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Catalyzed Claisen-Schmidt Reaction by Protonated Aluminate Mesoporous Silica Nanomaterial Focused on the (*E*)-Chalcone Synthesis as a Biological Active Compound

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The mesoporous silica structure (MSN) was synthesized using sol gel method followed by aluminium grafting and protonation which denoted HAlMSN (Si/Al=18.9). N_2 physisorption confirmed mesoporous structure with a pore diameter of 3.38 nm. ^{27}Al NMR showed the presence of framework and extra-framework aluminium structures which led to the formation of the strong Lewis and Brønsted acidic sites. HAlMSN catalyzed synthesis of (*E*)-chalcones through Claisen-Schmidt reaction. Chalcone derivatives have been applied as biologically active compounds with anti-cancer, anti-inflammatory and diuretic pharmacological activities. The products were produced via reactions on the protonic acid sites of HAlMSN. The significant advantages were high yield, easy work up, short time reaction and also compatibility with various ranges of the organic solvents. The products were obtained in the excellent conversion of 97% at 298 K. The results showed the electron donated substitutes exhibited higher conversion in comparison with electron withdraw substitutes. The stability of catalyst was investigated by reusing five times in (*E*)-chalcone production which showed a bit decrease in its activity. The highest product of (*E*)-chalcone was observed with 1:2 molar ratio of benzaldehyde/acetophenone. A comparative study in chalcone synthesis using the heterogeneous catalysts exhibited that HAlMSN has significantly the highest activity at the low temperature.

Introduction

The hierarchically mesoporous siliceous nanostructures (MSN) with specific properties such as high internal surface areas (500–1000 m^2g^{-1}), large uniform pore dimensions (2–50 nm) and large pore volumes had been attention by researchers[1]. These properties make them suitable for various applications in the different fields of science e.g. drug delivery, environmental refinery, petroleum science and chemical reactions[2]. In these catalysts, the presence of the acid sites show the main role in their catalytic activities and since the pure MSN do not show the Lewis and Brønsted acid sites in its structure, it cannot use as a strong acid catalyst[3]. In order to improve its acid sites and subsequently to modify its catalytic activity, incorporation of some metals such as aluminium[4], nickel[1] and platinum[5] into the MSNframework have been reported by scientists. These metals are effective to create Brønsted acid site in the structures[3,6,7]. However, this method is limited in making moderate Brønsted acid site strength. The pure MCM-41 is a mesoporous silica material which is widely used in the various applications as catalyst. Introduction of aluminium into MCM-41 increased its catalytic activity due to the generation of Lewis and Brønsted acid sites in their structures[8]whichusedasasolidacid catalyst[9].Inaddition,some transition metals like Pt, Zr, Ni, Ir and Zn are able to improve the activity of nanomaterials[4,9-13]. The mesopore silica nanoparticles are capable to catalyze the synthesis of some chemical compounds[9], especially in the pharmaceutical industries and medicinal chemistry[4, 12]. Therefore, Al-grafted MCM-41 can be used as for the synthesis of (*E*)-chalcone derivatives which have been used in the pharmaceutical science[14].

(*E*)-Chalcone family ((*E*)-1,3-Diaryl-2-propenone) is a subgroup of the flavonoid component which has been displayed as biological active compound. These materials could act as anti-cancer, anti-mitotic, anti-inflammatory, tyrosinase inhibition, and nitric oxide inhibition[14-16]. In addition, chalcone is a starting material for the synthesis of several biologically heterocycles such as benzothiazepine, pyrazolines, and flavones[17]. Therefore, this family has been noticed by researchers either in order to design of new derivatives or to obtain more yields of these products. The other attempts are carrying out in order to find new pathways for synthesizing these compounds in easier and faster way.

Claisen-Schmidt Condensation reaction is the best method to synthesize chalcone derivatives by using strong base or acid such as sodium and potassium hydroxide, dry HCl, and aluminiumchloride[18]. Some of the organometallic catalysts such as Zn(bpy)(OAc)[19,2] also were reported as catalysts for this reaction.

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Moreover, chalcone can be synthesized by using Suzuki reaction[20]. Although there are several pathways to prepare the chalcones, various disadvantages have been reported for these methods such as long reaction times (14 h to 5 days), high temperature, expensive catalysts and reagents, production of the poison substances, use of hazardous solvents, production of the several by-products and neutralization process. Therefore, several studies were carried out to replace heterogeneous materials instead of the conventional and commercial catalysts. These catalysts were able to do reactions in the mild conditions with more advantages in the saving time, energy and were environmentally friendly properties. Mesoporous silica nanomaterials such as MCM-41 and SBA-15 were introduced as suitable catalysts for Claisen-Schmidt Condensation reaction[21,22]. The Claisen-Schmidt reaction can be carried out with or without presence of the solvent. Recently, the Claisen-Schmidt reactions under solvent-free condition by using mesoporous silica materials were reported as green chemistry way in order to reduce the environmental pollution and bring down the handling costs due to the simplification of work up technique[21].

In the recent study, Romanelli *et al.*[22] synthesized aminopropylated nanosilica by a sol-gel process using tetraethyl orthosilicate (TEOS) as a source of Si followed by functionalizing with different amounts of 3-aminopropyltriethoxysilane (APTES) under toluene reflux. Then this modified nanoparticles catalyzed synthesis of chalcones through the Claisen-Schmidt reaction under solvent-free conditions with high selectivity. The result showed that the activity of catalyst increased over amino modified of silica. In another research, Wang and cooperatives[23] studied Claisen-Schmidt condensation between benzaldehyde and acetophenone, and subsequently intramolecular over the aminopropyl-functionalized SBA-15 with well-ordered hexagonally structure. This catalyst synthesized by one-pot condensation of TEOS and APTES using amphiphilic block copolymer as the template under acidic condition. The results exhibited a good activity and high selectivity for chalcone synthesis over this catalyst in the solvent-free condition, while the use of organic solvents decreased the catalytic activity and selectivity.

In the present study, we synthesized protonated aluminate mesoporous silica nanoparticles (HAlMSN) as a solid acid catalyst and used in order to improve the conditions of Claisen-Schmidt condensation reaction. (*E*)-Chalcone derivatives as a biologically active family were selected due to their importance in the pharmaceutical science. Initially, MSN was prepared through the sol-gel process. Then, HAlMSN solid catalyst was prepared through aluminium loading on MSN by the post-synthesis method followed by protonation. Pyridine adsorbed FTIR spectroscopy was used to investigate the acid strength of this catalyst. Physical properties of the samples were carried out by nitrogen physisorption, XRD, FTIR and ^{27}Al solid state NMR. The mechanism of (*E*)-chalcone synthesis in Claisen-Schmidt condensation over the HAlMSN solid acid catalyst under solvent-free condition was studied in detail. The advantages of using the HAlMSN catalysts such as high activity, short time and low temperature in this reaction were studied in details and a comparison of its activity with the commercial and the different heterogeneous catalysts was carried out.

Experimental

Catalyst Synthesis

The synthesis of pure MSN followed the procedure of the previous report[3]. MSN was prepared as described below. Cetyltrimethylammonium bromide (CTAB, 1.17 g) was dissolved in a solution containing double distilled water (180 g) and 1,2-propanediol (30 mL) in an aqueous ammonia solution (7.2 mL, 25%). After vigorous stirring for approximately 30 min at 323 K, tetraethylorthosilicate (TEOS, 1.43 mL) and 3-aminopropyl triethoxysilane (APTES, 0.263 mL) were added to the mixture. The resulting mixture was stirred for an additional 2 h at 323 K and allowed to rest for 20 h at the same temperature. The gel composition used in the synthesis of MSN was 1TEOS:0.17APTES:0.5CTAB:13.5NH3:85.2PD:1042H2O. The sample was collected by centrifugation at 20,000 rpm for 30 min and washed with deionized water and absolute ethanol three times. The surfactant was removed by heating MSN (1 g) in an NH_4NO_3 (0.3 g) and ethanol (40 mL) solution at 333 K. The surfactant-free product was collected by centrifugation and dried at 383 K overnight prior to calcination in air at 823 K for 3 h. The acidic sites of the sample were prepared by aluminium-grafting (calculated Si/Al=20) on the template-free MSN at 353 K for 10 h followed by centrifugation and dried at 383 K overnight prior to calcination in air at 823 K for 3 h. Sodium aluminate (Sigma-Adrich) was used as a precursor of aluminium. The aluminium-grafted MSN was denoted as AlMSN. Whereas, the protonated AlMSN (HAlMSN) was prepared by protonation of AlMSN (1 g) using aqueous solution of NH4NO3 (2.5 g in 50 mL of double distilled water) at 333 K K for 16 h followed by removal of solution, drying at 383 K overnight and calcination at 823 K for 3 h in air.

Catalyst Characterization

The crystallinity of catalysts was measured with a Bruker Advance D8 X-ray powder diffractometer with Cu Kα (⍰=1.5418 Å) radiation as the diffracted monochromatic beam at 40 kV and 40 mA. Nitrogen physisorption analysis was conducted on a Quantachrome Autosorb-1 at 77 K. Before the measurement, the sample was evacuated at 573 K for 3 h. While the elemental analysis of the catalyst measured with Agilent 4100 Microwave Plasma-Atomic Emission Spectrometer. ^{27}Al MAS NMR spectra were recorded on a BrukerAvance 400 MHz spectrometer at 104.3 MHz with 0.3 s recycle delays and spun at 7 kHz to determine the chemical statusof aluminium in the silicate framework of catalysts.

Fourier Transform Infra-Red (FTIR) measurements were carried out using Agilent Carry 640 FTIR Spectrometer. The catalyst was prepared as a self-supported wafer and activated under H_2 stream (F_{H2}=100 ml min^{-1}) at 623 K for 3 h, followed by vacuum at 623 K for 1 h[24]. To determine the catalyst acidity, the activated samples were exposed to 2 Torr pyridine at 423 K for 30 min, followed by evacuation at 473 K for 1 h to remove physisorbed pyridine on the samples. All spectra were recorded at room temperature. In order to compare the surface coverage of the adsorbed species between different wafer thicknesses, all spectra were normalized using the overtone and combination vibrations of the lattice of MSN between 2200 and 1300 cm^{-1} after activation, particularly the lattice peaks at 1855 cm^{-1}[25].

The bulk Si/Al ratio of HAlMSN was determined by Bruker S4 Explorer X-ray Fluorescence Spectroscopy (XRF) using Rh as anode target material operated at 20 mA and 50 kV. The analysis showed that the Si/Al ratio of the HAlMSN framework was 18.9.

The concentration of pyridine adsorbed on Brønsted and Lewis acid sites was determined based on the report of Emeis[26]. The number of Brønsted and Lewis acid sites was calculated using the integrated molar adsorption coefficient values. The resulting values were ε_{1545} = 1.67 cm µmol^{-1} for the band at 1545 cm^{-1} which is characteristic of pyridine on a Brønsted acid sites and ε_{1455} = 2.22 cm µmol^{-1} for the 1455 cm^{-1} band of pyridine on a Lewis acid sites.

Catalytic Activity

The catalytic activity of HAlMSN catalyst was investigated by using Claisen-Schmidt condensation reaction. The details of this study have explained according to the below section:

Typical Experimental Protocol

To a stirring mixture of aldehyde (0.02 mol), ketone (0.04 mol) and dichloromethane (0.15 mol), HAlMSN (0.01 wt%) was added at room temperature and continued the stirring for 30 min. The mixture was heated at 323 K under an air atmosphere for 3h. The samples were taken at regular intervals and the concentrations of ketones (acetophenone derivatives) and chalcones were identified by GC-Mass spectrometry (detector HP 5971) and analysed using chrompak CP 9000 GC equipped with an RTX-50 capillary column and a flame ionization detector. The dodecane was chosen for the internal standard.

The conversion of ketone to chalcone ($X_{chalcone}$%), the yield of chalcone ($Y_{chalcone}$%), the selectivity of chalcone ($S_{chalcone}$%) were calculated according to the Eq.(1) to Eq.(3), respectively:

$$X_{Cumene}(\%) = \frac{[KET]_i - [KET]_f}{[KET]_f} \times 100 \qquad (1)$$

$$Y_{Cumene}(\%) = \frac{n_y}{n_c} \times 100 \qquad (2)$$

$$S_{Cumene}(\%) = \frac{n_y}{n_i - n_f} \times 100 \qquad (3)$$

Where $[KET]_i$ and $[KET]_f$ are the concentration of ketone at the initial and final reaction time, n_y and n_c are the number of molars of the yielded and calculated (*E*)-chalcones, and n_i and $n_f$are the number of molars of ketone at the initial and final reaction time, respectively.

Reusability Testing

Reusability test of the HAlMSN catalyst was carried out for the (*E*)-chalcone production (%) at 298 K during five times reusing[27]. The reactivity was carried out by using washing with hot toluene (3×10 mL) and was dried under vacuum at 343 K for 4 h. In this method the weight of catalyst, its catalytic activity and produced product were measured after each reaction. After reusability testing, the catalyst was subjected to XRD and FTIR in order to study its properties.

Results and Discussion

Catalyst characterization

Fig. 1 shows the XRD patterns of MSN and HAlMSN. These catalysts have presented three peaks of 100, 110 and 200 at the range of 2.30°, 4.20° and 4.70°, respectively. The sharp peaks at 2.30° reveal the high order crystalline structures for the catalysts and confirmed the two-dimensional hexagonal (*p*6mm) structure with d_{100}-spacing of approximately 3.8 nm and an average lattice constant (a_o) of 4.4 nm (Table 1).

In addition, this peak illustrates the long ordered structure in MSN[28]. The intense peak at 2.30° decreased in HAlMSN and shifted to 2.25° that indicated to the loading of Al into the HAlMSN framework which led to an increase in the interplanar spacing of MSN. This shifting in the intense peak is probably due to the presence of a residual sodium atom which interacted with the Si atom through the O atom7. Decrease the intense peak in HAlMSN shows the less uniform crystal structure in compare to MSN.

Table 1 shows the physical characteristics of the MSNand HAlMSN catalysts. The surface area of MSN and HAlMSN are 995 and 639 m^{2}g^{-1}, respectively. Change of the BET specific surface area probably is due to alter in the pore size distributions and change of the two dimensional hexagonal structure of MSN. The grafting of MSN with sodium aluminate has plugged MSN at a pore diameter of around 2–5 nm (Fig. 2).

Table 1
Physical properties of MSN and HAlMSN

Sample	d_{100} (nm)	a_o (nm)	*S* (m^2/g)	*Vp* (cm^3/g)	*W* (nm)	*t* (nm)
MSN	3.84	4.43	995	0.84	3.38	1.06
HAlMSN	3.76	4.34	639	0.54	3.38	0.96

d_{100}, *d*-value 100 reflections; a_0, pore center distance is equal to d_{100}x2/√3; *S*, BET surface area (m^2/g) obtained from N_2 adsorption; V_p, total pore volume (ml/g); *W*, pore size (nm) obtained from BJH method; *t*, pore-wall thickness is equal to a_0-*W*

However, the protonation of AlMSN removed this plugging from MSN, therefore, their pore sizes remained in a constant value. This result also is in good agreement with the alteration of total pore volume and pore-wall thickness of MSN obtained from the BJH method analyses (Table 1).

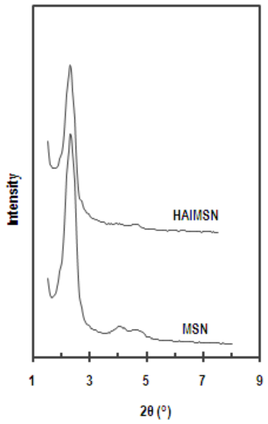


Fig. 1 XRD patterns of MSN and HAlMSN

The plugging of MSN decreased the total pore volume from 0.84 to 0.54 cm^{3}g^{-1}. Whereas, the pore-wall thickness shrank from 1.06 to 0.96 nm is due to the widening of the pore size of MSN. These revealed that Al and residual Na located inside and outside of the pores in HAlMSN. Decrease in d_{100}-spacing value and unit cell parameter indicating to the immobilizing Al into the framework and changing the HAlMSN structure[29].

Fig. 2 shows the nitrogen sorption isotherms and the pore size distribution of MSN and HAlMSN. Fig. 2A exhibited that the mesoporous silica of MSN represented isotherm can be classified as Type IV with a Type H4 hysteresis loop which can be attributed to the mesoporous structures. The isotherm for MSN illustrates the properties of an intense inflection of the capillary condensation within uniform pores at P/P_0 = 0.2–0.4 which indicates the presence of MSN small pore diameter and volume[30]. At P/P_0 = 0.8-1.0 the increase of adsorbed nitrogen illustrates an important external surface area contribution. At relative pressure of P/P_0 less than 0.2, gradual and rounded transitions showed the presence of a small number of non-slit-like micropores, whereas the pore size distribution confirmed the presence of a narrow peak at a pore diameter of 2.5-2.8 nm, Fig. 2B. In HAlMSN, the inflection of the isotherm at P/P_0 of 0.8–1.0 increased gradually, indicated the presence of extra-framework Al which contributed to the external surface area and the inflection at $P/P_0<0.2$ decreased due to the presence of Al species inside the microporous MSN.

In agreement with our results, On et al. immobilized Al into an MCM-41 mesoporous framework with the Si/Al of 33 [31]. The X-ray diffraction result showed that the ordered hexagonal structure of the parent MCM-41 did not change and exhibited a d-spacing of ca. 40 and 41 Å for MCM-41 and Al-MCM-41, respectively. Both samples represented the narrow pore size distributions of around 28 Å with the surface areas of 1050 and 815 m^{2}g^{-1} for MCM-41 and Al-MCM41, respectively.

Fig. 2C shows the peak of ^{27}Al MAS NMR spectrum of the HAlMSN solid catalyst. Here, no peak was observed for MSN, while the peaks at approximately 53 and 0 ppm were observed for HAlMSN which are responsible for the octahedral and tetrahedral Al atoms, respectively[32]. The peaks of 6-coordinate structure (extra-framework) illustrates that a small part of the aluminium dislodged into the aluminosilicate framework[33,34]. The most of Al species remained in 4-coordinate structure (framework) which is promising for the catalytic reactions. Chen et al. reported the synthesis of Al-MCM-41 by loading method in the various Si/Al ratios and showed two types of Al structure in the MCM-41 frameworks[33].

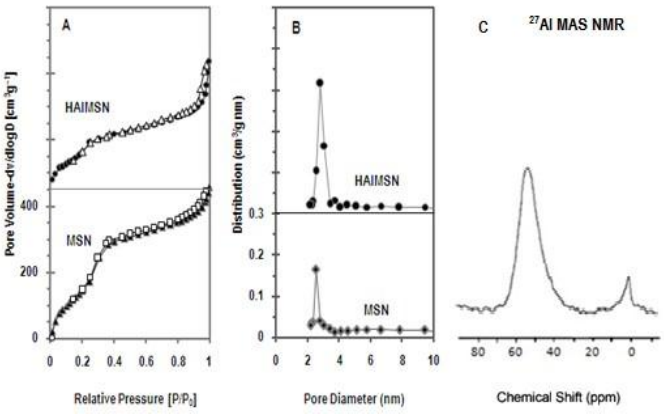


Fig. 2 (A) Nitrogen sorption isotherm and (B) pore size distributions for MSN and HAlMSN; and (C) ^{27}Al MAS NMR spectrum of HAlMSN

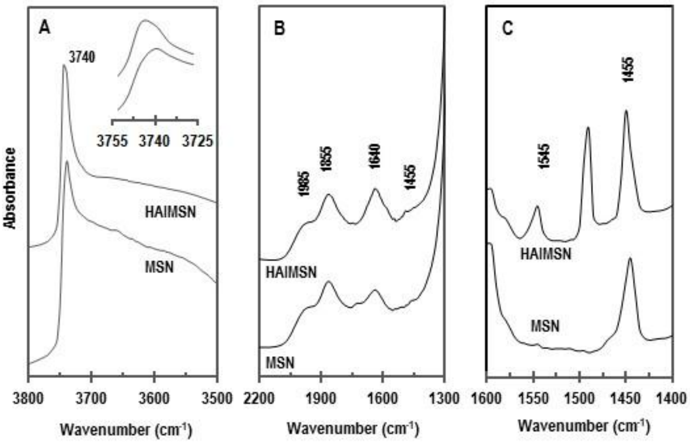


Fig. 3 FTIR spectra of MSN and HAlMSN (A) in the region of 3800-3500 cm^{-1}, (B) in the region of 2200-1300 cm^{-1}, (C) pyridine adsorbed FTIR

FTIR and pyridine adsorbed FTIR spectroscopies of MSN and HAlMSN were shown in Fig. 3. The pure MSN catalyst did not show the Brønsted acid sites due to its electrically neutral property. The non-acidic silanol groups of MSN observed at the range of 3800–3500 cm^{-1} which has shown in Fig. 3A. The sharp band at 3740 cm^{-1} is attributed to the non-acidic terminal silanol groups (ΞSiOH) placed on the external surface of MSN[35].

Introduction Al into the mesoporous silica decreased H-bonds of the hydroxyl groups at the terminal and on the structural defects. The intensity of band at 3740 cm^{-1} shifted to 3745 cm^{-1} after protonation indicated the production of geminalsilanol groups due to the dislodging of Al from the framework[12]. There are no significant differences in the band intensities in the region of 3740 cm^{-1} for MSN and HAlMSN which illustrates that they have a comparable primary particle size and have no significant differences in the d_{100}-spacing or pore diameters. Fig. 3B shows the vibrational lattice stretching frequency of the mesoporous silica catalysts in the region of 2200–1300 cm^{-1}. The bands were observed at 1855 and 1640 cm^{-1} probably correspond to Si-O-Si bonds. Aluminium loading and protonation intensified the band at 1640 cm^{-1}, which may correspond to increase in the concentration of Si atom connected to Al or H atom through O atom.

The number and strength of the catalyst acid sites was evaluated using pyridine adsorptions monitored by IR spectroscopy. IR spectra of the adsorbed pyridine on MSN and HAlMSN at the region of 1600–1400 cm^{-1} are shown in Fig. 3C. The presence of absorbance bands at 1455 and 1545 cm^{-1} demonstrated to the Lewis and Brønsted acid sites, respectively, while the absorbance band at around1495 cm^{-1} is attributed to the combination of the Lewisand Brønsted acid sites[35,36].

The pure MSN possessesonly Lewis acid sites at 1455 cm^{-1} which is belonging tothe electron pair acceptor sites from silanol groups. Incorporation Al increased Lewis acidity and protonation of Al-grafted MSN generated strong Brønsted acid sites at 1545 cm^{-1} which probably correspond to the formation of acidic hydroxyl groups (OH groups which bound Si or Al in the framework) and/or bridging hydroxyl (Si(OH)Al) groups[36,37].

The concentration of Brønsted and Lewis acid sites for HAlMSN was calculated 96 μmol g^{-1} for the Brønsted sites and 189 μmol g^{-1} for Lewis acid sites[3].

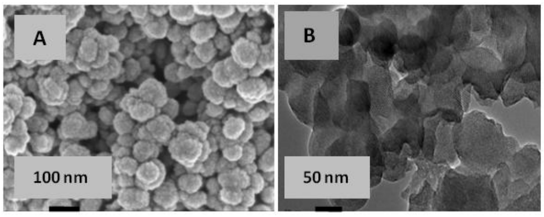


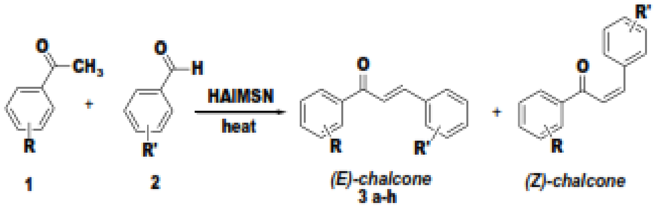
Fig. 4 FESEM and TEM images of HAlMSN

These values were measured in terms of amounts of the pyridine ion for the Brønsted sites with corresponding band at 1545 cm^{-1} and for Lewis acid sites with corresponding band at 1455 cm^{-1}[26].

The morphology of the HAlMSN was observed using FESEM and TEM images. Fig. 4 shows the HAlMSN as a uniform spherical particle with particle size of 70-120 nm. The 2D hexagonal mesostructure was confirmed by TEM image. The TEM images clearly determined well-ordered pores with parallel and cylindrical channels and honeycomb structures, which indicates a 2D hexagonal *p*6mm mesostructure for HAlMSN[38]. These results are in accordance with those measured from the low-angle XRD patterns and N_2 sorption analysis.

Catalytic activity

Chalcones are usually synthesized by using Claisen–Schmidt condensation reaction under basic or acidic conditions at the presence of a polar solvent. This reaction involves difficult purification process as the condensation reaction often led to a complex mixture[39,40]. HAlMSNcatalysed the (*E*)-chalcones (**3a-h**) synthesis which carried out with acetophenone (**1**) and benzaldehydes derivatives (**2**) under solvent-free condition at the low temperatures with excellent yield and selectivity without generation of any side product in a short time (**scheme 1**). In these reactions the (*Z*) isomers were synthesized as by-products in the small amounts. These one-pot reactions occurred by focusing on the optimizing the reaction conditions in terms of the amounts of products, temperature and reaction time.



Scheme 1 Reagents and conditions for (*E*)-chalcones synthesis

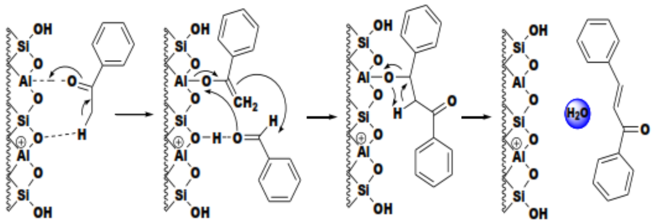
To compare the obtain results in the presence and absence of the catalyst, this reaction occurred for (*E*)-chalcone through the traditional method without catalyst at 323 K. No improvement in yield of reaction was observed. The use of high polarity solvents such as light alcohols gives a little yield of product which probably due to the solvent effect[23].

Table 2
Synthesis of (*E*)-chalcones (**3a-h**) using the HAlMSN solid acid catalyst

Entry	R	R′	Time (h)	Conv. (%)	Select. E-isomer (%)	Yield (%)	Ref.
1[a]	H	H	3	97	94	91	38
2[b]	H	4-Cl	3	94	87	82	24
3[c]	H	2-OH	3	96	90	86.5	24
4[d]	4-OMe	4-OMe	3	96	95	91	37
5[e]	4-OH	4-OCH_3	3	98	94	92	37
6[f]	H	4-OCH_3	3	97	91	88	24
7[i]	4-OMe	H	3	98	90	88	39
8[k]	H	2,6-Cl	3	97	88	85.4	37
9[g]	4-OH	H	3	96	91	87.4	39
10[h]	4-Me	3-Cl	3	95	92	87.4	37

a-h are the various (E)-chalcones with the various substitutions of R and R’

The HAlMSN solid acid catalyzed the synthesis of (*E*)-chalcone derivatives. The production of (*E*)-1,3-diphenyl-2-propenone derivatives is smoothly in the high yield and the selectivity. The proposed mechanism described the formation of enolate intermediate through the bond formation between carbonyl groups and oxygen atom of Al-O bands in HAlMSN (scheme 2).



Scheme 2 Supposed mechanism of the (*E*)-chalcone synthesis over HAlMSN

This mechanism suggested that the bond formation occurred by the reaction of Al^{3+} ion species with oxygen of the aryl ketone carbonyl group in order to generate enolate intermediate by the abstraction of proton from α-carbon of aryl ketone. The reaction goes ahead through the future coordinates with the arylaldehyde and raises electrophilicity of the aldehyde carbonyl group and makes it susceptible for intramolecularnucleophillic attack of enolate ion. Further dehydration process produces the resultant products (**3a-h**). The catalyst was recovered and can be recycled five times without appreciable loss of reactivity.

Reuse of the catalyst

In order to investigate the reusable properties of the HAlMSN catalyst, recycle experiment was conducted and the result is shown in Fig. 5. Reusing method was carried out by the explained technique. After reaction, the catalyst was recycled by washing with hot toluene (3×10 mL) and dried under vacuum at 343 K for 4 h. The catalyst was reused five times without a serious loss in the catalyst weight, catalytic activity and product selectivity during each recycles.

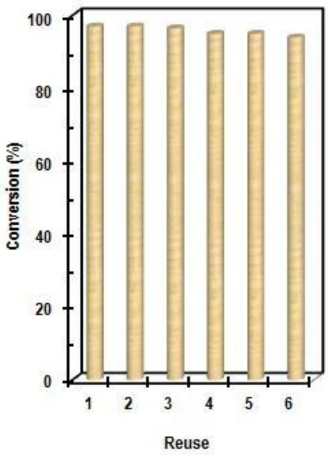


Fig. 5 Stability of HAlMSN in Claisen-Schmidt reaction at 298 K during five times reusing

Decrease of the conversion of the substrate to (*E*)-chalcone was not noticeable and reduced from (97 to 94%) which showed the good reusability of this catalyst under these conditions[41].

XRD results (not shown) of HAlMSN before and after the Claisen-Schmidt reactions indicated that there is no significant change after the reaction; however, the presence of two weak bands corresponds to the vibration of C-H stretching were observed at 2860 and 2930 cm^{-1} confirmed the presence of the C-H stretching vibration, which may be related to the plugging of the unreacted acetophenone or/and remained chlcone molecules on the pores. Removal of the plug by washing with toluene carried out which reduced these two bands at 2860 and 2930 cm^{-1} to the initial values. Fig. 6 has shown the FTIR spectra of the fresh HAlMSN, after Claisen-Schmidt reaction at 473 K for 3 h and after washing with toluene at the end of the final step.

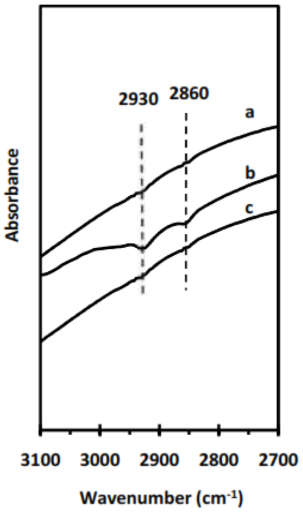


Fig. 6. FTIR spectra of (a) fresh, (b) used and (c) washed HAlMSN in the C-H stretching regions. Chalcone production was done at 473 K for 3 h.

Table 3 shows the comparison study of the (*E*)-chalcone synthesis over several types of heterogeneous catalysts[41-45]. The results indicated to higher activity of HAlMSN in (*E*)-chalcone synthesis in comparison with the other catalysts such as traditional catalysts, pure MSN, ZSM-5, SBA-15, MCM-41 and MgO. This probably is due to the presence of stronger Lewis and Brønsted acid sites in HAlMSN. Larger pore size and surface area of this catalyst also provides an enough space for reaction of the reactants with the active sites inside the catalyst wall. The reported results in Table 3 showed that HAlMSN exhibited more activity in comparison with the mentioned catalysts based on shorter reaction time (3h), lower temperature and higher yield of (*E*)-chalcone synthesized.

Table 3

Comparison of (*E*)-chalcone yield over HAlMSN and the other homogeneous and heterogeneous catalysts

catalyst	Conv. (%)	Yield (%)	Select.* (%)	Time (h)	Temp. (K)	Ref.
Blank	13.1	12.9	98.5	6	423	43
H_2SO_4	98	71.2	72.7	6	423	41
$NaHCO_3$	-	62.2	-	24	393	44
HAlMSN	97	92	95	3	298	This study
MSN	10.5	7.2	68.2	6	423	This study
SiO_2(230-280 mesh)	6	2.6	-	6	413	45
Zn-Al(6)	66.4	34.1	-	6	413	45
SBA-15	9.7	6.2	63.9	6	423	41
ZSM-5	17.7	10.9	61.6	6	423	41
MCM-49	13.7	13.7	100	6	423	41
SBA-15-SO_3H	50	41.7	83.4	6	423	41
Al(11)SBA-15-SO_3H	88.7	87.3	98.4	6	423	41
MgO	40	-	-	18	523	42

*The selectivity of (*E*)-chalcone

In fig. 7A the conversion of reaction with the different substitutes (**3**) versus reaction time are presented. The results show the (*E*)-chalcones with donor electron substitute exhibit higher conversion of Claisen-Schmidt in compare with that of electron withdraw substitutes. The time of reaction for donor electron substitute is less than electron withdraw substitute. The lone pair electron with enough activation energy react with Lewis acid sites of HAlMSN and consequently the conversion of starting material to the product occurred with higher yield and selectivity.

Fig. 7B shows the mole of (*E*)-chalcone and starting materials which produced or consumed during Claisen-Schmidt reaction. Here, the consumption of starting materials and production of (*E*)-chalcone was investigated. The mole of benzaldehyde and acetophenone reduced while the mole of (*E*)-chalcone increased. In this reaction, acetophenone is a limiting reagent and as it expect, the amount of acetophenone almost consume thoroughly while the molecules of benzaldehyde remained in the container. The result confirms that the amount of the product depends on the amount of acetophenone compound as the controlling compound.

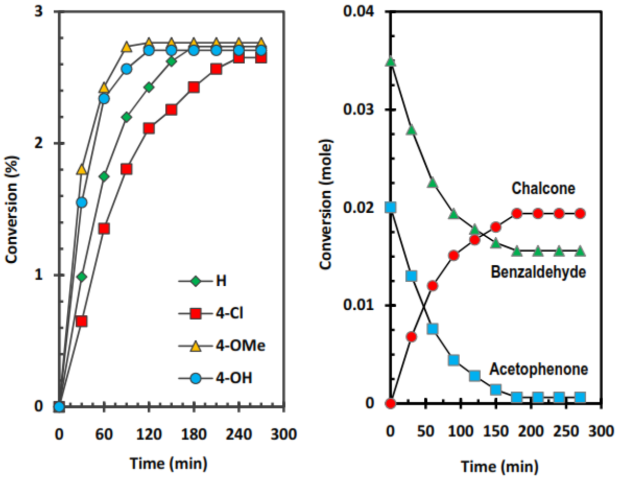


Fig. 7 (A) Development of the production (E)-chalcone derivatives during the reaction time, (B) The mole of bezaldehyde, acetophenone and (E)-chalcone during the process of Claisen-Schmidt reaction

In the (*E*)-chalcone synthesis, the turnover frequency (TOF) is the number of (*E*)-chalcone mole that a mole of HAlMSN can be produced per unit time before coming inactivated. Here, TOF was determined from the rate of (*E*)-chalcone synthesis and the number of the Brønsted acid site. TOF of (*E*)-chalcone synthesis over HAlMSN was shown in Fig. 8. Though the TOF increased with the time reaction, this amount became constant after 180 minute which this indicated that the highest yield of (*E*)-chalcone obtained after 3 h.

The effect of benzaldehyde to acetophenone (B/A) molar ratio

The influence of benzaldehyde/acetophenone (B/A) molar ratio on the conversion of acetophenone to (*E*)-chalcone using HAlMSN is shown in Fig. 9. The effect of B/A molar ratios of 1:1, 1:2, 2:1, 3:1 and 4:1 on the production of (*E*)-chalcone in Claisen-Schmidt condensation were studied. After condensation reaction for 3 h, the yield of (*E*)-chalcone decreased from 97% to 68% from the B/A ratio of 1:2 to 4:1, respectively.

This result probably is due to the presence of the excess benzaldehyde surrounded the active sites which could make a blocking-effect on improving the catalytic activity of Claisen-Schmidt reaction. On the other hand, the excess of benzaldehyde diluted the concentration of acetophenone in media, consequently decreased the contact probability between acetophenone molecules and the active acid sites on the surface of HAlMSN. The results showed that the highest product of (*E*)-chalcone synthesis was observed with 1:2 molar ratio of B/A.

The obtained results strongly are in agreement with Li *et al.*[27] results. They synthesized chalcone via condensation reaction over the Al-SBA-15-SO_3H acid catalyst under solvent-free condition. They reported the amount of acetophenone decreased from 89.0 % to 72.1 % by using the molar ratio of B/A from 1:2 to 5:1 ratios. The yield of synthesized chalcone decreased from 86.9 % to 66.1%.

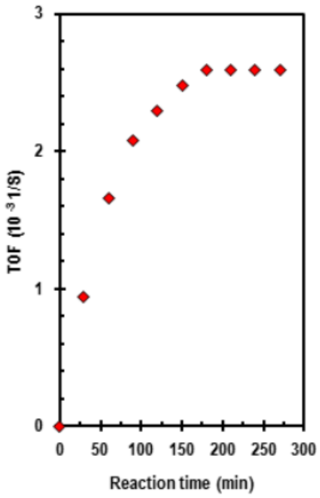


Fig. 8 Turnover frequency of (*E*)-chalcone production during Claisen-Schmidt reaction

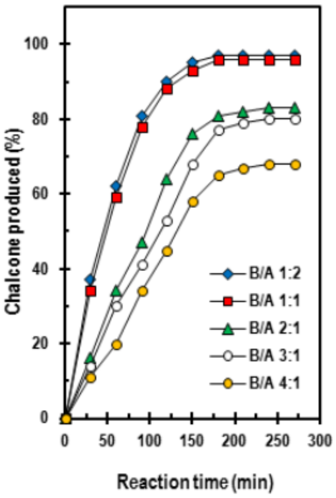


Fig. 9 The effects of the molar ratio of benzaldehyde/acetophenone(B/A) on the conversion of acetophenone in (*E*)-chalcone synthesis

Conclusions

The HAlMSN solid acid catalyst was synthesized by using post-synthesis method from MSN followed by protonation. X-ray diffraction and N_2 sorption results confirmed the ordered mesoporous structure with pore diameter of 3.38 nm and surface area of 995 and 639 m^2g^{-1} for MSN and HAlMSN, respectively. ^{27}Al solid state NMR and IR results confirmed that Al grafting followed by protonation produce extra-framework aluminium atoms which led to the generation of strong Brønsted and Lewis acid sites in which the pyridine probe molecules remained after outgassing at 473 K.

HAlMSN catalyzed Claisen-Schmidt condensation reaction as a strong solid acid. The (*E*)-chalcone derivatives with biologically activity were synthesized over this catalyst with excellent yield and selectivity. The outstanding advantages of this solid catalyst included high yield and selectivity, low temperature, fast work up and short reaction time. This catalyst is also capable to be compatible with both solvent and solvent-free conditions.

The conversion of ketone to chacone was 97% at 298 K in the presence of the HAlMSN as a solid acid catalyst. HAlMSN reused for five times with high yield production of (*E*)-chalcone which indicated to the high stability of this catalyst. The highest product of (*E*)-chalcone synthesis was observed with 1:2 molar ratio of B/A. The result of Claisen-Schmidt reaction indicates that HAlMSN is able to catalyze the chemical reactions under mild conditions with high sufficient, reduce reaction time, saving consumption energy and environmental friendly.

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Table of content

Catalyzed Claisen-Schmidt Reaction by Protonated Aluminate Mesoporous Silica Nanomaterial Focused on the (*E*)-Chalcone Synthesis as a Biological Active Compound

HAlMSN catalyzed Claisen-Schmidt reaction in (*E*)-chalcones synthesis with high yield, low temperature, short reaction time, saving energy and reusable properties