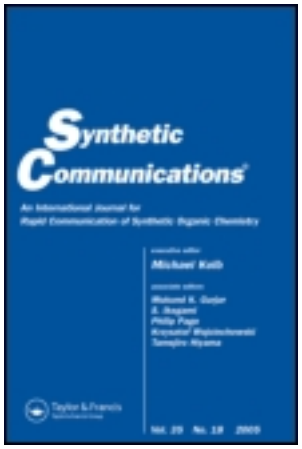

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M. B. Deshmukh [a], Suresh S. Patil [b], S. D. Jadhav [b] & P. B. Pawar [b]

[a] Department of Chemistry, Shivaji University, Kolhapur, India

[b] Department of Chemistry, PDVP College, Sangli, India

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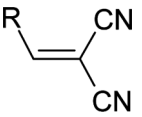
GREEN APPROACH FOR KNOEVENAGEL CONDENSATION OF AROMATIC ALDEHYDES WITH ACTIVE METHYLENE GROUP

M. B. Deshmukh,[1] Suresh S. Patil,[2] S. D. Jadhav,[2] and P. B. Pawar[2]

[1]*Department of Chemistry, Shivaji University, Kolhapur, India*
[2]*Department of Chemistry, PDVP College, Sangli, India*

GRAPHICAL ABSTRACT



Abstract *An ecofriendly and economical method of Knoevenagel condensation of aromatic aldehydes with malononitrile catalyzed by lemon juice, a natural catalyst, in the absence of any solvent is described.*

Keywords Knoevenagel condensation; lemon juice; malononitrile

INTRODUCTION

Concern for the environment demands the development of ecofriendly and economical processes wherein even slightly hazardous by-products are not desirable. In the development of new syntheses, ecological points of view must be taken into account. A number of organic reactions employing natural catalysts such as clay[1,2] and phosphates[3–5] are reported in literature. In accordance with this, we report the Knoevenagel condensation of active methylene compound with aromatic aldehydes in the presence of lemon juice, a natural catalyst, without any solvent (Scheme 1).

Citrus limonium, *Citrus aurantium*, and *Citrus indica* are some important species of citrus family, commonly known as the lemon. The lemon is indigenous to the northwestern regions of India and is also cultivated in Asia and Europe. It is now widely grown in all tropical and subtropical countries. In India, it is also cultivated in home gardens.

For the present work, we used the extract of *Citrus limonium* as a natural catalyst. The main ingredients of this extract are moisture (85%), citric acid (5–7%), carbohydrates (11.1%), vitamin C (0.4%), protein (1%), fat (0.9%), minerals

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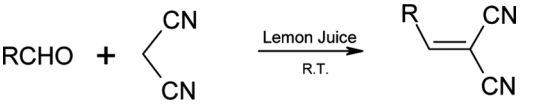
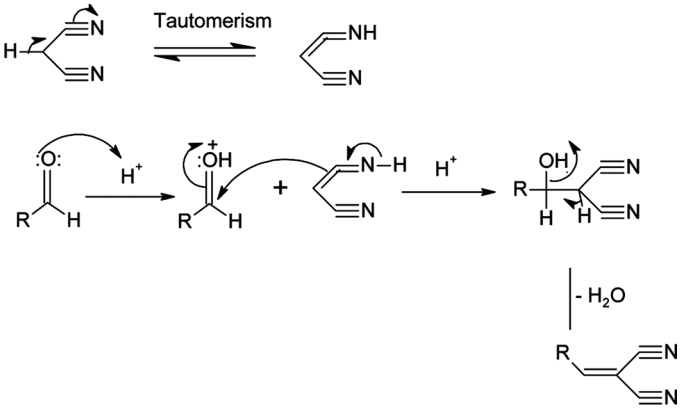
Address correspondence to Suresh S. Patil, Department of Chemisty, PDVP College, Tasgaon District, Sangli 416312, India. E-mail: sanyujapatil@yahoo.com



Scheme 1. Knoevenagel condensation of aromatic aldehydes with malononitrile.



Scheme 2. Mechanism for acid catalyzed Knoevenagel condensation.

(0.3%), fibers (1.7%), and some free and combined organic acids. As lemon juice is acidic in nature (pH about 2–3) and the percentage of citric acid is 5–7%, it will be worked as acid catalyst for condensation (Scheme 2).

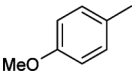
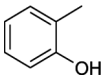
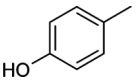
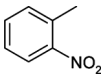
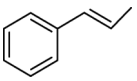
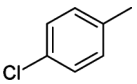
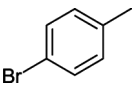
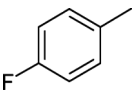
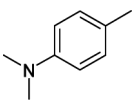
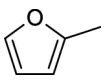
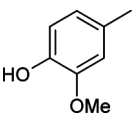
The Knoevenagel condensation of aldehydes with active methylene compounds is an important method used for the synthesis of different pharmaceutically important organic compounds.[6] The Knoevenagel condensation reaction is mostly catalyzed by bases such as amines or their ammonium salts, ammonia in organic solvents, and dimethylaminopyridine.[7]

The importance of Knoevenagel condensation for carbon–carbon bond formation in organic synthesis has attracted renewed attention. A number of improved

Table 1. Comparison of different catalysts used for synthesis of 2-(phenyl)methylenemalononitrile ($R = C_6H_4$)

Sr. no.	Catalyst	Solvent	Time	Condition	Yield (%)	Reference
1	USY Zeolite	Benzene	12 hr.	Reflux	92	8
2	$AlPO_4$-Al_2O_3	–	$\frac{1}{4}$ hr.	Stirred at RT	80	10
3	$LaCl_3 \cdot 7H_2O$	–	1 hr.	Heated at 80 °C	95	11
4	I_2/K_2CO_3	EtOH/DMF	12 min	RT	80	14
5	CTMAB	Water	1.5 hr.	Stirred at RT	90.6	15
6	TEBA	–	10 min	Ground at RT	90	16
7	NH_4OAc & Basic Alumina	–	6 min	MW (850 Watt)	80	17
8	$H_3PW_{12}O_{40}$	Water	15 min	Refluxed	91	18
9	NaF & LiCl	–	1 min	MW	96	20
10	$MgBr_2 \cdot OEt_2$	TEA, THF	1–2 hr.	Stirred at RT	98	22
11	Lemon Juice	–	2 hr.	Stirred at RT	91	–

Table 2. Lemon juice catalyzed Knoevengel condensation of aromatic aldehydes and malononitrile

Product	R	Color	Time (min)	Yield (%)	M.P. °C	
					Found	Reported
1		Light brown crystals	120	91	82	84[25]
2		Yellow crystals	15	90	118	115[25]
3		Yellow crystals	05	86	158	160[25]
4		Light Yellow crystals	15	91	182	188[25]
5		Orange crystals	120	85	142	138[25]
6		Yellow crystals	05	88	129	128[17]
7		Colourless solid	60	87	164	163[25]
8		Colourless solid	10	95	158	155[16]
9		Yellow crystals	05	92	124	127[25]
10		Orange crystals	30	82	179	182[16]
11		Faint brown crystals	120	82	74	72[17]
12		Lemon yellow solid	20	92	132	135[25]

procedures have been reported for the Knoevenagel condensation. Some green methods have been reported using catalysts in the absence of solvent. However, high reaction temperatures and long reaction times were required for complete reactions. There are also some new reported methods employing catalysts, such as USY zeolites,[8] calcium hydroxyapatite,[9] $AlPO_4 \cdot Al_2O_3$,[10] and $LaCl_3 \cdot 7H_2O$.[11] The reaction is also carried out by using catalysts such as the methane sulfonic acid (MSA)/morphine system,[12] basic alumina,[13] I_2/K_2CO_3,[14] cetyltrimethylammoniumbromide

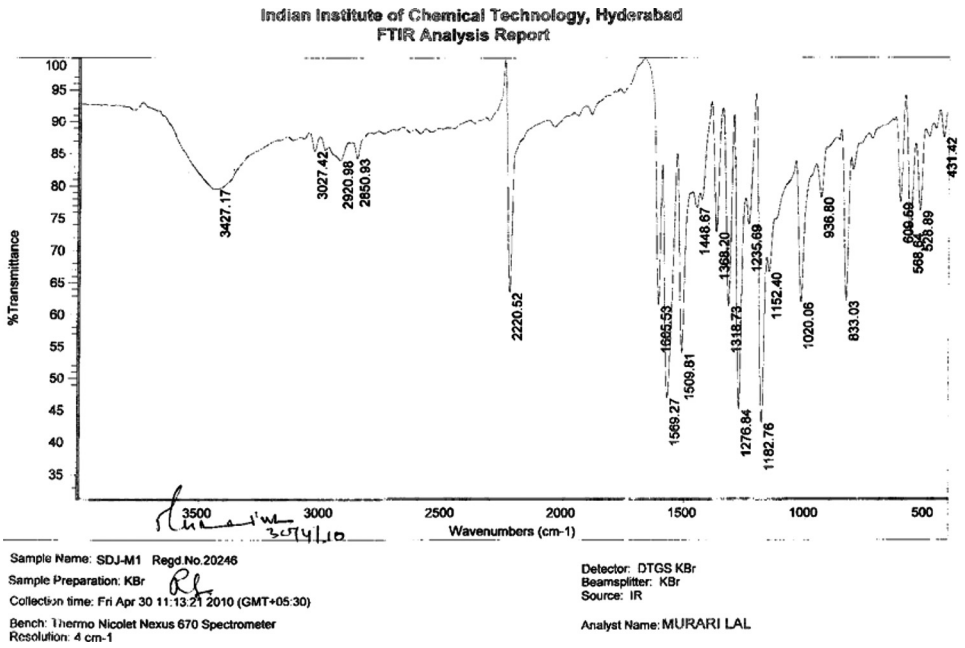


Figure 1. IR spectrum of **2**.

(CTMAB),[15] triethylbenzylammonium (TEBA),[16] ammonium acetate–basic alumina,[17] 12-tungstophosphoric acid,[18] $(NH_4)_2HPO_4$,[19] NaF and LiCl,[20] $ZnCl_2$,[21] $MgBr_2 \cdot OEt_2$, and triethylamine (TEA),[22] and ionic liquids.[23] The condensation is also carried out in presence of various solvents.[24] These methods have various drawbacks such as prolonged reaction time, toxicity, poor recovery, and use of harmful organic solvents (Table 1). Therefore, introduction of clean procedures and eco-friendly green catalysts have attracted attention of workers.

RESULTS AND DISCUSSION

We herein report a Knoevenagel condensation of aromatic aldehydes with active methylene groups using a catalytic amount of lemon juice under solvent-free conditions. In addition to its simplicity, this catalyst resulted in better yields for the products (Table 2) in the Knoevenagel condensation. A stoichiometric amount of catalyst was sufficient to obtain good yields.

The synthesis of 2-(p-methoxyphenyl)methylenemalononitrile (**2**) is described as a representative example: A mixture of 10 mmol (1.36 g) of p-methoxybenzaldehyde, 10 mmol (0.66 g) of malononitrile, and 1 ml lemon juice was stirred at room temperature for 15 min with monitoring by thin-layer chromatography (TLC). Then the reaction mixture was filtered, and the pure yellow crystalline product was recovered by crystallization with ethanol. Its identity was confirmed by infrared (IR) spectrum (Fig. 1), NMR spectrum (Fig. 2), and its melting point.

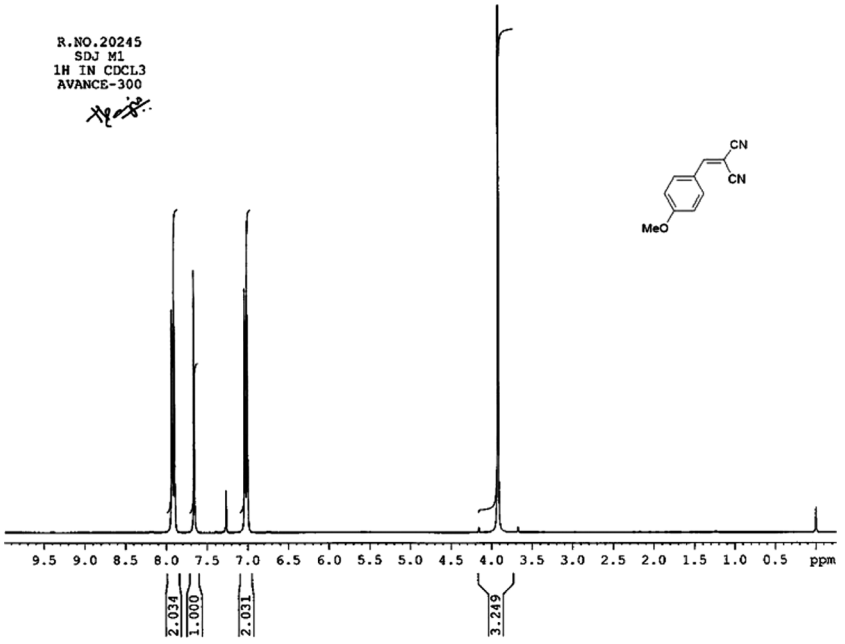


Figure 2. NMR spectrum of **2**.

Compound **2** is a yellow crystalline product, yield 90%, mp 118 °C; IR (KBr): 2220, 1665, 1318, 1276, 936, 833 cm^{-1}; ^1H NMR ($CDCl_3$): 3.9 (3H, s, $-OCH_3$), 7.0 (2H, d, Ar-H), 7.6 (1H, s, =CH), 7.9 (2H, d, Ar-H).

The experimental procedure is followed for the appropriate time to synthesize all the products listed in Table 2.

CONCLUSION

We have developed an ecofriendly and economical method for the Knoevenagel condensation by lemon juice catalyst with good yields. This solvent-free approach is nonpolluting and does not employ any toxic materials, quantifying it as a green approach to Knoevenagel condensation. In addition to this, it involved mild reaction conditions and simple workup.

ACKNOWLEDGMENT

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