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Catalysis Today 114 (2006) 183–187
CATALYSIS TODAY
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Sonocatalysis in solvent free conditions: An efficient eco-friendly methodology to prepare chalcones using a new type of amino grafted zeolites

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Available online 10 February 2006

Abstract

The synthesis of chalcones via Claisen-Schmidt condensation between benzaldehyde and acetophenone by sonochemical and thermally-activated reactions over a new type of zeolite as catalyst is reported. The catalysts were prepared by grafting amino groups on sodium and cesium exchanged X zeolite. In this green, solvent free procedure, chalcones are selectively produced in very high yields (>95%) when cesium exchanged X-NH_2 is employed under ultrasound activation

Keywords: Amino-zeolites; Green chemistry; Sonocatalysis; Basicity; Chalcone synthesis; Claisen-Schmidt condensation

1. Introduction

The members of the chalcone and flavonid family have attracted a great deal of interest due to their applications as antibacterial, anti-inflammatory and anticancer pharmacological agents [1,2]. Chalcones are important intermediates in the synthesis of many pharmaceuticals. They are commonly synthesized via the Claisen-Schmidt condensation between acetophenone and benzaldehyde. This reaction is catalyzed by acids and bases under homogeneous conditions. Homogeneous reactions present several hurdles, such as catalyst recovery and waste disposal problems. In this respect, heterogeneous catalysts are considered as an eco-friendly alternative. The utilization of heterogeneous catalysts for the production of chalcones was reported in the literature [3–9], but there is no report for the use of zeolites as catalysts in combination with ultrasounds.

Ultrasonic irradiation leads to the acceleration of numerous catalytic reactions as well as in homogeneous and heterogeneous systems [10]. Furthermore, significant improvements can be realized as regards to the yields [11,12]. The sonochemical phenomena originate from the interaction between a suitable field of acoustic waves and a potentially reacting chemical system; the interaction takes place through the intermediate phenomenon of acoustic cavitation. Three important factors have to be considered when an ultrasonic induced reaction is performed: the acoustic field, the bubbles field and the chemical system [13,14].

The chemical effects of ultrasounds have been attributed to implosive collapse of the cavitation period of the sound waves. The bubbles are generated at localized sites in the liquid mixture that contain small amounts of dissolved gases. Trapped within a microbubble, the reactants are exposed to a high pressure and temperature upon implosion, and the molecules are fractured, forming highly reactive species with a great

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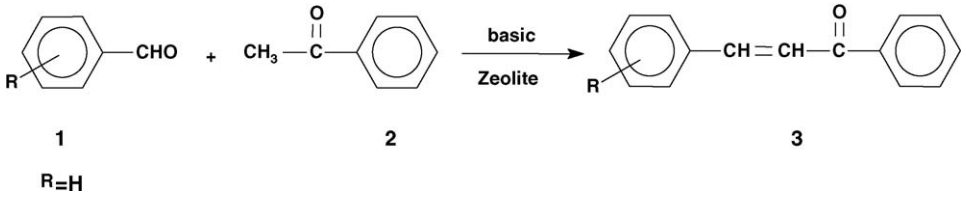
doi:10.1016/j.cattod.2006.01.003



Scheme 1. Claisen-Schmidt condensation between benzaldehyde (**1**) and acetophenone (**2**) to yield the chalcone (**3**).

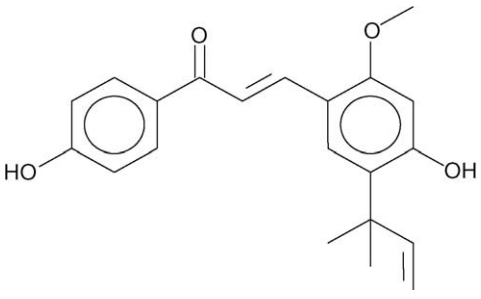
tendency to react with the surrounding molecules. When one of the phases is a solid, the ultrasonic irradiation has several additional enhancement effects, and this is especially useful when the solid acts as a catalyst [15]. The cavitation effects form microjects of solvent, which bombard the solid surface. This fact causes the exposition of unreacted surfaces of solid, increasing the interphase surface able to react. In general, the sonication presents beneficial effects on the chemical reactivity, such as to accelerate the reaction, to reduce the induction period, and to enhance the catalyst efficiency.

Base-catalysed processes such as Claisen-Schmidt condensation are commonly used for the manufacture of fine chemicals. Indeed the development of environmentally friendly solid catalysts has recently experienced growing interest and several review articles have been devoted to catalysis by solid bases, such as alkali-exchange zeolites, clays, oxides, carbonates [9].

Alkali-exchanged zeolites, sepiolites and alkali-doped carbons possess only middle basic strength. Our group has recently reported the preparation of a new type of basic zeolite obtained by grafting amino groups onto NaX and CsNaX zeolites [16]. These zeolites exhibit excellent catalytic activities for the Knoevenagel condensation probe reaction [17].

The present paper reports experimental results obtained in a heterogeneous reaction (benzaldehyde condensation with acetophenone; liquid phase) catalyzed by amino-zeolites (solid phase) under ultrasonic activation, and in the absence of any solvent (Scheme 1). For comparison, the results obtained under thermal activation are also presented. We have also investigated the influence of different factors during the reaction, such as basicity of the catalyst, catalyst amount and reaction temperature.

Finally, the method employed in this study (combination of sonocatalysis and NH_2-zeolites) has been used for the synthesis of commercial chalcones with the structure of Licochalcone A (Scheme 2) which exhibit pharmacological activities against *Staphylococcus Aureus* [18].



Scheme 2. Licochalcone A.

2. Experimental

2.1. Catalysts preparation and characterization

The Faujasite X zeolite powders were purchased from Aldrich chemicals. The zeolite powder was ground, sieved and calcined prior to use, in order to obtain a uniform catalyst powder free of moisture and adsorbed organic contaminants. The CsNaX was prepared by ion exchange of NaX powder with 0.5 M cesium chloride solution at 353 K for 6 h. This procedure was repeated three times to obtain the maximum Cs exchange (Cs/Si loading of 0.32). An active CsNaX catalyst was obtained after pre-treatment in air at 673 K for 4 h. The NaX-NH_2 and CsNaX-NH_2 were prepared by grafting 3-aminopropyl-trimethoxysilane (APTS) onto NaX and CsNaX zeolites, respectively. Five grams of zeolite powders were refluxed in a dry toluene solution (250 ml) containing 18 ml of APTS (97%, Aldrich Chemicals) at 383 K for 18 h. The catalysts were recovered by filtration after washing in dry toluene, distilled deionized water and acetonitrile. The powders were dried in an oven at 373 K and stored for later use. The structure and composition of the zeolite catalysts were analyzed by electron microscopy (SEM, JEOL 6300), X-ray diffraction (XRD, Philips PW1830), X-ray fluorescence spectroscopy (XRF, JEOL JSX-3201Z) and X-ray photoelectron spectroscopy (XPS, Physical Electronics, PHI 5600). The amount of grafted organic amino groups was measured by thermal gravimetric and differential thermal analyses (TGA/DTA, Setaram).

2.2. Reaction procedure

2.2.1. Ultrasonic induced reactions

Benzaldehyde (5 mmol) and acetophenone (5 mmol) which are liquid reactants, were mixed in a flask in the absence of solvent. The flask was suspended into the ultrasonic water bath at the reaction temperature (303, 323 and 343 K). The corresponding amino-zeolite (NaX-NH_2 and CsNaX-NH_2) was then added (0.3 g of zeolite) and the reaction times started. The reactions were performed in an ultrasonic bath (Selecta Ultrasound-H, 40 kHz, 550 W).

2.2.2. Thermal induced reactions

The conventional heating experiments were carried out in a batch reactor. The same ratio of reactants as that for ultrasound

activation was used. The mixture was heated up to the reaction temperature (303, 323 and 343 K), and the reaction was followed by gas chromatography-mass spectrometry, using a 60 m-long phenyl-silicone capillary column and a flame ionization detector. The conversion is expressed in terms of amount of chalcone (**3**) in wt% (Scheme 1).

In prior experiments it was found that for stirring speeds above 1000 rpm, and particle sizes below 0.250 mm diameter, no control by external or internal diffusion exists.

2.2.3. Synthesis of Licochalcone A derivatives

4′-Hydroxy-2,4-dichloro-chalcone and 4′-carboxy-2,4-dichloro-chalcone were obtained following the general procedure under sonic or non-sonic activation. (Scheme 3).

3. Results and discussion

3.1. Catalyst characterization

The Faujasite zeolite powders obtained after crushing, sieving and calcination had an average particle size of 2 μm and formed aggregate clusters of about 6 μm in diameter. Analyses by electron microscopy revealed mostly spherical particles with poorly formed facets. Despite the lack of particles with the characteristic bipyramidal shape of Faujasite crystals, X-ray diffraction data indicated the absence of impurities. There was no detectable change in the size and shape of zeolite particles after ion exchange with cesium (i.e., CsNaX, CsNaX-NH_2) and addition of aminopropyl group (i.e., NaX-NH_2, CsNaX-NH_2). Fig. 1 displays the X-ray diffraction patterns of the original and modified NaX zeolites. The calcined NaX powder displays the characteristic diffraction pattern of dehydrated NaX zeolite [19]. Ion exchange with $CsCl_2$ led to weaker peak intensities and disappearance of (3 3 1) and (4 4 0) diffraction lines. The presence of new diffraction peaks at 2θ = 12, 25.5, and 27.5 that had been assigned to Cs-exchanged NaX [20] is a strong evidence of a successful catalyst preparation. Grafting aminopropyl groups onto NaX and CsNaX also resulted in lower X-ray peak intensities, but no new diffraction peaks appeared in these samples (Fig. 1).

Elemental analyses of the zeolite samples by XPS and XRF detected a decrease in the sodium content of the zeolite and the appearance of cesium after the ion exchange (Table 1). Over 60% of the original sodium in NaX zeolite was exchanged for cesium (i.e., Cs/(Cs + Na) = 0.60). A slight decrease in the surface area (i.e., 430–400 m^2/g) was observed after cesium ion exchange. Similar observations was made by Both Rodriguez et al. [21] and Lasperas et al. [22]. They suggested that the loss

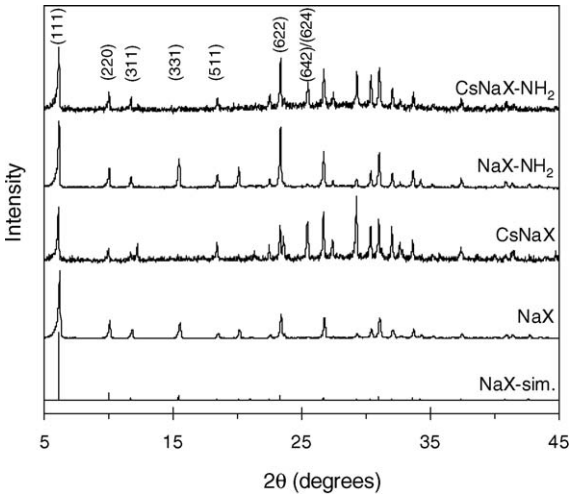
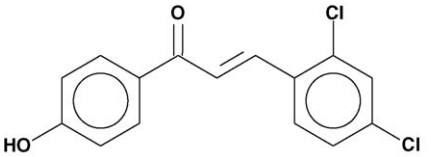


Fig. 1. X-ray diffraction pattern of zeolite catalysts.

of surface area was caused by breakage of Si–O–Si bonds leading to pore collapse, but it was also possible that the smaller surface area was due to the restricted access to the zeolite pore channel caused by the presence of large cesium counterions [23]. The amount of grafted organic amino groups was found by thermal gravimetric and differential thermal analyses (Setaram) to be 1.4 and 1.2 mmoles/g for NaX-NH_2 and CsNaX-NH_2, respectively. A decrease in the Na/Si signal was observed by XPS and XRF after the RNH_2 groups were grafted onto the zeolites (Table 1). In addition, the catalyst surface areas were also smaller than the original NaX and CsNaX zeolite precursors. Nitrogen physisorption and TGA/DTA analyses suggested that for NaX-NH_2 most of the aminopropyls resided inside the zeolite pores. This may explain the small BET surface area measured for this sample.

3.2. Sonochemical synthesis of chalcones via Claisen-Schmidt condensation

The Claisen-Schmidt condensation between benzaldehyde (**1**) and acetophenone (**2**) (Scheme 1) was carried out at 303, 323 and 343 K, in the absence of solvent using 0.3 g of zeolites for 3 h. The reaction gives *trans*-chalcone (**3**). The yield of chalcone is showed in Fig. 2 and compared with that obtained using ultrasound activation. No side-products were observed, indicating that ketone autocondensation or Cannizaro reaction does not take place under these experimental conditions. Fig. 2 shows a clear improvement in the catalytic activity when the reaction takes place under ultrasounds. It is also observed that ultrasound enhance the activity, keeping the selectivity



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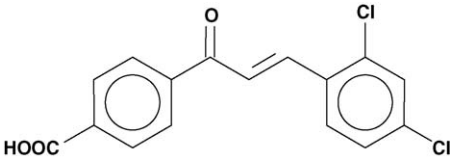

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Scheme 3. Structure of 4′-hydroxy-2,4-dichloro-chalcone (**4**) and 4′-carboxy-2,4-dichloro-chalcone (**5**) with antibacterial properties.

Table 1
Physical and chemical properties of the zeolite catalysts

Physical and chemical properties	NaX	CsNaX	NaX-NH_2	CsNaX-NH_2
Average particle size[a] (μm)	2.1	1.9	2.1	1.8
BET[b] surface area (m^2/g)	430	400	80	200
Cs/Si ratio[c], bulk (surface)	0 (0)	0.32 (0.20)	0 (0)	0.24 (0.10)
Cs/(Na + Cs) ratio[c], bulk (surface)	0 (0)	0.60 (0.63)	0 (0)	0.60 (0.67)
N/Si ratio[c], bulk (surface)	0 (0)	0.10 (0)	3.0 (0.21)	3.1 (0.29)
Amino groups[d] (mmole/g)	0	0	1.4	1.2

[a] The average particle size was measure from the scanning electron microscope pictures.
[b] The BET surface area was obtained after the zeolite sample was calcined in air at 773 K for 8 h to burn away the organic groups.
[c] The bulk and surface compositions were calculated from the XRF and XPS data, respectively.
[d] The amount of organic moieties on the zeolites was determined from the TGA/DTA data.

constant. This increase of activity due to ultrasounds is attributed to the cavitation phenomena during the induced sonochemical reactions. This trend is observed at all the tested temperatures using 0.3 g of catalysts. These results show that the order of activity is NaX-NH_2 < CsNaX-NH_2 under sono-activation or thermal activation.

In Fig. 3, yields of chalcone (**3**) versus time at different temperatures are presented when using the CsNaX-NH_2 zeolite. These results show that using CsNaX-NH_2 catalysts under ultrasound conversions around 99% are attained after 3 h reaction time. This value is around 80% when the reaction takes place under silent conditions.

The mass spectrum of the reaction product (MS m/s: 208 (M^+), 179, 103, 77(100), 65, 51, 32) confirms that, under our experimental conditions, *trans*-chalcone of type (**3**) is obtained selectively.

Based on the results showen in the previous part of the work, we carried out the Claisen-Schmidt condensation between benzaldehyde and 4′-hydroxy and 4′-carboxy acetophenones under sono-activation of the zeolites to obtain the corresponding chalcones. The resultant chalcones are important antibacterial compounds.

3.2.1. Preparation of chalcones with antibacterial activity using amino grafted zeolites under sonochemical activation

Claisen-Schmidt condensation of hydroxy acetophenones or carboxy acetophenones with benzaldehyde has been described in the literature using basic catalysts [24]. Licochalcone A

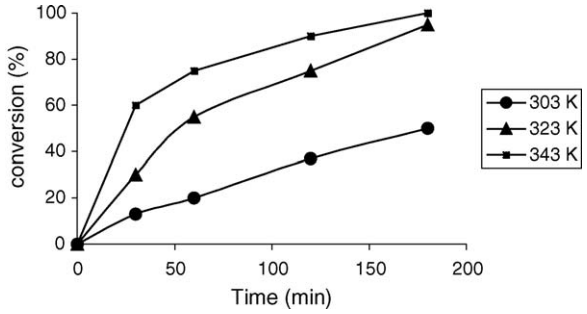

Fig. 3. Effect of the reaction temperature during the solventless condensation between acetophenone and benzaldehyde in the presence of 0.3 g of CsNaX-NH_2.

posses antibacterial activity against *S. Aureus*. The exchange of the 4′-hydroxy group with carboxy acids increases aqueous solubility of the chalcones improving their in vitro antibacterial activity against *Staphylococcus Aureous*. Traditionally, the synthesis of these chalcones is carried out by Claisen-Schmidt condensation between benzaldehyde and acetophenone using 1.5 eq of sodium hydroxide under ethanol reflux. However, the use of organic solvents or liquid catalysts would be avoided using a ‘‘green’’ methodology. In this sense, the present work optimizes the use of amino grafted zeolites as heterogeneous catalysts under ultrasound activation. This methodology has improved the yields of chalcones which exhibit antibacterial activity such as 4′-hydroxy- and 4′-carboxy-Licochalcone A derivatives. Fig. 4 shows the conversion values obtained. Using

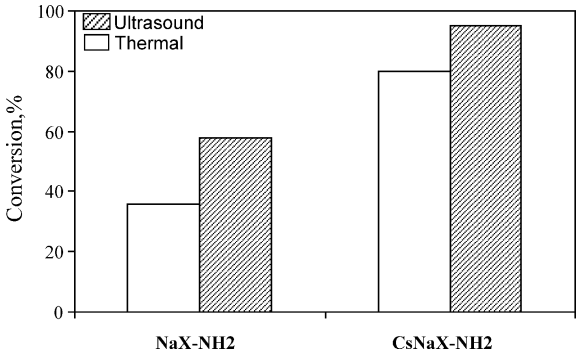

Fig. 2. Influence of the sonication during the chalcone formation using NaX-NH_2 and CsNaX-NH_2 zeolites (0.3 g). Reaction time: 3 h. Reaction temperature: 323 K.

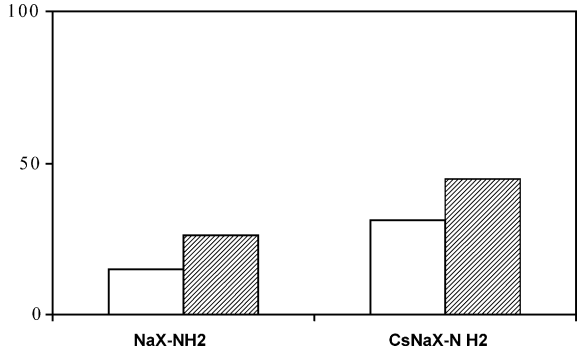

Fig. 4. Influence of sonic activation vs. non-sonic activation during the solventless synthesis of (A) 4′-hydroxy and (B) 4′-carboxy-chalcones. Reaction temperature: 343 K, catalyst: NaX-NH_2 and CsNaX-NH_2 (0.6 g). Reaction time: 5 h.

both zeolites, the preparation of these types of chalcones has been achieved successfully. In fact, with CsNaX-NH_2 zeolite and under ultrasound activation, it is possible to achieve 45% conversion of 4′-hydroxy and 65% conversion of 4′-carboxy-chalcone in only 5 h. When these reactions were performed under thermal activation using the same reaction conditions, lower conversions (around 20 and 35%, respectively) were obtained, indicating that ultrasound present positive effect during the reaction. It is important to remark that conversions around 13% for 4′-hydroxy-chalcone and 46% for 4′-carboxy-chalcone are obtained following the traditional method (18 h and NaOH/EtOH reflux).

4. Conclusions

The main noticeable result is the marked increase of basicity in the amino grafted zeolites. This basicity is exhibited during the Claisen-Schmidt condensation, under sonic and non-sonic activation. The results demonstrate that this methodology (combination of a new type of basic zeolite with ultrasound) is a mild and effective method for the preparation of chalcones with nearly 100% conversion in only 3 h. This method thus offers a practical alternative to conventional heating catalysis and the process itself is environmentally friendly with minimal waste.

Amino grafted zeolites can successfully be employed to obtain chalcones with antibacterial activities. These solid catalysts can compete with the traditionally used NaOH/EtOH.

Acknowledgements

E.P.R. thanks the University of Carabobo (Venezuela) for a Ph.D. fellowship. The authors would like to thank the Hong Kong Research Grant Council (HKUST6021/01P and HKUST6009/02P) and the Institute for Integrated Microsystems (I2MS-01/02.EG02) for funding this research. We also would like to acknowledge the Material Preparation and Characterization Facility (MCPF) of Hong Kong University of Science and Technology.

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