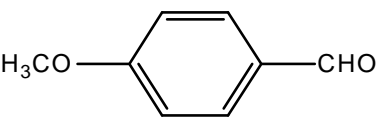
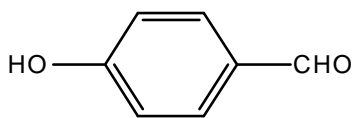
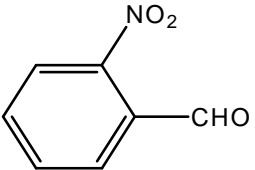
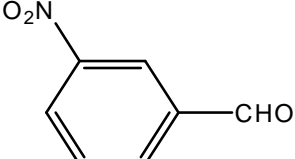


Scheme 1

Table 1 **Microwave assisted Knoevenagel reaction between various aldehydes and ethylcyanoacetate**

Compd. no.	substrate	product	Watt/ Time(sec)	Yield(%)	Mp ^o C
1a			300/50	86	85-85 ^o C
1b			300/120	75	78-80 ^o C
1c			300/60	75	172-173 ^o C
1d			300/60	70	100-102 ^o C
1e			300/60	90	125-127 ^o C

Table 2 Similar products obtained by other workers by conventional method

Entry	Substrate	Product	Conventional method	
			Time(h)	Yield(%)
1		1a	3.0	85
2		1b	4.5	82
3		1c	5.0	78
4		1d	--	--
55		1e	5.0	80

CONCLUSION

We have investigated the microwave-assisted Knoevenagel condensation of aromatic aldehydes with ethylcyanoacetate catalyzed by NH_4OAc . The procedure are considered as environmentally benign procedure because harmful organic solvents were avoided during the reaction process.

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