The use of chitosan as a solid base catalyst for the chalcones synthesis

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Abstract. In the present work, chitosan was modified through the hydrogel synthesis. Chitosan catalyst was characterized for its physicochemical properties. The catalytic activity of chitosan was evaluated in chalcones synthesis via Claisen-Schmidt condensation reaction. The reaction was conducted by varying the amount of chitosan catalyst (50 mg, 100 mg, 200 mg) and temperature variations (room temperature, 40 °C, 50 °C, 60 °C). The best chalcones results were obtained in the operating conditions of 100 mg and 60 °C with the yield obtained at 45.50%.

1. Introduction

In recent years development of new heterogeneous catalytic systems for the synthesis of fine chemicals has become a major research area [1]. The use of a heterogeneous catalyst can provide industrial process with easy handling, regeneration, and reusability of catalyst. Moreover, the heterogeneous catalyst also can afford the need for products separation, thus making a significant endowment on the environmental enforcement for the synthetic methods. Most of this novel catalyst is silica-based material which has a high surface area, good accessibility and easy anchoring of organic groups but has poor stability in alkaline conditions [2]. Therefore, the use of biopolymers as polymeric supports for catalysis playing an important key role in organic synthesis.

Chitosan is a linear biopolymer of glucosamine and N-acetyl and glucosamine. Chitosan is produced by extensive alkaline N-deacetylation of chitin [3], which is the second most abundant natural polymer after cellulose. Chitosan, which is obtained by extensive alkaline deacetylation of chitin, has been used most widely as a support for catalytic applications [4,5]. The presence of amino and hydroxyl groups in the chitosan scaffold (Figure 1) makes it have the potential to act as a base catalyst [6].

Chitosan and chitosan derived catalysts have attracted increasing interest in their use as solid catalysts for numerous organic synthesis [4]. For example, chitosan aerogel was utilized as a heterogeneous organocatalyst for asymmetric aldol condensation [1]. Moreover chitosan derived catalyst have been reported as heterogeneous catalyst for cycloaddition reactions of azide-alkyne [7], nitriles hydration to amides[8], transformation of amino nitriles and imines [9], synthesis of hexahydropyrimidines [10], Suzuki-Miyaura cross-coupling [11], Ullmann C-N coupling [12], C-C bond formation [13], C-S coupling [14], C-N cross-coupling [15], and Sonogashira cross-coupling [16]. Chitosan-based catalyst has also been used as a heterogeneous catalyst for the synthesis of some
heterocyclic compounds like alkylaminophenols [17], substituted imidazoles [18], spiropiperidine [19], and benzimidazoles and benzodiazepines [20].

![Chemical structure of chitosan](image)

**Figure 1.** Chemical structure of chitosan

Chalcones are aromatic ketones with two aromatic groups bridged by an enone linkage. Chalcones have gained great interest due to various pharmacological applications. Chalcones are usually synthesized via the Claisen–Schmidt condensation [21]. The condensation between acetophenone and benzaldehyde is catalyzed by bases or acids. Chalcones are the main precursors for the biosynthesis of flavonoids and heterocyclic compounds of biological significance [22,23]. In the present work, the catalytic activity of chitosan hydrogel was studied using the Claisen-Schmidt condensation reaction in ethanol.

2. Materials and methods

2.1 Material
Low molecular-weight chitosan (Product number 417963) was purchased from Sigma–Aldrich (USA). HCl, NaOH, acetophenone, benzaldehyde, ethanol, n-hexane, and ethyl acetate were obtained from Merck (Germany). All the chemicals used are pro analysis as received without further purification.

2.2 Catalyst preparation
The chitosan hydrogel catalyst was prepared by the following method reported in the literature[6,24]. A number of chitosan (1 g) was dissolved in HCl 0.1M (100 mL) and stirred at room temperature. The chitosan solution was poured dropwise into a 0.1M NaOH solution (300 mL). The chitosan hydrogel was kept for 1 h aging at room temperature and then filtered. After completion chitosan found in the form of hydrogel was washed with excess distilled water until neutral. The NaOH excess in the filtrate was monitored by phenolphthalein. The obtained hydrogel was dried at 80 ◦C and then was powdered by using a mortar and pestle.

2.3 Catalyst characterization
Fourier transform infrared spectra (FT-IR) were recorded with Shimadzu Prestige 21 using KBr pellet. Powder XRD patterns were collected using a Malvern Pananalytical X’pert3 powder diffractometer. The data were collected between 5° and 80°. Thermogravimetric analysis (TGA) was measured on a Mettler TGA/DTA 851e. Surface area analysis was performed at 77.4 K in a comptometer (ASAP 2010, Micromeritics). The sample was degassed at 80 ◦C for four h before the sorption analysis. Surface morphology was studied using Hitachi SU 3500 scanning electron microscopy (SEM). Basicity of the catalyst is counted as a number of accessible amino groups. The number of accessible amino groups was determined by GC method [6] as previously reported.

2.4 Condensation reaction
The Claisen-Schmidt condensation was afforded by the reaction of acetophenone and benzaldehyde in ethanol. A number of chitosan catalyst (50 mg, 100 mg, 200 mg) was added to the mixture and stirred at various temperature (room temperature, 40 °C, 50 °C, 60 °C) overnight. The end of the reaction was monitored by thin-layer chromatography (TLC). After the completion of the reaction, the mixture was
then poured onto the crushed ice and neutralized with 2 M HCl solution. The precipitate obtained was filtered, washed with aquadest and dried over, then weighed to determine the yield percent.

3. Results and discussions

3.1 Characterization of the catalyst

The FT-IR spectrum for the catalyst is shown in figure 2. The band that appeared at 3437 cm\(^{-1}\) related to the -O-H vibrational stretching. The broad peak in the region 3000–3400 cm\(^{-1}\) also indicated that the hydroxyl groups are hydrogen-bonded [24–26] and there would exist the overlapped contribution of the amino group [27]. The band at 2956 cm\(^{-1}\) corresponds to the C–H stretching of methylene (–CH2) groups. The band at 1602 cm\(^{-1}\) is due to the –NH2 bending, related to the presence of glucosamine resulting from chitin deacetylation. The absorption bands at 1154 cm\(^{-1}\) is indicated anti-symmetric C–O–C bond stretching vibrations. The peak at 1073 cm\(^{-1}\) and 1026 cm\(^{-1}\) were shown skeletal vibration involving the C–O stretching is characteristics of its saccharide structure [28]. From the FTIR Spectra, the degree of chitosan deacetylation can be calculated using the equation developed by Domszy and Roberts [29]. The results obtained reveal that the degree of deacetylation of chitosan found to be 93%.

![Figure 2. The FT-IR spectrum of the chitosan catalyst.](image)

The thermal behaviour of chitosan catalyst was shown in the TGA curve figure 3. The curves obtained correspond to the chitosan TGA curve pattern, as reported by Sudheesh et al., 2010 [24]. Chitosan catalyst has two main weight losses. The first stage in the region of 80–150 °C reveals 5% weight loss corresponds with the loss of volatile compounds and adsorbed water. The second stage between 260 and 400 °C weight loss is related to the decomposition of the polysaccharide chain. Weight loss monitored in the second stage was 60%. This result reveals that the chitosan catalyst has high thermal stability [27,30]. Chitosan catalyst could be used at various temperatures.
The powder XRD pattern of the chitosan catalyst is shown in figure 4. It could be seen that the chitosan catalyst had two characteristic peaks at $2\theta = 10.5^\circ$ and $2\theta = 20.5^\circ$. These two broad diffraction peaks are generally associated as fingerprints characteristic of semi-crystalline chitosan [31,32].

The surface morphology of the chitosan catalyst is shown in figure 5. SEM image reveals that the chitosan catalyst has a layered scaffold. The BET surface area analysis shown that chitosan catalyst has a narrow surface area. The BET surface area was found to be $0.47$ m$^2$/g with a pore diameter of 38.80 nm. Accessible free amines were determined by mixing the chitosan catalyst with solution salicylaldehyde in ethanol. The salicylaldehyde forms a yellow Schiff base complex with the free amino group on the chitosan catalyst. GC analyzed the residual salicylaldehyde. Nitrobenzene was used as the internal standard. The accessible free amino group was found to be 35%. A similar result was reported by Valentin et al. (2003), which found lower chitosan surface area $\leq 1$m$^2$/g with high an accessible amine 27% [33]. The lower surface area, even with the high number of accessible amine group was because of the protic solvent. The ethanol is a protic solvent acts as an excellent swelling agent for the chitosan polysaccharide framework [34]. The chitosan catalyst that swells causes the availability of amine that is more accessible in higher percentages.
3.2 Catalytic activity

The catalytic activity of the chitosan catalyst was evaluated for the chalcone synthesis by Claisen-Schmidt condensation. The corresponding result is listed in table 1. The experiment was carried out in detail with ten mmol of acetophenone and benzaldehyde. The effect of reaction temperature was investigated in the range from room temperature to 60 °C. It was observed that the yield was increased with an increase in temperature.

The effect of the chitosan catalyst amount on the conversion was studied by varying the catalyst amount from 50 mg to 200 mg. The yield of chalcone was observed to be 17.15 % for 50 mg and room temperature. The yield was increased to 45.50 % at 100 mg and 60 °C. No significant change in the yield on further increase in the chitosan catalyst amount to 200 mg. This result is still too low when compared to the use of NaOH base catalysts, which give yields above 60% [35].

**Table 1.** Effect of reaction temperature and the chitosan catalyst amount on the chalcone synthesis

| No | Reaction Temperature (°C) | Chitosan catalyst amount (mg) | Weight (g) | TLC area (%) | Yield (%) |
|----|----------------------------|-------------------------------|------------|-------------|-----------|
| 1  | Rt                        | 50                            | 0.54       | 35.52       | 17.15     |
|    |                            | 100                           | 0.62       | 37.42       | 20.23     |
|    |                            | 200                           | 0.63       | 38.50       | 22.50     |
| 2  | 40                        | 50                            | 0.65       | 35.52       | 23.55     |
|    |                            | 100                           | 0.64       | 47.73       | 28.28     |
|    |                            | 200                           | 0.70       | 48.53       | 27.59     |
| 3  | 50                        | 50                            | 0.64       | 35.52       | 37.35     |
|    |                            | 100                           | 0.84       | 57.42       | 40.23     |
|    |                            | 200                           | 0.87       | 58.55       | 40.50     |
| 4  | 60                        | 50                            | 0.66       | 45.52       | 37.25     |
|    |                            | 100                           | 1.64       | 73.42       | 45.50     |
|    |                            | 200                           | 1.56       | 74.50       | 45.40     |
4. Conclusion

The use of chitosan catalysts on the chalcone synthesis has found to be able to catalyze Claisen-Schmidt condensation. The catalyst is operative on the amount of catalyst 100 mg and reaction temperature 60 °C under ethanol solvent giving chalcones 45.50% in yield.

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References

[1] Ricci A, Bernardi L, Gioia C, Vierucci S, Robitzer M, and Quignard F 2010 Chem. Commun. 46 6288
[2] Cozzi F 2006 Adv. Synth. Catal. 348 1367–90
[3] Poeloengasih C D, Hernawan, and Angwar M 2008 Indones. J. Chem. 8 189–92
[4] Guibal E 2005 Prog. Polym. Sci. 30 71–109
[5] El Kadib A 2014 ChemSusChem 8 217–44
[6] Reddy K R, Rajigopal K, Maheswari C U, and Lakshmi Kantam M 2006 New J. Chem. 30 1549–52
[7] Baig R B N and Varma R S 2013 Green Chem. 15 1839–43
[8] Baig R B N, Nadagouda M N, and Varma R S 2014 Green Chem. 16 2122–7
[9] Dekamin M G, Azimoshan M and Ramezani L 2013 Green Chem. 15 811–20
[10] Ahmed N, Tarannum S, and Siddiqui Z N 2015 RSC Adv. 5 50691–700
[11] Affrose A, Suresh P, Azath I A, and Pitchumani K 2015 RSC Adv. 5 27533–9
[12] Yang B, Mao Z, Zhu X, and Wan Y 2015 Catal. Commun. 60 92–5
[13] Hajipour A R, Boostani E, and Mohamadsaleh F 2015 RSC Adv. 5 24742–8
[14] Shen C, Xu J, Yu W, and Zhang P 2014 Green Chem. 16 3007–12
[15] Bodhak C, Kundu A, and Pramanik A 2015 Tetrahedron Lett. 56 419–24
[16] Frindy S, Primo A, Lachini M, Bousmina M, Garcia H and El Kadib A 2015 Green Chem. 17 1893–8
[17] Reddy S R S, Reddy B R P, and Reddy P V G 2015 Tetrahedron Lett. 56 4984–9
[18] Khan K and Siddiqui Z N 2015 Ind. Eng. Chem. Res. 54 6611–8
[19] Ahmed N and Siddiqui Z N 2015 ACS Sustain. Chem. Eng. Chem. Eng. 27–8
[20] Maleki A, Ghamari N, and Kamalzare M 2014 RSC Adv. 4 9416–23
[21] Romanelli G, Pasquale G, Sathicq Á, Thomas H, Autino J, and Vázquez P 2011 J. Mol. Catal. A Chem. 340 24–32
[22] Albuquerque H M T, Santos C M M, Cavaleiro J A S, and Silva A M S 2015 Curr. Org. Chem. 18 2750–75
[23] Kulkarni P 2015 Curr. Microw. Chem. 2 144–9
[24] Sudheesh N, Sharma S K, and Shukla R S 2010 J. Mol. Catal. A Chem. 321 77–82
[25] Hernawan, Nurhayati S, Nisa K, Indriangnsih A W, Darsih C, and Kismurtono M 2013 Indones. J. Chem. 13
[26] Hernawan H, Hayati S N, Nisa K, Indriangnsih A W, Darsih C, and Kismurtono M 2017 IOP Conf. Series: Earth and Environmental Science vol 101 p 012018
[27] Phan N T S, Le K K A, Nguyen T V, and Le N T H 2012 ISRN Org. Chem. 2012 1–9
[28] Jose T, Sudheesh N, and Shukla R S 2010 J. Mol. Catal. A Chem. 333 158–66
[29] Khan T A, Peh K K, and Ch’ng H S 2002 J. Pharm. Pharm. Sci. 5 205–12
[30] Klaykruayat B, Siralertmukul K, and Sirikulkit K 2010 Carbohydr. Polym. 80 197–207
[31] Kang B, Dai Y dong, Zhang H Qian, and Chen D 2007 Polym. Degrad. Stab. 92 359–62
[32] Bangyekan C, Aht-Ong D, and Srikulkit K 2006 Carbohydr. Polym. 63 61–71
[33] Valentin R, Molvinger K, Quignard F, and Brunel D 2003 New J. Chem. 27 1690–2
[34] Quignard F, Valentin R, and Di Renzo F 2008 New J. Chem. 32 1300–10
[35] Syahri J, Yuanita E, Nurohmah B A, Armunanto R, and Purwono B 2017 Asian Pac. J. Trop. Biomed. 7 675–9