

Nano-MgO / Bulk-MgCl₂: An Efficient Catalyst For Knoevenagel Condensation

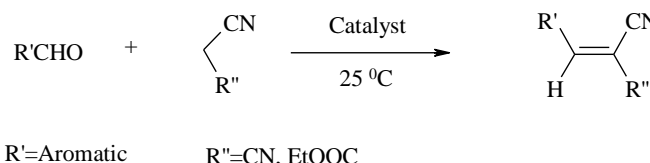
J. B. Hameeda, G. T. Chandrappa, M. A. Pasha

Abstract: An efficient procedure for Knoevenagel condensation of araldehydes with malononitrile has been developed using a mixture of environmentally friendly nano MgO and commercial MgCl₂ as catalyst. The reactions were carried out at 25 °C using *grindstone technique*. The protocol developed is advantageous as it follows the green-chemistry norms avoiding the use of any organic solvent and affording excellent yield of the products.

Index Terms: Arylmethylidene malononitrile, green Chemistry, grindstone technique, Knoevenagel condensation, Nano MgO/commercial MgCl₂, solvent-free reaction.

1 INTRODUCTION

Knoevenagel condensation is a reaction between an araldehydes with a variety of active methylene compounds and is named after Emil Knoevenagel [1865-1921]. Usually the reaction is catalyzed by bases or Lewis acids [1]. Knoevenagel condensation has been extensively studied as an important carbon-carbon bond forming reaction [2]. The reaction catalyzed by PEG400/K₂CO₃ [3], ZnCl₂ [4], silica gel functionalized with amine groups has been used under heterogeneous catalysis conditions [5]. Recently, Bigi's group described the same reaction in water without any catalyst [6]. The reaction is also catalyzed by various organic bases [7]. Various other catalysts used for the purpose are Al₂O₃ [8], CdI₂ [9], KF–Al₂O₃ [10], AlPO₄–Al₂O₃ [11], bulk MgO and ZnO [12], modified inorganic reagents have also been reported such as MCM-41 [13], resins [14], phase-transfer agents [15]. Many reports are based on microwave and ultrasonic irradiation [16-18]. Though a number of reports are available on the Knoevenagel condensation, yet there is need of for a much more efficient catalyst and a synthetic procedure which matches the green chemistry protocols, hence, the present reaction is carried out using *grindstone technique* at 25 °C. Grindstone method was introduced by Toda [19] in the year 1987 in which the solid reactants are ground together using a pestle and a mortar to get the desired products in the absence of any solvent. The method is advantageous over the other methods as the yields of the products are high, the reactions go to completion in short durations, and use of solvents can be avoided. Most of the chemists are tempted to try this technique as the method is Green. The method reported herein, is the synthesis of arylmethylidene malononitrile catalyzed by a mixture of Nano MgO and bulk MgCl₂ under grindstone method. Nano materials provide large surface [20] and contact area and hence, the rate of reaction can be opted as desired because of the changes in surface properties such as surface defects. Recently, the nanocrystalline inorganic oxides have gained interest. Nano MgO has very different physical and chemical properties when compared with the bulk MgO. It is a versatile smart material potentially used as catalyst, in nano electronics, and in biomedicines etc. Nano-MgO being a porous basic catalyst is non-volatile, non-hygroscopic, odourless, and white crystalline solid with versatile physical properties and stability [21].



Scheme 1: Synthesis of arylmethylidene malononitrile using grindstone method

2. Materials and methods

2.1 Materials and instrument

Commercially available reagent grade chemicals were used without further purification. Melting points were determined on a Perfit melting apparatus. GC-Mass spectra were obtained using a Shimadzu GC-MS QP 5050A equipped with a 30 meter length and 0.32 mm of diameter BP-5 column with the column temperature 80–15–250 °C. All the reactions were monitored by TLC and all the products were characterized by comparison with authentic samples on TLC, or by IR, ¹HNMR spectral analysis, and by comparison of melting points with authentic samples prepared according to the reported methods. All the reactions were performed in open vessels without any mechanical stirring.

2.2 Preparation of MgO nanoparticles

Nano-MgO was prepared by the solution combustion technique [21]. An aqueous solution of Mg(NO₃)₆H₂O And NH₂CH₂COOH (corresponding F/O ratio of 1.75 (φ)) was taken in a Petri dish. It was then heated to obtain a semi-solid. The dish was then introduced into a muffle furnace maintained at 400 ± 10 °C. Initially, the semi-solid underwent dehydration and then smoldering combustion occurred at one end which quickly got and propagated throughout the mass. A voluminous black porous nano crystalline product became white on leaving it in the muffle furnace at the same temperature for another 30 min.

2.3 General procedure for the synthesis of arylmethylidene malononitriles by the Knoevenagel condensation between araldehydes and malononitrile

A mixture of aromatic aldehyde (1 mmol), malononitrile (1 mmol), bulk MgCl₂ (0.09g) and Nano MgO (0.02g) was ground well using a pestle and a mortar, the progress of the reaction was monitored by TLC. After the completion of the reaction (see Table 1 for time), 10 mL of EtOAc was added, filtered to remove nano MgO and MgCl₂, after washing the residue with

- J. B. Hameeda, G. T. Chandrappa, M. A. Pasha
- Department of Studies in Chemistry, Central College Campus, Bangalore University, Bengaluru-560 001, INDIA E-mail: mafasha@gmail.com

EtOAc (2 × 5 mL), the filtrate was dried over anhydrous Na₂SO₄. The solvent was evaporated under reduced pressure get a solid, which was then recrystallized from hot aq. ethanol to afford the pure product. In order to synthesize arylmethylidene malononitriles, we carried out a few preliminary experiments. We chose anisaldehyde and malononitrile as the model reactants to carry out further investigations. Anisaldehyde (1 mmol), malononitrile (1 mmol) was subjected to grinding using various amounts of the catalysts and a mixture of catalysts under different conditions and the results are presented in the Table-1.

Table 1. Optimization of the amount of catalyst for the Knoevenagel condensation^a

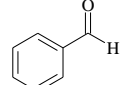
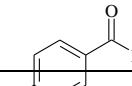
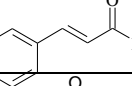
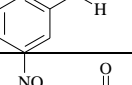
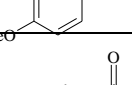
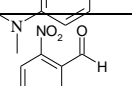
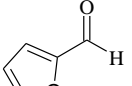
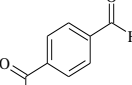
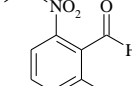
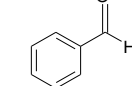
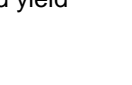
Sl. No	Catalyst	Amount (g)	Duration (min)	Yield (%)
1	MgO [bulk]	0.04	30	20
2	MgCl ₂ [bulk]	0.45	35	50
3	MgCl ₂ [bulk]	1.0	30	50
4	Nano MgO	0.05	45	60
5	Nano MgO	0.15	45	60
6	Bulk MgCl ₂ + Nano MgO	0.05 + 0.45	35	85
7	Bulk MgCl ₂ + Nano MgO	0.25 + 0.05	25-30	90
8	Bulk MgCl ₂ + Nano MgO	0.09 + 0.02	20	95

^a Reaction conditions: All the reactions are carried out using anisaldehyde (1 mmol), malononitrile (1 mmol) using a pestle and a mortar.

In a preliminary experiment, bulk MgO (0.04g) was grinded with above mentioned amount of the reactant for 30 min and the yield of the product was very poor (Table 1, entry 1). Then the reaction was carried out using MgCl₂ (0.45g), which also gave less yield, and there was no increase in the yield with continued grinding and increase in the amount of MgCl₂ (up to 1g, Table 1, entries 2 and 3). As mentioned earlier, the nano materials provide large surface and contact area and thus with the intension of increasing the rate of reaction, the present reaction was carried out by grinding the substrates in the presence of nano MgO (0.05g) as a catalyst for 45 min (Table 1, entry 4). The yield was increased from 20% to 60% and then remained constant even after increasing the amount of nano MgO to 0.15g (Table 1, entry 5). As the reaction was studied using two different catalysts, without much satisfactory yields, it was decided to use a mixture of both the catalysts; and anisaldehyde and malononitrile were subjected to grinding using a pestle and mortar in the presence of this catalyst mixture. By trial and error method optimization of the amount of catalyst was done, and finally a mixture of nano MgO

(0.02g) and commercial MgCl₂ (0.09g) was found to have considerable effect on increase in the yield (95%) of the desired product in just 20 min (Table 1, entry 8). Encouraged by this result, the method was extended to synthesize a variety of arylmethylidene derivatives from a series of aromatic aldehydes and active methylene substrates in the presence of a mixture of nano MgO and bulk MgCl₂ as catalyst in the absence of any solvent at 25 °C to get the respective product in high purity and in excellent yield within 15–25 minutes. The products were characterized by the IR spectral analysis which showed a characteristic signal for C=N between 2210–2260 cm⁻¹ and the other between 1600–1670 cm⁻¹ for C=C. Further, characterization of most of the products was done by ¹H NMR spectral analysis.

Table 2. [Nano MgO/bulk MgCl₂] catalyzed synthesis of arylmethylidene derivatives

Sl. No	Aldehyde (R')	R''	Time (min)	Yield (%) ^a	Melting point (°C)
a		CN	15	98	80–82
b		CN	20	95	161-163
c		CN	25	88	127-129
d		CN	20	90	102-104
e		CN	20	95	112-114
f		CN	15	93	179-180
g		CN	30	90	89-91
h		CN	15	98	69-71
i		CN	20	95	162-165
J		EtOOC	20	92	108-110
k		EtOOC	15	95	51-53

^a Isolated yield

3 CONCLUSIONS

We have developed a simple and economically viable method for the synthesis of arylmethylidene derivatives by a Knoevenagel condensation between araldehydes and malononitrile. The reaction is catalyzed by a mixture of nano MgO and bulk MgCl₂ and works well under grindstone technique, which matches with the Green Chemistry norms. The present method is advantageous as it does not involve any organic solvents and works at 25 °C. As the products are obtained by grinding the substrates and the catalyst mixture, there is scope for use of 'Ball mills' in future for the production of the said products in large scale.

4. ACKNOWLEDGEMENT

Authors acknowledge the financial assistance by the VGST, Dept. of Science & Technology, Government of Karnataka for the CESEM Award Grant No. 24 (2010-2011).

REFERENCES

- [1] T. Sugino, K. Tanaka, Solvent-Free Coumarin Synthesis. *Chem. Lett.* Vol.30, pp. 110-111, 2001.
- [2] B. M. Trost, *Comprehensive Organic Synthesis*, Pergamon, Oxford.: pp. 133–238, 1991.
- [3] Y. Q. Cao, Z. Dai, R. Zhang, B. H. Chen, A Practical Knoevenagel Condensation Catalyzed by PEG400 and Anhydrous K₂CO₃ without Solvent. *Synth. Commun.* Vol. 34, pp. 2965–2971, 2004.
- [4] R. V. S. Rao, Venkataratnam, Zinc chloride as a new catalyst for Knoevenagel condensation. *Tetrahedron Lett.* Vol. 32, pp. 5821–5822, 1991.
- [5] E. Angeletti, C. Canepa, G. Martinetti, P. Venturello, Silica gel functionalized with amino groups as a new catalyst for Knoevenagel condensation under heterogeneous catalysis conditions. *Tetrahedron Lett.* Vol. 29, pp. 2261–2264, 1988.
- [6] F. Bigi, M. L. Conforti, R. Maggi, A. Piccinno, G. Sartori, Clean synthesis in water: uncatalysed preparation of Ylidenemalononitriles. *Green Chem.* Vol. 2, pp. 101–103, 2000
- [7] G. Jones, The Knoevenagel condensation reaction in organic reactions; *John Wiley: New York.* Vol. 15, pp. 204–599, 1967
- [8] F. Texier-Boullet, A. Foucaud, Knoevenagel condensation catalysed by aluminium oxide. *Tetrahedron Lett.* Vol. 23, 4927–4928, 1982
- [9] D. Prajapati, J. S. Sandhu, Cadmium iodide as a new catalyst for Knoevenagel condensation. *J. Chem. Soc. Perkin Trans 1.* Vol. 1, pp. 739–740, 1993.
- [10] G. Dai, D. Shi, L. Zhou, Y. Huaxue, Knoevenagel condensation catalyzed by potassium fluoride/alumina. *Chin. J. Appl. Chem.* Vol. 12, pp. 104–108, 1995.
- [11] J. A. Cabello, J. M. Campelo, A. Garcia, D. Luna, J. M. Marinas, Knoevenagel condensation in the heterogeneous phase using aluminum phosphate-aluminum oxide as a new catalyst. *J. Org.Chem.* Vol. 49, pp. 5195–5197, 1984.
- [12] T. I. Reddy, R. S. Varma, Rare-earth (RE) exchanged NaY zeolite promoted Knoevenagel condensation. *Tetrahedron Lett.* Vol. 38, pp. 1721–1724, 1997.
- [13] Y. V. S. Rao, D. E. De Vos, P. A. Jacobs, Montmorillonite KSF as an inorganic, water stable, and reusable catalyst for the Knoevenagel synthesis of coumarin-3-carboxylic acids. *J. Org. Chem.* Vol. 64, pp. 1033–1035, 1999.
- [14] J. Simpson, D. L. Rathbone, D. C. Billington, New solid phase Knoevenagel catalyst. *Tetrahedron Lett.* Vol. 40, pp. 7031–7033, 1999.
- [15] N. Taha, Y. Sasson, M. Chidambaram, Phase transfer methodology for the synthesis of substituted stilbenes under Knoevenagel condensation condition. *Appl. Catal. A: Gen.* Vol. 350, pp. 217–224, 2008.
- [16] P. De la Cruz, E. Diez-Barra, A. Loupy, F. Langa, Silica gel catalysed Knoevenagel condensation in dry media under microwave irradiation. *Tetrahedron Lett.* Vol. 37, pp. 1113–1116, 1996.
- [17] X. S. Wang, J. T. Li, W. Z. Yang, T. S. Li, Synthesis of ethyl α -cyanocinnamates catalyzed by KF-Al₂O₃ under ultrasound irradiation. *Ultrason. Sonochem.* Vol. 9, pp. 159–163, 2002.
- [18] Y. Q. Peng, G. H. Song, Combined microwave and ultrasound accelerated Knoevenagel-Doebner reaction in aqueous media: A green route to 3-aryl acrylic acids. *Green Chem.* Vol. 6, pp. 704–706, 2003.
- [19] T. Tanaka, F. Toda, Solvent-Free Organic Synthesis. *Chem. Rev.* Vol. 100, pp. 1025–1074, 2000.
- [20] D. W. Bahnemann, S. N. Kholuiskaya, R. Dillert, A. I. Kulak, A. I. Kokorin, Photodestruction of dichloroacetic acid catalyzed by nano-sized TiO₂ particles. *Appl. Catal.B: Environ.* Vol. 36, pp. 161, 2002.
- [21] B. Nagappa, G. T. Chandrappa, Mesoporous nanocrystalline magnesium oxide for environmental remediation. *Micropor. Mesopor. Mater.* Vol. 106, pp. 212–218, 2007.