Microwave-assisted Knoevenagel condensation in aqueous over triazine-based microporous network

Mohd Bismillah Ansari · Mst. Nargis Parvin · Sang-Eon Park

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Abstract A high nitrogen-containing triazine-based microporous polymeric (TMP) network was used as an efficient metal-free catalyst for Knoevenagel condensation of ethylcyanoacetate with aromatic aldehydes. The reactions were performed in water as an environmentally benign medium, under microwave irradiation within a short reaction time of 10 min. The conversions of substituted aromatic aldehydes and selectivities for Knoevenagel products were found to be in the ranges of 44–99 and 65–99 %, respectively. The electron-withdrawing substituent showed higher conversion and selectivity as compared to electron-donating substituents. The TMP network can be readily recovered and reused up to three runs without loss in catalytic activity and selectivity.

Keywords Triazine · Microporous polymer network · Aqueous media · Knoevenagel condensation · Microwave

Introduction

Green catalysis has attained a major status in scientific disciplines for the development of clean and benign chemical processes [1]. Current emphasis on green processes involves utilization of safer solvents and the design for energy-efficient and time-saving methodologies. The choice of green solvent is not only based upon its abundance but also the following factors should be taken into consideration, such as energy to manufacture, cumulative energy demand, and impact on health and the environment. In this regard, there is widespread current debate over relative "greenness", and undoubtedly water can be regarded as the cleanest solvent

M. B. Ansari · Mst. N. Parvin · S.-E. Park (🖂)

Laboratory of Nano-Green Catalysis and Nano Center for Fine Chemicals Fusion Technology, Department of Chemistry, Inha University, Inchon 402-751, Korea e-mail: separk@inha.ac.kr

available [2]. On the other hand, for many chemical processes, a major adverse effect on the environment is the consumption of energy for heating and cooling. To overcome these problems, it is highly desirable to develop efficient methods that use alternative energy sources such as ultrasound or microwave irradiation to facilitate chemical reactions. In this context, microwaves hold superiority as most of the reactions can be performed in a very short time and, moreover, they provide significant energy savings in most of the chemical transformations compared to heating by conduction and convection currents [3, 4]. An important perspective for greenness is the design and development of methodologies using metal-free heterogeneous catalysts for clean organic transformations under microwave irradiation in water [5].

Knoevenagel condensation is a base catalyzed reaction for the synthesis of α , β unsaturated carbonyl compounds by condensation of aldehydes or ketones with C–H acidic methylene group-containing compounds [6]. Metal-free Knoevenagel reactions have been well investigated in homogenous reactions using nitrogenous molecules such as aliphatic amines, urea, and piperidine or their corresponding ammonium salts and amino acids as catalyst [7, 8]. These homogenous reactions are prone to problems of catalyst recovery and separation. In order to overcome these limitations, enormous efforts have been dedicated to the immobilization of amines and ionic liquids over silica support [9–11]. However, these materials are associated with the drawback of fewer active sites and leaching of anchored catalysts. In this context, it is desirable to design a catalyst which possesses inbuilt catalytic functionalities as a part of a nanoporous framework, and one such promising design of catalysts is porous organic polymers (POPs) [12–14].

In regard to these perspectives, here we report the catalytic performance of a nitrogen-containing triazine-based microporous polymer network as an efficient base catalyst for Knoevenagel condensation in aqueous under microwave irradiation.

Experimental

Chemicals

All chemicals were of analytical grade and were used without further purification. Aldehydes, terephthalaldehyde, and ethylcyanoacetate were purchased from Sigma Aldrich. Melamine was purchased from TCI. The water was deionized by aqua MaxTM basic water purification system (Young Lin, Korea).

Synthesis of TMP-network

The 1,3,5-triazine-based microporous network was synthesized by our earlier reported procedure [12]. The TMP network was synthesized by condensation reaction between terephthalaldehyde and melamine at 180 °C up to 48 h under an inert atmosphere (Scheme 1). The isolated TMP network gave 75 % yield. The

detailed synthetic procedure and characterization of TMP network have been reported by us elsewhere [12].

Catalytic activity

Knoevenagel condensation

The Knoevenagel condensation reactions were carried out under green solvent (water) at 120 °C using single mode microwave irradiation (power 300 W). A flame-dried two-necked round-bottom flask fitted with a condenser and a magnetic stirring bar was charged with 1 mmol of aldehyde and 1 mmol of active methylene compound ethylcyanoacetate. To this mixture, 20 mg of catalyst was added and stirred for 2 min, followed by addition of 2 ml solvent. The reaction mixture was maintained in inert atmosphere and air was removed by flushing nitrogen in order to prevent oxidation of the aldehyde to acid.

The temperature of the reaction mixture was raised to 120 °C within 1.5 min and maintained for an appropriate time (max. 12 min). After completion of the reaction, the mixture was cooled to room temperature, diluted with dichloromethane, and poured into a separating funnel. The organic layer was collected and dried over anhydrous sodium sulfate, filtered, concentrated by rota-evaporator, and subjected to GC and GC–MS analysis (Agilent Technologies 5975). From the aqueous layer, the catalyst was recovered by filtration and washed with water, followed by subsequent washing with acetone, and dried at 120 °C in a vacuum oven for reuse. A similar procedure was followed for subsequent cycles.

The conversions were calculated on the basis of mole percent of aldehyde; the initial mole percent of aldehyde was divided by initial area percent (CYA peak area from GC) to get the response factor. The unreacted moles of aldehyde remaining in the reaction mixture were calculated by multiplying the response factor by the area percentage of the GC peak for the CYA obtained after the reaction. The conversion and selectivity were calculated as follows:

Aldehyde Con. $(mol\%) = [(Initial mol\% - Final mol\%)/initial mol\%] \times 100,$

Knoevenagel product Sel.%

= (GC peak area of aldehyde/ Σ GC peak area of all products) \times 100.

Results and discussion

The TMP network was synthesized by catalyst-free polymerization by our earlier reported procedure with 75 % yield. The detailed synthesis and characterization procedure is presented elsewhere [12]. The TMP network is nitrogen-enriched (elemental analysis C, 41.03; H, 4.55; N, 40.30; S, 1.3 %) and can be used as a base catalyst in Knoevenagel condensation reaction. As an initial step, we investigated the effect of various solvents in microwave-assisted Knoevenagel condensation.



Scheme 1 Synthesis of TMP network

Effect of solvent

The investigations on the effect of the solvent over the reaction revealed that the highest conversion of benzaldehyde (99 and 85 %; Table 1, entries 1 and 4) was found in the case of ethanol and water, respectively, whereas the lowest conversion was observed in toluene (34 %) and chloroform (54 %). The selectivity for the Knoevenagel product in all the cases was approximately 99 %.

These observations revealed that the solvent plays a significant role in the reaction. Polar protic solvents such as ethanol and water give better conversions due to δ H hydrogen bonding interaction and dipole interaction with the intermediate formed during the course of the reaction. The acetonitrile and DMF are considered to be polar aprotic solvents lacking hydrogen bonding interaction and depicting a little lower conversion. The lowest conversion in the case of toluene and chloroform is attributed to their relative non-polar nature. The effect of solvent property on the conversion of benzaldehyde can be summarized in the following order: polar protic solvent > polar aporotic solvent > non-polar solvent [15].

In the absence of solvent, the conversion of benzaldehyde was 55 % (Table 1, entry 7), and without catalyst, 10 % conversion (Table 1, entry 8) was observed. These results suggested that microwave-assisted Knoevenagel condensation reactions described here are purely catalytic in nature.

Effect of reaction time

The difference in the conversion of ethanol and water has only a small deviation, owing to the eco-friendly and green nature of water as solvent, and further investigation on the effect of time over the reaction was investigated in condensation reactions between benzaldehyde and ethylcyanoacetae. The increase in reaction time showed an increase in conversion. Maximum conversion of benzaldehyde (99 %) and selectivity of Knoevenagel product (99 %) was observed at 12 min of microwave irradiation time (Table 2, entry 5).

 Table 1
 TMP-catalyzed Knoevenagel condensation of benzaldehyde with ethylcyanoacetate in different solvents



S. no.	Solvent	Benzaldehyde conversion (%) ^a	Knoevenagel product selectivity (%) ^a
1	Water	85	99
2	Acetonitrile	68	99
3	DMF	71	99
4	Ethanol	99	99
5	Toulene	34	99
6	Chloroform	54	99
7	No	54	99
8	Ethanol ^b	10	96

Reaction conditions: catalyst 20 mg, benzaldehyde 1 mmol, ethylcyanoacetate 1 mmol, solvent 2 ml, microwave irradiation 300 W, temperature 120 °C and time 10 min

^a Analyzed by GC and GC–MS

^b Without catalyst

S. no.	Time (min)	Benzaldehyde conversion (%) ^a	Knoevenagel product selectivity (%) ^a
1	2.5	50	92
2	5	66	90
3	7.5	77	84
4	10	85	99
5	12	99	99

Table 2 Effect of microwave irradiation time in TMP catalyzed Knoevenagel condensation reactions

Reaction conditions: catalyst 20 mg, benzaldehyde 1 mmol, ethylcyanoacetate 1 mmol, solvent 2 ml, microwave irradiation 300 W, temperature 120 °C and time 2.5-12 min

^a Analyzed by GC and GC-MS

Effect of substituents

The effect of substituents over the aromatic ring of benzaldehyde was investigated with various electron-withdrawing and electron-donating groups at different

S. II.	<u>ح</u>	Substrate	WW irradiation10 min TMP 6 Benzaldehyde conversion (%) ^a	Knoevenagel product selectivity (%) ^a
_	Н	Benzaldehyde	85	66
2	2-CI	2-Chlorobenzaldehyde	66	84
3	4-CI	4-Chlorobenzaldehyde	66	66
4	4-NO ₂	4-Nitrobenzaldehyde	66	66
5	2-OH	Salicylaldehyde	60	66
9	4-OH	4-Hydroxybenzaldehyde	80	06
7	2-OMe	2-Methoxybenzaldehyde	44	72
8	4-OMe	4-Methoxybenzaldehyde	51	93
6	4- <i>i</i> Pr	4- <i>Iso</i> propylbenzaldehyde	55	65
10	3-OPh	3-Phenoxybenzaldehyde	75	95
Reaction condi 10 min	tions: catalyst 20 mg.	, benzaldehyde 1 mmol, ethylcyanoace	tate 1 mmol, solvent 2 ml, microwave irradia	tion (300 W), temperature 120 °C and time
^a Analvzed bv	GC and GC–MS			

Table 3 Effect of substituents over the aromatic ring in TMP-catalyzed Knoevenagel condensation reactions

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Fig. 1 Recyclability of the TMP network in Knoevenagel condensation of benzaldehyde and ethylcyanoacetate



Fig. 2 Plausible mechanism for TMP-catalyzed Knoevenagel condensation of benzaldehyde and ethylcyanoacetate

positions (Table 3). The conversions of aromatic aldehydes were obtained in the range of 44–99 %, whereas the selectivities for Knoevenagel products were in the range of 65–99 % within a short reaction time of 10 min. These results indicated that the TMP network can be used as an efficient catalyst with substrate versatility.

Electron-withdrawing groups such as -Cl and $-NO_2$ on the the aromatic ring (Table 3, entries 2–4) increases the conversion due to the -I effect (electron-withdrawing inductive effect). A slight decrease in conversion was observed for the 4-hydroxybenzaldehyde, 4-methoxybenzaldehyde, and 3-phenoxybenzaldehyde (Table 3, entries 6, 8 and 10) due to the cumulative role of +M (electron-donating mesomeric effect) and the -I effect. In the case of salicylaldehyde, the intramolecular hydrogen bonding between carbonyl "O" and hydroxyl "H" restricts the reaction. The electron-donating group such as 4-*iso*propyl-(Table 3, entry 9) on the aromatic ring decreases the yields due to the existence of +I (electron-donating inductive effect) effect. These reaction results are in agreement with those reported earlier [16–19]. The catalyst recyclability was tested for three cycles (Fig. 1) in Knoevenagel condensation between benzaldehyde and ethyl-cyanoacetate, and no significant loss in catalytic activity was observed.

Plausible mechanism

As mentioned earlier, the TMP is nitrogen-enriched which plays a role as a Lewis base site for Knoevenagel condensation. Figure 2 depicts a plausible mechanism for the TMP-catalyzed Knoevenagel condensation of benzaldehyde with ethylcyanoacetate. The amine nitrogen from the TMP network abstracts the acidic proton from the active methylene group of ethylcyanoacetate. The generated anion makes a nuleophilic attack on the carbonyl-carbon atom of the benzaldehyde to form oxyanion. The oxyanion abstracts H^+ from the protonated amine group of TMP network and the catalyst is regenerated. The formed hydroxyl molecule eliminates the water molecule, leading to the formation of Knoevenagel product [20].

Conclusion

In summary, we have developed a new metal-free heterogeneous catalyst for microwave-mediated Knoevenagel condensation operative under water as a green solvent media. The TMP catalyst exhibited a wide substrate scope for Knoevenagel condensation reaction with high to optimum conversions and selectivities. The catalyst can be easily recovered and reused without loss of its catalytic activity and selectivity.

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